Organolithium/Chiral Lewis Base/BF_3: a Versatile Combination for the Enantioselective Desymmetrization of *meso*-Epoxides

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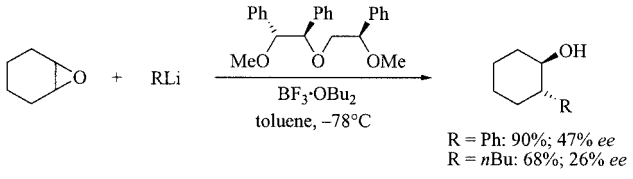
BF_3 can be used in combination with organolithium/strong Lewis base complexes for the enantioselective nucleophilic ring-opening or the carbenoidic rearrangement of various *meso*-oxiranes with excellent yields and *ee* values of up to 87 %. Mechanistic aspects of these reactions are considered.

Introduction

The concept of the combination of an organolithium reagent and a chiral Lewis base for enantioselective reactions has been widely explored. Similarly, the combination of an organolithium and BF_3 has also been extensively studied.[1] Thus, we wondered if it would be possible to use a combination of these two methodologies (i.e. RLi + ligand + BF_3) in order to take advantage of the enantioselective possibilities arising from the chiral ligand and the dramatic improvements often induced by the presence of BF_3. A good application field of this concept is the enantioselective opening of *meso*-epoxides. Indeed, many methodologies using asymmetric catalytic systems have been successfully developed for the enantioselective opening of *meso*-oxiranes by non-carbon nucleophiles (including the CN group).[2] In contrast, there are only a few reports of efficient processes involving organometallic species (RMgX, R_2CuLi, R_3Al, RZnX etc.) for such a reaction, the best results being obtained with organolithium reagents.[3–9] A significant advance was achieved in 1996 by Tomioka et al., who used an organolithium/homochiral ether combination in the presence of BF_3, as depicted in Scheme 1.[4,5]



Scheme 1.

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Since BF_3 is known to promote the nucleophilic addition of a wide range of organometallic reagents to epoxides in a simple and effective way,[10–14] this approach appears to be a practical and versatile methodology. Among all the chiral ligands tested with organolithium reagents, strong Lewis base donors such as amino alcohols, amino alkoxides, or diamines give the best results in term of enantioselectivity.[15] However, as we started this work, the compatibility between strong Lewis base/organolithium complexes and strong Lewis acids had never been addressed.[16,17] Therefore, we decided to explore the scope and the generality of such a reaction. Here, we wish to report all our results obtained during this study.[6]

Results and Discussion

Among the most usual chiral ligands used for organolithium reagents, (–)-sparteine appears to be an excellent typical diamine for such a study.[18] It is cheap, commercially available, and very efficient in a number of reactions. At first glance, it could seem incongruous to mix a strong Lewis base (sparteine is a diamine) with a strong Lewis acid such as $BF_3{\cdot}Et_2O$ as competition for the Lewis acid should favor the diamine moiety instead of the oxygen of the epoxide. Despite this fact, we assumed that the kinetics of these two competitive reactions (nucleophilic addition of the organolithium reagents to the oxirane vs. irreversible complexation of the Lewis acid and the diamine) might be similar enough to afford at least small amounts of the desired alcohols. We were thus very pleased to notice that when 1.5 equiv. of $BF_3{\cdot}Et_2O$ was added dropwise to an ethereal solution of salt-free PhLi, complexed by 2 equiv. of (–)-sparteine and 1 equiv. of cyclohexene oxide **1** (this stoichiometry corresponds to that used by Tomioka et al.), a very clean reaction took place to afford enantioenriched *trans*-phenylcyclohexanol (**2**) in near quantitative yield (48% *ee*;[19,20] Scheme 2).

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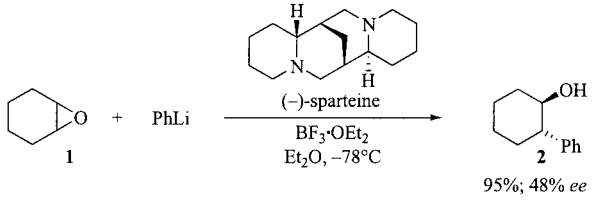


Scheme 2.

Encouraged by this result, a study of the influence of the different reaction parameters was initiated. It has been reported in the literature that the temperature of formation of the RLi/chiral ligand complex may have a dramatic effect on its aggregation state, and thus affect the enantioselectivity.[21–23] However, we did not observe such an effect − similar yields and enantioselectivities were obtained for temperatures of formation of the (–)-sparteine/PhLi complex ranging from –78 °C to 25 °C. On the other hand, the addition of the Lewis acid at higher temperatures (–10 °C) results in a dramatic drop in the selectivity (Table 1, Entry 2). This is a general observation of our studies: the selectivities were always strictly dependent on the temperature of the reaction mixture. An intriguing solvent effect was observed when hexane was used as cosolvent, both the yields and selectivities decreasing proportionally to the hexane/diethyl ether ratio (Table 1, Entries 3–5 vs. Entry 1). Interestingly, the optimum selectivities were restored when toluene was used instead of diethyl ether (Table 1, Entry 6). As reported by Tomioka,[5] the selectivity was totally lost in THF as its strong Lewis basicity might compete with the diamine, thereby disrupting the formation of the sparteine/PhLi complex (Table 1, Entry 7).

Table 1. Solvent effect on enantioselectivity.

Entry	Solvent	*T* [°C]	Yield [%][a]	*ee* [%][b]
1	Et_2O	–78	>95	49
2	Et_2O	–10	70	20
3	Et_2O/hexane[c]	–78	85	30
4	Et_2O/hexane[d]	–78	80	38
5	hexane	–78	12	19
6	toluene/hexane[c]	–78	>95	49
7	THF	–78	>95	0

[a] Isolated by column chromatography on silica gel. [b] Determined by ^{31}P NMR spectroscopy according to ref.[19] [c] Ratio: 5:1. [d] Ratio: 10:1.

Any variation of the number of equivalents of (–)-sparteine with respect to the organolithium reagents gave lower *ee* values. The optimum is a 1:1 ratio (Table 2, Entries 1–3). If a PhLi·LiBr complex is used, additional (–)-sparteine is needed, without enhancement of the *ee*. However, a lower yield is observed due to the formation of bromocyclohexanol by competitive nucleophilic attack of the Br anion (Table 2, Entry 4). In the absence of BF_3·Et_2O, no reaction was observed at –78 °C, even if (–)-sparteine (Table 2, Entry 5) is present. In this case, an increase of the temperature to 0 °C for 3 d was needed to give a 34% yield of *trans*-phenylcyclohexanol (**2**) with 5% *ee*. Similarly, a 1:2 BF_3/epoxide ratio allows the formation of **2** in only 49% yield, and with a much lower selectivity (Table 2, Entry 6). This result could be due to participation of the enantiomerically enriched product in the enantioselective recognition. The addition of varying catalytic amounts of enantiomerically enriched *trans*-phenylcyclohexanol (**2**) to the reaction mixture had no effect on the enantioselectivity, which rules out the envisaged self-induction. The selectivity appears to depend only on the BF_3·Et_2O/(–)-sparteine ratio, an optimum result being reached for values above or equal to one (Table 2, Entries 5–7).

Table 2. Reaction of PhLi reagents/(–)-sparteine with cyclohexene oxide and BF_3·Et_2O in diethyl ether or toluene/hexane mixtures as solvent.

Entry	ArLi	RLi/sparteine/epoxide/BF_3	Yield [%][a]	*ee* [%][b]
1	PhLi[c]	2:2:1:1.5	>95	49
2	PhLi	2:4:1:1.5	87	30
3	PhLi	2:1:1:1.5	94	37
4	PhLi·LiBr	2:4:1:1.5	50[d]	47
5	PhLi[c]	2:2:1:5	>95	47
6	PhLi	2:2:1:0.5	48	25
7	PhLi	1:1:1:0.5	49	39

[a] Isolated by column chromatography on silica gel. [b] Determined by ^{31}P NMR spectroscopy according to ref.[19] [c] Salt-free reagent. [d] Racemic *trans*-bromocyclohexanol was also obtained in 17% yield.

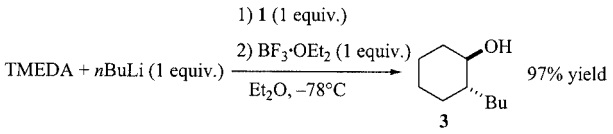
Next, we screened a variety of organolithium reagents to check quickly the scope of this reaction. As shown in Table 3, only aryllithium reagents give significant *ee* values, the use of alkyl-, alkenyl-, or alkynyllithium species giving the corresponding alcohols with no selectivity (Entries 1–6). However, the conversion is excellent for most of the organolithium reagents tested.

Table 3. Enantioselective nucleophilic ring-opening of **1**.

Entry	RLi	Product	Yield [%][a]	*ee* [%][b]
1	Ph[c]	2	>95	49
2	Bu[c]	3	97	0
3	Me[c]	4	96	6
4	$PhCH_2$[d]	5	87[e]	5
5	1-cyclohexenyl[f]	6	98	0
6	1-hexynyl[f]	7	42[e]	0

[a] Isolated by column chromatography on silica gel. [b] Determined by ^{31}P NMR spectroscopy according to ref.[19] [c] Salt-free reagent. [d] Obtained by metalation with *n*BuLi. [e] This yield corrects the previous reported one in ref.[6] [f] Obtained by halogen/Li exchange with *n*BuLi.

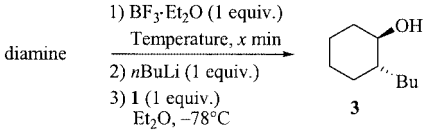
These results outline the surprising behavior of the Lewis acid towards the diamine. This observation prompted us to further study the addition of *n*BuLi to cyclohexene oxide **1** in the presence of BF_3·Et_2O and diamines as a model reaction. First, the less bulky TMEDA was employed instead of (–)-sparteine, under standard reaction conditions. No effect on the yield was observed and the corresponding *trans*-butylcyclohexanol (**3**) was obtained almost quantitatively (Scheme 3).



Scheme 3.

