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Enantioselective Synthesis of Phosphine Boranes via Crystallization-Induced Dynamic Resolution of Lithiated Intermediate by Understanding the Underlying Epimerization Process

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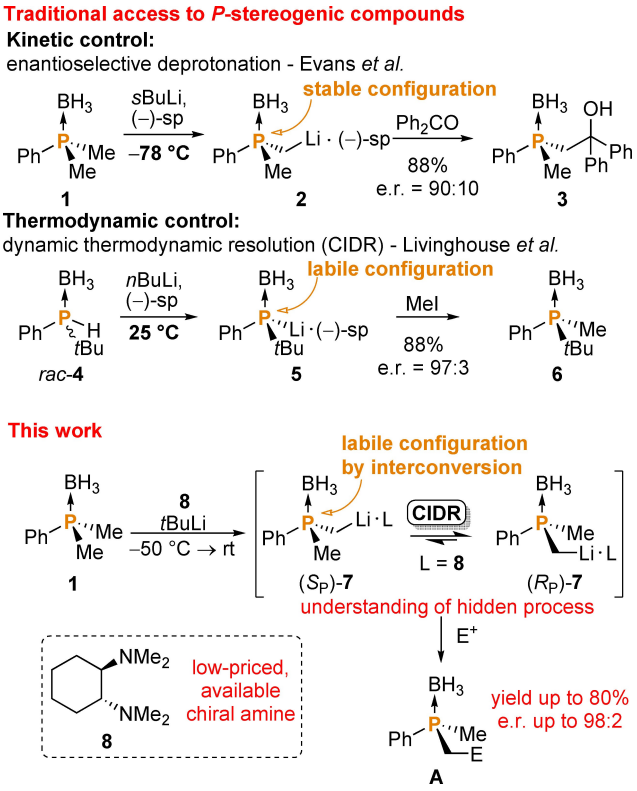
Abstract: Described herein is the successful crystallization-induced dynamic resolution (CIDR) of an α-lithiated phosphine borane utilizing the easily accessible and inexpensive ligand (*R*,*R*)-TMCDA. Starting from the essential *P*-prochiral building block dimethyl phenyl phosphine borane we were able to obtain phosphine boranes in yields up to 80% and e.r. up to 98:2 by crystallization of the lithiated intermediate prior to the trapping reaction. NMR-based deuterium labeling experiments indicate that the epimerization in solution is based on the intermolecular proton transfer between nonlithiated phosphine borane and the corresponding lithiated intermediate, rendering the presence of the remaining starting compound in an optimized solvent mixture the main factor for successful enantioselective synthesis. Quantum chemical calculations using different model systems based on solid state structures confirm these experimental results. By gaining insights into the epimerization mechanism, essential principles for CIDR of lithiated phosphine boranes are elucidated that may be expanded to other important *P*-stereogenic compounds and simple chiral amines.



Scheme 1. Literature known (−)-sparteine [(−)-sp] mediated synthesis of *P*-stereogenic phosphines and our approach.

***P*-stereogenic compounds have seen widespread applications in various fields but particularly play an essential role as ligands for asymmetric metal catalysis.[1] Their asymmetric synthesis itself is thereby crucial and relies in most cases on various resolution techniques, mostly in combination with chiral auxiliaries.[1] Two of the most commonly used protocols for the synthesis of *P*-stereogenic phosphines utilize (−)-sparteine [(−)-sp] as chiral ligand (Scheme 1).[2] Since Evans's initial approach in 1995 to deprotonate prochiral dimethyl phenyl phosphine borane (**1**) with *s*-BuLi in the presence of (−)-sp at −78 °C, this method of kinetically controlled asymmetric lithiation-trapping at low temperatures plays an important role in asymmetric synthesis of *P*-stereogenic compounds. Livinghouse et al. described the dynamic thermodynamic resolution of the secondary phosphide borane **5** obtained after deprotonation of racemic *tert*-butylphenyl phosphine borane **4** with *n*-BuLi in presence of (−)-sp at 25 °C.[3] It was found that increased temperatures, elongated reaction times, and the formation of a suspension during the reaction were crucial for successful enantioenrichment.[4] For these kinds of resolution techniques, one of the formed enantiomers must be preferred either kinetically, thermodynamically, or by other means and provide appropriate configurational stability.[5] In the special case of the preferred crystallization of one intermediate, one can consider this process as crystallization-induced dynamic resolution (CIDR).[6,7]

