ELSEVIER

Journal of Organometallic Chemistry 624 (2001) 96–104

Journal of Organometallic Chemistry

www.elsevier.nl/locate/jorganchem

Synthesis of enantioenriched indene-derived bicyclic alcohols and tricyclic cyclopropanes via (−)-sparteine-mediated lithiation of a racemic precursor and kinetic resolution during the cyclocarbolithiation

H. Laqua, R. Fröhlich [1], B. Wibbeling[1], D. Hoppe *

Organisch-Chemisches Institut der Universität Münster, Corrensstraße 40, D-48149 Münster, Germany

Received 12 September 2000; accepted 24 October 2000

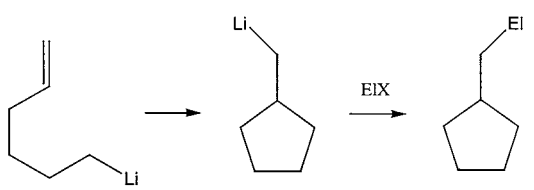
Dedicated to Professor J.F. Normant on the occasion of his 65th birthday

Abstract

By treatment of the racemic 3-(indenyl)alkyl carbamate *rac*-8 with *sec*-BuLi–(−)-sparteine, cyclocarbolithiation occurs, which is accompanied by kinetic resolution during the cyclisation step. After addition of electrophiles, the stereohomogeneous optically active benzobicyclo[3.3.0]octenols of type **13** are obtained. Increasing the temperature from −78 to −40°C or the application of TMEDA instead of (−)-sparteine yields the formation of the tricyclic cyclopropane **14**. © 2001 Elsevier Science B.V. All rights reserved.

Keywords: Chiral carbanions; Cyclocarbolithiation; (−)-Sparteine; Kinetic resolution; Lithiated alkyl carbamates

Based on the work of Drozd et al. [1] and, more important, of Bailey et al. [2], the intramolecular cyclocarbolithiation of 5-alkenyllithium and related compounds became a powerful synthetic tool in the construction of five-membered carbo- and hetereocycles (Scheme 1) [3]. The cyclisation of **A** proceeds readily in a 5-*exo*-trig ring-closure [4] and the intermediate **B** can be trapped either by protons or other electrophiles.



A **B** **C**

Scheme 1.

Inspired by the seminal work of Normant and Marek [5], who found that the (−)-sparteine complexes of achiral alkyllithiums add with high enantiofacial selectivity onto the double bond of 3-heterosubstituted 1-phenyl-1-propenes, we applied our method of (−)-sparteine-mediated enantioselective deprotonation of alkyl carbamates [6b] successfully to achieve the goal of asymmetric cyclocarbolithiation starting from 5-alkenyl carbamates (Scheme 2) [7–9].

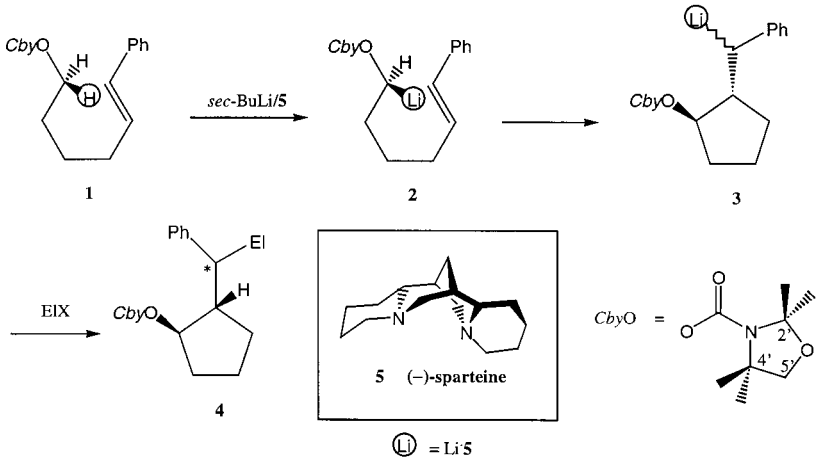
Starting from the achiral alkene **1**, the base *sec*-butyllithium–(−)-sparteine (**5**) removes almost exclusively the α-*pro*-*S* proton and leads to the intermediate **2** which cyclises to form the cyclic benzyllithium compound **3** with both high enantio- and diastereoselectivity in respect to the stereogenic centers at the five-membered ring [7a,b]. Despite the fact that the benzylic position in **3** is configuratively labile, it is trapped by most electrophiles with formation of the nearly stereohomogeneous cyclopentanol derivatives **4**, bearing three consecutive stereocenters.

When starting from racemic alkenyl carbamates, the generation of two enantioenriched epimers, both with

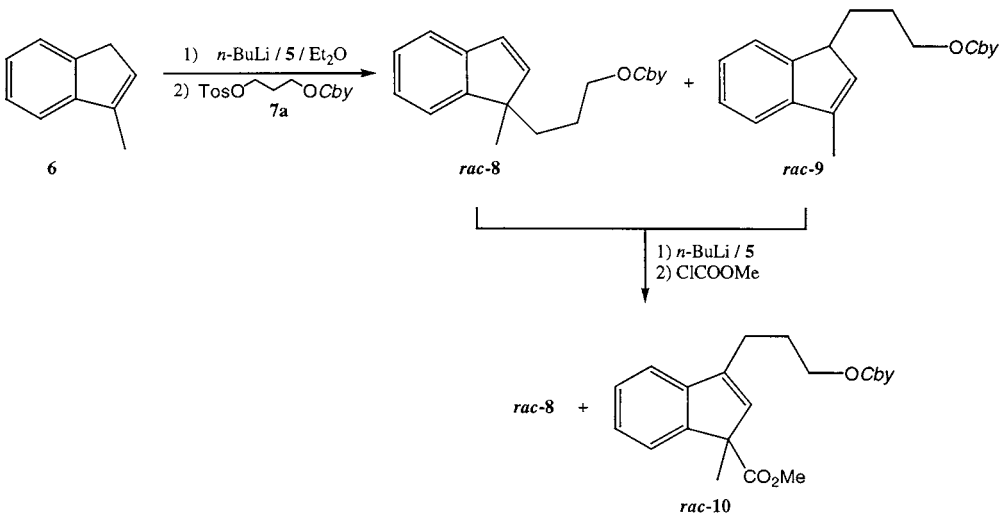
* Corresponding author. Fax: +49-251-8339772.
E-mail address: dhoppe@uni-muenster.de (D. Hoppe).

[1] X-ray crystal structure analysis.

PII: S0022-328X(00)00832-9



Scheme 2.



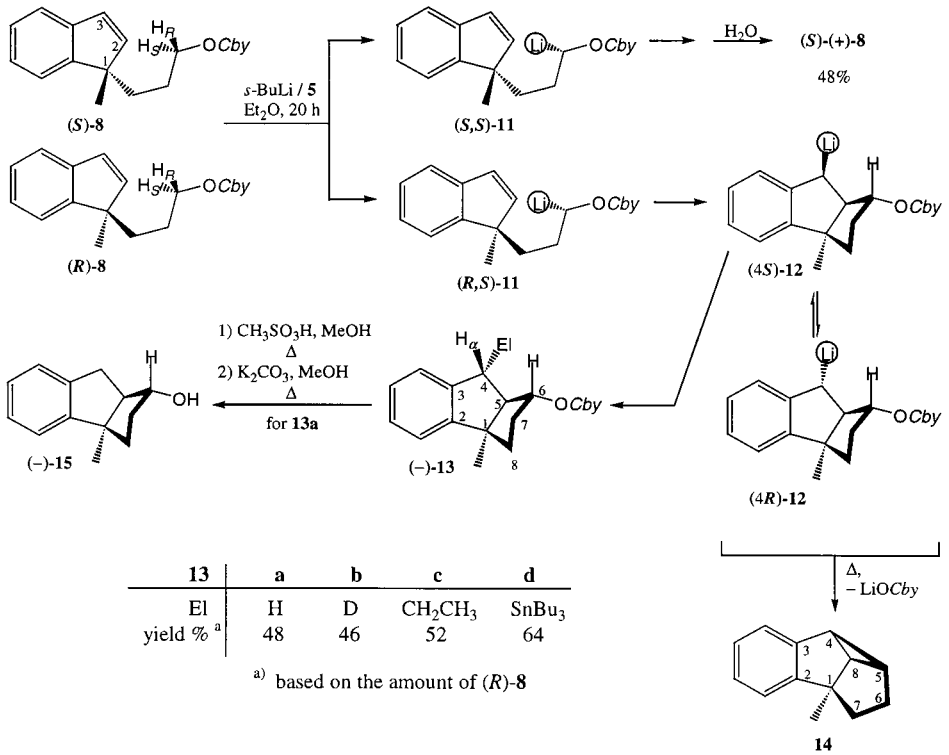
Scheme 3.

