Stereoselective Synthesis of Highly Substituted Bicyclic γ-Lactones Using Homoaldol Addition of 1-(1-Cycloalkenyl)methyl Carbamates

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Dedicated to Professor Wilhelm Flitsch on the occasion of his 80th birthday

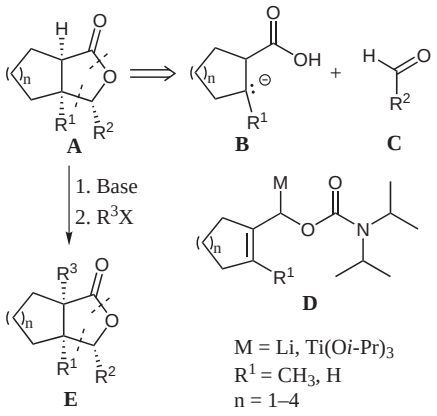
Abstract: Stereoselective addition of aldehydes **4** to metallated 1-(1-cycloalkenyl)methyl *N*,*N*-diisopropylcarbamates **1** gave cyclic homoaldol adducts **6**. By applying the (–)-sparteine method, enantiomerically enriched products were obtained. These were oxidatively cyclized to diastereomerically pure γ-lactones **8** via the γ-lactol ethers **7**. After deprotonation of γ-lactones **8** with lithium hexamethyldisilazide, a further substitution was achieved. By trapping the lactone enolates **11** with β-naphthylmethyl bromide, single diastereomers of γ-lactones **12** were produced.

Key words: asymmetric synthesis, 1-alkenyl carbamates, homoaldol addition, (–)-sparteine, bicyclic lactones

A few enantiomerically enriched 1-heterosubstituted allyllithium compounds are readily accessible by (–)-sparteine-induced deprotonation of achiral precursors.[2,3] After lithium-titanium exchange, a chiral homoenolate is produced, which adds stereoselectively to aldehydes and ketones.

We recently published the generation of enantioenriched (1-lithiomethyl)-1-cycloalkenylmethyl *N*,*N*-diisopropylcarbamates **D** and their asymmetric homoaldol reaction with *p*-bromobenzaldehyde to serve as equivalents for homoenolate synthons **B** (Scheme 1).[4] The application of this methodology to the synthesis of bicyclic γ-lactones **A** from aldehydes **C** and their further elaboration to highly substituted lactones of type **E** through introduction of a further residue R^3 by means of enolate chemistry are reported in this paper.

For the synthesis of the racemic adducts **6** (Scheme 2), the deprotonation of (cycloalkenyl)methyl diisopropylcarbamates **1a**–**1f** (*Cb* = diisopropylcarbamate) was carried out by treatment with *n*-butyllithium–*N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA) in toluene (Conditions A). The intermediate lithium compound *rac*-**2**·TMEDA was converted to the (triisopropoxy)titanium derivative *rac*-**3** with three equivalents of Ti(O*i*-Pr)$_4$; aldehyde **4** was then added.[5] According to the Zimmerman-Traxler transition state[6] **TS5** the *Z*-*anti*-diastereomers *rac*-**6** were formed with diastereoselectivities greater then 95:5. When *n*-butyllithium–(–)-sparteine was used for the deprotonation of **1** (Conditions B), the *pro*-*S* proton was removed to form (*S*)-**2**·(–)-sparteine with selectivities exceeding 90:10.[3] However, with the exception of the configurationally stable γ-methyl-substituted derivatives **2b** and **2d**, an epimerisation to form substantial amounts of (*R*)-**2**·(–)-sparteine competes with the lithium-titanium exchange, which proceeds stereospecifically with inversion of configuration. Since the reaction of Ti(O*i*-Pr)$_4$ was sluggish, we applied the more reactive ClTi(O*i*-Pr)$_3$.[5] Although the yields of adducts **6** were quite low,[7,8] a reasonable degree of chirality transfer was maintained (Table 1).



Scheme 1 Strategy for the synthesis of bicyclic γ-lactones

Methanolysis of **6** in the presence of catalytic mercuric acetate provided the γ-lactol ethers **7** as anomeric mixtures.[9] Grieco oxidation[9,10] then furnished the bicyclic γ-lactones **8**. Substrates with annulated five- and six-membered rings gave products as essentially pure diastereomers (Table 2). Larger rings, such as cycloheptane and cyclooctane gave rise to mixtures of *cis*- and *trans*-fused bicycles (*rac*-**8ei** and *rac*-**8fi**, entries 13 and 14). The relative configuration could be unambiguously assigned due to NOE effects in ^{1}H NMR between the bridgehead proton and the CH_3 group.

The vinyl carbamate **6df** (82% ee), bearing a mercuric salt-sensitive unsaturated side chain, required a more elaborate strategy previously applied by us in the synthesis of the pheromone (+)-eldanolide.[11] Conversion of **6df** to the silyl ether **9**, vinyl deprotonation and subsequent quenching of the vinyllithium intermediate with dimethyldisulfide, afforded the monothioacetal **10**. Compound **10** was solvolized by aqueous MeOH–methanesulfonic acid to yield in 56% lactone **8df** with 82% ee (Scheme 3).

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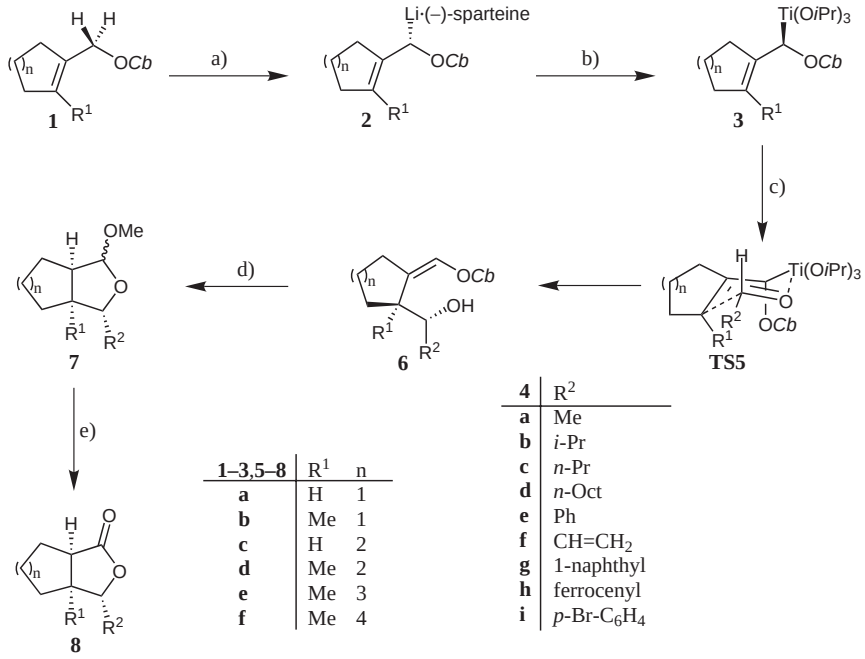


1–3,5–8	R^1	n
a	H	1
b	Me	1
c	H	2
d	Me	2
e	Me	3
f	Me	4

4	R^2
a	Me
b	*i*-Pr
c	*n*-Pr
d	*n*-Oct
e	Ph
f	$CH=CH_2$
g	1-naphthyl
h	ferrocenyl
i	*p*-Br-C_6H_4

Scheme 2 *Reagents and conditions:* a) *s*-BuLi, TMEDA, toluene, –78 °C for racemates (Conditions A) or *n*-BuLi, (–)-sparteine, toluene, –78 °C for enantioenriched products (Conditions B). b) $Ti(OiPr)_4$ or $ClTi(OiPr)_3$, 3 equiv c) i. R^2CHO (**4**), ii. 2 N HCl. d) $Hg(OAc)_2$ (5–10 mol%), $MeSO_3H$ (2 equiv) in MeOH. e) *m*-$ClC_6H_4CO_3H$–$BF_3{\cdot}OEt_2$.

Table 1 Prepared Homoaldol Products

Entry	Substrates	Conditions	Ti-Reagent	Product[a,b]	Yield (%)	er[c]	$[\alpha]_D$[d]
1	**1a** + **4a**	A	$Ti(O$*i*-$Pr)_4$	*rac*-**6aa**	83	–	–
2	**1a** + **4b**	A	$Ti(O$*i*-$Pr)_4$	*rac*-**6ab**	79	–	–
3	**1a** + **4c**	A	$Ti(O$*i*-$Pr)_4$	*rac*-**6ac**	69	–	–
4	**1a** + **4d**	A	$Ti(O$*i*-$Pr)_4$	*rac*-**6ad**	71	–	–
5	**1b** + **4b**	B	$Ti(O$*i*-$Pr)_4$	**6bb**	79	87:13	+29.6
6	**1b** + **4b**	A	$Ti(O$*i*-$Pr)_4$	*rac*-**6bb**	77	–	–
7	**1b** + **4e**	B	$Ti(O$*i*-$Pr)_4$	**6be**	70	86:14	+82.7
8	**1b** + **4e**	A	$Ti(O$*i*-$Pr)_4$	*rac*-**6be**	77	–	–
9	**1b** + **4f**	B	$Ti(O$*i*-$Pr)_4$	**6bf**	57	85:15	+70.1
10	**1b** + **4f**	A	$Ti(O$*i*-$Pr)_4$	*rac*-**6bf**	59	–	–
11	**1b** + **4i**	B	$ClTi(O$*i*-$Pr)_3$	**6bi**[f]	29	96:4	+113
12	**1b** + **4i**	A	$Ti(O$*i*-$Pr)_4$	*rac*-**6bi**	79	–	–
13	**1c** + **4b**	B	$Ti(O$*i*-$Pr)_4$	**6cb**	70	77:23	+18.1
14	**1c** + **4b**	A	$Ti(O$*i*-$Pr)_4$	*rac*-**6cb**	68	–	–
15	**1c** + **4e**	B	$Ti(O$*i*-$Pr)_4$	**6ce**	82	76:24	–36.2
16	**1c** + **4e**	A	$Ti(O$*i*-$Pr)_4$	*rac*-**6ce**	88	–	–
17	**1d** + **4b**	B	$ClTi(O$*i*-$Pr)_3$	**6db**	40	94:6	+48.1
18	**1d** + **4b**	A	$Ti(O$*i*-$Pr)_4$	*rac*-**6db**	80	–	–
19	**1d** + **4c**	B	$ClTi(O$*i*-$Pr)_3$	**6dc**	25	89:11	+61.7