Two possible explanations were proposed to explain this: either there is no complexation of the $BF_3{\cdot}Et_2O$ with the diamines (sparteine or TMEDA) in the reaction conditions, or an equilibrium may allow the reaction to proceed. In order to check these hypotheses, a precomplexation of $BF_3{\cdot}Et_2O$ with the diamines was performed under different conditions. The addition of $BF_3{\cdot}Et_2O$ to an ethereal solution of (–)-sparteine at room temperature leads to the exothermic formation of a complex, as a white precipitate, which is unable to achieve the transformation (Table 4, Entry 1), which invalidates the hypothesis of an equilibrium. It is noteworthy that the commercially available $BF_3{\cdot}NEt_3$ reagent was also unable to promote the reaction, thus corroborating this hypothesis (Table 4, Entry 5).The formation of the Lewis acid/sparteine complex needed 1 h at low temperature to ensure complete inhibition of the nucleophilic ring-opening reaction (Table 4, Entries 2 and 3). The complexation of $BF_3{\cdot}Et_2O$ to TMEDA is very fast even at –78 °C (Table 4, Entry 4). The kinetics of the complexation are thus strongly dependent on both the temperature and the steric hindrance of the diamine.

Table 4. Effect of complexation of $BF_3{\cdot}Et_2O$ with diamines on nucleophilic ring-opening of **1** by *n*BuLi.



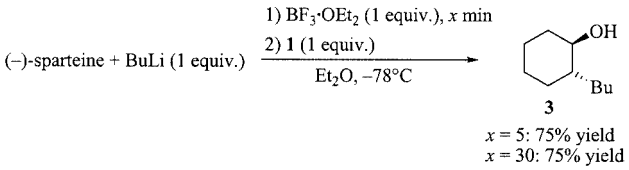
Entry	Diamine	Temp [°C]	Time [min]	Yield [%][a]
1	sparteine	25	5	0
2	sparteine	–78	5	80
3	sparteine	–78	60	0
4	TMEDA	–78	5	0
5[b]	NEt_3	–	–	0

[a] Determined by GC using decane as internal standard. [b] Commercially available $BF_3{\cdot}NEt_3$ was used.

In contrast, the complex formed when $BF_3{\cdot}Et_2O$ was added to a preformed sparteine/*n*BuLi aggregate at –78 °C was reactive, and subsequent addition of **1** after 5 or 30 min yielding alcohol **3** cleanly. (Scheme 4). These observations suggest a possible protection of the diamine from the Lewis acid by the organolithium reagent.

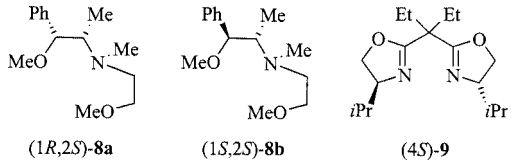
Despite the strong Lewis basicity of these two diamines, the excellent yields obtained validate our approach, which allows the use of an extensive number of chiral auxiliaries. We therefore decided to test other chiral ligands, such as amino ethers **8a** and **8b** and bis(oxazoline) **9**, as depicted in Table 5.

The two amino ethers **8a** and **8b** are easily obtained in three steps from (1*R*,2*S*)-ephedrine or (1*S*,2*S*)-pseudoephedrine. Despite their similar structures, the use of these two chiral ligands, in association with PhLi, resulted in different selectivities (Table 5, Entries 2 and 4). Moreover, the *trans*-butylcyclohexanols **2** obtained with (1*R*,2*S*)-**8a** or (1*S*,2*S*)-**8b** are of opposite absolute configuration, which emphasizes the dramatic effect of the absolute configuration of the benzylic carbon atom of these ligands (Table 5, Entries 1 and 3). Although modest, the 38% *ee* obtained with the *n*BuLi/(1*R*,2*S*)-**8b** complex is, to the best of our knowledge, the best described in the literature. In the presence of the bis(oxazoline) **9**, similar results to those observed with (–)-sparteine were obtained: no selectivity with *n*BuLi, and 54% *ee* with PhLi (Table 5, Entries 5 and 6). Importantly, even this very strong Lewis base ligand is compatible with BF_3 under our reaction conditions, as shown by the high yield obtained.



Scheme 4.

Table 5. Ligand effects on enantioselectivity.



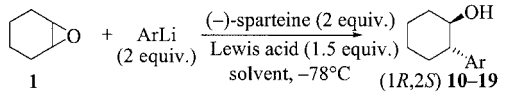
Entry	Ligand	RLi[a]	Solvent	Product	Yield [%][b]	*ee* [%][c]
1[e]	**8a**	*n*Bu	tol/hex[d]	3	78	38
2[e]	**8a**	Ph	tol/hex[d]	2	60	0
3[e]	**8b**	*n*Bu	tol/hex[d]	3	70	22
4[e]	**8b**	Ph	tol/hex[d]	2	75	35
5[e]	**9**	*n*Bu	Et_2O	3	85	0
6[e]	**9**	Ph	Et_2O	2	93	54

[a] Salt-free reagent. [b] Isolated by column chromatography on silica gel. [c] Determined by ^{31}P NMR spectroscopy according to ref.[19] [d] In a 5:1 ratio. [e] RLi ligand/epoxide/BF_3 ratio of 1.2:1.2:1:1.5.

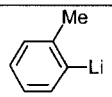
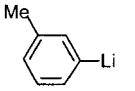
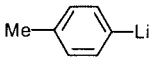
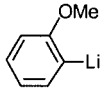
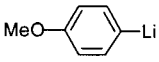
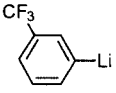
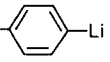
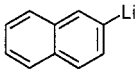
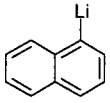
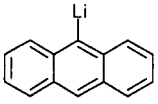
Since optically pure phenylcyclohexanol is a useful chiral auxiliary,[24] we screened other aryllithium reagents which would afford other arylcyclohexanols. These compounds may, in turn, serve as new chiral auxiliaries. The results are summarized in Table 6.

All the arylcyclohexanol derivatives **10**–**19** obtained have a (1*R*,2*S*) absolute configuration,[25] which results from a nucleophilic attack on the (*S*)-carbon atom of the epoxide ring. A comparison of the results obtained with the three isomers of tolyllithium shows that an *ortho* substituent causes a marked increase in the enantioselectivity (Table 6, Entry 1). However, an *ortho*-methoxy substituent has a detrimental effect, probably due to internal coordination of the lithium cation by the oxygen atom (Table 6, Entry 4). The

Table 6. Formation of arylcyclohexanols by reaction of aryllithiums reagents with cyclohexene oxide.



1 (1*R*,2*S*) **10–19**

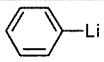
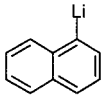
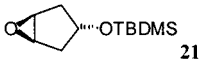
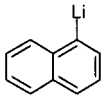
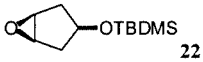
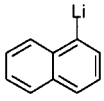
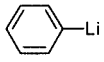
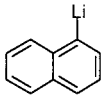
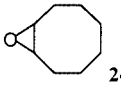
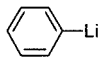
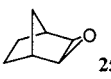
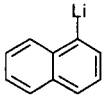
Entry	Ar-Li	Solvent	Product	Yield [%][a]	*ee* [%][b]
1[c]		Et_2O	**10**	91	65
2[d]		Et_2O/hexane[f] toluene/hexane[f]	**11**	82 0[i]	36 –
3[a]		Et_2O	**12**	85	52
4[c]		Et_2O/hexane[f] toluene/hexane[f]	**13**	84 85	15 23
5[d]		Et_2O/hexane[f] toluene/hexane[f]	**14**	95 96	44 43
6[d]		toluene/hexane[f]	**15**	92	60
7[d]		toluene/hexane[f]	**16**	95	53
8[d]		toluene/hexane[f]	**17**	90	70
9[d]		Et_2O/hexane[f] toluene/hexane[f] toluene/hexane[f]	**18**	81 91 87[g]	22 85 87[g]
10[d]		toluene/hexane[f]	**19**	80	41

[a] Isolated by column chromatography on silica gel. [b] Determined by ^{31}P NMR spectroscopy according to ref.[19] [c] Salt-free reagent. [d] Obtained by halogen/Li exchange with *n*BuLi. [e] Obtained by metalation with *n*BuLi. [f] In a 5:1 ratio. [g] ArLi/sparteine/epoxide/BF_3 ratio of 1:1:1:1. [i] ArLi/sparteine mixture insoluble in the reaction conditions.

electronic nature of the *para* substituent plays a moderate role, since the *ee* values are in the same range (43–53%). The same may be roughly said about a *meta* substituent, although we note the 60% *ee* obtained with a CF_3 moiety (Table 6, Entry 6). Both 1- and 2-naphthyllithium are extremely interesting cases (Table 6, Entries 8 and 9) as they give the corresponding alcohols **17** and **18** with 70 and 85% *ee*, respectively. Once again, as for the PhLi, an important solvent effect is observed in diethyl ether/hexane mixtures which disappears in toluene (see Table 6, Entries 4 and 9, and Table 1). An *ee* of 87% was obtained in a large-scale experiment (5 g of final material **18**), showing that the method has some preparative value. Moreover, enantiomerically pure **18** (>98% *ee*) can be obtained in 78.5% yield after one recrystallization. Similarly, compound **19** with 96% *ee* was obtained after one recrystallization. An increase of the steric effects with anthracenyllithium (Table 6, Entry 10) resulted in a lower *ee*.

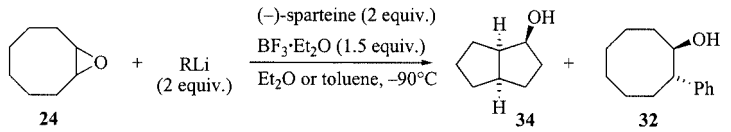
We next examined the behavior of other epoxides with PhLi and 1-naphthyllithium reagents. The absolute configuration of the obtained alcohols could be determined by derivatization with (+)- and (–)-methoxymandelic acid.[26] The observed results indicate that, again, in every case the nucleophilic attack takes place at the (*S*)-carbon atom of the oxiranyl ring. As previously observed, 1-naphthyllithium give better *ee* values than PhLi (Table 7, Entries 1, 2, 5, and 6). Although the *ee* values are lower than those obtained with cyclohexene oxide (**1**), it is interesting to note that a rather flat epoxide, such as cyclopentene oxide (**20**), gave a result as good as cycloheptene oxide (**23**) or norbornene oxide (**25**; Table 7, Entries 2, 6, and 8). Moreover, the enantioselectivity depends on the substitution on the carbocyclic ring: whereas the presence on the cyclopentene oxide derivative **21** of a substituent *anti* to the epoxide ring decreases the *ee* from 53 to 24%, a higher *ee* (62%) is observed for its *syn* isomer **22** (Table 7, Entries 2–4).

Table 7. Nucleophilic opening of various epoxides by an ArLi/sparteine/BF_3·Et_2O combination in toluene/hexane.