(*S*)-configuration at the metal-bearing stereocenter will occur, although in different amounts through a kinetic resolution, due to a matched and mismatched situation [10] in the deprotonation step [9,11] (for the principle, see Scheme 4).

We report here on another type of efficient kinetic resolution, namely, that which is involved in the cyclisation step. A suitable cyclisation precursor *rac*-**8** was prepared from 3-methyl-1*H*-indene (**6**) and the 3-tosyloxypropyl carbamate (**7a**) (Scheme 3) by deprotonation of **6** by means of *n*-butyllithium–(−)-sparteine [12,13]. As expected [12], both regioisomers *rac*-**8** and *rac*-**9** (ratio 1:1) were obtained as racemates. For facilitating the separation, the mixture was deprotonated again and trapped by methyl chloroformate. Only *rac*-**9**, still bearing an acidic proton, was converted into the ester *rac*-**10**, and *rac*-**8** remained unchanged.

rac-**8** was kept with *sec*-butyllithium/(−)-sparteine (1.5 equivalents) in diethyl ether for 20 h at −78°C before the reaction mixture was quenched by addition of water (Scheme 4). Chromatographic separation afforded the benzobicyclo[3.3.0]-octenyl carbamate (−)-**13a** (24%; only one diastereomer could be detected by ^{1}H-NMR and TLC), the optically active starting material (+)-**8** (48%), and traces of the impure tricyclic cyclopropane **14** (Scheme 4). From carbamate (−)-**13a**, the alcohol (−)-**15** was liberated [14] and converted to the (*R*) Mosher ester [15]. The samples appeared homogeneous; no evidence for diastereomeric impurities could be detected in GC, ^{1}H- and ^{19}F-NMR. From this it must be concluded that (−)-**15** and (−)-**13a** have high enantiomeric purities. This is in accordance with what is expected, since it is determined by the *pro*-*S*-selectivity in the deprotonation step, which was always found to be higher than 97%.

Crystalline (−)-**13a** could be subjected to single-crystal structure analysis [16] (Fig. 1) which revealed the relative configuration. Since we had demonstrated with numerous examples that the (−)-sparteine deprotonation of alkyl carbamates leads without any excep-



13	a	b	c	d
El	H	D	CH_2CH_3	$SnBu_3$
yield % [a]	48	46	52	64

[a] based on the amount of (*R*)-**8**

Scheme 4.

tion [6b] to the removal of the *pro*-*S* proton and, in addition, the carbolithiation takes place with stereoretention [6,7], C-6 has the (*R*)-configuration and can be taken as the reference stereocenter for assigning the absolute configuration (1*R*,5*R*,6*R*) to (−)-**13a**. The precursor of (−)-**13a** is solely the lithium intermediate (*R*,*S*)-**11**, since no diastereomer of (−)-**13a** was detected. Thus, recovered (+)-**8** must arise from the epimer (*S*,*S*)-**11** and have the (*S*)-configuration. In order to exclude the unlikely event that stereodiscrimination had already occurred in the deprotonation step, the reaction mixture was trapped with $DOCH_3$ and, as expected, [1D]-(+)-**8** was isolated.

From these results, it can be concluded that the epimer (*S*,*S*)-**11** does not cyclize under the conditions where the cyclocarbolithiation of (*R*,*S*)-**11** proceeds easily. The difference in both transition states is that in the syn-addition of C–Li to the double bond, for formation of (4*S*)-**12** from (*R*,*S*)-**11** the complexing carbamoyloxy residue can occupy a favourable position in the developing roof-like *cis*-bicyclus, whereas for (*S*,*S*)-**11** this group has to be placed in a congested endo-position [17]. The originally formed benzyllithium derivative (4*S*)-**12** is not expected to be configurationally stable [6b] and presumably exists in equilibrium with its epimer (4*R*)-**12**. By addition of electrophiles, such as ethyl iodide or tributyltin chloride, the stereohomogeneous substitution products (−)-**13c** and (−)-**13d** are isolated. Due to the rigid structure of **13a**, the ^{1}H-NMR spectroscopic stereochemical assignment is no problem: the coupling constants $^3J_{H5,H4\alpha}$ (2.4 Hz) and $^3J_{H5,H4\beta}$ (10.2 Hz) are of very different sizes. In (−)-**13c** (4.2 Hz) and (−)-**13d** (2.9 Hz), only a small coupling constant remained, indicating that the introduced substituent occupies the β-position. Consequently, the electrophile had approached from the less shielded *exo*-face. Since alkylations and stannylations in benzylic position were found to proceed with stereoinversion, most likely, lithium compound (4*S*)-**12** is the direct precursor. Deuteration of the benzyllithium intermediate **12** with $DOCH_3$ is less diastereoselective, leading to a 69:31 mixture of the β- and α-D isotopomers **13b**; spectroscopic configurational assignment is based on the same ^{1}H-NMR arguments. Possibly, CH_3OD, being a very rapid electrophile, reacting with stereoretention [18], traps the equilibrium mixture of (4*S*)- and (4*R*)-**12**.

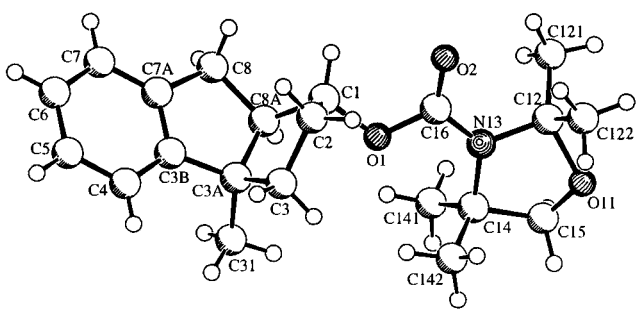
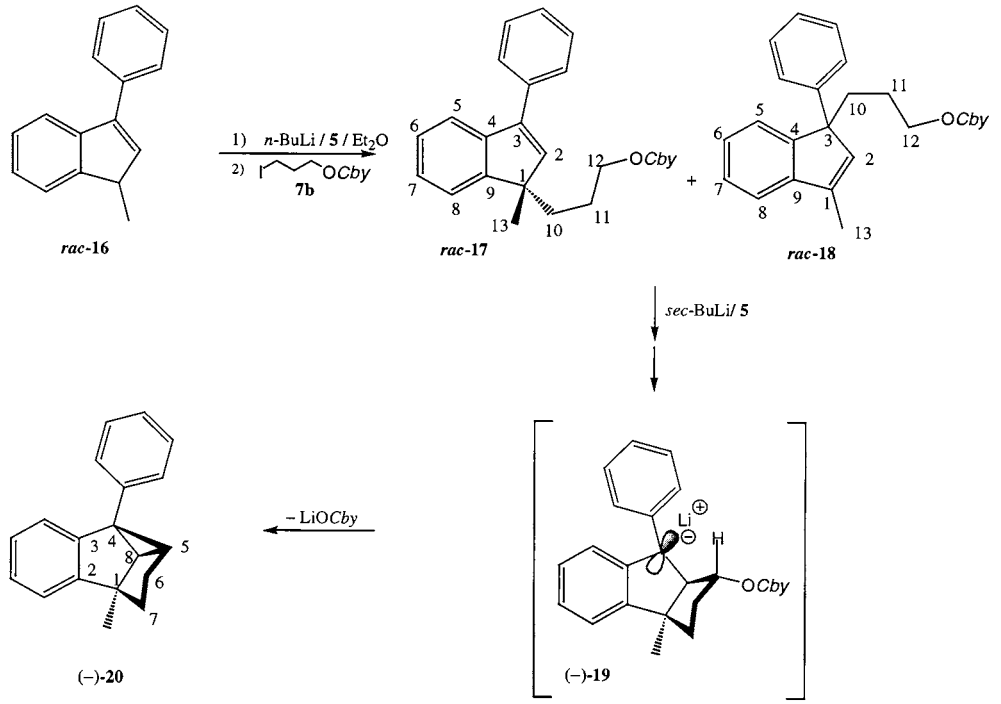


