[15] D. Kummer, L. Diehl, *Angew. Chem.* **1970**, *82*, 881; *Angew. Chem. Int. Ed. Engl.* **1970**, *9*, 895; J. D. Corbett, *Chem. Rev.* **1985**, *85*, 383.

[16] L. Diehl, K. Khodadadeh, D. Kummer, J. Strähle, *Chem. Ber.* **1976**, *109*, 3404.

[17] [2.2.2]Crypt = 4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]hexacosane.

[18] J. D. Corbett, *Structure and Bonding* **1997**, *87*, 157.

[19] R. G. Teller, L. J. Krause, R. C. Haushalter, *Inorg. Chem.* **1983**, *22*, 1809.

[20] Crystal structure determination: Crystals were mounted in glass capillaries. Structure solution (SHELXS-97) and refinement (SHELXL-97) was carried out with direct and full-matrix least-square methods based on F^2 for all atoms with anisotropic displacement parameters. **1**: crystal dimensions $0.12 \times 0.45 \times 0.50$ mm^3, lattice constants at 243 K: $a = 10.220(2)$, $b = 14.957(3)$, $c = 23.690(5)$ Å, $\alpha = 99.86(3)$, $\beta = 91.43(3)$, $\gamma = 103.79(3)^\circ$, $V = 3456(1)$ Å^3; space group $P\bar{1}$ (no 2), $Z = 2$, $\rho_{calcd} = 1.996$ g cm^{-3}, $\mu = 3.489$ mm^{-1}; Data collection: STOE IPDS, $Mo_{K\alpha}$ radiation, $2\Theta_{max} = 48.18^\circ$ (imaging plate distance 80 mm); of 20081 total reflections, 10171 were independent ($R_{int.} = 0.052$); $R_1 = 0.046$ and $wR = 0.123$ for 620 parameters and 10168 reflections with $I > 2\sigma(I)$; max./min. residual electron density 1.57/ – 1.32 e Å^{-3}. **2**: crystal dimensions $0.24 \times 0.34 \times 0.46$ mm^3, lattice constants at 193 K: $a = 14.839(3)$, $b = 22.012(4)$, $c = 14.910(3)$ Å, $\beta = 108.97(3)^\circ$, $V = 4605(2)$ Å^3; space group $P2_1$ (no. 4), $Z = 2$, $\rho_{calcd} = 1.645$ g cm^{-3}, $\mu = 2.631$ mm^{-1}; data collection: STOE IPDS, $Mo_{K\alpha}$ radiation, $2\Theta_{max} = 48.18^\circ$ (imaging plate distance 80 mm); of 26456 total reflections, 13778 were independent ($R_{int.} = 0.051$); $R_1 = 0.078$ and $wR = 0.209$ for 766 parameters and 13321 reflections with $I > 2\sigma(I)$; max./min. residual electron density 1.86/ – 1.05 e Å^{-3}. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-102741 (**1**) and CCDC-102742 (**2**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44)1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

[21] R. Burns, J. D. Corbett, *Inorg. Chem.* **1985**, *24*, 1489.

[22] KSn contains discrete, tetrahedral Sn_4^{4-} units: I. F. Hewaidy, E. Busmann, W. Klemm, *Z. Anorg. Allg. Chem.* **1964**, *328*, 283.

[23] The sum of van der Waals radii is 3.30 Å: A. Bondi, *J. Phys. Chem.* **1964**, *68*, 441.

[24] K. Wade, *Adv. Inorg. Chem. Radiochem.* **1976**, *18*, 1.

[25] J. D. Corbett, P. A. Edwards, *J. Am. Chem. Soc.* **1977**, *99*, 3313.

[26] S. C. Critchlow, J. D. Corbett, *J. Am. Chem. Soc* **1983**, *105*, 5715.

[27] M. E. O'Neill, K. Wade, *Polyhedron* **1983**, *2*, 963; T. F. Fässler in *Metal Clusters in Chemistry* (Eds.: P. Braunstein, L. A. Oro, P. R. Raithby), WILEY-VCH, submitted.

