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(–)-Myrtenyl *N*,*N*-Diisopropylcarbamate: Stereochemistry of Lithiation and Electrophilic Substitution Directed by Dynamic Kinetic Diastereoisomer Resolution

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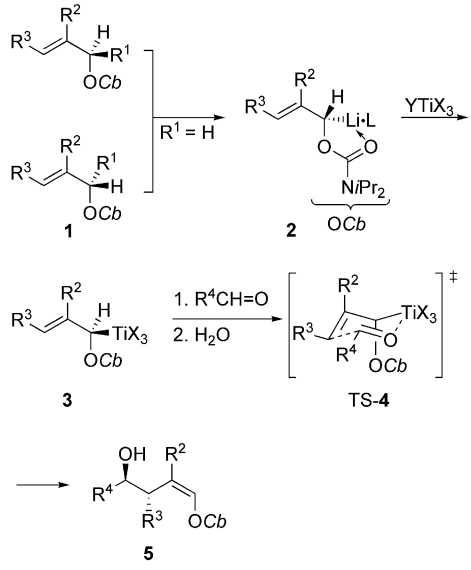
(–)-Myrtenyl *N*,*N*-diisopropylcarbamate was lithiated by butyllithium in the presence of achiral and chiral ligands, followed by quench with several electrophiles. The ratio of diastereomeric products allows conclusions regarding the configurational stability of both diastereomeric lithium intermediates and the influence of kinetic diastereoisomer resolution in the substitution step.

Introduction

Metallated alk-2-en-1-yl *N*,*N*-diisopropylcarbamates like **2** turned out to be valuable homoenolate reagents,[1] in particular for enantioselective homoaldol reactions with aldehydes (or ketones).[2] The reagents are either accessible by stereospecific deprotonation of enantiopure starting materials by means of butyllithium/tetramethylethylenediamine (TMEDA),[3] by deprotonation of achiral precursors with butyllithium/(–)-sparteine[4] or chiral surrogates,[5] or by kinetic resolution of racemates[6] (Scheme 1).

The stereoselectivity in the formation of addition products **5** via a pericyclic Zimmerman–Traxler transition state[7] is dramatically enhanced by lithium/titanium exchange (**2** → **3**),[8] which usually – but not in all cases[9] – proceeds with inversion of configuration from the *endo*-α-lithioallyl carbamate, thus furnishing a high degree of chirality transfer.

The efficiency of the enantiomeric excess depends on the selectivity of proton transfer and the configurational stability of the lithium intermediate **2**. Configurationally labile intermediates undergo an equilibrium of the diastereoisomers **2** and may form essentially one diastereoisomer in a dynamic thermodynamic resolution according to P. Beak.[10] The stereochemical outcome is even less predicable if the equilibrium between **2** and *epi*-**2** is rather mobile, and its rate is similar to that of the addition step – giving rise to a dynamic kinetic resolution. Here, any simple relationship between the configurational ratio in intermediates and products is lost.



Scheme 1. Enantio- and diastereoselective homoaldol reaction of **1**.

We now studied the lithiation and the electrophilic substitution of the more complex allyl carbamate **6** more closely.

Results and Discussion

Deprotonation, Silylation, and Related Reactions

(–)-Myrtenyl *N*,*N*-diisopropylcarbamate (**6**) was investigated in our group on several occasions (Scheme 2).[11] A smooth deprotonation of **6** was already observed by A. Brönneke during his dissertation in 1983.[12] In principle, resulting from two diastereoisomers **7** and *epi*-**7**, the six diastereoisomers/regioisomers **8**–**12** are possible, of which the γ-addition products **10** and **12** are less likely since for their

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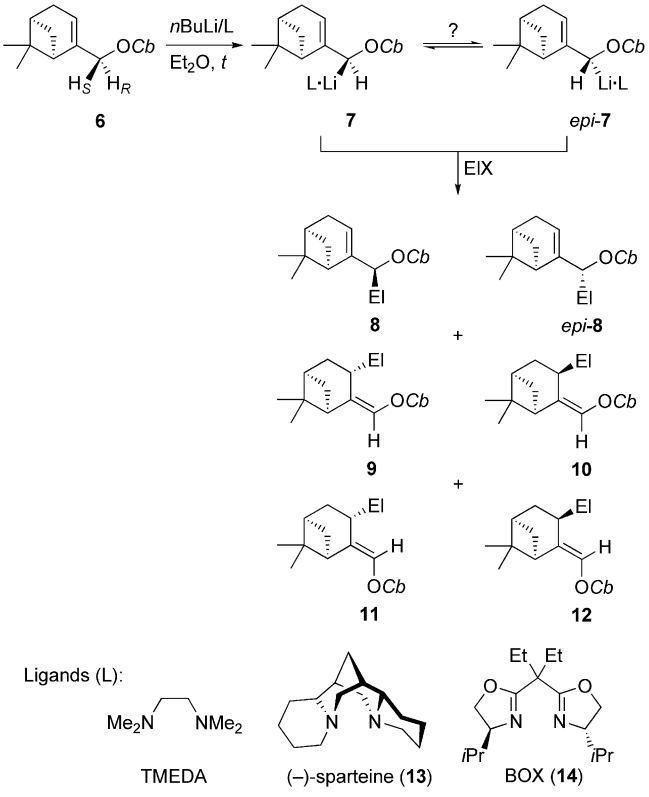
formation the attack of the electrophile at the six-membered ring has to occur from the front face bearing the bulky isopropylidene bridge. Compounds **11** and **12** arise from the unfavorable *exo* conformation of **7**.



Scheme 2. Possible isomers formed after deprotonation of **6** in the presence of different diamines and following reaction with electrophiles (ElX).

First, myrtenyl carbamate **6** was deprotonated in the presence of different ligands, and the diastereomeric lithium compounds were trapped with electrophiles (Scheme 2, Table 1).

Due to several previous investigations, the configuration of the products allow for a direct conclusion on the lithium precursor: silylation and stannylation in the α-position proceed with inversion.[1f,13] The stereochemistry of borylation depends on the structure: retention for boric esters,[14] inversion for trialkylboranes.[15]

Essentially complete attack of silicon electrophiles from the more shielded top face of the enollithium component forming **8a** and **8b** was observed independently of the diamine ligand used: TMEDA (Entries 1, 2 and 6), (–)-sparteine (**13**) (Entry 3) or bulky C_2-symmetrical bis(oxazoline) ligand (BOX) **14**[16] (Entries 4 and 7). Surprisingly, BOX ligand *ent*-**14** causes a similar ratio (Entry 5), indicating that its chiral sense has less influence on the ratio than its both residues. The configuration of the newly formed stereogenic centres was confirmed by derivatisation (see below).

Similar results are found for the stannylation (Entries 8–10), but interestingly a second γ-isomer **11c** is found, having (*E*) configuration of the double bond. This fact counts for *epi*-**7** as the intermediate; for an *anti*-S_E' attack from the less hindered face the "carbanion" has to occupy its *exo* confuguration. The configuration of both, the introduced stereogenic centre and the double bond, was confirmed by means of NOE experiments (Figure 1).

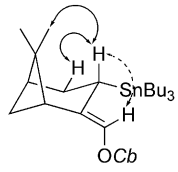
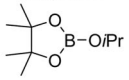
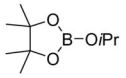


Figure 1. NOE enhancements of **11c**.

A further argument for the overwhelming reaction of diastereoisomer *epi*-**7** is the formation of essentially pure boronate *epi*-**8e** (Entries 11 and 12). We recently found that boronic esters, such as **15**, react with lithiated allyl carbamates with retention of the configuration,[14] presumably

Table 1. Metal exchange in **7**/*epi*-**7**.

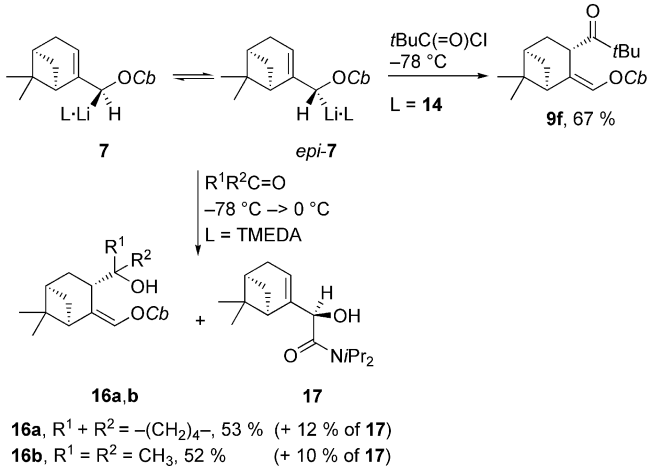
Entry	L	ElX	Deprotonation time (*t*)	Products	Yield (%)	Ratio
1	TMEDA	Me_3SiCl	2 h	**8a**, *epi*-**8a**	87[a]	56:44[b]
2	TMEDA	Me_3SiOTf	4 h	**8a**, *epi*-**8a**	55	90:10[b]
3	(–)-sparteine (**13**)	Me_3SiCl	30 min	**8a**, *epi*-**8a**	84	74:26[b]
4	BOX (**14**)	Me_3SiCl	4 h	**8a**, *epi*-**8a**	81	> 97:3[b]
5	BOX (*ent*-**14**)	Me_3SiCl	4 h	**8a**, *epi*-**8a**	77	93:7[c]
6	TMEDA	Et_3SiCl	2 h	**8b**, *epi*-**8b**	69	8:92[b]
7	BOX (**14**)	Et_3SiCl	4 h	**8b**, *epi*-**8b**	87	93:7[b]
8	TMEDA	Bu_3SnCl	2 h	**8c**, **11c**	89	74:26[c]
9	BOX (**14**)	Bu_3SnCl	4 h	**8c**, **11c**	71[d]	85:15[c]
10	BOX (**14**)	Ph_3SnCl	4 h	**8d**	63	≥ 97:3[c]
11	TMEDA	 **15**	2 h	*epi*-**8e**	69[e]	≥ 97:3[c]
12	BOX (**14**)	 **15**	4 h	*epi*-**8e**	65	≥ 97:3[c]

[a] Conversion, determined by ^{1}H NMR analysis of the crude product. [b] Determined by GC analysis of the crude product. [c] Determined by ^{1}H NMR analysis of the crude product. [d] Yield calculated on the isolated major isomer. [e] In addition, 16% of **17** was isolated (see below).

due to a bonding interaction of the alkoxy group with the lithium cation in the transition state. This reaction course was also confirmed by Aggarwal et al.[14,15]

Homoaldol Reactions

The lithium compounds add ketones, aldehydes, and even bulky acyl chlorides onto the less hindered "rear face" to afford the homoaldol products **16a**, **16b**, or **9f**, which result from the γ-*syn* addition reaction of diastereoisomers *epi*-**7** (Scheme 3). Since the reaction mixture with ketones was warmed up to 0 °C, carboxamide **17** was formed in 10–12% yield and a 95:5 *dr*. This migration of the carbamoyl group has been observed several times and was first reported by Nakai et al.[17]



Scheme 3. Reaction of lithiated myrtenyl carbamate **6** with ketones and acyl chlorides.