Fig. 1. Structure of (−)-**13a** in the crystal.



Scheme 5.

1. Cyclopropane formation

In an attempt to prepare a racemic sample of **13a**, TMEDA was used as a ligand instead of **5** for the deprotonation of *rac*-**8**. To our surprise, after protonolysis at −78°C not *rac*-**13a**, but the tricyclic cyclopropane *rac*-**14** was isolated with 48% yield, in addition to recovered starting material *rac*-**8**. The structure of *rac*-**14** was elucidated by C,H correlation NMR experiments (see Section 2); *rac*-**14** arises by the intramolecular 1,3-alkylation in the benzyllithium intermediates *rac*-**12**. Cyclopropane formation by intramolecular nucleophilic substitution of a *N*,*N*-dialkylcarbamoyloxy group is a common reaction, which was reported first by us in 1993 [7,9,19]. Apart from the stereochemical situation [19] in the precursor, the ligand at the lithium cation has a great influence on the ease of cycloelimination. Whereas the TMEDA complex of **12** undergoes the reaction even at −78°C, for the (−)-sparteine complex temperatures of −40°C are required to achieve complete cyclopropane formation. A case, using the different rates of cyclopropane formation for kinetic resolution of diastereomers on the stage of a cyclisation product, derived from a lithiated alkyl carbamate, was reported by Nakai et al. [7e].

When the 1-methyl-3-phenylindenyl-substituted propyl carbamate *rac*-**17** accompanied by its 1,3-regioisomery *rac*-**18** was subjected to the usual conditions of (−)-sparteine-assisted deprotonation, the optically active analogue (−)-**20** was formed with 36% yield (Scheme 5). Even, when the reaction was carried out at −90°C, no intermediate could be trapped. Presumably, the benzhydryllithium **19** is more reactive than **12** due to its larger ion-pair separation [20].

Altogether, the combination of alkylating an alkylindene by the 3-(tosyloxy)-alkyl carbamate (**7a**), (−)-sparteine-assisted deprotonation, followed by cyclocarbolithiation, which is accompanied by kinetic resolution, provides facile access to optically active benzobicyclo[3.3.0]octenols of type **13** and to tricyclic cyclopropanes such as **14** or **20**.

2. Experimental

All reactions involving water- or air-sensitive chemicals were carried out in distilled and dried solvents under argon. Diethyl ether was distilled from sodium 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 were used as purchased. Melting points: Gallenkamp melting point apparatus (uncorrected). IR: Perkin–Elmer PE 298. ^{1}H- and ^{13}C-NMR: Bruker AM 300, ARX 400 and Varian 600. Shifts are reported relative to tetramethylsilane as an internal reference. $CDCl_3$ was used as solvent. Numbering according to IUPAC rules. Elemental analysis: Perkin–Elmer 240. Flash chromatography: Merck Silica Gel 60 (40–63 μm) (100 g for 1 g of material to be separated). Thin-layer chromatography (TLC): Macherey, Nagel & Co. Sil G/UV_{254}.

2.1. (3-Tosylpropyl)2,2,4,4-tetramethyl-1,3-oxazolidine-3-carboxylate (**7a**)

Tosyl chloride (4.60 g, 24.0 mmol) was added to a stirred solution of (3-hydroxypropyl)-2,2,4,4-tetramethyl-1,3-oxazolidin-3-carboxylate [6] (4.62 g, 20.0 mmol) in 30 ml of dichloromethane. After addition of pyridine (3.9 ml, 48.0 mmol), the mixture was stirred for 16 h at room temperature (r.t.) and then 10 ml 2 M HCl were added. After separation of the layers and threefold extraction of the aqueous layer with 10 ml of diethyl ether, the organic layers were dried with Na_2SO_4. After column chromatography with diethyl ether–petroleum ether (4:1), the tosyl carbamate **7a** (6.71 g, 87%) was obtained as a white solid. M.p. 60–61°C. Anal. Calc. for $C_{18}H_{27}NO_6S$ (385.86): C, 56.08; H, 7.06; N, 3.63. Found: C, 56.09; H, 7.25; N, 3.67%. IR ($\tilde{\nu}$/cm^{-1}, KBr): 2980 (m); 2934 (m); 2881 (w); 1687 (s); 1366 (s); 1187 (s); 949 (m); 866 (s). ^{1}H-NMR (300 MHz): $\delta = 1.28$ [1.39] (s, 6H, 4′-CH_3); 1.53 [1.43] (s, 6H, 2′-CH_3); 2.00–2.04 (m, 2H, 2-H); 2.44 (s, 3H, 5″-H); 4.10–4.15 (m, 4H, 3-H, 1-H); 7.32–7.37 (m, 2H, 3″-H); 7.77–7.81 (m, 2H, 2″-H). ^{13}C-NMR (75 MHz): $\delta = 21.9$ q (C-5″); 25.6 [24.4] q (4′-*C*H$_3$); 25.6 [26.8] q (2′-*C*H$_3$); 29.1 t (C-2); 60.0 [60.6] s (C-4′); 60.6 t (C-3); 67.6 t (C-1); 76.6 [76.4] t (C-5′); 96.2 [95.1] s (C-2′); 128.2 d (C-2″); 130.2 d (C-3″); 133.4 s (C-1″); 145.2 s (C-4″); 152.6 [151.9] s (N*C*=O). EI-MS (*m*/*z* (%)): 370 (100) [(M − CH$_3$)$^+$]; 326 (23) [(M − C$_3$H$_7$O)$^+$]; 213 (78) [(M − OCby)$^+$]; 198 (7) [(M − OCby − CH$_3$)$^+$]; 155 (87) [C$_7$H$_7$O$_2$S$^+$]; 114 (15) [C$_7$H$_{14}$O$^+$]; 91 (61) [C$_7$H$_7^+$].

