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Enantioselective, (−)-sparteine-mediated deprotonation of geranyl and neryl *N*,*N*-diisopropylcarbamate: configurational stability of the intermediate lithium compounds

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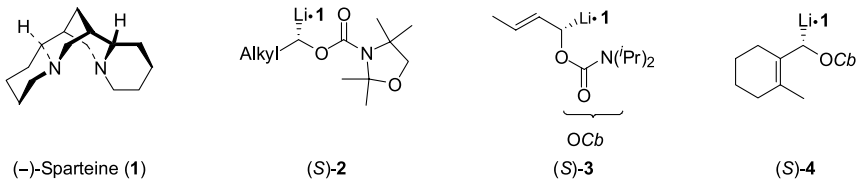
Abstract—(*E*)/(*Z*)-Isomeric allylic carbamate esters were deprotonated by *n*-butyllithium/(−)-sparteine in toluene. Trapping experiments with chlorotrimethylsilane afforded the α-substitution products, with (*R*)-configuration, revealing that the *pro-S* proton is removed predominantly to form the corresponding (*S*)-lithium·(−)-sparteine derivatives; $k_S/k_R > 15{:}1$ and $>7{:}1$, respectively. A slow (*S*)→(*R*)-epimerization occurs at −78 °C ($T_{1/2} > 60$ min). The allylic double bond is stable to (*Z*)–(*E*) isomerization under these conditions.

1. Introduction

Chiral carbanionic species play an important role in modern stereoselective synthesis.[1] In particular, the (−)-sparteine-mediated deprotonation of suitable substrates provides an efficient, rapid access to enantioenriched lithium intermediates.[2] As we found several years ago, *O*-alkyl-,[3] *O*-2-alkenyl-,[4] *O*-benzyl-,[5] and *O*-2-alkynyl[6] carbamates react with *n*-butyl- or *s*-butyllithium/(−)-sparteine (**1**) with preferential abstraction of the *pro-S*-proton (Fig. 1). The method was extended by Beak et al. to several *N*-carbamates[7] and benzylic compounds.[2b] The lithium complexes (*S*)-**2**, formed from alkyl carbamates at −78 °C with selectivities (*S*)/(*R*) between 50 to 100:1, are configurationally stable below −70 °C and react with all electrophiles with complete retention of the configuration.[3] However, the epimeric ion pairs (*S*) and (*R*)-**3** of the lithiated crotyl carbamate turned out to be configurationally unstable even in pentane solution at −78 °C. In the presence of cyclohexane, a selective crystallization of complex (*S*)-**3** takes place. As a consequence of the dynamic thermodynamic resolution[8] nearly all of the material is converted into (*S*)-**3**.[4] It can be transformed stereospecifically via metal exchange with complete stereoinversion to the corresponding tris(isopropoxy)-titanium intermediate. On the other hand, the trisubstituted cyclic allyllithium derivative (*S*)-**4** undergoes epimerization only very slowly ($T_{1/2} > 10$ h at −78 °C), rendering (*S*)-**4** and related lithium intermediates synthetically very useful.[9]

Although the mechanism of the epimerization is not known yet, it became clear that a high degree of substitution at the allylic moiety and, usually, a secondary carbanionic center support high configurational stability. Further information on the configurational behaviour of the lithiated 2-alkenyl carbamates is required. Unfortunately, the system is not suitable for NMR investigation at low temperature, although these (−)-sparteine complexes are monomeric even in the



(–)-Sparteine (**1**) (*S*)-**2** (*S*)-**3** (*S*)-**4**

Figure 1.

Keywords: (−)-Sparteine; Allyllithium; Asymmetric deprotonation; Stereoselectivity.
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† X-ray structure analysis.

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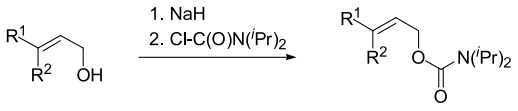
solid (for a representative X-ray structure analysis see Ref. 10), line broadenings and splittings of the *N*,*N*-diisopropylcarbamoyl group, due to slow rotation and diastereotopicity, hamper NMR investigation severely.[11]

We have now studied the *E*/*Z*-isomers geranyl- and neryl *N*,*N*-diisopropylcarbamate [(*E*)- and (*Z*)-**6**], which both were prepared by our standard procedure from the pure alcohols (*E*)- and (*Z*)-**5** (Scheme 1), by applying lithiation and trapping experiments. The results are presented herein.



(*E*)-**5**, (*E*)-**6**: R^1=$(CH_3)_2CCH(CH_2)_2$-, R^2=CH_3, yield: 76%
(*Z*)-**5**, (*Z*)-**6**: R^1=CH_3, R^2=$(CH_3)_2CCH(CH_2)_2$-, yield: 76%

Scheme 1.