Table 1 Prepared Homoaldol Products (continued)

Entry	Substrates	Conditions	Ti-Reagent	Product[a,b]	Yield (%)	er[c]	$[\alpha]_D$[d]
20	**1d** + **4c**	A	$Ti(Oi\text{-}Pr)_4$	*rac*-**6dc**	83	–	–
21	**1d** + **4d**	B	$ClTi(Oi\text{-}Pr)_3$	**6dd**	41	–[e]	+45.4
22	**1d** + **4d**	A	$Ti(Oi\text{-}Pr)_4$	*rac*-**6dd**	66	–	–
23	**1d** + **4e**	B	$ClTi(Oi\text{-}Pr)_3$	**6de**	34	96:4	–34.3
24	**1d** + **4e**	A	$Ti(Oi\text{-}Pr)_4$	*rac*-**6de**	85	–	–
25	**1d** + **4f**	B	$ClTi(Oi\text{-}Pr)_3$	**6df**	34	91:9	+30.4
26	**1d** + **4f**	A	$Ti(Oi\text{-}Pr)_4$	*rac*-**6df**	57	–	–
27	**1d** + **4g**	B	$ClTi(Oi\text{-}Pr)_3$	**6dg**	33	88:12	+6.8
28	**1d** + **4g**	A	$Ti(Oi\text{-}Pr)_4$	*rac*-**6dg**	48	–	–
29	**1d** + **4h**	B	$ClTi(Oi\text{-}Pr)_3$	**6dh**	27	–[e]	+166
30	**1d** + **4h**	A	$Ti(Oi\text{-}Pr)_4$	*rac*-**6dh**	65	–	–
31	**1d** + **4i**	B	$ClTi(Oi\text{-}Pr)_3$	**6di**[f]	35	94:6	–46.3
32	**1d** + **4i**	A	$Ti(Oi\text{-}Pr)_4$	*rac*-**6di**[f]	76	–	–
33	**1e** + **4i**	B	$ClTi(Oi\text{-}Pr)_3$	**6ei**[f]	22	75:25	+34.4
34	**1e** + **4i**	A	$Ti(Oi\text{-}Pr)_4$	*rac*-**6ei**	71	–	–
35	**1f** + **4i**	B	$ClTi(Oi\text{-}Pr)_3$	**6fi**[f]	21	69:31	+6,8
36	**1f** + **4i**	A	$Ti(Oi\text{-}Pr)_4$	*rac*-**6fi**	72	–	–

[a] For R^1, R^2, R^3, and n, see Scheme 2.
[b] In all cases, no second diastereomer was found by ^1H NMR. Thus, the diastereomeric ratios are assumed to be >95:5.
[c] Determined by ^1H NMR shift experiment or by chiral GC.
[d] c = 0.19–0.52 in $CHCl_3$.
[e] Not determined.
[f] These compounds have already been reported in the literature.[4]

Table 2 Prepared Lactones **8**

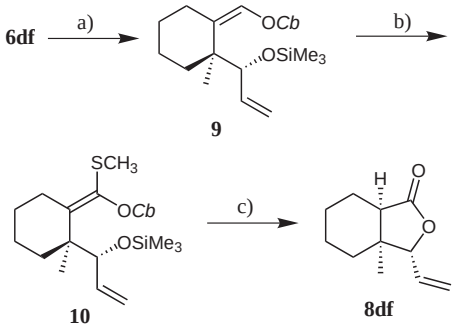
Entry	Starting material[a]	Product[a]	Yield (%)	er[b,c]	$[\alpha]_D$[d]
1	*rac*-**6aa**	*rac*-**8aa**	45	–	–
2	*rac*-**6ab**	*rac*-**8ab**	73[e]	–	–
3	*rac*-**6ac**	*rac*-**8ac**	71	–	–
4	*rac*-**6ad**	*rac*-**8ad**	83	–	–
5	**6bb**	**8bb**	54	87:13	+21.3
6	**6be**	**8be**	56	90:10	–6.2
7	**6bi**	**8bi**	49	96:4	–3.0
8	*rac*-**6dc**	*rac*-**8dc**	75	–	–
9	**6dd**	**8dd**	78	–[f]	+25.4
10	**6df**	**8df**	56	91:9	+33.6
11	**6dg**	**8dg**	80	88:12	–85.5
12	**6di**	**8di**	73	94:6	–15.8

Table 2 Prepared Lactones **8** (continued)

Entry	Starting material[a]	Product[a]	Yield (%)	er[b,c]	$[\alpha]_D$[d]
13	*rac*-**6ei**	*rac*-**8ei**	67	–	–
14	*rac*-**6fi**	*rac*-**8fi**	62	–	–

[a] For R^1, R^2, R^3, and n, see Scheme 2.
[b] The ee value of the starting enol carbamate **8** is given, since a racemisation is not possible.
[c] Diastereomeric ratios of *rac*-**8ei** and *rac*-**8fi** are 66:34 and 75:25, respectively. In all other cases, no second diastereomer was found by ^1H NMR. Thus, the diastereomeric ratios are assumed to be >95:5.
[d] c = 0.10–1.34 in $CHCl_3$.
[e] Crude.
[f] Not determined.

The lactones **8bi** and **8di**, containing bromine as a heavy atom, were crystalline. These were subjected to X-ray crystal structure analysis with anomalous diffraction (Figures 1 and 2) in order to elucidate their absolute configurations. These structures correlated well with those predicted and therefore confirm the proposed configurations of the intermediates and related derivatives reported in this paper.



Scheme 3 *Reagents and conditions*: a) $ClSiMe_3$, Et_3N, CH_2Cl_2, 0 °C → r.t., 15 h. b) i. *n*-BuLi. ii. MeSSMe, THF, 3 h, –78 °C. c) $MeSO_3H$, MeOH, 15 h, 50 °C.

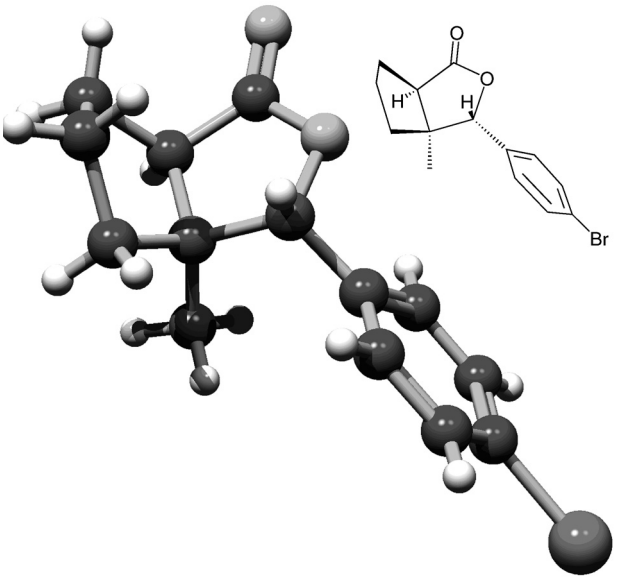


Figure 1 Structure of **8bi**[12]

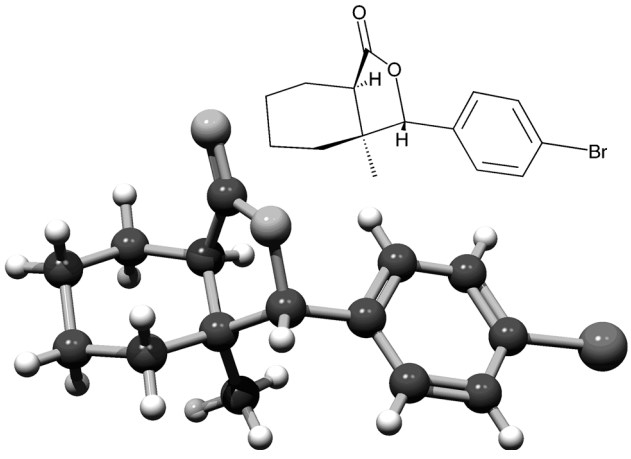
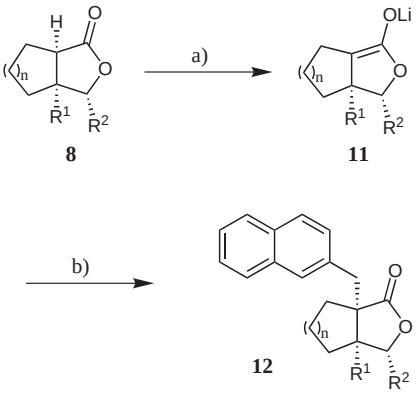


