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mpi

Development of Efficient Methods for Metal-Free C–H Bond Functionalization

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5. <u>Luis Bering</u>, Kirujan Jeyakumar and Andrey P. Antonchick, "Metal-Free C–O Bond Functionalization: Catalytic Intra- and Intermolecular Benzylation of Arenes", *Org. Lett.* **2018**, *20*, 3911–3914.

4. <u>Luis Bering</u>, Felix M. Paulussen and Andrey P. Antonchick, "Metal-Free, and Catalytic Dehydrogenative Coupling of Heterocycles: *En Route* to Hedgehog Signaling Pathway Inhibitors", *Org. Lett.* **2018**, *20*, 1978–1981.

3. <u>Luis Bering</u>, Srimanta Manna and Andrey P. Antonchick, "Sustainable, Oxidative, and Metal-Free Annulation", *Chem. Eur. J.* **2017**, *23*, 10936–10946.

2. <u>Luis Bering</u> and Andrey P. Antonchick, "Selective Transition Metal-Free *Vicinal cis*-Dihydroxylation of Saturated Hydrocarbons", *Chem. Sci.* **2017**, *8*, 452–457.

1. <u>Luis Bering</u> and Andrey P. Antonchick, "Regioselective Metal-Free Cross-coupling of Quinoline *N*-Oxides with Boronic Acids", *Org. Lett.* **2015**, *17*, 3134–3137.

dedicated to my mother

Table of Contents

Abstract

The development of novel and efficient methods for the transition metal-free functionalization of inert and abundant C–H bonds offers striking advantages in terms of step- and atom economy under environmentally benign reaction conditions. Metal-free reactions serve as environmentally friendly substitutes for cost intensive and harmful transition metal-catalyzed reactions. However, oxidative coupling reactions under metal-free conditions face some unsolved problems. High molecular weight oxidants, which are often used in stoichiometric amounts, lead to the undesired generation of large quantities of waste. Additionally, some organic oxidants are toxic, explosive or corrosive. Consequently, the development of catalytic and metal-free methods for the functionalization of C–H bonds attracted significant interest.
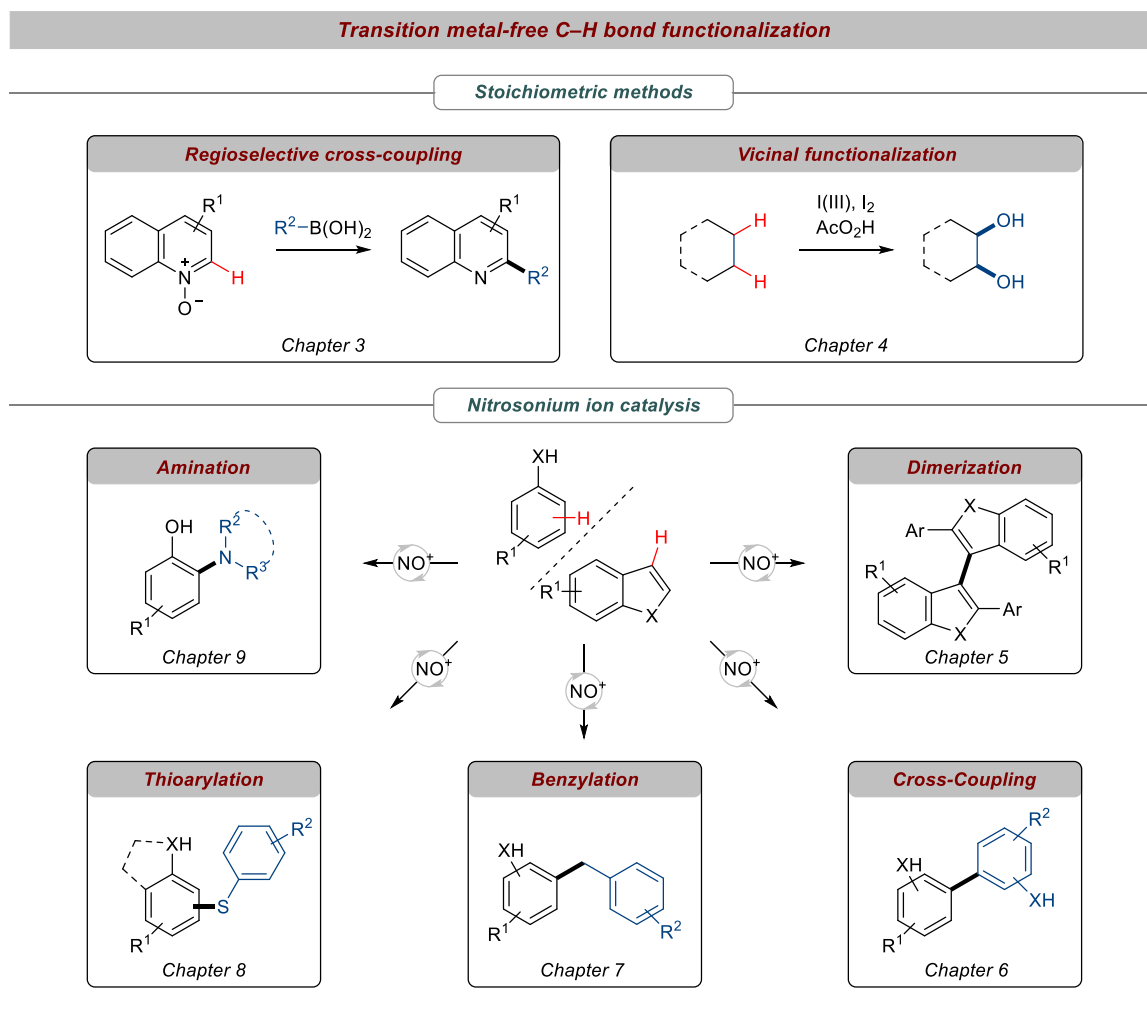
Figure 1 Overview of the projects described in this thesis.

With the aim to develop novel transition metal-free reactions and to address the aforementioned challenges, different methods have been established (Figure 1). Initially, the coupling of

quinoline *N*-oxides with boronic acids has been studied (Chapter 3). This unprecedented transformation is based on the Petasis-Borono-Mannich reaction, which has never been applied for the functionalization of heterocycles before. Further, the functionalization of unreactive C_{sp}^{3}–H bonds of simple alkanes was achieved (Chapter 4). Radical iodination mediated by hypervalent iodine(III) reagents was combined with a cascade of oxidation steps, introducing *vicinal* diols into saturated hydrocarbons. The developed reaction conditions were further applied for the functionalization of iodoalkanes. In these processes, iodine serves as a transient directing group for the functionalization of the starting materials.

The application of nitrosonium salts for the non-directed coupling of arenes under aerobic reaction conditions remained almost untouched in the past decade. Early reports found that nitrosonium species are regenerated when the reaction is exposed to ambient air, allowing the use of nitrosonium salts as catalysts. Molecular oxygen serves as terminal oxidant and water is produced as by-product. Due to the sustainable features of nitrosonium ion catalysis, different catalytic oxidative coupling reactions have been studied.

Guided by the oxidation potential of benzofurans, the catalytic coupling of different arylated heteroarenes was established (Chapter 5). The developed method allowed the efficient synthesis of different dimeric products, leading to the identification of novel bioactive compounds. Further, the homo- and cross-coupling of phenols and anilides has been developed (Chapter 6). For the first time, nitrosonium salts were successfully applied as catalysts for oxidative cross-coupling, including the unprecedented phenol-anilide cross-dehydrogenative coupling.

Furthermore, the application of nitrosonium salts as Lewis-acid catalysts has been uncovered (Chapter 7). The intramolecular rearrangement of benzyl aryl ethers has been studied, which served as template for the development of an intermolecular Friedel-Crafts reaction, using benzyl alcohols and arenes as the coupling partners.

Finally, two applications of nitrosonium ions for the formation of carbon-heteroatom bonds *via* C–H/S–H and C–H/N–H cross-dehydrogenative coupling have been developed. Radical-radical recombination allowed the selective cross-coupling of phenols and indoles with thiophenols (Chapter 8) and phenothiazines (Chapter 9) utilizing nitrosonium ions as efficient catalyst for the desired transformation. Notably, the C–H bond amination was achieved under mild and environmentally benign reaction conditions, omitting halogenated solvents and reagents.

Zusammenfassung

Die Entwicklung neuer und effizienter Methoden zur übergangsmetallfreien Funktionalisierung von inerten C–H Bindungen bietet wichtige Vorteile, wie die verbesserte Syntheseschritt- und Atomökonomie unter umweltfreundlichen Reaktionsbedingungen. Metallfreie Reaktionen dienen als Ersatz für teure und toxische Übergangsmetall-katalysierte Reaktionen. Oxidative Kupplungen unter metallfreien Bedingungen bringen jedoch einige ungelöste Probleme mit sich. Der Einsatz von Oxidationsmitteln mit hohem Molekulargewicht verursacht große Mengen an Abfall. Zudem sind viele organische Oxidationsmittel toxisch, explosiv oder korrosiv. Die Entwicklung von katalytischen und metallfreien Methoden zur Funktionalisierung von C–H-Bindungen gewann deshalb an großer Bedeutung.
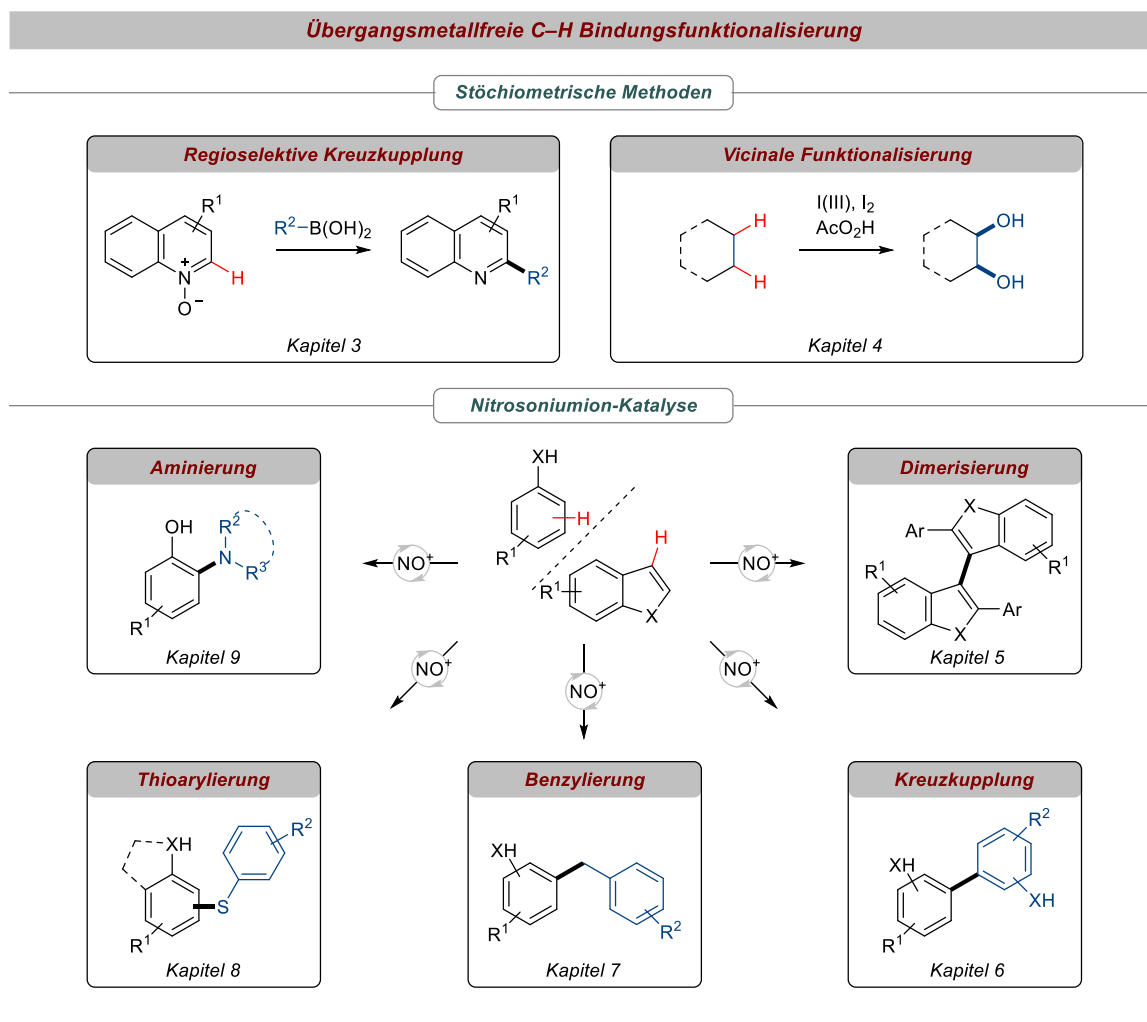

Abbildung 1 Übersicht der in dieser Arbeit beschriebenen Projekte.

Mit dem Ziel neue übergangsmetallfreie Reaktionen zu entwickeln und die zuvor genannten Probleme zu adressieren, wurden verschiedene Methoden etabliert (Abbildung 1). Zu Beginn

wurde die Kupplung von Chinolin *N*-Oxiden mit nukleophilen Boronsäuren studiert (Kapitel 3). Diese neue Transformation basiert auf Petasis-Boronsäure-Mannich-Reaktion, die zuvor noch nicht zur Funktionalisierung von Heterozyklen angewendet wurde. Zudem wurde die Funktionalisierung wenig reaktiver C_{sp}^3–H-Bindungen von Alkanen entwickelt (Kapitel 4). Radikalische Iodierung mittels hypervalenter Iod(III)-Reagenzien wurde mit einer Kaskade aus Oxidationsschritten kombiniert, um *vicinal*e Diole in gesättigte Kohlenwasserstoffe einzuführen. Die entwickelten Reaktionsbedingungen wurden darüber hinaus zur Dihydroxylierung von Iodalkanen genutzt. In diesen Prozessen dient Iod als transiente dirigierende Gruppe zur Funktionalisierung der Startmaterialien.

Die Verwendung von Nitrosoniumsalzen in der nicht-dirigierten Kupplung von Aromaten unter aeroben Reaktionsbedingungen verblieb nahezu unberührt im letzten Jahrzehnt. Frühe Studien beschrieben eine Regenerierung von Nitrosoniumspezies, wenn die Reaktion unter Luftatmosphäre durchgeführt wurde, wodurch der Einsatz von Nitrosoniumsalzen als Katalysator möglich war.

Geleitet durch das Oxidationspotential von Benzofuranen wurde die katalytische Kupplung von arylierten Heteroarenen etabliert (Kapitel 5). Die Reaktionsbedingungen erlaubten die effiziente Synthese von komplexen und bioaktiven Dimeren. Ebenso wurde die Homo- und Kreuzkupplung von Phenolen und Aniliden studiert (Kapitel 6). Zum ersten Mal wurden Nitrosoniumsalze erfolgreich als Katalysatoren für oxidative Kreuzkupplungen eingesetzt, einschließlich der nicht beschriebenen Phenol-Anilid-Kreuz-dehydrierenden Kupplung.

Des Weiteren wurde der Einsatz von Nitrosoniumsalzen als Lewis-Säure Katalysator aufgedeckt (Kapitel 7). Dafür wurde die intramolekulare Umlagerung von Benzylaryl-Ethern studiert, was als Vorlage für die Entwicklung einer intermolekularen Friedel-Crafts-Reaktion diente, bei der Benzylalkohole und nukleophile Aromaten als Kupplungspartner eingesetzt wurden.

Nitrosoniumionen konnten in zwei weiteren Anwendungen als Katalysatoren zur Bildung von Kohlenstoff-Heteroatombindungen durch C–H/S–H und C–H/N–H-Kreuz-dehydrierende Kupplung erfolgreich eingesetzt werden. Radikal-Radikal-Rekombination erlaubte die selektive Kreuzkupplung von Phenolen und Indolen mit Thiophenolen (Kapitel 8) und Phenothiazinderivaten (Kapitel 9). Insbesondere die C–H-Aminierung von Phenolen konnte unter besonders milden und umweltfreundlichen Bedingungen durchgeführt werden, da halogenierte Lösungsmittel und Reagenzien vermieden wurden.

Introduction

1 Introduction

1.1 The interplay of metal-free chemistry and C–H bond functionalization

Metal-free chemistry has observed steadily increasing interest in the past decades.[1] Several approaches of synthetic organic chemistry are covered within this field. Organocatalysis is the most prominent representative. Additionally, radical chemistry, photochemistry, electrochemistry, and oxidative coupling have emerged as modern approaches for metal-free synthesis.[2] Metal-free reactions serve as a powerful alternative, since transition metal-catalyzed reactions are to some extend still limited in application and face particular challenges. Pharmaceuticals, which are often synthesized applying transition metal-catalysis, might be contaminated with residual metal impurities. Removal of those impurities can be challenging, expensive and time intensive.[3] Metal-based impurities might alter the physical properties of organic molecules, which potentially causes problems in materials science application.[4] Toxicity, high prices, oxygen- and moister sensitivity are downsides associated with transition metal catalysts.[5] In the context of C–H bond functionalization, a sacrificial oxidant in stoichiometric amounts is often required.[6] However, metal-free approaches face disadvantages as well. Regioselectivity issues are common drawbacks and the requirement of stoichiometric amounts of high molecular weight oxidants is detrimental, since some organic oxidants are toxic, explosive or corrosive.[2]

C–H bond functionalization represents a highly efficient approach in order to increase molecular complexity.[7] Step-intensive pre-functionalization of starting materials is avoided, since abundant carbon-hydrogen bonds are functionalization in a direct manner. Therefore, the step- and atom-economy is dramatically improved and the amount of produced waste is decreased.[8] Due to its advantages, the construction of carbon-carbon and carbon-heteroatom bonds through functionalization of C–H bonds has observed tremendous attention in the past decades.[9] However, the selective functionalization of inert and abundant C–H bonds is still demanded. Oxidative functionalization of C_{sp}^2–H and C_{sp}–H bonds is considered to be easier than functionalization of the inert C_{sp}^3–H bonds.[10] The strong and localized C–H bonds in saturated molecules have no empty low energy orbitals or filled high energy orbitals that could readily participate in chemical reactions.[11] Many methods for C–H bonds functionalization utilize transition metal-catalysts, which are not unrestrictedly applicable, due to the aforementioned reasons. Consequently, metal-free reaction methodologies for C–H bond functionalization represent an efficient and sustainable strategy for the functionalization of

organic molecules. Several points for *green and sustainable* chemistry can be fulfilled by combining both approaches.[12]

1.2   Synthetic application of nitrosonium ions in organic synthesis

Due to the special emphasis towards novel applications of nitrosonium ions as catalysts within this thesis, synthetic methodologies based on the application of nitrosonium ions are summarized.

Nitrosonium ions are reactive intermediates and of wide application in organic chemistry. The nitrosonium cation is a strong single-electron oxidants with an oxidation potential of $E° = 1.28$ V (vs SCE in MeCN).[13] Nitrosonium ions can be generated using nitrosonium salts with different counterions (e.g. BF_4^-, PF_6^-, HSO_4^-, ClO_4^-), nitrous acid, nitrogen-oxygen gases (e.g. NO_x, N_2O_3, N_2O_4), nitrites and pre-functionalized ionic liquids.[14] A common method to generate nitrosonium ions is the treatment of sodium nitrite with strong acids (e.g. acetic acid, trifluoroacetic acid, triflic acid). Nitrosonium salts are inexpensive, stable and safe in handling, which makes them attractive reagents in organic chemistry.[15] Additionally, reactive nitrogen species can be found in every living cell and undertake important functions as messenger molecules and as transient post-translational protein modifications.[16]

Classically, enolizable C–H bonds undergo nitrosation in the presence of nitrosonium salts.[17] Nitrosonium ions react with primary, secondary and tertiary amines under N–N bond formation.[18] Additionally, nitrosonium salts were also applied for the diazotization of anilines.[19] Diazonium salts are important precursors for radical reactions, transition metal-catalyzed reactions and substitution reactions.[20] However, *tert*-butyl nitrite (TBN) has supersede nitrosonium salts for N–N bond formation due to its superior solubility in organic solvents, facile handling and functional group tolerance.[21] Under certain conditions, the nitrosonium ion is able to form stable complexes with sterically demanding alkenes, aromatic compounds and heteroatom-centered ligands.[22]

1.2.1   Oxidative carbon-carbon and carbon-heteroatom bond functionalization

Due to the oxidative character of nitrosonium ions, a great number of applications roots in the oxidative functionalization of carbon-heteroatom bonds. For numerous applications of nitrosonium salts, George Olah holds a pioneer position. Olah's group reported the C–O bond activation of methyl ethers (**1**) with nitronium tetrafluoroborate for the synthesis of ketones (**2**)

(Scheme 1.1a). Initially, the nitrosonium ion activates the ether bond by forming intermediate **1A**. Reductive elimination of nitrous acid leads to the formation of intermediate **1B** and subsequent hydrolysis gives the desired ketone (**2**).[23] This work served as a template for several other oxidation reactions. Using the same conditions, alcohols, silyl protected alcohols, and stannyl-protected alcohols were converted to the corresponding carbonyl analogues.[24] The mixture of $NaNO_2$-TfOH is capable to oxidize primary alcohols to the corresponding carboxylic acids (**3**). Additionally, cyclohexanol was converted to adipic acid in one step (Scheme 1.1b).[25] Later, Wu and co-workers developed the removal of TBS and THP protecting groups from alcohols using nitrosonium tetrafluoroborate as catalyst.[26] The method was also suitable for the deprotection of aliphatic and phenolic hydroxy groups.
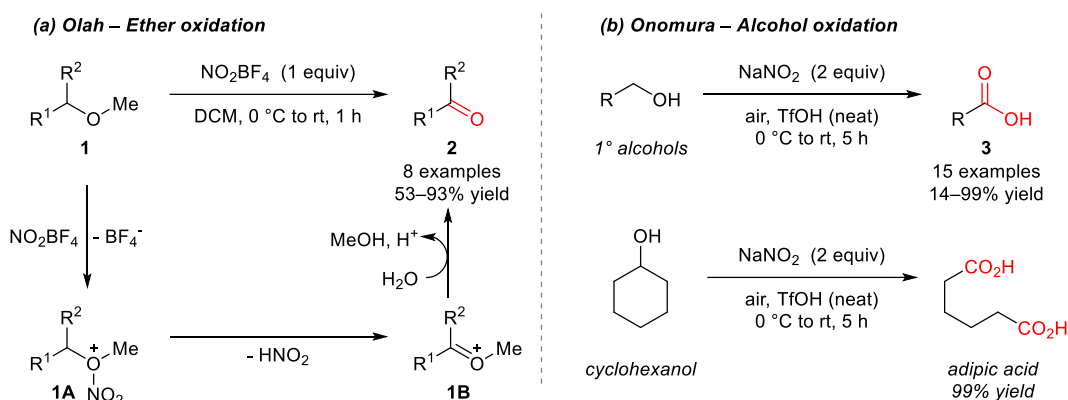
Scheme 1.1 Oxidation of C–O bonds with nitrosonium ions. (a) Olah's oxidation of methyl ethers. (b) Conversion of primary and secondary alcohols to carboxylic acids.

In 1993, Carrión and co-workers reported the pinacol-pinacolone rearrangement initiated by substoichiometric amounts of nitrosonium tetrafluoroborate (Scheme 1.2).[27] This reaction represents an interesting application, since other oxidants usually favour the glycol cleavage.
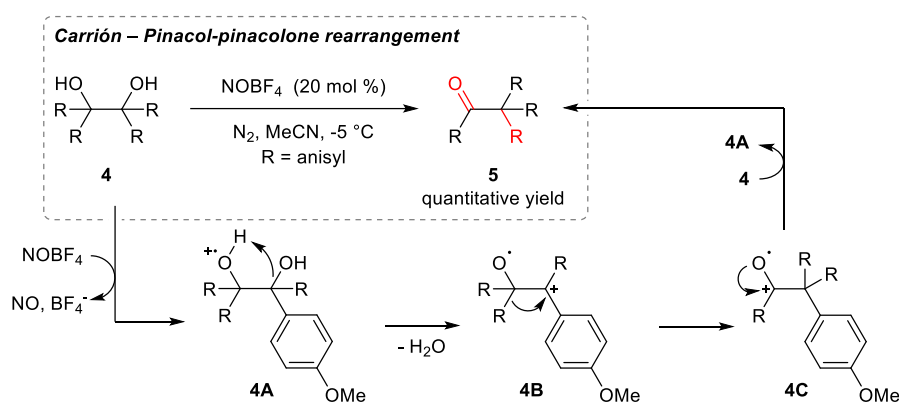
Scheme 1.2 Oxidative pinacol-pinacolone rearrangement using sodium tetrafluoroborate as initiator.

According to the proposed mechanism, a single-electron-transfer (SET) initiates the reaction to form **4A**. Elimination of water delivers intermediate **4B**, which is followed by 1,2-migration of the anisyl group to afford **4C**. Radical transfer of **4C** to pinacol (**4**) leads to the formation of pinacolone (**5**) and allows the propagation of the reaction. The oxidation potential of pinacol **4** was determined with cyclic voltammetry. A potential of 1.32 V and 1.46 V (vs Ag/Ag$^+$ in MeCN) was determined, which supports the proposed SET process. Consequently, no product was formed when the anisyl groups were replaced with *para*-chlorophenyl groups.

Olah and co-workers reported the oxidative displacement of alkyl halides (**6**) with stoichiometric amounts of nitrosonium tetrafluoroborate (Scheme 1.3a). It was proposed that the nitrosonium ion oxidizes the halide to generate a better leaving group. Different nitriles were used as trapping reagents. Aqueous work up of **6A** yields the corresponding amides **7** *via* a Ritter-type reaction.[28] Bach and co-workers reported comparable results (Scheme 1.3b). The employment of secondary alkyl halides yielded *vicinal* nitro amides through activation of the halide. Interestingly, 2-methylbutane (**8**) as a substrate yielded the same product *via* hydride abstraction at the tertiary carbon atom. According to the proposed mechanism, **8A** is formed upon oxidation of the tertiary C–H bond. Elimination leads to formation of **8B** and the nitronium ion is attacked by the double bond. Finally, **8C** is scavenged by the solvent to form **8D**. Aqueous work up gives the *vicinally* functionalized product **9**.[29] Further, oxidation of propellanes and other simple alkanes was successfully reported in the following years.[30]
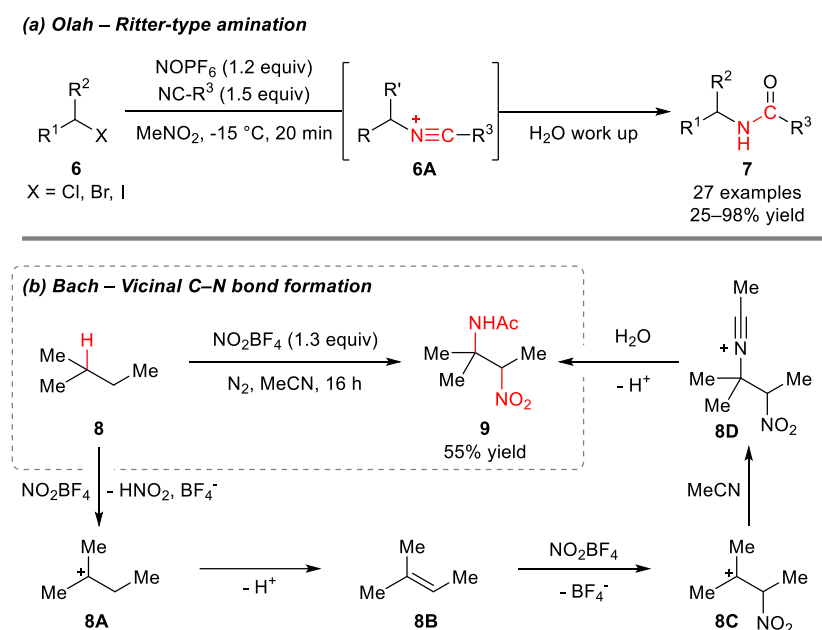
Scheme 1.3 Oxidative functionalization of carbon-halide and C$_{sp}^3$–H bonds. (a) Ritter-type amination of secondary alkylhalides. (b) *Vicinal* C–N bond formation by oxidation of inert C$_{sp}^3$–H bonds.

In addition, Olah's group reported the oxidative fluorination of thioethers (**10**) and dithiolanes (**12**) (Scheme 1.4).[31] Initially, *S*-nitrosation for the formation of **10A** leads to the activation of the C–S bond, followed by the nucleophilic attack of fluoride to form **11**. PPHF (hydrogen fluoride pyridine) serves as fluoride source in this reaction. The method allowed the mono-functionalization of thioethers as well as the synthesis of *geminal* difluorinated products (**13**) using thioacetals (**12**). In the absence of a fluoride donor, the sulfides are converted to the corresponding ketones.[32]

Olah – Fluorination of thioethers and dithiolanes
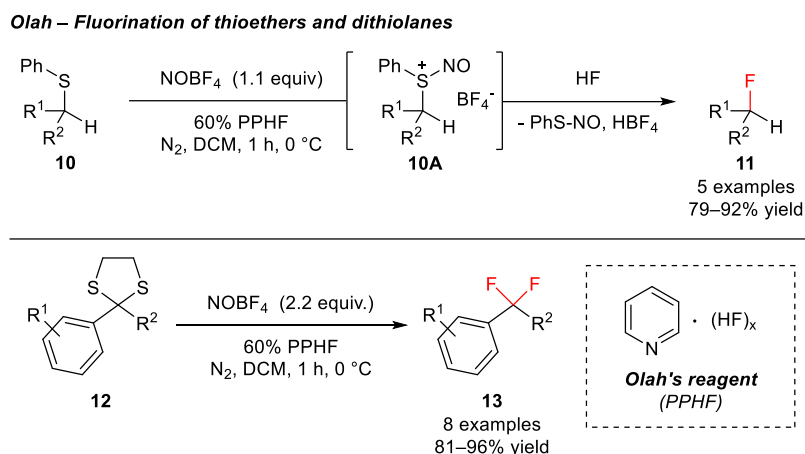
Scheme 1.4 Fluorination of thioethers and dithiolanes using nitrosonium tetrafluoroborate.

The conversion of nitroalkanes (**14**) to ketones (**15**) and oximes (**16**) with sodium nitrite was reported by Mioskowski and co-workers (Scheme 1.5a).[33] The authors proposed the *in situ* formation of nitrosonium ions, which are involved in the oxidation of the starting materials. The synthesis of ketones or oximes from secondary nitroalkanes is also known as Nef reaction.[34] Despite the synthetic applicability, the mode of action of sodium nitrite, in particular the exact role of the nitrosonium ion could not be conclusively uncovered yet. However, conversion of oximes to ketones is known to involve nitrosonium species.[35]

Using related reaction conditions, Reddy and co-workers reported the synthesis of naphthalenes **18** from arylated nitroalkanes **17** (Scheme 1.5b).[36] The authors proposed a Friedel-Crafts-like reaction mechanism upon functionalization of the nitroalkane. Oxime **17A** was proposed as intermediate, which undergoes nitrosation in order to form **17B**. Intramolecular nucleophilic attack and formation of **17C** induces the Friedel-Crafts-type reaction. In the following, elimination of 1,2-dihydroxydiazene as leaving group occurs and the product is formed. The diazene further decomposes to water and nitrous acid.

(a) Mioskowski – Synthesis of ketones and oximes

NaNO$_2$ (2 equiv.)

7:1 DMSO / H$_2$O
rt or 65 °C, 21 h

NaNO$_2$ (2 equiv.)

7:1 DMSO / H$_2$O
rt or 65 °C, 21 h

15
5 examples
65–86% yield

nitroalkanes (14)

16
2 examples
99% yield

electron rich substrates

75%

quant.

electron deficient substrate

quant.

(b) Reddy – Friedel-Crafts alkylation

NaNO$_2$ (1 equiv)

DMF, 100 °C, 6-10 h

17

18
23 examples
14–92% yield

key intermediates

NO$^+$

17A

17B

17C
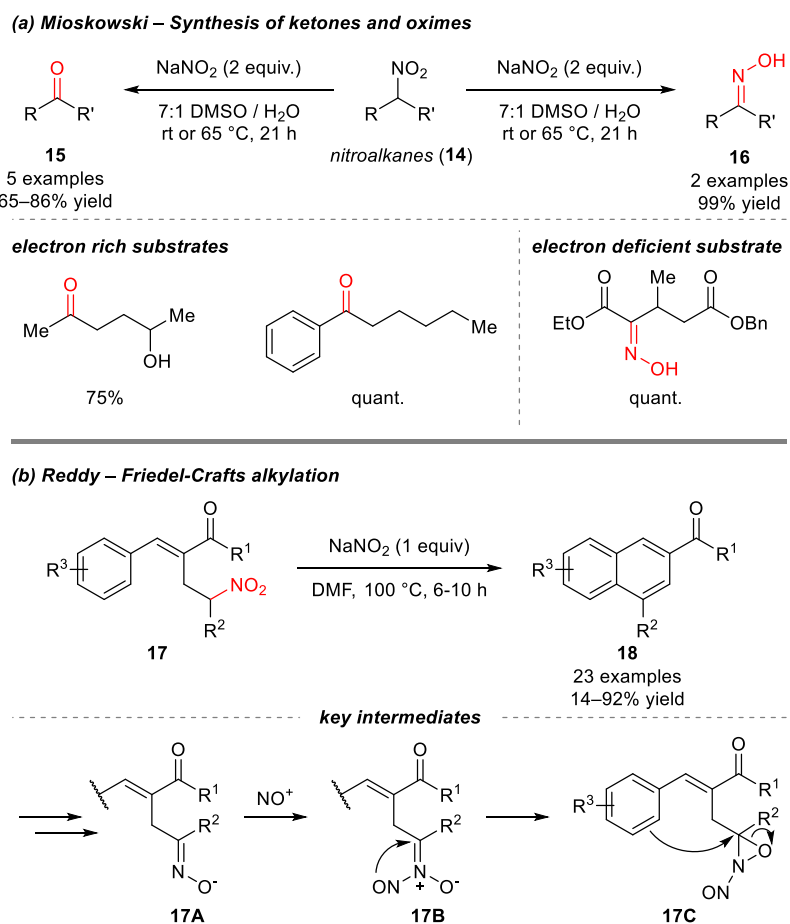
Scheme 1.5 Sodium nitrite mediated functionalization of secondary nitroalkanes. (a) Synthesis of ketones and oximes from nitroalkanes. (b) Friedel-Crafts-like synthesis of naphthalenes.

In 2014, Molander and Cavalcanti reported the efficient nitrosation of aromatic boronates (**19**) with nitrosonium tetrafluoroborate (Scheme 1.6a).[37] The reported reaction conditions allowed the synthesis of a broad number of nitroso arenes (**20**), including challenging heteroarenes. For the majority of substrates, the formation of products occurred within 30 seconds. The transformation is also suitable for aryl boronic acids and aryl boronic esters, but with reduced yields.

In 2018, Hilt and co-workers reported a related transformation for the nitrosodesilylation of **21** (Scheme 1.6b).[38] A shared feature of both methods is the fast reaction rate. According to the proposed mechanism for both approaches, a shared pathway for the nitrosation exists *via ipso*-substitution of the leaving group. Precise control of the amount of nitrosonium salt was crucial, in order to avoid poly-nitrosation. By using trimethylsilyl-substituted fluorobenzene as model substrate, ^{19}F-NMR studies revealed that more equivalents of nitrosonium tetrafluoroborate lead to the addition of a second nitronium ion to the nitroso group.
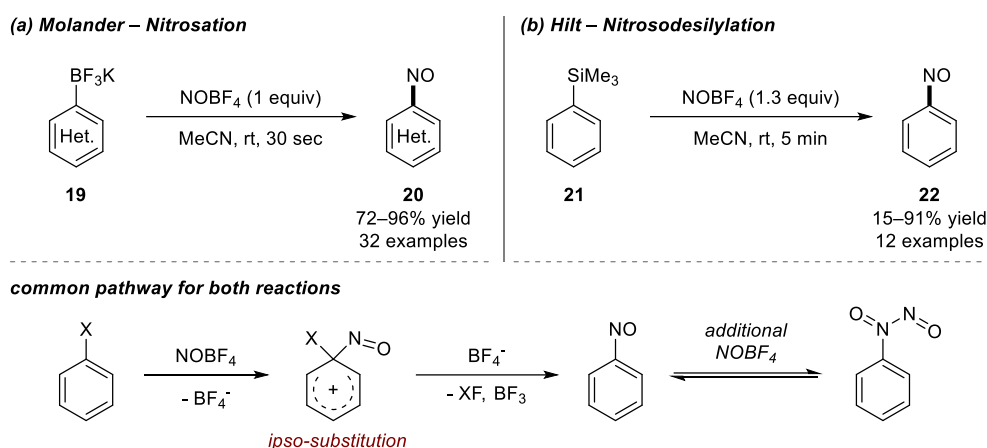
Scheme 1.6 Nitrosation of weak C_{sp}^2-heteroatom bonds. (a) Nitrosation of heteroaryl borates with nitrosonium tetrafluoroborate. (b) Synthesis of nitrosobenzene *via* nitrosodesilylation.

Zefirov and co-workers converted the halogenated cyclopropanes **23** to fluorinated pyrimidine *N*-oxides (**24**) under incorporation of a nitrosonium ion and an organic nitrile molecule (Scheme 1.7a).[39] According to the proposed mechanism, the nitrosonium ion reacts with the strained C–C bond of the cyclopropanes **23**. Ring opening gives the positively charged intermediate **23A**, which is subsequently scavenged by the nitrile to form **23B**. Nucleophilic attack at the nitrile carbon leads to the formation of **23C**. Finally, aromatization with elimination of HBr affords the pyrimidine *N*-oxide **24**.
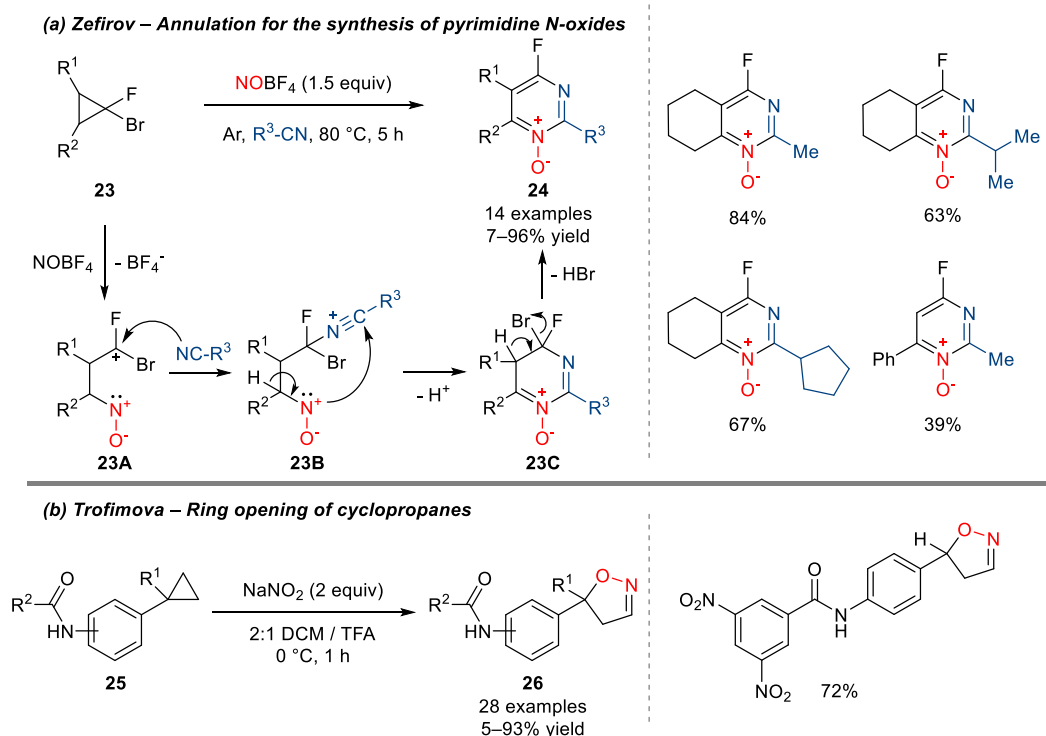
Scheme 1.7 Oxidative C–C bond functionalization of cyclopropanes. (a) Nitrosation of *geminal*-bromofluorocyclopropanes for the synthesis of pyrimidine *N*-oxides. (b) Synthesis of aniline-fused isoxazolines.

Trofimova reported the functionalization of cyclopropyl substituted anilines **25** (Scheme 1.7b). Oxidative addition of the nitrosonium ion to the cyclopropane unit yielded isoxazolines **26**.[40] Sodium nitrite served as source for nitrosonium ions, since they were generated *in situ* under the acidic reaction conditions. However, undesired nitration, formation of benzoxazines, and formation of quinolines as by-products limited the synthetic applicability. In analogy to the work of Trofimova's group, synthesis of halogenated isoxazoles was reported by Zyk and co-workers.[41]

Recently, Tu's group reported the incorporation of nitrosonium tetrafluoroborate using silyl allyl ethers **27** (Scheme 1.8).[42] The developed reaction conditions allowed the synthesis of different polycyclic oximes (**28**) in good yields and short reacting times *via* a semipinacol rearrangement. According to the proposed mechanism, the nitrosonium cation reacts with the enolic double bond (**27A**), inducing the C–C bond migration of the cyclobutan moiety to form intermediate **27B**. The TBS-protecting group is released upon H-elimination and intramolecular attack, whereupon the final product **28** is formed with high relative stereoselectivity. Depending on the ring size, the reaction stopped without intramolecular cyclization, giving access to polycyclic ketones instead of oximes.
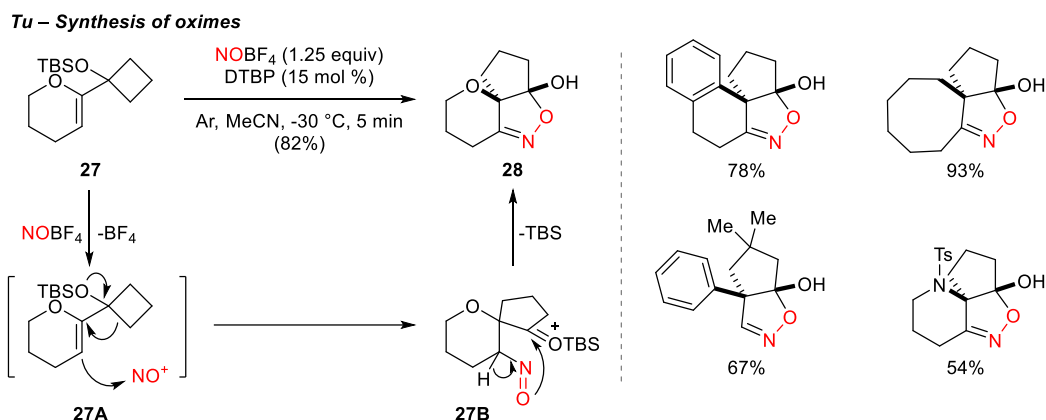
Scheme 1.8 Tu's synthesis of oximes *via* ring opening of cyclobutanes.

1.2.2 Functionalization of π-bonds

The reactivity of nitrosonium and nitronium ions towards various π-bonds has been studied in the past decades. Functionalization occurs under incorporation of the nitrosonium ion into the target structure or in a catalytic fashion. In 1971, Scheinbaum and co-workers reported the Ritter-type functionalization of propylene (**29**) and butene (Scheme 1.9).[43] The product formation results from the addition of the nitronium ion to the alkene and subsequent

nucleophilic attack of the solvent. Hydrolysis converts the intermediate **29A** to the corresponding amide **30**. In the absence of a scavenging nucleophile, nitrosonium salts act as initiators for alkene polymerization.[44]
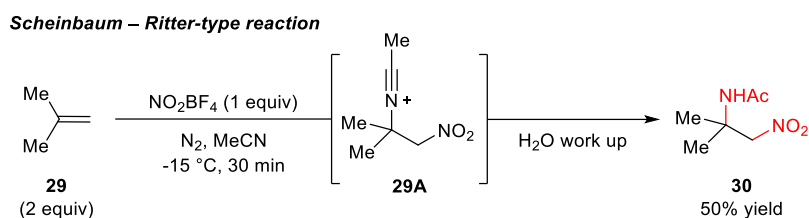
Scheme 1.9 Ritter-type functionalization of propylene with nitronium tetrafluoroborate.

Kim and co-workers applied nitrosonium tetrafluoroborate for the synthesis of 2-isooxazolines (**32**) using unsaturated esters **31** (Scheme 1.10a).[45] According to the proposed mechanism, the double bond attacks the nitrosonium ion to generate the positively charged intermediate **31A**. The neighbouring ester group scavenges the positive charge to form cyclic intermediate **31B**. Finally, intramolecular attack of the nitroso group forms the isoxazoline **32**. The developed strategy was later applied by Macritchie within the synthesis of racemic Brevioxime.[46]
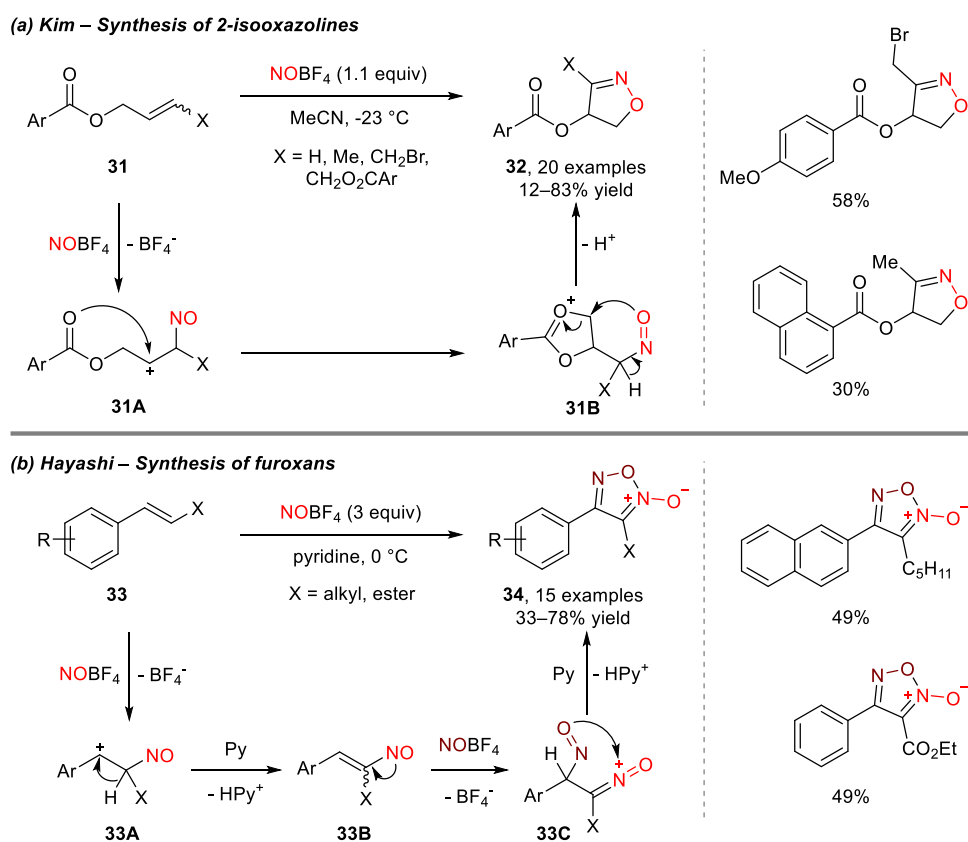
Scheme 1.10 Functionalization of π-bonds under incorporation of nitrosonium ions. (a) Synthesis of 2-isooxazolines using unsaturated aryl ether. (b) Synthesis of furoxanes in pyridine.

Hayashi and co-workers achieved the incorporation of two nitrosonium ions for the regioselective synthesis of furoxans **34** (Scheme 1.10b). Regioselectivity was reasoned through the stability of the benzylic cation **33A** and steric effects favouring the deprotonation by pyridine at the less hindered position to form **33B**. Intermediate **33B** reacts with a second equivalent of the nitrosonium ion to form **33C**, which undergoes ring closure to form furoxanes **34**.[47] The same results were achieved using the $NaNO_2$-AcOH system.[48]

Wu and co-workers contributed with an interesting example of a radical annulation reaction of imines (**35**) with electron-rich alkenes (**36**) (Scheme 1.11a).[49] In this Povarov-type reaction, the nitrosonium cation acts as an initiator and not as a catalyst. The nitrosonium ion oxidizes the vinyl starting material through a SET, followed by a nucleophilic attack of imine **35**. The formed intermediate **35A** undergoes radical transfer with another molecule of the vinyl starting material in order to form intermediate **35B** and to propagate the reaction. In the last step, intramolecular attack takes place to form the annulated product **37**. Analogously, the coupling of **36** with oximes was reported by the same group.[50]
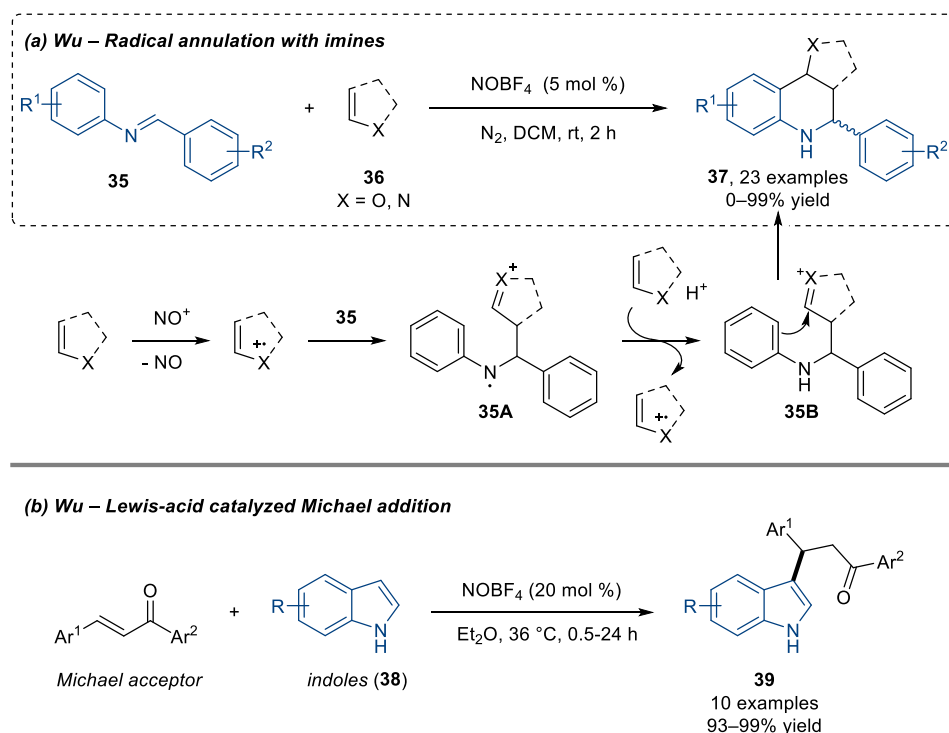
**Scheme 1.11** Nitrosonium salts as initiator and catalyst for synthetic transformation. (a) Nitrosonium initiated Povarov-type reaction of imines with electron-rich alkenes. (b) Michael addition of indoles to enones catalyzed by nitrosonium tetrafluoroborate.

Later on, the same group studied an alternative mode of action for nitrosonium tetrafluoroborate. Nitrosonium ions were found to efficiently catalyze the Michael addition of

indoles (**38**) with α,β-unsaturated ketones for the synthesis of C3-alkylated indoles **39** (Scheme 1.11b).[51] Within this reaction, nitrosonium tetrafluoroborate acts as an oxophilic Lewis-acid, underlining the variability of nitrosonium salts to promote different types of transformation.

In 2008, Neumann and co-worker reported the catalytic hydroarylation of alkenes (**41**) with simple arenes (**40**) for the synthesis of **42** (Scheme 1.12). Within this study, the authors generated a soluble nitrosonium catalyst by adding an organic counter ion to the reaction. For some examples, a more reactive heterogeneous phosphotungsten catalyst (POM) proved to give better results. In the absence of an arene as coupling partner, alkene dimerization was identified as the outcome of the reaction by GC-MS analysis. Unfortunately, no mechanism for this transformation was proposed, although it was assumed that alkene dimerization included a double bond nitrosation step.[52]
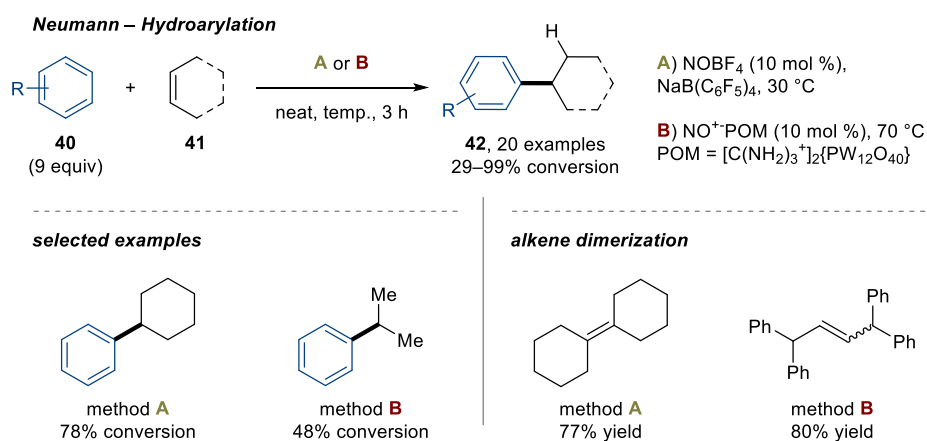
Scheme 1.12 Catalytic functionalization of alkenes with homogeneous and heterogeneous nitrosonium catalysts.

Winum and co-workers reported the catalytic Ferrier rearrangement achieving *N*-glycosylation of glycals (**43**) (Scheme 1.13).[53] Five glycals were converted into 2,3-unsaturated glycosides **45**, albeit without selectivity for the formation of the anomeric center. According to the mechanism, a SET process initiates the transformation to generate the oxocarbenium radical **43A**. Elimination of an acetate radical leads to formation of **43B** and upon charge delocalization, intermediate **43C** reacts with the hydroxysulfamide (**44**) to form the unsaturated glycoside **45**. The released acetate radical regenerates the nitrosonium ion to maintain the catalytic activity. Importantly, the obtained products revealed inhibitory activities against different isoforms of the enzyme carbonic anhydrase.
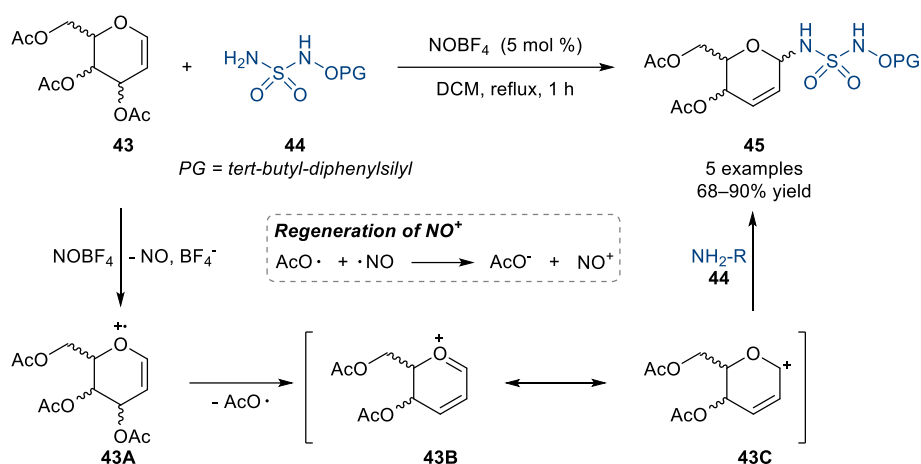
Scheme 1.13 Catalytic Ferrier rearrangement for the catalytic *N*-glycosylation of glycals.

Another pioneer in the field of nitrosonium salt chemistry was Finn Radner. His group reported the *vicinal* iodo-functionalization of cyclohexene (**46**) using nitrosonium tetrafluoroborate as catalyst (Scheme 1.14a).[54] According to the proposed mechanism, the nitrosonium ion oxidizes elemental iodine to generate highly electrophilic IBF₄. The activation of iodine leads to addition of the I$^+$ species to cyclohexene (**46**) to form halonium ion intermediate **46A**, which undergoes *trans*-selective ring opening with various nucleophiles to form **47**. Iodine, acetate, nitrile- and thiocyanate were successfully applied as nucleophiles. Importantly, ambient oxygen served as terminal oxidant in the reaction.
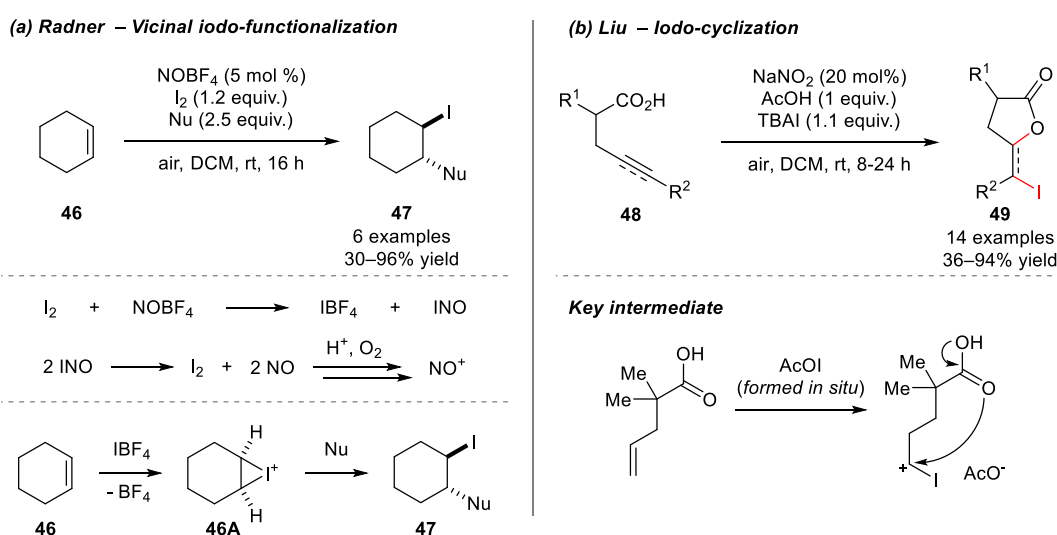
Scheme 1.14 Catalytic iodo-functionalization of π-bonds. (a) 1,2-Iodo-functionalization of cyclohexane. (b) Catalytic iodo-cyclization for the synthesis of lactones.

Later, Liu and co-workers developed the iodo-cyclizations of alkenes and alkynes (**48**) for the synthesis of lactons (**49**) (Scheme 1.14b). Acetyl hypoiodite (AcOI) was proposed as key

intermediate in accordance to the work by Radner.[55] Sodium nitrite serves as the source for nitrosonium ions and ambient air as oxidant to regenerate the reactive nitrogen species.

In 1994, Olah and co-workers reported the fluorination of diarylacetylenes **50**. PPHF (Olah's reagent) was applied as the source for fluoride nucleophiles (Scheme 1.15a).[56] According to the proposed mechanism, the nitrosonium ion adds to the triple bond leading to the first attack of fluoride to form intermediate **50A**. Formation of intermediate **50B** induces the formation a benzylic cation, which also reacts with fluoride. Nitrosation of the oxime **50C** and subsequent fluorination of **50D** is followed by elimination of 1,2-dihydroxydiazene (**50E**) in order to form **50F**. The diazene further decomposes to water and nitrous acid. Thereby, fluoride attacks the benzylic cation of **50E** to give the perfluorinated product **51**.
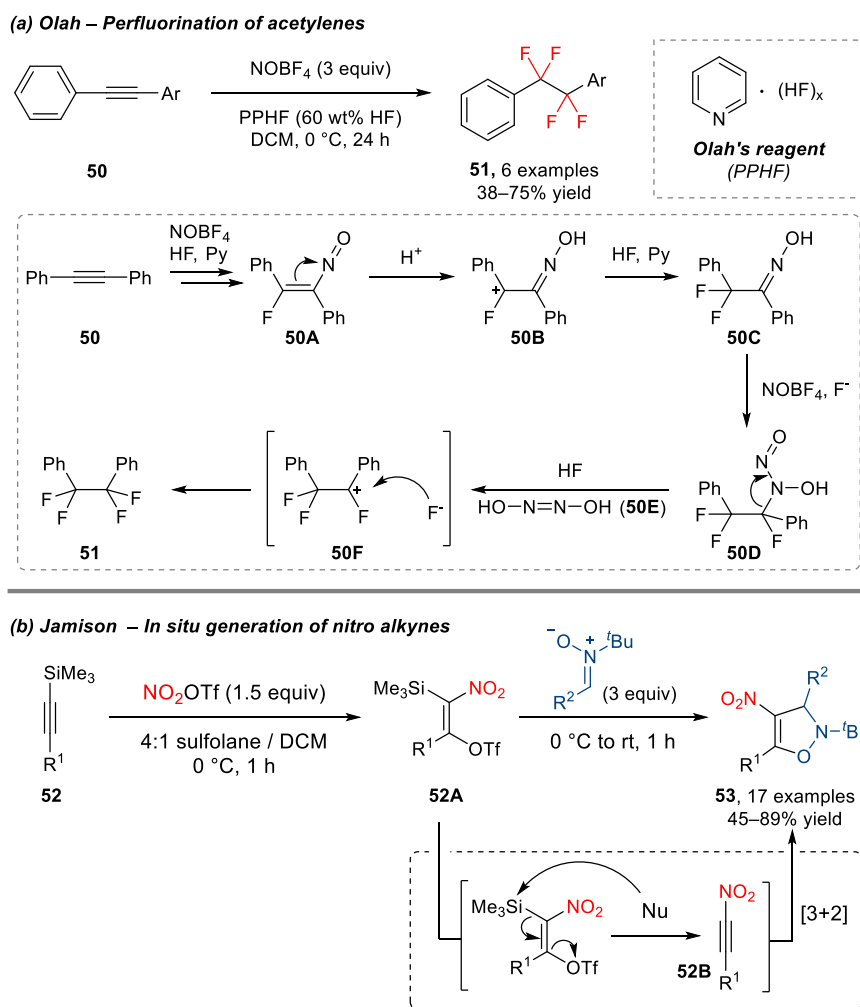
Scheme 1.15 Functionalization of acetylenes. (a) Fluorination of diarylacetylenes. (b) Silyl triflates as nitro alkyne equivalents for the synthesis of heterocycles in batch and continuous flow.

Recently, the generation of silyl triflates **52A** derived from trimethylsilyl alkynes **52** as equivalents of nitro alkynes was reported by Jamison and co-worker in batch and continuous

flow (Scheme 1.15b).[57] Nitro alkynes suffer from poor stability and the application in organic synthesis appeared to be illusive. Jamison's group reported that treatment of alkynes **52** with a solution of nitronium triflate in sulfolane leads to the *in situ* formation of nitro alkynes **52B**, which smoothly undergo [3+2] cycloaddition with nitrones to form stable 4-nitro-4-isoxazolines (**53**). Online NMR spectroscopy indicated the formation of a silyl triflate **52A** as a key intermediate. The application of a flow reactor bypasses the danger of working with hazardous and potentially explosive intermediates for the synthesis of useful heterocycles.

1.2.3 C–H bond functionalization of arenes

In 1946, Ingold and Hudges considered the nitronium cation as a reactive electrophile for aromatic nitration reactions.[58] In the following years an alternative mechanism based on a SET process and recombination of the radical species was discovered (Scheme 1.16a).[59] Nowadays, the possibility for a SET mechanism is supported by theoretical calculation.[60] The co-existence of the polar mechanism and the SET mechanism for the nitrosation of activated arenes was proposed by other groups.[61]

In-depth mechanistic studies by Kochi and Radner for the C–H bond nitrosation translated into a general methodology for the functionalization of anisole derivatives and poly-methylated arenes (**54**) (Scheme 1.16b).[62] Typically, the nitrosated products **55** were isolated as single regioisomers. Interestingly, *meta*-xylene underwent the nitrosation with good yields, while no product was formed when *ortho*-xylene was used as substrate. A strong kinetic isotope effect was determined and UV/Vis spectroscopy allowed the identification of a charge-transfer-complex. The experimental findings support the nitrosation *via* a radical pathway. Nitration of arenes can be achieved under the same reaction conditions using nitronium- instead of nitrosonium tetrafluoroborate.[63]

In the following years, nitration of phenols was achieved using various inorganic and organic nitrates.[64] Treatment of 18-crown-6 ether with gaseous N_2O_4 gives a stable nitrosonium complex, which was applied for the nitration of phenols as well.[65] In the following years, *tert*-butyl nitrite (TBN) replaced nitrosonium salts in the nitrosation of arenes due to the aforementioned advantages.[66] Recently, Düsel and König reported the photocatalytic nitration of anilides.[67] Sodium nitrite served in this reaction as the source for NO_2 radicals. However, the course of reaction does not include the formation of reactive nitronium or nitrosonium species.
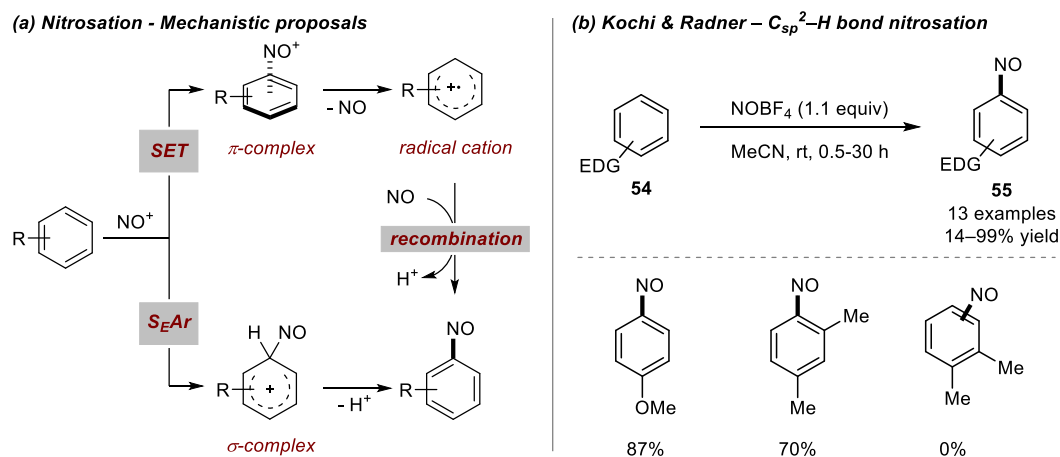
Scheme 1.16 Nitrosation of arenes. (a) Proposed pathways for aromatic nitrosation of arenes. (b) Nitrosation of anisole derivatives and poly-methylated arenes.

In 1988, Radner and co-workers were the first to report the catalytic iodination of simple arenes (**56**) using NOBF$_4$ as catalyst under aerobic conditions (Scheme 1.17a).[68] The reaction proceeds in a Friedel-Crafts fashion through the oxidation of iodide to I$^+$ species, followed by electrophilic aromatic substitution for the synthesis of iodoarenes (**57**) (also see Scheme 1.14). This system was also applied for bromination and chlorination, using NH$_4$Br and NH$_4$Cl, respectively. Based on control experiments, the *in situ* formation of I$^+$ species and the regeneration of the nitrosonium ions by ambient oxygen was proposed. The distribution of regioisomers was in accordance to expected trends for an electrophilic aromatic substitution. Inspired by the pioneer work of Radner, several groups reported the combination of sodium nitrite and strong Brønsted-acids for the sustainable halogenation of arenes, enolizable C–H bonds, and alkenes.[69] In accordance to the proposed mechanism by Radner, these transformations proceed *via* the *in situ* generation of nitrosonium ions and oxidation of the halogens to generate electrophilic species.

Li and co-workers reported a related transformation for the efficient iodination of electron-rich arenes **58** yielding iodoarenes **59** (Scheme 1.17b).[70] Interestingly, gaseous nitrogen dioxide was applied as catalyst for the transformation. According to the proposed mechanism, nitrogen dioxide is in equilibrium with nitrosonium species. The nitrosonium ion oxidizes iodine, which undergoes electrophilic aromatic substitution with the arene. The formed nitrogen dioxide is re-oxidized by ambient air to maintain the catalytic activity. To proof the involvement of nitrosonium ions, the reaction was repeated with nitrosonium tetrafluoroborate in substoichiometric amounts. The identical outcome was observed, suggesting the generation of nitrosonium ions during the course of reaction. Additionally, no biaryl formation took place in

the absence of iodine, which suggested that only iodine was oxidized. Later, the same group expanded the developed reaction to the oxidative thiocyanation of electron-rich arenes **60** by employing gaseous nitrogen dioxide as the catalyst (Scheme 1.17c).[71] The reaction proceeds through generation of a radical cation intermediate, which reacts with the thiocyanate. Subsequent oxidation and rearomatization affords the corresponding arylthiocyanate **61**. The developed reaction proceeds analogously with nitrosonium tetrafluoroborate as the catalyst.
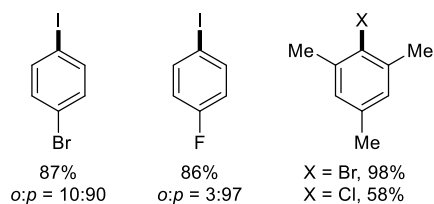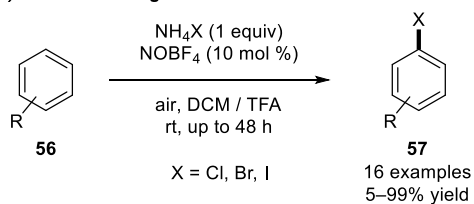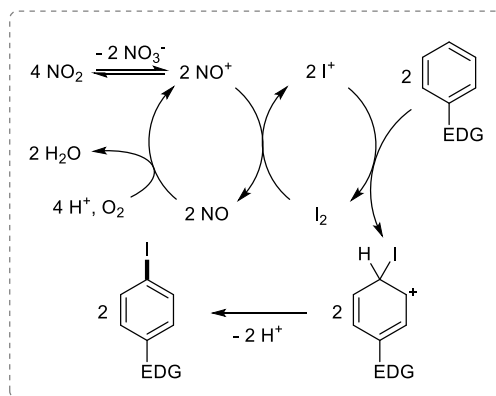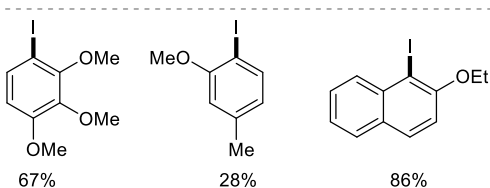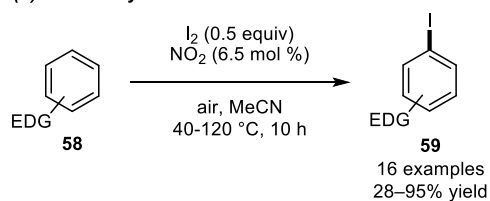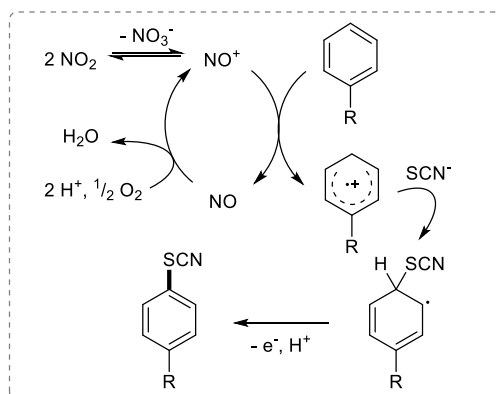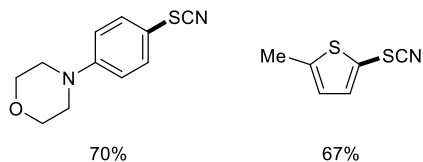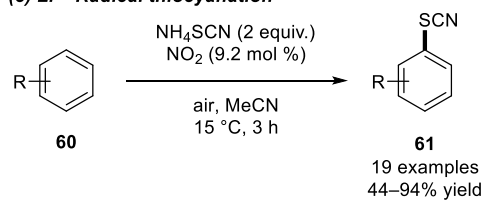
Scheme 1.17 Catalytic C–H bond functionalization of arenes. (a) Radner's aerobic and catalytic halogenation of arenes. (b) Nitrogen dioxide-catalyzed electrophilic iodination of anisole derivatives. (c) Radical thiocyanation of electron-rich arenes.

1.2.4 Non-directed coupling of arenes under aerobic conditions

The formation of radical species *via* single-electron-transfer (SET) processes is a key step for the non-directed functionalization of aromatic compounds (Figure 1.1). The radical cation reacts with a second nucleophilic arene (often itself). A second oxidation step is followed by rearomatization to give the biaryl product. This process allows the two-fold C–H bond functionalization, since no leaving group is required on both coupling partners. The ability of nitrosonium salts to oxidize electron-rich arenes to radical cations has been studied intensively in the past decades.[72] Shine and Bandlish were the first to isolate and characterize stable radical cation salts generated by treating polycyclic aromatic compounds with stoichiometric amounts of nitrosonium tetrafluoroborate.[73]
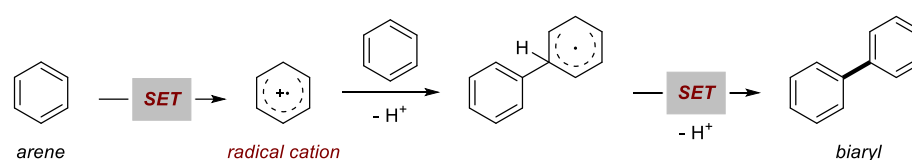
Figure 1.1 Non-directed C–H bond functionalization of arenes *via* SET for the generation of radical intermediates.

Despite the insights into the oxidation processes mediated by nitrosonium salts, practical application for oxidative coupling of arenes using nitrosonium ions are comparably less intensively studied. The first example of a nitrosonium ion catalyzed coupling reaction of naphthalenes **62** was reported by Radner's group in 1988 (Scheme 1.18a). The homo-coupled products **63** were obtained by employing ambient oxygen as the terminal oxidant.[74] The formation of π-complexes and subsequent radical cation formation for the biaryl coupling was later confirmed by Shubin's group by means of NMR-studies. This study provided the first evidence for a common pathway of nitrosation and biaryl coupling of arenes.[75]

Souma and co-workers continued the initial studies on the non-directed biaryl coupling of naphthalenes (**64**) for the synthesis of binaphthalenes (**65**) (Scheme 1.18b).[76] Treatment of NaNO$_2$ with triflic acid allowed the *in situ* generation of reactive nitrosonium species. Depending on the reactivity of the naphthalene, the temperature had to be adjusted to avoid decomposition of starting material. Ambient oxygen maintained the catalytic cycle. Importantly, loading of acid was crucial to suppress undesired nitration of the starting material and the product.[63] A conclusive cycle for the regeneration of nitrosonium ions was proposed (Scheme 1.18c). Formed nitrogen monoxide is oxidized by ambient oxygen to form nitrogen dioxide. Nitrogen dioxide is in equilibrium with dinitrogen tetroxide, which undergoes

disproportionation to form labile nitrosonium nitrite. In the presence of a strong acid protonation takes place to release a nitrosonium ion, a nitronium ion and water. The nitrosonium ion is able to oxidize nitrogen monoxide, whereupon nitrogen dioxide is able to re-enter the catalytic cycle.[77]
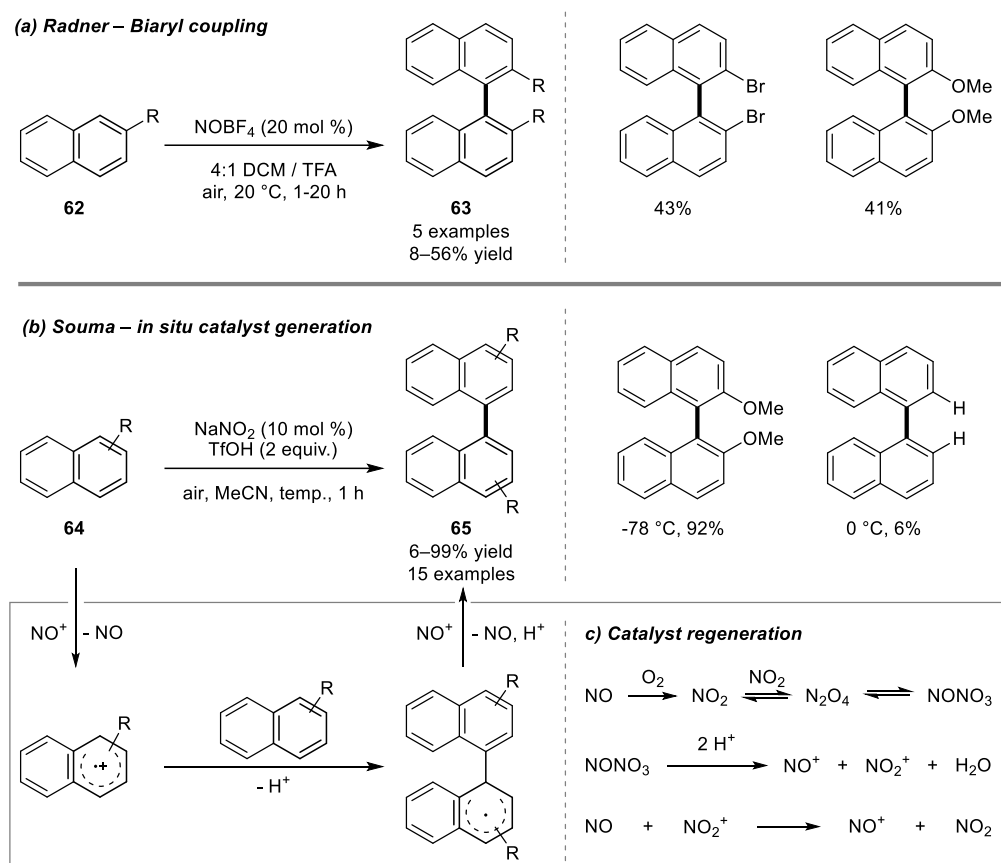
Scheme 1.18 Catalytic oxidative coupling of naphthalenes. (a) First catalytic biaryl coupling (b) *In situ* generation of nitrosonium ions for the catalytic coupling of naphthalenes. (c) Proposed catalytic cycle.

Oxidative biaryl coupling catalyzed by nitrosonium ions remained untouched for several decades. In 2012, Wang and co-workers reported the synthesis of electron-rich phenanthrene rings **67** *via* intramolecular C–C bond formation employing **66** as starting material (Scheme 1.19a).[78] The scope for the oxidative coupling reaction was also extended to the intermolecular homo-coupling of 1,2,4-trimethoxybenzene. Additionally, the same group reported the catalytic intramolecular arene-phenol coupling of **68** under aerobic conditions for the synthesis of spiro-cyclohexadienones **69** (Scheme 1.19b).[79] According to the proposed mechanism, a SET-process and subsequent deprotonation initiates the reaction to form a hexadienone radical (**68A**). Intramolecular attack to form **68B** is followed by a second SET process and rearomatization yields the spirocyclic dienone motif. Oxidation of the starting material leads to the formation of nitrogen monooxide, which is oxidized by ambient air. Two molecules of

nitrogen dioxide dimerize to form dinitrogen tetroxide. Finally, dinitrogen tetroxide is in equilibrium with nitrosonium nitrite, which serves as source for nitrosonium ions. The proposed regenerative cycle for the nitrosonium ion is in agreement with the aforementioned studies by Radner and Souma (Scheme 1.18a).

(a) Wang – Phenanthrene ring derivatives

66
R = CO$_2$H, CO$_2$R, CN, Me

NaNO$_2$ (20 mol %)
4:1 MeCN / TFA
air, rt, 30-60 min

67
16 examples
29–99% yield

(b) Wang – Spiro-cyclization

68

NaNO$_2$ (20 mol %)
4:1 DCM / TFA
air, 1 h, rt

69
20 examples
18–99% yield

NO$^+$ | - NO, H$^+$

68A

68B

NO$^+$ | - NO, H$^+$

2 NO $\xrightarrow{O_2}$ 2 NO$_2$ $\longrightarrow$ N$_2$O$_4$ $\rightleftharpoons$ NO$^+$NO$_3^-$
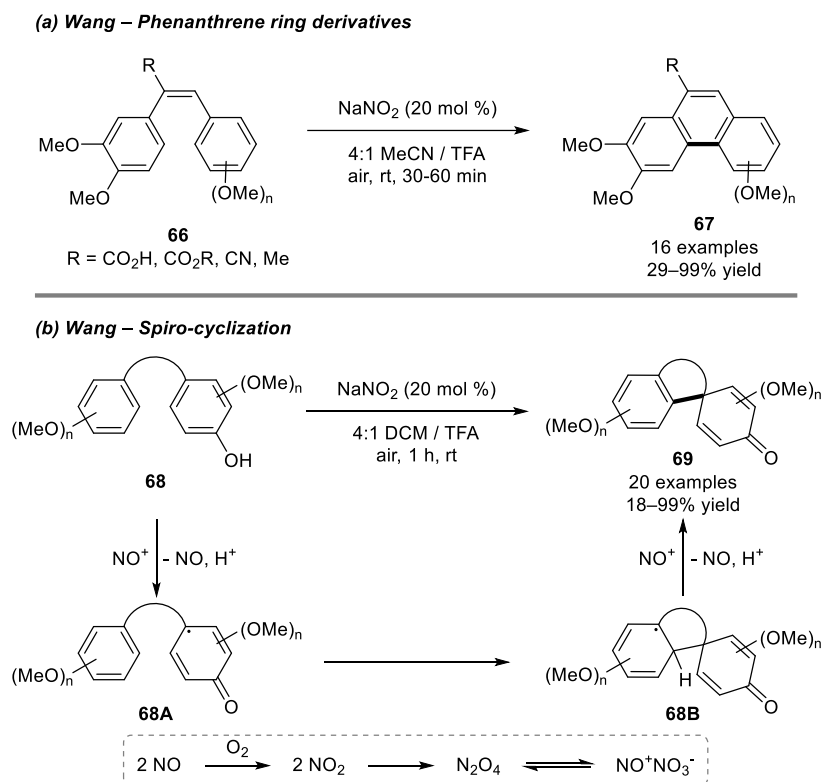
Scheme 1.19 Catalytic intramolecular biaryl coupling (a) Sodium nitrite catalyzed aerobic synthesis of polymethoxyphenanthrene rings. (b) Nitrosonium catalyzed spiro-cyclization of phenols.

Recently, König and co-workers reported the attempt for a selective cross-coupling reaction of phenol **70** with electron-rich arene **71** under photochemical reaction conditions (Scheme 1.20). Initially, LiNO$_3$ was hypothesized to serves as a radical donor under photochemical conditions. However, systematic optimization revealed that neither the photocatalyst nor blue light was required for the synthesis of **72**. In fact, it was found that under the acidic reaction condition LiNO$_3$ serves as a source for nitrosonium ions, which mediate the transformation.[80]

König – Nitrosonium-mediated phenol-arene coupling

70

71
(3 equiv)

LiNO$_3$ (0.5 equiv)
photocatalyst
9:1 HCO$_2$H / MeOH
air, rt, 4 h, blue LED

hidden NO$^+$ catalysis

72
78% yield
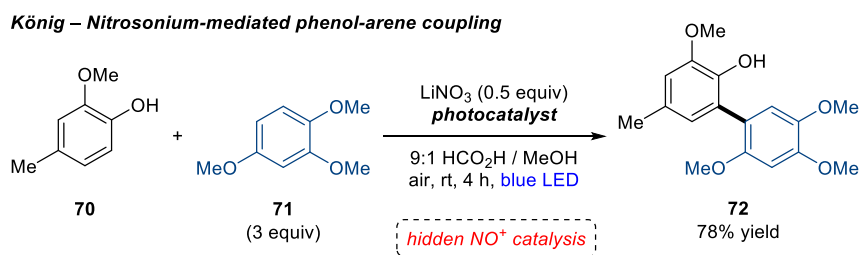
Scheme 1.20 Attempts for the oxidative coupling of phenols and arenes.

Introduction |

Objectives

2   Objectives

The interplay of metal-free reaction methodologies and strategies towards the selective functionalization of inert and abundant C–H bonds can serve as a guiding principle for the development of novel and environmentally benign reaction conditions. Thereby, metal-free chemistry can be applied to address diverse synthetic challenges. Ultimately, step- and atom economy is increased, and the generated waste is decreased. Most importantly, toxic and cost intensive transition metal-catalysts can be omitted.

The aim of this thesis was the development of novel methods for the functionalization of C–H bonds under transition metal-free conditions. On the one hand, novel transformations for the functionalization of $C_{sp}{}^2$–H bonds and challenging $C_{sp}{}^3$–H bonds should be developed. On the other hand, novel applications of nitrosonium salts as catalysts should be established, targeting the non-directed oxidative coupling of arenes. In order to achieve this goal, carbon-carbon bond formation *via* C–H/C–H cross-coupling should be studied. Based on the obtained results, C–H /X–H (with X = S, N) cross-coupling should be addressed to expand the scope of available coupling methodology using nitrosonium salts as catalysts.

Preliminary experiments of Antonchick and co-workers revealed the possibility to achieve reagent-less cross-coupling of quinoline *N*-oxides and boronic acids (Scheme 2.1). This reaction represents the first application of the Petasis reaction for the functionalization of heterocycles. The aim of this project was the systematic optimization of reaction conditions, followed by the examination of the scope of both coupling partners.
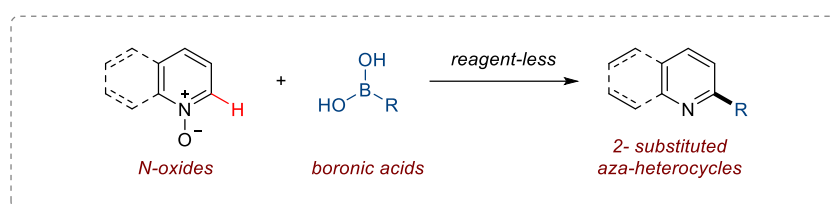
Scheme 2.1 Regioselective cross-coupling of heterocyclic *N*-Oxides with boronic acid.

The direct dihydroxylation of simple alkanes represents an unprecedented transformation. Although the functionalization of hydrocarbons gained significant interest, the *vicinal* dioxygenation under transition metal-free conditions has never been reported before. It was hypothesized that radical iodination might serve as entry into further oxidative functionalization steps of alkanes. The aim of this project was the development of an efficient method for the radical iodination of alkanes and the conversion into diols in a one-pot fashion

(Scheme 2.2). The developed reaction conditions should be applied to various saturated hydrocarbons in order to study the scope of the reaction.
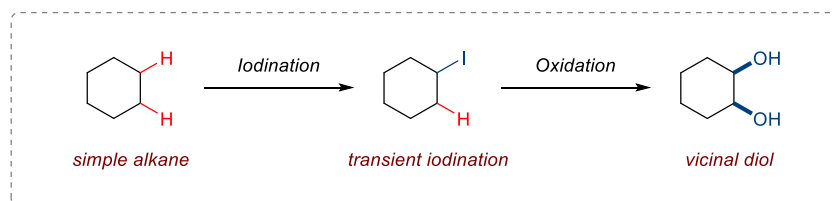
Scheme 2.2 *Vicinal* dihydroxylation of saturated hydrocarbons using hypervalent iodine(III) reagents.

Non-directed coupling of arenes catalyzed by nitrosonium ions remained almost untouched within the past decade. The application of nitrosonium salts was envisioned as an efficient and sustainable approach for non-directed coupling of arenes, since molecular oxygen serves as the terminal oxidant and water is produced as a by-product. In order to achieve this aim, the oxidative coupling of electron-rich heteroarenes should be studied (Scheme 2.3). Systematic optimization should provide mild and efficient conditions for the coupling reaction, which should serve as an alternative strategy to known methods.
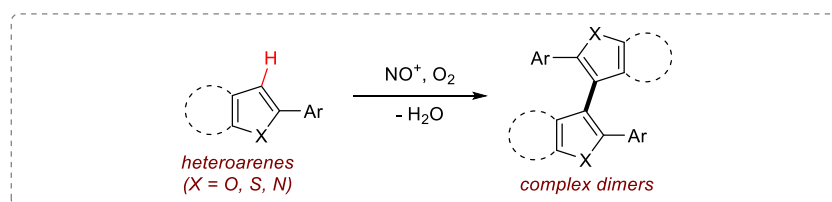
Scheme 2.3 Non-directed coupling of electron-rich heteroarenes.

The selective cross-coupling of arenes represents a great challenge. Electron-rich arenes, such as phenols, protected anilines (anilides) and indoles should be employed as starting materials in order to achieve homo- and cross-coupling, catalyzed by nitrosonium salts (Scheme 2.4). Additionally, the possibility to achieve carbon-heteroatom bond formation should be examined (Scheme 2.4). Systematic optimization of reaction conditions should be performed, the synthetic applicability should be demonstrated and the mechanism should be studied by suitable control experiments for all successful chemical transformations.
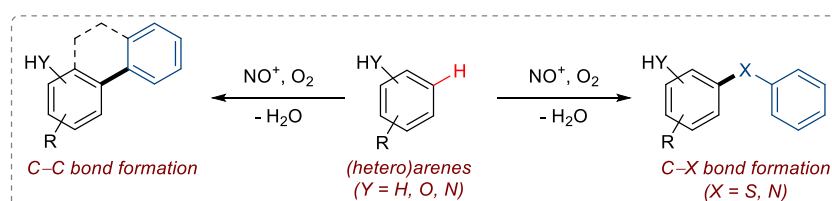
Scheme 2.4 Application of nitrosonium salts as catalysts for the non-directed oxidative coupling of arenes.

Regioselective Cross-coupling of Quinoline *N*-Oxides with Boronic Acids

3 Cross-coupling of Quinoline *N*-Oxides with Boronic Acids

3.1 Introduction

Quinolines are important molecular scaffolds for pharmaceuticals, natural products and material science.[81] Notably, quinoline-derived compounds are well known for their antimalarial and antimicrobial activities.[82] Due to the importance of quinoline scaffold, the selective functionalization is highly demanded. Palladium-catalyzed cross-coupling of heteroaromatic halides with boronic acids is a frequently used approach for the construction of carbon-carbon bonds (Figure 3.1a).[83] The required halides are accessible by utilizing *N*-oxides and phosphoryl chloride or phosphoryl bromide as starting materials (Figure 3.1b). However, the synthesis of halides is associated with low yields, insufficient regioselectivity and poor functional group tolerance.[84] Alternatively, metalation strategies can be applied.[85]
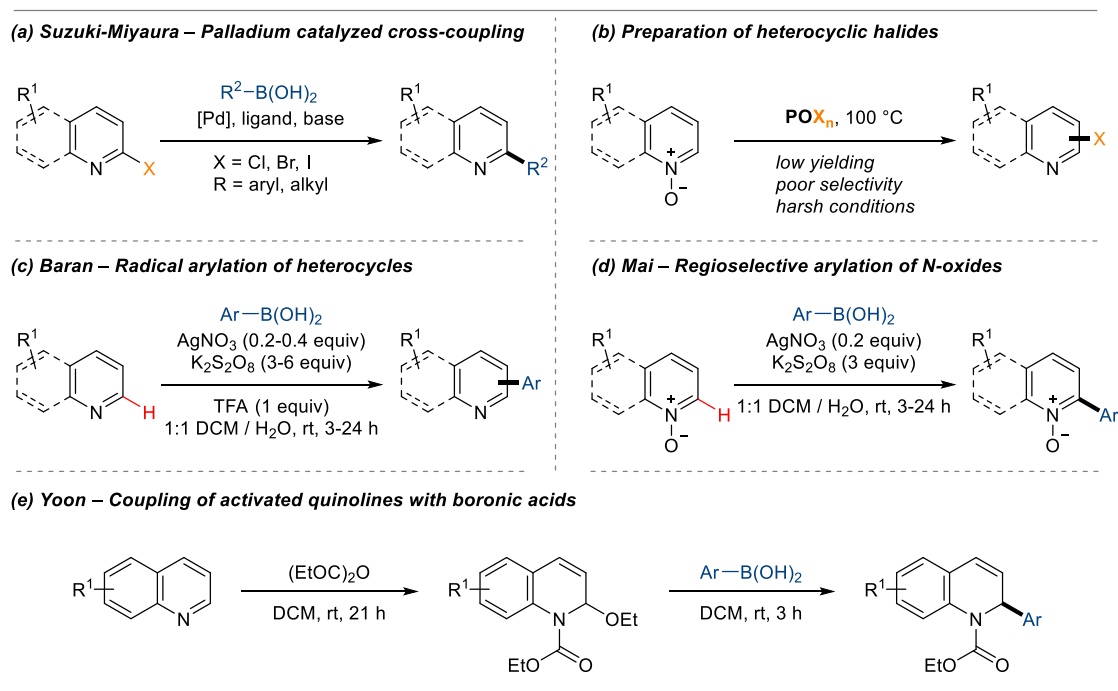
Figure 3.1 Progress towards synthetic strategies for the cross-coupling of heterocycles with boronic acids.

To overcome the requirement for step intensive pre-functionalization of starting materials, the selective C–H bond functionalization of quinolines gained significant attention.[86] Various methods for the metal-catalyzed C–H bond functionalization of quinoline *N*-oxides have been reported.[87] Baran's group reported the silver-catalyzed arylation using boronic acids for the functionalization of electron-deficient heterocycles (Figure 3.1c).[88] In this Minisci-type reaction, aryl radicals are generated from the boronic acids, which attack the electron-deficient heterocycle. Additional protonation is required to increase the electrophilicity of the

heterocycles. However, unsubstituted pyridines and quinolines suffer from C2:C4-regioselectivity issues. Based on the pioneer work by Baran's group, Mai and co-workers employed heterocyclic *N*-oxides under related reaction conditions (Figure 3.1d).[89] The employment of *N*-oxides avoids the requirement for a strong acid and improved the regioselectivity towards the C2-position. However, initial oxidation of the starting materials and an additional deprotection step of the *N*-oxide is required to obtain the functionalized *N*-heterocycles. Yoon and co-workers reported the metal-free coupling reaction of activated quinolines with boronic acids (Figure 3.1e). The reaction yielded protected dihydroquinolines, which demand further processing to obtain regioselectively functionalized quinolines.[90]

3.2 Motivation and aim of the project

Boronic acids commonly serve as organometallic nucleophiles in transition metal-catalyzed coupling reactions.[91] Nevertheless, boronic acids were also employed for the construction of carbon-carbon bonds in the absence of a transition metal-catalyst.[92] The Petasis reaction and its variants are well known approaches towards this transformation.[93] In a simplified way, the Petasis-Borono-Mannich reaction is represented by the multicomponent reaction of glyoxylic acid, amines and boronic acids (Figure 3.2). Gois and co-workers proposed a concise reaction mechanism based on density-functional-theory (DFT) calculations.[94] In the first step, glyoxylic acid and the amine form the iminium ion **73** upon condensation. The carboxylic acid coordinates the boronic acid **74** to form **75**. Induced by the proximity of the reaction partner, aryl migration occurs to form the carbon-carbon bond at the *alpha*-position of the iminium ion. Aqueous work up of **76** releases boric acid and yields the *alpha*-amino acid.
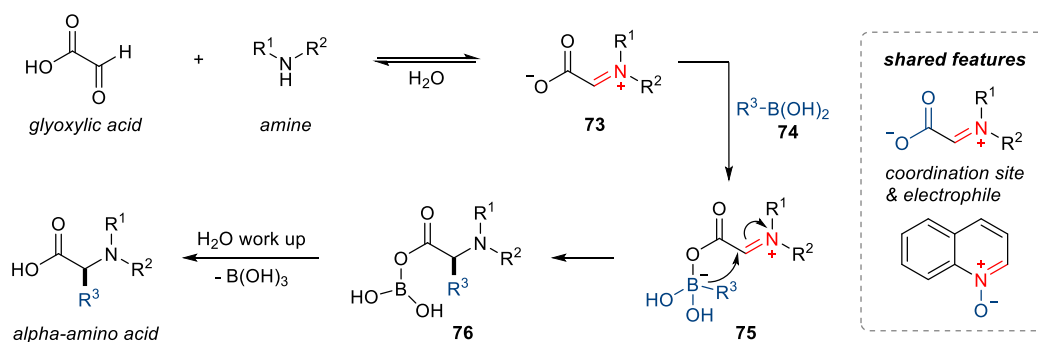
Figure 3.2 Reaction proposal for the cross-coupling of quinoline *N*-oxides and boronic acids based on the analogy with Petasis-Borono-Mannich multicomponent reaction and quinoline *N*-oxides.

Hypothetically, heterocyclic *N*-oxides offer both structural features, which are essential for the Petasis-Borono-Mannich reaction (Figure 3.2). On the one hand, the *N*-oxide serves as a coordination site for the boronic acid. On the other hand, the reactivity at the C2-position

towards nucleophiles is increased due to the polarization induced by the nitrogen-oxygen bond. Upon coordination of the boronic acid by the *N*-oxides, the resulting proximity of reaction partners should induce aryl migration *via* nucleophilic attack at the C2-position. Rearomatization and elimination of boric acids would lead to the formation of the cross-coupling product.

3.3 Initial results and optimization

The hypothesized analogy between iminium ion **73** and heterocyclic *N*-oxides served as template for the reaction design. Key step for the desired transformation was the aryl migration and subsequent cleavage of the weak nitrogen-oxygen bond to obtain the functionalized quinoline in a one-pot fashion. In order to achieve a selective cross-coupling reaction, quinoline *N*-oxide (**77a**) and nucleophilic 2-furanyl-boronic acid (**74a**) were selected as model system.

Initially, different solvents were tested in the cross-coupling reaction at elevated temperatures (Table 3.1). The polar aprotic solvents DMF and NMP afforded the desired product **78a** in 41% and 58% yield, respectively (entry 1-2). Initial testing revealed that high concentration of starting materials was crucial for the course of reaction. Screening of several nonpolar and protic solvents did not provide satisfying results (entry 3-8). Competing coordination of the solvent or low solubility of the boronic acid appeared to be unfavourable for the course of reaction. Polar aprotic solvents proved to be beneficial for the outcome of the reaction (entry 9-10). The employment of DMSO as solvent achieved a distinct improvement, affording product **78a** in 73% yield and short reaction times (entry 11). Acidic and basic solvents did not yield the product (entry 13-14). To further improve the outcome of the coupling reaction, different temperatures were tested (entry 15-18). However, 110 °C as operating temperature was already optimal. Finally, the amount of boronic acid was systematically changed (entry 19-21). However, high loading of boronic acid **74a** was required to maintain product formation.

Although the optimized conditions provided product **78a** in good yield, the deprotected quinoline could be identified as the main by-product in the reaction. The interaction of the boronic acid with quinoline *N*-oxide led to an unproductive cleavage of the weak nitrogen-oxygen bond to some extent. For further improvement of the reaction outcome, different additives were tested. Tartaric acid was used to generate a boronic ester prior to the coupling step, however no product was formed. Employment of potassium trifluoroborates did not yield the coupling product either. Further, elemental iodine, sulfur and Hantzsch ester were added to the reaction, but no conversion of starting material was observed. The presence of different

Lewis-acids did not improve the outcome of the reaction and also the presence of inorganic bases supressed the product formation. Since no further improvement was achieved, the scope of reaction was studied.

Table 3.1 Representative conditions of the optimization for the cross-coupling of *N*-oxides and boronic acids.[a]
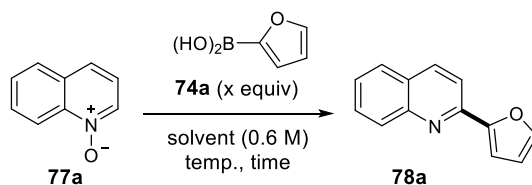
Entry	Solvent	Temp. / °C	74a (equiv)	Time / h	Yield / %[b]
1	DMF	110	3	3	41
2	NMP	110	3	3	58
3	Toluene	110	3	8	Traces
4	Chlorobenzene	110	3	8	Traces
5	EtOH	110	3	14	25
6	Water	110	3	24	Traces
7	Ethylene glycol	110	3	24	n.d.
8	Diethylene glycol	110	3	24	Traces
9	Diglyme	110	3	24	48
10	1,4-Dioxane	110	3	6	38
11	**DMSO**	**110**	**3**	**3**	**73**
12	Sulfolane	110	3	8	27
13	AcOH	110	3	24	n.d.
14	Pyridine	110	3	24	Traces
15	DMSO	80	3	12	26
16	DMSO	100	3	3	66
17	DMSO	120	3	2	56
18	DMSO	140	3	2	34
19	DMSO	110	1.5	3	56
20	DMSO	110	2	3	63
21	DMSO	110	3.5	3	70

[a] Reaction conditions: **77a** (0.2 mmol, 1 equiv), **74a** (see table), DMSO (0.6 M), under argon atmosphere, 110 °C. [b] Yields are given for isolated products after column chromatography.