2.2. (3-Iodopropyl)2,2,4,4-tetramethyl-1,3-oxazolidine-3-carboxylate (**7b**)

A 0.8 M solution of iodine in DMF was added to a stirred solution of (3-hydroxypropyl)-2,2,4,4-tetramethyl-1,3-oxazolidin-3-carboxylate (3.00 g, 13.0 mmol) and 3.75 g (14.3 mmol) triphenylphosphine in 20 ml of DMF until the colour of the solution remained brown. After 1 h, 10 ml of saturated aqueous $Na_2S_2O_3$ solution were added. After separation of the layers and threefold extraction of the aqueous layer with 10 ml of diethyl ether the organic layers were dried with Na_2SO_4. After column chromatography with diethyl ether–petroleum ether (1:6) the carbamate **7b** (3.73 g, 85%) was obtained as a colourless oil. Anal. Calc. for $C_{11}H_{20}INO_3$ (341.19): C, 38.72; H, 5.91; N, 4.11. Found: C, 38.57; H, 6.32; N, 4.11%. IR ($\tilde{\nu}$/cm^{-1}, film): 2981 (s); 2869 (m); 1696 (s); 1406 (m); 1360 (m); 1258 (m); 1104 (m). ^{1}H-NMR (300 MHz): $\delta = 1.37$ [1.42] (s, 6H, 4′-CH_3); 1.55 [1.52] (s, 6H, 2′-CH_3); 2.18 (tt, 2H, 2-H); 3.24 (t, 2H, 3-H); 3.73 (s, 2H, 5′-H); 4.17 (t, 2H, 1-H). $^3J_{1,2} = 6.5$; $^3J_{2,3} = 6.7$ Hz. ^{13}C-NMR (75 MHz): $\delta = 1.6$ t (C-3); 25.3 [24.1] q (4′-*C*H$_3$); 25.4 [26.6] q (2′-*C*H$_3$); 32.8 t (C-2); 59.7 [60.6] s (C-4′); 64.3 t (C-1); 76.3 [76.1] t (C-5′); 96.6 [94.6] s (C-2′); 152.6 [152.1] s (N*C*=O). EI-MS (*m*/*z* (%)): 326 (100) [(M − CH$_3$)$^+$]; 169(24) [(M − OCby)$^+$]; 114 (8) [C$_7$H$_{14}$O].

2.3. General procedure for the lithiation and substitution of the indenes **6** and rac-**16**

n-Butyllithium (one equivalent, 1.6 M in *n*-hexane) was added drop-wise with stirring at −78°C to a solution of the indene (one equivalent) and (−)-sparteine (**5**) (one equivalent) in diethyl ether (2 ml mmol^{-1}). The electrophile was added and stirring continued for 4 h at −78°C. After addition of 2 M HCl (1 ml mmol^{-1}) the mixture was warmed to room temperature and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 10 ml) and the combined ethereal phases were washed with water (10 ml). After the solution had been dried (Na_2SO_4), the solvent was evaporated under reduced pressure, and the products were separated on silica gel with diethyl ether–petroleum ether.

2.4. Carbamates rac-**8** and rac-**10**

3-Methyl-1*H*-indene (2.60 g, 20.0 mmol), 4.70 g (20.0 mmol) (−)-sparteine, 12.5 ml (20.0 mmol) *n*-BuLi, 7.71 g (20.0 mmol) **7a**, column chromatography with diethyl ether–petroleum ether (1:4); yield: 75% (colourless oil; rac-**8**/rac-**10** = 1:1).

The mixture (5.18 g, 15.1 mmol) was lithiated again with 2.34 g (10.0 mmol) (−)-sparteine and 6.25 ml (10.0 mmol) *n*-BuLi; 1.0 ml (12.0 mmol) methyl chlorofomate was added. Column chromatography with diethyl ether–petroleum ether (1:4) produced rac-**8** (43%) and rac-**10** (32%) as colourless oils.

2.5. Carbamate rac-**8**

Anal. Calc. for $C_{21}H_{29}NO_3$ (343.47): C, 73.44; H, 8.51; N, 4.08. Found: C, 73.32; H, 8.48; N, 3.94%. IR ($\tilde{\nu}$/cm^{-1}, film): 3065 (m); 2973 (s); 2868 (s); 1710 (s); 1479 (m); 1414 (s); 1348 (s); 1269 (m); 1111 (s); 755 (s). ^{1}H-NMR (300 MHz): $\delta = 1.31$ (s, 3H, 13-H); 1.33–1.53 (m, 14H, 2′-CH_3–4′-CH_3–10-H); 1.86 (tt, 2H, 11-H); 3.71 (s, 2H, 5′-H); 3.94 (t, 2H, 12-H); 6.29 (d, 1H, 2-H); 6.68 (d, 1H, 3-H); 7.14–7.29 (m, 4H, Ph–H). $^3J_{2,3} = 5.5$; $^3J_{10,11} = 5.6$; $^3J_{11,12} = 6.2$ Hz. ^{13}C-NMR (75 MHz): $\delta =$ 24.0 q (C-13); 24.9 t (C-11); 25.7 [24.6] q (4′-*C*H$_3$); 25.7 [27.0] q (2′-*C*H$_3$); 35.4 t (C-10); 53.4 s (C-1); 59.2 [60.5] s (C-4′); 65.2 t (C-12); 77.6 t (C-5′); 96.1 [94.6] s (C-2′); 121.6, 121.7 d (C-5/C-8); 125.5 d (C-7); 127.0 d (C-6); 129.7 d (C-2); 143.8 s (C-9); 145.2 s (C-4); 145.3 d (C-3); 152.1 s (N=*C*O). EI-MS (*m*/*z* (%)): 343 (1) [M$^+$]; 328 (55) [(M − CH$_3$)$^+$]; 171 (100) [(M − OCby)$^+$]; 156 (59) [(M − OCby − CH$_3$)$^+$]; 143 (38) [C$_{11}$H$_{11}^+$]; 129 (88) [C$_{10}$H$_9^+$].

2.6. Carbamate rac-**10**

Anal. Calc. for $C_{23}H_{31}NO_5$ (401.50): C, 68.80; H, 7.78; N, 3.49. Found: C, 68.81; H, 7.87; N, 3.25%. IR ($\tilde{\nu}$/cm^{-1}, film): 2987 (s); 2934 (m); 2875 (m); 1736 (s); 1703 (s); 1460 (m); 1420 (m); 1368 (m); 1104 (s); 1071 (m); 788 (m). ^{1}H-NMR (300 MHz): $\delta = 1.41–1.57$ (m, 12H, 4′-CH_3–2′-CH_3); 1.58 (d, 3H, 10-H_3); 2.06 (tt, 2H, 12-H_2); 2.62 (t, 2H, 11-H_2); 3.61 (s, 3H, OCH_3); 3.74 (s, 2H, 5′-H_2); 4.20 (t, 2H, 13-H_2); 6.18 (q, 1H, 2-H); 7.20–7.33 (m, 4H, Ph–H). $^4J_{2,10} = 1.2$; $^3J_{11,12} = 7.7$; $^3J_{12,13} = 6.4$ Hz. ^{13}C-NMR (75 MHz): $\delta = 22.5$ q (C-10); 24.6 t (C-12); 25.8 [24.7] q (4′-CH$_3$); 25.8 [27.1] q (2′-CH$_3$); 27.6 t (C-11); 52.7 q (OCH$_3$); 58.5 s (C-1); 59.3 [60.1] s (C-4′); 64.5 t (C-13); 77.4 t (C-5′); 95.8 [94.8] s (C-2′); 119.7 d (C-5); 123.4 d (C-8); 126.3 d (C-7); 127.9 d (C-6); 134.9 d (C-2); 143.3 s (C-9); 143.9 s (C-4); 148.0 s (C-3); 152.9 s (NC=O); 174.6 s (COOCH$_3$). EI-MS (m/z (%)): 386 (14) [(M − CH$_3$)$^+$]; 342 (2) [(M − COOCH$_3$)$^+$]; 327 (1) [(M − CH$_3$ − COOCH$_3$)$^+$]; 229 (20) [(M − OCby)$^+$]; 228 (100) [(M − H − OCby)$^+$]; 169 (91); 115 (6) [$C_9H_7^+$].

