Comprehensive Experimental and Theoretical Studies of Configurationally Labile Epimeric Diamine Complexes of α-Lithiated Benzyl Carbamates

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Abstract: Different primary benzyl-type carbamates were deprotonated by *sec*-butyllithium in the presence of a *tert*-leucinol-derived bis(oxazoline) ligand. The resulting configurationally labile epimeric complexes equilibrated and one diastereomer was strongly favored in the equilibria. After dynamic thermodynamic resolution, the complexes could be trapped with different classes of electrophiles to yield highly enantioenriched secondary benzyl carbamates. The stereochemical course of the substitution reactions was elucidated. High-level quantum chemical investigations were performed and allowed a prediction of both the favored complex and the enantiomeric excess that could be expected within the reactions.

Key words: asymmetric synthesis, carbanions, lithium, bis(oxazoline) ligands, quantum chemical calculations

One of the most important and most challenging features within the field of asymmetric synthesis via chiral carbanions is the configurational stability of the metalated carbanionic species.[1,2] Several research groups have investigated different classes of such metalated carbanions concerning their configurational stability and the possibility to use them as valuable precursors for the synthesis of highly enantioenriched compounds.[3,4]

Configurationally stability is a rare feature, especially if mesomeric stabilization of the carbanion is possible. Nevertheless, if the carbanionic center is a tertiary one, synthetically useful configurational stability, despite possible mesomeric stabilization of the carbanion, can be found [Figure 1, (*R*)-**1**,[5] **2**,[5] (*R*)-**3**,[6] (*S*)-**4**,[3b] (*S*)-**5**,[3c,d,7] (*S*)-**6**[8]]. The complexing abilities of the moieties connected to the carbanionic center, usually by heteroatoms, are important and may even influence the enantiodetermining step of an asymmetric substitution reaction in the very end.[9,10] Only a few configurationally stable benzyllithium derivatives are known [Figure 1, (*R*)-**1**,[5] **2**,[5] (*R*)-**3**,[6] (*S*)-**5**,[3c,d,7] (*S*)-**6**[8]]. More often these compounds exhibit distinct configurational lability. An increasing planarization of the carbanionic center as a result of the stabilization of the anion by resonance[11–14] is usually accompanied by a higher tendency for the formation of solvent-separated ion pairs.[15] Both factors probably facilitate the migration of the lithium cation from one enantiotopic face to the other by complex intra- and intermolecular processes, thus leading to epimerization. Short-lived benzyl anions have been

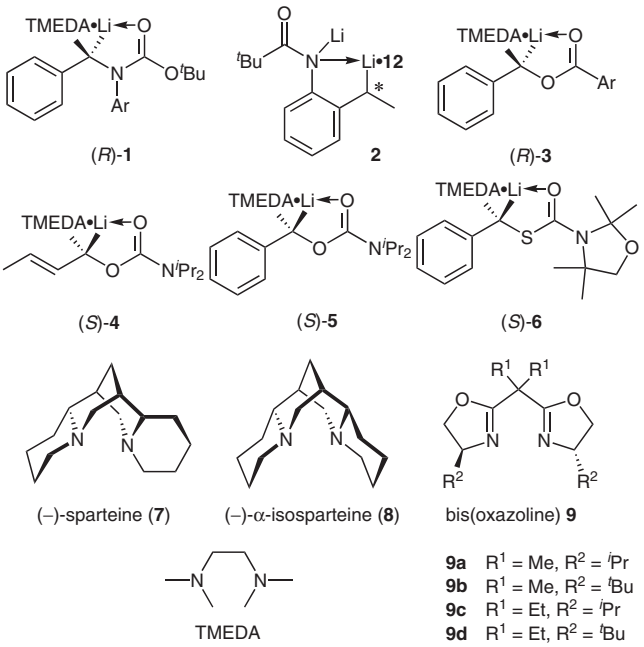

Figure 1 Configurationally stable diamine complexes of α-heterosubstituted, α-lithiated mesomerically stabilized carbanions and diamine ligands used

trapped in situ with high enantiomeric excess by deprotonation/reprotonation of optically active phenyl alkanes[14b] as well as in the Haller–Bauer cleavage of tertiary benzyl phenyl ketones.[14a,16] Chiral α-oxybenzyl anions are trapped as short-lived intermediates in the Brook[17] and the reverse Brook rearrangements.[18,19] Nevertheless, highly enantioenriched substitution products were obtained using configurationally labile benzyllithium compounds (Figure 2): Nakai and co-workers presented the asymmetric substitution of bis(oxazoline) containing lithium complexes like **13/14**.[20–22] Toru and co-workers successfully worked on different aryl benzyl sulfides **16**–**18**.[9]

Deprotonating primary benzyl carbamate **19**[23] yields α-lithiated benzyl carbamate **15**, which seemed to be configurationally stable within the timescale set by the Hoffmann test.[24] We recently reported our initial studies on the bis(oxazoline) complexes **15**·**9d** (Table 1, entry 1) and proved that the epimeric complexes equilibrate and that the R_C-configured complex (R_C)-**15**·**9d** is energetically strongly favored within the equilibrium.[25] In addition we showed that the equilibrium position and the enantiomeric excess can be predicted by calculating ΔΔE and ΔΔH (0 K),[26] using high level quantum chemical methods

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(SCS-MP2/TZVPP//B97-D/TZVP).[27] For other recent attempts to compute stereoselectivity, see, for example, ref. 28. We now wish to demonstrate the general applicability of the experimental and computational methods developed.[25,29]

Substitution reactions employing parent carbamate **19**: First, we were interested in further substitution products employing the parent system **19** and its diamine complexes **15**·**9d**. Employing different classes of electrophiles, we were especially interested in the stereochemical pathways of the substitution reactions, since all electrophiles employed so far reacted with inversion of configuration.[25] Employing standard conditions as outlined in Table 1, we synthesized various substitution products. The results are summarized in Table 1.

Like methylation,[25] allylation worked fine, took place with inversion of configuration, and afforded α-allylated compound (–)-(*S*)-**20c** in 75% yield (Table 1, entry 3). The enantiomeric excess decreased to 62% ee most probably due to a radical pathway. The *S*-configuration was proven after decarbamoylation to (*S*)-**34** (Table 3).[30]

We then used different acid chlorides as electrophiles (Table 1, entries 4–6). Methyl chloroformate reacted smoothly so that ester (–)-(*R*)-**20d** was isolated in high yield (95%) and with high enantiomeric excess of 91%. The absolute configuration of (–)-(*R*)-**20d** was deter-

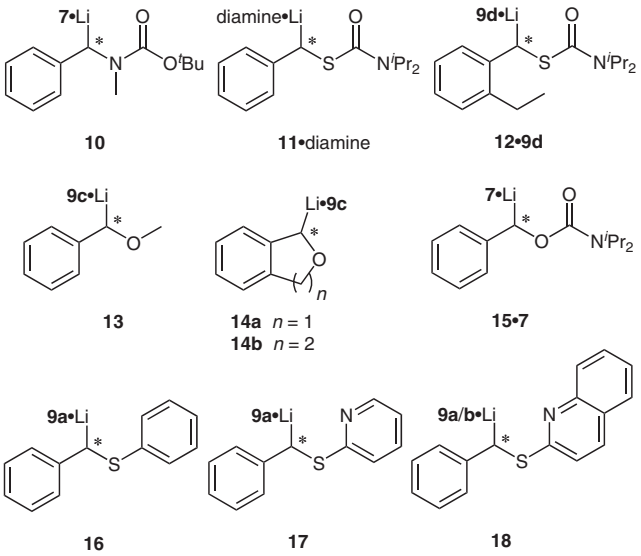
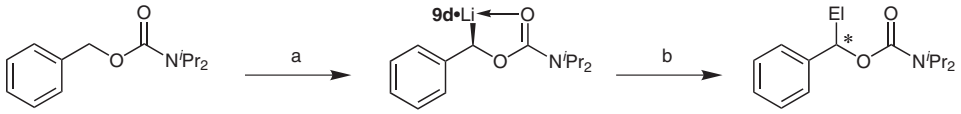


Figure 2 Some configurationally labile diamine complexes of α-hetero-substituted benzyllithium derivatives

Table 1 Substitution Reactions with Benzyl Carbamate **19** in the Presence of Chiral Bis(oxazoline) **9d**[a]



Entry	ElX	Diamine	Product	Yield (%)	ee[b] (%)	$[\alpha]_D^{20}$ (*c*, solvent)	Config	Inversion /retention
1	Bu_3SnCl	**9d**	**20a**	98	98[c]	–19.7 (1.1, $CHCl_3$)	*S*	inversion
2	Me_3SiCl	**8**[d]	**20b**	67	30[c]	+8.5 (1.0, $CHCl_3$)[c]	*R*[d]	inversion[d]
3	$H_2C{=}CHCH_2Br$	**9d**	**20c**	75	62	–2.3 (0.12, $CHCl_3$)	*S*	inversion
4	MeOC(O)Cl	**9d**	**20d**	95	91	–93.3 (1.00, MeOH)	*R*	inversion
5	*t*-BuC(O)Cl	**9d**	**20e**	87	63	–155.1 (0.97, $CHCl_3$)	*R*	inversion
6	4-$BrC_6H_4C(O)Cl$	**9d**	**20f**	24	96	–134.6 (0.40, $CHCl_3$)	*R*	inversion
7	Me_2CO	**9d**	**20g**	28	54	–8.4 (0.98, $CHCl_3$)	*S*	retention
8	Ph_2CO	**9d**	**20h**	81	94	+196.2 (0.50, $CHCl_3$)	*R*	inversion
9	*t*-BuCHO	**9d**	**20i**	70 (dr 1.1:1)[e]	32[f]	–	*S*[f]	retention
10	4-BrC_6H_4CHO	**9d**	**20j**	80 (dr 1.3:1)[g]	97[f]	–	*R*[f]	inversion

[a] *Reagents and conditions*: (a) bis(oxazoline) **9d**, *s*-BuLi, toluene, –78 °C, 2.5 h; electrophile (ElX), –78 °C, 2 h. *Products*: **20a**: El = $SnBu_3$; **20b**: El = $SiMe_3$; **20c**: El = $CH_2CH{=}CH_2$; **20d**: El = CO_2Me; **20e**: El = C(O)*t*-Bu; **20f**: El = 4-BrC_6H_4CO; **20g**: El = $C(OH)Me_2$; **20h**: El = $C(OH)Ph_2$; **20i**: El = CH(OH)*t*-Bu; **20j**: El = 4-$BrC_6H_4CH(OH)$.

[b] Determined by HPLC on chiral phase; see the experimental section for details.

[c] Determined by GC on chiral phase; see the experimental section for details.

[d] Here the S_C-configured complex is favored in the equilibrium of epimeric complexes. Invertive silylation affords the *R*-configured silane **20b** in this case.

[e] Yield of mixture of diastereomers. Diastereomeric ratio determined by ^1H NMR; (1*S*,2*S*)-isomer favored.

[f] Determined after the diastereomeric mixture of alcohols was oxidized by PDC into (*S*)-**20e** and (*R*)-**20f**, respectively; see the experimental section for details.

[g] Yield of mixture of diastereomers. Diastereomeric ratio determined by ^1H NMR; (1*R*,2*R*)-isomer favored.