Fortunately, **9f** gave suitable crystals for X-ray analysis (Figure 2) to allow the determination of the configuration of the newly formed stereogenic centre (*R*) and of the double bond (*Z*).

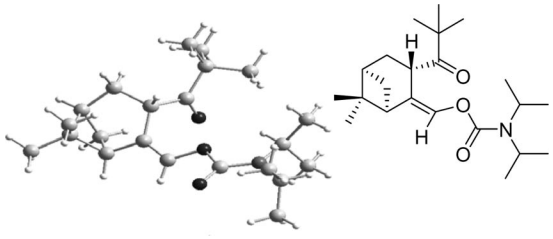
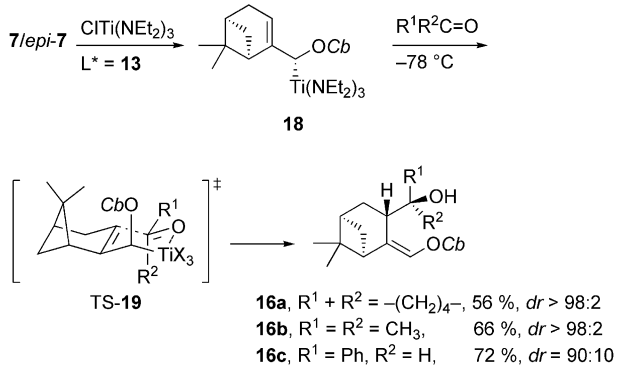


Figure 2. X-ray structure of **9f**.[18,19]

After titanium exchange with $ClTi(NEt_2)_3$, the reaction with cyclopentanone as well as with acetone led to the formation of **16a** and **16b** as single products in 56% and 66% yield, respectively (Scheme 4). These moderate yields are probably due to the steric hindrance of the large residues in the Zimmerman–Traxler transition state TS-**19**. Surprisingly, the configuration of both homoallylic alcohols arising from the lithium and the titanium method, are identical, which means that a dynamic kinetic resolution must play a major role either in the lithium/titanium exchange or in the carbonyl addition. On the other hand, the reaction with benzaldehyde furnished **16c** in 72% yield and a diastereomeric ratio of 90:10 (Scheme 4). The configuration of the newly formed stereogenic centres, as well as the (*Z*) configuration of the double bond, were determined by X-ray crystallography (Figure 3).



Scheme 4. Titanium-mediated homoaldol reaction of myrtenyl carbamate **6**.

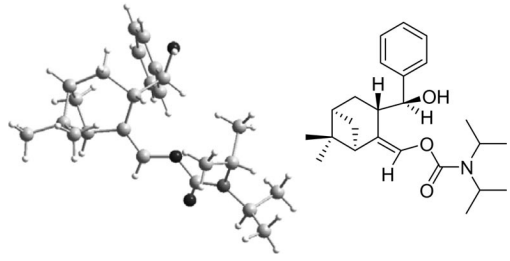
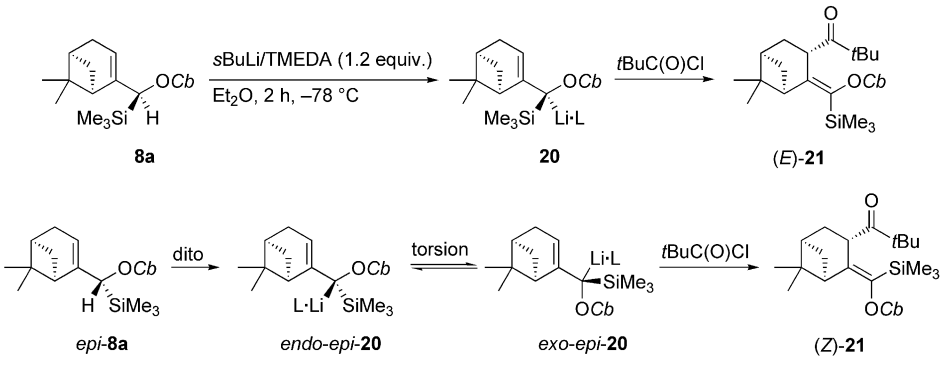


Figure 3. X-ray structure of **16c**.[18,20]

Stereochemistry of the Silylated Substitution Products

It was desirable to compare the stereochemical properties of similar, but configurationally stable ion pairs with those of unpersistent ones described below. In our previous study we gained evidence for the fact that α-silyl groups in the lithiated allyl carbamates enhance the configurational stability.[21] The acidic proton α to the silicon residue[22] of **8a** and *epi*-**8a** was removed with *sec*-butyllithium, which is expected to proceed with retention of the configuration. This leads to the diastereoisomeric lithium carbanions **20**, *endo*-*epi*-**20** and *exo*-*epi*-**20**, which react with pivaloyl chloride to form ketones (*E*)- and (*Z*)-**21** in distinguished ratios (92:8 and 82:18, respectively) (Scheme 5). The attack of the acyl chloride has to take place in a pericyclic reaction from the less hindered face. The intermediate *endo*-*epi*-**20** must turn the O*Cb* group to the *exo* face. The different double-bond geometries as well as the relative configuration at the γ-C atom were proven by NOE experiments (Figure 4).

For comparison, (*E*)-**21** (87%, *dr* > 98:2) was also formed from vinylsilane **22** (Scheme 6) by γ-deprotonation.[11b] This result and further mechanistic investi-



8a/*epi*-8a[a]	Yield (%)	(*E*)-21/(*Z*)-21
87:13	83	92:8
91:9	86	82:18

[a] Determined by GC analysis. [b] Determined by GC analysis of the crude product.

Scheme 5. Deprotonation of **8a** and *epi*-**8a** followed by reaction with pivaloyl chloride.

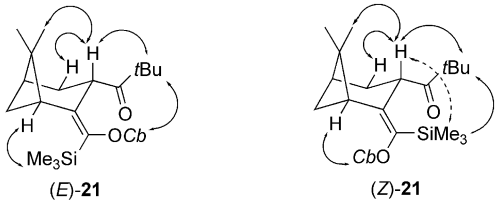
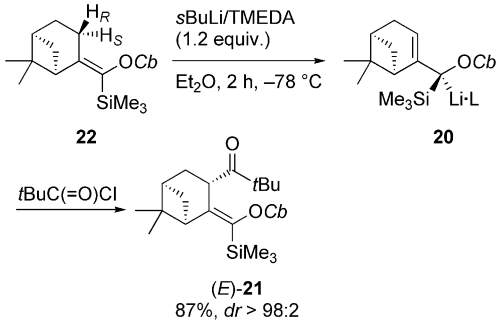


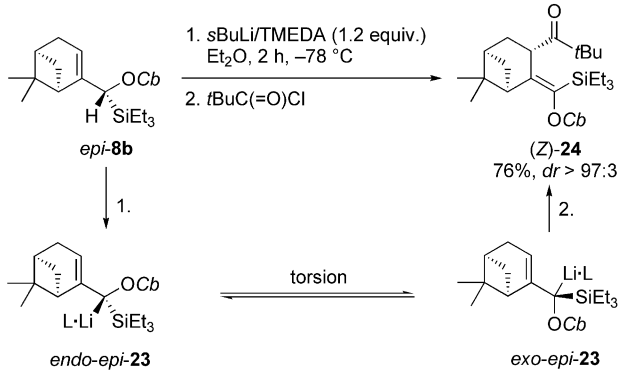
Figure 4. NOE enhancements for (*E*)-**21** and (*Z*)-**21**.

gations[23] allow to consider the lithiated intermediate **20** as configurationally stable, which confirmed the proposed configuration of **8a** and *epi*-**8a**.



Scheme 6. Synthesis of (*E*)-**21** by γ-deprotonation of **22**.

The triethylsilane *epi*-**8b** (*dr* > 97:3) afforded analogously the ketone (*Z*)-**24** in 76% yield and a very good diastereomeric ratio of 95:5 (Scheme 7). This was a further argument for the configuration of *epi*-**8b** and the proposed stereochemical pathway.



Scheme 7. Reaction of *epi*-**8b** with pivaloyl chloride.

Conclusions

Lithiation of the myrtenyl carbamate **6** leads to two diastereoisomers, which are, even at –78 °C, interconverting. Thus, the influence of ligands at the lithium cation on the equilibrium can not be determined. The selectivity is mainly governed by a kinetic diastereomer resolution. However, the high diastereoselectivities (> 97:3) in the substitution reactions in the presence of the bulky BOX ligand **14** point to the following assumption: the equilibrium **7**/*epi*-**7** is shifted to the side of the less hindered complex *epi*-**7**, and the equilibration proceeds slowly. Substitution of the lithium compound **7** by electrophiles proceeds in a way that can be explained by stereochemical preference of the particular electrophile. Due to the very different accessibilities of both faces at the six-membered ring, γ-substitution proceeds exclusively from the face of the methylene bridge.

