Experimental and Theoretical Investigations of Lithio-Indenyl Carbamate/(−)-Sparteine and (−)-α-Isosparteine Complexes

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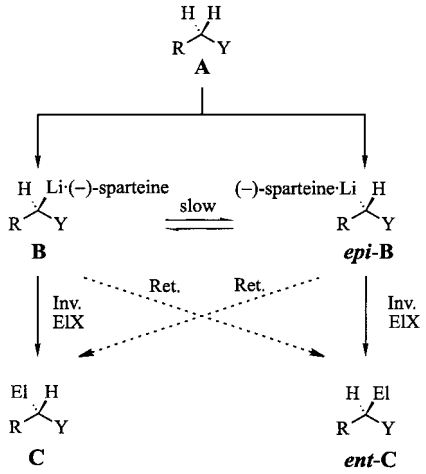
Dedicated to Dr. Pol Bamelis on the occasion of his 60th birthday

Abstract: 1-Carbamoyloxy-1-lithio-indene complexes of (−)-sparteine and (−)-α-isosparteine **5**/*epi*-**5** and **6**/*epi*-**6** were prepared and found to be configurationally unstable on the macroscopic time scale. Ratios of epimers and the rates of interconversion, including some activation parameters, were determined by temperature-dependent line shape analysis in the ^{1}H NMR spectrum. The highest barrier for interconversion ($\Delta\Delta H^{\ddagger} > 25$ kcal mol^{-1}) was recorded for the 2-methylindenide/(−)-sparteine complexes **5b**/*epi*-**5b**, whereas the activation energy for the epimerisation of the indenide/(−)-α-isosparteine complex **6a**/*epi*-**6a** is too low to be recorded by this method. Trapping of the lithium compounds **5**/*epi*-**5** and **6**/*epi*-**6** proceeds with methyl iodide in an *anti*-S_E' process. The obtained enantiomeric ratios correlate roughly with the observed epimeric ratios in the lithium intermediates. The absolute configurations of the methylation products **7c** and **7d** have been established by chemical correlation with the known (+)-(*S*)-3-methyl-1*H*-indan-1-one. The ratios correspond well to those predicted by semiempirical PM3 calculations on the relative stability of the diastereomeric complexes.

Keywords: chiral carbanions · line shape analysis · lithiation · semiempirical calculations · (−)-sparteine

Introduction

Although enantioenriched, chiral organolithium compounds became important tools in enantioselective synthesis,[1, 2] quantitative information on the features of configurational stability is still very scarce. Besides of some types of sp^3-carbanion lithium-(−)-sparteine complexes which are configurationally stable in solution at least at −70 °C,[3] the mesomerically stable sp^2-carbanion counterparts usually are configurationally unstable with few exceptions.[4] The diastereomeric ion pairs, which differ in the configuration of the carbanionic part, may equilibrate under the reaction conditions (Scheme 1). Provided that the substitution step by the electrophile occurs stereospecifically, either with complete inversion or retention at the former carbanionic center, and in addition, proceeds much more rapidly than the equilibration, the enantiomeric ratio in the products **C** and *ent*-**C** reflects the diastereomeric ratio in the organometallic intermediates **B** and *epi*-**B**.[5]



Scheme 1. (−)-Sparteine-mediated generation, epimerisation, and trapping of chiral lithium compounds.

When the epimeric organolithium complexes **B** and *epi*-**B** remain in solution (and the equilibrium is not disturbed through dynamic kinetic resolution[6] by the preferred crystallisation of one diastereomer[7]), their ratio directly correlates with their difference in free energy $\Delta\Delta G$.

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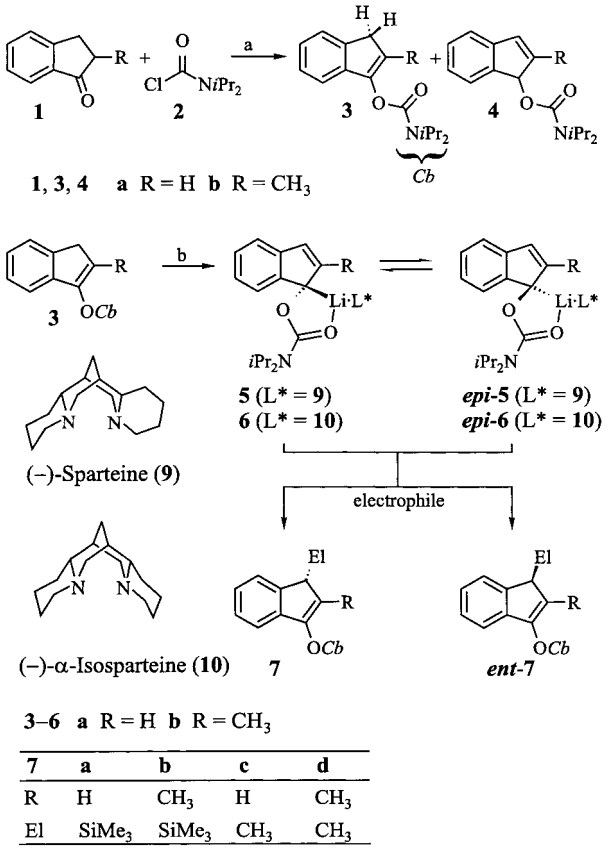
In this work we studied few chiral ion pairs, formed by chiral diamine-assisted deprotonation of *O*-indenyl carbamates,[8] including trapping experiments, ^{1}H NMR investigations on the equilibria, their interconversion rates, and the suitability of semiemipirical quantum-chemical calculation predicting the relative energies.

Results and Discussion

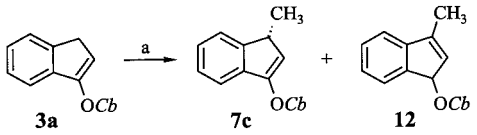
The 1*H*-inden-3-yl carbamates **3a**,**b** were prepared from the corresponding indanones **1a**,**b** and *N*,*N*-diisopropylcarbamoyl chloride (**2**) by heating in neat pyridine (Scheme 2). Small amounts of the 1*H*-inden-1-yl isomers **4a**,**b** (rel. 3–4%) are formed presumably by a base-induced 1,3-proton shift; **4b** was separated easily by chromatography on silica gel. The deprotonation of the enol carbamates **3a**,**b** in the presence of 1.0 equiv (−)-sparteine (**9**) or (−)-α-isosparteine (**10**),[9] respectively, in toluene with a 1.6 M solution of *n*-butyllithium (1.0 equiv) proceeded smoothly and was completed after stirring for 30 min at −78 °C. The carbanionic intermediates were trapped with 3 equiv of trimethylsilyl chloride or methyl iodide at −78 °C; neutralisation of the reaction mixture with acetic acid and aqueous workup afforded the optically active γ-substitution products **7** in good yields. Noteworthy, the exchange of (−)-sparteine (**9**) with (−)-α-isosparteine (**10**) results in an inversion of the sense of stereoselectivity and an increase in efficiency (Scheme 2 and Table 1).