Entry	Oxirane	Ar–Li	Product	Yield [%][a]	*ee*[%][b]
1[c]	 **20**		**26**	95	37[e]
2[d]	 **20**		**27**	78	53[f]
3[d]	 **21**		**28**	75	24[h]
4[d]	 **22**		**29**	76	62[h]
5[c]	 **23**		**30**	95	29[h]
6[d]	 **23**		**31**	71	49[f],[g]
7[c]	 **24**		**32**	32	62[h]
8[d]	 **25**		**33**	63	34[i]

[a] Isolated by column chromatography on silica gel. [b] Determined by ^{31}P NMR spectroscopy according to ref.[19] [c] Salt-free reagent. [d] Obtained by halogen/Li exchange with *n*BuLi. [e] Absolute configuration (1*R*,2*S*) determined by polarimetry and comparison with the literature (see Exp. Sect.). [f] Absolute configuration (1*R*,2*S*) estimated by comparison of the ^{31}P NMR spectra of the derivatives. [g] This value corrects the previous one reported in ref.[6] [h] Absolute configuration (1*R*,2*S*) established according to ref.[26] [i] Absolute configuration (1*R*,2*S*) established according to ref.[26]

Eight-membered-ring epoxides are of particular interest. We have already observed that the cyclooctene oxide **24**



R = PhLi: 45%, 22% *ee* 32%, 62% *ee* (toluene)
R = *s*BuLi: 98%, 61% *ee* – (Et_2O)

Scheme 5.

provides a mixture of the expected arylcyclooctanol **32** and the (–)-*endo*-*cis*-fused bicyclic alcohol **34**, as a single diastereoisomer, under our reaction conditions with PhLi.[27,28] This latter compound was first obtained by Cope,[29] starting from the same epoxide and using strongly basic conditions ($LiNEt_2$, boiling Et_2O, 48 h), and was rationalized as a result of an α-deprotonation followed by a transannular C–H insertion of the transient carbenoid species.[30–33] In our conditions at –78 °C, using stronger bases than PhLi and in diethyl ether instead of toluene, the reaction was chemoselective, yielding exclusively the rearranged alcohol **34** in quantitative yields (Scheme 5). As for the nucleophilic opening, the presence of the BF_3 allows a strong acceleration of the carbenoid rearrangement, complete conversion being observed after the addition of the last drop of 1 equiv. of the Lewis acid. Presumably, this accelerating effect can be interpreted in this case by the higher acidity of the oxiranyl protons, or by an enhanced carbenoid character of the lithiooxirane intermediate, or both. Note that the RLi/(–)-sparteine complex causes the α-deprotonation of the (*R*)-carbon atom of the oxiranyl ring, whereas the (*S*) center is preferentially attacked during nucleophilic opening. This fact may be due to a difference between the transition states of these two processes.

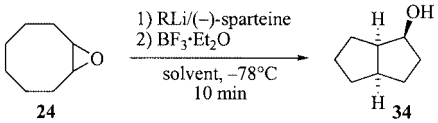
An enantioselective version of this reaction has been reported by Hodgson et al., using alkyllithium bases in the presence of (–)-sparteine.[34–36] Under their optimum conditions (*i*PrLi, Et_2O, –98 °C, 6 h to room temperature, 12 h) the alcohol **34** was obtained in good yield with an *ee* of up to 84%. For our part, we decided to perform a brief study of the influence of the different experimental parameters for the carbenoid rearrangement of epoxide **24** with the RLi/(–)-sparteine/BF_3 combination. The results are summarized in Table 8.

The results obtained contrast with our observations made for the nucleophilic ring-opening reaction of cyclohexene oxide (**1**). Indeed, similar *ee* values were obtained for alcohol **34** either in Et_2O/hexane or cumene/hexane mixtures (Table 8, Entries 1 and 2). Variation of the (–)-sparteine/*n*BuLi ratio from 1:1 to 2:1 or of the BF_3/(–)-sparteine ratio from 2.5:1 to 0.25:1 have no significant effect on the enantioselectivity (Table 8, Entries 3–5). The use of LiBr as additive has no beneficial influence on the *ee* values, additional (–)-sparteine being needed in order to overcome the 1:1 Li cation/ligand ratio (Table 8, Entries 6 and 7).

The reverse addition of epoxide **24** to a preformed mixture of *n*BuLi/sparteine complex and BF_3·Et_2O gave alcohol **34** with no change in the selectivity (Table 8, Entry 1), which points to the crucial role of the Lewis acid in this enantioselective process (Scheme 6).

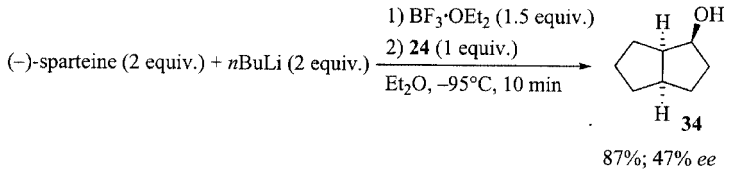
A slight enhancement of the *ee* values was observed by increasing the steric hindrance of the organolithium used (48% for *n*BuLi to 61% for *s*BuLi; Table 8, Entries 1, 9, and 10). These values are slightly different to Hodgson's results: they are higher for *n*BuLi (48% vs. 31%) and lower for the secondary organolithium reagents (61% vs. 77% for *s*BuLi and 56% vs. 84% for *i*PrLi).[34–36] In our case, *s*BuLi gave the best selectivity, whereas without the assistance of BF_3,

Table 8. Influence of some reaction parameters on yield and enantioselectivity.



Entry	RLi	RLi/sparteine/epoxide/BF_3	Solvent	Yield [%][a]	*ee* [%][b]
1	*n*BuLi	2:2:1:1.5	Et_2O/hexane[c]	98	48
2	*n*BuLi	2:2:1:1.5	cumene/hexane[c]	60	45
3	*n*BuLi	2:4:1:1.5	Et_2O/hexane[c]	85	48
4	*n*BuLi	2:2:1:0.5	Et_2O/hexane[c]	45	48
5	*n*BuLi	2:2:1:5	Et_2O/hexane[c]	98	47
6	*n*BuLi, LiBr	2:2:1:1.5	Et_2O/hexane[c]	78[e]	27
7	*n*BuLi, LiBr	2:4:1:1.5	Et_2O/hexane[c]	72[e]	45
8	MeLi	2:2:1:1.5	Et_2O/hexane[c]	0	–
9	*i*PrLi	2:2:1:1.5	Et_2O/hexane[c]	96	56
10	*s*BuLi	2:2:1:1.5	Et_2O/hexane[c]	98	61

[a] Isolated by column chromatography on silica gel. [b] Determined by ^{31}P NMR spectroscopy according to ref.[19] [c] In a 6:1 ratio. [d] Racemic *trans*-bromocyclooctanol was also obtained in 20% yield.



Scheme 6.

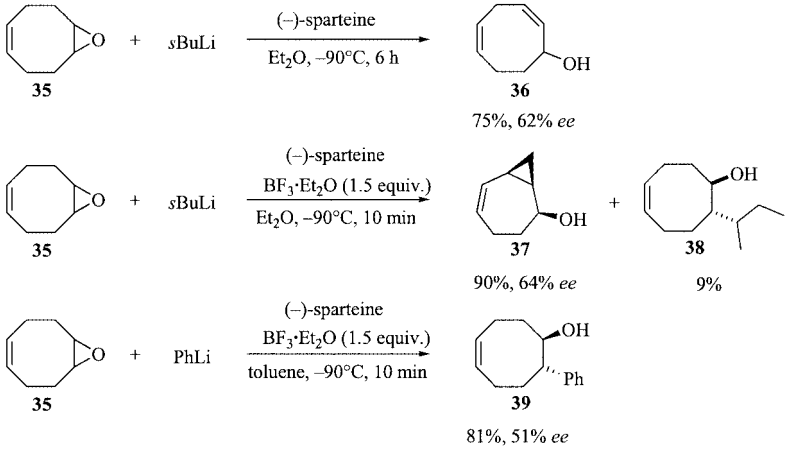
as reported by Hodgson, *i*PrLi gave the best *ee*. Therefore, the BF_3 not only has an influence on the kinetics of the reaction, but also on the enantioselectivity. This effect illustrates possible differences in the transition states of theses two processes. Indeed, the α-deprotonation is known to proceed through the complexation of the organolithium with the oxirane, the deprotonation taking place into an epoxide/RLi oligomer.[30,31,33,37] The formation of this oligomeric structure should be strongly disrupted by the complexation of the Lewis acid to the oxygen atom of the oxiranyl ring, thus inducing a probable intermolecular transition state.

The presence of the BF_3 and the basicity of the organolithium reagent used can thus have a profound effect on the course of the reaction. In all cases, a strong Lewis base can be used as chiral ligand without any erosion of the conversion, and, in this way, various valuable enantiomerically enriched products can be synthesized. The application of this methodology to the synthesis of *meso*-cycloocta-1,5-diene oxide (**35**) illustrates the above concept well. As shown in Scheme 7, addition of **35** to a 1:1 *s*BuLi/(–)-sparteine mixture at –90 °C gives, after 6 h, the allylic alcohol **36** in 85% yield, with an *ee* of up to 62% (the absolute configuration was not determined). Note that under the same reaction conditions, its saturated analog **24** gave exclusively the α-deprotonation product **34**. This difference of behavior has been rationalized by Crandall[38] as a result of a steric decongestion of the carbocyclic ring, induced by the presence of the double bond, which may increase the flexibility and allows a suitable conformation for the postulated β-elimination process.[39] In the same manner, this steric decongestion could reduce the strain energy of the epoxide ring, thus decreasing the acidity of the α-proton.[32]

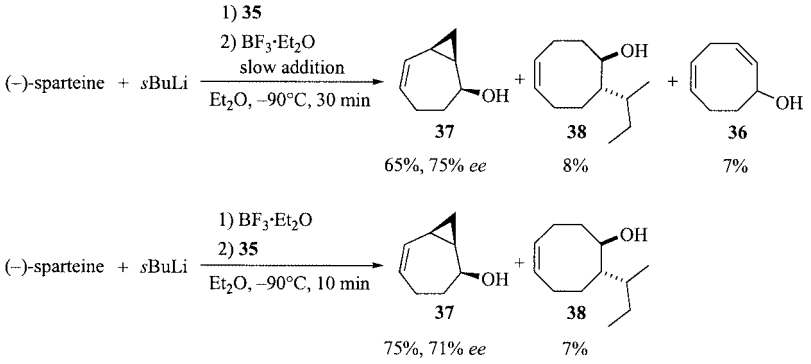
Under the same conditions, but in the presence of $BF_3{\cdot}Et_2O$, the course of the reaction changes dramatically: the major compound, obtained in 90% yield, is the alcohol **37**, as a single diastereoisomer and with an interesting 64% *ee*. As previously, the absolute configuration could be assessed by derivatization with (+)- and (–)-methoxymandelic acids,[26] and was found to be (1*S*,2*R*,3*S*), which is in good agreement with an abstraction of the α-proton from the (*R*)-carbon atom of the oxiranyl ring. Moreover, the obtention of a single diastereoisomer supports the hypothesis of a concerted carbenoid rearrangement. These observations are in good accordance with an enhancement of the oxiranyl proton acidity induced by the complexation with the Lewis acid.