2.7. Carbamate rac-**17** (65:35 mixture with the γ-regioisomer rac-**18**)

1-Methyl-3-phenyl-1H-indene (0.69 g, 2.0 mmol), 0.47 g (2.0 mmol) (−)-sparteine, 1.25 ml (2.0 mmol) n-BuLi, 0.68 g (2 mmol) carbamate **7b**; column chromatography with diethyl ether–petroleum ether (1:4) produced a mixture of rac-**17** and rac-**18** (66%, α/γ = 65:35) as a colourless oil. This mixture was used without further separation. Anal. Calc. for $C_{27}H_{33}NO_3$ (419.57): C, 77.29; H, 7.93; N, 3.34. Found: C, 77.19; H, 8.03; N, 3.23%. IR ($\tilde{\nu}$/cm^{-1}, film): 2987 (s); 2868 (m); 1697 (s); 1453 (m); 1407 (s); 1348 (s); 1269 (m); 1098 (s); 762 (s). ^{1}H-NMR (300 MHz, γ-isomere in curly brackets): $\delta = 1.25–1.59$ (m, 15H, 2′-CH_3, 4′-CH_3, 11-H_2, 10-H_a); 1.40 {2.16} (s {d}, 3H, 13-H_3); 1.93 {2.38} (m, 1H, 10-H_b); 3.70 (s, 2H, 5′-H_2); 3.96 {4.00} (t, 2H, 12-H_2); 6.35 {6.19} (s {q}, 1H, 2-H); 7.13–7.59 (m, 9H, Ph–H). $^3J_{11,12} = 6.2$ Hz; {$^4J_{2,13} = 1.4$ Hz}. ^{13}C-NMR (75 MHz, γ-isomere in curly brackets): $\delta = 13.2$ {15.7} q (C-13); 24.6 [24.1] q (4′-CH$_3$); 25.0 t (C-11); 25.8 [27.0] q (2′-CH$_3$); 35.9 {34.3} t (C-10); 52.1 s (C-1); 59.6 [60.3] s (C-4′); {61.2 s (C-3)}; 65.3 {66.2} t (C-12); 76.8 t (C-5′); 95.8 [94.8] s (C-2′); 119.8/121.1/123.2/125.9/126.7/126.8/127.0/127.2/128.0/128.8/ 136.2/139.2/142.0/142.9 s/d (Ph–C, C-3, {C-3}, C-2, {C-2}); 153.1 [152.5] s (N=CO). EI-MS (m/z (%)): 419 (6) [M$^+$]; 404 (4) [(M − CH$_3$)$^+$]; 246 (65) [(M − OCby − H)$^+$]; 231 (58) [(M − H − CH$_3$ − OCby)$^+$]; 205 (51) [(M − C_3H_6OCby)$^+$]; 156 (100) [Cby$^+$].

2.8. General procedure for the cyclocarbolithiation of the indenes rac-**8** and rac-**17** and substitution by electrophiles

sec-Butyllithium [1.5 equivalents 1.08 M in cyclohexane–n-hexane (92:8)] was added drop-wise with stirring at −78°C to a solution of the indene (one equivalent) and (−)-sparteine (**5**) (1.5 equivalents) in diethyl ether. After 20 h at −78°C the electrophile was added and stirring continued for 5 h while the temperature was slowly raised to r.t. After addition of 2 M HCl (2 ml) the layers were separated, the aqueous layer was extracted with diethyl ether (3 × 10 ml) and the combined ethereal phases were washed with water (10 ml). After the solution had been dried (Na_2SO_4), the solvent was evaporated under reduced pressure, and the products were separated on silica gel with diethyl ether–petroleum ether.

2.9. (1R,5R,6R)-1-Methyl-2,3-benzobicyclo[3.3.0]oct-2-ene-6-yl2,2,4,4-tetramethyl-1,3-oxazolidine-3-carboxylate (**13a**)

rac-**8** (117 mg, 0.34 mmol), 120 mg (0.51 mmol) (−)-sparteine, 0.48 ml (0.51 mmol) *sec*-BuLi, 5 ml diethyl ether, column chromatography with diethyl ether–petroleum ether (1:4) produced (−)-**13a** (24%) as a white solid. M.p. 82–83°C. $[\alpha]_D^{20} = -62.6$ (c = 0.77, CH_2Cl_2). Anal. Calc. for $C_{21}H_{29}NO_3$ (343.47): C, 73.44; H, 8.51; N, 4.08. Found: C, 73.70; H, 8.80; N, 3.86%. IR ($\tilde{\nu}$/cm^{-1}, KBr): 2980 (s); 2960 (s); 2875 (s); 1683 (s); 1413 (s); 1348 (s); 1262 (s); 1210 (m); 1104 (s); 1065 (s); 912 (w); 861 (w); 775 (s); 538 (w). ^{1}H-NMR (600 MHz): $\delta = 1.44–1.69$ (m, 16H, 7-H_β, 1-CH_3, 2′-CH_3, 4′-CH_3); 1.82 (m, 1H, 7-H_α); 1.97–2.00 (m, 2H, 8-H_2); 2.50 (ddd, 1H, 5-H); 2.80 (dd, 1H, 4-H_β); 3.37 (dd, 1H, 4-H_α); 3.74 (s, 2H, 5′-H_2); 4.90 (ddd, 1H, 6-H); 7.12–7.18 (m, 4H, Ph–H). $^3J_{6,7\alpha} = 4.2$; $^3J_{6,7\beta} = 2.4$; $^3J_{5,6} = 1.8$; $^2J_{4\alpha,4\beta} = 17.4$; $^3J_{4\alpha,5} = 10.2$; $^3J_{4\beta,5} = 2.4$ Hz. ^{13}C-NMR (150 MHz): $\delta = 25.3$ [24.1] q (4′-CH$_3$); 25.6 [25.3] q (2′-CH$_3$); 26.8 q (1-CH$_3$); 31.9 t (C-7); 36.4 t (C-8); 39.7 t (C-4); 55.9 s (C-1); 56.3 d (C-5); 59.4 [60.3] s (C-4′); 76.3 t (C-5′); 84.5 d (C-6); 95.8 [94.8] s (C-2′); 122.8 d, 124.2 d, 126.3 d, 126.8 d, 141.6/150.5 s (Ph–C); 152.2 s (NC=O). EI-MS (m/z (%)): 343 (1) [M$^+$]; 328 (14) [(M − CH$_3$)$^+$]; 171 (78) [(M − OCby)$^+$]; 170 (100) [(M − H − OCby)$^+$]; 155 (64) [(M − H − OCby − CH$_3$)$^+$]; 129 (73) [$C_{10}H_9^+$]; 114 (39) [$C_9H_6^+$].

Besides the cyclisation product, 48% of the enantioenriched educt (−)-**8** could be reisolated [21].

The deuterated product (−)-**13b** was synthesized as described above: 343 mg (1.0 mmol) rac-**8**, 351 mg (1.5 mmol) (−)-sparteine, 1.39 ml (1.5 mmol) *sec*-BuLi, 10 ml diethyl ether, 0.5 ml (12.3 mmol) methanol-[D_1]; column chromatography with diethyl ether–petroleum ether (1:4) produced (−)-**13b** (23%) as a white solid

(d.r., 69:31). The physical data are identical with those of (−)-**13a**. $^3J_{4\alpha,5} = 10.8$; $^3J_{4\beta,5} = 2.3$ Hz.