7	a	b	c	d
R	H	CH_3	H	CH_3
El	$SiMe_3$	$SiMe_3$	CH_3	CH_3

Scheme 2. a) Pyridine, Δ; b) i) −78 °C, 1.0 equiv *n*BuLi, 1.0 equiv L*; ii) electrophile (−78 °C).

The lithium compounds prepared from **3a** and *n*BuLi/(−)-sparteine required higher temperatures for a complete reaction with methyl iodide and were allowed to warm to room temperature before neutralisation (yield 59%, 11% *ee*). The formation of the by-product **12** (16%), which arises from a double bond shift in the primary product **7c**, may indicate the occurrence of a competing racemisation under the basic reaction conditions (Scheme 3). Nearly complete conversion of the carbanionic intermediate is an important issue, otherwise a kinetic resolution of the diastereomers **5**/**6** and *epi*-**5**/**6** may occur.[10] This feature was demonstrated, when carrying the mixture **5a**/*epi*-**5a** and methyl iodide to only 16% conversion: The opposite enantiomer *ent*-**7c** (11% *ee*) was formed preferentially.



Scheme 3. a) i) −78 °C, 1.0 equiv *n*BuLi, 1.0 equiv L*; ii) MeI (−78 °C to RT).

Enantiomeric ratios in all products could easily be determined by ^{1}H NMR-spectroscopy in the presence of the optically active shift reagent tris-[(3-heptafluoropropylhydroxymethylen)-(+)-camphorato]europium(III). The assignments of absolute configurations in the products **7a** and **7b** are tentative,[11] since we were unable to accomplish any useful transformation of the sensitive silanes **7** for stereochemical correlation.

The carbamate moiety of indene **7c** and *ent*-**7d** could be removed by hydrolysis under acidic conditions (Scheme 4). The transformation of **7c** to the known (−)-(*R*)-3-methyl-1*H*-1-indanone (**13**) establishes the predominant (*R*)-configuration in the alkylation product **7c**. Indanone **13** could be alkylated to ketone **14** and **15** in an 89:11 diastereomeric ratio.

Table 1. Trapping experiments with lithiated indenes **5** and **6**.

Starting materials	Solvent	Product	R	El	Yield [%]	$[\alpha]_D$ (*c*, solvent)	*er* **7**/*ent*-**7**	*ee* [%]
3a, (−)-sparteine (**9**), Me_3SiCl	Et_2O	**7a**	H	Me_3Si	80	+22.4 (0.8, acetone)	58:42	16
3a, (−)-α-isosparteine (**10**), Me_3SiCl	Et_2O	*ent*-**7a**	H	Me_3Si	81	−22.0 (1.2, CH_2Cl_2)	32:68	32
3a, (−)-sparteine (**9**), MeI	Et_2O	**7c**	H	CH_3	59[a]	−11.7 (0.9, CH_2Cl_2)	56:44	12
3a, (−)-sparteine (**9**), MeI	toluene	**7c**	H	CH_3	45[a]	−8.9 (0.8, CH_2Cl_2)	54:46	8
3b, (−)-sparteine (**9**), Me_3SiCl	toluene	**7b**	CH_3	Me_3Si	84	−4.1 (1.2, Et_2O)	52:48	4
3b, (−)-α-isosparteine (**10**), Me_3SiCl	toluene	*ent*-**7b**	CH_3	Me_3Si	63	+48.1 (1.0, Et_2O)	24:76	52
3b, (−)-sparteine (**9**), MeI	Et_2O	**7d**	CH_3	CH_3	83	0.0 (0.8, acetone)	–	–
3b, (−)-α-isosparteine (**10**), MeI	Et_2O	*ent*-**7d**	CH_3	CH_3	68	+11.5 (1.1, CH_2Cl_2)	30:70	40

[a] The reaction mixture was allowed to warm to room temperature prior to neutralisation.

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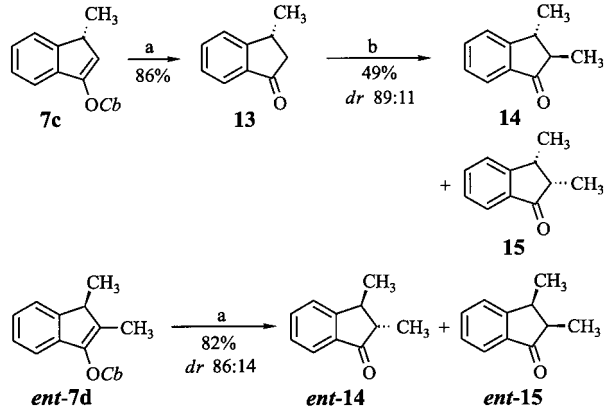

Scheme 4. a) 6N aq. H_2SO_4, THF, Δ; b) i) −78 °C, LDA; ii) MeI (−78 °C to RT); yields and ratios see Table 1.

This reaction allows to assign the (*S*)-configuration in the alkylation product *ent*-**7d** via the ketone *ent*-**14**.

^{1}H NMR spectroscopic investigations: In 1971, the first NMR studies on the exchange reaction of (−)-sparteine/magnesium complexes were published.[13] Later, several experiments showed the importance of NMR line shape analysis for the investigation of the kinetic behavior of lithiated compounds.[14] In this work, we determined the epimerisation of the lithiated indenides **5** and **6** by ^{1}H NMR spectroscopy. Figure 1 shows the 3-H signal of compound **6b** at various temperatures. At 295 K the signals of both epimers **6b** and *epi*-**6b** are averaged to one single absorption peak. Cooling of the sample results in the separation of two singlets due to slower epimerisation. Line shape analysis[15] with the density matrix formalism gives the rates of epimerisation. The activation parameters $\Delta H^{\neq} = 8.0 - 8.5$ kcal mol^{-1} and $\Delta S^{\neq} = -25.1$ cal mol^{-1} K^{-1} were obtained from the Eyring plot shown in Figure 2.