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Even though the above mentioned approaches result in highly enriched products and good yields, the purification of stereoisomers can be challenging.[8] Also, for chelating diastereomeric phosphorus ligands (e.g. MiniPHOS), higher *ee* ratios in the preliminary compounds may be necessary, so that the enhancement of stereoselectivity remains an important goal, especially in simple, easy to functionalize pro-*P*-stereogenic building blocks like **1** and **4**.

Moreover, (−)-sp has experienced a very variable global supply shortage during the last decades and still exhibits scarce commercial availability and high cost.[9] Therefore, the use of a more easily accessible and cheaper ligand in these types of reactions is a clear advantage.

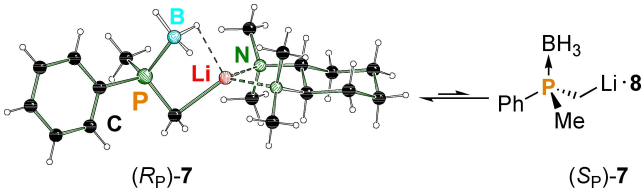
Here we present our results for the successful asymmetric lithiation-trapping of the important *P*-prochiral building block dimethyl phosphine borane (**1**) via the CIDR of its *α*-lithiated derivative **7** utilizing the easily accessible and cheap ligand (*R*,*R*)-TMCDA (**8**) (Scheme 1).[10] Additional quantum chemical studies, deuterium labeling experiments and X-ray structural analysis give insights into the underlying epimerization mechanism. These insights prove our method to be an interesting opportunity for enantioselective synthesis of further phosphine boranes with various chiral auxiliaries.

To start, the utilization of (*R*,*R*)-TMCDA for the synthesis of *P*-stereogenic compounds was tested following Evans' approach of asymmetric lithiation of **1** by using different alkyl lithium reagents in presence of **8** and subsequent trapping with benzophenone (Table 1, entry 1–3). The results indicate that the degree of asymmetric induction afforded by **8** is low. Lowering the temperature, as expected for a kinetically controlled process, enhances the selectivity slightly (Table 1, entry 4). Density functional theory (DFT) calculations of the diastereomeric transition states (TS) for the deprotonation of **1** show no energetic preference, which reflects the experimental findings (for details, see the Supporting Information).[11] In conclusion, **8** did not lead to a sufficient kinetical preference in enantioselective deprotonation.

During the X-ray structural studies of several single crystals of the intermediate *α*-lithiated phosphine borane, we observed only the diastereomer (R_P)-**7** in the solid state (Scheme 2). Based on this, it seems that **8** does favor the predominant crystallization of one lithiated diastereomeric intermediate **7**, which paves the way for CIDR techniques.

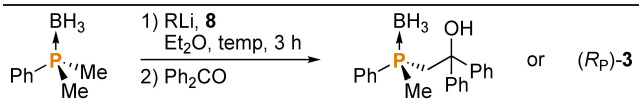
With these assumption in hand, further stereochemical studies were carried out. Subsequently, two different trapping experiments by reaction with benzophenone were conducted after cooling the reaction mixture to −80 °C: once before and once after separation of the crystals and the mother liquor. The first experiment provided (R_P)-**3** and (S_P)-**3** in a high e.r. of 84:16, already indicating an enrichment by crystallization (Table 2, entry 1). By trapping the isolated crystals, highly enriched (R_P)-**3** with e.r. = 98:2 and 60 % yield was obtained (Table 2, entry 2). Trapping the mother liquor resulted in an e.r. of 56:44 (Table 2, entry 3), displaying an epimerization process of (S_P)-**7** in solution reproducing (R_P)-**7** that is crystallizing continuously. The trapping reaction of the isolated crystals was repeated multiple times to determine the stereoselectivity using different trapping electrophiles. High enantioselectivity with e.r. from 96:4 to 98:2 and up to 80 % yield was achieved (Table 2, entries 4–5).