3.4 Scope of heterocyclic *N*-oxides and boronic acids

With the optimized conditions in hand, the scope of the transition metal-free cross-coupling reaction was studied. All required *N*-oxides were synthesized by treating the heterocycles with *meta*-chloroperbenzoic acid (*m*CPBA).[95] Initially, the scope of heterocyclic *N*-oxides was studied (Scheme 3.1). Different functional groups at the C3-position were well tolerated, covering halogens, arenes and alkynes (**78b-e**). Electron-withdrawing substituents improved the outcome of the reaction in terms of yield and reaction time.
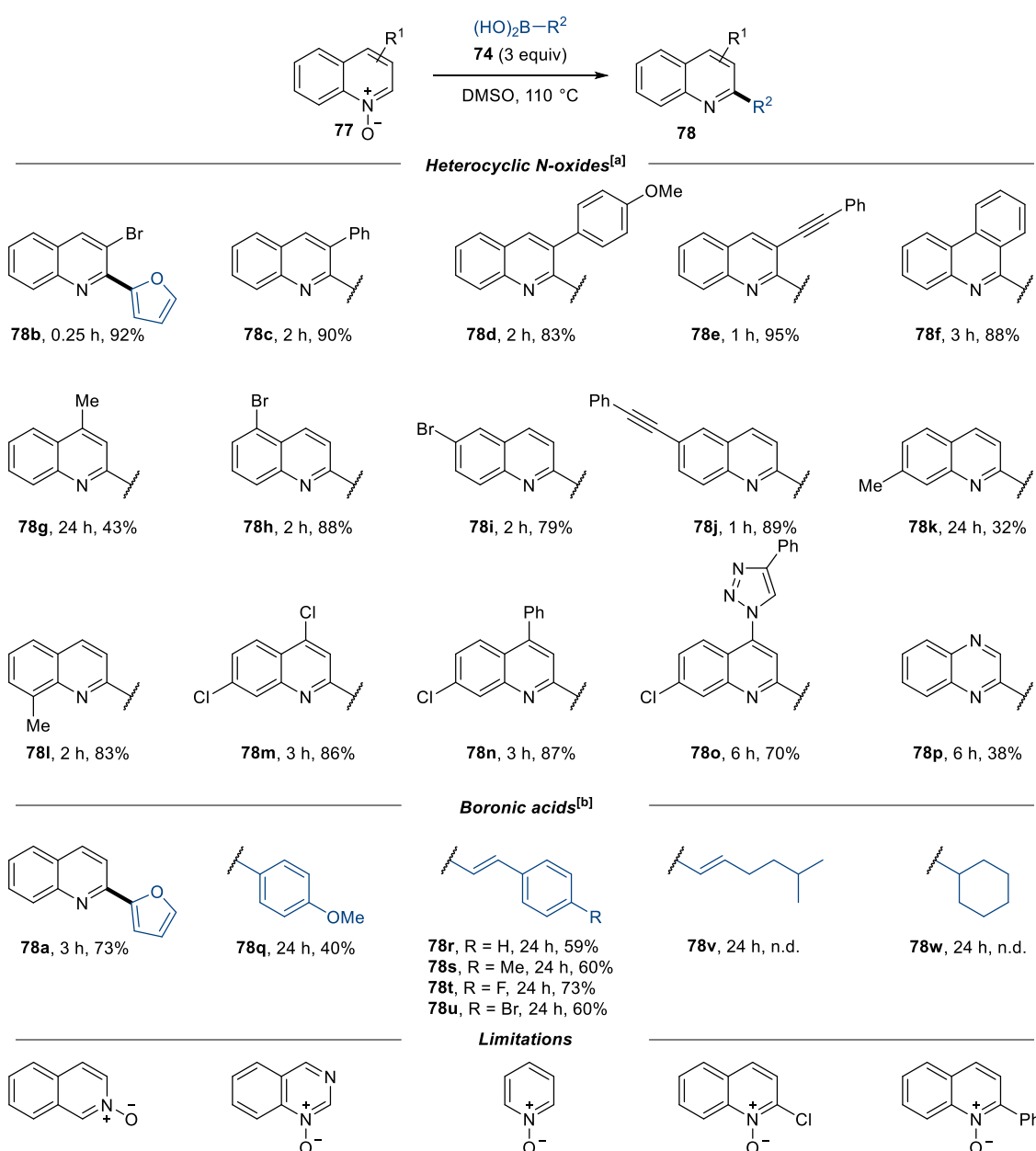
Scheme 3.1 Scope and limitation of the cross-coupling of heterocyclic *N*-oxides **77** with boronic acids **74**. [a] Reaction conditions: **77** (0.3 mmol, 1 equiv), **74a** (3 equiv), DMSO (0.6 M), under argon atmosphere, 110 °C. [b] Reaction conditions: **77a** (0.2 mmol, 1 equiv), **74** (3 equiv), DMSO (0.6 M), under argon atmosphere, 110 °C. Yields are given for isolated compounds after column chromatography.

Phenanthridine *N*-oxide underwent the coupling smoothly in 88% yield (**78f**). Further, differently substituted quinolines were systematically tested (**78g-l**). The desired products were isolated in moderate to excellent yields. Functional groups with an electron-withdrawing effect proved to be beneficial on all tested positions. Electron-donating groups yielded the coupling products in lower yields, even if the reaction time was prolonged to 24 h. Cleavage of the nitrogen-oxygen bonds and release of the quinoline was identified as the dominant side reaction. Next, a set of poly-functionalized products (**78m-o**) was synthesized in good to excellent yields. Finally, quinoxaline *N*-oxide was found as the only additional class of heterocycle, which afforded the desired product **78p** in moderate yield. Unfortunately, isoquinoline, quinazoline and pyridines *N*-oxides did not yield the desired products. Neither did the employment of 2-substituted quinoline *N*-oxides lead to conversion of starting materials. The scope of the cross-coupling reaction of different boronic acids with quinoline *N*-oxide (**77a**) was investigated in the next step (Scheme 3.1). It was found that the scope was limited to electron-rich aromatic (**78q**) and alkenyl boronic acids (**78r-u**), which yielded the desired products in a moderate to good range. Vinyl boronic acids and alkyl boronic acids did not yield the desired products (**78v-w**), presumably because of their insufficient nucleophilicity. This observation is in agreement with the analogy to the Petasis reaction, which is tied to the nucleophilic properties of the boronic acid.

In order to stress the utility of the developed reaction, the stepwise and selective C–H bond functionalization of quinoline **79** was performed. Selective cross-dehydrogenative coupling with aldehyde **80** afforded intermediate **81** as a single regioisomer.[96] Subsequent *N*-oxidation (product **77x**) and cross-coupling with boronic acid **74a** yielded the poly-functionalized product **78x** in good yield. The functionalization was achieved without pre-functionalization of starting material or utilization of metal-containing reagents.
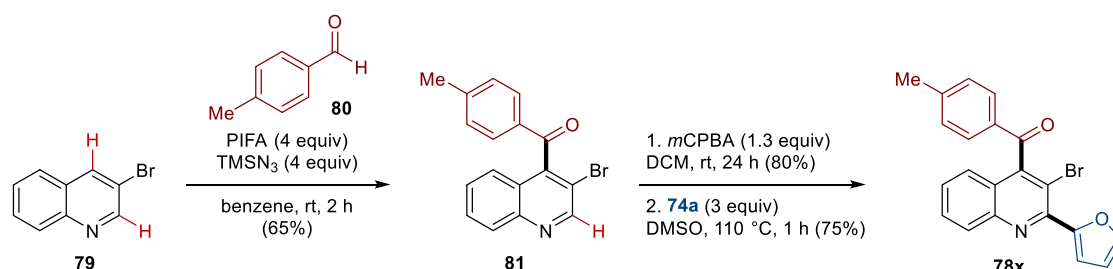
Scheme 3.2 Sequence for a regioselective stepwise C–H bond functionalization of 3-bromoquinoline (**79**). Reaction conditions: i) **79** (0.4 mmol, 1 equiv), **80** (4 equiv), PIFA (4 equiv), TMSN$_3$ (4 equiv) in benzene, room temperature, 2 h; ii) **81** (0.15 mmol, 1 equiv), *m*CPBA (1.3 equiv), DCM (0.2 M), room temperature, 24 h; iii) **77x** (0.1 mmol, 1 equiv), **74a** (3 equiv), DMSO (0.6 M), under argon atmosphere, 110 °C, 1 h.

3.5 Mechanistic considerations

Control experiments were conducted to obtain a better understanding of the mechanism (Figure 3.3). Subjecting quinoline **82** instead of the corresponding *N*-oxide to the optimized reaction conditions did not yield product **78a**. This result supports the assumption that the *N*-oxide is required for the pre-activation of the heterocycle. Further, the reaction was performed in the presence of radical trap **83**. However, cross-coupling product **78a** was formed unaffectedly. A mechanism was proposed based on the control experiments and by considering the aforementioned DFT-studies by Gois and co-workers (Figure 3.3). In the first step, quinoline *N*-oxide coordinates the boronic acid to form intermediate **77A**. Initiated by the proximity of the coupling partners, aryl migration *via* a nucleophilic attack at the C2-position takes place to form **77B**. Finally, rearomatization and elimination of boric acids leads to formation of the cross-coupling product. Notably, the nucleophilic attack occurs with high regioselectivity, since no C4 regioisomers could be identified during the studies on the substrate scope.
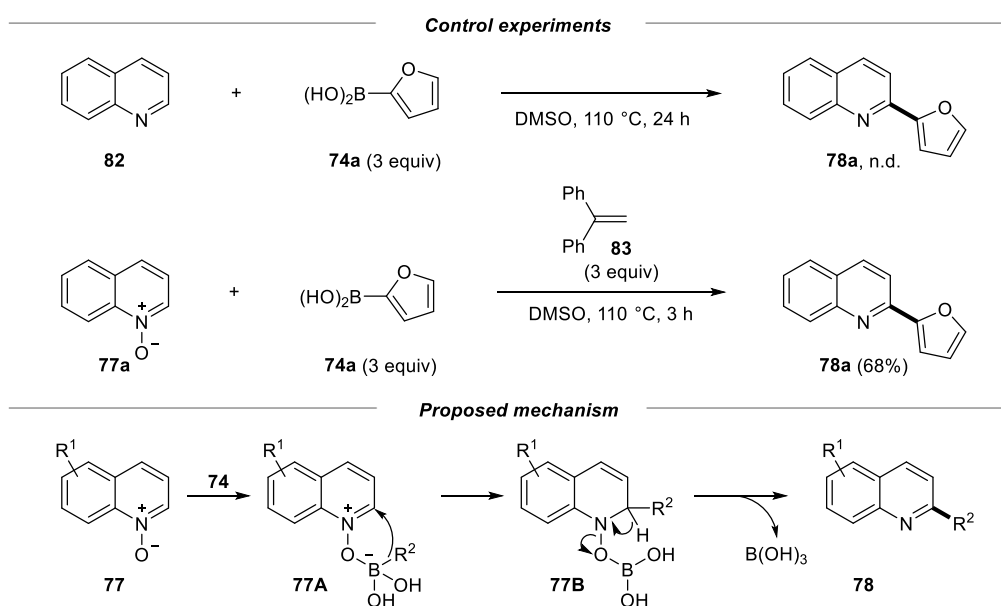
Figure 3.3 Control experiments and mechanism of the cross-coupling of quinoline *N*-oxides with boronic acid.

3.6 Conclusion

In summary, a novel and transition metal-free method for the regioselective cross-coupling of quinoline *N*-oxides with boronic acids has been developed. A broad range of C2-substituted quinolines was obtained with excellent regioselectivity. The cross-coupling revealed good functional group tolerance and electron-deficient substituents were beneficial for the outcome of the reaction. The scope of boronic acid was limited to electron-rich 2-aryl and 2-alkenyl groups, but consistent with the hypothesized analogy to the Petasis reaction.

Cross-coupling of Quinoline N-Oxides with Boronic Acids |

Dihydroxylation of Saturated Hydrocarbons

4 Dihydroxylation of Saturated Hydrocarbons

4.1 Introduction

The selective functionalization of unreactive C–H bonds of saturated hydrocarbons is a longstanding goal in organic chemistry research.[97] Hydrocarbons are derived from petroleum and natural gases, which are abundant and low cost feedstocks.[98] The old name for alkanes is *paraffins* meaning '*not enough affinity'*. Selective functionalization of hydrocarbons represents a significant challenge, because their participation in chemical reactions often requires high temperatures and highly reactive transition metal-complexes.[10] Important aims in the field of hydrocarbon functionalization are the conversion of gases to liquids, the production of more valuable products from simple starting materials and utilizing hydrocarbons as building blocks in organic synthesis.[99] C–H bond halogenation, alkylation, amidation, dehydrogenation and borylation have been reported in the past.[100] C–H bond oxygenation has gained significant interest, due to the importance of polyols as synthetic precursors, structural motifs in natural products and their relevance in industrial application.[101]

Different methods for hydrocarbon oxidation have been reported, covering metal-based, cytochrome P-450 inspired and metal-free methodologies.[102] Already in 1983, Barton and co-workers pioneered the iron-mediated oxyfunctionalization of hydrocarbons (GIF-chemistry) (Figure 4.1a).[103] More recently, White's group developed the iron-catalyst Fe(PDP), which is capable to selectively oxidize aliphatic C–H bonds (Figure 4.1b).[104] Impressively, cyclohexane was converted to cyclohexanone by using the alkane as limiting reagent. Moody's group reported the oxidation of hydrocarbons by employing a hydrogen peroxide urea complex as oxidant (Figure 4.1c).[105] According to the proposed mechanism, cyclohexanol is formed upon oxidation, but undergoes acidic dehydration. Alternatively, utilization of dimethyldioxirane (DMDO) gives access to cyclohexanone from cyclohexane in the absence of a metal-reagent.[106]

A common outcome for the functionalization of hydrocarbons is the over-oxidation to ketones. Oxidation to an alcohol lowers the BDE of the neighbouring C–H bond, which becomes more prompt to oxidation.[107] Additionally, metal-free methods often require acidic reaction conditions, which lead to dehydration of the formed alcohols. The generated cation is scavenged by the solvent or undergoes elimination and further functionalization (Figure 4.1).

Despite the progress towards methods for the mono-functionalization of hydrocarbons, the difunctionalization is comparably less explored. Barluenga and co-workers reported an interesting approach for the *vicinal* functionalization of cycloalkanes (Figure 4.1d). [108] The PhI(OAc)$_2$-I$_2$ system in *tert*-BuOH yielded iodocyclohexane, which was converted to *trans*-iodocyclohexyl acetate by adding an excess of the hypervalent iodine reagent PhI(OAc)$_2$. According to the proposed mechanism, oxidation of iodoalkanes leads to the formation of alkenes as intermediates, which subsequently undergo *trans*-addition with acetyl hypoiodite. The same results were reported by Sudalai's group, using the NaIO$_4$-KI system.[109]

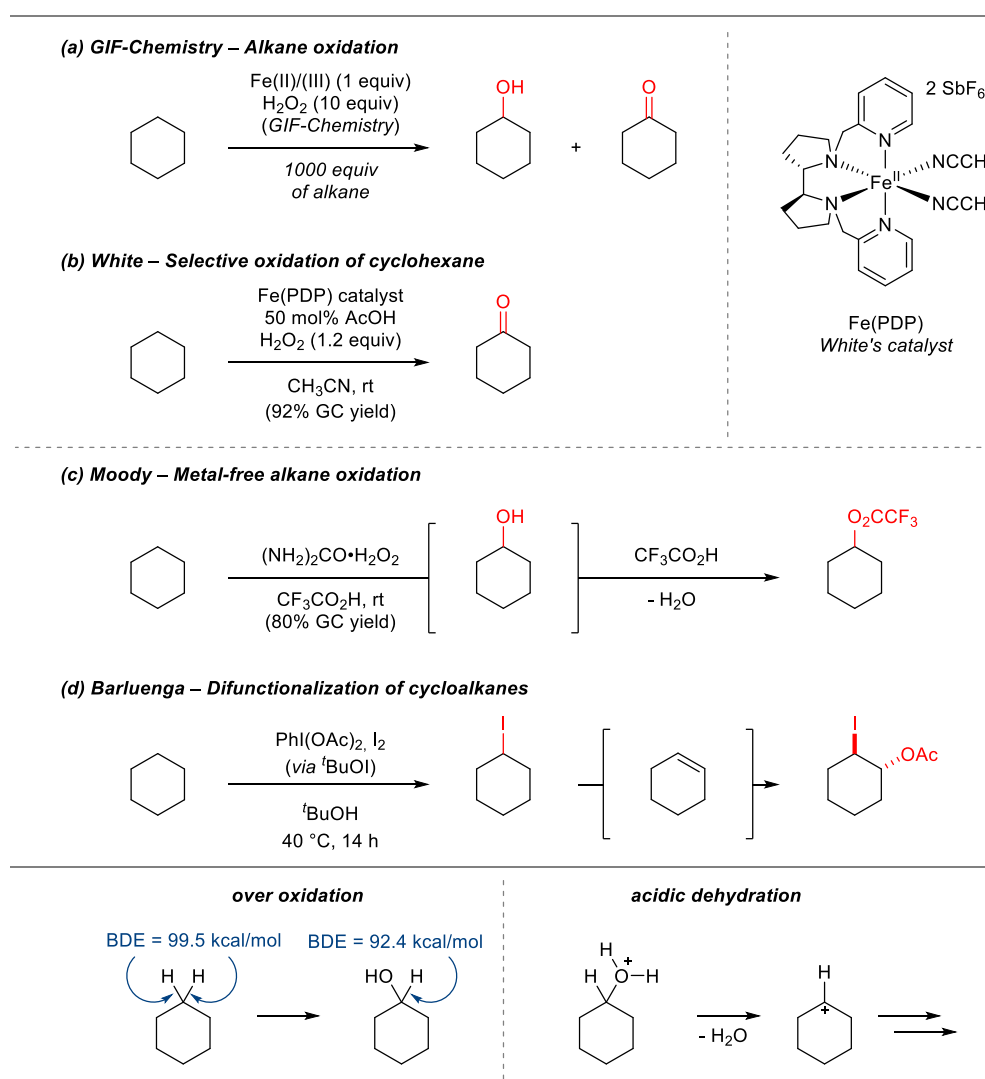**Figure 4.1** Synthetic methodologies for the direct oxygenation of C$_{sp}{}^3$–H bonds of hydrocarbons.

4.2 Motivation and aim of the project

As described, the mono-oxidation of alkanes has been intensively studied. However, the difunctionalization is comparably less explored and a direct *vicinal* oxygenation of alkanes has never been reported before. This approach faces the challenge of overcoming the tendency of mono-oxidized products to undergo acidic dehydrations and over-oxidation, due to the lowered C–H bond dissociation energy. Inspired by the work of Barluenga, it was hypothesized that radical iodination followed by oxidative elimination of acetyl hypoiodite could serve as an entry for *vicinal* dihydroxylation (Figure 4.2). As described, iodoalkanes form alkenes as intermediates in the presence of hypervalent iodine reagents. Therefore, it was assumed that the presence of a suitable oxidant might allow the conversion of the formed double bond into protected alcohols by epoxidation and subsequent ring opening.
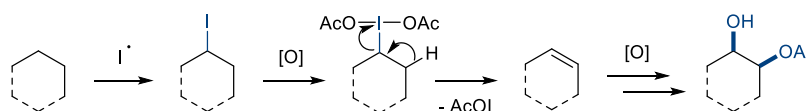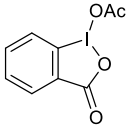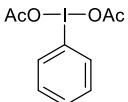

Figure 4.2 Proposed course of reaction for the *vicinal* functionalization of alkanes.

4.3 Initial results and optimization

Inspired by precedented literature, different combinations of radical iodination conditions and oxidants were tested in a one-pot reaction, but a satisfying formation of a *vicinal* functionalized hydrocarbon was not observed. Therefore, iodination and subsequent oxidation were examined as individual steps with hope to find suitable systems that can be combined as a one-pot reaction. Different combinations of hypervalent iodine reagents and azides were tested for the conversion of cyclohexane (**84**) to iodocyclohexane (**85**) (Table 4.1). As reported by Barluenga, utilizing the hypervalent iodine reagent 1-acetoxy-1,2-benziodoxol-3-(1*H*)-one and TMSN$_3$ afforded **85** in quantitative yields (entry 1).[108b] In contrast, the PhI(OAc)$_2$-I$_2$-*tert*-BuOH system did not yield the desired product (entry 2).[108a] The use of sodium periodate and sodium azide yielded **85** in quantitative yield at room temperature (entry 3). Further, the combination of hypervalent iodine(III) reagent PhI(OAc)$_2$ and different azides was tested (entry 4-7). By using an excess of sodium azide, cyclohexane was quantitatively converted to iodocyclohexane at room temperature (entry 7). If the ratio of hypervalent iodine(III) reagent and azide was changed, unspecific over-oxidation of iodocyclohexane was observed. The PhI(OAc)$_2$-I$_2$-NaN$_3$ is an unprecedented iodination system for the functionalization of hydrocarbons at room temperature under mild reaction conditions.

Table 4.1 Radical iodination of cyclohexane mediated by hypervalent iodine reagents.[a]
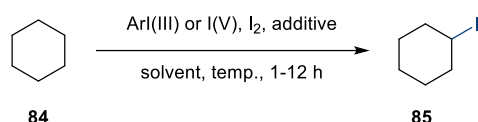
Entry	ArI(III) or I(V)	Solvent	Additive	Temp.	GC-yield / %[b]
1	(1,1-diacetoxy-1,2-benziodoxol-3-one, OAc)	DCE	$TMSN_3$ (1.1 equiv)	60 °C	quant.
2	AcO—I—OAc (PhI(OAc)$_2$ = PIDA)	DCE	*tert*-BuOH (1.1 equiv)	40 °C	-
3	$NaIO_4$	AcOH	NaN_3 (2.5 equiv)	rt	quant.
4	$PhI(OAc)_2$	DCM	$TMSN_3$ (1 equiv)	rt	< 15
5	$PhI(OAc)_2$	DCM	$TMSN_3$ (2.5 equiv)	rt	< 15
6	$PhI(OAc)_2$	DCM	NaN_3 (1 equiv)	rt	< 15
7	$PhI(OAc)_2$	DCM	NaN_3 (2.5 equiv)	rt	quant.

[a] Reaction conditions: ArI(III) or I(V) (0.2 mmol, 1 equiv), cyclohexane (12.5 equiv), I_2 (1 equiv), azide (see table), solvent (0.1 M), room temperature. [b] Yields were calculated by GC-MS-FID using iodobenzene as internal standard.

Having a robust system for the radical iodination in hand, the transformation of iodocyclohexane (**85**) in the presence of different oxidants was studied (Table 4.2). According to the reaction proposal, the conversion to a mono-acetylated diol was expected *via* the transient formation of a double bond upon oxidation of the iodine atom, followed by elimination and epoxidation. Surprisingly, $PhI(OAc)_2$ and sodium periodate did not achieve any conversion of the starting material (entry 1-2). A large excess of peracetic acid converted **85** to the mono-acetylated diol **86** in good yield (entry 3). Surprisingly, the more reactive PIDA analogue PIFA (phenyliodo bistrifluoroacetate) did not afford a productive outcome of the reaction (entry 4). Further variation of oxidants did not lead to a productive outcome of the reaction (entry 5-6).

Table 4.2 Oxidative transformation of iodocyclohexane in the presence of different oxidants.[a]
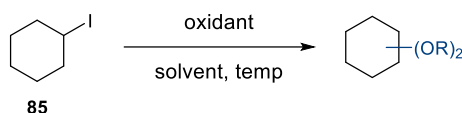
| Entry	Oxidant	Equiv	Solvent	Temp.	Product	Yield / %[b]
1	PhI(OAc)$_2$	3.5	DCM	rt	-	-
2	NaIO$_4$	3.5	AcOH	rt	-	-
3	AcO$_2$H	16.5	AcOH	0 °C to rt	**86**	76
4	(PhI(O$_2$CCF$_3$)$_2$ = PIFA)	3.5	DCM	rt	-	-
5	(F$_5$-PIFA)	3.5	DCM	rt	-	-
6	*m*CPBA	3.5	DCM	rt	-	-
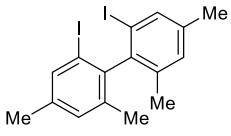
[a] Reaction conditions: **85** (0.2 mmol, 1 equiv), oxidant (see table), solvent (0.1 M) at the given temperature. [b] Yields are given for isolated products after column chromatography.

Finally, the identified systems for the iodination of cyclohexane and the conversion to the mono-protected diol **86** were combined in a one-pot reaction (Scheme 4.1). Delightfully, the desired product **86** was isolated in 72% yield. ^{1}H-NMR analysis allowed the assignment of the isomers. In accordance to precedented literature, the major diastereomer was identified as the *cis*-isomer, while the minor isomer was the *trans*-isomer.[110] The relative configuration provided the first evidence that the reaction did not proceed *via* epoxidation, since the *trans*-isomer would be the major product.
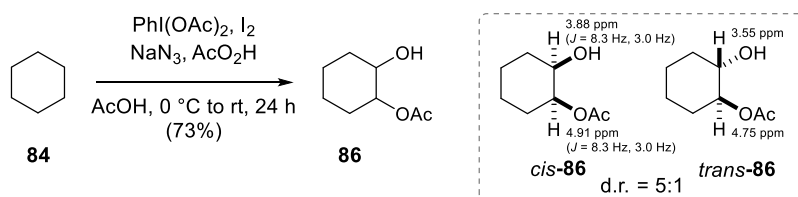
Scheme 4.1 Merging the systems for radical iodination and oxidation for the synthesis of mono-acetylated diol **86**. Reaction conditions: PhI(OAc)$_2$ (0.6 mmol, 1 equiv), Ac$_2$OH (16.5 equiv), cyclohexane (12.5 equiv), I$_2$ (1 equiv), NaN$_3$ (2.5 equiv), AcOH (0.1 M), room temperature, 24 h.

Table 4.3 Representative conditions of the optimization for the dihydroxylation of cyclohexane.[a]
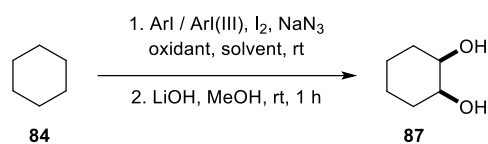
Entry	Oxid. (equiv)	84 (equiv)	ArI / ArI(III)	Solvent	Yield / %[b]	d.r.[c]
1	AcO_2H (16.5)	12.5	$PhI(OAc)_2$	AcOH	72	5.3:1
2	AcO_2H (16.5)	12.5	$PhI(OAc)_2$	HCO_2H	32	7:1
3	AcO_2H (16.5)	12.5	$PhI(OAc)_2$	HFIP	18	1.5:1
4	AcO_2H (16.5)	12.5	$PhI(OAc)_2$	MeCN	16	1.5:1
5	AcO_2H (16.5)	12.5	$PhI(OAc)_2$	DCM	20	1.5:1
6	AcO_2H (16.5)	12.5	$PhI(OAc)_2$	neat	17	4.3:1
7	H_2O_2 (16.5)	12.5	$PhI(OAc)_2$	AcOH	n.d.	-
8	TBHP (16.5)	12.5	$PhI(OAc)_2$	AcOH	n.d.	-
9	*m*CPBA (16.5)	12.5	$PhI(OAc)_2$	AcOH	n.d.	-
10	$Na_2S_2O_8$ (16.5)	12.5	$PhI(OAc)_2$	AcOH	Traces	-
11	AcO_2H (12.5)	12.5	$PhI(OAc)_2$	AcOH	77	5.3:1
12	AcO_2H (12.5)	12.5	$PhI(O_2CCF_3)_2$	AcOH	53	5:1
13	AcO_2H (12.5)	12.5		AcOH	97	5:1
14	AcO_2H (12.5)	12.5	4-Me-C_6H_4I	AcOH	99	6:1
15	AcO_2H (12.5)	12.5	4-F-C_6H_4I	AcOH	79	6.3:1
16	AcO_2H (12.5)	12.5	3,5-Me-C_6H_4I	AcOH	58	4:1
17	AcO_2H (12.5)	12.5	2-Me-C_6H_4I	AcOH	53	5:1
18	AcO_2H (12.5)	12.5	4-I-C_6H_4I	AcOH	52	5:1
19	AcO_2H (12.5)	12.5	2-$CO_2HC_6H_4I$	AcOH	8	10:1
20	**AcO_2H (12.5)**	**8.5**	**4-Me-C_6H_4I**	**AcOH**	**99**	**6.5:1**
21	AcO_2H (12.5)	6	4-Me-C_6H_4I	AcOH	86	6:1
22	AcO_2H (12.5)	1	4-Me-C_6H_4I	AcOH	8	n.c.

[a] Reaction conditions: 1. ArI or ArI(III) (0.6 mmol, 1 equiv), oxidant (see table), cyclohexane (12.5 equiv), I_2 (0.8 equiv), NaN_3 (2.5 equiv), AcOH (0.1 M), room temperature, 24 h; 2. LiOH (2 equiv), MeOH (0.2 M), room temperature, 1 h. [b] Yields are given for isolated products after column chromatography. [c] Diastereomeric ratio (d.r.) according to ^{1}H-NMR.

With the newly discovered system for the *vicinal* functionalization of cyclohexane in hand, the systematic optimization of reaction conditions was initiated (Table 4.3). The reaction sequence was extended by a hydrolysis step in order to reduce the structural complexity of the obtained products. Initially, a set of solvents was tested, but no improvement was observed, and acetic acid proved to be superior (entry 1-6). Different oxidants were reinvestigated, but exclusively peracetic acid achieved the desired transformation (entry 7-10). The loading of oxidant could be reduced to 12.5 equivalents of peracetic acid (entry 11). However, further lowering of oxidant loading decreased the yield of product **87**. Next, different hypervalent iodine reagents and iodoarenes were tested (entry 12-19). Iodoarenes were oxidized *in situ* to form the required hypervalent iodine reagent. Employment of 4-iodotoluene gave a drastic improvement, affording **87** in 99% yield with a diastereoselectivity of 6.5:1 (entry 14). The loading of cyclohexane was stepwise reduced to 8.5 equivalents, without altering the yield of the product (entry 20-22). Additionally, different loadings of potassium iodide and tetrabutylammonium iodide (TBAI) as alternative iodine sources were tested without improvement. Substoichiometric amounts of iodine (0.8 equiv) gave the best results. The amount of azide was found to be already optimal.

4.4   Scope with respect to saturated hydrocarbons

Having the optimized conditions in hand, the scope of the *vicinal* oxygenation of different saturated hydrocarbons was explored (Table 4.4). Alkanes with different ring sizes (5, 7, and 8) afforded the desired products in good to moderate yields (entry 1-4). Cyclopentanediol (**89**) was formed in 86% yield and with a diastereoselectivity of 6.3:1. With increasing ring size of the hydrocarbons, the diastereoselectivity was noticeably improved. Only trace amounts of the *trans*-isomer of cycloheptanediol (**91**) were identified by ^{1}H-NMR and cyclooctane (**92**) yielded exclusively the *cis*-diol (**93**). It appeared that the relative stereochemistry was influenced by the neighbouring group effect of the acetate group, which became less dominant with increasing ring size of the alkane. Next, substituted cyclic alkanes were tested, carrying a tertiary (3°) carbon atom. It should be noted that the position of the radical iodination and the subsequent elimination of iodine determines the position of the *vicinal* diol, potentially at different positions. Although iodination predominantly occurred on the 3° positions, minor functionalization of secondary (2°) positions occurred as well. In order to facilitate the isolation and separation of the functionalized products, an additional benzoylation step was applied. Benzoylation allowed the separation from unassigned regioisomers, which were formed due to of the functionalization of 2° positions.

Table 4.4 Scope of the *vicinal* C_{sp}^3–H bond oxygenation of various saturated hydrocarbons.[a]

Entry	Alkane	Products[b]	r.r.[c]	Yield / %[d]
1	**84**	**87** (d.r. = 6.5:1)	-	99
2	**88**	**89** (d.r. = 6.3:1)	-	86
3	**90**	**91** (d.r. = 20:1)	-	85
4	**92**	**93** (d.r. > 20:1)	-	37
5[e]	**94**	**95a** (d.r. = 3.5:1) + **95b**	21 :1	68
6[e]	**96**	**97a** (d.r. = 5:1) + **97b**	19 : 1	73
7[e]	**98**	**99a** (d.r. = 12:1) + **99b**	20 : 1	86
8[e]	**100**	**101a**, C2 / C3 (d.r. = 3:1); **101b**, C3 / C4 (d.r. = 2:1); **101c**, C1 / C2	6.5 : 1.5 : 1	68
9[e]	**102**	**103a**, C2/C3 (d.r. = 3:1); **103b**, C3/C4 (d.r. = 2:1); **103c**, C1/C2	5.5 : 2 : 1	73
10[e]	**104**	**105a** (d.r. = 1.3:1) + **105b**	8 : 1	55
11[e]	**106**	**107a** + **107b**	8 : 1	20

[a] Reaction conditions: 1. 4-MeC$_6$H$_4$I (0.3-0.9 mmol, 1 equiv), alkane (8.5 equiv), I$_2$ (0.8 equiv), NaN$_3$ (2.5 equiv) and AcO$_2$H (12.5 equiv) in AcOH (0.1 M), room temperature, 24 h; 2. LiOH (2 equiv) in MeOH (0.1 M), room temperature. [b] Diastereomeric ratio (d.r.) according to ^{1}H-NMR. The major isomer is shown. [c] Regioisomeric ratio (r.r.) according to ^{1}H-NMR. [d] Yields are given for isolated products. [e] BzCl (2.5 equiv) and DMAP (5 mol %) in 1:1 DCM / Py (0.45 M).

The sequence of oxidation, hydrolysis and benzoylation allowed the isolation of **95a, b** and **97a, b** in good yields (entry 5-6). The major products resulted due to the iodination of 3° positions and elimination of iodine to the thermodynamically more stable double bond. However, elimination and subsequent functionalization of exocyclic double bonds could not be completely bypassed (**95b** and **97b**). 1,4-Dimethylcyclohexane (**98**) was functionalized with excellent regioselectivity (entry 7). The presence of two identical 3° carbon atoms with high probability for radical iodination reduced the functionalization of the other C–H positions. Minor product **99b** is a result of the elimination of iodine with formation of an exocyclic double bond or iodination of the 1° carbon atom, which occurred only in traces. Consequently, product **99a** was isolated in good yields and excellent regioselectivity.

The *vicinal* oxygenation of linear alkanes was achieved in good yields (entry 8 and 9). Benzoylation of 2° hydroxyl groups was applied in order to facilitate the handling of the volatile products. The major products were identified as a result of the iodination of 2° carbon atoms and further transformation to form **101a, b** and **103a, b**. Although oxidation predominantly occurred at the 2° carbon atoms, minor product formation as a result of either 1° C–H bond iodination or elimination to a terminal double bond was identified (**101c** and **103c**). The absence of a 3° positions resulted in the formation of regioisomers *via* iodination and elimination, however it should be noted that among all possible oxidation products exclusively *vicinal* oxidation was observed and over oxidation to ketones was not detected.

Finally, branched alkanes containing 3° carbon atoms were tested in the reaction. 3-Methylpentane (**104**) yielded products **105** in 55% yield and demonstrated regioselectivity in a comparable manner to the previous examples. Interestingly, products **107** revealed an opposite tendency for the formation of the regioisomer, presumably due to steric hindrance. Attempts to use aliphatic ethers, esters or carboxylic acids remained unsuccessful under the developed conditions.

4.5   Mechanistic considerations

In order to gain better insights into the mechanism, the reaction was carefully monitored and quantified by GC-MS-FID analysis (Figure 4.3). 4-Iodotoluene was replaced with 2,3-dichloroiodobenzene to avoid signal overlap the in the GC-traces. This experiment allowed the identification of important intermediates, which are transiently formed during the course of reaction. Initially, iodocyclohexane (**85**) was formed, which rapidly decreased in concentration again. With a short delay in time, *trans*-iodocyclohexane acetate (**109**) appeared as the second

reaction intermediate. The conversion of **85** to **109** *via* elimination and *trans*-addition of acetyl hypoiodite is in good agreement with the results reported by Barluenga's group.[108a] This intermediate decreased, while product **86** begins to form. Interestingly, the reaction plot revealed that both intermediates are almost steadily produced and converted to product **86** over the course of several hours. The observed *cis*-selectivity for the formation of product **86** can be explained by another oxidative displacement step of **109** under inversion of configuration.
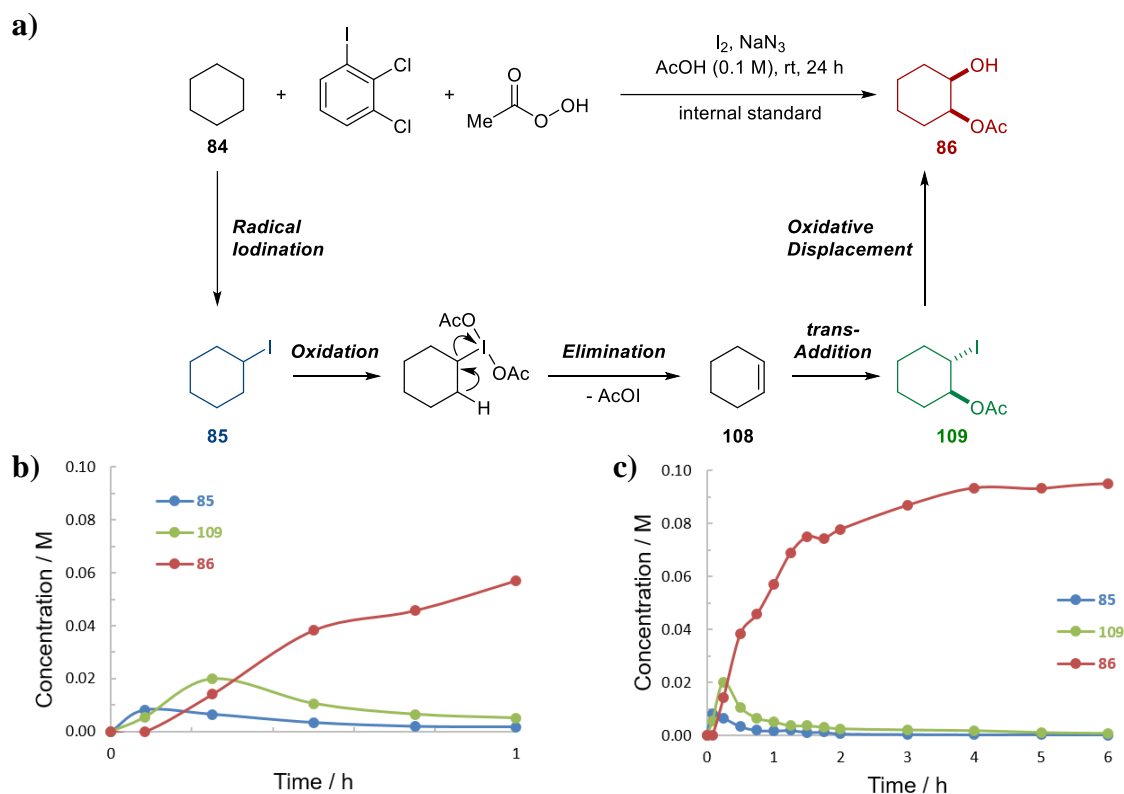
Figure 4.3 Reaction profile of the *vicinal* difunctionalization of cyclohexane (**84**). a) Schematic presentation of the course of reaction. 1,3-Bis(trifluoromethyl)-5-bromobenzene was used as internal standard. b) GC-MS-FID time course of the functionalization of **84** over the course of 1 h. c) GC-MS-FID time course of the functionalization of **84** over the course of 6 h.

Next, different control experiments were conducted (Figure 4.4). No product formation was detected by leaving out the iodoarene, iodine or sodium azide. The employment of iodocyclohexane (**85**) instead of cyclohexane (**84**) yielded the expected product **87** in 98% yield after hydrolysis. To exclude the formation of an epoxide and subsequent ring opening, cyclohexene was oxidized with peracetic acid in the absence of acetyl hypoiodite. *trans*-Cyclohexane-diol (**110**) was isolated as a single isomer. Additionally, a strong kinetic isotope effect was observed (KIE = 7.4), by using d_{12}-cyclohexane and **84**. Consequently, the abstraction of hydrogen from cyclohexane is the rate-limiting step.
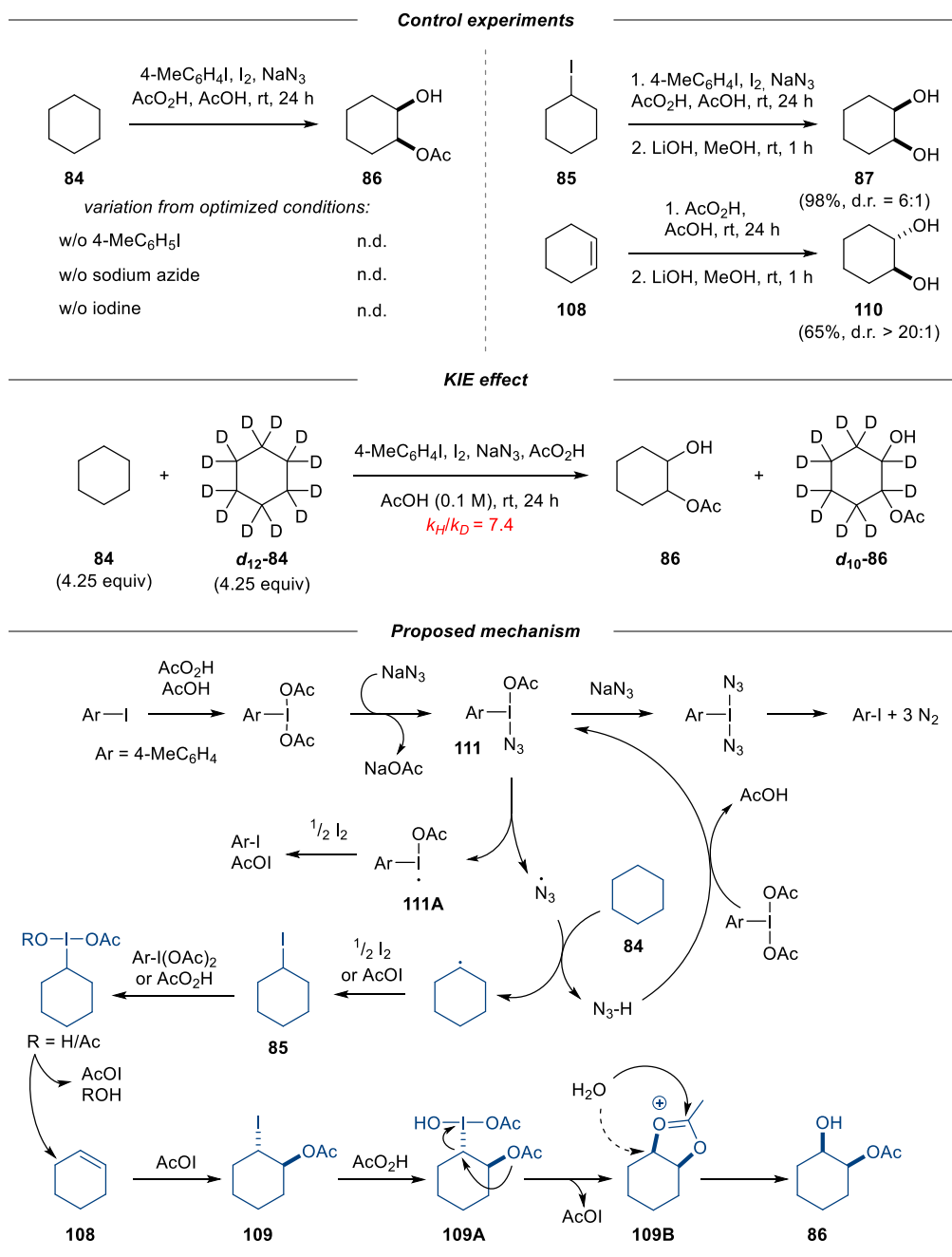
Figure 4.4 Control experiments, determination of the KIE effect and proposed mechanism for the *vicinal* oxygenation of saturated hydrocarbons.

A mechanism was proposed based on the conducted control experiments and the obtained reaction profile (Figure 4.4). Initially, 4-iodotoluene is oxidized by peracetic acid, while acetic acid serves as ligand for the hypervalent iodine(III) reagent. Ligand exchange with sodium azide leads to formation of intermediate **111**, which undergoes thermolysis at ambient temperature to give an azide radical and iodine centred radical **111A**.[111] **111A** is scavenged by iodine whereupon AcOI and 4-iodotoluene are formed. The azide radical reacts with alkane **84** providing a cyclohexyl radical. This transformation is the rate limiting step of the cascade

reaction. Radical recombination with iodine gives iodocyclohexane (**85**). Subsequent oxidation and reductive elimination of AcOI leads to the formation of cyclohexene (**108**). Next, *trans*-addition of AcOI to **108** provides **109**. Further **109** is oxidized by peracetic acid to form **109A** and oxidative displacement gives product **86**. The stereochemical outcome of the reaction can be reasoned with a competing hydrolysis step of intermediate **109B**, which can occur in *cis*- and *trans*-fashion. As the studies on the scope revealed, the diastereoselectivity is strongly influenced by the ring strained of the hydrocarbons.

The selective C–H bond functionalization of complex molecules is of great interest and offers unique advantages in terms of efficiency and atom economy. However, the required excess of starting material in this method negotiates those advantages. Based on the results obtained during the studies on the reaction mechanism, it was hypothesized that iodoalkanes offer the opportunity to selectively introduce *vicinal* diols into more complex substrates by mimicking the developed reaction conditions. In this process, radical iodination is excluded and the iodine atom in iodoalkanes serves as sacrificial directing group for transition metal-free dihydroxylation.
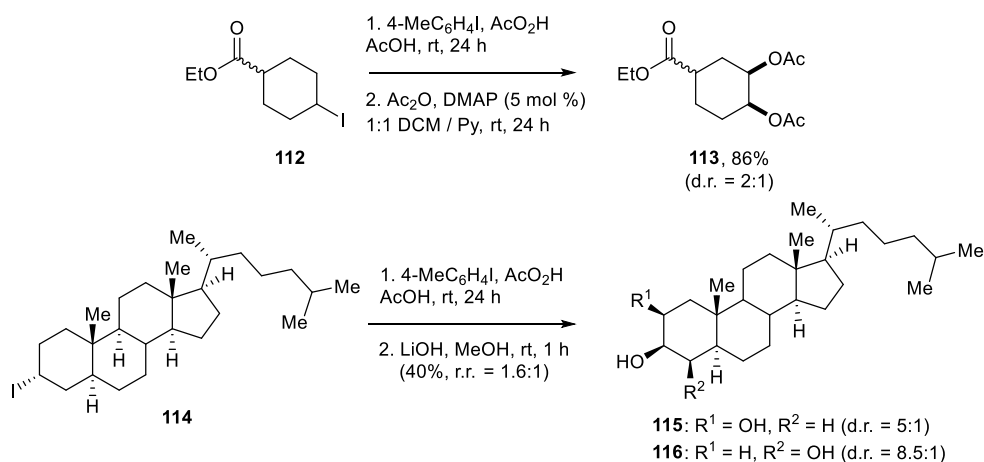
Scheme 4.2 Iodoalkanes as traceless directing group for dihydroxylation. Reaction conditions: iodoalkane (0.5 mmol, 1 equiv), 4-MeC$_6$H$_4$I (0.6 equiv) AcO$_2$H (39% solution in AcOH, 7.35 equiv) in AcOH (0.1 M), room temperature, 24 h; acetylation: Ac$_2$O (3 equiv), DMAP (5 mol%), 1:1 DCM / Py (0.2 M), room temperature, 24 h; hydrolysis: LiOH (2 equiv), MeOH (0.5 M), room temperature, 1 h.

Accordingly, ester **112** yielded the dioxygenated product **113** in good yields (Scheme 4.2). Furthermore, the functionalization of complex molecules was addressed by using iodinated cholestane derivative **114**. The dihydroxylated products were isolated with good *cis*-selectivity after hydrolysis in 40% yield (Scheme 4.2). Notably, **114** contains 7 weak tertiary C–H bonds, which were untouched under the applied reaction conditions. Despite the imperfect formation of regioisomers, the achieved functionalization represents a sustainable strategy. Common

reaction routes include multiple reaction steps and the use of expensive and toxic metal reagents.[112]

4.6 Conclusion

In summary, the first efficient and scalable method for the transition metal-free double C_{sp}^3–H bond functionalization of saturated hydrocarbons has been developed. Cyclic, linear and branched alkanes were converted selectively to *vicinal* diols under ambient reaction conditions. Furthermore, iodoalkanes were utilized as traceless directing group for transition metal-free dihydroxylation. The reaction is grounded on complex cascade reaction, which represents a unique interplay of radical reaction methodology and oxidative functionalization of weak carbon-heteroatom bonds.

Dihydroxylation of Saturated Hydrocarbons |

Oxidative Coupling of Electron-rich Heteroarenes

5 Oxidative Coupling of Electron-rich Heteroarenes

5.1 Introduction

The selective C–H bond functionalization under oxidative reaction conditions represents an efficient strategy for the construction of carbon-carbon bonds.[113] Various methods are based on the employment of transition metal-catalysts and directing groups.[114] Non-directed oxidative coupling serves as an alternative strategy.[115] Consequently, step-intensive pre-functionalization of starting material is avoided. Already in 1988, Radner pioneered the oxidative coupling of naphthalene derivatives. The reaction was catalyzed by nitrosonium tetrafluoroborate, while oxygen served as the stoichiometric oxidant (Figure 5.1a).[74] Kita and co-workers reported the dimerization of naphthalenes mediated by hypervalent iodine(III) reagents. Similarly to the work of Radner, it was proposed that oxidative coupling was initiated by means of a SET process and subsequent nucleophilic attack of the naphthalene (for details see Scheme 1.18).[116]
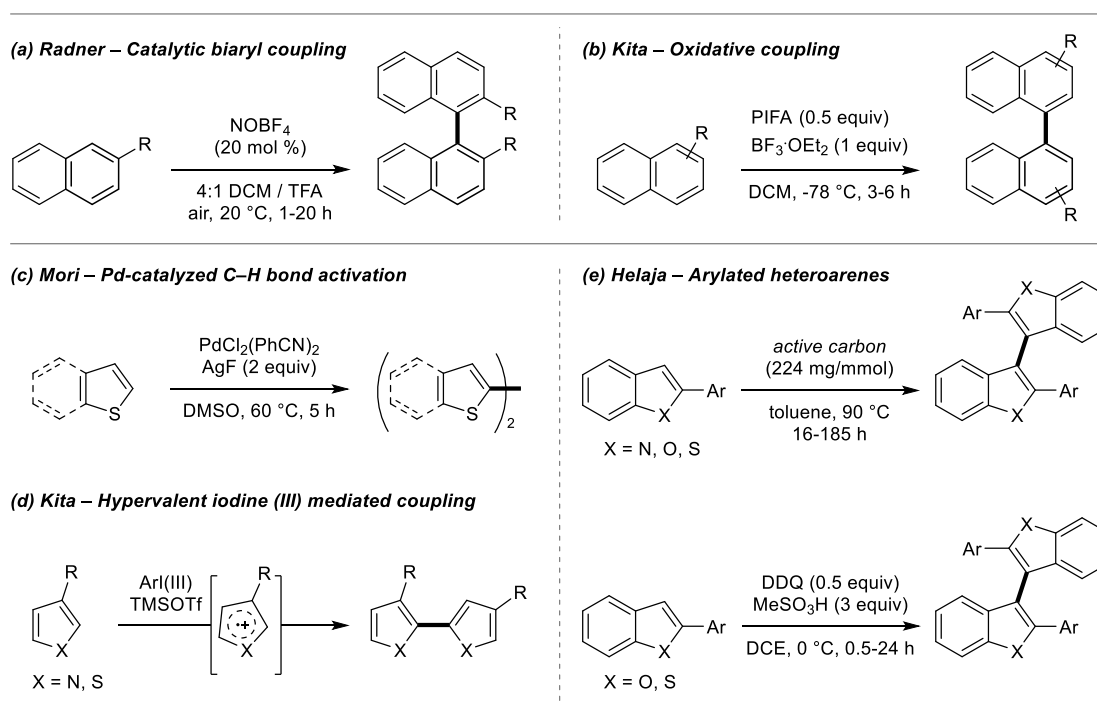

(a) Radner – Catalytic biaryl coupling

NOBF$_4$ (20 mol %)

4:1 DCM / TFA air, 20 °C, 1-20 h

(b) Kita – Oxidative coupling

PIFA (0.5 equiv) BF$_3$·OEt$_2$ (1 equiv)

DCM, -78 °C, 3-6 h

(c) Mori – Pd-catalyzed C–H bond activation

PdCl$_2$(PhCN)$_2$ AgF (2 equiv)

DMSO, 60 °C, 5 h

(d) Kita – Hypervalent iodine (III) mediated coupling

ArI(III) TMSOTf

X = N, S

(e) Helaja – Arylated heteroarenes

active carbon (224 mg/mmol)

toluene, 90 °C 16-185 h

X = N, O, S

DDQ (0.5 equiv) MeSO$_3$H (3 equiv)

DCE, 0 °C, 0.5-24 h

X = O, S

Figure 5.1 Construction of carbon-carbon bonds *via* two-fold C–H bond functionalization.

Early on, palladium salts were employed for the oxidative coupling of different heterocycles.[117] Mori's group reported the dimerization of thiophenes based on a palladium catalyzed C–H bond activation strategy. However, the reaction required an excess of sacrificial metal oxidant (Figure 5.1c).[118] Later, different transition metal-free variants for the non-

directed coupling of heteroarenes have been developed. Kita's group reported a metal-free variant employing hypervalent iodine(III) reagents for the oxidative coupling of thiophenes. It was proposed that oxidative coupling proceeds through SET and subsequent nucleophilic attack of the starting material (Figure 5.1d).[119] Helaja and co-workers utilized active carbon material for the oxidative dimerization of arylated heteroarenes. Although a broad substrate scope and the recycling of the active carbon material were achieved, the reaction suffered from long reaction times (up to 185 h) at elevated temperatures. Further, the same group utilized DDQ for the oxidative coupling reaction of benzofurans and benzothiophenes (Figure 5.1e).[120] Despite the progress in the field of metal-free oxidative coupling of heteroarenes, the employment of organic oxidants results in large quantities of waste in the coupling reaction.

5.2 Motivation and aim of the project

The application of nitrosonium salts as catalysts for non-directed oxidative coupling remained almost untouched within the past decade. Nitrosonium salts as catalyst offer the great potential of employing ambient oxygen as terminal oxidant (see Chapter 1.2.4). Oxygen is considered as the ideal oxidant, due to its natural occurrence and safe properties.[121] Further, hypervalent iodine(III) reagents and nitrosonium salts have comparable oxidation potential as well, which suggested a shared substrate spectrum for oxidative coupling.[62a, 122] Naphthalenes and arylated benzofurans entail a comparable oxidation potential (approx. 0.9-1.3 V, strongly depending on the solvent).[120c, 123] Therefore, it was hypothesized that arylated heteroarenes, such as benzofurans, benzothiophenes and indoles, might serve as substrate for non-directed oxidative coupling, catalyzed by nitrosonium salts.

5.3 Initial results and optimization

The oxidative dimerization of 2-phenylbenzofuran (**117a**) was selected as model system (Table 5.1). The desired coupling product **118a** was isolated in 39% yield by applying the conditions developed by Radner (entry 1). In the absence of acid, no product formation was detected (entry 2-3). By using the acidic solvent HFIP, product **118a** was formed in moderate yield (entry 4). Next, different solvents in combination with TFA were tested (entry 5-15). The solvent system consisting out of MeCN / TFA allowed the isolation of **118a** in 85% yield (entry 11). Conducting the reaction in AcOH or TFA without the addition of organic solvents gave only insufficient results (entry 16-17). Sodium nitrite served as nitrosonium ion source in the presence of the strong acid TfOH, achieving 62% yield (entry 18).

Table 5.1. Initial results and representative conditions of the reaction optimization.[a]
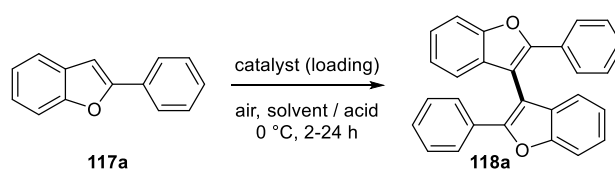
Entry	Solvent	Acid (% v/v)	Catalyst (mol %)	Yield / %[b]
1	DCM	TFA (20)	NOBF$_4$ (10)	39
2	DCM	-	NOBF$_4$ (10)	Traces
3	MeCN	-	NOBF$_4$ (10)	Traces
4	HFIP	-	NOBF$_4$ (10)	31
5	DCE	TFA (20)	NOBF$_4$ (10)	62
6	PhCl	TFA (20)	NOBF$_4$ (10)	80
7	C$_6$H$_5$F	TFA (20)	NOBF$_4$ (10)	30
8	TFE	TFA (20)	NOBF$_4$ (10)	Traces
9	MeNO$_2$	TFA (20)	NOBF$_4$ (10)	62
10	THF	TFA (20)	NOBF$_4$ (10)	n.d.
11	**MeCN**	**TFA (20)**	**NOBF$_4$ (10)**	**85**
12	DMF	TFA (20)	NOBF$_4$ (10)	n.d.
13	DMSO	TFA (20)	NOBF$_4$ (10)	n.d.
14	EtOAc	TFA (20)	NOBF$_4$ (10)	72
15	Me$_2$CO	TFA (20)	NOBF$_4$ (10)	n.d.
16	-	TFA (100)	NOBF$_4$ (10)	14
17	-	AcOH (100)	NOBF$_4$ (10)	n.d.
18	MeCN	TfOH (2 equiv)	NaNO$_2$ (20)	62
19	MeCN	TFA (20)	NaNO$_2$ (20)	5
20	MeCN	TfOH (2 equiv)	NOBF$_4$ (10)	21
21	MeCN	TFA (20)	NO$_2$BF$_4$ (10)	78
22	MeCN	TFA (10)	NOBF$_4$ (10)	79
23	MeCN	TFA (33)	NOBF$_4$ (10)	64
24	MeCN	TFA (20)	NOBF$_4$ (20)	82
25	MeCN	TFA (20)	NOBF$_4$ (5)	32
26[c]	MeCN	TFA (20)	NOBF$_4$ (10)	n.d.

[a] Reaction conditions: **117a** (0.1 mmol, 1 equiv), NOBF$_4$ (10 mol %), solvent (0.1 M), 0 °C, 2-24 h, under air atmosphere. [b] Yields are given for isolated products after column chromatography. [c] Reaction performed under O$_2$ atmosphere.

TFA did not allow an efficient utilization of sodium nitrite (entry 19). The combination of nitrosonium tetrafluoroborate and TfOH gave **118a** in only 21% yield (entry 20). Nitronium tetrafluoroborate was tested as catalyst, but gave slightly reduced yields (entry 21).

Next, different ratios of MeCN and TFA were tested, but no improvement was found (entry 22-23). In order to further improve the coupling reaction, the catalyst loading was varied. 20 and 5 mol % of catalyst were tested respectively, but the initial amount of nitrosonium tetrafluoroborate proved to be ideal (entry 24-25). Also different temperatures and concentrations were explored, but no further improvements were found. Finally, the reaction was performed under oxygen atmosphere (entry 26). Surprisingly, **118a** was not detected in the reaction, presumably because of uncontrolled over-oxidation.

5.4 Scope of benzofurans, benzothiophenes and indoles

With the optimized conditions in hand, the scope of the coupling reaction was studied. The required starting materials (**117a-s**) were synthesized in a metal-free fashion according to the work by Olofsson's group.[124]

A broad number of substituted bibenzofurans was successfully synthesized (Scheme 5.1). All accessible positions of the 2-phenyl group were systematically decorated with different functional groups, covering different electronic and steric properties (**118b-k**). Several starting materials were highly nonpolar and suffered from poor solubility in acetonitrile. Changing the solvent to dichloromethane allowed the isolation of the products in satisfying yields and short reaction times. Next, synthesis of a set of poly-substituted products was achieved in good to excellent yields. Electron-donating substituents led to higher yields and shorter reaction times (**118l-p**). Product **118p** was selectively formed, while the naphthalene substituent remained nonfunctionalized under the reaction conditions. The oxidative coupling of 5-substituted benzofurans was successfully performed as well (**118q-s**). In order to stress the synthetic utility of the developed method, the oxidative coupling was repeated using 5 mmol of **117a**. Product **118a** was isolated in only slightly reduced yield, demonstrating the scalability of the coupling reaction.

After disclosing the scope of 2-arylbenzofurans, the oxidative coupling of structurally related benzothiophenes was studied (Scheme 5.1). In contrast to 2-arylbenzofurans, the required starting materials were synthesized by a Suzuki-Miyaura cross-coupling reaction.[125] Products **118t-w** were isolated in good yields and short reaction times. Dichloromethane was used as

solvent, due to the nonpolar properties of starting material. The functional groups covered electron-rich groups, sterically demanding groups and halogens. The products revealed similar trends in functional group compatibility, albeit in moderate yields.
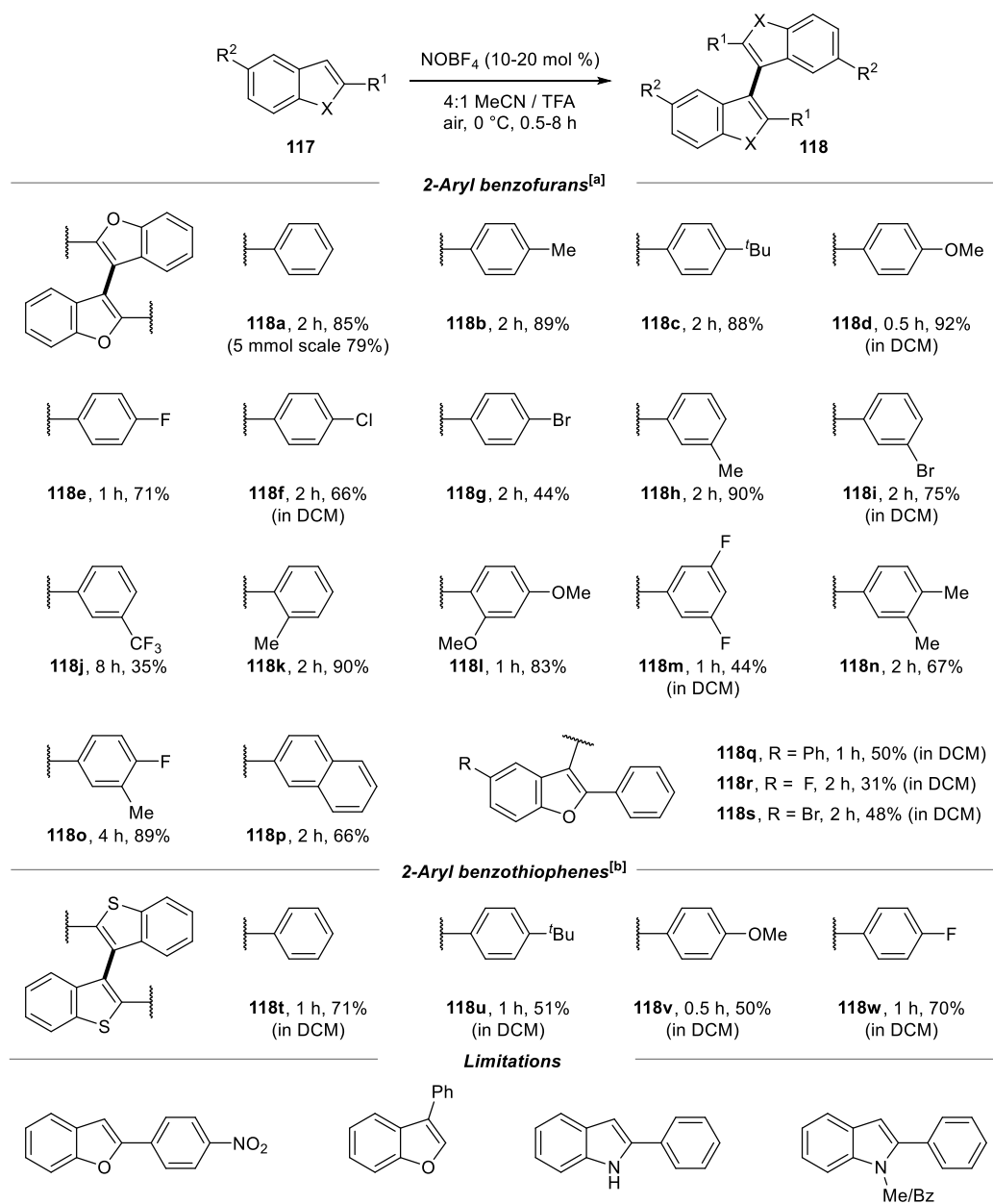

Scheme 5.1 Scope and limitation for the oxidative coupling of arylated benzofurans and benzothiophenes. [a] Reaction conditions: **117** (0.2 mmol, 1 equiv), NOBF$_4$ (10-20 mol %), 4:1 MeCN / TFA (0.1 M), 0 °C, 1-8 h under air atmosphere. [b] Reaction conditions: **117** (0.2 mmol, 1 equiv), NOBF$_4$ (10 mol %), 4:1 DCM / TFA. Yields are given for isolated products after column chromatography.

The developed methods faced some limitations. Starting materials with highly electron deficient groups did not undergo conversion to the desired products. 3-Phenylbenzofuran proved to be unreactive under the reaction conditions as well. Additionally, the coupling reaction of 2-functionalized indoles was tested. However, independently of the substitution

patterns and protecting groups, no product formation was achieved. In contrast, 3-arylindoles were successfully coupled to the desired products (Scheme 5.2). The oxidative coupling gave the best results by excluding TFA. Functional groups with electron-donating or electron-withdrawing effects were well tolerated on the 3-phenylring and the 5-position of indole (**120a-f**). While the coupling of unprotected indoles did not require any acid, products **120g** and **120h** were synthesized using the optimized reaction conditions. An efficient non-directed coupling of 3-arylindoles *via* twofold C–H bond functionalization has not been described before.

Dimeric scaffolds can be found in natural products and represent a promising source for the discovery of biologically active compounds.[126] All starting materials (**117**, **119**) and products (**118**, **120**) were tested in different cell-based screening assays. Bisindoles **120b, 120c, 120e** were identified as moderately active modulators of the hedgehog (HH) signaling pathway (Scheme 5.1). Inhibition of the HH signaling pathway is a promising approach for the treatment of cancer, such as basal cell carcinoma and medulloblastoma.[127] A primary structure activity relationship was obtained with IC_{50} values in the micromolar range. Importantly, the monomeric starting materials remained inactive. This finding highlights the importance of homo-dimerization processes.
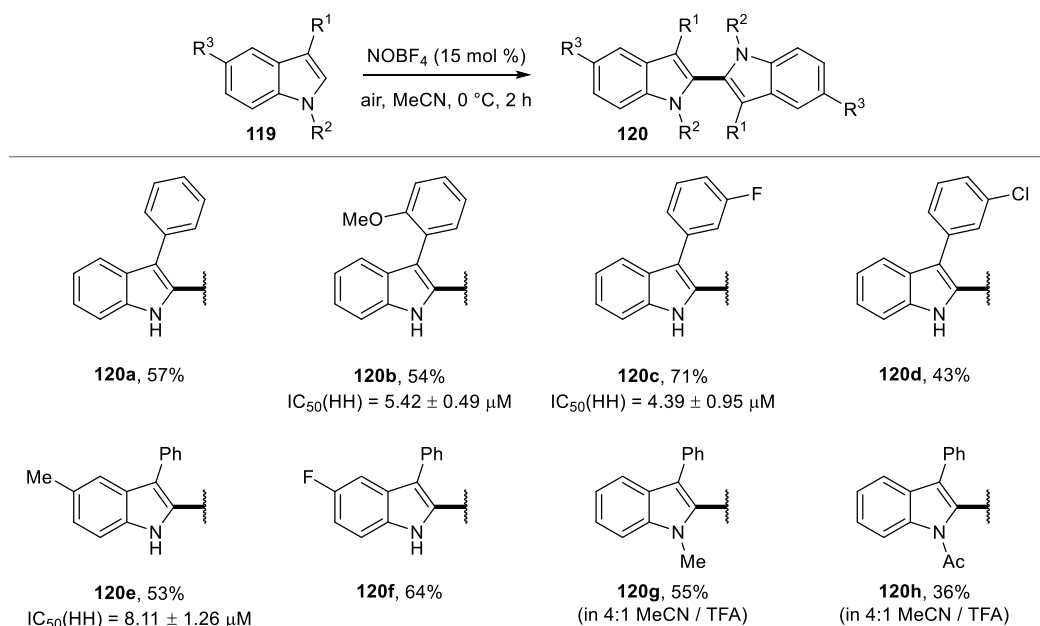
Scheme 5.2 Scope for the oxidative coupling of arylated indoles and identified bioactivity. Reaction conditions: **119** (0.2 mmol, 1 equiv), NOBF$_4$ (15 mol %), MeCN (0.1 M), 0 °C, 2 h under air atmosphere. Yields are given for isolated products after column chromatography. Mean IC_{50} value for the modulation of the Hedgehog signaling pathway (provided by the COMAS Dortmund).

In the next step, cross-coupling experiments with differently substituted benzofurans were performed. Benzofurans were selected according to their electronic properties (**117a** and **117d**) and subjected to the optimized reaction conditions (Figure 5.2a). The conversion of starting materials and the formation of products were monitored and quantified by GC-MS-FID.

The reaction profile for the conversion of starting materials clearly reflects that the more electron-rich starting material **117d** was selectively converted, while the fraction of the less reactive compound **117a** remained almost untouched (Figure 5.2b). This result shows that nitrosonium ions entail a high preference for starting materials with a lower oxidation potential. In parallel, the homo-dimerization of **118d** was identified as the major outcome of the cross-coupling experiment (Figure 5.2c). Formation of the desired cross-coupling product **118x** occurred only in 6%. Surprisingly, the homo-dimerization of benzofuran **117a** occurred only in traces as well. Presumably, the nitrosonium ion undergoes undesired nitrosation of starting materials or products, which stops the catalytic cycle.[63] Generally speaking, this finding is in accordance to the general tendency that substrates with low oxidation potentials entail higher nucleophilicity and preferentially undergo homo-coupling.
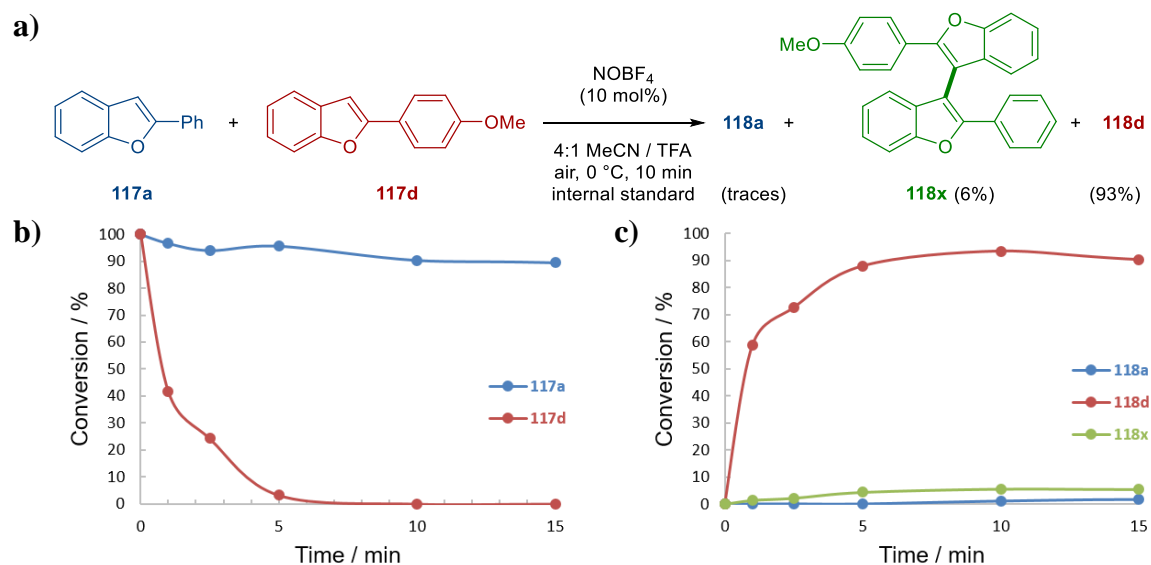
Figure 5.2 Reaction profile of the cross-coupling reaction of 2-arylbenzofurans **117a** and **117d**. 1,3-Bis(trifluoromethyl)-5-bromobenzene was used as internal standard. a) Schematic presentation of the reaction. b) GC-MS-FID time course of the conversion of starting materials over the course of 15 min. c) GC-MS-FID time course of the formation of coupling products over the course of 15 min.

5.5 Mechanistic considerations

Control experiments were conducted in order to gain insights into the mechanism (Figure 5.3). Only traces of products **118a** were detected when the coupling reaction was performed under argon atmosphere. This result underlines the importance of oxygen to maintain the catalytic

cycle. Next, commonly used radical traps were subjected to the reaction conditions. However, only butylated hydroxytoluene (BHT) did not reveal any reactivity towards nitrosonium tetrafluoroborate. By performing the radical scavenging experiment, product **118a** was not detected in the presence of BHT, but the formation of a radical scavenging product **118y** could be confirmed by GC-MS analysis.

Based on the conducted control experiments and precedent literature a reaction mechanism was proposed (Figure 5.3). Initially, **117** is oxidized *via* a single-electron-transfer (SET) process to generate radical cation **117A** and nitrogen monoxide. Next, **117A** reacts with a second molecule of starting material **117** by means of radical S_EAr to generate intermediate **117B**. A second SET process leads to rearomatization and formation of product **118**. The second oxidation step affords another molecule of nitrogen monoxide.
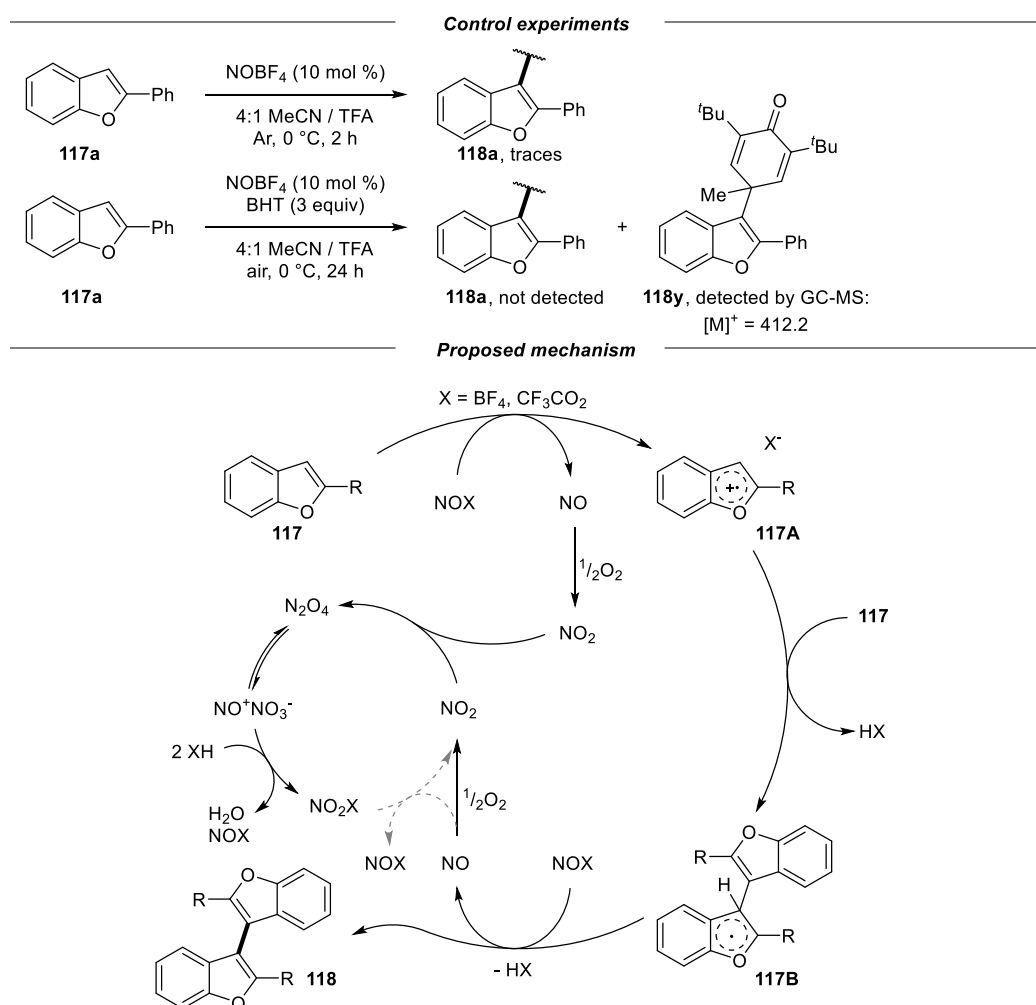
Figure 5.3 Control experiments and proposed reaction mechanism for the oxidative coupling reaction.

Oxidation of nitrogen monoxide by ambient oxygen generates nitrogen dioxide. Released nitrogen dioxide dimerizes to form dinitrogen tetroxide, which is in equilibrium with nitrosonium nitrate through disproportionation.[76] Under the acidic reaction conditions nitrosonium and a nitronium ions are released and water is generated as by-product. Finally, the nitronium ion is able to oxidize nitrogen monoxide instead of molecular oxygen in order to maintain the catalytic cycle.[77]

5.6   Conclusion

In summary, the regioselective nitrosonium salt catalyzed oxidative coupling of arylated heteroarenes under mild conditions has been developed. The desired products were formed smoothly within short reaction times using molecular oxygen as the terminal oxidant. In accordance to precedented literature, water is produced as the stoichiometric by-product. A comprehensive scope covering different heterocycles was demonstrated revealing a good functional group tolerance. Oxidative coupling of heteroarenes allowed the straightforward synthesis of dimeric scaffolds, which translated into the discovery of novel HH-modulators.

Oxidative Coupling of Electron-rich Heteroarenes |

Aerobic Coupling of Phenols and Anilides

6 Aerobic Coupling of Phenols and Anilides

6.1 Introduction

Non-directed oxidative coupling represents the ideal strategy for the construction of the biaryl skeleton, since forging of C–C bonds proceeds by twofold C–H bond functionalization.[5, 128] Biphenols and bisanilides are of importance, due to their frequent occurrence in natural products, organic synthesis and materials science.[129] The selective homo- and cross-coupling of phenols has received tremendous attention in the past decades. However, selective coupling of phenols under oxidative conditions represents a significant challenge, due to the high intrinsic nucleophilicity of phenols and the resulting tendency to preferentially undergo homo-coupling.

In 1968, Nakaya and co-workers reported the oxidative homo-coupling of phenols utilizing metal-reagents in stoichiometric amounts. The authors proposed that the reaction proceeds through generation of a phenoxy radical intermediate, which reacts with a second phenol molecule (Figure 6.1a).[130] In the following years, various methods for the homo-coupling of phenols have been reported.[131]

Pappo and co-workers developed a predictive model for the phenol-phenol cross-coupling by considering the oxidation potential (E_{ox}) and the global nucleophilicity (N) of the starting materials (Figure 6.1b).[132] The oxidation potential reflects the energy which is required to abstract an electron from the phenol. An oxidant with a matching potential will selectively oxidize the phenol with the lower oxidation potential in the presence of a less reactive phenol. The global nucleophilicity is a measure for the ability of a phenol to react with reactive intermediates *via* a radical $S_E Ar$. Selective cross-coupling can be achieved if a "complementary" pair of phenols entails a sufficient difference in oxidation potential ($E_{ox}\textbf{A} < E_{ox}\textbf{B}$), while the phenol with a higher potential is more nucleophilic ($\Delta N \gg 0$). This complementary reactivity is possible, since the oxidation potential of phenols correlates with the O−H bond dissociation energy (BDE), which is influenced by the substitution pattern and electronic properties of the adjacent functional groups.[133] The global nucleophilicity correlates with the energy of the highest occupied molecular orbital (HOMO), which is a global molecular property.[134] The less reactive phenol can be used in excess to overcompensate homo-coupling, if the difference in nucleophilicity is not pronounced enough. Taking advantage of the developed model, Pappo's group reported the application of different iron-catalysts, which efficiently catalyzed the cross-coupling of phenols.[135]
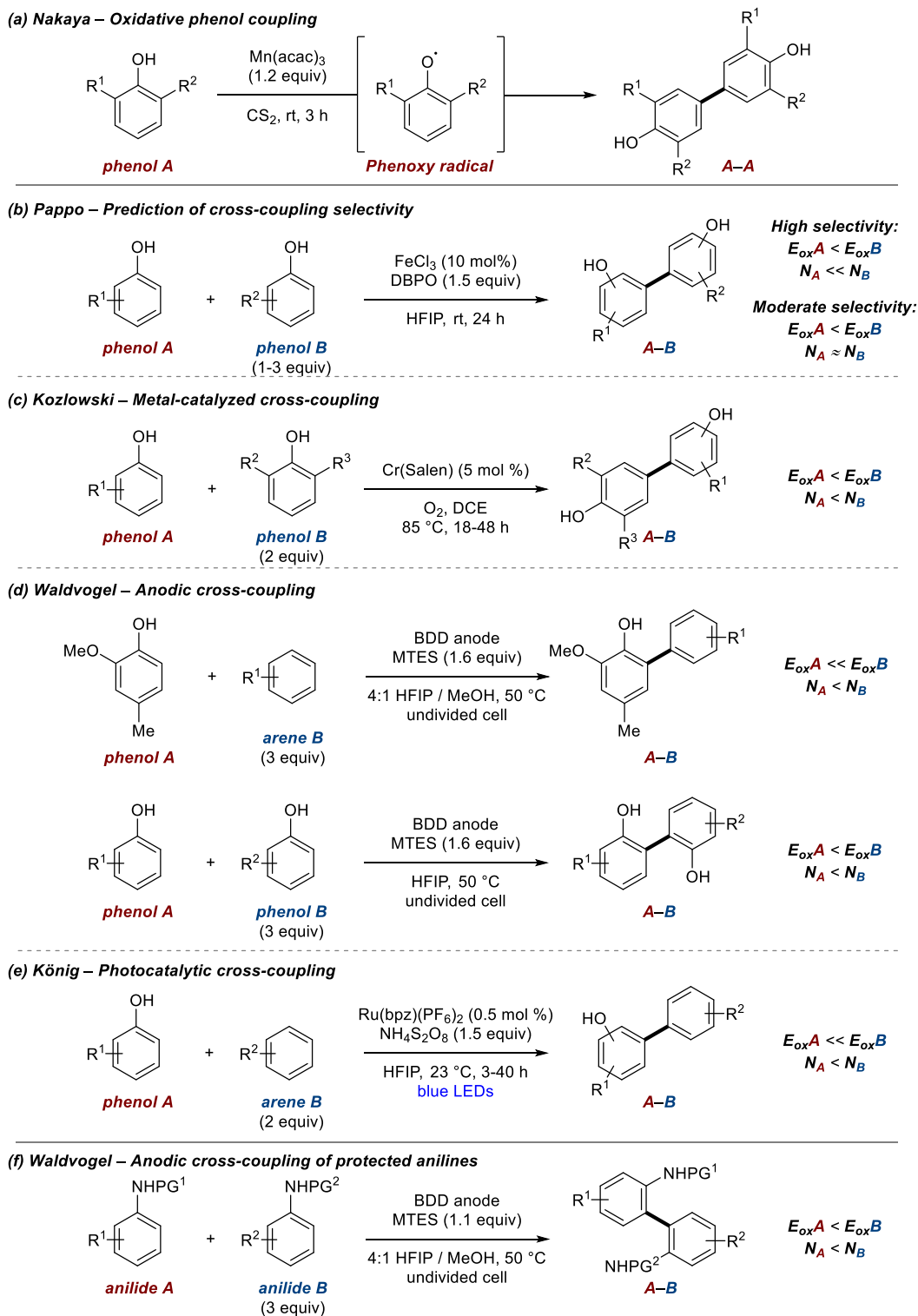
Figure 6.1 Overview of oxidative coupling methodology of phenols and anilides *via* a radical pathway. Abbreviations: MTES = Methyltriethylammonium methylsulfate; BDD = boron doped diamond.

Kozlowski's group reported the Cr(Salen) catalyzed homo- and cross-coupling of phenols under aerobic conditions (Figure 6.1c).[136] The achieved selectivity within the cross-coupling reaction can be reasoned with the model developed by Pappo and co-workers. A variety of phenols were selectively coupled with 2,6-substituted phenols. The 2,6-substituted phenols

were assigned to be more nucleophilic, while successful cross-coupling was achieved if a phenol with a lower oxidation potential was employed as the coupling partner. The group of Waldvogel actively contributed to the field of anodic coupling chemistry. Initially, phenols and nucleophilic arenes were coupled under mild reaction conditions utilizing boron doped diamond (BDD) anodes (Figure 6.1d). The lack of a hydroxy-group increases the oxidation potential of the arenes and allows the selective activation of phenols. If the arene is nucleophilic enough, cross-coupling can be achieved *via* a radical S_EAr.[137] The strategy of employing phenols and nucleophilic arenes, including heteroarenes, was reported for a variety of cross-coupling applications.[138] The anodic coupling with BDD anodes allowed the phenol-phenol cross-coupling by using complementary coupling partners.[139] The same logic for cross-coupling was applied by König and co-workers for the phenol-arene cross-coupling under photochemical reaction conditions (Figure 6.1e).[140] Alternatives for the cross-coupling concept by Pappo have been developed as well. The equipment of the more reactive coupling partner with a sterically demanding protecting group disfavours the undesired homo-coupling.[141] Employment of hypervalent iodine(III) reagents achieved the cross-coupling of phenols following a dearomatization pathway.[142]

The oxidative coupling of anilides in the absence of a metal-reagent is less explored compared to phenols. The increased oxidation potential and intrinsic nucleophilicity often leads to undesired polymerization of anilides or to formation of diazenes.[141b, 143] Waldvogel and co-workers reported the efficient cross-coupling of protected anilines under electrochemical conditions (Figure 6.1f). By carefully selecting appropriate protecting groups and substitution patterns on the anilides, a selective cross-coupling reaction was achieved in good agreement with the rational by Pappo's group.[144]

6.2 Motivation and aim of the project

As described, the low O−H bond dissociation energy (BDE) of phenols allows the initiation of radical coupling reactions *via* generation of phenoxy radicals and subsequent radical S_EAr. Considering the low oxidation potential of phenols, it was hypothesized that such an oxidative coupling reaction can be catalyzed by nitrosonium ions under aerobic conditions. Photoredox catalysis and organo electrochemistry represent clean and efficient approaches for the synthesis of biaryls and fulfill some of the requirements for green and sustainable chemistry. However, scaling limitations, the lack of standardized instrumentation with improved reproducibility and reduced pricing remain major obstacles.[145] In the case of electrochemistry, addition of

supporting electrolytes in high concentrations is often required to avoid current gradients in batch reactors.[146] Consequently, a transition metal-free and catalytic methodology, covering the selective oxidative coupling of phenols and anilides using inexpensive and readily available reagents without the requirement of specialized equipment and the production of stoichiometric amounts of harmful waste, would be a valuable addition to the portfolio of oxidative coupling reactions.

6.3   Initial results and optimization

The homo-coupling of phenol **121a** was chosen as a model reaction, by treating the starting material with substoichiometric amounts of nitrosonium salts under aerobic conditions (Table 6.1). Initially, different solvents were tested, but only decomposition of starting materials was observed (entry 1-4). Changing the solvent to a 1:1 mixture of DCM and HFIP, afforded the desired product **122a** in 15% yield (entry 5). The homo-coupling product **122a** revealed an unusual *ortho-meta* connectivity - and not the expected *ortho-ortho*-connectivity - with high regioselectivity. Presumably, the regioselectivity was controlled by the directing effect of the substituents, rather than a radical-radical recombination pathway. Additionally, compound **123a** was isolated as the major side product of the reaction. The formation of ketone **123a** was realized as an additional oxidation step of homo-coupling product **122a**.[147] In order to improve the outcome of the reaction, different combinations of solvent and TFA were tested (entry 6-12). However, only decomposition of starting material or the formation of ketone **123a** was observed. Lowering the amount of TFA did not improve the outcome of the reaction (13-15). Next, the loading of nitrosonium tetrafluoroborate was reduced, which was found to be optimal by using 2.5 mol %, affording homocoupling product **122a** in 58% yield (entry 16-18). Further, lowering of concentration improved the homocoupling up to 73% yield (entry 19-21). Finally, the optimized conditions were found by lowering the temperature to -15 °C (entry 22). The temperature could not be further lowered, since it fell below the melting point of TFA. The reaction was repeated under oxygen atmosphere, which did not improve outcome (entry 23).

Next, different additives were tested in order to improve the homo-coupling reaction of **121a** (Table 6.2). In accordance to precedented literature, it was expected that a counterion exchange could be achieved through precipitation of tetrafluoroborate salts.[52] Among all tested boronate salts, only the use of the perfluorinated $B(C_6F_5)_4$-anion yielded the desired product, albeit in lower yields (entry 1-3). Increasing the catalyst loading did not improve the outcome of the reaction while using the DCM / TFA solvent system (entry 4).

Table 6.1 Initial results and representative conditions of the optimization for the nitrosonium ion catalyzed homo-coupling of phenols.[a]
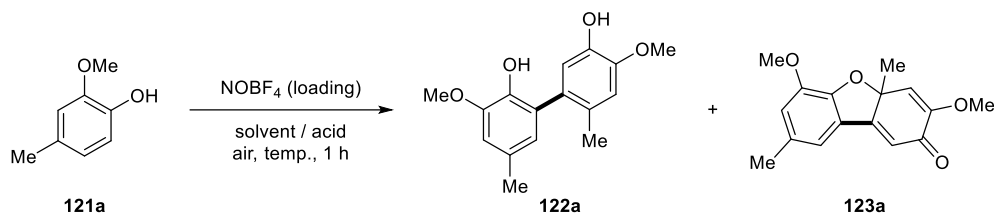
Entry	Solvent	TFA / % v/v	NOBF$_4$ / mol %	Conc. / M	122a : 123a Yield / %[b]
1	MeCN	-	10	0.1	- : -
2	DCM	-	10	0.1	- : -
3	TFE	-	10	0.1	- : -
4	HFIP	-	10	0.1	- : -
5	1:1 DCM / HFIP	-	10	0.1	15 : 32
6	1,4-dioxane	20	10	0.1	- : -
7	MeNO$_2$	20	10	0.1	- : -
8	EtOAc	20	10	0.1	- : -
9	PhCl	20	10	0.1	- : -
10	-	100	10	0.1	- : -
11	MeCN	20	10	0.1	- : -
12	DCM	20	10	0.1	- : 33
13	DCM	10	10	0.1	- : 29
14	DCM	5	10	0.1	- : 32
15	DCM	2.5	10	0.1	- : 14
16	DCM	20	5	0.1	33 : -
17	DCM	20	2.5	0.1	58 : -
18	DCM	20	1	0.1	44 : -
19	DCM	20	2.5	0.2	30 : -
20	DCM	20	2.5	0.05	73 : -
21	DCM	20	2.5	0.025	51 : -
22[c]	**DCM**	**20**	**2.5**	**0.05**	**84 : -**
23[c,d]	DCM	20	2.5	0.05	55 : -

[a] Reaction conditions: phenol **121a** (0.2 mmol, 1 equiv) in solvent (see table), at the given temperature, 1 h under air atmosphere. [b] Yields are given for isolated products after column chromatography. [c] Performed at -15 °C. [d] Under O$_2$ atmosphere.

Surprisingly, the desired product was still formed in the absence of TFA, which indicated that the boronate counterion slightly improved the course reaction (entry 5). Based on this finding, HFIP was reinvestigated as the solvent (entry 6-9). The loading of nitrosonium tetrafluoroborate could be increased back to 10 mol % without decomposition of starting material and product (entry 8). However, the yield of **122a** could not be further improved. Albeit the best conditions for the oxidative coupling of **121a** were found by using low loading of NOBF₄ (Table 6.1, entry 22), it was assumed that the use of boronate salts might represent an alternative for the coupling of even more reactive starting materials, which otherwise undergo decomposition under the optimized reaction conditions.

Table 6.2 Screening of additives for the homo-coupling of phenols.[a]
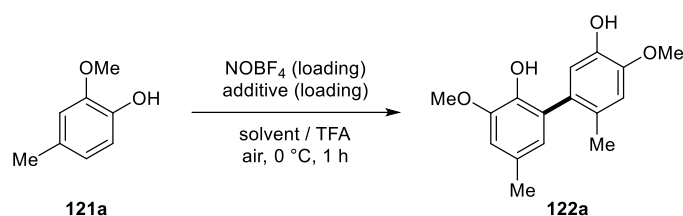
Entry	Solvent	TFA / % v/v	NOBF₄ / mol %	Additive / mol %	Yield / %[b]
1	DCM	20	2.5	KB(Ph)₄ (5)	Traces
2	DCM	20	2.5	KBPhF₃ (5)	Traces
3	DCM	20	2.5	KB(C₆F₅)₄ (5)	55
4	DCM	20	5	KB(C₆F₅)₄ (10)	37
5	DCM	-	2.5	KB(C₆F₅)₄ (5)	14
6	HFIP	-	2.5	KB(C₆F₅)₄ (5)	30
7	HFIP	-	5	KB(C₆F₅)₄ (10)	36
8	**HFIP**	**-**	**10**	**KB(C₆F₅)₄ (20)**	**58**
9	HFIP	-	20	KB(C₆F₅)₄ (40)	58

[a] Reaction conditions: phenol **121a** (0.2 mmol, 1 equiv), additive (see table), in solvent (see table), at 0 °C, 1 h under air atmosphere. [b] Yields are given for isolated products after column chromatography.

6.4 Scope of the oxidative coupling of phenols and anilides

Having the optimized conditions in hand, the scope of the homo-coupling of phenols was studied (Scheme 6.1). Homo-coupling of 2,4-substituted phenols was achieved in good yields. The usage of KB(C₆F₅)₄ as an additive proved to be beneficial for the synthesis of **122b** and **122c**. Notably, exclusive selectivity for *ortho-ortho*-coupling was observed, revealing a shift of selectivity controlled by the most nucleophilic position of the phenol. 2,6-Substituted

phenols yielded the corresponding diketones **122d-f** in good to excellent yields through *para-para*-coupling and controlled oxidation. Interestingly, product **122g** revealed *para-meta*-selectivity as a single regioisomer in a comparable manner to product **122a**, directed by the methoxy substituents. Homo-coupling of naphthols was achieved in good yields (**122h-i**) and short reaction times as well. Electron deficient product **122j** was smoothly formed using sodium nitrite as source for nitrosonium ions and TfOH instead of TFA.
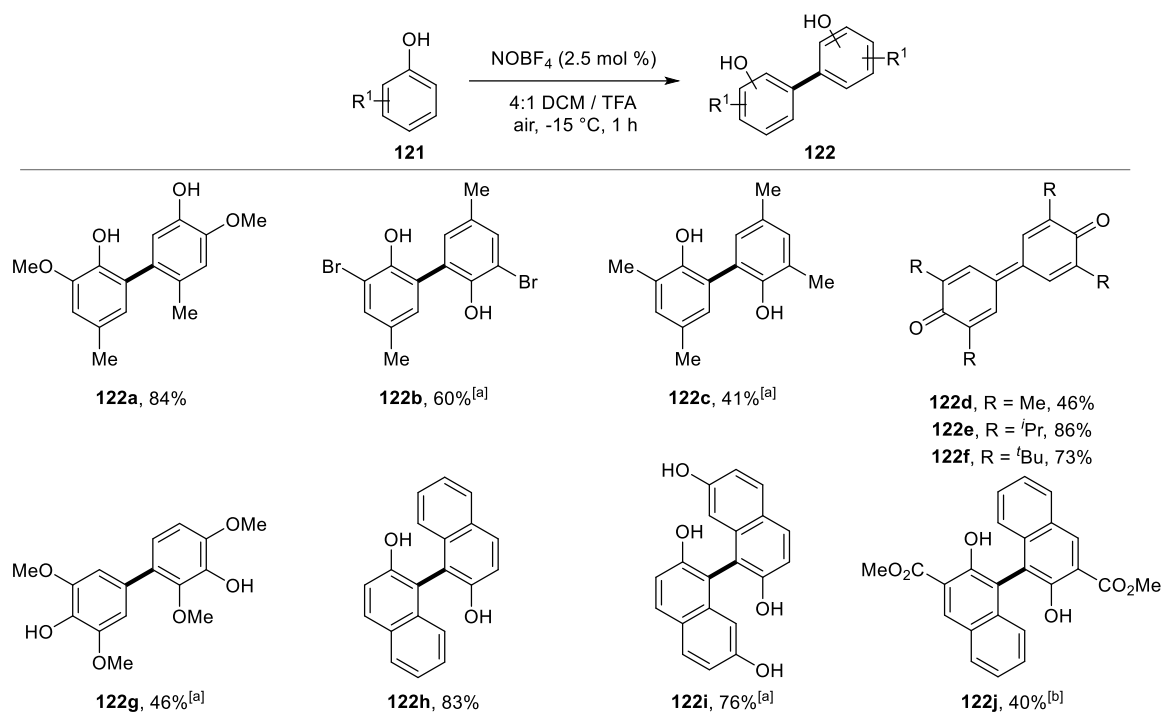
Scheme 6.1 Scope of the oxidative homo-coupling of phenols. Reaction conditions: **121** (0.5 mmol, 1 equiv), NOBF$_4$ (2.5 mol %) in 4:1 DCM / TFA (0.05 M), -15 °C, 1 h, under air atmosphere. [a] **121** (0.2 mmol, 1 equiv), NOBF$_4$ (10 mol %), KB(C$_6$F$_5$)$_4$ (20 mol %) in HFIP (0.05 M), 0 °C, 1 h under air atmosphere. [b] Using NaNO$_2$ (30 mol %), TfOH (2 equiv) in MeCN. Yields are given for isolated products after column chromatography.
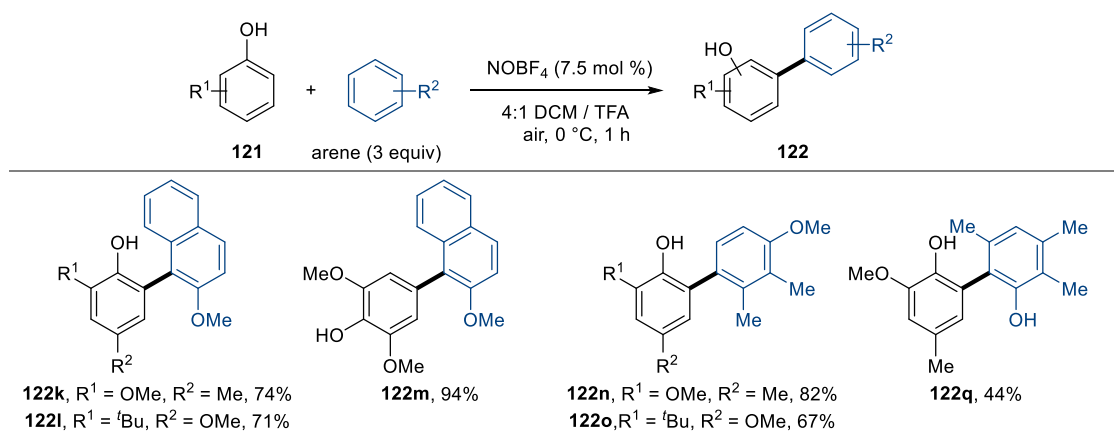
Scheme 6.2 Scope of the oxidative cross-coupling of phenols. Reaction conditions: **121** (0.25 mmol, 1 equiv), arene (3 equiv), NOBF$_4$ (7.5 mol %) in 4:1 DCM / TFA (0.1 M), 0 °C, 1 h under air atmosphere. Yields are given for isolated products after column chromatography.

Based on the aforementioned work by Pappo and co-workers, the selective cross-coupling of phenols and nucleophilic arenes was performed, using the developed reaction conditions (Scheme 6.2). Successful cross-coupling required only a slight increase of catalyst loading, yielding the desired products as single regioisomers in high yields and short reaction times (**122k-o**). Notably, the phenol-phenol cross-coupling was performed as well (**122q**).

As described, the formation of over-oxidation product **123a** was identified during the systematic optimization of the reaction conditions (Figure 6.2). The unusual connectivity is in contrast to the known formation of Pummerer-ketones, which commonly proceeds *via ortho-para*-coupling of phenols and subsequent 1,4-addition.[147] Increasing the loading of nitrosonium tetrafluoroborate to 15 mol % in 1:1 DCM / HFIP allowed the conversion of **121a** to **123a** in a one-pot reaction. Additionally, homo-coupling product **122a** was converted to ketone **123a** in good yield in order to reveal the course of reaction. This annulation reaction represents an unprecedented example of oxidative coupling for the synthesis of inverse Pummerer-type ketones, controlled by the connectivity achieved within the first coupling step.
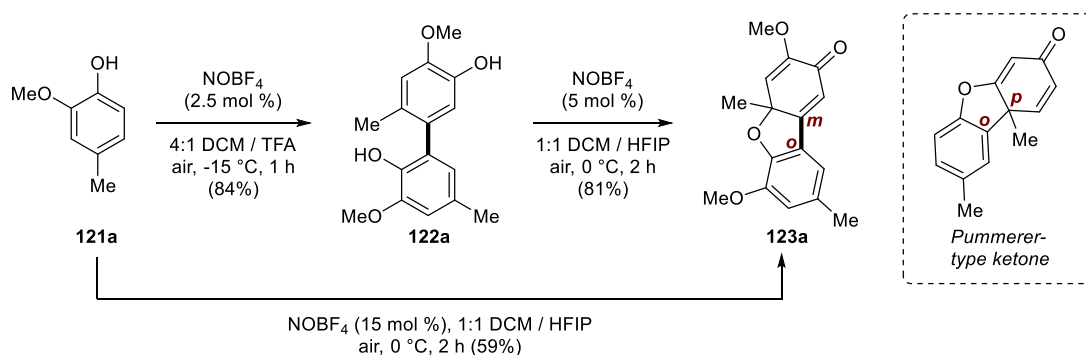
Figure 6.2 Synthesis of inverse Pummerer-type ketone *via* stepwise and one-pot oxidative annulation.