The NMR signals of the protons 2-H and 3-H in indenide **5a** is shown in Figure 3. At 345 K averaging results in one signal set for both epimers. At 285 K the two sets of dubletts corresponding to indenides **5a** and *epi*-**5a** are clearly separated. Comparison of observed and calculated line shapes provided the rates of epimerisation, and through the Eyring plot in Figure 4 activation parameters $\Delta H^{\neq}$ and $\Delta S^{\neq}$ of 13.5 kcal mol^{-1} and −8 cal mol^{-1} K^{-1}, respectively, were obtained. In addition, NMR investigations of compound **5b** and **6a** were performed. Unfortunately, line shape analyses were not possible in these cases. Obviously, the interconversion between the epimeric (−)-sparteine complexes **5b** and *epi*-**5b** was slow as the signals of proton 3-H remain separated up to temperatures of 363 K. In contrast, the rates of epimerisation were very high in the (−)-α-isosparteine complexes **6a** and *epi*-**6a** because the NMR spectra showed averaged signals down to temperatures of 200 K.[16]

The comparison of the kinetic data for lithiated indenides **5** and **6** (Table 2) shows that (−)-α-isosparteine decreases the configurational stability compared with (−)-sparteine. This may result from longer carbon–lithium bonds caused by the greater steric bulk of this ligand.[18] With either ligand, the indenides substituted with a methyl group in position 2 (**5b**, **6b**) show slower epimerisation than the corresponding unsubstituted compounds **5a** and **6a**.

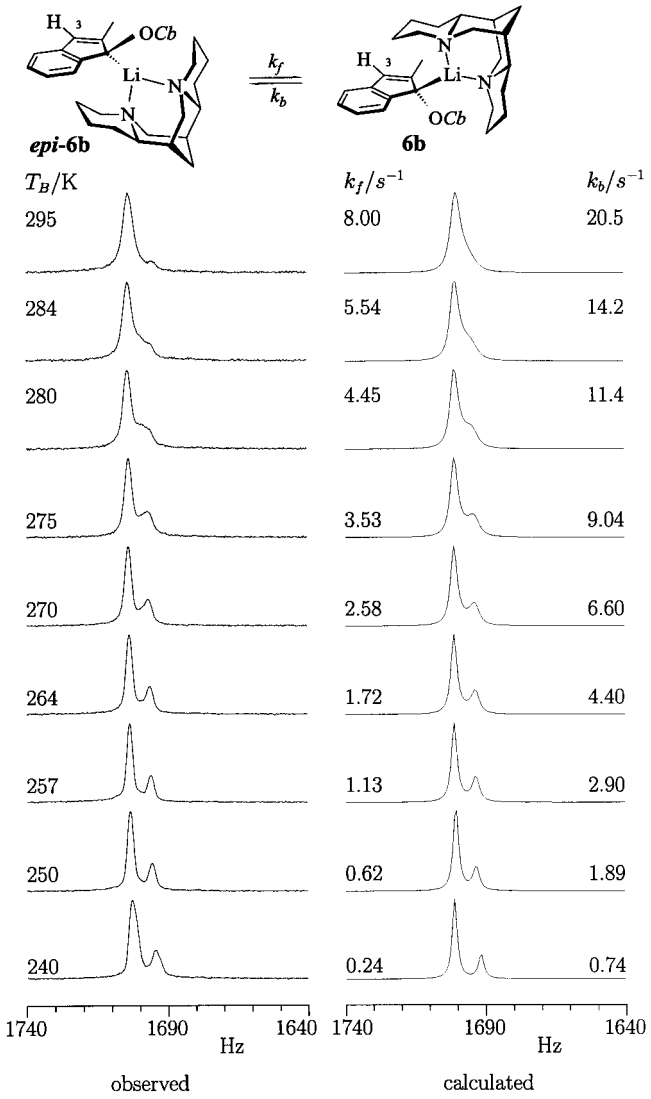

Figure 1. 300 MHz ^{1}H NMR spectra, line shapes of 3-H absorption of **6b**/*epi*-**6b** observed (left) in [D_{10}]diethyl ether and different temperatures; calculated (right).

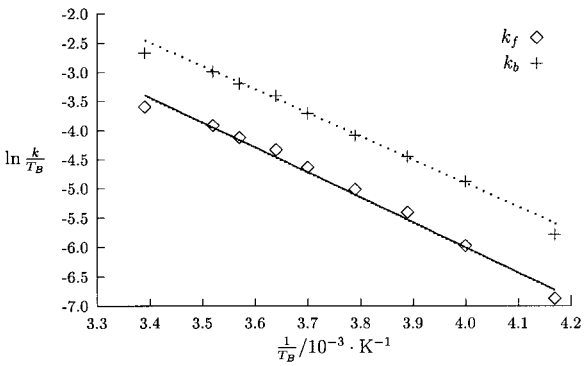

Figure 2. Eyring plot for epimerisation of **6b** (k_f, k_b: rate constants, T_b: temperature, see also Figure 1).

Semiempirical calculations (MOPAC,[19] PM3[20]): In the beginning of our work, semiempirical calculations of the lithiated indenides **5** were performed in order to estimate the

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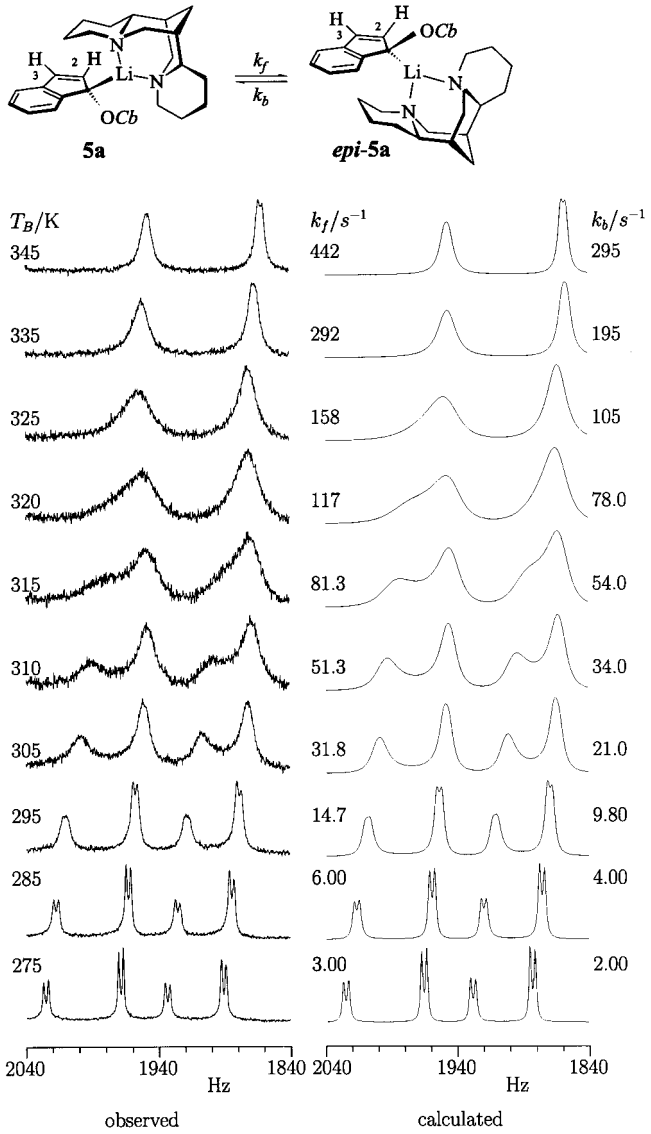

Figure 3. 300 MHz ^{1}H NMR spectra, line shapes of 2-H and 3-H absorption of **5a**/*epi*-**5a** observed (left) in [D_8]toluene and different temperatures; calculated (right).