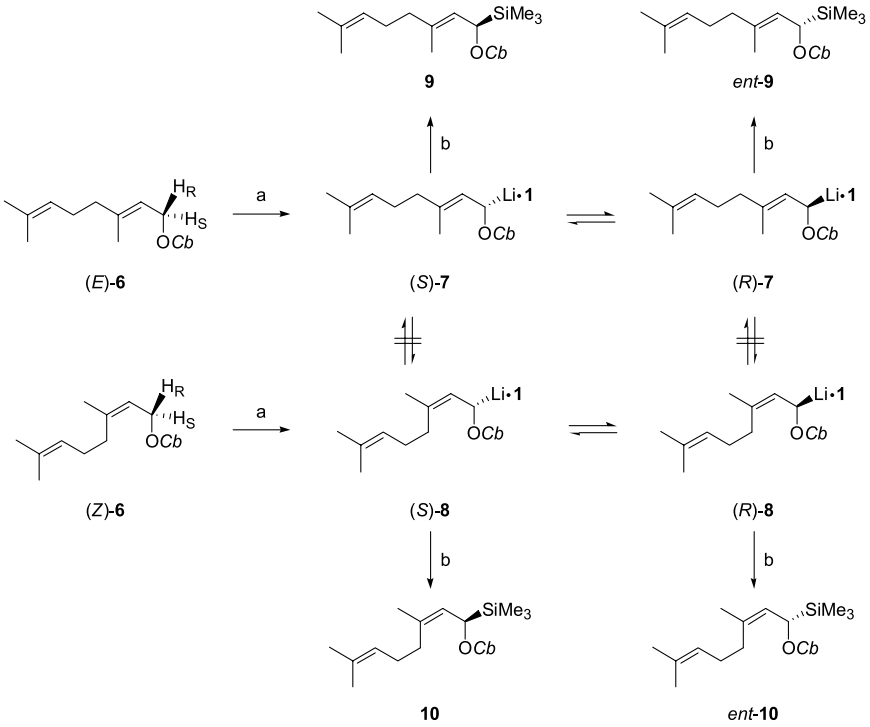
2. Results and discussion

The following questions were addressed (Scheme 2):

(1) What is the direction and magnitude of enantiotopos-differentiating deprotonation of (*E*)- and (*Z*)-**6** in the presence of (−)-sparteine?
(2) How rapidly do the intermediate diastereomer pairs (*R*)- and (*S*)-**7**, (*R*)- and (*S*)-**8** epimerize under the reaction conditions?
(3) Is there an interconversion of **7** and **8** occurring by *E*–*Z* isomerization of the allylic double bond as we have observed for an α-silyl-substituted derivative?[12]

For question (1) we used an in situ experiment[13] by deprotonating either (*E*)- or (*Z*)-**6** in toluene at −78 °C with *n*-butyllithium/(−)-sparteine (**1**) (each 1.5 equiv) in the presence of excess chlorotrimethylsilane (entry 1 and 6, Table 1). The silylation of the carbanionic intermediates (*S*)/(*R*)-**7** or **8** is highly α-selective and proceeds with strict inversion of the configuration[11a,14] producing the α-silyl-alkenyl carbamates (*S*)/(*R*)-**9** and (*S*)/(*R*)-**10**, respectively. The ratios of enantiomers were determined by ^{1}H NMR shift experiments in the presence of (+)-Eu(hfc)$_3$. The *R*/*S*-ratio expresses the minimum of kinetically controlled enantiotopic differentiation in the deprotonation step. In principle, errors might arise by a renewed deprotonation of silanes **9** or **10**. These could be excluded by control experiments: Firstly, *n*-butyllithium/**1** is not able to deprotonate **9** and **10** under the reaction condition. Secondly, the lithium compounds, derived from silanes **9** and **10**, undergo only very slow epimerization. Enantiomeric ratios up to 93.5:6.5 (87% ee) for (*S*)-**9**, starting from (*E*)-**6**, and up to 87.5:12.5 (75% ee) for (*S*)-**10** from (*Z*)-**6** could be obtained. Using pentane as a solvent under the same conditions (entry 1 and 6, Table 2) these selectivities are diminished: 72% ee from (*E*)-**6** and 61% ee from (*Z*)-**6**.

For finding an answer to question (2), the reaction mixture was allowed defined times for deprotonation before the trapping agent Me_3SiCl was added. Whereas the yields increased (due to a higher degree of deprotonation), the er decreased, giving evidence for configurational lability of the lithium compounds in toluene at −78 °C. After 30 min, the er of (*R*)/(*S*)-**9** was 84.5:15.5 (69% ee, Table 1, entry 4), and after 240 min (entry 5), the ratio 55.5:44.5 (11% ee) presumably closely reflects the thermodynamically determined ratio of the epimers (*S*)- and (*R*)-**7**. Applying a lower



Scheme 2. Reagents: (a) **1**, *n*-BuLi, −78 °C. (b) $ClSiMe_3$; MeOH.