Figure 2 Structure of **8di**[12]

In order to demonstrate the further synthetic diversity offered by the bicyclic lactones **8**, we investigated the preparation and alkylation of a selection of examples (Scheme 4, Table 3). Lactones *rac*-**8** were converted with lithium hexamethyldisilazide (LiHMDS) into the lactone-enolates **11** and alkylated by treatment with 2-(bromomethyl)naphthalene to furnish the unpolar products **12a**–**f** as single diastereomers. Exemplary, a ^1H NMR investigation of compound **12f** revealed the *cis*-configuration by an NOE effect between the 3a-CH_3 and the 7a-CH_2 groups. As predicted, the bicyclic enolate **11** is attacked exclusively from the convex face.[13]

In conclusion, the asymmetric deprotonation of achiral 2-substituted (1-cycloalkenyl)methyl carbamates, with subsequent homoaldol reaction and enolate alkylation provides a versatile brick-box system for the synthesis of highly substituted bicyclic lactones. Some examples for more complex elaboration will be found in ref.[14]



Scheme 4 *Reagents and conditions:* a) LiHMDS, THF, 1 h, –78 °C. b) 2-(bromomethyl)naphthalene, THF, –78 °C → r.t., 15 h.

Table 3 Prepared γ-Lactones **12**

Entry	Starting material	Product	n	R^1	R^2	Yield (%)
1	*rac*-**8aa**	*rac*-**12a**	1	H	Me	45
2	*rac*-**8ab**	*rac*-**12b**	1	H	*i*-Pr	42
3	*rac*-**8ac**	*rac*-**12c**	1	H	*n*-Pr	46
4	*rac*-**8ad**	*rac*-**12d**	1	H	*n*-Oct	48
5	*rac*-**8ae**	*rac*-**12e**	1	H	Ph	46
6	*rac*-**8bc**	*rac*-**12f**	2	Me	*n*-Pr	52

n-BuLi (1.6 M in hexane) and *s*-BuLi [1.4 M in hexane–cyclohexane (92:8)] were used. Aldehydes were distilled prior to use. (–)-Sparteine was kept under Ar in a refrigerator after the original bottles had been opened. All reactions, which are sensitive to moisture or air, were carried out under Ar using the septum-and-syringe techniques. All solvents were purified by distillation or dried (toluene, Et_2O ether) prior to use. Flash chromatography was carried out with silica gel (40–63 μm) using an Ar pressure of 1.2–1.4 bar. Chiral GC was carried out with a Beta-Dex™ 120 capillary column, 30 m, Supelco. ^1H and ^{13}C NMR spectra were recorded on ARX 300, Bruker.

Chemical shifts in brackets refer to the minor isomer caused by *E*/*Z*-isomerism in the OCS group. $CDCl_3$ was used as solvent, chemical shifts are reported in ppm (δ); ^1H shifts are related to TMS and ^{13}C shifts to $\delta_c = 77.0$. Ψ indicates pseudo multiplicities. IR absorption spectra were recorded using a Perkin-Elmer 298 and a FT-IR 5DXC (Nicolet, Offenbach a. M.). Mass spectrocopy was performed using a MAT 8200 (Finnigan, Bremen) or a Quattro LC-Z (Micromass).

Homoaldol Reaction of Allyl Carbamates 1; General Procedure (GP1)

To a solution of allyl carbamate **1** (1.0 mmol) and diamine (1.1–1.2 mmol) in toluene (3–10 mL) at –78 °C was added dropwise *n*-BuLi (1.6 M in hexane) or *s*-BuLi (0.97–1.20 M in hexane) (1.1–1.2 mmol) under vigorous stirring. The reaction mixture was stirred at this temperature for 10–120 min and then a precooled (–78 °C) solution of tetraisopropoxytitanium (TiPT) or chlorotriisopropoxytitanium (Cl-TiPT) (1 M in hexane, 1.1–3.6 mmol) was added. The reaction mixture was stirred for 1 h at –78 °C and then, the aldehyde (1.5–3.0 mmol), dissolved in toluene (1 mL), was added. Finally, the reaction mixture was stirred for 1 h at –78 °C before it was allowed to warm to r.t. The solution was poured into ice-cooled mixture of Et_2O (15 mL) and aq 2 N HCl (15 mL). The aqueous layer was extracted with Et_2O (3 × 15 mL). The combined organic extracts were dried over anhyd $MgSO_4$ and concentrated in vacuo. The residue was purified by silica gel flash column chromatography.

rac-{1*Z*,1[2*RS*,2(1*SR*)]}-1-[2-(1-Hydroxyethyl)cyclopentylidene]methyl *N*,*N*-Diisopropylcarbamate (*rac*-6aa)

According to GP1, allyl carbamate **1a** (1.13 g, 5.00 mmol) and TMEDA (640 mg, 5.50 mmol) were dissolved in toluene (15 mL) and cooled to –78 °C before 1.2 M *s*-BuLi (4.6 mL, 5.50 mmol) was added. The reaction mixture was stirred for 30 min after which TiPT (4.27 g, 15.0 mmol) was added. The orange-coloured solution was stirred for 1 h at –78 °C and then ethanal (**4a**, 275 mg, 6.25 mmol), dissolved in toluene (1.0 mL) was added. After workup, the residue was purified by flash chromatography (petroleum ether–Et_2O, 2:1) to give *rac*-**6aa** (1.12 g, 83%) as a colourless oil; R_f 0.40 (petroleum ether–Et_2O, 2:1).

IR (film): 3461 (OH), 1701 (C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.13 (d, *J* = 6.3 Hz, 3 H), 1.23 [1.22] (d, *J* = 6.8 Hz, 12 H), 1.40–1.96 (m, 4 H), 2.14–2.34 (m, 2 H), 2.85–2.96 (m, 1 H), 3.75 (dq, *J* = 6.3, 7.7 Hz, 1 H), 3.91 (m, 2 H), 7.01 (m_c, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.0 (CH_3), 20.8 (CH_3), 24.7 (CH_2), 28.0 (CH_2), 29.4 (CH_2), 46.3 (CH), 47.8 (CH), 69.7 (CH), 126.4 (C_q), 130.4 (CH), 152.7 (C=O).

Anal. Calcd for $C_{15}H_{27}NO_3$ (269.38): C, 66.88; H, 10.10; N, 5.20. Found: C, 66.70; H, 9.88; N, 5.33.

rac-{1*Z*,1[2*RS*,2(1*SR*)]}-1-[2-(1-Hydroxy-2-methylpropyl)cyclopentylidene]methyl *N*,*N*-Diisopropylcarbamate (*rac*-6ab)

According to GP1, allyl carbamate **1a** (225 mg, 1.00 mmol) and TMEDA (128 mg, 1.10 mmol) were dissolved in toluene (3 mL) and cooled to –78 °C before 1.30 M *sec*-BuLi (0.85 mL, 1.10 mmol) was added. The reaction mixture was stirred for 30 min after which TiPT (835 mg, 3.00 mmol) was added. The orange-coloured solution was stirred for 1 h at –78 °C then 2-methylpropanal (**4b**, 90 mg, 1.25 mmol), dissolved in toluene (0.5 mL), was added. After workup and flash chromatography (petroleum ether–Et_2O, 2:1) *rac*-**6ab** (236 mg (79%)) was obtained as a colourless oil; R_f 0.19 (petroleum ether–Et_2O, 4:1).

IR (film): 3499 (OH), 1705 (C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.85, 0.97 (d, *J* = 6.9 Hz, 6 H), 1.20 (m_c, 12 H), 1.33–1.57 (m, 2 H), 1.70–1.74 (m, 2 H), 1.88 (m_c, 2 H), 2.19–2.23 (m, 2 H), 2.87–2.95 (m, 1 H), 3.13 (dt, *J* = 2.4, 9.9 Hz, 1 H), 3.89 (m_c, 2 H), 7.02 (m_c, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.3 (CH_3), 20.7 (CH_3), 24.3 (CH_2), 28.8 (CH_2), 28.9 (CH_2), 29.9 (CH), 43.8 (CH), 46.2 (CH), 77.5 (CH), 126.8 (C_q), 130.4 (CH), 152.4 (C=O).

Anal. Calcd for $C_{17}H_{31}NO_3$ (297.43): C, 68.65; H, 10.51; N, 4.71. Found: C, 68.61; H, 10.63; N, 4.73.

rac-{1*Z*,1[2*RS*,2(1*SR*)]}-1-[2-(1-Hydroxybutyl)cyclopentylidene]methyl *N*,*N*-Diisopropylcarbamate (*rac*-6ac)

According to GP1, allyl carbamate **1a** (1.13 g, 5.00 mmol) and TMEDA (640 mg, 5.50 mmol) were dissolved in toluene (15 mL) and cooled to –78 °C before 1.2 M *s*-BuLi (4.6 mL, 5.50 mmol) was added. The reaction mixture was stirred for 30 min after which TiPT (4.27 g, 15.0 mmol) was added. The orange-coloured solution was stirred for 1 h at –78 °C then butanal (**4c**, 450 mg, 6.25 mmol), dissolved in toluene (1.0 mL), was added. After workup, and flash chromatography (petroleum ether–EtOAc, 4:1) **6ac** (1.28 g, 69%) was obtained as a colourless oil; R_f 0.39 (petroleum ether–EtOAc, 4:1).

