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Configurationally Labile Lithiated *O*-Benzyl Carbamates: Application in Asymmetric Synthesis and Quantum Chemical Investigations on the Equilibrium of Diastereomers

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Dedicated to Professor Volker Jäger on the occasion of his 65th birthday

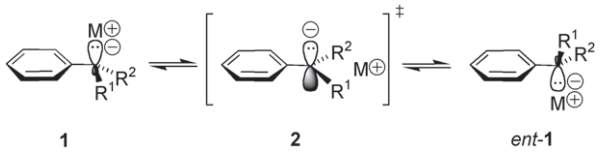
Abstract: The title compounds were generated by deprotonation of different benzyl-type carbamates with *sec*-butyllithium in the presence of chiral diamines (−)-sparteine or diisopropyl and di-*tert*-butyl bis(oxazoline)s. These lithiated species exhibit configurational lability at −78 °C. In the case of the chiral di-*tert*-butyl bis(oxazoline), the equilibrium of the epimeric complexes can be used synthetically to obtain highly enantioenriched secondary benzyl carbamates. The enantiodetermining step was proven to be a dynamic thermodynamic resolution. The absolute configurations of the products were determined, and the stereochemical pathways of selected substitution reactions were thus elucidated. High-level quantum chemical investigations were performed to gain insight into the experimentally investigated system. To obtain an accuracy for the energy difference ($\Delta\Delta H$) between two epimeric complexes of about 0.5 kcal mol^{-1} as well as the correct sign, a theoretical procedure was established. It included geometry optimization at the dispersion-corrected DFT level, computation of zero-point vibrational energies, and single-point SCS-MP2 energy calculations with large atomic-orbital basis sets.

Keywords: asymmetric synthesis · bis(oxazoline) ligands · lithium · quantum chemical calculations · stereochemistry

Introduction

Chiral benzylic, α-heterosubstituted carbanions are of great interest because of both their usefulness in enantioselective synthesis and their challenging behavior with regard to their configurational stability.[1]

Chiral secondary benzyl alkali-metal derivatives **1** racemize in solution with great ease, most probably via a planar transition state **2** (Scheme 1); therefore, the chiral information introduced during their generation is lost, and the final substitution product is formed with poor or even no enantioselectivity.[2–4] Lithiated secondary *O*-benzyl *N*,*N*-diisopropylcarbamate (*S*)-**6** (Scheme 2), which belongs to the small group of benzyllithium compounds that exhibit configurational stability in solution at low temperatures, turned out to be a versatile intermediate in the enantioselective synthesis of highly enantioenriched chiral tertiary benzylalcohol derivatives.[5,6] Nevertheless, different groups also gained success in the use of configurationally labile benzyllithium compounds (**7**–**10**; Scheme 3) as intermediates in enantioselective synthesis by employing different classes of chiral ligands and by using different enantiodetermining steps.[9–12] Bis(oxazoline) ligands such as **12**, in particular, were successfully employed by Nakai[10] and Toru[12] and their co-workers in



Scheme 1. Possible racemization mechanism of metallated benzylic carbanions **1**.

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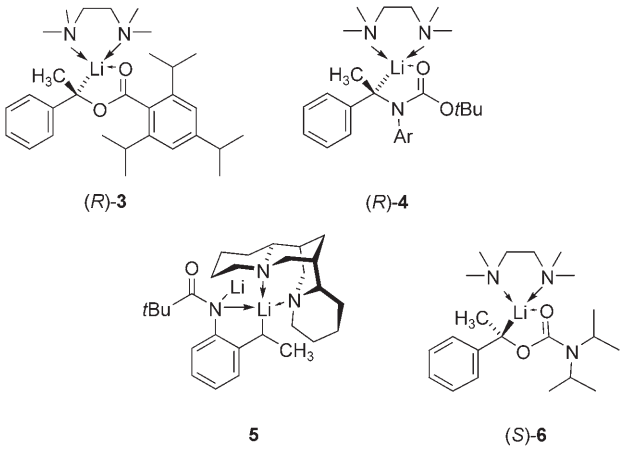
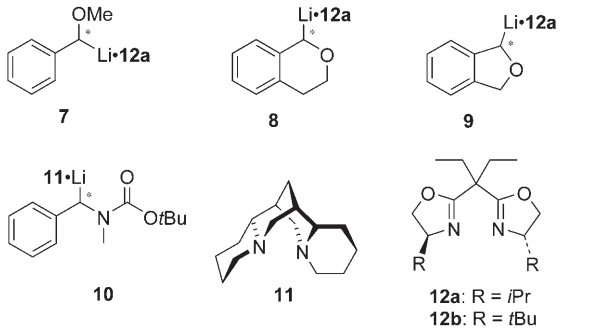


Scheme 2. Configurationally stable benzyl lithium complexes (*R*)-**3**,[7] (*R*)-**4**,[8] **5**,[8] and (*S*)-**6**.[5]



Scheme 3. Successfully employed configurationally labile benzyl lithium complexes **7**–**9**[11] and **10**.[12] Chiral diamine ligands used: (−)-sparteine (**11**), diisopropyl bis(oxazoline) **12a**, and di-*tert*-butyl bis(oxazoline) **12b**.

Abstract in German: Prochirale Benzylcarbamate werden mittels *sec*-Butyllithium in der Gegenwart eines chiralen Diamins ((−)-Spartein oder Bisoxazoline) deprotoniert. Die resultierenden lithiierten Spezies sind bei −78 °C konfigurativ labil. Im Falle des chiralen di-*tert*-Butyl-Bisoxazolin-Liganden setzen sich die epimeren Komplexe in ein Gleichgewicht, in dem ein Lithiumkomplex im großen Überschuss vorliegt (dynamisch-thermodynamische Resolution). Umsetzungen mit verschiedenen Elektrophilen liefern hoch enantiomerenangereicherte sekundäre Benzylcarbamate. Der stereochemische Verlauf der Substitutionen wird anhand der Absolutkonfiguration der Produkte aufgeklärt. Zudem werden die experimentell untersuchten Epimerengleichgewichte mit quantenchemischen Methoden erfasst. Um bei der Bestimmung der Energiedifferenz $\Delta\Delta H$ zwischen zwei epimeren Komplexen eine Genauigkeit von ungefähr 0.5 kcal mol^{-1} und ein korrektes Vorzeichen zu erhalten, wurde eine theoretische Vorgehensweise entwickelt. Diese beinhaltet Geometrieoptimierungen auf Dispersions-korrigiertem DFT-Level, Berechnung der Nullpunktschwingungsenergien und SCS-MP2-Energie Einzelpunktberechnungen unter Verwendung großer AO-Basissätze.

asymmetric substitutions of benzyl ethers and aryl benzyl sulfides, respectively. Lithiated benzyl carbamates such as **14** (see scheme in Table 1),[13] although configurationally stable in the Hoffmann test,[14] have not been employed in the synthesis of highly enantioenriched secondary benzyl alcohols.[1a]

Herein we report our initial results with epimeric complexes of lithiated secondary benzyl carbamates **14** as intermediates in the synthesis of highly enantioenriched α-substituted benzyl alcohols. We present the elucidation of the enantiodetermining step and the stereochemical pathway of important substitution reactions. High-level quantum chemical methods allow insight into the energetic situation of the intermediate epimeric complexes.