Besides the major product **37**, trace amounts (9%) of *sec*-butyl-substituted cyclooctanol **38** were detected. Such a compound, which results from a nucleophilic ring-opening reaction, has never been observed when cyclooctene oxide **24** is submitted to the same reaction conditions. The formation of this side product is consistent with the above hypothesis upon the effect of the double bond, which probably affects the oxiranyl proton acidity. To check it, the less basic PhLi was used instead of *s*BuLi under otherwise similar conditions, and, as expected, the nucleophilic ring-opening product **39** was obtained in 81% yield with an *ee* of up to 51%. The absolute configuration, assigned after hydrogenation of the double bond and comparison of the optical rotation of the resulting product with alcohol **32**, was found to be (1*R*,2*S*).

In order to improve the *ee* of bicyclic alcohol **37**, a slow (30 min) addition of BF_3 with a syringe pump was realized in a scaled-up trial (20 mmol). A slight enhancement of the selectivity, from 64 to 75% *ee*, was observed, which could



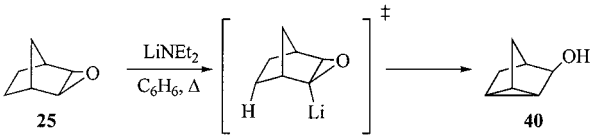
Scheme 7.



Scheme 8.

be explained by a better control of the reaction temperature. However, the allylic alcohol **36** appears as a new side product. To avoid its formation, the Lewis acid was added prior to the oxirane, giving the alcohol **37** cleanly with a non-optimized 71% *ee* (Scheme 8).

Finally, we tried to extend our methodology to the highly reactive *endo*-norbornene oxide **25**. This epoxide is known to give the 1,3-carbenoid C–H insertion product (alcohol **40**) upon treatment with organolithium reagents (Scheme 9).[36,40–42]



Scheme 9.

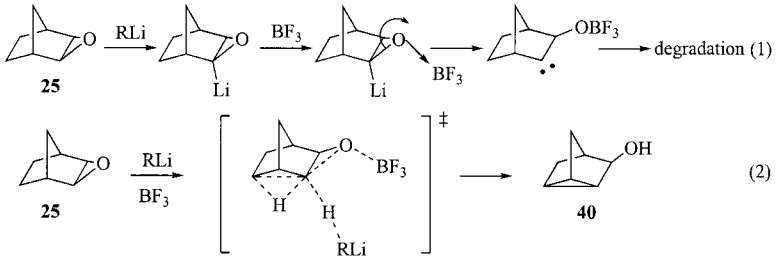
An attempt to develop an enantioselective version of this reaction with our RLi/sparteine/BF_3 combination, under standard conditions, resulted in the degradation of the starting material. However, a 70% yield of the desired alcohol **40** was obtained when the Lewis acid was added to the *s*BuLi/(–)-sparteine mixture before the oxirane, but unfortunately without selectivity. These results highlight the mechanism of the base-promoted rearrangement of medium-sized-ring epoxides in the presence of BF_3. The enhanced acidity of *endo*-norbornene oxide **25** is well known.[32] Therefore, under the standard conditions, the formation of the transient carbenoid species should occur before the addition of BF_3. The obtention of degradation products would thus reflect the instability of the carbenoid in the presence of BF_3 [Scheme 10, Equation (1)]. Consequently, when the epoxide is treated simultaneously with RLi and BF_3, the α-deprotonation step and the transannular rearrangement may be compressed into a single, concerted process, thus avoiding the formation of a real carbenoid intermediate [Scheme 10, Equation (2)]. This type of model could be applicable to all medium-sized-ring epoxides to explain their observed behavior towards our RLi/sparteine/BF_3 combination.

Conclusions

We have demonstrated that strong Lewis bases, such as (–)-sparteine, are compatible with strong Lewis acids, such as BF_3, as long as they are protected by coordination to an organolithium reagent. Moreover, when the Lewis base is chiral, good enantioselectivity can be attained in the nucleophilic desymmetrization of *meso*-epoxides. The role of the Lewis acids has been demonstrated to be exclusively directed towards the activation of the epoxides, to enhance the reaction rate.

Experimental Section

General Considerations: Experiments involving organometallic reagents were carried out under dry argon. All glassware was dried at 120 °C and assembled while hot under a stream of dry nitrogen. All moisture-sensitive reactants were handled under argon. Low-temperature experiments were carried out by cooling a three-necked, round-bottomed flask with an acetone (–80 °C) or diethyl ether (–95 °C) bath frozen with liquid nitrogen. The flask was equipped with an internal thermometer, an argon inlet, and a septum cap. Diethyl ether and tetrahydrofuran were distilled from so-



Scheme 10.

dium/benzophenone ketyl. Organolithium reagents were titrated with 2-butanol (1 M solution in toluene) using 1,10-phenanthroline as indicator. (–)-Sparteine was freshly distilled from calcium hydride before use. Column chromatography was performed on silica gel Si 60 (0.015–0.040 or 0.040–0.063 mesh). Thin-layer chromatography (TLC) was performed on silica gel (0.25 mm, F-254) and visualized under a UV lamp (254 and 366 nm) or by spraying with a 10% phosphomolybdic acid solution in ethanol (heating), vanillin reagent (heating), or Dragendorf reagent. Optical rotations were measured at 20 °C. ^{1}H NMR spectra were recorded at 200 or 400 MHz, ^{13}C NMR spectra were recorded at 50 or 100 MHz, ^{31}P NMR spectra were recorded at 162 MHz, and ^{19}F NMR spectra were recorded at 376 MHz, in $CDCl_3$ as solvent. Chemical shifts are reported in ppm (reference $CDCl_3$ for ^{1}H and ^{13}C, H_3PO_4 for ^{31}P and $CFCl_3$ for ^{19}F).

Preparation of the Epoxides: All the epoxides have already been described. Epoxides **1**, **20**, and **23**–**25** are commercially available. Epoxide **35** was prepared according to the procedure of Crandall et al.[43] Epoxides **21** and **22** were prepared according to the procedure of Asami.[44]

(2-Methoxyethyl)[(1*R*,2*S*)-2-methoxy-1-methyl-2-phenylethyl]methylamine (1*R*,2*S*)-8a: A solution of methoxyacetyl chloride (1.53 mL, 16.85 mmol) in dichloromethane (10 mL) was added at 0 °C under nitrogen to a solution of (1*R*,2*S*)-*O*-methylephedrine[45] (3 g, 16.9 mmol) and triethylamine (7 mL, 50 mmol) in dichloromethane (60 mL). The reaction mixture was stirred at room temperature for 16 h and then poured into a saturated solution of NH_4Cl. The aqueous layer was extracted with dichloromethane (2 × 50 mL) and the combined organic phases were washed with brine, dried with K_2CO_3, and filtered. The solvents were removed under reduced pressure to afford the crude product (4.03 g, 95%) which was then slowly added without further purification to a solution of $LiAlH_4$ (1.25 g, 33.7 mmol) in diethyl ether (100 mL). The reaction mixture was heated under reflux for 3 d and was then hydrolyzed at 0 °C with an aqueous solution of sodium/potassium tartrate (100 mL). The mixture was stirred for 16 h and then the aqueous layer was extracted with diethyl ether (3 × 50 mL). The combined organic layers were dried with K_2CO_3, filtered, and the solvent was removed under reduced pressure. The product was purified by column chromatography on silica gel with cyclohexane/ethyl acetate/NEt_3 (50:45:5) as eluent to afford the title compound (2.94 g, 11.66 mmol, 69% 2 steps) as a colorless oil. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.30 (m, 5 H), 4.32 (d, J = 3.95 Hz, 1 H), 3.40 (t, J = 11 Hz, 2 H), 3.23 and 3.34 (2 s, 6 H), 2.76 (m, 3 H), 2.36 (s, 3 H), 1.02 (d, J = 6.8 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 141.6, 128.1, 127.0, 126.8, 85.0, 71.6, 64.6, 58.8, 56.7, 53.0, 39.4, 8.8 ppm. $C_{14}H_{23}NO_2$: calcd. C 70.85, H 9.77, N 5.90; found C 70.77, H 9.75, N 5.90. $[\alpha]_D^{20}$ = –53.08 (c = 1.32, $CHCl_3$).

(2-Methoxyethyl)[(1*S*,2*S*)-2-methoxy-1-methyl-2-phenylethyl]methylamine (1*S*,2*S*)-8b: A solution of methoxyacetyl chloride (5.56 mL, 60 mmol) in dichloromethane (30 mL) was added dropwise over 30 min, in order to keep the temperature at –20 °C, to a solution of (1*S*,2*S*)-(+)-pseudoephedrine (9.9 g, 60 mmol) and triethylamine (11.15 mL, 80 mmol) in dichloromethane (130 mL). The reaction mixture was stirred at this temperature for 2 h and then poured into a saturated solution of NH_4Cl. The aqueous layer was extracted with dichloromethane (2 × 50 mL) and the combined organic phases were washed with brine, dried with $MgSO_4$, and filtered off. The solvents were removed under reduced pressure to afford the acetamide derivative as a white solid (9.95 g) which was used without further purification. A solution of the acetamide (8.40 g) in THF (70 mL) was added dropwise over 1 h to a slurry of potassium hydride (2.2 g, 55 mmol) in THF (200 mL). The mixture was stirred for 16 h, after which a solution of MeI (5.08 g, 35.5 mmol) in THF (50 mL) was added. After a further 3 h, the reaction was carefully quenched by addition of ice-cold water (400 mL), and the aqueous layer extracted with diethyl ether (3 × 150 mL). The organic layer was dried with K_2CO_3 and filtered. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel using cyclohexane/ethyl acetate (50:50) as eluent to afford the methoxy-acetamide derivative (5.02 g, 55%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33 (m, 5 H), 4.21 (m, 1 H), 4.07 (m, 1 H), 3.99 (m, 1 H), 3.39, 3.38, 3.15, and 3.12 (4s, 6 H), 2.87 and 2.91 (2s, 3 H, H_6), 0.98 (d, J = 5.8 Hz) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.6, 169.6, 139.5, 139.3, 129.0, 128.8, 128.7, 127.9, 127.8, 85.1, 84.9, 72.2, 59.3, 59.1, 57.2, 56.7, 27.3, 15.9, 14.3 ppm. The methoxy acetamide derivative (5.02 g, 20 mmol) was slowly added to a solution of $LiAlH_4$ (1.52g, 40 mmol) in diethyl ether (120 mL) and the reaction mixture was heated under reflux for 3 d. The hydrolysis was carried out at 0 °C with an aqueous solution of sodium/potassium tartrate (100 mL). The mixture was stirred for 16 h and then the aqueous layer was extracted with diethyl ether (3 × 50 mL). The combined organic layers were dried with K_2CO_3, filtered, and the solvent was removed under reduced pressure. The product was purified by column chromatography on silica gel with cyclohexane/ethyl acetate/NEt_3 (50:45:5) as eluent to afford amino ether **8b** (3.79 g, 80%) as a colorless oil. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.31 (m, 5 H), 4.02 (d, J = 8.9 Hz, 1 H), 3.50 (t, J = 6.3 Hz, 2 H), 3.36 (s, 3 H), 3.13 (s, 3 H), 2.97 (m, 1 H), 2.86 (m, 1 H), 2.75 (m, 1 H), 2.42 (s, 3 H), 0.67 (d, J = 6.8 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.9, 128.3, 127.8, 126.7, 86.5, 71.8, 63.6, 59.9, 56.4, 52.9, 39.0, 11.9 ppm. $C_{14}H_{23}NO_2$: calcd. C 70.85, H 9.77, N 5.90; found C 70.89, H 9.81, N 5.72. $[\alpha]_D^{20}$ = +86.05 (c = 1.45, $CHCl_3$).