IR (film): 3491 (OH), 1703 (C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.90 (t, *J* = 6.9 Hz, 3 H), 1.23 [1.23] (d, *J* = 6.9 Hz, 12 H), 1.28–1.86 (m, 8 H), 2.11–2.35 (m, 2 H), 2.80–2.90 (m, 1 H), 3.75 (dt, *J* = 2.5, 8.0 Hz, 1 H), 3.91 (sept, *J* = 6.9 Hz, 2 H), 7.02 (m_c, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.2 (CH_3), 19.0 (CH_2), 20.8 (CH_3), 24.7(CH_2), 28.3(CH_2), 29.5 (CH_2), 36.3 (CH_2), 46.3 (CH), 46.5 (CH), 73.3 (CH), 126.4 (C_q), 130.3 (CH), 152.7 (C=O).

Anal. Calcd for $C_{17}H_{31}NO_3$ (297.43): C, 68.65; H, 10.51; N, 4.71. Found: C, 68.53; H, 10.54; N, 5.03.

rac-{1*Z*,1[2*RS*,2(1*SR*)]}-1-[2-(1-Hydroxynonyl)cyclopentylidene]methyl *N*,*N*-Diisopropylcarbamate (*rac*-6ad)

According to GP1, allyl carbamate **1a** (1.35 g, 6.0 mmol) and TMEDA (698 mg, 6.60 mmol) were dissolved in toluene (15.00 mL) and cooled to –78 °C before 0.97 M *s*-BuLi (6.8 mL, 6.60 mmol) was added. The reaction mixture was stirred for 30 min after which TiPT (4.27 g, 15.0 mmol) was added. The orange-coloured solution was stirred for 1 h at –78 °C then *n*-nonanal (**4d**, 1.12 g, 7.50 mmol), dissolved in toluene (1.0 mL), was added. After workup and flash chromatography (petroleum ether–Et_2O, 2:1) *rac*-**6ad** (1.57 g, 71%) was obtained as a colourless oil; R_f 0.47 (petroleum ether–Et_2O, 2:1).

IR (film): 3489 (OH), 1706 (C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.84 (t, *J* = 6.8 Hz, 3 H), 1.22 [1.22] (d, *J* = 6.8 Hz, 12 H), 1.12–1.84 (2 × m, 18 H), 2.13–2.33 (m, 2 H), 2.85–2.95 (m, 1 H), 3.54 (m_c, 1 H), 3.90 (m_c, 2 H), 7.01 (m_c, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0 (CH_3), 20.8 (CH_3), 22.6 (CH_2), 24.7 (CH_2), 25.8 (CH_2), 28.3 (CH_2), 29.2 (CH_2), 29.4 (CH_2), 29.6 (CH_2), 29.8 (CH_2), 31.9 (CH_2), 34.0 (CH_2), 46.3 (CH), 46.4 (CH), 73.5 (CH), 126.4 (C_q), 130.3 (CH), 152.7 (C=O).

Anal. Calcd for $C_{22}H_{41}NO_3$ (367.57): C, 71.89; H, 11.24; N, 3.81. Found: C, 72.00; H, 11.53; N, 4.13.

{1*Z*,1[2*S*,2(1*R*)]}-1-[2-(1-Hydroxy-2-methylpropyl)-2-methylcyclopentylidene]methyl *N*,*N*-Diisopropylcarbamate (6bb)

According to GP1, allyl carbamate **1b** (239 mg, 1.00 mmol) and (–)-sparteine (281 mg, 1.20 mmol) were dissolved in toluene (5.00 mL) and cooled to –78 °C before 1.6 M *n*-BuLi (0.75 mL, 1.20 mmol) was added. The reaction mixture was stirred for 30 min before TiPT (853 mg, 3.00 mmol) was added. The orange-coloured solution was stirred for 1 h at –78 °C and then 2-methylpropanal (**4b**, 144 mg, 2.00 mmol), dissolved in toluene (1.00 mL), was add-

ed. After workup, the residue was purified by flash chromatography (petroleum ether–Et_2O, 4:1) to give **6bb** (247 mg, 79%) as a colourless solid; R_f 0.39 (petroleum ether–EtOAc, 4:1); mp 56 °C (petroleum ether–EtOAc); $[\alpha]_D^{20}$ = +29.6 (*c* = 0.26, $CHCl_3$); 73% ee.[15]

IR (KBr): 3493 (OH), 1695 (C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.93 (d, *J* = 6.7 Hz, 3 H), 0.94 (d, *J* = 6.9 Hz, 3 H), 1.14–1.32 (m, 12 H), 1.28 (s, 3 H), 1.37–2.00 (2 × m, 5 H), 2.27–2.22 (m, 2 H), 3.39–4.41 (br s, 2 H), 3.67 (br s, 1 H), 6.89 (dd, *J* = 1.6, 2.2 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.5 (CH_3), 20.7 (CH_3), 23.1 (CH_3), 24.4 (CH_3), 23.9 (CH_2), 30.1 (CH), 32.2 (CH_2), 36.7 (CH_2), 46.3 (CH), 50.6 (C_q), 80.7 (CH), 128.9 (CH), 130.8 (C_q), 151.8 (C=O).

Anal. Calcd for $C_{18}H_{33}NO_3$ (311.46): C, 69.41; H, 10.68; N, 4.50. Found: C, 69.46; H, 10.67; N, 4.22.

Carbamate *rac*-**6bb** was prepared by applying the analogous procedure with *sec*-BuLi–TMEDA (1.2 equiv). Allyl carbamate **1b** (239 mg, 1.00 mmol) gave *rac*-**6bb** (240 mg, 77%).

{1*Z*,1[2*S*,2(1*R*)]}-1-[2-(1-Hydroxy-1-phenylmethyl)-2-methylcyclopentylidene]methyl *N*,*N*-Diisopropylcarbamate (6be)

According to GP1, allyl carbamate **1b** (160 mg, 0.67 mmol) and (–)-sparteine (188 mg, 0.80 mmol) were dissolved in toluene (5 mL) and cooled to –78 °C before 1.6 M *n*-BuLi (0.50 mL, 0.80 mmol) was added. The reaction mixture was stirred for 30 min after which TiPT (682 mg, 2.40 mmol) was added. The orange-coloured solution was stirred for 1 h at –78 °C and then benzaldehyde (**4e**, 144 mg, 1.01 mmol), dissolved in toluene (1 mL), was added. After workup, the residue was purified by flash chromatography (petroleum ether–Et_2O, 10:1) to give **6be** (162 mg, 70%) as a colourless oil; R_f 0.16 (petroleum ether–Et_2O, 10:1); $[\alpha]_D^{20}$ = +82.7 (*c* = 0.52, $CHCl_3$), 72% optical purity.

IR (film): 3483 (OH), 1686 (C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.22–1.54 (m, 2 H), 1.31 (d, *J* = 6.4 Hz, 12 H), 1.41 (s, 3 H), 1.77–2.01 (m, 2 H), 2.13–2.30 (m, 2 H), 3.75 [4.19] (br s, 2 H), 5.00 (s, 1 H), 6.97 (dd, *J* = 1.7 H, 2.2 Hz, 1 H), 7.19–7.40 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.8 (CH_3), 22.7 (CH_3), 23.7 (CH_2), 31.7 (CH_2), 36.3 (CH_2), 50.7 (C_q), 46.4 (CH), 77.7 (CH), 127.1 (CH), 127.5 (CH), 127.5 (CH), 129.5 (CH), 130.5 (C_q), 141.7 (C_q), 151.9 (C=O).

Anal. Calcd for $C_{21}H_{31}NO_3$ (345.48): C, 73.01; H, 9.04; N, 4.05. Found: C, 73.10; H, 9.28; N, 3.85.

Carbamate *rac*-**6be** was prepared by applying the analogous procedure with *s*-BuLi–TMEDA (1.2 equiv). Allyl carbamate **1b** (287 mg, 1.20 mmol) gave *rac*-**6be** (319 mg, 77%).

{1*Z*,1[2*S*,2(1*R*)]}-1-[2-(1-Hydroxy-2-propenyl)-2-methylcyclopentylidene]methyl *N*,*N*-Diisopropylcarbamate (6bf)

According to GP1, allyl carbamate **1b** (1.00 g, 4.18 mmol) and (–)-sparteine (1.18 g, 5.00 mmol) were dissolved in toluene (20 mL) and cooled to –78 °C before 1.6 M *n*-BuLi (3.10 mL, 5.00 mmol) was added. The reaction mixture was stirred for 30 min after which TiPT (4.28 g, 15.0 mmol) was added. The orange-coloured solution was stirred for 30 min at –78 °C and then 2-propenal (**4f**, 351 mg, 6.27 mmol), dissolved in toluene (1 mL), was added. After workup, the residue was purified by flash chromatography (petroleum ether–Et_2O, 6:1) to give **6bf** (683 mg, 57%) as a colourless oil; R_f 0.23 (petroleum ether–EtOAc, 6:1); $[\alpha]_D^{20}$ = +70.1 (*c* = 0.37, $CHCl_3$). GC: Supelco β-Dex© 120 (70% ee); the major enantiomer appears at lower retention time.