Next, the attention was pointed to the oxidative coupling of anilides. Oxidative coupling of phenols is known to proceed *via* homolytic O–H bond cleavage and generation of phenoxy radicals. Phenols and electron-rich anilides share structural similarities and also entail comparable oxidation potentials. Consequently, anilides were expected to be suitable substrates for the developed methodology. It was assumed that the coupling proceeds by an initial N–H bond cleavage. Delightfully, *N*-phenylacetamide (**124a**) efficiently formed the dimeric product **125a** in 65% yield using 20 mol % of the nitrosonium tetrafluoroborate (Table 6.3, entry 1). Changing the solvent to MeCN resulted in a decreased yield of **125a** (entry 2-3). A stronger tendency for electrophilic nitration of starting material was observed, due to the higher nucleophilicity. The undesired nitration could be bypassed by increasing the solvent / acid-

ratio (entry 4-6). Homo-coupling product **125a** was isolated in 94% yield under the optimized reaction conditions using 20 mol % of the nitrosonium salt in 2:1 DCM / TFA as the solvent system (entry 5).

Table 6.3 Focussed optimization for the oxidative homo-coupling of anilides.[a]

Entry	Solvent	TFA / % v/v	NOBF₄ / mol %	Yield / %[b]
1	DCM	20	20	65
2	MeCN	20	10	34
3	MeCN	20	20	52
4	DCM	10	20	48
5	**DCM**	**33**	**20**	**94**
6	DCM	50	20	26

[a] Reaction conditions: **124a** (0.2 mmol, 1 equiv) in solvent / TFA (see table), 0 °C, 1 h, under air atmosphere.
[b] Yields are given for isolated products after column chromatography.

With the optimized conditions in hand, the scope for the oxidative coupling of anilides was studied as well (Scheme 6.3). Acetylated anilines afforded the desired products **125b** and **125c** in good yields. However, anilides with electron-withdrawing substituents were not reactive under the developed reaction conditions. Next, different protecting groups on the nitrogen atom were tested. Coupling of *N*-phenylbenzene-sulfonamide afforded product **125d** in 53% yield.

Anilides equipped with different benzoyl groups were also suitable for the coupling reaction (**125e-h**). The highly electron-withdrawing nitro group on the benzoyl moiety was well tolerated (**125f**). Additionally, the highly sterically demanding adamantyl group did not alter the outcome of the reaction, yielding product **125i** in 75% yield. Product **125j** was obtained as a single regioisomer, while the naphthyl substituent was not reactive under the developed reaction conditions. To stress the utility of the developed oxidative coupling, the coupling of anilide **124a** was repeated on 1 g scale. The product **125a** was formed unaffectedly in short reaction time and only slightly reduced yield.
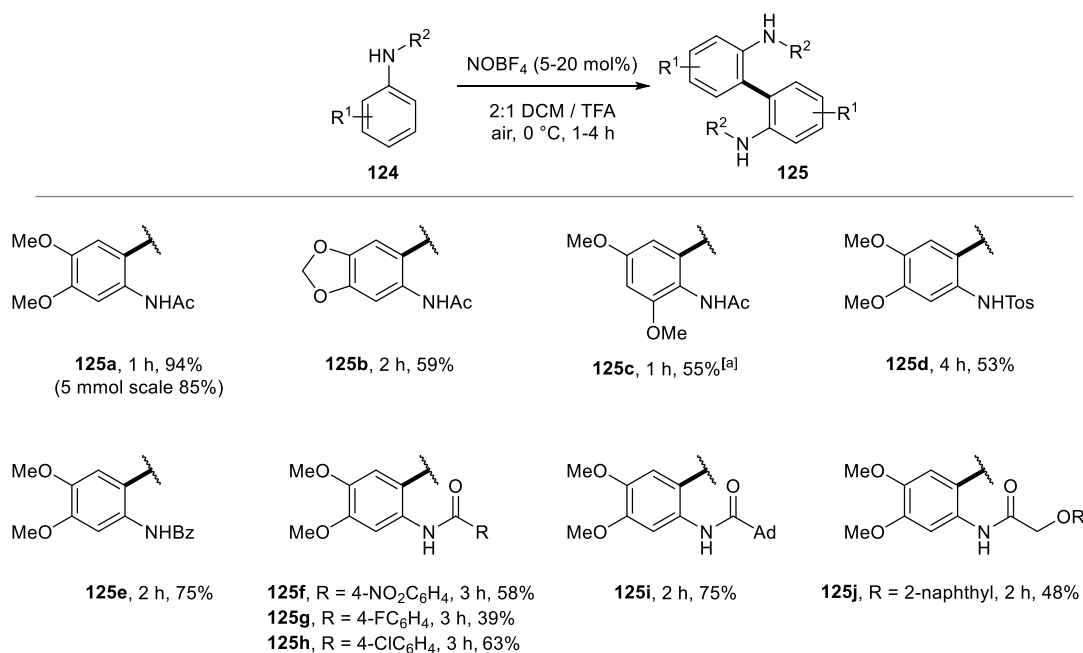
Scheme 6.3 Scope the oxidative homo-coupling of anilides. Reaction conditions: **124** (0.2 mmol, 1 equiv), NOBF$_4$ (20 mol %) in 2:1 DCM / TFA (0.1 M), 0 °C, under air atmosphere. [a] NOBF$_4$ (5 mol %). Yields are given for isolated products after column chromatography.

By judging the results of the scope experiments, it was assumed that phenols entail a lower oxidation potential than anilides, but anilides are more nucleophilic. Therefore, phenols and anilides should represent a complementary pair for cross-coupling chemistry. According to that hypothesis, a set of selective phenol-anilide cross-coupling reactions was successfully performed (Scheme 6.4). The unprecedented cross-coupling products **125k-n** were obtained in good yields, excellent selectivity and short reaction times.
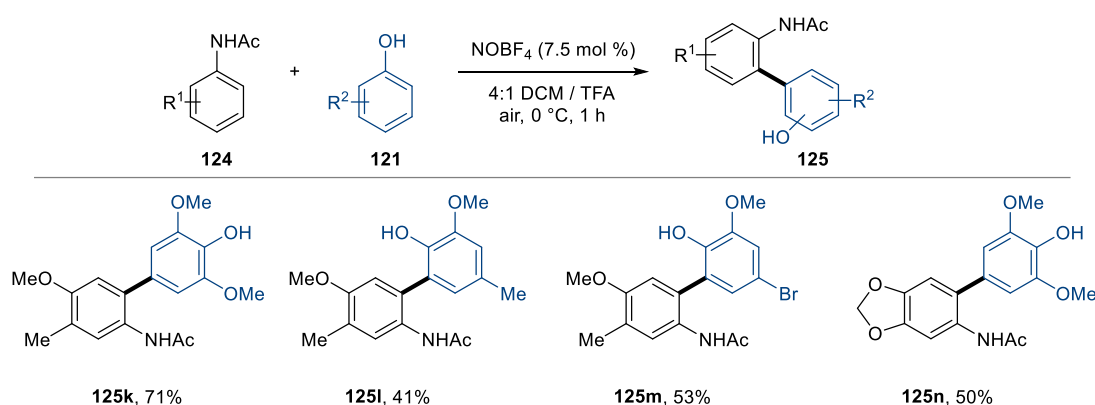
Scheme 6.4 Scope the oxidative cross-coupling of anilides and phenols. Reaction conditions: **121** (0.2 mmol, 1 equiv), **124** (3 equiv), NOBF$_4$ (7.5 mol %) in 4:1 DCM / TFA (0.1 M), 0 °C, 1 h, under air atmosphere. Yields are given for isolated products after column chromatography.

6.5   Mechanistic considerations

After disclosing the scope of the catalytic coupling reaction, the reaction mechanism was studied (Figure 6.3). When conducting the reaction under argon atmosphere and by carefully removing residual oxygen from the solvent, no product was formed for both phenols and anilides. According to the initial hypothesis, oxidative coupling is initiated by homolytic cleavage of O–H bond or N–H bonds. The heteroatoms were functionalized by methylation, in order to study the importance of weak heteroatom-hydrogen bonds for the coupling reaction. For both substrates no conversion was detected, which excludes the formation of a radical cation species through a direct single electron transfer.
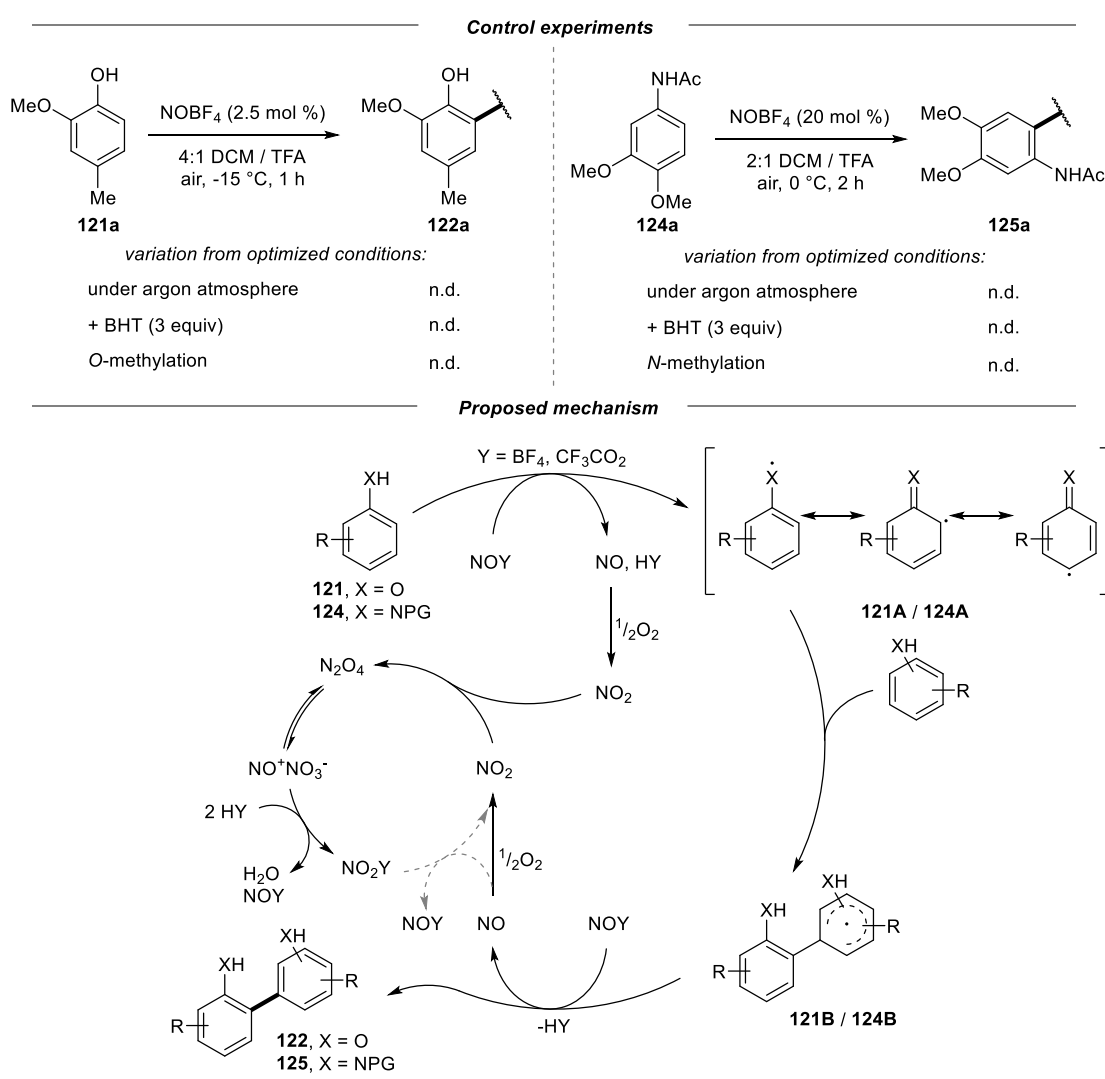
Figure 6.3 Control experiments and proposed mechanism for the oxidative coupling of phenols and anilides.

Finally, the oxidative coupling was repeated in the presence of radical trap butylated hydroxytoluene (BHT). While no homo-coupling product was detected, the formation of

scavenging adducts was observed respectively. These results support the proposed homology between phenol- and anilide-coupling under the reaction conditions.

Based on the control experiments, a mechanism was outlined in Figure 6.3. Initially, the substrates are oxidized by means of homolytic heteroatom-hydrogen bond cleavage to form **121A** or **124A**. Intermediates **A** react with a second equivalent of the substrate, or a nucleophilic arene in the case of cross-coupling, by means of radical S_EAr and subsequent rearomatization generates intermediate **121B** or **124B**. A second oxidation step by nitrosonium tetrafluoroborate leads to aromatization and formation of the products **122** or **125** respectively.

Nitrogen monoxide, which is formed upon oxidation of the starting material, is oxidized by molecular oxygen, forming nitrogen dioxide. Nitrogen dioxide dimerizes to form dinitrogen tetroxide, which is in equilibrium with nitrosonium nitrate by means of disproportionation. Nitrosonium and nitronium ions are released under the acidic reaction conditions and water is generated as the by-product. Finally, the nitronium ion is able to oxidize nitrogen monoxide instead of molecular oxygen to maintain the catalytic cycle.[77]

6.6   Conclusion

In summary, the first catalytic and transition metal-free coupling reaction of phenols and anilides using nitrosonium salts as catalyst and ambient oxygen as the terminal oxidant has been developed. Phenols were efficiently homo-coupled with unusual selectivities for the biaryl formation. The unusual connectivity translated into the synthesis of an unprecedented inverse Pummerer-type ketone in good yields. Additionally, the phenol-arene cross-coupling was performed in excellent yield and selectivity. Finally, mechanistic studies suggested that phenols and anilides share a similar pathway in oxidative coupling. Based on this analogy, a set of dimerized anilides was synthesized and the unprecedented phenol-anilide cross-coupling was successfully performed. The application of nitrosonium salts represents a sustainable and unprecedented entry into oxidative coupling methodology. The developed reaction conditions offer some advantages compared to known methods, due to the accessibility and low costs of nitrosonium salts and the exclusion of the requirement for any specialized equipment or reagents.

Intra- and Intermolecular Benzylation of Arenes

7 Intra- and Intermolecular Benzylation of Arenes

7.1 Introduction

The electrophilic activation of hydroxyl groups and Friedel-Crafts reactions on non-activated systems have been elected as top priorities for green chemistry research.[148] C–O bonds are omnipresent in nature and the development of novel chemical methods for the transformation of C–O bonds into C–C bonds are of high demand.[149] In contrast to organo halides, alcohols, and ethers are inexpensive readily available and non-toxic.[150]
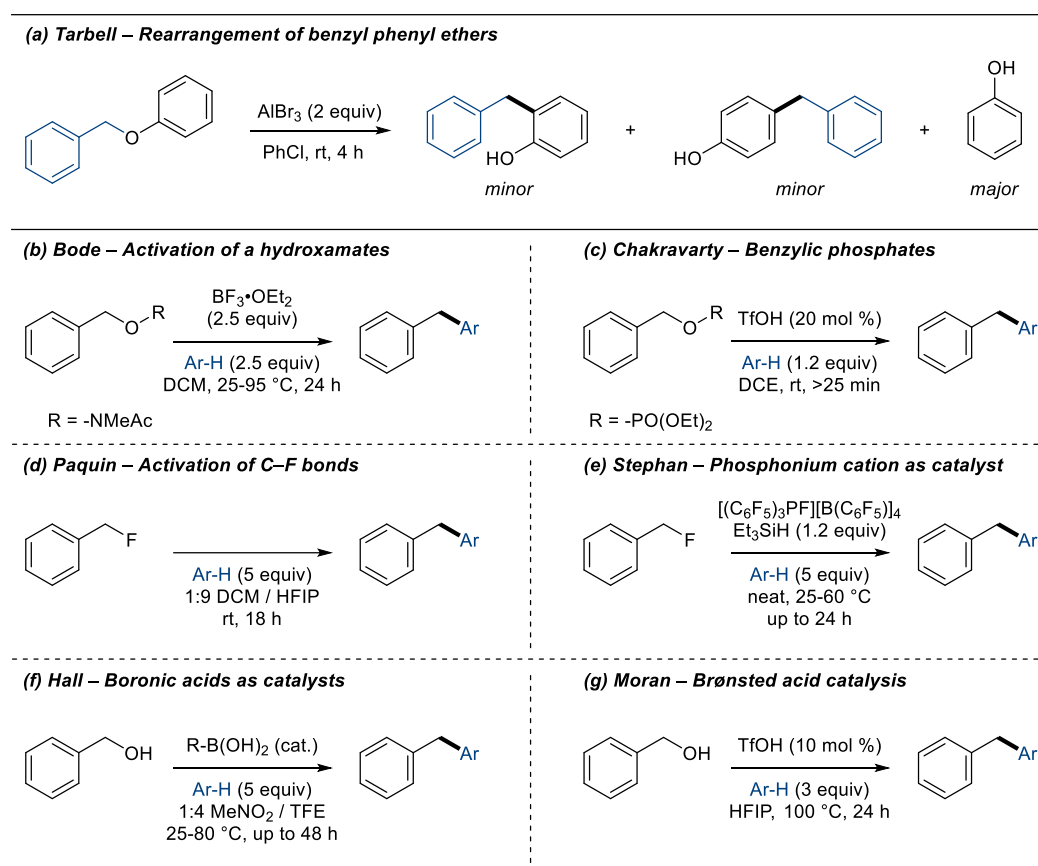
Figure 7.1 Overview of transition metal-free approaches towards the synthesis of diarylmethanes.

In 1952, Tarbell and Petropoulos reported the rearrangement of benzyl phenyl ethers using stoichiometric amounts of AlBr$_3$ affording a mixture of benzylated phenols and deprotected phenol (Figure 7.1a).[151] Later on, different methods for the synthesis of benzylated phenols have been described. However, the restriction to electron-rich substrates accompanied with harsh reaction conditions are still limitation for this transformation.[152] Friedel-Craft reactions enable the efficient C–C bond formation *via* functionalization of C$_{sp}^2$–H bonds, but usually require metal-based Lewis-acids, harsh reaction conditions or lead to the undesired production of halohydric acid as by product.[153] Recently, different strategies for the transition metal-free

synthesis of diarylmethanes have been reported. Diarylmethanes are important building blocks for pharmaceuticals, agrochemicals and materials.[154] Cross-coupling methods enable the regioselective synthesis of diarylmethanes, but require additional activating groups on both coupling partners.[92, 155]

Bode and co-workers developed the arylation of benzyl hydroxamates mediated by BF$_3\cdot$OEt$_2$ (Figure 7.1b).[156] Later, the application of alkyl phosphates was reported by Chakravarty's group (Figure 7.1c).[157] Paquin and co-workers developed the Friedel-Crafts alkylation with benzyl fluorides *via* the *in situ* generation of HF (Figure 7.1d).[158] Stephan's group disclosed the activation of benzyl fluorides in the presence of electrophilic organofluorides and stoichiometric amounts of Et$_3$SiH as a reductant (Figure 7.1e).[159] However, benzyl fluorides must be generated from the corresponding alcohols using stoichiometric amounts of fluorination reagent.[160] Consequently, the direct employment of benzyl alcohols overcomes the drawbacks of the corresponding fluorides. Hall and co-workers explored the application of electron-deficient boronic acids (Figure 7.1f)[161] and later, Moran's group demonstrated the Brønsted acid-catalyzed functionalization of arenes with benzyl alcohols (Figure 7.1b).[162] In contrast, the application of nitrosonium salts in C–O bond activation is limited to protecting group removal and oxidation reaction.[24c, 26, 29a]

7.2   Motivation and aim of the project

Structurally tailored biaryls can serve as template for intramolecular coupling reactions. Usually favoured homo-coupling might be overcome, due to the proximity of both arenes (see Scheme 1.19). Towards this concept, benzyl ethers were selected as substrates to forge new carbon-carbon bonds intramolecularly (see Table 7.1). However, the treatment of benzyl ether **126a** with nitrosonium tetrafluoroborate yielded the rearranged product in the same manner as described by Tarbell and co-workers.[151] Since the reaction proceeded rapidly and in the absence of any activation group, the systematic optimization was performed. Further, the developed conditions were used as template for the development of an intermolecular transition metal-free Friedel-Crafts reaction.

7.3   Initial results and optimization

As described, the intramolecular oxidative coupling reaction of benzyl aryl ethers was targeted in order to form a new carbon-carbon bond (Table 7.1). However, treating **126a** with substoichiometric amounts of nitrosonium tetrafluoroborate induced the formation of the regioisomeric mixture of **127a** as the only product in the reaction. A set of solvents was tested,

but solely HFIP afforded **127a** in low yields albeit with 4:1 regioselectivity (entry 1-13). By employing a 1:1 mixture of DCM / HFIP, the yield could be improved to 50% with an *ortho* : *para*-selectivity of 6:1 (entry 14). The yield dropped to 27% by changing the solvent system to the more acidic component TFA (entry 15).

Table 7.1 Initial results and representative conditions for the solvent screening.[a]
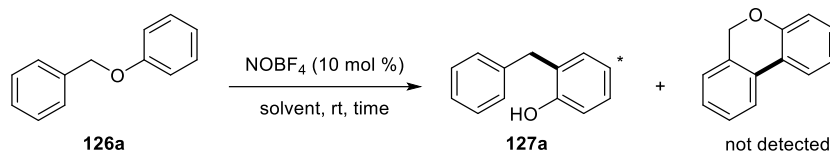
Entry	Solvent	Time / h	Yield / %[b]	*o:p*[c]
1	DCM	24	Traces	-
2	MeCN	24	-	-
3	HFIP	< 0.5	14	4:1
4	PhF	24	-	-
5	TFE	24	-	-
6	DMF	24	-	-
7	DCE	24	-	-
8	EtOAc	24	-	-
9	MeOH	24	-	-
10	THF	24	-	-
11	1,4-dioxane	24	-	-
12	toluene	24	-	-
13	DMSO	24	-	-
14	1:1 DCM / HFIP	3	50	6:1
15	4:1 DCM / TFA	3	27	6:1
16	4:1 MeCN / TFA	24	-	-
17	2:1 DCM / HFIP	1	54	6:1
18	3:1 DCM / HFIP	1	46	6:1
19	10:1 DCM / HFIP	10	27	4:1
20	1:2 DCM / HFIP	1	17	4:1

[a] Reaction conditions: **126a** (0.1 mmol, 1 equiv), NOBF$_4$ (10 mol %), solvent (0.1 M), rt. [b] Yields are given for isolated products after column chromatography. [c] *o:p* ratio according to ^{1}H-NMR. * Denotes minor regioisomer.

Exchanging DCM to MeCN did not afford the desired product (entry 16). Further, the solvent ratio of DCM / HFIP was systematically varied (entry 17-20). The highest yield was obtained in a 2:1 mixture of solvents, affording **127a** in 54% yield. Unfortunately, the regioselectivity was not affected by the choice of solvent. However, with a selectivity of 6:1, the reaction reveals acceptable selectivity for the *ortho*-position. This selectivity is higher than the statistical distribution of regioisomers in a Friedel-Craft reaction. A possible explanation is the proximity of the *ortho*-position of the phenol relative to the cleavage site, favouring the recombination at this site prior to the nucleophilic attack of the *para*-position of the phenol.

In order to improve the outcome of the reaction, the identified conditions were further optimized (Table 7.2). A drastic improvement of yield was observed while lowering the loading of the nitrosonium salt (entry 1-6). By using low loading of nitrosonium tetrafluoroborate, the rearranged product **127a** was isolated in 84% yield (entry 5). However, the regioisomeric ratio did not improve. Additionally, different additives were tested (entry 7-9). In accordance to precedented literature, it was expected that a counterion exchange would lead to precipitation of the tetrafluoroborate salts.[52] However, no improvement was found. Finally, different concentrations and temperatures were tested, but no beneficial effect could be identified.

Table 7.2 Representative conditions for the optimization of the catalytic system.[a]
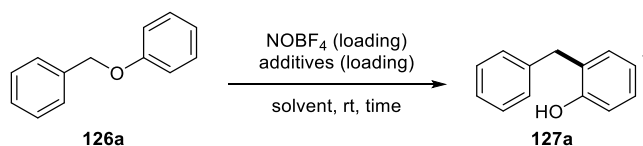
Entry	NOBF$_4$ / mol %	Additive (mol %)	Time / h	Yield / %[b]	o:p[c]
1	10	-	0.5	56	6:1
2	5	-	0.5	69	6:1
3	2.5	-	0.5	68	6:1
4	1	-	1	80	6:1
5	**0.5**	**-**	**1**	**84**	**6:1**
6	0.2	-	10	36	6:1
7	0.5	NaBPh$_4$ (1.5)	1	78	6:1
8	0.5	KB(C$_6$F$_5$)$_4$ (1.5)	24	60	5:1
9	0.5	KPhBF$_3$ (1.5)	24	80	5:1

[a] Reaction conditions: **126a** (1 mmol, 1 equiv), NOBF$_4$ (0.5 mol %), 2:1 DCM / HFIP (0.1 M), rt. [b] Yields are given for isolated products after column chromatography. [c] *o*:*p* ratio according to ^{1}H-NMR. * Denotes minor regioisomer.

7.4 Scope of the rearrangement of benzyl ethers

With the optimized conditions in hand, the scope of the catalytic rearrangement of various benzyl aryl ethers was explored (Scheme 7.1). The reaction proved to be robust and allowed the synthesis of a large set of benzylated phenols in short reaction times and with predictable selectivities.
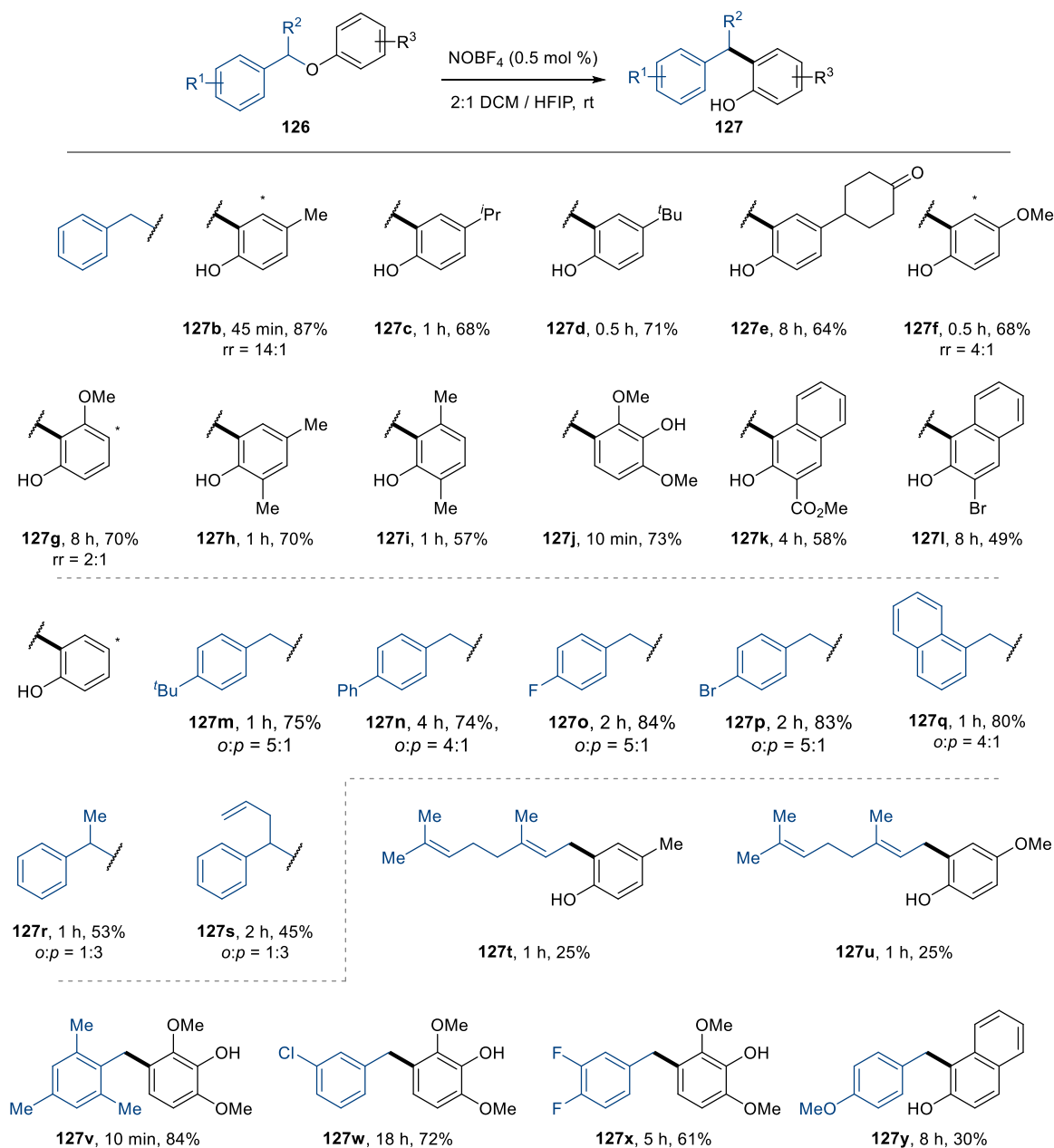
Scheme 7.1 Scope of the intramolecular rearrangement of benzyl aryl ethers. Reaction conditions: **126** (0.5 mmol, 1 equiv), NOBF$_4$ (0.5 mol %), 2:1 DCM / HFIP (0.1 M), room temperature, 0.16-18 h. Yields are given for isolated products after column chromatography. Regioisomer ratio according to GC-MS-FID. * Denotes minor regioisomer.

Benzyl aryl ethers, equipped with substituents at the 4-position of phenol, afforded the desired products in high yields and good to excellent regioselectivities (**127b-e**). Methoxy groups at the 3 or 4-position of the phenol yielded the rearranged products in high yields, but as a mixture of regioisomers. The obtained isomers could be separated in a straightforward manner (**127f-g**). A set of polysubstituted phenols was tested, allowing the synthesis of various products with good selectivities and high yields (**127h-j**). Naphthol derivatives underwent the rearrangement under the developed reaction conditions, affording the products **127k** and **127l** in good yields and excellent regioselectivities.

The rearrangement of benzyl aryl ethers bearing substituents on the benzyl moiety was also demonstrated. Functional groups with electron-donating and electron-withdrawing effects were well tolerated. The desired products were formed in high yields, but as a mixture of *ortho*- and *para*-isomers (**127m-q**). Substrates with highly electron-withdrawing groups did not yield the desired products. Further, products **127r** and **127s** proved the compatibility of secondary benzyl groups, even tolerating a terminal double bond. Interestingly, the *para*-regioisomer was isolated as the major product. The rearrangement of allylic groups was also explored. Geranylated products **127t** and **127u** were isolated as single isomers, albeit in reduced yields. Next, a set of polysubstituted starting materials was tested, bearing functional groups on the phenol and benzyl moiety (**127v-y**). The desired products were isolated in moderate to good yields, but with excellent regioselectivities.

7.5 Scope of the intermolecular benzylation of arenes

Next, the development of an intermolecular variant was targeted, based on the developed reaction conditions of the catalytic rearrangement of benzyl aryl ethers. The direct employment of benzylic alcohols was found to be suitable for the intermolecular Friedel-Crafts reaction using slightly adjusted reaction conditions (Scheme 7.2). The most simplified coupling reaction was performed by means of diphenylmethane synthesis (**130a**). Benzylation using benzene as nucleophile was achieved in good yield, while using nitrosonium tetrafluoroborate as catalyst and producing water as the stoichiometric by-product.

The scope of the catalytic Friedel-Crafts reaction was explored by testing secondary and tertiary benzyl alcohols. Products **130b-d** were isolated in high yields and short reaction times. Electron-neutral and deactivated diarylmethanes were successfully synthesized in good yields, revealing no restriction to electron-rich starting materials (**130e-i**). Even poly-halogenated arenes (**130j**) and benzyl alcohols (**130k**) afforded the desired products.

The combination of two electron-rich coupling partners yielded products **130l-o** in high yield and selectivity. Further, a set of diarylmethanes was synthesized using polysubstituted arenes as coupling partners (**130p-u**). Arylation of dibenzylic alcohols was also demonstrated and the corresponding diarylated products were obtained good yields (**130v-w**).

130a, 63% **130b**, 76% **130c**, 78% **130d**, 91%

130e, R = *t*Bu, 69%, *o:p* = 1:2
130f, R = F, 59%, *o:p* = 3:1
130g, R = Cl, 68%, *o:p* = 1:2
130h, R = Br, 78%, *o:p* = 1:2
130i, R = I, 70%, *o:p* = 1:3

130j, 78% **130k**, 59%

130l, 98% **130m**, 75% **130n**, 98% **130o**, 85%

130p, 67% **130q**, 88% **130r**, 77% **130s**, 58%, rr = 7:1

130t, 43% **130u**, 60% **130v**, 60%
R = *p*-xylyl
130w, 69%
R = mesityl
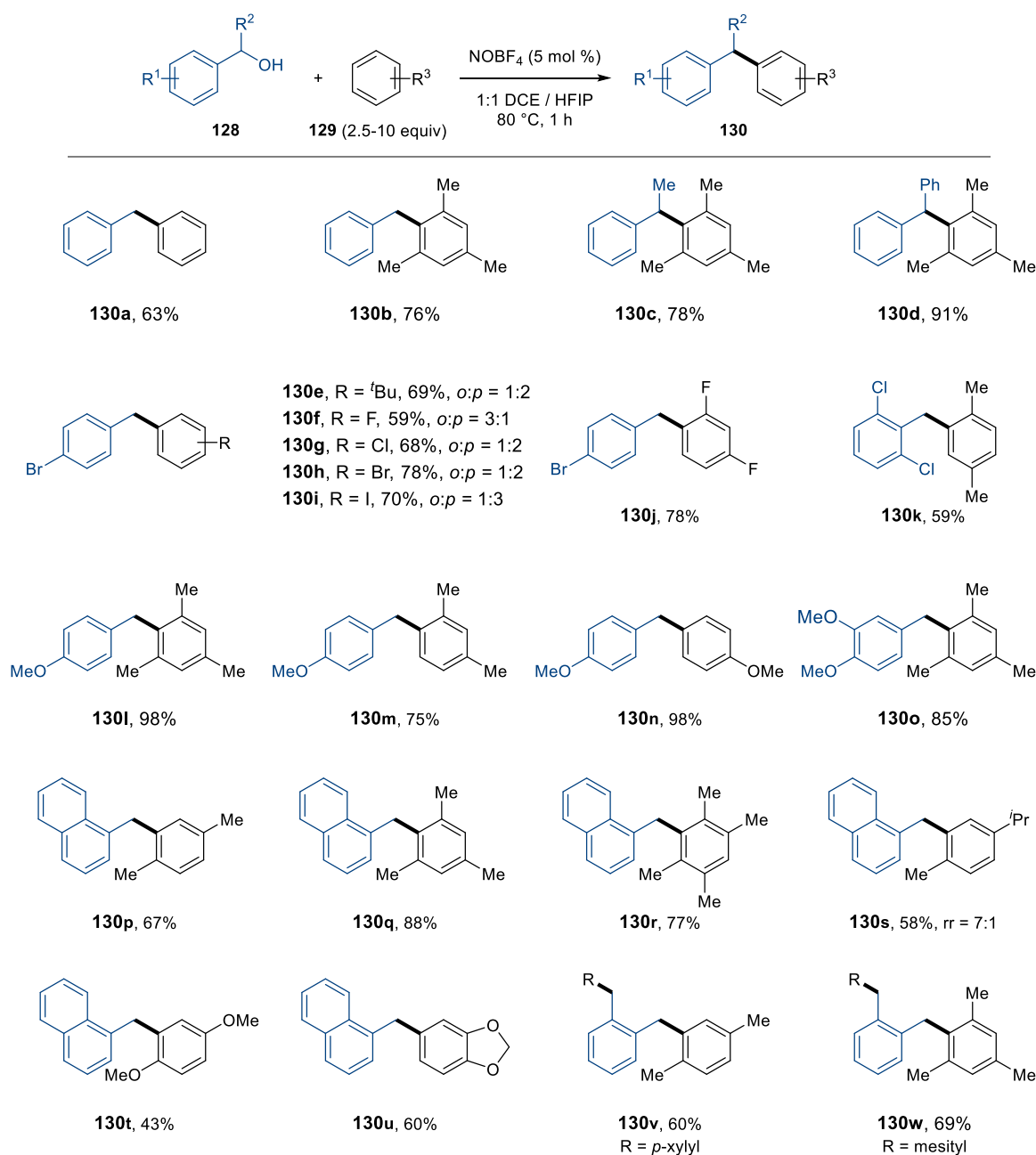
Scheme 7.2 Scope of the intermolecular benzylation of arenes with benzyl alcohols. Reaction conditions: **128** (0.2 mmol, 1 equiv), **129** (2.5 equiv or 10 equiv) NOBF$_4$ (5 mol %), 1:1 DCE / HFIP (0.1 M), 80 °C, 1 h. Yields are given for isolated products after column chromatography. Regioisomer ratio according to ^{1}H-NMR. * Denotes minor regioisomer.

Afterwards, the coupling of complex starting materials, including heterocycles, was explored (Scheme 7.3). Functionalization of indoles was successfully achieved in good to excellent

yields (**130x-z**). Late-stage functionalization of unprotected estrone afforded the natural product-derived compound **130aa** in a regioselective manner in 92% yield. Synthesis of oxindole **130ab** proceeded with perfect yield and regioselectivity using anisole and protected 3-hydroxy-2-oxindole as coupling partners. Incorporation of heterocyclic groups such as benzothiophene, chromone and furan was achieved in good to excellent yield (**130ac-ae**). To further explore the utility of the developed reaction conditions, we targeted the transition metal-free synthesis of drug molecules. Phenprocoumon (**130af**) and Nafenopin (**130ag**) were synthesized in satisfying yields as single regioisomers. Notably, Nafenopin is commonly synthesized using stoichiometric amounts of aluminium chloride.[163]
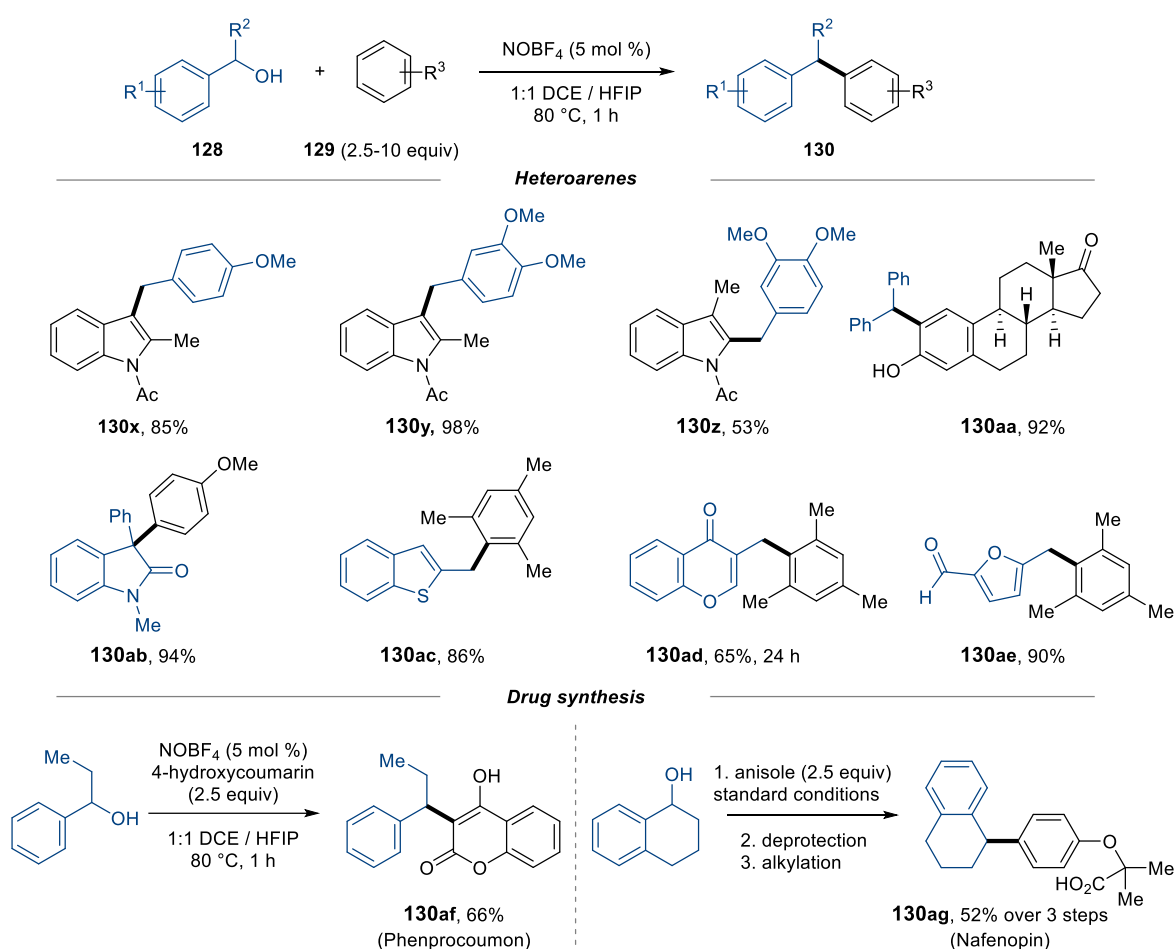
Scheme 7.3 Scope for the intermolecular benzylation of heteroarenes with benzyl alcohols and synthesis of drug molecules applying the developed reaction conditions. Reaction conditions: **128** (0.2 mmol, 1 equiv), **129** (2.5 equiv or 10 equiv) NOBF₄ (5 mol %), 1:1 DCE / HFIP (0.1 M). Yields are given for isolated products after column chromatography.

Next, the developed system for the Friedel-Crafts alkylation reaction was compared with other Brønsted-acid catalysts, including triflic acid and HBF₄ (Table 7.3). The results revealed the efficacy of different acid catalysts for the Friedel-Crafts alkylation reaction under standard

conditions. However, no acid proved to be superior to nitrosonium tetrafluoroborate. Additionally, the possibility for the release of fluorine was examined. However, the use of Olah's reagent yielded only small amounts of product.

Table 7.3 Efficacy testing of various Brønsted-acid catalysts.[a]
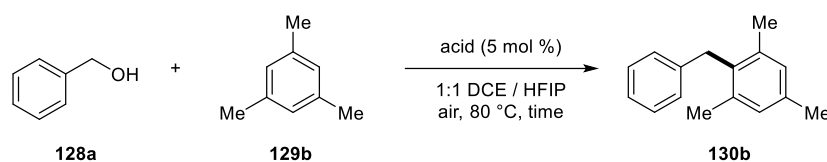
Entry	Acid	Time / h	Yield / %[b]
1	AcOH	24	-
2	TFA	24	Traces
3	p-TsOH	2	49
4	TfOH	2	57
5	HBF_4	2	48
6	H_2SO_4	2	26
7	$HClO_4$	2	28
8	Olah's reagent	24	<10

[a] Reaction conditions: **128a** (0.2 mmol, 1 equiv), **129b** (10 equiv), acid (5 mol %), 1:1 DCE / HFIP (0.1 M), 80 °C, 2-24 h. [b] Yields are given for isolated products after column chromatography.

7.6 Mechanistic Considerations

Initially, the mechanism for the intramolecular rearrangement of benzyl ethers was studied. However, a Brønsted acid-based mechanism through the *in situ* formation of HBF_4 could not be conclusively ruled out. Nevertheless, the importance of the nitrosonium ion and a Lewis acid-based mechanism for the intramolecular Friedel-Crafts reaction was confirmed (Figure 7.2). Initially, the reaction was repeated under inert gas atmosphere, but product **130b** was formed unaffectedly. In order to rule out the generation of radical intermediates, the reaction was repeated in the presence of radical trap butylated hydroxytoluene (BHT). However, **130b** was formed unaffectedly. Neither the employment of nitronium tetrafluoroborate nor variation of the counter ion affected the outcome of the reaction. Oxidation of reactive nitrogen-oxygen species appeared to be unlikely, due to the inefficient performance of nitric acid. NOCl as the catalyst yielded the desired product unaffectedly, which supports a Lewis acid-based mechanism. Notably, when hydrochloric acid and nitric acid were used individually, only small amounts of product were isolated. The presence of the nitrosonium ion in solution appeared to

be crucial for the reaction. The formation of a benzylic cation appeared to be reasonable, since racemization was observed upon functionalization of an enantiopure starting material. The proposed course of reaction is outlined in Figure 7.2. Nitrosonium tetrafluoroborate activates benzylic alcohol (**128a**) by generating intermediate **128A**. Formation of intermediate **128B** is followed by intermolecular S_EAr with the arene nucleophile (**129b**). The released NO^+ species are scavenged by HBF_4 to generate water and to maintain the catalytic cycle.
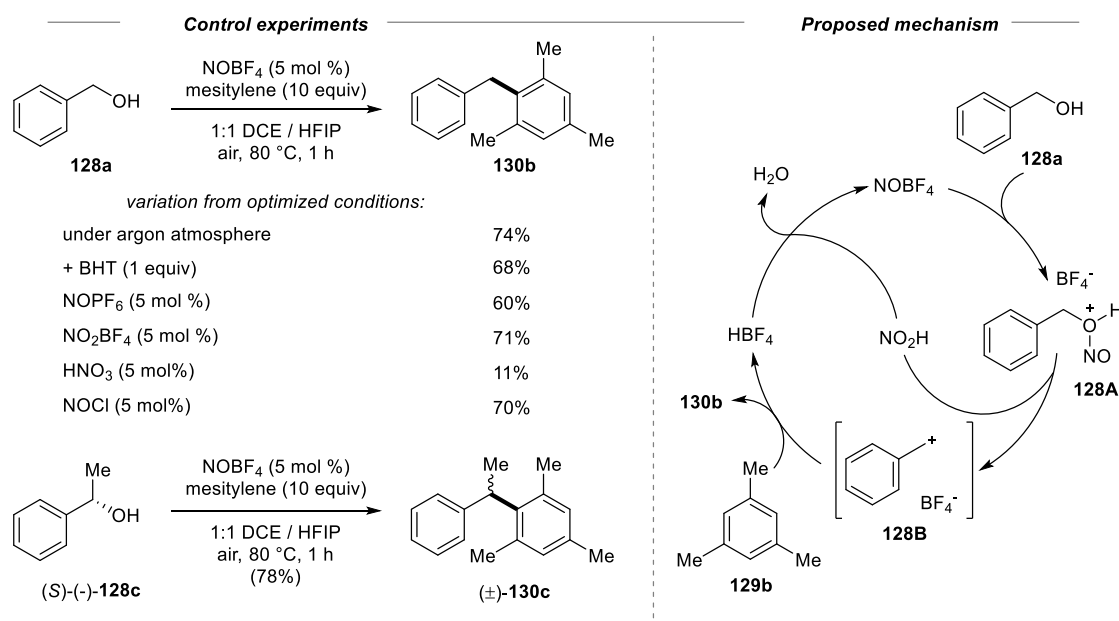
Figure 7.2 Control experiments and proposed mechanism.

7.7 Conclusion

In summary, the transition metal-free intramolecular rearrangement of benzyl aryl ethers with low loading of nitrosonium tetrafluoroborate as catalyst has been developed under mild conditions. A broad scope was demonstrated revealing good functional group tolerance, predictable selectivities and short reaction times. Furthermore, the developed reaction conditions converted into the catalytic and transition metal-free Friedel-Crafts alkylation for the synthesis of various diarylmethanes using benzyl alcohols and nucleophilic arenes. A comprehensive scope was demonstrated, covering electron-deficient coupling partners and complex molecules, including natural products. Strikingly, the developed method was successfully applied for the synthesis of the drug molecules Phenprocoumon and Nafenopin.

Thioarylation of Phenols and Indoles

8 Cross-Dehydrogenative Thioarylation of Phenols and Indoles

8.1 Introduction

Carbon-sulfur bonds are essential structural features in natural products, pharmaceuticals and material science.[164] Consequently, methods for the construction of C–S bonds are of high importance.[165] Transition metal-catalyzed synthesis of diaryl sulfides has been widely reported.[166] However, high costs, toxicity and oxygen sensitivity limit the general applicability of transition metal-catalysts.[5, 167] Most importantly, thiophenols tend to poison metal-catalysts and are prompt to undergo oxidation.[168]
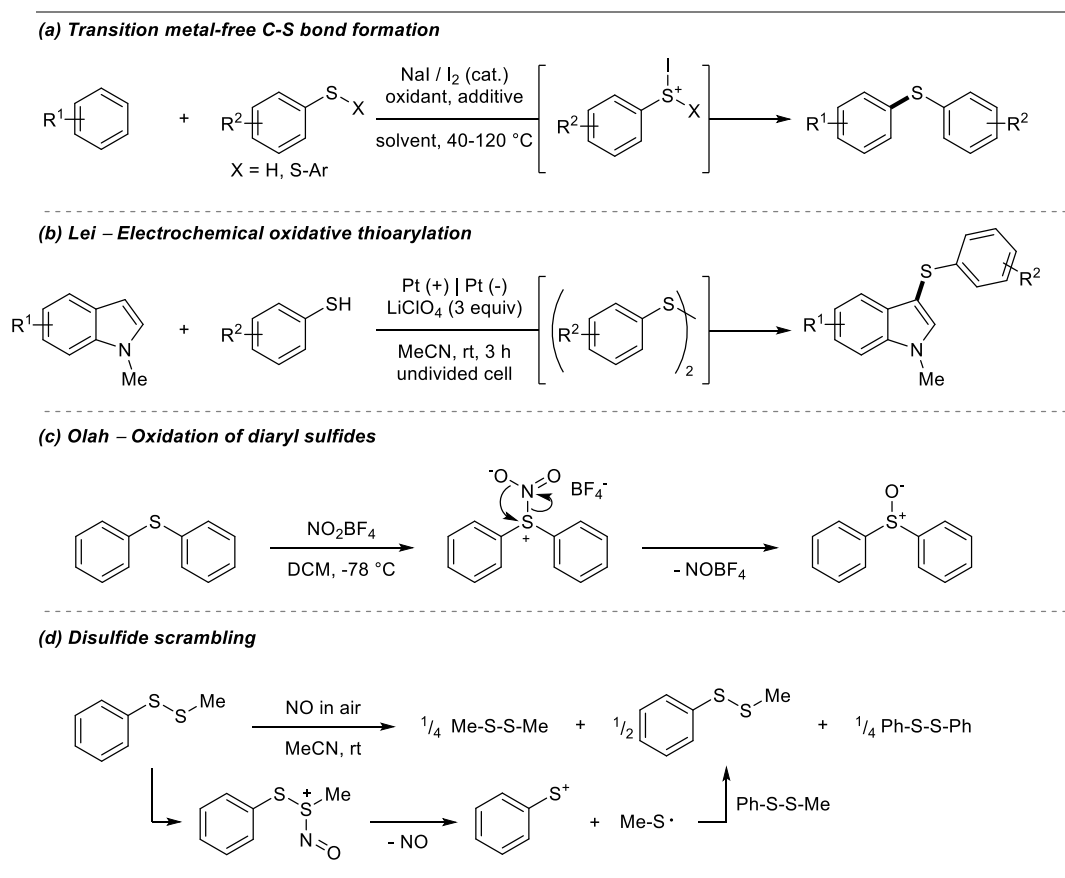
Figure 8.1 Transition metal-free synthesis and functionalization of aryl-thioethers and disulfides.

Towards general coupling conditions, transition metal-free approaches for C–S bond formation have been developed.[169] To overcome the requirement for pre-functionalized starting materials, cross-dehydrogenative coupling (CDC) under transition metal-free conditions has emerged as a green and sustainable alternative (Figure 8.1a).[71, 170] Typically, these reactions proceed in a Friedel-Crafts-type fashion. High temperatures, excess of oxidant and restriction to highly nucleophilic arenes are common drawbacks. Recently, Lei and co-workers have

reported an efficient and clean approach for the oxidative cross-dehydrogenative coupling of indoles and thiophenols under electrochemical reaction conditions (Figure 8.1b).[171] However, for this method LiClO$_4$ (4 equiv) is required as supporting electrolyte. Consequently, a catalytic and transition metal-free C–H/S–H bond cross-dehydrogenative coupling reaction at ambient temperature with reduced waste is still of significant interest.

The oxidation of diaryl sulfides with stoichiometric amounts of nitronium tetrafluoroborate is a well-known application (Figure 8.1c).[172] Gaseous nitrogen monoxide has been applied for the shuffling of disulfides, yielding an imperfect mixture of recombined products. The activation of disulfides results from the transient *S*-nitrosation, leading to a disulfide exchange reaction *via* a cationic or radical pathway (Figure 8.1d).[173] In fact, *S*-nitrosation is a dynamic and ubiquitous post-translational modification of all classes of proteins in living cells, which can promote or inhibit the formation of disulfides.[16, 174]

8.2 Motivation and aim of the project

As described in the previous chapters, the oxidative cleavage of weak heteroatom-hydrogen bonds serves as entry for radical cross-coupling reaction. Consequently, the possibility for a radical-radical recombination reaction of thiophenols with phenols for C–S bond formation was hypothesized. The dynamic behaviour of thiophenols in the presence of NO species supported the possibility for a radical-recombination pathway. However, the tendency of phenols to undergo homo-coupling and undesired *S*-oxidation had to be overcome.

8.3 Initial results and optimization

The coupling reaction of phenol **131a** and thiophenol **132a** was selected as model system for the systematic optimization (Table 8.1). Nitrosonium tetrafluoroborate was added in substoichiometric amounts to the reaction. A large number of available solvents were tested, but exclusively HFIP and TFA yielded the desired products. Cross-dehydrogenative coupling in HFIP yielded product **133a** in 44% yield (entry 1). The acidic character and the unique ability of HFIP to stabilize radical intermediates appeared to be crucial for the course of reaction.[175] Varying the counterion of the nitrosonium salt did not improve the reaction (entry 2-3). Surprisingly, nitronium tetrafluoroborate as catalyst yielded product **133a** in 76% yield (entry 4). Next, different concentrations were tested, but no improvement was found (entry 5-7). Loading of catalyst was found to be optimal by using 15 mol % of the nitronium salt to furnish **133a** in 91% yield (entry 8-11). Further, the ratio of phenol and thiophenol was varied, which was found to be already optimal (entry 12-15). HBF$_4$ was used to exclude a hidden

Brønsted-acid catalysis, but no conversion of starting materials was observed (entry 16). Next, the reaction was repeated in the dark, but **133a** was formed unaffectedly (entry 17). Finally, the reaction was also conducted at elevated temperatures, however no improvement was found (entry 18).

Table 8.1 Representative conditions of the optimization for the thioarylation of phenols.[a]
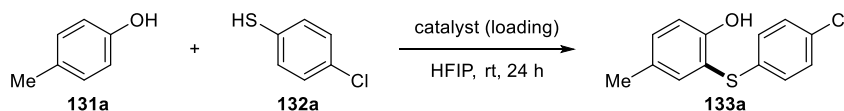
Entry	Catalyst (mol %)	131a : 132a	Conc. / M	Temp.	Yield / %[b]
1	NOBF$_4$ (10)	1 : 2	0.05	rt	44
2[c]	NOCl (10)	1 : 2	0.05	rt	20
3	NOPF$_6$ (10)	1 : 2	0.05	rt	43
4	NO$_2$BF$_4$ (10)	1 : 2	0.05	rt	76
5	NO$_2$BF$_4$ (10)	1 : 2	0.2	rt	16
6	NO$_2$BF$_4$ (10)	1 : 2	0.1	rt	36
7	NO$_2$BF$_4$ (10)	1 : 2	0.025	rt	Traces
8	NO$_2$BF$_4$ (2.5)	1 : 2	0.05	rt	Traces
9	NO$_2$BF$_4$ (5)	1 : 2	0.05	rt	48
10	**NO$_2$BF$_4$ (15)**	**1 : 2**	**0.05**	**rt**	**91**
11	NO$_2$BF$_4$ (20)	1 : 2	0.05	rt	88
12	NO$_2$BF$_4$ (10)	1 : 1	0.05	rt	52
13	NO$_2$BF$_4$ (10)	1 : 2.5	0.05	rt	84
14	NO$_2$BF$_4$ (10)	1 : 3	0.05	rt	Traces
15	NO$_2$BF$_4$ (10)	2 : 1	0.05	rt	68
16	HBF (15)	1 : 2	0.05	rt	-
17[d]	NO$_2$BF$_4$ (15)	1 : 2	0.05	rt	90
18	NO$_2$BF$_4$ (15)	1 : 2	0.05	50 °C	64

[a] Reaction conditions: **131a** (0.1 mmol, 1 equiv), **132a** (see table), solvent (see table), at the given temperature under air atmosphere. [b] Yields are given for isolated products after column chromatography. [c] NOCl was generated *in situ* using HNO$_3$ (65% in H$_2$O, 10 mol %) and HCl (37% in H$_2$O, 30 mol %). [d] Reaction performed in the dark.

8.4 Scope of the thioarylation of phenols

With the optimized conditions in hand, the scope for the cross-coupling of phenols and thiophenols was studied (Scheme 8.1). Initially, the reaction was scaled to 1 mmol, which did

not alter the outcome of the reaction. Products **133b-d** were isolated in good yields, bearing functional groups at the *para*-position of phenols. 2,4-Substituted phenols yielded products **133e-g** in good to excellent yield, covering electron-rich and sterically demanding functional groups.
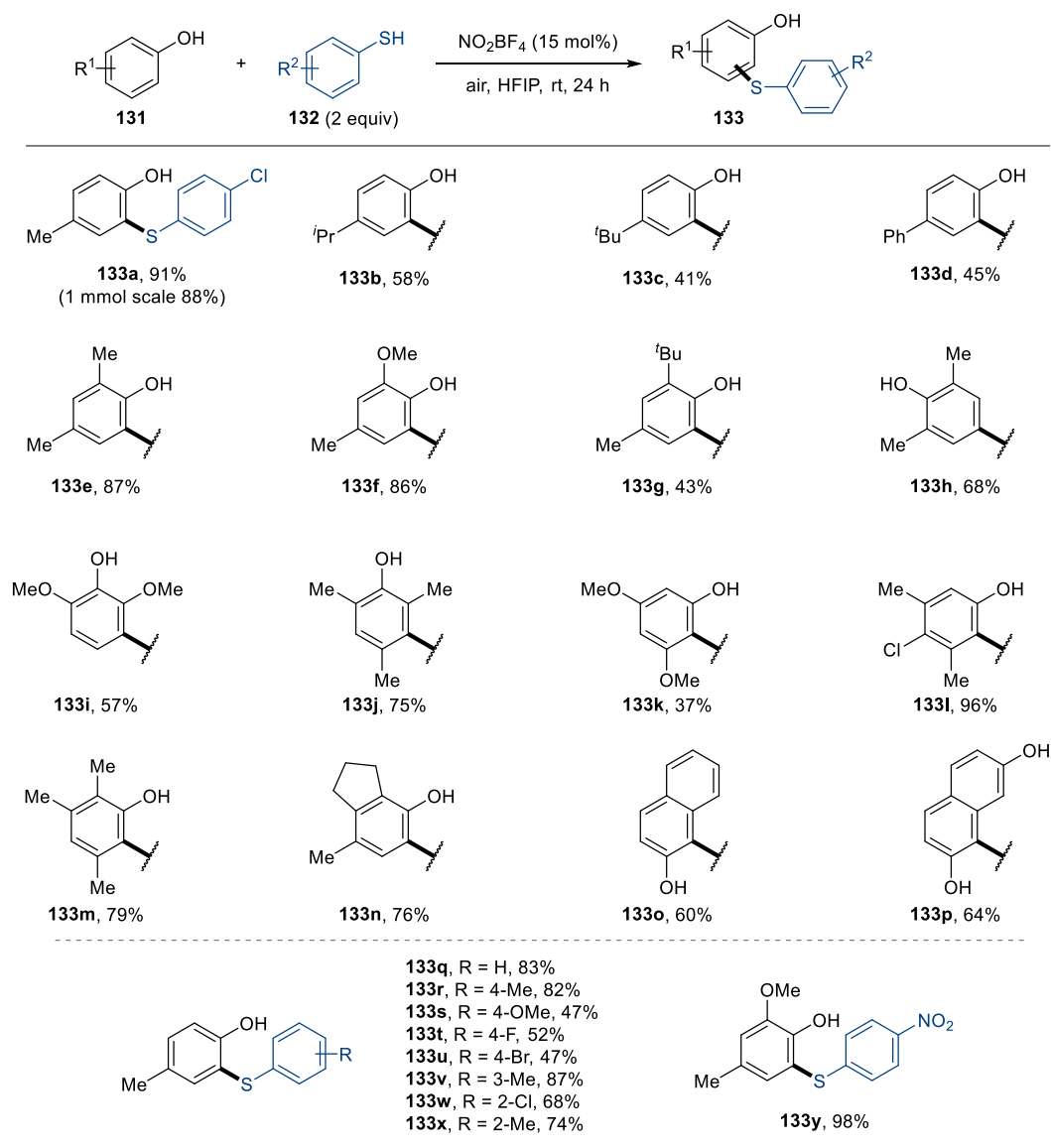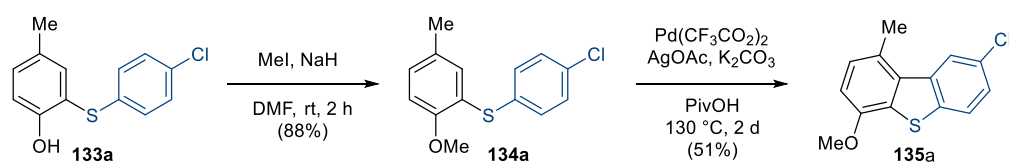
Scheme 8.1 Scope of the catalytic C–H bond thioarylation of phenols. Reaction conditions: **131** (0.1 mmol, 1 equiv), **132** (2 equiv), HFIP (0.05 M), at room temperature under air atmosphere. Yields are given for isolated products after column chromatography. [a] 1. **133a** (0.3 mmol, 1 equiv), MeI (1.5 equiv), NaH (1.2 equiv) in DMF (0.1 M) at room temperature; 2. **134a** (0.25 mmol, 1 equiv)(CF₃CO₂)₂Pd (20 mol %), AgOAc (5 equiv), K₂CO₃ (1.5 equiv) in PivOH (0.3 M) at 130 °C for 2 d.

Product **133h** demonstrates the possibility to functionalize the *para*-position of phenols. Interestingly, electron-rich product **133i** revealed coupling selectivity for the *meta*-position of the phenol. The same outcome was observed for product **133j** by blocking the *ortho-* and *para*-positions. Dearomatization and subsequent 1,4-addition appeared to be an alternative pathway. Further, **133k** was isolated in moderate yield, using a 3,5-substituted phenol.

Polysubstituted phenols allowed the isolation of products **133l-n** in 76-98% yield. Naphthol derivatives were compatible, giving access to product **133o** and **133p**. Next, substituted thiophenols were tested. Different functional groups on the *para*-position were tolerated, albeit in lower yields (**133q-u**). Alkyl or chloro substituents at the *ortho-* and *meta*-position gave products **133v-x** in good yields. Equipping the thiophenol with a nitro-group gave product **133y** in quantitative yield.

All products were formed as single regioisomers under the developed reaction conditions. Double thioarylation was not observed either. Usage of alkyl and benzyl thiols did not yield the desired products. Finally, to stress the utility of the obtained products, **133a** was transformed into polysubstituted benzothiophene **135a** by applying a dual C–H bond activation strategy.[176]

8.5   Scope of the thioarylation of indoles

The generality of the developed reaction conditions was further explored by studying the thioarylation of indoles (Scheme 8.2). Unprotected indoles gave notably better results than *N*-protected analogues. This result makes the reaction conditions more attractive for other applications.

The cross-coupling of indole **136a** and thiophenol **132a** yielded product **137a** in 77% yield. Scaling the reaction to 1 mmol gave **137a** unaffectedly. Functional groups with different electronic properties at the indole skeleton were well tolerated (**137b-f**). Further, thiophenols were systematically decorated with functional groups at the *para-* (**137h-j**), *ortho-* (**137k-l**) and *meta-* position (**137m**). Product **137n** was isolated in 51% yield bearing a naphthyl moiety. Additionally, a set of polysubstituted products was synthesized. Products **137o-s** were synthesized in good yields, including combinations of electron-rich and electron-deficient functional groups. Next, substituted pyrroles were employed under the developed reaction conditions. Product **137t** was isolated in 64% yield. 2-Substituted pyrrole yielded the double functionalized product **137v** in good yield. To further stress the applicability, **137l** was

transformed into the indole-fused benzothiophenes **138a** using a C–H bond activation methodology.[177] 3-Methyl indole and structurally related heterocycles did not afford the desired product under the developed reaction conditions.
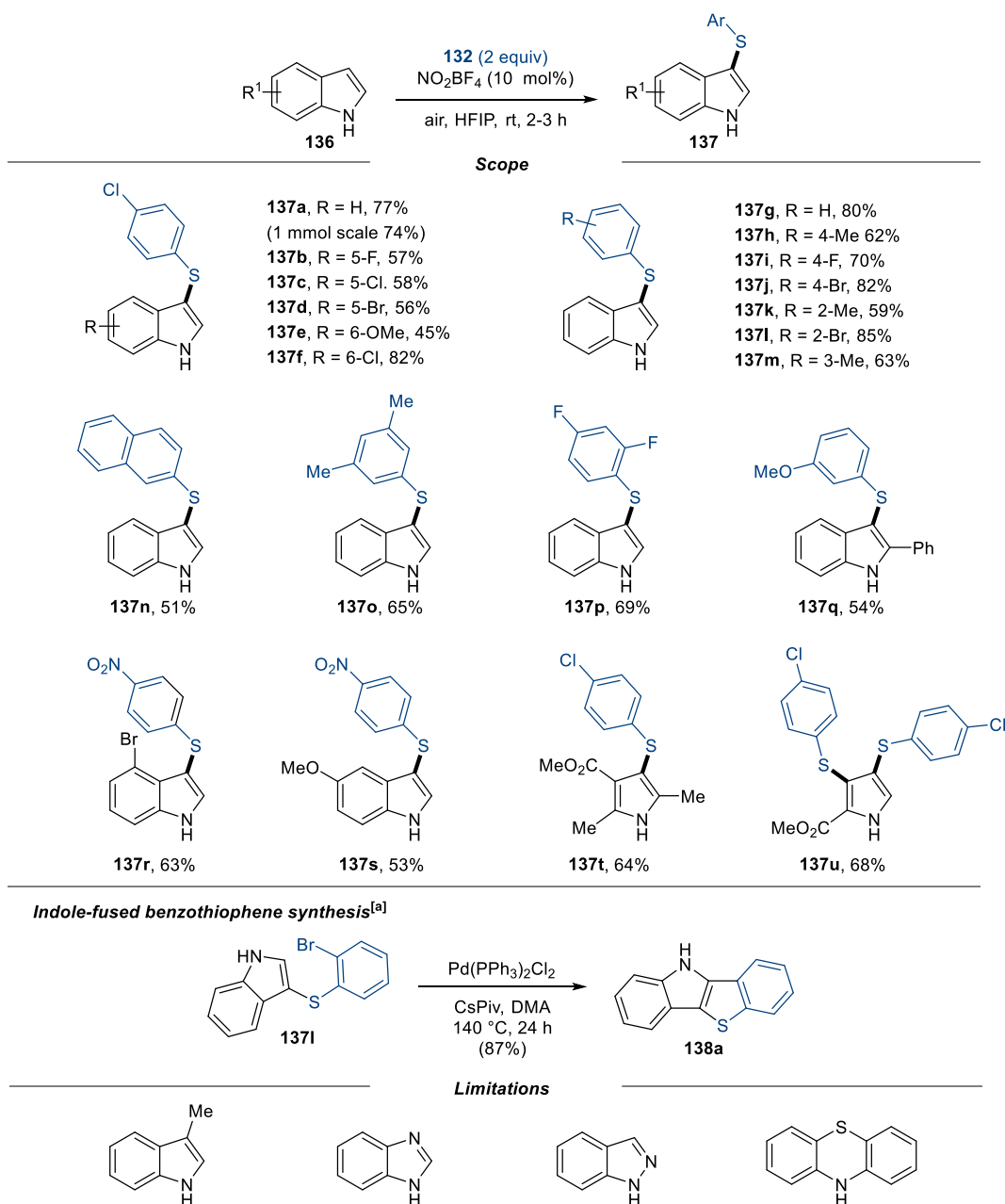
Scheme 8.2 Scope of the catalytic C–H bond thioarylation of indoles. Reaction conditions: **136** (0.1 mmol, 1 equiv), **137** (2 equiv), HFIP (0.05 M), at room temperature under air atmosphere. Yields are given for isolated products after column chromatography. [a] **137l** (0.08 mmol, 1 equiv), Pd(PPh$_3$)$_2$Cl$_2$ (5 mol%), CsPiv (2 equiv) in *N,N*-dimethylacetamide (0.1 M).

8.6   Mechanistic consideration

Next, control experiments were conducted in order to obtain a better understanding of the reaction mechanism (Figure 8.2). No product was formed in presence of the radical trap

butylated hydroxytoluene (BHT). Additionally, product formation was inhibited under inert gas atmosphere. Ambient oxygen was crucial to maintain the catalytic activity. The possibility for the oxidation of weak heteroatom–hydrogen bonds was studied through methylation of phenol **131a**. No conversion was observed under the optimized reaction conditions.
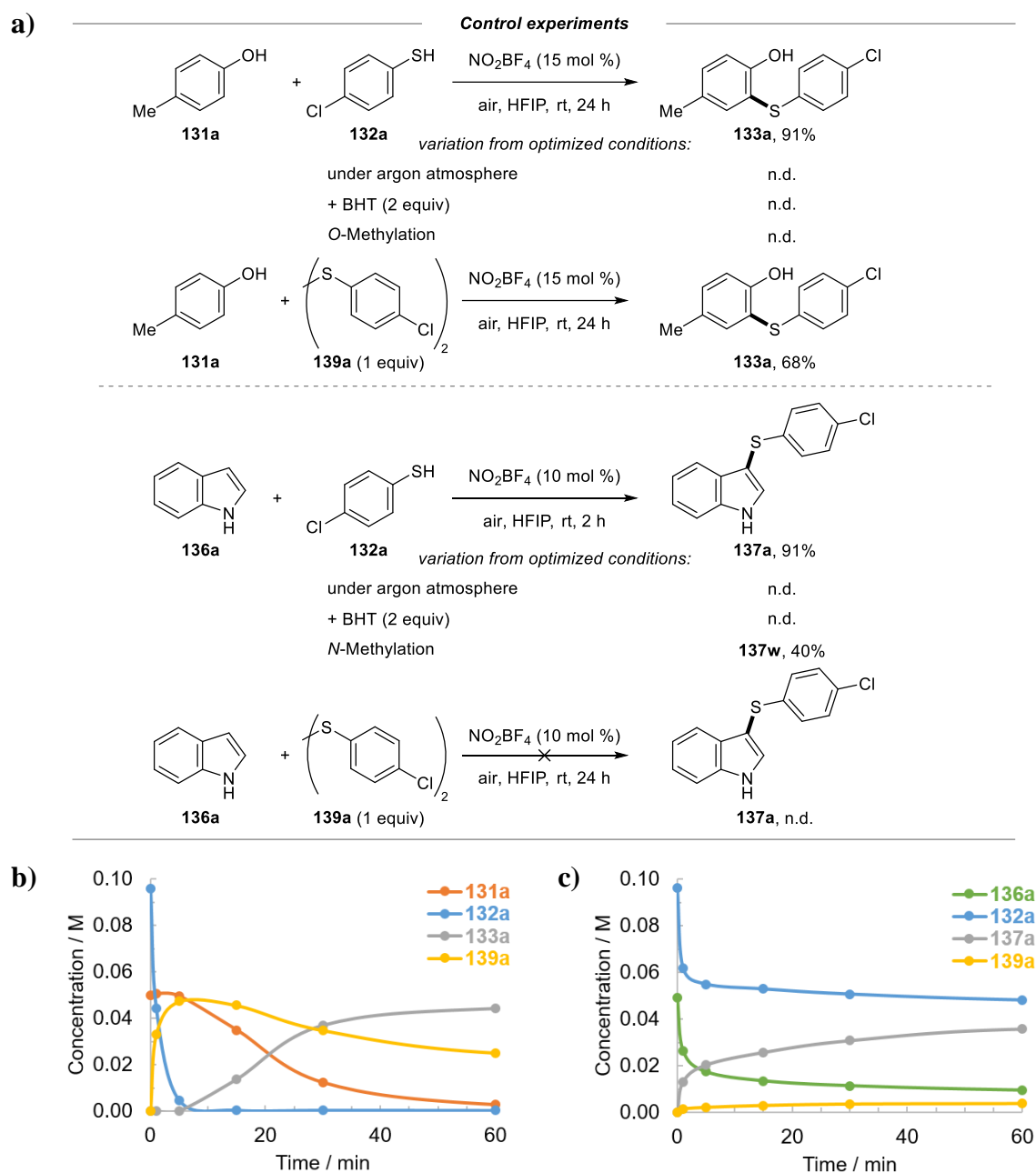
Figure 8.2 Mechanistic investigation and reaction profile. 1,3-Bis(trifluoromethyl)-5-bromobenzene was used as internal standard. a) Control experiments for the cross-coupling of thiophenols with phenols and indoles. b) GC-MS-FID time course of the cross-dehydrogenative coupling of phenol **131a** with thiophenol **132a**. c) GC-MS-FID time course of the cross-dehydrogenative coupling of indole **136a** with thiophenol **132a**.

Conducting the same control experiments with indole **136a** gave comparable results (Figure 8.2a). Thiophenol **132a** was oxidized quantitatively to disulfide **139a** in the presence of

nitronium tetrafluoroborate. Conversion to disulfide **139a** was tied to the presence of air and did not take place in the presence of radical trap BHT. The cross-coupling reaction of **131a** with disulfide **139a** yielded product **133a**, which indicates that disulfides are intermediates in the cross-coupling of phenols and thiophenols. In contrast, indole **136a** did not show any reactivity towards disulfide **139a** under the optimized reaction conditions. This difference in recombination selectivity is in good agreement with the obtained reaction profiles (Figure 8.2b,c). The reaction profile for the cross-coupling of phenol **131a** revealed that first the thiol **132a** is fully converted to the corresponding disulfide **139a**, before cross-coupling takes places (Figure 8.2b). In contrast, cross-coupling of indole **136a** showed that conversion of starting materials occurs synchronously and formation of the disulfide does not take place prior to the coupling step (Figure 8.2c).
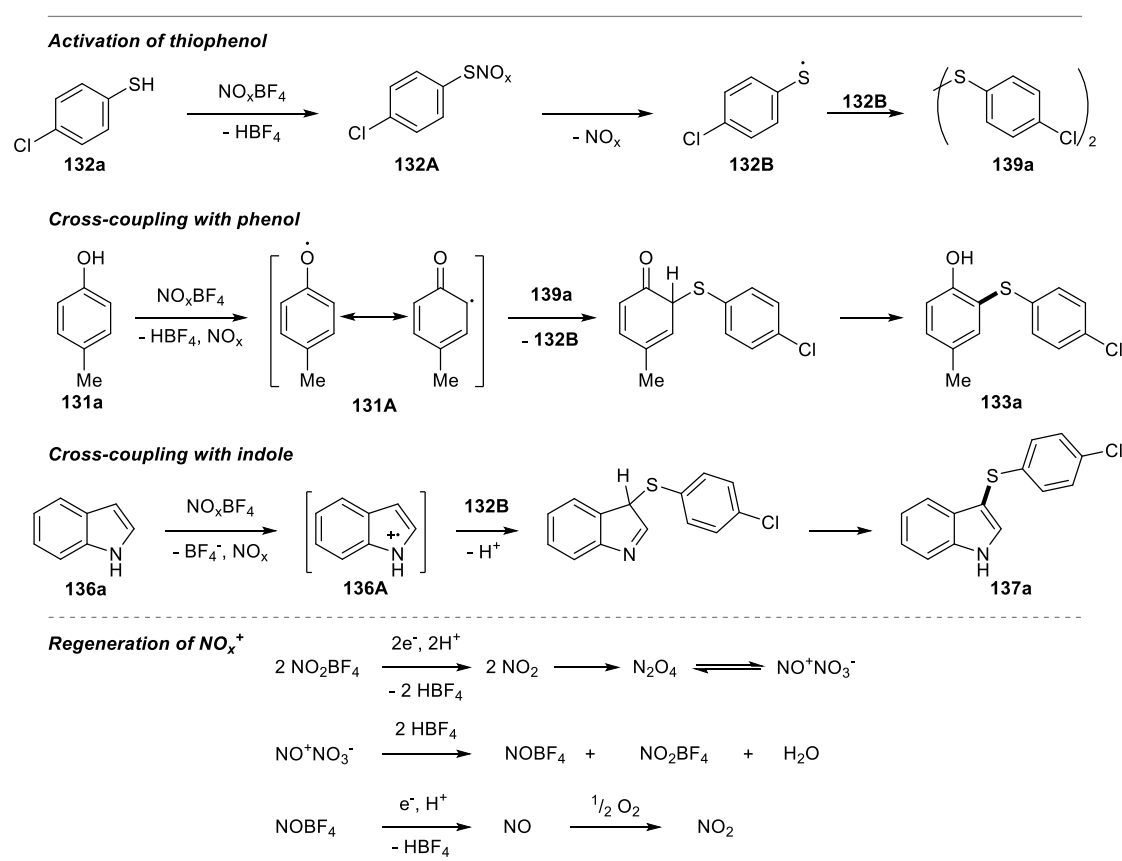
Figure 8.3 Proposed course of reaction for the C–H/S–H cross-dehydrogenative coupling of thiophenols with phenols and indoles.

Based on the control experiments, a mechanism for the dehydrogenative cross-coupling of phenol **131a** and indole **136a** with thiophenol **132a** was proposed (Figure 8.3). Initially, intermediate **132A** is formed by *S*-nitrosylation of **132a**.[173] Homolytic cleavage releases thiophenol radical **132B**, which forms disulfide **132a** by recombination with itself. Phenol **131a**

is oxidized to generate a phenoxy radical. Delocalization of the phenoxy radical and attack at the disulfide bond leads to release of radical **132B**. Rearomatization furnishes the cross-coupling product **133a**. Oxidation of indole **136a** gives intermediate **136A**, which undergoes recombination with **132B**. Oxidation of indole **136a** and thiophenol **132a** occurs synchronously, leading to the formation of **137a** before disulfide **139a** begins to form.

Initially, nitronium tetrafluoroborate oxidizes the starting materials to form nitrogen dioxide. Further, nitrogen dioxide dimerizes to form dinitrogen tetroxide, which undergoes disproportionation to nitrosonium nitrate.[73, 178] Water is released upon protonation by HBF_4 and nitrosonium and nitronium tetrafluoroborate are regenerated. Nitrosonium tetrafluoroborate is capable of oxidizing the substrates in the same way as the nitronium salt. Oxidation of substrates results in the formation of nitrogen monoxide, which is oxidized by ambient oxygen, before it rejoins the catalytic cycle.[77]

8.7 Conclusion

In summary, the first application of nitronium tetrafluoroborate as efficient and environmentally friendly catalyst for the cross-dehydrogenative coupling of phenols and indoles with thiophenols has been developed. The operationally simple protocol enables the efficient and catalytic C–S bond construction through C–H bond functionalization at room temperature. Ambient oxygen serves as stoichiometric oxidant and water is generated as by-product. A broad scope for (hetero)arenes and thiophenols was demonstrated in good yields and regioselectivities. The obtained products were transformed into complex benzothiophenes using C–H bond activation strategies. While phenols react selectively with formed disulfides, indoles react synchronously with thiophenols *via* a radical-radical recombination pathway.

Cross-Dehydrogenative Thioarylation of Phenols and Indoles |

Sustainable C–H Bond Amination of Phenols

(Parts of this chapter have already been published: <u>Luis Bering</u>, Laura D'Ottavio, Gierdre Sirvinskaite, and Andrey P. Antonchick, *submitted manuscript.*)

9 Sustainable C–H Bond Amination of Phenols

9.1 Introduction

The construction of C–N bonds is a fundamental challenge in organic synthesis, due to the importance of arylamines in natural products, pharmaceuticals and materials.[179] Traditionally, C–N bonds are installed by nucleophilic substitution, Ullmann–Goldberg condensations or by applying Buchwald-Hartwig conditions.[180] However, pre-functionalized starting materials, transition metal-catalysts and complex ligands are usually required.[181] Consequently, dehydrogenative C_{sp}^2–H/N–H cross-coupling represents an efficient and economical alternative.[182]
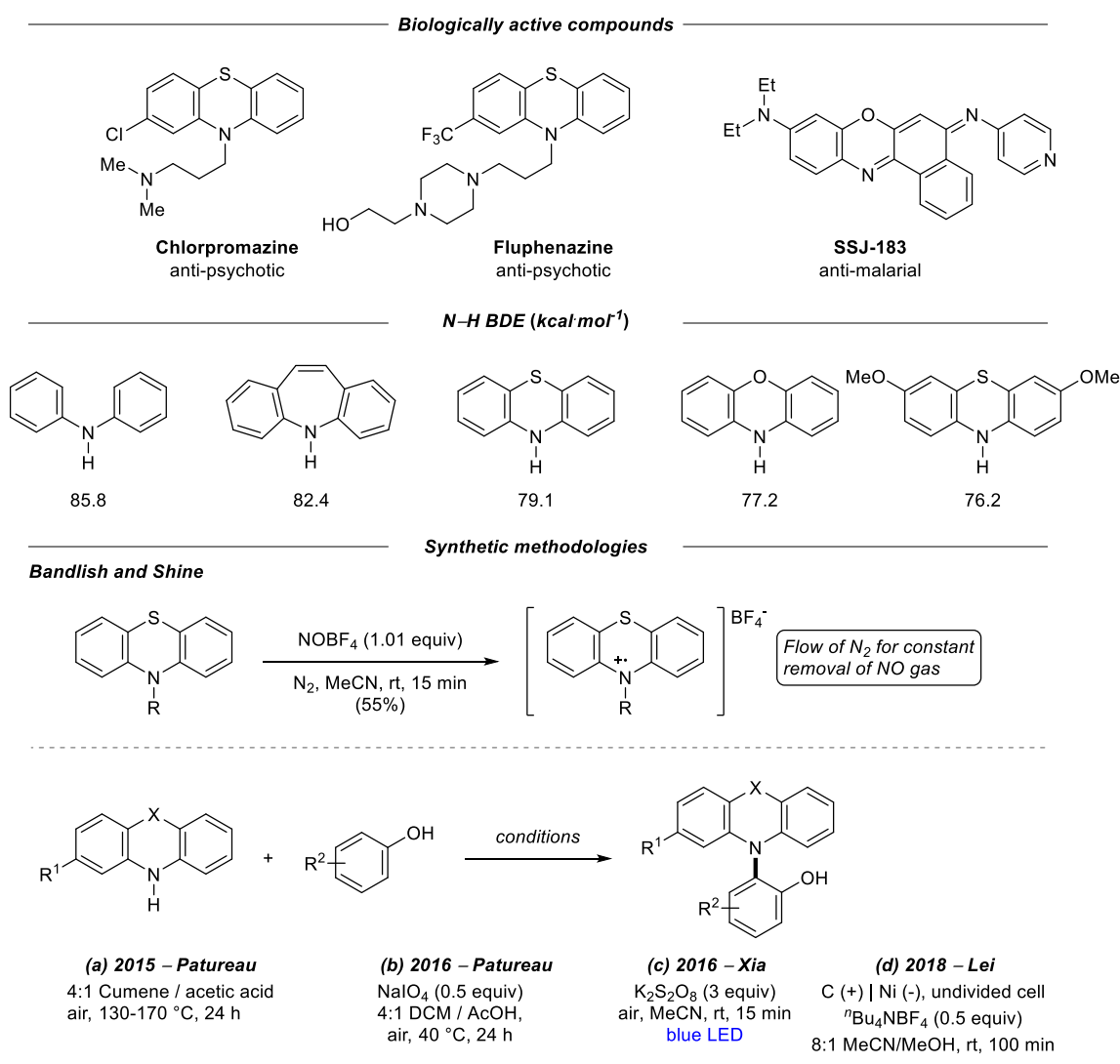
Figure 9.1 Biological relevance and synthetic strategies for the functionalization of phenothiazines and phenoxazines.

Phenothiazines and phenoxazines are compounds with diverse useful biological activities.[183] Consequently, phenothiazine derivatives can be found in the WHO list of essential medicines (Figure 9.1).[184] Phenoxazines are associated with useful biological activities as well.[185] Further, the applications as photocatalysts, electroluminescent organic semiconductors and solar cell materials have been reported.[186]

Recently, the employment of phenothiazines and phenoxazines in cross-dehydrogenative coupling has received much attention. The possibility of applying phenoxazines and phenothiazines in radical-cross-coupling methodology roots in the low N–H bond dissociation energy, which allows the generation of *N*-centred radicals by means of homolytic nitrogen-hydrogen bond breakage with mild oxidants (Figure 9.1).[187] Additionally, formed radicals are long-lived, which gives phenoxazines and phenothiazines a persistent radical character.[188] The ability to stabilize radical intermediates is tied to the presence of a bridging heteroatom, which drastically improves the stability of formed radical intermediates.[189] The bridging heteroatom between the two aryl units rigidifies the overall structure, whereby delocalization of the formed radical is improved. This property leads to less reactive and more stable *N*-centred radicals.

Already in 1976, Bandlish and Shine reported the synthesis and isolation of stable radical cations derived from heteroaromatic compounds (Figure 9.1).[73] By treating phenothiazines with nitrosonium tetrafluoroborate, the corresponding radical cationic salts were isolated. The reaction mixture was continuously degassed with a flow of nitrogen to remove formed nitrogen monoxide gas in order to avoid any undesired radical recombination. In 2015, Patureau's group reported the radical-coupling reaction of phenothiazines and phenoxazines with various phenols (Figure 9.1a).[190] This pioneer study represents a unique reagent-less transformation mediated by ambient oxygen. However, temperatures beyond 130 °C and long reaction times had to be applied in order to achieve efficient coupling. Later, the same group reported the coupling of phenothiazines with phenols using sodium periodate as oxidant (Figure 9.1b).[191] Albeit the reaction was conducted under milder conditions, undesired high molecular weight oxidants in stoichiometric amounts and halogenated solvents were used. In the same year, Xia and co-workers applied the usage of potassium peroxosulfate as mediator for the radical coupling of phenothiazines and phenols (Figure 9.1c).[192] Generation of peroxosulfate radicals as mediator for the coupling reaction was induced by irradiating the reaction with blue light. Recently, Lei's group reported to the cross-dehydrogenative C–N bond formation under oxidative electrochemical reaction conditions (Figure 9.1d).[193]

9.2 Motivation and aim of the project

The precedented literature for the cross-dehydrogenative coupling of phenothiazines and phenols suggested that coupling of phenothiazines and phenols is rather limited to the combination of starting materials, but not to the utilized oxidants. However, the reported methodologies do not fully address the principles of green and sustainable chemistry[12a], since high temperatures, toxic reagents and solvents or undesired electrolytes were required.

Consequently, it was hypothesized that nitrosonium ion catalysis might overcome current drawbacks for the cross-dehydrogenative coupling of phenothiazines and phenols. As demonstrated in the previous chapters, nitrosonium ion catalysis offers the striking advantage of producing water as the sole by-product. However, in order to develop a truly sustainable alternative to known methods, the usage of environmentally benign reagents and solvents was additionally considered during the systematic optimization of reaction conditions.

9.3 Initial results and optimization

The investigations were initiated by selecting the coupling reaction of phenothiazine **140a** and phenol **141a** as the model system (Table 9.1). Nitrosonium tetrafluoroborate was added in substoichiometric amounts to the reaction. Initially, a large number of available solvents in combination with different acids were tested, but exclusively the combination of DCM and acetic acid yielded the desired product.

Cross-dehydrogenative coupling in 4:1 DCM / AcOH yielded product **142a** in 52% yield (entry 1). Next, the solvent was varied by using polar, protic or aromatic solvents (entry 2-9). Delightfully, changing the solvent to toluene afforded **142a** in 63% yield (entry 4). Thereby, the use of undesired polychlorinated solvent was avoided. Further, different benzene-derived solvents were tested, but no improvement was found (entry 10-15). In order to further improve the reaction, different catalysts were tested (entry 16-18). Strikingly, sodium nitrite as source for nitrosonium ions afforded the desired cross-coupling product in 80% yield (entry 18). Sodium nitrite represents an environmentally friendly substitute for nitrosonium tetrafluoroborate, since the poly-fluorinated boronate counterion is excluded from the reaction. Next, different carboxylic acids were tested, whereby pivalic acid led to a slight increase in yield (entry 19-22). Additionally, the concentration, temperature, solvent / acid ratio and catalyst loading were systematically studied. However, no improvement was found. In summary, systematic optimization provided "green" and mild reaction conditions for the catalytic cross-dehydrogenative coupling of phenothiazines and phenols.

Table 9.1 Representative conditions of the systematic optimization for the catalytic C–H/N–H cross-dehydrogenative coupling of phenothiazines and phenols.[a]
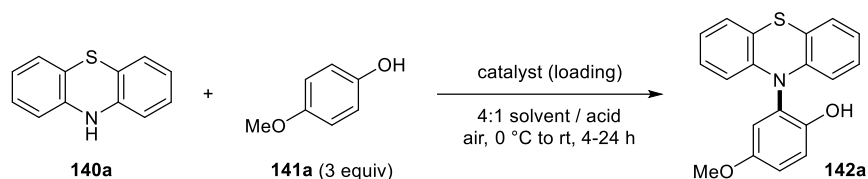
Entry	Solvent	Acid (20% v/v)	Catalyst (7.5 mol%)	Yield / %[b]
1	DCM	AcOH	$NOBF_4$	52
2	MeCN	AcOH	$NOBF_4$	54
3	MeOH	AcOH	$NOBF_4$	34
4	Toluene	AcOH	$NOBF_4$	63
5	THF	AcOH	$NOBF_4$	Traces
6	HIFP	AcOH	$NOBF_4$	10
7	DMSO	AcOH	$NOBF_4$	27
8	DMF	AcOH	$NOBF_4$	Traces
9	Benzene	AcOH	$NOBF_4$	Traces
10	Chlorobenzene	AcOH	$NOBF_4$	41
11	*p*-Xylene	AcOH	$NOBF_4$	37
12	Fluorobenzene	AcOH	$NOBF_4$	-
13	Nitrobenzene	AcOH	$NOBF_4$	30
14	Mesitylene	AcOH	$NOBF_4$	11
15	Cumene	AcOH	$NOBF_4$	Traces
16	Toluene	AcOH	NO_2BF_4	63
17[c]	Toluene	AcOH	NOCl	Traces
18	Toluene	AcOH	$NaNO_2$	80
19	Toluene	Formic acid	$NaNO_2$	Traces
20	**Toluene**	**PivOH**	**$NaNO_2$**	**82**
21	Toluene	Butyric acid	$NaNO_2$	56
22	Toluene	Optanoic acid	$NaNO_2$	47

[a] Reaction conditions: **140a** (0.2 mmol, 1 equiv), **141a** (3 equiv), 4:1 solvent / acid (0.05 M), 0 °C to room temperature under air atmosphere. [b] Yields are given for isolated products after column chromatography. [c] NOCl was generated *in situ* using HNO_3 (65% in H_2O, 10 mol %) and HCl (37% in H_2O, 30 mol %).

9.4 Scope of the C–H bond amination of phenols

With the optimized conditions in hand, the scope of the catalytic C–H bond amination of phenols was studied (Scheme 9.1). Initially, the cross-coupling of 4-methoxyphenol (**142a**) and different commercially available phenothiazines was studied. Products **142a-d** were isolated in good yields, revealing functional group tolerance for halogenated substituents and ketones.
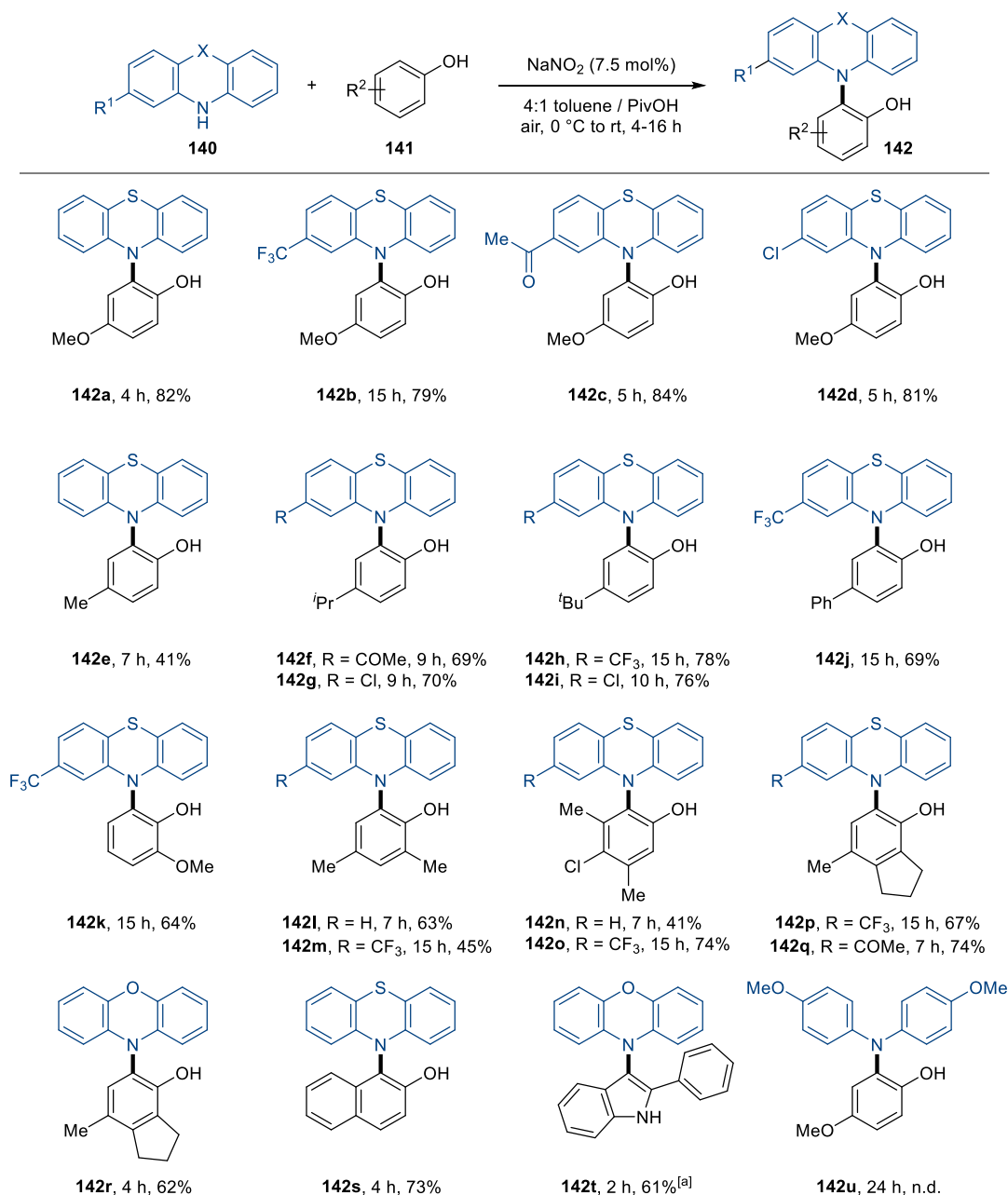
Scheme 9.1 Scope of the oxidative C–H bond amination. Reaction conditions: **140** (0.2 mmol, 1 equiv), **141** (3 equiv), 4:1 toluene / PivOH (0.05 M), 0 °C to room temperature under air atmosphere. Yields are given for isolated products after column chromatography. [a] NOBF$_4$ (0.02 mmol, 10 mol%) was used as catalyst.

Further, various phenols were tested in the coupling reaction. 4-Substituted phenols afforded the desired products in moderate to excellent yield, covering aliphatic, sterically demanding

and aromatic functional groups (**142e-j**). Strikingly, cross-coupling with differently substituted phenothiazines was achieved for several phenols as well. Interestingly, product **142k** was isolated in good yield as single regioisomer, without functionalization of the *para*-position.

Next, different poly-functionalized phenols were coupled with different phenothiazines. Products **142l-q** were isolated in moderate to good yields, demonstrating the possibility of synthesizing a large set of structurally diverse products. Phenoxazine proved to be compatible for the cross-coupling reaction as well (**142r**). 2-Naphthol yielded the desired product **142s** in 73% yield and short reaction time. Finally, the cross-coupling of 2-phenylindole and phenoxazine was also successfully performed. However, synthesis of **142t** worked superior if nitrosonium tetrafluoroborate was used as catalyst. Attempts for the synthesis of **142u** failed, presumably because of the increased N–H bond dissociation energy and the decreased ability to stabilize radical intermediates in the absence of a bridging heteroatom. Various attempts synthesizing and testing of different phenothiazines failed, due to their low stability and poor synthetic accessibility.

9.5 Mechanistic considerations

Next, control experiments were conducted in order to obtain better insights into the reaction mechanism (Figure 9.2). In analogy to the previously conducted studies, the product formation was inhibited when the reaction was conducted under inert gas atmosphere. Ambient oxygen was crucial to maintain the catalytic activity of nitrosonium ions. Further, product formation was fully suppressed in the presence of radical trap butylated hydroxytoluene (BHT). Unfortunately, the mass of a radical trapping adduct could not be identified by mass spectrometry. In order to study if the cross-coupling reaction of phenothiazine (**140a**) and 4-methoxyphenol (**141a**) is mediated by a homolytic heteroatom-hydrogen bond cleavage, both starting materials were functionalized by means of *N*- and *O*-methylation. No product formation was observed when the methylated analogues were used. This finding supports the assumption that the coupling reactivity is mediated by the low bond dissociation energy of both coupling partners. Finally, the reaction was repeated in the absence of sodium nitrite. As expected, no conversion of staring materials was observed.

Based on the conducted control experiments and in agreement with precedented literature a mechanism was proposed (Figure 9.2). Initially, sodium nitrite is converted to nitrosonium pivalate under the acidic reaction conditions. The nitrosonium ion is capable of oxidizing both starting materials *via* homolytic heteroatom-hydrogen bond cleavage in order to form radical

intermediates **140A** and **141A**. Delocalization of the phenoxy radical is followed by subsequent radical-radical recombination to form intermediate **141B**. The formed intermediate **141B** undergoes rearomatization to form product **142**.
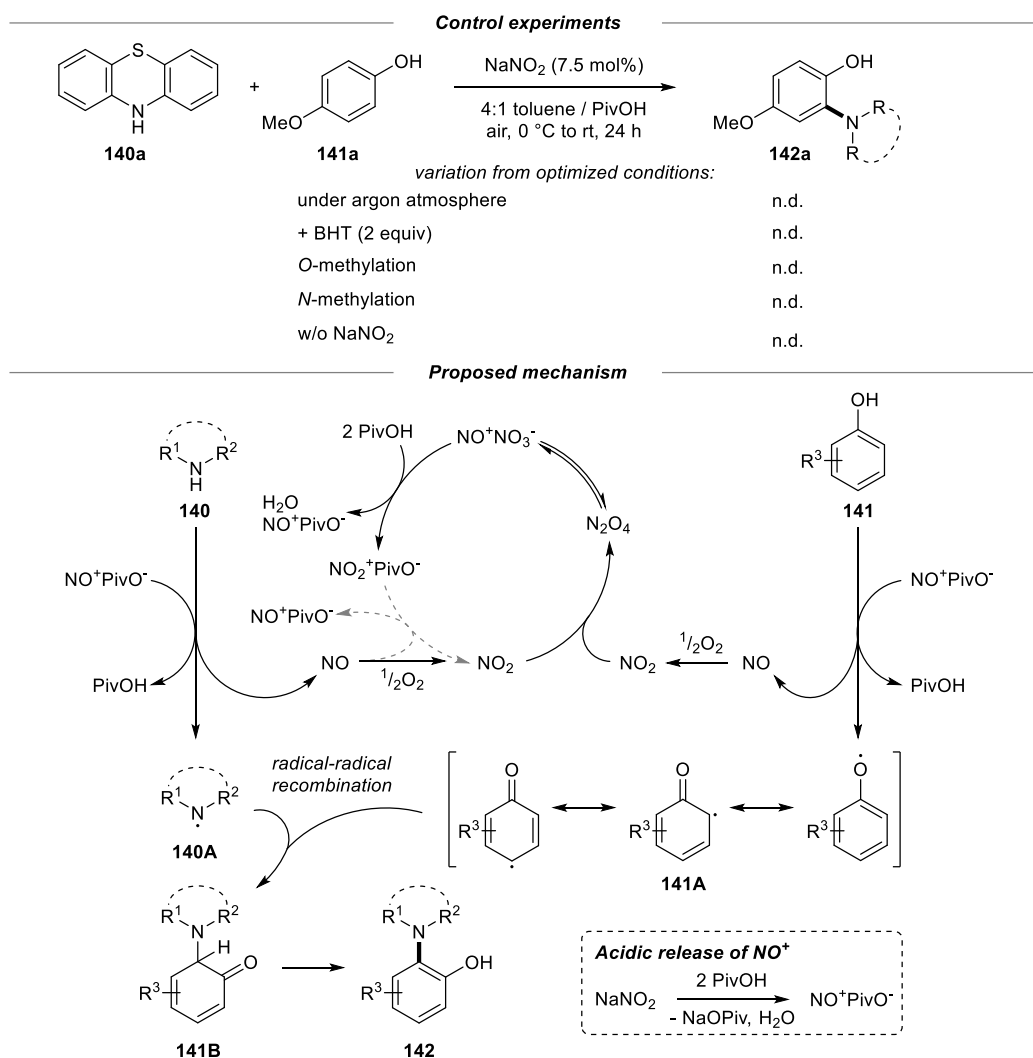
Figure 9.2 Control experiments and proposed mechanism for the C–H/N–H cross-dehydrogenative coupling of phenothiazines and phenols.