Experimental Section

General Remarks: All solvents were dried and purified prior to use: toluene and Et_2O were distilled from sodium/benzophenone, THF was distilled from potassium/benzophenone, and CH_2Cl_2 was distilled from powdered CaH_2. *N*,*N*,*N*′,*N*′-Tetramethylethylenediamine (TMEDA) was distilled from powdered CaH_2 and stored under Ar in the dark. (–)-Sparteine (**13**) was kept under Ar in a refrigerator after the original bottles had been opened. Solutions of *sec*-butyllithium (ca. 1.3 M in cyclohexane/hexane, 92:8) were filtered through Celite under Ar and stored in glass bottles sealed with septa. The exact concentration was determined by titration with diphenylacetic acid.[24] *n*-Butyllithium (1.6 M in hexanes) and all other commercially available reagents were used as received. All reactions were performed under Ar in flame-dried glassware sealed with a rubber septum. Flash column chromatography (FCC) was performed on Merck 60 silica gel (40–63 μm) and monitored by thin-layer chromatography (TLC) on Merck 60 F254 TLC plates. NMR: ^1H and ^{13}C NMR spectra were measured with Bruker AV300, ARX300, DPX300, AV400 and ARX400 instruments and Varian 500 Inova and 600 Unity Plus spectrometers. ^1H shifts are related to $SiMe_4$ (δ_H = 0.00 ppm) or to the residual content of $CHCl_3$ (δ_H = 7.24 ppm) and ^{13}C shifts to $CDCl_3$ (δ_C = 77.0 ppm). Peak multiplicities in the ^1H NMR spectra are abbreviated as s (singlet), d (doublet), t (triplet), m (multiplet), and br. (broad). Diastereotopic methylene protons with different chemical shifts are abbreviated as H_A and H_B. IR: Varian 3100 Excalibur Series with Specac Golden Gate Single Reflection ATR. MS: Bruker MicroTof (ESI). Optical rotations: Perkin–Elmer 341. Melting points: Stuart Scientific SMP3. Melting points are not corrected. Elemental analyses: Elementar-Analysensysteme Vario EL III. GC: Agilent 6890; 30 m × 0.32 mm HP-5; 1.5 mL min^{-1} H_2; start at 50 °C, 10 °C min^{-1}, end at 300 °C, 15 min at 300 °C.

Deprotonation of 6 and Substitution with Electrophiles

General Procedure: *n*BuLi (1.2 equiv.) was added dropwise to a solution of myrtenyl carbamate **6** (1.0 equiv.) and the applied diamine ligand (1.2 equiv.) in Et_2O (7 mL mmol^{-1}) at –78 °C. After a certain deprotonation time, the corresponding electrophile (1.5–3.0 equiv.) was added slowly within 5 min. The mixture was stirred for a certain additional time and was quenched by addition of a satd. aq. NH_4Cl solution (15 mL mmol^{-1}). After warming up to room temp. and addition of Et_2O or TBME (15 mL mmol^{-1}), the organic layer was removed. The aqueous phase was extracted three times with Et_2O or TBME (15 mL mmol^{-1} each). The combined organic layers were dried with $MgSO_4$ and concentrated under reduced pressure. Purification by column chromatography yielded the corresponding product.

Reaction with TMSCl: (*S*)- and (*R*)-{(1*R*,5*R*)-6,6-Dimethylbicyclo[3.1.1]hept-2-en-2-yl}(trimethylsilyl)methyl *N*,*N*-Diisopropylcarbamate (8a and *epi*-8a)

Deprotonation with TMEDA: According to the General Procedure, **6** (422 mg, 1.5 mmol, 1.0 equiv.) was deprotonated with *n*BuLi (1.1 mL, 1.8 mmol, 1.3 equiv.) and TMEDA (208 mg, 1.8 mmol, 1.2 equiv.) for 2 h and treated with TMSCl (485 mg, 4.4 mmol, 3.0 equiv.) for 4 h. Conversion and *dr* were determined by ^1H NMR analysis of the crude product (87% conversion, *dr* = 56:44).

Deprotonation with (–)-Sparteine (13): According to the General Procedure, **6** (279 mg, 1.3 mmol, 1.0 equiv.) was deprotonated with *n*BuLi (0.81 mL, 1.3 mmol, 1.3 equiv.) and **13** (305 mg, 1.3 mmol, 1.3 equiv.) for 30 min and treated with TMSCl (163 mg, 1.5 mmol, 1.5 equiv.) for 1 h to yield after purification by column chromatography (Et_2O/PE, 1:20) *epi*-**8a** (79 mg, 0.22 mmol, 22%) and **8a** (215 mg, 0.68 mmol, 68%) (*dr* = 74:26).

Deprotonation with BOX Ligand 14: According to the General Procedure, **6** (87 mg, 0.31 mmol, 1.0 equiv.) was deprotonated with *n*BuLi (0.25 mL, 0.4 mmol, 1.3 equiv.) and **14** (139 mg, 0.47 mmol, 1.5 equiv.) for 4 h and treated with TMSCl (97 mg, 0.89 mmol, 2.8 equiv.) for 2 h to yield after column chromatography (Et_2O/PE, 1:20) **8a** (87 mg, 0.25 mmol, 81%, *dr* ≥ 97:3) as a colorless liquid.

Deprotonation with BOX Ligand *ent*-14: According to the General Procedure, **6** (88 mg, 0.31 mmol, 1.0 equiv.) was deprotonated with *n*BuLi (0.25 mL, 0.4 mmol, 1.3 equiv.) and *ent*-**14** (110 mg, 0.37 mmol, 1.2 equiv.) for 4 h and treated with TMSCl (99 mg, 0.91 mmol, 2.9 equiv.) for 2 h to furnish after column chromatography (Et_2O/PE, 1:20) **8a** (86 mg, 0.24 mmol, 77%) as a colorless liquid (*dr* = 93:7). t_R = 16.7 min (HP5). R_F = 0.51 (Et_2O/PE, 1:4). $[\alpha]_D^{20}$ = –31.2 (*c* = 0.97, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 0.05 (s, 9 H, 2′-H), 0.83 (s, 3 H, 8/9-H), 1.20 (br. s and m, 13 H, 7-H_A, CH_3-*Cb*), 1.23 (s, 3 H, 8/9-H), 2.06 (m, 1 H, 5-H), 2.18 (t, $^3J_{H,H}$ = 5.4 Hz, 1 H, 1-H), 2.25 (br. s, 2 H, 4-H), 2.38 (ddd, $^3J_{H,H}$ = 5.6, $^2J_{H,H}$ = 8.4 Hz, 1 H, 7-H_B), 3.77, 4.04 (2 br. s, 2 H, CH-*Cb*), 5.03 (s, 1 H, 1′-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = –2.7 (C-2′), 20.7, 21.6 (CH_3-*Cb*), 21.3, 26.4 (C-8, C-9), 31.4 (C-4), 32.0 (C-7), 37.6 (C-6), 40.8 (C-5), 43.6 (C-1), 45.2, 46.3 (CH-*Cb*), 72.8 (C-1′), 117.1 (C-3), 146.1 (C-2), 155.8 (C_{CO}-*Cb*) ppm. IR (ATR): $\tilde{\nu}$ = 2962, 2929, 2831 (C–H), 1699 (C=O), 1650 (C=C) cm^{-1}. MS (ESI): *m*/*z* = 374.25 [M + Na^+]. $C_{20}H_{37}NO_2Si$ (351.60): calcd. C 68.32, H 10.61, N 3.98; found C 68.33, H 10.70, N 3.86.

***epi*-8a:** t_R = 16.3 min (HP5). R_F = 0.57 (Et_2O/PE, 1:4). $[\alpha]_D^{20}$ = +15.0 (*c* = 1.04, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ = 0.05 (s, 9 H, 2′-H), 0.87 (s, 3 H, 8/9-H), 1.15 (d, $^2J_{H,H}$ = 8.5 Hz, 1 H, 7-H_A), 1.21 (d, $^3J_{H,H}$ = 6.5 Hz, 12 H, CH_3-*Cb*), 1.26 (s, 3 H, 8/9-H), 2.03–2.06 (m, 2 H, 1-H, 5-H), 2.20 (dm, $^2J_{H,H}$ = 17.4 Hz, 1 H, 4-H_A), 2.29 (dm, 1 H, 4-H_B), 2.34 (dt, $^3J_{H,H}$ = 5.6 Hz, 1 H, 7-H_B), 3.92 (br. s, 2 H, CH-*Cb*), 4.90 (s, 1 H, 1′-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = –2.9 (C-2′), 20.7, 21.5 (CH_3-*Cb*), 21.3, 26.5 (C-8, C-9), 31.2 (C-4), 31.5 (C-7), 38.0 (C-6), 40.8 (C-5), 44.6 (C-1), 45.7, 46.2 (CH-*Cb*), 72.3 (C-1′), 115.0 (C-3), 147.0 (C-2), 155.4 (C_{CO}-*Cb*) ppm. IR (ATR): $\tilde{\nu}$ = 2965, 2926, 2873, 2826 (C–H), 1696 (C=O) cm^{-1}. MS (ESI): *m*/*z* = 374.25 [M + Na^+]. $C_{20}H_{37}NO_2Si$ (351.60): calcd. C 68.32, H 10.61, N 3.98; found C 68.19, H 10.72, N 3.80.

Reaction with TMSOTf: According to the General Procedure, **6** (84 mg, 0.30 mmol, 1.0 equiv.) was deprotonated with *n*BuLi (0.25 mL, 0.4 mmol, 1.3 equiv.) and TMEDA (40 mg, 0.34 mmol, 1.2 equiv.) for 4 h and treated with TMSOTf (0.18 mL, 0.9 mmol, 3.0 equiv.) for 1 h to furnish after column chromatography (Et_2O/PE, 1:20) **8a** (61 mg, 0.17 mmol, 55%) as a colorless liquid (*dr* = 90:10). For analytical data, see above.

Reaction with TESCl: (*S*)- and (*R*)-{(1*R*,5*R*)-6,6-Dimethylbicyclo[3.1.1]hept-2-en-2-yl}(triethylsilyl)methyl *N*,*N*-Diisopropylcarbamate (8b and *epi*-8b)

Deprotonation with TMEDA: According to the General Procedure, **6** (143 mg, 0.51 mmol, 1.0 equiv.) was deprotonated with *n*BuLi (0.38 mL, 0.61 mmol, 1.2 equiv.) and TMEDA (75 mg, 0.65 mmol, 1.3 equiv.) for 2 h and treated with TESCl (235 mg, 1.56 mmol, 3.1 equiv.) for 2 h to yield after column chromatography (Et_2O/PE, 1:15) *epi*-**8b** (136 mg, 0.35 mmol, 69%) as a colorless liquid (*dr* = 92:8).