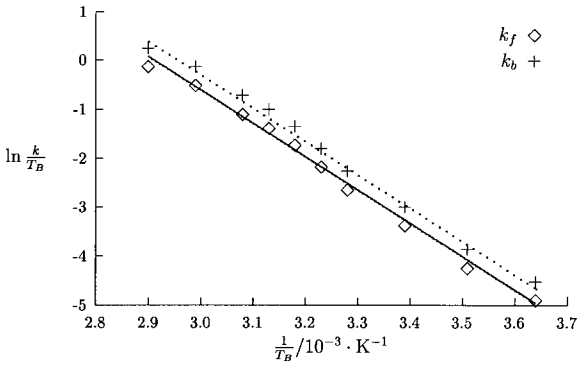

Figure 4. Eyring plot for epimerisation of **5a** (k_f, k_b: rate constants, T_b: temperature, see also Figure 3).

relative stabilities of the epimers. All calculations were performed on IBM-Risc 6000 computers with the PM3 parameters[20] by Stewart and lithium parameters by Anders et al. by using the MOPAC[19] program. The convergence criteria "GNORM = 0.1" was used. All structures were geometry-optimized with a fixed planar geometry of the carbamate nitrogen to avoid another center of asymmetry as found in all X-ray structures. The character of the stationary points on the hyperface was exemplarily determined by frequency analysis. The diastereomeric ratios in the lithiated indenides **5** and **6** determine the enantioenrichment in the substitution products **7**. For this reason the free energies of the ground states ΔG have to be considered. The calculations give the enthalpies ΔH, but the differences between the $\Delta\Delta G$ and $\Delta\Delta H$ values, resulting from the entropy term, should be very small, because very similar diastereomeric structures are compared.

Table 2. Activation parameters for epimerisation of lithiated indenes **5** and **6**.

Compound	*dr*[a]	$\Delta H^{\neq}$	$\Delta S^{\neq}$
5a	55:45	13.5 kcal mol^{-1}	-8 cal mol^{-1} K^{-1}
6a	–[b]	<5 kcal mol^{-1}	–[c]
5b	60:40	>25 kcal mol^{-1}	–[c]
6b	18:82	8.0–8.5 kcal mol^{-1}	-25.1 cal mol^{-1} K^{-1}

[a] Isomer appearing at lower field at left. [b] The diastereomeric ratio could not be determined due to fast epimerisation. [c] Line shape analysis not possible.

Since (−)-sparteine is not C_2-symmetric, the lithium cation is stereogenic and four diastereomers of **5** have to be considered (Figure 5). The data in Table 3 shows that in the case of the unsubstituted indenide **5a** the *like*-configured diastereomers S_CS_{Li}-**5a** and R_CR_{Li}-**5a** are more stable than the *unlike*-configured compounds S_CR_{Li}-**5a** and R_CS_{Li}-**5a**. The

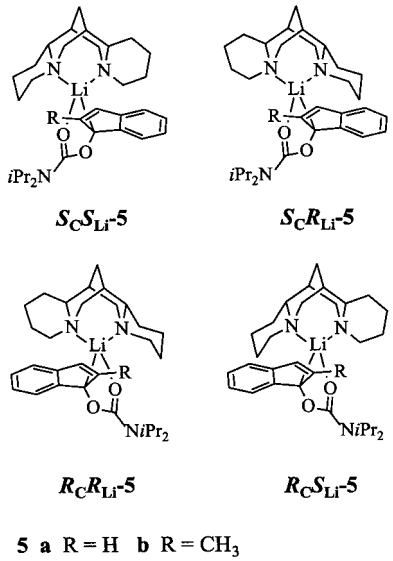

Figure 5. Diastereomeric (−)-sparteine/indenide complexes **5**.

Table 3. Calculated heat of formation (ΔH) for lithiated indenes **5** and **6**.

ΔH [kcal mol^{-1}]	**5a**	**5b**	ΔH [kcal mol^{-1}]	**6a**	**6b**
S_CS_{Li}	−66.3	−72.8	S_C	−60.3	−64.5
R_CR_{Li}	−66.0	−69.0	R_C	−61.6	−65.1
S_CR_{Li}	−64.2	−68.7			
R_CS_{Li}	−65.6	−73.0			
observed[a]	S_C	S_C		R_C	R_C

[a] Derived by chemical correlation of alkylation products **7c** and **7d**.

small energetic difference of 0.3 kcal mol^{-1} between the favored diastereomers S_CS_{Li}-**5a** (−66.3 kcal mol^{-1}) and R_CR_{Li}-**5a** (−66.0 kcal mol^{-1}) is too low to be significant. In contrast, the difference between the 2-methyl substituted indenide complexes S_CS_{Li}-**5b** and R_CR_{Li}-**5b** is 3.8 kcal mol^{-1}, respectively.[21] But in this case, the *unlike*-configured complexes are more stable and S_CS_{Li}-**5b** and R_CS_{Li}-**5b** possess nearly the same enthalpy.[22] In other words, the possibility of stereoisomerisation at the lithium cation levels the energy difference which results from the interaction of the chiral ligand and the carbanionic moiety. When applying a C_2-symmetric ligand, such as (−)-α-isosparteine (**10**), these complications do not exist. Isosparteine **10** causes a non-stereogenic lithium atom; only two diastereomers which differ in the configuration of the carbanionic moiety have to be considered. The PM3 calculations on the (−)-α-isosparteine complexes **6a** and **6b** predicts differences of −1.3 and −0.6 kcal mol^{-1}, respectively, in favor of the R_C-epimers (corresponding to *epi*-**6**). The experiments resulted in an improvement from 8 to 51% *ee* (see above). Except for indenide **5b**, the calculated most stable isomers match the experimental correlation (Table 3), but the deviation for compounds **5a** and **5b** (0.2 and 0.3 kcal mol^{-1}) are at best at the magnitude of error for this calculation.