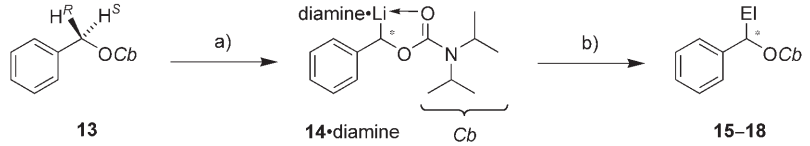
Results and Discussion

Benzyl carbamate **13** was deprotonated and subsequently stannylated with tributyltin chloride as electrophile under different conditions (Table 1). The configurational lability of the lithiated species was thereby revealed (Table 1, entries 1 and 2): Whereas stannane (+)-(*R*)-**15**[15] was formed with 32% *ee* after the lithiated species was stirred for 3 h at −78 °C, (+)-(*R*)-**15**, which was significantly more enantioenriched, was obtained when we stirred the lithiated species for 3 h at −94 °C. We then applied chiral bis(oxazoline) **12a**[16] as the chiral ligand and obtained stannane (−)-(*S*)-**15** with high enantiomeric excess (90% *ee*). Changing the ligand once more to sterically more demanding bis(oxazoline) **12b** finally yielded (−)-(*S*)-**15** with an excellent 98% *ee* (Table 1, entry 4). Control experiments revealed and proved the enantiodetermining step: We first trapped the epimeric (−)-sparteine complex **14·11** with trimethylsilyl chloride at −78 °C and isolated the silane (−)-(*R*)-**16** with a moderate 27% *ee* (Table 1, entry 5).[17] An in situ trapping experiment with (−)-sparteine as diamine yielded (−)-(*R*)-**16** with a significantly higher enantiomeric excess (54% *ee*; Table 1, entry 6) than those obtained in the preceding experiments. This indicates that the diastereomer ratio resulting from enantiotopic differentiation by (−)-sparteine must be better than that of **14·11** after stirring, which means that the complexes equilibrated as expected.

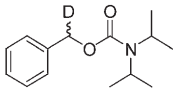
We then performed essentially the same experiments with bis(oxazoline) **12b** as the chiral ligand (Table 1, entries 7 and 8). As the in situ experiment indicates, enantiotopic differentiation by the chiral bis(oxazoline) **12b** in the deprotonation step is poor; it yielded silane (−)-(*S*)-**16** with only 9% *ee*. With prolonged reaction times (Table 1, entry 7), the epimeric complex-ion pairs equilibrated, thereby forming one diastereomer essentially exclusively, which was trapped with electrophiles to yield highly enantioenriched substitution products. Therefore, enantioselectivity most probably originates from a dynamic thermodynamic resolution[9] after the deprotonation step.[18]

Final proof was obtained by deprotonating deuterated benzyl carbamate *rac*-[D]**13** ([D] > 95%) in the presence of

Table 1. General deprotonation–substitution sequence and results obtained for different conditions with carbamate **13**.[a]



13 **14**•diamine **15–18**

Entry	Substrate	Diamine	T [°C]	Config. of **14**	ElX (product)	Yield [%]	e.r.[b]	Config. of product[c]
1	**13**	**11**	−78	S_C	Bu_3SnCl (**15**)	91	66:34	*R*
2	**13**	**11**	−94	S_C	Bu_3SnCl (**15**)	87	72:28	*R*
3	**13**	**12a**	−78	R_C	Bu_3SnCl (**15**)	88	5:95	*S*
4	**13**	**12b**	−78	R_C	Bu_3SnCl (**15**)	88	1:99	*S*
5	**13**	**11**	−78	S_C	Me_3SiCl (**16**)	87	64:36[d]	*R*
6	**13**	**11**	−78	S_C	Me_3SiCl (**16**) in situ	51	77:23[d]	*R*
7	**13**	**12b**	−78	R_C	Me_3SiCl (**16**) in situ	50	45.5:54.5[d]	*S*
8	**13**	**12b**	−78	R_C	Me_3SiCl (**16**)	98	>1:99[d]	*S*
9[e]		**12b**	−78	R_C	Bu_3SnCl ([D]**15**)	87 ([D] > 95%)	4:96	*S*
10	**13**	**12b**	−78	R_C	MeI (**17**)	98	98:2	*S*
11[f]	**13**	**12b**	−78	R_C	CO_2 (**18**)	99	2.5:97.5	*R*

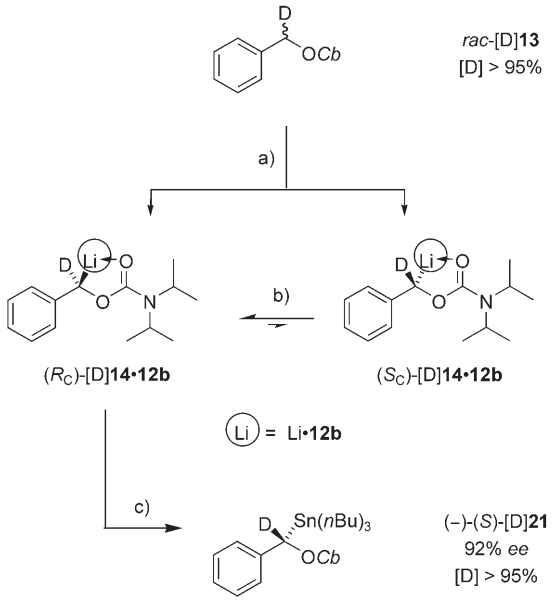
[a] Reaction conditions: a) Diamine, *s*BuLi, −78 °C, 2.5 h, toluene; b) electrophile (ElX), −78 °C, 2 h. [b] Enantiomer ratio (e.r.) determined by HPLC on chiral phase; see Experimental Section for details. [c] All the electrophiles used so far reacted under inversion of configuration. [d] Determined by GC on chiral phase; see Experimental Section for details. [e] Grade of deuteration determined by ^{1}H NMR spectroscopy. [f] The corresponding acid was converted into the methyl ester with diazomethane before the enantiomeric excess was determined.

chiral bis(oxazoline) **12b** under the previously used conditions (Scheme 4 and Table 1, entry 9). α-Deuterated α-stannylated carbamate (−)-(*S*)-[D]**15** was obtained in high yield with 92% *ee* and was deuterated to >95%. These results indicate that the proton in *rac*-[D]**13** is removed with high preference to lead to a 1:1 mixture of lithium complexes [D]**14·12b** and *epi*-[D]**14·12b**. The reasons for this are a large kinetic H/D isotope effect[19,20] and low enantiotopic discrimination in the kinetically controlled deprotonation step. An efficient equilibration of the epimeric carbanionic species [D]**14·12b** and *epi*-[D]**14·12b** has to take place to yield highly enantioenriched stannane (−)-(*S*)-[D]**15**.

A possible kinetic resolution of the epimeric complexes by the electrophiles used can be excluded. The reaction of the bis(oxazoline) lithium complexes **14·12b** with methyl iodide and carbon dioxide—two electrophiles with completely different characteristics—yielded methyl-substituted benzyl carbamate **17** and ester **18**, respectively, in high yields and enantiomeric excesses (Table 1, entries 10 and 11). These results are comparable to those obtained with trimethylsilyl chloride and tributyltin chloride.

Determination of the Absolute Configuration and Elucidation of the Stereochemical Pathway

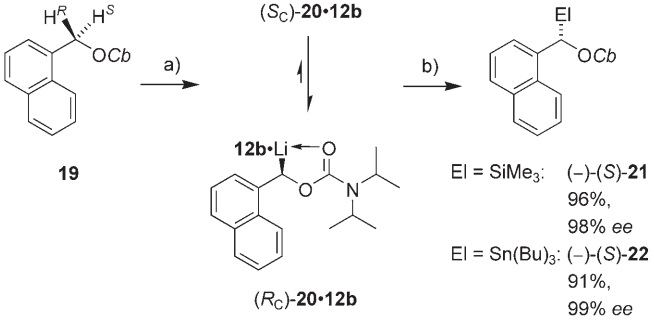
The absolute stereochemistry of the stereogenic carbon atom in the favored complex was deduced from silylation experiments. Silylation is expected to proceed with inversion of configuration here; this can be concluded from silylation experiments that employ similar substrates.[5] Therefore, on the basis of silane (−)-(*S*)-**16**, whose absolute configuration was deduced by comparison of the optical rotation of the corresponding alcohol with literature values,[17] the stereogenic carbon atom of the favored epimeric complex was assigned to be R_C-configured. The assignment of the absolute configuration of the stereogenic benzylic carbon atom of the favored complexes **14·12b** was also underlined by the findings with regard to the stereochemical courses of the methylation and carboxylation: The determination of the absolute configuration of the substitution products (−)-(*S*)-**17** and (−)-(*R*)-**18** was