The regeneration of nitrosonium ions was assumed to work analogously to the previous developed transformation. Nitrogen monoxide is formed upon oxidation of the starting material and is subsequently oxidized by molecular oxygen to generate nitrogen dioxide. Nitrogen dioxide dimerizes to form dinitrogen tetroxide, which is in equilibrium with nitrosonium nitrate by means of disproportionation. Nitrosonium and nitronium ions are released under the acidic reaction conditions and water is generated as by-product. This step reflects the key step for the formation of the stoichiometric by-product. Finally, the nitronium ion is able to oxidize nitrogen monoxide instead of molecular oxygen to maintain the catalytic cycle.[77]

It should be noted that a radical-propagation step *via* radical transfer from **140A** to phenols **141** was proposed as an alternative pathway. However, the radical-radical recombination and regeneration of nitrosonium species would occur in the same manner.[188]

9.6 Conclusion

In summary, the cross-dehydrogenative coupling of phenothiazines and phenoxazines with phenols under environmentally friendly conditions has been developed. For the first time, nitrosonium nitrate was found as efficient and sustainable catalyst for the oxidative formation of C–N bonds *via* N–H/C–H bond cross-dehydrogenative coupling. A notable number of phenothiazines and phenols was successfully employed under the developed conditions, affording >20 examples. The developed reaction conditions can be considered as truly green and sustainable, since halogenated solvents and reagents were avoided under mild reaction conditions, while water was produced as the sole by-product.

Summary

10 Summary

The development of novel and efficient methodologies for the metal-free functionalization of inert and abundant C–H bonds offers unique advantages in terms of step- and atom economy under environmentally benign reaction conditions.[3] By considering additional aspects, such as safety of reagents, by-product formation, employed solvents and energy consumption, several aspects of green and sustainable chemistry can be addressed.[12a] Although toxic and cost intensive transition metal-catalysts are omitted, metal-free reactions face some particular challenges. Often stoichiometric amounts of high molecular weight oxidant are required, which leads to the undesired generation of harmful waste. Additionally, some organic oxidants are toxic, explosive or corrosive.[2] Consequently, transition metal-free and catalytic processes for the functionalization of C–H bonds, which employ ambient oxygen as terminal oxidant, while producing water as the stoichiometric by-product, present a drastic improvement compared to known methods. Molecular oxygen is considered as the ideal oxidant, due to its natural occurrence and safe properties.[121a] Towards this goal, different transition metal-free transformations for the functionalization of C_{sp}^2–H and C_{sp}^3–H bonds were developed. The studies were initiated by developing unprecedented methods for the transition metal-free functionalization of heteroarenes and simple alkanes. Afterwards, different applications of nitrosonium salts for the catalytic functionalization of (hetero)arenes were studied. By applying nitrosonium ion catalysis, carbon-carbon and carbon-heteroatom bond formation *via* C–H bond functionalization was successfully covered. Strikingly, the developed coupling conditions employed ambient oxygen as oxidant and water was produced as the stoichiometric by-product, leading to unprecedented transformations and affording environmentally benign alternatives to known transformations.

The cross-coupling of quinoline *N*-oxides (**77**) with boronic acids (**74**) was established under external oxidant-free conditions (Scheme 10.1). The developed methodology was based on a hypothesized analogy between Petasis-Borono-Mannich reaction and heterocyclic *N*-oxides. Quinoline *N*-oxides entail a coordination site for boronic acids and a strongly polarized carbon nitrogen-bond, comparable to an iminium ion. Coordination of the boronic acid induces an aryl migration *via* nucleophilic attack of the boronic acid at the C2-position of the quinoline. Rearomatization under elimination of boric acid affords the functionalized quinoline in a regioselective fashion. According to the reaction proposal, various quinoline *N*-oxides were successfully coupled with nucleophilic boronic acids under the optimized reaction conditions.
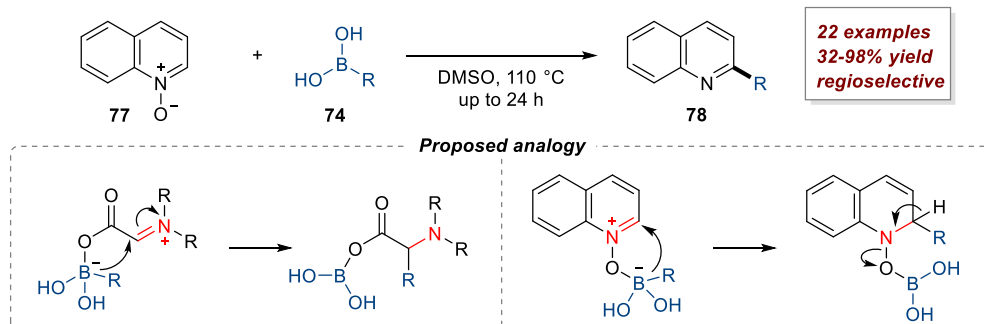
Scheme 10.1 Regioselective cross-coupling of quinoline *N*-oxides with boronic acids.

Next, the *vicinal* dioxygenation of simple alkanes (**84**) was established under transition metal-free conditions (Scheme 10.2). In this reaction, radical iodination serves as transient modification for the functionalization of alkanes. In order to achieve this transformation an unprecedented system for radical iodination of alkanes under mild reaction conditions was established. Further, the conversion of iodoalkanes (**85**) into mono-protected diols (**86**) was discovered. By combining both reactions, alkanes were successfully converted into the desired products in a one-pot reaction. Subsequent hydrolysis afforded the *vicinal* diols in good yield and selectivity. The reaction conditions were successfully applied to the functionalization of different cyclic, linear, and branched saturated hydrocarbons.
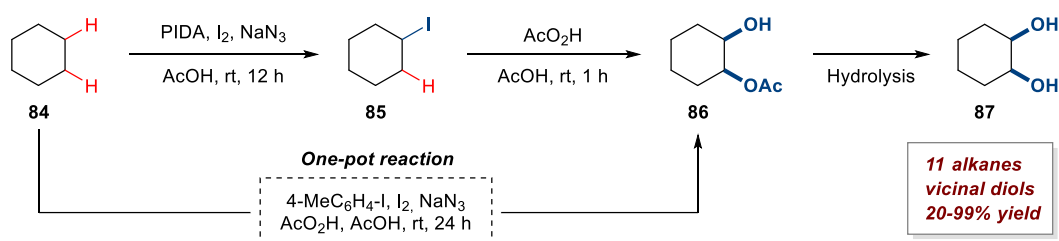
Scheme 10.2 *Vicinal* dioxygenation of saturated hydrocarbons using hypervalent iodine(III) reagents.

The utilization of nitrosonium salts as catalysts for non-directed oxidative coupling of arenes remained almost untouched within the past decade. Guided by the oxidation potential of substrates, the oxidative coupling of arylated benzofurans and structurally related heterocycles was studied (Scheme 10.3). A large number of 2-arylated benzofurans and benzothiophenes (**117**) was successfully converted into the corresponding 3,3'-dimers (**118**) in high yields and short reaction times. Additionally, 3-arylated indoles (**119**) underwent the dimerization process smoothly, giving access to biological active dimeric compounds (**120**). Mechanistic studies support the assumption that ambient oxygen serves as terminal oxidant and water is produced as the stoichiometric by-product.
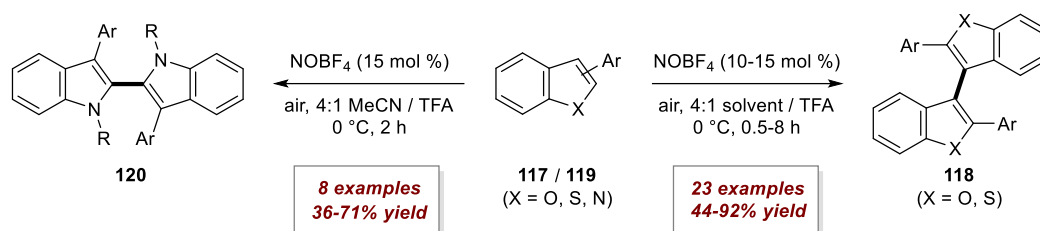
Scheme 10.3 Oxidative coupling of arylated heteroarenes using ambient oxygen as terminal oxidant.

In order to achieve intramolecular cross-coupling of arenes, benzyl aryl ethers (**126**) were treated with substoichiometric amounts of nitrosonium salts. While no intramolecular ring closure was detected, the formation of benzylated phenols (**127**) occurred in the presence of nitrosonium salts *via* an intramolecular rearrangement (Scheme 10.4). Under the optimized reaction conditions, various benzyl aryl ethers were converted into benzylated phenols in good yields and short reaction times. The discovered transformation served as template for the development of an intermolecular benzylation reaction of nucleophilic arenes. Under adjusted reaction conditions, benzyl alcohols (**128**) were employed as reagents for C–H bond benzylation of arenes producing water as the by-product. Mechanistic studies support the role of nitrosonium ions as Lewis-acid catalysts
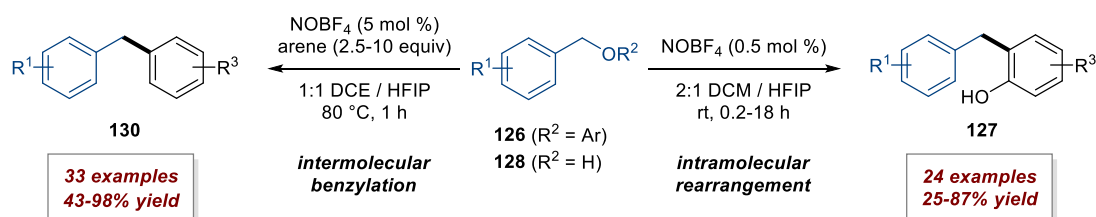
Scheme 10.4 Nitrosonium salts as Lewis-acid catalyst: Intra- and intermolecular benzylation of arenes.

Phenols were employed as substrates for oxidative homo- and cross-coupling based on the correlation between the oxidation potential and the heteroatom-hydrogen bond dissociation energy (Scheme 10.5). Nitrosonium salts proved to be capable to catalyze the phenol-phenol (**122a-j**) and phenol-arene (**122k-j**) coupling under aerobic reaction conditions. Further, also protected anilines (**124**) underwent the homo-coupling, catalyzed by nitrosonium tetrafluoroborate. The coupling of protected anilines revealed a significant difference in reactivity relative to phenols, which lead the unprecedented phenol-anilide (**125k-n**) cross-coupling. Mechanistic studies suggested that the coupling reaction is initiated by homolytic cleavage of the O–H or N–H bond respectively.

Since thiophenols represent a third class of aromatic compounds entailing weak heteroatom-hydrogen bonds, the C–H/S–H cross-coupling for the synthesis of **133** was studied (Scheme

10.5). The developed reaction conditions were also applied for the cross-coupling of indoles (**136**) and thiophenols (**132**) under mild conditions. All developed transformations shared the same feature of employing ambient oxygen as the oxidant in order to maintain the catalytic activity of nitrosonium and nitronium salts.
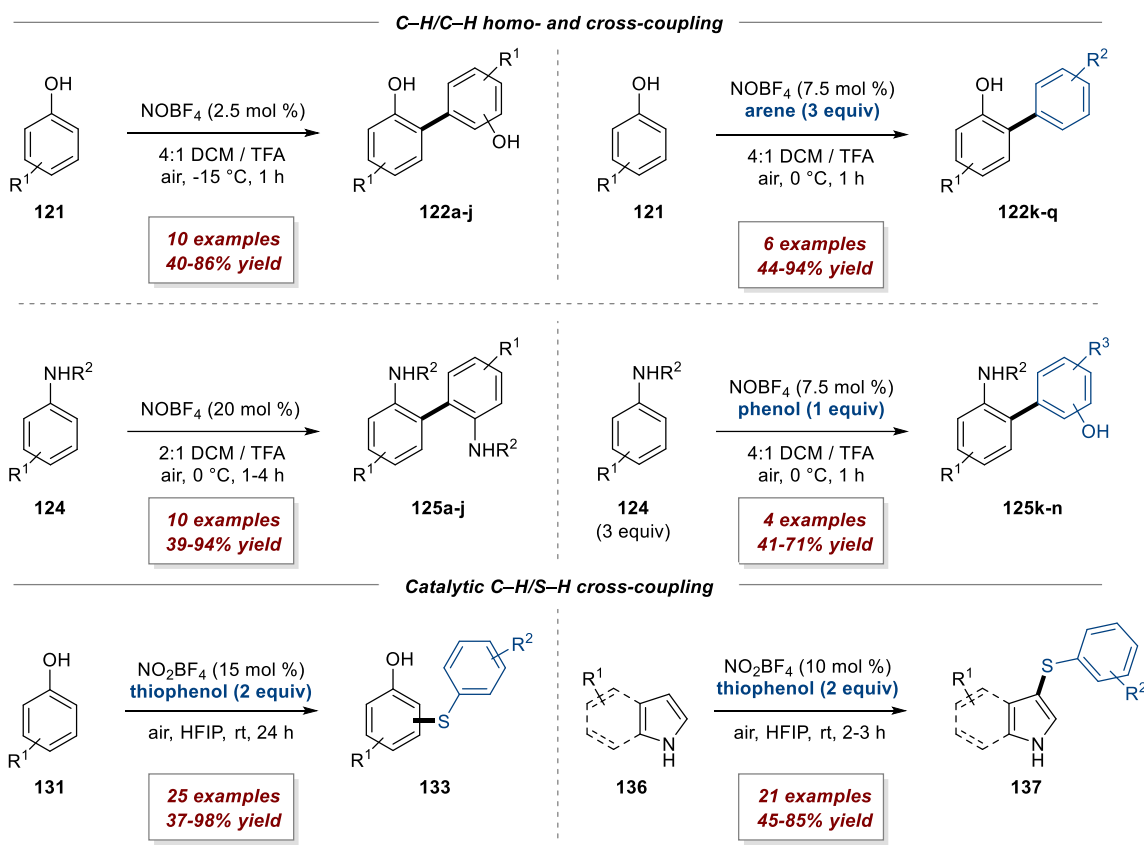
Scheme 10.5 Nitrosonium salts as efficient catalyst for C–H/C–H and C–H/S–H cross-coupling reactions.

Finally, the C–H bond amination of phenols was studied. Sodium nitrite served as source for nitrosonium ions under the acidic reaction conditions (Scheme 10.6). The optimized reaction conditions omitted the use of halogenated solvents and reagents. Thereby, the C–H/N–H cross-coupling for the synthesis of **142** was achieved under mild and environmentally benign reaction conditions, meeting the criteria for green and sustainable chemistry.
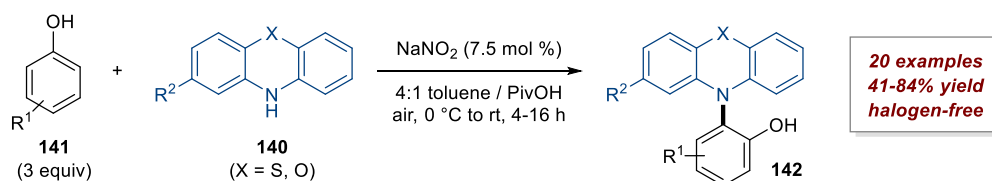
Scheme 10.6 Sustainable C–H/N–H cross-coupling for the C–H bond amination of phenols.

Experimental

11 Experimental

11.1 General

Reagents and solvents

Commercially available chemicals were purchased from *Sigma-Aldrich*, *Acros Organics*, *Alfa Aesar*, *VWR Germany*, *ABCR* or *TCI Germany*. Unless otherwise noted, all commercially available compounds and solvents were used as provided without any further purification. Dry dichloromethane was purified by the solvent purification system *M-BRAUN SPS-800*. Solvents for chromatography were laboratory grade. Nitrosonium tetrafluoroborate was purchased from *VWR Germany* with a claimed purity of 98%. Nitronium tetrafluoroborate was purchased from *VWR Germany* with a claimed purity of 95%.

Chromatography

Analytical thin-layer chromatography (TLC) was performed on Merck silica gel aluminium plates with F-254 indicator, visualized by irradiation with UV light (254 nm) and staining with $KMnO_4$-solution (1.5 g $KMnO_4$, 10 g K_2CO_3, 1.25 mL 10% NaOH in 150 mL H_2O) or staining with *para*-anisaldehyde staining solution (5 mL glacial sulfuric acid, 1.5 mL glacial acetic acid and 3.7 mL *para*-anisaldehyde in 135 mL absolute EtOH).

Column chromatography was performed using silica gel Merck 60 (particle size 0.040-0.063 mm). Solvent mixtures are understood as volume/volume.

Mass spectrometry

Low resolution mass spectra (MS-EI, 70 eV) were collected using an *Agilent Technologies 7890A GC-System* (column: HP-5MS, 30 m × 0.250 mm × 0.25 μm) equipped with an *Agilent Technologies 5975C inert XL MSD with Triple-Axis Detector*.

Low resolution mass spectra (MS-ESI) were collected using a *Waters Corp. LC-MS system* (column: LC revers phase CC Nucleodur C4 Gravity, 5 µm from Macherey-Nagel) equipped with an *UV-Waters 2487 Dual Absorbance Detector* and *Waters Micromass ZQ 2000 ESCI+ Multi-Mode-Ionisation MS-Detector*.

High resolution mass spectra were recorded on a *LTQ Orbitrap* mass spectrometer coupled to an *Accela HPLC System* (HPLC column: Hypersyl GOLD, 50 mm × 1 mm, 1.9 μm).

Nuclear magnetic resonance spectroscopy (NMR)

^{1}H-NMR and ^{13}C-NMR were recorded on *Bruker DRX400* (400 MHz), *DRX500* (500MHz), *DRX600* (600MHz) and *DRX700* (700 MHZ) spectrometers in CD_2Cl_2, $CDCl_3$, Aceton-d_6 or DMSO-d_6. Data are reported in the following order: chemical shift (δ) in ppm; multiplicities are indicated s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet); coupling constants (*J*) are given in Hertz (Hz).

Fourier transform infrared spectroscopy

Fourier transform infrared spectroscopy (FT-IR) spectra were obtained with a *Bruker Tensor 27* spectrometer (ATR, neat) and are reported in terms of frequency of absorption (cm^{-1}).

Optical rotations

Optical rotation [α] was measured in a *Schmidt + Haensch Polartronic HH8* polarimeter in cuvettes with a path length of 10 cm at ambient temperature. The concentration is given as g/100 mL

Elemental analysis

Elemental analysis was conducted on a *Leco* elemental analysis instrument (*Leco CHNS–932 and O–Analysator VTF–900*).

11.2 Experimental part for the cross-coupling of quinoline *N*-oxides with boronic acids

11.2.1 General procedures

General procedure A: Synthesis of quinoline *N*-oxides
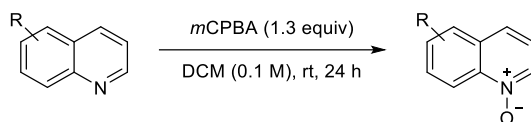
To a solution of quinoline (1 equiv) in DCM (10 mL/mmol) *meta*-chloroperbenzoic acid (1.3 equiv) was added and the reaction was stirred for 24 h at room temperature.[95] The residual *m*CPBA was removed by adding 1 M KOH solution. The aqueous phase was extracted three times with dichloromethane and the combined organic layers were dried over $MgSO_4$. Column chromatography provided the pure product (eluent: ethyl acetate / methanol).

General procedure B: Cross-coupling of quinoline *N*-oxides with boronic acids
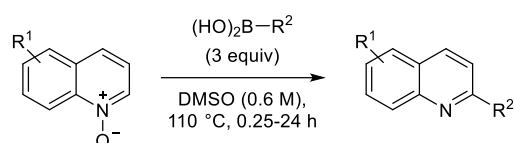
To a solution of quinoline *N*-oxides (0.2-0.3 mmol, 1 equiv) in DMSO (0.6 M) boronic acid was added (3 equiv) and the reaction was stirred at 110 °C for the indicated time (Scheme 3.1). Afterwards the reaction was cooled to room temperature and diluted with dichloromethane. Column chromatography provided pure product (eluent: Petroleum ether / ethyl acetate).

11.2.2 Physical data of starting materials
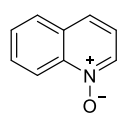
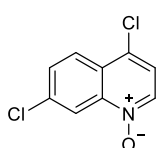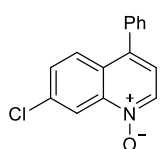**Quinoline 1-oxide (77a).** Prepared according to the general procedure A using quinoline (1.81 mL, 15 mmol, 1 equiv) and *meta*-chloroperbenzoic acid (77%, 4.42 g, 19.5 mmol, 1.3 equiv) in DCM (20 mL); the product was obtained as a pale yellow solid (1.58 g, 10.8 mmol, 72%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.74 (d, *J* = 8.8 Hz, 1H), 8.67 (d, *J* = 6.0 Hz, 1H), 7.90 (d, *J* = 8.2 Hz, 1H), 7.86 (d, *J* = 8.4 Hz, 1H), 7.84 – 7.78 (m, 1H), 7.72 – 7.65 (m, 1H), 7.36 ppm (dd, *J* = 8.4, 6.0 Hz, 1H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 141.20, 136.41, 131.20, 130.66, 129.19, 128.33, 128.01, 121.07, 119.81 ppm.
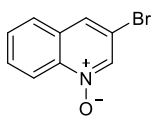
**3-Bromoquinoline 1-oxide (77b).** Prepared according to the general procedure A using 3-bromoquinoline (130 µL, 1 mmol, 1 equiv) and *meta*-chloroperbenz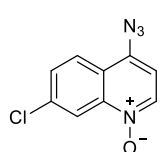oic acid (77%, 291 mg, 1.3 mmol, 1.3 equiv); the product was obtained as a pale white solid (155 mg, 0.69 mmol, 72%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.67 (dd, *J* = 4.8, 3.3 Hz, 2H), 7.93 (s, 1H), 7.85 – 7.73 (m, 2H), 7.72 – 7.63 ppm (m, 1H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 140.23, 137.77, 131.15, 130.42, 130.19, 129.36, 127.52, 119.93, 114.46 ppm.
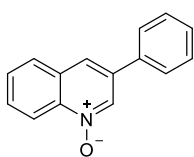
3-Phenylquinoline 1-oxide (77c). Conducted according to a literature procedure.[194] Prepared according to the general procedure A using 3-phenylquinoline (205 mg, 1 mmol, 1 equiv) and *meta*-chloroperbenzoic acid (77%, 291 mg, 1.3 mmol, 1.3 equiv); The product was obtained as a white solid (190 mg, 0.86 mmol, 86%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.90 (d, *J* = 1.1 Hz, 1H), 8.73 (d, *J* = 8.7 Hz, 1H), 8.00 – 7.87 (m, 2H), 7.81 – 7.71 (m, 1H), 7.70 – 7.60 (m, 3H), 7.51 (d, *J* = 7.4 Hz, 2H), 7.49 – 7.42 ppm (m, 1H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 140.13, 135.82, 135.44, 135.07, 130.57, 130.41, 129.52, 129.34, 129.17, 128.49, 127.19, 124.48, 119.74 ppm.
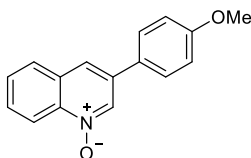
3-(4-Methoxyphenyl)quinoline 1-oxide (77d). Conducted according to a literature procedure.[194] Prepared according to the general procedure A using 3-(4-Methoxyphenyl)quinoline (235 mg, 1 mmol, 1 equiv) and *meta*-chloroperbenzoic acid (77%, 291 mg, 1.3 mmol, 1.3 equiv); the product was obtained as a white solid (163 mg, 0.65 mmol, 65%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.90 (s, 1H), 8.71 (d, *J* = 8.9 Hz, 1H), 7.90 (d, *J* = 8.9 Hz, 2H), 7.74 (d, *J* = 7.5 Hz, 1H), 7.66 (d, *J* = 7.5 Hz, 1H), 7.59 (d, *J* = 8.7 Hz, 2H), 7.03 (d, *J* = 8.7 Hz, 2H), 3.86 ppm (s, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 160.63, 139.66, 135.50, 134.70, 131.01, 130.73, 130.40, 129.33, 128.37, 128.03, 124.19, 119.66, 115.03, 114.30, 55.57 ppm.
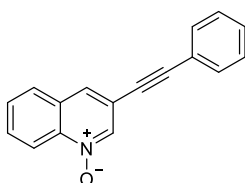
3-(Phenylethynyl)quinoline 1-oxide (77e). Conducted according to a literature procedure.[195] Prepared according to the general procedure A using 3-(Phenylethynyl)quinoline (254 mg, 1 mmol, 1 equiv) and *meta*-chloroperbenzoic acid (77%, 291 mg, 1.3 mmol, 1.3 equiv); the product was obtained as a white solid (218 mg, 0.89 mmol, 89%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.76 – 8.67 (m, 2H), 7.98 (d, *J* = 14.2 Hz, 1H), 7.85 (t, *J* = 10.3 Hz, 1H), 7.81 – 7.76 (m, 1H), 7.68 (d, *J* = 7.5 Hz, 1H), 7.60 – 7.53 (m, 2H), 7.45 – 7.34 ppm (m, 3H). **^{13}C NMR** (126 MHz,

CDCl$_3$) δ 140.73, 140.56, 137.73, 132.10, 132.00, 131.47, 129.96, 129.74, 129.52, 128.69, 128.25, 121.85, 119.84, 118.11, 93.96, 84.16 ppm.
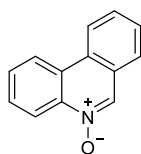
Phenanthridine 5-oxide (77f). Prepared according to the general procedure A using phenanthridine (179 mg, 1 mmol, 1 equiv) and *meta*-chloroperbenzoic acid (77%, 291 mg, 1.3 mmol, 1.3 equiv); the product was obtained as a white solid (173 mg, 0.89 mmol, 89%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 9.02 (s, 1H), 8.95 – 8.86 (m, 1H), 8.58 (dd, J = 6.8, 2.5 Hz, 1H), 8.51 (d, J = 8.2 Hz, 1H), 7.83 (dd, J = 7.2, 4.1 Hz, 3H), 7.80 – 7.74 (m, 1H), 7.72 – 7.64 ppm (m, 1H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 138.88, 135.69, 130.32, 129.95, 129.65, 129.15, 127.49, 126.80, 126.73, 126.44, 122.93, 122.27, 120.71 ppm.
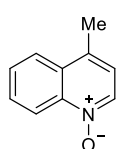
4-Methylquinoline 1-oxide (77g). Prepared according to the general procedure A using 4-methylquinoline (132 µL, 1 mmol, 1 equiv) and *meta*-chloroperbenzoic acid (77%, 291 mg, 1.3 mmol, 1.3 equiv); the product was obtained as a white solid (64 mg, 0.4 mmol, 40%). **^{1}H NMR** (500 MHz, CDCl3) δ 8.81 (d, J = 8.7 Hz, 1H), 8.51 (d, J = 6.1 Hz, 1H), 7.99 (d, J = 8.7 Hz, 1H), 7.86 - 7.74 (m, 1H), 7.76 - 7.64 (m, 1H), 7.16 (d, J = 6.1 Hz, 1H), 2.69 ppm (s, 3H). **^{13}C NMR** (126 MHz, CDCl3) δ 140.90, 135.93, 135.49, 130.55, 130.02, 128.78, 124.90, 121.58, 120.48, 18.58.
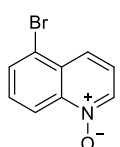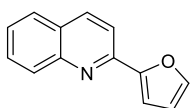
5-Bromoquinoline 1-oxide (77h). Prepared according to the general procedure A using 5-bromoquinoline (208 mg, 1 mmol, 1 equiv) and *meta*-chloroperbenzoic acid (77%, 291 mg, 1.3 mmol, 1.3 equiv); the product was obtained as a pale orange solid (211 mg, 0.94 mmol, 94%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.80 - 8.70 (m, 2H), 8.25 (d, J = 8.8 Hz, 1H), 7.97 (dd, J = 7.5, 0.9 Hz, 1H), 7.66 (dd, J = 8.8, 7.5 Hz, 1H), 7.48 ppm (dd, J = 8.8, 6.1 Hz, 1H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 142.08, 136.90, 133.23, 131.31, 130.15, 127.89, 122.70, 121.90, 119.68 ppm.
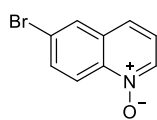
6-Bromoquinoline 1-oxide (77i). Prepared according to the general procedure A using 6-bromoquinoline (208 mg, 1 mmol, 1 equiv) and *meta*-chloroperbenzoic acid (77%, 291 mg, 1.3 mmol, 1.3 equiv); the product was obtained as a pale orange solid (210 mg, 0.94 mmol, 94%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.61 (dd, J = 7.4, 6.1Hz, 2H), 8.06 (d, J = 2.0 Hz, 1H), 7.84 (dd, J = 7.4, 2.0 Hz, 1H), 7.73 (d, J = 8.5 Hz, 1H), 7.37 ppm (dd, J = 8.5, 6.1 Hz, 1H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 140.10, 136.45, 134.39, 131.72, 130.28, 126.29, 123.68, 122.33, 121.76 ppm.
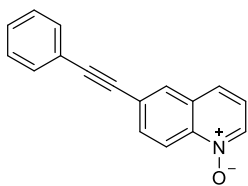
**6-(Phenylethynyl)quinoline 1-oxide (77j).** Conducted according to a literature procedure.[195] Prepared according to the general procedure A using 6-(phenylethynyl)quinoline (229 mg, 1 mmol, 1 equiv) and *meta*-chloroperbenzoic acid (77%, 291 mg, 1.3 mmol, 1.3 equiv); the product was obtained as a pale white solid (164 mg, 0.67 mmol, 67%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.72 (d, J = 9.0 Hz, 1H), 8.64 (d, J = 5.9 Hz, 1H), 8.06 (d, J = 1.3 Hz, 1H), 7.89 (dd, J = 9.0, 1.3 Hz, 1H), 7.81 (d, J = 8.4 Hz, 1H), 7.61 – 7.53 (m, 2H), 7.44 – 7.34 ppm (m, 4H) **^{13}C NMR** (126 MHz, CDCl$_3$) δ 140.39, 136.70, 133.84, 131.94, 131.09, 130.55, 129.18, 128.65, 127.36, 124.77, 122.49, 121.82, 120.05, 92.77, 87.85 ppm.
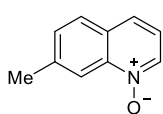
7-Methylquinoline 1-oxide (77k). Prepared according to the general procedure A using 7-methylquinoline (143 mg, 1 mmol, 1 equiv) and *meta*-chloroperbenzoic acid (77%, 291 mg, 1.3 mmol, 1.3 equiv); the product was obtained as a pale white solid (150 mg, 0.94 mmol, 94%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.61 (d, J = 6.0 Hz, 1H), 8.53 (s, 1H), 7.77 (m, 2H), 7.54 – 7.46 (m, 1H), 7.28 (dd, J = 8.0, 6.0 Hz, 1H), 2.60 ppm (s, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 142.44, 141.17, 136.41, 131.31, 128.82, 128.04, 127.78, 120.07, 118.71, 22.28 ppm.
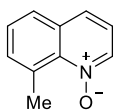
8-Methylquinoline 1-oxide (77l). Prepared according to the general procedure A using 8-methylquinoline (200 mg, 1.4 mmol, 1 equiv) and *meta*-chloroperbenzoic acid (77%, 406 mg, 1.82 mmol, 1.3 equiv); the product was obtained as a pale white solid (72 mg, 0.45 mmol, 32%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.49 (d, J = 5.5 Hz, 1H), 7.71 (d, J = 8.2 Hz, 1H), 7.67 (d, J = 4.8 Hz, 1H), 7.45 (d, J = 5.5 Hz, 2H), 7.22 (dd, J = 8.2, 4.8 Hz, 1H), 3.18 ppm (s, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 141.20, 137.90, 134.01, 133.64, 132.60, 128.42, 128.01, 127.00, 120.76, 24.99 ppm.

4,7-Dichloroquinoline 1-oxide (77m). Prepared according to the general procedure A using 4,7-dichloroquinoline (200 mg, 1 mmol, 1 equiv) and *meta*-chloroperbenzoic acid (77%, 291 mg, 1.3 mmol, 1.3 equiv); the product was obtained as a reddish solid (200 mg, 0.93 mmol, 93%). **^{1}H NMR** 300 MHz, CDCl$_3$) δ 8.79 (d, J = 1.8 Hz, 1H), 8.47 (d, J = 6.6 Hz, 1H), 8.17 (d, J = 9.0 Hz, 1H), 7.71 (dd, J = 9.0, 1.8 Hz, 1H), 7.39 ppm (d, J = 6.6 Hz, 1H). **^{13}C NMR** (75 MHz, CDCl$_3$) δ 142.39, 138.57, 136.28, 131.05, 130.58, 126.95, 126.69, 121.35, 120.06 ppm.

7-Chloro-4-phenylquinoline 1-oxide (77n). Conducted according to a literature procedure.[194] Prepared according to the general procedure A using 7-chloro-4-phenylquinoline (240 mg, 1 mmol, 1 equiv) and *meta*-chloroperbenzoic acid (77%, 291 mg, 1.3 mmol, 1.3 equiv; the product was obtained as a reddish solid (205 mg, 0.8 mmol, 80%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.85 (d, J = 1.9 Hz, 1H), 8.68 (d, J = 6.3 Hz, 1H), 7.91 (d, J = 9.0 Hz, 1H), 7.59 – 7.49 (m, 4H), 7.46 (dd, J = 7.8, 1.9 Hz, 2H), 7.30 ppm (d, J = 6.3 Hz, 1H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 141.54, 140.63, 137.84, 136.47, 136.37, 130.16, 129.61, 129.28, 129.14, 128.52, 127.37, 121.60, 119.61 ppm.
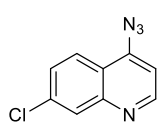
4-Azido-7-chloroquinoline. To a solution of 4,7-dichloroquinoline (1 g, 5.05 mmol, 1 equiv) in DMF (7.5 mL) sodium azide (656 mg, 10.1 mmol, 2 equiv) was added and the reaction mixture was stirred at 85 °C for 8 h. After cooling to room temperature, the crude reaction was purified by column chromatography (eluent: petroleum ether / ethyl acetate); the product was obtained as a yellow solid (946 mg, 4.62 mmol, 92%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.83 (d, J = 5.0 Hz, 1H), 8.13 (d, J = 2.1 Hz, 1H), 8.07 – 7.95 (m, 1H), 7.51 (dd, J = 8.9, 2.1 Hz, 1H), 7.16 ppm (d, J = 5.0 Hz, 1H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 150.74, 148.82, 147.42, 137.34, 128.09, 127.72, 123.99, 120.09, 108.83 ppm.

4-Azido-7-chloroquinoline 1-oxide. Prepared according to the general procedure A using 4-azido-7-chloroquinoline (930 mg, 4.55 mmol, 1 equiv) and and *meta*-chloroperbenzoic acid (77%, 1.32 g, 5.91 mmol, 1.3 equiv) in DCM (20 mL); the product was obtained as a reddish solid (830 mg, 3.76 mmol, 83%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.73 (d, J = 1.6 Hz, 1H), 8.52 (d, J = 6.6 Hz, 1H), 8.02 (d, J = 8.9 Hz, 1H), 7.60 (dd, J = 8.9, 1.8 Hz, 1H), 7.05 ppm (d, J = 6.6 Hz, 1H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 142.04, 138.77, 136.63, 136.29, 130.12, 124.93, 121.69, 119.69, 109.06 ppm.
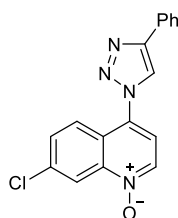
7-Chloro-4-(4-phenyl-1H-1,2,3-triazol-1-yl)quinoline 1-oxide (77o). To a solution of 4-azido-7-chloroquinoline 1-oxide (88 mg, 0.4 mmol, 1 equiv) in 1:1 H$_2$O / ^{t}BuOH (1 mL) was subsequently added phenylacetylene (65 µL, 0,6 mmol, 1.5 equiv), sodium *L*-ascorbate (24 mg, 0.12 mmol, 0.3 equiv), and CuSO$_4$•5 H$_2$O (10 mg, 0.04 mmol, 0.1 equiv). The reaction mixture was vigorously stirred at room temperature for 24 h. On completion, the reaction mixture was poured in to ice-cold water (10 mL). The aqueous phase was extracted with dichloromethane (3x50 mL) and the combined organic layers were dried over MgSO$_4$. Column chromatography provided the pure product

(eluent: EtOAc / MeOH); the product was obtained as a white solid (91 mg, 0.28 mmol, 71%).
¹H NMR (500 MHz, DMSO) δ 9.23 (s, 1H), 8.86 (d, J = 6.6 Hz, 1H), 8.64 (d, J = 2.1 Hz, 1H), 8.08 (d, J = 9.1 Hz, 1H), 8.03 – 7.94 (m, 2H), 7.94 – 7.85 (m, 2H), 7.53 (d, J = 7.7 Hz, 2H), 7.42 ppm (d, J = 7.7 Hz, 1H). **¹³C NMR** (126 MHz, DMSO) δ 146.88, 141.77, 136.36, 136.00, 130.76, 129.74, 129.05, 128.94, 128.36, 126.63, 125.40, 123.75, 123.11, 118.68, 118.57 ppm.
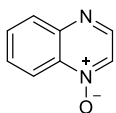
Quinoxaline 1-oxide (77p). Prepared according to the general procedure A using quinoxaline (117 µL, 1 mmol, 1 equiv) and and *meta*-chloroperbenzoic acid (77%, 291 mg, 1.3 mmol, 1.3 equiv); the product was obtained as a white solid (57 mg, 0.4 mmol, 40%). **¹H NMR** (500 MHz, CDCl₃) δ 8.68 (d, J = 3.5 Hz, 1H), 8.59 (d, J = 8.7 Hz, 1H), 8.37 (d, J = 3.5 Hz, 1H), 8.16 (d, J = 8.7 Hz, 1H), 7.88 – 7.81 (m, 1H), 7.81 – 7.72 ppm (m, 1H). **¹³C NMR** (126 MHz, CDCl₃) δ 145.94, 145.89, 132.03, 130.48, 130.17, 129.46, 119.14 ppm.
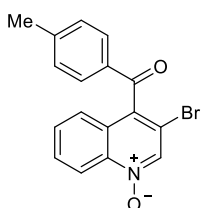
3-Bromo-4-(4-methylbenzoyl)quinoline 1-oxide (77x). Conducted according to a literature procedure.[96] Prepared according to the general procedure A using 3-bromo-4-(4-methylbenzoyl)quinoline (90 mg, 0.14 mmol, 1 equiv) and *meta*-chloroperbenzoic acid (77%, 40 mg, 0.18 mmol, 1.3 equiv) in DCM (3 mL); the product was obtained as a yellow solid (37 mg, 0.11 mmol, 80%). **¹H NMR** (500 MHz, CDCl₃) δ 8.86 (s, 1H), 8.76 (d, J = 8.8 Hz, 1H), 7.84 (dd, J = 11.4, 4.2 Hz, 1H), 7.74 (d, J = 7.9 Hz, 2H), 7.67 – 7.57 (m, 2H), 7.30 (d, J = 8.3 Hz, 2H), 2.45 ppm (s, 3H). **¹³C NMR** (126 MHz, CDCl₃) δ 192.50, 146.48, 137.66, 132.75, 131.35, 130.57, 129.98, 129.96, 127.88, 125.65, 119.96, 111.70, 21.84 ppm.

11.2.3 Physical data of products

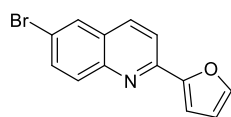**2-(Furyl)quinoline (78a).** Prepared according to general procedure B using quinoline 1-oxide (43.5 mg, 0.3 mmol, 1 equiv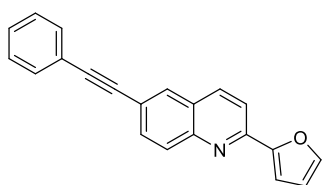) and 2-furanylboronic acid (100 mg, 0.9 mmol, 3 equiv); the product was obtained as a pale white solid (43 mg, 0.22 mmol, 73%). **¹H NMR** (500 MHz, CDCl₃) δ 8.36 (d J = 8.6 Hz, 1H), 8.02 (d, J = 8.6 Hz, 1H), 7.92 (dd, J = 8.3, 5.7 Hz, 2H), 7.81 – 7.77 (m, 1H), 7.75 (s, 1H), 7.56 (d, J = 7.0 Hz, 1H), 7.32 (d, J = 3.4 Hz, 1H), 6.68 ppm (dd, J = 3.4, 1.7 Hz, 1H). **¹³C NMR** (126 MHz, CDCl₃) δ 154.99, 149.90, 149.06, 145.17, 137.70, 130.73, 129.94, 128.72, 128.16, 127.06, 117.93, 113.19, 110.71 ppm. **FT-IR:** v = 3143, 3063, 1730, 1620, 1558, 1487 cm⁻¹. **HR-MS:** calc. for [M+H]⁺ $C_{13}H_9NO$ = 196.07828; found 196.07521.
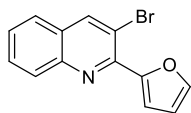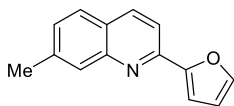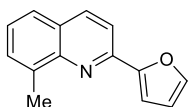
3-Bromo-2-(furyl)quinoline (78b). Prepared according to general procedure B using 3-bromo-quinoline 1-oxide (67 mg, 0.3 mmol, 1 equiv) and 2-furanylboronic acid (100 mg, 0.9 mmol, 3 equiv); the product was obtained as a pale reddish solid (75.5 mg, 0.28 mmol, 92%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.67 (s, 1H), 8.04 (dd, J = 8.5, 0.8 Hz, 1H), 7.90 (d, J = 8.5 Hz, 1H), 7.84 (dd, J = 1.7, 0.8 Hz, 1H), 7.79 (m, 1H), 7.64 – 7.55 (m, 1H), 7.49 (dd, J = 3.5, 0.8 Hz, 1H), 6.69 ppm (dd, J = 3.5, 1.7 Hz, 1H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 152.60, 147.45, 147.11, 145.26, 141.84, 131.31, 129.89, 128.70, 128.41, 127.72, 115.02, 114.25, 112.50 ppm. **FT-IR:** v = 3097, 3055, 2965, 2360, 2342, 1616, 1486, 1366 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{13}$H$_9$ON^{79}Br = 273.98620; found 273.98748; [M+H]$^+$ C$_{13}$H$_9$ON^{81}Br = 275.98416; found 275.98490.
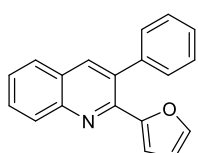
2-(Furyl)-3-phenylquinoline (78c). Prepared according to general procedure B using 3-phenylquinoline 1-oxide (66 mg, 0.3 mmol, 1 equiv) and 2-furanylboronic acid (100 mg, 0.9 mmol, 3 equiv); the product was obtained as a white solid (83 mg, 0.27 mmol, 90%). **^{1}H NMR** (500 MHz, CD$_2$Cl$_2$) δ 8.14 (d, J = 8.5 Hz, 1H), 8.05 (s, 1H), 7.83 (d, J = 8.1 Hz, 1H), 7.75 (dd, J = 8.5, 6.9, 1H), 7.56 (m, 1H), 7.52 – 7.42 (m, 4H), 7.43 – 7.31 (m, 2H), 6.35 (dd, J = 3.5, 1.7 Hz, 1H), 6.10 ppm (dd, J = 3.5, 0.6 Hz, 1H). **^{13}C NMR** (126 MHz, CD$_2$Cl$_2$) δ 153.37, 148.12, 147.71, 143.99, 140.66, 138.18, 133.99, 130.37, 129.81, 129.68, 129.00, 128.34, 128.05, 127.33, 113.78, 111.91 ppm. **FT-IR:** v = 3056, 2971, 2901, 2361, 2341, 1604, 1488, 1368, 1336, 1158 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{19}$H$_{14}$ON = 272.10699; found 272.10699.
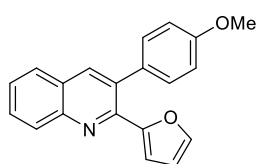
2-(Furyl)-3-(4-methoxyphenyl)quinoline (78d). Prepared according to general procedure B using 3-(4-methoxyphenyl)quinoline 1-oxide (75 mg, 0.3 mmol, 1 equiv) and 2-furanylboronic acid (100 mg, 0.9 mmol, 3 equiv) in DMSO (0.5 mL); the product was obtained as a white solid (75 mg, 0.25 mmol, 83%). **^{1}H NMR** (500 MHz, CD$_2$Cl$_2$) δ 8.11 (d, J = 8.5 Hz, 1H), 8.03 (s, 1H), 7.82 (d, J = 8.3 Hz, 1H), 7.73 (m, 1H), 7.54 (m, 1H), 7.50 (dd, J = 1.6, 0.6 Hz, 1H), 7.35 – 7.26 (m, 2H), 7.03 – 6.95 (m, 2H), 6.36 (dd, J = 3.4, 1.7 Hz, 1H), 6.11 (dd, J = 3.4, 0.6 Hz, 1H), 3.88 ppm (s, 3H). **^{13}C NMR** (126 MHz, CD$_2$Cl$_2$) δ 160.10, 153.44, 148.45, 147.59, 143.95, 138.16, 133.75, 132.82, 130.94, 130.21, 129.66, 127.97, 127.40, 127.26, 114.45, 113.79, 111.90, 55.88 ppm. **FT-IR:** v = 2970, 2836, 2360, 2341, 1734, 1653, 1511, 1286, 1032 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{20}$H$_{15}$O$_2$N = 302.11756; found 302.11773.
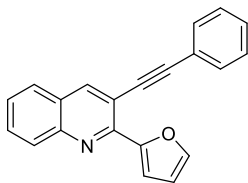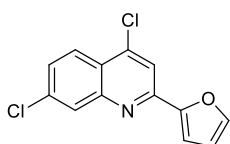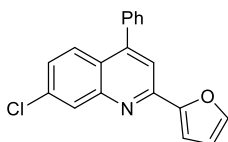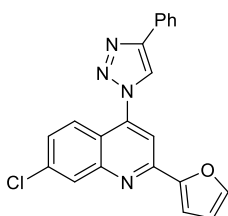
2-(Furyl)-3-(phenylethynyl)quinoline (78e). Prepared according to general procedure B using 3-(phenylethynyl)quinoline 1-oxide (75 mg, 0.3 mmol, 1 equiv) and 2-furanylboronic acid (100 mg, 0.9 mmol, 3 equiv) in DMSO (0.5 mL); the product was obtained as a yellow oil (85 mg, 0.29 mmol, 95%). **^{1}H NMR** (500 MHz, Acetone) δ 8.60 (s, 1H), 8.06 (d, J = 8.5 Hz, 1H), 7.96 (d, J = 8.1 Hz, 1H), 7.88 (d, J = 0.8 Hz, 1H), 7.85 – 7.75 (m, 1H), 7.72 (d, J = 3.4 Hz, 1H), 7.70 – 7.65 (m, 2H), 7.61 (t, J = 7.4 Hz, 1H), 7.54 – 7.42 (m, 3H), 6.73 ppm (dd, J = 3.4, 1.6 Hz, 1H). **^{13}C NMR** (126 MHz, Acetone) δ 153.43, 148.59, 147.71, 145.32, 142.39, 132.33, 131.68, 130.02, 129.94, 129.67, 128.33, 128.02, 126.93, 123.73, 114.42, 114.36, 112.73, 95.54, 88.23 ppm. **FT-IR:** v = 3055, 2924, 2361, 2341, 2210, 1616, 1488, 1004 cm^{-1}. **HR-MS:** calc. for [M+Na]$^+$ C$_{21}$H$_{13}$ON = 318.08897; found 318.08923.
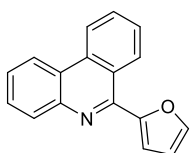
6-(Furyl)-phenanthridine (78f). Prepared according to general procedure B using phenanthridine 1-oxide (58.5 mg, 0.3 mmol, 1 equiv) and 2-furanylboronic acid (100 mg, 0.9 mmol, 3 equiv) in DMSO (0.5 mL); the product was obtained as a yellow oil (65 mg, 0.27 mmol, 88%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.81 (d, J = 8.3 Hz, 1H), 8.66 (d, J = 8.3 Hz, 1H), 8.55 (d, J = 8.3 Hz, 1H), 8.33 (d, J = 6.9 Hz, 1H), 7.93 – 7.82 (m, 1H), 7.82 – 7.69 (m, 3H), 7.69 – 7.62 (m, 1H), 7.37 (s, 1H), 6.69 ppm (dd, J = 3.3, 1.8 Hz, 1H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 149.42, 144.52, 133.92, 131.06, 129.98, 129.19, 128.23, 127.80, 127.37, 124.12, 123.80, 122.41, 122.04, 112.03 ppm. **FT-IR:** v = 3065, 2361, 2341, 2210, 1609, 1350, 1012 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ Chemical Formula: C$_{17}$H$_{11}$ON = 246.09208; found 246.09208.
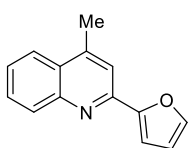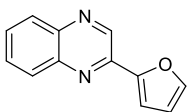
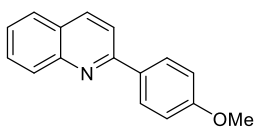**2-(Furyl)-4-methylquinoline (78g).** Prepared according to general procedure B using 4-methylquinoline 1-oxide (48 mg, 0.3 mmol, 1 equiv) and 2-furanylboronic acid (100 mg, 0.9 mmol, 3 equiv) in DMSO (0.5 mL); the product was obtained as a yellow oil (27 mg, 0.13 mmol, 43%). **^{1}H NMR** (500 MHz, Acetone) δ 8.03 (ddd, J = 21.8, 8.4, 0.6 Hz, 2H), 7.82 – 7.75 (m, 2H), 7.72 (dd, J = 5.6, 4.2 Hz, 1H), 7.59 – 7.52 (m, 1H), 7.29 (dd, J = 3.4, 0.6 Hz, 1H), 6.66 (dd, J = 3.4, 1.8 Hz, 1H), 2.75 ppm (s, 3H). **^{13}C NMR** (126 MHz, Acetone) δ 155.12, 149.58, 148.98, 145.87, 144.96, 130.53, 130.34, 128.10, 126.81, 124.84, 118.35, 113.10, 110.48, 18.78 ppm. **FT-IR:** v = 3064, 2921, 2360, 2342, 1600, 1088, 1007 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{14}$H$_{12}$ON = 210.09134; found 210.09236.
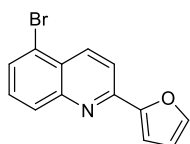
5-Bromo-2-(furyl)quinoline (78h). Prepared according to general procedure B using 5-bromo-quinoline 1-oxide (67 mg, 0.3 mmol, 1 equiv) and 2-furanylboronic acid (100 mg, 0.9 mmol, 3 equiv) in DMSO (0.5 mL); the product was obtained as a pale reddish solid (72 mg, 0.26 mmol, 88%). **^{1}H NMR** (500 MHz, Acetone) δ 8.57 (dd, J = 8.9, 0.9 Hz, 1H), 8.08 – 7.99 (m, 1H), 7.86 (dd, J = 7.5, 0.9 Hz, 1H), 7.84 – 7.79 (m, 1H), 7.67 (dd, J = 8.4, 7.5 Hz, 1H), 7.36 (dd, J = 3.4, 0.9 Hz, 1H), 6.70 (dd, J = 3.4, 1.7 Hz, 1H), 6.70 ppm (dd, J = 3.4, 1.7 Hz, 1H). **^{13}C NMR** (126 MHz, Acetone) δ 154.28, 150.63, 149.83, 145.74, 136.65, 131.25, 130.84, 130.15, 127.13, 122.15, 119.31, 113.38, 111.71 ppm. **FT-IR:** v = 3134, 2926, 2362, 2343, 1592, 1499, 1387, 1283, 1086, 1010 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ $C_{13}H_9ON^{79}Br$ = 273.98620; found 273.98678; [M+H]$^+$ $C_{13}H_9ON^{81}Br$ = 275.98416; found 275.98403.
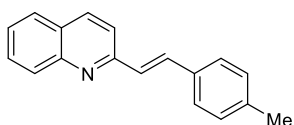
6-Bromo-2-(furyl)quinoline (78i). Prepared according to general procedure B using 6-bromo-quinoline 1-oxide (67 mg, 0.3 mmol, 1 equiv) and 2-furanylboronic acid (100 mg, 0.9 mmol, 3 equiv) in DMSO (0.5 mL); the product was obtained as an orange solid (65 mg, 0.24 mmol, 79%). **^{1}H NMR** (500 MHz, Acetone) δ 8.33 (d, J = 8.7 Hz, 1H), 8.14 (d, J = 2.1 Hz, 1H), 7.94 (dd, J = 11.9, 8.7 Hz, 2H), 7.83 – 7.81 (m, 2H), 7.33 (dd, J = 3.4, 0.6 Hz, 1H), 6.69 ppm (dd, J = 3.4, 1.7 Hz, 1H). **^{13}C NMR** (126 MHz, Acetone) δ 154.61, 150.35, 147.64, 145.51, 136.87, 133.91, 131.92, 130.78, 129.28, 120.09, 118.87, 113.31, 111.28 ppm. **FT-IR:** v = 3052, 2924, 2360, 2341, 1493, 1283, 1084, 1005 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ $C_{13}H_9ON^{79}Br$ = 273.98710; found 273.98620; [M+H]$^+$ $C_{13}H_9ON^{81}Br$ = 275.98416; found 275.98437.

2-(Furyl)-6-(phenylethynyl)quinoline (78j). Prepared according to general procedure B using 6-(phenylethynyl)quinoline 1-oxide (73.5 mg, 0.3 mmol, 1 equiv) and 2-furanylboronic acid (100 mg, 0.9 mmol, 3 equiv) in DMSO (0.5 mL); the product was obtained as a pale white solid (79 mg, 0.27 mmol, 89%). **^{1}H NMR** (500 MHz, Acetone) δ 8.38 (d, J = 8.7 Hz, 1H), 8.13 (d, J = 1.5 Hz, 1H), 8.00 (dd, J = 22.3, 8.7 Hz, 2H), 7.85 (dd, J = 8.7, 1.8 Hz, 1H), 7.81 (s, 1H), 7.67 – 7.56 (m, 2H), 7.45 (dd, J = 4.7, 2.4 Hz, 3H), 7.35 (d, J = 3.4 Hz, 1H), 6.70 ppm (dd, J = 3.4, 1.8 Hz, 1H). **^{13}C NMR** (126 MHz, Acetone) δ 154.78, 150.50, 148.54, 145.54, 137.49, 133.18, 132.43, 131.98, 130.31, 129.63, 129.55, 127.96, 123.86, 121.66, 118.73, 113.35, 111.33, 91.23, 89.86 ppm. **FT-IR:** v = 3044, 2971, 2922, 2360, 2340, 1948, 1595, 1492, 1139, 1004 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ $C_{21}H_{14}ON$ = 296.10699; found 296.10742.

2-(Furyl)-7-methylquinoline (78k). Prepared according to general procedure B using 7-methylquinoline 1-oxide (48 mg, 0.3 mmol, 1 equiv) and 2-furanylboronic acid (100 mg, 0.9 mmol, 3 equiv) in DMSO (0.5 mL); the product was obtained as a white solid (24 mg, 0.11 mmol, 38%). **^{1}H NMR** (500 MHz, Acetone) δ 8.29 (d, J = 8.6 Hz, 1H), 7.85 (d, J = 8.6 Hz, 1H), 7.80 (m, 2H), 7.77 (m, 1H), 7.39 (dd, J = 8.3, 1.3 Hz, 1H), 7.28 (dd, J = 3.4, 0.7 Hz, 1H), 6.67 (dd, J = 3.4, 1.7 Hz, 1H), 2.55 ppm (s, 3H). **^{13}C NMR** (126 MHz, Acetone) δ 155.18, 149.88, 149.33, 145.00, 140.94, 137.26, 129.22, 128.96, 128.38, 126.23, 117.09, 113.14, 110.42, 29.84, 21.83 ppm. **FT-IR:** v = 3136, 3115, 2922, 2360, 1597, 1495 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{14}$H$_{12}$ON = 210.09164; found 210.09134.
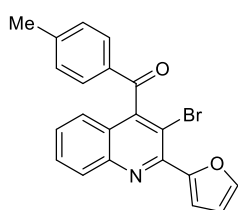
2-(Furyl)-8-methylquinoline (78l). Prepared according to general procedure B using 8-methylquinoline 1-oxide (48 mg, 0.3 mmol, 1 equiv) and 2-furanylboronic acid (100 mg, 0.9 mmol, 3 equiv) in DMSO (0.5 mL); the product was obtained as a yellow oil (52 mg, 0.25 mmol, 83%). **^{1}H NMR** (500 MHz, Acetone) δ 8.31 (d, J = 8.6 Hz, 1H), 7.91 (d, J = 8.6 Hz, 1H), 7.78 (dd, J = 1.7, 0.8 Hz, 1H), 7.74 (d, J = 8.1 Hz, 1H), 7.60 (d, J = 7.0 Hz, 1H), 7.48 – 7.37 (m, 1H), 7.33 (dd, J = 3.4, 0.8 Hz, 1H), 6.68 (dd, J = 3.4, 1.7 Hz, 1H), 2.79 ppm (s, 3H). **^{13}C NMR** (126 MHz, Acetone) δ 155.38, 148.81, 147.89, 144.98, 137.91, 137.67, 130.74, 128.08, 126.85, 126.65, 117.54, 113.15, 110.41, 17.83 ppm. **FT-IR:** v = 3151, 3043, 2916, 2361, 1600, 1505, 1093, 1007 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{14}$H$_{12}$ON = 210.09314; found 210.09134.

4,7-Dichloro-2-(furyl)quinoline (78m). Prepared according to general procedure B using 4,7-dichloroquinoline 1-oxide (64 mg, 0.3 mmol, 1 equiv) and 2-furanylboronic acid (100 mg, 0.9 mmol, 3 equiv) in DMSO (0.5 mL); the product was obtained as a white solid (68 mg, 0.26 mmol 86%). **^{1}H NMR** (500 MHz, CD$_2$Cl$_2$) δ 8.10 (d, J = 8.9 Hz, 1H), 8.03 (d, J = 1.9 Hz, 1H), 7.90 (s, 1H), 7.64 (s, 1H), 7.52 (dd, J = 8.9, 1.9 Hz, 1H), 7.25 (d, J = 3.3 Hz, 1H), 6.62 ppm (dd, J = 3.3, 1.9 Hz, 1H). **^{13}C NMR** (126 MHz, CD$_2$Cl$_2$) δ 153.20, 150.44, 149.92, 145.31, 143.40, 137.24, 128.88, 128.38, 126.03, 124.32, 118.06, 113.13, 111.81 ppm. **FT-IR:** v = 3110, 2924, 2360, 1608, 1479, 1400, 1072 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{13}$H$_8$ON^{35}Cl = 263.99775; found 263.99862; [M+H]$^+$ C$_{13}$H$_9$ON^{37}Cl = 265.99480; found 265.99509.

7-Chloro-2-(furyl)-4-phenylquinoline (78n). Prepared according to general procedure B using 7-chloro-4-phenylquinoline 1-oxide (77 mg, 0.3 mmol, 1 equiv) and 2-furanylboronic acid (100 mg, 0.9 mmol, 3 equiv) in DMSO (0.5 mL); the product was obtained as a white solid (80 mg, 0.26 mmol, 87%). **^{1}H NMR** (500 MHz, CD$_2$Cl$_2$) δ 8.11 (d, J = 2.0 Hz, 1H), 7.81 (d, J = 9.0 Hz, 1H), 7.79 (s, 1H), 7.68 – 7.62 (m, 1H), 7.61 – 7.49 (m, 5H), 7.40 (dd, J = 9.0, 2.2 Hz, 1H), 7.28 (dd, J = 3.4, 0.6 Hz, 1H), 6.63 ppm (dd, J = 3.4, 2.0 Hz, 1H). **^{13}C NMR** (126 MHz, CD$_2$Cl$_2$) δ 154.28, 150.13, 149.80, 149.72, 144.91, 138.25, 136.02, 130.03, 129.25, 128.91, 127.85, 127.45, 124.86, 118.27, 112.94, 111.14 ppm. **FT-IR:** v = 3111, 3056, 2901, 2360, 2341, 1618, 1488, 1158, 1011 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{19}$H$_{12}$ONCl = 306.06802; found 306.06864.

7-Chloro-2-(furyl)-4-(4-phenyl-1H-1,2,3-triazol-1-yl)quinoline (78o). Prepared according to general procedure B using 7-chloro-4-(4-phenyl-1H-1,2,3-triazol-1-yl)quinoline 1-oxide (48 mg, 0.15 mmol, 1 equiv) and 2-furanylboronic acid (50 mg, 0.45 mmol, 3 equiv) in DMSO (0.25 mL); the product was obtained as a yellow solid (39 mg, 0.1 mmol, 70%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.32 (s, 1H), 8.26 (d, J = 1.3 Hz, 1H), 8.04 – 7.90 (m, 4H), 7.64 (s, 1H), 7.55 – 7.46 (m, 3H), 7.42 (d, J = 7.4 Hz, 2H), 6.63 ppm (dd, J = 3.3, 1.3 Hz, 1H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 152.14, 149.97, 149.86, 148.67, 145.34, 141.91, 137.66, 129.68, 129.22, 129.04, 128.87, 128.42, 126.15, 124.77, 121.32, 119.56, 113.05, 112.66, 112.41 ppm. **FT-IR:** v = 3088, 2924, 2360, 2341, 1601, 1304, 1022 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{21}$H$_{13}$ON$_4$^{35}Cl = 373.08507; found 373.08582.

2-(Furyl)quinoxaline (78p). Prepared according to general procedure B using heterocyclic quinoxaline 1-oxide (44 mg, 0.3 mmol, 1 equiv) and 2-furanylboronic acid (100 mg, 0.9 mmol, 3 equiv); the product was obtained as a pale reddish solid (22 mg, 0.11 mmol, 38%). **^{1}H NMR** (500 MHz, Acetone) δ 9.31 (s, 1H), 8.06 – 8.04 (m, 2H), 7.89 (dd, J = 1.7, 0.7 Hz, 1H), 7.83 (m, 1H), 7.78 (m, 1H), 7.46 (dd, J = 3.5, 0.7 Hz, 1H), 6.74 (dd, J = 3.5, 1.7 Hz, 1H), 6.74 ppm (dd, J = 3.5, 1.7 Hz, 1H). **^{13}C NMR** (126 MHz, Acetone) δ 152.80, 146.37, 144.86, 142.92, 142.85, 142.25, 131.38, 130.22, 130.11, 129.94, 113.45, 112.76 ppm. **FT-IR:** v = 3137, 2924, 2361, 1552, 1496, 1081, 1001 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{12}$H$_8$ON$_2$ = 197.07094; found 197.07170.

2-(4-Methoxyphenyl)quinoline (78q). Prepared according to general procedure B using quinoline 1-oxide (29 mg, 0.2 mmol, 1 equiv) and (4-methoxyphenyl)boronic acid (91 mg, 3 equiv, 0.6 mmol) in DMSO (0.33 mL); the product was obtained as a white solid (19 mg, 0.08 mmol, 40% in yield). **¹H NMR** (500 MHz, Acetone) δ 8.35 (d, J = 8.7 Hz, 1H), 8.29 (d, J = 8.7 Hz, 1H), 8.06 (dd, J = 8.7, 4.4 Hz, 2H), 7.92 (d, J = 8.5 Hz, 1H), 7.74 (t, J = 7.5 Hz, 1H), 7.54 (t, J = 7.5 Hz, 1H), 7.10 (d, J = 8.7 Hz, 3H), ppm 3.89 (s, 1H). **¹³C NMR** (126 MHz, Acetone) δ 162.07, 157.17, 149.18, 137.57, 132.70, 130.40, 130.22, 129.57, 128.52, 127.96, 126.76, 118.97, 114.97, 55.74 ppm. **FT-IR:** v = 3039, 2961, 2841, 2360, 1596, 1516, 1289, 1175, 1028 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{16}$H$_{14}$NO = 236.10699; found 236.10800.
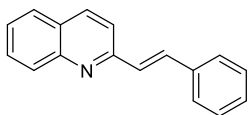
(*E*)-2-styrylquinoline (78r). Prepared according to general procedure B using quinoline 1-oxide (43.5 mg, 0.3 mmol, 1 equiv) and (*E*)-styrylboronic acid (133 mg, 0.9 mmol, 3 equiv) in DMSO (0.5 mL); the product was obtained as a yellow solid (41 mg, 0.18 mmol, 59%). **¹H NMR** (500 MHz, Acetone) δ 8.29 (d, J = 8.6 Hz, 1H), 8.03 (d, J = 8.6 Hz, 1H), 7.93 – 7.85 (m, 2H), 7.81 (d, J = 8.6 Hz, 1H), 7.75 (dd, J = 10.2, 4.5 Hz, 3H), 7.54 (dd, J = 11.0, 3.9 Hz, 1H), 7.48 (d, J = 16.3 Hz, 1H), 7.44 (t, J = 7.6 Hz, 2H), 7.35 ppm (t, J = 7.6 Hz, 1H). **¹³C NMR** (126 MHz, Acetone) δ 156.73, 149.22, 137.67, 137.17, 134.95, 130.45, 130.05, 129.82, 129.70, 129.44, 128.56, 128.35, 128.11, 126.96, 120.73 ppm. **FT-IR:** v = 3057, 3033, 2923, 2852, 2361, 2342, 1611, 1553 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{17}$H$_{14}$N = 232.11897; found 232.11305.

(*E*)-2-(4-Methylstyryl)quinoline (78s). Prepared according to general procedure B using quinoline 1-oxide (43.5 mg, 0.3 mmol, 1 equiv) and (*E*)-methylstyrylboronic acid (146 mg, 0.9 mmol, 3 equiv) in DMSO (0.5 mL); the product was obtained as a yellow solid (44 mg, 0.18 mmol, 60%). **¹H NMR** (500 MHz, Acetone) δ 8.27 (d, J = 8.6 Hz, 1H), 8.02 (d, J = 8.4 Hz, 1H), 7.89 (d, J = 8.0 Hz, 1H), 7.85 (d, J = 16.3 Hz, 1H), 7.79 (d, J = 8.6 Hz, 1H), 7.73 (m, 1H), 7.62 (d, J = 8.0 Hz, 2H), 7.53 (m, 1H), 7.42 (d, J = 16.3 Hz, 1H), 7.25 (d, J = 7.9 Hz, 2H), 2.36 ppm (s, 3H). **¹³C NMR** (126 MHz, Acetone) δ 156.92, 149.23, 139.43, 137.10, 134.96, 134.92, 130.41, 130.36, 130.00, 128.83, 128.54, 128.29, 128.09, 126.84, 120.66, 29.84 ppm. **FT-IR:** v = 3022, 2921, 2854, 2361, 2342, 2198, 1592, 1500, 1424 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{18}$H$_{16}$N = 246.12895; found 246.12895.
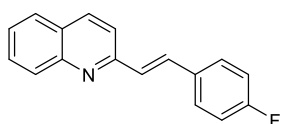
(E)-2-(4-Fluorostyryl)quinoline (78t). Prepared according to general procedure B using quinoline 1-oxide (29 mg, 0.2 mmol, 1 equiv) and (E)-(4-fluorostyryl)boronic acid (100 mg, 0.6 mmol, 3 equiv) in DMSO (0.33 mL); the product was obtained as a pale orange solid (36.5 mg, 0.15 mmol 73%). **^{1}H NMR** (500 MHz, Acetone) δ 8.29 (d, J = 8.5 Hz, 1H), 8.02 (d, J = 8.5 Hz, 1H), 7.91 (d, J = 8.2 Hz, 1H), 7.87 (d, J = 16.3 Hz, 1H), 7.83 – 7.76 (m, 3H), 7.74 (dd, J = 11.3, 4.0 Hz, 1H), 7.54 (t, J = 7.5 Hz, 1H), 7.43 (d, J = 16.3 Hz, 1H), 7.21 ppm (t, J = 8.5 Hz, 2H). **^{13}C NMR** (126 MHz, Acetone) δ 164.75, 162.79, 156.65, 149.25, 137.18, 134.21 (d, J_{CF} = 3.27 Hz), 133.65, 130.47, 130.04 (d, J_{CF} = 7.82 Hz), 129.79 (d, J_{CF} = 2.34 Hz), 128.57, 128.37, 126.98, 120.74, 116.61 ppm. **FT-IR:** v = 3034, 2925, 2853, 2360, 2341, 1684, 1612, 1507, 1315 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{17}$H$_{12}$NF = 250.10265; found 250.10375.
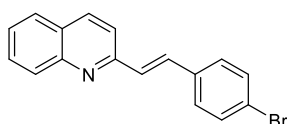
(E)-2-(4-Bromostyryl)quinoline (78u). Prepared according to general procedure B using quinoline 1-oxide (29 mg, 0.2 mmol, 1 equiv) and (E)-(4-bromostyryl)boronic acid (136 mg, 0.6 mmol, 3 equiv) in DMSO (0.33 mL); the product was obtained as a pale orange solid (37 mg, 0.12 mmol, 60%). **^{1}H NMR** (500 MHz, Acetone) δ 8.30 (d, J = 8.5 Hz, 1H), 8.03 (d, J = 8.5 Hz, 1H), 7.91 (d, J = 8.1 Hz, 1H), 7.85 (d, J = 16.3 Hz, 1H), 7.81 (d, J = 8.5 Hz, 1H), 7.78 – 7.72 (m, 1H), 7.70 (d, J = 8.5 Hz, 2H), 7.61 (d, J = 8.5 Hz, 2H), 7.55 (t, J = 7.5 Hz, 1H), 7.51 ppm (d, J = 16.3 Hz, 1H). **^{13}C NMR** (126 MHz, Acetone) δ 156.45, 149.25, 137.25, 136.99, 133.53, 132.78, 130.76, 130.52, 130.11, 129.92, 128.59, 128.44, 127.10, 122.75, 120.86 ppm. **FT-IR:** v = 3042, 2923, 2361, 2342, 1612, 1553, 1179, 1068 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{17}$H$_{12}$N^{79}Br = 310.02559; found 310.02355; [M+H]$^+$ C$_{17}$H$_{12}$N^{81}Br = 312.02054; found 312.02082.

(3-Bromo-2-(furyl)quinolin-4-yl)(p-tolyl)methanone (78v). Prepared according to general procedure B using 3-bromo-quinolin-4-yl)(p-tolyl)methanone 1-oxide (34 mg, 0.1 mmol, 1 equiv) and 2-furanylboronic acid (33.5 mg, 0.3 mmol, 3 equiv) in DMSO (0.15 mL); the product was obtained as a pale reddish solid (29.5 mg, 0.08 mmol, 75%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.31 (d, J = 8.6 Hz, 1H), 7.76 (dd, J = 7.1, 2.9 Hz, 4H), 7.61 (d, J = 3.5 Hz, 1H), 7.47 (d, J = 3.7 Hz, 2H), 7.29 (d, J = 8.0 Hz, 2H), 6.63 (dd, J = 3.5, 1.7 Hz, 1H), 2.43 ppm (s, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 193.93, 150.35, 148.59, 146.63, 145.98, 144.82, 132.73, 130.78, 129.90, 129.84, 129.48, 128.15, 124.84, 124.57, 115.79, 111.72, 110.38, 21.82 ppm. **FT-IR:** v = 2921, 2361, 2341, 1666, 1601, 1236, 1053 cm^{-1}. **HR-MS:** calc. for

$[M+H]^+$ $C_{21}H_{14}O_2N^{79}Br$ = 392.2815; found 392.02815; $[M+H]^+$ $C_{21}H_{14}O_2N^{79}Br$ = 394.02602; found = 394.02530.

11.3 Experimental part for the dihydroxylation of saturated hydrocarbons

11.3.1 General procedures

General procedure C: Synthesis of *vicinal* diols

1. 4-MeC$_6$H$_4$-I (1 equiv), I$_2$ (0.8 equiv)
   NaN$_3$ (2.5 equiv), AcO$_2$H (12.5 equiv)
   AcOH (0.1 M), 0 °C to rt, 24 h

2. LiOH (2 equiv), MeOH (0.1 M), 1 h
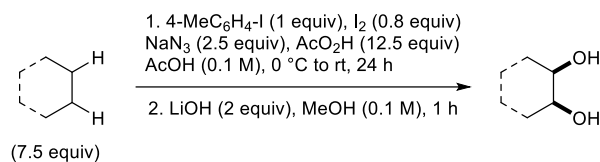
(7.5 equiv)

To a solution of 4-iodotoluene (65 mg, 0.3 mmol, 1 equiv) in glacial acetic acid (1.4 mL), peracetic acid (704 µL of 39% solution in acetic acid, 3.75 mmol, 12.5 equiv), alkane (2.55 mmol, 8.5 equiv) and iodine (61 mg, 0.24 mmol, 0.8 equiv) were added. When iodine was dissolved (usually within 10 – 15 minutes), NaN$_3$ (49 mg, 0.75 mmol, 2.5 equiv) was added portionwise over a time period of 15 minutes. The reaction was vigorously stirred for 24 hours at room temperature. After completion, the reaction was diluted with dichloromethane, neutralized with 1 M NaOH solution (25 mL) and washed with saturated Na$_2$SO$_3$ solution (10 mL). The aqueous phase was extracted two times with dichloromethane (2x20 mL) and the combined organic layers were dried over Na$_2$SO$_4$ and concentrated under reduced pressure. The crude mixture was dissolved in 3 mL MeOH, whereupon LiOH (14.5 mg, 0.6 mmol, 2 equiv) was added and the reaction was stirred at room temperature. After completion, HCl (1.25 M) in MeOH (0.5 mL) was added and MeOH was removed under reduced pressure. Column chromatography purification on silica provided the pure products (eluent: dichloromethane / MeOH).

General procedure D: Synthesis of benzoylated diols

1. 4-MeC$_6$H$_4$-I (1 equiv), I$_2$ (0.8 equiv)
   NaN$_3$ (2.5 equiv), AcO$_2$H (12.5 equiv)
   AcOH (0.1 M), 0 °C to rt, 24 h

2. LiOH (2 equiv), MeOH (0.1 M), 1 h
3. BzCl (2.5 equiv), DMAP (5 mol %)
   1:1 DCM / Py, rt, 24 h
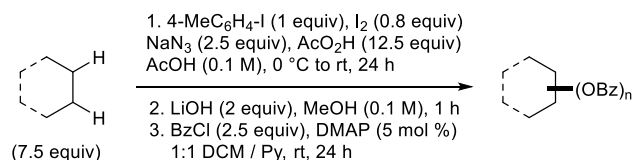
(7.5 equiv)

To a solution of 4-iodotoluene (200 mg, 0.9 mmol, 1 equiv) in glacial acetic acid (4.2 mL), peracetic acid (2.1 mL of 39% solution in acetic acid, 11.25 mmol, 12.5 equiv), alkane (7.65 mmol, 8.5 equiv) and iodine (183 mg, 0.72 mmol, 0.8 equiv) were added. When iodine was dissolved (usually within 10 – 15 minutes), NaN$_3$ (147 mg, 2.25 mmol, 2.5 equiv) was added portionwise over a time period of 15 minutes under water bath cooling. Afterwards, the reaction was vigorously stirred for 24 hours at room temperature. After completion, the reaction

was diluted with dichloromethane, neutralized with 1 M NaOH solution (75 mL) and washed with saturated Na_2SO_3 solution (30 mL). The aqueous phase was extracted two times with dichloromethane (2x50 mL) and the combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The crude reaction mixture was dissolved in MeOH (9 mL) whereupon LiOH (44 mg, 1.8 mmol, 2 equiv) was added and the reaction was stirred at room temperature. Afterwards, the reaction mixture was quenched with HCl (1.25 M) in MeOH (3 mL) and MeOH was removed under reduced pressure. The crude reaction mixture was purified by column chromatography (eluent: petroleum ether / EtOAc). The obtained diols were dissolved in dichloromethane/pyridine (5 mL, 1:1) and 4-(dimethylamino)-pyridine (5.5 mg, 5 mol %, 0.05 mmol) was added. Benzoyl chloride (261 µL, 2.25 mmol, 2.5 equiv) was added dropwise at 0°C to the reaction mixture and the reaction was stirred for 12 h at room temperature. The excess of benzoyl chloride was quenched by adding 25% NH_4OH solution (1 mL) and the crude reaction was diluted with dichloromethane and washed with saturated $NaHCO_3$ solution (15 mL). The aqueous phase was extracted two times with dichloromethane (2x25 mL) and dried over Na_2SO_4. Column chromatography (eluent: petroleum ether : EtOAc) provided the products.

11.3.2 Physical data of products
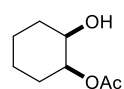
2-Hydroxycyclohexyl acetate (86). To a solution of $PhI(OAc)_2$ (193 mg, 0.6 mmol, 1 equiv) in glacial acetic acid (2.8 mL) peracetic acid (1.875 mL 39% solution in acetic acid, 10 mmol, 16.5 equiv), cyclohexane (810 µL, 7.5 mmol, 12.5 equiv) and iodine (127 mg, 0.5 mmol, 0.8 equiv) were added. After 15 minutes, NaN_3 (98 mg, 1.5 mmol, 2.5 equiv) was added portion wise over a time period of 15 minutes. Then the reaction was vigorously stirred for 24 hours at room temperature. Afterwards, the reaction was diluted with dichloromethane, slowly neutralized with NaOH solution (1 M, 50 mL) and washed with saturated Na_2SO_3 solution (20 mL). The aqueous phase was extracted two times with dichloromethane (2x40 mL) and the combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. Column chromatography provided the pure product (eluent: petroleum ether / EtOAc); the product was obtained as a colourless oil (69 mg, 0.43 mmol, 73%). **Selectivity:** d.r. = 5.3:1. **^{1}H NMR** (500 MHz, CDCl₃, # denotes major-, * minor diastereomer signals) δ 4.91# (dd, J = 8.0, 2.7 Hz, 1H), 4.57* (dd, J = 10.1, 4.7 Hz, 1H), 3.88# (dd, J = 6.8, 3.2 Hz, 1H), 3.62 – 3.47* (m, 1H), 2.09# (s, 2H), 2.08* (s, 3H), 1.84* (m, 4H), 1.81 – 1.72* (m, 4H), 1.62# (m, 4H), 1.42 – 1.21# ppm (m, 4H). **^{13}C NMR** (126 MHz, CDCl₃) δ

170.90, 78.43[*], 74.39[#], 72.95[*], 69.29[#], 33.23[*], 30.48[#], 30.13[*], 27.00[#], 24.04[*], 23.93[*], 22.22[#], 21.44[#], 21.08[#] ppm. **FT-IR:** v = 3436, 2937, 2863, 2360, 1716, 1237 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_8$H$_{15}$O$_3$ = 159.10157; found 159.10186. The spectral data were matching with reported.[196]
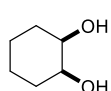
cis-**Cyclohexane-1,2-diol (87).** Prepared according to the general procedure C using cyclohexane (276 µL, 2.55 mmol, 8.5 equiv) as starting material; the product was obtained as a white crystalline solid (34.5 mg, 0.3 mmol, 99%). **Selectivity:** d.r. = 6.5:1. **^{1}H NMR** (400 MHz, CDCl3) δ 3.78 (dd, J = 5.7, 2.5 Hz, 1H), 1.91 (br. s, 2H), 1.82 – 1.69 (m, 2H), 1.69 – 1.49 (m, 4H), 1.40 – 1.21 ppm (m, 2H). **^{13}C NMR** (101 MHz, CDCl3) δ 70.77, 30.06, 21.55 ppm. **FT-IR:** v = 3392, 3260, 2929, 2851 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_6$H$_{13}$O$_2$: 117.0966; found 117.09025. The spectral data are matching with reported.[197]
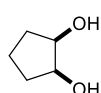
cis-**Cyclopentane-1,2-diol (89).** Prepared according to the general procedure C using cyclopentane (241 µL, 2.55 mmol, 8.5 equiv) as the starting material; the product was obtained as a colourless solid (26.5 mg, 0.26 mmol, 86%). **Selectivity:** d.r. = 6.3:1. **^{1}H NMR** (500 MHz, CDCl$_3$) δ 4.02 (q, J = 4.4 Hz, 2H), 2.77 (br. s, 2H), 1.96 – 1.76 (m, 3H), 1.75 – 1.38 ppm (m, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 74.05, 31.19, 19.89 ppm. **FT-IR:** v = 3348, 2963 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_5$H$_{11}$O$_2$ = 103.07536; found 103.07518. The spectral data are matching with reported.[198]
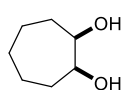
Cycloheptane-*cis*-1,2-diol (91). Prepared according to the general procedure C using cycloheptane (271 µL, 2.55 mmol, 8.5 equiv) as the starting material; the product was obtained as a white crystalline solid (33 mg, 0.26 mmol, 85%). **Selectivity:** d.r. = 20:1. **^{1}H NMR** (400 MHz, CDCl$_3$) δ 3.86 (dd, J = 4.0, 1.4 Hz, 2H), 2.18 (br. s, 2H), 1.74 (m, 7H), 1.56 - 1.30 ppm (m, 3H). **^{13}C NMR** (101 MHz, CDCl$_3$) δ 73.93, 31.11, 28.00, 22.00 ppm. **FT-IR:** v = 3333, 2920, 2858 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_7$H$_{15}$O$_2$ = 131.10666; found 131.10593. The spectral data are matching with reported.[198]
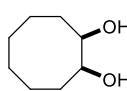
Cyclooctane-*cis*-1,2-diol (93). Prepared according to the general procedure C using cyclooctane (340 µL, 2.55 mmol, 8.5 equiv) as the starting material; the product was obtained as a colourless solid (16 mg, 0.11 mmol, 37%). **Selectivity:** d.r. > 20:1. **^{1}H NMR** (500 MHz, CDCl$_3$) δ 3.93 – 3.83 (m, 2H), 2.09 – 1.36 ppm (m, 14H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 71.75, 33.47, 30.58, 22.45 ppm. **FT-IR:** v = 3316, 2924, 2857 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_8$H$_{17}$O$_2$ = 145.12231; found 145.12177. The spectral data are matching with reported.[199]
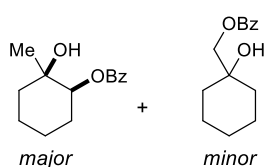
Regioisomeric mixture of 2-hydroxy-2-methyl-cyclohexyl benzoate (95a) and (1-hydroxycyclohexyl)-methyl benzoate (95b). Prepared according to the general procedure D using methylcyclohexane (975 µL, 7.65 mmol, 8.5 equiv) as the starting material. The products were obtained as colourless oil (143 mg, 0.61 mmol, 68%). **Selectivity:** r.r. > 20(**95a**):1(**95b**). d.r. = 3.5:1 (**95a**). **^{1}H NMR** (400 MHz, CDCl$_3$, # denotes major-, * minor diastereomer signals) δ 8.13 – 7.94 (m, 2H), 7.55 (t, J = 6.8, 4.1, Hz, 1H), 7.50 – 7.30 (m, 2H), 4.96 (dd, J = 8.9, 4.1 Hz, 1H, **95a***), 4.92 (dd, J = 8.5, 5.8 Hz, 1H, **95a**#), 4.23 (s, 2H, **95b**), 2.02 (br. s, 1H), 1.90 – 1.79 (m, 2H), 1.79 – 1.54 (m, 2H), 1.44 (m, 2H), 1.31 (s, 3H, **95a***), 1.24 ppm (s, 3H, **95a**#). **^{13}C NMR** (101 MHz, CDCl$_3$, # denotes major-, * minor diastereomer signals) δ 166.37 (**95a**#), 166.01 (**95a**#), 133.11 (**95a**#), 133.05 (**95a***), 130.58 (**95a***), 130.43 (**95a**#), 129.69 (**95a***), 129.67 (**95a**#), 128.50 (**95a**#), 128.45 (**95a***), 78.87 (**95a***), 78.37 (**95a**#), 77.16 (**95a***), 72.05 (**95a**#), 71.08, 38.13, 37.58, 28.32, 27.32, 27.00, 23.59, 22.89, 22.51, 21.69, 21.29 ppm. **FT-IR:** v = 3500, 2935, 2862, 1699, 1268, 1108 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{14}$H$_{19}$O$_3$ = 235.13287; found 235.13245.
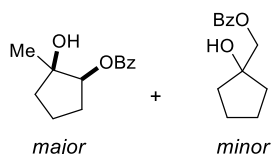
Regioisomeric mixture of 2-Hydroxy-2-methyl-cyclopentyl benzoate (97a) and (1-Hydroxycyclopentyl)-methyl benzoate (97b). Prepared according to the general procedure D using methylcyclopentane (858 µL, 7.65 mmol, 8.5 equiv) as the starting material. The products were obtained as pale yellow oil (145 mg, 0.66 mmol, 73%). **Selectivity:** r.r. = 18.5(**97a**):1(**97b**), d.r. = 5:1 (**97a**). **^{1}H NMR** (500 MHz, CDCl$_3$, # denotes major-, * minor diastereomer signals) δ 8.09 – 7.96 (m, 2H), 7.56 (m, 1H), 7.44 (t, J = 7.7 Hz, 2H), 5.15 – 5.07 (m, 1H, **97a***), 4.99 (t, J = 6.8 Hz, 1H, **97a**#), 4.33 (s, 2H, **97b**), 2.28 – 1.59 (m, 3H), 1.33 (s, 3H, **97a**#), 1.31 ppm (s, 3H, **97a***). **^{13}C NMR** (126 MHz, CDCl$_3$, # denotes major-, * minor diastereomer signals) δ 166.93 (**97a***), 166.78 (**97b**), 166.33 (**97a**#), 133.23, 130.17, 129.67, 128.52, 84.19 (**97a***), 81.26 (16d), 81.00 (**97a**#), 80.37 (**97a***), 78.60 (**97a**#), 71.37 (**97a***), 38.68, 37.38, 36.81 (**97a**#), 30.46, 28.77 (**97a**#), 25.42 (**97a**#), 24.16, 23.25, 20.62, 19.36 (**97a**#) ppm. **FT-IR:** v = 3512, 2965, 1713, 1269, 1109 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{13}$H$_{17}$O$_3$ = 221.11722; found 221.11723.
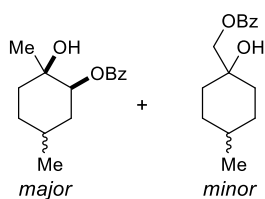
Regioisomeric mixture of 2-hydroxy-2,5-dimethyl cyclohexyl benzoate (99a) and (1 hydroxy-4-methylcyclohexyl) methyl benzoate (99b). Prepared according to the general procedure D using 1,4-dimethylcyclohexane (1.09 mL, 7.65 mmol, 8.5 equiv) as the starting material. The products were obtained as colourless solid (191 mg, 0.77 mmol, 86%). **Selectivity:** r.r. > 20(**99a**):1(**99b**), d.r. = 12:1 (**99a**). **^{1}H NMR** (500 MHz, CDCl$_3$, # denotes major-, * minor diastereomer signals) δ 8.11 – 7.98 (m, 2H), 7.63 – 7.50 (m, 1H7.45 (t, J = 7.7 Hz, 2H), 5.01 (m, 1H, **99a***), 4.92 (dd, J = 11.3, 4.6 Hz, 1H, **99a$^#$**), 4.19 (s, 2H, **99b**), 1.87 – 1.81 (m, 2H), 1.63 – 1.30 (m, 5H), 1.24 (s, 3H, **99a***), 1.23 (s, 3H, **99a$^#$**), 0.93 (s, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$, $^#$ denotes major diastereomer signals) δ 166.76, 165.99, 165.75 (**99a***), 133.20 (**99a$^#$**), 133.11, 133.01, 130.61, 130.35, 130.17, 129.68 (**99a$^#$**), 129.63, 128.55 (**99a$^#$**), 128.47, 78.35 (**99a$^#$**), 76.15, 70.54 (**99a$^#$**), 70.21, 63.31, 41.39, 37.46 (**99a$^#$**), 35.39 (**99a$^#$**), 34.69, 31.32 (**99a$^#$**), 30.65, 30.07, 29.69, 29.59, 29.42 (**99a$^#$**), 27.49 (**99a$^#$**), 27.14, 26.23, 21.98 (**99a$^#$**), 21.78, 19.37. **FT-IR:** v = 3520, 2929, 2862, 1696, 1600, 1452, 1266, 1110 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{15}$H$_{21}$O$_3$ = 249.14852; found 249.14911.
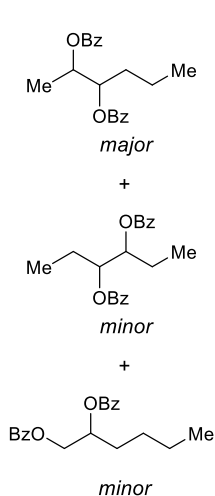
Regioisomeric mixture of heptane-2,3-diyl dibenzoate (101a), heptane-3,4-diyl dibenzoate (101b) and heptane-1,2-diyl dibenzoate (101c). Prepared according to the general procedure D using n-hexane (998 µL, 7.65 mmol, 8.5 equiv) as the starting material; the product was obtained as a colourless oil (200 mg, 0.61 mmol, 68%). **Selectivity:** r.r. = 6.5(**101a**):1.5(**101b**):1(**101c**), d.r. = 3:1 (**101a**), d.r. = 2:1 (**101b**). **^{1}H NMR** (500 MHz, CDCl$_3$, $^#$ denotes major-, * minor diastereomer signals) δ 8.14 – 7.91 (m, 4H), 7.62 – 7.48 (m, 2H), 7.50 – 7.35 (m, 4H), 5.51 (m, 2H, **101a***), 5.45 (dt, J = 9.1, 3.9 Hz, 2H, **101a$^#$**), 5.42 – 5.33 (m, 2H, **101b$^#$**), 5.26 – 5.09 (m, 2H, **101b***), 4.52 (ddd, J = 18.6, 11.9, 5.1 Hz, 2H, **101c**), 4.52 (ddd, J = 18.6, 11.9, 5.1 Hz, 1H, **101c**), 4.27 – 4.18 (m, 1H), 2.12 – 1.96 (m, 4H, **101c**), 1.89 – 1.65 (m, 2H), 1.45 (d, J = 6.5 Hz, 3H, **101a***), 1.40 (d, J = 6.5 Hz, 3H, **101a$^#$**), 1.40 – 1.24 (m, 2H), 1.05 – 0.88 ppm (m, CH$_3$, **101a, b, c**). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 166.32, 166.02, 133.09, 133.07, 133.06, 133.03, 130.35, 130.25, 129.78, 129.76, 129.75, 128.51, 128.48, 128.46, 128.44, 77.16, 76.91, 76.00, 75.63, 75.39, 75.12, 72.35, 71.95, 71.61, 33.00, 32.46, 27.46, 24.23, 23.31, 22.66, 18.92, 18.64, 16.75, 15.25, 14.07, 14.05, 10.08, 9.82, 9.70 ppm. FT-IR: v = 3064, 2961, 2875, 1715, 1260, 1095 cm^{-1}. **FT-IR:** v = 2958, 2931, 2872, 1716, 1261, 1095 cm^{-1}.
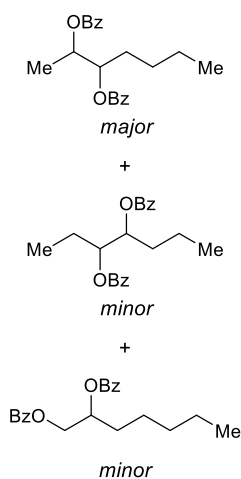
Regioisomeric mixture of heptane-2,3-diyl dibenzoate (103a), heptane-3,4-diyl dibenzoate (103b) and heptane-1,2-diyl dibenzoate (103c). Prepared according to the general procedure D using *n*-heptane (1.12 mL, 7.65 mmol, 8.5 equiv) as the starting material. The products were obtained as colourless oil (224 mg, 0.66 mmol, 73%). **Selectivity:** r.r. = 5.5(**103a**):2(**103b**):1(**103c**), d.r. = 2:1 (**103a**), d.r. = 2.5:1 (**103b**). **^{1}H NMR** (500 MHz, CDCl$_3$, $^\#$ denotes major-, * minor diastereomer signals) δ 8.14 – 7.91 (m, 4H), 7.62 – 7.49 (m, 2H), 7.50 – 7.35 (m, 4H), 5.54 – 5.48 (m, 2H, **103b***), 5.43 (ddd, *J* = 10.5, 7.2, 2.8 Hz, 2H, **103b**$^\#$),

5.41 – 5.36 (m, 2H, **103a**$^\#$), 5.36 – 5.30 (m, 2H, **103a***), 4.52 (ddd, *J* = 18.6, 11.9, 5.0 Hz, 2H, **103c**), 4.23 (ddd, *J* = 18.6, 11.9, 5.0 Hz, 1H, **103c**), 1.90 – 1.59 (m, 2H), 1.44 (d, *J* = 6.2 Hz, 3H, **103a***), 1.40 (d, *J* = 6.2 Hz, 3H, **103a**$^\#$), 1.39 – 1.24 (m, 4H), 1.02 – 0.96 (t, *J* = 7.2 Hz, 3H, **103b**$^\#$), 0.94 (t, *J* = 3.7 Hz, 3H, **103b***), 0.93 – 0.86 ppm (m, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 166.33, 166.29, 166.16, 166.03, 133.09, 133.07, 133.06, 130.47, 130.36, 130.26, 129.80, 129.79, 129.76, 129.74, 128.52, 128.49, 128.46, 128.44, 77.16, 76.91, 76.04, 75.65, 75.36, 74.14, 71.94, 71.57, 33.27, 30.57, 30.10, 27.76, 27.45, 24.26, 22.66, 18.69, 16.76, 15.20, 14.06, 14.04, 14.02, 9.83 ppm. **FT-IR:** v = 2958, 2931, 2872, 1716, 1261, 1095 cm^{-1}.
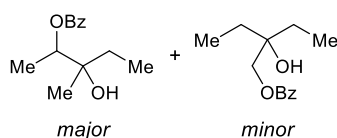
Regioisomeric mixture of 3-hydroxy-3-methylpentan-2-yl benzoate (105a) and 2-ethyl-2-hydroxybutyl benzoate (105b). Prepared according to the general procedure D using 3-methylpentane (992 µL, 7.65 mmol, 8.5 equiv) as the starting material. The products were obtained as colourless oil (110 mg, 0.49 mmol, 55%). **Selectivity**: r.r. = 7.7(**105a**):1(**105b**), d.r. = 1.3:1 (**105b**). **^{1}H NMR** (500 MHz, CDCl$_3$, $^\#$ denotes major-, * minor diastereomer signals) δ 8.12 – 7.97 (m, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.7 Hz, 2H), 5.11 (dd, *J* = 12.5, 6.4 Hz, 1H), 4.25 (s, 2H, 22b), 1.91 (br. s, 1H), 1.71 – 1.52 (m, 2H), 1.34 (d, 6.8 Hz, 3H, **105a**$^\#$), 1.32 (d, 6.6 Hz, 3H, **105a***), 1.23 (s, 3H, **105a**$^\#$), 1.22 (s, 3H, **105a***), 1.01 – 0.91 ppm (m, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$, $^\#$ denotes major-, * minor diastereomer signals, $\sim$ denotes minor regioisomer signals) δ 166.73 (**105b**), 166.21 (**105a**$^\#$), 166.08 (**105a***), 133.25 (**105b**), 133.14, 130.46 (**105b**), 130.04, 129.71 (**105b**), 129.67, 128.54 (**105b**), 128.52, 76.50, 76.15, 74.43, 74.16, 74.05, 69.39, 31.71, 30.48, 28.76, 22.75, 21.69, 14.98, 14.59, 7.84, 7.77, 7.76 ppm. **FT-IR:** v = 3496, 2974, 2941, 2882, 1699, 1269 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{13}$H$_{19}$O$_3$ = 223.13287; found 223.13241.
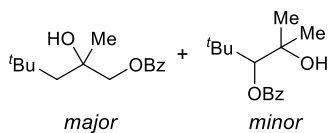
Regioisomeric mixture of 2-hydroxy-2,4,4-trimethyl-pentyl benzoate (107a) and 2-hydroxy-2,4,4-trimethyl-pentan-3-yl benzoate (107b). Prepared according to the general procedure D using 2,2,4-trimethylpentane (1.26 mL, 7.65 mmol, 8.5 equiv) as the starting material. The products were obtained as colourless oil (45 mg, 0.18 mmol, 20%). **Selectivity**: r.r. = 8(**107a**):1(**107b**). d.r. = 1.3:1. ^{1}**H NMR** (500 MHz, CDCl$_3$) δ 8.13 – 7.97 (m, 2H), 7.58 (d, J = 7.4 Hz, 1H), 7.47 (t, J = 7.7 Hz, 2H), 4.23 (dd, J = 38.5, 11.0 Hz, 2H), 3.49 (s, 1H, 26b), 1.63 (q, J = 14.8 Hz, 2H), 1.39 (s, 2H), 1.27 (m, 2H), 1.10 (s, 9H). ^{13}**C NMR** (126 MHz, CDCl$_3$) δ 166.66, 133.32, 130.08, 129.74, 128.62, 73.43, 72.78, 51.18, 31.68, 31.36, 26.16 ppm. **FT-IR:** v = 3489, 2953, 2360, 2105, 1718, 1270, 1111 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{15}$H$_{23}$O$_3$: 251.16417; found 251.16373.
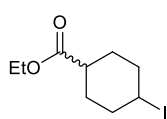
4-Iodocyclohexane-1-carboxylate (112). To a stirring solution of ethyl 4-hydroxycyclohexane-1-carboxylate (344 mg, 2 mmol, 1 equiv) in dichloromethane (8 mL) triphenylphosphine (788 mg, 1.5 mmol, 1.5 equiv), imidazole (204 mg, 1.5 mmol, 1.5 equiv) and iodine (762 mg, 1.5 mmol, 1.5 equiv) were successively added and the reaction was stirred for 3 h at rt. Afterwards, the reaction was diluted with DCM (20 mL) and quenched with saturated Na$_2$SO$_3$ solution (10 mL). The aqueous phase was extracted two times with dichloromethane (2x20 mL), the combined organic layers were dried over MgSO$_4$ and concentrated under reduced pressure. Column chromatography provided the pure product (eluent: petroleum ether); the product was obtained as a colourless oil (276 mg, 0.98 mmol, 49%). **Selectivity:** d.r. = 2.5:1. ^{1}**H NMR** (500 MHz, CD$_2$Cl$_2$$^\#$ denotes major-, * minor diastereomer signals) δ 4.68$^\#$ (s, 1H), 4.17* (td, J = 7.6, 3.8 Hz, 1H), 4.09 (m, 2H), 2.43 – 2.31 (m, 1H), 2.14 – 1.70 (m, 6H), 1.53 (2H), 1.28 – 1.18 (m, 3H). ^{13}**C NMR** (126 MHz, CD$_2$Cl$_2$) δ 175.15, 60.83, 42.01, 39.53, 36.44, 33.98, 31.26, 26.73, 14.57, 14.52 ppm.
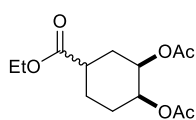
4-(Ethoxycarbonyl)cyclohexane-1,2-diyl diacetate (113). Conducted according to a literature procedure.[200] To a stirring solution of 4-MeC$_6$H$_4$I (66.7 mg, 0.3 mmol, 0.6 equiv) and AcO$_2$H (704 μL of a 39% solution in AcOH, 3.75 mmol, 7.35 equiv) in glacial acetic acid (1.8 mL) ethyl 4-iodocyclohexane-1-carboxylate (254 mg, 0.5 mmol, 1 equiv) was added portionwise over a time period of 15 minutes under waterbath cooling. After that time, the reaction was stirred for 24 h at rt. The reaction was diluted with DCM (20 mL) and slowly neutralized with 1 M NaOH (10 mL). The aqueous phase was extracted two times with dichloromethane (2x20 mL), the combined

organic layers were dried over MgSO$_4$ and concentrated under reduced pressure. The crude reaction was dissolved in DCM-Py (1:1, 3 mL) and 4-(dimethylamino)-pyridine (2.75 mg, 5 mol %, 0.025 mmol) was added. Ac$_2$O (144 µL, 1.5 mmol, 3 equiv) was added dropwise at 0 °C and the reaction was stirred at rt for 24 h. Column chromatography (eluent: petroleum ether : EtOAc) provided the pure products. The reaction was diluted with DCM (20 mL) and washed with 1 M HCl solution. The aqueous phase was extracted two times with dichloromethane (2x20 mL), the combined organic layers were dried over MgSO$_4$ and concentrated under reduced pressure. Column chromatography (eluent: petroleum ether : EtOAc) provided the pure product; the product was obtained as a colourless oil (119 mg, 0.44 mmol, 86%). **Selectivity:** *cis* (major) : trans (minor) = 2.5:1. **^{1}H NMR** (600 MHz, CDCl$_3$, # denotes major-, * minor diastereomer signals) δ 5.34 – 5.27* (m, 1H), 5.24 – 5.17* (m, 1H), 5.00# (dd, J = 9.1, 5.6 Hz, 1H), 4.88 – 4.79# (m, 3H), 4.13 (m, 2H), 2.69 – 2.22 (m, 1H), 2.20 – 1.94 (m, 7H), 1.75 (m, 4H), 1.30 – 1.18 (m, 3H). **^{13}C NMR** (151 MHz, CDCl$_3$) δ 174.98, 174.90, 174.34, 173.92, 170.73, 170.68, 170.64, 170.58, 170.46, 170.32, 170.04, 73.44, 72.98, 71.55, 71.44, 69.96, 69.50, 68.85, 68.81, 61.05, 60.96, 60.95, 60.83, 43.73, 43.02, 41.11, 40.93, 37.98, 37.54, 33.14, 32.69, 31.42, 30.17, 30.10, 29.41, 29.33, 28.67, 27.89, 26.71, 26.41, 25.86, 25.51, 23.72, 22.74, 21.46, 21.45, 21.43, 21.40, 21.37, 21.33, 14.54, 14.52, 14.49 ppm. **FT-IR:** v = 2955, 1729, 1444, 1367, 1227, 1107, 1028 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{13}$H$_{21}$O$_6$ = 273.13326; found 273.13333.
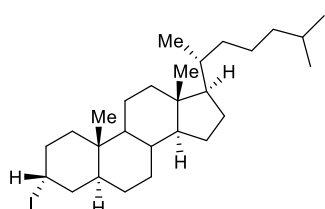
3α-Iodo-5α-cholestane (114). Conducted according to a literature procedure.[200] To a stirring solution of 5α-cholestane-3β-ol (389 mg, 1 mmol, 1 equiv) in dichloromethane (4 mL) triphenylphosphine (394 mg, 1.5 mmol, 1.5 equiv), imidazole (102 mg, 1.5 mmol, 1.5 equiv) and iodine (381 mg, 1.5 mmol, 1.5 equiv) were successively added and the reaction was stirred for 3 h at rt. Afterwards, the reaction was diluted with DCM (20 mL) and quenched with saturated Na$_2$SO$_3$ solution (10 mL). The aqueous phase was extracted two times with dichloromethane (2x20 mL), the combined organic layers were dried over MgSO$_4$ and concentrated under reduced pressure. Column chromatography provided the pure product (eluent: petroleum ether); the product was obtained as a pale yellow solid (339 mg, 0.68 mmol, 68%). **Selectivity:** d.r. > 20:1. **^{1}H NMR** (500 MHz, CDCl$_3$) δ 4.95 (s, 1H), 2.02 – 1.75 (m, 3H), 1.66 (m, 4H), 1.49 (m, 6H), 1.28 (m, 8H), 1.18 – 0.92 (m, 9H), 0.90 (d, J = 6.6 Hz, 3H), 0.86 (dd, J = 6.6, 2.5 Hz, 6H), 0.82 (m, 1H), 0.79 (s, 3H), 0.64 ppm (s, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 56.54, 56.35, 53.88, 42.69, 42.13, 40.05, 39.63, 38.88, 38.59,

36.66, 36.28, 35.97, 35.53, 34.47, 32.85, 31.90, 28.39, 28.15, 27.89, 24.30, 24.00, 22.99, 22.72, 20.91, 18.79, 13.53, 12.21 ppm.