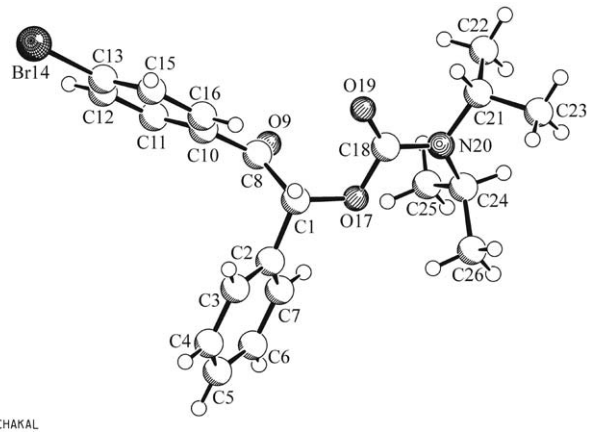


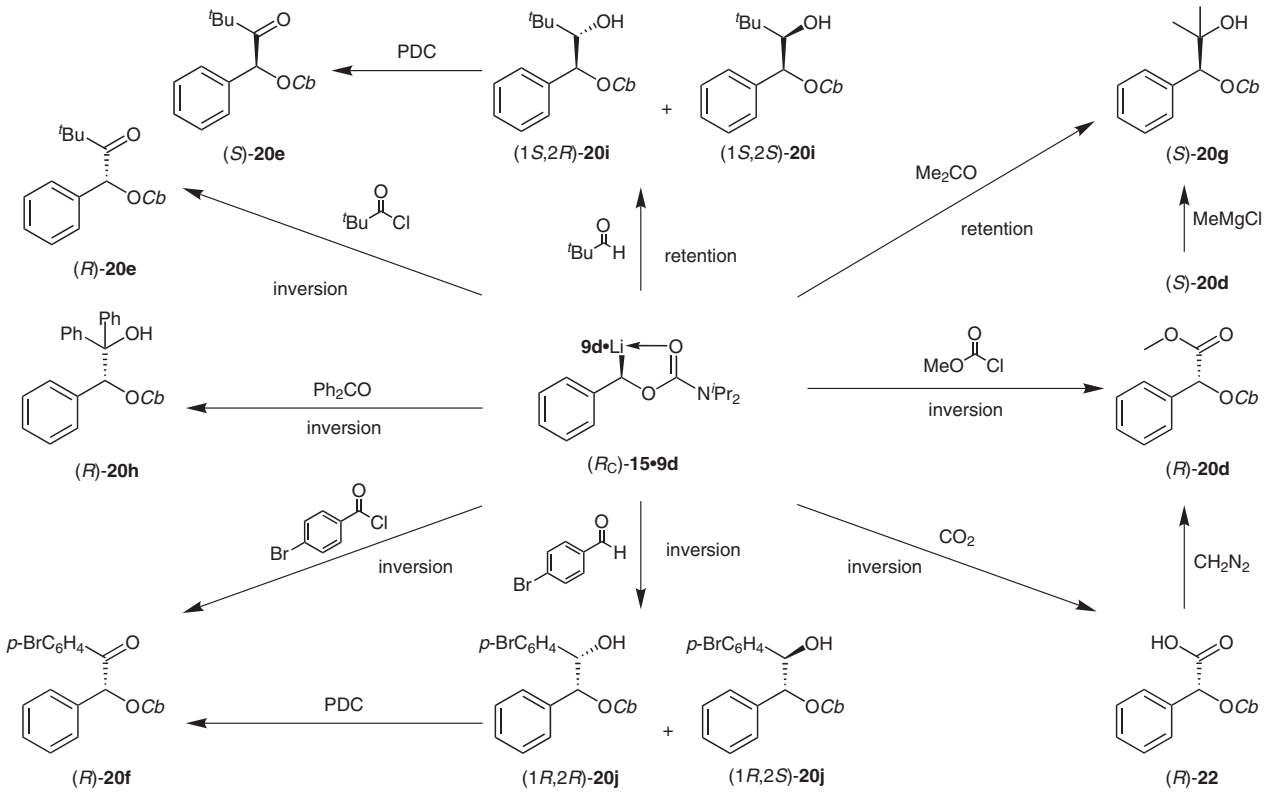
Figure 3 X-ray crystal structure of (–)-(*R*)-**20f**[32]

mined by comparing its optical rotation with that reported in the literature ($[\alpha]_D^{20}$ –93.3 (*c* 1.00, MeOH), ref.[25] $[\alpha]_D^{20}$ –107.6 (*c* 0.99, MeOH), 95% ee). Therefore, reaction with inversion of configuration must be concluded. The same stereochemical course is assumed when pivaloyl chloride is reacted with the equilibrated lithiated complexes **15**·**9d** (Table 1, entry 5);[31] ketone (–)-(*R*)-**20e** was obtained in 87% yield. The enantiomeric ratio of 81.5:17.5 is comparably low, indicating a nonhomogeneously stereochemical course for this particular electrophile. However, aromatic acid chlorides react with defined stereochemistry as shown by employing 4-bromobenzoyl chloride as trapping reagent (Table 1, entry 6). Albeit in moderate yield (24%), the desired (–)-(*R*)-**20f** is formed with 96% ee. Since we obtained single crystals of (–)-(*R*)-**20f** suitable for X-ray crystal structure analysis with anomalous dispersion, we determined the stereogenic carbon atom in ketone **20f** to be *R*-configured (Figure 3). Again, the acid chloride reacted with inversion of configuration.[31]

When employing ketones as carbonyl electrophiles, the stereochemical course of the substitution reactions highly depends on the nature of the ketone (Table 1, entries 7, 8). In contrast to the electrophiles used so far, acetone, as representative for aliphatic ketones, reacted predominantly with retention of configuration (28% yield, 54% ee, Table 1, entry 7). The *S* configuration of (–)-**20g** was proven by reacting known ester (+)-(*S*)-**20d**[33] with excess methylmagnesium chloride as outlined in Scheme 1. Aromatic ketones react highly stereospecifically with inversion of configuration as trapping of the equilibrated lithiated complexes **15**·**9d** with benzophenone shows (Table 1, entry 8). The desired alcohol (+)-(*R*)-**20h** was obtained in good yield (81%) with a very good enantiomeric ratio of 97:3 in favor of the *R*-configured enantiomer. Determination of the absolute configuration was achieved once more by decarbamoylation of the product, which led to the corresponding known diol (+)-(*R*)-**21** (Table 3).[34]

The same divergence in stereochemistry was found when different aldehydes were used (Table 1, entries 9, 10). Trapping the lithiated species with pivaldehyde, we found reaction with retention of configuration; the two possible diastereomeric alcohols **20i** were obtained in the form of an inseparable ~1:1 mixture (Table 1, entry 9). Oxidation of these alcohols by means of pyridinium dichromate[35] yielded ketone **20e** with the *S*-configured enantiomer enriched. Therefore, the favored configuration of the benzylic carbon in the starting alcohol must have been *S*-configured, corresponding to predominant reaction with retention of configuration (Scheme 1). The enantioenrichment of only 32% ee determined at the stage of the ketone (*S*)-**20e** revealed that the aliphatic aldehyde did not react with particular stereoselectivity with equilibrated lithium complexes **15**·**9d**. When 4-bromobenzaldehyde was used as the electrophile, a 1.3:1-mixture of the diastereomeric alcohols **20j** was obtained (Table 1, entry 10). Corey's pyridinium dichromate oxidation[35] delivered the well known ketone (–)-(*R*)-**20f** with an enantiomeric excess of 97%. These two facts indicate that the reaction of the aromatic aldehyde took place with high stereospecificity and with inversion of configuration (Scheme 1).

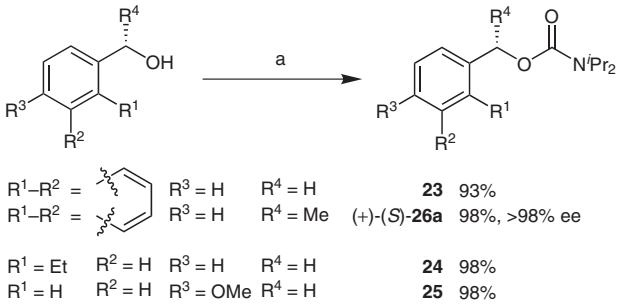
Discussion of the stereochemistry observed: The observed stereochemical course of the different substitution reactions and the stereodivergence observed may be understood by having a closer look at the reacting benzylic center, the reacting electrophile, and the leaving group. The benzylic carbanionic center of the different complexes is not perfectly tetrahedral, but slightly flattened; this can be concluded from our quantum chemical investigations (*vide infra*, ref. 25). For example, the sum of angles Li–$C_{benzylic}$–O, Li–$C_{benzylic}$–C_{ipso}, and O–$C_{benzylic}$–C_{ipso} in complex **15**·**9d** amounts to 314.8° (the ideal values for sp^3 hybridization are 328.4°, for sp^2 hybridization 300.0°).[36] This causes enhanced electron density at the rear face and enables the electrophile to attack from the rear face, thereby avoiding hindrance by the lithium cation. This fact corresponds to an antarafacial reaction, i.e. a reaction with inversion of configuration. This reaction pathway should be preferred by every electrophile exhibiting an energetically low LUMO in addition to lacking a good complexing group for the lithium cation; these features are found, for example, in silyl and stannyl chlorides and in acid chlorides. Both methyl iodide and allyl bromide also fit this interpretation as invertive reactions are found.[3c,d,7,25] According to our investigations, aromatic aldehydes and ketones as well as carbon dioxide belong to this group. However, aliphatic aldehydes and ketones are known to posses an energetically higher LUMO and to have better complexing abilities, thereby enhancing the complexation of the lithium cation by the carbonyl oxygen atom, and, thus, they prefer the suprafacial reaction pathway.[3c,d,7a] Nevertheless, the fact that the enantiomeric ratios of the corresponding substitution products are comparably low indicates that these electrophiles still react antarafacially to a significant degree. Although regarded as being unlikely, it cannot be excluded that kinetic resolution takes place in the substitution step [both epimeric complexes (R_C)-**15**·**9d** and (S_C)-**15**·**9d** remain in solution], in particu-



Scheme 1 Addition of aldehydes, ketones, and acid chlorides and stereochemical correlations; for reagents and conditions, see the experimental section. For the synthesis of acid (*R*)-**22** and its subsequent transformation into ester (*R*)-**20d** and for information on the stereochemical pathway of the substitution reaction, see ref. 25.

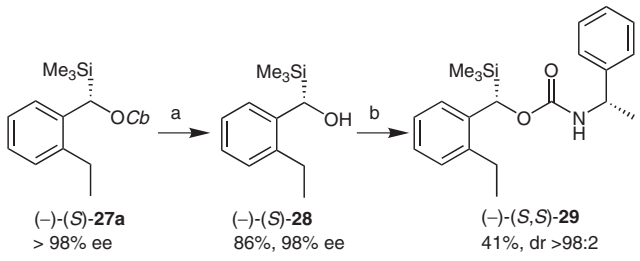
lar if it is a slow reaction and the minor diastereomer is reacting faster.

Further extension of the methodology: We then tested further benzylic substrates. We were especially interested in sterically more demanding and electronically differing benzyl carbamates like **23**,[25] **24**, and **25**.[23a] All these were synthesized in greater than 90% yield from the corresponding benzyl alcohols using sodium hydride as the base and *N*,*N*-diisopropylcarbamoyl chloride (*Cb*Cl) (Scheme 2). Relying on the results obtained for the silylation and stannylation of 1-naphthylmethyl carbamate **23**[25] for which we have already determined the R_C-configured complex to be energetically favored within an equilibrium of epimers, we tried methylation [(+)-(*S*)-**26a**], allylation [(+)-(*S*)-**26b**], and carboxylation [(–)-(*R*)-**26c**]. We obtained the desired substitution products in good yields and high enantiomeric excesses (Table 2, entries 1–3). The absolute configuration of the methylated product (+)-(*S*)-**26a** (77%, 93% ee) was determined by comparing its optical rotation {$[\alpha]_D^{20}$ +34.4 (*c* 1.05, $CHCl_3$), 93% ee} with the value obtained from a sample of **26a**, which was prepared by carbamoylating a commercially available sample of the corresponding enantioenriched tertiary alcohol {$[\alpha]_D^{20}$ +34.9 (*c* 1.0, $CHCl_3$), 98% ee} (Scheme 2). The *S* configuration of allylation product (+)-**26b** (80%, 78% ee) was elucidated after decarbamoylation and comparison of the optical rotation of the corresponding tertiary alcohol (–)-**35** with literature values (Table 3, entry 3).[30] Carboxylation of **23** to give (*R*)-**26c** is also assumed to proceed with inversion of configuration (65%, 90% ee).[25]



Scheme 2 Synthesis of the primary benzyl-type carbamates **23**–**25**, **26a**. *Reagents and conditions*: (a) NaH, *Cb*Cl, THF, r.t., 2 d.

2-Ethylbenzyl carbamate (**24**) was substituted via the same mechanism (Table 2, entries 4–7). Stereochemical aspects were clarified by a silylation experiment (Table 2, entry 5; Scheme 3). Liquid silane (–)-(*S*)-**27b** was formed in 97% yield with an enantiomeric excess of >98% ee. Removal of the carbamoyl group to give (–)-**28** and forming new monocarbamate (–)-**29** as a single diastereomer (dr >98%, determined by ^{1}H NMR of the crude product) by using enantiomerically pure (*S*)-1-phenylethyl isocyanate yielded single crystals of **29** suitable for X-ray crystal structure analysis under anomalous dispersion (Scheme 3, Figure 4) from which we determined the absolute configuration to be *S*,*S*. Therefore silylated benzyl carbamate (–)-**27b** must also be *S*-configured, indicating an energetically favored R_C-configured complex (R_C)-**32**·**9d** within the equilibrium, since silylation is expected to occur with inversion of configuration. The same stereochemical



Scheme 3 Synthesis of monocarbamate (–)-(*S*,*S*)-**29**. *Reagents and conditions*: (a) DIBAL-H, THF, reflux, 2 d (TLC control); (b) (*S*)-1-phenylethyl isocyanate, cat. DMAP, DMF, r.t., 1 d.

course was assumed for the stannylation [(–)-(*S*)-**27a**], methylation [(–)-(*S*)-**27c**], and carboxylation [(–)-(*R*)-**27d**] in analogy to the results obtained so far. The enantiomeric excesses obtained were above 90% ee with the exception of carboxylation (70% ee). We do not want to exclude downstream racemization of a higher enantiomerically enriched product at the moment.