IR (film): 3480 (OH), 1700 (C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.16–1.28 (m, 12 H), 1.30 (s, 3 H), 1.33–1.84 (m, 4 H), 2.20 (dddd, *J* = 2.4, 7.4, 9.8, 15.1 Hz, 1 H), 2.34 (ddddd, *J* =1.4, 1.4, 4.1, 8.4,13.7 Hz, 1 H), 3.40–4.25 (br s, 2 H), 4.41 (m_c, 1 H), 5.14 (ddd, *J* = 1.7, 1.7, 10.6 Hz, 1 H), 5.24 (ddd, *J* = 17.2, 1.7, 1.7 Hz, 1 H), 5.93 (ddd, *J* = 5.0, 10.6, 17.3 Hz, 1 H), 6.91 (dd, *J* = 1.6, 2.3 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.7 (CH_3), 22.6 (CH_3), 24.0 (CH_2), 32.0 (CH_2), 36.1 (CH_2), 46.3 (CH), 49.6 (C_q), 77.1 (CH), 115.3 (CH_2), 129.2 (CH), 129.9 (C_q), 138.3 (CH), 151.9 (C=O).

Anal. Calcd for $C_{17}H_{29}NO_3$ (295.42): C, 69.12; H, 9.89; N, 4.74. Found: C, 69.03; H, 9.83; N, 4.65.

Carbamate *rac*-**6bf** was prepared by applying the analogous procedure with *s*-BuLi–TMEDA (1.2 equiv). Allyl carbamate **1b** (239 mg, 1.00 mmol) gave *rac*-**6bf** (174 mg, 59%).

{1*Z*,1[2*S*,2(1*R*)]}-1-[2-(1-Hydroxy-2-methylpropyl)cyclohexylidene]methyl *N*,*N*-Diisopropylcarbamate (6cb)

According to GP1, allyl carbamate **1c** (144 mg, 0.60 mmol) and (–)-sparteine (155 mg, 0.66 mmol) were dissolved in toluene (3 mL) and cooled to –78 °C before 1.6 M *n*-BuLi (0.41 mL, 0.66 mmol) was added. The reaction mixture was stirred for 1 h after which TiPT (0.53 mL, 1.80 mmol) was added. The orange-coloured solution was stirred for 1 h at –78 °C and then 2-methylpropanal (**4b**, 0.11 mL, 1.20 mmol), dissolved in toluene (1 mL), was added. After workup, the residue was purified by flash chromatography (petroleum ether–Et_2O, 2:1) to give **6cb** (132 mg, 70%) as a colourless oil; R_f 0.62 (petroleum ether–Et_2O, 3:1); $[\alpha]_D^{20}$ = +18.1, 53% ee.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.87 (d, *J* = 6.7 Hz, 3 H), 1.06 (d, *J* = 6.7 Hz, 3 H), 1.24 (d, *J* = 6.7 Hz, 12 H), 1.35–1.60 (m, 4 H), 1.65–1.95 (m, 3 H), 2.00–2.20 (m, 3 H), 2.85–3.00 (m, 1 H), 3.73 (dd, *J* = 2.1, 10.5 Hz, 1 H), 3.70–4.20 (m, 2 H), 6.98 (d, *J* = 1.6 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.4 (CH_3), 19.5 (CH_3), 20.7 (CH_2), 26.7 (CH_2), 27.4 (CH_2), 27.6 (CH_2), 28.8 (CH), 38.1 (CH), 46.0 (CH), 72.2 (CH), 123.0 (C_q), 131.3 (CH), 153.1 (C=O).

Anal. Calcd for $C_{18}H_{33}NO_3$ (311.46): C, 69.41; H, 10.68; N, 4.50. Found: C. 69.45: H. 10.80: N. 4.51.

Carbamate *rac*-**6cb** was prepared applying the analogous procedure with *s*-BuLi–TMEDA (1.2 equiv). Allyl carbamate **1c** (1.093 g, 4.57 mmol) gave *rac*-**6cb** (0.966 g, 68%).

{1*Z*,1[2*S*,2(1*R*)]}-1-[2-(1-Hydroxymethyl-1-phenyl)cyclohexylidene]methyl *N*,*N*-Diisopropylcarbamate (6ce)

According to GP1, allyl carbamate **1c** (165 mg, 0.60 mmol) and (–)-sparteine (155 mg, 0.66 mmol) were dissolved in toluene (3 mL) and cooled to –78 °C before 1.6 M *n*-BuLi (0.41 mL, 0.66 mmol) was added. The reaction mixture was stirred for 1 h after which TiPT (0.53 mL, 1.80 mmol) was added. The orange-coloured solution was stirred for 1 h at –78 °C and then benzaldehyde (**4e**, 0.11 mL, 1.20 mmol), dissolved in toluene (1 mL), was added. After workup, the residue was purified by flash chromatography (petroleum ether–Et_2O, 2:1) to give **6ce** (196 mg, 82%) as a colourless oil; R_f 0.39 (petroleum ether–Et_2O, 2:1); $[\alpha]_D^{20}$ = –36.2; 52% ee; mp 92–94 ºC (petroleum ether–Et_2O).

^1H NMR (300 MHz, $CDCl_3$): δ = 1.10–1.47 (m, 15 H), 1.47–1.70 (m, 1 H), 2.15–2.35 (m, 3 H), 2.85–2.95 (m, 1 H), 3.06–3.13 (m, 1 H), 3.8–4.2 (m, 2 H), 4.50 (d, *J* = 7.7 Hz, 1 H), 4.81 (d, *J* = 10.5 Hz, 1 H), 7.12 (d, *J* = 1.7 Hz, 1 H), 7.25–7.42 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.4 (CH_3), 21.6 (CH_2), 26.8 (CH_2), 27.4 (CH_2), 27.7 (CH_2), 43.2 (CH), 44.5 (CH), 72.8 (CH), 122.0 (C_q), 126.9 (CH), 127.6 (CH), 128.2 (CH), 132.4 (CH), 142.9 (C_q), 153.2 (C=O).

Anal. Calcd for $C_{21}H_{31}NO_3$ (345.48): C, 73.01; H, 9.04; N, 4.05. Found: C, 72.87; H, 9.39; N, 4.12.

Carbamate *rac*-**6ce** was prepared by applying the analogous procedure with *s*-BuLi–TMEDA (1.2 equiv). Allyl carbamate **1c** (244 mg, 1.02 mmol) gave *rac*-**6ce** (307 mg, 76%).

{1*Z*,1[2*S*,2(1*R*)]}-1-[2-(1-Hydroxy-2-methylpropyl)-2-methylcyclohexylidene]methyl *N*,*N*-Diisopropylcarbamate (6db)

According to GP1, allyl carbamate **1d** (116 mg, 0.46 mmol) and (–)-sparteine (129 mg, 0.55 mmol) were dissolved in toluene (2 mL) and cooled to –78 °C before 1.6 M *n*-BuLi (0.97 mL, 1.55 mmol) was added. The reaction mixture was stirred for 1 h after which 1.0 M Cl-TiPT solution in toluene (1.6 mL, 1.65 mmol) was added. The dark solution was stirred for 1 h at –78 °C and then 2-methylpropanal (**4b**, 33 mg, 0.46 mmol), dissolved in toluene (0.5 mL), was added. After workup, the residue was purified by flash chromatography (petroleum ether–Et_2O, 4:1) to give **6dc** (60 mg, 40%) as a thick colourless oil. Crystallisation from petroleum ether–Et_2O gave colourless crystals; R_f 0.44 (petroleum ether–Et_2O, 4:1); $[\alpha]_D^{20}$ = +48.1 (88% op); mp 53–54 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.97 (d, *J* = 6.7 Hz, 3 H), 1.04 (d, *J* = 6.7 Hz, 3 H), 1.15–1.44 (m, 17 H), 1.48–1.57 (m, 2 H), 1.67–1.80 (m, 3 H), 1.92 (septd, *J* = 2.9, 6.7 Hz, 1 H), 2.00–2.08 (m, 1 H), 2.14–2.26 (m, 1 H), 3.74 (d, *J* = 2.9 Hz, 1 H), 3.50–4.30 (m, 2 H), 6.87 (d, *J* = 1.7 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.0 (CH_3), 21.0 (CH_3), 21.6 (CH_3), 22.7 (CH_2), 24.2 (CH_2), 26.8 (CH_2), 28.3 (CH_2), 29.4 (CH), 36.9 (CH), 45.2 (CH), 77.8 (CH), 125.8 (C_q), 132.2 (CH), 156.6 (C=O).

Anal. Calcd for $C_{19}H_{35}NO_3$ (325.49): C, 70.11; H, 10.84; N, 4.30. Found: C, 69.76; H, 10.97; N, 4.41.

Carbamate *rac*-**6db** was prepared by applying the analogous procedure with *s*-BuLi–TMEDA (1.2 equiv). Allyl carbamate **1d** (622 mg, 2.45 mmol) gave *rac*-**6db** (639 mg, 80%).