[28] A cluster with a similar structure is also observed in $[Na_4(en)_7]Sn_9$[16] and for the isoelectronic cation Bi_9^{5+}.[29]

[29] A. Hershaft, J. D. Corbett, *Inorg. Chem.* **1963**, *2*, 979; R. M. Friedman, J. D. Corbett, *Inorg. Chem.* **1973**, *12*, 1134.

[30] Distances [Å] in **1**: Sn1–Sn2 3.355(2), Sn5–Sn6 3.412(2), Sn7–Sn8 3.722(2), Sn1–Sn5 3.116(1), Sn1–Sn7 3.014(1), Sn5–Sn7 2.951(1), Sn2–Sn6 3.081(1), Sn2–Sn8 2.993(1), Sn6–Sn8 3.019(1), Sn1–Sn3 2.915(1), Sn2–Sn3 2.985(1), Sn7–Sn3 2.939(1), Sn8–Sn3 2.944(1), Sn1–Sn4 2.925(1), Sn2–Sn4 2.975(1), Sn5–Sn4 2.932(2), Sn6–Sn4 2.940(1), Sn5–Sn9 2.952(1), Sn6–Sn9 2.938(2) Sn7–Sn9 2.942(1), Sn8–Sn9 2.906(1); K1–Sn2,Sn4,Sn6 4.438(2), 3.544(2), 4.074(3); K2–Sn2,Sn3,Sn8 4.353(2), 3.535(2), 4.072(2); K3–Sn5,Sn7,Sn9 4.039(3), 4.021(2), 3.542(3). Sn–Sn distances [Å] in **2** (same order as for **1**): 3.335(2), 3.450(2), 3.531(2), 3.045(2), 3.010(2), 2.990(2), 3.038(2), 3.030(2), 2.987(2), 2.974(2), 2.959(2), 2.930(2), 2.923(2), 2.958(2), 2.980(2), 2.930(2), 2.928(2), 2.942(2), 2.984(2), 2.982(2), 2.941(2).

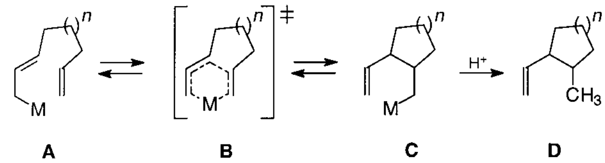
[31] For the controversial discussion on the charge allocation to the nonequivalent anions in $[K([2.2.2]crypt)]_6Ge_9Ge_9$, see C. H. E. Belin, J. D. Corbett, A. Cisar, *J. Am. Chem. Soc.* **1977**, *99*, 7163; T. F. Fässler, U. Schütz, *Inorg. Chem.*, in press; and references [10, 18].

Chiral Induction by Elimination-Coupled Lithium–Ene Reaction: Synthesis of (+)-(3*R*,4*R*)-1,2-Dihydromultifidene**

Alexander Deiters and Dieter Hoppe*

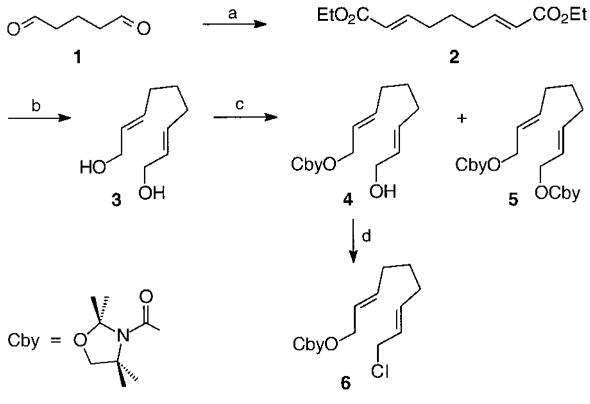
Dedicated to Professor Bernt Krebs on the occasion of his 60th birthday

Intramolecular metallo–ene reactions are efficient methods for the construction of substituted ring systems.[1] As the Type 1 metallo–ene reaction illustrates, $2,(\omega-1)$-alkadienylmetal compounds **A** cyclize via the cyclic conjugated transition state **B** to form a (2-vinylcycloalkyl)methylmetal intermediate **C**, which is then protonated to give cycloalkanes **D** (Scheme 1). One problem is the poorly developed equilibrium state. Moreover, the previously described metallo–ene reaction where M = Li[2] and M = MgHal[3] give racemic products.[1, 4]



Scheme 1. Metallo–ene reaction of Type 1 ($n = 1, 2$; M = Li, MgHal).