As a last substrate, we investigated 4-methoxy-substituted benzyl carbamate **25** (Table 2, entries 8–10). Using bis(oxazoline) **9d** to bring in chiral information, silylation and stannylation yielded the desired substitution products in 80% and 64% yield, respectively (Table 2, entries 8, 10). Whereas stannane (–)-(*S*)-**30a** exhibited a satisfying enantiomeric excess of 92%, silane (–)-(*S*)-**30b** was enantioenriched up to 78%. As there was no sterical hindrance compared to the parent system **19**, the low enantiomeric excesses must be explained by complex electronic effects induced by the 4-methoxy group. This assumption is underlined by the results obtained during the theoretical treatment of the complex **33**·**9d** (cf. Table 4), in which we found a significantly lower energy difference than for the parent system **15**·**9d**.

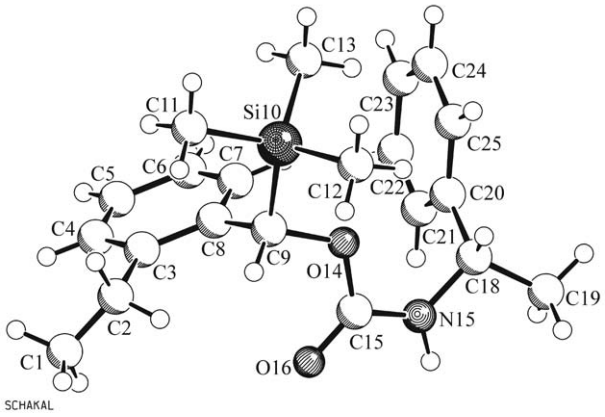
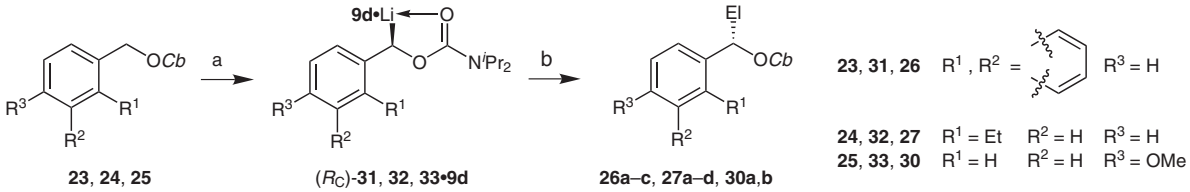


Figure 4 X-ray crystal structure of (–)-(*S*,*S*)-**29**[37]

Cleavage of substituted benzyl carbamates: Removal of the diisopropylcarbamoyl protecting group was achieved by refluxing the benzyl carbamates in the presence of a

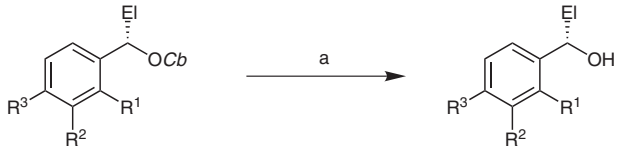
Table 2 Substitution Reactions with Benzyl Carbamates **23**–**25** in the Presence of Chiral Bis(oxazoline) **9d**[a]



Entry	Substrate	Diamine	ElX	Product	Yield (%)	ee[b] (%)	$[\alpha]_D^{20}$ (*c*, solvent)	Config	Inversion /retention
1	**23**	**9d**	MeI	**26a**	77	93	+34.4 (1.04, $CHCl_3$)	*S*	inversion
2	**23**	**9d**	H_2C=$CHCH_2Br$	**26b**	80	78	+21.5 (1.08, $CHCl_3$)	*S*	inversion
3[c]	**23**	**9d**	CO_2	**26c**	65	90	–142.2 (0.61, $CHCl_3$)	*R*	inversion
4	**24**	**9d**	Bu_3SnCl	**27a**	92	92	–46.1 (1.01, $CHCl_3$)	*S*	inversion
5	**24**	**9d**	Me_3SiCl	**27b**	97	>98	–38.9 (0.96, $CHCl_3$)	*S*	inversion
6	**24**	**9d**	MeI	**27c**	36	92	–2.3 (1.04, $CHCl_3$)	*S*	inversion
7[c]	**24**	**9d**	CO_2	**27d**	70	78	–101.0 (0.96, $CHCl_3$)	*R*	inversion
8	**25**	**9d**	Bu_3SnCl	**30a**	64	92	–17.8 (1.03, $CHCl_3$)	*S*	inversion
9	**25**	**7**[d]	Me_3SiCl	**30b**	96	40	+14.2 (1.00, $CHCl_3$)[d]	*R*[d]	inversion
10	**25**	**9d**	Me_3SiCl	**30b**	80	78	–26.9 (1.02, $CHCl_3$)	*S*	inversion

[a] *Reagents and conditions*: (a) bis(oxazoline) **9d**, *s*-BuLi, toluene, –78 °C, 2.5 h; electrophile (ElX), –78 °C, 2 h. *Products*: **26a**/**27c**: El = Me; **26b**: El = CH_2CH=CH_2; **26c**/**27d**: El = CO_2Me; **27a**/**30a**: El = $SnBu_3$; **27b**/**30b**: El = $SiMe_3$.
[b] Determined by HPLC on chiral phase; see the experimental section for details.
[c] The initially formed crude acid was converted into the methyl ester with diazomethane before yield and enantiomeric excess were determined.
[d] Here the S_C-configured complex is favored in the equilibrium of epimeric complexes. Invertive silylation affords the *R*-configured silane **20b** in this case.

Table 3 Deprotection of Selected Benzyl Carbamates[a]



20c R^1 = H R^2 = H R^3 = H El = $CH_2CH{=}CH_2$ **34**
20h R^1 = H R^2 = H R^3 = H El = $Ph_2C(OH)$ **21**
26b R^1–R^2 =  R^3 = H El = $CH_2CH{=}CH_2$ **35**
27b R^1 = Et R^2 = H R^3 = H El = $SiMe_3$ **28**

Entry	Substrate (ee)	Yield (%)	ee[b] or op	$[\alpha]_D^{20}$	Product
1	(*S*)-**20c** (62%)	75	60% ee	–32.9 (1.08, benzene)	(*S*)-**34**[30]
2	(*R*)-**20h** (94%)	69	>84% op	+179.7 (1.01, EtOH)	(*R*)-**21**[34]
3	(*S*)-**26b** (78%)	81	74% op	–72.8 (1.04, benzene)	(*S*)-**35**[30]
4	(*S*)-**27b** (>98%)	86	98% ee	–95.9 (0.64, $CHCl_3$)	(*S*)-**28**

[a] *Reagents and conditions*: DIBAL-H, THF, reflux, 12 h.
[b] Determined by HPLC on chiral phase; see the experimental section.

Table 4 Experimental and Calculated Results for Different Diamine-Containing Lithium Complexes

Complex	Experimental			SCS-MP2/TZVPP//B97-D/TZVP		
	Config	er[a]	ΔΔG[a] (kcal mol^{-1})	Config	er[b]	ΔΔE[c] (kcal mol^{-1})
15·**8**	S_C	35:65	–0.26	S_C	5:95	–1.15
15·**9d**	R_C	98:2	1.51	R_C	96:4	1.21
32·**9d**	R_C	99:1	1.78	R_C	>>99:1	2.56
33·**7**	S_C	30:70	–0.32	S_C	15:87	–0.72
33·**9d**	R_C	93:7	0.97	R_C	63:37	0.20
11·**7**	S_C	42:58	–0.13	S_C	40:60	–0.15
11·**9d**	R_C	98:2	1.51	R_C	>>99:1	2.92
12·**9d**	R_C	99:1	1.78	R_C	>>99:1	3.28

[a] Experimentally derived.
[b] Predicted quantum chemically.
[c] $\Delta E(S_C) - \Delta E(R_C)$.

tenfold excess of diisobutylaluminum hydride (DIBAL-H) in tetrahydrofuran (Table 3).[38] The stereogenic center is usually not touched under these conditions.

Quantum chemical calculations: In addition, we again were able to determine the energy differences in the equilibriums of the different epimeric complexes quantum chemically as outlined in Table 4.[27,39,40] Within the dynamic thermodynamic resolution taking place, ΔΔG can be determined experimentally from the enantiomeric ratios of the trapping products **26**, **27**, and **30**.[26] The values are comparable to the quantum chemically derived ΔΔE values as temperature and entropy effects are negligibly small due to structural similarities of the complexes.[25,26] Zero-point vibrational energy contributions as well as solvent effects are also negligible as we have already shown (see ref. 25 for a detailed description of the theoretical procedure). For all the calculated complexes the most stable epimer was found correctly by the theoretical treatment in comparison to experimental findings. Concerning quantitative aspects we can state that again we can estimate the amount of enantioenrichment that can be expected when using a special substrate–ligand system, provided that the electrophile reacts stereospecifically with the complexes. Experimentally detectable small changes within the position of the equilibrium that emanate most probably from electronic effects brought in by the choice of substrate are reproduced by the calculations (Table 4, complex **33**·**9d**). The ratio of the analogous (–)-sparteine

complexes **33·7** was computed with high accuracy. Simulation of the epimeric complexes obtained when employing tricyclic, C_2-symmetric diamine (–)-α-isosparteine (**8**) worked satisfying as well (Table 4, complex **15·8**). Although the S_C-configured complex (S_C)-**15·8** is quantum chemically more favored than determined experimentally, the results are still within estimated error bars of our computations of about 0.5–1 kcal·mol^{-1}.

We have already investigated epimeric lithium complexes of *S*-benzyl thiocarbamates and shown the utility of bis(oxazoline) **9d** containing complexes in enantioselective synthesis.[29] As shown in Table 4 (complexes **11·7**, **11·9d**, **12·9d**) these systems can also be described very accurately by quantum chemical means.

Altogether, the synthetic methodology developed provides an easy access to different highly enantioenriched user-defined secondary benzyl alcohols. These compounds can be used as chiral precursors in further transformations.[3c,d,41] The broad applicability of the quantum chemical methodology developed[25] is proven.

All solvents were dried and purified prior to use. Toluene was distilled over Na/benzophenone. Me_3SiCl was distilled from powdered CaH_2 and stored under argon. *s*-BuLi was filtered through Celite before use and its concentration was determined by titration against Ph_2CHCO_2H.[42] A soln of CH_2N_2 in Et_2O was obtained as described in literature,[43] stored under argon in the refrigerator and used without determination of its concentration. Bis(oxazoline) ligand **9d** was prepared according to ref. 22. All reactions were performed under argon atmosphere in flame-dried glassware using septum and syringe techniques. Flash column chromatography (FCC) was performed on Merck 60 silica gel, 0.040–0.063 mm, using an argon pressure of 1.2–1.4 bar, and monitored by TLC on Merck 60 F254 silica gel. Gas chromatography was performed on Agilent 6890 plus, Agilent, Böblingen. HP-5 was used as an achiral column (HP-5: 30 m long, 0.32 μm diameter, 0.25 mm thick stationary phase, N_2 as the mobile phase, 106 kPa pressure, 290 °C injection temperature, 300 °C detector temperature, program: 50 °C start temperature, 10 °C min^{-1} heating rate, 300 °C final temperature for 15 min) and Supelco β-DEX 120 was used as chiral stationary phase (Supelco β-DEX 120, 30 m long, 0.32 μm diameter, 0.25 mm thick stationary phase, N_2 as the mobile phase, 14.5 kPa pressure, 240 °C injection temperature, 260 °C detector temperature). Melting points were measured on an SMP3 melting point apparatus purchased from Stuart Scientific, UK (uncorrected values). The optical rotations were measured in a 10-cm cuvette on a polarimeter 341 purchased from Perkin-Elmer. Unless otherwise stated, ^{1}H and ^{13}C NMR data were recorded on Bruker ARX 300 and AMX 400 spectrometers; spectra were obtained from solns in $CDCl_3$ (δ_C = 77.0) and were calibrated relative to residual content of $CHCl_3$ (δ_H = 7.24) or TMS (δ_H = 0.0). Diastereotopic methylene protons with different chemical shifts are abbreviated as H_A and H_B. IR: Nicolet 5DCX, Bruker IFS 28 or Varian 3100 Excalibur Series spectrophotometer with Specac Golden Gate Single Reflection ATR. Elemental analyses were performed at the Microanalytical Section of the Organisch-Chemisches Institut, WWU Münster, on a Vario El III, purchased from Elementar Analysen Systeme, Hanau (Germany). MS data were obtained on Finnigan MAT 8230 (EI); Micromass Quattro LCZ (ESI), Micromass MAT 8200 (GC-TOF/HRMS). HPLC: Waters 600E Multisolvent Delivery System and 996 PDA detector. Crystallographic data: Data sets were collected with a Nonius KappaCCD diffractometer. Programs used: data collection COLLECT (Nonius B.V., 1998), absorption correction SORTAV,[44] Denzo,[45] structure solution SHELXS-97,[46] structure refinement SHELXL-97,[47] graphics SCHAKAL.[48] All given CCDC data contain the supplementary crystallographic data for this paper.[49] Known compounds have not been fully re-characterized.