{1*Z*,1[2*S*,2(1*R*)]}-1-[2-(1-Hydroxybutyl)-2-methylcyclohexylidene]methyl *N*,*N*-Diisopropylcarbamate (6dc)

According to GP1, allyl carbamate **1d** (329 mg, 1.30 mmol) and (–)-sparteine (366 mg, 1.56 mmol) were dissolved in toluene (5 mL) and cooled to –78 °C before 1.6 M *n*-BuLi (0.98 mL, 1.56 mmol) was added. The reaction mixture was stirred for 1 h after which 1.0 M Cl-TiPT solution in toluene (4.7 mL, 4.7 mmol) was added. The dark solution was stirred for 1 h at –78 °C and then *n*-butanal (**4c**, 141 mg, 1.95 mmol), dissolved in toluene (1 mL), was added. After workup, the residue was purified by flash chromatography (petroleum ether–Et_2O, 7:1) to give **6dc** (107 mg, 25%) as a colourless oil; R_f 0.33 (petroleum ether–Et_2O, 7:1); $[\alpha]_D^{20}$ = +61.7 (*c* = 0.36, $CHCl_3$); GC: Supelco β-Dex 120 (77% ee); major enantiomer appears at lower retention time.

IR (film): 3508 (OH), 1700 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.93 (t, *J* = 7.0 Hz, 3 H), 1.05–1.79 (m, 22 H), 1.19 (s, 3 H), 1.99–2.26 (m, 2 H), 3.58 [4.14] (br s, 2 H), 3.88 (dd, *J* = 2.5, 8.9 Hz, 1 H), 6.89 (d, *J* = 1.4 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.2 (CH_3), 20.4 (CH_2), 20.7 (CH_3), 20.7 (CH_3), 21.2 (CH_2), 26.8 (CH_2), 29.0 (CH_2), 31.9 (CH_2), 36.4 (CH_2), 44.0 (C_q), 46.5 (CH), 72.4 (CH), 124.1 (C_q), 132.1 (CH), 152.3 (C=O).

Anal. Calcd for $C_{19}H_{35}NO_3$ (325.49): C, 70.11; H, 10.84; N, 4.30. Found: C, 70.00; H, 11.02; N, 4.40.

Carbamate *rac*-**6dc** was prepared by applying the analogous procedure with *s*-BuLi–TMEDA (1.2 equiv). Allyl carbamate **1d** (622 mg, 2.45 mmol) gave *rac*-**6dc** (674 mg, 83%).

{1*Z*,1[2*S*,2(1*R*)]}-1-[2-(1-Hydroxyoctyl)-2-methylcyclohexylidene]methyl *N*,*N*-Diisopropylcarbamate (6dd)

According to GP1, allyl carbamate **1d** (329 mg, 1.30 mmol) and (–)-sparteine (366 mg, 1.56 mmol) were dissolved in toluene (5 mL) and cooled to –78 °C before 1.6 M *n*-BuLi (0.98 mL, 1.56 mmol) was added. The reaction mixture was stirred for 1 h after which 1.0 M Cl-TiPT solution in toluene (4.7 mL, 4.7 mmol) was added. The dark solution was stirred for 1 h at –78 °C and then *n*-nonanal (**4d**, 277 mg, 1.95 mmol), dissolved in toluene (1 mL), was added. After workup, the residue was purified by flash chromatography (petroleum ether–Et_2O, 4:1) to give **6dd** (213 mg, 41%) as a colourless oil; R_f 0.32 (petroleum ether–Et_2O, 4:1); $[\alpha]_D^{20}$ = +45.4 (*c* = 0.52, $CHCl_3$).

IR (film): 3497 (OH), 1716 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.86 (t, *J* = 7.0 Hz, 3 H), 1.01–1.79 (m, 32 H), 1.19 (s, 3 H), 1.97–2.23 (m, 2 H), 3.58 [4.17] (br s, 2 H), 3.86 (dd, *J* = 2.2, 9.1 Hz, 1 H), 6.89 (d, *J* = 1.4 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1 (CH_3), 20.7 (CH_3), 21.2 (CH_3), 21.2 (CH_2), 22.6 (CH_2), 26.8 (CH_2), 26.8 (CH_2), 27.4 (CH_2), 29.0 (CH_2), 29.3 (CH_2), 29.7 (CH_2), 29.8 (CH_2), 31.9 (CH_2), 36.5 (CH_2), 44.0 (C_q), 45.6 [46.8] (CH), 72.7 (CH), 124.5 (C_q), 132.1 (CH), 152.3 (C=O).

Anal. Calcd for $C_{24}H_{45}NO_3$ (395.62): C, 72.86; H, 11.46; N, 3.54. Found: C, 73.17; H, 11.55; N, 3.52.

Carbamate *rac*-**6dd** was prepared by applying the analogous procedure with *s*-BuLi–TMEDA (1.2 equiv). Allyl carbamate **1d** (228 mg, 0.90 mmol) gave *rac*-**6dd** (253 mg, 66%).

{1*Z*,1[2*S*,2(1*R*)]}-1-[2-(1-Hydroxymethyl-1-phenyl)-2-methylcyclohexylidene]methyl *N*,*N*-Diisopropylcarbamate (6de)

According to GP1, allyl carbamate **1d** (297 mg, 1.17 mmol) and (–)-sparteine (328 mg, 1.40 mmol) were dissolved in toluene (3 mL) and cooled to –78 °C before 1.6 M *n*-BuLi (0.88 mL, 1.40 mmol) was added. The reaction mixture was stirred for 1 h after which 1.0 M Cl-TiPT solution in toluene (3.51 mL, 3.51 mmol) was added. The dark solution was stirred for 1 h at –78 °C and then benzaldehyde (**4e**, 124 mg, 1.17 mmol), dissolved in toluene (1.0 mL), was added. Flash chromatography yielded **6de** (139 mg, 34%) as a colourless oil; R_f 0.26 (petroleum ether–Et_2O, 4:1); $[\alpha]_D^{20}$ = –34.3 (92% ee).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.13 (s, 3 H), 1.15–1.47 (m, 14 H), 1.53–1.65 (m, 1 H), 1.71–1.91 (m, 2 H), 2.09–2.35 (m, 3 H), 3.40–4.40 (m, 2 H), 5.07 (s, 1 H), 6.98 (d, *J* = 1.7 Hz, 1 H), 7.21–7.40 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.0 (CH_3), 21.0 (CH_3), 21.6 (CH_3), 22.7 (CH_2), 24.2 (CH_2), 26.8 (CH_2), 28.3 (CH_2), 29.4 (CH) 36.9 (CH), 45.2 (CH), 77.8 (CH), 125.8 (C_q), 132.2 (CH), 156.6 (C=O).

Anal. Calcd for $C_{22}H_{33}NO_3$ (359.51): C, 73.50; H, 9.25; N, 3.90. Found: C, 73.31; H, 9.20; N, 3.85.

Carbamate *rac*-**6de** was prepared by applying the analogous procedure with *s*-BuLi–TMEDA (1.2 equiv). Allyl carbamate **1d** (137 mg, 0.54 mmol) gave *rac*-**6de** (165 mg, 85%).

{1*Z*,1[2*S*,2(1*R*)]}-1-[2-(1-Hydroxy-2-propenyl)-2-methylcyclohexylidene]methyl *N*,*N*-Diisopropylcarbamate (6df)

According to GP1, allyl carbamate **1d** (820 mg, 3.24 mmol) and (–)-sparteine (909 mg, 3.88 mmol) were dissolved in toluene (10 mL) and cooled to –78 °C before 1.6 M *n*-BuLi (2.43 mL, 3.88 mmol) was added. The reaction mixture was stirred for 1 h after which Cl-TiPT (3.03 g 11.6 mmol), dissolved in toluene (1 mL), was added. The dark solution was stirred for 1 h at –78 °C and then 2-propenal (**4f**, 272 mg, 4.86 mmol), dissolved in toluene (1 mL), was added. After workup, the residue was purified by flash chroma-

tography (petroleum ether–Et_2O, 4:1) to give **6df** (342 mg, 34%) as a colourless oil, which crystallised after 2 weeks at r.t.; R_f 0.22 (petroleum ether–EtOAc, 6:1); $[\alpha]_D^{20}$ = +30.4 (*c* = 0.40, $CHCl_3$). HPLC: β-Dextrin-column (β-Dex 120) (82% ee); the major enantiomer appears at lower retention time.

IR (film): 3483 (OH), 1712 (C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.96–2.23 (m, 23 H), 3.56 [4.18] (br s, 2 H), 4.42 (d, *J* = 6.7 Hz, 1 H), 5.12 (d, *J* = 10.5 Hz, 1 H), 5.28 (d, *J* = 17.3 Hz, 1 H), 5.84 (dddd, *J* = 2.5, 6.7, 10.5, 17.3 Hz, 1 H), 6.89 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.7 (CH_3), 21.4 (CH_3), 21.2 (CH_2), 26.7 (CH_2), 29.1 (CH_2), 36.4 (CH_2), 43.7 (C_q), 45.6 [47.1] (CH), 74.3 (CH), 117.1 (CH_2), 124.2 (C_q), 132.3 (CH), 136.3 (CH), 152.3 (C=O).

Anal. Calcd for $C_{18}H_{31}NO_3$ (309.44): C, 69.86; H, 10.10; N, 4.53. Found: C, 69.67; H, 10.23; N, 4.54.

Carbamate *rac*-**6df** was prepared by applying the analogous procedure with *s*-BuLi–TMEDA (1.2 equiv). Allyl carbamate **1d** (760 mg, 3.0 mmol) gave *rac*-**6df** (529 mg, 57%).