Scheme 4. Stannylation of carbamate *rac*-[D]**13**. a) **12b**, *s*BuLi, −78 °C, toluene; b) 2.5 h, −78 °C; c) Bu_3SnCl, −78 °C, 2 h, 87%.

achieved by comparing their optical rotation with those reported in literature ((−)-(*S*)-**17**: $[\alpha]_D^{20} = -5.7$ ($c = 1.4$, $CHCl_3$), ref.: $[\alpha]_D^{20} = -5.5$ ($c = 1.2$, CH_2Cl_2), ≥97% *ee*;[5b] (−)-(*R*)-**18**: $[\alpha]_D^{20} = -107.6$ ($c = 0.99$, MeOH), ref.: $[\alpha]_D^{20} = -119.5$ ($c = 0.74$, MeOH), ≥95% *ee*[21]). There are examples reported in the literature that methylation at a benzylic carbanionic position with methyl iodide proceeds with inversion of configuration,[5] which again indicates an R_C-configured lithium-bearing carbon atom in the reaction complex **14·12b**. Consequently, carboxylation must proceed with inversion of configuration as well.[22]

We then changed the substrate to 1-naphthylmethyl carbamate **19** to estimate the generality of the method. Deprotonation of **19** under the same conditions as for benzyl carbamate **13**, followed by silylation with trimethylsilyl chloride, yielded silane (−)-(*S*)-**21** in 96% yield and with 98% *ee* (Scheme 5). We were able to obtain single crystals of (−)-



Scheme 5. Substitution of carbamate **19**. a) **12b**, *s*BuLi, −78 °C, toluene, 2.5 h; b) ElCl, −78 °C, 2 h.

(*S*)-**21** suitable for X-ray analysis with anomalous dispersion (Figure 1). This allowed us to determine that the stereogenic carbon atom in silane **20** is *S*-configured. Essentially the same stereochemical course as for the silylation and stannylation of **13** must be concluded for this sytem. Silylation is expected to proceed with inversion of configuration here as

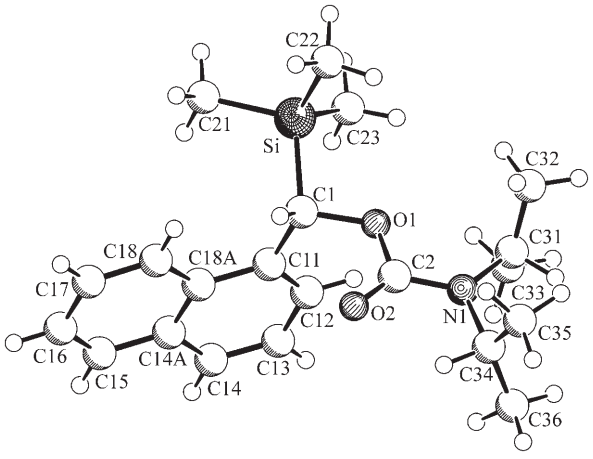


Figure 1. X-ray crystal structure of silane (−)-(*S*)-**21**.[23]

well;[5] therefore, an R_C-configured stereogenic carbon atom of the favored epimeric complex is indeed most probable. An analogously performed stannylation reaction with carbamate **19** and tributyltin chloride afforded 91% of the corresponding stannane (−)-(*S*)-**22** with 99% *ee*, thus proving some generality of the method.

Quantum Chemical Investigations of the Equilibrium of the Intermediate Epimeric Complexes

These results led to the question of why the bis(oxazoline) ligand **12b** is more efficient than (−)-sparteine with regard to its influence on the equilibration of the epimeric complexes. To gain deeper insight into the system, we performed high-level quantum chemical calculations on the epimeric complexes **14·11**, **20·11**, **14·12b**, and **20·12b** (Figure 2).[24,25] A theoretical investigation of the equilibrium of the diastereomers is possible here as there is a dynamic thermodynamic resolution taking place. No precipitate formed during the deprotonation, and though the lithiated species was stirred, the equilibrium was not disturbed by any means. Therefore, $\Delta\Delta G$ can be derived by the equation $\Delta\Delta G = RT\ln(\text{e.r.})$. From the experimentally determined enantiomer ratios of ≥98:2 in the trapping products **15**–**18**, a $\Delta\Delta G$ value of ≥1.5 kcal mol^{-1} between the epimeric intermediates **14·12b** and *epi*-**14·12b** at −78 °C was determined (Table 2). A slightly higher value was found for the naphthyl system. Significantly lower values were obtained for the (−)-sparteine-containing complexes **14·11** and **20·11**, in which only moderate enantiomer ratios reflect $\Delta\Delta G$ values of 0.26 and 0.05 kcal mol^{-1}, respectively.

The results for $\Delta\Delta G$ in the range 0–2 kcal mol^{-1} make computational treatment very demanding, especially when the size and complexity of the systems are taken into account. For meaningful results, the error of the calculation should not exceed 0.5 kcal mol^{-1} for the energy difference between the epimeric complexes. Therefore, the structures were fully optimized at the DFT-D level (B97-D/TZVP).[25a–c] Single-point energy computations with SCS-MP2/TZVPP followed.[25c,d] Geometries optimized with a density functional without dispersion correction (BP86[25e,f]) led to results for $\Delta\Delta E$ that did not agree even qualitatively with the experiments (results not shown). This important finding emphasizes the role of intramolecular van der Waals effects in large molecules.[26] Also, it is not sufficient to optimize the structures with B97-D and to calculate the energies with more-approximate methods than SCS-MP2, such as the density functionals PBE[25g,h] or B3-LYP.[25i–k] $\Delta\Delta E$ in this case is also not in qualitative agreement with the experimental data (results shown in the Supporting Information). If an accuracy of better than 0.5 kcal mol^{-1} is needed, relatively small contributions such as solvent effects and the zero-point vibrational energy (ZPVE)[28] have to be taken into account. The experiments were carried out in toluene. Thus, simulations of solvent effects were carried out by using both the COSMO[29] and the PCM model[30] to estimate the influence of the solvent. However, owing to the relatively nonpo-