Benzyl Carbamates 23, 24, 26a; General Procedure A (GPA)

NaH (60% in mineral oil, 920 mg, 23 mmol, 1.15 equiv) was suspended in anhyd THF (30 mL). The mixture was cooled to 0 °C and the corresponding benzyl alcohol (20 mmol, 1.0 equiv) dissolved in anhyd THF (5 mL), was slowly added. When the evolution of H_2 ceased, a soln of *Cb*Cl (3.76 g, 23 mmol, 1.15 equiv) in anhyd THF (10 mL) was added in such a way that the temperature did not rise. The mixture was allowed to warm to r.t. and stirred at this temperature for 2 d. The reaction flask was then immersed in an ice bath and H_2O (25 mL) and 2 M HCl (3 mL) were added to obtain a clear yellowish soln. TBME (50 mL) was added, the phases were separated, and the aqueous phase was extracted with TBME (3 × 20 mL). The combined organic layers were washed successively with sat. $NaHCO_3$ and brine. The soln was dried (anhyd $MgSO_4$), filtered through glass wool, and the solvent was removed to give the crude product, which was subjected to column chromatography (Et_2O–pentane) to obtain the pure benzyl carbamates.

Asymmetric Lithiation and Substitution of 19 and 23–25; General Procedure B (GPB)

Benzyl-type carbamate **19**, **23**–**25** (71 mg/86 mg/79 mg/80 mg, 0.30 mmol, 1.00 equiv) was dissolved in toluene (3 mL), ligand **9d** (0.36 mmol, 1.20 equiv) was added and the reaction flask was cooled to –78 °C. To this mixture, 1.2–1.3 M *s*-BuLi in hexane–cyclohexane (92:8) (0.36 mmol, 1.20 equiv) was injected in a dropwise manner. The mixture was stirred at –78 °C for 2.5 h and then the appropriate electrophile (0.36–1.50 mmol, 1.2–5.0 equiv) was injected and the mixture was stirred for 2 h. The reaction was quenched with MeOH (0.5 mL) followed by H_2O (1 mL) and 2 M HCl (0.5 mL). The layers were separated and the aqueous layer was extracted with TBME (3 × 10 mL). The combined organic layers were washed with sat. $NaHCO_3$, dried ($MgSO_4$), filtered through glass wool, and concentrated under reduced pressure to obtain the crude product. This was subjected to column chromatography (Et_2O–pentane) to obtain the pure products.

2-Ethylbenzyl *N*,*N*-Diisopropylcarbamate (24)

According to GPA, reaction of 2-ethylbenzyl alcohol (2.72 g, 20.00 mmol) with *Cb*Cl (3.76 g, 23.00 mmol) afforded **24** as colorless liquid; yield: 5.17 g (98%); R_f = 0.86 (Et_2O–pentane, 1:1); t_R = 14.1 min.

IR (film): 3065, 2969, 2934, 2876, 1694, 1435, 1368, 1310, 1289, 1217, 1188, 1100, 1052, 1049, 757, 618, 597 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.21 [d, $^3J_{(H3C)2CH,(H3C)2CH}$ = 6.8 Hz, 12 H, $(H_3C)_2CH$], 1.24 (t, $^3J_{CH3CH2,CH3CH2}$ = 7.2 Hz, 3 H, CH_3CH_2), 2.73 (q, 2 H, CH_3CH_2), 3.94 [ps s, 2 H, $(H_3C)_2CH$], 5.18 (s, 2 H, $H_{benzylic}$), 7.15–7.40 (m, 4 H, H_{aryl}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.1 (CH_3CH_2), 20.8 [$(H_3C)_2CH$], 25.2 (CH_3CH_2), 45.9 [$(H_3C)_2CH$], 64.1 ($C_{benzylic}$), 125.8 (C3), 127.0 (C2), 128.4 (C4), 129.2 (C5), 134.3 (C6), 142.6 (C1), 155.4 (NC=O).

MS (EI, 70 eV): *m*/*z* (%) = 248 [M – CH_3]$^+$ (1), 204 (10), 153 (1), 146 (8), 128 [*Cb*]$^+$ (4), 119 [$(H_5C_2)C_6H_4CH_2$]$^+$ (100), 104 (14), 91 [C_7H_7]$^+$ (53), 77 [C_6H_5]$^+$ (19), 58 (13), 43 [C_3H_7]$^+$ (32).

Anal. Calcd for $C_{16}H_{25}NO_2$: C, 72.96; H, 9.57; N, 5.32. Found: C, 72.74; H, 9.39; N, 5.25.

1-(1-Naphthyl)ethyl *N*,*N*-Diisopropylcarbamate [(*S*)-26a]

Via carbamoylation: According to GPA, a downscaled reaction of (*S*)-1-(1-naphthyl)ethanol (>99% ee) (172 mg, 1.00 mmol) with NaH (60% in mineral oil, 46 mg, 1.15 mmol) and *Cb*Cl (188 mg, 1.15 mmol) gave (*S*)-**26a** as a colorless oil; yield: 292 mg (98%); R_f = 0.49 (Et_2O–pentane, 1:4); t_R = 17.30 min.

HPLC [CHIRA-GROM 1 (2·250 mm), hexane–*i*-PrOH (2000:1), 0.3 mL·min^{-1}, λ = 210 nm]: t_R = 18.6 (–), 21.9 min (+); 98% ee.

$[\alpha]_D^{20}$ +34.9 (*c* 1.0, $CHCl_3$).

IR (film): 3050, 2970, 2933, 2874, 1692, 1598, 1537, 1511, 1433, 1368, 1189, 1157, 1131, 1090, 1073, 1047, 799, 777, 735 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.21 [d, $^3J_{(H3C)2CH,(H3C)2CH}$ = 7.3 Hz, 12 H, $(H_3C)_2CH$], 1.71 (d, $^3J_{Hbenzylic,H3C}$ = 6.7 Hz, 3 H, H_3C), 3.94 [ps s, 2 H, $(H_3C)_2CH$], 6.64 (q, 1 H, $H_{benzylic}$), 7.35–7.54 (m, 3 H, H3, H2, H7), 7.59 (dd, $^3J_{H5,H6}$ = 8.1 Hz, $^3J_{H6,H7}$ = 6.7 Hz, 1 H, H6), 7.77 (m, 1 H, H4), 7.85 (dd, $^4J_{H5,H7}$ = 1.4 Hz, 1 H, H5), 8.13 (dd, $^3J_{H7,H8}$ = 8.5 Hz, $^4J_{H6,H8}$ = 0.9 Hz, 1 H, H8).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.9 [$(H_3C)_2HC$], 22.3 (CH_3), 45.9 [$(H_3C)_2HC$], 69.6 (C9), 122.9 (C8), 123.4 (C2), 125.3 (C3), 125.5 (C6), 126.0 (C7), 128.0 (C4), 128.7 (C5), 130.4 (C8a), 133.8 (C4a), 138.7 (C1), 154.9 (NC=O).

MS (ESI): *m*/*z* = 322.3 [M + Na]$^+$.

Anal. Calcd for $C_{19}H_{25}NO_2$: C, 76.22; H, 8.42; N, 4.68. Found: C, 76.03; H, 8.63; N, 4.82.

Via asymmetric substitution: According to GPB, a mixture of carbamate **23** (86 mg, 0.30 mmol) and **9d** (116 mg, 0.36 mmol) was treated with *s*-BuLi (0.26 mL, 0.36 mmol) and then MeI (51 mg, 0.36 mmol) was added; yield: 69 mg (77%); 93% ee.

$[\alpha]_D^{20}$ +34.4 (*c* 1.04, $CHCl_3$).

(+)-(*R*)-Phenyl(trimethylsilyl)methyl *N*,*N*-Diisopropylcarbamate [(*R*)-20b]

According to GPB, a mixture of carbamate **19** (118 mg, 0.50 mmol) and **8** (141 mg, 0.60 mmol) was treated with *s*-BuLi (0.44 mL, 0.60 mmol). The mixture was stirred at –78 °C for 3 h and then Me_3SiCl (65 mg, 0.60 mmol) was added; yield: 103 mg (67%); R_f = 0.38 (Et_2O–pentane, 1:8); t_R = 14.1 min (HP-5).

GC [chiral phase; temperature program 94/1/1/ 95/999]: t_R = 938 (–), 958 min (+); 30% ee.

$[\alpha]_D^{20}$ +8.5 (*c* 1.0, CH_2Cl_2).

(–)-(*S*)-1-Phenylbut-3-enyl *N*,*N*-Diisopropylcarbamate [(*S*)-20c]

According to GPB, a mixture of carbamate **19** (118 mg, 0.50 mmol) and **9d** (193 mg, 0.60 mmol) was treated with *s*-BuLi (0.49 mL, 0.60 mmol) and then allyl bromide (91 mg, 0.6 mmol) was added; **20c** was obtained as a colorless oil; yield: 102 mg (75%); R_f = 0.65 (Et_2O–pentane, 1:1); t_R = 14.4 min.

HPLC [CHIRA GROM 1 (2·250 mm), hexane–*i*-PrOH (1000:1), 0.3 mL·min^{-1}, λ = 210 nm]: t_R = 13.5 (+), 14.9 min (–); 62% ee.

$[\alpha]_D^{20}$ –2.3 (*c* 0.12, $CHCl_3$).

IR (ATR): 3078, 3066, 3034, 2999, 2970, 2934, 2876, 1691, 1643, 1495, 1476, 1434, 1368, 1336, 1302, 1290, 1215, 1190, 1157, 1133, 1051, 980, 914, 767, 634 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.08 [br d, $^3J_{(H3C)2CH,(H3C)2CH}$ = 6.4 Hz, 12 H, $(H_3C)_2CH$], 2.42–2.66 (m, 2 H, H_2CCHCH_2), 3.80 [ps s, 2 H, $(H_3C)_2CH$], 4.90–5.06 (m, 2 H, H_2CCHCH_2), 5.55–5.75 (m, 2 H, $H_{benzylic}$, H_2CCHCH_2), 7.07–7.24 (m, 5 H, H_{phenyl}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.6 [$(H_3C)_2CH$], 41.3 (H_2CCHCH_2), 45.5 [$(H_3C)_2CH$], 75.6 ($C_{benzylic}$), 117.6 (H_2CCHCH_2), 126.5 (C2), 127.5 (C4), 128.2 (C3), 133.8 (H_2CCHCH_2), 141.1 (C1), 154.9 (NC=O).

MS (ESI): *m*/*z* = 298.1778 [M + Na]$^+$.

Anal. Calcd for $C_{17}H_{25}NO_2$: C, 74.14; H, 9.15; N, 5.09. Found: C, 74.11; H, 9.22; N, 4.78.

(–)-(*R*)-Methyl 2-(Diisopropylcarbamoyloxy)-2-phenylacetate [(*R*)-20d]

According to GPB, a mixture of carbamate **19** (71 mg, 0.30 mmol) and **9d** (116 mg, 0.36 mmol) was treated with *s*-BuLi (0.26 mL, 0.36 mmol) and then methyl chloroformate (85 mg, 0.90 mmol) was added; yield: 84 mg (95%); R_f = 0.13 (Et_2O–pentane, 1:8); t_R = 16.3 min (HP-5).

HPLC [CHIRA-GROM 1 (2·250 mm), hexane–*i*-PrOH (1000:1), 0.2 mL·min^{-1}, λ = 210 nm]: t_R = 25.1 (+), 35.3 min (–); 91% ee.

$[\alpha]_D^{20}$ –93.3 (*c* 1.00, MeOH).

(–)-(*R*)-3,3-Dimethyl-2-oxo-1-phenylbutyl *N*,*N*-Diisopropylcarbamate [(*R*)-20e]

According to GPB, a mixture of carbamate **19** (71 mg, 0.30 mmol) and **9d** (116 mg, 0.36 mmol) was treated with *s*-BuLi (0.26 mL, 0.36 mmol) and then pivaloyl chloride (182 mg, 1.50 mmol) was added; **20e** was obtained as a colorless solid; yield: 83 mg (87%); mp 79 °C (Et_2O); R_f = 0.37 (Et_2O–pentane, 1:3); t_R = 14.5 min.

HPLC [CHIRA-GROM 2 (2·250 mm), hexane–*i*-PrOH (1000:1), 0.2 mL·min^{-1}, λ = 210 nm]: t_R = 11.6 (+), 12.8 min (–); 63% ee.

$[\alpha]_D^{20}$ –155.1 (*c* 0.97, $CHCl_3$).