Deprotonation with BOX Ligand 14: According to the General Procedure, **6** (85 mg, 0.31 mmol, 1.0 equiv.) was deprotonated with *n*BuLi (0.25 mL, 0.40 mmol, 1.3 equiv.) and **14** (113 mg,

0.38 mmol, 1.2 equiv.) for 4 h and treated with TESCl (145 mg, 0.96 mmol, 3.1 equiv.) for 2 h to yield after purification by column chromatography (Et_2O/PE, 1:20) **8b** (136 mg, 0.20 mmol, 87%) as a colorless liquid (*dr* = 93:7).

8b: t_R = 19.0 min (HP5). R_F = 0.59 (Et_2O/PE, 1:4). $[\alpha]_D^{20}$ = –33.8 (*c* = 0.95, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 0.61 (dddd, $^2J_{H,H}$ = 11.6, $^3J_{H,H}$ = 7.9, $^4J_{H,H}$ = 3.1 Hz, 6 H, 2′-H), 0.81 (s, 3 H, 8-H), 0.97 (t, 3 H, 3′-H), 1.19 (m, 13 H, CH_3-*Cb*, 7-H_A), 1.23 (s, 3 H, 9-H), 2.06 (m, 2 H, 5-H), 2.17 (dt, $^3J_{H,H}$ = 5.6 Hz, 1 H, 1-H), 2.25 (m, 2 H, 4-H), 2.38 (dt, $^2J_{H,H}$ = 8.5 Hz, 1 H, 7-H_B), 3.85, 3.93 (2 br. s, 2 H, CH-*Cb*), 5.20 (d, $^4J_{H,H}$ = 0.9 Hz, 1 H, 1′-H), 5.34 (dd, $^3J_{H,H}$ = 2.6, $^3J_{H,H}$ = 1.4 Hz, 1 H, 3-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 2.6 (C-2′), 7.5 (C-3′), 20.7 (CH_3-*Cb*), 21.3 (C-8), 21.4 (CH_3-*Cb*), 26.4 (C-9), 31.4 (C-4), 32.0 (C-7), 37.6 (C-6), 40.7 (C-5), 43.4 (C-1), 45.6 (CH-*Cb*), 45.8 (CH-*Cb*), 70.6 (C-1′), 117.5 (C-3), 146.3 (C-2), 155.2 (C_{CO}-*Cb*) ppm. IR (ATR): $\tilde{\nu}$ = 2953 (C–H), 1698 (C=O), 1427, 1322, 1157, 1046, 633 cm^{-1}. MS (ESI): *m*/*z* = 416.30 [M + Na^+]. $C_{23}H_{43}NO_2Si$ (393.68): calcd. C 70.17, H 11.01, N 3.56; found C 69.80, H 11.23, N 3.47.

***epi*-8b:** t_R = 18.8 min (HP5). R_F = 0.66 (Et_2O/PE, 1:4). $[\alpha]_D^{20}$ = +20.0 (*c* = 1.00, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 0.61 (q, $^3J_{H,H}$ = 7.9 Hz, 6 H, 2′-H), 0.87 (s, 3 H, 8-H), 0.94 (t, 3 H, 3′-H), 1.16 (d, $^2J_{H,H}$ = 8.5 Hz, 1 H, 7-H_A), 1.22 (d, $^3J_{H,H}$ = 6.7 Hz, 12 H, CH_3-*Cb*), 1.27 (s, 3 H, 9-H), 2.02 (m, 2 H, 1-H, 5-H), 2.22 (m, 2 H, 4-H), 2.34 (m, 1 H, 7-H_B), 3.78, 4.06 (2 br. s, 2 H, CH-*Cb*), 5.00 (d, $^4J_{H,H}$ = 1.7 Hz, 1 H, 1′-H), 5.23 (dd, $^3J_{H,H}$ = 2.9 Hz, 1 H, 3-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 2.3 (C-2′), 7.4 (C-3′), 20.9 (CH_3-*Cb*), 21.2 (C-8, CH_3-*Cb*), 26.4 (C-9), 31.3 (C-7), 31.5 (C-4), 38.1 (C-6), 40.8, 44.6 (C-1,C-5), 45.8 (CH-*Cb*), 69.8 (C-1′), 114.7 (C-3), 147.0 (C-2), 154.8 (C_{CO}-*Cb*) ppm. IR (ATR): $\tilde{\nu}$ = 2953, 2913 (C–H), 1699 (NC=O), 1427, 1377, 1321, 1046, 1030, 723 cm^{-1}. MS (ESI): *m*/*z* = 416.30 [M + Na^+]. $C_{23}H_{43}NO_2Si$ (351.60): calcd. C 70.17, H 11.01, N 3.56; found C 69.94, H 11.13, N 3.37.

Reaction with Bu_3SnCl: (*S*)-{(1*R*,5*R*)-6,6-Dimethylbicyclo[3.1.1]-hept-2-en-2-yl}(tributylstannyl)methyl *N*,*N*-Diisopropylcarbamate (8c) and {(1*R*,2*E*,3*S*,5*R*)-6,6-Dimethyl-3-(tributylstannyl)bicyclo-[3.1.1]hept-2-ylidene}methyl *N*,*N*-Diisopropylcarbamate (11c)

Deprotonation with TMEDA: According to the General Procedure, **6** (1.410 g, 5.05 mmol, 1.0 equiv.) was deprotonated with *n*BuLi (3.9 mL, 6.24 mmol, 1.2 equiv.) and TMEDA (705 mg, 6.06 mmol, 1.2 equiv.) for 2 h and treated with Bu_3SnCl (2.489 g, 7.65 mmol, 1.5 equiv.) for 3 h to yield after purification by column chromatography (Et_2O/PE, 1:50) **8c** and **11c** as two yellowish liquids: (i) pure **8c** (354 mg, 0.62 mmol, 12%); (ii) mixtures **8c/11c** (ratio = 77:23) (1.200 g, 2.11 mmol, 42%) and **11c/8c** (ratio = 81:19) (1.012 g 1.78 mmol, 35%). Total yield: 2.212 g, 3.89 mmol, 89%, **8c/11c** = 74:26. **11c** was purified by a second column chromatography for analysis.

Deprotonation with BOX Ligand 14: According to the General Procedure, **6** (152 mg, 0.52 mmol, 1.0 equiv.) was deprotonated with *n*BuLi (0.41 mL, 0.66 mmol, 1.3 equiv.) and **14** (191 mg, 0.65 mmol, 1.3 equiv.) for 4 h and treated with Bu_3SnCl (256 mg, 0.79 mmol, 1.5 equiv.) for 2 h to yield after purification by column chromatography (Et_2O/PE, 1:50) **8c** (212 mg, 0.37 mmol, 71%) as a colorless liquid (**8c/11c** = 85:15).

8c: R_F = 0.80 (Et_2O/PE, 1:4). $[\alpha]_D^{20}$ = –6.6 (*c* = 1.33, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 0.89 (m, 18 H, 8-H, 2′-H, 5′-H), 1.20 (d, $^3J_{H,H}$ = 6.9 Hz, 13 H, 7-H_A, CH_3-*Cb*), 1.29 (m, 9 H, 9-H, 4′-H), 1.49 (m, 6 H, 3′-H), 2.09 (m, 2 H, 1-H, 5-H), 2.27 (m, 2 H, 4-H), 2.38 (m, 1 H, 7-H_B), 3.86 (br. s, 2 H, CH-*Cb*), 5.20 (d, $^4J_{H,H}$ = 1.4 Hz, 1 H, 3-H), 5.32 (m, 1 H, 1′-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 10.3 (C-2′), 13.7 (C-5′), 20.6 (CH_3-*Cb*), 21.4 (CH_3-*Cb*), 21.4 (C-8), 26.3 (C-9), 27.5 (C-4′), 29.1 (C-3′), 31.2 (C-4), 31.9 (C-7), 37.9 (C-6), 40.9 (C-1/5), 43.8 (C-1/5), 45.2, 46.0 (CH-*Cb*), 73.4 (C-1′), 113.0 (C-3), 148.5 (C-2), 155.6 (C_{CO}-*Cb*) ppm. IR (ATR): $\tilde{\nu}$ = 2955, 2919 (C–H), 2872, 1673 (NC=O), 1434, 1335, 1308, 1047 cm^{-1}. MS (ESI): *m*/*z* = 592.32 [M + Na^+]. $C_{29}H_{55}NO_2Sn$ (568.46): calcd. C 61.27, H 9.75, N 2.46; found C 61.34, H 9.48, N 2.43.

11c: R_F = 0.64 (Et_2O/PE, 1:4). $[\alpha]_D^{20}$ = +178.3 (*c* = 1.06, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 0.74 (s, 3 H, 8-H), 0.86 (m, 15 H, 2′-H, 5′-H), 1.28 (m, 18 H, 4′-H, CH_3-*Cb*), 1.47 (m, 7 H, 7-H_A, 3′-H), 2.02 (m, 2 H, 1/5-H, 4-H_A), 2.21 (m, 1 H, 4-H_B), 2.30 (m, 2 H, 1/5-H, 7-H_B), 2.55 (dd, $^3J_{H,H}$ = 9.7, $^4J_{H,H}$ = 1.6, $^2J_{H,Sn}$ = 42.2 Hz, 1 H, 3-H), 3.68, 4.16 (2 br. s, 2 H, CH-*Cb*), 6.56 (dd, $^4J_{H,Sn}$ = 12.6 Hz, 1 H, 1′-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 9.9 (C-2′, $^1J_{H,Sn}$ = 151.4 Hz), 13.7 (C-5′), 16.6 (C-3), 20.8 (CH_3-*Cb*), 21.8 (C-8), 25.6 (C-9), 26.5 (C-7), 27.4 (C-4), 27.6 (C-3′/4′), 29.1 (C-3′/4′), 41.5 (C-1/5), 41.6 (C-6), 45.6 (CH-*Cb*), 46.4 (CH-*Cb*), 46.8 (C-1/5), 124.4 (C-1′), 129.0 (C-2), 152.2 (C_{CO}-*Cb*) ppm. IR (ATR): $\tilde{\nu}$ = 2956, 2919 (C–H), 2871, 1712 (NC=O), 1430, 1328, 1302, 1143, 1095, 1045 cm^{-1}. MS (ESI): *m*/*z* = 592.31 [M + Na^+]. $C_{29}H_{55}NO_2Sn$ (568.46): calcd. C 61.27, H 9.75, N 2.46; found C 61.25, H 9.59, N 2.38.