Table 1. Enantioselective deprotonation and silylation of (*E*)- and (*Z*)-**6** in toluene

Entry	Starting material	Conditions	Time (min)	Product(s)	Yield (%)	Ratio (*R*)/(*S*)	% ee
1	(*E*)-**6**	In situ[a], −78 °C	(360)[b]	**9**	76	88.5:11.5	77
2	(*E*)-**6**	In situ[a], −78 °C	(90)[b]	**9**	37	93.5:6.5	87
3	(*E*)-**6**	−78 °C	15	**9**	47	86.5:13.5	73
4	(*E*)-**6**	−78 °C	30	**9**	59	84.5:15.5	69
5	(*E*)-**6**	−78 °C	240	**9**	85	55.5:44.5	11
6	(*E*)-**6**	In situ[a], −95 °C	(90)[b]	**9**	30	87.5:12.5	75
7	(*Z*)-**6**	In situ[a], −78 °C	(180)[b]	**10**	43	87.5:12.5	75
8	(*Z*)-**6**	−78 °C	15	**10**	75	84.5:15.5	69
9	(*Z*)-**6**	−78 °C	120	**10**	84	72.0:28.0	44
10	(*Z*)-**6**	−78 °C	240	**10**	87	56.0:44.0	12
11	(*Z*)-**6**	−78 °C	360	**10**	87	52.0:48.0	4
12	(*Z*)-**6**	−78 °C	480	**10**	88	50.5:49.5	1
13	(*Z*)-**6**	In situ[a], −95 °C	(90)[b]	**10**	31	90.5:9.5	81

[a] Deprotonation was carried out in the presence of Me_3SiCl.
[b] The reaction time is not identical with the standing time of **7** or **8**.

Table 2. Enantioselective deprotonation and silylation of (*E*)- and (*Z*)-**6** in pentane at −78 °C

Entry	Starting material	Conditions	Product(s)	Yield (%)	Ratio (*R*)/(*S*)	% ee
1	(*E*)-**6**	In situ[a], (90)[b]	**9**	49	86.0:14.0	72
2	(*E*)-**6**	5 min	**9**	52	87.0:13.0	74
3	(*E*)-**6**	15 min	**9**	59	94.5:5.5	89[c]
4	(*E*)-**6**	30 min	**9**	54	79.5:20.5	59
5	(*E*)-**6**	60 min	**9**	61	78.0:22.0	56
6	(*Z*)-**6**	In situ[a], (90)[b]	**10**	44	80.5:19.5	61
7	(*Z*)-**6**	5 min	**10**	66	80.0:20.0	60
8	(*Z*)-**6**	15 min	**10**	70	75.0:25.0	50
9	(*Z*)-**6**	60 min	**10**	79	68.0:32.0	36
10	(*Z*)-**6**	120 min	**10**	81	63.0:37.0	26

[a] *n*-Butyllithium was added to a solution of **6** and **1**.
[b] Reaction time does not represent the standing time of the lithium compound.
[c] A crystallization was observed which disappeared after 30 min.

temperature −95 °C (entry 6), both rates of deprotonation and epimerization are diminished.

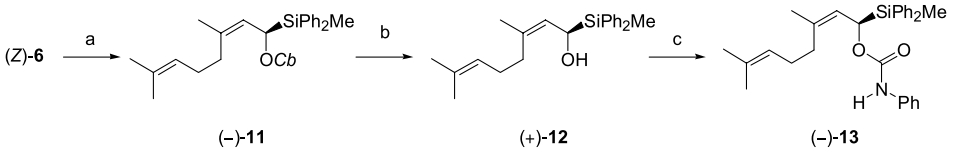
The situation is similar for the experiments with (*Z*)-**6** (entries 7–13), but the level of kinetically controlled stereoselection (entry 7) of 87.5:12.5 (75% ee) is somewhat lower. A kinetic resolution during the silylation step could be excluded by the following experiment: neryl carbamate (*Z*)-**6** was deprotonated in toluene by *sec*-butyllithium at −78 °C in the absence of any diamine, and later, (−)-sparteine (1.5 equiv) was added before the chlorosilane was introduced. The enantiomeric ratio (*R*/*S*) of silane **10** was 51:49 (59% yield). This result demonstrates that only a very slow interconversion of the epimers **8** and *epi*-**8** takes place.

A surprising result applying (*E*)-**6** was obtained, when the same series of experiments were carried out in *n*-pentane (Table 2). The er of (*S*)-**9** (94.5:5.5, 89% ee) after 15 min reaction time (entry 3) exceeded the kinetically controlled ratio (entry 1), 86:14 (72% ee); but it dropped again after prolonged reaction times (entry 4 and 5). After 15 min, a precipitate was observed in the reaction mixture, which subsequently dissolved again. We have no sound explanation for the phenomenon. Certainly, a dynamic thermodynamic resolution of the diastereomers occurred,[8] but the nature of the precipitating associate remains unknown.[15]

Concerning the question (3) of double bond (*Z*)–(*E*) isomerization in the lithium compounds **7** and **8**, we carefully investigated the reaction mixture by GC. In no case, more than 2% of the opposite silane **9** or **10**, respectively, was found. So, at −78 °C, the 2,3-double bond is perfectly stable against isomerization. This also turned out for the corresponding lithium–TMEDA complexes in toluene, pentane, and ether. Usually, substituted allyllithium compounds undergo facile isomerization of the 2,3-double bond.[16,17] Here again, the five-membered chelate complex, accomplishing a strong contact of the lithium cation with the α-carbon atom, causes an improved configurational stability both of the stereogenic α-carbon atom and the adjacent double bond.