We report here the first asymmetric lithium–ene reaction, the basis of which is the enantioselective (–)-sparteine-induced deprotonation of 2-alkenyl carbamates.[5, 6] We selected (2*E*,7*E*)-9-chloronona-2,7-dienyl carbamate (**6**)[7] as substrate in order to compensate for the unfavorable equilibrium state of the cyclization with an irreversible elimination step.[8] Compound **6** was obtained from pentanedial (**1**) by standard methods (Scheme 2). Treatment of **6** (E:Z = 98:2)

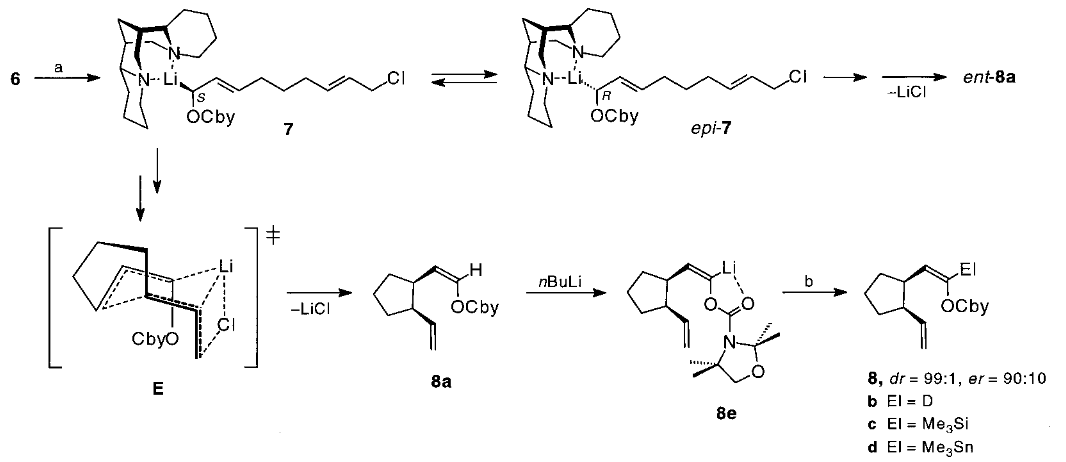


Scheme 2. Synthesis of **6**. a) $EtO_2CCH_2PO(OEt)_2$ (2.2 equiv), K_2CO_3 (5.0 equiv), H_2O, 35%;[9a] b) DIBAH (5.0 equiv), $PhCH_3$, 92%; c) NaH (1.1 equiv), CbyCl (1.0 equiv), THF, 19% **3**, 39% **4**, and 22% **5**;[9b] d) LiCl (5.0 equiv), *n*BuLi (1.0 equiv), CH_3SO_2Cl (1.1 equiv), THF, 90%.[26] DIBAH = diisobutylaluminum hydride.