Reaction with Ph_3SnCl: (*S*)-{(1*R*,5*R*)-6,6-Dimethylbicyclo[3.1.1]-hept-2-ylidene)(triphenylstannyl)methyl *N*,*N*-Diisopropylcarbamate (8d): According to the General Procedure, **6** (89 mg, 0.32 mmol, 1.0 equiv.) was deprotonated with *n*BuLi (0.25 mL, 0.44 mmol, 1.4 equiv.) and **14** (140 mg, 0.48 mmol, 1.5 equiv.) for 4 h and treated with Ph_3SnCl (347 mg, 0.90 mmol, 2.8 equiv.) dissolved in Et_2O (1.5 mL) for 3 h to yield after purification by column chromatography (Et_2O/PE, 1:50) **8d** (89 mg, 0.22 mmol, 65%) as a colorless oil (*dr* ≥ 97:3).

8d: R_F = 0.64 (Et_2O/PE, 1:4). $[\alpha]_D^{20}$ = +17.3 (*c* = 0.93, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 0.46 (d, $^2J_{H,H}$ = 8.7 Hz, 1 H, 7-H_A), 0.77 (s, 3 H, 8-H), 1.03 (m, 12 H, CH_3-*Cb*), 1.15 (s, 3 H, 9-H), 1.90 (m, 1 H, 5-H), 1.97 (dt, $^3J_{H,H}$ = 5.7 Hz, 1 H, 7-H_B), 2.18 (m, 3 H, 1-H, 4-H), 3.68, 3.88 (2 br. s, CH-*Cb*), 5.38 (m, 1 H, 1′-H), 5.40 (d, $^4J_{H,H}$ = 1.0 Hz, 1 H, 3-H), 7.32 (m, 9 H, H_{Ar}), 7.59 (br. m, 6 H, H_{Ar}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.3 (CH_3-*Cb*), 20.3 (CH_3-*Cb*), 21.2 (CH_3-*Cb*), 21.2 (CH_3-*Cb*), 21.4 (C-8), 26.2 (C-9), 31.0 (C-7), 31.1 (C-4), 37.9 (C-6), 40.4 (C-5), 44.1 (C-1), 45.2 (CH-*Cb*), 46.3 (CH-*Cb*), 76.1 (C-3), 116.8 (C-1′), 128.0 (CH_{Ar}), 128.4 (CH_{Ar}), 137.4 (CH_{Ar}), 141.1 (C_{Ar}), 146.8 (C-2), 156.2 (C_{CO}-*Cb*) ppm. IR (ATR): $\tilde{\nu}$ = 3063 (C–H_{Ar}), 2970, 2916 (C–H), 1656 (NC=O), 1480, 1428, 1330, 1308, 1157, 1073, 1046, 726 (C–H_{Ar}), 697 (C–H_{Ar}) cm^{-1}. MS (ESI): *m*/*z* = 652.22 [M + Na^+]. $C_{35}H_{43}NO_2Sn$ (628.43): calcd. C 66.89, H 6.90, N 2.23; found C 67.03, H 7.24, N 2.18.

Reaction with 2-Isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane: (*R*)-{(1*R*,5*R*)-6,6-Dimethyl-bicyclo[3.3.1]hept-2-en-2-yl)(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl *N*,*N*-Diisopropylcarbamate (*epi*-8e)

Deprotonation with TMEDA: According to the General Procedure, **6** (289 mg, 2.97 mmol, 1.0 equiv.) was deprotonated with *n*BuLi (2.3 mL, 3.68 mmol, 1.2 equiv.) and TMEDA (407 mg, 3.50 mmol, 1.2 equiv.) for 2 h and treated with **15** (1.665 g, 8.95 mmol, 3.0 equiv.) for 2 h to furnish after column chromatography (Et_2O/PE, 1:2) *epi*-**8e** (816 mg, 2.01 mmol, 67%) as a colorless solid (*dr* ≥ 97:3) and side product **17** (132 mg, 0.47 mmol, 16%) as a colorless solid.

Deprotonation with BOX Ligand 14: According to the General Procedure, **6** (95 mg, 0.34 mmol, 1.0 equiv.) was deprotonated with

*n*BuLi (0.28 mL, 0.45 mmol, 1.3 equiv.) and **14** (142 mg, 0.48 mmol, 1.4 equiv.) for 4 h and treated with **15** (171 mg, 0.92 mmol, 2.7 equiv.) for 2 h to furnish after purification by column chromatography (Et_2O/PE, 1:2) *epi*-**8e** (89 mg, 0.22 mmol, 65%) as a colorless solid (*dr* ≥ 97:3).

***epi*-8e:** R_F = 0.33 (Et_2O/PE, 1:1). M.p. 73–75 °C (Et_2O). $[\alpha]_D^{20}$ = –13.5 (*c* = 0.98, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ = 0.91 (s, 3 H, 8-H), 1.16 (s, 6 H, 3′-H), 1.18 (s, 6 H, 3′-H), 1.26 (m, 15 H, 9-H, CH_3-*Cb*), 1.41 (d, $^2J_{H,H}$ = 8.6 Hz, 1 H, 7-H_A), 2.05 (m, 2 H, 1-H, 5-H), 2.20 (m, 1 H, 4-H_A), 2.33 (m, 2 H, 4-H_B, 7-H_B), 3.93, 4.04 (2 m, 2 H, CH-*Cb*), 4.13 (d, $^4J_{H,H}$ = 2.13 Hz, 1 H, 1′-H), 5.20 (m, 1 H, 3-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.3, 20.5, 20.6, 20.8 (CH_3-*Cb*), 21.2 (C-8), 25.2 (C-3′), 26.4 (C-9), 31.0 (C-4), 31.5 (C-7), 37.9 (C-6), 40.9 (C-1/5), 43.6 (C-1/5), 46.8 (CH-*Cb*), 48.2 (CH-*Cb*), 80.0 (C-1′, C-2′), 112.0 (C-3), 146.5 (C-2), 162.4 (C_{CO}-*Cb*) ppm. IR (ATR): $\tilde{\nu}$ = 2971, 2916 (C–H), 1614 (NC=O), 1499 (B–C), 1449, 1366 (B–O), 1195, 1154, 1112, 1033 cm^{-1}. MS (ESI): *m*/*z* = 428.29 [M + Na^+]. $C_{23}H_{40}BNO_4$ (405.38): calcd. C 68.15, H 9.95, N 3.46; found C 68.08, H 10.04, N 3.42.

17: For analytical data, see below.

Reaction with Pivaloyl Chloride: {(1*R*,2*Z*,3S,5*R*)-3-(2,2-Dimethylpropanoyl)-6,6-dimethylbicyclo[3.1.1]hept-2-ylidene]methyl *N*,*N*-Diisopropylcarbamate (9f): According to the General Procedure, **6** (85 mg, 0.30 mmol, 1.0 equiv.) was deprotonated with *n*BuLi (0.25 mL, 0.40 mmol, 1.3 equiv.) and **14** (129 mg, 0.44 mmol, 1.4 equiv.) for 4 h and treated with pivaloyl chloride (105 mg, 0.96 mmol, 2.9 equiv.) for 3 h to furnish after column chromatography (Et_2O/PE, 1:15 → 1:10) **9f** (72 mg, 0.20 mmol, 67%) as a colorless solid (*dr* = 95:5).

9f: t_R = 21.7 min (HP5). R_F = 0.34 (Et_2O/PE, 1:4). M.p. 80 °C (Et_2O). $[\alpha]_D^{20}$ = +63.8 (*c* = 0.86, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ = 0.79 (s, 3 H, 8-H), 1.21 (m, 12 H, CH_3-*Cb*), 1.23 (s, 3 H, 9-H), 1.26 (s, 9 H, 4′-H), 1.52 (d, $^2J_{H,H}$ = 5.5 Hz, 1 H, 7-H_A), 1.79 (dt, $^2J_{H,H}$ = 13.6, $^3J_{H,H}$ = 3.6 Hz, 1 H, 4-H_A), 1.97 (m, 1 H, 5-H), 2.25 (ddt, $^3J_{H,H}$ = 11.5 Hz, 1 H, 4-H_B), 2.31 (m, 1 H, 7-H_B), 2.43 (t, $^3J_{H,H}$ = 5.5 Hz, 1 H, 1-H), 3.63, 3.95 (2 br. s, 2 H, CH-*Cb*), 4.03 (ddd, $^4J_{H,H}$ = 1.8 Hz, 1 H, 3-H), 6.68 (d, 1 H, 1′-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.7 (CH_3-*Cb*), 21.7 (C-8), 25.6 (C-9), 26.9 (C-7), 28.1 (C-4), 28.2 (C-4′), 38.6 (C-3), 40.6 (C-6), 40.7 (C-5), 44.1 (C-3′), 46.5 (C-1, CH-*Cb*), 123.2 (C-2), 130.5 (C-1′), 151.7 (C_{CO}-*Cb*), 215.8 (C-2′) ppm. IR (ATR): $\tilde{\nu}$ = 2970, 2930 (C–H), 1700 (NC=O), 1436, 1333, 1309, 1140, 1105, 1043, 964, 758 cm^{-1}. MS (ESI): *m*/*z* = 386.27 [M + Na^+]. $C_{22}H_{37}NO_3$ (363.53): calcd. C 72.69, H 10.26, N 3.85; found C 72.33, H 10.21, N 3.73.

Lithium-Mediated Homoaldol Reaction of 6

General Procedure: 6 (1.0 equiv.) and TMEDA (1.3 equiv.) were dissolved in Et_2O (3.0 mL $mmol^{-1}$). At –78 °C *n*BuLi (1.3 equiv.) was added, and stirring was continued at –78 °C for 2 h. The ketone (3.0 equiv.) was added dropwise, and the solution was stirred at –78 °C for 10 h. The reaction solution was then warmed up to 0 °C over a period of 9 h and quenched at 0 °C by addition of a satd. aq. NH_4Cl solution (5 mL $mmol^{-1}$). The layers were separated, and the aqueous phase was extracted with TBME three times (5 mL $mmol^{-1}$). The combined organic layers were dried with $MgSO_4$, and the solvent was removed under vacuum. Purification of the crude product was accomplished by column chromatography.