General Procedure A. Nucleophilic Ring-Opening of *meso*-Epoxides by Organolithium/(–)-Sparteine/BF_3·Et_2O: A solution of salt-free RLi (4 mmol) was added dropwise, under argon, to a cooled (–78 °C) solution of (–)-sparteine (0.92 mL, 4 mmol) in the required solvent (12 mL). After stirring for 30 m at this temperature, the epoxide (2 mmol) was injected with a syringe. A solution of BF_3·Et_2O (0.38 mL, 3 mmol) in the appropriate solvent (2 mL) was slowly (over 5 min) added in order to maintain the temperature at –78 °C. After stirring for 10 min, the reaction was quenched with MeOH (2 mL) and NEt_3 (3 mL) and then the mixture was allowed to reach room temperature. An aqueous solution of 5% H_2SO_4 (10 mL) was then slowly added to the reaction mixture. The aqueous layer was extracted with Et_2O (3 × 50 mL), the combined organic phases were washed with brine, dried with $MgSO_4$, and filtered. The solvents were removed under reduced pressure and the product was then subjected to flash chromatography (FC) on SiO_2. The enantiomeric excess of the compounds was determined by ^{31}P NMR spectroscopy, as reported previously.[19]

(1*R*,2*S*)-*trans*-2-Phenyl-1-cyclohexanol (2):[5] The product was isolated by FC (pentane/diethyl ether, 80:20) as a white solid. The NMR spectra of **2** are identical to those reported previously.[5] ^{31}P NMR [162 MHz, (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine, $CDCl_3$]: δ = 141.60 (s, 74.5%), 142.98 (s, 25.5%) ppm. *ee* = 49%. $[\alpha]_D^{20}$ = –24 (c = 1.26, benzene) for 49% *ee* {ref.[5] $[\alpha]_D^{20}$ = –22.4 (c = 1.26, benzene) for 47% *ee*}. M.p. 57 °C (ref.[46] 56–57 °C).

***trans*-2-Butyl-1-cyclohexanol (3):**[5] The product was isolated by FC (pentane/diethyl ether, 85:15) as a colorless oil. The NMR spectra of **3** are identical to those reported previously.[5] ^{31}P NMR [162 MHz, (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanedi-

amine, $CDCl_3$]: δ = 143.38 (s, 50%), 140.07 (s, 50%) ppm. *ee* = 0%.

***trans*-2-Methyl-1-cyclohexanol (4):**[47] The product was isolated by FC (pentane/diethyl ether, 85:15) as a colorless oil. The NMR spectra of **4** are identical to those reported previously.[47] ^{31}P NMR [162 MHz, (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine, $CDCl_3$]: δ = 143.32 (s, 51.5%), 140.14 (s, 48.5%) ppm. *ee* = 3%.

***trans*-2-Benzyl-1-cyclohexanol (5):**[48] The product was isolated by FC (pentane/diethyl ether, 80:20) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28 (m, 5 H), 3.23 (m, 1 H), 3.10 (dd, ^3J = 3.9, ^2J = 13 Hz, 1 H), 2.38 (dd, ^3J = 9.2, ^2J = 13 Hz, 1 H), 1.99 (m, 1 H), 1.54 (m, 6 H), 1.12 (m, 1 H), 0.93 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.7, 129.4, 128.1, 74.5, 125.7, 47.0, 39.0, 35.8, 29.9, 25.4, 24.9 ppm. ^{31}P NMR [162 MHz, (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine, $CDCl_3$]: δ = 143.55 (s, 50%), 140.46 (s, 50%) ppm; *ee* = 0%. M.p. 76 °C (ref.[48] 76–77 °C).

***trans*-2-(1-Cyclohexenyl)-1-cyclohexanol (6):**[49] The product was isolated by FC (pentane/diethyl ether, 85:15) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.59 (br. s, 1 H), 3.40 (dt, *J* = 4.2, 10 Hz, 1 H), 1.23 (m, 5 H), 2.03 (m, 3 H), 1.92 (m, 3 H), 1.66 (m, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.7, 124.9, 70.8, 55.4, 34.3, 30.2, 35.2, 26.2, 25.6, 23.3, 23.0 ppm. ^{31}P NMR [162 MHz, (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine, in the presence of S_8, $CDCl_3$]: δ = 82.60 (s, 50%), 81.94 (s, 50%) ppm. *ee* = 0%.

***trans*-2-(1-Hexynyl)-1-cyclohexanol (7):**[50] The product was isolated by FC (pentane/diethyl ether, 90:10) as a colorless oil. The NMR spectra of **7** are identical to those reported previously.[50] ^{31}P NMR [162 MHz, (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine, $CDCl_3$]: δ = 140.91 (s, 50%), 139.71 (s, 50%) ppm. *ee* = 0%.

(1*R*,2*S*)-*trans*-2-(2-Methylphenyl)-1-cyclohexanol (10):[51] The product was isolated by FC (pentane/diethyl ether, 85:15) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.21 (m, 4 H), 4.02 (dt, *J* = 4.3, 9.7 Hz, 1 H), 2.81 (ddd, *J* = 3.4, 10, 12 Hz, 1 H), 2.42 (s, 3 H), 2.14 (m, 1 H), 1.86 (m, 2 H), 1.83 (m, 2 H), 1.41 (m, 4 H) ppm. ^{13}C NMR (200 MHz, $CDCl_3$): δ = 141.4, 137.1, 130.5, 126.4, 126.1, 125.4, 74.3, 47.7, 34.5, 33.1, 26.2, 25.1, 19.8 ppm. ^{31}P NMR [162 MHz, (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine, $CDCl_3$]: δ = 143.22 (s, 82.5%), 141.67 (s, 17.5%) ppm. *ee* = 65%. $[\alpha]_D^{20}$ = –42 (*c* = 1.28, $CHCl_3$) for 65% *ee* {ref.[51] $[\alpha]_D^{20}$ =–63.9 (*c* = 1.26, benzene) for 90% *ee*}.

(1*R*,2*S*)-*trans*-2-(3-Methylphenyl)-1-cyclohexanol (11):[52] The product was isolated by FC (pentane/diethyl ether, 80:20) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.08 and 7.26 (2 m, 4 H), 3.67 (dt, *J* = 4.2, 10 Hz, 1 H), 2.40 (m, 1 H), 2.37 (s, 3 H), 2.15 (m, 1 H), 1.86 (m, 2 H), 1.77 (m, 1 H), 1.61 (m, 1 H), 1.55 (m, 1 H), 1.43 (m, 3 H) ppm. ^{13}C NMR (200 MHz, $CDCl_3$): δ = 143.0, 138.3, 128.6, 127.5, 124.8,. 74.3, 53.1, 34.3, 33.2, 26.0, 25.0, 21.4 ppm. ^{31}P NMR [162 MHz, (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine, $CDCl_3$]: δ = 141.35 (s, 32%), 143.18 (s, 68%) ppm. *ee* = 36%. $[\alpha]_D^{20}$ = –9 (*c* = 0.90, $CHCl_3$) for 36% *ee*.

(1*R*,2*S*)-*trans*-2-(4-Methylphenyl)-1-cyclohexanol (12):[51] The product was isolated by FC (pentane/diethyl ether, 80:20) as a white solid.^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.15 (m, 4 H), 3.67 (m, 1 H), 2.41 (ddd, *J* = 3.5, 9.9, 12.3 Hz, 1 H), 2.35 (s, 3 H), 2.14 (m, 1 H), 1.86 (m, 2 H), 1.71 (m, 1 H), 1.39 (m, 5 H) ppm. ^{13}C NMR (200 MHz, $CDCl_3$): δ = 140.4, 136.3, 129.4, 127.8, 74.3, 52.7, 34.4, 33.4, 26.0, 25.0, 21.0 ppm. ^{31}P NMR [162 MHz, (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine, $CDCl_3$]: δ = 143.18 (s, 76%), 141.58 (s, 24%) ppm. *ee* = 52%. $[\alpha]_D^{20}$ = –31 (*c* = 1.28, MeOH) for 52% *ee* {ref.[51] $[\alpha]_D^{20}$ = –59.5 (*c* = 1.37, MeOH) for 99% *ee*}. M.p. 70–71 °C (ref.[53] 72–73 °C).

(1*R*,2*S*)-*trans*-2-(2-Methoxyphenyl)-1-cyclohexanol (13): The product was isolated by FC (pentane/diethyl ether, 70:30) as a pale-yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.25–6.97 (m, 4 H), 3.83 (s, 3 H), 3.75 (m, 1 H), 3.03 (m, 1 H), 2.16 (m, 1 H), 1.78 (m, 4 H), 1.44 (m, 4 H) ppm. ^{13}C NMR (200 MHz, $CDCl_3$): δ = 159.8, 131.5, 127.3, 120.9, 111.9, 73.8, 55.4, 45.9, 35.1, 32.3, 26.1, 25.1 ppm. ^{31}P NMR [162 MHz, (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine, in the presence of S_8, $CDCl_3$]: δ = 82.25 (s, 57.5%), 82.13 (s, 42.5%) ppm. *ee* = 15%. $[\alpha]_D^{20}$ = –5 (*c* = 1.52, MeOH) for 15% *ee*. IR: $\tilde{\nu}$ = 3392, 2929, 2853, 1599, 1492, 1461, 1240, 1052, 752 cm^{-1}. M.p. 50–51 °C. $C_{13}H_{18}O_2$: calcd. C 75.69, H 8.80; found C 75.68, H 8.76.