{1*Z*,1[2*S*,2(1*R*)]}-1-{2-[1-Hydroxy-1-(1-naphthyl)methyl]-2-methylcyclohexylidene}methyl *N*,*N*-Diisopropylcarbamate (6dg)

According to GP1, allyl carbamate **1d** (329 mg, 1.30 mmol) and (–)-sparteine (366 mg, 1.56 mmol) were dissolved in toluene (5 mL) and cooled to –78 °C before 1.6 M *n*-BuLi (0.98 mL, 1.56 mmol) was added. The reaction mixture was stirred for 1 h after which 1.0 M Cl-TiPT solution in toluene (4.7 mL, 4.7 mmol) was added. The dark solution was stirred for 1 h at –78 °C and then naphthalene-1-carbaldehyde (**4g**, 314 mg, 1.95 mmol, 97 proc.), dissolved in toluene (1 mL), was added. After workup, the residue was purified by flash chromatography (petroleum ether–Et_2O, 4:1) to give **6dg** (177 mg, 33%) as a colourless oil; R_f 0.14 (petroleum ether–CH_2Cl_2–EtOAc, 32:7:1); $-[\alpha]_D^{20}$ = +6.8 (*c* = 0.44, $CHCl_3$). Shift experiment: er 88.0:12.0 (76% ee), 11.6 mg + 21 mol% $Eu(hfc)_3$ in $CDCl_3$, Δδ (Ar-H at 8.32 ppm) = 0.18 ppm; major enantiomer appears at lower field.

IR (KBr): 3490 (OH), 1687 (C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.90–1.61 (m, 20 H), 1.22 (s, 3 H), 3.52 [3.95] (br s, 2 H), 5.80 (s, 1 H), 6.98 (d, *J* = 1.3 Hz, 1 H), 7.34–7.50 (m, 3 H), 7.71 (d, *J* = 7.4 Hz, 1 H), 7.76 (d, *J* = 8.1 Hz, 1 H), 7.79–7.86 (m, 1 H), 8.32 (d, *J* = 7.9 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.7 (CH_3), 23.4 (CH_3), 22.4 (CH_2), 26.6 (CH_2), 30.1 (CH_2), 37.4 (CH_2), 45.5 (C_q), 73.4 (CH), 124.4(C_q), 124.6 (C_q), 124.9 (CH), 125.9 (CH), 125.3 (CH), 126.8 (CH), 128.0 (CH), 128.8 (CH), 132.4 (CH), 132.4 (CH), 132.4 (C_q), 133.9 (C_q), 152.0 (C=O).

Anal. Calcd for $C_{26}H_{35}NO_3$ (409.56): C, 76.25; H, 8.61; N, 3.42. Found: C, 76.43; H, 8.70; N, 3.26.

Carbamate *rac*-**6dg** was prepared by applying the analogous procedure with *s*-BuLi–TMEDA (1.2 equiv). Allyl carbamate **1d** (228 mg (0.90 mmol) gave *rac*-**6dg** (198 mg, 57%).

{1*Z*,1[2*S*,2(1*S*)]}-1-[2-(1-Hydroxy-1-ferrocenylmethyl)-2-methylcyclohexylidene]methyl *N*,*N*-Diisopropylcarbamate (6dh)

According to GP1, allyl carbamate **1d** (177 mg, 0.70 mmol) and (–)-sparteine (212 mg, 0.91 mmol) were dissolved in toluene (5 mL) and cooled to –78 °C before 1.6 M *n*-BuLi (0.57 mL, 0.91 mmol) was added. The reaction mixture was stirred for 1 h after which Cl-TiPT (710 mg, 2.73 mmol), dissolved in toluene (1 mL), was added. The dark solution was stirred for 1 h at –78 °C and then ferrocenecarbaldehyde (**4h**, 226 mg, 1.05 mmol), dissolved in toluene (1 mL), was added. After workup, the residue was purified by flash chromatography (petroleum ether–Et_2O, 40:1) to give **6dh** (87 mg, 27%) as red oil, which crystallised after 2 weeks at r.t.; R_f 0.22 (petroleum ether–EtOAc, 6:1); $[\alpha]_D^{20}$ = +166 (*c* = 0.40, $CHCl_3$): mp 135 °C (petroleum ether–Et_2O).

IR (KBr): 3484 (OH), 1683 (C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.09 (s, 3 H), 1.10–1.39 (m, 18 H), 1.99–2.06 (m, 1 H), 2.07 (d, *J* = 1.5 Hz, 1 H), 2.11–2.22 (m, 1 H), 3.58 [3.98–4.43] (br s, 2 H), 4.08–4.13 (m, 2 H), 4.15–4.20 (m, 6 H), 4.27–4.30 (m, 1 H), 4.73 (s, 1 H), 6.91 (d, *J* = 1.8 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.8 (CH_3), 21.2 (CH_2), 22.1 (CH_3), 26.4 (CH_2), 29.2 (CH_2), 36.0 (CH_2), 43.6 (C_q), 45.5 (CH), 66.6 (CH), 67.3 (CH), 67.3 (CH), 68.5 (CH), 69.0 (CH), 72.2 (CH), 89.5(C_q), 124.3 (C_q), 131.7 (CH), 152.2 (C=O).

Anal. Calcd for $C_{26}H_{37}FeNO_3$ (467.43): C, 66.81; H, 7.98; N, 3.00. Found: C, 66.92; H, 7.87; N, 2.84.

{1*Z*,1[2*S*,2(1*S*)]}-1-{[2-(4-Bromophenyl)-1-hydroxy]-2-methylcycloheptylidene}methyl *N*,*N*-Diisopropylcarbamate (6ei)

According to GP1, allyl carbamate **1e** (188 mg, 0.70 mmol) and (–)-sparteine (196 mg, 0.84 mmol) were dissolved in toluene (5 mL) and cooled to –78 °C before 1.32 M *s*-BuLi (0.64 mL, 0.84 mmol) was added. The reaction mixture was stirred for 15 min after which Cl-TiPT (657 mg, 2.52 mmol), dissolved in toluene (1 mL), was added. The dark solution was stirred for 1 h at –78 °C and then *p*-bromobenzaldehyde (**4i**, 194 mg, 1.05 mmol), dissolved in toluene (1 mL), was added. After workup, the residue was purified by flash chromatography (petroleum ether–Et_2O, 40:1) to give **6ei** (87 mg, 27%) as a colourless solid; R_f 0.08 (petroleum ether–Et_2O, 20:1); $[\alpha]_D^{20}$ = +34.4 (*c* = 0.22, $CHCl_3$). Shift experiment: er 74.9:25.1 (50% ee), 6.2 mg + 7.3 mol% $Eu(hfc)_3$ in $CDCl_3$, Δδ (H at 4.64 ppm); mp 166 °C (petroleum ether–Et_2O).

IR (KBr): 3445 (OH), 1691 (C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.98–1.75 (m, 20 H), 1.37 (s, 3 H), 1.75–2.88 (m, 1 H), 1.94–2.07 (m, 1 H), 2.25 (s, 1 H), 3.68 [4.11] (br s, 2 H), 4.64 (s, 1 H), 6.94 (s, 1 H), 7.20 (m_c, 2 H), 7.38 (m_c, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.8 (2 × CH_3), 22.3 (CH_3), 23.6 (CH_2), 29.9 (CH_2), 31.8 (CH_2), 32.0 (CH_2), 35.8 (CH_2), 46.5 (CH), 46.5 (C_q), 78.9 (CH), 121.1 (C_q), 128.4 (C_q), 129.8 (CH), 130.4 (CH), 135.4 (CH), 140.0 (C_q), 152.0 (C=O).

Anal. Calcd for $C_{23}H_{34}BrNO_3$ (452.43): C, 61.06; H, 7.57; N, 3.10. Found: C, 61.88; H, 7.73; N, 2.84.

Carbamate *rac*-**6ei** was prepared by applying the analogous procedure with *s*-BuLi–TMEDA (1.2 equiv). Allyl carbamate **1e** (294 mg, 1.1 mmol) gave *rac*-**6ei** (323 mg, 71%).

{1*Z*,1[2*S*,2(1*S*)]}-1-{[2-(4-Bromophenyl)-1-hydroxy]-2-methylcyclooctylidene}methyl *N*,*N*-Diisopropylcarbamate (6fi)

According to GP1, allyl carbamate **1f** (197 mg, 0.70 mmol) and (–)-sparteine (196 mg, 0.84 mmol) were dissolved in toluene (5 mL) and cooled to –78 °C before 1.32 M *s*-BuLi (0.64 mL, 0.84 mmol) was added. The reaction mixture was stirred for 15 min after which Cl-TiPT (657 mg, 2.52 mmol), dissolved in toluene (1 mL), was added. The dark solution was stirred for 1 h at –78 °C and then *p*-bromobenzaldehyde (**4i**, 194 mg, 1.05 mmol), dissolved in toluene (1 mL), was added. After workup, the residue was purified by flash chromatography (petroleum ether–Et_2O, 40:1) to give **6fi** (66 mg, 21%) as a colourless solid; R_f 0.12 (petroleum ether–Et_2O, 20:1); $[\alpha]_D^{20}$ = +6.8 (*c* = 0.19, $CHCl_3$). Shift experiment: er = 68.3:31.7 (37% ee), 6.0 mg + 7.8 mol% $Eu(hfc)_3$ in $CDCl_3$, Δδ (H at 4.40 ppm); mp 66 °C (petroleum ether–Et_2O).