While the isolated crystals provided very good enantiomeric ratios, little to no stereoenrichment could be observed in the mother liquor (Table 2, entry 3). To verify this observation, we investigated the deprotonation of **1** at higher temperatures and in the presence of an excess respectively deficient amount of **1**, experimentally (Table 3) and theoretically. Quantum chemical calculations showed no thermodynamic preference for the computed energy difference of the intermediates (S_P)-**7** and (R_P)-**7**, so that no distinct stereoselectivity was predicted for the deprotonation of **1** at higher temperatures (for details, see the Supporting Information).



Scheme 2. Crystal structure of (R_P)-**7** and interconversion of the lithiated intermediates (S_P)-**7** and (R_P)-**7**.

Table 1: Kinetically controlled lithiation-trapping of phosphine borane **1**.



entry	RLi	equiv. RLi	T [°C]	e.r. (R:S)[a]
1	*t*-BuLi	1.1	−80 °C	38:62
2	*s*-BuLi	1.1	−80 °C	33:67
3	*n*-BuLi	1.1	−80 °C	30:70
4	*n*-BuLi	1.1	−100 °C	25:75

The absolute configuration of **3** was determined by X-ray diffraction combined with CSP-HPLC (for details, see the Supporting Information). [a] Determined by CSP-HPLC.

Table 2: Trapping experiments after lithiation of phosphine borane **1** and subsequent crystallization of **7** according to Scheme 1 (cr. = isolated crystals; ml. = separated mother liquor).

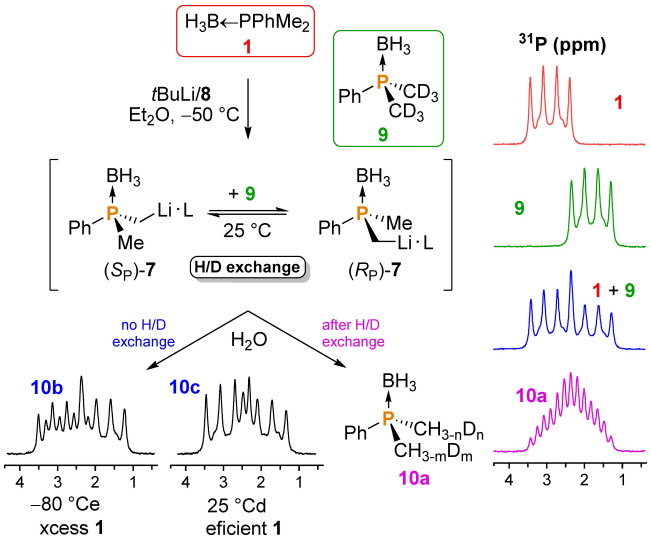
entry	E	experiment	product	yield [%][a]	e.r. (R:S)[c]
1	Ph_2CO	cr. and ml.	**3**	95[b]	84:16
2	Ph_2CO	cr.	**3**	60	98:2
3	Ph_2CO	ml.	**3**	16[b]	56:44
4	*n*-Bu_3SnCl	cr.	**14**	43[b]	2:98[d]
5	PhSSPh	cr.	**15**	80	4:96[d]

[a] Isolated yield. [b] Determined by NMR. [c] Determined by CSP-HPLC. [d] Configuration inverts due to a Cahn-Ingold-Prelog priority change.

Table 3: Lithiation-trapping of phosphine borane **1** at elevated temperatures.

entry	RLi	equiv. RLi	T [°C]	e.r. (R:S)[a]
1	*n*-BuLi	0.4	0 °C	55:45
2	*n*-BuLi	1.6	0 °C	39:61
3	*n*-BuLi	0.4	25 °C	55:45
4	*n*-BuLi	1.6	25 °C	41:59

The absolute configuration of product **3** was determined by X-ray diffraction combined with CSP-HPLC (for details, see the SI). [a] Determined by CSP-HPLC.



Scheme 3. Deuterium labeling experiments for the intermolecular proton transfer between lithiated intermediate **7** and nonlithiated deuterated **9**.