Reaction with Cyclopentanone: {(1*R*,2*Z*,3*S*,5*R*)-3-(1-Hydroxycyclopentyl)-6,6-dimethylbicyclo[3.1.1]hept-2-ylidene}methyl *N*,*N*-Diisopropylcarbamate (16a): According to the General Procedure, **6** (837 mg, 3.00 mmol, 1.0 equiv.) was deprotonated with *n*BuLi (2.4 mL, 3.90 mmol, 1.3 equiv.) and TMEDA (468 mg, 3.90 mmol, 1.3 equiv.) for 2 h and treated with cyclopentanone (756 mg, 9.0 mmol, 3.0 equiv.) to yield after column chromatography (twice: TBME/PE, 1:2 then 1:4) products **16a** and **17** (674 mg, **16a**/**17** = 82:18, *dr* = 95:5). Calculated yield: **16a**: 552 mg, 1.5 mmol, 53%; **17**: 122 mg, 0.44 mmol, 12%.

16a: t_R = 19.8 min (HP5). R_F = 0.13 (Et_2O/PE, 1:4). $[\alpha]_D^{20}$ = –17.9 (*c* = 1.00, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 0.71 (s, 3 H, 8/9-H), 1.26 (br. s, 12 H, CH_3-*Cb*), 1.24 (s, 3 H, 8/9-H), 1.55–1.87 (m, 9 H, 5-H, 3′-H, 4′-H), 1.90–2.05 (m, 3 H, 4-H, 7-H_A), 2.16–2.38 (m, 2 H, 1-H, 7-H_B), 2.99 (ddd, $^3J_{H,H}$ = 10.3, $^3J_{H,H}$ = 3.0, *J* = 1.6 Hz, 1 H, 3-H), 3.78, 4.10 (2 br. s, 2 H, CH-*Cb*), 6.72 (d, $J_{H,H}$ = 1.7 Hz, 1 H, 1′-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.8 (CH_3-*Cb*), 21.7, 25.7 (C-8, C-9), 23.0, 23.2 (C-4′), 26.3 (C-7), 27.8 (C-4), 38.0, 40.5 (C-3′), 39.7 (C-3), 40.7 (C-5), 42.7 (C-6), 46.2 (CH-*Cb*), 47.7 (C-1), 86.2 (C-2′), 125.5 (C-2), 131.7 (C-1′), 152.4 (C_{CO}-*Cb*) ppm. IR (KBr): $\tilde{\nu}$ = 3509 (OH), 2973, 2909, 2861 (C–H), 1696 (C=O) cm^{-1}. MS (ESI): *m*/*z* = 386.2673 [M + Na^+]. $C_{22}H_{37}NO_3$ (362.53): calcd. C 72.69, H 10.26, N 3.85; found C 72.53, H 10.24, N 3.73.

(2*R*)-2-{(1*R*,5*S*)-6,6-Dimethylbicyclo[3.1.1]hept-2-en-2-yl}-2-hydroxy-*N*,*N*-diisopropylacetamide (17): t_R = 15.3 min (HP5). R_F = 0.48 (TBME/PE, 1:6). M.p. 68 °C (TBME/PE). $[\alpha]_D^{20}$ = –17.1 (*c* = 1.01, $CHCl_3$, *dr* = 97:3). ^1H NMR (400 MHz, $CDCl_3$): δ = 0.83, 1.29 (2 s, 6 H, 8-H, 9-H), 1.13 (br. d, $^2J_{H,H}$ = 8.8 Hz, 1 H, 7-H_A), 1.15, 1.18 (2 d, $^3J_{H,H}$ = 6.6 Hz, 6 H, 4′-H), 1.43, 1.45 (2 d, 6 H, 4′-H), 2.10 (m, 1 H, 5-H), 2.26–2.30 (m, 2 H, 4-H), 2.34 (dt, $^3J_{H,H}$ = 5.6, *J* = 1.4 Hz, 1 H, 1-H), 2.40 (dt, $^2J_{H,H}$ = 8.8, $^3J_{H,H}$ = 5.6 Hz, 1 H, 7-H_B), 3.44, 3.89 (2 sept, 2 H, 3′-H), 3.66 (br. s 1 H, OH), 4.48 (s, 1 H, 2′-H), 5.41 (s, 1 H, 3-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.4, 20.3, 20.5, 21.0 (C-4′), 21.5, 26.0 (C-8, C-9), 31.3 (C-4), 31.8 (C-7), 37.9 (C-6), 40.6 (C-5), 43.8 (C-1), 46.2, 47.8 (C-3′), 71.5 (C-2′), 120.3 (C-3), 146.7 (C-2), 170.5 (C-1′) ppm. IR (ATR): $\tilde{\nu}$ = 3391 (OH), 2987, 2968, 2934, 2912, 2877 (C–H), 1635 (C=O) cm^{-1}. MS (ESI): *m*/*z* = 302.2093 [M + Na^+]. $C_{17}H_{29}NO_2$ (279.42): calcd. C 73.07, H 10.46, N 5.01; found C 73.07, H 10.50, N 4.85.

Reaction with Acetone: {(1*R*,2*Z*,3*S*,5*R*)-3-(1-Hydroxy-1-methylethyl)-6,6-dimethylbicyclo[3.1.1]hept-2-ylidene}methyl *N*,*N*-Diisopropylcarbamate (16b): According to the General Procedure, **6** (837 mg, 3.00 mmol, 1.0 equiv.) was deprotonated with *n*BuLi (2.4 mL, 3.90 mmol, 1.3 equiv.) and TMEDA (468 mg, 3.90 mmol, 1.3 equiv.) for 2 h and treated with acetone (522 mg, 9.0 mmol, 3.0 equiv.) to yield after column chromatography (TBME/PE, 1:4) products **16b** and **17** (144 mg, **16b**/**17** = 57:43, *dr* = 95:5; 465 mg, **16b**/**17** = 93:7). Calculated yield: **16b**: 514 mg, 1.5 mmol, 52%; **17**: 82 mg, 0.33 mmol, 10%. t_R = 17.5 min (HP5). R_F = 0.12 (Et_2O/PE, 1:4). M.p. 104 °C (Et_2O/PE). $[\alpha]_D^{20}$ = –23.9 (*c* = 0.99, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.72, 1.24 (2 s, 6 H, 8-H, 9-H), 1.25, 1.26 (2 br. s, 12 H, CH_3-*Cb*), 1.29, 1.30 (2 s, 6 H, 3′-H), 1.69 (br. d, $^2J_{H,H}$ = 10.0 Hz, 1 H, 7-H_A), 1.83 (dt, $^3J_{H,H}$ = 3.5, $^2J_{H,H}$ = 13.8, $^3J_{H,H}$ = 3.5 Hz, 1 H, 4-H_A), 1.90–2.06 (m, 2 H, 4-H_B, 7-H_B), 2.18–2.30 (m, 2 H, 5-H, OH), 2.34 (t, $^3J_{H,H}$ = 5.6 Hz, 1 H, 1-H), 2.89 (ddd, $^3J_{H,H}$ = 10.4, *J* = 1.9 Hz, 1 H, 3-H), 3.94 (br. s, 2 H, CH-*Cb*), 6.79 (d, *J* = 1.8 Hz, 1 H, 1′-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.7 (CH_3-*Cb*), 21.7, 25.7 (C-8, C-9), 26.3 (C-7), 27.6 (C-4), 28.6, 29.5 (C-3′), 40.7 (C-5), 41.8 (C-3), 42.6 (C-6), 46.3 (CH-*Cb*), 47.9 (C-1), 74.4 (C-2′), 124.7 (C-2), 131.8 (C-1′), 152.2 (C_{CO}-*Cb*) ppm. IR (KBr): $\tilde{\nu}$ = 3504 (OH), 2978, 2969, 2926, 2909, 2865 (C–H), 1996 (C=O) cm^{-1}. MS (ESI): *m*/*z* = 360.2523 [M + Na^+]. $C_{20}H_{35}NO_3$ (337.49): calcd. C 71.18, H 10.45, N 4.15; found C 71.07, H 10.61, N 4.09.

Titanium-Mediated Homoaldol Reaction of 6

General Procedure: 6 (1.0 equiv.) and (–)-sparteine (**13**) (1.3 equiv.) were dissolved in Et_2O (3.0 mL mmol^{-1}). At –78 °C *n*BuLi (1.3 equiv.) was added, and stirring was continued at –78 °C for 2 h. A solution of $ClTi(NEt_2)_3$ (2.0 equiv.) in Et_2O (0.5 mL mmol^{-1}) was added in a dropwise fashion, and the solution was stirred at –78 °C for additional 3 h. The carbonyl compound (3.0 equiv.) was added dropwise, and the solution was stirred at –78 °C for 3 or 4 h. The reaction was quenched at –78 °C by addition of a satd. aq. NH_4Cl solution (3 mL mmol^{-1}) and warmed up to room temp.; a 2 M HCl solution was added until the titanium salts were fully dissolved. The layers were separated, and the aqueous phase was extracted with TBME three times (5 mL mmol^{-1}). The combined organic layers were dried with $MgSO_4$, and the solvent was removed under vacuum. Purification of the crude product was accomplished by column chromatography.

Reaction with Cyclopentanone: {(1*R*,2*Z*,3*S*,5*R*)-3-(1-Hydroxycyclopentyl)-6,6-dimethylbicyclo[3.1.1]hept-2-ylidene}methyl *N*,*N*-Diisopropylcarbamate (16a): According to the General Procedure, **6** (837 mg, 3.0 mmol, 1.0 equiv.) was deprotonated with *n*BuLi (2.43 mL, 3.90 mmol, 1.3 equiv.) and **13** (912 mg, 3.90 mmol, 1.3 equiv.), transmetalleted with $ClTi(NEt_2)_3$ (1.8 g, 6.0 mmol, 2.0 equiv.) and treated with cyclopentanone (756 mg, 9.0 mmol, 3.0 equiv.) for 3 h to yield after purification by column chromatography (Et_2O/PE, 1:2) **16a** (607 mg, 1.67 mmol, 56%) as a colorless solid. For analytical data see above.