2.1. Determination of the absolute configuration

All attempts to convert the optically active silanes (+)-**9** or (−)-**10** into crystalline derivates, suitable for X-ray analysis with anomalous dispersion, failed. Finally, the neryl carbamate (*Z*)-**6** was transformed with *n*-butyllithium/**1** and chloromethyldiphenylsilane to (−)-**11** (Scheme 3), followed by DIBAL-H-mediated decarbamoylation,[18] and, subsequently, the α-silyl alcohol (+)-**12** was added to phenyl isocyanate to furnish the crystalline *N*-phenylurethane (−)-**13**. The X-ray structure analysis with anomalous dispersion of (−)-**13** (Fig. 2) clearly shows the (*R*)-configuration of the major enantiomer.[19]



Scheme 3. Reagents: (a) $ClSiPh_2Me$, **1**, *n*-BuLi (in situ procedure); 70%. (b) DIBAL-H in hexane (8 equiv), THF, 6 h, rt, 78%. (*c*) PhN=C=O, toluene, pyridine, 70 °C, 4d, 77%.

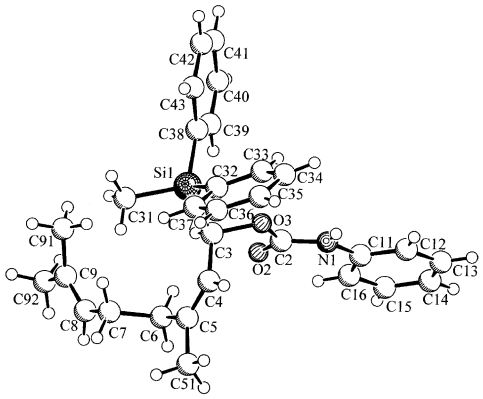
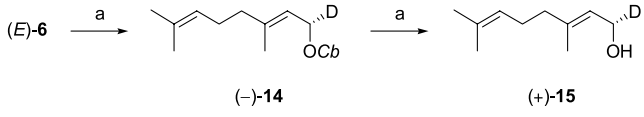


Figure 2. X-ray crystal structure analysis of (−)-**13**.[19]

Since all reported silylations of lithiated allyl carbamates[14,2c] are known to proceed with inversion of the configuration, the major epimer of lithium compounds **8** is likely to have the (*S*) configuration.

The similar reaction sequence applied to (*E*)-**6** did not lead to crystalline urethanes. However, (*S*)-1D-geraniol [(+)-**15**] (Scheme 4) is a known compound.[20,21] Hence, (*E*)-**6b** was deprotonated by means of *n*-butyllithium/(−)-sparteine (Scheme 4), and addition of MeOD yielded the α-deuterated carbamate (−)-**14**, followed by reductive cleavage with DIBAL-H reduction to form (*S*)-1D-geraniol (+)-**15**.[18] The specific rotation of the sample ($[\alpha]_D^{20} = +0.97$, $c = 1.75$ in cyclopentane) matches well with the reported data +0.44 ($c = 1.23$)[21] and +1.38 ($c = 1.70$).[20] Since all known protonation reactions of lithiated carbamates proceed with retention, it is very likely that the major intermediate of **7** has the (*S*)-configuration.



Scheme 4. Reagents: (a) *n*-BuLi, **1**; MeOD at −78 °C, 92%. (b) DIBAL-H in hexane (8 equiv), THF, 8 h, rt, 78%.

3. Conclusion

The kinetically controlled deprotonation of geranyl and neryl carbamate (*E*)- and (*Z*)-**6** by *n*-butyllithium/(−)-sparteine removes preferentially the *pro-S* proton, leading to the lithium intermediates (*S*)-**7** and (*S*)-**8**, respectively. These epimerize only slowly and have been employed in synthetically useful enantioselective homoaldol reactions.[22]

4. Experimental

4.1. General

All organometallic reactions were performed under argon at −78 °C with exclusion of air and moisture. Toluene was distilled from sodium benzophenone ketyl before use and THF was dried by refluxing over potassium/benzophenone. Pentane was dried over CaH_2 by refluxing overnight, distilled, and stored over 4 Å molecular sieves under an argon atmosphere; (−)-sparteine and TMEDA were dried over CaH_2 prior to use. LC separations were carried out at 0.5–1.5 bar on silica gel 40–63 μm (Merck, Darmstadt) with petroleum ether (PE)/Et_2O. Melting point: Gallenkamp melting point apparatus MFB-595; value uncorrected. Optical rotations: Perkin-Elmer 341 polarimeter. IR: Nicolet 5 DXC. Infrared spectra were recorded on a Fourier transform spectrometer and data were reported in wave numbers (cm^{-1}). NMR: Bruker ARX 300, AM 360, or AMX 400. All NMR spectra were recorded using $CDCl_3$ as the solvent with reference to residual $CHCl_3$ (^1H at 7.24 ppm and ^{13}C at 77.0 ppm). The ^1H NMR shift experiments were performed by addition of (+)-Eu(hfc)$_3$ to a solution of enantioenriched product (20 mg) in $CDCl_3$ (0.7 mL). Elemental analyses: Elementar Analysensysteme Vario EL III. All new compounds gave satisfactory elemental analyses (C, H ±0.3%).