As expected from the trapped mother liquor reaction, we observed little to no stereoselectivity, but lithiated **1** did show inverted selectivity—although marginal as expected regarding the DFT calculations—in dependency of excess/deficient nonlithiated **1** (Table 3, entry 1–4). The epimerization process seemed to be dependent on excess non-lithiated species **1**. An analogous behavior for dimethyl phosphine sulfides was reported by O'Brien et al. and our group.[12] These lithiated sulfide species have proven to be configurationally unstable and show a selectivity change at temperatures above −20 °C. This only occurred in the presence of remaining starting material, indicating a non-selective proton transfer between the latter species and the lithiated intermediate as one of the plausible reaction steps suggested for this process.[12] However, in similar initial studies phosphine boranes like *t*-butyl-dimethylphosphine borane turned out to be configurationally stable and thus seemed to behave differently from the sulfides.[13]

To further review this assumption, we performed deuterium labeling experiments to probe the nonselective proton transfer between the lithiated intermediate **7** and non-lithiated substrate **1**. Deuterated dimethyl phenyl phosphine borane (**9**) was added to a solution of lithiated intermediate **7** in diethyl ether and stirred at room temperature for several hours. The course of the reaction was followed by ^{31}P NMR and mass spectrometry (EI-MS) analysis. Scheme 3 (top) shows the related reaction scheme and essential spectra before and after completion of the reaction. An initially nearly equimolar mixture of **1** and **9** results in a distribution of different partially deuterated dimethyl phosphine boranes (**10a**) after the reaction, clearly indicating a H/D exchange between these species. Subsequently, the same procedure was repeated multiple times while omitting the amine ligand at −80 °C and using a deficient amount of **1**. An analogous intermolecular H/D exchange occurs in thf, diethyl ether, toluene (in the presence of amine ligand), but neither at −80 °C (**10b**) nor without the presence of excess reactant (**10c**) (Scheme 3, bottom; for experimental details and further spectra see the Supporting Information).

To further strengthen these results, DFT calculations of the intermolecular deprotonation were performed. Suitable model systems for the calculations were derived from X-ray structural analysis of several adducts of lithiated dimethylphenyl phosphine borane (**1**). We observed three different types of aggregates: with TMEDA a polymeric species (**11**), in diethyl ether (**12**) or mtbe (**13**) a dimeric species and with the sterically demanding **8** the monomeric species (R_P)-**7** is formed (Scheme 2, for details, see Supporting Information).

In all molecular structures the lithium center is coordinated by borane hydrides in both an intra- and intermolecular fashion, which is typical for this class of compounds.[14] Based on this information, it is reasonable to assume the formation of a precoordination complex of the nonlithiated phosphine **1** with the lithiated intermediate **7** via the borane unit bringing the methyl groups into proximity prior to deprotonation. Based on this, two simplified model systems were chosen for the DFT calculations: the deprotonation of nonlithiated phosphine borane via precoordination to a monomeric (TS1) and a dimeric (TS2) lithiated intermediate (Figure 1).[11] The lithium center is coordinatively saturated by TMEDA (shown here) for the monomeric structure motif as well as by dimethyl ether molecules for both monomeric and dimeric systems (for further details, see Supporting Information).The calculations show that TS1 is 7 kJ·mol^{-1} lower in energy than TS2. With calculated barriers of 84 kJ·mol^{-1} for TS1 and 91 kJ·mol^{-1} for TS2 respectively, the intermolecular deprotonation should only proceed at elevated temperatures, thus further confirming the experimental findings described above.

Supported by our studies we conclude that the interconversion of lithiated *P*-stereogenic dimethyl phosphine boranes can be attributed to the intermolecular proton transfer between nonlithiated methyl phosphine boranes and their lithiated counterparts. This reaction only occurs at elevated temperatures and in the presence of an excess amount of the nonlithiated species, rendering the configuration of the here used *α*-lithiated phosphine borane not stable, in contrast to the initial observations by Evans et al.. The interconversion of the target intermediates (S_P)-**7** and (R_P)-**7** in solution constitutes one basic requirement for a successful CIDR process, together with the preferred