Dihydroxylation of 3α-iodo-5α-cholestane. To a stirring solution of 4-MeC$_6$H$_4$I (66.7 mg, 0.3 mmol, 0.6 equiv) and AcO$_2$H (704 μL of a 39% solution in AcOH, 3.75 mmol, 7.35 equiv) in glacial acetic acid (1.8 mL) 3α-iodo-5α-cholestane (254 mg, 0.5 mmol, 1 equiv) was added portionwise over a time period of 15 minutes under waterbath cooling. After that time, the reaction was stirred for 24 h at rt. The reaction was diluted with DCM (20 mL) and slowly neutralized with 1 M NaOH (10 mL). The aqueous phase was extracted two times with dichloromethane (2x20 mL), the combined organic layers were dried over MgSO$_4$ and concentrated under reduced pressure. The crude mixture was dissolved in 5 mL MeOH, whereupon LiOH (24 mg, 1 mmol, 2 equiv) was added and the reaction was stirred at room temperature. After completion, HCl (1.25 M) in MeOH (0.85 mL) was added and MeOH was removed under reduced pressure. Column chromatography (eluent: petroleum ether : EtOAc) provided the pure products in the following order:
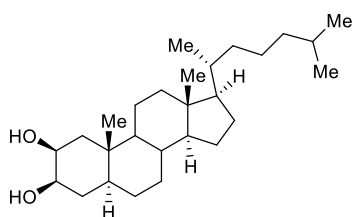
Cholestane-2β,3β-diol (115). The product was obtained as a white solid (52 mg, 0.13 mmol, 25%). **Selectivity:** *cis* (2β,3β) : trans (2α,3β) = 5:1. **MS-EI:** *m/z* (%): 404.1 (100) [M]$^+$. **^{1}H NMR** (500 MHz, CDCl$_3$, $^\#$ denotes major-, * minor diastereomer signals) δ 4.01$^\#$ (d, *J* = 2.8 Hz, 1H), 3.73* (m, 1H), 3.62$^\#$ (dt, *J* = 11.3, 4.1 Hz, 1H), 3.58 – 3.50* (m, 1H), 2.35 (br. s, 2H), 2.00 (dd, *J* = 43.9, 15.0 Hz, 2H), 1.85 – 1.42 (m, 7H), 1.43 – 0.91 (m, 27H), 0.92 – 0.77 (m, 12H), 0.64 (s, 3H), 0.61 – 0.51 ppm (m, 1H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 74.92, 72.54, 72.45, 70.32, 56.66, 56.51, 56.36, 56.33, 55.32, 48.90, 45.44, 43.26, 42.73, 42.69, 40.14, 40.00, 39.62, 36.98, 36.27, 35.91, 35.58, 35.50, 35.35, 34.93, 32.56, 32.51, 32.08, 29.85, 28.46, 28.37, 28.14, 26.01, 25.98, 24.34, 24.30, 23.95, 22.97, 22.70, 21.41, 20.70, 18.77, 14.79, 14.69, 14.29, 12.22, 12.19 ppm. **FT-IR:** *v* = 3387, 2926, 2865, 2359, 1711, 1457, 1382, 1078, 1051 cm^{-1}. The spectral data are matching with reported.[201]
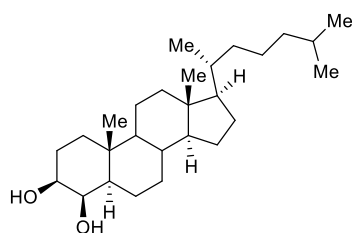
Cholestane-3β,5β-diol (116). Procedure: The product was obtained as a white solid (28 mg, 0.07 mmol, 15%). **Selectivity:** *cis* (3β,4β): trans (3α,4β) = 8.5:1. **MS-EI:** *m/z* (%): 404.1 (100) [M]$^+$. **^{1}H NMR** (500 MHz, CDCl$_3$, $^\#$ denotes major-, * minor diastereomer signals) δ 3.42$^\#$ (d, *J* = 1.9 Hz, 1H), 3.37$^\#$ (d, *J* = 2.4 Hz, 1H), 3.26* (m, 1H), 3.12* (m, 1H), 1.58 (m, 1H), 1.35 (m, 4H), 1.23 – 0.79 (m, 15H), 0.79

– 0.39 (m, 22H), 0.27 ppm (s, 4H). ^{13}**C NMR** (126 MHz, CDCl$_3$, $^{#}$ denotes major-, * minor diastereomer signals) δ 74.89*, 70.47$^{#}$, 69.46*, 69.35$^{#}$, 56.16, 56.04, 55.77, 54.81, 54.72, 43.32, 42.07, 42.00, 39.61, 39.48, 39.23, 38.97, 38.32, 35.63, 35.33, 35.05, 34.45, 31.96, 31.53, 31.36, 30.71, 27.75, 27.67, 27.44, 24.84, 23.55, 23.24, 21.91, 21.65, 20.29, 19.67, 17.84, 13.37, 13.25, 11.27, 11.22 ppm. **FT-IR:** ν = 3378, 2926, 2865, 2359, 1711, 1456, 1382, 1078, 1050 cm^{-1}. Assigned according to reported spectra.[201-202]

11.4 Experimental part for the catalytic oxidative coupling of heteroarenes

11.4.1 General procedures

General procedure E: Metal-free synthesis of 2-arylbenzofurans
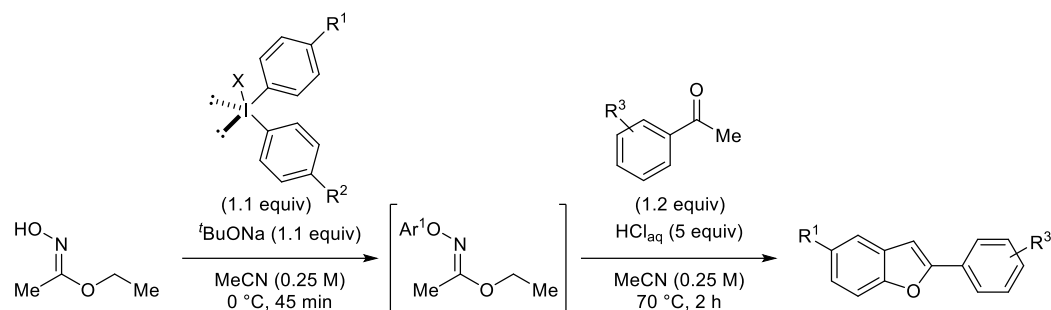
Conducted according to a literature procedure.[124] Ethyl acetohydroxamate (103 mg, 1 mmol, 1 equiv) was added to an oven dried screw cap vial and dissolved in anhydrous MeCN (4.0 mL). ^{t}BuONa (105 mg, 1.1 mmol, 1.1 equiv) was added in one portion at 0 °C and the mixture was vigorously stirred at room temperature for 15 min. The reaction vial was then submerged into an ambient temperature water bath and iodonium salt (1.1 equiv) was added in one portion. The reaction mixture was vigorously stirred at room temperature for 30 minutes. The ketone (1.2 mmol, 1.2 equiv) was added and the vial was purged with argon and submerged into an ambient temperature water bath. Then HCl (37%, 411 µL, 5 mmol, 5 equiv) was added dropwise. The vial was purged with argon, sealed, stirred at room temperature for 15 minutes and then stirred at 70 °C for 2 hours. After cooling to room temperature, the reaction mixture was diluted with DCM (20 mL), quenched with 1 M NaOH (10 mL), extracted two more times with DCM (2x10 mL), dried over MgSO$_4$ and the crude reaction was concentrated onto silica. The crude product was purified by column chromatography (eluent: petroleum ether / DCM or petroleum ether / ethyl acetate).

General procedure F: synthesis of 2-arylbenzofuran and –thiophenes
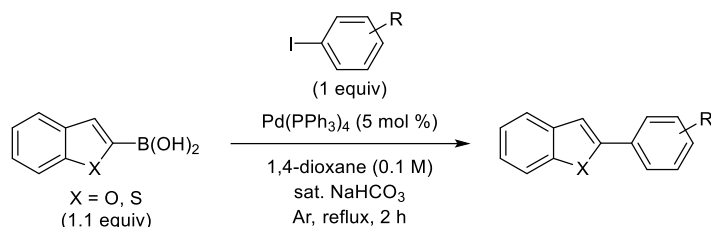
Conducted according to a literature procedure.[125] An oven dried Schlenk tube with stirring bar was charged with Pd(PPh$_3$)$_4$ (58 mg, 0.05 mmol, 5 mol %), evacuated and backfilled with argon three times and closed with a rubber septum. Successively, dry and degassed 1,4-dioxane (8 mL) and the iodoarene (1 mmol, 1 equiv) were added and the reaction was stirred for

20 minutes at room temperature. After this time, a degassed saturated NaHCO₃ solution (1.4 mL) and the boronic acid (1.1 mmol, 1.1 equiv) were added. The rubber septum was replaced with a glass stopper and the resulting mixture was refluxed for 2 h. The reaction mixture was allowed to cool to room temperature, diluted with H_2O (4 mL) and extracted with DCM (3×15 mL). The combined organic layers were washed with 1 M NaOH (5 mL) and dried over $MgSO_4$ and the crude reaction was concentrated onto silica. The crude product was purified by silica gel column chromatography (eluent: petroleum ether / DCM).

General procedure G: Oxidative coupling of heteroarenes
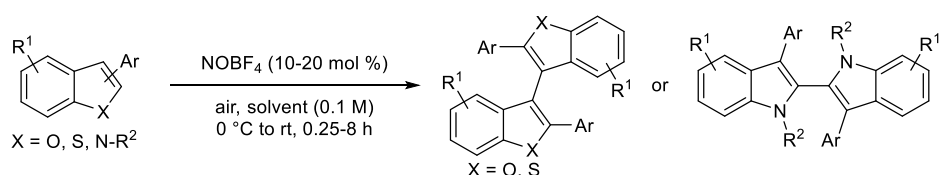
To a stirring solution of heteroarenes (0.2 mmol, 1 equiv) in the given solvent (2 mL), NOBF₄ (0.02-0.04 mmol, 10-20 mol) was added at 0 °C. The reaction was vigorously stirred until full conversion of starting material was monitored by TLC. The reaction was slowly quenched with saturated NaHCO₃ solution (10 mL) and extracted three times with DCM (3x15 mL). The combined organic layers were dried over $MgSO_4$ and the crude reaction mixture was concentrated onto silica. The crude product was purified by silica gel column chromatography (eluent: petroleum ether / DCM or petroleum ether / ethyl acetate).

11.4.2 Physical data of starting materials

Diphenyliodonium triflate. Conducted according to a literature procedure.[203] *meta*-Chloroperbenzoic acid (77%, 2.46 g, 11 mmol, 1.1 equiv) and iodobenzene (1.14 mL, 10 mmol, 1 equiv) were dissolved in dry DCM (44 mL) in an open flask. Benzene (0.98 mL, 11 mmol, 1.1 equiv) was added and the solution was cooled 0 °C followed by dropwise addition of CF_3SO_3H (2.7 mL, 30 mmol, 3 equiv). The solution was stirred at room temperature for 10 minutes and concentrated under reduced pressure while still cold. Et₂O (100 mL) was added and the mixture was stirred at room temperature for 30 minutes to precipitate an off-white solid. The flask was stored in a freezer for 1 h, after that time the solid was filtered off, washed with cold Et₂O and dried under vacuum. The compound was obtained as white solid (4.1 g, 9.53 mmol, 95%). **Mp.:** 184.3 °C. **¹H NMR** (500 MHz, DMSO) δ 8.20 (m, 4H), 7.62 (dd, J = 10.7 Hz, 2H), 7.48 ppm (dd, J = 10.7 Hz, 4H). **¹³C NMR** (126 MHz, DMSO) δ 135.23, 132.19, 131.83, 122.01, 119.44, 116.58 ppm.
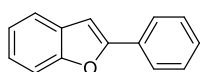
2-Phenylbenzofuran (117a). Prepared according to the general procedure E using diphenyliodonium triflate (473 mg, 1.1 mmol, 1.1 equiv) and acetophenone (140 µL, 1.2 mmol, 1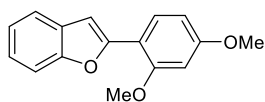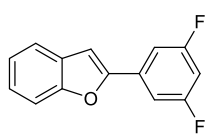.2 equiv); the product was obtained as a white solid (160 mg, 0.82 mmol, 82 %). **^{1}H NMR** (400 MHz, CDCl$_3$) δ 7.88 (d, J = 7.3 Hz, 2H), 7.62 – 7.57 (m, 1H), 7.54 (d, J = 7.9 Hz, 1H), 7.46 (dd, J = 10.5, 4.7 Hz, 2H), 7.36 (dd, J = 8.3, 6.4 Hz, 1H), 7.32 – 7.26 (m, 1H), 7.26 – 7.21 (m, 1H), 7.04 ppm (s, 1H). **^{13}C NMR** (101 MHz, CDCl$_3$) δ 156.07, 155.04, 130.63, 129.36, 128.93, 128.69, 125.08, 124.40, 123.07, 121.04, 111.32, 101.44 ppm.
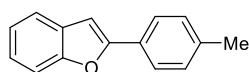
2-(*p*-Tolyl)benzofuran (117b). Prepared according to the general procedure E using diphenyliodonium triflate (473 mg, 1.1 mmol, 1.1 equiv) and 1-(*p*-tolyl)ethan-1-one (161 mg, 1.2 mmol, 1.2 equiv); the product was obtained as a white solid (135 mg, 0.65 mmol, 66%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.64 (d, J = 8.2 Hz, 2H), 7.42 (m, 2H), 7.18 – 7.07 (m, 4H), 6.83 (d, J = 0.7 Hz, 1H), 2.27 ppm (s, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 156.27, 154.86, 138.68, 129.59, 129.46, 127.83, 124.98, 124.11, 122.97, 120.86, 111.20, 100.67, 21.50 ppm.
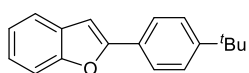
2-(4-(*tert*-Butyl)phenyl)benzofuran (117c). Prepared according to the general procedure F using benzofuran-2-boronic acid (178 mg, 1.1 mmol, 1.1 equiv) and 1-(*tert*-butyl)-4-iodobenzene (176 µL, 1 mmol, 1 equiv); the product was obtained as a light yellow solid (223 mg, 0.89 mmol, 89%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.70 (d, J = 8.3 Hz, 2H), 7.47 (d, J = 7.7 Hz, 1H), 7.43 (d, J = 8.3 Hz, 1H), 7.37 (d, J = 8.3 Hz, 2H), 7.19 – 7.10 (m, 2H), 6.87 (s, 1H), 1.26 (s, 9H) ppm. **^{13}C NMR** (126 MHz, CDCl$_3$) δ 156.27, 154.94, 151.90, 129.48, 127.85, 125.87, 124.86, 124.12, 122.97, 120.89, 111.26, 100.81, 34.90, 31.38 ppm.
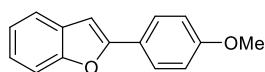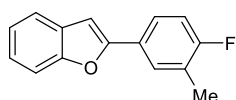
2-(4-Methoxyphenyl)benzofuran (117d). Prepared according to the general procedure F using benzofuran-2-boronic acid (178 mg, 1.1 mmol, 1.1 equiv) and 4-iodoanisol (120 mg, 1 mmol, 1 equiv); the product was obtained as a pale-yellow solid (196 mg, 0.87 mmol, 87%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.81 (d, J = 8.9 Hz, 2H), 7.55 (m, 2H), 7.31 – 7.19 (m, 2H), 6.99 (d, J = 8.9 Hz, 2H), 6.90 (s, 1H), 3.87 ppm (s, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 160.07, 156.15, 154.80, 129.61, 126.53, 123.86, 123.43, 122.95, 120.70, 114.35, 111.11, 99.79, 55.47 ppm.
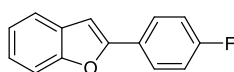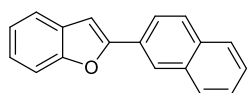
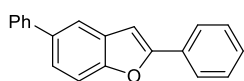**2-(4-Fluorophenyl)benzofuran (117e).** Prepared according to the general procedure E using diphenyliodonium triflate (473 mg, 1.1 mmol,

1.1 equiv) and 1-(4-fluorophenyl)ethan-1-one (150 μL, 1.2 mmol, 1.2 equiv); the product was obtained as a white solid (181 mg, 0.85 mmol, 85%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.88 – 7.82 (m, 2H), 7.59 (dd, J = 7.6, 0.6 Hz, 1H), 7.53 (dd, J = 8.1, 0.6 Hz, 1H), 7.34 – 7.28 (m, 1H), 7.27 – 7.22 (m, 1H), 7.15 (dd, J = 9.7, 7.8 Hz, 2H), 6.99 – 6.94 ppm (m, 1H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 162.99 (d, J = 248.7 Hz), 155.13, 154.95, 129.30, 126.89 (d, J_{CF} = 8.2 Hz), 124.42, 123.15, 121.02, 116.10 (d, J_{CF} = 22.0 Hz), 115.93, 111.27, 101.12 ppm (d, J_{CF} = 1.5 Hz).
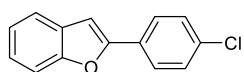
2-(4-Chlorophenyl)benzofuran (117f). Prepared according to the general procedure E using diphenyliodonium triflate (473 mg, 1.1 mmol, 1.1 equiv) and 1-(4-chlorophenyl)ethan-1-one (160 μL, 1.2 mmol, 1.2 equiv); the product was obtained as a white solid (189 mg, 0.83 mmol, 83%). **^{1}H NMR** (400 MHz, CDCl$_3$) δ 7.82 – 7.77 (m, 2H), 7.59 (dd, J = 7.6, 0.6 Hz, 1H), 7.54 – 7.49 (m, 1H), 7.46 – 7.39 (m, 2H), 7.34 – 7.27 (m, 1H), 7.23 (dd, J = 7.4, 0.9 Hz, 1H), 7.01 ppm (d, J = 0.5 Hz, 1H). **^{13}C NMR** (101 MHz, CDCl$_3$) δ 155.05, 154.92, 134.46, 129.21, 129.19, 129.13, 126.28, 124.71, 123.24, 121.15, 111.35, 101.89 ppm.
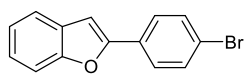
2-(4-Bromophenyl)benzofuran (117g). Prepared according to the general procedure E using diphenyliodonium triflate (473 mg, 1.1 mmol, 1.1 equiv) and 1-(4-bromophenyl)ethan-1-one (239 mg, 1.2 mmol, 1.2 equiv); the product was obtained as a pale yellow solid (210 mg, 0.77 mmol, 77 %). **^{1}H NMR** (600 MHz, CDCl$_3$) δ 7.75 – 7.71 (m, 2H), 7.60 – 7.56 (m, 3H), 7.52 (dd, J = 8.2, 0.7 Hz, 1H), 7.30 (m, 1H), 7.24 (td, J = 7.7, 0.9 Hz, 1H), 7.03 ppm (d, J = 0.7 Hz, 1H). **^{13}C NMR** (151 MHz, CDCl$_3$) δ 155.05, 154.93, 132.12, 129.56, 129.19, 126.52, 124.76, 123.26, 122.65, 121.17, 111.36, 102.00 ppm.
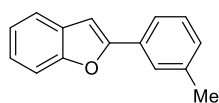
2-(*m*-Tolyl)benzofuran (117h). Prepared according to the general procedure F using benzofuran-2-boronic acid (178 mg, 1.1 mmol, 1.1 equiv) and 3-iodotoluene (128 μL, 1 mmol, 1 equiv); the product was obtained as a white solid (184 mg, 0.88 mmol, 88%). **^{1}H NMR** (700 MHz, CDCl$_3$) δ 7.60 (s, 1H), 7.57 (d, J = 7.8 Hz, 1H), 7.48 (d, J = 7.7 Hz, 1H), 7.43 (d, J = 8.2 Hz, 1H), 7.23 (t, J = 7.6 Hz, 1H), 7.20 – 7.16 (m, 1H), 7.15 – 7.11 (m, 1H), 7.07 (d, J = 7.5 Hz, 1H), 6.90 (s, 1H), 2.33 ppm (s, 3H). **^{13}C NMR** (176 MHz, CDCl$_3$) δ 156.24, 154.99, 138.56, 130.52, 129.51, 129.40, 128.82, 125.67, 124.30, 123.02, 122.27, 120.98, 111.27, 101.32, 21.63 ppm.
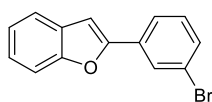
2-(3-Bromophenyl)benzofuran (117i). Prepared according to the general procedure E using diphenyliodonium triflate (473 mg, 1.1 mmol, 1.1 equiv) and 1-(3-bromophenyl)ethan-1-one (239 mg, 1.2 mmol, 1.2 equiv); the product was obtained as a pale yellow solid (230 mg, 0.84 mmol, 84%). **^{1}H NMR** (400 MHz, CDCl$_3$) δ 8.02 (t, J = 1.7 Hz, 1H), 7.78 (d, J = 7.8 Hz, 1H), 7.60 (d, J = 7.4 Hz, 1H), 7.53 (d, J = 8.1 Hz, 1H), 7.47 (dd, J = 8.0, 0.7 Hz, 1H), 7.31 (t, J = 7.9 Hz, 2H), 7.27 – 7.23 (m, 1H), 7.05 ppm (s, 1H). **^{13}C NMR** (101 MHz, CDCl$_3$) δ 155.11, 154.32, 132.59, 131.49, 130.46, 129.05, 127.95, 124.93, 123.54, 123.29, 123.12, 121.29, 111.42, 102.55 ppm.
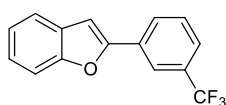
2-(3-(trifluoromethyl)phenyl)benzofuran (117j). Prepared according to the general procedure E using diphenyliodonium triflate (473 mg, 1.1 mmol, 1.1 equiv) and 1-(3,5-difluorophenyl)ethan-1-one (193 mg, 1.2 mmol, 1.2 equiv); the product was obtained as a white solid (167 mg, 0.73 mmol, 73 %). **^{1}H NMR** (400 MHz, CDCl$_3$) δ 8.12 (s, 1H), 8.03 (d, J = 7.5 Hz, 1H), 7.66 – 7.49 (m, 4H), 7.33 (m, 1H), 7.26 (m, 1H), 7.12 ppm (d, J = 0.7 Hz, 1H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 155.13, 154.33, 132.12 – 130.83 (m), 129.47, 128.99, 128.03, 128.02, 125.20, 125.17 – 125.01 (m), 123.38, 123.04, 121.77 (q, J_{CF} = 3.9 Hz), 121.38, 111.47, 102.79 ppm.
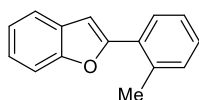
2-(*o*-Tolyl)benzofuran (117k). Prepared according to the general procedure F using benzofuran-2-boronic acid (178 mg, 1.1 mmol, 1.1 equiv) and 1-iodo-2-methylbenzene (231 mg, 1 mmol, 1 equiv); the product was obtained as a colourless oil (64 mg, 0.31, 31%). **^{1}H NMR** (600 MHz, CDCl$_3$) δ 8.01 (d, J = 7.3 Hz, 1H), 7.74 (d, J = 7.3 Hz, 1H), 7.67 (d, J = 8.1 Hz, 1H), 7.48 – 7.34 (m, 5H), 7.01 (d, J = 0.6 Hz, 1H), 2.70 ppm (s, 3H). **^{13}C NMR** (151 MHz, CDCl$_3$) δ 155.73, 154.48, 135.87, 131.36, 130.00, 129.30, 128.58, 128.23, 126.19, 124.34, 122.89, 121.02, 111.18, 105.21, 22.03 ppm.

2-(2,4-Dimethoxyphenyl)benzofuran (117l). Prepared according to the general procedure F using benzofuran-2-boronic acid (178 mg, 1.1 mmol, 1.1 equiv) and 1-iodo-2,4-dimethoxybenzene (263 mg, 1 mmol, 1 equiv); the product was obtained as a pale yellow solid (216 mg, 0.85 mmol, 85 %). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.99 (d, J = 8.6 Hz, 1H), 7.57 (dd, J = 7.5, 0.8 Hz, 1H), 7.52 – 7.47 (m, 1H), 7.25 – 7.17 (m, 3H), 6.63 (dd, J = 8.6, 2.4 Hz, 1H), 6.58 (d, J = 2.4 Hz, 1H), 3.98 (s, 3H), 3.87 ppm (s, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 161.01, 157.89, 153.79, 152.55, 130.13, 128.09, 123.69, 122.66, 120.83, 112.86, 110.75, 104.89, 104.39, 98.88, 55.63, 55.61 ppm.

2-(3,5-Difluorophenyl)benzofuran (117m). Prepared according to the general procedure E using diphenyliodonium triflate (473 mg, 1.1 mmol, 1.1 equiv) and 1-(3,5-difluorophenyl)ethan-1-one (193 mg, 1.2 mmol, 1.2 equiv); the product was obtained as a white solid (167 mg, 0.73 mmol, 73 %). **^{1}H NMR** (400 MHz, CDCl$_3$) δ 7.61 (d, J = 7.6 Hz, 1H), 7.53 (d, J = 7.6 Hz, 1H), 7.40 – 7.30 (m, 3H), 7.26 (m, 1H), 7.06 (s, 1H), 6.79 ppm (m, 1H). **^{13}C NMR** (101 MHz, CDCl$_3$) δ 164.75 (d, J = 13.0 Hz), 162.28 (d, J = 12.9 Hz), 155.12, 153.60, 133.57 (t, J = 10.5 Hz), 128.82, 125.37, 123.47, 121.50, 111.51, 108.50 – 106.81 (m), 104.62 – 102.64 ppm (m). ^{19}F NMR (377 MHz, CDCl$_3$) δ -112.50 (dd, J = 8.1, 3.3 Hz) ppm.
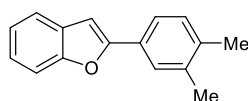
2-(3,4-Dimethylphenyl)benzofuran (117n). Prepared according to the general procedure E using diphenyliodonium triflate (473 mg, 1.1 mmol, 1.1 equiv) and 1-(3,4-dimethylphenyl)ethan-1-one (178 mg, 1.2 mmol, 1.2 equiv); the product was obtained as a white solid (113 mg, 0.51 mmol, 51%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.72 (s, 1H), 7.69 – 7.56 (m, 3H), 7.36 – 7.23 (m, 3H), 7.01 (d, J = 0.5 Hz, 1H), 2.39 (s, 3H), 2.36 ppm (s, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 156.43, 154.85, 137.45, 137.11, 130.15, 129.51, 128.19, 126.18, 124.02, 122.93, 122.58, 120.82, 111.17, 100.57, 19.99, 19.82 ppm.

2-(4-Fluoro-3-methylphenyl)benzofuran (117o). Prepared according to the general procedure E using diphenyliodonium triflate (473 mg, 1.1 mmol, 1.1 equiv) and 1-(4-fluoro-3-methylphenyl)ethan-1-one (188 mg, 1.2 mmol 1.2 equiv); the product was obtained as a white solid (178 mg, 0.79 mmol, 79 %). **^{1}H NMR** (400 MHz, CDCl$_3$) δ 7.70 (d, J = 7.3 Hz, 1H), 7.68 – 7.62 (m, 1H), 7.60 – 7.55 (m, 1H), 7.51 (d, J = 8.0 Hz, 1H), 7.31 – 7.26 (m, 1H), 7.23 (td, J = 7.4, 0.9 Hz, 1H), 7.08 (t, J = 8.9 Hz, 1H), 6.94 (s, 1H), 2.36 ppm (d, J = 1.7 Hz, 3H). **^{13}C NMR** (101 MHz, CDCl$_3$) δ 161.67 (d, J_{CF} = 247.5 Hz), 155.43, 154.96, 129.40, 128.26 (d, J_{CF} = 5.3 Hz), 126.60 (d, J_{CF} = 3.6 Hz), 125.56 (d, J_{CF} = 18.0 Hz), 124.30 (t, J_{CF} = 4.1 Hz), 123.11, 120.96, 115.76, 115.53, 111.24, 100.94 (d, J_{CF} = 1.5 Hz), 14.80 (d, J_{CF} = 3.6 Hz) ppm.

2-(Naphthalen-2-yl)benzofuran (117p). Prepared according to the general procedure E using diphenyliodonium triflate (473 mg, 1.1 mmol, 1.1 equiv) and 1-(naphthalen-2-yl)ethan-1-one (204 mg, 1.2 mmol, 1.2 equiv); the product was obtained as a white solid (102 mg, 0.42 mmol, 42%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.41 (s, 1H), 7.97 – 7.89 (m, 3H), 7.89 – 7.85 (m, 1H), 7.63 (dd, J = 15.8, 7.8 Hz, 2H), 7.54 (dd, J =

6.8, 1.4 Hz, 2H), 7.39 – 7.32 (m, 1H), 7.29 (td, J = 7.6, 0.8 Hz, 1H), 7.15 ppm (s, 1H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 156.05, 155.12, 133.53, 133.37, 129.40, 128.61, 128.54, 127.91, 127.80, 126.76, 126.58, 124.54, 123.93, 123.12, 122.91, 121.09, 111.29, 102.06 ppm.

2,5-diphenylbenzofuran (117q). Prepared according to the general procedure F using 5-bromo-2-phenylbenzofuran (273 mg, 1 mmol, 1 equiv) and phenylboronic acid (134 mg, 1.1 mmol, 1.1 equiv); The product was obtained as a pale yellow solid (194 mg, 0.72 mmol, 72 %). ^{1}**H NMR** (500 MHz, CDCl$_3$) δ 7.93 – 7.86 (m, 2H), 7.78 (d, J = 1.4 Hz, 1H), 7.64 (dd, J = 8.2, 1.1 Hz, 2H), 7.57 (s, 1H), 7.53 (d, J = 1.8 Hz, 1H), 7.49 – 7.43 (m, 4H), 7.36 (d, J = 8.9 Hz, 2H), 7.08 ppm (d, J = 0.6 Hz, 1H). ^{13}**C NMR** (126 MHz, CDCl$_3$) δ 156.73, 154.65, 141.80, 136.78, 130.52, 129.89, 128.97, 128.90, 128.80, 127.58, 127.03, 125.10, 124.15, 119.53, 111.42, 101.60 ppm.
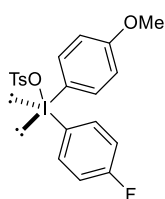
(4-Fluorophenyl)(4-methoxyphenyl)iodonium tosylate. Conducted according to a literature procedure.[203] 1-Fluoro-4-iodobenzene (231 µL, 2 mmol, 1 equiv) and *meta*-chloroperbenzoic acid (77 %, 531 mg, 2.4 mmol, 1.2 equiv) were dissolved in DCM (10 mL) in an open flask. Then anisol (260 µL, 2.4 mmol, 1.2 equiv) was added and the solution cooled to 0 °C followed by addition of *p*-toluenesulfonic acid monohydrate (457 mg, 2.4 mmol, 1.2 equiv). The reaction mixture was stirred at room temperature for 30 minutes and subsequently concentrated under reduced pressure while still cold. Et$_2$O (10 mL) was added and the mixture was stirred at room temperature for 10 min to precipitate a white solid. To ensure complete precipitation, the flask was stored in the freezer for 1 h before the solid was filtered off, washed with Et$_2$O and dried under reduced pressure; the product was obtained as a white solid (754 mg, 1.51 mmol, 73 %). **Mp.:** 140.6 °C. ^{1}**H NMR** (600 MHz, CDCl$_3$) δ 7.95 (dd, J = 8.9, 4.9 Hz, 2H), 7.90 (d, J = 9.0 Hz, 2H), 7.42 (d, J = 8.1 Hz, 2H), 6.99 (d, J = 8.0 Hz, 2H), 6.92 (t, J = 8.6 Hz, 2H), 6.77 (d, J = 9.0 Hz, 2H), 3.75 (s, 3H), 2.29 ppm (s, 3H). ^{13}**C NMR** (151 MHz, CDCl$_3$) δ 164.42 (d, J_{CF} = 253.8 Hz), 162.37, 142.19, 139.79, 137.54, 137.50 (d, J_{CF} = 6.4 Hz), 128.64, 126.06, 118.92 (d, J_{CF} = 22.7 Hz), 117.44, 109.65 (d, J_{CF} = 3.2 Hz), 104.64, 55.65, 21.3 ppm.
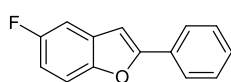
5-Fluoro-2-phenylbenzofuran (117r). Prepared according to the general procedure E using (4-fluorophenyl)(4-methoxyphenyl)iodonium tosylate (550 mg, 1.1 mmol, 1.1 equiv) and acetophenone (144 mg, 1.2 mmol, 1.2 equiv); the product was obtained as a pale yellow solid (153 mg, 0.72 mmol, 72 %). ^{1}**H NMR** (500 MHz, CDCl$_3$) δ 7.88 – 7.83 (m, 2H), 7.50 – 7.42 (m, 3H), 7.38 (t, J = 7.4 Hz, 1H), 7.24 (dd, J = 8.5, 2.6 Hz,

1H), 7.04 – 6.96 (m, 2H) ppm. ^{13}C NMR (126 MHz, CDCl$_3$) δ 160.40, 158.51, 157.82, 151.24, 130.34 – 130.00 (m), 129.02 (d, J = 7.2 Hz), 125.14, 112.10, 112.01 – 111.74 (m), 106.57, 106.37, 101.56 (d, J = 4.0 Hz) ppm.
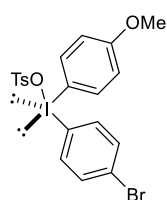
(4-Bromophenyl)(4-methoxyphenyl)iodonium tosylate. Conducted according to a literature procedure.[203] 1-Bromo-4-iodobenzene (566 mg, 2 mmol, 1 equiv) and *meta*-chloroperbenzoic acid (77 %, 531 mg, 2.4 mmol, 1.2 equiv) were dissolved in DCM (10 mL) in an open flask. Then anisol (260 µL, 2.4 mmol, 1.2 equiv) was added and the solution cooled to 0 °C followed by addition of *p*-toluenesulfonic acid monohydrate (457 mg, 2.4 mmol, 1.2 equiv). The reaction mixture was stirred at room temperature for 30 minutes and subsequently concentrated under reduced pressure while still cold. Et$_2$O (10 mL) was added and the mixture was stirred at room temperature for 10 min to precipitate a white solid. To ensure complete precipitation, the flask was stored in the freezer for 1 h before the solid was filtered off, washed with cold Et$_2$O and dried under vacuum; the product was obtained as a white solid (963 mg, 1.72 mmol, 86 %). **Mp.:** 195.6 °C. ^{1}**H NMR** (600 MHz, CDCl$_3$) δ 7.89 (d, J = 8.9 Hz, 2H), 7.78 (d, J = 8.6 Hz, 2H), 7.57 – 7.52 (m, 2H), 7.40 (d, J = 8.5 Hz, 2H), 7.07 (d, J = 7.9 Hz, 2H), 6.84 (d, J = 8.7 Hz, 2H), 3.80 (s, 3H), 2.33 ppm (s, 3H). ^{13}**C NMR** (151 MHz, CDCl$_3$) δ 162.74, 140.53, 137.61, 136.14, 134.83, 133.48, 128.88, 126.95, 126.20, 117.82, 113.95, 103.80, 55.77, 21.50 ppm.
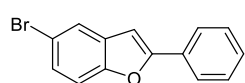
5-Bromo-2-phenylbenzofuran (117s). Prepared according to the general procedure E using (4-bromophenyl)(4-methoxyphenyl)iodonium tosylate (617 mg, 1.1 mmol, 1.1 equiv) and acetophenone (144 mg, 1.2 mmol, 1.2 equiv); the product was obtained as a light yellow solid (126 mg, 0.46 mmol, 46 %). ^{1}**H NMR** (500 MHz, CDCl$_3$) δ 7.88 – 7.82 (m, 2H), 7.71 (d, J = 1.4 Hz, 1H), 7.46 (dd, J = 10.5, 4.7 Hz, 2H), 7.42 – 7.34 (m, 3H), 6.97 ppm (s, 1H). ^{13}**C NMR** (126 MHz, CDCl$_3$) δ 157.36, 153.74, 131.35, 130.03, 129.17, 129.01, 127.22, 125.20, 123.61, 116.12, 112.76, 100.77 ppm.
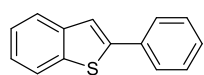
2-Phenylbenzo[*b*]thiophene (117t). Prepared according to the general procedure F using benzo[*b*]thiophen-2-ylboronic acid (99 mg, 0.55 mmol, 1.1 equiv) and iodobenzene (57 µL, 0.5 mmol, 1 equiv); the product was obtained as a white solid (100 mg, 0.48 mmol, 95%). ^{1}**H NMR** (500 MHz, CDCl$_3$) δ 7.84 (d, J = 7.9 Hz, 1H), 7.78 (d, J = 7.5 Hz, 1H), 7.76 – 7.71 (m, 2H), 7.56 (s, 1H), 7.44 (dd, J = 10.4, 4.8 Hz, 2H), 7.40 –

7.29 ppm (m, 3H). **¹³C NMR** (126 MHz, CDCl₃) δ 144.37, 140.82, 139.62, 134.42, 129.10, 128.41, 126.63, 124.65, 124.46, 123.71, 122.42, 119.58 ppm.
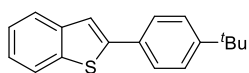
2-(4-(*tert*-Butyl)phenyl)benzo[*b*]thiophene (117u). Prepared according to the general procedure F using benzo[*b*]thiophen-2-ylboronic acid (99 mg, 0.55 mmol, 1.1 equiv) and 1-(*tert*-butyl)-4-iodobenzene (133 mg, 0.5 mmol, 1 equiv); the product was obtained as a white solid (121 mg, 0.45 mmol, 91%). **¹H NMR** (500 MHz, CDCl₃) δ 7.82 (d, *J* = 7.8 Hz, 1H), 7.77 (d, *J* = 7.6 Hz, 1H), 7.69 – 7.64 (m, 2H), 7.52 (s, 1H), 7.48 – 7.44 (m, 2H), 7.37 – 7.33 (m, 1H), 7.31 (dd, *J* = 7.8, 1.0 Hz, 1H), 1.36 ppm (s, 9H). **¹³C NMR** (126 MHz, CDCl₃) δ 151.64, 144.44, 140.91, 139.52, 131.63, 126.36, 126.04, 124.58, 124.26, 123.57, 122.38, 119.05, 34.84, 31.40 ppm.
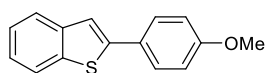
2-(4-Methoxyphenyl)benzo[*b*]thiophene (117v). Prepared according to the general procedure F using benzo[*b*]thiophen-2-ylboronic acid (178 mg, 1 mmol, 1.1 equiv) and 4-iodoanisol (239 mg, 1 mmol, 1 equiv); the product was obtained as a white solid (122 mg, 0.51 mmol, 51%). **¹H NMR** (500 MHz, CDCl₃) δ 7.64 (d, *J* = 7.7 Hz, 1H), 7.57 (d, *J* = 7.7 Hz, 1H), 7.51 – 7.44 (m, 2H), 7.14 (m, 2H), 7.09 (s, 1H), 6.82 – 6.77 (m, 2H), 3.69 ppm (s, 3H). **¹³C NMR** (126 MHz, CDCl₃) δ 159.91, 144.27, 141.02, 139.30, 127.89, 127.18, 124.59, 124.08, 123.39, 122.33, 118.33, 114.48, 55.55 ppm.
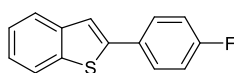
2-(4-Fluorophenyl)benzo[*b*]thiophene (117w). Prepared according to the general procedure F using benzo[*b*]thiophen-2-ylboronic acid (99 mg, 0.55 mmol, 1.1 equiv) and 1-fluoro-4-iodobenzene (59 µL, 0.5 mmol, 1 equiv). **¹H NMR** (500 MHz, CDCl₃) δ 7.83 (d, *J* = 7.9 Hz, 1H), 7.77 (d, *J* = 7.5 Hz, 1H), 7.71 – 7.65 (m, 2H), 7.48 (s, 1H), 7.44 – 7.44 (m, 2H), 7.13 ppm (t, *J* = 8.7 Hz, 2H). **¹³C NMR** (126 MHz, CDCl₃) δ 162.89 (d, *J* = 248.4 Hz), 143.19, 140.79, 139.55, 128.31 (d, *J* = 8.1 Hz), 124.75, 124.52, 123.69, 122.39, 119.57 (d, *J* = 1.2 Hz), 116.19, 116.01 ppm.
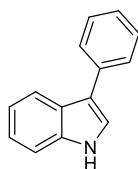
3-Phenyl-1*H*-indole (119a). Conducted according to a literature procedure.[204] A mixture of phenylacetaldehyde (583 µL, 5 mmol, 1 equiv) and phenylhydrazine (492 µL, 5 mmol, 1 equiv) was stirred for 1 h and then heated to 100°C for 30 min. A solution of ZnCl₂ (1.23 g, 9 mmol, 1.8 equiv) in ethanol (5.4 mL) was added to the reaction mixture and stirred at 100°C for 1 h. After cooling to room temperature, the reaction mixture was filtered and the solvent was removed under reduced pressure. HCl (4%, 40 mL) was added to the residue and extracted with DCM (3×30 mL). The combined organic layers were dried over MgSO₄ and concentrated under reduced pressure. Purification

by silica gel column chromatography (eluent: petroleum ether / DCM) afforded the product. The compound was obtained as pale an orange solid (830 mg, 4.3 mmol, 86%). **1H NMR** (700 MHz, CDCl$_3$) δ 8.21 (s, 1H), 7.97 (d, J = 8.0 Hz, 1H), 7.70 (d, J = 7.2 Hz, 2H), 7.50 – 7.41 (m, 3H), 7.37 (d, J = 2.4 Hz, 1H), 7.31 (t, J = 7.4 Hz, 1H), 7.27 (t, J = 7.4 Hz, 1H), 7.24 – 7.20 ppm (m, 1H). **13C NMR** (176 MHz, CDCl$_3$) δ 136.80, 135.69, 128.90, 127.65, 126.13, 125.91, 122.57, 121.88, 120.47, 119.97, 118.54, 111.53 ppm.
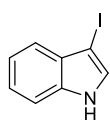
3-Iodo-1*H*-indole. Conducted according to a literature procedure.[205] A solution of I$_2$ (2.17 g, 8.54 mmol, 1 equiv) in DMF (10 mL) was added dropwise to a solution of 1*H*-indole (1 g, 8.54 mmol, 1 equiv) and KOH (1.19 g, 21.34 mmol) in DMF (10 mL) at room temperature and stirred for 1 h. The reaction mixture was poured into ice and water (100 mL) containing ammonia (0.5%) and sodium metabisulphite (0.1% aqueous solution). The precipitate was filtered, washed with cold water and dried under vacuum. The compound was obtained as an orange solid (1.746 g, 7.18 mmol, 84%). **1H NMR** (500 MHz, CDCl$_3$) δ 8.31 (s, 1H), 7.48 (d, J = 7.7 Hz, 1H), 7.37 (d, J = 7.7 Hz, 1H), 7.26 ppm (m, 3H). **13C NMR** (126 MHz, CDCl$_3$) δ 135.69, 129.87, 128.51, 123.31, 121.11, 120.93, 111.38, 57.69 ppm.
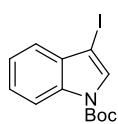
***tert*-Butyl 3-iodo-1*H*-indole-1-carboxylate.** Conducted according to a literature procedure.[206] 3-Iodo-1*H*-indole (1.74 g, 7.18 mmol, 1 equiv) was dissolved in DCM (33 mL), treated with Boc$_2$O (1.725 g, 7.9 mmol), NEt$_3$ (3 mL), and DMAP (44 mg, 0.36 mmol, 0.05 equiv) and stirred at room temperature for 1 h. The solution was then washed twice with sodium metabisulphite (5% aqueous solution), dried over MgSO$_4$ and concentrated under reduced pressure. The residue was purified by silica gel chromatography (petroleum ether / EtOAc). The compound was obtained as an orange oil (2.38 g, 6.94 mmol, 96%). **1H NMR** (500 MHz, CDCl$_3$) δ 8.13 (d, J = 6.5 Hz, 1H), 7.73 (s, 1H), 7.38 (m, 2H), 7.32 (td, J = 7.6, 1.0 Hz, 1H), 1.67 ppm (s, 9H). **13C NMR** (126 MHz, CDCl$_3$) δ 148.85, 134.97, 132.21, 130.21, 125.49, 123.46, 121.63, 115.19, 84.46, 65.59, 28.29 ppm.
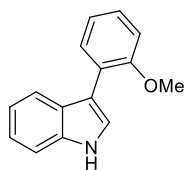
3-(2-Methoxyphenyl)-1*H*-indole (119b). Conducted according to a literature procedure.[207] A suspension of *tert*-butyl 3-iodo-1*H*-indole-1-carboxylate (343 mg, 1 mmol, 1 equiv), Pd(PPh$_3$)$_4$ (58 mg, 0.05 mmol, 0.05 equiv), 3-chlorophenylboronic acid (181 mg, 1.1 mmol, 1.1 equiv) and sodium carbonate (216 mg, 2 mmol, 2 equiv) in a 3:1 mixture of 1,4-dioxane and water (10 mL) was degassed with a stream of nitrogen for 10 minutes. The reaction was heated at reflux for 3 h.

DCM (10 mL) and water (10 mL) were added and the layers were separated. The aqueous phase was two more times extracted with DCM (2x10 mL) and the combined organic layers were dried over MgSO$_4$. The filtrate was concentrated under reduce pressure and the residue was purified by column chromatography (eluent petroleum ether / DCM). The purified material was dissolved in dry DCM (5 mL), trifluoroacetic acid (1.5 mL, 20 mmol, 20 equiv) was added at 0 °C and stirring was continued for 2 h at room temperature. After that time, the solvent was removed under reduced pressure and the products were purified by silica gel column chromatography (eluent petroleum ether / DCM). The compound was obtained as white solid (37 mg, 0.17 mmol, 17%). **^{1}H NMR** (700 MHz, CDCl$_3$) δ 8.22 (s, 1H), 7.80 (d, J = 8.1 Hz, 1H), 7.64 (dd, J = 7.5, 1.6 Hz, 1H), 7.49 (d, J = 2.4 Hz, 1H), 7.41 (d, J = 8.1 Hz, 1H), 7.31 (dd, J = 8.1, 1.6 Hz, 1H), 7.23 (dd, J = 11.1, 4.0 Hz, 1H), 7.19 – 7.15 (m, 1H), 7.08 (td, J = 7.4, 0.9 Hz, 1H), 7.05 (d, J = 8.2 Hz, 1H), 3.87 ppm (s, 3H). **^{13}C NMR** (176 MHz, CDCl$_3$) δ 156.79, 136.19, 130.65, 127.39, 126.77, 124.34, 124.24, 122.16, 120.84, 120.66, 120.05, 113.62, 111.34, 111.30, 55.60 ppm.
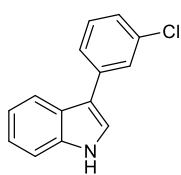
3-(3-Chlorophenyl)-1*H*-indole (119c). Conducted according to a literature procedure.[207] A suspension of *tert*-butyl 3-iodo-1*H*-indole-1-carboxylate (343 mg, 1 mmol, 1 equiv), Pd(PPh$_3$)$_4$ (58 mg, 0.05 mmol, 0.05 equiv), 3-chlorophenylboronic acid (181 mg, 1.1 mmol, 1.1 equiv) and sodium carbonate (216 mg, 2 mmol, 2 equiv) in a 3:1 mixture of 1,4-dioxane and water (10 mL) was degassed with a stream of nitrogen for 10 minutes. The reaction was heated at reflux for 3 h. DCM (10 mL) and water (10 mL) were added and the layers were separated. The aqueous phase was two more times extracted with DCM (2x10 mL) and the combined organic layers were dried over MgSO$_4$. The filtrate was concentrated under reduce pressure and the residue was purified by column chromatography (eluent petroleum ether / DCM). The purified material was dissolved in dry DCM (5 mL) and trifluoroacetic acid (1.5 mL, 20 mmol, 20 equiv) was added at 0 °C and stirring was continued for 2 h at room temperature. After that time, the solvent was removed under reduced pressure and the products were purified by silica gel column chromatography (eluent petroleum ether / DCM). The compound was obtained as yellow solid (61.5 mg, 0.27 mmol, 27%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.27 (s, 1H), 7.94 (d, J = 7.9 Hz, 1H), 7.67 (t, J = 1.6 Hz, 1H), 7.57 (d, J = 7.7 Hz, 1H), 7.45 (d, J = 8.1 Hz, 1H), 7.41 – 7.34 (m, 2H), 7.31 – 7.26 (m, 2H), 7.24 ppm (dd, J = 11.1, 4.0 Hz, 1H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 137.54, 136.72, 134.66, 130.11, 127.40, 126.04, 125.60, 125.53, 122.80, 122.31, 120.75, 119.70, 117.17, 111.65, ppm.
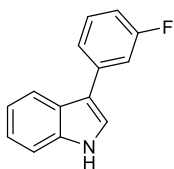
3-(3-Fluorophenyl)-1*H*-indole (119d). Conducted according to a literature procedure.[207] A suspension of *tert*-butyl 3-iodo-1*H*-indole-1-carboxylate (343 mg, 1 mmol, 1 equiv), Pd(PPh$_3$)$_4$ (58 mg, 0.05 mmol, 0.05 equiv), 3-fluorophenylboronic acid (162 mg, 1.1 mmol, 1.1 equiv) and sodium carbonate (216 mg, 2 mmol, 2 equiv) in a 3:1 mixture of 1,4-dioxane and water (10 mL) was degassed with a stream of nitrogen for 10 minutes. The reaction was heated at reflux for 3 h. DCM (10 mL) and water (10 mL) were added and the layers were separated. The aqueous phase was two more times extracted with DCM (2x10 mL) and the combined organic layers were dried over MgSO$_4$. The filtrate was concentrated under reduce pressure and the residue was purified by column chromatography (eluent petroleum ether / DCM). The purified material was dissolved in dry DCM (5 mL) and trifluoroacetic acid (1.5 mL, 20 mmol, 20 equiv) was added at 0 °C and stirring was continued for 2 h at room temperature. After that time, the solvent was removed under reduced pressure and the products were purified by silica gel column chromatography (eluent petroleum ether / DCM). The compound was obtained as brown solid (42.5 mg, 0.2 mmol, 20%). **¹H NMR** (400 MHz, CDCl$_3$) δ 8.25 (s, 1H), 7.96 (d, *J* = 7.9 Hz, 1H), 7.54 – 7.33 (m, 5H), 7.34 – 7.18 (m, 2H), 7.00 ppm (td, *J* = 8.2, 2.0 Hz, 1H). **¹³C NMR** (101 MHz, CDCl$_3$) δ 163.39 (d, *J* = 244.8 Hz), 137.95 (d, *J* = 8.3 Hz), 136.78, 130.29 (d, *J* = 8.7 Hz), 125.59, 123.10 (d, *J* = 2.7 Hz), 122.79, 122.30, 120.75, 119.76, 117.43 (d, *J* = 2.3 Hz), 114.16 (d, *J* = 21.7 Hz), 112.79 (d, *J* = 21.2 Hz), 111.65 ppm.
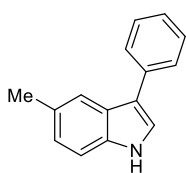
5-Methyl-3-phenyl-1*H*-indole (119e). Conducted according to a literature procedure.[204] A mixture of phenylacetaldehyde (246 µL, 2.5 mmol, 1 equiv) and tolylhydrazine hydrochloride (397 mg, 2.5 mmol, 1 equiv) was stirred for 1 h and was then heated to 100°C for 30 min. A solution of ZnCl$_2$ (613 mg, 4.5 mmol, 1.8 equiv) in ethanol (2.7 mL) was added to the reaction mixture and stirred at 100°C for 1 h. After cooling to room temperature, the reaction mixture was filtered and the solvent was removed under reduced pressure. HCl (4%, 20 mL) was added to the residue and extracted with DCM (3×15 mL). The combined organic layers were dried over MgSO$_4$ and concentrated under reduced pressure. Purification by silica gel column chromatography (eluent: petroleum ether / DCM) afforded the product. The compound was obtained as yellow solid. **¹H NMR** (700 MHz, CDCl$_3$) δ 8.12 (s, 1H), 7.74 (s, 1H), 7.68 (d, *J* = 7.4 Hz, 2H), 7.46 (t, *J* = 7.7 Hz, 2H), 7.35 – 7.31 (m, 2H), 7.30 (t, *J* = 7.4 Hz, 1H), 7.09 (d, *J* = 8.2 Hz, 1H), 2.49 ppm (s, 3H). **¹³C NMR** (176 MHz, CDCl$_3$) δ 135.86, 135.12, 129.76, 128.86, 127.65, 126.14, 126.02, 124.16, 122.03, 119.56, 118.07, 111.16, 21.76 ppm.
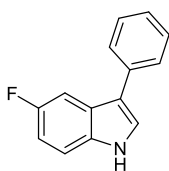
5-Fluoro-3-phenyl-1*H*-indole (119f). Conducted according to a literature procedure.[204] A mixture of phenylacetaldehyde (246 µL, 2.5 mmol, 1 equiv) and 4-fluorophenylhydrazine hydrochloride (406 mg, 2.5 mmol, 1 equiv) was stirred for 1 h and was then heated to 100°C for 30 min. A solution of $ZnCl_2$ (613 mg, 4.5 mmol, 1.8 equiv) in ethanol (2.7 mL) was added to the reaction mixture and stirred at 100°C for 1 h. After cooling to room temperature, the reaction mixture was filtered and the solvent was removed under reduced pressure. HCl (4%, 20 mL) was added to the residue and extracted with DCM (3×15 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by silica gel column chromatography (eluent: petroleum ether / DCM) afforded the product. The compound was obtained as pale orange solid (830 mg, 4.3 mmol, 86%). **^{1}H NMR** (700 MHz, $CDCl_3$) δ 8.22 (s, 1H), 7.63 (d, J = 7.4 Hz, 2H), 7.59 (dd, J = 9.9, 2.3 Hz, 1H), 7.46 (t, J = 7.7 Hz, 2H), 7.41 (d, J = 2.5 Hz, 1H), 7.35 (m, 1H), 7.31 (t, J = 7.4 Hz, 1H), 7.01 ppm (m, 1H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 158.58 (d, J_{CF} = 234.9 Hz), 135.21, 133.29, 129.01, 127.43, 126.34, 126.29 (d, J_{CF} = 9.8 Hz), 123.54, 118.76 (d, J_{CF} = 4.7 Hz), 112.13 (d, J_{CF} = 9.7 Hz), 111.03 (d, J_{CF} = 26.4 Hz), 104.97 ppm (d, J_{CF} = 24.1 Hz).
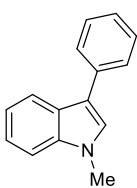
1-Methyl-3-phenyl-1*H*-indole (119g). Under argon atmosphere, 3-phenyl-1*H*-indole (195 mg, 1 mmol, 1 equiv) was dissolved in dry DMF (4 mL) and NaH, 60% dispersion in mineral oil (60 mg, 1.5 mmol, 1 equiv) was added at 0 °C in portions. Stirring was continued at 0 °C for 30 minutes and after that time methyl iodide (126 µL, 2 mmol, 2 equiv) was added dropwise to the reaction. The reaction mixture was stirred at room temperature for 12 h. Afterwards, the reaction was poured into cold water (50 mL) and extracted three times with EtOAc (3x15 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Silica gel column chromatography proved the pure product (eluent: petroleum ether / ethyl acetate). The compound was obtained as pale yellow oil (184 mg, 0.89 mmol, 89%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.96 (d, J = 8.0 Hz, 1H), 7.67 (dd, J = 8.2, 1.1 Hz, 2H), 7.45 (t, J = 7.7 Hz, 2H), 7.38 (d, J = 8.2 Hz, 1H), 7.32 – 7.23 (m, 3H), 7.23 – 7.18 (m, 1H), 3.85 ppm (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 137.57, 135.78, 128.88, 127.45, 126.69, 126.25, 125.83, 122.09, 120.06, 120.01, 116.81, 109.67, 33.05 ppm.
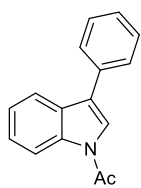
1-(3-Phenyl-1*H*-indol-1-yl)ethan-1-one (119h). Under argon atmosphere, 3-phenyl-1*H*-indole (195 mg, 1 mmol, 1 equiv) was dissolved in dry DMF (4 mL) and NaH, 60% dispersion in mineral oil (60 mg, 1.5 mmol, 1 equiv) was added at 0 °C in portions. Stirring was continued at 0 °C for 30 minutes and after that time acetyl chloride (144 μL, 2 mmol, 2 equiv) was added dropwise to the reaction. The reaction mixture was stirred at room temperature for 12 h. Afterwards, the reaction was poured into cold water (50 mL) and extracted three times with EtOAc (3x15 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Silica gel column chromatography proved the pure product (eluent: petroleum ether / ethyl acetate). The compound was obtained as pale yellow solid (231 mg, 0.89 mmol, 89%). **¹H NMR** (500 MHz, $CDCl_3$) δ 8.53 (d, *J* = 7.4 Hz, 1H), 7.82 (d, *J* = 7.8 Hz, 1H), 7.70 – 7.60 (m, 2H), 7.50 (dd, *J* = 14.3, 6.9 Hz, 3H), 7.46 – 7.37 (m, 2H), 7.38 – 7.32 (m, 1H), 2.69 ppm (s, 3H). **¹³C NMR** (126 MHz, $CDCl_3$) δ 168.74, 136.41, 133.47, 129.15, 129.07, 128.11, 127.70, 125.68, 124.18, 124.10, 122.18, 120.02, 116.99, 24.27 ppm.

11.4.3 Physical data of products
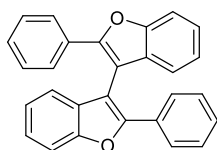
2,2'-Diphenyl-3,3'-bibenzofuran (118a). Prepared according to the general procedure F using 2-phenylbenzofuran (39 mg, 0.2 mmol, 1 equiv) and $NOBF_4$ (2.4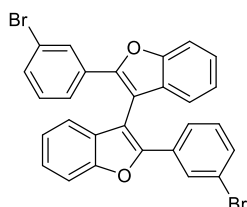 mg, 0.02 mmol, 10 mol %) in 4:1 MeCN / TFA; the product was obtained as a white solid (33 mg, 0.085 mmol, 85%). **MS-EI:** *m/z* (%): 386.1 (100) [M]⁺. **¹H NMR** (500 MHz, $CDCl_3$) δ 7.80 (dd, *J* = 7.9, 1.7 Hz, 4H), 7.66 (d, *J* = 8.3 Hz, 2H), 7.36 (s, 2H), 7.31 – 7.23 (m, 6H), 7.21 – 7.11 ppm (m, 4H). **¹³C NMR** (126 MHz, $CDCl_3$) δ 154.46, 152.07, 130.55, 129.57, 128.71, 128.65, 126.34, 125.05, 123.13, 120.83, 111.35, 107.78 ppm. **FT-IR:** v = 3060, 2161, 1589, 1545 cm⁻¹. The spectral data were matching with reported.[120b, 120c]

Scale up experiment: In a 250 mL round-bottom flask 2-phenylbenzofuran (1 g, 5.15 mmol, 1 equiv) was dissolved in 4:1 MeCN / TFA (51.5 mL) and cooled to 0 °C. To the stirring solution $NOBF_4$ (74 mg, 0.62 mmol, 0.12 equiv) was added at 0 °C and stirring was continued for 2 h. Afterwards, the reaction was slowly quenched with 1 M NaOH solution (150 mL) and extracted three times with DCM (3x150 mL). The combined organic layers were dried over $MgSO_4$ and the crude reaction was concentrated onto silica. The crude product was purified by silica gel column chromatography (eluent: petroleum ether / DCM), affording the title compound as white solid (790 mg, 2.05 mmol, 79%).
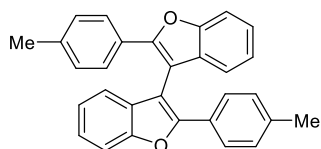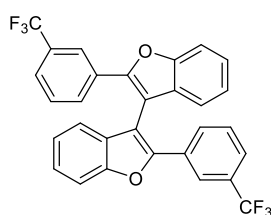
2,2'-Di-*p*-tolyl-3,3'-bibenzofuran (118b). Prepared according to the general procedure F using 2-(*p*-tolyl)benzofuran (42 mg, 0.2 mmol, 1 equiv) and NOBF$_4$ (4.6 mg, 0.04 mmol, 20 mol %) in 4:1 MeCN / TFA; the product was obtained as a white solid (37 mg, 0.09 mmol, 89%). **MS-EI:** *m/z* (%): 414.1 (100) [M]$^+$. **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.68 (d, *J* = 8.3 Hz, 4H), 7.62 (d, *J* = 8.2 Hz, 2H), 7.34 – 7.29 (m, 2H), 7.15 – 7.08 (m, 4H), 7.06 (d, *J* = 8.1 Hz, 4H), 2.29 ppm (s, 6H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 154.24, 152.23, 138.56, 129.65, 129.34, 127.72, 126.14, 124.65, 122.92, 120.61, 111.12, 107.01, 21.37 ppm. **FT-IR:** *v* = 1450, 1340, 1254, 1067 cm^{-1}. The spectral data were matching with reported.[120b, 120c]
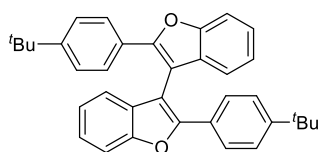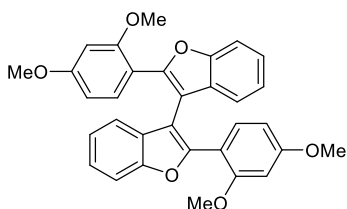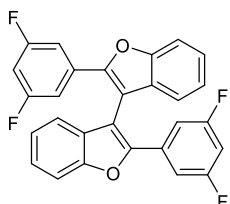

2,2'-Bis(4-(*tert*-butyl)phenyl)-3,3'-bibenzofuran (118c). Prepared according to the general procedure F using 2-(4-(tert-butyl)phenyl)benzofuran (50 mg, 0.2 mmol, 1 equiv) and NOBF$_4$ (3.4 mg, 0.03 mmol, 30 mol %) in 4:1 MeCN / TFA; the product was obtained as a white solid (44 mg, 0.09 mmol, 88%). **MS-EI:** *m/z* (%): 498.3 (100) [M]$^+$. **^{1}H NMR** (600 MHz, CDCl$_3$) δ 7.63 – 7.59 (m, 4H), 7.55 (d, *J* = 8.3 Hz, 2H), 7.26 – 7.23 (m, 2H), 7.19 – 7.17 (m, 4H), 7.10 – 7.07 (m, 2H), 7.05 – 7.02 (m, 2H), 1.17 ppm (s, 18H). **^{13}C NMR** (151 MHz, CDCl$_3$) δ 154.38, 152.34, 151.71, 130.10, 127.81, 126.03, 125.69, 124.77, 123.07, 120.68, 111.25, 107.19, 34.80, 31.26 ppm. **FT-IR:** *v* = 1609, 1451, 1255, 1207, 1030 cm^{-1}.The spectral data were matching with reported.[120b, 120c]
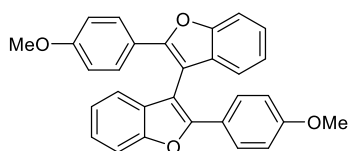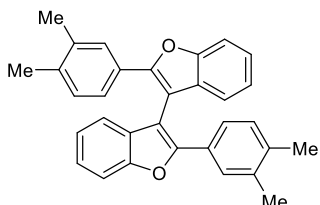

2,2'-Bis(4-methoxyphenyl)-3,3'-bibenzofuran (118d). Prepared according to the general procedure F using 2-(4-methoxyphenyl)benzofuran (45 mg, 0.2 mmol,1 equiv) and NOBF$_4$ (2.3 mg, 0.02 mmol, 10 mol %) in 4:1 DCM / TFA; the product was obtained as a white solid (41 mg, 0.092 mmol, 92%). **MS-EI:** *m/z* (%): 446.2 (100) [M]$^+$. **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.75 – 7.69 (m, 4H), 7.60 (d, *J* = 8.2 Hz, 2H), 7.30 (m, 2H), 7.15 – 7.07 (m, 4H), 6.81 – 6.76 (m, 4H), 3.75 ppm (s, 6H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 159.86, 154.27, 152.22, 129.89, 127.83, 124.50, 123.37, 123.01, 120.58, 114.17, 111.12, 106.17, 55.34 ppm. **FT-IR:** *v* = 1608, 1493, 1419, 1246, 1037 cm^{-1}. The spectral data were matching with reported.[120b, 120c]
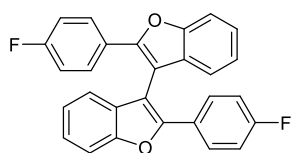
2,2'-Bis(4-fluorophenyl)-3,3'-bibenzofuran (118e). Prepared according to the general procedure F using 2-(4-fluorophenyl)benzofuran (42 mg, 0.2 mmol, 1 equiv) and NOBF$_4$ (4.6 mg, 0.04 mmol, 20 mol %) in 4:1 MeCN / TFA; the product was obtained as a white solid

(30 mg, 0.07 mmol, 71%). **MS-EI:** m/z (%): 422.1 (100) [M]$^+$. **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.75 – 7.69 (m, 4H), 7.62 (d, J = 8.3 Hz, 2H), 7.38 – 7.32 (m, 2H), 7.14 (d, J = 4.0 Hz, 4H), 6.94 (t, J = 8.7 Hz, 4H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 162.85 (d, J = 249.7 Hz), 154.44, 151.27, 129.37, 128.27 (d, J = 8.2 Hz), 126.75 (d, J = 3.3 Hz), 125.21, 123.31, 120.76, 115.90 (d, J = 21.8 Hz), 111.42, 107.24. **FT-IR:** v = 1608, 1452, 1066, 831 cm^{-1}. The spectral data were matching with reported.[120c]
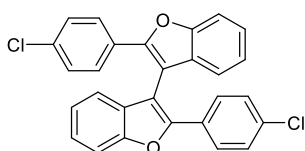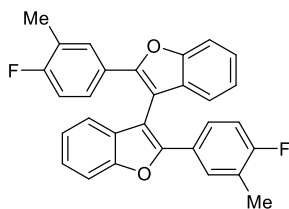
2,2'-Bis(4-chlorophenyl)-3,3'-bibenzofuran (118f). Prepared according to the general procedure F using 2-(4-chlorophenyl)benzofuran (46 mg, 0.2 mmol, 1 equiv) and NOBF$_4$ (4.6 mg, 0.04 mmol, 20 mol %) in 4:1 DCM / TFA; the product was obtained as a white solid (30 mg, 0.07 mmol, 66%). **MS-EI:** m/z (%): 454.1 (100) (C$_{28}$H$_{16}$^{35}Cl$_2$O$_2$) [M]$^+$, 456.1 (80) (C$_{28}$H$_{16}$^{35}Cl^{37}ClO$_2$) [M]$^+$, 458.1 (10) (C$_{28}$H$_{16}$^{37}Cl$_2$O$_2$) [M]$^+$. **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.99 (t, J = 1.7 Hz, 2H), 7.64 (d, J = 8.3 Hz, 2H), 7.51 (d, J = 8.0 Hz, 2H), 7.38 (m, 2H), 7.36 – 7.33 (m, 2H), 7.16 (dd, J = 8.0, 5.3 Hz, 4H), 7.03 ppm (t, J = 8.0 Hz, 2H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 154.55, 150.36, 132.32, 131.61, 130.24, 129.12, 129.05, 125.73, 124.87, 123.48, 122.91, 120.98, 111.60, 108.50 ppm. **FT-IR:** v = 1493, 1482, 1452, 1092 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{28}$H$_{15}$O$_2$Cl$_2$ = 453.04436; found 453.03096.
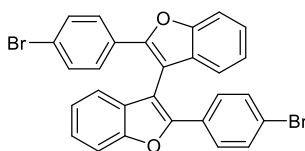
2,2'-Bis(4-bromophenyl)-3,3'-bibenzofuran (118g). Prepared according to the general procedure F using 2-(4-bromophenyl)benzofuran (55mg, 0.2 mmol, 1 equiv) and NOBF$_4$ (9.2 mg, 0.08 mmol, 0.4 equiv) in 4:1 MeCN / TFA; the product was obtained as a white solid (24 mg, 0.045 mmol, 44%). **MS-EI:** m/z (%): 541.9 (60) (C$_{28}$H$_{16}$^{79}Br$_2$O$_2$) [M]$^+$, 543.9 (100) (C$_{28}$H$_{16}$^{79}Br^{81}BrO$_2$) [M]$^+$, 545.9 (65) (C$_{28}$H$_{16}$^{81}Br$_2$O$_2$) [M]$^+$. **^{1}H NMR** (700 MHz, CDCl$_3$) δ 7.62 (dt, J = 8.3, 0.8 Hz, 2H), 7.61 – 7.57 (m, 4H), 7.38 – 7.34 (m, 6H), 7.17 – 7.09 ppm (m, 4H). **^{13}C NMR** (176 MHz, CDCl$_3$) δ 154.52, 151.03, 132.00, 129.33, 129.21, 127.73, 125.57, 123.48, 123.03, 120.82, 111.53, 108.09 ppm. **FT-IR:** v = 1450, 1255, 1206, 1071 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{28}$H$_{15}$O$_2$Br$_2$ = 544.94333; found 544.94305
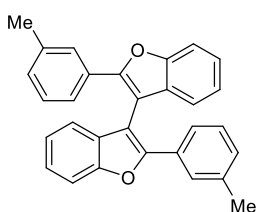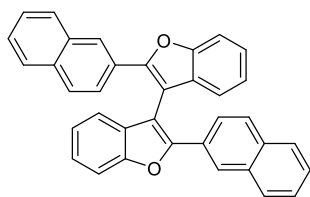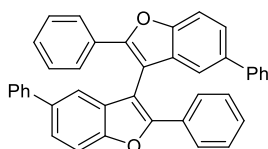
2,2'-Di-m-tolyl-3,3'-bibenzofuran (118h). Prepared according to the general procedure F using 2-(m-tolyl)benzofuran (42 mg, 0.2 mmol, 1 equiv) and NOBF$_4$ (3.6 mg, 0.03 mmol, 15 mol %) in 4:1 MeCN / TFA; the product was obtained as a yellow solid (36 mg, 0.09 mmol, 86%). **MS-EI:** m/z (%): 414.2 (100) [M]$^+$. **^{1}H NMR** (700 MHz, CDCl$_3$) δ 7.67 – 7.60 (m, 4H), 7.49

(d, J = 7.8 Hz, 2H), 7.33 (t, J = 1.3 Hz, 2H), 7.17 – 7.06 (m, 6H), 7.04 (s, 2H), 2.25 ppm (s, 6H). **^{13}C NMR** (176 MHz, CDCl$_3$) δ 154.43, 152.25, 138.24, 130.54, 129.67, 129.44, 128.58, 126.94, 124.92, 123.69, 123.04, 120.89, 111.27, 107.78, 21.59 ppm. **FT-IR:** v = 1450, 1256, 1182, 1063, 933 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{30}$H$_{21}$O$_2$ = 413.15361; found 413.15449.
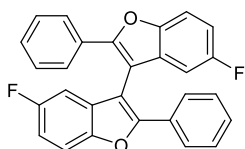
2,2'-Bis(3-bromophenyl)-3,3'-bibenzofuran (118i). Prepared according to the general procedure F using 2-(3-bromophenyl)benzofuran (55 mg, 0.2 mmol, 1 equiv) and NOBF$_4$ (4.6 mg, 0.04 mmol, 20 mol %) in 4:1 DCM / TFA; the product was obtained as a white solid (41 mg, 0.075 mmol, 75%). **MS-EI:** m/z (%): 541.9 (60) (C$_{28}$H$_{16}$^{79}Br$_2$O$_2$) [M]$^+$, 543.9 (100) (C$_{28}$H$_{16}$^{79}Br^{81}BrO$_2$) [M]$^+$, 545.9 (50) (C$_{28}$H$_{16}$^{81}Br$_2$O$_2$) [M]$^+$. **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.00 (t, J = 1.6 Hz, 2H), 7.65 (d, J = 8.3 Hz, 2H), 7.51 (d, J = 8.0 Hz, 2H), 7.40 – 7.33 (m, 4H), 7.20 – 7.14 (m, 4H), 7.04 ppm (t, J = 8.0 Hz, 2H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 154.54, 150.36, 132.31, 131.61, 130.23, 129.11, 129.04, 125.72, 124.86, 123.47, 122.91, 120.97, 111.60, 108.49 ppm. FT-IR: v = 1590, 1470, 1450, 1339, 1060, 923 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{28}$H$_{15}$O$_2$Br$_2$ = 544.94333; found 544.94414.

2,2'-Bis(3-(trifluoromethyl)phenyl)-3,3'-bibenzofuran (118j). Prepared according to the general procedure F using 2-(3-(trifluoromethyl)phenyl)benzofuran (52 mg, 0.2 mmol, 1 equiv) and NOBF$_4$ (9.2 mg, 0.08 mmol, 40 mol %) in 4:1 DCM / TFA; the product was obtained as a white solid (18 mg, 0.035 mmol, 35%). **MS-EI:** m/z (%): 522.1 (100) [M]$^+$. **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.07 (s, 2H), 7.75 (d, J = 8.0 Hz, 2H), 7.68 (d, J = 8.3 Hz, 2H), 7.46 (d, J = 7.8 Hz, 2H), 7.41 (m, 2H), 7.29 (t, J = 7.9 Hz, 2H), 7.24 – 7.16 ppm (m, 4H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 154.65, 150.35, 131.35, 131.10, 129.26 (d, J = 6.7 Hz), 128.95, 125.96, 125.19 (q, J = 3.7 Hz), 124.96, 123.62, 123.06 (q, J = 4.0 Hz), 122.80, 121.01, 111.74, 108.69 ppm. **FT-IR:** v = 1449, 1284, 1256, 1120 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{30}$H$_{15}$O$_2$F$_6$ = 521.09708; found 521.09762.
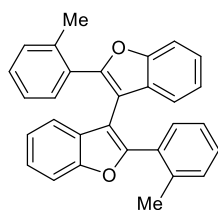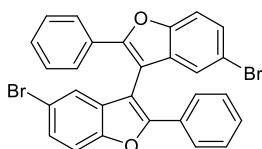
2,2'-Di-*o*-tolyl-3,3'-bibenzofuran (118k). Prepared according to the general procedure F using 2-(*o*-tolyl)benzofuran (42 mg, 0.2 mmol, 1 equiv) and NOBF$_4$ (3.6 mg, 0.03 mmol, 15 mol %) in 4:1 MeCN / TFA; the product was obtained as a white solid (38 mg, 0.09 mmol, 90%). **MS-EI:** m/z (%): 414.2 (100) [M]$^+$. **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.47 (d, J = 8.2 Hz, 2H), 7.45 – 7.42 (m, 2H), 7.30 – 7.25 (m, 2H), 7.18 (dd, J = 11.5, 4.5 Hz, 2H), 7.06 – 7.00 (m, 2H), 6.92 (d, J

= 7.7 Hz, 2H), 6.82 – 6.80 (m, 4H), 1.84 (s, 6H) ppm. **^{13}C NMR** (126 MHz, CDCl$_3$) δ 154.82, 154.21, 137.84, 130.32, 130.26, 129.95, 129.19, 128.91, 125.52, 124.47, 122.93, 120.82, 111.47, 109.47, 20.12 ppm. **FT-IR:** v = 1610, 1449, 1251, 1207, 1031 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{30}$H$_{21}$O$_2$ = 413.15361; found 413.14221.

2,2'-Bis(2,4-dimethoxyphenyl)-3,3'-bibenzofuran **(118l).** Prepared according to the general procedure F using 2-(2,4-dimethoxyphenyl)benzofuran (50 mg, 0.2 mmol, 1 equiv) and NOBF$_4$ (2.4 mg, 0.02 mmol, 10 mol %) in 4:1 MeCN / TFA; the product was obtained as a white solid (41.5 mg, 0.08 mmol, 83 %). **MS-EI:** *m/z* (%): 506.1 (100) [M]$^+$. **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.45 (d, *J* = 8.2 Hz, 2H), 7.23 (d, *J* = 7.7 Hz, 2H), 7.17 (dd, *J* = 9.7, 5.1 Hz, 2H), 7.11 (d, *J* = 8.5 Hz, 2H), 7.04 (t, *J* = 7.4 Hz, 2H), 6.23 (dd, *J* = 8.5, 2.3 Hz, 2H), 6.19 (d, *J* = 2.2 Hz, 2H), 3.68 (s, 6H), 3.29 ppm (s, 6H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 161.43, 158.43, 154.65, 150.70, 131.70, 129.50, 123.78, 122.47, 120.55, 113.14, 111.06, 110.11, 104.59, 98.61, 55.47, 55.06 ppm. **FT-IR:** v = 1610, 1437, 1208, 1029 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{32}$H$_{27}$O$_6$ = 507.18022; found 507.18029.

2,2'-Bis(3,5-difluorophenyl)-3,3'-bibenzofuran **(118m).** Prepared according to the general procedure F using 2-(3,5-difluorophenyl)benzofuran (46 mg, 0.2 mmol, 1 equiv) and NO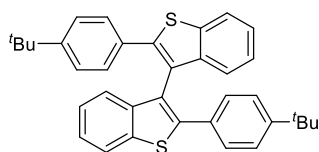BF$_4$ (4.672 mg, 0.04 mmol, 20 mol %) in 4:1 DCM / TFA; the product was obtained as a white solid (20 mg, 0.045 mmol, 44%). **MS-EI:** *m/z* (%): 458.1 (100) [M]$^+$. **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.66 (d, *J* = 8.3 Hz, 2H), 7.42 (m, 2H), 7.25 – 7.15 (m, 8H), 6.69 ppm (m, 2H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 164.16 (d, *J* = 13.0 Hz), 162.18 (d, *J* = 13.0 Hz), 154.52, 149.59 (d, *J* = 3.5 Hz), 133.06 (t, *J* = 10.6 Hz), 128.80, 126.34, 123.80, 120.91, 111.83, 109.09 (dd, *J* = 21.1, 6.8 Hz), 104.21 ppm (t, *J* = 25.5 Hz). **FT-IR:** v = 1623, 1597, 1454, 1241, 1118, 1082 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{28}$H$_{13}$O$_2$F$_4$ = 457.08462; found 457.08481.

2,2'-Bis(3,4-dimethylphenyl)-3,3'-bibenzofuran **(118n).** Prepared according to the general procedure F using 2-(3,4-dimethylphenyl)benzofuran (43 mg, 0.2 mmol, 1 equiv) and NOBF$_4$ (4.8 mg, 0.02 mmol, 20 mol %)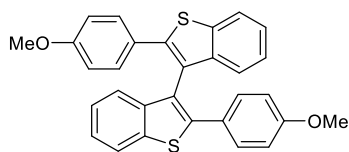 in 4:1 MeCN / TFA; the product was obtained as a white solid (29 mg, 0.07 mmol, 67%). **MS-EI:** *m/z* (%): 442.1 (100) [M]$^+$. **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.63 (s, 2H), 7.61 (d, *J* = 8.3 Hz, 2H), 7.42 (dd, *J* = 7.9, 1.6 Hz, 2H), 7.30 (m, 2H), 7.15 – 7.07 (m, 4H), 6.95 (d, *J* = 8.0 Hz, 2H), 2.19 (s, 6H), 2.16 ppm (s,

6H). ^{13}**C NMR** (126 MHz, CDCl$_3$) δ 154.29, 152.42, 137.38, 136.83, 129.98, 129.85, 128.22, 127.37, 124.63, 124.00, 122.94, 120.73, 111.15, 107.10, 19.96, 19.78 ppm. **FT-IR:** ν = 1610, 1450, 1207, 1030 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{32}$H$_{27}$O$_2$ = 443.20056; found 443.20068.

2,2'-Bis(4-fluoro-3-methylphenyl)-3,3'-bibenzofuran **(118o).** Prepared according to the general procedure F using 2-(4-fluoro-3-methylphenyl)benzofuran (45 mg, 0.2 mmol, 1 equiv) and NOBF$_4$ (4.6 mg, 0.04 mmol, 20 mol %) in 4:1 MeCN / TFA; the product was obtained as a white solid (40 mg, 0.09 mmol, 89%). **MS-EI:** m/z (%): 450.1 (100) [M]$^+$. ^{1}**H NMR** (500 MHz, CDCl$_3$) δ 7.65 (dd, J = 7.4, 1.5 Hz, 2H), 7.62 (d, J = 8.3 Hz, 2H), 7.50 – 7.42 (m, 2H), 7.34 (m, 2H), 7.14 (dd, J = 5.1, 1.2 Hz, 4H), 6.83 (t, J = 9.0 Hz, 2H), 2.19 ppm (s, 6H). ^{13}**C NMR** (126 MHz, CDCl$_3$) δ 162.47, 160.49, 154.37, 151.46, 129.70 – 129.38 (m), 126.47 (d, J = 3.6 Hz), 125.76 (d, J = 8.2 Hz), 125.30 (d, J = 17.8 Hz), 125.03, 123.19, 120.80, 115.45 (d, J = 22.9 Hz), 111.32, 107.16, 14.73 (d, J = 3.4 Hz) ppm. **FT-IR:** ν = 1490, 1452, 1234, 1117 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{30}$H$_{21}$O$_2$F$_2$ = 451.15041; found 451.15085.

2,2'-di(naphthalen-2-yl)-3,3'-bibenzofuran **(118p).** Prepared according to the general procedure F using 2-(naphthalen-2-yl)benzofuran (49 mg, 0.2 mmol, 1 equiv) and NOBF$_4$ (4.6 mg, 0.04 mmol, 20 mol %) in 4:1 MeCN / TFA; the product was obtained as a white solid (32 mg, 0.07 mmol, 66%). **ESI-MS:** calc. for [M]$^+$ C$_{36}$H$_{22}$O$_2$: 486.3; found: 486.2. ^{1}**H NMR** (500 MHz, CDCl$_3$) δ 8.40 (s, 2H), 7.82 (dd, J = 8.7, 0.9 Hz, 2H), 7.74 (dd, J = 6.7, 2.7 Hz, 2H), 7.72 – 7.68 (m, 4H), 7.63 (d, J = 8.7 Hz, 2H), 7.45 – 7.40 (m, 4H), 7.38 – 7.33 (m, 2H), 7.19 (d, J = 7.7 Hz, 2H), 7.13 – 7.07 ppm (m, 2H). ^{13}**C NMR** (126 MHz, CDCl$_3$) δ 154.62, 152.26, 133.29, 133.18, 129.77, 128.66, 128.41, 128.01, 127.74, 126.72, 126.52, 125.86, 125.24, 123.81, 123.26, 120.94, 111.38, 108.37 ppm. **FT-IR:** ν = 1451, 1257, 1055, 818 cm^{-1}. **HR-MS:** [M-H]$^-$ C$_{36}$H$_{21}$O$_2$ = 485.15361; found 485.15372.

2,2',5,5'-Tetraphenyl-3,3'-bibenzofuran (118q). Prepared according to the general procedure F using 2,5-diphenylbenzofuran (54 mg, 0.2 mmol, 1 equiv) and NOBF$_4$ (4.6 mg, 0.04 mmol, 20 mol %) in 4:1 DCM / TFA; the product was obtained as a white solid (27 mg, 0.05 mmol, 50%). **MS-EI:** m/z (%): 537.2 (100) [M]$^+$. ^{1}**H NMR** (700 MHz, CD$_2$Cl$_2$) δ 7.85 – 7.81 (m, 3H), 7.72 (d, J = 8.5 Hz, 2H), 7.60 (dd, J = 8.5, 1.9 Hz, 2H), 7.42 – 7.37 (m, 4H), 7.36 – 7.27 (m, 13H), 7.25 ppm (d, J = 7.3 Hz, 2H). ^{13}**C NMR** (126 MHz, CDCl$_3$) δ 156.73, 154.65, 141.80, 136.78,

130.52, 129.89, 128.97, 128.90, 128.80, 127.58, 127.03, 125.10, 124.15, 119.53, 111.42, 101.60 ppm. **FT-IR:** v = 2162, 1603, 1464, 1267 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{40}$H$_{25}$O$_2$ = 537.18491; found 537.18553.

5,5'-Difluoro-2,2'-diphenyl-3,3'-bibenzofuran (118r). Prepared according to the general procedure F using 5-fluoro-2-phenylbenzofuran (42 mg, 0.2 mmol, 1 equiv) and NOBF$_4$ (9.2 mg, 0.08 mmol, 0.4 equiv) in 4:1 MeCN / TFA; the product was obtained as a white solid (13 mg, 0.03 mmol, 31%). **MS-EI:** m/z (%): 422.1 (100) [M]$^+$. **^{1}H NMR** (400 MHz, CD$_2$Cl$_2$) δ 7.79 – 7.70 (m, 4H), 7.59 (dd, J = 8.9, 4.0 Hz, 2H), 7.29 (dd, J = 6.7, 3.6 Hz, 6H), 7.07 (td, J = 9.1, 2.6 Hz, 2H), 6.77 ppm (dd, J = 8.4, 2.6 Hz, 2H). **^{13}C NMR** (101 MHz, CD$_2$Cl$_2$) δ 159.99 (d, J = 238.7 Hz), 154.60, 151.24, 130.87 (d, J = 10.5 Hz), 130.54, 129.64, 129.26, 126.80, 113.27 (d, J = 26.6 Hz), 112.68 (d, J = 9.5 Hz), 107.88, 106.33 (d, J = 25.5 Hz) ppm. **FT-IR:** v = 2161, 1466, 1246, 1149 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{28}$H$_{15}$O$_2$F$_2$ = 421.10346; found 421.10307.

5,5'-Dibromo-2,2'-diphenyl-3,3'-bibenzofuran (118s). Prepared according to the general procedure F using 5-bromo-2-phenylbenzofuran (55 mg, 0.2 mmol, 1 equiv) and NOBF$_4$ (4.6 mg, 0.04 mmol, 20 mol %) in 4:1 DCM / TFA; the product was obtained as a white solid (26 mg, 0.05 mmol, 48%). **MS-EI:** m/z (%):542.0 (50) (C$_{28}$H$_{16}$^{79}Br$_2$O$_2$) [M]$^+$, 544.0 (100) (C$_{28}$H$_{16}$^{79}Br^{81}BrO$_2$) [M]$^+$, 546.0 (50) (C$_{28}$H$_{16}$^{81}Br$_2$O$_2$) [M]$^+$. **^{1}H NMR** (400 MHz, CD$_2$Cl$_2$) δ 7.79 – 7.69 (m, 4H), 7.55 (d, J = 8.7 Hz, 2H), 7.46 (dd, J = 8.7, 2.0 Hz, 2H), 7.28 ppm (dt, J = 9.7, 2.8 Hz, 8H). **^{13}C NMR** (101 MHz, CD$_2$Cl$_2$) δ 154.17, 153.77, 132.10, 130.27, 129.78, 129.33, 128.58, 126.76, 123.31, 116.80, 113.49, 106.91 ppm. **FT-IR:** v = 1578, 1439, 1259, 1204, 1065 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{28}$H$_{15}$O$_2$Br$_2$ = 544.94333; found 544.94181.
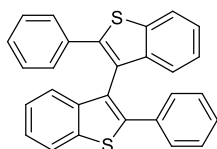
2,2'-Diphenyl-3,3'-bibenzo[*b*]thiophene (118t). Prepared according to the general procedure F using 2-phenylbenzo[*b*]thiophene (42 mg, 0.2 mmol, 1 equiv) and NOBF$_4$ (4.6 mg, 0.04 mmol, 20 mol %) in 4:1 DCM / TFA; the product was obtained as a white solid (30 mg, 0.07 mmol, 71%). **MS-EI:** m/z (%): 418.1 (100) [M]$^+$. **^{1}H NMR** (600 MHz, CDCl$_3$) δ 7.91 (d, J = 8.0 Hz, 2H), 7.37 (dd, J = 16.2, 7.8 Hz, 4H), 7.28 – 7.24 (m, 2H), 7.12 (t, J = 6.9 Hz, 2H), 7.05 ppm (m, 8H). **^{13}C NMR** (151 MHz, CDCl$_3$) δ 142.48, 140.80, 138.94, 134.18, 128.48, 128.37, 127.78, 126.54,

124.75, 124.66, 123.77, 122.33 ppm. **FT-IR:** v = 2519, 2363, 2159, 1976 cm^{-1}. The spectral data were matching with reported.[120b, 120c]

2,2'-Bis(4-(*tert*-butyl)phenyl)-3,3'-bibenzo[*b*]thiophene (118u). Prepared according to the general procedure F using 2-(4-(*tert*-butyl)phenyl)benzo[*b*]thiophene (53 mg, 0.2 mmol, 1 equiv) and NOBF$_4$ (2.6 mg, 0.02 mmol, 10 mol %) in 4:1 DCM / TFA; the product was obtained as a white solid (27 mg, 0.05 mmol, 51%). **LC-MS:** calc. for [M+H]$^+$ C$_{36}$H$_{34}$S$_2$: 531.2; found: 531.4. **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.90 (d, J = 8.0 Hz, 2H), 7.37 (dd, J = 17.7, 7.6 Hz, 4H), 7.26 (m, 2H), 7.05 (d, J = 8.5 Hz, 4H), 6.92 (d, J = 8.5 Hz, 4H), 1.24 ppm (s, 18H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 150.61, 142.48, 140.98, 138.76, 131.27, 128.09, 126.21, 125.23, 124.56, 123.78, 122.26, 34.60, 31.31 ppm. **FT-IR:** v = 1451, 1285, 1207, 1028 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{36}$H$_{35}$S$_2$ = 531.21747; found 531.21897.

2,2'-Bis(4-methoxyphenyl)-3,3'-bibenzo[*b*]thiophene (118v). Prepared according to the general procedure F using 2-(4-methoxyphenyl)benzo[*b*]thiophene (48 mg, 0.2 mmol, 1 equiv) and NOBF$_4$ (2.3 mg, 0.02 mmol, 10 mol %) in 4:1 DCM / TFA; the product was obtained as a white solid (24 mg, 0.05 mmol, 50 %). **MS-EI:** m/z (%): 478.2 (100) [M]$^+$. **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.88 (d, J = 8.0 Hz, 2H), 7.36 – 7.28 (m, 4H), 7.25 – 7.20 (m, 2H), 7.10 – 7.05 (m, 4H), 6.67 – 6.59 (m, 4H), 3.71 ppm (s, 6H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 159.31, 142.13, 140.95, 138.54, 129.58, 126.79, 125.68, 124.59, 124.48, 123.49, 122.19, 113.89, 55.32 ppm. **FT-IR:** v = 1606, 1503, 1242, 1173 cm^{-1}. The spectral data were matching with reported.[120b, 120c]
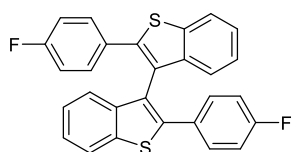
2,2'-Bis(4-fluorophenyl)-3,3'-bibenzo[*b*]thiophene (118w). Prepared according to the general procedure F using 2-(4-fluorophenyl)benzo[*b*]thiophene (46 mg, 0.2 mmol, 1 equiv) and NOBF$_4$ (2.3 mg, 10 mol %) in 4:1 DCM / TFA; the product was obtained as a white solid (32 mg, 0.07 mmol, 70 %). **MS-EI:** m/z (%): 454.1 (100) [M]$^+$. **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.99 (t, J = 1.7 Hz, 2H), 7.64 (d, J = 8.3 Hz, 2H), 7.51 (d, J = 8.0 Hz, 2H), 7.38 (m, 2H), 7.36 – 7.33 (m, 2H), 7.16 (dd, J = 8.0, 5.3 Hz, 4H), 7.03 ppm (t, J = 8.0 Hz, 2H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 152.46 (d, J = 526.2 Hz), 132.32, 131.61, 130.24, 129.08 (d, J = 8.8 Hz), 125.73, 124.87, 123.48, 122.91, 120.98, 111.60, 108.50 ppm. **FT-IR:** v = 1593, 1502, 1432, 1216, 1157 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{28}$H$_{17}$F$_2$S$_2$ = 455.07342; found 455.07394.
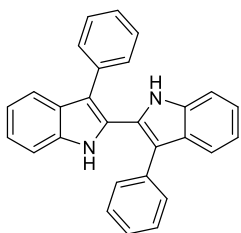
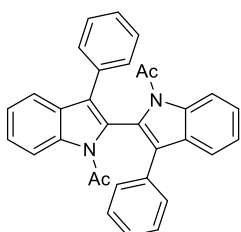**3,3'-Diphenyl-1*H*,1'*H*-2,2'-biindole (120a).** Prepared according to the general procedure F using 3-phenyl-1*H*-indole (39 mg, 0.2 mmol, 1 equiv) and NOBF$_4$ (3.6 mg, 0.03 mmol, 15 mol %) in MeCN; the product was obtained as a white solid (22 mg, 0.06 mmol, 57%). **^{1}H NMR** (700 MHz, DMSO) δ 11.56 (s, 2H), 7.64 (d, *J* = 8.0 Hz, 2H), 7.42 (d, *J* = 8.0 Hz, 2H), 7.22 – 7.14 (m, 10H), 7.12 – 7.05 ppm (m, 4H). **^{13}C NMR** (176 MHz, DMSO) δ 136.29, 134.83, 128.37, 128.14, 126.80, 126.48, 125.39, 122.14, 119.74, 118.85, 116.06, 111.67 ppm. **FT-IR:** v = 3393, 3371, 3063, 2961, 2926, 2511, 2159, 2029, 1976 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{28}$H$_{21}$N$_2$ = 385.16993; found 385.16988.
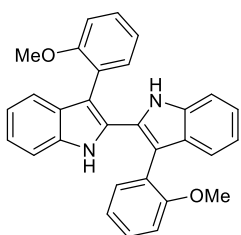
3,3'-Bis(2-methoxyphenyl)-1*H*,1'*H*-2,2'-biindole (120b). Prepared according to the general procedure F using 3-(2-methoxyphenyl)-1*H*-indole (22.5 mg, 0.1 mmol, 1 equiv) and NOBF$_4$ (1.8 mg, 0.015 mmol, 10 mol %) in MeCN; the product was obtained as a white solid (12 mg, 0.027 mmol, 54%). **^{1}H NMR** (400 MHz, Acetone) δ 10.16 (s, 2H), 7.35 (dd, *J* = 8.0, 3.8 Hz, 4H), 7.23 – 7.15 (m, 2H), 7.15 – 7.07 (m, 4H), 6.99 (t, *J* = 7.6 Hz, 2H), 6.91 (d, *J* = 8.2 Hz, 2H), 6.79 (t, *J* = 7.4 Hz, 2H), 3.50 ppm (s, 6H). **^{13}C NMR** (101 MHz, Acetone) δ 158.33, 137.45, 132.77, 129.47, 129.31, 128.47, 124.73, 122.56, 121.09, 120.82, 120.05, 113.26, 112.07, 111.89, 55.30 ppm. **FT-IR:** v = 3346, 2972, 2926, 2513, 2343, 2159, 2096, 2029, 1976 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{30}$H$_{25}$O$_2$N$_2$ = 445.19105; found 445.19023.
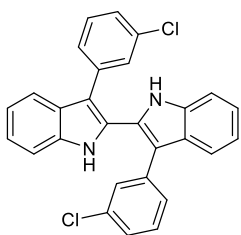
3,3'-Bis(3-chlorophenyl)-1*H*,1'*H*-2,2'-biindole (120c). Prepared according to the general procedure F using 3-(3-chlorophenyl)-1*H*-indole (23 mg, 0.1 mmol, 1 equiv) and NOBF$_4$ (1.8 mg, 0.015 mmol, 10 mol %) in MeCN; the product was obtained as a white solid (16 mg, 0.035 mmol, 71%). **^{1}H NMR** (600 MHz, Acetone) δ 10.77 (s, 2H), 7.64 (d, *J* = 8.0 Hz, 2H), 7.50 (d, *J* = 8.2 Hz, 2H), 7.27 – 7.20 (m, 2H), 7.19 – 7.11 (m, 8H), 7.08 ppm (m, 2H). **^{13}C NMR** (101 MHz, Acetone) δ 137.13, 137.02, 133.46, 129.71, 128.68, 127.65, 127.11, 126.82, 125.57, 122.86, 120.38, 118.83, 115.41, 111.70 ppm. **FT-IR:** v = 3386, 2972, 2926, 2513, 2362, 2342, 2159, 2096.89, 2029, 1976 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{28}$H$_{19}$N$_2$Cl$_2$ = 453.09198; found 453.09146 and C$_{28}$H$_{19}$N$_2$Cl^{37}Cl = 455.08903; found 455.08855.
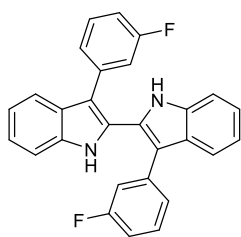
3,3'-Bis(3-fluorophenyl)-1*H*,1'*H*-2,2'-biindole (120d). Prepared according to the general procedure F using 3-(3-fluorophenyl)-1*H*-indole (21 mg, 0.1 mmol, 1 equiv) and NOBF$_4$ (1.8 mg, 0.015 mmol, 10 mol %) in MeCN; the product was obtained as a white solid (9 mg, 0.022 mmol, 43%). **^{1}H NMR** (400 MHz, Acetone) δ 10.71 (s, 2H), 7.69 (d, *J* = 8.1 Hz, 2H), 7.49 (d, *J* = 8.1 Hz, 2H), 7.27 – 7.17 (m, 4H), 7.14 (t, *J* = 7.5 Hz, 2H), 7.04 (d, *J* = 7.7 Hz, 2H), 6.96 – 6.82 ppm (m, 4H). **^{13}C NMR** (101 MHz, Acetone) δ 163.65 (d, J_{CF} = 242.7 Hz), 138.40 (d, J_{CF} = 8.4 Hz), 137.86, 130.75 (d, J_{CF} = 8.7 Hz), 127.83 (d, J_{CF} = 23.9 Hz), 125.94 (d, J_{CF} = 2.6 Hz), 123.70, 121.22, 119.85, 116.54 (d, *J* = 2.3 Hz), 116.23 (d, J_{CF} = 21.6 Hz), 113.12 (d, J_{CF} = 21.2 Hz), 112.57, 112.52 ppm. **FT-IR:** *v* = 3363, 2972, 2924, 2526, 2361, 2342, 2159, 2029, 1976 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{28}$H$_{19}$N$_2$F$_2$ = 421.15108; found 421.15057.
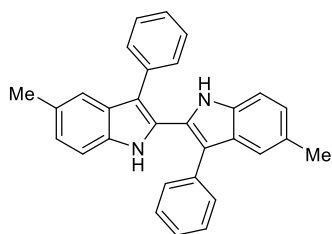
5,5'-Dimethyl-3,3'-diphenyl-1*H*,1'*H*-2,2'-biindole (120e). Prepared according to the general procedure F using 4-methyl-3-phenyl-1*H*-indole (41.5 mg, 0.2 mmol, 1 equiv) and NOBF$_4$ (3.6 mg, 0.03 mmol, 10 mol %) in MeCN; the product was obtained as a yellow solid (22 mg, 0.06 mmol, 53%). **^{1}H NMR** (400 MHz, DMSO) δ 11.41 (s, 2H), 7.42 (s, 2H), 7.29 (d, *J* = 8.2 Hz, 2H), 7.21 – 7.14 (m, 8H), 7.08 (m, 2H), 7.01 (d, *J* = 8.4 Hz, 2H), 2.38 ppm (s, 6H). **^{13}C NMR** (101 MHz, DMSO) δ 135.09, 134.68, 128.38, 128.32, 128.12, 127.02, 126.74, 125.27, 123.76, 118.38, 115.56, 111.42, 21.37 ppm. **FT-IR:** *v* = 3381, 2972, 2924, 2901, 2511, 2444, 2362, 2342, 2159, 2096, 2029, 1976 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{30}$H$_{25}$N$_2$ = 413.20123; found 413.20054.
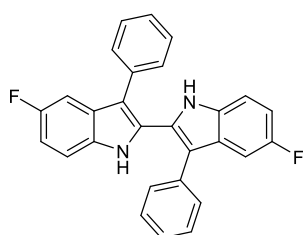
5,5'-Difluoro-3,3'-diphenyl-1*H*,1'*H*-2,2'-biindole (120f). Prepared according to the general procedure F using 4-fluoro-3-phenyl-1*H*-indole (42 mg 0.2 mmol, 1 equiv) and NOBF$_4$ (3.6 mg, 0.03 mmol, 15 mol %) in MeCN; the product was obtained as a white solid (27 mg, 0.07 mmol, 64%). **^{1}H NMR** (400 MHz, DMSO) δ 11.72 (s, 2H), 7.42 (dd, *J* = 8.8, 4.6 Hz, 2H), 7.32 (dd, *J* = 10.1, 2.3 Hz, 2H), 7.22 – 7.00 ppm (m, 12H). **^{13}C NMR** (101 MHz, DMSO) δ 157.59 (d, J_{CF} = 232.6 Hz), 134.24, 133.02, 128.43, 128.33, 128.25, 126.64 (d, J_{CF} = 9.8 Hz), 125.70, 116.41 (d, J_{CF} = 4.8 Hz), 112.90 (d, J_{CF} = 9.6 Hz), 110.64 (d, J_{CF} = 26.0 Hz), 103.50 ppm (d, J_{CF} = 23.8 Hz). **FT-IR:** *v* = 3392, 2971, 2925, 2523, 2159, 2096, 2030, 1976 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{28}$H$_{19}$N$_2$F$_2$ = 421.15108; found 421.15067.
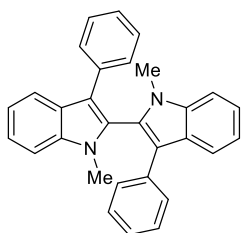
1,1'-Dimethyl-3,3'-diphenyl-1H,1'H-2,2'-biindole **(120g).** Prepared according to the general procedure F using 1-methyl-3-phenyl-1H-indole and NOBF$_4$ (3.6 mg, 0.03 mmol, 15 mol %) in 4:1 MeCN / TFA; the product was obtained as a yellow solid (23 mg, 0.055 mmol, 55%). **^{1}H NMR** (400 MHz, CDCl$_3$) δ 7.98 (d, J = 8.0 Hz, 2H), 7.40 (d, J = 7.3 Hz,

4H), 7.34 (d, J = 3.1 Hz, 4H), 7.27 (m, 6H), 7.20 (d, J = 7.3 Hz, 2H), 3.30 ppm (s, 6H). **^{13}C NMR** (101 MHz, CDCl$_3$) δ 137.80, 135.27, 128.81, 128.49, 127.67, 126.47, 126.01, 122.81, 120.43, 120.07, 118.47, 110.04, 30.37 ppm. **FT-IR:** v = 3345, 2972, 2924, 2512, 2363, 2342, 2159, 2028, 1976 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{30}$H$_{25}$N$_2$ = 413.20123; found 413.20096.