4.1.1. (*Z*)-3,7-Dimethylocta-2,6-dienyl *N*,*N*-diisopropylcarbamate (*Z*)-6. A solution of nerol (12.6 g, 81.7 mmol) in THF (100 mL) was added to a suspension of NaH (3.9 g, 60% in mineral oil) in THF (40 mL) under an argon atmosphere. After refluxing for 2.5 h, *Cb*Cl (15.5 g, 1.17 equiv) in THF (40 mL) was added dropwise and the mixture was refluxed for 17 h. Cooled with ice (50 g), diluted with diethyl ether (60 mL), quenched with 2 N HCl (15 mL), the reaction mixture was extracted with diethyl ether. The combined organic layers were washed by saturated $NaHCO_3$ and brine, dried over $MgSO_4$. Evaporation of the solvents gave the crude product which was purified by distillation under reduced pressure to yield (*Z*)-**6** (17.5 g, 76%) as colourless oil. bp 112 °C (0.2 torr). IR (film) ν 2973, 2933, 2882, 1703 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 1.20 (d, 12H, *Cb*-CH_3, $^3J_{2',1'} = 6.8$ Hz), 1.60, 1.67, 1.76 (each s, 9H, 3-CH_3, 7-CH_3, 8-H_3), 2.04–2.12 (m, 4H, 4-H_2, 5-H_2), 3.68–3.91 (m, 2H, *Cb*-CH), 4.58 (d, 2H, 1-H, $J = 6.8$ Hz), 5.08–5.14 (m, 1H, 6-H), 5.38 (t, 1H, 2-H, $J = 6.8$ Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 18.0, 26.0, 23.8, 27.1, 32.6, 46.1, 61.6, 120.8, 124.1, 132.3, 141.2, 156.2. ESI-MS (*m*/*e*) 304.4 [M^+ + Na]. $C_{17}H_{31}NO_2$ calcd. C 72.55 H 11.10 N 4.98; found C 72.55 H 11.42 N 4.83.

4.1.2. (*E*)-3,7-Dimethylocta-2,6-dienyl *N*,*N*-diisopropylcarbamate (*E*)-6. The carbamate (*E*)-**6** (18.8 g, 76%) was

obtained from geraniol (12.9 g, 83.8 mmol) and *Cb*Cl (17.5 g, 1.27 equiv) according to the procedure for (*Z*)-**6**. Colourless oil; bp 100 °C (0.1 torr). IR (film) ν 2950, 2910, 1685 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 1.20 (d, 12 H, *Cb*-CH_3, $^3J_{2',1'}=6.9$ Hz), 1.60, 1.67, 1.70 (each s, 9H, 3-CH_3, 7-CH_3, 8-H_3), 2.05–2.13 (m, 4H, 4-H_2, 5-H_2), 3.70–3.91 (m, 2H, *Cb*-CH), 4.60 (d, 2H, 1-H, $J=6.9$ Hz), 5.07–5.13 (m, 1H, 6-H), 5.38 (t, 1H, 2-H, $J=6.9$ Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.5, 19.9, 24.5, 25.2, 38.4, 44.6, 60.3, 118.5, 122.8, 130.4, 139.6, 154.8. ESI-MS (*m/e*) 304.3 [M^++Na]. $C_{17}H_{31}NO_2$ calcd. C 72.55 H 11.10 N 4.98; found C 72.60 H 11.14 N 4.86.

4.2. General procedure for the lithiation and silylation of (*E*)- or (*Z*)-6

n-Butyllithium (1.5 equiv) was added dropwise with vigorous stirring to a solution of allyl carbamate **6** (1.0 mmol) and diamine (1.5 equiv) in toluene (5 mL) at −78 °C under an argon atmosphere. After this had been stirred for a given time (Tables 1 and 2) at the same temperature, the electrophile (1.5 equiv) was added. The mixture was stirred for a given time (see Tables 1 and 2) at −78 °C, after which it was quenched with MeOH (1 mL) at the same temperature, and saturated NH_4Cl solution (10 mL) was added. The aqueous layer was extracted with diethyl ether (3×15 mL). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, and concentrated in vacuum. The residues were purified by silica gel flash column chromatography.

4.3. General procedure for the in situ lithiation and silylation of (*E*)- or (*Z*)-6

To a pre-dried one-necked round bottomed flask under argon atmosphere, was added allyl carbamate **6** (1.0 mmol), (−)-sparteine (1.5 equiv), toluene (5 mL), and the chlorosilane (1.5 equiv). After the reaction mixture was cooled to −78 °C, 1.6 M *n*-BuLi (1.5 equiv) was added slowly while stirring. Stirring was continued for a given time (Tables 1 and 2), the reaction was quenched with methanol (1 mL) at −78 °C. Saturated NH_4Cl solution was added to the reaction mixture. The aqueous layer was extracted with diethyl ether (3×15 mL). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, and then concentrated in vacuum; the crude product was purified by silica gel flash column chromatography.