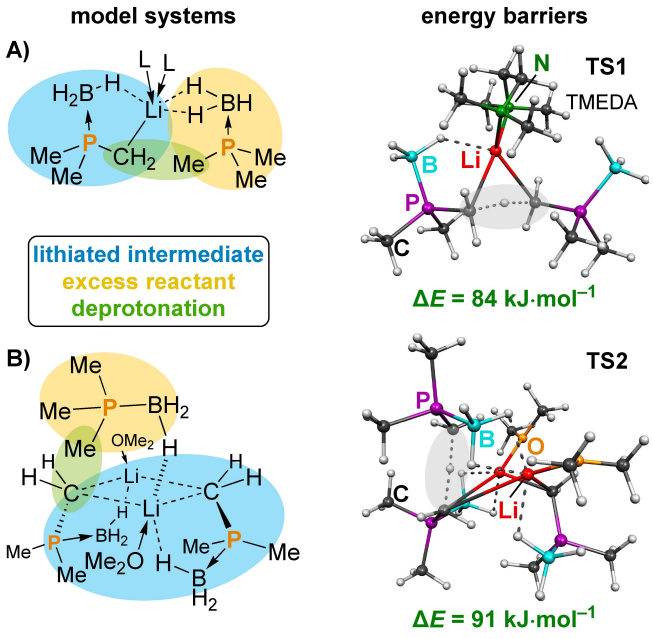


Figure 1. Calculated transition states for the deprotonation of a methyl phosphine borane by a monomeric (A) and dimeric (B) lithiated intermediate [M062X/6-311++G(d,p)/PCM(THF)].[10]

crystallization of one diastereomer, brought about by the ligand (*R*,*R*)-TMCDA.

Although the crystallization of (R_P)-**7** at −30 °C overnight is easy to carry out, a synthetic protocol for the CIDR-process realized at ambient temperature would be an even more desirable alternative. Since the lithiated intermediate **7** is soluble in diethyl ether at room temperature, we decided to use *n*-pentane to reduce its solubility. Thus, after lithiation of **1** in diethyl ether the solvent was removed and *n*-pentane was added. The obtained suspension was stirred at room temperature overnight and subsequently trapped with benzophenone.

Initially, the resolution did not occur as expected and gave (R_P)-**3** with an e.r. of 65:35, presumably because the low solubility of **7** slows down the epimerization process (Table 4, entry 1). However, the addition of small amounts of diethyl ether (3–5 %) to *n*-pentane proved to be sufficient in order to maintain a fast interconversion process under the same conditions. Subsequent trapping of the suspension provided (R_P)-**3** and (S_P)-**3** in an e.r. of 81:19 (Table 4, entry 2). Highly enriched (R_P)-**3** with e.r. = 96:4 and in 52 % yield was generated by trapping the isolated solid in diethyl ether (Table 4, entry 3). In this way, the CIDR of intermediate **1** is also viable at room temperature just by optimizing the solvent mixture to *n*-pentane/diethyl ether. By this means, a more convenient method also leads to a comparably good stereoselectivity.

Table 4: Trapping experiments after lithiation of phosphine borane **1** and subsequent crystallization of **7**.

entry	diethyl ether (%)	E	experiment	yield [%]	e.r. (R:S)[b]
1	–	Ph_2CO	cr. and ml.	nd	65:35
2	5	Ph_2CO	cr. and ml.	nd	81:19
3[c]	3	Ph_2CO	cr.	52[a]	96:4

cr. = isolated crystals; ml. = separated mother liquor. [a] Determined by NMR. [b] Determined by CSP-HPLC. [c] trapping in diethyl ether.

In conclusion, we reported the successful enantioselective synthesis of phosphine boranes in satisfactory yields via CIDR of the α-lithiated phosphine borane intermediates with the inexpensive ligand (*R*,*R*)-TMCDA. Due to the obtained mechanistic insights into the underlying epimerization process in solution, the reaction conditions were determined: the presence of remaining starting material, the correct solvent-mixture, and the configurational instability of the α-lithiated phosphine borane at elevated temperatures became the relevant reaction conditions for a successful dynamic resolution process. Usual kinetic deprotonation conditions for the used dimethyl phenyl phosphine borane do not need to be applied, as higher enantioselective ratios can be obtained by our CIDR method. Our studies demonstrate the importance of focusing on the isolation and careful study of the reactive intermediate as part of chiral resolution. Dimethyl phosphine boranes have been thoroughly studied in the past with regard to asymmetric lithiation-trapping, where (−)-sparteine and its surrogates have been applicated successfully.[4b,15] In contrast, many other easily-prepared chiral amines were not very effective.[15d,g,i] However, during the studies with these ligands little or no attention has been given to the isolation and/or CIDR of the lithiated intermediates. We believe that there is still much hidden potential to enhance stereoselectivity as demonstrated in the present work with the example of **8**. Our current focus is on the utilization of **8** and other easily accessible ligands for the CIDR of lithiated secondary phosphine boranes including **5**.