1,1'-(3,3'-Diphenyl-1H,1'H-[2,2'-biindole]-1,1'-diyl)bis(ethan-1-one) **(120h).** Prepared according to the general procedure F using 1-(3-phenyl-1H-indol-1-yl)ethan-1-one (47 mg, 0.2 mmol, 1 equiv) and NOBF$_4$ (3.6 mg, 0.03 mmol, 15 mol %) in 4:1 MeCN / TFA; the product was obtained as an orange solid (17 mg, 0.035 mmol, 36%). **^{1}H NMR** (600 MHz,

CDCl$_3$) δ 8.31 (d, J = 8.5 Hz, 2H), 7.54 (d, J = 7.8 Hz, 2H), 7.47 – 7.41 (m, 2H), 7.33 – 7.27 (m, 2H), 7.22 – 7.13 (m, 6H), 6.91 (dd, J = 8.0, 1.4 Hz, 4H), 2.43 ppm (s, 6H). **^{13}C NMR** (151 MHz, CDCl$_3$) δ 169.81, 136.70, 132.40, 129.10, 128.80, 128.54, 127.44, 126.63, 126.24, 126.23, 124.01, 120.58, 116.49, 25.84 ppm. **FT-IR:** v = 3372, 3055, 2925, 2854, 2523, 2363, 2159, 2029, 1976, 1694, 1603 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{32}$H$_{25}$O$_2$N$_2$ = 469.19105; found 469.19057.

11.5 Experimental part for the aerobic coupling of phenols and anilides

11.5.1 General procedures

General procedure G: Protection of anilines
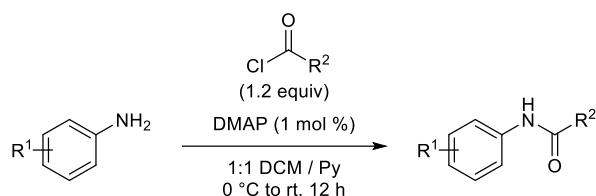
To a solution of the amine (2 mmol, 1 equiv) and 4-(dimethylamino)pyridine (0.02 mmol, 1 mol %) in 1:1 DCM / pyridine (10 mL) the acyl chloride (2.4 mmol, 1.2 equiv) was slowly added at 0 °C and the reaction was stirred at room temperature for 12 h. The reaction was neutralized adding 1 M HCl solution (40 mL), the aqueous phase was extracted three times with DCM (3x50 mL) and the combined organic layers were dried over $MgSO_4$. The crude product was purified by silica gel column chromatography (eluent: petroleum ether / EtOAc).

General procedure H: Synthesis of biphenols
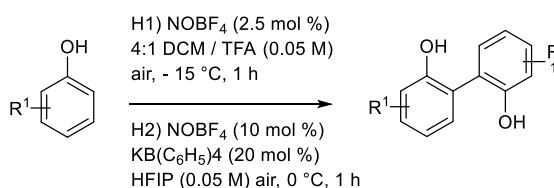
H1) To a stirring solution of phenol (0.5 mmol, 1 equiv) in 4:1 DCM / TFA (10 mL), $NOBF_4$ (1.5 mg, 12.5 μmol, 2.5 mol %) was added at -15 °C. The reaction was vigorously stirred for 1 h. The reaction was slowly quenched with saturated $NaHCO_3$ solution (30 mL) and extracted three times with DCM (3x40 mL). The combined organic layers were dried over $MgSO_4$ and the crude product was purified by silica gel column chromatography (eluent: petroleum ether / EtOAc).

H2) To a stirring solution of $KB(C_6F_5)_4$ (28 mg, 0.04 mmol, 20 mol %) in HFIP (4 mL) was added $NOBF_4$ (2.34 mg, 0.02 mmol, 10 mol %) at room temperature. The reaction mixture was stirred at room temperature for 15 Minutes and subsequently cooled to 0 °C. The reaction was vigorously stirred for 1 h. The solvent was removed under reduced pressure and the crude product was purified by silica gel column chromatography (eluent: petroleum ether / EtOAc).

General procedure I: Cross-dehydrogenative coupling of phenols
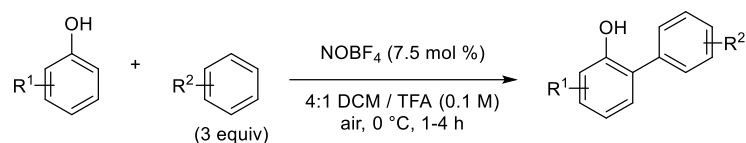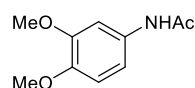
To a stirring solution of phenol (0.25 mmol, 1 equiv) and arene (0.75 mmol, 3 equiv) in 4:1 DCM / TFA (2.5 mL), NOBF₄ (2.24 mg, 18.5 µmol, 7.5 mol %) was added at 0 °C. The reaction was vigorously stirred until full conversion of starting material was monitored by TLC. The reaction was slowly quenched with saturated NaHCO₃ solution (15 mL) and extracted three times with DCM (3x20 mL). The combined organic layers were dried over MgSO₄ and the crude product was purified by silica gel column chromatography (eluent: petroleum ether / EtOAc). Phenol-anilide cross-coupling was conducted in the same manner, using phenol (0.2 mmol, 1 equiv) and anilide (0.6 mmol, 3 equiv) in 4:1 DCM / TFA (2 mL).

General procedure J: Synthesis of bisanilides
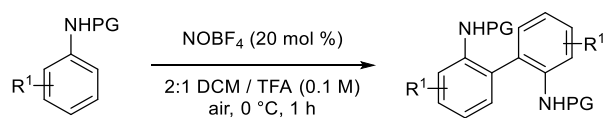
To a stirring solution of anilide (0.2 mmol, 1 equiv) in 2:1 DCM / TFA (2 mL), NOBF₄ (4.76 mg, 0.04 mmol, 20 mol %) was at 0 °C. The reaction was vigorously stirred until full conversion of starting material was monitored by TLC. The reaction was slowly quenched with saturated NaHCO₃ solution (10 mL) and extracted three times with DCM (3x20 mL). The combined organic layers were dried over MgSO₄ and the crude product was purified by silica gel column chromatography (eluent: petroleum ether / EtOAc or DCM / MeOH).
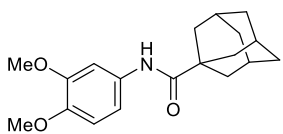
11.5.2 Physical data of starting materials

N-(3,4-dimethoxyphenyl)acetamide (124a). Prepared according to the general procedure G using 3,4-dimethoxyanilide (306 mg, 2 mmol, 1 equiv) and acetyl chloride (170 µL, 2.4 mmol, 1.2 equiv); the product was obtained as a brownish solid (223 mg, 1.14 mmol, 57%). **¹H NMR** (500 MHz, DMSO) δ 9.78 (s, 1H), 7.26 (d, J = 2.4 Hz, 1H), 7.06 (dd, J = 8.6, 2.4 Hz, 1H), 6.86 (d, J = 8.6 Hz, 1H), 3.70 (s, 3H), 3.70 (s, 3H), 1.99 ppm (s, 3H). **¹³C NMR** (126 MHz, DMSO) δ 173.00, 153.66, 149.80, 138.20, 117.20, 116.05, 109.42, 60.89, 60.50, 29.12 ppm.
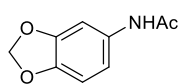
N-(benzo[d][1,3]dioxol-5-yl)acetamide (124b). Prepared according to the general procedure G using benzo[d][1,3]dioxol-5-amine (306 mg, 2 mmol, 1 equiv) and acetyl chloride (170 µL, 2.4 mmol, 1.2 equiv); the product was obtained as a brownish solid (304 mg, 1.7 mmol, 85%). **^{1}H NMR** (500 MHz, DMSO) δ 9.84 (s, 1H), 7.28 (d, J = 2.0 Hz, 1H), 6.92 (dd, J = 8.4, 2.0 Hz, 1H), 6.82 (d, J = 8.4 Hz, 1H), 5.96 (s, 2H), 1.99 ppm (s, 3H). **^{13}C NMR** (126 MHz, DMSO) δ 168.34, 147.42, 143.09, 134.24, 112.14, 108.46, 101.67, 101.34, 24.35 ppm.
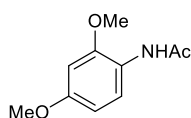
N-(2,4-dimethoxyphenyl)acetamide (124c). Prepared according to the general procedure G using 2,3-dimethoxyanilide (306 mg, 2 mmol, 1 equiv) and acetyl chloride (170 µL, 2.4 mmol, 1.2 equiv); the product was obtained as a brownish solid (304 mg, 1.7 mmol, 85%). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.01 (s, 1H), 7.64 (d, J = 8.7 Hz, 1H), 6.59 (d, J = 2.7 Hz, 1H), 6.46 (dd, J = 8.7, 2.7 Hz, 1H), 3.80 (s, 3H), 3.74 (s, 3H), 2.02 ppm (s, 3H). **^{13}C NMR** (126 MHz, DMSO) δ 168.23, 156.75, 151.53, 124.01, 120.44, 103.97, 98.73, 55.66, 55.32, 23.59 ppm.
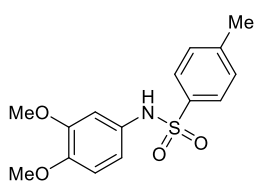
N-(3,4-dimethoxyphenyl)-4-methylbenzenesulfonamide (124d). To a solution of 3,4-dimethoxyanilide (383 mg, 2.5 mmol, 1 equiv) in distilled water (25 mL) *para*-toluenesulfonyl chloride (572, 3 mmol, 1 equiv) was added and the reaction was stirred for overnight at room temperature. The aqueous phase was three times extracted with EtOAc (3x30 mL) and the combined organic layers were washed with brine and dried over MgSO4. The crude product was purified by silica gel column chromatography (eluent: petroleum ether / EtOAc); the product was obtained as a white solid (369 mg, 1.2 mmol, 48%). **^{1}H NMR** (500 MHz, DMSO) δ 9.85 (s, 1H), 7.58 (d, J = 8.3 Hz, 2H), 7.33 (d, J = 8.3 Hz, 2H), 6.77 (d, J = 8.7 Hz, 1H), 6.67 (d, J = 2.5 Hz, 1H), 6.53 (dd, J = 8.7, 2.5 Hz, 1H), 3.65 (s, 3H), 3.62 (s, 3H), 2.33 ppm (s, 3H). **^{13}C NMR** (126 MHz, DMSO) δ 148.69, 145.97, 143.08, 136.57, 130.64, 129.60, 126.85, 113.31, 111.96, 106.25, 55.54, 55.35, 20.99 ppm.
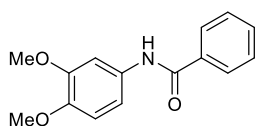
N-(3,4-dimethoxyphenyl)benzamide (124e). Prepared according to the general procedure G using 3,4-dimethoxyanilide (306 mg, 2 mmol, 1 equiv) and benzoyl chloride (277 µL, 2.4 mmol, 1.2 equiv); the product was obtained as a brownish solid (253 mg, 0.98 mmol, 48%). **^{1}H NMR** 600 MHz, DMSO) δ 10.10 (s, 1H), 8.08 – 7.86 (m, 2H), 7.57 (d, J = 7.3 Hz, 1H), 7.52 (t, J = 7.3 Hz, 2H), 7.48 (d, J = 2.3 Hz, 1H), 7.34 (dd, J = 8.7, 2.3 Hz, 1H), 6.93 (d, J = 8.7 Hz, 1H), 3.75 (s, 3H), 3.74 ppm

(s, 3H). **¹³C NMR** (151 MHz, DMSO) δ 165.55, 148.89, 145.61, 135.51, 133.18, 131.87, 128.82, 127.98, 112.78, 112.34, 105.96, 56.18, 55.85 ppm.
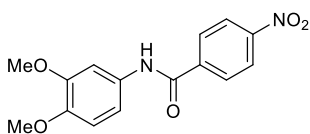
***N*-(3,4-dimethoxyphenyl)-4-nitrobenzamide (124f).** Prepared according to the general procedure G using 3,4-dimethoxyanilide (306 mg, 2 mmol, 1 equiv) and 4-nitrobenzoyl chloride (445 mg, 2.4 mmol, 1.2 equiv); the product was obtained as a yellow solid (235 mg, 0.78 mmol, 39%). **¹H NMR** (500 MHz, DMSO) δ 10.44 (s, 1H), 8.37 (d, J = 8.8 Hz, 2H), 8.17 (d, J = 8.8 Hz, 2H), 7.46 (d, J = 2.3 Hz, 1H), 7.34 (dd, J = 8.8, 2.3 Hz, 1H), 6.96 (d, J = 8.8 Hz, 1H), 3.75 ppm (s, 6H). **¹³C NMR** (126 MHz, DMSO) δ 163.84, 149.53, 148.87, 145.95, 141.15, 132.61, 129.54, 124.03, 112.92, 112.22, 105.87, 56.11, 55.85 ppm.
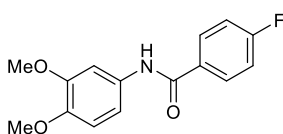
***N*-(3,4-dimethoxyphenyl)-4-fluorobenzamide (124g).** Prepared according to the general procedure G using 3,4-dimethoxyanilide (306 mg, 2 mmol, 1 equiv) and 4-fluorobenzoyl chloride (284 µL, 2.4 mmol, 1.2 equiv); the product was obtained as a white solid (290 mg, 1.05 mmol, 53%). **¹H NMR** (500 MHz, DMSO-d_6) δ 10.20 (s, 1H), 8.10 (dd, J = 8.7, 5.5 Hz, 2H), 7.53 (d, J = 2.4 Hz, 1H), 7.44 (t, J = 8.8 Hz, 2H), 7.39 (dd, J = 8.7, 2.4 Hz, 1H), 7.01 (d, J = 8.7 Hz, 1H), 3.83 (s, 3H), 3.81 ppm (s, 3H). **¹³C NMR** (126 MHz, DMSO) δ 164.43 (d, J_{CF} = 248.7 Hz), 164.42, 148.83, 145.61, 133.00, 131.90, 130.68 (d, J_{CF} = 9.1 Hz), 115.77 (d, J_{CF} = 21.8 Hz), 112.78, 112.23, 105.89, 56.13, 55.82 ppm.
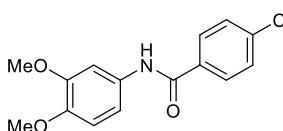
4-chloro-*N*-(3,4-dimethoxyphenyl)benzamide (124h). Prepared according to the general procedure G using 3,4-dimethoxyanilide (306 mg, 2 mmol, 1 equiv) and 4-chlorobenzoyl chloride (307 µL, 2.4 mmol, 1.2 equiv); the product was obtained as a brownish solid (319 mg, 1.63 mmol, 82%). **¹H NMR** (500 MHz, DMSO-d_6) δ 10.19 (s, 1H), 7.98 (d, J = 8.6 Hz, 2H), 7.61 (d, J = 8.6 Hz, 2H), 7.46 (d, J = 2.4 Hz, 1H), 7.33 (dd, J = 8.7, 2.4 Hz, 1H), 6.94 (d, J = 8.7 Hz, 1H), 3.76 (s, 3H), 3.74 ppm (s, 3H). **¹³C NMR** (126 MHz, DMSO) δ 164.41, 148.85, 145.69, 136.71, 134.16, 132.90, 129.96, 128.91, 112.82, 112.23, 105.89, 56.12, 55.82 ppm.

***N*-(3,4-dimethoxyphenyl)adamantane-1-carboxamide (124i).** Prepared according to the general procedure G using 3,4-dimethoxyanilide (306 mg, 2 mmol, 1 equiv) and 1-adamantanecarbonyl chloride (394 µL, 2.4 mmol, 1.2 equiv); the product was obtained as a white solid (520 mg, 1.64 mmol, 82%). **¹H NMR** (500 MHz, DMSO) δ 8.95 (s, 1H), 7.34 (d,

J = 2.3 Hz, 1H), 7.21 (dd, J = 8.7, 2.3 Hz, 1H), 6.84 (d, J = 8.7 Hz, 1H), 3.71 (s, 3H), 3.70 (s, 3H), 2.01 – 1.70 ppm (m, 15H). **^{13}C NMR** (126 MHz, DMSO) δ 176.0, 148.7, 145.06, 133.44, 112.32, 112.14, 105.64, 56.12, 55.75, 41.24, 38.94, 38.85, 36.51, 28.16, 27.84 ppm.
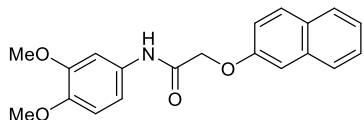
***N*-(3,4-dimethoxyphenyl)-2-(naphthalen-2-yloxy)acetamide (124j).** To a solution of 3,4-dimethoxyanilide (306 mg, 2 mmol, 1 equiv) and 2-bromoacetic acid (417 mg, 3 mmol, 1.5 equiv) in THF (4 mL) a solution of ethylcarbodiimide hydrochloride (421.7 mg, 2.2 mmol, 1.1 equiv) and 4-aminopyridine (2.44 mg, 0.02 mmol, 1 mol %) was added dropwise at 0 °C and the reaction was stirred for 12 h at room temperature. The reaction was acidified with 1 M HCl solution (50 mL) and the aqueous phase was three times extracted with EtOAc (3x50 mL). The combined organic layers were washed with brine and dried over MgSO₄. The solvent was removed under reduced pressure and the crude product was subjected to the next reaction step without further purification. To the solution of the crude 2-bromo-*N*-(3,4-dimethoxyphenyl)acetamide in acetone (8 mL) successively 2-naphthol (284 µL, 2.4 mmol, 1.2 equiv) and K₂CO₃ (553 mg, 4 mmol, 2 equiv) were added and the reaction was stirred at 60 °C for overnight. Then, the reaction mixture was quenched with water (20 mL) and three times extracted with DCM (3x30 mL). The combined organic layers were dried over MgSO₄ and the crude product was purified by column chromatography; the product was obtained as an orange solid (493 mg, 1.3 mmol, 65%). **^{1}H NMR** (500 MHz, DMSO) δ 10.00 (s, 1H), 7.88 (d, J = 8.9 Hz, 1H), 7.85 (d, J = 8.2 Hz, 1H), 7.80 (d, J = 8.2 Hz, 1H), 7.49 – 7.44 (m, 1H), 7.35 (m, 4H), 7.21 (dd, J = 8.7, 2.4 Hz, 1H), 6.91 (d, J = 8.7 Hz, 1H), 4.79 (s, 2H), 3.72 (s, 3H), 3.72 ppm (s, 3H). **^{13}C NMR** (126 MHz, DMSO) δ 166.43, 156.16, 148.93, 145.60, 134.50, 132.36, 129.86, 129.22, 128.02, 127.24, 126.99, 124.37, 119.17, 112.34, 112.17, 107.67, 105.32, 67.68, 56.12, 55.82 ppm.
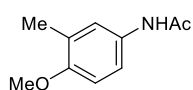
***N*-(4-Methoxy-3-methylphenyl)acetamide.** Prepared according to the general procedure G using 4-methoxy-3-methylaniline (354 mg, 2.5 mmol, 1 equiv) and acetyl chloride (213 µL, 3 mmol, 1.2 equiv); the product was obtained as a white solid (430 mg, 2.4 mmol, 96%). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.87 (s, 1H), 7.26 (d, J = 1.8 Hz, 1H), 7.06 – 6.98 (m, 2H), 3.73 (s, 3H), 2.07 (s, 3H), 2.02 ppm (s, 3H). **^{13}C NMR** (126 MHz, DMSO) δ 168.58, 157.56, 138.91, 130.54, 120.37, 110.99, 102.22, 55.42, 24.48, 16.00 ppm.
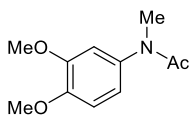
_N_-(3,4-dimethoxyphenyl)-_N_-methylacetamide. To a solution of _N_-(3,4-dimethoxyphenyl)acetamide (78 mg, 0.4 mmol, 1 equiv) in DMF (2 mL) was added NaH, 60% in mineral oil (24 mg, 0.6 mmol, 1.5 equiv) at 0 °C in portions. The reaction was stirred for 30 Minutes at 0 °C and after that time iodomethane (37 μL, 0.6 mmol, 1.5 equiv) was added and the reaction was stirred at 60 °C for overnight. After cooling to room temperature, water (20 mL) and DCM (10 mL) were successively added and the phases were separated. The aqueous phase was two more times extracted with DCM (2x10 mL), the combined organic layers were dried over MgSO$_4$ and the crude product was purified by silica gel column chromatography (eluent: petroleum ether / EtOAc); the product was obtained as an orange solid (52 mg, 0.25 mmol, 62%). **^{1}H NMR** (500 MHz, DMSO) δ 6.96 (m, 2H), 6.83 (dd, _J_ = 8.4, 2.3 Hz, 1H), 3.76 (s, 3H), 3.76 (s, 3H), 3.10 (s, 3H), 1.75 ppm (s, 3H). **^{13}C NMR** (126 MHz, DMSO) δ 169.80, 149.57, 148.33, 137.78, 119.46, 112.27, 111.48, 56.10, 56.05, 37.12, 22.59 ppm.
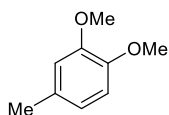
1,2-Dimethoxy-4-methylbenzene. To a solution of 2-methoxy-4-methylphenol (258 μL, 2 mmol, 1 equiv) in DMF (5 mL) was added NaH, 60% in mineral oil (120 mg, 3 mmol, 1.5 equiv) at 0 °C in portions. The reaction was stirred for 30 Minutes at 0 °C and after that time iodomethane (254 μL, 4 mmol, 2 equiv) was added and the reaction was stirred at 60 °C for overnight. After cooling to room temperature, water (50 mL) and DCM (30 mL) were successively added and the phases were separated. The aqueous phase was two more times extracted with DCM (2x30 mL), the combined organic layers were dried over MgSO$_4$ and the crude product was purified by silica gel column chromatography (eluent: petroleum ether / EtOAc); the product was obtained as a yellow oil (292 mg, 1.92 mmol, 96%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 6.77 (d, _J_ = 8.6 Hz, 1H), 6.71 (m, 2H), 3.87 (s, 3H), 3.85 (s, 3H), 2.31 ppm (s, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 148.67, 124.81, 130.40, 120.74, 112.37, 111.16, 55.96, 55.77, 21.03 ppm.

11.5.3 Physical data of products
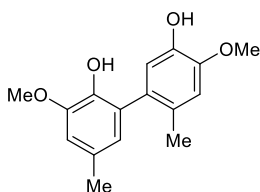
3,4'-Dimethoxy-5,6'-dimethyl-[1,1'-biphenyl]-2,3'-diol (122a). Prepared according to the general procedure H1 using 2-methoxy-4-methylphenol (64.5 μL, 0.5 mmol, 1 equiv); the product was obtained as a white solid (57 mg, 0.21 mmol, 84%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 6.82 (s, 1H), 6.78 (s, 1H), 6.70 (d, _J_ = 1.6 Hz, 1H), 6.57 (d, _J_ = 1.6 Hz, 1H), 3.92 (s, 6H), 2.32 (s, 3H), 2.15 ppm (s, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 146.26, 145.82, 143.20, 140.39,

129.99, 128.75, 128.37, 127.38, 123.35, 116.16, 112.32, 110.58, 55.98, 55.92, 21.10, 19.53 ppm. **FT-IR:** v = 2524, 2161, 2032, 1978 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{16}$H$_{19}$O$_4$ = 275.1277; found 275.1279. Spectral data matched literature characterization.[208]

**3,3'-Dibromo-5,5'-dimethyl-[1,1'-biphenyl]-2,2'-diol (122b).** Prepared according to the general procedure H2 using 2-bromo-4-methylphenol (25.5 µL, 0.2 mmol, 1 equiv); the product was obtained as a white solid (22 mg, 0.06 mmol, 60%). **¹H NMR** (500 MHz, CDCl$_3$) δ 7.28 (d, J = 2.1 Hz, 2H), 6.94 (d, J = 2.1 Hz, 2H), 5.74 (s, 2H), 2.23 ppm (s, 6H). **¹³C NMR** (126 MHz, CDCl$_3$) δ 147.13, 132.63, 131.67, 131.50, 125.36, 110.99, 20.31 ppm. **FT-IR:** v = 2493, 2344, 2159, 2030, 1976 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{14}$H$_{13}$O$_2$^{79}Br$_2$ = 370.9276; found 370.8924, C$_{14}$H$_{13}$O$_2$^{81}Br$_2$ = 372.9256; found 372.9079. Spectral data matched literature characterization.[208]
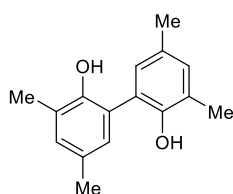
3,3',5,5'-Tetramethyl-[1,1'-biphenyl]-2,2'-diol (122c). Prepared according to the general procedure H2 using 2,4-dimethylphenol (24 µL, 0.2 mmol. 1 equiv); the product was obtained as a white solid (10 mg, 0.041 mmol, 41%). **¹H NMR** (600 MHz, CDCl$_3$) δ 6.93 (d, J = 2.2 Hz, 2H), 6.79 (d, J = 2.2 Hz, 2H), 5.01 (s, 2H), 2.21 (s, 6H), 2.20 ppm (s, 6H). **¹³C NMR** (151 MHz, CDCl$_3$) δ 149.16, 132.03, 130.03, 128.51, 125.18, 122.16, 20.45, 16.18 ppm. **FT-IR:** v = 2524, 2444, 2159, 2096, 2029, 1976 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{16}$H$_{19}$O$_2$ = 243.1379; found 243.1379. Spectral data matched literature characterization.[208]
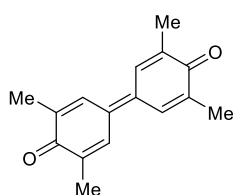
3,3',5,5'-Tetramethyl-[1,1'-bi(cyclohexylidene)]-2,2',5,5'-tetraene-4,4'-dione (122d). Prepared according to the general procedure H2 using 2,6-dimethylphenol (25 mg, 0.2 mmol, 1 equiv); the product was obtained as a red crystalline solid (11 mg, 0.046 mmol, 46%). **¹H NMR** (500 MHz, DMSO-d_6) δ 8.04 (s, 4H), 2.07 ppm (s, 12H). **¹³C NMR** (126 MHz, DMSO) δ 186.95, 138.47, 136.31, 130.80, 16.56 ppm. **FT-IR:** v = 2523, 2159, 2030, 1976, 1588 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{16}$H$_{17}$O$_2$ = 241.1223; found 241.1223. Spectral data matched literature characterization.[209]
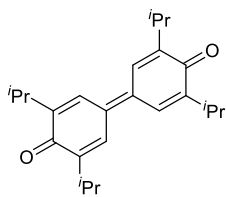
3,3',5,5'-Tetraisopropyl-[1,1'-bi(cyclohexylidene)]-2,2',5,5'-tetraene-4,4'-dione (122e). Prepared according to the general procedure H1 using 2,6-diisopropylphenol (76 mg, 0.43 mmol, 1 equiv); the product was obtained as a red crystalline solid (76 mg, 0.22 mmol, 86%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.59 (s, 4H), 3.25 – 3.07 (m, 4H), 1.15 ppm (d, J = 6.9 Hz, 24H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 185.45, 148.51, 136.38, 125.60, 27.70, 22.03 ppm. **FT-IR:** v = 2523, 2159, 2029, 1976, 1585 cm^{-1}. **HR-MS:** calc. for [M+H]$^{+}$ C$_{24}$H$_{33}$O$_2$ = 353.2475; found 353.2475. Spectral data matched literature characterization.[209]
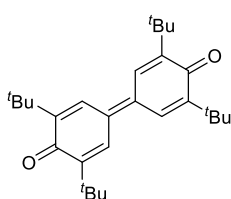
3,3',5,5'-Tetra-*tert*-butyl-[1,1'-bi(cyclohexylidene)]-2,2',5,5'-tetraene-4,4'-dione (122f). Prepared according to the general procedure H1 using 2,6-di-*tert*-butylphenol (105 mg, 0.5 mmol, 1 equiv); the product was obtained as a red amorphous solid (75 mg, 0.185 mmol, 73%). **^{1}H NMR** (400 MHz, CDCl$_3$) δ 7.64 (s, 4H), 1.29 ppm (s, 36H). **^{13}C NMR** (101 MHz, CDCl$_3$) δ 186.61, 150.59, 136.28, 126.16, 36.18, 29.75 ppm. **FT-IR:** v = 2522, 2159, 2029, 1976, 1637, 1602 cm^{-1}. **HR-MS:** calc. for [M+H]$^{+}$ C$_{28}$H$_{41}$O$_2$ = 409.3101; found 409.3098. Spectral data matched literature characterization.[210]
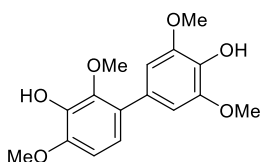
2,3',4,5'-Tetramethoxy-[1,1'-biphenyl]-3,4'-diol (122g). Prepared according to the general procedure H2 using 2,6-dimethoxyphenol (31.5 mg, 0.2 mmol, 1 equiv); the product was obtained as a white solid (14 mg, 0.046 mmol, 46%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 6.76 (d, J = 8.5 Hz, 1H), 6.72 (s, 2H), 6.65 (d, J = 8.5 Hz, 1H), 5.68 (s, 1H), 5.49 (s, 1H), 3.86 (s, 3H), 3.85 (s, 6H), 3.50 ppm (s, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 146.87, 122.55, 138.73, 133.84, 129.25, 127.97, 120.23, 106.91, 105.68, 77.25, 60.54, 56.36, 56.29 ppm. **FT-IR:** v = 2520, 2492, 2446, 2159, 2096, 2029, 1976 cm^{-1}. **HR-MS:** calc. for [M+H]$^{+}$ C$_{16}$H$_{19}$O$_6$ = 307.1176; found 307.1177. Spectral data matched literature characterization.[208]
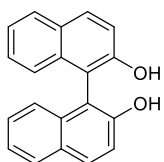
[1,1'-Binaphthalene]-2,2'-diol (122h). Prepared according to the general procedure H1 using 2-naphthol (73.5 mg, 0.5 mmol, 1 equiv); the product was obtained white solid (60 mg, 0.21 mmol, 83%). **^{1}H NMR** (400 MHz, CDCl$_3$) δ 7.88 (d, J = 8.9 Hz, 2H), 7.80 (d, J = 8.0 Hz, 2H), 7.29 (m, 4H), 7.22 (td, J = 7.6, 6.9, 1.2 Hz, 2H), 7.07 (d, J = 8.4 Hz, 2H), 4.97 ppm (s, 2H). **^{13}C NMR** (101 MHz, CDCl$_3$) δ 152.75, 133.41, 131.44, 129.46, 128.42, 127.50, 124.22, 124.06, 117.77, 110.84 ppm. **FT-**

IR: v = 2522, 2159, 2029, 1976 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{20}$H$_{15}$O$_2$ = 287.1066; found 287.1067. Spectral data matched literature characterization.[208]
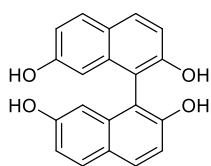
[1,1'-Binaphthalene]-2,2',7,7'-tetraol (122i). Prepared according to the general procedure H1 using naphthalene-2,7-diol (82.5 mg, 0.5 mmol, 1 equiv); the product was obtained white solid (60.5 mg, 0.19 mmol, 76%). **^{1}H NMR** (500 MHz, Acetone-d_6) δ 8.41 (s, 2H), 7.75 (m, 6H), 7.10 (d, J = 8.8 Hz, 2H), 6.89 (dd, J = 8.8, 2.4 Hz, 2H), 6.37 (d, J = 2.4 Hz, 2H). **^{13}C NMR** (126 MHz, Acetone) δ 156.82, 154.83, 137.19, 130.43, 130.11, 124.73, 116.27, 115.87, 113.65, 107.29 ppm. **FT-IR:** v = 2557, 2159, 2031, 1976, 1617 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{20}$H$_{15}$O$_4$ = 319.0964; found 319.0967. Spectral data matched literature characterization.[208]
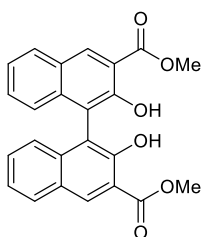
Dimethyl 2,2'-dihydroxy-[1,1'-binaphthalene]-3,3'-dicarboxylate (122j). To a stirring solution of methyl 3-hydroxy-2-naphthoate (41.3 mg, 0.2 mmol, 1 equiv) and sodium nitrite (2.7 mg, 0.04 mmol, 20 mol %) in MeCN (2 mL) CF$_3$SO$_3$H (36 µL, 0.4 mmol, 2 equiv) was added at 0 °C. Stirring was continued for 1 h and the reaction was slowly quenched with saturated NaHCO$_3$ solution (15 mL) and extracted three times with DCM (3x20 mL). The combined organic layers were dried over MgSO$_4$ and the crude product was purified by silica gel column chromatography (eluent: petroleum ether / EtOAc); the product was obtained as a white solid (16 mg, 0.04 mmol, 40%). **^{1}H NMR** (400 MHz, CDCl$_3$) δ 10.63 (s, 2H), 8.61 (s, 2H), 7.89 – 7.77 (m, 2H), 7.26 (dd, J = 6.3, 3.3 Hz, 4H), 7.08 (dd, J = 6.0, 3.6 Hz, 2H), 3.97 ppm (s, 6H). **^{13}C NMR** (101 MHz, CDCl$_3$) δ 170.57, 154.02, 137.20, 132.90, 129.80, 129.46, 127.20, 124.69, 123.98, 116.99, 114.16, 52.74 ppm. **FT-IR:** v = 2521, 2161, 2031, 1978 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{24}$H$_{19}$O$_6$ = 403.1176; found 403.1174. Spectral data matched literature characterization.[211]
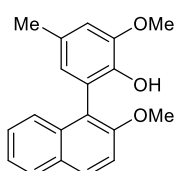
2-Methoxy-6-(2-methoxynaphthalen-1-yl)-4-methylphenol (122k). Prepared according to the general procedure I using 2-methoxy-4-methylphenol (37.2 µL, 0.25 mmol, 1 equiv) and 2-methoxynaphthalene (122 mg, 0.75 mmol, 3 equiv) in MeCN / TFA; the product was obtained as a white solid (54 mg, 0.185 mmol, 74%). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 8.02 (s, 1H), 7.94 (d, J = 9.0 Hz, 1H), 7.87 (dd, J = 6.4, 3.0 Hz, 1H), 7.48 (d, J = 9.0 Hz, 1H), 7.35 – 7.28 (m, 2H), 7.27 – 7.20 (m, 1H), 6.82 (d, J = 1.6 Hz, 1H), 6.48 – 6.36 (m, 1H), 3.84 (s, 3H), 3.77 (s, 3H), 2.26 ppm (s, 3H). **^{13}C NMR** (126 MHz, DMSO) δ 153.95, 147.47, 142.09, 133.15, 128.72,

128.50, 127.77, 127.22, 126.02, 125.01, 123.81, 123.16, 122.87, 121.56, 114.16, 111.56, 56.24, 55.64, 20.77 ppm. **FT-IR:** v = 2523, 2159, 2030, 1976 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ $C_{19}H_{19}O_3$ = 295.1328; found 295.1330. Spectral data matched literature characterization.[142d]
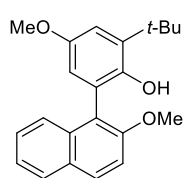
2-(*tert*-Butyl)-4-methoxy-6-(2-methoxynaphthalen-1-yl)phenol **(122l).** Prepared according to the general procedure I using 3-*tert*-butyl-4-hydroxyanisole (46 mg, 0.25 mmol, 1 equiv) and 2-methoxynaphthalene (122 mg, 0.75 mmol, 3 equiv); the product was obtained as a colourless oil (60 mg, 0.18 mmol, 71%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.85 (d, J = 9.1 Hz, 1H), 7.78 – 7.72 (m, 1H), 7.44 – 7.38 (m, 1H), 7.33 – 7.24 (m, 3H), 6.92 (d, J = 3.1 Hz, 1H), 6.52 (d, J = 3.1 Hz, 1H), 4.69 (s, 1H), 3.80 (s, 3H), 3.66 (s, 3H), 1.37 ppm (s, 9H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 154.68, 152.49, 146.51, 137.86, 133.80, 130.56, 129.45, 128.09, 127.16, 125.11, 124.11, 123.19, 118.97, 114.11, 113.62, 112.84, 56.79, 55.63, 35.13, 29.60 ppm. **FT-IR:** v = 2514, 2159, 2029, 1976 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ $C_{22}H_{25}O_3$ = 337.1798; found 337.1788.
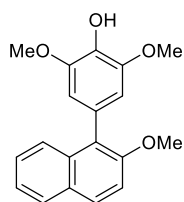
2,6-Dimethoxy-4-(2-methoxynaphthalen-1-yl)phenol **(122m).** Prepared according to the general procedure I using 2,6-dimethoxyphenol (40 mg, 0.25 mmol, 1 equiv) and 2-methoxynaphthalene (122 mg, 0.75 mmol, 3 equiv); the product was obtained as a white solid (73 mg, 0.24 mmol, 93%). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 8.44 (s, 1H), 7.95 (d, J = 9.0 Hz, 1H), 7.88 (d, J = 7.5 Hz, 1H), 7.49 (d, J = 9.0 Hz, 1H), 7.44 (d, J = 8.2 Hz, 1H), 7.38 – 7.29 (m, 2H), 6.49 (s, 2H), 3.80 (s, 3H), 3.73 ppm (s, 6H). **^{13}C NMR** (126 MHz, DMSO) δ 154.08, 148.31, 135.07, 133.80, 129.25, 128.97, 128.29, 126.79, 126.34, 125.30, 125.28, 123.76, 114.62, 108.51, 56.84, 56.49 ppm. **FT-IR:** v = 2526, 2161, 2031, 1978 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ $C_{19}H_{19}O_4$ = 311.1277; found 311.1278. Spectral data matched literature characterization.[142c]
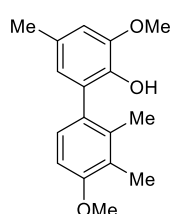
3,4'-Dimethoxy-2',3',5-trimethyl-[1,1'-biphenyl]-2-ol **(122n).** Prepared according to the general procedure I using 2-methoxy-4-methylphenol (37.2 µL, 0.25 mmol, 1 equiv) and 2,3-dimethoxyanisole (107 µL, 0.75 mmol, 3 equiv); the product was obtained as a colourless oil (56 mg, 0.21 mmol, 82%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.08 (d, J = 8.4 Hz, 1H), 6.81 (d, J = 8.4 Hz, 1H), 6.72 (d, J = 2.0 Hz, 1H), 6.60 (d, J = 2.0, 1H), 5.41 (s, 1H), 3.93 (s, 3H), 3.87 (s, 3H), 2.35 (s, 3H), 2.25 (s, 3H), 2.13 ppm (s, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 156.98, 146.27, 140.62, 136.67, 129.95, 128.73, 128.45, 127.69, 125.23, 123.65, 110.46, 107.66, 56.00, 55.54,

21.19, 17.21, 12.19 ppm. **FT-IR:** v = 2515, 2159, 2029, 1976 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ $C_{17}H_{21}O_3$ = 273.1485; found 273.1485.
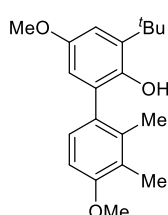
3-(*tert*-Butyl)-4',5-dimethoxy-2',3'-dimethyl-[1,1'-biphenyl]-2-ol (122o). Prepared according to the general procedure I using 3-*tert*-butyl-4-hydroxyanisole (46 mg, 0.25 mmol, 1 equiv) and and 2,3-dimethoxyanisole (107 µL, 0.75 mmol, 3 equiv); the product was obtained as a white solid (53 mg, 0.17 mmol, 67%). **¹H NMR** (500 MHz, CDCl$_3$) δ 7.03 (d, J = 8.3 Hz, 1H), 6.81 (d, J = 3.1 Hz, 1H), 6.75 (d, J = 8.3 Hz, 1H), 6.43 (d, J = 3.1 Hz, 1H), 4.59 (s, 1H), 3.79 (s, 3H), 3.67 (s, 3H), 2.14 (s, 3H), 1.98 (s, 3H), 1.34 ppm (s, 9H). **¹³C NMR** (126 MHz, CDCl$_3$) δ 157.61, 152.26, 145.62, 137.38, 136.96, 129.02, 128.60, 128.33, 126.19, 113.22, 111.76, 108.34, 55.64, 55.60, 34.99, 29.46, 16.83, 12.17 ppm. **FT-IR:** v = 2515, 2159, 2029, 1976 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ $C_{20}H_{27}O_3$ = 315.1954; found 315.1950.
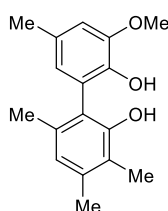
3-Methoxy-2',3',5,6'-tetramethyl-[1,1'-biphenyl]-2,4'-diol (122p). Prepared according to the general procedure I using 2-methoxy-4-methylphenol (37.2 µL, 0.25 mmol, 1 equiv) and 2,3,5-trimethylphenol (105 mg, 0.75 mmol, 3 equiv); the product was obtained as a white solid (30 mg, 0.11 mmol, 44%). **¹H NMR** (400 MHz, CDCl$_3$) δ 6.61 (d, J = 1.9 Hz, 1H), 6.50 (s, 1H), 6.35 (d, J = 1.9 Hz, 1H), 3.84 (s, 3H), 2.23 (s, 3H), 2.09 (s, 3H), 1.90 ppm (s, 6H). **¹³C NMR** (101 MHz, CDCl$_3$) δ 152.78, 146.52, 140.38, 137.03, 135.07, 129.16, 129.05, 127.16, 123.34, 119.92, 114.07, 110.45, 55.87, 21.19, 20.32, 17.30, 11.90 ppm. **FT-IR:** v = 2523, 2159, 2030, 1976 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ $C_{17}H_{21}O_3$ = 273.1485; found 273.1486.
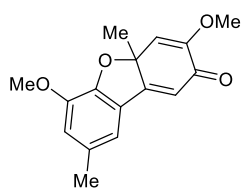
3,6-Dimethoxy-4*a*,8-dimethyldibenzo[*b*,*d*]furan-2(4*a*H)-one (123a). A) To a stirring solution of 2-methoxy-4-methylphenol (25 µL, 0.2 mmol, 1 equiv) in 1:1 DCM / HFIP (2 mL), NOBF$_4$ (3.6 mg, 0.3 mmol, 15 mol %) was added with the help of a glass capillary at 0 °C. The reaction was vigorously stirred until full conversion of starting material was monitored by TLC. The solvent was reduced under reduced pressure and the crude product was purified by silica gel column chromatography (eluent: petroleum ether / EtOAc); the product was obtained as a yellow solid (16 mg, 0.12 mmol, 59%). B) To a stirring solution of 3,4'-dimethoxy-5,6'-dimethyl-[1,1'-biphenyl]-2,3'-diol (55 mg, 0.2 mmol, 1 equiv) in in 1:1 DCM / HFIP (4 mL), NOBF$_4$ (1.2 mg, 0.1 mmol, 5 mol %) was added with the help of a glass capillary at 0 °C. The reaction was vigorously stirred until full conversion of starting material was monitored by TLC. The solvent

was reduced under reduced pressure and the crude product was purified by silica gel column chromatography (eluent: petroleum ether / EtOAc); the product was obtained as a yellow solid (44 mg, 0.081 mmol, 81%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 6.94 (s, 1H), 6.78 (s, 1H), 6.32 (s, 1H), 6.16 (s, 1H), 3.91 (s, 3H), 3.70 (s, 3H), 2.36 (s, 3H), 1.74 ppm (s, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 180.73, 167.62, 151.57, 151.19, 145.61, 133.02, 123.65, 116.70, 115.11, 114.80, 112.20, 87.90, 56.20, 55.55, 33.29, 21.49 ppm. **FT-IR:** v = 2525, 2159, 2029, 1976, 1652, 1610 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{16}$H$_{17}$O$_4$ = 273.1121; found 273.1122.
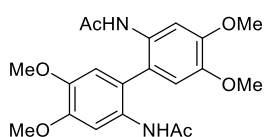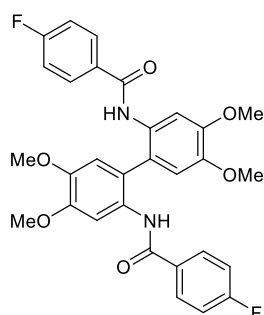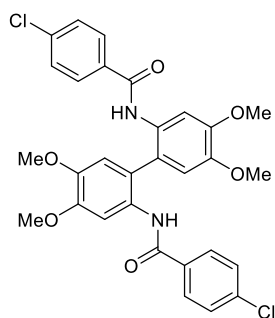
 N,N'-(4,4',5,5'-tetramethoxy-[1,1'-biphenyl]-2,2'-diyl)diacetamide (125a). Prepared according to the general procedure J using N-(3,4-dimethoxyphenyl)acetamide (39 mg, 0.2 mmol, 1 equiv); the product was obtained as a brownish solid (37 mg, 0.094 mmol, 94%). **^{1}H NMR** (500 MHz, DMSO) δ 8.65 (s, 2H), 7.19 (s, 2H), 6.71 (s, 2H), 3.75 (s, 6H), 3.73 (s, 6H), 1.83 ppm (s, 6H). **^{13}C NMR** (101 MHz, DMSO) δ 169.33, 148.29, 146.43, 129.38, 125.15, 114.33, 110.21, 56.13, 56.04, 23.56 ppm. **FT-IR:** v = 2509, 2159, 2030, 1976, 1674 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{20}$H$_{25}$N$_2$O$_6$: 389.1701; found: 389.1707. Spectral data matched literature characterization.[212]

Scale up experiment: In a 250 mL round-bottom flask N-(3,4-dimethoxyphenyl)acetamide (1 g, 5.12 mmol, 1 equiv) was dissolved in 2:1 MeCN / TFA (51.2 mL) and cooled to 0 °C. To the stirring solution NOBF$_4$ (122 mg, 1.02 mmol, 0.2 equiv) was added at 0 °C and stirring was continued for 1 h. After that time, the reaction was slowly quenched with 1 M NaOH solution (150 mL) and extracted three times with DCM (3x150 mL). The combined organic layers were dried over MgSO$_4$ and the crude product was purified by silica gel column chromatography (eluent: petroleum DCM/ MeOH), affording the title compound as brownish solid (850 mg, 2.19 mmol, 85%).
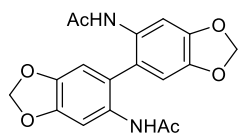
 N,N'-([5,5'-bibenzo[d][1,3]dioxole]-6,6'-diyl)diacetamide (125b). Prepared according to the general procedure J using N-(benzo[d][1,3]dioxol-5-yl)acetamide (36 mg, 0.2 mmol, 1 equiv); the product was obtained as an orange solid (21 mg, 0.06 mmol, 59%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.46 (s, 2H), 6.99 (s, 2H), 6.60 (s, 2H), 6.01 (dd, J = 8.2, 1.2 Hz, 4H), 1.96 (s, 6H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 169.45, 147.93, 145.22, 129.58, 122.84, 109.79, 105.53, 101.75, 23.91 ppm. **FT-IR:** v = 2509, 2363, 2343, 2161, 2031, 1978 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{18}$H$_{17}$N$_2$O$_6$: 357.1081; found: 357.1077.
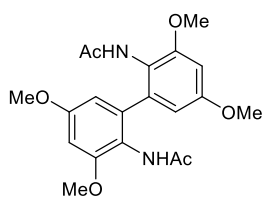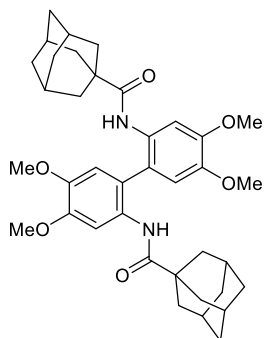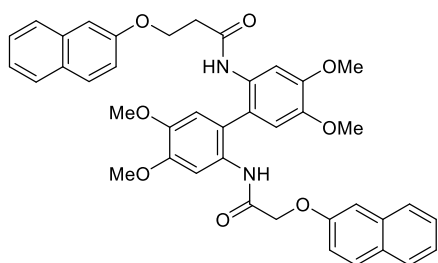
_N,N'_-(3,3',5,5'-tetramethoxy-[1,1'-biphenyl]-2,2'-diyl)diacetamide (125c). Prepared according to the general procedure J using _N_-(2,4-dimethoxyphenyl)acetamide (39 mg, 0.2 mmol, 1 equiv) using NOBF$_4$ (1.19 mg, 0.01 mmol, 5 mol %); the product was obtained as a brownish solid (21.5 mg, 0.055 mmol, 55%). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.03 (s, 2H), 7.49 (s, 2H), 6.72 (s, 2H), 3.88 (s, 6H), 3.71 (s, 6H), 2.02 ppm (s, 6H). **^{13}C NMR** (126 MHz, DMSO) δ 168.55, 154.38, 150.89, 126.24, 120.06, 118.77, 97.02, 56.29, 56.26, 24.02 ppm. **FT-IR:** v = 2523, 2159, 2030, 1976 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{20}$H$_{25}$O$_6$N$_2$ = 389.1707; found: 389.1710.
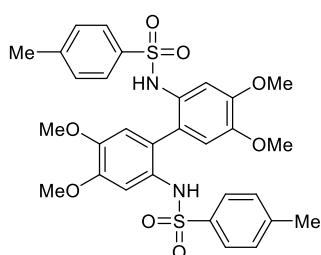
_N,N'_-(4,4',5,5'-tetramethoxy-[1,1'-biphenyl]-2,2'-diyl)bis(4-methylbenzenesulfonamide) (125d). Prepared according to the general procedure J using _N_-(3,4-dimethoxyphenyl)-4-ethylbenzenesulfon-amide (61 mg, 0.2 mmol, 1 equiv); the product was obtained as a brownish solid (33 mg, 0.053 mmol, 53%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.62 (d, J = 8.2 Hz, 4H), 7.36 (d, J = 8.2 Hz, 4H), 6.24 (s, 2H), 5.99 (s, 2H), 4.03 (s, 6H), 3.81 (s, 6H), 2.55 ppm (s, 6H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 149.57, 146.62, 144.34, 136.24, 129.82, 127.93, 127.14, 120.82, 112.88, 106.34, 56.13, 56.02, 21.64 ppm. **FT-IR:** v = 2522, 2159, 2029, 1976, 1507 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{30}$H$_{33}$N$_2$O$_8$S$_2$: 613.1672; found: 613.1679.
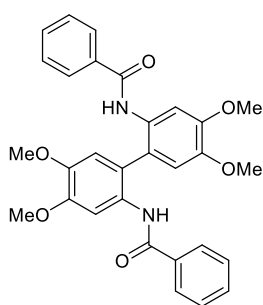
_N,N'_-(4,4',5,5'-tetramethoxy-[1,1'-biphenyl]-2,2'-diyl)dibenzamide (125e). Prepared according to the general procedure J using _N_-(3,4-dimethoxyphenyl)benzamide (51 mg, 0.2 mmol, 1 equiv); the product was obtained as a light brown solid (38 mg, 0.075 mmol, 75%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.11 (s, 2H), 7.87 (s, 2H), 7.57 (d, J = 7.4 Hz, 4H), 7.47 (t, J = 7.4 Hz, 2H), 7.38 (t, J = 7.6 Hz, 4H), 6.79 (s, 2H), 4.00 (s, 6H), 3.85 ppm (s, 6H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 165.66, 149.24, 146.17, 134.20, 132.01, 129.58, 128.90, 126.77, 120.09, 112.77, 106.35, 56.22, 56.18 ppm. **FT-IR:** v = 2529, 2360, 2342, 2159, 2030, 1976, 1654. cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{30}$H$_{29}$N$_2$O$_6$: 513.2020; found: 513.2016. Spectral data matched literature characterization.[212]
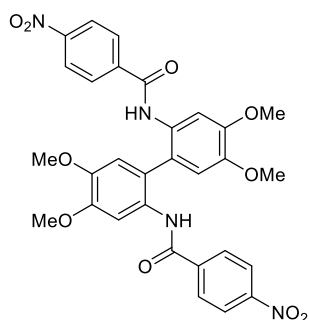
N,N′-(4,4′,5,5′-tetramethoxy-[1,1′-biphenyl]-2,2′-diyl)bis(4-nitrobenzamide) (125f). Prepared according to the general procedure J using *N*-(3,4-dimethoxyphenyl)-4-nitrobenzamide (60 mg, 0.2 mmol, 1 equiv); the product was obtained as a yellow solid (34 mg, 0.058 mmol, 58%). **^{1}H NMR** (400 MHz, DMSO) δ 9.99 (s, 2H), 8.64 (d, *J* = 8.7 Hz, 4H), 8.27 (d, *J* = 8.7 Hz, 4H), 7.52 (s, 2H), 7.16 (s, 2H), 4.10 (s, 6H), 4.04 ppm (s, 6H). **^{13}C NMR** (101 MHz, DMSO) δ 164.82, 149.64, 148.55, 147.20, 140.42, 129.19, 128.55, 127.56, 124.12, 113.98, 111.01, 56.14 ppm. **FT-IR:** v = 2519, 2364, 2344, 2161, 2031, 1978 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{30}$H$_{27}$N$_4$O$_{10}$: 603.1721; found: 603.1728.

N,N'-(4,4',5,5'-tetramethoxy-[1,1'-biphenyl]-2,2'-diyl)bis(4-fluorobenzamide) (125g). Prepared according to the general procedure J using *N*-(3,4-dimethoxyphenyl)-4-fluorobenzamide (55 mg, 0.2 mmol, 1 equiv) in MeCN / TFA; the product was obtained as a reddish solid (21 mg, 0.04 mmol, 39%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.91 (s, 2H), 7.81 (s, 2H), 7.60 – 7.55 (m, 4H), 7.04 (t, *J* = 8.6 Hz, 4H), 6.76 (s, 2H), 3.96 (s, 6H), 3.83 ppm (s, 6H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 165.46 (d, *J$_{CF}$* = 142.6 Hz), 164.02, 149.30, 146.50, 130.35 (d, *J$_{CF}$* = 3.1 Hz), 129.61 – 128.60 (m), 121.13, 116.11, 115.94, 112.90, 106.96, 56.29, 56.22 ppm. **FT-IR:** v = 2521, 2362, 2342, 2159, 2029, 1976, 1683 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{30}$H$_{27}$F$_2$N$_2$O$_6$: 549.1831; found: 549.1833.

N,N′-(4,4',5,5'-tetramethoxy-[1,1'-biphenyl]-2,2'-diyl)bis(4-chlorobenzamide) (125h). Prepared according to the general procedure J using 4-chloro-*N*-(3,4-dimethoxyphenyl)benzamide (58 mg, 0.2 mmol, 1 equiv); the product was obtained as a yellow solid (37 mg, 0.065 mmol, 63%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.92 (s, 2H), 7.79 (s, 2H), 7.50 (d, *J* = 8.5 Hz, 4H), 7.34 (d, *J* = 8.5 Hz, 4H), 6.76 (s, 2H), 3.97 (s, 6H), 3.84 ppm (s, 6H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 164.88, 149.37, 146.58, 138.44, 132.55, 129.23, 129.21, 128.33, 121.05, 112.91, 106.93, 56.33, 56.26 ppm. **FT-IR:** v = 2514, 2361, 2342, 2159, 2027, 1976 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{30}$H$_{27}$Cl$_2$N$_2$O$_6$: 581.1240; found: 581.1246.

***N,N'*-(4,4',5,5'-tetramethoxy-[1,1'-biphenyl]-2,2'-diyl)bis(1-adamantan-1-yl)formamide) (125i).** Prepared according to the general procedure J using *N*-(3,4-dimethoxyphenyl)adamantane-1-carboxamide (63 mg, 0.2 mmol, 1 equiv); the product was obtained as a brownish solid (49 mg, 0.075 mmol, 75%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.08 (s, 2H), 7.19 (s, 2H), 6.69 (s, 2H), 3.95 (s, 6H), 3.85 (s, 6H), 1.68 – 1.54 ppm (m, 30H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 176.26, 149.10, 145.51, 129.92, 118.88, 112.56, 105.60, 56.19, 56.15, 41.55, 38.96, 36.26, 27.93 ppm. **FT-IR:** v = 2518, 2361, 2341, 2159, 2029, 1976 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{38}$H$_{49}$N$_2$O$_6$: 629.3585; found: 629.3573.

***N,N'*-(4,4',5,5'-tetramethoxy-[1,1'-biphenyl]-2,2'-diyl)bis(2-(naphthalen-2-yloxy)acetamide) (125j).** Prepared according to the general procedure J using *N*-(3,4-dimethoxyphenyl)-2-(naphthalen-2-yloxy)acetamide (50 mg, 0.15 mmol, 1 equiv) in MeCN / TFA; the product was obtained as a white solid (24 mg, 0.05 mmol, 48%). **^{1}H NMR** (500 MHz, DMSO) δ 8.80 (s, 2H), 7.81 (dd, *J* = 23.0, 8.5 Hz, 4H), 7.75 – 7.67 (m, 4H), 7.41 (dt, *J* = 40.3, 7.1 Hz, 4H), 7.18 (d, *J* = 2.1 Hz, 2H), 6.91 (dd, *J* = 8.9, 2.4 Hz, 2H), 6.82 (s, 2H), 4.58 (q, *J* = 14.9 Hz, 4H), 3.82 (s, 6H), 3.65 (s, 6H). **^{13}C NMR** (126 MHz, DMSO) δ 166.50, 155.32, 148.82, 146.29, 134.36, 129.83, 129.28, 128.90, 128.02, 127.21, 127.00, 124.47, 122.21, 118.41, 114.01, 107.94, 107.46, 67.40, 56.10, 55.40 ppm. **FT-IR:** v = 2525, 2361, 2341, 2159, 2027, 1976, 1673 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{40}$H$_{37}$N$_2$O$_8$: 673.2544; found: 673.2557.
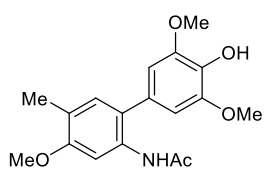
***N*-(4'-Hydroxy-3',4,5'-trimethoxy-5-methyl-[1,1'-biphenyl]-2-yl)acetamide (125k).** Prepared according to the general procedure I using 2,6-dimethoxyphenol (31 mg, 0.2 mmol, 1 equiv) and *N*-(4-methoxy-3-methylphenyl)acetamide (108 mg, 0.6 mmol, 3 equiv); the product was obtained as a white solid (47 mg, 0.14 mmol, 71%). **^{1}H NMR** (500 MHz, DMSO-*d$_6$*) δ 9.13 (s, 1H), 8.39 (s, 1H), 7.12 (s, 1H), 7.07 (s, 1H), 6.57 (s, 2H), 3.76 (s, 3H), 3.75 (s, 6H), 2.15 (s, 3H), 1.92 ppm (s, 3H). **^{13}C NMR** (126 MHz, DMSO) δ 169.25, 156.47, 148.23, 135.06, 133.80, 132.01, 129.21, 128.98, 123.47, 109.44, 106.76, 56.41, 55.84, 23.62, 16.10 ppm. **FT-IR:** v = 2159, 2028, 1976, 1678 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{18}$H$_{22}$O$_5$N = 332.1492; found: 332.1494.
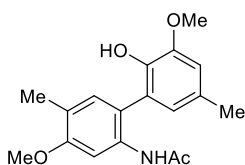
N-(2'-Hydroxy-3',4-dimethoxy-5,5'-dimethyl-[1,1'-biphenyl]-2-yl)acetamide (125l). Prepared according to the general procedure I using 2-methoxy-4-methylphenol (26 µL, 0.2 mmol, 1 equiv) and *N*-(4-methoxy-3-methylphenyl)acetamide (108 mg, 0.6 mmol, 3 equiv); the product was obtained as a white solid (26 mg, 0.08 mmol, 41%). **^{1}H NMR** (600 MHz, DMSO-d_6) δ 8.67 (s, 1H), 8.54 (s, 1H), 7.32 (s, 1H), 6.97 (s, 1H), 6.80 (s, 1H), 6.50 (s, 1H), 3.83 (s, 3H), 3.77 (s, 3H), 2.25 (s, 3H), 2.13 (s, 3H), 1.90 ppm (s, 3H). **^{13}C NMR** (151 MHz, DMSO) δ 168.01, 156.14, 147.60, 140.68, 134.32, 132.36, 128.04, 125.42, 123.50, 123.47, 121.57, 111.72, 106.50, 55.87, 55.27, 23.83, 20.71, 15.60 ppm. **FT-IR:** v = 2516, 2159, 2029, 1976, 1666 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ $C_{18}H_{22}O_4N$ = 316.1543; found: 316.1550.
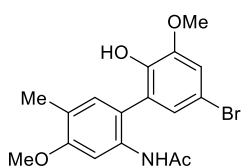
N-(5'-Bromo-2'-hydroxy-3',4-dimethoxy-5-methyl-[1,1'-biphenyl]-2-yl)acetamide (125m). Prepared according to the general procedure I using 4-bromo-2-methoxyphenol (40 mg, 0.2 mmol, 1 equiv) and *N*-(4-methoxy-3-methylphenyl)acetamide (108 mg, 0.6 mmol, 3 equiv); the product was obtained as a yellow solid (40 mg, 0.11 mmol, 53%). **^{1}H NMR** (600 MHz, CDCl$_3$) δ 7.95 (s, 1H), 7.71 (s, 1H), 7.03 (s, 1H), 6.94 (d, *J* = 8.5 Hz, 1H), 6.68 (d, *J* = 8.5 Hz, 1H), 6.56 (s, 1H), 3.81 (s, 3H), 3.77 (s, 3H), 2.08 (s, 3H), 2.03 ppm (s, 3H). **^{13}C NMR** (151 MHz, CDCl$_3$) δ 168.40, 154.14, 151.21, 145.67, 138.34, 128.25, 124.10, 122.15, 120.49, 120.15, 116.58, 116.12, 103.51, 56.38, 55.95, 25.02, 16.00 ppm. **FT-IR:** v = 2510, 2362, 2159, 2030, 1675 cm^{-1}.**HR-MS:** calc. for [M+H]$^+$ $C_{17}H_{19}O_4N^{79}Br$ = 380.0492; found: 380.0497; $C_{17}H_{19}O_4N^{81}Br$ = 382.0471; found: 382.0476.
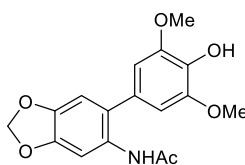
N-(6-(4-hydroxy-3,5-dimethoxyphenyl)benzo[*d*][1,3]dioxol-5-yl)acetamide (125n). Prepared according to the general procedure I using 2,6-dimethoxyphenol (31 mg, 0.2 mmol, 1 equiv) and *N*-(benzo[*d*][1,3]dioxol-5-yl)acetamide (106 mg, 0.6 mmol, 3 equiv); the product was obtained as a pale white solid (33 mg, 0.1 mmol, 50%). **^{1}H NMR** (600 MHz, DMSO-d_6) δ 9.10 (s, 1H), 8.41 (s, 1H), 6.98 (s, 1H), 6.91 (s, 1H), 6.57 (s, 2H), 6.04 (s, 2H), 3.76 (s, 6H), 1.89 ppm (s, 3H). **^{13}C NMR** (151 MHz, DMSO) δ 169.41, 148.19, 146.32, 145.63, 135.32, 131.08, 129.18, 128.89, 109.83, 108.53, 106.93, 101.79, 56.41, 23.40 ppm. **FT-IR:** v = 2511, 2341, 2159, 2029, 1976, 1721 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ $C_{17}H_{18}O_6N$ = 332.1128; found: 332.1129.

11.6 Experimental Part for the Intra- and Intermolecular Benzylation of Arenes

11.6.1 General procedures

General procedure K: Benzylation of phenols
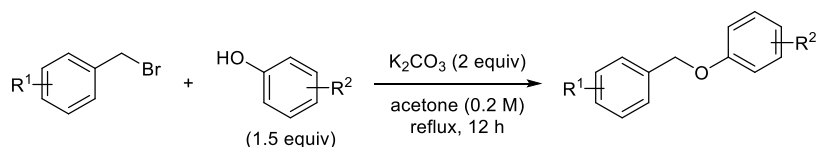
To a solution of benzyl bromide (2 mmol, 1 equiv) and phenol (3 mmol, 1.5 equiv) in Acetone (10 mL) was added K_2CO_3 (4 mmol, 2 equiv) and the reaction was refluxed for 12 h. After cooling to room temperature, the reaction was filtered, and the solvent was removed under reduced pressure. Silica gel column chromatography afforded the desired product (eluent: petroleum ether / ethyl acetate).

Preparation of the nitrosonium tetrafluoroborate stock solution

Under nitrogen atmosphere in a flame dry Schlenk flask, $NOBF_4$ was dissolved in sulfolane (1 mL/23.36 mg $NOBF_4$), sealed with a glass stopper and placed in an ultrasonic bath for 30 Minutes. The stock solution was used for up to three days.

General procedure L: Catalytic rearrangement of benzyl ethers
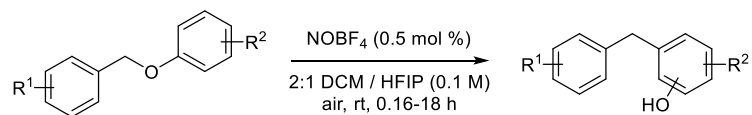
To a stirring solution of benzyl ether (0.5 mmol, 1 equiv) in 2:1 DCM / HFIP (5 mL) $NOBF_4$ (0.2 M in sulfolane, 12.5 µL, 2.5 µmol, 0.5 mol %) was added. The reaction was stirred at room temperature until full conversion of starting material was monitored by TLC and the regioisomeric ratio was determined by GC-MS-FID. The reaction was diluted with DCM, concentrated on silica and purified by silica gel column chromatography to afford the desired products (eluent: petroleum ether / dichloromethane).

General procedure M: Catalytic benzylation of arenes
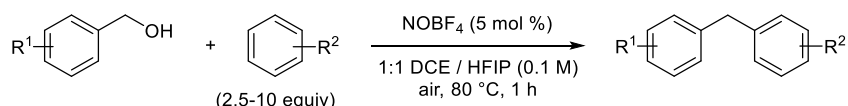
To a stirring solution of benzyl alcohol (0.2 mmol, 1 equiv) and arene (2.5 equiv or 10 equiv) in 1:1 DCE / HFIP (2 mL) $NOBF_4$ (0.2 M in sulfolane, 50 µL, 10 µmol, 5 mol %) was added at room temperature and the reaction was stirred at 80 °C for 1 h. After cooling to room

temperature, the solvents were removed under reduced pressure and the crude reaction was purified by silica gel column chromatography to afford the desired products (eluent: petroleum ether / ethyl acetate).

11.6.2 Physical data of starting materials
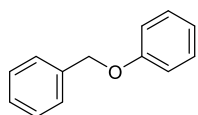
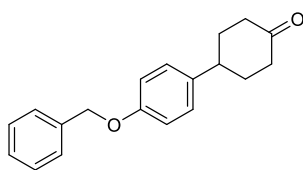**(Benzyloxy)benzene (126a).** Prepared according to general procedure K using phenol (0.98 mL, 11.3 mmol, 1.5 equiv) and benzyl bromide (0.89 mL, 7.5 mmol, 1 equiv). The compound was obtained as a white solid (360 mg, 1.95 mmol, 95%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.47 (d, J = 7.5 Hz, 2H), 7.41 (t, J = 7.5 Hz, 2H), 7.38 – 7.29 (m, 3H), 7.05 – 6.95 (m, 3H), 5.09 ppm (s, 2H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 158.88, 137.17, 129.61, 128.71, 128.07, 127.62, 121.05, 114.94, 70.00 ppm.
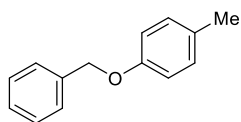
1-(Benzyloxy)-4-methylbenzene (126b). Prepared according to general procedure K using p-cresol (320 µL, 3 mmol, 1.5 equiv) and benzyl bromide (238 µL, 2 mmol, 1 equiv). The compound was obtained as a white solid (378 mg, 1.91 mmol, 95%). **^{1}H NMR** (700 MHz, CDCl$_3$) δ 7.51 – 7.45 (m, 2H), 7.43 (m, 2H), 7.39 – 7.33 (m, 1H), 7.13 (dd, J = 6.0, 2.8 Hz, 2H), 6.97 – 6.90 (m, 2H), 5.08 (s, 2H), 2.34 ppm (m, 3H). **^{13}C NMR** (176 MHz, CDCl$_3$) δ 156.83, 137.41, 130.26, 130.04, 128.67, 127.98, 127.57, 114.84, 70.19, 20.61 ppm.
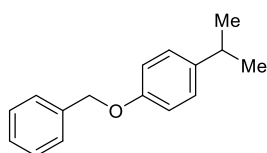
1-(Benzyloxy)-4-isoproptylbenzene (126c). Prepared according to general procedure K using 4-isopropylphenol (408 mg, 3 mmol, 1.5 equiv) and benzyl bromide (238 µL, 2 mmol, 1 equiv). The compound was obtained as a yellow oil (452 mg, 2 mmol, quant). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.44 (d, J = 7.4 Hz, 2H), 7.39 (t, J = 7.5 Hz, 2H), 7.33 (t, J = 7.2 Hz, 1H), 7.16 (d, J = 8.5 Hz, 2H), 6.92 (d, J = 8.5 Hz, 2H), 5.05 (s, 2H), 2.87 (m, 1H), 1.23 ppm (d, J = 6.9 Hz, 6H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 157.03, 141.46, 137.40, 128.70, 128.03, 127.64, 127.42, 114.72, 70.17, 33.42, 24.35 ppm.
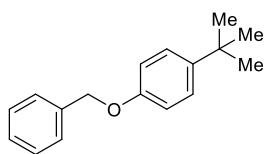
1-(Benzyloxy)-4-(*tert*-butyl)benzene (126d). Prepared according to general procedure K using 4-*tert*-butylphenol (450 mg, 3 mmol) and benzyl bromide (238 µL, 2 mmol). The compound was obtained as a white solid (471 mg, 2 mmol, quant.). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.45 (d, J = 7.4 Hz, 2H), 7.39 (t, J = 7.5 Hz, 2H), 7.35 – 7.30 (m, 3H), 6.95 – 6.91 (m, 2H), 5.05 (s, 2H), 1.31 ppm (s,

9H). **¹³C NMR** (126 MHz, CDCl₃) δ 156.70, 143.71, 137.40, 128.70, 128.03, 127.64, 126.40, 114.35, 70.12, 34.22, 31.66 ppm.

4-(4-(Benzyloxy)phenyl)cyclohexan-1-one (126e). Prepared according to general procedure K using 4-(4-hydroxyphenyl)cyclohexanone (571 mg, 3 mmol, 1.5 equiv) and benzyl bromide (238 µL, 2 mmol, 1 equiv). The compound was obtained as a white solid (486 mg, 1.73 mmol, 87%). **¹H NMR** (400 MHz, CDCl₃) δ 7.47 – 7.36 (m, 4H), 7.33 (t, J = 7.1 Hz, 1H), 7.20 – 7.12 (m, 2H), 6.98 – 6.91 (m, 2H), 5.05 (s, 2H), 2.99 (tt, J = 12.1, 3.3 Hz, 1H), 2.59 – 2.44 (m, 4H), 2.27 – 2.14 (m, 2H), 1.91 ppm (m, 2H). **¹³C NMR** (101 MHz, CDCl₃) δ 211.42, 157.60, 137.31, 137.20, 128.72, 128.09, 127.73, 127.60, 115.04, 70.19, 42.06, 41.52, 34.31 ppm.
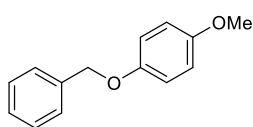
1-(Benzyloxy)-4-methoxybenzene (126f). Prepared according to general procedure K using 4-methoxyphenol (372 mg, 3 mmol, 1.5 equiv) and benzyl bromide (238 µL, 2 mmol, 1 equiv). The compound was obtained as a white solid (421 mg, 1.96 mmol, 98%). **¹H NMR** (500 MHz, CDCl₃) δ 7.43 (d, J = 7.3 Hz, 2H), 7.39 (t, J = 7.5 Hz, 2H), 7.32 (t, J = 7.2 Hz, 1H), 6.95 – 6.90 (m, 2H), 6.86 – 6.81 (m, 2H), 5.02 (s, 2H), 3.77 ppm (s, 3H). **¹³C NMR** (126 MHz, CDCl₃) δ 154.06, 153.05, 137.40, 128.69, 128.03, 127.62, 115.94, 114.75, 70.81, 55.85 ppm.
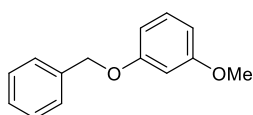
1-(Benzyloxy)-3-methoxybenzene (126g). Prepared according to general procedure K using 3-methoxyphenol (372 mg, 3 mmol, 1.5 equiv) and benzyl bromide (238 µL, 2 mmol, 1 equiv). The compound was obtained as a colourless oil (428 mg, 2 mmol, quant.). **¹H NMR** (400 MHz, CDCl₃) δ 7.50 – 7.29 (m, 5H), 7.19 (t, J = 8.1 Hz, 1H), 6.68 – 6.44 (m, 3H), 5.05 (s, 2H), 3.79 (s, 3H) ppm. **¹³C NMR** (101 MHz, CDCl₃) δ 160.98, 160.20, 137.11, 130.04, 128.73, 128.12, 127.67, 107.08, 106.74, 101.52, 70.18, 55.42 ppm.
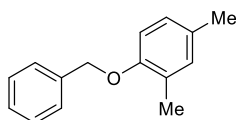
1-(Benzyloxy)-2,4-dimethylbenzene (126h). Prepared according to general procedure K using 2,4-dimethylphenol (362 µL, 3 mmol, 1.5 equiv) and benzyl bromide (238 µL, 2 mmol, 1 equiv). The compound was obtained as a yellow oil (424 mg, 2 mmol, quant.). **¹H NMR** (500 MHz, CDCl₃) δ 7.45 (d, J = 7.3 Hz, 2H), 7.39 (t, J = 7.5 Hz, 2H), 7.32 (t, J = 7.3 Hz, 1H), 6.99 (s, 1H), 6.95 (d, J = 8.3 Hz, 1H), 6.79 (d, J = 8.2 Hz, 1H), 5.06 (s, 2H), 2.27 ppm (s, 6H). **¹³C NMR** (126 MHz, CDCl₃)

δ 154.89, 137.82, 131.71, 129.92, 128.61, 127.80, 127.22, 127.03, 126.98, 111.61, 70.11, 20.60, 16.47 ppm.
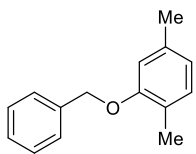
2-(Benzyloxy)-1,4-dimethylbenzene (126i). Prepared according to general procedure K using 2,5-dimethylphenol (367 mg, 3 mmol, 1.5 equiv) and benzyl bromide (238 µL, 2 mmol, 1 equiv). The compound was obtained as a yellow oil (424 mg, 2 mmol, quant.). **¹H NMR** (500 MHz, CDCl₃) δ 7.46 (d, J = 7.0 Hz, 2H), 7.40 (t, J = 7.4 Hz, 2H), 7.33 (t, J = 7.3 Hz, 1H), 7.05 (d, J = 7.3 Hz, 1H), 6.78 – 6.66 (m, 2H), 5.07 (s, 2H), 2.33 (s, 3H), 2.25 ppm (s, 3H). **¹³C NMR** (126 MHz, CDCl₃) δ 156.90, 137.73, 136.69, 130.57, 128.62, 127.83, 127.24, 124.02, 121.23, 112.51, 69.86, 21.58, 16.13 ppm.
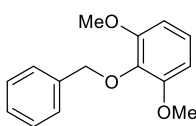
2-(Benzyloxy)-1,3-dimethoxybenzene (126j). Prepared according to general procedure K using 2,6-dimethoxyphenol (308 mg, 2 mmol, 1 equiv) and benzyl bromide (1.03 mL, 6 mmol, 3 equiv). The compound was obtained as a colourless oil (485 mg, 1.99 mmol, quant.). **¹H NMR** (500 MHz, CDCl₃) δ 7.50 (d, J = 7.1 Hz, 2H), 7.35 (t, J = 7.3 Hz, 2H), 7.29 (t, J = 7.3 Hz, 1H), 7.00 (t, J = 8.4 Hz, 1H), 6.58 (d, J = 8.4 Hz, 2H), 5.01 (s, 2H), 3.83 ppm (s, 6H). **¹³C NMR** (126 MHz, CDCl₃) δ 153.92, 138.01, 137.12, 128.64, 128.25, 127.92, 123.89, 105.36, 75.13, 56.20 ppm.
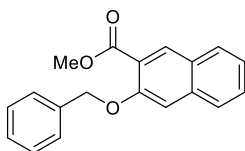
Methyl 3-(benzyloxy)-2-naphthoate (126k). Prepared according to general procedure K using methyl-3-hydroxy-naphtoate (606 mg, 3 mmol, 1.5 equiv) and benzyl bromide (238 µL, 2 mmol, 1 equiv). The compound was obtained as a white solid (526 mg, 1.8 mmol, 90%). **¹H NMR** (500 MHz, CDCl₃) δ 8.35 (s, 1H), 7.83 (d, J = 8.1 Hz, 1H), 7.72 (d, J = 8.2 Hz, 1H), 7.56 (d, J = 7.4 Hz, 2H), 7.54 – 7.49 (m, 1H), 7.40 (m, 3H), 7.33 (t, J = 7.4 Hz, 1H), 5.29 (s, 2H), 3.97 ppm (s, 3H). **¹³C NMR** (126 MHz, CDCl₃) δ 166.93, 154.76, 136.89, 136.14, 133.08, 128.85, 128.69, 128.53, 127.89, 127.82, 126.94, 126.63, 124.65, 122.25, 108.58, 70.51, 52.40 ppm.
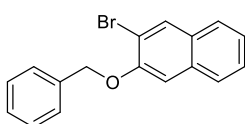
2-(Benzyloxy)-3-bromonaphthalene (126l). Prepared according to general procedure K using 3-bromo-2-naphthol (175 mg, 1.2 mmol, 1.2 equiv) and benzyl bromide (122 µL, 1 mmol, 1 equiv). The compound was obtained as a white solid (238 mg, 0.76 mmol, 76%). **¹H NMR** (500 MHz, CDCl₃) δ 8.10 (s, 1H), 7.70 (d, J = 8.9 Hz, 2H), 7.56 (d, J = 7.4 Hz, 2H), 7.45 (m, 3H), 7.40 – 7.32 (m, 2H), 7.22 (s, 1H), 5.27 ppm (s, 2H). **¹³C NMR** (126 MHz, CDCl₃) δ 152.69, 136.52, 133.53, 132.46, 129.64, 128.75, 128.09, 127.12, 126.85, 126.80, 126.78, 124.72, 114.00, 108.37, 70.76 ppm.
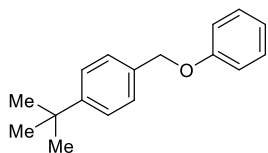
1-(*tert*-Butyl)-4-(phenoxymethyl)benzene **(126m).** Prepared according to general procedure K using phenol (264 µL, 3 mmol, 1.5 equiv) and 4-*tert*-butylbenzy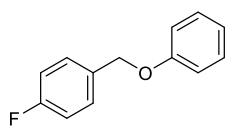l bromide (367 µL, 2 mmol, 1 equiv). The compound was obtained as a white, crystalline solid (173 mg, 0.72 mmol, 36%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.41 (dd, J = 20.2, 8.4 Hz, 4H), 7.30 (dd, J = 8.7, 7.4 Hz, 2H), 6.98 (dd, J = 18.5, 7.6 Hz, 3H), 5.03 (s, 2H), 1.34 (s, 9H) ppm. **^{13}C NMR** (126 MHz, CDCl$_3$) δ 159.02, 151.15, 134.09, 129.60, 127.62, 125.69, 120.96, 114.90, 69.88, 34.73, 31.49 ppm.
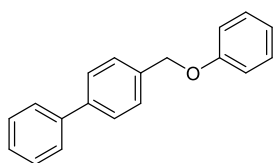
4-(Phenoxymethyl)-1,1'-biphenyl (126n). Prepared according to general procedure K using phenol (264 µL, 3 mmol, 1.5 equiv) and 4-(bromomethyl)-1,1'-biphenyl (742 mg, 3 mmol, 1 equiv). The compound was obtained as a white, crystalline solid (679 mg, 2.61 mmol, 87%). **^{1}H NMR** (600 MHz, CDCl$_3$) δ 7.65 – 7.59 (m, 4H), 7.52 (d, J = 8.3 Hz, 2H), 7.48 – 7.43 (m, 2H), 7.36 (m, 1H), 7.34 – 7.29 (m, 2H), 7.02 (m, 2H), 7.00 – 6.95 (m, 1H), 5.12 ppm (s, 2H). **^{13}C NMR** (151 MHz, CDCl$_3$) δ 158.72, 140.88, 140.74, 136.00, 129.44, 128.73, 127.91, 127.30, 127.07, 120.92, 114.79, 69.60 ppm.

1-Fluoro-4-(phenoxymethyl)benzene (126o). Prepared according to general procedure K using phenol (264 µL, 3 mmol, 1.5 equiv) and 4-fluorobenzyl bromide (374 µL, 2 mmol, 1 equiv). The compound was obtained as a white, crystalline solid (453 mg, 2.24 mmol, 75%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.42 (dd, J = 8.5, 5.5 Hz, 2H), 7.34 – 7.27 (m, 2H), 7.08 (t, J = 8.7 Hz, 2H), 7.02 – 6.95 (m, 3H), 5.03 ppm (s, 2H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 163.60, 161.64, 158.71, 132.91 (d, J_{CF} = 3.2 Hz), 129.66, 129.48 (d, J_{CF} = 8.2 Hz), 121.21, 115.71, 115.54, 114.93, 69.34 ppm.
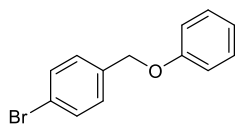
1-Bromo-4-(phenoxymethyl)benzene (126p). Prepared according to general procedure K using phenol (264 µL, 3 mmol, 1 equiv) and 4-bromobenzyl bromide (749 mg, 3 mmol, 1 equiv). The compound was obtained as a white solid (610 mg, 2.32 mmol, 77%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.51 (d, J = 8.4 Hz, 2H), 7.35 – 7.27 (m, 4H), 6.97 (dd, J = 13.2, 7.6 Hz, 3H), 5.02 ppm (s, 2H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 158.60, 136.22, 131.84, 129.68, 129.21, 121.97, 121.29, 114.93, 69.25 ppm.
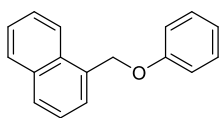
1-(Phenoxymethyl)naphthalene (126q). Prepared according to general procedure K using phenol (264 µL, 3 mmol, 1.5 equiv) and 1-(chloromethyl)naphthalene (301 µL, 2 mmol, 1.5 equiv). The compound was obtained as a white solid (150 mg, 0.64 mmol, 32%). **¹H NMR** (500 MHz, CDCl₃) δ 8.06 (d, J = 7.4 Hz, 1H), 7.93 – 7.89 (m, 1H), 7.87 (d, J = 8.3 Hz, 1H), 7.62 (d, J = 6.9 Hz, 1H), 7.58 – 7.51 (m, 2H), 7.48 (dd, J = 8.2, 7.1 Hz, 1H), 7.34 (dd, J = 8.6, 7.4 Hz, 2H), 7.08 (d, J = 7.8 Hz, 2H), 7.01 (t, J = 7.4 Hz, 1H), 5.50 (s, 2H) ppm. **¹³C NMR** (126 MHz, CDCl₃) δ 158.98, 133.92, 132.45, 131.67, 129.69, 129.16, 128.84, 126.76, 126.59, 126.06, 125.48, 123.87, 121.21, 115.02, 68.69 ppm.
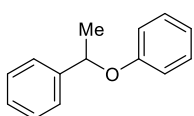
(1-Phenoxyethyl)benzene (126r). Conducted according to a literature procedure.[213] To an oven dried Schlenck flask under nitrogen was added (benzyloxy)benzene (184 mg, 1 mmol, 1 equiv) and anhydrous THF (5 mL). This solution was cooled to -78 °C and then *tert*-BuLi (0.760 mL of a 1.7 M solution in pentane, 1.3 equiv) was added. After 5 min at this temperature, the cooling bath was slowly warmed to -60 °C and the mixture was stirred for 20 min. Then, methyl iodide (83 µL, 1.3 mmol, 1.3 equiv) was added, and after 5 min, the cooling bath was removed Finally, the reaction mixture was quenched with H₂O (30 mL), and extracted with Et₂O (3×30 mL). The organic layers were combined, dried over MgSO₄ and concentrated under reduced pressure. Products were purified silica gel chromatography (hexane:ethyl acetate). The compound was obtained as colourless oil (152 mg, 0.77 mmol, 77%). **¹H NMR** (500 MHz, CDCl₃) δ 7.29 (d, J = 7.3 Hz, 2H), 7.24 (t, J = 7.6 Hz, 2H), 7.16 (t, J = 7.3 Hz, 1H), 7.13 – 7.07 (m, 2H), 6.78 (d, J = 8.2 Hz, 2H), 5.22 (q, J = 6.4 Hz, 1H), 1.55 ppm (d, J = 6.5 Hz, 3H). **¹³C NMR** (126 MHz, CDCl₃) δ 158.06, 143.37, 129.43, 128.73, 127.52, 125.65, 120.74, 116.01, 75.95, 24.64 ppm.
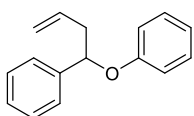
(1-Phenoxybut-3-en-1-yl)benzene (126s). Conducted according to a literature procedure.[213] To an oven dried Schlenck flask under nitrogen was added (benzyloxy)benzene (276 mg, 1.5 mmol, 1 equiv) and anhydrous THF (7.5 mL). This solution was cooled to -78 °C and then *tert*-BuLi (1.14 mL of a 1.7 M solution in pentane, 1.3 equiv) was added. After 5 min at this temperature, the cooling bath was slowly warmed to -60 °C and the mixture was stirred for 20 min. Then, allyl iodide (83 µL, 1.3 mmol, 1.3 equiv) was added, and after 5 min, the cooling bath was removed Finally, the reaction mixture was quenched with H₂O (40 mL), and extracted with Et₂O (3×40 mL). The organic layers were combined, dried over MgSO₄ and concentrated under reduced pressure. Products were purified silica gel chromatography (hexane:ethyl acetate). The compound was obtained

as colourless oil (193 mg, 0.86 mmol, 57%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.31 – 7.22 (m, 4H), 7.19 – 7.15 (m, 1H), 7.13 – 7.08 (m, 2H), 6.78 (dd, J = 12.9, 7.6 Hz, 3H), 5.86 – 5.73 (m, 1H), 5.10 – 4.96 (m, 3H), 2.74 – 2.63 (m, 1H), 2.52 ppm (m, 1H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 158.12, 141.47, 134.25, 129.32, 128.55, 127.59, 126.08, 120.75, 117.55, 116.00, 79.80, 42.95 ppm.
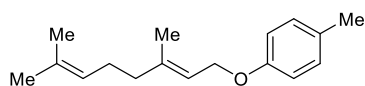

(*E*)-1-((3,7-dimethylocta-2,6-dien-1-yl)oxy)-4-methylbenzene (126t). Conducted according to a literature reference.[214] *p*-Cresol (313.5 μL, 3 mmol, 1 equiv), geraniol (780 μL, 4.5 mmol, 1.5 equiv) and triphenylphosphine (944 mg, 3.6 mmol, 1.2 equiv) were dissolved in THF (40 mL) and cooled to 0 °C. Diisopropyl azodicarboxylate (945 μL, 4.8 mmol, 1.6 equiv) was slowly added *via* syringe. The resulting clear yellow-orange-coloured solution was stirred at room temperature for 2 h. The volume of the solution was reduced by evaporation of THF. The residue (2-3 ml) was purified by flash chromatography to give the desired compounds. The compound was obtained as colourless oil (266 mg, 1.09 mg, 36%) **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.08 (d, J = 8.2 Hz, 2H), 6.82 (d, J = 8.6 Hz, 2H), 5.56 – 5.43 (m, 1H), 5.14 – 5.06 (m, 1H), 4.51 (d, J = 6.5 Hz, 2H), 2.29 (s, 3H), 2.15 – 2.05 (m, 4H), 1.73 (s, 3H), 1.68 (s, 3H), 1.61 ppm (s, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 156.85, 141.13, 131.94, 129.97, 129.90, 123.98, 119.81, 114.64, 65.01, 39.70, 26.44, 25.84, 20.62, 17.85, 16.79 ppm.
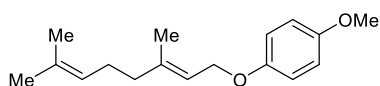

(*E*)-1-((3,7-dimethylocta-2,6-dien-1-yl)oxy)-4-methoxybenzene(126u). Conducted according to a literature reference.[214] 4-Methoxyphenol (372 mg, 3 mmol, 1 equiv), geraniol (780 μL, 4.5 mmol, 1.5 equiv) and triphenylphosphine (944 mg, 3.6 mmol, 1.2 equiv) were dissolved in THF (40 mL) and cooled to 0 °C. Diisopropyl azodicarboxylate (945 μL, 4.8 mmol, 1.6 equiv) was slowly added *via* syringe. The resulting clear yellow-orange-coloured solution was stirred at room temperature for 2 h. The volume of the solution was reduced by evaporation of THF. The residue (2-3 ml) was purified by flash chromatography (10% EtOAc/hexane) to give the desired compounds. The compound was obtained as colourless oil (564 mg, 2.17 mmol, 72%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 6.89 – 6.79 (m, 4H), 5.56 – 5.42 (m, 1H), 5.16 – 5.04 (m, 1H), 4.49 (d, J = 6.6 Hz, 2H), 3.77 (s, 3H), 2.20 – 2.01 (m, 4H), 1.73 (s, 3H), 1.68 (s, 3H), 1.61 ppm (s, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 153.83, 153.13, 141.13, 131.92, 123.97, 119.86, 115.75, 114.69, 65.58, 55.84, 39.69, 26.43, 25.84, 17.84, 16.78 ppm.
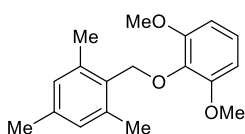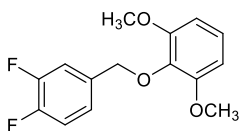
2-((2,6-Dimethoxyphenoxy)methyl)-1,3,5-trimethylbenzene (126v). Prepared according to general procedure K using 2,6-dimethoxyphenol (471 mg, 3 mmol, 1.5 equiv) and 2,4,6-trimethylbenzyl chloride (314 μL, 2 mmol, 1 equiv). The compound was obtained as a colourless oil (372 mg, 1.3 mmol, 65%). **¹H NMR** (400 MHz, CDCl₃) δ 7.02 (t, J = 8.4 Hz, 1H), 6.89 (s, 2H), 6.61 (d, J = 8.4 Hz, 2H), 5.01 (s, 2H), 3.84 (s, 6H), 2.52 (s, 6H), 2.29 ppm (s, 3H). **¹³C NMR** (101 MHz, CDCl₃) δ 154.39, 138.85, 137.85, 137.45, 131.06, 128.85, 123.80, 105.53, 68.79, 56.13, 21.15, 19.35 ppm.
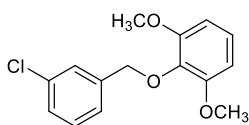
2-((3-Chlorobenzyl)oxy)-1,3-dimethoxybenzene (126w). Prepared according to general procedure K using 2,6-dimethoxyphenol (471 mg, 3 mmol, 1.5 equiv) and 3-chlorobenzyl chloride (267 μL, 2 mmol, 1 equiv). The compound was obtained as a colourless oil (550 mg, 1.97 mmol, 99%). **¹H NMR** (500 MHz, CDCl₃) δ 7.56 (s, 1H), 7.35 (dd, J = 6.1, 2.6 Hz, 1H), 7.30 – 7.23 (m, 2H), 7.01 (t, J = 8.4 Hz, 1H), 6.58 (d, J = 8.4 Hz, 2H), 4.98 (s, 2H), 3.84 ppm (s, 6H). **¹³C NMR** (126 MHz, CDCl₃) δ 153.77, 140.13, 136.82, 134.13, 129.50, 128.61, 127.98, 126.43, 124.11, 105.27, 74.25, 56.16 ppm.

**2-((3,4-Difluorobenzyl)oxy)-1,3-dimethoxybenzene (126x).** Prepared according to general procedure K using 2,6-dimethoxyphenol (471 mg, 3 mmol, 1.5 equiv) and 3,4-difluorobenzyl chloride (256 μL, 2 mmol, 1 equiv). The compound was obtained as a colourless oil (520 mg, 1.86 mmol, 93%). **¹H NMR** (500 MHz, CDCl₃) δ 7.45 – 7.36 (m, 1H), 7.20 – 7.15 (m, 1H), 7.11 (m, 1H), 7.01 (t, J = 8.4 Hz, 1H), 6.58 (d, J = 8.4 Hz, 2H), 4.95 (s, 2H), 3.84 ppm (s, 6H). **¹³C NMR** (126 MHz, CDCl₃) δ 153.73, 151.17 (dd, J_{CF} = 22.5, 12.6 Hz), 149.20 (dd, J_{CF} = 22.5, 12.7 Hz), 136.65, 135.19 (dd, J_{CF} = 5.7, 3.8 Hz), 124.34 (dd, J_{CF} = 6.4, 3.6 Hz), 124.19, 117.62, 117.48, 116.94, 116.80, 105.23, 73.81, 56.15 ppm.
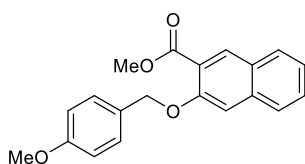
Methyl 3-((4-methoxybenzyl)oxy)-2-naphthoate (126y). Prepared according to general procedure K using methyl 3-hydroxy-2-naphthoate (309 mg, 1.5 mmol, 1.5 equiv) and 4-methoxybenzyl chloride (102 μL, 1 mmol, 1 equiv). The compound was obtained as a colourless solid (138 mg, 0.43 mmol, 43%). **¹H NMR** (500 MHz, CDCl₃) δ 8.33 (s, 1H), 7.82 (d, J = 8.2 Hz, 1H), 7.72 (d, J = 8.3 Hz, 1H), 7.53 – 7.45 (m, 3H), 7.38 (t, J = 7.5 Hz, 1H), 7.27 (s, 1H), 6.94 (d, J = 8.6 Hz, 2H), 5.21 (s, 2H), 3.95 (s, 3H), 3.82 ppm (s, 3H). **¹³C NMR** (126

MHz, CDCl₃) δ 166.95, 159.39, 154.84, 136.15, 132.99, 128.93, 128.85, 128.64, 128.50, 127.80, 126.63, 124.62, 122.36, 114.08, 108.72, 70.45, 55.43, 52.39 ppm.
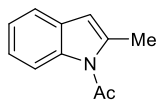
1-(2-Methyl-1H-indol-1-yl)ethan-1-one. To a stirring solution of 2-methylindole (0.5 g, 3.81 mmol. 1 equiv) in anhydrous DMF (15 mL) NaH (60% in mineral oil, 228 mg, 5.72 mmol, 1.5 equiv) was added portionwise at 0 °C and the stirring was continued for 30 minutes. Acetyl chloride (555 µL, 7.62 mmol, 2 equiv) was added dropwise and the reaction was allowed to warm to room temperature and stirred for 2 h. After that time, the reaction was quenched with saturated NaHCO₃ solution (50 mL) and three times extracted with EtOAc (3x50 mL). The combined organic layers were dried over MgSO₄ and concentrated under reduced pressure. Flash chromatography yielded the desired product. The compound was obtained as reddish solid (360 mg, 2.08 mmol, 54%). **¹H NMR** (500 MHz, CDCl₃) δ 8.02 (dd, J = 8.2, 1.2 Hz, 1H), 7.51 – 7.46 (m, 1H), 7.26 (m, 2H), 6.40 (s, 1H), 2.74 (s, 3H), 2.66 ppm (s, 3H). **¹³C NMR** (126 MHz, CDCl₃) δ 170.38, 137.38, 136.56, 129.80, 123.61, 123.19, 119.89, 115.33, 109.79, 27.43, 17.71 ppm.
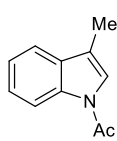
1-(3-Methyl-1H-indol-1-yl)ethan-1-one. To a stirring solution of 3-methylindole (0.5 g, 3.81 mmol. 1 equiv) in anhydrous DMF (15 mL) NaH (60% in mineral oil, 228 mg, 5.72 mmol, 1.5 equiv) was added portionwise at 0 °C and the stirring was continued for 30 minutes. Acetyl choride (555 µL, 7.62 mmol, 2 equiv) was added dropwise and the reaction was allowed to warm to room temperature and stirred for 2 h. After that time, the reaction was quenched with saturated NaHCO₃ solution (50 mL) and three times extracted with EtOAc (3x50 mL). The combined organic layers were dried over MgSO₄ and concentrated under reduced pressure. Flash chromatography yielded the desired product. The compound was obtained as pale yellow solid (559 mg, 3.23 mmol, 85%). **¹H NMR** (500 MHz, CDCl₃) δ 8.35 (s, 1H), 7.42 (m, 1H), 7.28 (m, 1H), 7.22 (m, 1H), 7.10 (s, 1H), 2.52 (s, 3H), 2.21 (s, 3H). **¹³C NMR** (126 MHz, CDCl₃) δ 168.35, 135.84, 131.43, 125.18, 123.40, 122.23, 118.84, 118.42, 116.61, 24.04, 9.74 ppm.
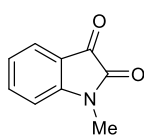
1-Methylindoline-2,3-dione. To a stirring solution of isatine (1.47 g, 10 mmol. 1 equiv) in anhydrous DMF (40 mL), NaH (60% in mineral oil, 600 mg, 15 mmol, 1.5 equiv) was added portionwise at 0 °C and the stirring was continued for 30 minutes. Methyl iodide (1.26 mL, 20 mmol, 2 equiv) was added dropwise and the reaction was allowed to warm to room temperature and stirred for 2 h. After that time, the reaction was quenched with water (100 mL) and three times extracted with EtOAc (3x100 mL). The

combined organic layers were dried over MgSO₄ and concentrated under reduced pressure. Flash chromatography yielded the desired product. The compound was obtained as orange solid (876 mg, 5.22 mmol, 52%). **¹H NMR** (500 MHz, CDCl₃) δ 7.59 – 7.48 (m, 2H), 7.06 (td, J = 7.6, 0.9 Hz, 1H), 6.84 (d, J = 7.9 Hz, 1H), 3.19 ppm (s, 3H). **¹³C NMR** (126 MHz, CDCl₃) δ 183.41, 158.25, 151.46, 138.49, 125.29, 123.88, 117.41, 110.00, 26.26 ppm.
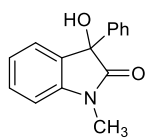
3-Hydroxy-1-methyl-3-phenylindolin-2-one. Conducted according to a literature reference.[215] *N*-methylisatin (644, 4 mmol, 1 equiv) was dissolved in anhydrous THF (6 mL) and cooled to 0 °C followed by dropwise addition of a PhMgBr (1 M in THF, 2.9 ml, 4.8 mmol, 1.2 equiv). Then, the ice-bath was removed, and the reaction was stirred for 30 Min at room temperature. The reaction mixture was quenched by the addition of 5 mL of MeOH, and then poured into saturated aqueous NH₄Cl (20 mL) and extracted with ethyl acetate (3×20 mL). The combined organic layers were dried over anhydrous MgSO₄ and concentrated under reduced pressure. Flash chromatography yielded the desired product. The compound was obtained as orange solid (765 mg, 3.2 mmol, 80%). **¹H NMR** (500 MHz, CDCl₃) δ 7.32 – 7.18 (m, 7H), 7.01 (t, J = 7.5 Hz, 1H), 6.83 (d, J = 7.8 Hz, 1H), 3.17 ppm (s, 3H). **¹³C NMR** (126 MHz, CDCl₃) δ 177.57, 143.52, 140.10, 131.58, 129.91, 128.62, 128.32, 125.37, 124.97, 123.59, 108.74, 78.00, 26.57 ppm.