---

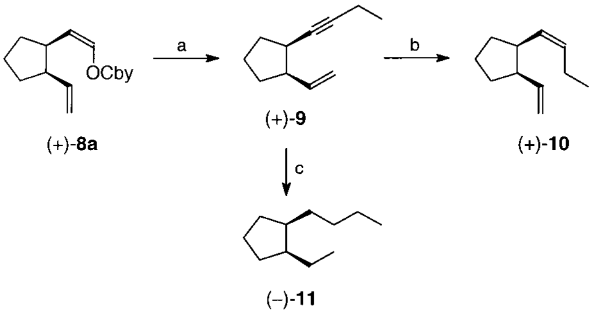
[*] Prof. Dr. D. Hoppe, Dipl.-Chem. A. Deiters
Organisch-chemisches Institut der Universität
Corrensstrasse 40, D-48149 Münster (Germany)
Fax: (+49)251-8339772

[**] This work was supported by the Fonds der Chemischen Industrie and the Studienstiftung des deutschen Volkes. We thank Prof. Dr. E.-U. Würthwein and Dr. C. Mück-Lichtenfeld for the semi-empirical calculations on the reaction pathway.

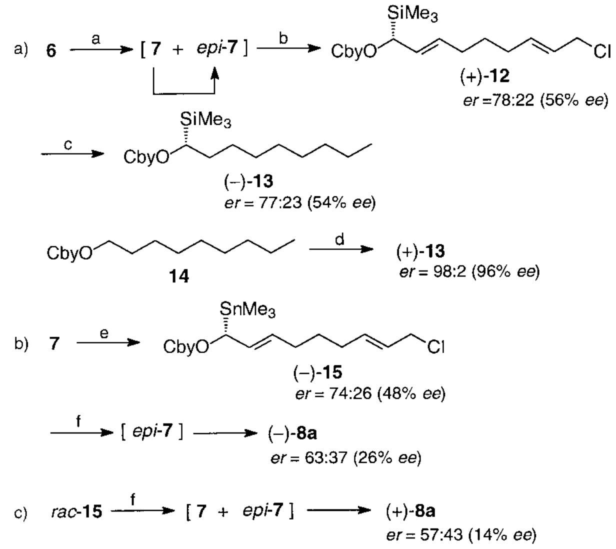


Scheme 3. Enantioselective lithium–ene reaction. a) *n*BuLi/(−)-sparteine (2.2 equiv), $PhCH_3$, −90 °C; b) ElX (5 equiv); **8a**: MeOH, 90%, *dr* = 99:1, *er* = 90:10 (80% *ee*); **8b**: MeOD, 90%; **8c**: Me_3SiCl, 84%; **8d**: Me_3SnCl, 75%.[26]

with 2.2 equivalents of *n*-butyllithium/(−)-sparteine in toluene at −90 °C and subsequent hydrolysis of the reaction mixture gave the cyclopentane (+)-**8a** in 90% yield with a diastereomeric ratio (*dr*) *cis*:*trans* of over 99:1 and an enantiomeric ratio (*er*) of 90:10 (80% *ee*; Scheme 3). At −78 °C (+)-**8a** was again obtained in 90%, but with only 66% *ee* (*er* = 83:17).[10–12] Reaction product **8a** is once more deprotonated under the reaction conditions,[13] and the intermediate vinyllithium compound **8e** can be captured by protons or other electrophiles with retention of the double bond geometry to yield **8b–d**. The absolute configuration (1*R*,2*R*) of (+)-**8a** was confirmed by conversion into the known (+)-(3*R*,4*R*)-1,2-dihydromultifidene (+)-**10** and the perhydro product (−)-**11** (Scheme 4).[14, 15] The key step is a Fritsch–Buttenberg–Wiechell rearrangement of the lithiated vinyl carbamate by the Kocienski method.[13]



Scheme 4. Stereochemical correlation of (+)-**8a**. a) 1. *n*BuLi/TMEDA (3.0 equiv), THF, −78 °C, 1.5 h; 2. 20 °C, 2 h; 3. 0 °C, EtI (4.0 equiv); 4. 40 °C, 12 h, 65%; b) H_2, 30 wt% Lindlar catalyst, quinoline, C_5H_{12}, 76%; c) H_2, 50 wt% Pt/C, C_5H_{12}, 82%.[26] TMEDA = *N*,*N*,*N*′,*N*′-tetramethylethylenediamine.