4.3.1. (1*R*,2*E*)-3,7-Dimethyl-1-(trimethylsilyl)-octa-2,6-dienyl *N*,*N*-diisopropylcarbamate (9).

As described under Section 4.3, the solution of (*E*)-**6** (281 mg, 1.0 mmol), TMSCl (162 mg, 1.5 equiv), and (−)-sparteine (351 mg, 1.5 mmol) was treated with *n*-BuLi (0.94 mL, 1.5 mmol, 1.6 M solution in hexane) at −78 °C. The reaction mixture was stirring for 90 min at −78 °C then quenched with MeOH. The described work-up procedure and a subsequent purification of the crude product by flash chromatography on silica gel (PE/E 20:1) furnished **9** (130 mg, 37%); colourless oil; $[\alpha]_D^{20}=+16.9$ (*c* 0.90 in MeOH); shift experiment: er=93.5:6.5 (87% ee), 17.9 mol % (+)-Eu(hfc)$_3$. R_f (PE/Et_2O, 8:1)=0.47. IR (film) ν 2967, 2931, 2883,1692. ^1H NMR (300 MHz, $CDCl_3$) δ 0.01 (s, 9H, Si–CH_3), 1.20 (d, 12H, *Cb*-CH_3, $^3J_{2',1'}=6.9$ Hz), 1.59, 1.66, 1.68 (each s, 9H, 3-CH_3, 7-CH_3, 8-H_3), 2.00–2.05 (m, 4H, 4-H_2, 5-H_2), 3.69–3.91 (m, 2H, *Cb*-CH), 5.06–5.10 (m, 1H, 1-H), 5.14–5.18 (m, 1H, 6-H), 5.35 (d, 1H, 2-H, $J=10.2$ Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ −3.6, 16.9, 17.6, 21.2, 25.7, 27.1, 39.9, 45.6, 67.4, 122.7, 126.3, 131.3, 135.7, 156.3. EI-MS (*m/e*) 353.2 [M^+], 338.2 [M^+−Me], 216.1 [M^+−*Cb*], 128.1 [Cb^+], 73.0 [$SiMe_3^+$]. $C_{20}H_{39}NO_2Si$ calcd. C 67.93 H 11.12 N 3.96; found C 68.21 H 11.14 N 4.24.

4.3.2. (1*R*,2*Z*)-3,7-Dimethyl-1-(trimethylsilyl)-octa-2,6-dienyl *N*,*N*-diisopropylcarbamate (10).

As described under Section 4.3, the solution of (*Z*)-**6** (281 mg, 1.0 mmol), TMSCl (162 mg, 1.5 mmol), and (−)-sparteine (351 mg, 1.5 mmol) was treated with *n*-BuLi (0.94 mL, 1.5 mmol, 1.6 M solution in hexane) at −78 °C. The reaction mixture was stirred for 180 min at −78 °C, and then quenched with MeOH. The described work-up procedure and a subsequent purification of the crude product by flash chromatography on silica gel (PE/E 15:1) furnished **10** (153 mg, 43%); colourless oil; $[\alpha]_D^{20}=-15.0$ (*c* 0.85 in MeOH); shift experiment: er=87.5:12.5 (75% ee), 23.5 mol % (+)-Eu(hfc)$_3$. R_f (PE/Et_2O, 8:1)=0.66. IR (film) ν 2968, 2933, 2871, 1708. ^1H NMR (400 MHz, $CDCl_3$) δ 0.00 (s, 9H, Si–CH_3), 1.21 (d, 12H, *Cb*-CH_3, $^3J_{2',1'}=6.8$ Hz), 1.61, 1.68, 1.74 (each s, 9H, 3-CH_3, 7-CH_3, 8-H_3), 2.10–2.20 (m, 4H, 4-H_2, 5-H_2), 3.68–3.89 (m, 2H, *Cb*-CH), 5.15–5.20 (m, 2H, 6-H, 1-H), 5.36 (d, 1H, 2-H, $J=11.2$ Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ −3.4, 17.5, 21.1, 23.4, 25.5, 26.7, 32.4, 45.2, 66.8, 124.4, 122.2, 131.2, 137.3, 156.0. ESI-MS (*m/e*) 376.4 [M^++Na], 729.7 [$2M^+$+Na]. $C_{20}H_{39}NO_2Si$ calcd. C 67.93 H 11.12 N 3.96; found C 67.78 H 11.23 N 3.75.

4.3.3. (1*R*,2*Z*)-3,7-Dimethyl-1-(methyldiphenylsilyl)-octa-2,6-dienyl *N*,*N*-diisopropylcarbamate (11).