2.10. (1R,4S,5R,8R)-1-Methyl-2,3-benzotricyclo[3.2.1.0^{4,8}]oct-2-ene (**14**)

Analogous conditions to the above were used, but after addition of the base the reaction mixture was warmed to −40°C. After column chromatography with diethyl ether/petroleum ether (1:4), **14** (26 mg, 45%) was produced as a colourless liquid. $[\alpha]_D^{20} = -31.7$ ($c = 2.20$, CH_3Cl). Anal. Calc. for $C_{13}H_{14}$ (170.26): C, 91.71; H, 8.29. Found: C, 91.65; H, 8.80%. IR ($\tilde{\nu}$/cm^{-1}, film): 3019 (m); 2960 (s); 2868 (m); 1479 (m); 1453 (w); 1019 (w); 745 (s). ^{1}H-NMR (600 MHz): $\delta = 1.07$ (dddd, 1H, 6-H$_\beta$); 1.49 (s, 3H, 1-CH_3); 1.58 (dd, 1H, 7-H$_\beta$); 1.78 (ddd, 1H, 6-H$_\alpha$); 1.88 (dddd, 1H, 5-H); 2.04 (ddd, 1H, 7-H$_\alpha$); 2.35 (dd, 1H, 4-H); 2.46 (dd, 1H, 8-H); 6.95–7.21 (m, 4H, Ph–H). $^2J_{7\alpha,7\beta} = 13.2$ Hz; $^2J_{8\alpha,8\beta} = 11.4$; $^3J_{7\alpha,8a} = 9.0$; $^3J_{7\beta,8\beta} = 6.0$; $^3J_{7\alpha,5} = 7.2$; $^3J_{7\beta,8\alpha} = 9.0$; $^3J_{7\beta,5} = 1.8$; $^3J_{4,5} = 7.2$; $^3J_{4,8} = 6.6$; $^3J_{5,8} = 6.6$ Hz. ^{13}C-NMR (150 MHz): $\delta = 21.6$ q (1-CH$_3$); 23.4 t (C-6); 30.2 d (C-5); 32.3 d (C-4); 43.6 d (C-8); 51.7 t (C-7); 54.7 q (C-1); 121.0 d, 123.5 d, 125.4 d, 126.3 d, 142.6/151.7 q (Ph–C). EI-MS (m/z (%)): 170 (47) [M$^+$]; 155 (58) [(M − CH$_3$)$^+$]; 142 (100) [(M − C$_2$H$_4$)$^+$]; 128 (70) [(M − C$_3$H$_6$)$^+$]; 115 (63) [(M − C$_4$H$_7$)$^+$]; 102 (12) [C$_8$H$_6^+$].

2.11. (1R,4R,5R,6R)-4-Ethyl-1-methyl-2,3-benzobicyclo[3.3.0]oct-2-ene-6-yl2,2,4,4-tetramethyl-1,3-oxazolidine-3-carboxylate (**13c**)

rac-**8** (120 mg, 0.35 mmol), 123 mg (0.53 mmol) (−)-sparteine, 0.49 ml (0.53 mmol) *sec*-BuLi, 5 ml diethyl ether, column chromatography with diethyl ether–petroleum ether (1:4) produced (−)-**13c** (26%) as a colourless oil. $[\alpha]_D^{20} = -56.3$ ($c = 0.24$, CH_2Cl_2). HR-MS calc. for $C_{23}H_{33}NO_3 + Na^+$: 394.2358. Found: 394.2312. IR ($\tilde{\nu}$/cm^{-1}, film): 2967 (m); 2934 (m); 2868 (m); 1695 (s); 1399 (m); 1339 (m); 1095 (s); 1065 (s); 775 (w). ^{1}H-NMR (600 MHz): $\delta = 1.03$ (t, 3H, Et–CH$_3$); 1.41–1.61 (m, 17H, 7-H$_\beta$, 1-CH_3, Et–CH$_{2\beta}$, 2′-CH_3, 4′-CH_3); 1.79–1.83 (m, 2H, 7-H$_\alpha$, Et–CH$_{2\alpha}$); 1.93–1.96 (m, 2H, 8-H$_2$); 2.15–2.19 (m, 1H, 5-H); 2.88 (dt, 1H, 4-H); 3.75 (s, 2H, 5′-H); 4.97 (m, 1H, 6-H); 7.12–7.23 (m, 4H, Ph–H). $^3J_{4,5} = 4.2$ Hz. ^{13}C-NMR (150 MHz): $\delta = 12.3$ q (Et–C); 25.8 [24.6] q (4′-CH$_3$); 25.9 [25.8] q (2′-CH$_3$); 30.1 q (1-CH$_3$); 31.1 t (Et–C); 32.3 t (C-7); 40.6 t (C-8); 51.9 d (C-4); 55.5 s (C-1); 59.5 s (C-4′); 63.0 d (C-5); 77.4 t (C-5′); 84.8 d (C-6); 95.9 s (C-2′); 123.4, 124.4 d, 127.1, 127.6 d, 145.5/150.4 s (Ph–C); 149.1 s (NC=O). EI-MS (m/z (%)): 356 (3) [(M − CH$_3$)$^+$]; 198 (100) [(M − H − OCby)$^+$]; 169 (34) [(M − H − C$_2$H$_5$ − OCby)$^+$]; 143 (32) [C$_{11}$H$_{11}^+$]; 129 (14) [C$_{10}$H$_9$].

2.12. (1R,4R,5R,6R)-1-Methyl-4-(trimethylstannyl)-2,3-benzobicyclo[3.3.0]oct-2-ene-6-yl2,2,4,4-tetramethyl-1,3-oxazolidine-3-carboxylate (**13d**)

398 mg (1.16 mmol) *rac*-**8**, 408 mg (1.74 mmol) (−)-sparteine, 1.61 ml (1.74 mmol) *sec*-BuLi, 15 ml diethyl ether, column chromatography with diethyl ether–petroleum ether (1:40) yielded (−)-**13d** (32%) as a colourless oil. $[\alpha]_D^{20} = -47.7$ ($c = 0.92$, CH_2Cl_2). Anal. calc. for $C_{33}H_{55}NO_3Sn$ (632.51): C, 62.68; H, 8.77; N, 2.21. Found: C, 62.09; H, 8.97; N, 2.29%. IR ($\tilde{\nu}$/cm^{-1}, film): 2955 (s); 2929 (s); 2871 (m); 1682 (s); 1470 (m); 1402 (s); 1375 (s); 1264 (m); 1063 (m); 757 (m). ^{1}H-NMR (600 MHz): $\delta = 0.82$–0.88 (m, 15H, SnBu$_3$–H); 1.20–1.58 (m, 28H, 7-H$_\beta$, 2′-CH_3, 4′-CH_3; 1-CH$_3$, SnBu$_3$–H); 1.75–1.80 (m, 1H, 7-H$_\alpha$); 1.94–1.98 (m, 2H, 8-H); 2.48 (bs, 1H, 5-H); 2.83 (d, 1H, 4-H); 3.74 (s, 2H, 5′-H); 4.84 (m, 1H, 6-H); 6.87–7.08 (m, 4H, Ph–H). $^3J_{4,5} = 2.9$ Hz. ^{13}C-NMR (150 MHz): $\delta = 9.9$ t, 14.0 q (SnBu$_3$–C); 25.8 [24.6] q (4′-CH$_3$); 26.1 [25.8] q (2′-CH$_3$); 27.0 t (SnBu$_3$–C); 28.7 q (1-CH$_3$); 29.6 t (SnBu$_3$–C); 32.2 t (C-7); 35.4 d (C-4); 41.1 t (C-8); 56.4 s (C-1); 59.8 [61.2] s (C-4′); 61.4 d (C-5); 76.6 t (C-5′); 86.6 d (C-6); 96.3 [95.0] s (C-2′); 122.2, 123.2, 124.9, 127.2 d, 148.1/148.6 s (Ph–C)); 152.0 [151.8] s (NC=O). EI-MS (m/z (%)): 575(60) [(M–C$_4$H$_9$)$^+$]; 404 (100) [C$_{21}$H$_{33}$Sn$^+$]; 290 (37) [C$_{12}$H$_{27}$Sn$^+$]; 233 (20) [C$_8$H$_{18}$Sn$^+$]; 177 (29) [C$_4$H$_{10}$Sn$^+$]; 170 (34) [(M − OCby − Sn(C$_{12}$H$_{27}$))$^+$].