Supporting Information

The authors have cited additional references within the Supporting Information.[16–26]

Acknowledgements

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Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

Keywords: asymmetric synthesis · chiral resolution · dynamic interconversion · lithiated intermediate · phosphine boranes

[1] For reviews on the synthesis, especially via non-reactive intermediates and further chiral auxillaries, of *P*-stereogenic compounds, see: a) O. Kolodiazhnyi, *Tetrahedron: Asymmetry* **2012**, *23*, 1; b) M. Dutartre, J. Bayardon, S. Jugé, *Chem. Soc. Rev.* **2016**, *45*, 5771; c) S. Lemouzy, L. Giordano, D. Hérault, G. Buono, *Eur. J. Org. Chem.* **2020**, *23*, 3351; d) X. Ye, L. Peng, X. Bao, C.-H. Tan, H. Wang, *Green Synth. Catal.* **2021**, *2*, 6.

[2] a) A. R. Muci, K. R. Campos, D. A. Evans, *J. Am. Chem. Soc.* **1995**, *117*, 9075; b) B. Wolfe, T. Livinghouse, *J. Am. Chem. Soc.* **1998**, *120*, 5116; see also c) T. Imamoto, J. Watanabe, Y. Wada, H. Masuda, H. Yamada, H. Tsuruta, S. Matsukawa, K. Yamaguchi, *J. Am. Chem. Soc.* **1998**, *120*, 1635. Since these initial works, the lithiation-trapping-based desymmetrization of phosphine boranes (and sulfides) has seen significant developments. Especially the contributions from the O'Brien and the Kann group deserve to be mentioned here. For an overview, see [1c–d] and [14a–h].

[3] For an overview of the synthesis of phosphine boranes, see: C. Alayrac, S. Lakhdar, I. Abdellah, A.-C. Gaumont, *Top. Curr. Chem.* **2015**, *361*, 1.

[4] a) B. S. Williams, P. Dani, M. Lutz, A. L. Spek, *Helv. Chim. Acta* **2001**, *84*, 3519; b) M. J. Dearden, M. J. McGrath, P. O'Brien, *J. Org. Chem.* **2004**, *69*, 5789; c) C. E. Headley, S. P. Marsden, *J. Org. Chem.* **2007**, *72*, 7185.

[5] In the first approach of kinetically controlled resolution, a stable configuration of the lithio phosphine borane **2** is essential and the preference for one enantiomer is solely dependent on the energy difference of the transition states of deprotonation. On the other hand, for the dynamic resolution access by Livinghouse et al. a labile configuration of the lithio phosphide needs to be assumed, so that the thermodynamically more stable deprotonation product **5** is dynamically reformed during the reaction.

[6] In the literature, different terms have been used to describe this process. In this paper, we use the term CIDR. For details, see: a) I. Coldham, N. S. Sheikh, *Top. Stereochem.* **2010**, *26*, 253; b) C. Wolf, in *Dynamic Stereochemistry of Chiral Compounds: Principles and Applications*, RSC Publishing, Cambridge, **2008**, pp. 337–344; c) E. Vedejs, M. Jure, *Angew. Chem. Int. Ed.* **2005**, *44*, 3974; *Angew. Chem.* **2005**, *117*, 4040; d) K. M. J. Brands, A. J. Davies, *Chem. Rev.* **2006**, *106*, 2711; e) N. G. Anderson, *Org. Process Res. Dev.* **2005**, *9*, 800; f) K. M. J. Brands, A. J. Davies, *Chem. Rev.* **2006**, *106*, 2711; g) A. Kolarovič, P. Jakubec, *Adv. Synth. Catal.* **2021**, *363*, 4110.