Conclusion

We were surprised that the experimental evidence matches well — even in the semiquantitative view — with the results of the semiempirical calculations. One reason might be that the lithiated carbamates of type **5** and **6** are monomeric, as has been demonstrated for a related complex even for the solid state,[23] and no equilibria between different aggregates are relevant under the reaction conditions. As predicted by the calculations

- the enantiomeric ratios in the products **7**/*ent*-**7** (corresponding to the diastereomeric ratios in the lithium compounds **5**/*epi*-**5** and **6**/*epi*-**6**) are increased by the exchange of the chiral ligand (−)-sparteine (**9**) for (−)-α-isosparteine (**10**), and
- the sense of stereoselectivity is reversed by this exchange and the relative configurations at the carbanionic center of the major epimer are predicted correctly when $\Delta\Delta H$ is more than 0.5 kcal mol^{-1}.

(−)-α-Isosparteine (**10**) is superior to (−)-sparteine (**9**) as a result of the larger energetic differences and its greater kinetic mobility when the equilibration between diastereomeric ion pairs in solution is the goal. However, when applying **10** to precursors of lower CH-acidity, its diminished ability in supporting the deprotonation step has to be taken into account.[24]

Experimental Section

General remarks: All reactions involving water- or air-sensitive chemicals were carried out in distilled and dried solvents under argon. Diethyl ether was distilled from sodium and THF from potassium immediately prior to use. Solvents [diethyl ether, petroleum ether (boiling range 35–40 °C)] used for chromatography were distilled prior to use. All other reagents and solvents were used as received. Melting points: Gallenkamp melting point apparatus (uncorrected). IR: Perkin–Elmer PE 298. ^{1}H and ^{13}C NMR: Bruker AM200, AM300 or AM360 or Avance 300. Shifts are reported relative to tetramethylsilane as an internal reference. $CDCl_3$ was used as solvent. The multiplicities of the ^{13}C NMR signals were determined with DEPT pulse sequences. Numbering according to IUPAC rules. Elemental analyses: Perkin–Elmer 240. TLC: Macherey, Nagel & Co. Sil G/UV$_{254}$; eluent given in brackets, diethyl ether (E)/pentane (P) (1:1) was used as solvent unless noted otherwise; detection by coloration with molybdato phosphoric acid (4% in ethanol). Flash chromatography (FC): Merck silica gel 60 (40–63 μm) (100 g for 1 g of material to be separated).

1*H*-Inden-3-yl *N*,*N*-diisopropylcarbamate (3a) and *rac*-1*H*-inden-1-yl *N*,*N*-diisopropyl-carbamate (4a): 1-Indanone (6.60 g, 50.0 mmol), dry pyridine (5.4 mL, 75.0 mmol), and *N*,*N*-diisopropylcarbamoyl chloride (8.15 g, 50.0 mmol) were stirred at 90 °C for 6 d. The reaction mixture was then chilled to room temperature and poured to a slurry of 6 N HCl (100 mL) and ice (20 g). The aqueous solution was extracted with Et_2O (3 × 30 mL) and the combined etheral phases were washed with sat. aqueous $NaHCO_3$ (40 mL). After the solution was dried ($MgSO_4$), the solvent was evaporated under reduced pressure, and the residue was purified by FC (silica gel, E/P 1:5) to yield **3a** and **4a** (6.67 g, 52%) as a 97:3 mixture.

Carbamate 3a: IR (film): $\tilde{\nu}$ = 1715 cm^{-1} (NCO); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.1–1.4 (m, 12H, 2′-H), 3.4 (dd, ^3J(1-H,2-H) = 2.4 Hz, ^4J(1-H,7-H) = 0.7 Hz, 2H, 1-H), 3.9–4.2 (m, 2H, 1′-H), 6.3 (t, 1H, 2-H), 7.2–7.5 (m, 4H, 4–7-H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C, TMS): δ = 21.0 (q, C-2′), 34.9 (t, C-1), 46.7 (d, C-1′), 113.8 (d, C-2), 118.1/124.1/125.4/126.2 (d, C-4–7), 140.0/142.1 (s, C-3a, C-7a), 149.6 (s, c-3), 152.7 (s, NCO); $C_{16}H_{21}NO_2$ (259.35): calcd C 74.03, H 8.09, found C 74.01, H 7.93.

Carbamate 4a: IR (film): $\tilde{\nu}$ = 1690 cm^{-1} (NCO); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.0–1.4 (m, 12H, 2′-H), 3.5–4.2 (m, 2H, 1′-H), 6.2 (d, ^3J(2-H,3-H) = 5.8 Hz, 1H, 3-H), 6.4 (dd, ^3J(1-H,2-H) = 2.0 Hz, 1H, 2-H), 6.8 (d, 1H, 1-H), 7.1–7.5 (m, 4–7-H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 21.0 (q, C-2′), 46.2 (d, C-1′), 77.8 (d, C-1), 121.4/124.2/126.1/128.5 (d, C-4–7), 133.8 (d, C-3), 134.8 (d, C-2), 142.9/143.1 (s, C-3a, C-7a), 155.8 (s, NCO).

(2-Methyl-1*H*-inden-3-yl) *N*,*N*-diisopropylcarbamate (3b) and *rac*-(2-methyl-1*H*-inden-1-yl) *N*,*N*-diisopropylcarbamate (4b): 2-Methyl-1-indanone (5.42 g, 42.0 mmol), dry pyridine (5.0 mL, 64.0 mmol), and *N*,*N*-diisopropylcarbamoyl chloride (6.85 g, 42.0 mmol) were stirred at 90 °C for 6 d. Then, the reaction mixture was chilled to room temperature and poured to a slurry of 6 N HCl (100 mL) and ice (20 g). The aqueous solution was extracted with diethyl ether (3 × 30 mL) and the combined etheral phases washed with sat. aqueous $NaHCO_3$ (40 mL). After the solution was dried ($MgSO_4$), the solvent was evaporated under reduced pressure, and the residue was purified by FC (silica gel, E/P 1:4) to yield **3b** (5.29 g, 46%) and **4b** (0.35 g, 3%) as colorless oils.