Scheme 5. Studies on the mechanism of the lithium–ene reaction. a) *n*BuLi/(−)-sparteine (1.5 equiv), $PhCH_3$, −78 °C; b) Me_3SiCl (1.5 equiv, present in (a)), 70%; c) H_2, 200 wt% Pd/C, NaOAc (10.0 equiv), MeOH, 90%; d) *s*BuLi/(−)-sparteine (1.5 equiv), Me_3SiCl (3.0 equiv), Et_2O, −78 °C, 80%; e) Me_3SnCl (2.5 equiv), 16% **15**, 7% **8d**, 53% **8a**, and 18% **6**; f) *n*BuLi/(−)-sparteine (2.0 equiv), $PhCH_3$, −78 °C, 100%.[26]

The details of the mechanism and the topology of the transition state which leads to (+)-**8** were elicited by further experiments (Scheme 5):

a) Deprotonation of **6** with *n*-butyllithium/(−)-sparteine in the presence of Me_3SiCl gave the silane (+)-(*R*)-**12**[16] with *er* = 78:22 (56% *ee*). The *R* configuration was confirmed by correlation with (+)-(*S*)-**13**, which was obtained by the (−)-sparteine method from the saturated alkyl carbamate **14**.[17] Since silylation and stannylation of lithiated allyl carbamates generally take place with inversion of configuration,[18] the predominant lithium compound **7** was assigned the 1*S* configuration.
b) The configuration of **7** was inverted to *epi*-**7** by trimethylstannylation to the tin compound (−)-(*R*)-**15** (49% *ee*)[18] and lithiodestannylation with *n*-butyllithium/(−)-sparteine.[19] In this way, (−)-(1*S*,2*S*)-**8a** (*er* = 63:37, 26% *ee*) was prepared in quantitative yield.
c) Starting from *rac*-**15**, (+)-**8a** (*er* = 57:43, 14% *ee*) was obtained in quantitative yield.

According to the stereochemical information that is "conserved" in the product (1*R*,2*R*; *cis* arrangement of the side chains, *Z* configuration of the vinyl carbamate unit),[20] the transition state which leads to the main product (+)-**8** is assigned the structure **E** (see Scheme 3).[21] It is probable that no discrete lithium intermediate is formed; instead *β*-elimination of lithium chloride occurs concurrently with its formation.[23] Experiments (b) and (c), illustrated in Scheme 5, suggest a comparably slow epimerization of **7** into *epi*-**7**, when the (−)-sparteine complex **7** cyclizes somewhat more rapidly than *epi*-**7**.[24] Overall, chiral induction by an elimination-coupled lithium–ene reaction offers a new and potentially useful route to enantiomerically enriched carbocycles.[25]

Experimental Section

Compound **6** (100 mg, 0.30 mmol) and (−)-sparteine (155 mg, 0.66 mmol) were dissolved in toluene (4 mL) under argon. After the solution had been cooled to −90°C, a 1.6 M hexane solution of *n*-butyllithium (0.41 mL, 0.66 mmol) was added slowly, and the solution was stirred at this temperature for 2 h. Methanol (1 mL) and saturated NH_4Cl solution (1 mL) were then added, and the reaction mixture was warmed to room temperature. The crude product was isolated by usual procedures and purified by column chromatography with Et_2O/pentane (1/5) to yield **8a** as a colorless oil (79 mg, 90%, 80% ee).[11, 26]

Received July 8, 1998 [Z12112]
German version: *Angew. Chem.* **1999**, *111*, 529–532

Keywords: asymmetric synthesis · carbocycles · ene reactions · metalations

---

[1] Review: W. Oppolzer, *Angew. Chem.* **1989**, *101*, 39–53; *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 38–52.

[2] A. D. Josey, *J. Org. Chem.* **1974**, *39*, 139–145.

[3] H. Felkin, J. D. Umpleby, E. Hagaman, E. Wenkert, *Tetrahedron Lett.* **1972**, 2285–2288.

[4] A single example of a Pd–ene reaction induced by a chiral ligand has been described (47% *ee*, *cis*:*trans* = 87:13): W. Oppolzer, D. L. Kuo, M. W. Hutzinger, R. Léger, J.-O. Durand, C. Leslie, *Tetrahedron Lett.* **1997**, *38*, 6213–6216.