2.13. (1R,4R,5R,8R)-1-Methyl-4-phenyl-2,3-benzotricyclo[3.2.1.0^{4,8}]oct-2-ene ((−)-**20**)

rac-**17** (198 mg, 0.47 mmol), accompanied by its 1,3-regioisomere *rac*-**18**, 165 mg (0.71 mmol) (−)-sparteine, 0.65 ml (0.71 mmol) *sec*-BuLi, column chromatography with diethyl ether–petroleum ether (1:4) produced (−)-**20** (36%) as a colourless liquid. HR-MS calc. for $C_{19}H_{18}$: 246.1409. Found: 246.1406. $[\alpha]_D^{20} = -11.7$ ($c = 0.61$, CH_2Cl_2). IR ($\tilde{\nu}$/cm^{-1}, film): 3033 (m); 2954 (s); 2875 (m); 1604 (w); 1460 (m); 1025 (w); 762 (s). ^{1}H-NMR (300 MHz): $\delta = 1.14$–1.27 (m, 1H, 6-H$_b$); 1.58 (s, 3H, 1-CH_3); 1.64 (dd, 1H, 7-H$_b$); 1.90 (ddd, 1H, 6-H$_a$); 2.10 (ddd, 1H, 7-H$_a$); 2.39 (ddd, 1H, 5-H); 2.60 (d, 1H, 8-H); 6.84–7.38 (m, 9H, Ph–H). $^2J_{6a,6b} = 13.4$; $^2J_{7a,7b} = 11.2$; $^3J_{6b,7b} = 6.1$; $^3J_{6a,7a} = {}^3J_{6b,7a} = 9.1$; $^3J_{6a,5} = {}^3J_{5,8} = 6.9$; $^3J_{6b,5} = 1.9$ Hz. ^{13}C-NMR (75 MHz): $\delta = 21.9$ q (1-CH$_3$); 24.4 t (C-6); 36.1 d (C-5); 47.8 s (C-1); 51.6 d (C-8); 51.9 t (C-7); 55.1 s (C-4); 121.3/124.4/126.2/126.9/127.5/128.4/130.3/142.2/145.5/151.7 s, d (Ph–C). EI-MS (m/z (%)): 246 (39) [M$^+$]; 170 (96) [(M − C$_6$H$_5$ + H)$^+$]; 155 (78) [(M − C$_6$H$_5$ + H − CH$_3$)$^+$]; 142 (100) [C$_{11}$H$_{10}^+$]; 129 (82) [C$_{10}$H$_9^+$].

2.14. Deprotection of carbamate **13a**; (1R,5R,6R)-1-methyl-2,3-benzobicyclo[3.3.0]-oct-2-ene-6-ol (**15**)

Methanesulfonic acid (21 mg, 0.23 mmol) was added to a solution of 77 mg (0.22 mmol) of the carbamate **13a** in 3 ml of methanol. After 2 h of refluxing, potassium carbonate (90 mg, 0.67 mmol) was added and the reaction mixture was refluxed for additional 2.5 h. The solvent was evaporated and the residue suspended in 5 ml of diethyl ether. The precipitate was filtered off and washed with diethyl ether. The solvent was removed from the filtrate and after column chromatography with diethyl ether/petroleum ether (1:4) the carbamate (−)-**15** (27 mg, 66%) was obtained as a colourless oil. HR-MS Calc. for $C_{13}H_{16}O$: 188.1199. Found: 188.1196. $[\alpha]_D^{20} = -63.0$ ($c = 0.61$, CH_2Cl_2). IR ($\tilde{\nu}$/cm^{-1}, film): 3368 (s); 2921 (s); 2861 (s); 1453 (m); 1019 (w); 769 (m). ^{1}H-NMR (600 MHz): $\delta = 1.43$ (s, 3H, 1-CH_3); 1.57–1.63 (m, 2H, 7-H$_\beta$, OH); 1.66–1.71 (m, 1H, 7-H$_\alpha$); 1.90 (ddd, 1H, 8-H$_\beta$); 2.06 (ddd, 1H, 8-H$_\alpha$); 2.31 (m, 1H, 5-H); 2.70 (dd, 1H, 4-H$_\beta$); 3.26 (dd, 1H, 4-H$_\alpha$); 4.00 (m, 1H, 6-H); 7.12–7.20 (m, 4H, Ph–H). $^3J_{6,7\alpha} = 4.2$; $^3J_{6,7\beta} = 3.6$; $^2J_{8\alpha,8\beta} = 12.6$; $^3J_{8\beta,7\beta} = 2.4$; $^3J_{8\alpha,7\alpha} = 7.2$; $^2J_{4\alpha,4\beta} = 17.2$; $^3J_{4\alpha,5} = 9.6$; $^3J_{4\beta,5} = 2.4$ Hz. ^{13}C-NMR (150 MHz): $\delta = 29.1$ q (1-CH_3); 34.7 t (C-7); 35.5 d (C-4); 38.8 t (C-8); 55.6 s (C-1); 58.7 d (C-5); 81.5 d (C-6); 123.0 d, 124.4 d, 126.5 d, 126.9 d, 141.5 s, 151.7 s (Ph–C). EI-MS (m/z (%)): 188 (38) [M^+]; 173 (13) [$(M - CH_3)^+$]; 159 (77) [$(M - C_2H_5)^+$]; 130 (100) [$(M - C_3H_5OH)^+$]; 115 (21) [$(M - C_3H_5OH - CH_3)^+$].

2.15. (R) Mosher ester of (−)-**15**

Pyridine (0.1 ml) was added to 8 mg (0.04 mmol) of the alcohol (−)-**15** in 0.5 ml of dichloromethane. After addition of 10 mg (0.04 mmol) of (*R*)-α-methoxy-α-trifluoromethylphenylacetyl chloride, the mixture was stirred for 24 h. Direct chromatographic separation [diethyl ether–petroleum ether (1:4)] afforded 16 mg (100%) of the Mosher ester of (−)-**15** as a colourless oil. ESI-HR-MS calc. for $C_{23}H_{33}NO_3 + Na^+$: 427.1560. Found: 427.1585. ^{1}H-NMR (600 MHz): $\delta = 1.51$ (s, 3H, 1-CH_3); 1.56–1.71 (m, 2H, 7-H$_2$); 1.82–1.96 (m, 2H, 8-H$_2$); 2.43 (m, 1H, 5-H); 2.76 (m, 1H, 4-H$_\beta$); 3.35 (dd, 1H, 4-H$_\alpha$); 3.57 (s, 3H, OCH_3); 5.16 (m, 1H, 6-H); 7.10–7.58 (m, 9H, Ph–H). ^{19}F-NMR (564 MHz): $\delta = -71.85$ (s, 3F, CF_3). No second diastereomer could be detected. ESI-MS (m/z (%)): 427 (100) [$M^+ + Na$]; 171 (32) [$(M - C_{10}H_8F_3O_3)^+$].

3. Supplementary material

Crystallographic data (excluding structure factors) for the structural analysis have been deposited with the Cambridge Crystallographic Data Centre, CCDC no. 149313. Copies of this information may be obtained free of charge from the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

References

[1] (a) V.N. Drozd, Y.A. Ustynyuk, M.A. Tsel'eva, L.B. Dmitriev, J. Gen. Chem. USSR 1968, 38, 2047; Zh. Obsch. Khim. 38 (1968) 2144. (b) V.N. Drozd, Y.A. Ustynyuk, M.A. Tsel'eva, L.B. Dmitriev, J. Gen. Chem. USSR 39 (1969) 1951; Zh. Obsch. Khim. 39 (1969) 1991.