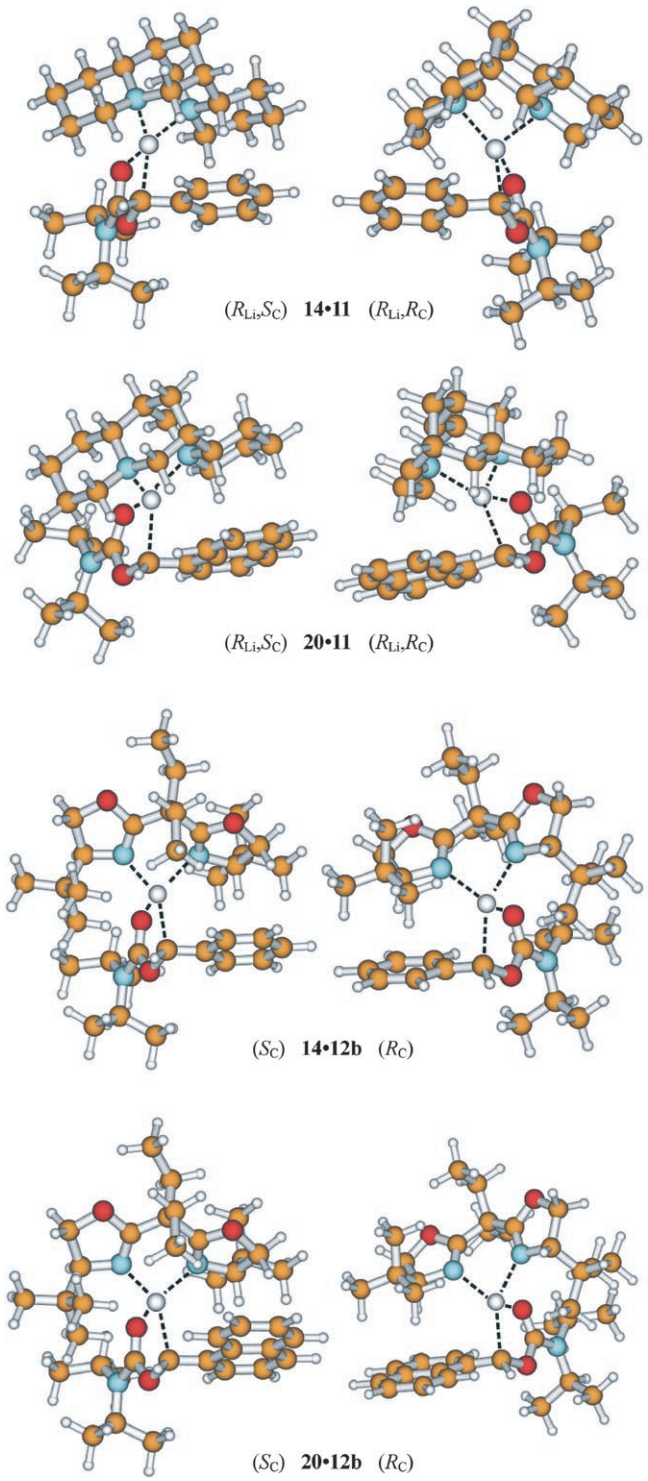


Figure 2. Calculated structures of the epimeric complexes. C = orange, N = blue, O = red, Li = grey, H = white.

lar nature of the solvent, the contribution of the solvent effects was negligibly small (0.1–0.2 kcal mol^{-1}). Taking into account the ZPVE contributions led to $\Delta\Delta H$(0 K) instead of $\Delta\Delta E$. As seen in Table 2, the ZPVE contributions are also in the range 0.1–0.2 kcal mol^{-1}. In the following discussion, these results for $\Delta\Delta H$(0 K), with solvent effects neglected,

Table 2. Experimental and calculated results for complexes **14·11/12b** and **20·11/12b**.

Complex	Experimental			SCS-MP2/TZVPP//B97-D/TZVP		
	Config.	e.r.[a]	$\Delta\Delta G$[a] [kcal mol^{-1}]	Config.	e.r.[b]	$\Delta\Delta H$(0 K)[c] [kcal mol^{-1}]
14·11	S_C	34:66	−0.26	S_C	7:93	−1.01 (−0.96)
20·11[d]	R_C	53:47	0.05	R_C	81:19	0.56 (0.53)
14·12b	R_C	98:2	1.51	R_C	98:2	1.56 (1.21)
20·12b	R_C	99:1	1.78	R_C	⩾99:1	3.65 (3.53)

[a] Experimentally derived. [b] Predicted quantum chemically. [c] ΔH(0 K)(S_C)−ΔH(0 K)(R_C); $\Delta\Delta E$ values are given in parentheses. [d] Experiment: Silane (−)-(*S*)-**21** was obtained in 95% yield and with 4–6% *ee*.[27]

are compared to the experimentally determined $\Delta\Delta G$, assuming that temperature and entropy effects are negligibly small ($\Delta\Delta H(0\,\mathrm{K}) \approx \Delta\Delta G = \Delta\Delta H - T\Delta\Delta S$). This is a reasonable assumption because the structures of each of the two epimers of the same complex are very similar.

For all the calculated complexes, the most stable epimer was found correctly by our theoretical treatment. In the following paragraphs, the quantitative results are discussed in more detail.

At first glance, the quantitative description is not sufficient. The parent system **14·12b**/*epi*-**14·12b** can be described correctly in this way, but $\Delta\Delta H$(0 K) for the naphthyl system **20·12b**/*epi*-**20·12b** is strongly overestimated. This discrepancy can be understood with a closer look at the single experiments and the connection between experiment and theory: $\Delta\Delta G$ was determined out of an average enantiomer ratio calculated from different experiments with different electrophiles. This was done to minimize the influence of the individual electrophile, as some electrophiles exhibit a stronger kinetically driven distortion of the enantiomer ratio than others. Besides that, there are technical limits with regard to the determination of enantiomeric excess. It was impossible to determine enantiomeric excesses higher than 99% with HPLC or GC on chiral phase. If some kinetic differentiation by the electrophile during its reaction with the epimeric complexes is taken into consideration, the ratio of these complexes can be assumed to be greater than 99:1. Furthermore, given that the relationship between $\Delta\Delta G$ and the enantiomer ratio is logarithmic in nature, the doubts with regard to the quantum chemical results derived for the naphthylmethyl system diminish. In the four diastereomeric complexes of **14·11**, the pair of diastereomers with an *R*-configured lithium cation is energetically strongly favored, thus ruling out the pair of S_{Li}-configured complexes. For the remaining complex pair, the S_C-configured complex is clearly the more stable. Although an estimated error of about 0.5 kcal mol^{-1} usually has to be taken into consideration for the computed results, even the results for the most complicated (−)-sparteine-containing naphthylmethyl carbamate complexes **20·11** are mirrored correctly. Again, one pair of diastereomers (R_{Li}-configured) is clearly favored. Here, the R_{Li},R_C-configured complex is favored.

We can thus conclude that the quantum chemical method chosen for the treatment of these epimeric complexes is reli-

able and delivers authentic energy differences. We can state that substrate–ligand systems (configurationally labile α-lithiated benzyl type *O*-carbamates as substrates) that show a quantum chemically derived $\Delta\Delta H(0\,K)$ (SCS-MP2/TZVPP//B97-D/TZVP) of ≥ 1.4 kcal mol^{-1} are worth testing experimentally in lithiation–substitution reactions as they will deliver highly enantioenriched products when appropriate electrophiles are employed.

Our calculated structures are in good agreement with previous findings with regard to the structural aspects of benzyllithium complexes: Boche and co-workers reported X-ray crystal-structure analyses of different benzyllithium species as well as quantum chemical calculations on these structures.[31] A common feature is the pyramidal benzylic carbon atom. In all our calculations, the stereogenic benzylic carbon atom is pyramidal and bears an η^1-bound lithium atom regardless of the aromatic system or the ligand (Figure 2), which is in agreement with previous findings.[31a,b]

Conclusions

We gained access to highly enantioenriched secondary benzyl carbamates via the configurationally labile benzyllithium complexes **14·12b** and **20·12b**. We determined the absolute configuration of the substitution products obtained and deduced the absolute configuration of the sterogenic carbon atom in the favored diamine complex. From the enantiomer ratios of the substitution products, we determined the energy differences $\Delta\Delta G$ of the epimeric complexes. SCS-MP2 calculations allowed a first insight into the equilibrium of these complexes and their structural properties. We found a promising way of simulating equilibrated epimeric mixtures of lithiated benzyl-type carbamates, so as to describe correctly such complex systems both qualitatively and quantitatively. Further results with regard to substitution reactions and quantum chemical investigations will be published in due course.[32]