IR (KBr): 3065, 2975, 2928, 1714, 1684, 1586, 1499, 1478, 1441, 1386, 1368, 1304, 1243, 1208, 1189, 1134, 1091, 1055, 969, 906, 867, 812, 768, 723, 701 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.09 [s, 9 H, $(H_3C)_3C$], 1.13 [d, $^3J_{(H3C)2CH,(H3C)2CH}$ = 7.0 Hz, 12 H, $(H_3C)_2CH$], 3.72 [ps s, 1 H, $(H_3C)_2CH$], 4.07 [ps s, 1 H, $(H_3C)_2CH$], 6.35 (s, 1 H, $H_{benzylic}$), 7.30–7.45 (m, 5 H, H_{phenyl}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.0 [$(H_3C)_2CH$], 27.2 [$(H_3C)_3C$], 43.7 [$(H_3C)_3C$], 46.0 [$(H_3C)_2CH$], 76.7 ($C_{benzylic}$), 128.8 (C2), 128.9 (C4), 129.3 (C3), 134.5 (C1), 154.7 (NC=O), 210.4 (C=O).

MS (ESI): *m*/*z* = 320.2220 [M + H]$^+$, 342.2042 [M + Na]$^+$.

Anal. Calcd for $C_{19}H_{29}NO_3$: C, 71.44; H, 9.15; N, 4.38. Found: C, 71.44; H, 9.29; N, 4.24.

(+)-(*S*)-3,3-Dimethyl-2-oxo-1-phenylbutyl *N*,*N*-Diisopropylcarbamate [(*S*)-20e]

Via Corey's PDC oxidation: Epimeric alcohols **20i** (51 mg, 0.16 mmol) were dissolved CH_2Cl_2 (2 mL). PDC (67 mg, 0.18 mmol) was added and the mixture was stirred at r.t. for 20 h. The solids were filtered off and the solvents removed in vacuo to give a crude product that was purified by column chromatography (Et_2O–pentane, 1:6); yield: 21 mg (41%); 32% ee.

$[\alpha]_D^{20}$ +79.7 (*c* 0.38, $CHCl_3$).

(–)-(*R*)-2-(4-Bromophenyl)-2-oxo-1-phenylethyl *N*,*N*-Diisopropylcarbamate [(*R*)-20f]

According to GPB, a mixture of carbamate **19** (71 mg, 0.30 mmol) and **9d** (116 mg, 0.36 mmol) was treated with *s*-BuLi (0.26 mL, 0.36 mmol) and then 4-bromobenzoyl chloride (329 mg, 1.50 mmol) was added; **20f** was obtained as a colorless solid; yield: 30 mg (24%); mp 131 °C (Et_2O); R_f = 0.34 (Et_2O–pentane, 1:2); t_R = 21.4 min.

HPLC [CHIRA-GROM 2 (2·250 mm), *n*-hexane–*i*-PrOH (1000:1), 0.3 mL·min^{-1}, λ = 210 nm]: t_R = 58.0 (–), 79.1 min (+); 96% ee.

$[\alpha]_D^{20}$ –134.6 (*c* 0.40, $CHCl_3$).

IR (KBr): 3069, 3002, 2968, 2933, 2861, 1698, 1686, 1588, 1475, 1456, 1436, 1397, 1367, 1297, 1256, 1227, 1211, 1187, 1131, 1090, 1068, 1010, 971, 954, 907, 856, 826, 769, 728, 695 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.21 [d, $^3J_{(H3C)2CH,(H3C)2CH}$ = 6.7 Hz, 12 H, $(H_3C)_2CH$], 3.90 [ps s, 1 H, $(H_3C)_2CH$], 4.02 [ps s, 1 H, $(H_3C)_2CH$], 6.25 (s, 1 H, $H_{benzylic}$), 6.75–6.85 (m, 5 H, H_{phenyl}), 7.05–7.21 (m, 4 H, H_{aryl}).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.6 [$(H_3C)_2CH$], 46.4 [$(H_3C)_2CH$], 78.7 ($C_{benzylic}$), 121.2, 122.8, 127.5, 127.9, 129.2, 130.1, 136.3, 136.8 (C_{phenyl}, C_{aryl}), 154.9 (NC=O), 191.8 (C=O).

MS (ESI): *m*/*z* = 420.1001 $[M + H]^+$, 442.0841 $[M + Na]^+$.

Anal. Calcd for $C_{21}H_{24}BrNO_3$: C, 60.29; H, 5.78; N, 3.35. Found: C, 60.09; H, 5.67; N, 3.24.

Via Corey's PDC oxidation: Epimeric alcohols **20j** (168 mg, 0.40 mmol) were dissolved CH_2Cl_2 (2 mL). PDC (168 mg, 0.45 mmol) was added and the mixture was stirred at r.t. for 12 h. The solids were filtered off and the solvent removed in vacuo to give a crude product that was purified by column chromatography (Et_2O–pentane, 1:6); yield: 56 mg (33%); 97% ee.

$[\alpha]_D^{20}$ –134.6 (*c* 0.40, $CHCl_3$).

(–)-(*S*)-2-Hydroxy-2-methyl-1-phenylpropyl *N*,*N*-Diisopropylcarbamate [(*S*)-20g]

According to GPB, a mixture of carbamate **19** (71 mg, 0.30 mmol) and **9d** (116 mg, 0.36 mmol) was treated with *s*-BuLi (0.26 mL, 0.36 mmol) and then acetone (87 mg, 1.50 mmol) was added; **20g** was obtained as a colorless oil; yield: 25 mg (28%); R_f = 0.32 (Et_2O–pentane, 1:2); t_R = 14.0 min.

HPLC [CHIRA-GROM 2 (2·250 mm), hexane–*i*-PrOH (400:1), 0.3 mL·min^{-1}, λ = 210 nm]: t_R = 25.3 (–), 33.2 min (+); 54% ee.

$[\alpha]_D^{20}$ –8.4 (*c* 0.98, $CHCl_3$).

IR (ATR): 3461, 3088, 3065, 3033, 2972, 2935, 2876, 1682, 1495, 1436, 1369, 1323, 1300, 1213, 1157, 1135, 1054, 962, 905, 866, 818, 768, 735, 701, 650 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.13 (s, 3 H, H_3C), 1.15 (s, 3 H, H_3C), 1.17 [br d, $^3J_{(H3C)2CH,(H3C)2CH}$ = 6.1 Hz, 12 H, $(H_3C)_2CH$], 2.11 (br s, 1 H, OH), 3.90 [sept, 2 H, $(H_3C)_2CH$], 5.56 (s, 1 H, $H_{benzylic}$), 7.16–7.35 (m, 5 H, H_{phenyl}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.7 [$(H_3C)_2CH$], 25.3 (H_3C), 26.7 (H_3C), 45.9 [$(H_3C)_2CH$], 72.7 [$(H_3C)_2C(OH)$], 82.8 ($C_{benzylic}$), 127.8 (C2), 127.9 (C4), 128.0 (C3), 138.0 (C1), 155.0 (NC=O).

MS (ESI): *m*/*z* = 316.1881 $[M + Na]^+$.

Anal. Calcd for $C_{17}H_{27}NO_3$: C, 69.59; H, 9.28; N, 4.77. Found: C, 69.34; H, 9.39; N, 4.60.

(+)-(*R*)-2-Hydroxy-1,2,2-triphenylethyl *N*,*N*-Diisopropylcarbamate [(*R*)-20h]

According to GPB, a mixture of carbamate **19** (71 mg, 0.30 mmol) and **9d** (116 mg, 0.36 mmol) was treated with *s*-BuLi (0.26 mL, 0.36 mmol) and then benzophenone (82 mg, 0.45 mmol) was added; **20h** was obtained as a colorless solid; yield: 100 mg (81%); mp 104 °C (Et_2O); R_f = 0.56 (Et_2O–pentane, 1:1); t_R = 23.6 min.

HPLC [Chiralcel OD-H (4.6·250 mm), hexane–*i*-PrOH (200:1), 1.0 mL·min^{-1}, λ = 210 nm]: t_R = 14.1 (–), 15.4 min (+); 94% ee.

$[\alpha]_D^{20}$ +196.2 (*c* 0.50, $CHCl_3$).

IR (ATR): 3446, 3090, 3059, 3034, 2971, 2935, 2875, 1668, 1495, 1442, 1369, 1230, 1299, 1214, 1156, 1134, 1048, 1035, 999, 828, 761, 729, 697, 674, 625 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.87 [ps s, 3 H, $(H_3C)(H_3C)CH$], 1.05 [ps s, 3 H, $(H_3C)(H_3C)CH$], 1.14 [ps s, 6 H, $(H_3C)_2CH$], 2.63 (s, 1 H, OH), 3.74 [ps s, 1 H, $(H_3C)_2CH$], 3.86 [ps s, 1 H, $(H_3C)_2CH$], 6.73 (s, 1 H, $H_{benzylic}$), 7.00–7.38 (m, 13 H, H_{phenyl}), 7.56–7.66 (m, 2 H, H_{phenyl}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.5 [$(H_3C)_2CH$], 46.3 [$(H_3C)_2CH$], 79.3 ($C_{benzylic}$), 80.8 [$(H_5C_6)_2C(OH)$], 126.2, 126.4, 126.9, 127.0, 127.4, 127.6, 127.7, 128.2, 128.4, 136.5, 143.0, 145.2 (C_{phenyl}), 153.9 (NC=O).

MS (ESI): *m*/*z* = 440.2194 $[M + H]^+$.

Anal. Calcd for $C_{27}H_{31}NO_3$: C, 77.67; H, 7.48; N, 3.35. Found: C, 77.52; H, 7.68; N, 3.35.

(–)-2-Hydroxy-3,3-dimethyl-1-phenylbutyl *N*,*N*-Diisopropylcarbamate [(1*S*,2*R*)-20i, (1*S*,2*S*)-20i]

According to GPB, a mixture of carbamate **19** (71 mg, 0.30 mmol) and **9d** (116 mg, 0.36 mmol) was treated with *s*-BuLi (0.26 mL, 0.36 mmol) and then pivaldehyde (78 mg, 0.90 mmol) was added; (1*S*,2*R*)-**20i**/(1*S*,2*S*)-**20i** was obtained as a colorless liquid; yield: 67 mg (70%); R_f = 0.49 (Et_2O–pentane, 1:1); t_R = 15.6 min (1*S*,2*R*), 15.7 min (1*S*,2*S*) (HP 5). 32% ee was determined by conversion into (*S*)-**20e**.

$[\alpha]_D^{20}$ +2.0 (*c* 0.67, $CHCl_3$).

IR (film): 3486, 3082, 3064, 3032, 2969, 2872, 2713, 1684, 1586, 1486, 1479, 1436, 1368, 1320, 1300, 1217, 1157, 1135, 1100, 1048, 984, 905, 848, 767, 734, 700, 604 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.93 [s, 9 H, $(H_3C)_3C$ (1*S*,2*S*)], 0.96 [s, 9 H, $(H_3C)_3C$ (1*S*,2*R*)], 1.15–1.27 [m, 24 H, $(H_3C)_2CH$ (1*S*,2*R*), (1*S*,2*S*)], 1.55 [d, $^3J_{CH(OH),OH}$ = 5.0 Hz 1 H, OH (1*S*,2*S*)], 2.16 [d, $^3J_{CH(OH),OH}$ = 7.2 Hz, 1 H, OH (1*S*,2*R*)], 3.49 [dd, $^3J_{Hbenzylic,CH(OH)}$ = 3.0 Hz, 1 H, C*H*(OH) (1*S*,2*S*)], 3.71 [dd, $^3J_{Hbenzylic,CH(OH)}$ = 5.0 Hz, 1 H, C*H*(OH) (1*S*,2*R*)], 3.91 [ps s, 4 H, $(H_3C)_2CH$ (1*S*,2*R*), (1*S*,2*S*)], 5.85 [d, 1 H, $H_{benzylic}$ (1*S*,2*S*)], 6.00 [d, 1 H, $H_{benzylic}$ (1*S*,2*R*)], 7.18–7.43 [m, 10 H, H_{phenyl} (1*S*,2*R*), (1*S*,2*S*)].

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.6 [$(H_3C)_2CH$ (1*S*,2*R*), (1*S*,2*S*)], 26.4 [$(H_3C)_3C$ (1*S*,2*R**)], 26.5 [$(H_3C)_3C$ (1*S*,2*S**)], 45.9 [(*C*H(OH) (1*S*,2*R**)], 46.1 [(*C*H(OH) (1*S*,2*S**)], 46.0 [$(H_3C)_2CH$ (1*S*,2*R*), (1*S*,2*S*)], 74.8 [$C_{benzylic}$ (1*S*,2*R**)], 76.7 [$C_{benzylic}$ (1*S*,2*S**)], 80.3 [$(H_3C)_3C$ (1*S*,2*S**)], 82.0 [$(H_3C)_3C$ (1*S*,2*R**)], 126.8 [C2 (1*S*,2*R**)], 127.7 [C2 (1*S*,2*S**)], 128.1 [C4 (1*S*,2*R**)], 128.3 [C4 (1*S*,2*S**)], 128.4 [C3 (1*S*,2*R**)], 128.5 [C3 (1*S*,2*S**)], 138.7 [C1 (1*S*,2*R**)], 140.7 [C1 (1*S*,2*S**)], 153.7 [NC=O (1*S*,2*R**)], 154.0 [NC=O (1*S*,2*S**)].

MS (ESI): *m*/*z* = 344.2213 $[M + Na]^+$.