As described under Section 4.3, the solution of (*Z*)-**6** (562 mg, 2.0 mmol), chloromethyldiphenylsilane (1.420 g, 2.0 equiv), and (−)-sparteine (701 mg, 1.5 mmol) was treated with *n*-BuLi (1.87 mL, 3.0 mmol, 1.6 M solution in hexane) at −78 °C. The reaction mixture was stirred for 210 min at −78 °C, and then quenched with MeOH. The described work-up procedure and a subsequent purification of the crude product by flash chromatography on silica gel (PE/E 15:1) furnished **11** (920 mg, 70%); colourless oil; $[\alpha]_D^{20}=-10.7$ (*c* 1.04 in MeOH). R_f (PE/Et_2O, 8:1)=0.57. Determination of the enantiomeric excess failed by using (+)-Eu(hfc)$_3$ or (+)-Pr(hfc)$_3$ in $CDCl_3$. IR (film) ν 2973, 2934, 2874, 1690. ^1H NMR (300 MHz, $CDCl_3$) δ 0.63 (s, 3H, Si–CH_3), 1.21 (d, 12H, *Cb*-CH_3, $^3J_{2',1'}=6.9$ Hz), 1.51, 1.63, 1.68 (each s, 9H, 3-CH_3, 7-CH_3, 8-H_3), 2.00–2.05 (m, 4H, 4-H_2, 5-H_2), 3.70–3.90 (m, 2H, *Cb*-CH), 5.00–5.05 (m, 1H, 6-H), 5.30 (d, 1H, 1-H, $J=10.8$ Hz), 5.98 (d, 1H, 2-H, $J=10.8$ Hz), 7.18–7.40 (m, 10H, Ph). ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.9, 17.7, 21.0, 23.4, 25.5, 26.3, 32.4, 45.7, 65.9, 121.9, 124.6, 127.6, 127.9, 129.3, 129.9, 131.1, 134.0, 134.3, 155.4. ESI-MS (*m/e*) 537.7 [M^++Na+K], 500.6 [M^++Na]. $C_{30}H_{43}NO_2Si$ calcd. C 75.42 H 9.07 N 2.93; found C 75.24 H 9.12 N 2.91.

4.3.4. (1*R*,2*Z*)-3,7-Dimethyl-1-(methyldiphenylsilyl)-octa-2,6-dien-1-ol (12).

DIBAL-H (1.0 M in hexane, 12.0 mL) was added dropwise to a solution of the carbamate

(*R*)-**11** (826 mg, 1.89 mmol) in anhydrous THF (14 mL) at 0 °C. The reaction mixtures were stirred for 6 h at room temperature. After it had been again cooled to 0 °C, MeOH (20 mL) was added, followed by saturated solution of NH_4Cl (30 mL). The aqueous phase was extracted with Et_2O (3×30 mL). The combined organic layers were washed with saturated $NaHCO_3$ and brine, dried over anhydrous $MgSO_4$. Purification of the crude product by flash chromatography on silica gel (PE/E, 4:1) yielded alcohol (*R*)-**12** (515 mg, 78%) as a colourless liquid. $[\alpha]_D^{20}=+31.5$ (*c* 1.08 in MeOH). R_f (PE/Et_2O, 2:1) =0.43. Attempts to determine the ee failed by using (+)-Eu(hfc)$_3$ or (+)-Pr(hfc)$_3$ in $CDCl_3$. IR (film) ν 3384, 2965, 2929, 2833, 1602. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.52 (s, 3H, Si–CH_3), 1.56, 1.69, 1.73 (each s, 9H, 3-CH_3, 7-CH_3, 8-H_3), 1.96–2.04 (m, 4H, 4-H_2, 5-H_2), 4.66 (d, 1H, 1-H, J= 10.8 Hz), 5.00–5.06 (m, 1H, 6-H), 5.37 (d, 1H, 2-H, J= 10.8 Hz), 7.25–7.40 (m, 10H, Ph). ^{13}C NMR (75 MHz, $CDCl_3$) δ −6.4, 15.2, 17.6, 23.4, 25.6, 49.5, 66.8, 124.0, 125.3, 127.3, 127.7, 128.8, 129.7, 131.9, 134.0. EI-MS (*m*/*e*) 350.3 [M^+], 335.2 [M^+-CH_3], 268.2 [$M^+-C_6H_{10}$], 197.1 [$SiPh_2Me^+$], 121.1 [$SiPhMe^+$], 69.1 [$C_5H_9^+$]. $C_{23}H_{30}OSi$ calcd. C 78.80 H 8.63; found C 78.78 H 8.75.