Experimental Section

General

All solvents were dried and purified prior to use. Toluene was distilled over sodium/benzophenone. TMSCl was distilled from powdered CaH_2 and stored under argon. *sec*-Butyllithium was filtered through cellite before use, and its concentration was determined by titration against diphenylacetic acid.[33] Ethereal solutions of diazomethane were obtained as described in the literature,[34] stored under argon in the refrigerator, and used without determination of concentration. (−)-Sparteine (**11**) was purchased from Aldrich and used without further purification. The bis(oxazoline) ligands were prepared according to reference [15]. E = Et_2O, P = pentane, TBME = *tert*-butyl methyl ether. All reactions were performed under argon atmosphere in flame-dried glassware with septum and syringe techniques. Flash column chromatography (FCC) was performed on Merck 60 silica gel, 0.040–0.063 mm, with an argon pressure of 1.2–1.4 bar, and monitored by thin-layer chromatography (TLC) on Merck 60 F254 silica gel. Gas chromatography was performed on an Agilent 6890 plus chromatograph (Agilent, Böblingen). HP-5 was used as the achiral column (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 detection 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 the chiral stationary phase (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 detection temperature). Melting points (uncorrected) were measured on an SMP3 melting-point apparatus purchased from Stuart Scientific, UK. Optical rotations were measured in a 10-cm cuvette on a Perkin–Elmer 341 polarimeter. Unless otherwise stated, ^{1}H and ^{13}C NMR data were recorded on Bruker ARX 300, AVANCE II 300, AM 360, AMX 400, and AVANCE II 400 spectrometers; spectra were obtained from solutions in $CDCl_3$ ($\delta_C = 77.0$ ppm) and were calibrated relative to the residual content of $CHCl_3$ ($\delta_H = 7.24$ ppm) or $SiMe_4$ ($\delta_H = 0.0$ ppm). Peak multiplicities in ^{1}H NMR spectra are abbreviated as s (singlet), d (doublet), t (triplet), q (quartet), sept (septet), m (multiplet), and br (broad). Diastereotopic methylene protons with different chemical shifts are abbreviated as H_A and H_B. IR spectra were obtained on Nicolet 5DCX, Bruker IFS 28, or Varian 3100 Excalibur Series spectrometers with Specac golden gate single reflection ATR (attenuated total reflection). Elemental analysis was performed at the Microanalytical Section of the Organisch-Chemisches Institut, WWU Münster, on a Vario El III instrument purchased from Elementar Analysen Systeme, Hanau (Germany). Mass spectrometric data were obtained on Finnigan MAT 8230 (EI), Micromass Quattro LCZ (ESI), or Micromass MAT 8200 (GC-TOF/HRMS) spectrometers. HPLC: Waters 600E multisolvent delivery system and 996 PDA detector. Crystallographic data: Data sets were collected with a Nonius Kappa CCD diffractometer. Programs used: data collection COLLECT (Nonius B.V., 1998), data reduction Denzo-SMN,[35] absorption correction SORTAV,[36] Denzo,[37] structure solution SHELXS-97,[38] structure refinement SHELXL-97,[39] graphics SCHAKAL.[40] CCDC-657926 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre at http://www.ccdc.cam.ac.uk/data_request/cif.

Syntheses

19: NaH (60 % in mineral oil, 920 mg, 23 mmol, 1.15 equiv) was suspended in absolute THF (30 mL). The mixture was cooled to 0 °C, and benzyl alcohol (2.48 g, 20 mmol, 1.0 equiv) dissolved in dry THF (5 mL) was slowly added. After generation of hydrogen stopped, a solution of *N*,*N*-diisopropylcarbamoyl chloride (3.76 g, 23 mmol, 1.15 equiv) in dry THF (10 mL) was added such that the reaction temperature did not rise. The reaction mixture was allowed to warm to room temperature and was stirred at this temperature for 2 days. The reaction flask was then immersed in an ice bath, and water (25 mL) and HCl (2 N, 3 mL) were added to give a clear yellowish solution. TBME (50 mL) was added, and after separation of phases, the aqueous phase was extracted with TBME (3 × 20 mL). The combined organic layers were washed with saturated $NaHCO_3$ and brine successively. After drying over anhydrous $MgSO_4$, filtering through glass wool, and removal of the solvent, the crude product was subjected to column chromatography (E/P = 1:4) to give pure *N*,*N*-diisopropylcarbamic acid (naphthalen-1-yl)methyl ester (**19**; 3.96 g, 14 mmol, 93 %), after purification by column chromatography (E/P = 1:8→1:4), as a slightly yellow crystalline solid. $R_f = 0.76$ (E/P = 1:1); t_R = 17.3 min (HP-5); m.p.: 66 °C (E/P = 1:4); IR (KBr): $\tilde{\nu}$ = 3062 (m, C−H_{arom}), 2971, 2930, 2898 (s, C−H_{aliph}), 1670 (s, NC=O), 1600 (m), 1511 (m), 1289 (s), 1189 (m), 1160 (m), 1135 (m), 1082 (s), 1060 (s), 796 (m), 780 cm^{-1} (s); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.16$ (d, $^3J_{N,H} = 6.8$ Hz, 12 H, $((H_3C)_2HC)_2N$), 3.91 (br s, 2 H, $((H_3C)_2HC)_2N$), 5.58 (s, 2 H, $CH_{benzylic}$), 7.42 (d, $^3J_{2\text{-}H,3\text{-}H} = 7.0$ Hz, 2 H, 2-H), 7.46 (dd, $^3J_{3\text{-}H,4\text{-}H} = 8.2$ Hz, $^3J_{2\text{-}H,3\text{-}H} = 7.0$ Hz, 1 H, 3-H), 7.49–7.53 (m, 1 H, 7-H), 7.54 (ddd, $^3J_{5\text{-}H,6\text{-}H} = 8.4$ Hz, $^3J_{6\text{-}H,7\text{-}H} = 6.7$ Hz, $^4J_{6\text{-}H,8\text{-}H} = 1.6$ Hz, 1 H, 6-H), 7.82 (d, $^3J_{3\text{-}H,4\text{-}H} = 8.2$ Hz, 1 H, 4-H), 7.86 (dd, $^4J_{5\text{-}H,7\text{-}H} = 2.2$ Hz, $^3J_{5\text{-}H,6\text{-}H} = 8.4$ Hz, 1 H, 5-H), 8.06 ppm (dd, $^3J_{7\text{-}H,8\text{-}H} = 8.2$ Hz, $^4J_{6\text{-}H,8\text{-}H} = 1.6$ Hz, 1 H, 8-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 20.8$ $(((H_3C)_2HC)_2N)$, 46.0 $(((H_3C)_2HC)_2N)$, 64.8 ($C_{benzylic}$), 123.9 (C8), 125.3 (C2), 125.8 (C3), 126.2 (C6), 127.0 (C7), 128.6 (C4), 128.8 (C5), 131.8 (C8a), 132.6 (C4a), 133.7 (C1), 155.4 ppm (NC=O); GC–MS (EI, 70 eV): *m/z* (%) = 285 $[M]^+$ (12), 267 (3), 226 (21), 157 (8), 141 $[C_{10}H_7-CH_2]^+$ (100), 128 $[Cb]^+$ (27), 115 $[C_9H_7]^+$ (81), 102

$[C_8H_6]^+$ (9), 89 (24), 86 (42), 70 (54), 63 (29), 58 (26), 51 $[C_4H_3]^+$ (25), 43 $[C_3H_7]^+$ (57); elemental analysis: calcd (%) for $C_{18}H_{23}NO_2$ (285.38): C 75.76, H 8.12, N 4.91; found: C 75.68, H 7.95, N 4.68.

General procedure for the asymmetric lithiation and substitution of **13**, [D]**13**, and **19** (GPA): Benzyl carbamate **13**/[D]**13**/**19** (71/71/86 mg, 0.30 mmol, 1.0 equiv) was dissolved in toluene (3 mL), the appropriate ligand (0.36 mmol, 1.2 equiv) was added, and the reaction flask was cooled to −78 °C. *s*BuLi (1.2–1.3 M in hexane/cyclohexane = 92:8, 0.36 mmol, 1.2 equiv) was injected in a dropwise manner into this mixture. The reaction mixture was stirred at −78 °C for 2.5 h. The appropriate electrophile (0.45–1.5 mmol, 1.5–5.0 equiv) was injected, and the reaction mixture was stirred for 2 h. The reaction was then quenched with methanol (0.5 mL) followed by water (1 mL) and HCl (2 N, 0.5 mL). The layers were separated, and the aqueous layer was extracted with TBME (3 × 10 mL). The collective organic phase was washed with saturated $NaHCO_3$, dried over anhydrous $MgSO_4$, filtered through glass wool, and concentrated under reduced pressure to obtain the crude product, which was subjected to column chromatography (E/P) to give the pure products.