Anal. Calcd for $C_{27}H_{31}NO_3$: C, 70.99; H, 9.72; N, 4.36. Found: C, 70.87; H, 9.81; N, 4.28.

(+)-2-(4-Bromophenyl)-2-hydroxy-1-phenylethyl *N*,*N*-Diisopropylcarbamate [(1*R*,2*S*)-20j, (1*R*,2*R*)-20j]

According to GPB, a mixture of carbamate **19** (71 mg, 0.30 mmol) and **9d** (116 mg, 0.36 mmol) was treated with *s*-BuLi (0.26 mL, 0.36 mmol) and then 4-bromobenzaldehyde (275 mg, 1.50 mmol) was added; (1*R*,2*S*)-**20j**/(1*R*,2*R*)-**20j** was obtained as a colorless solid; yield: 168 mg (80%); mp 84 °C (Et_2O); R_f = 0.31 (Et_2O–pentane, 1:1); t_R = 21.5 min (1*R*,2*S*), 21.6 min (1*R*,2*R*) (HP 5). 97% ee was determined by conversion into (*R*)-**20f**.

$[\alpha]_D^{20}$ +19.2 (*c* 0.87, $CHCl_3$).

IR (KBr): 3408, 3065, 3001, 2974, 2932, 1659, 1590, 1480, 1445, 1398, 1384, 1368, 1299, 1213, 1197, 1158, 1137, 1074, 1010, 980, 957, 899, 858, 822, 767, 719, 701, 614 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.08–1.28 [m, 24 H, $(H_3C)_2CH$ (1*R*,2*S*), (1*R*,2*R*)], 3.68 [ps s, 1 H, OH (1*R*,2*S*)], 3.75 [ps s, 1 H, OH (1*R*,2*R*)], 3.82–3.96 [m, 4 H, $(H_3C)_2CH$ (1*R*,2*S*), (1*R*,2*R*)], 4.89 [d, $^3J_{Hbenzylic,CH(OH)}$ = 7.4 Hz, 1 H, C*H*(OH) (1*R*,2*R*)], 4.95 [d, $^3J_{H1,H8}$ = 3.9 Hz, 1 H, C*H*(OH) (1*R*,2*S*)], 5.79 [d, 1 H, $H_{benzylic}$

(1*R*,2*R*)], 6.25 [d, 1 H, $H_{benzylic}$ (1*R*,2*S*)], 6.87–7.45 [m, 9 H, H_{phenyl}, H_{aryl} (1*R*,2*S*), (1*R*,2*R*)].

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.7 [$(H_3C)_2CH$ (1*R*,2*S*), (1*R*,2*R*)], 46.0 [$(H_3C)_2CH$ (1*R*,2*S*), (1*R*,2*R*)], 65.8 [(*C*H(OH) (1*R*,2*S**)], 77.3 [(*C*H(OH) (1*R*,2*R**)], 80.1 [$C_{benzylic}$ (1*R*,2*R**)], 81.2 [$C_{benzylic}$ (1*R*,2*S**)], 121.6, 127.1, 127.4, 127.5, 128.0, 128.1, 128.2, 128.9, 129.0, 129.1, 130.7, 130.9, 131.1, 136.8, 136.9, 138.5, 139.0 [C_{phenyl}, C_{aryl} (1*R*,2*S*), (1*R*,2*R*)], 155.0 [NC=O (1*R*,2*R**)], 155.5 [NC=O (1*R*,2*S**)].

MS (ESI): *m*/*z* = 422.0979 $[M + H]^+$, 444.0961 $[M + Na]^+$.

Anal. Calcd for $C_{21}H_{26}BrNO_3$: C, 60.00; H, 6.23; N, 3.33. Found: C, 59.92; H, 6.47; N, 3.23.

(+)-(*S*)-1-(1-Naphthyl)but-3-enyl *N*,*N*-Diisopropylcarbamate [(*S*)-26b]

According to GPB, a mixture of carbamate **23** (143 mg, 0.50 mmol) and **9d** (193 mg, 0.60 mmol) was treated with *s*-BuLi (0.49 mL, 0.60 mmol) and then allyl bromide (301 mg, 2.50 mmol) was added; **26b** was obtained as a colorless liquid; yield: 130 mg (80%); R_f = 0.64 (Et_2O–pentane, 1:1); t_R = 17.5 min (HP 5).

HPLC [CHIRA GROM 1 (2·250 mm), hexane–*i*-PrOH (1000:1), 0.3 mL·min^{-1}, λ = 210 nm]: t_R = 13.7 (–), 16.5 min (+); 78% ee.

$[\alpha]_D^{20}$ +21.5 (*c* 1.08, $CHCl_3$).

IR (ATR): 3075, 3051, 2998, 2970, 2934, 2875, 1686, 1643, 1598, 1511, 1475, 1431, 1375, 1339, 1309, 1294, 1215, 1189, 1157, 1132, 1046, 974, 914, 775, 734 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.24 [br d, $^3J_{(H3C)2CH,(H3C)2CH}$ = 6.5 Hz, 12 H, $(H_3C)_2CH$], 2.45–2.55 [m, 2 H, H_2CCHCH_2], 3.98 [ps s, 2 H, $(H_3C)_2CH$], 5.04 [ddd, $^3J_{H2CCHCH2,HcisHtransCCHCH2}$ = 10.1 Hz, $^2J_{HcisHtransC=CH,HcisHtransC=CH}$ = 2.1 Hz, $^4J_{H2C=CHCH2,HcisHtransC=CH}$ = 1.1 Hz, 1 H, $H_{cis}H_{trans}C=CHCH_2$), 5.10 (ddd, $^3J_{H2C=CHCH2,HcisHtransC=CH}$ = 17.1 Hz, $^4J_{H2C=CHCH2,HcisHtransC=CH}$ = 2.1 Hz, 1 H, $H_{cis}H_{trans}C=CHCH_2$), 5.69 (m, 1 H, H13), 6.62 (t, $^3J_{H2C=CHCH2,Hbenzylic}$ = 6.3 Hz, 1 H, $H_{benzylic}$), 7.43–7.50 (m, 7 H, $H_{naphthyl}$).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.2 [$(H_3C)_2CH$], 40.8 ($H_2C=CHCH_2$), 46.0 [$(H_3C)_2CH$], 72.5 ($C_{benzylic}$), 117.5 ($H_2C=CH$), 134.1 ($H_2C=CH$) 123.4, 123.6, 125.2, 125.5, 126.1, 128.0, 128.8, 130.4, 133.8, 137.1 ($C_{naphthyl}$), 154.7 (NC=O).

MS (ESI): *m*/*z* = 348.1933 $[M + Na]^+$.

Anal. Calcd for $C_{21}H_{27}NO_2$: C, 77.50; H, 8.36; N, 4.30. Found: C, 77.31; H, 8.49; N, 4.20.

(–)-(*R*)-Methyl 2-(Diisopropylcarbamoyloxy)-2-(1-naphthyl)-acetate [(*R*)-26c]; Typical Procedure

As described in GPB, the lithiated species was synthesized by deprotonating **23** (143 mg, 0.50 mmol) in the presence of **9d** (193 mg, 0.60 mmol) and equilibrated. As electrophile, dried and pre-cooled gaseous CO_2 was bubbled through the mixture over a period of 10–15 min. The mixture was stirred at –78 °C for an additional 1 h, then the reaction was carefully quenched with MeOH (0.5 mL) and H_2O (1 mL). Workup was performed as described in GPB. The crude acid was directly dissolved in Et_2O and a soln of CH_2N_2 in Et_2O was added at r.t. until a yellowish color of the mixture remained. The soln was stirred for 1 h. In order to destroy the remaining CH_2N_2, silica gel (ca. 1 g) was added and the suspension was stirred for 1 h. The solvent was removed under reduced pressure and, thereby, the crude product adsorbed on the silica gel. This was directly submitted to column chromatography (Et_2O–pentane, 1:4) to yield **26c** as a colorless crystalline solid; yield: 111 mg (65%); mp 93 °C (Et_2O); R_f = 0.55 (Et_2O–pentane, 1:1); t_R = 18.2 min (HP 5).

HPLC [CHIRA-GROM 1 (2·250 mm), hexane–*i*-PrOH (1000:1), 0.3 mL·min^{-1}, λ = 210 nm]: t_R = 38.2 (+), 43.5 min (–); 90% ee.

$[\alpha]_D^{20}$ –142.2 (*c* 0.61, $CHCl_3$).

IR (ATR): 3069, 2978, 2970, 2935, 1753, 1688, 1513, 1434, 1371, 1332, 1300, 1222, 1209, 1160, 1138, 1064, 1042, 1007, 930, 906, 868, 806, 786, 764, 736, 641, 621, 572 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.19 [ps s, 6 H, $(H_3C)_2CH$], 1.27 [br d, $^3J_{(H3C)2CH,(H3C)2CH}$ = 7.4 Hz, 6 H, $(H_3C)_2CH$], 3.69 (s, 3 H, H_3CO), 3.95 [ps s, 2 H, $(H_3C)_2CH$], 6.73 (s, 1 H, $H_{benzylic}$), 7.42–7.60 (m, 3 H, H2, H3, H7), 7.63 (ps dd, $^3J_{H5,H6}$ = $^3J_{H6,H7}$ = 7.1 Hz, $^4J_{H6,H8}$ = 1.1 Hz, 1 H, H6), 7.83–7.89 (m, 2 H, H5, H6), 8.26 (dd, $^3J_{H7,H8}$ = 8.5 Hz, 1 H, H8).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.9 [$(H_3C)_2CH$], 46.2 [$(H_3C)_2CH$], 52.4 (H_3CO), 72.7 ($C_{benzylic}$), 124.1, 125.2, 125.9, 126.7, 127.3, 128.7, 129.7, 131.0, 131.2, 134.0 ($C_{naphthyl}$), 154.4 (NC=O), 170.7 (C12).

MS (ESI): *m*/*z* = 366.1682 $[M + Na]^+$.

Anal. Calcd for $C_{20}H_{25}NO_4$: C, 69.95; H, 7.34; N, 4.08. Found: C, 69.87; H, 7.37; N, 3.95.

(–)-(*S*)-(2-Ethylphenyl)(tributylstannyl)methyl *N*,*N*-Diisopropylcarbamate [(*S*)-27a]

According to GPB, a mixture of carbamate **24** (79 mg, 0.30 mmol) and **9d** (116 mg, 0.36 mmol) was treated with *s*-BuLi (0.26 mL, 0.36 mmol) before Bu_3SnCl (117 mg, 0.36 mmol) was added; **27a** was obtained as a colorless liquid; yield: 153 mg (92%); R_f = 0.56 (Et_2O–pentane, 1:12); t_R = 20.6 min (HP 5).

HPLC [EC250/4 Nucleosil 100-5 Chiral-2 (4·250 mm), hexane–*i*-PrOH–TFA (1000:1:0.5), 0.3 mL·min^{-1}, λ = 210 nm]: t_R = 20.1 (+), 23.4 min (–); 92% ee.

$[\alpha]_D^{20}$ –46.1 (*c* 1.01, $CHCl_3$).

IR (ATR): 3063, 2959, 2930, 2871, 2853, 1681, 1602, 1493, 1463, 1433, 1377, 1331, 1310, 1216, 1157, 1135, 1048, 951, 936, 865, 771, 755 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.81 (t, $^3J_{H3CCHH,(H3C)CH2}$ = 6.9 Hz, 3 H, H_3CCH_2), 0.83 [t, $^3J_{(H3C)CH2CH2CH2,(H3C)CH2CH2CH2}$ = 7.3 Hz, 9 H, $(H_3C)CH_2CH_2CH_2$], 1.13–1.48 [m, 18 H, $(H_3C)CH_2CH_2CH_2$], 1.24 [d, $^3J_{(H3C)2CH,(H3C)2CH}$ = 6.6 Hz, 12 H, $(H_3C)_2CH$], 2.61 (dq, $^2J_{H3CCHH,(H3C)CHH}$ = 14.5 Hz, 1 H, H_3CCHH], 2.65 (dq, 1 H, H_3CCHH), 3.98 [sept, 2 H, $(H_3C)_2CH$], 5.90 (s, 1 H, $H_{benzylic}$), 6.99–7.32 (m, 4 H, H_{aryl}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.5 [$(H_3C)CH_2CH_2CH_2$], 13.6 [$(H_3C)CH_2CH_2CH_2$], 14.3 (H_3CCH_2), 20.9 [$(H_3C)_2CH$], 25.5 (H_3CCH_2), 27.4 [$(H_3C)CH_2CH_2CH_2$], 28.8 [$(H_3C)CH_2CH_2CH_2$], 45.9 [$(H_3C)_2CH$], 71.2 ($C_{benzylic}$), 124.7 (C5), 124.9 (C6), 125.9 (C4), 127.7 (C3), 137.1 (C2), 144.0 (C1), 155.6 (NC=O).