[7] For CIDR comprising secondary respectively tertiary phosphines and phosphine oxides, see: a) M. Pabel, A. C. Willis, S. B. Wild, *Angew. Chem. Int. Ed.* **1994**, *33*, 1835–1837; *Angew. Chem.* **1994**, *106*, 1971; b) A. Bader, M. Pabel, S. B. Wild, *J. Chem. Soc. Chem. Commun.* **1994**, 1405; c) M. Pabel, A. C. Willis, S. B. Wild, *Tetrahedron: Asymmetry* **1995**, *6*, 2369; d) A. Bader, M. Pabel, A. C. Willis, S. B. Wild, *Inorg. Chem.* **1996**, *35*, 3874; e) M. Pabel, A. C. Willis, S. B. Wild, *Inorg. Chem.* **1996**, *35*, 1244; f) E. Vedejs, Y. Donde, *J. Am. Chem. Soc.* **1997**, *119*, 9293; g) E. Vedejs, Y. Donde, *J. Org. Chem.* **2000**, *65*, 2337; h) F. A. Kortmann, M.-C. Chang, E. Otten, E. P. A. Couzjin, M. Lutz, A. J. Minnaard, *Chem. Sci.* **2014**, *5*, 1322.

[8] The products are often crystalline and thus may be further enriched by recrystallization, but for liquid or more complex products this is rather challenging, see: M. F. Cain, D. S. Glueck, J. A. Golen, A. L. Rheingold, *Organometallics* **2012**, *31*, 775.

[9] a) S. K. Ritter, *Chem. Eng. News* **2017**, *95*, 18; for examples of the synthesis of sparteine, see: b) B. T. Smith, J. A. Wendt, J. Aubé, *Org. Lett.* **2002**, *4*, 2577; c) J.-P. R. Hermet, M. J. McGrath, P. O'Brien, D. W. Porter, J. Gilday, *Chem. Commun.* **2004**, 1830; d) J.-P. R. Hermet, A. Viterisi, J. M. Wright, M. J. McGrath, P. O'Brien, A. C. Whitwood, J. Gilday, *Org. Biomol. Chem.* **2007**, *5*, 3614; e) J. D. Firth, S. J. Canipa, L. Ferris, P. O'Brien, *Angew. Chem. Int. Ed.* **2018**, *57*, 223; *Angew. Chem.* **2018**, *130*, 229.

[10] (*R*,*R*)-*N*,*N*,*N*',*N*'-Tetramethyl-1,2-cyclohexanediamine [(*R*,*R*)-TMCDA (**8**)] can be synthesized from 1,2-cyclohexanediamine, a byproduct derived during the purification of 1,6-hexanediamine, which is used in the synthesis of Nylon 6,6 and therefore readily available in both enantiomeric forms on a large scale. For details, see: a) T. A. Whitney, *J. Org. Chem.* **1980**, *45*, 4214; b) J. F. Larrow, E. N. Jacobsen, *J. Org. Chem.* **1994**, *59*, 1939; c) J.-C. Kizirian, N. Cabello, L. Pinchard, J.-C. Caille, A. Alexakis, *Tetrahedron* **2005**, *61*, 8939.

[11] a) M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson, H. Nakatsuji, X. Li, M. Caricato, A. Marenich, J. Bloino, B. G. Janesko, R. Gomperts, B. Mennucci, H. P. Hratchian, J. V. Ortiz, A. F. Izmaylov, J. L. Sonnenberg, D. Williams-Young, F. Ding, F. Lipparini, F. Egidi, J. Goings, B. Peng, A. Petrone, T. Henderson, D. Ranasinghe, V. G. Zakrzewski, J. Gao, N. Rega, G. Zheng, W. Liang, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, K. Throssell, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, T. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, J. M. Millam, M. Klene, C. Adamo, R. Cammi, J. W. Ochterski, R. L. Martin, K. Morokuma, O. Farkas, J. B. Foresman, D. J. Fox, Gaussian 09, Revision A.02, Gaussian, Inc., Wallingford CT (USA), **2016**; b) R. Dennington, T. A. Keith, J. M. Millam, GaussView, Version 6.1,, Semichem Inc., Shawnee Mission, KS (USA), **2016**.