4.3.5. (1*R*,2*Z*)-3,7-Dimethyl-1-(methyldiphenylsilyl)-octa-2,6-dienyl *N*-phenylcarbamate (13). Under argon, a solution of methyldiphenylsilyl alcohol (*R*)-**12** (158 mg, 0.45 mmol), phenyl isocyanate (126 mg, 1.06 mmol, 2.35 equiv) and pyridine (21 mg, 0.60 equiv) in toluene (1 mL) was stirred for 4 days at 70 °C. The solution was poured into a mixture of Et_2O (10 mL) and 2 N aq HCl (3 mL). The aqueous phase was extracted with Et_2O (3× 15 mL). The combined organic layers were washed with saturated $NaHCO_3$ and brine, dried over anhydrous Na_2SO_4, and then concentrated in vacuum. Flash chromatography (PE/Et_2O, 5:1) of the crude product gave (*R*)-**13** (163 mg, 77%) as a white solid. mp 105–106 °C (PE/Et_2O). $[\alpha]_D^{20}=-21.3$ (*c* 1.20 in MeOH). R_f (PE/Et_2O, 8:1)=0.27. IR (KBr) ν 3352, 2962, 2926, 2852, 1695, 1604, 1535. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.82 (s, 3H, Si–CH_3), 1.75, 1.82, 1.87 (each s, 9H, 3-CH_3, 7-CH_3, 8-H_3), 2.20–2.25 (m, 4H, 4-H_2, 5-H_2), 4.95–4.99 (m, 1H, 6-H), 5.19 (d, 1H, 1-H, J= 10.8 Hz), 5.87 (d, 1H, 2-H, J=10.8 Hz), 6.36 (s, 1H, N–H), 7.34–7.49 (m, 15H, Ph). ^{13}C NMR (75 MHz, $CDCl_3$) δ −5.8, 17.6, 22.6, 23.5, 26.4 (C-5), 39.8, 66.0, 118.8, 121.0, 123.2, 124.3, 127.8, 129.6, 131.4, 133.8, 134.4, 135.0, 138.1, 153.6. ESI-MS (*m*/*e*) 469.3 [M^+], 400.2 [$M^+-C_5H_9$], 256.1 [M^+-CH_3–$SiPh_2Me$], 197.1 [$SiPh_2Me^+$], 136.1 [$OCNHPh^+$], 69.1 [$C_5H_9^+$]. $C_{27}H_{37}NO_2Si$ calcd. C 76.71 H 7.51 N 2.98; found C 76.51 H 7.50 N 2.85.

4.3.6. (1*S*,2*E*)-1-Deuterio-3,7-dimethylocta-2,6-dienyl *N*,*N*-diisopropylcarbamate (14). As described under Section 4.1.1, the solution of (*E*)-**6** (281 mg, 1.0 mmol) and (−)-sparteine (351 mg, 1.5 mmol) was treated with *n*-BuLi (0.94 mL, 1.5 mmol, 1.6 M solution in hexane) at −78 °C. The reaction mixture was stirring for 30 min at −78 °C. MeOD (0.06 mL, 50 mg) was added to the solution and the mixture was stirred for 1 h. The usual work-up was done and a subsequent purification of the crude product by flash chromatography on silica gel (PE/E 10:1) furnished **15** (260 mg, 92%); deuterium content was >99% (mass spectral analysis); colourless liquid. $[\alpha]_D^{20}=-0.45$ (*c* 1.34 in MeOH). R_f (PE/Et_2O, 8:1)=0.47. IR (film) ν 2967, 2930, 2882, 1695. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.20 (d, 12 H, *Cb*-CH_3, $^3J_{2',1'}$=6.9 Hz), 1.60, 1.67, 1.69 (each s, 9H, 3-CH_3, 7-CH_3, 8-H_3), 2.03–2.10 (m, 4H, 4-H_2, 5-H_2), 3.70–3.92 (m, 2H, *Cb*-CH), 4.57 (d, 1H, 1-H, J=6.9 Hz), 5.05–5.09 (m, 1H, 6-H), 5.36 (d, 1H, 2-H, J=6.9 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.8, 21.4, 26.0, 26.7, 29.4, 39.9, 45.6, 61.8, 120.0, 124.3, 132.0, 141.1, 156.3. EI-MS (*m*/*e*) 282.3 [M^+], 213.2 [$M^+-C_5H_9$], 128.1 [Cb^+], 94.1 [$C_7H_{10}^+$], 86.1 [$C_4H_9NO^+$], 69.1 [$C_5H_9^+$]. $C_{17}H_{30}DNO_2$ calcd. C 72.29 H 11.42 N 4.96; found C 72.66 H 11.29 N 4.84.

4.3.7. (1*S*,2*E*)-1-Deuterio-3,7-dimethyl-octa-2,6-dien-1-ol (15). As described for (*R*)-**12**, DIBAL-H (1.0 M in hexane, 5.4 mL) was added dropwise to a solution of the carbamate (*S*)-**14** (190 mg, 0.67 mmol) in anhydrous THF (4 mL) at 0 °C. The reaction mixture was stirred for 8 h at room temperature. After it had been cooled to 0 °C, methanol (2 mL) was added, followed by saturated solution of NH_4Cl. The usual work-up was done and a subsequent purification of the crude product by flash chromatography on silica gel (PE/E 5:1) furnished **15** (81 mg, 78%) as a colourless liquid. Deuterium content was >99% (mass spectral analysis); $[\alpha]_D^{20}=+0.97$ (*c* 1.75 in cyclopentane). Other spectral data correspond to Refs. 20, 21.

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