(1*R*,2*S*)-*trans*-2-(4-Methoxyphenyl)-1-cyclohexanol (14):[51] The product was isolated by FC (pentane/diethyl ether, 70:30) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28 (m, 2 H), 6.91 (m, 2 H), 1.40 (m, 3 H), 3.83 (s, 3 H), 3.62 (m, 1 H), 2.39 (ddd, *J* = 3.5, 9.9, 12.2 Hz, 1 H), 2.15 (m, 1 H), 1.87 (m, 2 H), 1.85 (m, 1 H), 1.52 (m, 2 H) ppm. ^{13}C NMR (200 MHz, $CDCl_3$): δ = 158.8, 135.5, 129.1, 114.5, 74.9, 55.5, 52.7, 34.7, 33.8, 26.5, 25.4 ppm. ^{31}P NMR [162 MHz, (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine, $CDCl_3$]: δ = 141.65 (s, 72%), 142.98 (s, 28%) ppm. *ee* = 44%. $[\alpha]_D^{20}$ = –24 (*c* = 1.46, MeOH) for 44% *ee* {ref.[51] $[\alpha]_D^{20}$ = –55.4 (*c* = 1.46, MeOH) for 99% *ee*}. M.p. 70–71 °C (ref.[47] 70–71 °C).

(1*R*,2*S*)-*trans*-2-(3-Trifluoromethylphenyl)-1-cyclohexanol (15): The product was isolated by FC (pentane/diethyl ether, 80:20) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.53 (m, 2 H), 7.46 (m, 2 H), 3.62 (m, 1 H, H_1), 2.54 (ddd, *J* = 3.4, 10.1, 12.3 Hz, 1 H, H_2), 2.16 (m, 2 H), 1.80 (m, 2 H), 1.60 (m, 2 H), 1.43 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.7, 131.4, 129.1, 124.5, 123.7, 74.2, 53.0, 34.9, 33.4, 25.9, 25.0 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –62.97 ppm. ^{31}P NMR [162 MHz, (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine, $CDCl_3$]: δ = 143.78 (s, 80%), 141.81 (s, 20%) ppm. *ee* = 60%. $[\alpha]_D^{20}$ = –15 (*c* = 1.49, MeOH) for 60% *ee*. M.p. 53–54 °C. IR: $\tilde{\nu}$ = 3366, 2929, 1149, 1319, 1102, 801, 701 cm^{-1}. $C_{13}H_{15}F_3O$: calcd. C 63.93, H 6.19; found C 63.89, H 6.17.

(1*R*,2*S*)-*trans*-2-(4-Fluorophenyl)-1-cyclohexanol (16): The product was isolated by FC (pentane/diethyl ether, 80:20) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.25 (m, 2 H), 7.04 (m, 2 H), 3.62 (m, 1 H), 2.44 (ddd, *J* = 3.5, 9.9, 12.0 Hz, 1 H), 2.13–1.46 (m, 8 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.3, 161.0, 139.3, 129.6, 129.5, 116.0, 115.8, 74.9, 53.8, 34.9, 33.8, 26.3, 25.4 ppm.^{19}F NMR (376 MHz, $CDCl_3$): δ = –116.8 ppm. ^{31}P NMR [162 MHz, (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine, $CDCl_3$]: δ = 143.28 (s, 76.5%), 141.71 (s, 23.5%) ppm. *ee* = 53%. $[\alpha]_D^{20}$ = –12.3 (*c* = 1.52, MeOH) for 53% *ee*. M.p. 63–64 °C. IR: $\tilde{\nu}$ = 3319, 2935, 1064, 1509, 1227, 1059, 810 cm^{-1}. $C_{12}H_{15}FO$: calcd. C 74.20, H 7.78; found C 74.18, H 7.74.

(1*R*,2*S*)-*trans*-2-(2-Naphthyl)-1-cyclohexanol (17):[5] The product was isolated by FC (pentane/diethyl ether, 80:20) as a white solid. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.30–7.90 (m, 7 H), 3.62 (m, 1 H), 2.53 (m, 1 H), 1.30–2.30 (m, 8 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 133.6, 132.6, 128.4, 127.6, 127.6, 126.7, 126.1,125.9, 125.5, 74.2, 53.3, 34.5, 33.3, 26.0, 25.1 ppm. ^{31}P NMR [162 MHz, (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine, $CDCl_3$]: δ = 142.59 (s, 84.9%), 140.54 (s, 15.1%) ppm. *ee* = 70%. $[\alpha]_D^{20}$ = –20.2 (*c* = 1.035, $CHCl_3$) for 70% *ee* {ref.[5] $[\alpha]_D^{20}$ = –7.8 (*c* = 1.05, $CHCl_3$) for 33% *ee*}. M.p. 89 °C (2-propanol) (ref.[54] 90 °C, 2-propanol). Recrystallization from EtOH afforded white crystals

of racemic material. Subsequent filtration and concentration of the mother liquor under reduced pressure gave an enantiomerically enriched solid (96% *ee*). The enantiomeric excess was determined by ^{31}P NMR spectroscopy as well as by HPLC (Chiral OD; *i*PrOH/hexane, 2:98; 1 mL min^{-1}; 254 nm). ^{31}P NMR [162 MHz, (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine, $CDCl_3$]: δ = 142.59 (s, 97.9%), 140.54 (s, 2.1%) ppm. *ee* = 96%. $[\alpha]_D^{20}$ = –25.6 (*c* = 1.01, $CHCl_3$) for 96% *ee*.

(1*R*,2*S*)-*trans*-2-(1-Naphthyl)-1-cyclohexanol (18):[5] The product was isolated by FC (pentane/diethyl ether, 80:20) as a white solid. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.22–7.55 (m, 7 H), 4.02 (m, 1 H), 3.51 (br. s, 1 H), 2.27 (br. s, 1 H), 1.97 (m, 2 H), 1.85 (m, 1 H), 1.59 (m, 6 H) ppm. ^{13}C NMR (200 MHz, $CDCl_3$): δ = 139.6, 134.2, 132.7, 129.0, 126.1, 125.7, 125.8, 123.3, 74.3, 46.7, 34.8, 34.0, 26.5, 25.2 ppm. ^{31}P NMR [162 MHz, (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine, $CDCl_3$]: δ = 143.41 (s, 92.5%), 140.85 (s, 7.5%) ppm. *ee* = 85%. $[\alpha]_D^{20}$ = –60 (*c* = 1.46, MeOH) for 85% *ee* {ref.[51] $[\alpha]_D^{20}$ = –72.9 (*c* = 1.47, MeOH,) for 99% *ee*}. M.p.129–130 °C (ref.[55] 129–130 °C). Recrystallization from EtOH afforded white crystals of racemic material. Subsequent filtration andconcentration of the mother liquor under reduced pressuregave an enantiomerically enriched solid (*ee* > 98%). ^{31}P NMR [162 MHz, (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine, $CDCl_3$]: δ = 142.59 (s, >98%), 140.54 (s, <2%) ppm. *ee* > 98%. $[\alpha]_D^{20}$ = –71.5 (*c* = 1.38, MeOH) for 98% *ee*.

(1*R*,2*S*)-*trans*-2-(9-Anthracenyl)-1-cyclohexanol (19): The product was isolated by FC (pentane/diethyl ether, 80:20) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.61–7.54 (m, 8 H), 4.02 (dt, *J* = 4.4, 10.1 Hz, 1 H), 4.16 (ddd, *J* = 4, 10.2, 12.6 Hz, 1 H), 2.57 (m, 1 H), 2.35 (m, 1 H), 2.03 (m, 3 H), 1.67 (m, 4 H) ppm. ^{13}C NMR (200 MHz, $CDCl_3$): δ = 134.5, 132.4, 130.2, 129.7, 126.5, 125.0, 124.9, 126.2, 72.8, 48.7, 32.0, 30.1, 27.3, 25.5 ppm. ^{31}P NMR [162 MHz, (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine, $CDCl_3$]: δ = 143.35 (s, 70.5%), 139.76 (s, 29.5%) ppm. *ee* = 41%. $[\alpha]_D^{20}$ = –10.4 (*c* = 1.48, MeOH) for 41% *ee*. M.p. 69–70 °C. IR: $\tilde{\nu}$ = 3483, 2929, 1623, 1449, 1028, 741 cm^{-1}.

(1*R*,2*S*)-*trans*-2-Phenyl-1-cyclopentanol (26):[56] The product was isolated by FC (pentane/diethyl ether, 80:20) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32–7.26 (m, 4 H), 4.16 (q, *J* = 7.24 Hz, 1 H), 2.89 (dt, *J* = 7.5, 9.5 Hz, 1 H), 2.14 (m, 2 H), 1.80 (m, 6 H) ppm. ^{13}C NMR (200 MHz, $CDCl_3$): δ = 141.9, 127.1, 126.0, 124.9, 78.9, 52.9, 32.4, 30.4, 20.3 ppm. ^{31}P NMR [162MHz, (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine, $CDCl_3$]: δ = 141.85 (s, 68.5%), 138.69 (s, 31.5%) ppm. *ee* = 37%. $[\alpha]_D^{20}$ = –29.8 (*c* = 1.34, EtOH) for 37% *ee* {ref.[57] $[\alpha]_D^{20}$ = +83.6 (*c* = 1.565, EtOH) for (1*S*, 2*R*)-**28**, 99% *ee*}

(1*R*,2*S*)-*trans*-2-(1-Naphthyl)-1-cyclopentanol (27): The product was isolated by FC (pentane/diethyl ether, 80:20) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.25–7.53 (m, 7 H), 3.62 (q, *J* = 6.4 Hz, 1 H), 3.82 (dt, *J* = 6.7, 8.4 Hz, 1 H), 2.39–1.89 (m, 7 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.3, 139.9, 132.9, 129.2, 126.0, 125.9, 124.2, 122.8, 79.7, 49.5, 34.4, 32.1, 22.4 ppm. ^{31}P NMR [162 MHz, (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine, $CDCl_3$]: δ = 141.90 (s, 76.5%), 138.60 (s, 23.5%) ppm. *ee* = 53%. $[\alpha]_D^{20}$ = –18.7 (*c* = 1.05, $CHCl_3$) for 53% *ee*. M.p. 71–72 °C. IR: $\tilde{\nu}$ = 3244, 2952, 1596, 1397, 1056, 778 cm^{-1}. $C_{15}H_{16}O$: calcd. C 84.87, H 7.60; found C 84.98, H 7.53.