15: (−)-(*S*)-*N*,*N*-Diisopropylcarbamic acid (1-phenyl-1-tributylstannyl)-methyl ester: Colorless liquid, see Table 1 for yield. $R_f = 0.86$ (E/P = 1:4); $t_R = 20.5$ min (HP-5); $[\alpha]_D^{20} = -19.5$ ($c = 1.07$, $CHCl_3$); IR (film): $\tilde{\nu} = 3083$, 3061, 3023 (m, C−H_{arom}), 2997, 2957, 2927, 2871, 2853 (ms, C−H_{aliph}), 1678 (s, NC=O), 1493 (m), 1475 (m), 1435 (s), 1376 (m), 1348 (m), 1327 (m), 1309 (m), 1292 (s), 1248 (m), 1156 (m), 1136 (m), 1071 (s), 1048 (s), 950 (m), 864 (s), 770 (m), 756 (m), 668 cm^{-1} (m); ^1H NMR (300 MHz, $CDCl_3$): $\delta = 0.68$–0.93 (m, 9H, $(H_3C(CH_2)_3)_3Sn$), 1.13–1.46 (m, 24H, $((H_3C)HC(CH_3))_2N$, $(H_3C(CH_2)_3)_3Sn$), 3.94 (sept, $^3J_{N,H} = 6.7$ Hz, 2H, $((H_3C)_2HC)_2N$), 5.76 (s, 1H, $CH_{benzylic}$), 6.96–7.27 ppm (m, 5H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 10.1$ ($(H_3CCH_2CH_2CH_2)_3Sn$), 13.4 ($(H_3C(CH_2)_3)_3Sn$), 20.9 ($((H_3C)_2HC)_2N$), 27.4 ($(H_3CCH_2CH_2CH_2)_3Sn$), 29.0 ($(H_3CCH_2CH_2CH_2)_3Sn$), 45.6 ($((H_3C)_2HC)_2N$), 73.4 ($C_{benzylic}$), 123.6, 124.8, 128.3, 144.0 (Ph), 155.6 ppm (NC=O); MS (ESI): $m/z = 548.2525$ $[M+Na]^+$; elemental analysis: calcd (%) for $C_{26}H_{47}NO_2Sn$ (524.37): C 59.55, H 9.03, N 2.67; found: C 59.51, H 9.20, N 2.50; HPLC: EC250/4 Nucleosil 100–5 Chiral-2 (4 × 250 mm), $\lambda = 210$ nm, *n*-hexane/*i*PrOH/TFA (trifluoroacetic acid) = 1000:1:0.5, 0.3 mL min^{-1}, $t_R(+) = 24.1$ min, $t_R(-) = 27.9$ min, 98 % *ee* (with bis(oxazoline) **12b**; Table 1, entry 4).

21: (−)-(*R*)-*N*,*N*-Diisopropylcarbamic acid (1-phenyl-1-trimethylsilanyl)-methyl ester: GPA, colorless liquid, see Table 1 for yield. $R_f = 0.38$ (E/P=1:8); $t_R = 14.1$ min (HP-5); $[\alpha]_D^{20} = -22.8$ ($c = 0.93$, $CHCl_3$); IR (ATR): $\tilde{\nu} = 3085$, 3063, 3027 (m, C−H_{arom}), 2998, 2968, 2934, 2901 (s, C−H_{aliph}), 1693 (s, NC=O), 1368 (m), 1314 (m), 1292 (s), 1248 (m), 1157 (m), 1134 (m), 1074 (s), 1046 (s), 953 (m), 872 (s), 841 (s), 767 (s), 751 (m), 617 (m), 594 cm^{-1} (m); ^1H NMR (300 MHz, $CDCl_3$): $\delta = 0.00$ (s, 9H, $(H_3C)_3Si$), 1.21 (br s, 12H, $((H_3C)HC(CH_3))_2N$), 3.94 (br s, 2H, $((H_3C)_2HC)_2N$), 5.57 (s, 1H, $CH_{benzylic}$), 7.05–7.30 ppm (m, 5H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -3.7$ ($(H_3C)_3Si$), 21.0 ($((H_3C)_2HC)_2N$), 46.0 ($((H_3C)_2HC)_2N$), 72.0 ($C_{benzylic}$), 125.3, 125.8, 128.0, 141.1 (Ph), 155.5 ppm (NC=O); MS (ESI): $m/z = 330.1867$ $[M+Na]^+$, 637.3841 $[2M+Na]^+$; elemental analysis: calcd (%) for $C_{17}H_{29}NO_2Si$ (307.50): C 66.40, H 9.51, N 4.55; found: C 66.04, H 9.68, N 4.97; GC: β-DEX-120, temperature program: 94/1/1/95/999, $t_R(-) = (937 \pm 1)$ min, $t_R(+) = (958 \pm 1)$ min, > 98 % *ee* (with bis(oxazoline) **12b**; Table 1, entry 7).

In situ experiment with **12b**: Carbamate **13** (71 mg, 0.30 mmol, 1.0 equiv), bis(oxazoline) **12b** (116 mg, 0.36 mmol, 1.2 equiv), and trimethylsilyl chloride (65 mg, 0.6 mmol, 2 equiv) were dissolved in dry toluene (3 mL). The reaction flask was cooled to −78 °C, *s*BuLi (1.2–1.3 M in hexane/cyclohexane = 92:8, 0.60 mmol, 1.2 equiv) was injected in a dropwise manner, and the reaction mixture was stirred for 30 min. The reaction was then quenched with methanol (0.5 mL) followed by water (1 mL) and HCl (2 N, 0.5 mL). Workup was performed according to GPA. Yield: 50 %. GC: β-DEX-120, temperature program: 94/1/1/95/999, $t_R(-) = (937 \pm 1)$ min, $t_R(+) = (958 \pm 1)$ min, 9 % *ee*.

In situ experiment with **11**: Carbamate **13** (71 mg, 0.30 mmol, 1.0 equiv), (−)-sparteine (**11**; 84 mg, 0.36 mmol, 1.2 equiv), and trimethylsilyl chloride (65 mg, 0.6 mmol, 2 equiv) were treated together as described above. Yield: 51 %. GC: β-DEX-120, temperature program: 94/1/1/95/999, $t_R(-) = (937 \pm 1)$ min, $t_R(+) = (958 \pm 1)$ min, 54 % *ee*.

rac-[D]**13**: According to GPA, **13** (71 mg, 0.30 mmol, 1.0 equiv) was deprotonated by using *s*BuLi (0.30 mL, 1.22 M in cyclohexane/hexane, 0.36 mmol, 1.2 equiv) and *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA; 70 mg, 0.60 mmol, 1.2 equiv). The lithiated intermediate was trapped with an excess of H_3COD (0.5 mL) at −78 °C. After workup according to GPA, the crude product was subjected to column chromatography (E/P = 1:4) to yield *rac*-*N*,*N*-diisopropylcarbamic acid (1-deuterio-1-phenyl)methyl ester (*rac*-[D]**13**) as a colorless liquid. Yield: 97 %. $R_f = 0.54$ (E/P = 1:1); $t_R = 12.5$ min (HP-5); IR (ATR): $\tilde{\nu} = 3065$, 3032 (m, C−H_{arom}), 2998, 2970, 2934, 2875 (s, C−H_{aliph}), 1686 (s, C=O), 1498 (m), 1474 (m), 1433 (s), 1368 (m), 1327 (m), 1305 (m), 1282 (s), 1217 (s), 1157 (m), 1133 (m), 1079 (m), 1057 (s), 921 (m), 769 (s), 744 (m), 718 (m), 697 (s), 604 cm^{-1} (m); ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.20$ (d, $^3J_{N,H} = 6.8$ Hz, 12H, $((H_3C)_2HC)_2N$), 3.93 (br s, 2H, $((H_3C)_2HC)_2N$), 5.12 (s, 1H, $CH_{benzylic}$), 7.27–7.41 ppm (m, 5H, Ph); [D] ≥ 95 % according to integration of the signal of the benzylic protons; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 21.1$ ($((H_3C)_2HC)_2N$), 45.8 ($((H_3C)_2HC)_2N$), 66.2 (t, $C_{benzylic}$), 127.8, 127.9, 128.4 137.1 (Ph), 155.5 ppm (NC=O); MS (ESI): $m/z = 237.1716$ $[M+H]^+$, 259.1530 $[M+Na]^+$; elemental analysis: calcd (%) for $C_{14}H_{20}DNO_2$ (236.33): C 71.15, H 9.38, N 5.93; found: C 70.91, H 8.89, N 5.89.