[12] J. J. Gammon, V. H. Gessner, G. R. Barker, J. Granander, A. C. Whitwood, C. Strohmann, P. O'Brien, B. Kelly, *J. Am. Chem. Soc.* **2010**, *132*, 13922.

[13] V. H. Gessner, PhD thesis, TU Dortmund University (Germany), **2009**.

[14] a) K. Izod, C. Willis, W. Clegg, R. W. Harrington, *Dalton Trans.* **2007**, 3669; b) K. Izod, C. Willis, W. Clegg, R. W. Harrington, *Organometallics* **2007**, *26*, 2861; c) A. Staubitz, A. P. M. Robertson, M. E. Sloan, I. Manners, *Chem. Rev.* **2010**, *110*, 4023.

[15] a) M. J. Dearden, C. R. Firkin, J.-P. R. Hermet, P. O'Brien, *J. Am. Chem. Soc.* **2002**, *124*, 11870; b) J.-P. R. Hermet, D. W. Porter, M. J. Dearden, J. R. Harrison, T. Koplin, P. O'Brien, J. Parmene, V. Tyurin, A. C. Whitwood, J. Gilday, N. M. Smith, *Org. Biomol. Chem.* **2003**, *1*, 3977; c) M. J. Johansson, L. O. Schwartz, M. Amedjkouh, N. C. Kann, *Eur. J. Org. Chem.* **2004**, 1894; d) M. J. Johansson, L. O. Schwartz, M. Amedjkouh, N. C. Kann, *Tetrahedron: Asymmetry* **2004**, *15*, 3531; e) A. J. Dixon, M. J. McGrath, P. O'Brien, *Org. Synth.* **2006**, *83*, 141; f) P. O'Brien, *Chem. Commun.* **2008**, 655; g) D. Stead, P. O'Brien, A. Sanderson, *Org. Lett.* **2008**, *10*, 1409; h) J. D. Firth, P. O'Brien, L. Ferris, *Org. Biomol. Chem.* **2014**, *12*, 9357; i) V. M. Foley, R. Cano, G. P. McGlacken, *Tetrahedron: Asymmetry* **2016**, *27*, 1160.

[16] Y. Kuzu, Master thesis, TU Dortmund University (Germany), **2017**.
[17] G. M. Sheldrick, *Acta Crystallogr.* **2008**, *A64*, 112.
[18] O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard, H. Puschmann, *J. Appl. Crystallogr.* **2009**, *42*, 339.
[19] T. Kottke, D. Stalke, *J. Appl. Crystallogr.* **1993**, *26*, 615.
[20] D. Leusser, PhD thesis, Universität Würzburg, **2002**.
[21] G. M. Sheldrick, *Acta Crystallogr.* **2015**, *C71*, 3.
[22] G. M. Sheldrick, *Acta Crystallogr.* **2015**, *A71*, 3.
[23] a) Y. Zhao, D. G. Truhlar, *Theor. Chem. Acc.* **2008**, *120*, 215; b) A. D. Becke, *J. Chem. Phys.* **1993**, *98*, 5648–5652; c) C. Lee, W. Yang, R. G. Parr, *Phys. Rev. B.* **1988**, *37*, 785–789; d) J. Tomasi, B. Mennucci, R. Cammi, *Chem. Rev.* **2005**, *105*, 2999–3093; e) S. Grimme *WIREs Comput. Mol. Sci.* **2011**, *1*, 211.
[24] a) M. J. Frisch, J. A. Pople, J. S. Binkley, *J. Chem. Phys.* **1984**, *80*, 3265–3269; b) R. Ditchfield, W. J. Hehre, J. A. Pople, *J. Chem. Phys.* **1971**, *54*, 724–728.
[25] P. Flükiger, H. P. Lüthi, S. Portmann, J. Weber, MOLEKEL 4.3, Swiss Center for Scientific Computing, Manno (Schweiz), **2000**.
[26] Y. Kuzu, PhD thesis, TU Dortmund University (Germany), **2021**.
[27] Deposition Numbers 2304934 (for (R_P-**3**), 2304935 (for (R_P)-**7**), 2304933 (for **11**), 2304932 (for **12**), 2304931 (for **13**) contain the supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe Access Structures service.

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