Carbamate 3b: IR (film): $\tilde{\nu}$ = 1700 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.2–1.5 (m, 12H, C-2′), 2.0 (t, ^4J(1-H,2-CH_3) = 1.0 Hz, 3H, 2-CH_3), 3.3 (q, 2H, 1-H), 3.9–4.3 (m, 2H, C-1′), 7.0–7.4 (m, 4H, 4–7-H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 3.8 (q, 2-CH_3), 20.6/21.5 (q, C-2′), 38.9 (t, C-1), 46.4 (d, C-1′), 117.2/123.7/124.3/126.1 (d, C-4–7), 127.3 (s, C-2), 140.3/140.8/144.8 (s, C-3, C-3a, C-7a), 152.6 (s, NCO); $C_{17}H_{23}NO_2$ (273.37): calcd C 74.7, H 8.49; found C 74.83, H 8.40.

Carbamate 4b: IR (film) $\tilde{\nu}$ = 1690 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.0–1.4 (m, 12H, 2′-H), 2.0 (s, 3H, 2-CH_3), 3.6–4.3 (m, 2H, 1′-H), 6.2 (s, 1H, 1-H), 6.4 (s, 1H, 3-H), 7.0–7.5 (m, 4H, 4–7-H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C, TMS): δ = 14.2 (q, 2-CH_3), 21.1 (q, C-2′), 46.2 (d, C-1′), 78.7 (d, C-1), 120.1/124.5/124.9/128.4 (d, C-4–7), 143.1/143.2/145.7 (s, C-2, C-3a, C-7a), 155.9 (s, NCO).

General procedure for the lithiation of the indenes 3a and 3b: *n*-Butyllithium (1.0 mmol, 1.6 M in *n*-hexane) was added dropwise with stirring (30 min) at −78 °C to a solution of **3** (1.0 mmol) and (−)-sparteine (**9**) or (−)-α-isosparteine[9] (**10**) (1.0 mmol) in diethyl ether (2 mL) or toluene (4 mL). The electrophile was added and stirring continued for 4 h at −78 °C. Acetic acid (1 mL, 50% in ether) was added before warming the mixture to room temperature. The organic phase was washed with 2 N HCl (20 mL). After the phases were separated, the aqueous phase was extracted with diethyl ether (3 × 20 mL). The combined organic phases were washed

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with sat. aqueous $NaHCO_3$ (20 mL) and dried with sodium sulfate. The products were separated on silica gel with diethyl ether/petroleum ether. *ee*-Values were determined by 360 MHz ^{1}H NMR spectroscopy in the presence of the optically active shift reagent tris-[(3-heptafluoropropylhydroxymethylen)-(+)-camphorato]europium(III) in $CDCl_3$.

(+)-(*R*)-(1-Trimethylsilyl-1*H*-inden-3-yl) *N*,*N*-diisopropylcarbamate (7a): According to the general procedure indenyl carbamate **3a** (259 mg, 1.00 mmol) was lithiated with *n*-butyllithium (1.6 M, 0.63 mL, 1.00 mmol) in the presence of (−)-sparteine (**9**) (234 mg, 1.00 mmol) in diethyl ether (2 mL) for 30 min at −78 °C and treated 4 h with trimethylsilyl chloride (238 mg, 2.20 mmol). Flash chromatography on silica gel (40 g) with E/P 1:15 yielded silane **7a** (230 mg, 80 %) as a colorless oil with 16 % *ee* (main isomer at lower field). $[\alpha]_D^{20} = +22.4$ ($c = 0.8$ in acetone); IR (film) $\tilde{\nu} =$ 1720 cm^{-1} (NCO); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 0.0$ (s, 9H, Si-CH_3), 1.0–1.5 (m, 12H, 2′-H), 3.4 (d, ^3J(1-H,2-H) = 2.3 Hz, 1H, 1-H), 3.7–4.4 (m, 2H, 1′-H), 6.4 (d, 1H, 2-H), 7.2–7.5 (m, 4H, 4–7-H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C, TMS): $\delta = -2.4$ (q, Si-CH_3), 21.1 (q, C-2′), 41.8 (d, C-1), 46.5 (d, C-1′), 116.7/118.0/123.0/124.4/124.8 (d, C-2, C-4–7), 138.6/143.8/147.5 (s, C-3, C-3a, C-7a), 153.2 (s, NCO); HR-MS (70 eV): $C_{19}H_{29}NO_2Si$: calcd 331.1959; found 331.1953.

(−)-(*S*)-(1-Trimethylsilyl-1*H*-inden-3-yl) *N*,*N*-diisopropylcarbamate (*ent*-7a): According to the general procedure indenyl carbamate **3a** (259 mg, 1.00 mmol) was lithiated with *n*-butyllithium (1.6 M, 0.63 mL, 1.00 mmol) in the presence of (−)-α-isosparteine (**10**) (234 mg, 1.00 mmol) in diethyl ether (8 mL) for 30 min at −78 °C and treated 4 h with trimethylsilyl chloride (238 mg, 2.20 mmol). FC on silica gel (40 g) with E/P 1:15 yielded silane *ent*-**7a** (230 mg, 80 %) as a colorless oil with 32 % *ee* (main isomer at higher field). $[\alpha]_D^{20} = -22.0$ ($c = 1.2$ in CH_2Cl_2).

(−)-(*R*)-(2-Methyl-1-trimethylsilyl-1*H*-inden-3-yl) *N*,*N*-diisopropylcarbamate (7b): According to the general procedure indenyl carbamate **3b** (163 mg, 0.50 mmol) was lithiated with 3.0 M *n*-butyllithium (0.18 mL, 0.50 mmol) in the presence of (−)-sparteine (**9**) (118 mg, 0.50 mmol) in toluene (2 mL) for 30 min at −78 °C and treated 4 h with trimethylsilyl chloride (116 mg, 1.00 mmol). FC on silica gel (25 g) with E/P 1:15 yielded silane **7a** (146 mg, 84 %) as a colorless oil with 4 % *ee* (main isomer at lower field). M.p. 65 °C (diethyl ether); $[\alpha]_D^{20} = -4.1$ ($c = 1.2$ in diethyl ether); IR (film) $\tilde{\nu} = 1710$ cm^{-1} (NCO); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta =$ 0.0 (s, 9H, Si-CH_3), 1.2–1.5 (m, 12H, 2′-H), 2.0 (s, 3H, 2-CH_3), 3.3 (s, 1H, 1-H), 3.7–4.4 (m, 2H, 1′-H), 7.0–7.4 (m, 4H, 4–7-H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C, TMS): $\delta = -2.0$ (q, Si-CH_3), 13.1 (q, 2-CH_3), 20.8/21.5 (q, C-2′), 45.0 (d, C-1), 46.0/46.9 (d, C-1′), 117.0/123.0/123.2/124.9 (d, C-4–7), 130.2/139.4/142.3/143.4 (s, C-2, C-3, C-3a, C-7a), 153.2 (s, NCO); HR-MS (70 eV) $C_{20}H_{32}NO_2Si$: calcd 345.2115; found 345.2123.