[D]**15**: According to GPA, *rac*-[D]**13** (71 mg, 0.30 mmol, 1.0 equiv) was deprotonated in the presence of **12b** (116 mg, 0.36 mmol, 1.2 equiv) for 2.5 h and subsequently stannylated to yield the crude product, which was purified by column chromatography to give (−)-(*S*)-[D]*N*,*N*-diisopropylcarbamic acid (1-deuterio-1-phenyl-1-tributylstannyl)methyl ester ([D]**15**) as a colorless liquid. Yield: 87 %. $R_f = 0.86$ (E/P = 1:4); $t_R = 20.4$ min (HP-5); $[\alpha]_D^{20} = -19.0$ ($c = 1.07$, $CHCl_3$); IR (ATR): $\tilde{\nu} = 3030$ (m, C−H_{arom}), 2956, 2925, 2872, 2854 (ms, C−H_{aliph}), 1674 (s, NC=O), 1602 (m), 1493 (m), 1463 (m), 1433 (s), 1377 (m), 1331 (m), 1310 (m), 1216 (m), 1158 (m), 1136 (m), 1052 (s), 1027 (m), 1001 (m), 957 (m), 878 (s), 770 (m), 737 (m), 697 (m), 664 (m), 630 (s), 544 cm^{-1} (s); ^1H NMR (300 MHz, $CDCl_3$): $\delta = 0.80$ (t, $^3J_{Sn,H} = 7.0$ Hz, 9H, $(H_3C(CH_2)_3)_3Sn$), 1.13–1.48 (m, 24H, $((H_3C)HC(CH_3))_2N$, $(H_3C(CH_2)_3)_3Sn$), 3.97 (sept, $^3J_{N,H} = 7.0$ Hz, 2H, $((H_3C)_2HC)_2N$), 5.76 (s, 0.03H, $CH_{benzylic}$), 6.98–7.32 ppm (m, 5H, Ph); [D] > 95 % according to integration of the signal of the benzylic protons; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 10.2$ ($(H_3CCH_2CH_2CH_2)_3Sn$), 13.4 ($(H_3C(CH_2)_3)_3Sn$), 20.9 ($((H_3C)_2HC)_2N$), 27.3 ($(H_3CCH_2CH_2CH_2)_3Sn$), 28.7 ($(H_3CCH_2CH_2CH_2)_3Sn$), 45.8 ($((H_3C)_2HC)_2N$), 73.5 ($C_{benzylic}$), 123.7, 124.7, 128.3, 144.0 (Ph), 155.6 ppm (NC=O); MS (ESI): $m/z = 529.2585$ $[M+Na]^+$; elemental analysis: calcd (%) for $C_{26}H_{46}DNO_2Sn$ (525.37): C 59.44, H 9.21, N 2.67; found: C 59.48, H 9.00, N 2.62; HPLC: EC250/4 Nucleosil 100–5 Chiral-2 (4 × 250 mm), $\lambda = 210$ nm, *n*-hexane/*i*PrOH/TFA = 1000:1:0.5, 0.3 mL min^{-1}, $t_R(+) = 24.1$ min, $t_R(-) = 27.8$ min, 92 % *ee*.

17: (−)-(*S*)-*N*,*N*-Diisopropylcarbamic acid 1-phenylethyl ester: Colorless liquid, yield: 98 %. $R_f = 0.44$ (E/P = 1:4); $t_R = 12.5$ min (HP-5); $[\alpha]_D^{20} = -5.7$ ($c = 1.4$, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.20$ (d, $^3J_{N,H} = 6.9$ Hz, 12H, $((H_3C)_2HC)_2N$), 1.56 (d, $^3J_{C,Hbenzylic} = 6.7$ Hz, 3H, H_3C), 3.92 (br s, 2H, $((H_3C)_2HC)_2N$), 5.84 (q, $^3J_{Hbenzylic,C} = 6.7$ Hz, 1H, $CH_{benzylic}$), 7.20–7.38 ppm (m, 5H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 21.1$ ($((H_3C)_2HC)_2N$), 22.8 (H_3C), 45.8 ($((H_3C)_2HC)_2N$), 72.7 ($C_{benzylic}$), 126.0, 127.3, 128.3, 142.8 (Ph), 155.0 ppm (NC=O); spectroscopic data correspond to those in the literature;[5b] HPLC: CHIRA-GROM 1 (2 × 250 mm), $\lambda = 210$ nm, *n*-hexane/*i*PrOH = 1000:1, 0.3 mL min^{-1}, $t_R(-) = 11.3$ min, $t_R(+) = 15.1$ min, 96 % *ee*.

18: As described in GPA, the lithiated species was synthesized by deprotonating **13** (71 mg, 0.30 mmol, 1.0 equiv) in the presence of **12b** (116 mg, 0.36 mmol, 1.2 equiv) and was equilibrated. As the electrophile, dried and precooled gaseous carbon dioxide was bubbled through the reaction mixture over a period of 10–15 min. After a further hour of stirring at −78 °C, the reaction was carefully quenched with methanol (0.5 mL) and water (1 mL). Workup was performed as described in GPA. The crude acid was directly dissolved in Et_2O, and a solution of diazomethane in Et_2O was added at room temperature until the yellowish color of the reaction mixture remained. The solution was stirred for 1 h. To remove the

remaining diazomethane, silica gel was added, and the suspension was stirred for a further hour. The solvent was removed under reduced pressure, and the crude product was thus adsorbed onto the silica gel. This mixture was directly subjected to column chromatography (E/P = 1:3) to yield (−)-(*R*)-[*N*,*N*-(1-diisopropylcarbamoyloxy)]-1-phenyl acetic acid methyl ester (**18**) as a colorless liquid. Yield: 99 %. R_f = 0.13 (E/P = 1:8); t_R = 16.3 min (HP-5); $[\alpha]_D^{20} = -107.6$ (c = 0.99, MeOH); IR (ATR): $\tilde{\nu}$ = 3034 (m, C–H_{arom}), 2998, 2970, 2933, 2876, 2850 (s, C–H_{aliph}), 1757 (s, C=O), 1694 (s, NC=O), 1497 (m), 1476 (m), 1456 (m), 1436 (m), 1369 (m), 1294 (m), 1265 (m), 1213 (s), 1133 (m), 1086 (m), 1069 (s), 1046 (m), 1017 (m), 906 (m), 770 (m), 732 (m), 699 (s), 639 (m), 619 (m), 607 cm^{-1} (m); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.23 (br s, 12 H, $((H_3C)_2HC)_2N$), 3.64 (br s, 2 H, $((H_3C)_2HC)_2N$), 3.67 (s, 3 H, OCH_3), 5.22 (s, 1 H, $CH_{benzylic}$), 7.11–7.41 ppm (m, 5 H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.3 ($((H_3C)_2HC)_2N$), 48.5 ($((H_3C)_2HC)_2N$), 52.0 (OCH_3), 52.9 ($C_{benzylic}$), 128.2, 128.6, 128.8, 135.1 (Ph), 163.1 (NC=O), 171.6 ppm (C=O); MS (ESI): m/z = 316.1515 $[M+Na]^+$; elemental analysis: calcd (%) for $C_{16}H_{23}NO_4$ (293.56): C 65.51, H 7.90, N 4.77; found: C 65.73, H 7.90, N 5.40; HPLC: CHIRA-GROM 1 (2 × 250 mm), λ = 210 nm, *n*-hexane/*i*PrOH = 1000:1, 0.2 mL min^{-1}, $t_R(+)$ = 25.1 min, $t_R(-)$ = 35.3 min, 95 % *ee*.