Reaction with Acetone: {(1*R*,2*Z*,3*S*,5*R*)-3-(1-Hydroxy-1-metyhlethyl)-6,6-dimethylbicyclo[3.1.1]hept-2-ylidene}methyl *N*,*N*-Diisopropylcarbamate (16b): According to the General Procedure, **6** (837 mg, 3.0 mmol, 1.0 equiv.) was deprotonated with *n*BuLi (2.43 mL, 3.90 mmol, 1.3 equiv.) and **13** (912 mg, 3.90 mmol, 1.3 equiv.), transmetalleted with $ClTi(NEt_2)_3$ (1.8 g, 6.0 mmol, 2.0 equiv.) and treated with acetone (522 mg, 9.0 mmol, 3.0 equiv.) for 3 h to yield after purification by column chromatography (Et_2O/PE, 1:2) **16b** (665 mg 1.97 mmol, 66%) as a colorless solid. For analytical data see above.

Reaction with Benzaldehyde: {(1*R*,2*Z*,3*S*,5*R*)-3-[(*S*)- and (*R*)-Hydroxy(phenyl)methyl]-6,6-dimethylbicyclo[3.1.1]hept-2-ylidene}-methyl *N*,*N*-Diisopropylcarbamate (16c and *epi*-16c): According to the General Procedure, **6** (1.40 g, 5.0 mmol, 1.0 equiv.) was deprotonated with *n*BuLi (4.1 mL, 6.5 mmol, 1.3 equiv.) and **13** (1.52 g, 6.5 mmol, 1.3 equiv.), transmetalleted with $ClTi(NEt_2)_3$ (3.0 g, 10.0 mmol, 2.0 equiv.) and treated with benzaldehyde (1.6 g, 15.0 mmol, 3.0 equiv.) for 4 h to yield after purification by column chromatography (Et_2O/PE, 1:2) *epi*-**16c** (84 mg, 0.22 mmol, 4%) as a colorless solid and **16c**/*epi*-**16c** = 92:8 (1.307 g, 3.39 mmol, 68%) as a colorless crystalline solid. Total yield: 1.391 g (3.61 mmol, 72%). A single crystal of **16c** suitable for X-ray structure analysis was obtained by slow evaporation of the solvent from a saturated solution of **16c**/*epi*-**16c** (92:8) in Et_2O. After measuring, the crystal was dissolved in Et_2O and the retention time (HP5) compared to those of the diastereoisomers. The comparison clearly revealed that the crystal was the major diastereoisomer **16c**.

16c: t_R = 21.2 min (HP5). R_F = 0.32 (Et_2O/PE, 2:5). M.p. 115–116 °C (PE, **16**/*epi*-**16c** = 92:8). $[\alpha]_D^{20}$ = –54.9 (*c* = 1.02, $CHCl_3$, **16**/*epi*-**16c** = 92:8). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.72, 1.20 (2 s, 6 H, 8-H, 9-H), 0.84 (br. d, $^2J_{H,H}$ = 10.2 Hz, 1 H, 7-H_A), 1.29, 1.30 (2 br. s, 12 H, CH_3-*Cb*), 1.69 (m, 1 H, 4-H_A), 1.77 (m, 1 H, 4-H_B), 1.84 (m, 1 H, 5-H), 2.15 (dt, $^3J_{H,H}$ = 5.5, $^2J_{H,H}$ = 10.2 Hz, 1 H, 7-H_B), 2.35 (t, $^3J_{H,H}$ = 5.5 Hz, 1 H, 1-H), 2.63 (s, 1 H, OH), 3.30 (dt, $^3J_{H,H}$ = 1.6, $^3J_{H,H}$ = 8.6, $J_{H,H}$ = 1.9 Hz, 1 H, 3-H), 3.88, 4.18 (2 br. s, 2 H, CH-*Cb*), 4.89 (d, $^3J_{H,H}$ = 8.6 Hz, 1 H, 2′-H), 6.95 (s, 1 H, 1′-H), 7.27–7.41 (m, 5 H, H_{Ar}) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.6, 21.2 (CH_3-*Cb*), 21.7 (C-8,C-9), 25.6 (C-4) 26.3 (C-7), 38.0 (C-3), 40.5 (C-5), 42.0 (C-6), 46.3 (CH-*Cb*), 47.0 (C-1), 78.4 (C-2′), 124.5 (C-2), 127.6 (CH_{Ar}), 127.7 (CH_{Ar}), 128.8 (CH_{Ar}), 132.1 (C-1′), 142.7 (C_{Ar}), 152.5 (C_{CO}-*Cb*) ppm. IR (KBr): $\tilde{\nu}$ = 3491 (OH), 3091, 3061, 3030 (C–H_{Ar}), 2970, 2922, 2861 (C–H), 1700 (C=O) cm^{-1}. MS (ESI): *m*/*z* = 408.2521 [M + Na$^+$]. $C_{24}H_{35}NO_3$ (385.54): calcd. C 74.77, H 9.15, N 3.63; found C 74.73, H 9.01, N 3.47.

***epi*-16c:** t_R = 21.3 min (HP5). R_F = 0.32 (Et_2O/PE, 2:5). M.p. 96 °C. $[\alpha]_D^{20}$ = –72.2 (*c* = 1.03, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.75, 1.23 (2 s, 2 H, 8-H, 9-H), 0.89 (m, 1 H, 7-H_A), 1.28, 1.31 (2 br. s, 12 H, CH_3-*Cb*), 1.51 (m, 1 H, 4-H_A), 1.66–1.78 (m, 2 H, 4-H_B, 7-H_B), 1.87 (m, 1 H, 5-H), 2.21 (s, 1 H, OH), 2.36 (m, 1 H, 1-H), 3.29 (m, 1 H, 3-H), 3.80, 4.18 (2 br. s, 2 H, CH-*Cb*), 5.53 (s, 1 H, 2′-H), 6.84 (d, $J_{H,H}$ = 2.3 Hz, 1 H, 1′-H), 7.22–7.44 (m, 5 H, CH_{Ar}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.9 (CH_3-*Cb*), 21.7 (C-8, C-9), 24.8 (C-4), 25.9 (C-7), 37.8 (C-3), 40.3 (C-5), 41.2 (C-6), 46.4 (CH-*Cb*), 47.3 (C-1), 72.4 (C-2′), 125.6 (C-2), 125.5 (CH_{Ar}), 126.5 (CH_{Ar}), 128. 0 (CH_{Ar}), 130.4 (C-1′), 143.2 (C_{Ar}), 152.2 (C_{CO}, *Cb*) ppm. IR (KBr): $\tilde{\nu}$ = 3439 (OH), 3096, 3061, 3000 (C–H_{Ar}), 2974, 2930, 2896, 2861 (C–H), 1683 (C=O) cm^{-1}. MS (ESI): *m*/*z* = 408.2499 [M + Na$^+$]. $C_{22}H_{37}NO_3$ (362.53): calcd. C 74.77, H 9.15, N 3.63; found C 74.65, H 9.25, N 3.41.

Deprotonation of Silanes 8a, *epi*-8a, *epi*-8b and 23 Followed by Substitution with Pivaloyl Chloride

General Procedure: A solution of the carbamate (0.3 mmol, 1.0 equiv.) and TMEDA (1.2 equiv.) in Et_2O (2 mL) was cooled down to –78 C, *s*BuLi (1.28 M, 1.2 equiv.) was added slowly. After 2 h of deprotonation, pivaloyl chloride (3.0 equiv.) was added in a dropwise fashion within 5 min. After additional 3 h of stirring, the reaction was stopped by addition of a satd. aq. NH_4Cl solution (5 mL), and the mixture was warmed up to room temp. After addition of Et_2O or TBME (5 mL) and separation of the organic phase, the aqueous layer was extracted three times with Et_2O or TBME (10 mL of each). The combined organic phases were dried with $MgSO_4$, and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography.

Reaction of 8a: {(1*R*,2*E*,3*S*,5*R*)- and (1*R*,2*Z*,3*S*,5*R*)-3-(2,2-Dimethylpropanoyl)-6,6-dimethylbicyclo[3.1.1]hept-2-ylidene}(trimethylsilyl)methyl *N*,*N*-Diisopropylcarbamate [(*E*)- and (*Z*)-21]: According to the General Procedure, **8a** (*dr* = 87:13) (108 mg, 0.31 mmol, 1.0 equiv.) was deprotonated with *s*BuLi (0.30 mL, 0.38 mmol, 1.2 equiv.) and TMEDA (42 mg, 0.36 mmol, 1.2 equiv.) and treated with pivaloyl chloride (109 mg, 0.90 mmol, 2.9 equiv.) to yield after purification by column chromatography (Et_2O/PE, 1:15) (*E*)-**21** (106 mg, 0.24 mmol, 77%) as a colorless solid and (*Z*)-**21** (10 mg, 0.02 mmol, 6%) as a yellowish oil (*dr* = 92:8).

(*E*)-21: t_R = 20.1 min (HP5). R_F = 0.51 (Et_2O/PE, 1:4). M.p. 121–122 (Et_2O). $[\alpha]_D^{20}$ = +75.7 (*c* = 1.05, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.13 (d, 9 H, 2′-H), 0.86 (s, 3 H, 8-H), 1.12 (dd, 6 H, CH_3-*Cb*), 1.22 (s, 9 H, 5′-H), 1.27 (s, 3 H, 9-H), 1.33 (d, 6 H, CH_3-*Cb*), 1.61 (d, $^3J_{H,H}$ = 5.4 Hz, 1 H, 7-H_A), 1.74 (dt, $^3J_{H,H}$ = 3.0, $^2J_{H,H}$ = 13.6 Hz, 1 H, 4-H_A), 1.94 (m, 1 H, 5-H), 2.19 (dd, $^3J_{H,H}$ = 11.8 Hz, 1 H, 4-H_B), 2.28 (m, 1 H, 7-H_B), 2.77 (t, 1 H, 1-H), 3.40 (dt, $^3J_{H,H}$ = 6.7, $^4J_{H,H}$ = 3.0 Hz, 1 H, CH-*Cb*), 4.02 (dd, 1 H, 3-H), 4.30 (dt, 1 H, CH-*Cb*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 0.4 (C-2′), 20.5, 20.6, 21.0, 21.2 (CH_3-*Cb*), 21.8 (C-8), 25.6 (C-9), 25.9 (C-7), 27.8 (C-4), 28.4 (C-5′), 39.4 (C-3), 40.5 (C-5), 40.7 (C-6), 44.1 (C-4′), 44.7 (CH-*Cb*), 45.6 (C-1), 47.3 (CH-*Cb*), 143.4 (C-2), 147.5 (C-1′), 152.7 (C_{CO}-*Cb*), 216.2 (C-3′) ppm. IR (ATR): $\tilde{\nu}$ = 2961 (C–H), 2938, 2872, 1703 (C=O), 1686 (NC=O), 1478,

1425, 1369, 1314 (Si–CH_3), 1246, 1138, 1074, 1062, 1043, 988, 855, 839 (Si–CH_3), 761 cm^{-1}. MS (ESI): *m*/*z* = 458.31 [M + Na^+]. $C_{25}H_{45}NO_3Si$ (458.72): calcd. C 68.91, H 10.41, N 3.21; found C 68.70, H 10.31, N 3.16.