(+)-(*S*)-(2-Methyl-1-trimethylsilyl-1*H*-inden-3-yl) *N*,*N*-diisopropylcarbamate (*ent*-7b): According to the general procedure of indenyl carbamate **3b** (273 mg, 1.00 mmol) was lithiated with 3.0 M *n*-butyllithium (0.33 mL, 1.00 mmol) in the presence of (−)-α-isosparteine (**10**) (234 mg, 1.00 mmol) in toluene (7 mL) for 30 min at −78 °C and treated 4 h with trimethylsilyl chloride (324 mg, 3.00 mmol). FC on silica gel (40 g) with E/P 1:15 yielded silane **7a** (146 mg, 84 %) as a colorless oil with 52 % *ee* (main isomer at higher field). $[\alpha]_D^{20} = +48.1$ ($c = 1.0$ in diethyl ether).

(−)-(*R*)-(1-Methyl-1*H*-inden-3-yl) *N*,*N*-diisopropylcarbamate (7c): According to the general procedure indenyl carbamate **3a** (518 mg, 2.00 mmol) was lithiated with *n*-butyllithium (1.6 M, 1.26 mL, 2.00 mmol) in the presence of (−)-sparteine (**9**) (518 mg, 2.00 mmol) in diethyl ether (4 mL) for 30 min at −78 °C and treated 5 h with methyl iodide (710 mg, 5.00 mmol). In contrast to the general procedure, the reaction mixture was warmed to room temperature before neutralisation with 2 N HCl. FC on silica gel (60 g) with E/P 1:15 yielded indene **7c** (322 mg, 59 %) as a colorless oil (8 % *ee*, main isomer at lower field), isomer **12** (87 mg, 16 %) and starting material **3a** (57 mg, 11 %).

Carbamate 7c: $[\alpha]_D^{20} = -11.7$ ($c = 0.9$ in CH_2Cl_2); IR (film) $\tilde{\nu} = 1720$ cm^{-1} (NCO); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 1.1–1.5$ (m, 15H, 1-CH_3, 2′-H),3.6 (dq, ^3J(1-H,2-H) = 2.2 Hz, ^4J(1-H,1-CH_3) = 7.5 Hz, 1H, 1-H), 3.9–4.2 (m, 2H, 1′-H), 6.2 (d, 1H, 2-H), 7.1–7.4 (m, 4H, 4–7-H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 16.5$ (q, 1-CH_3), 21.1 (q, C-2′), 41.2 (d, C-1), 46.7 (d, C-1′), 118.7/120.5/123.9/125.6/128.1 (d, C-2, C-4–7), 142.3/147.6/148.3 (s, C-1, C-3a, C-7a), 152.6 (s, NCO); $C_{17}H_{23}NO_2$ (273.37): calcd C 74.69, H 8.48; found C 74.73, H 8.72.

Carbamate 12: IR (film) $\tilde{\nu} = 1680$ cm^{-1} (NCO); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 1.0–1.4$ (m, 12H, 2′-H), 2.1 (dd, ^4J(1-H,3-CH_3) = 1.8 Hz, ^4J(2-H,3-CH_3) = 1.8 Hz, 3H, 3-CH_3), 3.6–4.2 (m, 2H, 1′-H), 6.1 (dq, ^3J(1-H,2-H) = 1.8 Hz, 1H, 2-H), 6.2 (dq, 1H, 1-H), 7.1–7.5 (m, 4H, 4–7-H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 12.9$ (q, 3-CH_3), 21.0 (q, C-2′), 46.1 (d, C-1′), 76.9 (d, C-1), 119.1/123.2/126.0/128.5/129.5 (d, C-2, C-4–7), 142.0/143.7/144.5 (s, C-3, C-3a, C-7a), 155.9 (s, NCO); $C_{17}H_{23}NO_2$ (273.37): calcd C 74.69, H 8.48; found C 74.67, H 8.46.

(*RS*)-(1,2-Dimethyl-1*H*-inden-3-yl) *N*,*N*-diisopropylcarbamate (7d): According to the general procedure indenyl carbamate **3a** (273 mg, 1.00 mmol) was lithiated with *n*-butyllithium (1.6 M, 0.63 mL, 1.00 mmol) in the presence of (−)-sparteine (**9**) (234 mg, 1.00 mmol) in diethyl ether (2 mL) for 30 min at −78 °C and treated 5 h with methyl iodide (284 mg, 2.00 mmol). FC on silica gel (30 g) with E/P 1:10 yielded indene **7d** (239 mg, 83 %) as a colorless oil. $[\alpha]_D^{20} = 0.0$ ($c = 0.8$ in acetone); IR (film) $\tilde{\nu} =$ 1710 cm^{-1} (NCO); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 1.3–1.4$ (m, 12H, 2′-H), 1.3 (d, ^3J(1-H,1-CH_3) = 7.5 Hz, 3H, 1-CH_3), 1.9 (d, ^4J(1-H,2-CH_3) = 0.7 Hz, 3H, 2-CH_3), 3.3 (qq, 1H, 1-H), 3.9–4.2 (m, 2H, 1′-H), 7.0–7.4 (m, 4H, 4–7-H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 10.4$ (q, 1-CH_3), 15.5 (q, 2-CH_3), 21.5 (q, C-2′), 43.7 (d, C-1), 46.6 (d, C-1′), 117.3/122.5/124.5/126.4 (C-4–7), 132.5/139.7/144.0 (s, C-3, C-3a, C-7a), 152.8 (s, NCO); $C_{18}H_{25}NO_2$ (287.40): calcd C 75.23, H 8.77; found C 75.14, H 8.86.

(+)-(*S*)-(1,2-Dimethyl-1*H*-inden-3-yl) *N*,*N*-diisopropylcarbamate (*ent*-7d): According to the general procedure indenyl carbamate **3a** (273 mg, 1.00 mmol) was lithiated with *n*-butyllithium (1.6 M, 0.63 mL, 1.00 mmol) in the presence of (−)-α-sparteine (**9**) (234 mg, 1.00 mmol) in diethyl ether (2 mL) for 30 min at −78 °C and treated 4 h with methyl iodide (430 mg, 3.00 mmol). FC on silica gel (30 g) with E/P 1:10 yielded indene *ent*-**7d** (195 mg, 68 %) as a colorless oil with 40 % *ee* (main isomer at higher field). $[\alpha]_D^{20} = +11.5$ ($c = 1.1$ in CH_2Cl_2).