21: (−)-(*S*)-*N*,*N*-Diisopropylcarbamic acid 1-naphthalen-1-yl-1-trimethylsilanylmethyl ester: White solid, yield: 96 %. R_f = 0.81 (E/P = 1:8); t_R = 18.2 min (HP-5); m.p.: 111 °C (Et_2O); $[\alpha]_D^{20} = -6.0$ (c = 0.98, $CHCl_3$); IR (KBr): $\tilde{\nu}$ = 3048 (m, C–H_{arom}), 2999, 2965, 2933 (s, C–H_{aliph}), 1696 (s, NC=O), 1595 (m), 1577 (m), 1475 (m), 1408 (s), 1292 (m), 1258 (s), 1156 (m), 1140 (m), 1122 (m), 1082 (m), 1046 (s), 1009 (m), 950 (m), 842 (s), 795 (m), 778 (s), 701 cm^{-1} (m); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.00 (s, 9 H, $(H_3C)_3Si$), 1.24 (br s, 12 H, $((H_3C)_2HC)_2N$), 3.92–4.03 (br m, 2 H, $((H_3C)_2HC)_2N$), 6.49 (s, 1 H, $CH_{benzylic}$), 7.36 (d, $^3J_{2\text{-H},3\text{-H}}$ = 7.3 Hz, 2 H, 2-H), 7.38–7.44 (m, 2 H, 3-H, 7-H), 7.45 (ddd, $^3J_{5\text{-H},6\text{-H}}$ = 7.5 Hz, $^3J_{6\text{-H},7\text{-H}}$ = 6.8 Hz, $^4J_{6\text{-H},8\text{-H}}$ = 1.9 Hz, 1 H, 6-H), 7.65 (d, $^3J_{3\text{-H},4\text{-H}}$ = 7.8 Hz, 1 H, 4-H), 7.79 (dd, $^4J_{5\text{-H},7\text{-H}}$ = 2.3 Hz, $^3J_{5\text{-H},6\text{-H}}$ = 7.5 Hz, 1 H, 5-H), 8.06 ppm (dd, $^3J_{7\text{-H},8\text{-H}}$ = 7.8 Hz, $^3J_{6\text{-H},8\text{-H}}$ = 1.9 Hz, 1 H, 8-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = −2.9 ($(H_3C)_3Si$), 21.0 ($((H_3C)_2HC)_2N$), 46.0 ($((H_3C)_2HC)_2N$), 68.3 ($C_{benzylic}$), 122.9 (C8), 123.9 (C2), 125.2 (C3), 125.38 (C6), 125.4 (C7), 126.3 (C4), 128.6 (C5), 130.1 (C8a), 133.7 (C4a), 137.5 (C1), 155.4 ppm (NC=O); MS (ESI): m/z = 380.2013 $[M+Na]^+$, 737.4125 $[2M+Na]^+$; elemental analysis: calcd (%) for $C_{21}H_{31}NO_2Si$ (357.57): C 70.54, H 8.74, N 3.92; found: C 70.55, H 8.61, N 3.81; HPLC: CHIRA-GROM 1 (2 × 250 mm), λ = 210 nm, *n*-hexane/*i*PrOH = 1000:1, 0.2 mL min^{-1}, $t_R(+)$ = 11.5 min, $t_R(-)$ = 14.8 min, 98 % *ee*.

22: (−)-(*S*)-*N*,*N*-Diisopropylcarbamic acid 1-naphthalen-1-yl-1-tributylstannylmethyl ester: Colorless liquid, yield: 91 %. R_f = 0.86 (E/P = 1:8); t_R = 23.1 min (HP-5); $[\alpha]_D^{20} = -140.7$ (c = 1.02, $CHCl_3$); IR (film): $\tilde{\nu}$ = 3058 (m, C–H_{arom}), 2957, 2928, 2871, 2853 (s, C–H_{aliph}), 1681 (s, NC=O), 1593 (m), 1578 (m), 1509 (m), 1462 (m), 1433 (s), 1376 (m), 1336 (m), 1298 (m), 1198 (s), 1157 (m), 1135 (m), 1072 (m), 1048 (s), 793 (m), 774 (s), 689 cm^{-1} (m); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.76 (t, $^3J_{Sn,H}$ = 7.1 Hz, 9 H, $((H_3CCH_2CH_2CH_2)_3Sn)$, 1.00–1.35 (m, 24 H, $((H_3C)_2HC)_2N$, $((H_3CCH_2CH_2CH_2)_3Sn$, $((H_3CCH_2CH_2CH_2)_3Sn)$, 4.01 (br s, 2 H, $((H_3C)_2HC)_2N)$, 6.50 (s, 1 H, $CH_{benzylic}$), 7.36–7.48 (m, 4 H, 2-H, 3-H, 6-H, 7-H), 7.55–7.63 (m, 1 H, 4-H), 7.81 (dd, $^3J_{5\text{-H},6\text{-H}}$ = 6.6 Hz, $^4J_{5\text{-H},7\text{-H}}$ = 3.2 Hz, 1 H, 5-H), 7.87 ppm (dd, $^3J_{7\text{-H},8\text{-H}}$ = 6.4 Hz, $^4J_{6\text{-H},8\text{-H}}$ = 3.2 Hz, 1 H, 8-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.6 ($(H_3CCH_2CH_2CH_2)_3Sn$), 13.5 ($(H_3C(CH_2)_3)_3Sn$), 21.1 ($((H_3C)_2HC)_2N$), 27.3 ($(H_3CCH_2CH_2CH_2)_3Sn$), 28.7 ($(H_3CCH_2CH_2CH_2)_3Sn$), 46.0 ($((H_3C)_2HC)_2N$), 72.2 (C9), 120.3 (C8), 123.1 (C2), 125.2 (C3), 125.3 (C6), 125.5 (C7), 125.6 (C4), 128.6 (C5), 128.8 (C8a), 133.7 (C4a), 139.5 (C1), 155.3 ppm (NC=O); MS (ESI): m/z = 598.2685 $[M+Na]^+$, 1171.5475 $[2M+Na]^+$; elemental analysis: calcd (%) for $C_{30}H_{49}NO_2Sn$ (574.43): C 62.73, H 8.60, N 2.44; found: C 62.46, H 8.69, N 2.29; HPLC: EC250/4 Nucleosil 100–5 Chiral-2 (4 × 250 mm), λ = 210 nm, *n*-hexane/*i*PrOH:TFA = 1000:1:0.5, 0.3 mL min^{-1}, $t_R(+)$ = 36.6 min, $t_R(-)$ = 39.5 min, 99 % *ee*.

Computational Details

DFT calculations of the epimeric lithium complexes of phenylmethyl carbamate **13** and 1-naphthylmethyl carbamate **19**: Unless otherwise stated, the Turbomole 5.9 suite of programs[25l] was used for all calculations. The structures of the complexes were optimized at the DFT level by employing the B97-D functional,[25a,b] which included an empirical dispersion correction (DFT-D), with a Gaussian atomic-orbital (AO) basis set of triple-zeta quality with polarization functions on all atoms (TZVP)[25c] and numerical quadrature multiple grid ("grid m4" option in turbomole).[25m] The resolution of the identity (RI) approximation[25n–p] was applied for all DFT calculations. Single-point energies were computed with SCS-MP2[25d] by using the TZVPP basis set[25c] and employing the RI approximation.[25q–s] For comparison, single-point calculations at the DFT level with the functionals B3-LYP[25i–k] and PBE[25g,h] were performed. Solvent effects (SCS-MP2-level) were simulated with COSMO (ε(toluene) = 2.355).[29] Additional computations with the PCM model[30a] for solvent effects were carried out by using PBE/6–311G* and Gaussian 03.[30b] ZPVE contributions were determined at the B97-D[25d] level by using a split valence basis set (SV(P))[30b] in the harmonic approximation (unscaled) as numerical derivatives of analytically calculated nuclear gradients with the SNF program.[30]

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