MS (EI, 70 eV): *m*/*z* (%) = 552 $[M]^+$ (1), 496 $[M – Bu]^+$ (49), 440 $[M – 2 Bu]^+$ (4), 378 (2), 322 (2), 263 (12) $[M – SnBu_3]^+$, 175 (16), 119 (100) $[M – SnBu_3 – OCb]^+$.

Anal. Calcd for $C_{28}H_{51}NO_2Sn$: C, 60.88; H, 9.31; N, 2.54. Found: C, 61.00; H, 9.34; N, 2.44.

(–)-(*S*)-(2-Ethylphenyl)(trimethylsilyl)methyl *N*,*N*-Diisopropylcarbamate [(*S*)-27b]

According to GPB, a mixture of carbamate **24** (79 mg, 0.30 mmol) and **9d** (116 mg, 0.36 mmol) was treated with *s*-BuLi (0.26 mL, 0.36 mmol) and then Me_3SiCl (39 mg, 0.36 mmol) was added; **27b** was obtained as a colorless liquid; yield: 96 mg (97%); R_f = 0.45 (Et_2O–pentane, 1:6); t_R = 14.2 min (HP 5).

HPLC [CHIRA-GROM 1 (2·250 mm), hexane–*i*-PrOH (4000:1), 0.3 mL·min^{-1}, λ = 210 nm]: t_R = 6.5 (+), 7.0 min (–); >98% ee.

$[\alpha]_D^{20}$ –38.9 (*c* 0.96, $CHCl_3$).

IR (film): 3064, 2967, 2936, 2877, 1693, 1475, 1428, 1377, 1368, 1334, 1311, 1294 1260, 1188, 1157, 1135, 1045, 940, 877, 865, 840, 765, 617, 601 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.00 [s, 9 H, $(H_3C)_3Si$], 1.16–1.36 [br m, 15 H, $(H_3C)_2CH$, H_3CCH_2], 2.53 (dq, $^2J_{H3CCHH,H3CCHH}$ = 14.8 Hz, $^3J_{H3CCHH,(H3C)CHH}$ = 7.4 Hz, 1 H, H_3CCHH), 2.75 (dq, $^3J_{H3CCHH,(H3C)CHH}$ = 7.4 Hz, 1 H, H_3CCHH), 3.92 [ps s, 2 H, $(H_3C)_2CH$], 5.89 (s, 1 H, $H_{benzylic}$), 7.02–7.22 (m, 4 H, H_{aryl}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = –3.2 [$(H_3C)_3Si$), 14.5 (H_3CCH_2), 21.1 [$(H_3C)_2CH$], 25.4 (H_3CCH_2), 45.8 [$(H_3C)_2CH$], 65.7 ($C_{benzylic}$), 125.5 (C3), 125.9 (C5), 126.3 (C6), 128.0 (C4), 138.7 (C1), 139.6 (C2), 155.8 (NC=O).

MS (EI, 70 eV): *m*/*z* (%) = 321 [M – CH_3]$^+$ (5), 278 (8), 216 (48), 172 (54), 144 [O*Cb*]$^+$ (6), 130 (16), 119 [$(H_5C_2)C_6H_4CH_2$]$^+$ (9), 73 [$(H_3C)_3Si$]$^+$ (100), 43 [H_7C_3]$^+$ (32).

Anal. Calcd for $C_{19}H_{33}NO_2Si$: C, 68.01; H, 9.91; N, 4.17. Found: C, 67.87; H, 9.98; N, 4.06.

(–)-(*S*)-1-(2-Ethylphenyl)ethyl *N*,*N*-Diisopropylcarbamate [(*S*)-27c]

According to GPB, a mixture of carbamate **24** (263 mg, 1.00 mmol) and **9d** (387 mg, 1.20 mmol) was treated with *s*-BuLi (0.88 mL, 1.20 mmol) and then MeI (284 mg, 1.20 mmol) was added; **27c** was obtained as a colorless liquid; yield: 101 mg (36%); R_f = 0.50 (Et_2O–pentane, 1:3); t_R = 14.5 min (HP 5).

HPLC [CHIRA-GROM 1 (2·250 mm), hexane–*i*-PrOH (1000:1), 0.3 mL·min^{-1}, λ = 210 nm]: t_R = 5.8 (+), 6.4 min (–); 92% ee.

$[\alpha]_D^{20}$ –2.3 (*c* 1.04, $CHCl_3$).

IR (film): 3064, 2969, 2934, 1692, 1475, 1428, 1368, 1293, 1216, 1190, 1133, 1100, 1068, 1047, 906 (m), 757, 624, 600 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.02–120 [br m, 15 H, H_3CCH_2, $(H_3C)_2CH$], 1.39 (d, $^3J_{H3C,Hbenzylic}$ = 6.8 Hz, 3 H, H_3C), 2.61 (dq, $^2J_{H3CCHH,H3CCHH}$ = 14.8 Hz, $^3J_{H3CCHH,(H3C)CHH}$ = 7.5 Hz, 1 H, H_3CCHH), 2.65 (dq, $^3J_{H3CCHH,(H3C)CHH}$ = 7.5 Hz, 1 H, H_3CCHH), 3.79 [ps s, 2 H, $(H_3C)_2CH$], 5.99 (q, 1 H, $H_{benzylic}$), 7.00–7.34 (m, 4 H, H_{aryl}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.4 (H_3CCH_2), 21.0 [$(H_3C)_2CH$], 22.8 (H_3C), 25.4 (H_3CCH_2), 45.8 [$(H_3C)_2CH$], 68.9 ($C_{benzylic}$), 125.7 (C5), 126.0 (C6), 127.5 (C4), 128.5 (C3), 139.0 (C2), 140.6 (C1), 155.0 (NC=O).

MS (EI, 70 eV): *m*/*z* (%) = 277 [M]$^+$ (1), 218 (8), 146 (3), 133 [$(H_5C_2)C_6H_4CH(CH_3)$]$^+$ (100), 128 [O*Cb*]$^+$ (4), 117 [$(H_5C_2)C_6H_4CH_2$]$^+$ (100), 105 [$(H_5C_2)C_6H_4$]$^+$ (14), 91 [C_7H_7]$^+$ (53), 77 [C_6H_5]$^+$ (19), 43 [C_3H_7]$^+$ (32).

Anal. Calcd for $C_{17}H_{27}NO_2$: C, 73.61; H, 9.81; N, 5.05. Found: C, 73.58; H, 9.74; N, 4.92.

(–)-(*R*)-Methyl 2-(Diisopropylcarbamoyloxy)-2-(2-ethylphenyl)acetate [(*R*)-27d]

According to GPB, a mixture of carbamate **24** (79 mg, 0.30 mmol) and **9d** (116 mg, 0.36 mmol) was treated with *s*-BuLi (0.27 mL, 0.36 mmol) to generate the lithiated species. After 2.5 h the reaction was continued according to the synthesis of **26c**; **27d** was obtained as a highly viscous, colorless oil; yield: 67 mg (70%); R_f = 0.88 (Et_2O–pentane, 1:1); t_R = 15.9 min (HP 5).

HPLC [CHIRA-GROM 1 (2·250 mm), hexane–*i*-PrOH (1000:1), 0.2 mL·min^{-1}, λ = 210 nm]: t_R = 20.2 (+), 25.4 min (–); 78% ee.

$[\alpha]_D^{20}$ –101.0 (*c* 0.96, $CHCl_3$).

IR (film): 3064, 2970, 2936, 2877, 1758, 1692, 1493, 1436, 1369, 1297, 1263, 1213, 1188, 1159, 1134, 1075, 1046, 1017, 926, 906, 793, 757, 734, 627 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.14–1.34 [br m, 15 H, H_3CCH_2, $(H_3C)_2CH$], 2.80–2.86 (m, 2 H, H_3CCH_2), 3.69 (s, 3 H, H_3CO), 3.94 [br s, 2 H, $(H_3C)_2CH$], 6.23 (s, 1 H, $H_{benzylic}$), 7.17–7.29 (m, 2 H, H5, H3), 7.31 (ps dt, $^3J_{H3,H4}$ = $^3J_{H4,H5}$ = 7.9 Hz, $^4J_{H4,H6}$ = 1.3 Hz, 1 H, H4), 7.43 (dd, $^3J_{H5,H6}$ = 7.7 Hz, 1 H, H6).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.5 (H_3CCH_2), 21.0 [$(H_3C)_2CH$], 25.5 (H_3CCH_2), 46.8 [$(H_3C)_2CH$], 52.2 (H_3CO), 71.1 ($C_{benzylic}$), 126.2 (C5), 128.2 (C6), 129.0 (C4), 129.9 (C3), 132.6 (C2), 142.8 (C1), 154.5 (NC=O), 170.8 (C=O).

MS (EI, 70 eV): *m*/*z* (%) = 262 [M – $COOCH_3$]$^+$ (1), 177 [M – O*Cb*]$^+$ (65), 149 (25), 145 (30), 133 (31), 131 (38), 128 [*Cb*]$^+$ (4), 119 [$(H_5C_2)C_6H_4CH_2$]$^+$ (18), 117 (84), 115 (66), 105 [$(H_5C_2)C_6H_4$]$^+$ (23), 103 (41), 91 [C_7H_7]$^+$ (53), 84 (28), 77 [C_6H_5]$^+$ (47), 70 (81), 63 (31), 58 (26), 51 [C_4H_3]$^+$ (48), 42 [C_2H_2O]$^+$ (100).

Anal. Calcd for $C_{18}H_{27}NO_4$: C, 67.26; H, 8.47; N, 4.36. Found: C, 67.31; H, 8.52; N, 4.19.

(–)-(*S*)-(4-Methoxyphenyl)(tributylstannyl)methyl *N*,*N*-Diisopropylcarbamate [(*S*)-30a]

According to GPB, a mixture of carbamate **25** (80 mg, 0.30 mmol) and **9d** (116 mg, 0.36 mmol) was treated with *s*-BuLi (0.26 mL, 0.36 mmol) and then Bu_3SnCl (117 mg, 0.36 mmol) was added; **30a** was obtained as a colorless liquid; yield: 106 mg (64%); R_f = 0.24 (Et_2O–pentane, 1:12); t_R = 23.3 min (HP 5).

HPLC [EC250/4 Nucleosil 100-5 Chiral-2 (4·250 mm), hexane–*i*-PrOH–TFA (500:1:0.5), 0.3 mL·min^{-1}, λ = 210 nm]: t_R = 40.1 (+), 49.7 min (–); 92% ee.

$[\alpha]_D^{20}$ –17.8 (*c* 1.03, $CHCl_3$).

IR (ATR): 3060, 2998, 2956, 2926, 2872, 2853, 1673, 1609, 1509, 1460, 1438, 1377, 1346, 1312, 1298, 1245, 1213, 1157, 1135, 1048, 827, 772, 745, 659 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.83 [t, $^3J_{H3C(CH2)3,H3CCH2}$ = 7.1 Hz, 9 H, $H_3C(CH_2)_3$], 1.13–1.47 (m, 18 H, $H_3CCH_2CH_2CH_2$), 1.22 [d, $^3J_{(H3C)2CH,(H3C)2CH}$ = 7.1 Hz, 12 H, $(H_3C)_2CH$], 3.77 (s, 3 H, H_3CO), 3.94 [ps s, 2 H, $(H_3C)_2CH$], 5.72 (s, 1 H, $H_{benzylic}$), 6.81 (dd, $^3J_{H2,H3}$ = 8.8 Hz, $^4J_{H3,H3'}$ = 1.9 Hz, 2 H, H3), 7.04 (dd, $^4J_{H2,H2'}$ = 2.1 Hz, 2 H, H2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.1 ($H_3CCH_2CH_2CH_2$), 13.7 ($H_3CCH_2CH_2CH_2$), 21.1 [$(H_3C)_2CH$], 27.5 ($H_3CCH_2CH_2CH_2$), 29.0 ($H_3CCH_2CH_2CH_2$), 45.9 [$(H_3C)_2CH$], 55.3 (H_3CO), 73.1 ($C_{benzylic}$), 113.8 (C3), 125.3 (C2), 136.1 (C1), 155.7 (NC=O), 157.1 (C4).

MS (ESI): *m*/*z* = 578.2623 [M + Na]$^+$.

Anal. Calcd for $C_{27}H_{49}NO_3Sn$: C, 58.49; H, 8.91; N, 2.53. Found: C, 58.65; H, 9.02; N, 2.37.

(–)-(*S*)-(4-Methoxyphenyl)(trimethylsilyl)methyl *N*,*N*-Diisopropylcarbamate [(*S*)-30b]

According to GPB, a mixture of carbamate **25** (80 mg, 0.30 mmol) and **9d** (116 mg, 0.36 mmol) was treated with *s*-BuLi (0.26 mL, 0.36 mmol) and then Me_3SiCl (39 mg, 0.36 mmol) was added; **30b** was obtained as a colorless liquid; yield: 85 mg (80%); R_f = 0.43 (Et_2O–pentane, 1:4); t_R = 15.5 min (HP 5).