(*R*)-3-Methylindan-1-one (13): 6 N H_2SO_4 (3 mL) were added to a solution of indenyl carbamate **7d** (570 mg, 2.10 mmol) in THF (20 mL). After the solution was heated under reflux for 3 h, the chilled mixture was extracted with diethyl ether (3 × 20 mL). The combined organic phases were washed with sat. aqueous $NaHCO_3$ (20 mL) and dried with Na_2SO_4. FC on silica gel (60 g) with E/P 1:6 yielded known ketone **13**[25] (263 mg, 86 %) as a yellow oil. $[\alpha]_D^{20} = -1.4$ ($c = 0.8$ in acetone).

(2*R*,3*R*)-2,3-Dimethylindan-1-one (14) and (2*S*,3*R*)-2,3-dimethylindan-1-one (15): A solution of ketone **13** (147 mg, 1.02 mmol) in THF (3 mL) was added dropwise to a solution of lithium diisopropylamide [1.4 mmol, prepared from diisopropylamine (141 mg, 1.40 mmol) and *n*-butyllithium (1.6 M, 0.88 mL, 1.4 mmol) in THF (3 mL)] at −78 °C. After the solution was stirred for 2 h at −78 °C, methyl iodide (430 mg, 3.0 mmol) was allowed to react for 3 h with the lithiated compound, before the mixture was slowly warmed to room temperature. After neutralisation with 2 N HCl (10 mL) the aqueous phase was extracted 3 × each with diethyl ether(20 mL each). The combined organic phases were washed with sat. aqueous $NaHCO_3$ (20 mL) and dried with Na_2SO_4. FC on silica gel (40 g) with E/P 1:8 yielded indanone **14** (62 mg, 38 %) and a 1:1 mixture of indanones **14** and **15** (18 mg, 11 %). **14**: $[\alpha]_D^{20} = -1.7$ ($c = 1.5$ in CH_2Cl_2).

(2*S*,3*S*)-2,3-Dimethylindan-1-one (*ent*-14) and (2*R*,3*S*)-2,3-dimethylindan-1-one (*ent*-15): 6 N H_2SO_4 (1 mL) was added to a solution of indenyl carbamate *ent*-**7d** (270 mg, 0.94 mmol) in THF (5 mL). After the mixture was refluxed for 6 h, the chilled mixture was extracted 3 × with diethyl ether (20 mL each). The combined organic phases were washed with sat. aqueous $NaHCO_3$ (20 mL) and dried with Na_2SO_4. FC on silical gel (60 g) with E/P 1:8 yielded indanone *ent*-**14** (90 mg, 60 %) as a colorless oil and a 1:1-mixture of indanones *ent*-**14** and *ent*-**15** (33 mg, 22 %). *ent*-**14**: $[\alpha]_D^{20} = +7.0$ ($c = 0.7$ in CH_2Cl_2).

General procedure for the preparation of the NMR samples: *n*-Butyllithium (1.6 M, 0.19 mmol, in *n*-hexane) was added dropwise under stirring at −78 °C to a solution of **3** (0.2 mmol) and (−)-sparteine (**9**) or (−)-α-isosparteine (**10**) (0.2 mmol) in diethyl ether (2 mL). The solution was stirred for 30 min and the solvent was removed under reduced pressure. The remaining residue was washed with petroleum ether (2 × 1 mL) (as a result of the partial solubility of lithiated compounds **5** and **6** at room temperature, the petroleum ether was removed at −78 °C) and dried in vacuum. A 5 mm OD NMR tube attached to a 2 mm straight bore stopcock via a 12/30 standard joint was flamed out under vacuum, filled with argon, and transferred to the glove box (argon atmosphere). The lithiated

indenide **5** or **6** was weighed in the glove box and loaded into the NMR tube with a narrow nickel spatula. The stopcock was reattached and the assembly transferred to the vacuum line. Then deuterated solvent was transferred to the tube by bulb-to-bulb distillation. Finally the samples were sealed off under vacuum.

Carbamate 5a was prepared according to the general procedure from **3a** (57 mg, 0.22 mmol), (−)-sparteine (**9**) (54 mg, 0.23 mmol) and *n*-butyllithium (1.6 M, 0.15 mL) in diethyl ether (2 mL). Lithiated indenide **5a** (40 mg) was transferred into a NMR tube and [D_8]toluene (0.5 mL) was added before the sample was sealed off.

Carbamate 5b was prepared according to the general procedure from **3b** (62 mg, 0.23 mmol), (−)-sparteine (**9**) (57 mg, 0.24 mmol) and *n*-butyllithium (1.6 M, 0.16 mL) in diethyl ether (2 mL). Lithiated indenide **5b** (36 mg) was transferred into a NMR tube and [D_8]toluene (0.5 mL) was added before the sample was sealed off.

Carbamate 6a was prepared according to the general procedure from **3a** (30 mg, 0.12 mmol), (−)-α-isosparteine (**10**) (33 mg, 0.14 mmol) and *n*-butyllithium (1.6 M, 0.11 mL) in diethyl ether (2 mL). In contrast to the general procedure, the lithiated indenide **6a** was redissolved in diethyl ether (1 mL) after washing with petroleum ether and drying. 0.5 mL of this solution containing approx. 30 mg of lithiated indenide **6a** were transferred into a NMR tube with a syringe, the solvent was removed in vacuum and [D_{10}]diethyl ether (0.5 mL) was added before the sample was sealed off.

Carbamate 6b was prepared according to the general procedure from **3b** (55 mg, 0.20 mmol), (−)-α-isosparteine (**10**) (47 mg, 0.20 mmol) and *n*-butyllithium (1.6 M, 0.19 mL) in diethyl ether (2 mL). Lithiated indenide **6b** (36 mg) was transferred into a NMR tube and [D_{10}]diethyl ether (0.5 mL) was added before the sample was sealed off.

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[21] The NMR investigation shows a high configurational stability of complex **5b**. So the discussion of ground state calculations is at least difficult here. The main result, though, the correspondence of low selectivity with the missing C_2-symmetry of (−)-sparteine, should be transferable to the transition state of the lithiation.

[22] In this case the complexes with (S_{Li})-configuration are at least 3.8 kcal mol^{-1} more stable than those with (R_{Li})-configuration. But as the substitution step is assumed to follow an *anti*-S_E'-mechanism, no interaction between the electrophiles methyl iodide and trimethylsilyl chloride should exist and the configuration of the lithium should have no influence on the enantioenrichment in the substitution products. This configuration could have an influence in the reaction with carbonyl compounds, though, were a precoordination between the lithium and the carbonyl oxygen is supposed [ref. 2a].

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