11.6.3 Physical data of products
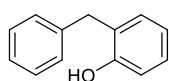
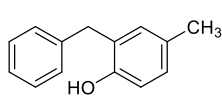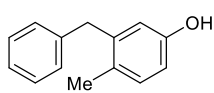**2-Benzylphenol (127a#).** Prepared according to general procedure L using (benzyloxy)benzene (184 mg, 1 mmol, 1 equiv). The compound was obtained as a colourless oil (129 mg, 0.7 mmol, 70%). **¹H NMR** (500 MHz, CDCl₃) δ 7.21 (m, 2H), 7.16 – 7.11 (m, 3H), 7.04 (d, J = 7.5 Hz, 2H), 6.81 (td, J = 7.5, 1.1 Hz, 1H), 6.69 (d, J = 7.5 Hz, 1H), 4.60 (s, 1H), 3.91 ppm (s, 2H). **¹³C NMR** (126 MHz, CDCl₃) δ 153.78, 139.96, 131.11, 128.81, 128.77, 127.97, 127.08, 126.49, 121.09, 115.83, 36.46 ppm. **FT-IR:** v = 3529, 3061, 3026, 2668, 2548 cm⁻¹. **HR-MS:** calc. for [M-H]⁻ C₁₃H₁₁O = 183.0815; found 183.0810.
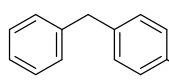
4-Benzylphenol (127a*). Prepared according to general procedure L using (benzyloxy)benzene (184 mg, 1 mmol, 1 equiv). The compound was obtained as a colourless solid (25 mg, 0.14 mmol, 14%). **¹H NMR** (500 MHz, CDCl₃) δ 7.29 (t, J = 7.4 Hz, 2H), 7.19 (dd, J = 13.9, 7.1 Hz, 3H), 7.08 – 7.04 (m, 2H), 6.78 – 6.74 (m, 2H), 3.92 ppm (s, 2H). **¹³C NMR** (126 MHz, CDCl₃) δ 153.87, 141.63, 133.57, 130.20, 128.94,

128.57, 126.14, 115.39, 41.13 ppm. **FT-IR:** v = 3184, 3020, 2903, 2844, 2686 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{13}$H$_{11}$O = 183.0815; found 183.0818.
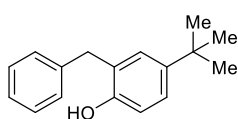
2-Benzyl-4-methylphenol (127b$^{\#}$). Prepared according to general procedure L using 1-(benzyloxy)-4-methylbenzene (99 mg, 0.5 mmol, 1 equiv). The compound was obtained as a colourless oil (80 mg, 0.4 mmol, 81%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.34 – 7.30 (m, 2H), 7.27 – 7.22 (m, 3H), 6.98 – 6.92 (m, 2H), 6.70 (d, J = 7.8 Hz, 1H), 4.57 (s, 1H), 3.99 (s, 2H), 2.28 ppm (s, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 151.52, 140.13, 131.67, 130.26, 128.77, 128.75, 128.32, 126.80, 126.43, 115.70, 36.48, 20.65 ppm. **FT-IR:** v = 3528, 3025, 2918, 2360, 2341 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{14}$H$_{13}$O = 197.0971; found 197.0974.

3-Benzyl-4-methylphenol (127b*). Prepared according to general procedure L using 1-(benzyloxy)-4-methylbenzene (99 mg, 0.5 mmol, 1 equiv). The compound was obtained as a colourless oil (6 mg, 0.03 mmol, 6%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.29 (dd, J = 10.3, 4.6 Hz, 2H), 7.21 (t, J = 7.3 Hz, 1H), 7.16 – 7.12 (m, 2H), 7.03 (d, J = 8.1 Hz, 1H), 6.63 (m, 1H), 6.56 (d, J = 2.7 Hz, 1H), 4.56 (s, 1H), 3.92 (s, 2H), 2.18 ppm (s, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 153.99, 140.82, 140.39, 131.56, 129.24, 128.83, 126.42, 117.12, 113.38, 39.77, 19.14 ppm. **FT-IR:** v = 3336, 3024, 2917, 2360, 2341 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{14}$H$_{13}$O = 197.0971; found 197.0974.
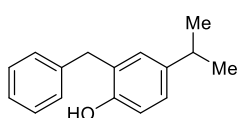
2-Benzyl-4-isopropyl-1-methylbenzene (127c). Prepared according to general procedure L using 1-(benzyloxy)-4-isopropylbenzene (113 mg, 0.5 mmol, 1 equiv). The compound was obtained as a colourless oil (77 mg, 0.34 mmol, 68%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.30 (t, J = 7.5 Hz, 2H), 7.22 (dd, J = 15.1, 7.3 Hz, 3H), 7.00 (d, J = 6.3 Hz, 2H), 6.74 – 6.71 (m, 1H), 4.51 (s, 1H), 3.99 (s, 2H), 2.83 (m, 1H), 1.22 ppm (d, J = 6.9 Hz, 6H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 151.82, 141.54, 140.11, 129.25, 128.76, 128.75, 126.61, 126.44, 125.60, 115.72, 36.78, 33.41, 24.39 ppm. **FT-IR:** v = 3527, 3026, 2955, 2360, 2341 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{16}$H$_{17}$O = 225.1284; found 225.1286.
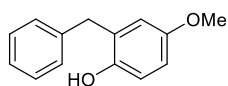
2-Benzyl-4-(*tert*-butyl)phenol (127d). Prepared according to general procedure L using 1-(benzyloxy)-4-(tert-butyl)benzene (120 mg, 0.5 mmol, 1 equiv). The compound was obtained as a colourless oil (85 mg, 0.35 mmol, 71%). **^{1}H NMR** (600 MHz, CDCl$_3$) δ 7.42 – 7.29 (m, 6H), 7.26 – 7.20 (m, 1H), 6.82 (d, J = 8.5 Hz, 1H), 4.10 (s, 2H), 1.39 (s, 9H). **^{13}C NMR** (151 MHz, CDCl$_3$) δ 151.61,

143.82, 140.18, 128.75, 128.72, 128.19, 126.43, 126.19, 124.73, 115.41, 37.00, 34.20, 31.70 ppm. **FT-IR:** v = 3528, 3026, 2960, 2904, 2360, 2341 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{17}$H$_{19}$O = 239.1441; found 239.1442.
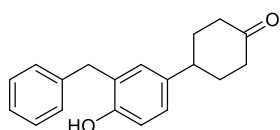
4-(3-Benzyl-4-hydroxyphenyl)cyclohexan-1-one (127e). Prepared according to general procedure L using 4-(4-(benzyloxy)phenyl)cyclohexan-1-one (140 mg, 0.5 mmol, 1 equiv). The compound was obtained as a white solid (90 mg, 0.32 mmol, 64%). **¹H NMR** (500 MHz, DMSO) δ 9.22 (s, 1H), 7.27 – 7.20 (m, 4H), 7.14 (t, J = 6.7 Hz, 1H), 6.98 (d, J = 2.1 Hz, 1H), 6.92 (dd, J = 8.2, 2.2 Hz, 1H), 6.73 (d, J = 8.2 Hz, 1H), 3.83 (s, 2H), 2.88 (m, 1H), 2.54 (dd, J = 14.1, 6.0 Hz, 1H), 2.21 (dd, J = 12.5, 1.9 Hz, 2H), 2.03 – 1.93 (m, 2H), 1.76 ppm (m, 2H). **¹³C NMR** (126 MHz, DMSO) δ 210.53, 153.31, 141.40, 135.62, 128.78, 128.66, 128.18, 127.12, 125.63, 125.04, 114.93, 40.92, 40.84, 35.45, 33.80 ppm. **FT-IR:** v = 3377, 2930, 2869, 2360, 2341, 1697 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{19}$H$_{19}$O$_2$ = 279.13905; found 279.1352.
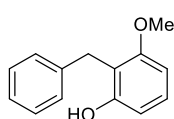
2-Benzyl-4-methoxyphenol (127f$^\#$). Prepared according to general procedure L using 1-(benzyloxy)-4-methoxybenzene (107 mg, 0.5 mmol, 1 equiv). The compound was obtained as a colourless oil (57 mg, 0.27 mmol, 53%). **¹H NMR** (500 MHz, CDCl$_3$) δ 7.30 (t, J = 6.5 Hz, 2H), 7.22 (m, 3H), 6.70 (m, 3H), 4.45 (s, 1H), 3.97 (s, 2H), 3.74 ppm (s, 3H). **¹³C NMR** (126 MHz, CDCl$_3$) δ 153.85, 147.8, 139.8, 128.8, 128.3, 126.5, 116.8, 116.5, 112.5, 55.8, 36.7 ppm. **FT-IR:** v = 3419, 3025, 2913, 2834, 2360, 2340 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{14}$H$_{13}$O$_2$ = 213.0921; found 213.0922.
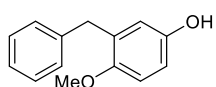
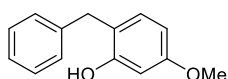**3-Benzyl-4-methoxyphenol (127f*).** Prepared according to general procedure L using 1-(benzyloxy)-4-methoxybenzene (107 mg, 0.5 mmol, 1 equiv). The compound was obtained as a colourless oil (16 mg, 0.07 mmol, 15%). **¹H NMR** (500 MHz, CDCl$_3$) δ 7.30 – 7.26 (m, 2H), 7.23 – 7.18 (m, 3H), 6.75 (d, J = 8.7 Hz, 1H), 6.65 (dd, J = 8.7, 3.1 Hz, 1H), 6.53 (d, J = 3.1 Hz, 1H), 4.48 (s, 1H), 3.93 (s, 2H), 3.77 ppm (s, 3H). **¹³C NMR** (126 MHz, CDCl$_3$) δ 151.70, 149.28, 140.72, 131.21, 129.18, 128.46, 126.05, 117.60, 113.31, 111.79, 56.19, 35.85 ppm. **FT-IR:** v = 3420, 3025, 2944, 2833, 2360, 2341 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{14}$H$_{13}$O$_2$ = 213.0921; found 213.0922.
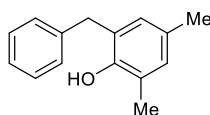
2-Benzyl-3-methoxyphenol (127g$^\#$). Prepared according to general procedure L using 1-(benzyloxy)-3-methoxybenzene (107 mg, 0.5 mmol, 1 equiv). The compound was obtained as a colourless oil (52 mg, 0.24 mmol, 48%). **¹H NMR** (500 MHz, CDCl$_3$) δ 7.24 – 7.20 (m, 2H), 7.17 – 7.11 (m, 3H), 6.95 (d, J = 8.3 Hz, 1H), 6.40

(dd, J = 8.3, 2.5 Hz, 1H), 6.32 (d, J = 2.5 Hz, 1H), 4.59 (s, 1H), 3.86 (s, 2H), 3.70 ppm (s, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 159.70, 154.71, 140.19, 131.56, 128.82, 128.66, 126.52, 119.19, 106.29, 102.20, 55.47, 35.92 ppm. **FT-IR:** v = 3379, 2923, 2853, 2360, 2341 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{14}$H$_{13}$O$_2$ = 213.0921; found 213.0897.
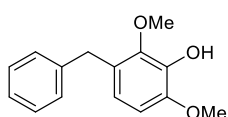
2-Benzyl-5-methoxyphenol (127g*). Prepared according to general procedure L using 1-(benzyloxy)-3-methoxybenzene (107 mg, 0.5 mmol, 1 equiv). The compound was obtained as a colourless oil (27 mg, 0.13 mmol, 25%). **^{1}H NMR** (400 MHz, CDCl$_3$) δ 7.27 – 7.14 (m, 5H), 7.08 (t, J = 8.2 Hz, 1H), 6.53 (d, J = 8.2 Hz, 1H), 6.44 (d, J = 8.1 Hz, 1H), 4.74 (s, 1H), 4.05 (s, 2H), 3.81 ppm (s, 3H). **^{13}C NMR** (101 MHz, CDCl$_3$) δ 158.75, 154.80, 140.68, 128.52, 127.66, 126.04, 115.71, 108.77, 103.56, 55.91, 28.82 ppm. **FT-IR:** v = 3384, 2930, 2836, 2360, 2341 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{14}$H$_{13}$O$_2$ = 213.0921; found 213.0922.

2-Benzyl-4,6-dimethylphenol (127h). Prepared according to general procedure L using 1-(benzyloxy)-2,4-dimethylbenzene (106 mg, 0.5 mmol, 1 equiv). The compound was obtained as a colourless oil (74 mg, 0.35 mmol, 70%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.33 – 7.28 (m, 2H), 7.26 – 7.22 (m, 3H), 6.86 (s, 1H), 6.82 (s, 1H), 4.45 (s, 1H), 3.97 (s, 2H), 2.25 (s, 3H), 2.20 (s, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 150.24, 140.34, 130.27, 129.90, 129.55, 129.07, 129.00, 126.76, 126.54, 123.99, 37.12, 20.88, 16.24 ppm. **FT-IR:** v = 3443, 3419, 3024, 3003, 2914, 2360, 2341 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{15}$H$_{15}$O = 211.1128; found 211.1129.
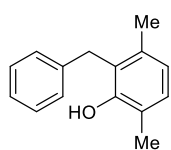
2-Benzyl-3,6-dimethylphenol (127i). Prepared according to general procedure L using 1-(benzyloxy)-2,5-dimethylbenzene (106 mg, 0.5 mmol, 1 equiv). The compound was obtained as a colourless oil (61 mg, 0.29 mmol, 57%). **^{1}H NMR** (500 MHz, Acetone) δ 7.19 (m, 4H), 7.11 (t, J = 7.2 Hz, 1H), 6.90 (d, J = 7.6 Hz, 1H), 6.64 (d, J = 7.6 Hz, 1H), 4.09 (s, 2H), 2.26 (s, 3H), 2.16 ppm (s, 3H). **^{13}C NMR** (126 MHz, Acetone) δ 153.97, 141.78, 136.35, 129.18, 129.07, 128.90, 126.68, 126.28, 122.50, 122.42, 32.53, 19.84, 16.76 ppm. **FT-IR:** v = 3446, 3025, 2969, 2921, 2360, 2341 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{15}$H$_{15}$O = 211.1128; found 211.1129.

3-Benzyl-2,6-dimethoxyphenol (127j). Prepared according to general procedure L using 2-(benzyloxy)-1,3-dimethoxybenzene (122 mg, 0.5 mmol). The compound was obtained as a yellow oil (89 mg, 0.36 mmol, 73%). **^{1}H NMR** (600 MHz, CDCl$_3$) δ 7.28 – 7.25 (m, 2H), 7.21 (d, J = 7.1 Hz,

2H), 7.17 (t, J = 7.2 Hz, 1H), 6.60 (d, J = 2.3 Hz, 2H), 5.53 (s, 1H), 3.95 (s, 2H), 3.87 (s, 3H), 3.76 ppm (s, 3H). **^{13}C NMR** (151 MHz, CDCl$_3$) δ 146.50, 145.50, 141.53, 138.80, 128.93, 128.42, 127.50, 125.97, 120.33, 106.40, 60.59, 56.35, 35.76 ppm. **FT-IR:** v = 3503, 2938, 2835, 2360, 2341 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{15}$H$_{15}$O$_3$ = 243.1026; found 243.1026.
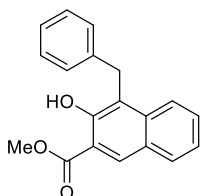
Methyl 4-benzyl-3-hydroxy-2-naphthoate (127k). Prepared according to general procedure L using methyl 3-(benzyloxy)-2-naphthoate (146 mg, 0.5 mmol, 1 equiv). The compound was obtained as a yellow solid (85 mg, 0.29 mmol, 58%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 10.83 (s, 1H), 8.48 (s, 1H), 7.90 (d, J = 8.7 Hz, 1H), 7.83 (d, J = 8.2 Hz, 1H), 7.50 (m 1H), 7.34 – 7.30 (m, 1H), 7.23 (dd, J = 12.1, 4.9 Hz, 4H), 7.14 (t, J = 6.8 Hz, 1H), 4.50 (s, 2H), 4.04 ppm (s, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 170.81, 154.12, 140.80, 136.86, 131.54, 130.24, 129.42, 128.47, 128.43, 127.23, 125.93, 123.67, 123.58, 120.68, 113.91, 52.81, 30.50 ppm. **FT-IR:** v = 3177, 3059, 3025, 2950, 2360, 2341, 1674 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{19}$H$_{15}$O$_3$ = 291.1026; found 291.1026.
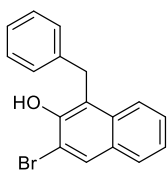
1-Benzyl-3-bromonaphthalen-2-ol (127l). Prepared according to general procedure L using 2-(benzyloxy)-3-bromonaphthalene (157 mg, 0.5 mmol, 1 equiv). The compound was obtained as a white crystalline solid (76 mg, 0.24 mmol, 49%). **^{1}H NMR** (400 MHz, CDCl$_3$) δ 8.00 (s, 1H), 7.91 (d, J = 8.6 Hz, 1H), 7.70 (d, J = 8.1 Hz, 1H), 7.45 (m, 1H), 7.39 – 7.29 (m, 1H), 7.26 – 7.11 (m, 5H), 5.79 (s, 1H), 4.53 ppm (s, 2H). **^{13}C NMR** (101 MHz, CDCl$_3$) δ 147.36, 140.34, 133.14, 130.06, 129.91, 128.56, 128.40, 127.76, 127.15, 126.13, 124.30, 123.88, 120.45, 112.95, 31.83 ppm. **FT-IR:** v = 3444, 3421, 3024, 2922, 2360, 2341 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{17}$H$_{12}$O^{79}Br = 311.00770; found 311.00351; C$_{17}$H$_{12}$O^{81}Br = 313.0056; found 313.0014.
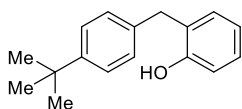
2-(4-(*tert*-Butyl)benzyl)phenol (127m$^\#$). Prepared according to general procedure L using 1-(*tert*-butyl)-4-(phenoxymethyl)benzene (120 mg, 0.5 mmol, 1 equiv). The compound was obtained as a colourless oil (72 mg, 0.3 mmol, 60%). **^{1}H NMR** (700 MHz, CDCl$_3$) δ 7.33 (d, J = 8.3 Hz, 2H), 7.19 – 7.12 (m, 4H), 6.91 (td, J = 7.5, 0.9 Hz, 1H), 6.80 (d, J = 7.5 Hz, 1H), 4.66 (s, 1H), 3.98 (s, 2H), 1.31 ppm (s, 9H). **^{13}C NMR** (176 MHz, CDCl$_3$) δ 154.11, 149.59, 136.85, 131.33, 128.57, 128.16, 127.32, 125.95, 121.28, 116.12, 36.27, 34.72, 31.69 ppm. **FT-IR:** v = 3527, 2960, 2903, 2867, 2360, 2341 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{17}$H$_{19}$O = 239.1441; found 239.1443.
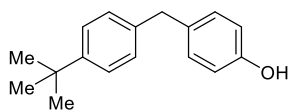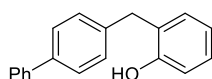
4-(4-(*tert*-Butyl)benzyl)phenol (127m*). Prepared according to general procedure L using 1-(*tert*-butyl)-4-(phenoxymethyl)benzene (120 mg, 0.5 mmol, 1 equiv). The 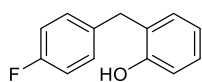compound was obtained as a colourless solid (18 mg, 0.07 mmol, 15%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.31 (d, J = 8.3 Hz, 2H), 7.10 (dd, J = 18.4, 8.3 Hz, 4H), 6.77 (d, J = 8.5 Hz, 2H), 3.89 (s, 2H), 1.31 ppm (s, 9H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 153.84, 148.89, 138.60, 133.69, 130.21, 128.49, 125.46, 115.37, 40.61, 34.48, 31.52 ppm. **FT-IR:** v = 3241, 2957, 2902, 2867, 2360, 2341 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{17}$H$_{19}$O = 239.1441; found 239.1442.

2-([1,1'-Biphenyl]-4-ylmethyl)phenol (127n#). Prepared according to general procedure L using 4-(phenoxymethyl)-1,1'-biphenyl (130 mg, 0.5 mmol, 1 equiv). The compound was obtained as a white solid (77 mg, 0.30 mmol, 59%). **^{1}H NMR** (600 MHz, CDCl$_3$) δ 7.58 (d, J = 7.1 Hz, 2H), 7.53 (d, J = 8.2 Hz, 2H), 7.43 (t, J = 7.7 Hz, 2H), 7.36 – 7.29 (m, 3H), 7.17 (m, 2H), 6.93 (td, J = 7.4, 1.1 Hz, 1H), 6.81 (dd, J = 7.9, 0.9 Hz, 1H), 4.71 (s, 1H), 4.05 ppm (s, 2H). **^{13}C NMR** (151 MHz, CDCl$_3$) δ 153.82, 141.08, 139.44, 139.15, 131.17, 129.22, 128.87, 128.05, 127.51, 127.26, 127.16, 127.04, 121.18, 115.88, 36.12 ppm. **FT-IR:** v = 3381, 3030, 2920, 2359, 2341 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{19}$H$_{15}$O = 259.1128; found 259.1127.
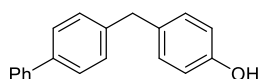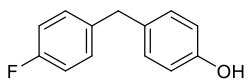
4-([1,1'-Biphenyl]-4-ylmethyl)phenol (127n*). Prepared according to general procedure L using 4-(phenoxymethyl)-1,1'-biphenyl (130 mg, 0.5 mmol, 1 equiv). The compound was obtained as a white solid (20 mg, 0.08 mmol, 15%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.57 (dd, J = 8.2, 1.1 Hz, 2H), 7.52 (d, J = 8.2 Hz, 2H), 7.43 (dd, J = 10.6, 4.8 Hz, 2H), 7.33 (t, J = 7.4 Hz, 1H), 7.25 (d, J = 8.2 Hz, 2H), 7.10 (d, J = 8.5 Hz, 2H), 6.78 (d, J = 8.5 Hz, 2H), 4.67 (s, 1H), 3.96 ppm (s, 2H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 153.97, 141.13, 140.78, 139.10, 133.44, 130.24, 129.33, 128.86, 127.34, 127.21, 127.15, 115.46, 40.79 ppm. **FT-IR:** v = 3417, 3027, 2912, 2848, 2359 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{19}$H$_{15}$O = 259.1128; found 259.1128.

2-(4-Fluorobenzyl)phenol (127o#). Prepared according to general procedure L using 1-fluoro-4-(phenoxymethyl)benzene (101 mg, 0.5 mmol, 1 equiv). The compound was obtained as a colourless oil (68 mg, 0.34 mmol, 67%). **^{1}H NMR** (400 MHz, CDCl$_3$) δ 7.23 – 7.08 (m, 4H), 7.02 – 6.94 (m, 2H), 6.91 (td, J = 7.4, 0.9 Hz, 1H), 6.78 (d, J = 8.0 Hz, 1H), 4.68 (s, 1H), 3.97 ppm (s, 2H). **^{13}C NMR** (101 MHz, CDCl$_3$) δ 162.83, 160.41, 153.63, 135.82 (d, J_{CF} = 3.2 Hz), 131.02, 130.23 (d, J_{CF} = 7.9 Hz), 128.04, 127.11, 121.20,

115.49 (t, J_{CF} = 23.9 Hz), 35.54 ppm. **FT-IR:** v = 3501, 3417, 3036, 2914, 2359, 2340 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ $C_{13}H_{10}OF$ = 201.0721; found 201.0723.

4-(4-Fluorobenzyl)phenol (127o*). Prepared according to general procedure L using 1-fluoro-4-(phenoxymethyl)benzene (101 mg, 0.5 mmol, 1 equiv). The compound was obtained as a colourless oil (17 mg, 0.08 mmol, 17%). **¹H NMR** (500 MHz, CDCl$_3$) δ 7.12 (dd, J = 8.5, 5.6 Hz, 2H), 7.04 (d, J = 8.5 Hz, 2H), 6.97 (t, J = 7.7 Hz, 2H), 6.79 – 6.74 (m, 2H), 4.66 (s, 1H), 3.88 ppm (s, 2H). **¹³C NMR** (126 MHz, CDCl$_3$) δ 161.48 (d, J_{CF} = 243.8 Hz), 153.96, 137.28 (d, J_{CF} = 3.1 Hz), 133.40, 130.28 (d, J_{CF} = 7.9 Hz), 130.11, 115.43 (d, J = 10.1 Hz), 115.22, 40.28 ppm. **FT-IR:** v = 3264, 3029, 2916.95, 2853, 2360, 2341 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ $C_{13}H_{10}OF$ = 201.0721; found 201.0723.
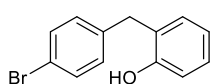
2-(4-Bromobenzyl)phenol (127p#). Prepared according to general procedure L using 1-bromo-4-(phenoxymethyl)benzene (132 mg, 0,5 mmol, 1 equiv). The compound was obtained as a white solid (88 mg, 0.33 mmol, 66%). **¹H NMR** (500 MHz, CDCl$_3$) δ 7.44 – 7.37 (m, 2H), 7.13 – 7.08 (m, 3H), 6.90 (td, J = 7.4, 1.0 Hz, 1H), 6.77 (dd, J = 8.0, 0.8 Hz, 1H), 4.72 (s, 1H), 3.94 ppm (s, 2H). **¹³C NMR** (126 MHz, CDCl$_3$) δ 153.56, 139.33, 131.66, 131.05, 130.60, 128.09, 126.73, 121.20, 120.12, 115.71, 35.72 ppm. **FT-IR:** v = 3500, 3034, 2918, 2361, 2342 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ $C_{13}H_{10}O^{81}Br$ = 262.9900; found 262.9893.
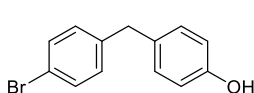
4-(4-bromobenzyl)phenol (127p*). Prepared according to general procedure L using 1-bromo-4-(phenoxymethyl)benzene (132 mg, 0,5 mmol, 1 equiv). The compound was obtained as an orange solid (22 mg, 0.08 mmol, 17%). **¹H NMR** (500 MHz, CDCl$_3$) δ 7.39 (d, J = 8.3 Hz, 2H), 7.03 (t, J = 8.3 Hz, 4H), 6.76 (d, J = 8.5 Hz, 2H), 4.76 (s, 1H), 3.86 (s, 2H). **¹³C NMR** (126 MHz, CDCl$_3$) δ 154.07, 140.63, 132.88, 131.61, 130.68, 130.16, 119.97, 115.51, 40.51 ppm. **FT-IR:** v = 3404, 2923, 2905, 2849, 2360, 2340 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ $C_{13}H_{10}O^{81}Br$ = 262.9900; found 262.9900.
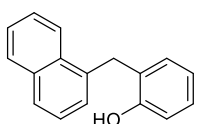
2-(Naphthalen-1-ylmethyl)phenol (127q#). Prepared according to general procedure L using 1-(phenoxymethyl)naphthalene (117 mg, 0.5 mmol, 1 equiv). The compound was obtained as a colourless solid (74 mg, 0.32 mmol, 63%). **¹H NMR** (500 MHz, Acetone) δ 8.59 (s, 1H), 8.16 – 8.11 (m, 1H), 7.92 – 7.87 (m, 1H), 7.79 (d, J = 8.2 Hz, 1H), 7.49 – 7.45 (m, 2H), 7.45 – 7.40 (m, 1H), 7.34 (d, J = 7.0 Hz, 1H), 7.06 (td, J = 7.9, 1.6 Hz, 1H), 6.97 (dd, J = 8.0, 1.0 Hz, 1H), 6.87 (dd, J = 7.6, 1.4 Hz, 1H), 6.70 (td, J = 7.5, 1.1 Hz, 1H), 4.46 ppm (s, 2H). **¹³C NMR** (126 MHz, Acetone) δ

155.54, 137.86, 134.84, 133.12, 130.97, 129.34, 127.99, 127.73, 127.71, 127.56, 126.59, 126.38, 126.29, 125.14, 120.36, 115.77, 32.89 ppm. **FT-IR:** v = 3526, 3039, 3010, 2902, 2359, 2341 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{17}$H$_{13}$O = 233.0971; found 233.0971.
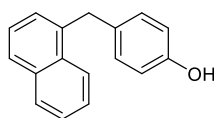
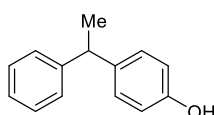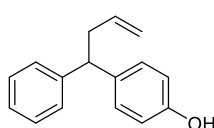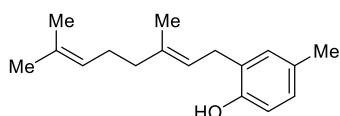**4-(Naphthalen-1-ylmethyl)phenol (127q*).** Prepared according to general procedure L using 1-(phenoxymethyl)naphthalene (117 mg, 0.5 mmol, 1 equiv). The compound was obtained as a colourless solid (20 mg, 0.09 mmol, 17%). **^{1}H NMR** (500 MHz, Acetone) δ 8.18 (s, 1H), 8.08 (d, J = 9.7 Hz, 1H), 7.89 (s, 1H), 7.79 (d, J = 8.2 Hz, 1H), 7.46 (m, 3H), 7.35 (d, J = 6.9 Hz, 1H), 7.07 (d, J = 8.6 Hz, 2H), 6.78 – 6.71 (m, 2H), 4.36 ppm (s, 2H). **^{13}C NMR** (126 MHz, Acetone) δ 156.52, 138.46, 135.00, 132.95, 132.36, 130.44, 129.40, 127.89, 127.71, 126.63, 126.40, 126.34, 125.26, 116.01, 115.92, 38.60 ppm. **FT-IR:** v = 3245, 3038, 2909, 2360, 2341 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{17}$H$_{13}$O = 233.0971; found 233.0972.

4-(1-Phenylethyl)phenol (127r$^{\#}$). Prepared according to general procedure L using (1-phenoxyethyl)benzene (99 mg, 0.5 mmol, 1 equiv). The compound was obtained as a colourless oil (40 mg, 0.2 mmol, 40%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.30 (t, J = 7.5 Hz, 2H), 7.20 (dd, J = 17.0, 7.6 Hz, 3H), 7.10 (d, J = 8.4 Hz, 2H), 6.76 (d, J = 8.6 Hz, 2H), 4.81 (s, 1H), 4.11 (q, J = 7.2 Hz, 1H), 1.62 ppm (d, J = 7.2 Hz, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 153.72, 146.84, 138.86, 128.86, 128.47, 127.65, 126.08, 115.25, 44.02, 22.18 ppm. **FT-IR:** v = 3395, 2961, 2923, 2360, 2341 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{14}$H$_{13}$O = 197.0971; found 197.0973.

4-(1-Phenylbut-3-en-1-yl)phenol (127s$^{\#}$). Prepared according to general procedure L using (1-phenoxybut-3-en-1-yl)benzene (112 mg, 0.5 mmol, 1 equiv). The compound was obtained as a colourless oil (38 mg, 0.17 mmol, 34%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.30 (t, J = 7.5 Hz, 2H), 7.25 (dd, J = 10.5, 3.6 Hz, 2H), 7.19 (t, J = 7.2 Hz, 1H), 7.12 (d, J = 8.4 Hz, 2H), 6.76 (d, J = 8.5 Hz, 2H), 5.81 – 5.65 (m, 1H), 5.05 (d, J = 18.5 Hz, 1H), 4.97 (d, J = 10.2 Hz, 1H), 3.97 (t, J = 7.9 Hz, 1H), 2.80 ppm (t, J = 7.4 Hz, 2H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 153.84, 144.97, 137.05, 136.94, 129.18, 128.51, 127.95, 126.24, 116.37, 115.34, 50.46, 40.24 ppm. **FT-IR:** v = 3336, 3024, 2922, 2360.12341 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{16}$H$_{15}$O = 223.1128; found 223.1129.

(E)-2-(3,7-Dimethylocta-2,6-dien-1-yl)-4-methylphenol (127t). Prepared according to general procedure L using (E)-1-((3,7-dimethylocta-2,6-dien-1-yl)oxy)-4-methylbenzene (122 mg,

0.5 mmol, 1 equiv). The compound was obtained as a colourless oil (30 mg, 0.12 mmol, 25%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 6.95 – 6.89 (m, 2H), 6.74 – 6.68 (m, 1H), 5.37 – 5.28 (m, 1H), 5.13 – 5.05 (m, 1H), 5.01 (s, 1H), 3.34 (d, J = 7.2 Hz, 2H), 2.27 (s, 3H), 2.11 (dq, J = 20.3, 7.2 Hz, 4H), 1.78 (s, 3H), 1.69 (s, 3H), 1.61 ppm (s, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 152.29, 138.43, 132.10, 130.65, 129.98, 128.02, 126.70, 123.97, 121.95, 115.79, 39.82, 29.98, 26.53, 25.84, 20.66, 17.85, 16.31 ppm. **FT-IR:** v = 3446, 2967, 2915, 2858, 2360, 2341 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{17}$H$_{23}$O = 243.1754; found 243.1754.
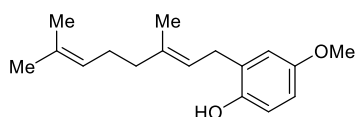

(E)-2-(3,7-Dimethylocta-2,6-dien-1-yl)-4-methoxyphenol (127u). Prepared according to general procedure L using (E)-1-((3,7-dimethylocta-2,6-dien-1-yl)oxy)-4-methoxybenzene (130 mg, 0.5 mmol, 1 equiv). The compound was obtained as a colourless oil (32 mg, 0.12 mmol, 25%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 6.75 (d, J = 8.6 Hz, 1H), 6.69 (d, J = 2.9 Hz, 1H), 6.66 (dd, J = 8.6, 3.0 Hz, 1H), 5.35 – 5.28 (m, 1H), 5.11 – 5.04 (m, 1H), 4.87 (s, 1H), 3.76 (s, 3H), 3.34 (d, J = 7.2 Hz, 2H), 2.10 (dq, J = 13.5, 6.9 Hz, 4H), 1.76 (s, 3H), 1.69 (s, 3H), 1.60 (s, 3H) ppm. **^{13}C NMR** (126 MHz, CDCl$_3$) δ 153.71, 148.43, 138.73, 132.14, 128.22, 123.94, 121.55, 116.50, 115.77, 112.13, 55.82, 39.80, 30.10, 26.56, 25.82, 17.84, 16.32 ppm. **FT-IR:** v = 3408, 2964, 2913, 2854, 2359, 2341 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{17}$H$_{23}$O$_2$ = 259.1703; found 259.1703.
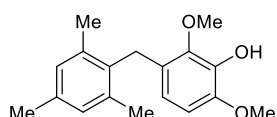
2,6-Dimethoxy-3-(2,4,6-trimethylbenzyl)phenol (127v). Prepared according to general procedure L using 2-((2,6-dimethoxyphenoxy)methyl)-1,3,5-trimethylbenzene (143 mg, 0.5 mmol, 1 equiv). The compound was obtained as an orange solid (120 mg, 0.42 mmol, 84%). **^{1}H NMR** (400 MHz, CDCl$_3$) δ 6.89 (s, 2H), 6.44 (d, J = 8.5 Hz, 1H), 6.03 (d, J = 8.5 Hz, 1H), 5.54 (s, 1H), 3.95 (d, J = 4.0 Hz, 5H), 3.83 (s, 3H), 2.30 (s, 3H), 2.18 ppm (s, 6H). **^{13}C NMR** (101 MHz, CDCl$_3$) δ 146.16, 145.38, 138.52, 137.33, 135.64, 133.65, 128.92, 126.05, 117.68, 106.34, 60.38, 56.28, 28.19, 21.05, 20.06 ppm. **FT-IR:** v = 3396, 2921, 2360, 2341 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{18}$H$_{21}$O$_3$ = 285.1496; found 285.1458.
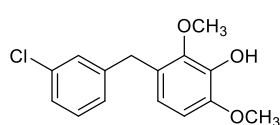
3-(3-Chlorobenzyl)-2,6-dimethoxyphenol (127w). Prepared according to general procedure L using 2-((3-chlorobenzyl)oxy)-1,3-dimethoxybenzene (139 mg, 0.5 mmol, 1 equiv). The compound was obtained as a yellow oil (101 mg, 0.36 mmol, 72%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.50 (s, 1H), 7.27 (t, J = 7.8 Hz, 1H), 7.22 (s, 1H), 7.20 – 7.14 (m, 2H), 6.65 (dd, J = 20.9, 8.4 Hz, 2H),

3.90 (s, 2H), 3.80 (s, 3H), 3.73 ppm (s, 3H). ^{13}**C NMR** (126 MHz, CDCl$_3$) δ 148.44, 146.69, 145.46, 140.45, 134.28, 130.61, 129.42, 128.12, 127.14, 126.51, 120.41, 107.56, 60.16, 56.44, 36.06 ppm. **FT-IR:** v = 3510, 2937, 2836, 2360, 2341 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{15}$H$_{14}$O$_3$^{35}Cl = 277.06370; found 277.05996; C$_{15}$H$_{14}$O$_3$^{37}Cl = 279.06075; found 279.0569.
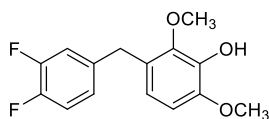
**3-(3,4-Difluorobenzyl)-2,6-dimethoxyphenol (127x).** Prepared according to general procedure L using 2-((3,4-difluorobenzyl)oxy)-1,3-dimethoxybenzene (140 mg, 0.5 mmol, 1 equiv). The compound was obtained as a yellow oil (85 mg, 0.3 mmol, 61%). ^{1}**H NMR** (400 MHz, CDCl$_3$) δ 7.08 – 6.94 (m, 2H), 6.90 (d, J = 6.5 Hz, 1H), 6.59 (s, 2H), 5.54 (s, 1H), 3.87 (s, 5H), 3.76 ppm (s, 3H). ^{13}**C NMR** (101 MHz, CDCl$_3$) δ 151.90 – 147.34 (m), 146.85, 145.37, 138.90, 138.78 – 138.53 (m), 126.55, 124.53 (dd, J_{CF} = 6.0, 3.5 Hz), 120.17, 117.55 (d, J_{CF} = 17.0 Hz), 116.95 (d, J_{CF} = 17.1 Hz), 106.34, 60.54, 56.37, 35.18 ppm. **FT-IR:** v = 3340, 2950, 2836, 2360, 2341 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{15}$H$_{13}$O$_3$F$_2$ = 279.0838; found 279.0800.
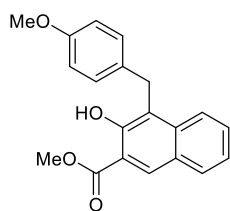
Methyl 3-hydroxy-4-(4-methoxybenzyl)-2-naphthoate (127y). Prepared according to general procedure L using methyl 3-((4-methoxybenzyl)oxy)-2-naphthoate (129 mg, 0.5 mmol, 1 equiv). The compound was obtained as a white solid (39 mg, 0.12 mmol, 30%). ^{1}**H NMR** (600 MHz, CD$_2$Cl$_2$) δ 10.84 (s, 1H), 8.49 (s, 1H), 7.87 (dd, J = 30.3, 8.4 Hz, 2H), 7.51 (d, J = 1.4 Hz, 1H), 7.38 – 7.29 (m, 1H), 7.15 (d, J = 8.7 Hz, 2H), 6.81 – 6.70 (m, 2H), 4.41 (s, 2H), 4.03 (s, 3H), 3.72 ppm (s, 3H). ^{13}**C NMR** (151 MHz, CD$_2$Cl$_2$) δ 171.31, 158.41, 154.37, 137.07, 133.34, 131.82, 130.69, 129.75, 129.70, 127.74, 124.11, 123.86, 121.50, 114.48, 114.20, 55.67, 53.23, 29.84 ppm. **FT-IR:** v = 3444, 3420, 2923, 2360, 2340, 1674 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{20}$H$_{17}$O$_4$ = 321.1132; found 321.1129.
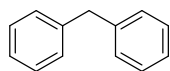
Diphenylmethane (130a). Prepared according to general procedure M using benzyl alcohol (21 µL, 0.2 mmol, 1 equiv) and benzene (178 µL, 2 mmol, 10 equiv). The compound was obtained as colourless solid (23 mg, 0.14 mmol, 68%). **MS-EI:** m/z (%): 167.1 (100) [M]$^{+•}$, 152.1 (30), 91.1 (20). ^{1}**H NMR** (500 MHz, CDCl$_3$) δ 7.30 (t, J = 7.6 Hz, 4H), 7.21 (m, 6H), 4.00 ppm (s, 2H). ^{13}**C NMR** (126 MHz, CDCl$_3$) δ 141.24, 129.07, 128.59, 126.20, 42.06 ppm. FT-IR: v = 3062, 2921, 2850, 2359, 2340 cm^{-1}. Spectral data matched literature characterization.[216]
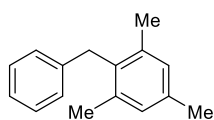
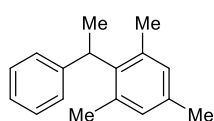**2-Benzyl-1,3,5-trimethylbenzene (130b).** Prepared according to general procedure M using benzyl alcohol (21 µL, 0.2 mmol, 1 equiv) and mesitylene (278 µL, 2 mmol, 10 equiv). The compound was obtained as colourless oil (32 mg, 0.15 mmol, 76%). **MS-EI:** *m/z* (%): 210.2 (70) [M]⁺, 195.1 (100), 180.1 (30), 165.1 (30). **¹H NMR** (500 MHz, CDCl₃) δ 7.28 (d, *J* = 7.3 Hz, 2H), 7.20 (t, *J* = 7.3 Hz, 1H), 7.06 (d, *J* = 7.3 Hz, 2H), 6.94 (s, 2H), 4.07 (s, 2H), 2.34 (s, 3H), 2.25 ppm (s, 6H). **¹³C NMR** (126 MHz, CDCl₃) δ 140.15, 137.09, 135.73, 133.84, 128.93, 128.40, 127.90, 125.71, 34.75, 20.99, 20.21 ppm. **FT-IR:** v = 3059, 2998, 2968, 2860 cm⁻¹. Spectral data matched literature characterization.[217]

1,3,5-Trimethyl-2-(1-phenylethyl)benzene (130c). Prepared according to general procedure M using 1-phenylethanol (24.5 µL, 0.2 mmol, 1 equiv) and mesitylene (278 µL, 2 mmol, 10 equiv). The compound was ob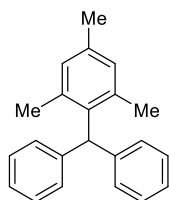tained as colourless oil (35 mg, 0.16 mmol, 78%). **MS-EI:** *m/z* (%): 224.2 (40) [M]⁺, 209.1 (100), 194.1 (20), 179.1 (30). **¹H NMR** (500 MHz, CDCl₃) δ 7.17 (t, *J* = 7.6 Hz, 2H), 7.11 – 7.06 (m, 3H), 6.74 (s, 2H), 4.56 (q, *J* = 7.3 Hz, 1H), 2.18 (s, 3H), 2.03 (s, 6H), 1.57 ppm (d, *J* = 7.3 Hz, 3H). **¹³C NMR** (126 MHz, CDCl₃) δ 145.51, 140.12, 136.57, 135.45, 130.04, 128.17, 126.87, 125.31, 37.83, 21.12, 20.82, 16.86 ppm. **FT-IR:** v = 3024, 2968, 2935 cm⁻¹. Spectral data matched literature characterization.[218]

(Mesitylmethylene)dibenzene (130d). Prepared according to general procedure M using diphenylmethanol (37 mg, 0.2 mmol, 1 equiv) and mesitylene (278 µL, 2 mmol, 10 equiv). The compound was obtained as white solid (52 mg, 0.18 mmol, 91%). **MS-EI:** *m/z* (%): 286.1 (70) [M]⁺, 271.1 (100), 193.1 (40), 165.1 (60). **¹H NMR** (500 MHz, CDCl₃) δ 7.17 (t, *J* = 7.5 Hz, 4H), 7.09 (d, *J* = 7.4 Hz, 2H), 7.01 (d, *J* = 7.2 Hz, 4H), 6.77 (s, 2H), 5.91 (s, 1H), 2.19 (s, 3H), 1.91 ppm (s, 6H). **¹³C NMR** (126 MHz, CDCl₃) δ 142.59, 137.65, 137.14, 136.08, 130.19, 129.38, 128.23, 125.98, 51.06, 22.08, 20.91 ppm. **FT-IR:** v = 3058, 2917, 2855 cm⁻¹. Spectral data matched literature characterization.[219]
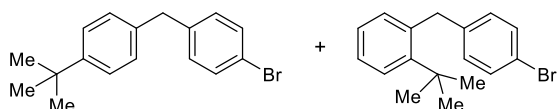
Regioisomeric mixture of 1-bromo-4-(4-(*tert*-butyl)benzyl)benzene and 1-(4-bromobenzyl)-2-(*tert*-butyl)benzene (130e). Prepared according to general procedure M using (4-bromophenyl)methanol (37.5 mg, 0.2 mmol, 1 equiv) and *tert*-butylbenzene (316 µL, 2 mmol, 10 equiv). The compound was obtained as

colourless oil (42 mg, 0.14 mmol, 69%). **Selectivity**: $o{:}p$ = 1:2. **MS-EI:** m/z (%): 302.1/304.1 (30) [M]$^+$, 287.0/289.0 (100), 169.0 (20). **^{1}H NMR** (400 MHz, CDCl$_3$, # denotes major-, * minor regioisomer signals) δ 7.33 – 7.21 (m, 3H), 7.15 – 7.11 (m, 1H), 6.99 (t, J = 8.3 Hz, 4H), 3.84* (s, 2H), 3.81$^\#$ (s, 2H), 1.22 ppm (s, 9H). **^{13}C NMR** (101 MHz, CDCl$_3$, # denotes major-, * minor regioisomer signals) δ 151.49*, 149.16$^\#$, 140.33*, 140.32*, 140.00*, 137.44*, 131.52$^\#$, 131.50$^\#$, 130.74$^\#$, 130.69$^\#$, 128.48$^\#$, 128.29*, 125.98*, 125.96*, 125.50$^\#$, 123.30$^\#$, 119.89*, 119.87*, 41.59*, 40.84$^\#$, 34.67*, 34.43$^\#$, 31.74*, 31.42$^\#$ ppm. **FT-IR:** v = 2960, 2902, 2866, 1738 cm^{-1}. **EA:** (%) calc. for C$_{17}$H$_{19}$Br = C 67.33, H, 6.32; found: C 67.2, H 6.3.
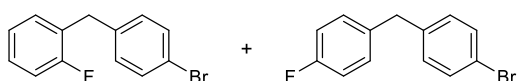
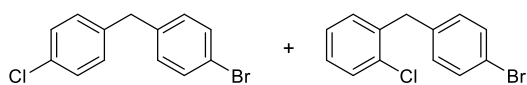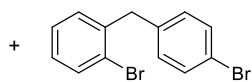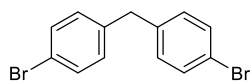**Regioisomeric mixture of 1-(4-bromobenzyl)-2-fluorobenzene and 1-bromo-4-(4-fluorobenzyl)benzene (130f).** Prepared according to general procedure M using (4-bromophenyl)methanol (37.5 mg, 0.2 mmol, 1 equiv) and fluorobenzene (191 µL, 2 mmol, 10 equiv). The compound was obtained as colourless oil (31 mg, 0.12 mmol, 59%). **Selectivity:** $o{:}p$ = 3:1. **MS-EI:** m/z (%): 264.0/266.0 (40) [M]$^+$, 183.1/185.1 (100), 165.1 (60). **^{1}H NMR** (400 MHz, CDCl$_3$, # denotes major-, * minor regioisomer signals) δ 7.32 (d, J = 8.5, 2H), 7.14 – 6.86 (m, 6H), 3.86$^\#$ (s, 2H), 3.81* ppm (s, 2H). **^{13}C NMR** (101 MHz, CDCl$_3$, # denotes major-, * minor regioisomer signals) 161.54$^\#$ (d, J_{CF} = 244.3 Hz), 160.93* (d, J_{CF} = 245.5 Hz), 139.94$^\#$, 138.89*, 139.94$^\#$, 136.12$^\#$ (d, J_{CF} = 3.2 Hz), 131.62$^\#$, 131.59*, 130.93* (d, J_{CF} = 4.5 Hz), 130.58*, 130.52*, 130.27$^\#$ (d, J_{CF} = 7.9 Hz), 128.26$^\#$ (d, J_{CF} = 8.0 Hz), 124.20* (d, J_{CF} = 3.5 Hz), 120.11$^\#$, 115.45* (d, J_{CF} = 21.9 Hz), 115.38$^\#$ (d, J_{CF} = 21.3 Hz) 40.47$^\#$, 34.34* ppm (d, J = 3.1 Hz). **FT-IR:** v = 3039, 2916, 2850, 1897, 1738 cm^{-1}. Spectral data matched literature characterization.[220]

Regioisomeric mixture of 1-bromo-4-(4-chlorobenzyl)benzene and 1-(4-bromobenzyl)-2-chlorobenzene (130g). Prepared according to general procedure M using (4-bromophenyl)methanol (37.5 mg, 0.2 mmol, 1 equiv) and chlorobenzene (207 µL, 2 mmol, 10 equiv). The compound was obtained as colourless oil (38 mg, 0.13 mmol, 68%). **Selectivity:** $o{:}p$ = 2:1. **MS-EI:** m/z (%): 280.0/282.0 (80) [M]$^+$, 245.0/247.0 (40), 201.0 (60), 165.1 (100). **^{1}H NMR** (400 MHz, CDCl$_3$, # denotes major-, * minor regioisomer signals) δ 7.36 – 7.29 (m, 2H), 7.21 – 6.91 (m, 6H), 3.97* (s, 2H), 3.81$^\#$ ppm (s, 2H). **^{13}C NMR** (101 MHz, CDCl$_3$, # denotes major-, * minor regioisomer signals) 139.55$^\#$, 138.92$^\#$, 138.53*, 138.04*, 134.23*, 132.19*, 131.66$^\#$, 131.56$^\#$, 130.98*, 130.66$^\#$, 130.61$^\#$, 130.21$^\#$, 129.68*, 128.71$^\#$, 127.96*,

126.97*, 120.21*, 120.13*, 40.62#, 38.68* ppm. **FT-IR:** v = 2970, 2952, 2911, 1738 cm^{-1}. Spectral data matched literature characterization.[221]

Regioisomeric mixture of bis(4-bromophenyl)methane and 1-bromo-2-(4-bromobenzyl)benzene (130h). Prepared according to general procedure M using (4-bromophenyl)methanol (37.5 mg, 0.2 mmol, 1 equiv) and bromobenzene (213 μL, 2 mmol, 10 equiv). The compound was obtained as colourless oil (51 mg, 0.16 mmol, 78%). **Selectivity:** o:p = 1:2. **MS-EI:** m/z (%): 323.9/325.9/327.9 (90) [M]$^+$, 245.0/247.0 (70), 165.1 (100). **^{1}H NMR** (400 MHz, CDCl$_3$, # denotes major-, * minor regioisomer signals) 7.49* (d, J = 7.9 Hz, 1H), 7.32# (d, J = 8.3 Hz, 4H), 7.15* (d, J = 7.3 Hz, 1H), 7.03* (m, 2H), 6.96 (m, 4H), 3.98* (s, 2H), 3.79# ppm (s, 2H). **^{13}C NMR** (101 MHz, CDCl$_3$) δ 139.73*, 139.44#, 138.51*, 133.02*, 131.67#, 131.57*, 131.06*, 130.71*, 130.61#, 128.19*, 127.61*, 124.87*, 120.23#, 120.16*, 41.20*, 40.69# ppm. **FT-IR:** v = 2911, 2849, 1900, 1738 cm^{-1}. Spectral data matched literature characterization.[222]
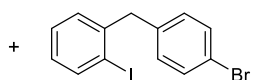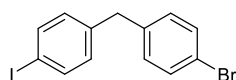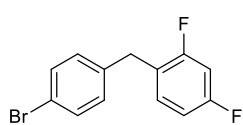

Regioisomeric mixture of 1-bromo-4-(4-iodobenzyl)benzene and 1-(4-bromobenzyl)-2-iodobenzene (130i). Prepared according to general procedure M using (4-bromophenyl)methanol (37.5 mg, 0.2 mmol, 1 equiv) and iodobenzene (227 μL, 2 mmol, 10 equiv). The compound was obtained as colourless oil (52 mg, 0.14 mmol, 70%). **Selectivity:** o:p = 1:3. **MS-EI:** m/z (%): 371.9/373.9 (90) [M]$^+$, 293.0 (50), 245.0/247.0 (30), 165.1 (100). **^{1}H NMR** (400 MHz, CDCl$_3$, # denotes major-, * minor regioisomer signals) δ 7.78* (dd, J = 7.9, 1.3 Hz, 1H), 7.56 – 7.49# (m, 2H), 7.33* (m, 4H), 7.32# (d, J = 8.4 Hz, 2H), 7.21* (d, J = 7.5 Hz, 1H), 7.02* (dd, J = 7.7, 1.7 Hz, 1H), 6.95# (t, J = 8.8 Hz, 2H), 6.85* (d, J = 7.6 Hz, 1H), 6.82# (d, J = 8.2 Hz, 2H), 3.97* (s, 2H), 3.78# ppm (s, 2H). **^{13}C NMR** (101 MHz, CDCl$_3$) δ 142.97*, 140.12*, 139.73*, 139.39*, 138.57*, 137.65#, 131.67#, 131.59#, 130.94#, 130.80#, 130.62#, 130.35*, 128.49*, 128.31*, 120.23#, 120.19*, 101.20*, 91.60#, 45.89*, 40.79# ppm. **FT-IR:** v = 2903, 2848, 1899, 1738 cm^{-1}. Spectral data matched literature characterization.[223]


2-(4-Bromobenzyl)-1,3-difluoro-4l3-benzene (130j). Prepared according to general procedure M using (4-bromophenyl)methanol (37.5 mg, 0.2 mmol, 1 equiv) and 1,3-difluorobenzene (396 μL, 4 mmol, 20 equiv). The compound was obtained as colourless oil (44 mg, 0.16 mmol, 78%). **Selectivity:** MS-EI: m/z (%): 284.1/282.1 [M]$^+$ (40), 201.1/203.1 (100), 183.1 (80). **^{1}H NMR** (400 MHz,

CDCl$_3$) δ 7.44 – 7.39 (m, 2H), 7.08 (dd, J = 14.1, 8.4 Hz, 3H), 6.81 (t, J_{CF} = 8.4 Hz, 2H), 3.91 ppm (s, 2H). **^{13}C NMR** (101 MHz, CDCl$_3$) δ 162.51 (dd, J_{CF} = 100.9, 11.8 Hz), 160.05 (dd, J_{CF} = 101.9, 11.7 Hz), 138.58, 131.67, 131.41 (dd, J_{CF} = 9.5, 6.2 Hz), 130.42, 123.34 (dd, J_{CF} = 16.1, 3.8 Hz), 120.27, 111.25 (dd, J_{CF} = 21.0, 3.8 Hz), 103.88 (t, J_{CF} = 25.7 Hz), 33.79 ppm (d, J = 2.5 Hz). **FT-IR:** ν = 3079, 2926, 2509, 2159, 2031, 1976, 1602, 1503 cm^{-1}. **EA** (%) calc. for C$_{13}$H$_9$BrF$_2$ = C 55.15, H, 3.20; found: C 55.2, H 3.5.
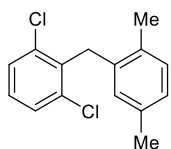
1,3-Dichloro-2-(2,5-dimethylbenzyl)benzene (130k). Prepared according to general procedure M using (2,6-dichlorophenyl)methanol (35.5 mg, 0.2 mmol, 1 equiv) and *para*-xylene (249 µL, 2 mmol, 10 equiv). The compound was obtained as white solid (31 mg, 0.12 mmol, 59%). **MS-EI:** *m/z* (%): 264.1 [M]$^+$ (80), 249.1 (100), 234.1 (10), 195.1 (20), 165.1 (20), 105 (15). **^{1}H NMR** (700 MHz, CDCl$_3$) δ 7.38 (dd, J = 8.1, 1.3 Hz, 2H), 7.19 (td, J = 8.1, 1.3 Hz, 1H), 7.10 (d, J = 7.6 Hz, 1H), 6.94 (d, J = 7.6 Hz, 1H), 6.37 (s, 1H), 4.23 (s, 2H), 2.41 (s, 3H), 2.18 ppm (s, 3H). **^{13}C NMR** (176 MHz, CDCl$_3$) δ 136.70, 136.58, 135.92, 135.49, 133.09, 129.97, 128.38, 128.29, 127.12, 126.96, 34.08, 21.28, 19.50 ppm. **FT-IR:** ν = 3226, 2971, 2922, 2525, 2159, 2030, 1976 cm^{-1}. Spectral data matched literature characterization.[224]
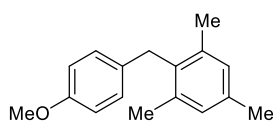
2-(4-Methoxybenzyl)-1,3,5-trimethylbenzene (130l). Prepared according to general procedure M using anisyl alcohol (28 mg, 0.2 mmol, 1 equiv) and mesitylene (278 µL, 2 mmol, 10 equiv). The compound was obtained as pale yellow solid (48 mg, 0.2 mmol, 99%). **MS-EI:** *m/z* (%): 240.2 (60) [M]$^+$, 225.1 (50), 132.1 (100). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 6.84 (d, J = 8.7 Hz, 2H), 6.80 (s, 2H), 6.69 (d, J = 8.7 Hz, 2H), 3.87 (s, 2H), 3.67 (s, 3H), 2.21 (s, 3H), 2.12 ppm (s, 6H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 157.67, 136.99, 135.61, 134.20, 132.07, 128.92, 128.76, 113.78, 55.26, 33.81, 20.97, 20.16 ppm. FT-IR: ν = 2959, 2917, 2852, 2360, 2340 cm^{-1}. Spectral data matched literature characterization.[225]
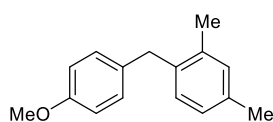
2-(4-Methoxybenzyl)-1,3-dimethy-lbenzene (130m). Prepared according to general procedure M using anisyl alcohol (28 mg, 0.2 mmol, 1 equiv) and *meta*-xylene (221 µL, 2 mmol, 1 equiv). The compound was obtained as colourless oil (34 mg, 0.15 mmol, 75%). **MS-EI:** *m/z* (%): 226.0 (100) [M]$^+$, 221.0 (100), 195.0 (20), 179.0 (15), 165.0 (20), 152.0 (15), 118.0 (80). **^{1}H NMR** (400 MHz, CDCl$_3$) δ 6.95 (d, J = 8.4 Hz, 2H), 6.92 – 6.85 (m, 3H), 6.72 (d, J = 8.5 Hz, 2H), 3.80 (s, 2H), 3.68 (s, 3H), 2.21 (s, 3H), 2.12 ppm (s, 3H). **^{13}C NMR** (101 MHz, CDCl$_3$) δ

157.83, 136.38, 136.35, 135.82, 132.77, 131.15, 129.77, 129.64, 126.61, 113.82, 55.27, 38.19, 20.97, 19.60 ppm. **FT-IR:** ν = 3002, 2917, 2854, 2834 cm^{-1}. Spectral data matched literature characterization.[226]
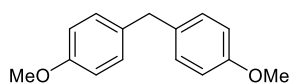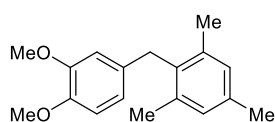
1-Methoxy-4-((4-methoxy-phenyl)methyl)benzene (130n). Prepared according to general procedure M using anisyl alcohol (28 mg, 0.2 mmol, 1 equiv) and anisole (221 µL, 2 mmol, 10 equiv). The compound was obtained as colourless oil (45 mg, 0.19 mmol, 98%). **MS-EI:** m/z (%): 228.0 (100) [M]$^{+}$, 213.0 (15), 197.0 (80), 121.1 (40). **^{1}H NMR** (400 MHz, CDCl$_3$) δ 7.00 (d, J = 8.6 Hz, 4H), 6.73 (d, J = 8.6 Hz, 4H), 3.77 (s, 2H), 3.68 ppm (s, 6H). **^{13}C NMR** (101 MHz, CDCl$_3$) δ 157.95, 133.77, 129.78, 113.89, 55.28, 40.16 ppm. **FT-IR:** ν = 2998, 2931, 2908, 2834 cm^{-1}. Spectral data matched literature characterization.[227]

2-(3,4-Dimethoxybenzyl)-1,3,5-trimethylbenzene (130o). Prepared according to general procedure M using (3,4-dimethoxyphenyl)methanol (34 mg, 0.2 mmol, 1 equiv) and mesitylene (278 µL, 2 mmol, 10 equiv). The compound was obtained as pale yellow solid (46 mg, 0.17 mmol, 85%): **^{1}H NMR** (500 MHz, CDCl$_3$) δ 6.80 (s, 2H), 6.63 (d, J = 8.2 Hz, 1H), 6.55 (d, J = 2.1 Hz, 1H), 6.39 – 6.34 (m, 1H), 3.88 (s, 2H), 3.74 (s, 3H), 3.72 (s, 3H), 2.21 (s, 3H), 2.13 ppm (s, 6H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 148.84, 147.06, 137.00, 135.65, 133.91, 132.64, 128.91, 119.38, 111.39, 111.12, 55.89, 55.80, 34.23, 20.97, 20.15 ppm. **FT-IR:** ν = 2968, 2928, 2838, 2360, 2341 cm^{-1}. **HR-MS:** calc. for [M+Na]$^{+}$ C$_{18}$H$_{22}$O$_2$Na = 293.1512; found 293.1522.
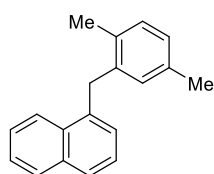
1-(2,5-Dimethylbenzyl)naphthalene (130p). Prepared according to general procedure M using naphthalen-1-ylmethanol (32 mg, 0.2 mmol, 1 equiv) and *para*-xylene (221 µL, 2 mmol, 10 equiv). The compound was obtained as colourless oil (33 mg, 0.13 mmol, 67%). **MS-EI:** m/z (%): 246.1 (100) [M]$^{+}$, 231.0 (60), 215.0 (50), 118.0 (60). **^{1}H NMR** (400 MHz, CDCl$_3$) δ 7.97 – 7.88 (m, 1H), 7.83 – 7.74 (m, 1H), 7.65 (d, J = 8.2 Hz, 1H), 7.45 – 7.35 (m, 2H), 7.27 (t, J = 7.6 Hz, 1H), 7.03 (d, J = 7.6 Hz, 1H), 6.91 (dd, J = 10.0, 7.6 Hz, 2H), 6.69 (d, J = 1.9 Hz, 1H), 4.27 (s, 2H), 2.17 (s, 3H), 2.12 ppm (s, 3H). **^{13}C NMR** (101 MHz, CDCl$_3$) δ 138.18, 136.31, 135.57, 133.81, 133.55, 132.30, 130.57, 130.10, 128.75, 127.14, 126.86, 126.30, 126.01, 125.68, 125.60, 123.88, 36.17, 21.05, 19.21 ppm. **FT-IR:** ν = 3041, 3013, 2917, 2855 cm^{-1}. Spectral data matched literature characterization.[228]
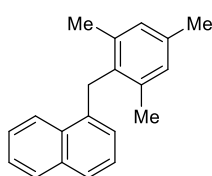
1-(2,4,6-Trimethylbenzyl)naphthalene (130q). Prepared according to general procedure M using naphthalen-1-ylmethanol (32 mg, 0.2 mmol, 1 equiv) and mesitylene (278 µL, 2 mmol, 10 equiv). The compound was obtained as white solid (46 mg, 0.18 mmol, 88%). **MS-EI:** m/z (%): 260.1 (100) $[M]^+$, 245.0 (70), 230 (40), 215.0 (30), 132.0 (90), 115.0 (20). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.16 (d, J = 8.4 Hz, 1H), 7.79 (dd, J = 8.1, 1.4 Hz, 1H), 7.59 (d, J = 8.1 Hz, 1H), 7.50 (m, 1H), 7.43 (m, 1H), 7.15 (t, J = 7.7 Hz, 1H), 6.86 (s, 2H), 6.58 (dd, J = 7.2, 1.4 Hz, 1H), 4.31 (s, 2H), 2.25 (s, 3H), 2.07 ppm (s, 6H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 137.56, 135.90, 135.40, 133.72, 133.19, 132.32, 128.99, 128.90, 126.57, 125.99, 125.86, 125.62, 123.59, 123.25, 31.50, 21.08, 19.96 ppm. **FT-IR:** v = 3049, 2915, 2855 cm^{-1}. Spectral data matched literature characterization.[229]

1-(2,3,5,6-Tetramethylbenzyl)naphthalene (130r). Prepared according to general procedure M using naphthalen-1-ylmethanol (32 mg, 0.2 mmol, 1 equiv) and 1,2,4,5 tetramethyl benzene (278 mg, 2 mmol, 10 equiv). The compound was obtained as white solid (42 mg, 0.15 mmol, 77%). **MS-EI:** m/z (%): 274.1 (100) $[M]^+$, 259.1 (50), 244.1 (40), 146.1 (100). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.18 (d, J = 8.4 Hz, 1H), 7.81 (dd, J = 8.2, 1.4 Hz, 1H), 7.60 (d, J = 8.2 Hz, 1H), 7.52 (m, 1H), 7.45 (m, 1H), 7.16 (dd, J = 8.2, 7.2 Hz, 1H), 6.91 (s, 1H), 6.60 (dd, J = 7.1, 1.3 Hz, 1H), 4.38 (s, 2H), 2.20 (s, 6H), 1.98 ppm (s, 6H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 136.11, 135.61, 133.81, 133.69, 133.59, 132.21, 130.16, 128.90, 126.54, 126.00, 125.83, 125.61, 124.10, 123.24, 32.59, 20.69, 15.75 ppm. **FT-IR:** v = 2997, 2963, 2938, 2917 cm^{-1}. **EA** (%) calc. for C$_{21}$H$_{22}$ = C 91.92, H 8.08; found: C 91.2, H 8.0.

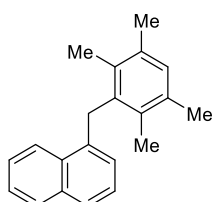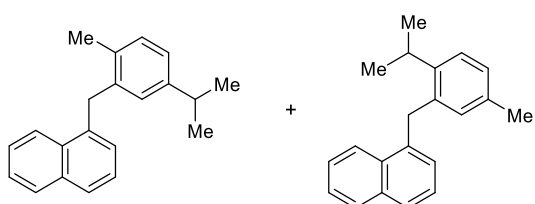**Regioisomeric mixture of 1-(5-isopropyl-2-methylbenzyl)naphthalene and 1-(2-isopropyl-5-methylbenzyl)naphthalene (130s).** Prepared according to general procedure M using naphthalen-1-ylmethanol (32 mg, 0.2 mmol, 1 equiv) and 5-isopropyl-*meta*-xylene (355 µL, 2 mmol, 10 equiv). The compound was obtained as colourless oil (32 mg, 0.12 mmol, 58%). **Selectivity:** rr = 7:1. **MS-EI:** m/z (%): 274.1 (100) $[M]^+$, 259.1 (50), 231.1 (60), 215.1 (50), 141.1 (100), 115.1 (50). **^{1}H NMR** (500 MHz, CDCl$_3$, # denotes major-, * minor regioisomer signals) δ 8.00 – 7.93 (m, 1H), 7.82 – 7.76 (m, 1H), 7.65 (d, J = 8.3 Hz, 1H), 7.46 – 7.37 (m, 2H), 7.29 – 7.23 (m, 1H), 7.19* (s, 1H), 7.09# (d, J = 7.7 Hz, 1H), 7.02* (d, J = 8.0 Hz, 1H), 6.98# (dd, J = 7.7, 1.5 Hz, 1H), 6.89# (d, J = 7.0 Hz, 1H), 6.87* (d, J = 7.3 Hz, 1H), 6.78# (d, J

= 2.0 Hz, 1H), 6.75* (d, *J* = 1.9 Hz, 1H), 4.36* (s, 2H), 4.31# (s, 2H), 3.03 – 2.92* (m, 1H), 2.69# (m, 1H), 2.16# (s, 3H), 2.15* (s, 3H), 1.11* (d, *J* = 6.8 Hz, 6H), 1.09 – 1.05# (m, 6H). **^{13}C NMR** (126 MHz, CDCl$_3$, # denotes major-, * minor regioisomer signals) *δ* 146.77#, 144.44*, 138.04#, 137.03*, 136.41*, 136.31#, 135.27*, 134.17#, 133.73#, 133.71*, 132.26#, 132.13*, 131.16*, 130.18#, 128.78*, 128.75#, 128.42#, 127.73*, 126.81#, 126.79*, 126.27*, 126.07#, 126.05*, 125.98#, 125.70#, 125.64*, 125.61#, 125.39*, 124.27#, 123.82#, 123.69*, 36.35#, 35.50*, 33.66#, 28.73*, 24.12#, 23.98*, 21.03*, 19.21# ppm. **FT-IR:** *ν* = 3044, 3005, 2957, 1738 cm^{-1}. **EA** (%) calc. for C$_{21}$H$_{22}$ = C 91.92, H 8.08; found: C 91.6, H 8.1.
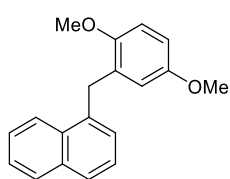
1-(2,5-Dimethoxybenzyl)naphthalene (130t). Prepared according to general procedure M using naphthalen-1-ylmethanol (32 mg, 0.2 mmol, 1 equiv) and 1,4-Dimethoxybenzene (70 mg, 0.5 mmol, 2.5 equiv). The compound was obtained as white solid (24 mg, 0.09 mmol, 43%). **MS-EI:** *m/z* (%): 278.1 (100) [M]$^+$. **^{1}H NMR** (400 MHz, CDCl$_3$) *δ* 7.94 – 7.88 (m, 1H), 7.79 – 7.75 (m, 1H), 7.66 (d, *J* = 8.2 Hz, 1H), 7.38 – 7.34 (m, 2H), 7.34 – 7.29 (m, 1H), 7.17 (d, *J* = 3.8 Hz, 1H), 6.76 (d, *J* = 8.8 Hz, 1H), 6.62 (dd, *J* = 8.8, 3.1 Hz, 1H), 6.38 (d, *J* = 3.1 Hz, 1H), 4.32 (s, 2H), 3.76 (s, 3H), 3.52 ppm (s, 3H). **^{13}C NMR** (101 MHz, CDCl$_3$) *δ* 153.56, 151.54, 136.42, 133.89, 132.32, 130.33, 128.60, 127.07, 126.96, 125.88, 125.59, 125.50, 124.34, 116.86, 111.09, 111.00, 56.09, 55.54, 32.62 ppm. **FT-IR:** *ν* = 3040, 2996, 2937, 2903, 2831 cm^{-1}. Spectral data matched literature characterization.[230]
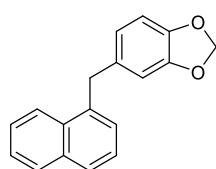
5-(Naphthalen-1-ylmethyl)benzo[*d*][1,3]dioxole (130u). Prepared according to general procedure M using naphthalen-1-ylmethanol (32 mg, 0.2 mmol, 1 equiv) and 1,3-benzodioxole (62 mg, 0.5 mmol, 2.5 equiv). The compound was obtained as white solid (31 mg, 0.12 mmol, 59%). **MS-EI:** *m/z* (%): 262.1 (100) [M]$^+$, 231.1 (40), 202.1 (50). **^{1}H NMR** (400 MHz, CDCl$_3$) *δ* 7.94 – 7.84 (m, 1H), 7.82 – 7.73 (m, 1H), 7.67 (d, *J* = 8.2 Hz, 1H), 7.40 – 7.30 (m, 3H), 7.20 (d, *J* = 7.0 Hz, 1H), 6.61 (dd, *J* = 19.3, 8.0 Hz, 3H), 5.80 (s, 2H), 4.27 ppm (s, 2H). **^{13}C NMR** (101 MHz, CDCl$_3$) *δ* 147.75, 145.85, 136.75, 134.55, 133.99, 132.09, 128.72, 127.27, 127.24, 126.02, 125.61, 125.57, 124.25, 121.59, 109.26, 108.23, 100.85, 38.79 ppm. **FT-IR:** *ν* = 2987, 2971, 2899, 2781, 2358, 2339 cm^{-1}. **EA** (%) calc. for C$_{18}$H$_{14}$O$_2$ = C 82.42, H 5.38, O 12.20; found: C 81.7, H 5.4.
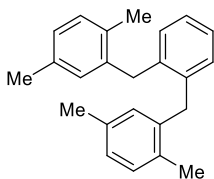
1,2-bis(2,5-Dimethylbenzyl)benzene (130v). Prepared according to general procedure M using 1,2-phenylenedimethanol (34.5 mg, 0.25 mmol, 1 equiv) and *para*-xylene (308 µL, 2.5 mmol, 10 equiv). The compound was obtained as pale yellow solid (54 mg, 0.14 mmol, 69%). **MS-EI:** m/z (%): 314.2 (20) [M]$^+$, 208.1 (10), 193.1 (100), 178.1 (30). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.16 (dd, J = 5.7, 3.5 Hz, 2H), 7.07 (d, J = 7.6 Hz, 2H), 6.98 (d, J = 2.0 Hz, 2H), 6.93 (dd, J = 5.7, 3.5 Hz, 2H), 6.75 (d, J = 2.0 Hz, 2H), 3.88 (s, 4H), 2.25 (s, 6H), 2.15 ppm (s, 6H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 137.73, 137.32, 135.83, 133.65, 129.03, 126.35, 126.08, 31.83, 21.11, 20.03 ppm. **FT-IR:** v = 3018.4, 2918.1, 2854 cm^{-1}. Spectral data matched literature characterization.[159]
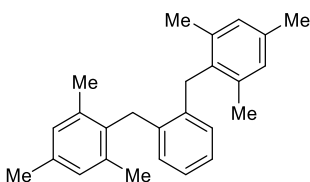
1,2-bis(2,4,6-Trimethylbenzyl)benzene (130w). Prepared according to general procedure M using 1,2-phenylenedimethanol (34.5 mg, 0.25 mmol, 1 equiv) and mesitylene (347 µL, 2.5 mmol, 10 equiv). The compound was obtained as pale yellow solid (51 mg, 0.12 mmol, 60%). **MS-EI:** m/z (%): 342.2 (5) [M]$^+$, 222.1 (15), 207.1 (100), 192 (20). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 6.97 (dd, J = 5.8, 3.4 Hz, 2H), 6.95 (s, 4H), 6.57 (dd, J = 5.8, 3.4 Hz, 2H), 4.05 (s, 4H), 2.33 (s, 6H), 2.21 ppm (s, 12H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 138.71, 138.19, 135.52, 133.61, 130.22, 130.11, 129.44, 127.05, 126.46, 36.52, 21.15, 19.22 ppm. **FT-IR:** v = 3021, 2917, 2852, 2730 cm^{-1}. Spectral data matched literature characterization.[230]
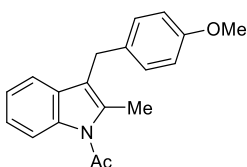
1-(3-(4-Methoxybenzyl)-2-methyl-1H-indol-1-yl)ethan-1-one (130x). Prepared according to general procedure M using anisyl alcohol (25 µL, 0.2 mmol, 1 equiv) and 1-(2-methyl-1*H*-indol-1-yl)ethan-1-one (88 mg, 0.5 mmol, 2.5 equiv). The compound was obtained as pale reddish solid (50 mg, 0.17 mmol, 85%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.86 (d, J = 8.3 Hz, 1H), 7.28 (dd, J = 7.8, 1.4 Hz, 1H), 7.17 – 7.12 (m, 1H), 7.09 (t, J = 7.4 Hz, 1H), 7.01 (d, J = 8.7 Hz, 2H), 6.69 (d, J = 8.6 Hz, 2H), 3.88 (s, 2H), 3.65 (s, 3H), 2.64 (s, 3H), 2.51 ppm (s, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 170.40, 157.96, 135.82, 133.71, 131.98, 130.62, 129.06, 123.80, 123.02, 118.83, 118.75, 115.04, 113.90, 55.27, 28.94, 27.70, 14.64 ppm. **FT-IR:** v = 2994, 2923, 2355, 2337, 1689 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{19}$H$_{20}$O$_2$N = 294.1488; found 294.1495.
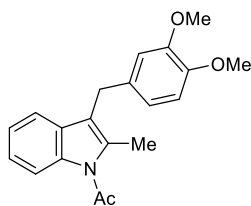
1-(3-(3,4-Dimethoxybenzyl)-2-methyl-1H-indol-1-yl)ethan-1-one (130y). Prepared according to general procedure M using 3,4-dimethoxybenzyl alcohol (30 µL, 0.2 mmol, 1 equiv) and 1-(2-methyl-1*H*-indol-1-yl)ethan-1-one (88 mg, 0.5 mmol, 2.5 equiv). The compound was obtained as pale reddish solid (64 mg, 0.19 mmol, 98%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.86 (d, J = 8.4 Hz, 1H), 7.29 (dd, J = 7.2, 1.2 Hz, 1H), 7.18 – 7.13 (m, 1H), 7.09 (m, 1H), 6.67 – 6.63 (m, 2H), 6.60 (dd, J = 8.2, 2.0 Hz, 1H), 3.90 (s, 2H), 3.73 (s, 3H), 3.71 (s, 3H), 2.65 (s, 3H), 2.53 ppm (s, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 170.42, 148.92, 147.39, 135.79, 133.79, 132.46, 130.63, 123.82, 123.02, 119.94, 118.74, 118.61, 115.02, 111.48, 111.17, 55.90, 55.86, 29.41, 27.71, 14.65 ppm. **FT-IR:** v = 2970, 2921, 2359, 2342, 1690 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{20}$H$_{22}$O$_3$N = 324.1594; found 324.1597.
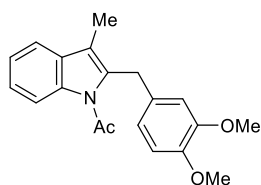
1-(2-(3,4-Dimethoxybenzyl)-3-methyl-1H-indol-1-yl)ethan-1-one (130z). Prepared according to general procedure M using 3,4-dimethoxybenzyl alcohol (30 µL, 0.2 mmol, 1 equiv) and 1-(3-methyl-1*H*-indol-1-yl)ethan-1-one (88 mg, 0.5 mmol, 2.5 equiv). The compound was obtained as pale yellow solid (34 mg, 0.11 mmol, 53%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.84 – 7.77 (m, 1H), 7.50 – 7.43 (m, 1H), 7.25 – 7.19 (m, 2H), 6.65 (d, J = 8.2 Hz, 1H), 6.62 (d, J = 1.5 Hz, 1H), 6.48 (d, J = 8.2 Hz, 1H), 4.30 (s, 2H), 3.74 (s, 3H), 3.73 (s, 3H), 2.54 (s, 3H), 2.22 ppm (s, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 169.89, 148.96, 147.42, 135.83, 134.85, 131.71, 131.05, 124.18, 122.88, 119.62, 118.74, 117.37, 114.98, 111.30, 111.18, 55.88, 55.86, 32.11, 27.37, 8.91 ppm. **FT-IR:** v = 2988, 2933, 2912, 2356, 2338, 1694 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{20}$H$_{22}$O$_3$N = 324.1594; found 324.1599.
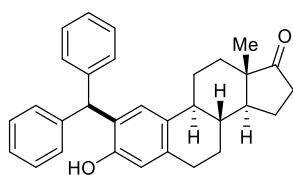
2-Benzhydryl-E (130aa). Prepared according to general procedure M using diphenylmethanol (37.5 mg, 0.2 mmol, 1 equiv) and estrone (135 mg, 0.5 mmol, 2.5 equiv). The compound was obtained as white solid (83 mg, 0.18 mmol, 92%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.24 (t, J = 7.6 Hz, 4H), 7.16 (d, J = 7.2 Hz, 2H), 7.08 (d, J = 7.6 Hz, 4H), 6.66 (s, 1H), 6.49 (s, 1H), 5.60 (s, 1H), 4.45 (s, 1H), 2.78 (dd, J = 9.7, 6.7 Hz, 2H), 2.41 (dd, J = 19.1, 8.7 Hz, 1H), 2.11 – 1.89 (m, 5H), 1.79 – 1.73 (m, 1H), 1.53 – 1.24 (m, 6H), 0.80 ppm (s, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 220.01, 151.38, 142.65, 142.63, 136.28, 131.91, 129.30, 128.61, 128.57, 127.71, 127.61, 126.70, 116.17, 51.13, 50.37, 48.02, 44.05, 38.35, 35.91, 31.50, 29.13, 26.51, 25.71, 21.58, 13.89 ppm. **FT-IR:** v = 3370, 3029, 2959, 2937, 2865, 1738, 1713 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{31}$H$_{31}$O$_2$ = 435.2329; found 435.2311.
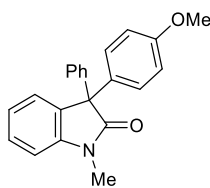
3-(4-Methoxyphenyl)-1-methyl-3-phenylindolin-2-one **(130ab).** Prepared according to general procedure M using 3-hydroxy-1-methyl-3-phenylindolin-2-one (49 mg, 0.2 mmol, 1 equiv) and anisole (247 µL, 2 mmol, 10 equiv). The compound was obtained as orange solid (62 mg, 0.19 mmol, 94%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.25 – 7.13 (m, 7H), 7.12 – 7.07 (m, 2H), 7.03 – 6.97 (m, 1H), 6.83 (d, J = 7.8 Hz, 1H), 6.77 – 6.70 (m, 2H), 3.67 (s, 3H), 3.20 ppm (s, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 177.87, 158.81, 143.03, 142.27, 133.78, 133.18, 129.64, 128.46, 128.34, 128.27, 127.25, 126.01, 122.86, 113.80, 108.57, 61.86, 55.29, 26.70 ppm. **FT-IR:** v = 2968, 2937, 2841, 1706 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{22}$H$_{20}$O$_2$N = 330.1488; found 330.1499.
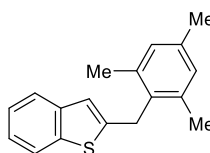
2-(2,4,6-Trimethylbenzyl)benzo[b]thiophene **(130ac).** Prepared according to general procedure M using benzothiophene-2-methanol (33.5 mg, 0.2 mmol, 1 equiv) and mesitylene (278 µL, 2 mmol, 10 equiv). The compound was obtained as white solid (46 mg, 0.17 mmol, 86%). **MS-EI:** m/z (%): 266.1 (100) [M]$^+$, 251.1 (40), 235.1 (20), 221.1 (20), 143.1 (30), 132.1 (50). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.62 (d, J = 7.9 Hz, 1H), 7.51 – 7.45 (m, 1H), 7.22 – 7.09 (m, 2H), 6.82 (s, 2H), 6.64 (d, J = 1.8 Hz, 1H), 4.11 (s, 2H), 2.21 ppm (s, 9H). **^{13}C NMR** (126 MHz, CDCl$_3$) 144.78, 140.16, 139.48, 136.88, 136.38, 133.12, 129.13, 124.10, 123.49, 122.81, 122.13, 120.54, 30.46, 21.06, 20.03 ppm. **FT-IR:** v = 2971, 2922, 2852, 1737 cm^{-1}. **EA** (%) calc. for C$_{18}$H$_{18}$S = C 81.15, H 6.81; found: C 81.1, H 6.9.
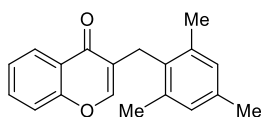
3-(2,4,6-Trimethylbenzyl)-4H-chromen-4-one **(130ad).** Prepared according to general procedure M using 3-(hydroxymethyl)-4H-chromen-4-one (35.5 mg, 0.2 mmol, 1 equiv), mesitylene (278 µL, 2 mmol, 10 equiv) and NOBF$_4$ (100 µL, 0.02 mmol, 0.1 equiv). The reaction was stirred for 24 h at 80 °C. The compound was obtained as white solid (36 mg, 0.13 mmol, 65%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.21 (dd, J = 8.0, 1.7 Hz, 1H), 7.56 (m, 1H), 7.36 – 7.27 (m, 2H), 6.97 – 6.92 (m, 1H), 6.83 (s, 2H), 3.75 (d, J = 1.7 Hz, 2H), 2.22 (s, 3H), 2.13 ppm (s, 6H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 178.02, 156.50, 152.10, 136.99, 136.21, 133.45, 130.85, 129.13, 125.89, 124.95, 123.46, 122.50, 118.09, 25.16, 20.95, 19.80 ppm. **FT-IR:** v = 2988, 2954, 2918, 1739, 1633 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{19}$H$_{19}$O$_2$ = 279.1379; found 279.1386.
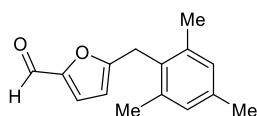
5-(2,4,6-Trimethylbenzyl)furan-2-carbaldehyde (130ae). Prepared according to general procedure M using 5-hydroxymethyl-2-

furfuraldehyde (26 mg, 0.2 mmol, 1 equiv) and mesitylene (278 µL, 2 mmol, 10 equiv). The compound was obtained as yellow oil (41 mg, 0.18 mmol, 90%). **^{1}H NMR** (400 MHz, CDCl$_3$) δ 9.44 (s, 1H), 7.03 (d, J = 3.5 Hz, 1H), 6.81 (s, 2H), 5.83 (d, J = 3.5 Hz, 1H), 3.96 (s, 2H), 2.20 (s, 3H), 2.19 ppm (s, 6H). **^{13}C NMR** (101 MHz, CDCl$_3$) δ 177.08, 161.95, 152.13, 136.84, 136.66, 129.70, 129.15, 109.11, 28.66, 20.91, 19.95 ppm. **FT-IR:** v = 2918, 2360, 2338, 1673, 1509 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{15}$H$_{17}$O$_2$ = 229.1223; found 229.1222.
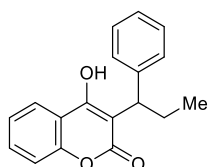
4-hydroxy-3-(1-phenylpropyl)-2H-chromen-2-one **(130af).** Prepared according to general procedure M using *alpha*-ethylbenzenemethanol (27 mg, 0.2 mmol, 1 equiv) and 4-hydroxycoumarin (82 mg, 0.5 mmol, 2.5 equiv). The compound was obtained as yellow solid (37 mg, 0.13 mmol, 66%). **^{1}H NMR** (400 MHz, CDCl$_3$) δ 7.72 (dd, J = 7.9, 1.6 Hz, 1H), 7.50 (td, J = 8.6, 1.3 Hz, 3H), 7.39 (t, J = 7.6 Hz, 2H), 7.33 – 7.27 (m, 2H), 7.25 – 7.20 (m, 1H), 6.67 (s, 1H), 4.54 (t, J = 7.7 Hz, 1H), 2.32 – 2.09 (m, 2H), 1.06 ppm (t, J = 7.3 Hz, 3H). **^{13}C NMR** (101 MHz, CDCl$_3$) δ 163.97, 160.21, 152.68, 141.41, 131.95, 129.64, 127.84, 127.65, 123.97, 123.00, 116.52, 116.17, 109.03, 41.86, 24.11, 12.49 ppm. **FT-IR:** v = 2967, 2926, 2513, 2364, 2342, 2159, 2028, 1976 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{18}$H$_{15}$O$_3$ = 279.1015; found 279.1027.
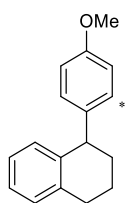
1-(4-Methoxy-phenyl)-1,2,3,4-tetrahydronaphthalene. Prepared according to general procedure M using 1,2,3,4-tetrahydronaphthalen-1-ol (60 mg, 0.4 mmol, 1 equiv) and anisole (111 µL, 1 mmol, 2.5 equiv); the product was obtained as a colourless oil (81 mg, 0.34 mmol, 85%). **Selectivity:** o:p = 1:10. **MS-EI:** m/z (%): 238.1 (40) [M]$^+$, 210.1 (15), 195.1 (10), 179.1 (20), 165.1 (20), 152.1 (10), 130.1 (100), 115.1 (20), 91.1 (10). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.20 – 7.08 (m, 5H), 6.93 (d, J = 7.7 Hz, 1H), 6.90 (d, J = 8.6 Hz, 2H), 4.14 (t, J = 6.8 Hz, 1H), 3.85 (s, 3H), 3.02 – 2.87 (m, 2H), 2.21 (dt, J = 13.0, 6.2 Hz, 1H), 1.98 – 1.79 ppm (m, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 157.89, 139.82, 139.75, 137.60, 130.23, 129.80, 129.04, 125.93, 125.71, 113.68, 55.29, 44.84, 33.44, 29.88, 21.06 ppm. Spectral data matched literature characterization.[231]
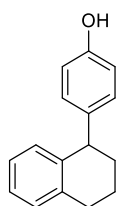
4-(1,2,3,4-Tetrahydronaphthalen-1-yl)phenol. To a solution of 1-(4-methoxy-phenyl)-1,2,3,4-tetrahydronaphthalene (81 mg, 0.34 mmol, 1 equiv) in dry dichloromethane (9 mL), BBr$_3$ (1.0 M solution in hexanes, 1.22 mL, 1.22 mmol, 3.5 equiv) was dropwise added and the reaction was allowed to warm to room temperature and stirred for 3 h. After that time, the reaction was quenched with water (25 mL), the phases were separated, and the aqueous phase was extracted two times with

dichloromethane (2x30 mL). The combined organic layers were dried over $MgSO_4$, the solvent was removed under reduced pressure and the crude product was purified by silica gel flash chromatography (eluent: petroleum ether / dichloromethane); the product was obtained as a white solid (64 mg, 0.28 mmol, 82%). **MS-EI:** m/z (%): 224.1 (40) [M]$^+$, 196.1 (30), 165.1 (20), 152.1 (15), 130.1 (100), 115.1 (20). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.13 (d, J = 6.1 Hz, 2H), 7.04 (dd, J = 9.7, 4.1 Hz, 1H), 6.97 (d, J = 8.4 Hz, 2H), 6.86 (d, J = 7.7 Hz, 1H), 6.76 (d, J = 8.4 Hz, 2H), 4.78 (s, 1H), 4.06 (t, J = 6.6 Hz, 1H), 2.96 – 2.78 (m, 2H), 2.18 – 2.09 (m, 1H), 1.95 – 1.71 ppm (m, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 153.75, 139.98, 139.80, 137.67, 130.24, 130.04, 129.07, 125.96, 125.73, 115.16, 44.85, 33.45, 29.88, 21.04 ppm. Spectral data matched literature characterization.[232]
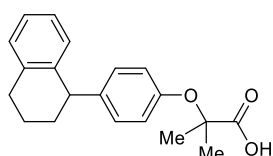
2-Methyl-2-(4-(1,2,3,4-tetrahydronaphthalen-1-yl)phenoxy)-propanoic acid (130ag). To a solution of 4-(1,2,3,4-tetrahydronaphthalen-1-yl)phenol (64 mg, 0.28 mmol, 1 equiv) in DMF (2 mL), $MgSO_4$ (35 mg, 0.29 mmol, 1 equiv), K_2CO_3 (157 mg, 1.12 mmol, 4 equiv) and *tert*-butyl α-bromoisobutyrate (266 µL, 1.4 mmol, 5 equiv) were added and the reaction was stirred at 100 °C for 24 h. After that time, the reaction was quenched with water (30 mL) and extracted three times with ethyl acetate (3x20 mL). The combined organic layers were dried over $MgSO_4$, the solvent was removed under reduced pressure and the crude product was purified by silica gel column chromatography (eluent: petroleum ether / ethyl acetate). The isolated compound was dissolved in dichloromethane (2 mL) and TFA (389 µL, 5.8 mmol, 20 equiv) was added dropwise at 0 °C. The reaction was allowed to warm to room temperature and stirred for 1 h. After that time, the solvent was removed under reduced pressure to provide the pure product; the product was obtained as a colourless oil, which became solid upon standing (64 mg, 0.21 mmol, 76%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.12 (d, J = 5.0 Hz, 2H), 7.07 – 7.01 (m, 1H), 6.99 (d, J = 8.4 Hz, 2H), 6.88 – 6.81 (m, 3H), 4.08 (t, J = 6.7 Hz, 1H), 2.87 (dtd, J = 22.7, 16.4, 6.4 Hz, 2H), 2.14 (dt, J = 12.9, 6.1 Hz, 1H), 1.92 – 1.71 (m, 3H), 1.60 ppm (s, 6H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 178.76, 152.57, 142.43, 139.48, 137.66, 130.25, 129.66, 129.10, 126.04, 125.74, 120.41, 79.57, 44.91, 33.31, 29.84, 25.24, 25.18, 20.95 ppm. **FT-IR:** v = 2918, 2855, 2541, 2159, 1976, 1694 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ $C_{20}H_{21}O_3$ = 309.1485; found 309.1494.

12 Experimental Part for the Thioarylation of Phenols and Indoles

12.1.1 General procedures

Preparation of the nitronium tetrafluoroborate stock solution

Under nitrogen atmosphere in a flame dry Schlenk flask, NO_2BF_4 was dissolved in sulfolane (1 mL/27 mg NO_2BF_4), sealed with a glass stopper and placed in an ultrasonic bath for 1 h. The stock solution was used for up to three days.

General procedure N: Cross-dehydrogenative coupling of phenols and thiophenols
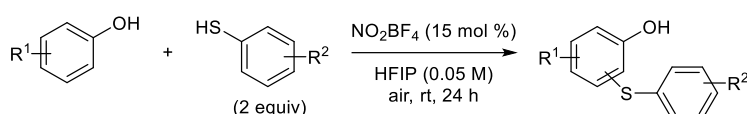
To a stirring solution of phenol (0.1 mmol, 1 equiv) and thiophenol (0.2 mmol, 2 equiv) in HFIP (2 mL), NO_2BF_4 (0.2 M in sulfolane, 75 µL, 15 mol %) was added. The reaction was stirred at room temperature for 24 h. After that time, the reaction was diluted with dichloromethane, concentrated on silica and purified by silica gel column chromatography to afford the desired product (eluent: petroleum ether / dichloromethane).

General procedure O: Cross-dehydrogenative coupling of indoles and thiophenols
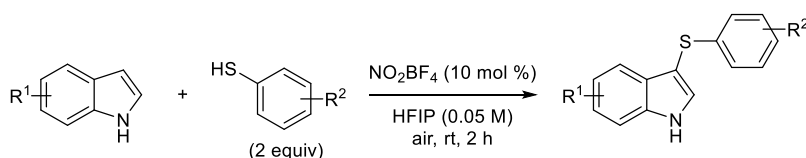
To a stirring solution of indole (0.2 mmol, 1 equiv) and thiophenol (0.2 mmol, 2 equiv) in HFIP (2 mL), NO_2BF_4 (0.2 M in sulfolane, 25 µL, 5 mol %) was added. The reaction was stirred for 1 h at room temperature and NO_2BF_4 (0.2 M in sulfolane, 25 µL, 5 mol %) was added again. Stirring was continued for 1 h at room temperature. After that time, the reaction was diluted with dichloromethane, concentrated on silica and purified by silica gel column chromatography to afford the desired product (eluent: petroleum ether / dichloromethane or petroleum ether / ethyl acetate).
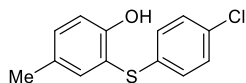
2-((4-Chlorophenyl)thio)-4-methylphenol (133a). Prepared according to the general procedure N using *p*-cresol (11 µL, 0.1 mmol, 1 equiv) and 4-chlorothiophenol (30 mg, 0.2 mmol, 2 equiv); the product was obtained as a colourless solid (23 mg, 0.09 mmol, 91%). **¹H NMR** (500 MHz, CDCl₃) δ 7.31 (d, J = 2.2 Hz, 1H), 7.22 – 7.16 (m, 3H), 6.99 (m, 3H), 6.27 (s, 1H), 2.29 ppm (s, 3H). **¹³C NMR** (126 MHz, CDCl₃) δ 155.07, 136.94, 134.79, 133.44, 132.10, 130.97, 129.41, 128.14, 115.55, 115.42, 20.46 ppm. **FT-IR:** ν = 2920, 1898, 1485, 1585, 1561 cm⁻¹. **HR-MS:** calc. for [M-H]⁻ C₁₃H₁₀OClS = 249.01354; found 249.01480.

Scale up experiment: In a 50 mL round-bottom flask *p*-cresol (106 µL, 0.10 mmol, 1 equiv) and 4-chlorothiophenol (298 mg, 0.2 mmol, 2 equiv) were dissolved in HFIP (20 mL). To the stirring solution NO₂BF₄ (0.2 M in sulfolane, 750 µL, 0.15 mmol, 15 mol %) was added and stirring was continued for 24 h. After that time, the reaction was diluted with dichloromethane, concentrated on silica and purified by silica gel column chromatography to afford the desired product (eluent: petroleum ether / dichloromethane); the product was obtained as a colourless solid (220 mg, 0.88 mmol, 88%).
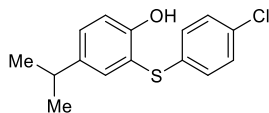
2-((4-Chlorophenyl)thio)-4-isopropylphenol (133b). Prepared according to the general procedure N using 4-isopropylphenol (14 mg, 0.1 mmol, 1 equiv) and 4-chlorothiophenol (30 mg, 0.2 mmol, 2 equiv); the product was obtained as a colourless oil (16 mg, 0.06 mmol, 58%). **¹H NMR** (500 MHz, CDCl₃) δ 7.35 (d, J = 2.0 Hz, 1H), 7.25 (d, J = 2.0 Hz, 1H), 7.20 (d, J = 8.6 Hz, 2H), 7.02 (s, 1H), 6.99 (d, J = 8.6 Hz, 2H), 6.25 (s, 1H), 2.86 (p, J = 6.9 Hz, 1H), 1.23 ppm (d, J = 6.9 Hz, 6H). **¹³C NMR** (126 MHz, CDCl₃) δ 155.28, 142.23, 134.86, 134.50, 132.04, 130.91, 129.42, 127.97, 115.60, 115.25, 33.32, 24.24 ppm. **FT-IR:** ν = 2158, 1604, 1577 cm⁻¹. **HR-MS:** calc. for [M-H]⁻ C₁₅H₁₄OClS = 277.04594; found 277.04590.
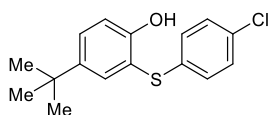
4-(*tert*-Butyl)-2-((4-chlorophenyl)thio)phenol (133c). Prepared according to the general procedure N using 4-*tert*-butylphenol (15.5 mg, 0.1 mmol, 1 equiv) and 4-chlorothiophenol (30 mg, 0.2 mmol, 2 equiv); the product was obtained as a white solid (21 mg, 0.04 mmol, 41%). **¹H NMR** (500 MHz, CDCl₃) δ 7.50 (d, J = 2.4 Hz, 1H), 7.42 (dd, J = 8.6, 2.4 Hz, 1H), 7.20 (d, J = 8.6 Hz, 2H), 7.01 (d, J = 8.6 Hz, 1H), 6.98 (d, J = 8.6 Hz, 2H), 6.24 (s, 1H), 1.30 ppm (s, 9H). **¹³C NMR** (126 MHz, CDCl₃) δ 155.00, 144.64, 134.91, 133.58, 132.00, 129.96, 129.42,

127.87, 115.30, 114.92, 34.38, 31.57 ppm. **FT-IR:** v = 2518, 2159, 2030, 1976, 1602, 1576 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{16}$H$_{16}$OClS = 291.06159; found 291.06152.