HPLC [CHIRA-GROM 1 (2·250 mm), hexane–*i*-PrOH (4000:1), 0.3 mL·min^{-1}, λ = 210 nm]: t_R = 11.8 (+), 17.1 min (–); 78% ee.

$[\alpha]_D^{20}$ –26.9 (*c* 1.02, $CHCl_3$).

IR (film): 3059, 2966, 2935, 2835, 1692, 1612, 1510, 1368, 1314, 1279, 1248, 1217, 1174, 1157, 1046, 877, 842, 767 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.00 [s, 9 H, $(H_3C)_3Si$], 1.22 [br s, 12 H, $(H_3C)_2CH$], 3.75 (s, 3 H, H_3CO), 3.94 [ps s, 2 H, $(H_3C)_2CH$], 5.52 (s, 1 H, $H_{benzylic}$), 6.81 (dd, $^3J_{H2,H3}$ = 8.7 Hz, $^4J_{H3,H3'}$ = 1.3 Hz, 2 H, H3), 7.07 (dd, $^4J_{H2,H2'}$ = 1.3 Hz, 2 H, H2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = –3.5 [$(H_3C)_3Si$], 21.2 [$(H_3C)_2CH$], 45.7 [$(H_3C)_2CH$], 55.1 (H_3CO), 71.5 ($C_{benzylic}$), 113.6 (C3), 126.7 (C2), 133.1 (C1), 155.6 (NC=O), 157.85 (C4).

MS (EI, 70 eV): *m*/*z* (%) = 322 [(M – CH_3)]$^+$ (6), 216 (28), 194 (14), 179 (49), 172 (28), 165 [$CH_3OC_6H_4CH_2OCO$]$^+$ (20), 158 (13), 144 [O*Cb*]$^+$ (6), 135 (10), 130 (12), 121 [$CH_3OC_6H_4CH_2$]$^+$ (19), 73 [$(CH_3)_3Si$]$^+$ (100), 43 [C_3H_7]$^+$ (23).

Anal. Calcd for $C_{18}H_{31}NO_3Si$: C, 64.05; H, 9.26; N, 4.15. Found: C, 63.88; H, 9.39; N, 4.00.

(+)-(*R*)-1-(4-Methoxyphenyl)-1-(trimethylsilyl)methyl *N*,*N*-Diisopropylcarbamate [(*R*)-30b]

According to GPB, a mixture of carbamate **25** (265 mg, 1.00 mmol) and **7** (282 mg, 1.20 mmol) was treated with *s*-BuLi (0.96 mL, 1.20 mmol) and then Me_3SiCl (130 mg, 1.20 mmol) was added; yield: 324 mg (96%); 40% ee.

$[\alpha]_D^{20}$ +14.2 (*c* 1.00, $CHCl_3$).

(–)-(*S*)-(2-Ethylphenyl)(trimethylsilyl)methanol [(*S*)-28]; Typical Procedure

To a soln of carbamate (–)-(*S*)-**27b** (168 mg, 0.50 mmol) in THF (5 mL) was added 1 M DIBAL-H in *n*-hexane (5.00 mL, 5.00 mmol). The mixture was refluxed for 16 h (TLC). The mixture was then cooled to r.t. and diluted with Et_2O (10 mL). 2 M HCl was added until the two-phase system became clear. The phases were separated and the aqueous phase was extracted with Et_2O (3 × 10 mL). The combined organic layers were washed with sat. $NaHCO_3$ and dried ($MgSO_4$). The solvents were removed in vacuo and the crude product was purified by column chromatography (silica gel, Et_2O–pentane, 1:4) to give the pure product as a colorless liquid; yield: 90 mg (86%); R_f = 0.61 (Et_2O–pentane, 1:1); t_R = 10.2 min (HP 5).

HPLC [Chiralcel OD-H (4.6·250 mm), hexane–*i*-PrOH (200:1), 1.0 mL·min^{-1}, λ = 210 nm]: t_R = 33.6 (+), 38.9 min (–); 98% ee.

$[\alpha]_D^{20}$ –95.9 (*c* 0.64, $CHCl_3$).

IR (ATR): 3419, 3066, 3022, 2962, 2930, 2875, 1669, 1601, 1483, 1452, 1407, 1377, 1290, 1247, 1212, 1140, 1055, 990, 946, 859, 838, 753, 695, 651, 611 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.03 [s, 9 H, $(H_3C)_3Si$], 1.21 (t, $^3J_{H3CCH2,H3CCH2}$ = 7.7 Hz, 3 H, H_3CCH_2), 1.54 (ps s, 1 H, OH), 2.47 (dq, $^2J_{H3CCHH,H3CCHH}$ = 14.9 Hz, 1 H, H_3CCHH), 2.60 (dq, 1 H, H_3CCHH), 4.83 (s, 1 H, $H_{benzylic}$), 7.09–7.25 (m, 3 H, H3, H4, H5), 7.39 (br d, $^3J_{H5,H6}$ = 7.4 Hz, 1 H, H6).

^{13}C NMR (75 MHz, $CDCl_3$): δ = –3.7 [$(H_3C)_3Si$], 14.8 (H_3CCH_2), 25.3 (H_3CCH_2), 65.9 ($C_{benzylic}$), 126.0 (br s, C4, C5, C6), 128.0 (C3), 139.3 (C2), 141.8 (C1).

MS (EI, 70 eV): *m*/*z* (%) = 208 [M]$^+$ (15), 179 [M – Et]$^+$ (72), 117 [C_9H_9]$^+$ (93), 95 (13), 73 [$(H_3C)_3Si$]$^+$ (100).

Anal. Calcd for $C_{12}H_{20}OSi$: C, 69.10; H, 9.67. Found: C, 68.99; H, 9.89.

(–)-(*S*,*S*)-[(2-Ethylphenyl)(trimethylsilyl)methyl] *N*-1-Phenylethylcarbamate [(*S*,*S*)-29]

A catalytic amount of DMAP was added to a soln of alcohol (–)-(*S*)-**28** (63 mg, 0.30 mmol, 98% ee) in DMF (5 mL). The mixture was stirred at r.t. until it became clear. Then, (–)-(*S*)-1-phenylethyl isocyanate (66 mg, 0.45 mmol) was added and the resulting mixture was stirred at 60 °C until no starting material was detected (TLC). Et_2O (5 mL) and H_2O (2 mL) were added prior to the addition of 2 M HCl (2 mL). The phases were separated and the aqueous phase was extracted with Et_2O (3 × 10 mL). The combined organic layers were washed with sat. $NaHCO_3$ and dried ($MgSO_4$). The solvents were removed in vacuo. Purification by column chromatography (silica gel, Et_2O–pentane, 1:6) yielded the colorless crystalline diastereomer (*S*,*S*)-**29** as single product; yield: 44 mg (41%); mp 109 °C (Et_2O); R_f = 0.44 (Et_2O–pentane, 1:1); t_R = 19.3 min (HP 5).

$[\alpha]_D^{20}$ –78.5 (*c* 0.28, $CHCl_3$).

IR (ATR): 3232, 3126, 3085, 3032, 2969, 2936, 2903, 2875, 1705, 1679, 1485, 1451, 1378, 1360, 1324, 1280, 1247, 1223, 1177, 1093, 1047, 1028, 1006, 1000, 882, 868, 833, 758, 700, 638, 609, 588 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.00 [s, 9 H, $(H_3C)_3Si$], 1.27 (t, $^3J_{H3CCH2,H3CCH2}$ = 7.5 Hz, 3 H, H_3CCH_2), 1.44 (d, $^3J_{H3C,Hbenzylic}$ = 7.4 Hz, 3 H, H_3C), 2.51–2.58 (m, 1 H, H_3CCHH), 2.69–2.73 (m, 1 H, H_3CCHH), 4.80 (dq, $^3J_{Hbenzylic,NH}$ = 7.3 Hz, 1 H, $H_{benzylic}$), 4.96 (ps s, 1 H, NH), 5.82 (s, 1 H, $H_{benzylic}$), 7.00–7.40 (m, 9 H, H_{aryl}, H_{phenyl}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = –3.4 [$(H_3C)_3Si$], 14.7 (H_3CCH_2), 25.7 (H_3C), 27.1 (H_3CCH_2), 50.8 ($C_{benzylic}$), 68.2 ($C_{benzylic}$), 125.6, 125.9, 126.1, 127.2, 128.0, 128.6 (C3, C4, C5, C6, C2′, C3′), 134.6 (C2), 138.1 (C1′), 141.0 (C1), 156.0 (NC=O).

MS (ESI): *m*/*z* = 378.1875 [M + Na]$^+$.

Anal. Calcd for $C_{21}H_{29}NO_2Si$: C, 69.90; H, 7.41; N, 4.29. Found: C, 69.64; H, 7.50; N, 4.26.

(–)-(*S*)-1-Phenylbut-3-en-1-ol [(*S*)-34]

According to the synthesis of (*S*)-**28**, benzyl carbamate (*S*)-**20c** (80 mg, 0.29 mmol) was decarbamoylated using 1 M DIBAL-H in *n*-hexane (2.90 mL, 2.90 mmol) in refluxing THF; (*S*)-**34** was obtained as a colorless liquid; yield: 32 mg (75%); R_f = 0.45 (Et_2O–pentane, 1:1); t_R = 9.0 min (HP 5).

$[\alpha]_D^{20}$ –32.9 (*c* 1.08, benzene).

(+)-(*R*)-1,1,2-Triphenylethane-1,2-diol [(*R*)-21]

According to the synthesis of (*S*)-**28**, benzyl carbamate (*R*)-**20h** (63 mg, 0.15 mmol) was decarbamoylated using 1 M DIBAL-H in *n*-hexane (2.25 mL, 2.25 mmol) in refluxing THF; (*R*)-**21** was obtained as a colorless solid; yield: 30 mg (69%); mp 128 °C (Et_2O); R_f = 0.63 (Et_2O–pentane, 1:1); t_R = 6.7 min (HP 5).

$[\alpha]_D^{20}$ +179.7 (*c* 1.01, EtOH).

(–)-(*S*)-1-(1-Naphthyl)but-3-en-1-ol [(*S*)-35]

According to the synthesis of (*S*)-**28**, 1-naphthylmethyl carbamate (*S*)-**26b** (98 mg, 0.30 mmol) was decarbamoylated using 1 M DIBAL-H in *n*-hexane (3.00 mL, 3.00 mmol) in refluxing THF; (*S*)-**35** was obtained as a colorless liquid; yield: 101 mg (81%); R_f = 0.70 (Et_2O–pentane, 1:1); t_R = 11.1 min (HP 5).

$[\alpha]_D^{20}$ –72.8 (*c* 1.04, benzene).

Computational details: For all calculations the Turbomole 5.9 suite of programs[39a] was used. The structures of the complexes were optimized at DFT level employing the B97-D functional[27a] including an empirical dispersion correction (DFT-D) using a Gaussian AO basis set of triple-zeta quality with polarization functions on all atoms (TZVP)[27b] and numerical quadrature multiple grid ('grid m4' option in Turbomole).[39b] The resolution of the identity (RI) approximation[39c] was applied for all DFT-calculations. Single point energies were computed with SCS-MP2[27c] using the TZVPP basis set[27b] and also employing the RI-approximation.[39d]

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(33) Ester (+)-(*S*)-**20d** was prepared by asymmetric lithiation of benzyl carbamate **19** in the presence of chiral diamine (–)-sparteine (**7**) in *n*-hexane at –78 °C (4 M soln). Trapping of the equilibrated and crystallized intermediate epimeric complex (S_C)-**15**·**7** with CO_2 at –78 °C after 4 h and subsequent esterification of the resulting carboxylic acid (*S*)-**22** with diazomethane yielded 78% of (+)-(*S*)-**20d** with 97% ee (HPLC) {$[\alpha]_D^{20}$ +107.2 (*c* 0.92, MeOH)}. Compare: (a) ref. 1a. (b) Retzow, S. *Diploma Thesis*; University of Kiel: Germany, **1990**.

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(37) X-ray crystal structure analysis for (*S*,*S*)-**29**: formula $C_{21}H_{29}NO_2Si$, M = 355.54, colorless crystals 0.25 × 0.06 × 0.05 mm, a = 22.666(1), b = 7.897(1), c = 12.669(1) Å, β = 108.45(1)°, V = 2151.1(3) Å^3, ρ_{calcd} = 1.0981 g cm^{-3}, μ = 10.52 cm^{-1}, empirical absorption correction (0.779 ≤ T ≤ 0.949), Z = 4, monoclinic, space group $C2$ (No. 5), λ = 1.54178 Å, T = 223 K, ω and ϕ scans, 5904 reflections collected (±h, ±k, ±l), [(sinθ)/λ] = 0.59 Å^{-1}, 2448 independent (R_{int} = 0.048) and 1962 observed reflections [I ≤ 2 σ(I)], 254 refined parameters, R = 0.052, R_w^2 = 0.122, Flack parameter 0.02 (6), max. residual electron density 0.17 (–0.23) e Å^{-3}, hydrogen atoms calculated and refined as riding atoms, CCDC 684785.

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