[5] a) O. Zschage, D. Hoppe, *Angew. Chem.* **1989**, *101*, 67–69; *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 67–69; b) O. Zschage, D. Hoppe, *Tetrahedron* **1992**, *48*, 8389–8392; c) H. Paulsen, C. Graeve, D. Hoppe, *Synthesis* **1996**, 141–144.

[6] Reviews: a) D. Hoppe, T. Hense, *Angew. Chem.* **1997**, *109*, 2376–2410; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2282–2316; b) P. Beak, A. Basu, D. J. Gallagher, Y. S. Park, S. Thayumanavan, *Acc. Chem. Res.* **1996**, *29*, 552–560.

[7] The *E* geometry of the double bonds of the diester **2** and the dicarbamate **5** were confirmed by the ^{1}H NMR coupling constants of the alkene protons (15.7 and 15.2 Hz)

[8] Previous attempts to cyclize simple 2,7-alkadienyl carbamates (**6**, H or C_6H_5 for CH_2Cl) by lithiation with *n*BuLi/TMEDA were unsuccessful. Only the dicarbamate **5** gave *rac*-**8a** in 10% yield.[10]

[9] a) J. Villieras, M. Raumbaud, M. Graff, *Synth. Commun.* **1986**, *16*, 149–156; b) F. Hintze, D. Hoppe, *Synthesis* **1992**, 1216–1218.

[10] A. Deiters, Diplomarbeit, Universität Münster, **1998**.

[11] **8a**: $[\alpha]_D^{20} = +50.7$ ($c = 0.34$ in $CHCl_3$) for *er* = 90:10 (80% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.21–1.65$ (m, 14H; CH_2, CH_3(Cby)), 1.76–1.85 (m, 4H; CH_2), 2.52–2.68 (m, 1H; CH), 2.97–3.15 (m, 1H; CH), 3.77 (s, 2H; CH_2(Cby)), 4.70 (dd, $^3J = 6.5$, 9.6 Hz, 1H; C*H*=CH–O), 4.95–5.03 (m, 2H; CH=C*H*$_2$), 5.72–5.84 (m, 1H; C*H*=CH_2), 6.96 (d, 1H; CH=C*H*–O). The *cis* arrangement of the alkyl groups in **8a**, **9**, and **10** was confirmed by NOE experiments. The *Z* geometry of the enol carbamate group in **8a** is derived from ^{1}H NMR coupling constants of the alkene protons at 6.5 Hz. The enantiomeric ratio was determined by gas chromatography on a chiral stationary phase (Beta-Dex 120, Supelco, USA).

[12] Compound *rac*-**8a** is also obtained in 90% yield with *n*BuLi/TMEDA. At least two equivalents of base are required because **8a** is deprotonated to **8e** under the reaction conditions: B. Peschke, Dissertation, Kiel University, **1991**; S. Sengupta, V. Snieckus, *J. Org. Chem.* **1990**, *55*, 5680–5683; H. Paulsen, D. Hoppe, *Tetrahedron* **1992**, *48*, 5667–5670 and reference [13].

[13] P. Kocienski, N. J. Dixon, *Synlett* **1989**, 52–54; P. Kocienski, C. Barber, *Pure Appl. Chem.* **1990**, *62*, 1933–1940.

[14] W. Boland, K. Mertes, L. Jaenicke, D. G. Müller, E. Fölster, *Helv. Chim. Acta* **1983**, *66*, 1905–1913.