(1*R*,2*S*,5*S*)-*trans*-4-(*tert*-Butyldimethylsiloxy)-2-(1-naphthyl)-1-cyclopentanol (28): The product was isolated by FC (pentane/diethyl ether, 80:20) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.29–7.50 (m, 7 H), 4.68 (q, *J* = 7.2 Hz, 1 H), 4.57 (m, 1 H), 3.76 (dt, *J* = 7.5, 9.0 Hz, 1 H), 2.58 (m, 1 H), 2.08 (m, 1 H), 1.94 (m, 1 H), 1.85 (m, 1 H), 0.95 (s, 9 H), 0.12 (s, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.6, 134.3, 132.7, 129.2, 126.2, 126.1, 125.8, 124.1, 78.8, 71.5, 48.3, 44.7, 42.9, 26.3, –4.3. ^{31}P NMR [162 MHz, (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine, $CDCl_3$]: δ = 142.43 (s, 62%), 137.09 (s, 38%) ppm. *ee* = 24%. $[\alpha]_D^{20}$ = +0.8 (*c* = 1.22, $CHCl_3$) for 24% *ee*. IR: $\tilde{\nu}$ = 3380, 3050, 2959, 1596, 1471, 1047, 777 cm^{-1}. $C_{21}H_{30}O_2Si$: calcd. C 73.63, H 8.20; found C 73.40, H 7.90. Derivatization of alcohol with (*R*)-(–)-2-methoxy-2-phenylacetic acid: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.91 (dt, *J* = 5.8, 8.6 Hz, 41%), 3.81 (dt, *J* = 5.8, 8.6 Hz, 59%), 3.26 (s, 61%), 3.22 (s, 39%) ppm. Derivatization of alcohol with (*S*)-(+)-2-methoxy-2-phenylacetic acid: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.98 (dt, *J* = 5.8, 8.6 Hz, 60.5%), 3.84 (dt, *J* = 5.8, 8.6 Hz, 39.5%), 3.31 (s, 38.5%), 3.27 (s, 61.5%) ppm.

(1*R*,2*S*,5*R*)-*trans*-(4-*tert*-Butyldimethylsiloxy)-2-(1-naphthyl)-1-cyclopentanol (29): The product was isolated by FC (pentane/diethyl ether, 80:20) as acolorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.37–7.25 (m, 7 H), 4.47 (m, 1 H), 4.17 (m, 1 H), 4.11 (dt, *J* = 3, 8.5 Hz, 1 H), 2.43–2.01 (m, 4 H), 0.98 (s, 9 H), 0.16 (s, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.2, 134.3, 132.7, 129.1, 126.4, 125.7, 124.5, 122.2, 80.4, 74.8, 49.1, 44.0, 42.5, 26.2, –4.3 ppm. ^{31}P NMR [162 MHz, (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine, $CDCl_3$]: δ = 142.95 (s, 81%), 139.28 (s, 19%) ppm. *ee* = 62%. $[\alpha]_D^{20}$ = –1.5 (*c* = 1.27, $CHCl_3$) for 62% *ee*. IR: $\tilde{\nu}$ = 3600, 3051, 2889, 1598, 1471, 1063, 777 cm^{-1}. $C_{21}H_{30}O_2Si$: calcd. C 73.63, H 8.20; found C 73.34, H 7.95. Derivatization of alcohol with (*R*)-(–)-2-methoxy-2-phenylacetic acid: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.29 (m, minor), 4.16 (dt, *J* = 7.5, 9.6 Hz, major), 3.22 (s, 81%), 3.16 (s, 19%) ppm. Derivatization of alcohol with (*S*)-(+)-2-methoxy-2-phenylacetic acid: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.39 (m, major), 4.25 (dt, *J* = 7.5, 9.6 Hz, minor), 3.31 (s, 20%), 3.25 (s, 80%) ppm.

(1*R*,2*S*)-*trans*-2-Phenyl-1-cycloheptanol (30): The product was isolated by FC (pentane/diethyl ether, 80:20) as acolorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37–7.25 (m, 5 H), 3.79 (dt, *J* = 3.5, 13.7 Hz, 1 H), 2.60 (dt, *J* = 3.1, 9.7 Hz, 1 H), 2.03–1.69 (2 m, 11 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.7, 128.7, 127.6, 126.5, 77.7 (C-1), 55.3 (C-2), 35.2, 32.0, 27.3, 26.7, 21.8. ^{31}P NMR [162 MHz, (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine, $CDCl_3$]: δ = 143.08 (s, 64.5%), 141.20 (s, 35.5%) ppm; *ee* = 29%. $[\alpha]_D^{20}$ = +2.52 (*c* = 0.99, $CHCl_3$) for 29% *ee*. IR: $\tilde{\nu}$ = 3400, 2910, 1440, 1010, 750, 690 cm^{-1}. $C_{13}H_{18}O$: calcd. C 82.06, H 8.41; found C 82.18, H 8.24. Derivatization of alcohol with (*R*)-(–)-2-methoxy-2-phenylacetic acid: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.26 (s, 65%), 3.11 (s, 35%), 2.85 (dt, *J* = 3.1, 10 Hz, minor), 2.80 (dt, *J* = 3.1, 10 Hz, major) ppm. Derivatization of alcohol with (*S*)-(+)-2-methoxy-2-phenylacetic acid: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.16 (s, 34%), 3.11 (s, 66%), 2.85 (dt, *J* = 3.1, 10 Hz, major), 2.79 (dt, *J* = 3.1, 10 Hz, minor) ppm.

(1*R*,2*S*)-*trans*-2-(1-Naphthyl)-1-cycloheptanol (31): The product was isolated by FC (pentane/diethyl ether, 80:20) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.22–7.53 (m, 7 H), 4.16 (br. s, 1 H), 3.58 (br. s, 1 H), 2.15–1.75 (m, 11 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.4, 132.5, 129.3, 127.3, 126.4, 126.1, 126.0, 123.8, 77.2, 48.7, 36.0, 33.1, 28.0, 27.4, 22.4 ppm. ^{31}P NMR [162 MHz, (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine, in the presence of S_8, $CDCl_3$]: δ = 143.08 (s, 25.5%), 81.16 (s, 74.5%) ppm; *ee* = 49%. ^{31}P NMR [162 MHz, (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine, $CDCl_3$]: δ = 140.57 (br. s, minor), 143.34 (br. s, major) ppm. $[\alpha]_D^{20}$ = –6.09 (*c* = 1.05, $CHCl_3$) for 49% *ee*. M.p. 98–99 °C. IR: $\tilde{\nu}$ = 3271, 2928, 1596, 1442, 1062, 777 cm^{-1}. $C_{17}H_{20}O$: calcd. C 84.96, H 8.39; found C 84.82, H 8.14.

(1*R*,2*S*)-*trans*-2-Phenyl-1-cyclooctanol (32): The product was isolated by FC (pentane/diethyl ether, 80:20) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28 (m, 5 H), 3.95 (m, 1 H), 2.76 (dt, J = 5.6, 10 Hz, 1 H), 2.02–1.68 (m, 13 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 146.2, 129.9, 129.3, 128.4, 127.0, 76.4, 51.7, 32.9, 32.4, 27.5, 27.4, 25.7, 23.5 ppm. ^{31}P NMR [162MHz, (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine, $CDCl_3$]: δ = 143.79 (s, 81%), 142.16 (s, 19%) ppm. *ee* = 62%.$[\alpha]_D^{20}$ = +4.95 (c = 1.07, $CHCl_3$) for 62% *ee*. IR: $\tilde{\nu}$ = 3960, 2930, 1640, 1470, 1052, 740 cm^{-1}. $C_{14}H_{20}O$: calcd. C 82.30, H 9.87; found C 82.12, H 9.75. Derivatization of alcohol with (*R*)-(–)-2-methoxy-2-phenylacetic acid: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.10 (s, 78%), 3.08 (s, 22%), 3.05 (ddd, minor), 3.02 (ddd, J = 2.6, 7.8, 11 Hz, major) ppm. Derivatization of alcohol with (*S*)-(+)-2-methoxy-2-phenylacetic acid: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.10 (s, 21%), 3.08 (s, 79%), 3.04 (ddd, J = 2.6, 7.8, 11 Hz, major), 3.02 (ddd, minor) ppm.

(1*R*,2*S*)-*trans*-2-(1-Naphthyl)norbornanol (33): The product was isolated by FC (pentane/diethyl ether, 80:20) as aviscous oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.12–7.51 (m, 7 H), 4.07 (br. s, 1 H), 3.58 (dd, J = 6.8, 8.8 Hz, 1 H), 2.54 (br. s, 1 H), 2.20–1.49 (m, 7 H) ppm. ^{13}C NMR (200 MHz, $CDCl_3$): δ = 142.1, 134.6, 132.7, 129.4, 127.0, 126.2, 125.8, 124.9, 123.5, 81.0, 45.6, 43.7, 41.9, 36.3, 28.8, 26.0 ppm. ^{31}P NMR [162 MHz, (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine, $CDCl_3$]: δ = 140.42 (s, 33%), 141.12 (s, 67%) ppm. *ee* = 34%. $[\alpha]_D^{20}$ = –14.07 (c = 1.6, $CHCl_3$) for 34% *ee*. IR: $\tilde{\nu}$ = 3380, 2970, 1590, 1390, 1062, 770, 720 cm^{-1}. $C_{17}H_{18}O$: calcd. C 85.67, H 7.61; found C 85.63, H 7.59. Derivatization of alcohol with (*R*)-(–)-2-methoxy-2-phenylacetic acid: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.49 (t, J = 7.4 Hz, 36%), 3.44 (t, J = 7.4 Hz, 64%), 3.18 (s, 35.5%), 3.15 (s, 64.5%) ppm. Derivatization of alcohol with (*S*)-(+)-2-methoxy-2-phenylacetic acid: ^{1}H NMR (400 MHz, $CDCl_3$) 3.49 (t, J = 7.4 Hz, 62.5%), 3.44 (t, J = 7.4 Hz, 37.5%), 3.18 (s, 71%), 3.15 (s, 19%) ppm.