3-((4-Chlorophenyl)thio)-[1,1'-biphenyl]-4-ol (133d). Prepared according to the general procedure N using 4-phenylphenol (17 mg, 0.1 mmol, 1 equiv) and 4-chlorothiophenol (30 mg, 0.2 mmol, 2 equiv); the product was obtained as a white solid (14 mg, 0.04 mmol, 45%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.77 (d, J = 2.3 Hz, 1H), 7.64 (dd, J = 8.5, 2.3 Hz, 1H), 7.54 (dd, J = 8.3, 1.3 Hz, 2H), 7.45 – 7.40 (m, 2H), 7.35 – 7.31 (m, 1H), 7.24 – 7.20 (m, 2H), 7.16 (d, J = 8.5 Hz, 1H), 7.10 – 7.02 (m, 2H), 6.45 ppm (s, 1H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 156.68, 139.75, 135.27, 134.93, 134.40, 132.38, 131.36, 129.52, 129.01, 128.33, 127.32, 126.78, 116.53, 116.21 ppm. **FT-IR:** v = 2518, 2159, 2030, 1976, 1602, 1576 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{18}$H$_{12}$OClS = 311.03029; found 311.02999. Spectral data matched literature characterization.[233]
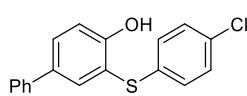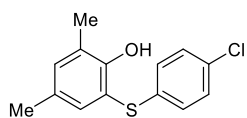
2-((4-Chlorophenyl)thio)-4,6-dimethylphenol (133e). Prepared according to the general procedure N using 2,4-dimethylphenol (12 µL, 0.1 mmol, 1 equiv) and 4-chlorothiophenol (30 mg, 0.2 mmol, 2 equiv); the product was obtained as a colourless oil (23 mg, 0.09 mmol, 87%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.19 (d, J = 8.6 Hz, 2H), 7.15 (s, 1H), 7.05 (s, 1H), 7.00 (d, J = 8.6 Hz, 2H), 6.37 (s, 1H), 2.27 (s, 3H), 2.25 ppm (s, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 153.22, 134.90, 134.62, 134.13, 131.90, 130.05, 129.26, 128.01, 124.87, 114.66, 20.34, 16.46 ppm. **FT-IR:** v = 2522, 2159, 2029, 1976, 1474 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{14}$H$_{12}$OClS = 263.03029; found 263.03028.
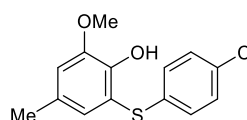
2-((4-Chlorophenyl)thio)-6-methoxy-4-methylphenol (133f). Prepared according to the general procedure N using 2-methoxy-4-methylphenol (13 µL, 0.1 mmol, 1 equiv) and 4-chlorothiophenol (30 mg, 0.2 mmol, 2 equiv); the product was obtained as a colourless solid (24 mg, 0.09 mmol, 86%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.18 (d, J = 8.7 Hz, 2H), 7.04 (s, 1H), 6.99 (d, J = 8.7 Hz, 2H), 6.78 (s, 1H), 5.49 (s, 1H), 3.91 (s, 3H), 2.30 ppm (s, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 147.40, 144.11, 136.76, 133.89, 131.31, 129.13, 128.78, 122.83, 121.16, 113.02, 56.10, 20.46 ppm. **FT-IR:** v = 2524, 2159, 2028, 1976, 1610, 1581 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{14}$H$_{12}$O$_2$ClS = 279.02410; found 279.02524.

2-(*tert*-Butyl)-6-((4-chlorophenyl)thio)-4-methoxyphenol **(133g).** Prepared according to the general procedure N using 3-*tert*-butyl-4-hydroxyanisole (18.5 mg, 0.1 mmol, 1 equiv) and 4-chlorothiophenol (30 mg, 0.2 mmol, 2 equiv); the product was obtained as a white solid (14 mg, 0.04 mmol, 43%). **¹H NMR** (500 MHz, CDCl₃) δ 7.21 (d, J = 8.5 Hz, 2H), 7.01 (d, J = 3.0 Hz, 1H), 6.98 (d, J = 8.5 Hz, 2H), 6.89 (d, J = 3.0 Hz, 1H), 6.57 (s, 1H), 3.75 (s, 3H), 1.40 ppm (s, 9H). **¹³C NMR** (126 MHz, CDCl₃) δ 152.75, 150.28, 138.33, 134.76, 132.06, 129.43, 127.89, 118.27, 116.49, 115.86, 55.91, 35.44, 29.35 ppm. **FT-IR:** v = 2500, 2159, 2029, 1976, 1579 cm⁻¹. **HR-MS:** calc. for [M-H]⁻ C₁₇H₁₈O₂ClS = 321.07215; found 321.07208.

4-((4-Chlorophenyl)thio)-2,6-dimethylphenol **(133h).** Prepared according to the general procedure N using 2,6-dimethylphenol (12.5 mg, 0.1 mmol, 1 equiv) and 4-chlorothiophenol (30 mg, 0.2 mmol, 2 equiv); the product was obtained as a colourless oil (18 mg, 0.07 mmol, 68%). **¹H NMR** (500 MHz, CDCl₃) δ 7.19 (d, J = 8.6 Hz, 2H), 7.13 (s, 2H), 7.07 (d, J = 8.6 Hz, 2H), 4.79 (s, 1H), 2.23 ppm (s, 6H). **¹³C NMR** (126 MHz, CDCl₃) δ 153.07, 137.88, 134.72, 131.44, 129.15, 129.06, 124.55, 122.72, 15.95 ppm. **FT-IR:** v = 2529, 2159, 2029, 1976, 1583, 1474 cm⁻¹. **HR-MS:** calc. for [M-H]⁻ C₁₄H₁₂OClS = 263.03029; found 263.03007.
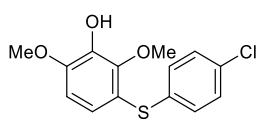
3-((4-Chlorophenyl)thio)-2,6-dimethoxyphenol **(133i).** Prepared according to the general procedure N using 2,6-dimethoxyphenol (16 mg, 0.1 mmol, 1 equiv) and 4-chlorothiophenol (30 mg, 0.2 mmol, 2 equiv); the product was obtained as a yellow solid (17 mg, 0.06 mmol, 57%). **¹H NMR** (500 MHz, CDCl₃) δ 7.20 (d, J = 8.6 Hz, 2H), 7.11 (d, J = 8.6 Hz, 2H), 6.90 (d, J = 8.6 Hz, 1H), 6.65 (d, J = 8.6 Hz, 1H), 5.64 (s, 1H), 3.91 (s, 3H), 3.86 ppm (s, 3H). **¹³C NMR** (126 MHz, CDCl₃) δ 148.83, 147.46, 139.48, 136.27, 131.89, 129.77, 129.14, 125.69, 118.53, 107.27, 61.16, 56.41 ppm. **FT-IR:** v = 2503, 2361, 2159, 2029, 1976, 1598, 1486 cm⁻¹. **HR-MS:** calc. for [M-H]⁻ C₁₄H₁₂O₃ClS = 295.02012; found 295.02000.
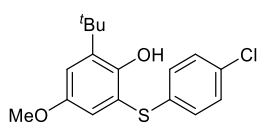
3-((4-Chlorophenyl)thio)-2,4,6-trimethylphenol **(133j).** Prepared according to the general procedure N using 2,4,6-trimethylphenol (14 mg, 0.1 mmol, 1 equiv) and 4-chlorothiophenol (30 mg, 0.2 mmol, 2 equiv); the product was obtained as a white solid (21 mg, 0.08 mmol, 75%). **¹H NMR** (700 MHz, CDCl₃) δ 7.13 (d, J = 8.6 Hz, 2H), 6.99 (s, 1H), 6.84 (d, J = 8.6 Hz, 2H), 4.60 (s, 1H), 2.36 (s, 3H), 2.32 (s, 3H), 2.27 ppm (s, 3H). **¹³C NMR** (176 MHz, CDCl₃) δ 150.95, 137.14,

135.47, 130.43, 130.35, 129.09, 128.52, 128.23, 126.90, 125.20, 21.28, 16.25, 14.33 ppm. **FT-IR:** v = 2474, 2159, 2030, 1976, 1570 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{15}$H$_{14}$OClS = 277.04594; found 277.04573.

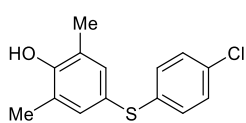**2-((4-Chlorophenyl)thio)-3,5-dimethoxyphenol (133k).** Prepared according to the general procedure N using 3,5-dimethoxyphenol (16 mg, 0.1 mmol, 1 equiv) and 4-chlorothiophenol (30 mg, 0.2 mmol, 2 equiv); the product was obtained as a white solid (11 mg, 0.04 mmol, 37%). **¹H NMR** (700 MHz, CDCl$_3$) δ 7.17 (d, J = 8.6 Hz, 2H), 6.98 (d, J = 8.6 Hz, 2H), 6.83 (s, 1H), 6.29 (d, J = 2.5 Hz, 1H), 6.13 (d, J = 2.5 Hz, 1H), 3.83 (s, 3H), 3.79 ppm (s, 3H). **¹³C NMR** (176 MHz, CDCl$_3$) δ 163.90, 161.98, 159.73, 134.98, 131.71, 129.21, 127.52, 95.54, 92.54, 92.27, 56.35, 55.68 ppm. **FT-IR:** v = 2510, 2159, 2028, 1976, 1607, 1576 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{14}$H$_{12}$O$_3$ClS = 295.02012; found 295.02002. Spectral data matched literature characterization.[171a]

4-Chloro-2-((4-chlorophenyl)thio)-3,5-dimethylphenol (133l). Prepared according to the general procedure N using 4-chloro-3,5-dimethylphenol (16 mg, 0.1 mmol, 1 equiv) and 4-chlorothiophenol (30 mg, 0.2 mmol, 2 equiv); the product was obtained as a white solid (29 mg, 0.04 mmol, 96%), **¹H NMR** (500 MHz, CDCl$_3$) δ 7.22 – 7.18 (m, 2H), 6.94 – 6.91 (m, 2H), 6.89 (s, 1H), 6.67 (s, 1H), 2.48 (s, 3H), 2.40 (s, 3H). **¹³C NMR** (126 MHz, CDCl$_3$) δ 155.88, 141.48, 140.90, 133.63, 132.18, 129.54, 127.55, 126.95, 115.10, 114.27, 21.55, 19.48 ppm. **FT-IR:** v = 2504, 2159, 2029, 1976, 1594 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{14}$H$_{11}$O^{35}Cl$_2$S = 296.99131; found 296.99089; C$_{14}$H$_{11}$O^{35}Cl^{37}ClS = 298.98836; found 298.98786.
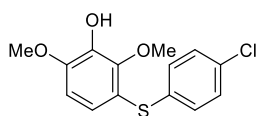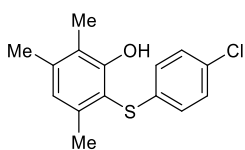
2-((4-Chlorophenyl)thio)-3,5,6-trimethylphenol (133m). Prepared according to the general procedure N using 2,3,5-trimethylphenol (14 mg, 0.1 mmol, 1 equiv) and 4-chlorothiophenol (30 mg, 0.2 mmol, 2 equiv); the product was obtained as a white solid (22 mg, 0.08 mmol, 79%). **¹H NMR** (500 MHz, CDCl$_3$) δ 7.18 (d, J = 8.6 Hz, 2H), 6.92 (d, J = 8.6 Hz, 2H), 6.85 (s, 1H), 6.73 (s, 1H), 2.29 (s, 3H), 2.28 (s, 3H), 2.20 ppm (s, 3H). **¹³C NMR** (126 MHz, CDCl$_3$) δ 155.59, 140.90, 140.36, 134.46, 131.65, 129.36, 127.34, 123.88, 120.59, 112.01, 20.80, 20.32, 12.52 ppm. **FT-IR:** v = 2535, 2161, 2030, 1978, 1602 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{15}$H$_{14}$OClS = 277.04594; found 277.04587.
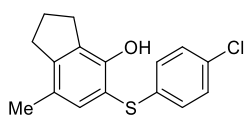
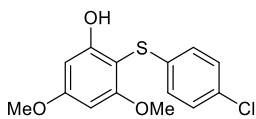**5-((4-Chlorophenyl)thio)-7-methyl-2,3-dihydro-1*H*-inden-4-ol (133n).** Prepared according to the general procedure N using 7-methyl-4-indanol (15 mg, 0.1 mmol, 1 equiv) and 4-chlorothiophenol (30 mg, 0.2 mmol, 2 equiv); the product was obtained as a white solid (22 mg, 0.08 mmol, 76%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.18 (d, J = 8.6 Hz, 2H), 7.12 (s, 1H), 7.00 (d, J = 8.6 Hz, 2H), 6.27 (s, 1H), 2.94 (t, J = 7.5 Hz, 2H), 2.87 (t, J = 7.5 Hz, 2H), 2.19 (s, 3H), 2.15 ppm (p, J = 7.5 Hz, 2H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 151.52, 149.19, 135.61, 135.25, 131.77, 129.92, 129.29, 127.90, 126.76, 112.29, 32.34, 30.02, 24.86, 18.45 ppm. **FT-IR:** v = 2535, 2159, 2030, 1976 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{16}$H$_{14}$OClS = 289.04594; found 289.04592.

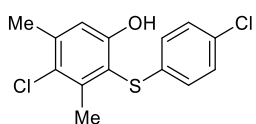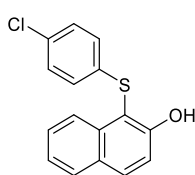**1-((4-Chlorophenyl)thio)naphthalen-2-ol (133o).** Prepared according to the general procedure N using 2-naphthol (15 mg, 0.1 mmol, 1 equiv) and 4-chlorothiophenol (30 mg, 0.2 mmol, 2 equiv); the product was obtained as a white solid (17 mg, 0.06 mmol, 60%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.16 (d, J = 8.4 Hz, 1H), 7.93 (d, J = 8.9 Hz, 1H), 7.83 (d, J = 8.4 Hz, 1H), 7.51 (t, J = 7.6 Hz, 1H), 7.39 (t, J = 7.6 Hz, 1H), 7.35 (d, J = 8.9 Hz, 1H), 7.14 (d, J = 8.7 Hz, 2H), 7.11 (s, 1H), 6.95 (d, J = 8.7 Hz, 2H) ppm. **^{13}C NMR** (126 MHz, CDCl$_3$) δ 157.14, 135.29, 134.04, 133.27, 131.97, 129.64, 129.43, 128.81, 128.26, 127.73, 124.57, 124.15, 117.05, 107.69 ppm. **FT-IR:** v = 2519, 2159, 2030, 1976 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{16}$H$_{10}$OClS = 285.01464; found 285.01458. Spectral data matched literature characterization.[234]
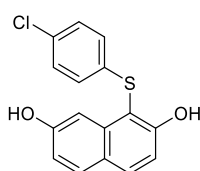
1-((4-Chlorophenyl)thio)naphthalene-2,7-diol (133p). Prepared according to the general procedure N using 2,7-dihydroxynaphthalene (16.5 mg, 0.1 mmol, 1 equiv) and 4-chlorothiophenol (30 mg, 0.2 mmol, 2 equiv); the product was obtained as a white solid (19 mg, 0.06 mmol, 64%). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 11.03 (s, 1H), 9.91 (s, 1H), 7.81 (d, J = 8.9 Hz, 1H), 7.69 – 7.65 (m, 2H), 7.62 – 7.55 (m, 4H), 6.98 (d, J = 8.9 Hz, 1H), 6.85 ppm (dd, J = 8.7, 2.4 Hz, 1H). **^{13}C NMR** (126 MHz, DMSO) δ 157.18, 156.82, 144.12, 134.64, 134.54, 132.69, 130.66, 129.20, 126.07, 122.98, 115.93, 115.83, 114.66, 104.71 ppm. **FT-IR:** v = 2516, 2159, 2029, 1976, 1633 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{16}$H$_{12}$O$_2$ClS = 303.0241; found 303.0244.
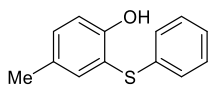
4-Methyl-2-(phenylthio)phenol (133q). Prepared according to the general procedure N using *p*-cresol (11 µL, 0.1 mmol, 1 equiv) and thiophenol (21 mg, 0.2 mmol, 2 equiv); the product was obtained as a colourless oil (18 mg, 0.08 mmol, 83%). **^{1}H NMR** (600 MHz, CDCl$_3$) δ 7.34 (d, J = 1.6 Hz, 1H), 7.24 (t, J = 7.7 Hz, 2H), 7.20 –

7.13 (m, 2H), 7.09 (d, J = 8.5 Hz, 2H), 6.98 (d, J = 8.5 Hz, 1H), 6.34 (s, 1H), 2.29 ppm (s, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 155.19, 137.06, 136.21, 133.16, 130.76, 129.32, 126.91, 126.16, 115.83, 115.37, 20.46 ppm. **FT-IR:** v = 2503, 2159, 2029, 1976 cm⁻¹. **HR-MS:** calc. for [M-H]⁻ $C_{13}H_{11}OS$ = 215.05251; found 215.05266. Spectral data matched literature characterization.[233]

4-Methyl-2-(p-tolylthio)phenol (133r). Prepared according to the general procedure N using *p*-cresol (11 µL, 0.1 mmol, 1 equiv) and 4-methylbenzenethiol (26 mg, 0.2 mmol, 2 equiv); the product was obtained as a colourless oil (19 mg, 0.08 mmol, 83%). **¹H NMR** (400 MHz, CDCl₃) δ 7.33 (d, J = 2.3 Hz, 1H), 7.15 (dd, J = 8.3, 2.3 Hz, 1H), 7.07 – 7.01 (m, 4H), 6.95 (d, J = 8.3 Hz, 1H), 6.36 (s, 1H), 2.29 (s, 3H), 2.28 ppm (s, 3H). **¹³C NMR** (101 MHz, CDCl₃) δ 155.01, 136.81, 136.30, 132.86, 132.49, 130.64, 130.10, 127.51, 116.72, 115.27, 21.06, 20.46 ppm. **FT-IR:** v = 2159, 2008, 1896, 1585 cm⁻¹. **HR-MS:** calc. for [M-H]⁻ $C_{14}H_{13}OS$ = 229.06926; found 229.06932. Spectral data matched literature characterization.[169a]

2-((4-Methoxyphenyl)thio)-4-methylphenol (133s). Prepared according to the general procedure N using *p*-cresol (11 µL, 0.1 mmol, 1 equiv) and 4-methoxythiolphenol (25 µL, 0.2 mmol, 2 equiv); the product was obtained as a colourless solid (14 mg, 0.06 mmol, 57%). **¹H NMR** (500 MHz, CDCl₃) δ 7.32 – 7.29 (m, 1H), 7.12 (m, 3H), 6.93 (d, J = 8.3 Hz, 1H), 6.82 – 6.78 (m, 2H), 6.40 (s, 1H), 3.76 (s, 3H), 2.26 ppm (s, 3H). **¹³C NMR** (126 MHz, CDCl₃) δ 158.82, 154.65, 136.35, 132.55, 130.58, 130.04, 126.42, 117.94, 115.21, 115.05, 55.49, 20.48 ppm. **FT-IR:** v = 2362, 2159, 2033, 1976 cm⁻¹. **HR-MS:** calc. for [M-H]⁻ $C_{14}H_{13}O_2S$ = 245.06417; found 245.06416. Spectral data matched literature characterization.[235]

2-((4-Fluorophenyl)thio)-4-methylphenol (133t). Prepared according to the general procedure N using *p*-cresol (11 µL, 0.1 mmol, 1 equiv) and 4-fluorothiophenol (22 µL, 0.2 mmol, 2 equiv); the product was obtained as a colourless oil (12 mg, 0.05 mmol, 51%). **¹H NMR** (400 MHz, CDCl₃) δ 7.31 (dd, J = 2.3, 0.9 Hz, 1H), 7.19 – 7.14 (m, 1H), 7.12 – 7.06 (m, 2H), 6.99 – 6.91 (m, 3H), 6.31 (s, 1H), 2.28 ppm (s, 3H). **¹³C NMR** (101 MHz, CDCl₃) δ 161.71 (d, J_{CF} = 246.1 Hz), 154.95, 136.76, 133.17, 131.16 (d, J_{CF} = 3.3 Hz), 130.87, 129.23 (d, J_{CF} = 8.0 Hz), 116.53 (d, J = 7.9 Hz), 116.35, 115.47, 20.46 ppm. **FT-IR:** v = 2511, 2159, 2029, 1976 cm⁻¹. **HR-MS:** calc. for [M-H]⁻ $C_{13}H_{10}OFS$ = 233.04419; found 233.04429.
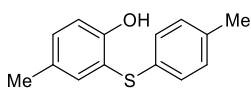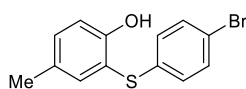
2-((4-Bromophenyl)thio)-4-methylphenol (133u). Prepared according to the general procedure N using *p*-cresol (11 µL, 0.1 mmol, 1 equiv) and 4-fluorothiophenol (38.5 mg, 0.2 mmol, 2 equiv); the product was obtained as a colourless solid (12 mg, 0.05 mmol, 47%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.34 (d, *J* = 8.6 Hz, 2H), 7.30 (s, 1H), 7.19 (d, *J* = 8.3 Hz, 1H), 6.97 (d, *J* = 8.3 Hz, 1H), 6.93 (d, *J* = 8.6 Hz, 2H), 6.24 (s, 1H), 2.29 ppm (s, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 155.10, 136.95, 135.53, 133.48, 132.31, 131.00, 128.40, 119.93, 115.57, 115.27, 20.46 ppm. **FT-IR:** ν = 2532, 2161, 2029, 1978 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{13}$H$_{10}$OBrS = 292.96412; found 292.96409; C$_{13}$H$_{10}$O^{81}BrS = 294.96205; found 294.96746. Spectral data matched literature characterization.[235]
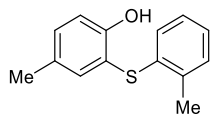
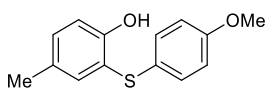**4-Methyl-2-(*o*-tolylthio)phenol (133v).** Prepared according to the general procedure N using *p*-cresol (11 µL, 0.1 mmol, 1 equiv) and *o*-toluenethiol (24 µL, 0.2 mmol, 2 equiv); the product was obtained as a colourless oil (20 mg, 0.09 mmol, 87%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.30 (s, 1H), 7.21 – 7.15 (m, 2H), 7.07 (t, *J* = 6.9 Hz, 1H), 7.03 (t, *J* = 7.3 Hz, 1H), 6.99 (d, *J* = 8.3 Hz, 1H), 6.67 (d, *J* = 7.7 Hz, 1H), 6.24 (s, 1H), 2.45 (s, 3H), 2.29 ppm (s, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 155.27, 137.08, 135.47, 135.29, 133.04, 130.88, 130.42, 126.91, 125.83, 125.72, 115.36, 115.25, 20.48, 20.20 ppm. **FT-IR:** ν = 2361, 2159, 2029, 1587 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{14}$H$_{13}$OS = 229.06926; found 229.06936.
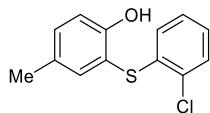
2-((2-Chlorophenyl)thio)-4-methylphenol (133w). Prepared according to the general procedure N using *p*-cresol (11 µL, 0.1 mmol, 1 equiv) and 2-chlorothiophenol (23.5 µL, 0.2 mmol, 2 equiv); the product was obtained as a white solid (17 mg, 0.07 mmol, 68%). **^{1}H NMR** (400 MHz, CDCl$_3$) δ 7.38 – 7.34 (m, 1H), 7.33 (d, *J* = 1.7 Hz, 1H), 7.23 (dd, *J* = 8.3, 1.9 Hz, 1H), 7.10 – 7.04 (m, 2H), 7.00 (d, *J* = 8.3 Hz, 1H), 6.67 – 6.60 (m, 1H), 6.22 (s, 1H), 2.30 (s, 3H). **^{13}C NMR** (101 MHz, CDCl$_3$) δ 155.51, 137.36, 135.56, 133.73, 131.49, 131.14, 129.79, 127.57, 126.89, 126.84, 115.69, 114.22, 20.47 ppm. **FT-IR:** ν = 2361, 2159, 2023, 1976 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{13}$H$_{10}$OClS = 249.01464; found 249.01464.
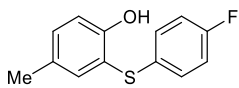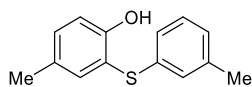
4-Methyl-2-(*m*-tolylthio)phenol (133x). Prepared according to the general procedure N using *p*-cresol (11 µL, 0.1 mmol, 1 equiv) and *m*-toluenethiol (25 µL, 0.2 mmol, 2 equiv); the product was obtained as a colourless oil (17 mg, 0.07 mmol, 74%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.33 (s, 1H), 7.19 – 7.16 (m, 1H), 7.12 (t, *J* = 7.7 Hz, 1H), 6.97 (dd, *J* = 7.7, 4.8 Hz, 2H), 6.93 (s, 1H), 6.87 (d, *J* = 7.7 Hz, 1H), 6.35 (s,

1H), 2.29 (s, 3H), 2.27 ppm (s, 3H). **13C NMR** (126 MHz, CDCl₃) δ 155.14, 139.21, 137.03, 135.88, 133.06, 130.68, 129.18, 127.57, 127.13, 124.05, 115.99, 115.29, 21.51, 20.48 ppm. **FT-IR:** v = 2461, 2362, 2159, 2028, 1976 cm^{-1}. **HR-MS:** calc. for [M-H]⁻ C₁₄H₁₃OS = 229.06926; found 229.06936.
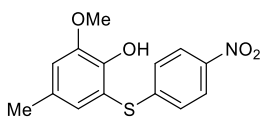
2-Methoxy-4-methyl-6-((4-nitrophenyl)thio)phenol (133y). Prepared according to the general procedure N using 2-methoxy-4-methylphenol (13 µL, 0.1 mmol, 1 equiv) and 4-nitrothiophenol (80%, 39 mg, 0.2 mmol, 2 equiv); the product was obtained as a yellow solid (28 mg, 0.1 mmol, 96%). **1H NMR** (400 MHz, CDCl₃) δ 8.03 (d, J = 9.0 Hz, 2H), 7.12 (s, 1H), 7.03 (d, J = 9.0 Hz, 2H), 6.85 (s, 1H), 5.57 (s, 1H), 3.94 (s, 3H), 2.29 ppm (s, 3H). **13C NMR** (101 MHz, CDCl₃) δ 149.35, 148.46, 145.02, 144.53, 135.30, 125.37, 124.12, 122.30, 119.57, 113.27, 56.14, 20.41 ppm. **FT-IR:** v = 2531, 2159, 2029, 1976, 1605, 1577 cm^{-1}. **HR-MS:** calc. for [M-H]⁻ C₁₄H₁₂O₄NS = 290.04925; found 290.04970.
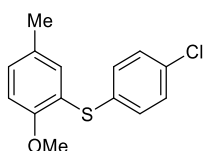
(4-Chlorophenyl)(2-methoxy-5-methylphenyl)sulfane (134a). To a stirring solution of 2-((4-chlorophenyl)thio)-4-methylphenol (**2a**) (75 mg, 0.3 mmol, 1 equiv) in DMF (3 mL) was NaH (60% in mineral oil, 15 mg, 0.36 mmol, 1.2 equiv) slowly added at 0 °C. The reaction was stirred for 30 min at room temperature and cooled again to 0 °C. Iodomethane (28.5 µL, 0.45 mmol, 1.5 equiv) was added and stirring was continued at 0 °C for 3 h. After that time, the reaction was diluted with water (30 mL) and extracted with EtOAc (3x15 mL). The combined organic layers were dried over MgSO₄ and concentrated under reduced pressure. Column chromatography provide the pure product (eluent: petroleum ether / DCM); the product was obtained as a pale yellow oil (70 mg, 0.26 mmol, 88%). **1H NMR** (600 MHz, CDCl₃) δ 7.26 – 7.23 (m, 2H), 7.22 – 7.19 (m, 2H), 7.09 (m, 1H), 7.03 (dd, J = 2.2, 0.8 Hz, 1H), 6.82 (d, J = 8.3 Hz, 1H), 3.82 (s, 3H), 2.24 (s, 3H) ppm. **13C NMR** (151 MHz, CDCl₃) δ 156.06, 134.35, 133.62, 132.53, 131.50, 130.84, 129.88, 129.22, 122.09, 111.20, 56.11, 20.47 ppm.
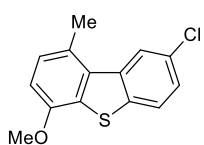
8-Chloro-4-methoxy-1-methyldibenzo[b,d]thiophene (135a). Conducted according to a literature reference.[236] Under an air atmosphere, (4-chlorophenyl)(2-methoxy-5-methylphenyl)sulfane (66 mg, 0.25 mmol, 1 equiv), Pd(CF₃CO₂)₂ (15 mg, 0.05 mmol, 20 mol %), AgOAc (209 mg, 1.25 mmol, 5 equiv), K₂CO₃ (53 mg, 0.38 mmol, 1.5 equiv), and PivOH (0.75 mL) were added into a Schlenk tube. After stirring the reaction for 10 Minutes at room temperature the mixture was stirred 130 °C

for 2 d. After that time, the reaction was cooled to room temperature, filtered through a Celite pad. The filtrate was washed with sat. NaHCO$_3$ solution and the aqueous phase was extracted with DCM (3x20 mL). The combined organic layers were dried over MgSO$_4$ and concentrated under reduced pressure. Column chromatography provide the pure product (eluent: petroleum ether / DCM); the product was obtained as a white solid (33.5 mg, 0.13 mmol, 51%). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 8.32 (d, J = 2.1 Hz, 1H), 8.11 (d, J = 8.5 Hz, 1H), 7.57 (dd, J = 8.5, 2.1 Hz, 1H), 7.31 – 7.26 (m, 1H), 7.07 (d, J = 8.1 Hz, 1H), 3.97 (s, 3H), 2.80 (s, 3H) ppm. **^{13}C NMR** (126 MHz, DMSO) δ 152.12, 137.69, 137.53, 133.25, 129.61, 128.41, 128.17, 126.88, 126.17, 124.80, 124.09, 107.62, 55.95, 20.96 ppm. **FT-IR:** v = 2522, 2361, 2159, 2029, 1976 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{14}$H$_{12}$OClS = 263.02919; found 263.02993. Spectral data matched literature characterization.[169k]
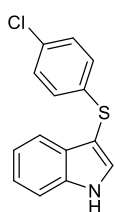
3-((4-Chlorophenyl)thio)-1H-indole (137a). Prepared according to the general procedure O using indole (12 mg, 0.1 mmol, 1 equiv) and 4-chlorothiophenol (30 mg, 0.2 mmol, 2 equiv); the product was obtained as a white solid (20 mg, 0.08 mmol, 77%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.43 (s, 1H), 7.58 (d, J = 8.0 Hz, 1H), 7.49 (d, J = 2.6 Hz, 1H), 7.45 (d, J = 8.0 Hz, 1H), 7.29 (t, J = 7.4 Hz, 1H), 7.19 (t, J = 7.4 Hz, 1H), 7.13 (d, J = 8.6 Hz, 2H), 7.03 ppm (d, J = 8.6 Hz, 2H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 137.92, 136.61, 130.86, 130.64, 128.90, 128.88, 127.19, 123.34, 121.19, 119.62, 111.81, 102.48 ppm. **FT-IR:** v = 2526, 2159, 2029, 1976 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{14}$H$_{11}$NClS = 260.02952; found 260.02951.

Scale up experiment: In a 50 mL round-bottom flask indole (120 mg, 1 mmol, 1 equiv) and 4-chlorothiophenol (298 mg, 0.2 mmol, 2 equiv) were dissolved in HFIP (20 mL). To the stirring solution NO$_2$BF$_4$ (0.2 M in sulfolane, 250 µL, 0.25 mmol, 5 mol %) was added and stirring was continued for 24 h. The reaction was stirred for 1 h at room temperature and NO$_2$BF$_4$ (0.2 M in sulfolane, 250 µL, 5 mol %) was added again. Stirring was continued for 1 h at room temperature. After that time, the reaction was diluted with dichloromethane, concentrated on silica and purified by silica gel column chromatography to afford the desired product (eluent: petroleum ether / dichloromethane); the product was obtained as a white solid (192 mg, 0.74 mmol, 74%).
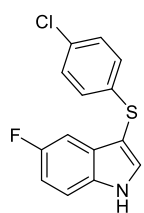
3-((4-Chlorophenyl)thio)-5-fluoro-1_H_-indole (137b). Prepared according to the general procedure O using 5-fluoroindole (14 mg, 0.1 mmol, 1 equiv) and 4-chlorothiophenol (30 mg, 0.2 mmol, 2 equiv); the product was obtained as a white solid (16 mg, 0.06 mmol, 57%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.46 (s, 1H), 7.53 (d, J = 2.6 Hz, 1H), 7.37 (dd, J = 8.8, 4.1 Hz, 1H), 7.21 (dd, J = 9.1, 2.5 Hz, 1H), 7.14 (d, J = 8.6 Hz, 2H), 7.05 – 6.98 (m, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 158.81 (d, J_{CF} = 237.2 Hz), 137.46, 133.01, 132.51, 130.89, 129.80 (d, J_{CF} = 10.0 Hz), 128.97, 127.26, 112.65 (d, J_{CF} = 9.5 Hz), 111.97 (d, J_{CF} = 26.6 Hz), 104.71 (d, J_{CF} = 24.3 Hz), 102.82 ppm (d, J_{CF} = 4.6 Hz). **FT-IR:** v = 2501, 2159, 2029, 1976 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{14}$H$_{10}$NClFS = 278.02010; found 278.02024.

5-Chloro-3-((4-chlorophenyl)thio)-1_H_-indole (137c). Prepared according to the general procedure O using 5-chloroindole (16 mg, 0.1 mmol, 1 equiv) and 4-chlorothiophenol (30 mg, 0.2 mmol, 2 equiv); the product was obtained as a white solid (17 mg, 0.06 mmol, 58%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.49 (s, 1H), 7.57 – 7.53 (m, 1H), 7.51 (d, J = 2.5 Hz, 1H), 7.36 (d, J = 8.6 Hz, 1H), 7.23 (dd, J = 8.7, 2.0 Hz, 1H), 7.14 (d, J = 8.6 Hz, 2H), 7.00 ppm (d, J = 8.6 Hz, 2H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 137.40, 134.94, 132.19, 130.94, 130.21, 129.01, 127.24, 127.21, 123.85, 119.12, 112.90, 102.55 ppm. **FT-IR:** v = 2502, 2159, 2029, 1976, 1474 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{14}$H$_{10}$N^{35}Cl$_2$S = 293.99055; found 293.99079; C$_{14}$H$_{10}$N^{35}Cl^{37}ClS = 295.98760; found 295.98772. Spectral data matched literature characterization.[170h]
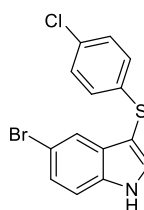
5-Bromo-3-((4-chlorophenyl)thio)-1_H_-indole (137d). Prepared according to the general procedure O using 5-bromoindole (20 mg, 0.1 mmol, 1 equiv) and 4-chlorothiophenol (30 mg, 0.2 mmol, 2 equiv); the product was obtained as a white solid (19 mg, 0.06 mmol, 56%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.49 (s, 1H), 7.71 (s, 1H), 7.49 (d, J = 2.5 Hz, 1H), 7.38 – 7.31 (m, 2H), 7.14 (d, J = 8.6 Hz, 2H), 6.99 ppm (d, J = 8.6 Hz, 2H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 137.39, 135.24, 132.04, 130.94, 130.80, 129.02, 127.22, 126.41, 122.21, 114.76, 113.30, 102.44 ppm. **FT-IR:** v = 2498, 2159, 2029, 1976 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{14}$H$_{10}$NBrClS = 337.94004; found 337.94030; C$_{14}$H$_{10}$N^{81}BrClS = 339.93799; found 339.93796. Spectral data matched literature characterization.[237]

3-((4-Chlorophenyl)thio)-6-methoxy-1*H*-indole (137e). Prepared according to the general procedure O using 6-methoxyindole (15 mg, 0.1 mmol, 1 equiv) and 4-chlorothiophenol (30 mg, 0.2 mmol, 2 equiv); the product was obtained as a white solid (13 mg, 0.04 mmol, 45%). **¹H NMR** (500 MHz, CDCl₃*d*) δ 8.31 (s, 1H), 7.42 (d, *J* = 8.7 Hz, 1H), 7.38 (d, *J* = 2.2 Hz, 1H), 7.12 (d, *J* = 8.7 Hz, 2H), 7.02 (d, *J* = 8.7 Hz, 2H), 6.92 (d, *J* = 2.2 Hz, 1H), 6.83 (dd, *J* = 8.7, 2.2 Hz, 1H), 3.86 ppm (s, 3H). **¹³C NMR** (126 MHz, CDCl₃) δ 157.42, 138.02, 137.43, 130.60, 129.62, 128.87, 127.15, 123.01, 120.29, 111.13, 102.42, 95.18, 55.83 ppm. **FT-IR:** v = 2525, 2159, 2029, 1976 cm⁻¹. **HR-MS:** calc. for [M+H]⁺ $C_{15}H_{13}ONClS$ = 290.04009; found 290.04026. Spectral data matched literature characterization.[238]
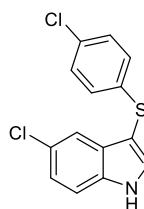
6-Chloro-3-((4-chlorophenyl)thio)-1*H*-indole (137f). Prepared according to the general procedure O using 6-chloroindole (16 mg, 0.1 mmol, 1 equiv) and 4-chlorothiophenol (30 mg, 0.2 mmol, 2 equiv); the product was obtained as a white solid (24 mg, 0.08 mmol, 82%). **¹H NMR** (500 MHz, CDCl₃) δ 8.43 (s, 1H), 7.48 (d, *J* = 2.5 Hz, 1H), 7.46 (d, *J* = 8.5 Hz, 1H), 7.45 – 7.43 (m, 1H), 7.17 – 7.10 (m, 3H), 7.03 – 6.97 ppm (m, 2H). **¹³C NMR** (126 MHz, CDCl₃) δ 137.41, 136.91, 131.38, 130.89, 129.37, 128.96, 127.47, 127.27, 122.01, 120.59, 111.80, 103.09 ppm. **FT-IR:** v = 2513, 2159, 2030, 1976 cm⁻¹. **HR-MS:** calc. for [M+H]⁺ $C_{14}H_{10}NCl^{37}ClS$ = 295.98760; found 295.98776; $C_{14}H_{10}N^{37}Cl_2S$ = 297.98465; found 297.98468.

3-(Phenylthio)-1*H*-indole (137g). Prepared according to the general procedure O using indole (12 mg, 0.1 mmol, 1 equiv) and thiophenol (21 µL, 0.2 mmol, 2 equiv); the product was obtained as a white solid (18 mg, 0.08 mmol, 80%). **¹H NMR** (500 MHz, CDCl₃) δ 8.39 (s, 1H), 7.63 (dd, *J* = 7.9, 1.0 Hz, 1H), 7.49 (d, *J* = 2.5 Hz, 1H), 7.46 – 7.43 (m, 1H), 7.28 (m, 1H), 7.20 – 7.14 (m, 3H), 7.14 – 7.10 (m, 2H), 7.09 – 7.04 ppm (m, 1H). **¹³C NMR** (126 MHz, CDCl₃) δ 139.33, 136.58, 130.83, 129.20, 128.83, 125.92, 124.89, 123.18, 121.03, 119.78, 111.71, 102.86 ppm. **FT-IR:** v = 2526, 2159, 2029, 1976 cm⁻¹. **HR-MS:** calc. for [M+H]⁺ $C_{14}H_{12}NS$ = 226.06850; found 226.06831. Spectral data matched literature characterization.[169c]

3-(*p*-Tolylthio)-1*H*-indole (137h). Prepared according to the general procedure O using indole (12 mg, 0.1 mmol, 1 equiv) and 4-methylbenzenethiol (26 mg, 0.2 mmol, 2 equiv); the product was obtained as a white solid (15 mg, 0.06 mmol, 63%). **^{1}H NMR** (400 MHz, Methylene Chloride-d_2) δ 8.57 (s, 1H), 7.55 (d, J = 7.9 Hz, 1H), 7.51 (d, J = 2.5 Hz, 1H), 7.47 (d, J = 8.2 Hz, 1H), 7.28 – 7.21 (m, 1H), 7.17 – 7.10 (m, 1H), 7.05 – 6.97 (m, 4H), 2.24 ppm (s, 3H). **^{13}C NMR** (101 MHz, CD$_2$Cl$_2$) δ 137.15, 136.00, 135.48, 131.29, 129.99, 129.52, 126.91, 123.45, 121.24, 119.81, 112.23, 103.80, 21.09 ppm. **FT-IR:** v = 2493, 2170, 1969 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{15}$H$_{14}$NS = 240.08415; found 240.083420. Spectral data matched literature characterization.[169k]

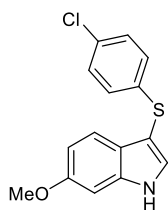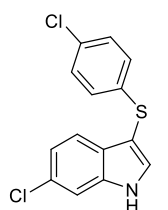**3-((4-Fluorophenyl)thio)-1*H*-indole (137i).** Prepared according to the general procedure O using indole (12 mg, 0.1 mmol, 1 equiv) and 4-fluorothiophenol (22 µL, 0.2 mmol, 2 equiv); the product was obtained as a white solid (17 mg, 0.07 mmol, 70%). **^{1}H NMR** (400 MHz, CDCl$_3$) δ 8.40 (s, 1H), 7.60 (d, J = 7.9 Hz, 1H), 7.49 (d, J = 2.5 Hz, 1H), 7.44 (d, J = 8.1 Hz, 1H), 7.30 – 7.26 (m, 1H), 7.21 – 7.15 (m, 1H), 7.10 (dd, J = 8.9, 5.1 Hz, 2H), 6.87 ppm (t, J = 8.7 Hz, 2H). **^{13}C NMR** (101 MHz, CDCl$_3$) δ 161.04 (d, J_{CF} = 243.8 Hz), 136.63, 134.13, 130.60, 129.00, 128.02 (d, J_{CF} = 7.8 Hz), 123.28, 121.12, 119.68, 115.87 (d, J_{CF} = 22.0 Hz), 111.75, 103.58 ppm. **FT-IR:** v = 2526, 2159, 2028, 19760 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{14}$H$_{11}$NFS = 244.05907; found 244.05895. Spectral data matched literature characterization.[169k]
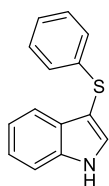
3-((4-Bromophenyl)thio)-1*H*-indole (137j). Prepared according to the general procedure O using indole (12 mg, 0.1 mmol, 1 equiv) and 4-bromothiophenol (38.5 mg, 0.2 mmol, 2 equiv); the product was obtained as a white solid (25 mg, 0.08 mmol, 82%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.44 (s, 1H), 7.56 (dd, J = 7.9, 1.0 Hz, 1H), 7.48 (d, J = 2.6 Hz, 1H), 7.44 (dt, J = 8.2, 1.0 Hz, 1H), 7.30 – 7.26 (m, 1H), 7.26 – 7.23 (m, 2H), 7.19 – 7.15 (m, 1H), 6.95 ppm (d, J = 8.6 Hz, 2H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 138.66, 136.62, 131.76, 130.89, 128.88, 127.48, 123.35, 121.21, 119.63, 118.41, 111.81, 102.33 ppm. **FT-IR:** v = 2518, 2159, 2030, 1976 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{14}$H$_{11}$NBS = 303.97901; found 303.97934; C$_{14}$H$_{11}$N^{81}BrS = 305.97696; found 305.97714. Spectral data matched literature characterization.[169k]

3-(*o*-Tolylthio)-1*H*-indole (137k). Prepared according to the general procedure O using indole (12 mg, 0.1 mmol, 1 equiv) and *o*-toluenethiol (25 µL, 0.2 mmol, 2 equiv); the product was obtained as a white solid (14 mg, 0.06 mmol, 59%). **^{1}H NMR** (600 MHz, CDCl$_3$) δ 8.41 (s, 1H), 7.60 (d, J = 7.9 Hz, 1H), 7.49 – 7.43 (m, 2H), 7.28 (t, J = 7.6 Hz, 1H), 7.17 (t, J = 7.5 Hz, 1H), 7.14 (d, J = 7.4 Hz, 1H), 6.99 (t, J = 7.8 Hz, 1H), 6.91 (t, J = 7.6 Hz, 1H), 6.73 (d, J = 7.9 Hz, 1H), 2.51 ppm (s, 3H). **^{13}C NMR** (151 MHz, CDCl$_3$) δ 138.40, 136.68, 134.47, 130.90, 129.95, 129.36, 126.38, 125.37, 124.58, 123.18, 121.02, 119.84, 111.72, 102.48, 20.04 ppm. **FT-IR:** v = 2489, 2159, 2029, 1976 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{15}$H$_{14}$NS = 240.08415; found 240.08398. Spectral data matched literature characterization.[170b]

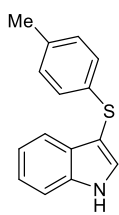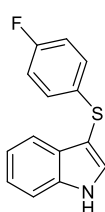**3-((2-Bromophenyl)thio)-1*H*-indole (137l).** Prepared according to the general procedure O using indole (12 mg, 0.1 mmol, 1 equiv) and 2-bromothiophenol (25 µL, 0.2 mmol, 2 equiv); the product was obtained as a white solid (26 mg, 0.09 mmol, 85%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.51 (s, 1H), 7.60 (dd, J = 7.9, 1.1 Hz, 1H), 7.53 – 7.45 (m, 3H), 7.30 (m, 1H), 7.19 (m, 1H), 6.98 (m, 1H), 6.91 (m, 1H), 6.63 ppm (dd, J = 7.9, 1.6 Hz, 1H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 140.55, 136.68, 132.64, 131.44, 129.01, 127.63, 126.47, 125.77, 123.40, 121.27, 119.74, 119.69, 111.85, 101.97 ppm. **FT-IR:** v = 2525, 2159, 2029, 1976 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{14}$H$_{11}$NBrS = 303.97901; found 303.97928; C$_{14}$H$_{11}$N^{81}BrS = 305.97696; found 305.97700. Spectral data matched literature characterization.[239]
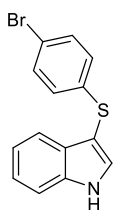
3-(*m*-Tolylthio)-1*H*-indole (137m). Prepared according to the general procedure O using indole (12 mg, 0.1 mmol, 1 equiv) and *m*-toluenethiol (25 µL, 0.2 mmol, 2 equiv); the product was obtained as a white solid (15 mg, 0.06 mmol, 63%). **^{1}H NMR** (600 MHz, CDCl$_3$) δ 8.39 (s, 1H), 7.64 (d, J = 7.9 Hz, 1H), 7.48 (d, J = 2.3 Hz, 1H), 7.44 (d, J = 8.2 Hz, 1H), 7.28 (d, J = 7.8 Hz, 1H), 7.17 (t, J = 7.5 Hz, 1H), 7.05 (t, J = 7.7 Hz, 1H), 6.99 (s, 1H), 6.92 – 6.85 (m, 2H), 2.23 ppm (s, 3H). **^{13}C NMR** (151 MHz, CDCl$_3$) δ 139.09, 138.59, 136.60, 130.77, 129.32, 128.71, 126.60, 125.89, 123.14, 121.00, 119.85, 111.66, 103.13, 21.51 ppm. **FT-IR:** v = 2489, 2159, 2029, 1976 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{15}$H$_{14}$NS = 240.08415; found 240.08405. Spectral data matched literature characterization.[239]
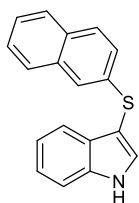
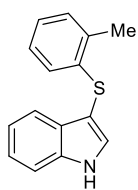**3-(Naphthalen-2-ylthio)-1*H*-indole (137n).** Prepared according to the general procedure O using indole (12 mg, 0.1 mmol, 1 equiv) and 2-naphthalenethiol (21 µL, 0.2 mmol, 2 equiv); the product was obtained as a white solid (14 mg, 0.05 mmol, 51%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.46 (s, 1H), 7.74 – 7.70 (m, 1H), 7.65 (d, *J* = 8.7 Hz, 1H), 7.62 (d, *J* = 8.0 Hz, 1H), 7.59 – 7.54 (m, 2H), 7.49 (d, *J* = 1.9 Hz, 1H), 7.47 (d, *J* = 8.2 Hz, 1H), 7.40 – 7.33 (m, 2H), 7.28 (m, 2H), 7.15 ppm (t, *J* = 7.5 Hz, 1H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 136.83, 136.66, 133.87, 131.44, 130.84, 129.22, 128.38, 127.81, 127.05, 126.47, 125.18, 124.88, 123.62, 123.23, 121.10, 119.84, 111.73, 102.93 ppm. **FT-IR:** ν = 2972, 2926, 2524, 2159, 2029, 1976 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{18}$H$_{14}$NS = 276.08415; found 276.08406. Spectral data matched literature characterization.[169g]
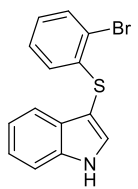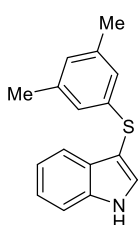
3-((3,5-Dimethylphenyl)thio)-1*H*-indole (137o). Prepared according to the general procedure O using indole (12 mg, 0.1 mmol, 1 equiv) and 3,5-dimethylbenzene-1-thiol (30 µL, 0.2 mmol, 2 equiv); the product was obtained as a white solid (16.5 mg, 0.07 mmol, 65%). **^{1}H NMR** (400 MHz, CDCl$_3$) δ 8.38 (s, 1H), 7.65 (d, *J* = 7.9 Hz, 1H), 7.47 (d, *J* = 2.4 Hz, 1H), 7.44 (m, 1H), 7.27 (t, *J* = 7.9 Hz, 1H), 7.17 (t, *J* = 7.5 Hz, 1H), 6.76 (s, 2H), 6.71 (s, 1H), 2.18 ppm (s, 6H). **^{13}C NMR** (101 MHz, CDCl$_3$) δ 138.86, 138.48, 136.58, 130.75, 129.41, 127.02, 123.79, 123.07, 120.95, 119.88, 111.62, 103.25, 21.38 ppm. **FT-IR:** ν = 2524, 2159, 2029, 1976 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{16}$H$_{16}$NS = 254.09980; found 254.09972.
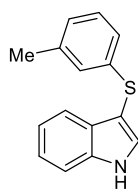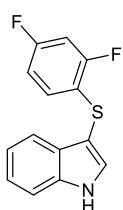
3-((2,4-Difluorophenyl)thio)-1*H*-indole (137p). Prepared according to the general procedure O using indole (12 mg, 0.1 mmol, 1 equiv) and 2,4-difluorobenzene-1-thiol (23 µL, 0.2 mmol, 2 equiv); the product was obtained as a white solid (18 mg, 0.07 mmol, 69%). **^{1}H NMR** (400 MHz, CDCl$_3$) δ 8.44 (s, 1H), 7.63 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.52 (d, *J* = 2.6 Hz, 1H), 7.45 (m, 1H), 7.31 – 7.26 (m, 1H), 7.22 – 7.17 (m, 1H), 6.88 – 6.77 (m, 2H), 6.66 – 6.60 ppm (m, 1H). **^{13}C NMR** (101 MHz, CDCl$_3$) δ 164.13 – 154.23 (m), 136.58, 131.16, 129.76 (dd, J_{CF} = 9.1, 3.7 Hz), 129.04, 123.37, 121.67 (dd, J_{CF} = 17.4, 3.9 Hz), 121.24, 119.53, 111.83, 111.80 (d, J_{CF} = 3.6 Hz), 111.59 (d, J_{CF} = 3.6 Hz), 104.06 (t, J_{CF} = 25.7 Hz), 101.42 ppm. **FT-IR:** ν = 2528, 2159, 20296, 1976 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{14}$H$_{10}$NF$_2$S = 262.04965; found 262.04963.
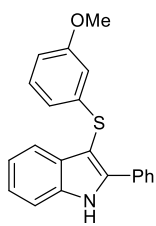
3-((3-Methoxyphenyl)thio)-2-phenyl-1*H*-indole (137q). Prepared according to the general procedure O using 2-phenylindole (20 mg, 0.1 mmol, 1 equiv) and 3-methoxythiophenol (25 µL, 0.2 mmol, 2 equiv); the product was obtained as a white solid (18 mg, 0.05 mmol, 54%). **^{1}H NMR** (700 MHz, CDCl$_3$) δ 8.56 (s, 1H), 7.76 (dd, J = 8.3, 1.3 Hz, 2H), 7.65 (d, J = 7.9 Hz, 1H), 7.44 (t, J = 7.4 Hz, 3H), 7.39 (t, J = 7.4 Hz, 1H), 7.28 (d, J = 7.4 Hz, 1H), 7.18 (t, J = 7.5 Hz, 1H), 7.08 (t, J = 8.0 Hz, 1H), 6.73 – 6.66 (m, 2H), 6.61 (dd, J = 8.3, 2.3 Hz, 1H), 3.68 ppm (s, 3H). **^{13}C NMR** (176 MHz, CDCl3) δ 160.09, 142.21, 140.94, 135.94, 131.54, 131.34, 129.76, 128.92, 128.84, 128.26, 123.51, 121.33, 120.10, 118.13, 111.38, 111.27, 110.36, 99.39, 55.26 ppm. **FT-IR:** v = 2501, 2159, 2029, 1976, 1589 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{21}$H$_{18}$ONS = 332.11036; found 332.11026.
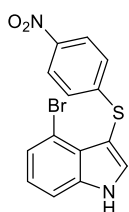
4-Bromo-3-((4-nitrophenyl)thio)-1*H*-indole (137r). Prepared according to the general procedure O using 4-bromoindole (20 mg, 0.1 mmol, 1 equiv) and 4-nitrothiophenol (80%, 39 mg, 0.2 mmol, 2 equiv); the product was obtained as a yellow solid (22 mg, 0.06 mmol, 63%). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 12.24 (s, 1H), 8.11 – 8.06 (m, 2H), 7.96 (d, J = 2.9 Hz, 1H), 7.56 (dd, J = 8.1, 0.9 Hz, 1H), 7.29 (dd, J = 7.6, 0.9 Hz, 1H), 7.18 – 7.15 (m, 2H), 7.13 ppm (t, J = 7.9 Hz, 1H). **^{13}C NMR** (126 MHz, DMSO) δ 151.97, 144.32, 138.30, 135.99, 125.25, 124.99, 124.91, 124.03, 123.76, 112.62, 112.51, 97.26 ppm. **FT-IR:** v = 2341, 2159, 2028, 1976, 1473 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{14}$H$_{10}$O$_2$N$_2$BrS = 348.96409; found 348.96428; C$_{14}$H$_{10}$O$_2$N$_2$^{81}BrS = 349.95422; found 349.95448.
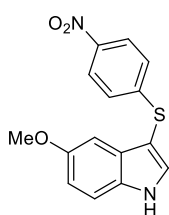
5-Methoxy-3-((4-nitrophenyl)thio)-1*H*-indole (137s). Prepared according to the general procedure O using 5-methoxyindole (15 mg, 0.1 mmol, 1 equiv) and 4-nitrothiophenol (80%, 39 mg, 0.2 mmol, 2 equiv); the product was obtained as a yellow solid (16 mg, 0.05 mmol, 53%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.56 (s, 1H), 8.04 – 7.98 (m, 2H), 7.50 (d, J = 2.6 Hz, 1H), 7.39 (dd, J = 8.7, 0.6 Hz, 1H), 7.17 – 7.09 (m, 2H), 6.98 – 6.92 (m, 2H), 3.79 ppm (s, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 155.61, 149.98, 145.01, 131.85, 131.51, 129.44, 125.10, 124.03, 114.18, 112.95, 100.43, 99.66, 55.91 ppm. **FT-IR:** v = 2159, 2028, 1976 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{15}$H$_{13}$O$_3$N$_2$S = 301.06414; found 301.06432.
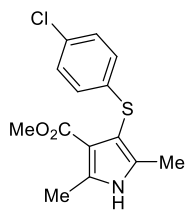
Methyl 4-((4-chlorophenyl)thio)-2,5-dimethyl-1*H*-pyrrole-3-carboxylate (137t). Prepared according to the general procedure O using methyl 2,5-dimethyl-1*H*-pyrrole-3-carboxylate (15.6 mmol, 0,1 mmol, 1 equiv) and 4-chlorothiophenol (29.5 mg, 0.2 mmol, 2 equiv); the product was obtained as a white solid (19 mg, 0.06 mmol, 64%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.41 (s, 1H), 7.14 – 7.10 (m, 2H), 6.99 – 6.94 (m, 2H), 3.67 (s, 3H), 2.50 (s, 3H), 2.24 (s, 3H) ppm. **^{13}C NMR** (126 MHz, CDCl$_3$) δ 165.31, 139.02, 135.70, 133.37, 130.07, 128.66, 126.93, 113.17, 106.25, 50.87, 14.19, 11.43 ppm. **FT-IR:** v = 2341, 2159, 2029, 1976, 1673 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{14}$H$_{13}$O$_2$NClS = 294.03610; found 294.03590.
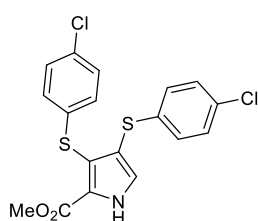
Methyl 3,4-bis((4-chlorophenyl)thio)-1H-pyrrole-2-carboxylate (137u). Prepared according to the general procedure O using methyl 2-pyrrolecarboxylate (13 mg, 0.1 mmol, 1 equiv) and 4-chlorothiophenol (29.5 mg, 0.2 mmol, 2 equiv); the product was obtained as a white solid (28 mg, 0.07 mmol, 68%). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 13.32 (s, 1H), 7.27 (d, J = 8.5 Hz, 2H), 7.23 (d, J = 8.7 Hz, 2H), 7.05 (d, J = 2.5 Hz, 1H), 7.04 – 6.98 (m, 4H), 3.80 (s, 3H) ppm. **^{13}C NMR** (126 MHz, DMSO) δ 160.10, 137.06, 135.41, 131.50, 130.59, 129.52, 129.50, 129.33, 128.56, 128.46, 126.45, 121.71, 118.40, 52.20 ppm. **FT-IR:** v = 2343, 2161, 2030, 1978, 1690 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{18}$H$_{12}$O$_2$N^{35}Cl$_2$S$_2$ = 407.96920; found 407.96915.
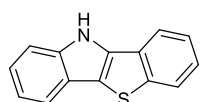
10-Benzo[4,5]thieno[3,2-*b*]indole (138a). Conducted according to literature reference.[240] To a degassed solution of 3-((2-Bromophenyl)thio)-1*H*-indole (**5l**) (25 mg, 0.08 mmol, 1 equiv) and caesium pivalate (38.5 mg, 0.16 mmol, 2 equiv) in *N*,*N*-dimethylacetamide (0.8 mL) was added PdCl$_2$(PPh$_3$)$_2$ (3 mg, 4 µmol, 5 mol %). The mixture was stirred for 24 h at 140 °C and then quenched by adding hydrochloric acid (1M, 7 mL). The resulting mixture was extracted with ethyl acetate (3×10 mL), washed with brine (3×20 mL), dried over MgSO$_4$, and concentrated under reduced pressure. Column chromatography provide the pure product (eluent: petroleum ether / DCM); the product was obtained as a pale brown solid (16 mg, 0.07 mmol, 87%). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 12.13 (s, 1H), 8.09 – 8.04 (m, 1H), 8.05 – 8.00 (m, 1H), 7.78 (dd, J = 8.0, 1.1 Hz, 1H), 7.62 – 7.57 (m, 1H), 7.49 (ddd, J = 8.0, 7.1, 1.1 Hz, 1H), 7.39 (ddd, J = 8.3, 7.1, 1.2 Hz, 1H), 7.28 (ddd, J = 8.1, 7.0, 1.2 Hz, 1H), 7.15 (ddd, J = 8.1, 7.0, 1.0 Hz, 1H) ppm. **^{13}C NMR** (126 MHz, DMSO) δ 141.98, 140.60, 137.50, 126.68, 124.58, 124.48, 124.34, 122.88, 121.52, 120.18, 119.40, 118.86, 113.83,

112.65 ppm. **FT-IR:** v = 2341, 2159, 2027, 1976 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{14}$H$_8$NS = 222.03829; found 222.03842. Spectral data matched literature characterization.[241]
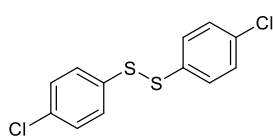
1,2-Bis(4-chlorophenyl)disulfane (139a). Prepared according to the general procedure N 4-chlorothiophenol (29.5 mg, 0.2 mmol, 1 equiv); the product was obtained as a white solid (28 mg, 0.1 mmol, 98%). **^{1}H NMR** (600 MHz, CDCl$_3$) δ 7.40 (d, J = 8.6 Hz, 4H), 7.28 (d, J = 8.6 Hz, 4H) ppm. 13CNMR (151 MHz, CDCl$_3$) δ 135.28, 133.79, 129.48, 129.46 ppm.
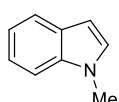
1-Methyl-1H-indole. To a solution of indole (500 µL, 5 mmol, 1 equiv) and powdered potassium hydroxide (1.4 g, 25 mmol, 5 equiv) in DMF (15 mL) was added iodomethane (623 µL, 10 mmol, 2 equiv). The reaction mixture was stirred at room temperature for 20 minutes. The mixture was filtered through a plug of silica gel, and H$_2$O (65 mL) was added to the filtrate. The water layer was extracted with DCM (2x30 mL). The combined organic layers were dried over MgSO$_4$ and the crude product was purified by silica gel chromatography (eluent: petroleum ether / ethyl acetate). The compound was obtained as yellow oil (600 mg, 4.57 mmol, 91%). **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.65 (d, J = 7.9 Hz, 1H), 7.34 (d, J = 8.2 Hz, 1H), 7.24 (t, J = 7.8 Hz, 1H), 7.12 (t, J = 7.5 Hz, 1H), 7.07 (d, J = 3.0 Hz, 1H), 6.50 (d, J = 2.9 Hz, 1H), 3.81 ppm (s, 3H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 136.77, 128.91, 128.55, 121.59, 120.97, 119.37, 109.30, 100.98, 32.96 ppm.
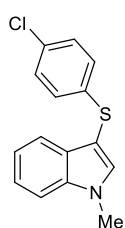
3-((4-Chlorophenyl)thio)-1-methyl-3a,7a-dihydro-1H-indole (137w). Prepared according to the general procedure O using 1-methyl-1H-indole (13 mg, 0.1 mmol, 1 equiv) and 4-chlorothiophenol (30 mg, 0.2 mmol, 2 equiv); the product was obtained as a white solid (11 mg, 0.04 mmol, 40%). **^{1}H NMR** (400 MHz, CDCl$_3$) δ 7.58 (m, 1H), 7.43 – 7.37 (m, 1H), 7.34 (s, 1H), 7.33 – 7.29 (m, 1H), 7.18 (m, 1H), 7.14 – 7.09 (m, 2H), 7.05 – 6.99 (m, 2H), 3.86 ppm (s, 3H). **^{13}C NMR** (101 MHz, CDCl$_3$) δ 138.42, 137.71, 135.20, 130.54, 129.67, 128.84, 127.10, 122.85, 120.79, 119.71, 109.96, 100.21, 33.31 ppm. **FT-IR:** v = 2514, 2159, 2030, 1976 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{15}$H$_{13}$NClS = 274.04517; found 274.04539. Spectral data matched literature characterization.[170i]

13 Experimental Part for the Sustainable C–H Bond Amination of Phenols
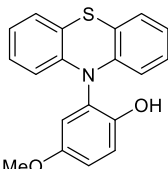
13.1 General procedure
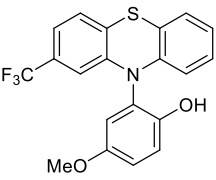
General procedure P: Amination of phenols
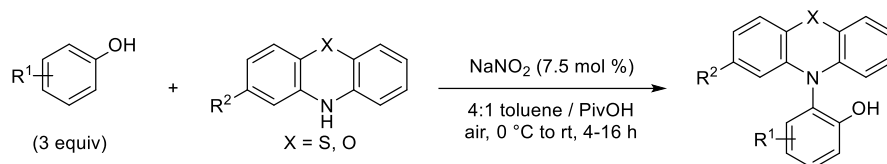
To a solution of phenothiazine (0.2 mmol, 1 equiv) and phenol (0.6 mmol, 3 equiv) in 4:1 toluene / pivalic acid (4 mL), $NaNO_2$ (7.5-20 mol %) was added at 0 °C under vigorous stirring. Stirring was continued at room temperature until full conversion of the starting material was monitored by TLC and uHPLC-MS analysis. The reaction was quenched with 1 M NaOH (20 mL) and extracted with DCM (3x50 mL). The combined organic layers were dried over $MgSO_4$ and concentrated on silica. The crude product was purified by silica gel flash chromatography (eluent: petroleum ether / DCM or petroleum ether / EtOAc).

13.2 Physical data of products

4-Methoxy-2-(10*H*-phenothiazin-10-yl)phenol (142a). Prepared according to general procedure P using phenothiazine (40.6 mg, 0.2 mmol, 1 equiv) and 4-methoxyphenol (76 mg, 0.6 mmol, 3 equiv); the product was obtained as a orange amorphous solid (51 mg, 0.16 mmol, 80%). **^{1}H NMR**(500 MHz, DMSO-*d6*) δ 9.47 (s, 1H), 7.07 (d, *J* = 8.9 Hz, 1H), 6.98 (dd, *J* = 7.6, 1.8 Hz, 3H), 6.93 – 6.87 (m, 2H), 6.82 – 6.77 (m, 3H), 6.09 (dd, *J* = 8.3, 1.2 Hz, 2H), 3.70 (s, 3H) ppm. **^{13}C NMR**(126 MHz, DMSO) δ 153.52, 149.30, 142.69, 127.28, 126.44, 126.19, 122.21, 118.27, 117.80, 116.21, 115.39, 115.37, 55.53 ppm. **FT-IR:** v = 3382, 2957, 1460, 1438, 1236 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$. $C_{19}H_{14}O_2NS$ = 320.07507; found 320.07423. Spectral data matched literature characterization.[190a]

4-Methoxy-2-(2-(trifluoromethyl)-10*H*-phenothiazin-10-yl)phenol (142b). Prepared according to general procedure P using 2-trifluoromethyl-phenothiazine (54.4mg, 0.2 mmol, 1 equiv) and 4-methoxyphenol (76 mg, 0.6 mmol, 3 equiv); the product was obtained as a yellow oil (66 mg, 0.17 mmol, 85%). **^{1}H NMR**(600 MHz, Methylene Chloride-*d2*) δ 7.17 – 7.10 (m, 3H), 7.06 – 7.01 (m, 2H), 6.97 – 6.89 (m, 3H), 6.56 (d, *J* = 1.7 Hz, 1H), 6.37 (dd, *J* =

8.0, 1.7 Hz, 1H), 5.58 (s, 1H), 3.79 ppm (s, 3H). **^{13}C NMR** δ 153.66, 149.07, 143.23, 141.94, 127.88 (d, J_{CF} = 31.7 Hz), 127.83, 127.02, 126.41, 125.59, 125.04, 124.21, 123.05, 122.88, 118.85 – 118.45 (m), 117.93, 117.42, 116.81, 115.82, 115.02, 110.80 ppm (d, J_{CF} = 4.1 Hz). **FT-IR:** v = 2959, 1500, 1409, 1324, 1215 cm^1. **HR-MS:** calc. for [M-H]$^-$ $C_{20}H_{13}O_2NF_3S$ = 388.06246; found 388.06121.
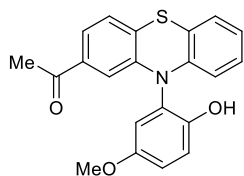
1-(10-(2-Hydroxy-5-methoxyphenyl)-10H-phenothiazin-2-yl)ethan-1-one (142c). Prepared according to general procedure P using 2-acetylphenothiazine (50.8mg, 0.2 mmol, 1 equiv) and 4-methoxyphenol (76 mg, 0.6 mmol, 3 equiv); the product was obtained as a white amorphous solid (62 mg, 0.17 mmol, 84%). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.52 (s, 1H), 7.42 (dd, J = 8.0, 1.8 Hz, 1H), 7.11 (dd, J = 9.8, 8.4 Hz, 2H), 7.05 – 6.96 (m, 2H), 6.91 (m, 1H), 6.85 – 6.77 (m, 2H), 6.59 (d, J = 1.8 Hz, 1H), 6.06 (dd, J = 8.3, 1.3 Hz, 1H), 3.70 (s, 3H), 2.36 ppm (s, 3H). **^{13}C NMR** (126 MHz, DMSO) δ 196.70, 153.55, 149.14, 142.64, 142.04, 135.82, 127.70, 126.22, 126.08, 125.98, 125.45, 123.19, 122.52, 117.92, 117.17, 116.42, 115.59, 115.21, 113.14, 55.54, 26.34 ppm. **FT-IR:** v = 3245, 1662, 1502, 1465, 1300, 1219 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ $C_{21}H_{16}O_3NS$ = 362.08454; found 362.08454.
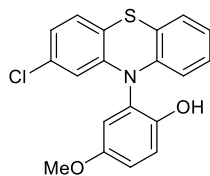
2-(2-Chloro-10H-phenothiazin-10-yl)-4-methoxyphenol (142d). Prepared according to general procedure P using 2-chlorophenothiazine (47 mg, 0.2 mmol, 1 equiv) and 4-methoxyphenol (76 mg, 0.6 mmol, 3 equiv); the product was obtained as a pale red oil (58 mg, 0.16 mmol, 81%). **^{1}H NMR** (500 MHz, Methylene Chloride-d_2) δ 7.13 (d, J = 9.0 Hz, 1H), 7.07 – 7.01 (m, 2H), 6.99 – 6.84 (m, 5H), 6.40 – 6.35 (m, 2H), 5.64 (s, 1H), 3.80 ppm (s, 3H). **^{13}C NMR** (126 MHz, CD$_2$Cl$_2$) δ 154.95, 147.69, 144.91, 143.00, 133.54, 128.03 (2C), 127.38, 126.24, 124.22, 123.54, 120.98, 119.98, 118.57, 117.38, 116.55, 116.30, 116.23, 56.40 ppm. **FT-IR:** v = 3216, 2927, 1568, 1500, 1235 cm^1. **HR-MS:** calc. for [M-H]$^-$ $C_{19}H_{13}O_2NClS$ = 354.03500; found 354.03505.

4-Methyl-2-(10H-phenothiazin-10-yl)phenol (142e). Prepared according to general procedure P using phenothiazine (40.6mg, 0.2 mmol, 1 equiv) and p-cresol (66 mg, 0.6 mmol, 3 equiv); the product was obtained as a white amorphous solid (30 mg, 0.08 mmol, 41%). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.70 (s, 1H), 7.17 (m, 1H), 7.04 – 7.01 (m, 2H), 6.98 (dd, J = 7.6, 1.6 Hz, 2H), 6.89 (m, 2H), 6.78 (m, 2H), 6.06 (dd, J = 8.2, 1.2 Hz, 2H), 2.25 ppm (s, 3H). **^{13}C NMR** (126 MHz, DMSO)

δ 153.22, 142.85, 131.31, 130.67, 130.02, 127.24, 126.17, 126.09, 122.14, 118.34, 117.02, 115.44, 19.90 ppm. **FT-IR:** v = 3374, 1462, 1441, 1342, 1225 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{19}$H$_{14}$ONS = 304.07906; found 304.07940.
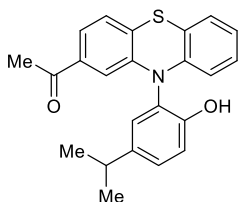
1-(10-(2-Hydroxy-5-isopropylphenyl)-10H-phenothiazin-2-yl)ethan-1-one (142f). Prepared according to general procedure P using 2-Acetylphenothiazine (50.8mg, 0.2 mmol, 1 equiv), 4-Isopropylphenol (83 mg, 0.6 mmol, 3 equiv); the product was obtained as a yellow oil (53 mg, 0.14 mmol, 69%). **^{1}H NMR** (500 MHz, Methylene Chloride-d_2) δ 7.41 (dd, J = 7.9, 1.8 Hz, 1H), 7.33 (dd, J = 8.4, 2.3 Hz, 1H), 7.26 (d, J = 2.3 Hz, 1H), 7.12 (dd, J = 16.5, 8.2 Hz, 2H), 7.04 (dd, J = 7.5, 1.7 Hz, 1H), 6.96 – 6.84 (m, 3H), 6.32 (dd, J = 8.1, 1.4 Hz, 1H), 6.03 (s, 1H), 3.04 – 2.89 (m, 1H), 2.32 (s, 3H), 1.29 ppm (d, J = 6.9 Hz, 6H). **^{13}C NMR** (126 MHz, CD$_2$Cl$_2$) δ 197.33, 151.70, 144.04, 143.51, 143.42, 136.75, 129.62, 129.23, 128.31, 128.24, 127.30, 127.09, 125.92, 123.97, 123.74, 120.30, 117.70, 116.58, 115.14, 33.91, 26.61, 24.51 ppm. **FT-IR:** v = 3267, 2958, 1662, 1464, 1403 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{23}$H$_{20}$O$_2$NS = 374.12093; found 374.12093.

2-(2-Chloro-10H-phenothiazin-10-yl)-4-isopropylphenol (142g). Prepared according to general procedure P using 2-chlorophenothiazine (47 mg, 0.2 mmol, 1 equiv) and 4-isopropylphenol (83 mg, 0.6 mmol, 3 equiv); the product was obtained as a pale red oil (52 mg, 0.14 mmol, 69%). **^{1}H NMR** (500 MHz, Methylene Chloride-d2) δ 7.32 (dd, J = 8.5, 2.2 Hz, 1H), 7.24 (d, J = 2.2 Hz, 1H), 7.12 (d, J = 8.4 Hz, 1H), 7.07 (dd, J = 7.3, 1.8 Hz, 1H), 6.99 (d, J = 8.1 Hz, 1H), 6.96 – 6.85 (m, 3H), 6.35 (dd, J = 8.0, 1.8 Hz, 2H), 5.77 (d, J = 1.2 Hz, 1H), 3.01 – 2.91 (m, 1H), 1.29 (d, J = 6.9 Hz, 6H) ppm. **^{13}C NMR** (126 MHz, CD$_2$Cl$_2$) δ 151.49, 145.31, 143.45, 143.41, 133.52, 129.65, 129.24, 128.06, 128.04, 127.41, 125.81, 124.18, 123.49, 121.31, 120.26, 117.65, 116.63, 116.46, 33.87, 24.46 ppm. **FT-IR:** v = 3396, 2958, 1503, 1458, 1393 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{21}$H$_{17}$ONClS = 366.07139; found 366.07143.
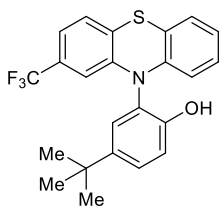
4-(*tert*-Butyl)-2-(2-(trifluoromethyl)-10H-phenothiazin-10-yl)phenol (142h). Prepared according to general procedure P using 2-trifluoromethyl-phenotiazine (54.4mg, 0.2 mmol, 1 equiv) and 4-*tert*-butylphenol (91 mg, 0.6 mmol, 3 equiv); the product was obtained as a yellow oil (64.4 mg, 0.16 mmol, 78%). **^{1}H NMR** (500 MHz, Methylene Chloride-d_2) δ 7.49 (dd, J = 8.6, 2.4 Hz, 1H), 7.39 (d, J = 2.4 Hz, 1H), 7.18 (dd, J = 7.9, 0.9 Hz, 1H), 7.15 – 7.11 (m, 2H), 7.08 (dd, J

= 7.1, 2.0 Hz, 1H), 6.98 – 6.91 (m, 2H), 6.56 (d, J = 1.8 Hz, 1H), 6.36 – 6.31 (m, 1H), 5.82 (s, 1H), 1.35 ppm (s, 9H). **^{13}C NMR** (126 MHz, Methylene Chloride-d_2) δ 151.14, 145.97, 144.73, 143.42, 130.28 – 129.37 (m), 128.93, 128.33, 128.18, 127.66, 127.47, 126.57, 125.27, 124.46 (d, J_{CF} = 272.0 Hz), 124.36, 120.58, 120.25 (q, J_{CF} = 3.8 Hz), 117.45, 116.66, 112.60 (q, J_{CF} = 4.0 Hz), 34.82, 31.70 ppm. **FT-IR:** v = 2960, 1506, 1441, 1326 cm^{-1}. **HR-MS:** calc. for [M+H]$^+$ C$_{23}$H$_{21}$ONF$_3$S = 416.12905; found 416.12774. Spectral data matched literature characterization.[190a]
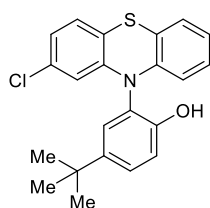
4-(*tert*-Butyl)-2-(2-chloro-10*H*-phenothiazin-10-yl) (142i). Prepared according to general procedure P using 2-chlorophenothiazine (47 mg, 0.2 mmol, 1 equiv) and 4-*tert*-butylphenol (91 mg, 0.6 mmol, 3 equiv); the product was obtained as a pale red solid (59 mg, 0.15 mmol, 76%). **^{1}H NMR** (500 MHz, Methylene Chloride-d_2) δ 7.48 (dd, J = 8.6, 2.4 Hz, 1H), 7.38 (d, J = 2.4 Hz, 1H), 7.13 (d, J = 8.6 Hz, 1H), 7.07 (dd, J = 7.3, 1.9 Hz, 1H), 7.00 (d, J = 8.2 Hz, 1H), 6.97 – 6.85 (m, 3H), 6.35 – 6.32 (m, 2H), 5.78 (s, 1H), 1.36 ppm (s, 9H). **^{13}C NMR** (126 MHz, CD$_2$Cl$_2$) δ 151.19, 145.89, 145.35, 143.44, 133.54, 129.52, 128.82, 128.16, 128.06, 127.42, 125.51, 124.16, 123.46, 121.24, 120.17, 117.33, 116.58, 116.44, 34.82, 31.76 ppm. **FT-IR:** v = 2959, 1566, 1504, 1458, 1393, 1041 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{22}$H$_{19}$ONClS = 380.08704; found 380.08693.

3-(2-(Trifluoromethyl)-10*H*-phenothiazin-10-yl)- [1,1'-biphenyl]-4-ol (142j). Prepared according to general procedure P using 2-trifluoromethyl-phenothiazine (54.4mg, 0.2 mmol, 1 equiv) and 4-phenylphenol (105 mg, 0.6 mm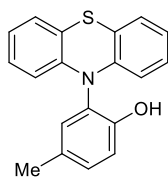ol, 3 equiv); the product was obtained as a yellow oil (61 mg, 0.14 mmol, 69%). **^{1}H NMR** (500 MHz, Methylene Chloride-d_2) δ 7.74 (dd, J = 8.5, 2.3 Hz, 1H), 7.68 (d, J = 2.3 Hz, 1H), 7.64 – 7.60 (m, 2H), 7.46 (dd, J = 8.4, 7.1 Hz, 2H), 7.36 (d, J = 7.3 Hz, 1H), 7.30 (d, J = 8.5 Hz, 1H), 7.20 (d, J = 8.3 Hz, 1H), 7.18 – 7.13 (m, 1H), 7.12 – 7.08 (m, 1H), 6.95 (td, J = 6.9, 1.8 Hz, 2H), 6.66 (d, J = 1.7 Hz, 1H), 6.49 – 6.41 (m, 1H), 6.09 ppm (s, 1H). **^{13}C NMR** (126 MHz, Methylene Chloride-d_2) δ 153.23, 144.45, 143.18, 140.14, 135.98, 130.52, 130.04, 129.96, 129.79, 128.35, 127.83, 127.76, 127.53, 127.17, 126.79, 125.52, 124.52, 120.67, 120.47 (q, J_{CF} = 3.9 Hz), 118.50, 116.79, 112.56 (q, J_{CF} = 4.0 Hz), 27.48 ppm. **FT-IR:** v = 3062, 1468, 1326 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{25}$H$_{15}$ONF$_3$S = 434.08210; found 434.08167
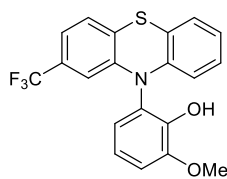
2-Methoxy-6-   (2-(trifluoromethyl)-10*H*-phenothiazin-10-yl)phenol (142k). Prepared according to general procedure P using 2-trifluoromethyl-phenothiazine (54.4mg, 0.2 mmol, 1 equiv), 2-methoxyphenol (76 mg, 0.60 mmol, 3 equiv) and sodium nitrite (2.8 mg, 0.04 mmol, 20 mol %); the product was obtained as a white solid (50 mg, 0.13 mmol, 64%). **^{1}H NMR** 500 MHz, DMSO-d_6) δ 9.57 (s, 1H), 7.22 (d, J = 8.3 Hz, 1H), 7.14 – 7.10 (m, 1H), 7.06 – 7.02 (m, 2H), 6.99 (d, J = 2.4 Hz, 1H), 6.96 – 6.91 (m, 1H), 6.86 (m, 2H), 6.31 (d, J = 1.8 Hz, 1H), 6.19 (dd, J = 8.3, 1.2 Hz, 1H), 3.77 ppm (s, 3H). **^{13}C NMR** (126 MHz, DMSO-d_6) δ 149.73, 146.97, 144.60, 143.12, 130.17, 127.78, 127.71 (d, J_{CF} = 31.8 Hz).127.15, 126.51, 124.95, 124.08, 123.11, 122.78, 118.72 (d, J_{CF} = 4.2 Hz), 117.28, 117.00, 115.99, 113.71, 110.76 (d, J_{CF} = 4.0 Hz), 55.94 ppm. **FT-IR:** v = 2963, 1509, 1441, 1328 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ $C_{20}H_{13}O_2NF_3S$ = 388.06136; found 388.06133.
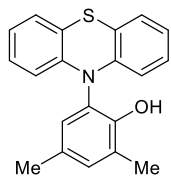
2,4-Dimethyl-6- (10*H*-phenothiazin-10-yl)phenol (142l). Prepared according to general procedure P using phenothiazine (40.6mg, 0.2 mmol, 1 equiv) and 2,4-dimethylphenol (75 mg, 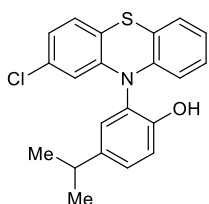0.6 mmol, 3 equiv); the product was obtained as a pale red amorphous solid (40 mg, 0.13 mmol, 63%). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 8.84 (s, 1H), 7.07 (d, J = 2.2 Hz, 1H), 6.94 (dd, J = 7.6, 1.6 Hz, 2H), 6.89 – 6.82 (m, 3H), 6.76 (m, 2H), 6.01 (dd, J = 8.2, 1.2 Hz, 2H), 2.25 (s, 3H), 2.21 ppm (s, 3H). **^{13}C NMR** (126 MHz, DMSO) δ 151.25, 142.68, 132.02, 129.82, 128.31, 127.20, 126.65, 126.50, 126.01, 122.02, 118.37, 115.47, 19.92, 16.60 ppm. **FT-IR:** v = 2918, 1461, 1441, 1310 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ $C_{20}H_{16}ONS$ = 318.09581; found 318.09477.
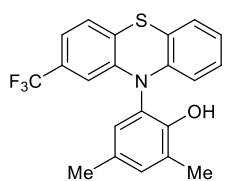
2,4-Dimethyl-6-   (2-(trifluoromethyl)-10H-phenothiazin-10-yl)phenol (142m). Prepared according to general procedure P using 2-trifluoromethyl-phenothiazine (54.4mg, 0.2 mmol, 1 equiv) and 2,4-dimethylphenol (75 mg, 0.6 mmol, 3 equiv); the product was obtained as a yellow oil (35 mg, 0.09 mmol, 45%). **^{1}H NMR** (500 MHz, Methylene Chloride-d_2) δ 7.20 – 7.10 (m, 3H), 7.10 – 7.00 (m, 2H), 6.98 – 6.89 (m, 2H), 6.60 (d, J = 1.8 Hz, 1H), 6.46 – 6.35 (m, 1H), 5.78 (s, 1H), 2.35 (s, 3H), 2.30 ppm (s, 3H). **^{13}C NMR** (126 MHz, Methylene Chloride-d_2) δ 149.48, 144.68, 143.39, 133.11, 131.19, 129.79 (q, J_{CF} = 32.4 Hz), 129.10, 128.22, 127.61, 127.40, 127.16, 127.07 – 126.78 (m), 125.14, 124.47 (d, J_{CF} = 272.0 Hz).124.40, 120.85, 120.32 (q, J_{CF} = 3.9 Hz), 116.92, 112.70 (q, J_{CF} = 4.0 Hz), 20.88, 16.39 ppm. **FT-IR:** v = 2923, 1467, 1441, 1409, 1322 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ $C_{21}H_{15}ONF_3S$ = 386.08319; found 386.08202.
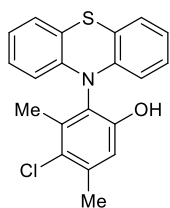
**4-Chloro-3,5-dimethyl-2-(10*H*-phenothiazin-10-yl)phenol (142n).** Prepared according to general procedure P using phenothiazine (40.6mg, 0.2 mmol, 1 equiv) and 4-chloro-3,4-dimethylphenol (96 mg, 0.6 mmol, 3 equiv); the product was obtained as a pale red solid (56 mg, 0.16 mmol, 79%). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 10.02 (s, 1H), 7.00 – 6.94 (m, 3H), 6.88 (m, 2H), 6.79 (m, 2H), 6.00 (dd, *J* = 8.2, 1.2 Hz, 2H), 2.36 (s, 3H), 2.20 ppm (s, 3H). **^{13}C NMR** (126 MHz, DMSO) δ 154.26, 141.55, 137.19, 136.09, 127.47, 126.29, 124.45, 124.37, 122.44, 118.41, 116.43, 114.89, 20.67, 15.31 ppm. **FT-IR:** *v* = 3218, 2959, 1464, 1306 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ $C_{20}H_{15}ONClS$ = 352.05574; found 352.05581.
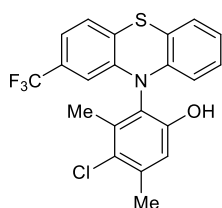
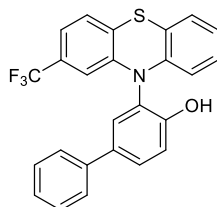**4-Chloro-3,5dimethyl-2-(2-(trifluoromethyl)-10*H*phenothiazin-10-yl)phenol (142o).** Prepared according to general procedure P using 2-trifluoromethyl-phenothiazine (54.5 mg, 0.2 mmol, 1 equiv) and 4-chloro-3,4-dimethylphenol (96 mg, 0.6 mmol, 3 equiv); the product was obtained as a pale red solid (62.4 mg, 0.15 mmol, 74%). **^{1}H NMR** (500 MHz, Methylene Chloride-d_2) δ 7.04 – 6.98 (m, 2H), 6.94 – 6.89 (m, 1H), 6.87 (t, *J* = 0.8 Hz, 1H), 6.85 – 6.77 (m, 2H), 6.22 (dd, *J* = 1.5, 0.8 Hz, 1H), 6.08 – 6.02 (m, 1H), 5.77 (s, 1H), 2.35 (d, *J* = 0.8 Hz, 3H), 2.15 – 2.10 ppm (m, 3H). **^{13}C NMR** (126 MHz, Methylene Chloride-d_2) δ 151.52, 142.34, 140.97, 139.18, 137.15, 129.55 (q, *J* = 32.5 Hz), 128.57 (d, *J* = 102.1 Hz), 127.97, 127.24, 127.10, 126.88, 125.47, 124.04, 123.20 123.82 (d, *J* = 272.0 Hz), 119.96 (q, *J* = 4.0 Hz), 116.36, 115.47, 111.23 (q, *J* = 4.0 Hz), 20.90, 16.24 ppm. **FT-IR:** *v* = 3276, 2927, 1499, 1471, 1489 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ $C_{21}H_{14}ONClF_3S$ = 420.04312; found 420.04274.
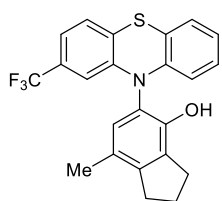
7-Methyl-5-(2-(trifluoromethyl)-10*H*-phenothiazin-10-yl)-2,3-dihydro-1*H*-inden-4-ol (142p). Prepared according to general procedure P using 2-trifluoromethyl-phenothiazine (54.4 mg, 0.2 mmol, 1 equiv) and 7-methyl-4-indanol (90 mg, 0.6 mmol, 3 equiv); the product was obtained as a yellow oil (56 mg, 0.13 mmol, 67%). **^{1}H NMR** (500 MHz, Methylene Chloride-d_2) δ 7.19 – 7.02 (m, 3H), 7.00 – 6.87 (m, 3H), 6.63 (d, *J* = 1.8 Hz, 1H), 6.40 (dd, *J* = 8.1, 1.5 Hz, 1H), 5.62 (s, 1H), 2.96 (q, *J* = 7.9 Hz, 4H), 2.28 (s, 3H), 2.19 ppm (p, *J* = 7.6 Hz, 2H). **^{13}C NMR** (126 MHz, Methylene Chloride-d_2) δ 147.67, 147.15, 144.94, 143.65, 132.02, 130.21 – 129.23 (m), 129.86, 128.17, 127.64, 127.53, 127.31, 126.84 – 126.66 (m), 125.62, 124.20, 123.51, 120.65, 120.11 (q, *J* = 4.0 Hz), 116.93, 112.69 (q, *J_{CF}* = 4.0 Hz), 32.56, 30.28, 25.36, 18.86 ppm. **FT-IR:** *v* = 2929, 1468, 1440, 1323 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ $C_{23}H_{17}ONF_3S$ = 412.09775; found 412.09759.
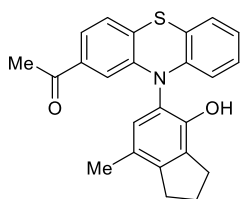
1-(10-(4-Hydroxy-7-methyl-2,3-dihydro-1*H*-inden-5-yl)-10H-phenothiazin-2-yl)ethan-1-one (142q). Prepared according to general procedure P using 2-acetylphenothiazine (50.8mg, 0.2 mmol, 1 equiv) and 7-methyl-4-indanol (90 mg, 0.6 mmol, 3 equiv); the product was obtained as a yellow amorphous solid (58 mg, 0.15 mmol, 74%). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.02 (s, 1H), 7.40 (dd, J = 7.9, 1.7 Hz, 1H), 7.08 (d, J = 7.9 Hz, 1H), 6.99 – 6.73 (m, 4H), 6.59 (d, J = 1.7 Hz, 1H), 6.02 (dd, J = 8.4, 1.3 Hz, 1H), 2.90 (m, 4H), 2.36 (s, 3H), 2.13 ppm (m, 5H). **^{13}C NMR** (126 MHz, DMSO) δ 196.87, 149.20, 145.41, 143.12, 142.45, 135.78, 131.49, 128.92, 127.64, 126.09, 125.98, 125.96, 125.64, 124.29, 123.14, 122.30, 117.29, 115.82, 113.14, 31.51, 30.06, 26.44, 24.35, 18.04 ppm. **FT-IR:** v = 2958, 1663, 1439, 1403, 1294, 1044 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{24}$H$_{20}$O$_2$NS = 386.12093; found 386.12088.
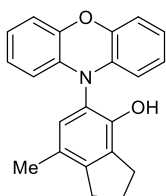
7-methyl-5-(10*H*-phenoxazin-10-yl)-2,3-dihydro-1H-inden-4-ol **(142r).** Prepared according to general procedure P using phenoxazine (37 mg, 0.2 mmol, 1 equiv) and 7-methyl-4-indanol (91 mg, 0.6 mmol, 1 equiv); the product was obtained as a white amorphous solid (42 mg, 0.13 mmol, 63%). **^{1}H NMR** (500 MHz, Methylene Chloride-d_2) δ 6.84 (d, J = 1.0 Hz, 1H), 6.73 – 6.63 (m, 6H), 6.04 (dd, J = 7.8, 1.4 Hz, 2H), 5.57 (s, 1H), 2.96 (t, J = 7.5 Hz, 2H), 2.91 (t, J = 7.5 Hz, 2H), 2.24 – 2.14 ppm (m, 5H). **^{13}C NMR** (126 MHz, CD$_2$Cl$_2$) δ 148.84, 146.73, 144.79, 134.10, 131.33, 129.51, 128.60, 128.06, 125.77, 124.07, 122.86, 122.48, 115.95, 114.35, 32.49, 30.22, 25.46, 18.75 ppm. **FT-IR:** v = 2961, 1483, 1463, 1334 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{22}$H$_{18}$O$_2$N = 328.13321; found 328.13331.
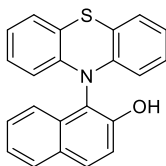
1-(10*H*-Phenothiazin-10-yl)naphthalen-2-ol (142s). Prepared according to general procedure P using phenothiazine (40.6mg, 0.2 mmol, 1 equiv) and 2-naphtol (87.3 mg, 0.6 mmol, 3 equiv); the product was obtained as a white amorphous solid (50 mg, 0.15 mmol, 73%). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.34 (s, 1H), 8.01 – 7.91 (m, 3H), 7.47 – 7.42 (m, 2H), 7.34 (m, 1H), 7.05 – 7.00 (m, 2H), 6.82 – 6.75 (m, 4H), 6.04 – 5.97 (m, 2H) ppm. **^{13}C NMR** (101 MHz, DMSO) δ 153.86, 142.16, 131.64, 130.31, 129.18, 128.46, 127.61, 127.37, 126.27, 123.53, 122.37, 120.96, 119.00, 118.90, 117.90, 115.33 ppm. **FT-IR:** v = 3057, 2962, 1597, 1573, 1487 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{22}$H$_{14}$ONS = 340.07906; found 340.07912.
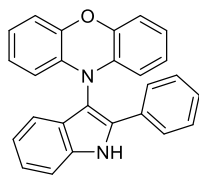
10-(2-phenyl-1H-indol-3-yl)-10H-phenoxazine (142t). Prepared according to general procedure P using phenothiazine (40.6mg, 0.2 mmol, 1 equiv) and 2-phenylindole (116 mg, 0.6 mmol, 3 equiv) and NOBF$_4$ (2.4 mg, 10 mol %); the product was obtained as a pale greenish solid (46 mg, 0.12 mmol, 61%). **^{1}H NMR** (500 MHz, Acetone-d_6) δ 11.08 (s, 1H), 7.95 – 7.86 (m, 2H), 7.58 (d, J = 8.2 Hz, 1H), 7.47 – 7.40 (m, 2H), 7.37 (d, J = 7.9 Hz, 1H), 7.33 (d, J = 7.4 Hz, 1H), 7.24 (m, 1H), 7.09 – 7.02 (m, 1H), 6.74 (dd, J = 7.9, 1.4 Hz, 2H), 6.65 (m, 2H), 6.57 (td, J = 7.7, 1.5 Hz, 2H), 6.07 ppm (dd, J = 8.0, 1.5 Hz, 2H). **^{13}C NMR** (126 MHz, Acetone) δ 145.13, 136.95, 136.04, 134.54, 131.73, 129.89, 129.14, 127.11, 125.65, 124.57, 123.86, 122.33, 121.11, 118.88, 116.18, 114.47, 112.98, 110.85 ppm. **FT-IR:** 3388, 2962, 2516, 2159, 2030, 1976 cm^{-1}. **HR-MS:** calc. for [M-H]$^-$ C$_{26}$H$_{17}$ON$_2$ = 373.13464; found 373.13223.
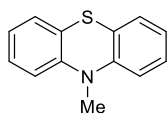
10-Methyl-10H-phenothiazine (140v). To a solution of phenothiazine (203 mg, 1 mmol, 1 equiv) in DMF (5 mL) was added NaH (60% dispersion in mineral oil, 48 mg, 1.2 mmol, 1.2 equiv) at 0 °C. After full addition, the reaction was stirred for 30 min at room temperature and subsequently cooled to 0 °C. Iodomethane (96 µL, 1.5 mmol, 1.5 equiv) was added dropwise and stirring was continued for 2 h. Afterwards, the reaction was poured into cold water (50 mL) and extracted three times with EtOAc (3x15 mL). The combined organic layers were dried over MgSO$_4$ and concentrated under reduced pressure. Silica gel column chromatography proved the pure product (eluent: petroleum ether / ethyl acetate). The compound was obtained as pale yellow oil (170 mg, 0.8 mmol, 80%). **^{1}H NMR** (500 MHz, Methylene Chloride-d_2) δ 7.18 (m, 2H), 7.13 (dd, J = 7.6, 1.5 Hz, 2H), 6.93 (m, 2H), 6.84 (dd, J = 8.2, 1.2 Hz, 2H), 3.36 ppm (s, 3H). **^{13}C NMR** (126 MHz, CD$_2$Cl$_2$) δ 146.39, 127.98, 127.48, 123.75, 122.90, 114.67, 35.73 ppm.

Experimental Part for the Sustainable C–H Bond Amination of Phenols |

Appendix

14 List of Abbreviations

Ac	acetyl
Ad	adamantyl
aq.	aqueous
Ar	argon
BDD	boron doped diamond
BDE	bond dissociation energy
BHT	butylated hydroxytoluene
Bu	butyl
calc.	calculated
CDC	cross-dehydrogenative coupling
COMAS	Compound Management and Screening Center
conc.	concentration
DCE	1,2-dichloroethane
DCM	dichloromethane
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
DFT	density-functional-theory
DMAP	4-dimethylaminopyridine
DME	dimethoxyethane
DMSO	dimethyl sulfoxide
DTBP	2,6-di-*tert*-butylpyridine
d.r.	diastereomeric ratio
EA	elemental analysis
EDG	electron-donating group
EI	electron ionization
ESI	electrospray ionization
Et	ethyl
et al.	*et alii* (and others)
equiv	equivalent

Fe(PDP)	(2S,2′S-(−)-[N,N′-Bis(2-pyridylmethyl)]-2,2′-bipyrrolidinebis(acetonitrile)iron(II) hexafluoroantimonate
FT-IR	Fourier-transform infrared spectroscopy
GC	gas chromatography
HH	Hedgehog
HFIP	1,1,1,3,3,3-hexafluoro-2-propanol
HOMO	highest occupied molecular orbital
HPLC	high performance liquid chromatography
HR-MS	high resolution mass spectrometry
^{i}Pr	isopropyl
IC_{50}	half maximal inhibitory concentration
KIE	kinetic isotope effect
LC-MS	liquid chromatography-mass spectrometry
m-	meta
$[M]^+$	molecular ion peak
Me	methyl
*m*CPBA	*meta*-chloroperoxybenzoic acid
mp	melting point
MTES	Methyltriethylammonium methylsulfate
MW	molecular weight
m/z	mass-to-charge ratio
n.d.	not detected
NMP	*N*-methylpyrrolidinone
NMR	nuclear magnetic resonance
Nu	nucleophile
o-	ortho
OTf	Triflate
p-	para
Ph	phenyl
PIDA	iodosobenzene diacetate

PIFA	iodosobenzene bis(trifluoroacetate)
Piv	pivaloyl
PPHF	hydrogen fluoride pyridine
*p*TsOH	*p*-toluenesulfonic acid
Pr	propyl
Py	pyridine / pyridyl
rt	room temperature
r.r.	regioisomeric ratio
Salen	Bis(salicyliden)ethylendiamin
SAR	structure activity relationship
SCE	saturated calomel electrode
SET	single electron transfer
S_EAr	electrophilic aromatic substitution
TBAI	tetrabutylammonium iodide
TBN	*tert*-butyl nitrite
TBS	*tert*-butyldimethylsilyl
TEMPO	2,2,6,6-tetramethylpiperidin-1-yloxy
TFA	trifluoroacetic acid
THF	tetrahydrofuran
THP	tetrahydropyranyl
TLC	thin layer chromatography
v/v	volume/volume percentage
$[\alpha]$	specific rotation

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8. Luis Bering and Andrey P. Antonchick, "Oxidative Heteroatom-Heteroatom Bond Formation", *Patai's Chemistry of Functional Groups*, edited by Ilan Marek, Berit Olofsson, Zvi Rappoport. John Wiley & Sons, Ltd: Chichester, UK, **2018**. DOI: 10.1002/9780470682531.pat0946 (invited book chapter).

7. Luis Bering and Oliver Koch, "Mycobacterium-Tuberculosis-Thioredoxin-Reductase Inhibitors as Anti-Tuberculotics", *Patent filed*, PCT/EP2018/066768, 22.06.**2018**.

6. <u>Luis Bering</u>, Melina Vogt, Felix M. Paulussen and Andrey P. Antonchick, "Selective, Catalytic and Metal-Free Coupling of Electron-Rich Phenols and Anilides Using Molecular Oxygen as Terminal Oxidant", *Org. Lett.* **2018**, *20*, 4077–4080.

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1. <u>Luis Bering</u> and Andrey P. Antonchick, "Regioselective Metal-Free Cross-Coupling of Quinoline *N*-Oxides with Boronic Acids", *Org. Lett.* **2015**, *17*, 3134–3137.

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