(*Z*)-21: t_R = 20.6 min (HP5). R_F = 0.34 (Et_2O/PE, 1:4). $[\alpha]_D^{20}$ = +10.2 (*c* = 0.84, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ = 0.13 (s, 9 H, 2′-H), 0.79 (s, 3 H, 8-H), 1.21 (m, 9 H, 9-H, CH_3-*Cb*), 1.24 (br. d, $^3J_{H,H}$ = 6.8 Hz, 6 H, CH_3-*Cb*), 1.32 (m, 10 H, 7-H_A, 5′-H), 1.96 (m, 1 H, 5-H), 2.17 (m, 2 H, 7-H_B, 4-H_A), 2.33 (m, 1 H, 4-H_B), 3.06 (t, $^3J_{H,H}$ = 5.6 Hz, 1 H, 1-H), 3.83 (br. s, 1 H, CH-*Cb*), 3.86 (dd, $^3J_{H,H}$ = 11.2, $^3J_{H,H}$ = 1.9 Hz, 1 H, 3-H), 4.04 (br. s, 1 H, CH-*Cb*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 0.2 (C-2′), 20.6, 20.6, 21.5, 21.5 (CH_3-*Cb*), 21.5 (C-8), 24.7 (C-4), 26.0 (C-9), 27.3 (C-7), 29.1 (C-5′), 41.2 (C-5), 41.4 (C-6/4′), 43.4 (C-3), 44.1 (C-6/4′), 44.3 (C-1), 45.6, 46.1 (CH-*Cb*),143.5 (C-2), 149.1 (C-1′), 154.1 (C_{CO}-*Cb*), 217.1 (C-3′) ppm. IR (ATR): $\tilde{\nu}$ = 2968 (C–H), 1696 (NC=O, C=O), 1429, 1367, 1321 (Si–CH_3), 1298, 1287, 1246, 1145, 1069, 1040, 839 (Si–CH_3) cm^{-1}. MS (ESI): *m*/*z* = 458.31 [M + Na^+]. $C_{25}H_{45}NO_3Si$ (435.72): calcd. C 68.91, H 10.41, N 3.21; found C 68.76, H 10.41, N 3.15.

Reaction of *epi*-8a: According to the General Procedure, *epi*-**8a** (*dr* = 91:9) (107 mg, 0.30 mmol, 1.0 equiv.) was deprotonated with *s*BuLi (0.30 mL, 0.38 mmol, 1.2 equiv.) and TMEDA (42 mg, 0.36 mmol, 1.2 equiv.) and treated with pivaloyl chloride (109 mg, 0.90 mmol, 3.0 equiv.) to yield after purification by column chromatography (Et_2O/PE, 1:10) (*Z*)-**21** (98 mg, 0.22 mmol, 73%) as a yellowish oil and (*E*)-**21** (19 mg, 0.04 mmol, 13%) as a yellowish solid (*dr* = 82:18). For analytical data see above.

Reaction of 23: According to the General Procedure, **23** (104 mg, 0.30 mmol, 1.0 equiv.) was deprotonated with *s*BuLi (0.30 mL, 0.38 mmol, 1.3 equiv.) and TMEDA (45 mg, 0.38 mmol, 1.3 equiv.) and treated with pivaloyl chloride (108 mg, 0.90 mmol, 3.0 equiv.) to furnish after column chromatography (Et_2O/PE, 1:15) (*E*)-**21** (113 mg, 0.26 mmol, 87%) as a colorless solid (*dr* > 97:3). For analytical data, see above.

Reaction of *epi*-8b: {(1*R*,2*Z*,3*S*,5*R*)-3-(2,2-Dimethylpropanoyl)-6,6-dimethylbicyclo[3.1.1]hept-2-ylidene}(triethylsilyl)methyl *N*,*N*-Diisopropylcarbamate [(*Z*)-24]: According to the General Procedure, *epi*-**8b** (*dr* > 97:3) (83 mg, 0.21 mmol, 1.0 equiv.) was deprotonated with *s*BuLi (0.21 mL, 0.27 mmol, 1.3 equiv.) and TMEDA (31 mg, 0.27 mmol, 1.32 equiv.) and treated with pivaloyl chloride (75 mg, 0.62 mmol, 2.9 equiv.) to yield after purification by column chromatography (Et_2O/PE, 1:20) (*Z*)-**24** (76 mg, 0.16 mmol, 76%) as a colorless solid (*dr* = 95:5).

(*Z*)-24: t_R = 22.4 min (HP5). R_F = 0.50 (Et_2O/PE, 1:4). M.p. 82–84 °C (Et_2O). $[\alpha]_D^{20}$ = –2.0 (*c* = 1.16, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 0.61 (m, 6 H, 2′-H), 0.82 (s, 3 H, 8-H), 0.96 (t, $^3J_{H,H}$ = 7.9 Hz, 9 H, 3′-H), 1.19 (m, 9 H, 9-H, CH_3-*Cb*), 1.26 (dd, $^3J_{H,H}$ = 6.8, $^4J_{H,H}$ = 0.8 Hz, 6 H, CH_3-*Cb*), 1.31 (s, 9 H, 6′-H), 1.33 (d, $^2J_{H,H}$ = 10.5 Hz, 1 H, 7-H_A), 1.96 (m, 1 H, 5), 2.15 (m, 2 H, 7-H_B, 4-H_A), 2.33 (m, 1 H, 4-H_B), 3.02 (t, $^3J_{H,H}$ = 5.6 Hz, 1 H, 1-H), 3.71 (m, 1 H, CH-*Cb*), 3.83 (dd, $^3J_{H,H}$ = 11.1, $^3J_{H,H}$ = 2.0 Hz, 1 H, 3-H), 4.12 (m, 1 H, CH-*Cb*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 3.6 (C-2′), 7.4 (C-3′), 20.6, 20.6, 21.3, 21.5 (CH_3-*Cb*), 21.7 (C-8), 24.8 (C-7), 26.0 (C-9), 27.2 (C-4), 29.0 (C-6′), 41.2 (C-5), 41.4 (C-6), 43.4 (C-3), 44.1 (C-5′), 44.5 (C-1), 45.3 (CH-*Cb*), 46.3 (CH-*Cb*), 144.8 (C-2), 148.1 (C-1′), 153.7 (C_{CO}-*Cb*), 216.9 (C-4′) ppm. IR (ATR): $\tilde{\nu}$ = 2952 (C–H), 2906, 2873, 1698 (C=O), 1673 (NC=O), 1477, 1439, 1367, 1296, 1286, 1220, 1129, 1069, 1040, 1003, 960, 951, 764, 717 cm^{-1}. MS (ESI): *m*/*z* = 500.35 [M + Na^+]. $C_{28}H_{51}NO_3Si$ (477.79): calcd. C 70.39, H 10.76, N 2.93; found C 70.06, H 10.50, N 2.91.

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[19] X-ray crystal structure analysis for **9f**: Formula $C_{22}H_{37}NO_3$, M = 363.53, colorless crystal $0.30 \times 0.25 \times 0.20$ mm, a = 6.1844(3), b = 34.3049(14), c = 10.4690(4) Å, β = 91.941(2)°, V = 2219.8(2) Å^3, $\rho_{calcd.}$ = 1.088 g cm^{-3}, μ = 0.556 mm^{-1}, empirical absorption correction ($0.851 \leq T \leq 0.897$), Z = 4, monoclinic, space group $P2_1$ (No. 4), λ = 1.54178 Å, T = 223 K, ω and ϕ scans, 18723 reflections collected ($\pm h$, $\pm k$, $\pm l$), $(\sin\theta)/\lambda$ = 0.60 Å^{-1}, 5594 independent (R_{int} = 0.051) and 5020 observed reflections [$I \geq 2\sigma(I)$], 487 refined parameters, R = 0.044, wR_2 = 0.117, Flack parameter 0.2(2), two almost identical molecules in the asymmetric unit, max. residual electron density 0.12 (–0.14) e Å^{-3}, hydrogen atoms calculated and refined as riding atoms.
[20] X-ray crystal structure analysis for **16c**: Formula $C_{24}H_{35}NO_3$, M = 385.53, colorless crystal $0.60 \times 0.20 \times 0.20$ mm, a = 6.986(1), b = 10.867(1), c = 15.321(1) Å, β = 101.93(1)°, V = 1138.0(2) Å^3, $\rho_{calcd.}$ = 1.125 g cm^{-3}, μ = 0.574 mm^{-1}, empirical absorption correction ($0.725 \leq T \leq 0.894$), Z = 2, monoclinic, space group $P2_1$ (No. 4), λ = 1.54178 Å, T = 223 K, ω and ϕ scans, 12418 reflections collected ($\pm h$, $\pm k$, $\pm l$), $(\sin\theta)/\lambda$ = 0.60 Å^{-1}, 2808 independent (R_{int} = 0.025) and 2794 observed reflections [$I \geq 2\sigma(I)$], 260 refined parameters, R = 0.037, wR_2 = 0.101, Flack parameter 0.0(2), max. residual electron density 0.11 (–0.09) e Å^{-3}, hydrogen atoms calculated and refined as riding atoms.
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