[15] The optical rotations corrected to 100% *ee* [(+)-**10**: $[\alpha]_{578}^{20} = +52.0$ ($c = 0.39$ in pentane); (−)-**11**: $[\alpha]_{578}^{20} = -3.5$ ($c = 2.84$ in pentane)] agree well with the literature values [(+)-**10**: $[\alpha]_{578}^{20} = +55.8$ ($c = 2.56$ in pentane); (−)-**11**: $[\alpha]_{578}^{20} = -7.1$ ($c = 0.64$ in pentane)].[14]

[16] The enantiomeric excesses of the silanes and stannanes (**12**, **13** and **15**) were determined by ^{1}H NMR shift experiments with [Eu(hfc)$_3$] (hfc = 3-(heptafluoropropylhydroxymethylene)-D-camphorate)). The rotations were: (+)-**12**: $[\alpha]_D^{20} = +11.7$ ($c = 0.73$ in $CHCl_3$); (+)-**13**: $[\alpha]_D^{20} = +7.1$ ($c = 2.08$ in $CHCl_3$); (−)-**13**: $[\alpha]_D^{20} = -3.9$ ($c = 2.55$ in $CHCl_3$); (−)-**15**: $[\alpha]_D^{20} = -9.5$ ($c = 0.40$ in $CHCl_3$).

[17] D. Hoppe, M. Paetow, F. Hintze, *Angew. Chem.* **1993**, *105*, 430–432; *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 394–396.

[18] For precedences on inversion of configuration during silylation and stannylation reactions with allyllithium-(−)-sparteine complexes, see K. Behrens, *Dissertation*, Münster University **1997** and reference [5c].

[19] For inversion of configuration of chiral benzyllithium compounds during stannylation (inversion) and lithium destannylation (retention), see A. Carstens, D. Hoppe, *Tetrahedron* **1994**, *50*, 6097–6108; G. A. Weisenburger, P. Beak, *J. Am. Chem. Soc.* **1996**, *118*, 12218–12219 and reference [18].

[20] The carbamoyloxy group in γ-monosubstituted lithiated allyl carbamates (e.g., **7**) preferentially adopts the *endo* configuration, which leads to a 1*Z* double bond in the products (e.g., **8a**): D. Hoppe, R. Hanko, A. Brönneke, F. Lichtenberg, E. von Hülsen, *Chem. Ber.* **1985**, *118*, 2822–2851.

[21] A previously unexplained discrepancy exists here: The transition state **E** requires (1*R*)-**7** as substrate, whereas the capture experiments suggest an excess of (1*S*)-**7**.[22] We tentatively speculate that the cyclization step is preceded by a lithium–lithium exchange with inversion of configuration, in which the Li^+/(−)-sparteine is replaced by a less sterically congested lithium cation, which in turn leads to a higher rate of reaction. Control experiments with the addition of lithium chloride or lithium butoxide lead to an enantiomeric enrichment factor of up to 1.2; these results agree with the proposed reaction pathway.

[22] We thank one of the referees for stimulating suggestions.

[23] The results of PM3 calculations suggest a reaction pathway with a lowest energy barrier in which the lithium atom comes into contact with C-8 and the chlorine atom. Accordingly, the reaction commences as a lithium–ene reaction which then merges into the reaction path of a *syn*-S_N' reaction: E.-U. Würthwein, C. Mück-Lichtenfeld, unpublished results.

[24] Experiments (b) and (c) in Scheme 5 gave the cyclopentanes (+)-**8a** and (−)-**8a** in quantitative yields. If the lithium intermediates **7** and *epi*-**7** were of unrestricted configurational stability, and if both complexes were to cyclize at the same rate, the same enantiomeric ratio would be expected in the product **8a** as in respective educts **15** (74:26 and 50:50, respectively). In both cases a shift in favor of the product (+)-**8a** would be recorded; that is, **7** is involved to a greater extent in product formation than *epi*-**7**.

[25] For the synthesis of enantiomer-enriched cyclopentanols by (−)-Sparteine-induced intramolecular carbolithiation, see M. J. Woltering, R. Fröhlich, D. Hoppe, *Angew. Chem.* **1997**, *109*, 1804–1805; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1764–1765; M. Oestreich, R. Fröhlich, D. Hoppe, *Tetrahedron Lett.* **1998**, *39*, 1745–1748.

[26] All new compounds gave satisfactory elemental analyses (C,H,N; ±0.4).