[2] (a) W.F. Bailey, J.J. Patricia, V.C. DelGobbo, R.M. Jarret, P.J. Okarma, J. Org. Chem. 50 (1985) 1999. (b) W.F. Bailey, T.T. Nurmi, J.J. Patricia, W. Wang, J. Am. Chem. Soc. 109 (1987) 2442. (c) W.F. Bailey, A.M. Khanolkar, K. Gavaskar, T.V. Ovaska, K. Rossi, Y. Thiel, K.B. Wiberg, J. Am. Chem. Soc. 113 (1991) 5720. (d) W.F. Bailey, M.J. Mealy, J. Am. Chem. Soc. 122 (2000) 6787. (e) G.S. Gil, U.M. Groth, J. Am. Chem. Soc. 122 (2000) 6789.

[3] Review: I. Marek, J. Chem. Soc. Perkin Trans. 1 (1999) 535.

[4] (a) J.E. Baldwin, J. Chem. Soc. Chem. Commun. (1976) 734. (b) Review: C.D. Johnson, Acc. Chem. Res. 26 (1993) 476.

[5] (a) S. Klein, I. Marek, J.-F. Normant, J. Org. Chem. 59 (1994) 2925. (b) S. Klein, I. Marek, J.-F. Poisson, J.-F. Normant, J. Am. Chem. Soc. 117 (1995) 8853. (c) S. Norsikian, I. Marek, J.-F. Poisson, J.-F. Normant, J. Org. Chem. 62 (1997) 4898. (d) C. Mück-Lichtenfeld, H. Ahlbrecht, Tetrahedron 52 (1996) 10025.

[6] (a) D. Hoppe, F. Hintze, P. Tebben, Angew. Chem. 102 (1990) 1457. (b) Review: D. Hoppe, T. Hense, Angew. Chem. 109 (1997) 2376; Angew. Chem. Int. Ed. Engl. 36 (1997) 2282.

[7] (a) M.J. Woltering, R. Fröhlich, D. Hoppe, Angew. Chem. 109 (1997) 1804; Angew. Chem. Int. Ed. Engl. 36 (1997) 1764. (b) M.J. Woltering, R. Fröhlich, B. Wibbeling, D. Hoppe, Synlett 1998, 797. (c) M.J. Woltering, M. Oestreich, R. Fröhlich, D. Hoppe, Helv. Chim. Acta 82 (1999) 1860. (d) S.H. Kleinfeld, E. Wegelius, D. Hoppe, Helv. Chim. Acta 82 (1999) 2413. (e) K. Tomooka, N. Komine, T. Nakai, Tetrahedron Lett. 38 (1997) 8939. (f) K. Tomooka, N. Komine, T. Sasaki, H. Shimizu, T. Nakai, Tetrahedron Lett. 39 (1998) 9715.

[8] The principle could also be applied to 5-alkynyl carbamates: D. Hoppe, M. Oestreich, Tetrahedron Lett. 39 (1998) 1745.

[9] Asymmetric cyclocarbolithiation reactions, using classical approaches to generate the enantioenriched, open-chain lithium intermediate: (a) I. Coldham, R. Hufton, D.J. Snowden, J. Am. Chem. Soc. 118 (1996) 5322. (b) I. Coldham, J.-C. Fernàndez, D.J. Snowden, Tetrahedron Lett. 40 (1999) 1819. (c) R.W. Hoffmann, R. Koberstein, K. Harms, J. Chem. Soc. Perkin Trans. 2 (1999) 183. (d) A. Krief, B. Kenda, B. Remacle, Tetrahedron Lett. 36 (1995) 7917.

[10] Review: S. Masamune, W. Choy, J.S. Petersen, L.R. Sita, Angew. Chem. 97 (1985) 1.

[11] Other examples for efficient kinetic resolutions: (a) J. Haller, T. Hense, D. Hoppe, Synlett (1993) 726. (b) T. Hense, D. Hoppe, Synthesis (1997) 1394.

[12] The (−)-sparteine complex of lithiomethylindene delivers carbonyl adducts with high enantiomeric excesses, but all attempts to achieve enantioselective alkylations have failed so far [13]. Despite that, (−)-sparteine was used, since better regioselectivities were observed in comparison to the lithium TMEDA complex.

[13] I. Hoppe, M. Marsch, K. Harms, G. Boche, D. Hoppe, Angew. Chem. 107 (1995) 2328; Angew. Chem. Int. Ed. Engl. 34 (1995) 2158.
[14] F. Hintze, D. Hoppe, Synthesis (1992) 1216.
[15] J.A. Dale, D.L. Dull, H.S. Mosher, J. Org. Chem. 34 (1969) 2543.
[16] X-ray crystal structure analysis of (−)-**13a**: formula $C_{21}H_{29}NO_3$, $M = 343.45$, colourless crystal $0.25 \times 0.20 \times 0.10$ mm, $a = 7.267(2)$, $b = 10.064(2)$, $c = 13.385(3)$ Å, $\beta = 94.51(2)°$, $V = 975.9(4)$ Å^3, $\rho_{calc} = 1.169$ g cm^{-3}, $\mu = 6.13$ cm^{-1}, empirical absorption correction via ψ scan data ($0.862 \leq T \leq 0.941$), $Z = 2$, monoclinic, space group $P2_1$ (no. 4), $\lambda = 1.54178$ Å, $T = 223$ K, $\omega/2\theta$ scans, 2274 reflections collected ($-h$, $+k$, $\pm l$), [(sin θ)/λ] = 0.62 Å^{-1}, 2109 independent ($R_{int} = 0.017$) and 1823 observed reflections [$I \geq 2\sigma(I)$], 242 refined parameters, $R = 0.037$, $wR^2 = 0.097$, max. residual electron density 0.14 (−18) e Å^{-3}, Flack parameter −0.1(3), positional disorder at 011, refined with split positions (0.74(1): 0.26(1)), hydrogens calculated and refined as riding atoms. Data set was collected with an Enraf–Nonius CAD4 diffractometer. Programs used: data collection EXPRESS (Nonius B.V., 1994), data reduction MOLEN (K. Fair, Enraf–Nonius B.V., 1990), structure solution SHELXS-97 (G.M. Sheldrick, Acta Crystallogr., Sect. A 46 (1990) 467), structure refinement SHELXL-97 (G.M. Sheldrick, Universität Göttingen, 1997), graphics SCHAKAL (E. Keller, Universität Freiburg, 1997).
[17] We have carried out PM3 calculations on the diastereomorphic transition states and found a difference of $\Delta\Delta H^{\ddagger}$ of 2.6 kcal mol^{-1} in favour of the observed reaction path. However, for the sake of simplicity, the ligand (−)-sparteine was removed from the model compounds.
[18] For benzylic substitution reactions see: (a) C. Derwing, D. Hoppe, Synthesis (1996) 149. (b) A. Carstens, T. Krämer, D. Hoppe, Angew. Chem. (1990) 102, 1455. (c) P. Beak, A. Basu, D.J. Gallagher, Y.S. Thayumanavan, Acc. Chem. Res. 29 (1996) 552. (d) F. Hammerschmidt, A. Hanninger, Chem. Ber. 128 (1995) 1069.
[19] (a) D. Hoppe, M. Paetow, F. Hintze, Angew. Chem. 105 (1993) 430; Angew. Chem. Int. Ed. Engl. 32 (1993) 394. (b) M. Paetow, M. Kotthaus, M. Grehl, R. Fröhlich, D. Hoppe, Synlett (1994) 1034. (c) S. Norsikian, I. Marek, S. Klein, J.F. Poisson, J.F. Normant, Chem. Eur. J. 5 (1999) 2055.
[20] The configuration and the enantiomeric purity of (−)-**18** or of its precursors could not be assessed. In analogy to the cyclopropane **14**, the proposed absolute configuration and a high enantiomeric excess are most likely.
[21] The enantiomeric excess could not be determined.