(1*R*,2*S*)-*trans*-2-Phenyl-5,6-cycloocten-1-ol (39): The product was isolated by FC (pentane/diethyl ether, 80:20) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.15 (m, 5 H), 5.79 (ddd, J = 1, 5.4, 16.8 Hz, 1 H), 5.60 (m, 1 H), 4.08 (ddd, J = 3.6, 5.7, 9.3 Hz, 1 H), 2.93 (ddd, J = 3.9, 9.4, 11.2 Hz), 1.67–2.34 (m, 9 H) ppm. ^{13}C NMR (200 MHz, $CDCl_3$): δ = 144.4, 131.9, 129.2, 128.8, 127.2, 74.6, 49.8, 34.1, 34.0, 25.2, 24.9 ppm. ^{31}P NMR [162MHz, (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine, $CDCl_3$]: δ = 145.59 (s, 75.5%), 142.35 (s, 24.5%) ppm; *ee* = 51%. $[\alpha]_D^{20}$ = +14.85 (c = 1.38, $CHCl_3$) for 51% *ee*. IR: $\tilde{\nu}$ = 3450, 2980, 1610, 1410, 1060, 720 cm^{-1}. $C_{14}H_{28}O$: calcd. C 83.12, H 8.97; found C 81.48, H 10.70.

Nucleophilic Opening of Cyclohexene Oxide by *n*BuLi/8a/BF_3·Et_2O To Give *trans*-2-Butyl-1-cyclohexanol (3): The reactions were performed according to the general procedure A but using (1*R*,2*S*)-**8a** instead of (–)-sparteine. ^{31}P NMR [162 MHz, (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine, $CDCl_3$]: δ = 143.11 (s, 71%), 139.78 (s, 31%) ppm. *ee* = 38%. $[\alpha]_D^{20}$ = –22.5 (c = 1.46, $CHCl_3$) for 35% *ee* {ref.[5] $[\alpha]_D^{20}$ = –6 (c = 1.08, $CHCl_3$) for 12% *ee*}.

Nucleophilic Opening of Cyclohexene Oxide by *n*BuLi/8b/BF_3·Et_2O To Give *trans*-2-Butyl-1-cyclohexanol (3): The reactions were performed according to the general procedure A but using (1*S*,2*S*)-**8b** instead of (–)-sparteine. ^{31}P NMR [162 MHz, (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine, $CDCl_3$]: δ = 143.22 (s, 39%), 139.96 (s, 61%) ppm; *ee* = 22%. $[\alpha]_D^{20}$ = +12.6 (c = 1.48, $CHCl_3$) for 22% *ee* {ref.[5] $[\alpha]_D^{20}$ = –6 (c = 1.08, $CHCl_3$) for 12% *ee*}.

Nucleophilic Opening of Cyclohexene Oxide by PhLi/9/BF_3·Et_2O To Give *trans*-2-Butyl-1-cyclohexanol (3): The reactions were performed according to the general procedure A but using (4*S*)-**9** instead of (–)-sparteine. ^{31}P NMR [162 MHz, (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine, $CDCl_3$]: δ = 143.02 (s, 23%), 141.71 (s, 77%) ppm; *ee* = 54%. $[\alpha]_D^{20}$ = +26.4 (c = 1.26, benzene) for 54% *ee* {ref.[5] $[\alpha]_D^{20}$ = –22.4 (c = 1.26, benzene) for 47% *ee*}.

1-Cycloocta-2,5-dienol (36):[58] A solution of *s*BuLi (3 mL, 1.3 M in hexane, 4 mmol) was added dropwise to a cooled (–90 °C) solution of (–)-sparteine (0.92 mL, 4 mmol) in Et_2O (10 mL) under argon. After stirring for 30 min at this temperature, a solution of 1,5-cyclooctadiene oxide **35** (248 mg, 2 mmol) in Et_2O (2 mL) was slowly added dropwise (over 5 min). After stirring at –90 °C for 6 h, the reaction was quenched with MeOH (2 mL) and an aqueous solution of 5% H_2SO_4 (10 mL). The aqueous layer was extracted with Et_2O (3 × 50 mL), the combined organic phases were washed with brine, dried with $MgSO_4$, and filtered off. The solvents were removed under reduced pressure and the product was purified by column chromatography on silica gel with pentane/diethyl ether (75:25) as eluent to afford alcohol **36** (186 mg, 75%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.65 (m, 2 H), 5.51 (m, 1 H), 5.37 (m, 1 H), 4.91 (m, 1 H), 2.84 (br. s, 2 H), 2.55 (m, 1 H), 2.09 (m, 1 H), 1.86 (m, 2 H), 1.42 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 134.0, 129.3, 128.9, 127.4, 69.3, 31.8, 29.3, 23.4 ppm. ^{31}P NMR [162 MHz, (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine, in the presence of S_8, $CDCl_3$]: δ = 83.20 (s, 81%), 83.03 (s, 19%) ppm. *ee* = 62%. $[\alpha]_D^{20}$ = –45.95 (c = 1.48, $CHCl_3$) for 62% *ee*. $C_8H_{12}O$: calcd. C 77.38, H 9.74; found C 77.30, H 9.90.

General Procedure B for the Carbenoid Rearrangement of *meso*-Epoxidesby *s*BuLi/(–)-sparteine/BF_3·Et_2O: A solution of *s*BuLi (3 mL, 1.3 M in hexane, 4 mmol) was added dropwise, under argon, to a cooled (–90 °C) solution of (–)-sparteine (0.92 mL, 4 mmol) in Et_2O (12 mL). After stirring for 30 min at this temperature, a solution of epoxide (2 mmol) in Et_2O (2 mL) was injected with a syringe. A solution of BF_3·Et_2O (0.38 mL, 3 mmol) in Et_2O (2 mL) was slowly (over 5 min) added in order to maintain the temperature at –90 °C. After stirring for 10 min, the reaction was quenched with MeOH (2 mL) and Et_3N (3 mL) and then the mixture was allowed to reach room temperature. An aqueous solution of 5% H_2SO_4 (10 mL) was then slowly added to the reaction mixture. The aqueous layer was extracted with Et_2O (3 × 50 mL), the combined organic phases were washed with brine, dried with $MgSO_4$, and filtered. The solvents were removed under reduced pressure and the product was then subjected to FC on SiO_2.

(1*S*)-*endo*-*cis*-Bicyclo[3.3.0]octan-2-ol (34):[36] The reaction was performed according to general procedure B. The product was isolated by FC (pentane/diethyl ether, 80:20) as a colorless oil. The NMR spectra of (1*S*)-**34** are identical to those reported previously.[36] ^{31}P NMR [162 MHz, (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine, $CDCl_3$]: δ = 138.72 (s, 19.5%), 140.76 (s, 80.5%) ppm. *ee* = 61%. $[\alpha]_D^{20}$ = –12.52 (c = 1.025, $CHCl_3$) for 61% *ee* {ref.[36] $[\alpha]_D^{20}$ = –19 (c = 1.0, $CHCl_3$) for 84% *ee*}.

General Procedure C for the Carbenoid Rearrangement of *meso*-Epoxidesby Organolithium/(–)-Sparteine/BF_3·Et_2O: A solution of *s*BuLi (3 mL, 1.3 M in hexane, 4 mmol) was added dropwise, under argon, to a cooled (–90 °C) solution of (–)-sparteine (0.92 mL, 4 mmol) in Et_2O (10 mL). After stirring at this temperature for 30 min, a solution of BF_3·Et_2O (0.38 mL, 3 mmol) in Et_2O (2 mL) was slowly (over 20 min) added in order to maintain the temperature at –90 °C. A solution of epoxide (2 mmol) in Et_2O (2 mL) was then slowly added dropwise (over 20 min). After stirring for 10 min, the reaction was quenched with MeOH (2 mL) and an aqueous solution of 5% H_2SO_4 (10 mL). The aqueous layer was extracted

with Et_2O (3 × 50 mL), the combined organic phases were washed with brine, dried with $MgSO_4$, and filtered. The solvents were removed under reduced pressure and the product was then subjected to FC on SiO_2.

Tricyclo[2.2.1.0]heptan-3-ol (40):[36] The reaction was performed according to general procedure B. The NMR spectra of **40** are identical to those reported previously.[36] ^{31}P NMR [162 MHz, (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine, $CDCl_3$]: δ = 138.86 (s, 52%), 137.02 (s, 48%) ppm. *ee* = 4%.

Cycloocta-2,5-dien-1-ol (36), (1*S*)-Bicyclo[3.3.1]heptan-3-ol (37), and *trans*-8-*sec*-Butylcyclooct-4-en-1-ol (38): The reaction was performed according to general procedure B. The residue was purified by column chromatography on silica gel with pentane/diethyl ether (75:25) as eluent. First to elute was alcohol **36** (173 mg, 7%, R_f = 0.33), then **37** (1.6 g, 65%, R_f = 0.25) and **38** (291 mg, 8%, R_f = 0.42) as colorless oils. **(1*S*)-37:**[59] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.78 (m, 1 H), 5.45 (ddd, *J* = 2.7, 7.6, 11 Hz, 1 H), 4.28 (m, 1 H), 1.39–2.03 (m, 7 H), 0.87 (dt, *J* = 4, 8.9 Hz, 1 H), 0.51 (dt, *J* = 4, 6.1 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 129.6, 127.9, 72.4, 34.2, 26.9, 24.3, 15.9, 11.8 ppm. ^{31}P NMR [162 MHz, (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine, in the presence of S_8, $CDCl_3$]: δ = 82.52 (s, 87.5%), 82.11 (s, 12.5%) ppm. *ee* = 75%. $[\alpha]_D^{20}$ = –86.16 (*c* = 1.03, $CHCl_3$) for 75% *ee*. Derivatization of alcohol with (*R*)-(–)-2-methoxy-2-phenylacetic acid: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.45 (s, 14%), 3.44 (s, 86%), 0.95 (dt, 86%), 0.73 (dt, 14%), 0.57 (dt, 87%), 0.43 (dt, 13%) ppm. Derivatization of alcohol with (*S*)-(+)-2-methoxy-2-phenylacetic acid: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.45 (s, 84%), 3.43 (s, 16%), 0.95 (dt, 13%), 0.73 (dt, 87%), 0.57 (dt, 15%), 0.43 (dt, 85%) ppm. **38:** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.66 (m, 1 H), 5.52 (m, 1 H), 3.75 (m, 1 H), 4.28 (m, 1 H), 1.24–2.27 (m, 14 H), 0.89 (t, *J* = 7.2 Hz, 3 H), 0.82 (d, *J* = 6.7 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 131.1, 130.5, 128.8, 128.2, 73.6, 47.2, 44.2, 36.6, 35.1, 34.3, 28.2, 25.6, 25.4, 25.0, 24.3, 24.1, 18.2, 14.2, 12.9, 12.7 ppm. IR: $\tilde{\nu}$ = 3380, 2903, 1450, 1030, 740 cm^{-1}. $C_{12}H_{22}O$: calcd. C 79.06, H 12.16; found C 79.08, H 12.14.

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