IR (KBr): 3462 (OH), 1693 (C = O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.03–1.95 (m, 23 H), 1.27 (s, 3 H), 2.08–2.22 (m, 1 H), 2.22 (br s, 1 H, OH), 3.65 [4.08] (br s, 2 H), 4.40 (s, 1 H), 6.93 (s, 1 H), 7.19 (m_c, 2 H), 7.38 (m_c, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 19,5 (CH_3), 20.8 (2 × CH_3), 23.7 (CH_2), 25.0 (CH_2), 26.3 (CH_2), 29.4 (CH_2), 31.3 (CH_2), 33.9 (CH_2), 46.1 (C_q), 46.5 (CH), 79.2 (CH), 121.2 (C_q), 126.9 (C_q), 130.0 (CH), 130.4 (CH), 136.6 (CH), 139.6 (C_q), 152.3 (C=O).

Anal. Calcd for $C_{24}H_{36}BrNO_3$ (466.45): C, 61.80; H, 7.78; N, 3.00. Found: C, 61.54; H, 7.81; N, 2.83.

Carbamate *rac*-**6fi** was prepared by applying the analogous procedure with *s*-BuLi–TMEDA (1.2 equiv). Allyl carbamate **1f** (321 mg, 1.14 mmol) gave *rac*-**6fi** (381 mg, 72%).

Converting Homoaldol Adducts 6 to Bicyclic Acetals 7; General Procedure (GP2)

To a solution of **6** (1 mmol) and $Hg(OAc)_2$ (0.05–0.20 mmol) in MeOH (10 mL) at 0 ºC was added dropwise $MeSO_3H$ (1–2 mmol) and stirred at 0 ºC for 15 h. Solid $NaHCO_3$ (2 equiv) was added to the reaction mixture and the solvent was removed under reduced pressure. The residue was dissolved in Et_2O (60 mL/mmol) and washed with water (20 mL/mmol). The organic layer was dried with $MgSO_4$ and concentrated in vacuo.

Oxidation of Bicyclic Acetals 7 to Bicyclic Lactones 8; General Procedure (GP3)

To a solution of acetal **7** (1.0 mmol) and *m*-CPBA (1.5–2.0 mmol, ca 60 proc.) in CH_2Cl_2 (5 mL), $BF_3{\cdot}OEt_2$ (1.0–2.7 mmol) was added dropwise at 0 °C. After stirring at r.t. for 15 h, Me_2S (100 μL) was added. The reaction mixture was stirred for an additional hour and poured into mixture of Et_2O (20 mL) and water (10 mL). The aqueous layer was extracted with Et_2O (3 × 15 mL). The combined organic extracts were dried over anhyd $MgSO_4$ and concentrated in vacuo. The residue was purified by silica gel flash column chromatography.

rac-(1*SR*,3*RS*,3a*SR*,6a*RS*)- and *rac*-(1RS,3RS,3aSR,6aRS)-1-Methoxy-3-methyl-hexahydrocyclopenta[*c*]furan (*rac*-α-7aa) and (*rac*-β-7aa)

According to GP2, *rac*-**6aa** (1.01 g, 3.80 mmol) was cyclised with $Hg(OAc)_2$ (242 mg, 0.76 mmol) and $MeSO_3H$ (730 mg, 7.60 mmol). After workup, the crude products were purified by flash chromatography (petroleum ether–Et_2O, 4:1) to give *rac*-**α-7aa** [97 mg (16%); R_f 0.56 (petroleum ether–Et_2O, 4:1)] and *rac*-**β-7aa** [288 mg (49%); R_f 0.47 (petroleum ether–Et_2O, 4:1)] as colourless oils.

rac-α-7aa

IR (film): 2953, 2879, 2829 (CH_{aliph}) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.25 (d, *J* = 6.2 Hz, 3 H), 1.21–1.62 (2 × m, 6 H), 2.23 (m, 1 H), 2.77 (m_c, 1 H), 3.30 (s, 3 H), 3.59 (dq, *J* = 8.1 Hz, 6.2 Hz, 1 H), 4.87 (d, *J* = 6.3 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.8 (CH_3), 26.6 (CH_2), 27.5 (CH_2), 29.3 (CH_2), 49.5 (CH), 51.9 (CH), 54.8 (CH_3), 78.1 (CH), 105.8 (CH).

rac-β-7aa

IR (film): 2953, 2866, 2835 (CH_{aliph}) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.27 (d, *J* = 6.4 Hz, 3 H), 1.41–1.80 (2 × m, 6 H), 2.38 (m_c, 1 H), 2.60 (m_c, 1 H), 3.30 (s, 3 H), 3.82 (dq, *J* = 4.4, 6.4 Hz, 1 H), 4.64 (d, *J* = 1.4 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.3 (CH_3), 25.8 (CH_2), 30.4 (CH_2), 32.5 (CH_2), 49.9 (CH), 51.6 (CH), 54.5 (CH_3), 83.7 (CH), 112.1 (CH).

rac-(3*RS*,3a*SR*,6a*RS*)-3-Methylhexahydrocyclopenta[*c*]furan-1-one (*rac*-8aa)

According to GP3, *rac*-**β-7aa** (211 mg, 1.42 mmol) was oxidized with *m*-CPBA (384 mg, 1.56 mmol, ca 60 proc.) and $BF_3{\cdot}OEt_2$ (199 μL, 1.42 mmol). After workup, the crude products were purified by flash chromatography (petroleum ether–EtOAc, 1:2) to yield *rac*-**8aa** (138 mg, 69%) as a colourless oil; R_f 0.44 (petroleum ether–EtOAc, 1:2).

IR (film): 1767 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.35 (d, *J* = 6.3 Hz, 3 H), 1.39–2.09 (m, 6 H), 2.49 (m_c, 1 H), 3.07 (m_c, 1 H), 4.21 (qd, *J* = 3.4, 6.3 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.2 (CH_3), 25.4 (CH_2), 30.6 (CH_2), 33.1 (CH_2), 45.0 (CH), 46.7 (CH), 82.3 (CH), 180.3 (C=O).

rac-(3*RS*,3a*SR*,6a*RS*)-3-Isopropylhexahydrocyclopenta[*c*]furan-1-one (8ab)

According to GP2, **6ab** (1.55 g, 5.25 mmol) was cyclized with $Hg(OAc)_2$ (169 mg, 0.53 mmol) and $MeSO_3H$ (1.01 g, 10.5 mmol). After workup, the organic layer was passed over silica gel. The solvent was removed under reduced pressure to give of a mixture of *rac*-**α-** and **β-7ab** (634 mg, 66%) which were used without further purification. According to GP3 a mixture of *rac*-**α-** and **β-7ab** (336 mg, 1.82 mmol) was oxidized with *m*-CPBA (492 mg, 2.00 mmol, ca 60 proc.) and $BF_3{\cdot}OEt_2$ (255 μL, 1.82 mmol). After workup, the residue was purified by flash chromatography (petroleum ether–Et_2O, 4:1) to give *rac*-**8ab** (244 mg, 73%) as a colourless oil: R_f 0.36 (petroleum ether–Et_2O, 2:1).

IR (film): 1769 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.91 (t, *J* = 6.3 Hz, 6 H), 1.44–1.90 (m, 6 H), 1.97–2.02 (m, 1 H), 2.58 (m_c, 1 H), 2.95 (dt, *J* = 3.0, 9.3 Hz, 1 H), 3.78 (dd, *J* = 3.9, 6.3 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.5 (CH_3), 25.4 (CH_2), 31.0 (CH_2), 33.3 (CH), 34.3 (CH_2), 42.1 (CH), 45.3 (CH), 91.3 (CH), 180.5 (C=O).

Anal. Calcd for $C_{10}H_{16}O_2$ (168.23): C, 71.39; H, 9.59. Found: C, 71.14; H, 9.76.

rac-(1*SR*,3*RS*,3a*SR*,6a*RS*)- and *rac*-(1*RS*,3*RS*,3a*SR*,6a*RS*)-1-Methoxy-3-propyl-hexahydrocyclopenta[*c*]furan (*rac*-α-7ac) and (*rac*-β-7ac)

According to GP2, *rac*-**6ac** (1.21 g, 4.10 mmol) was cyclized with $Hg(OAc)_2$ (261 mg, 0.82 mmol) and $MeSO_3H$ (788 mg, 8.20 mmol). After workup, the crude products were purified by flash chromatography (petroleum ether–Et_2O, 4:1) to yield *rac*-**α-7ac** [159 mg (21%); R_f 0.44 (petroleum ether–Et_2O, 4:1] and *rac*-**β-7ac** [480 mg (64%); R_f 0.54 (petroleum ether–Et_2O, 4:1] as colourless oils.

rac-α-7ac

IR (film): 2963, 2870, 2832 (CH_{aliph}) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.92 (t, *J* = 7.3 Hz, 3 H), 1.23–1.92 (m, 10 H), 2.23 (m_c, 1 H), 2.73 (m_c, 1 H), 3.30 (s, 3 H), 3.41–3.50 (m, 1 H), 4.85 (d, *J* = 6.0 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.2 (CH_3), 19.6 (CH_2), 26.4 (CH_2), 27.0 (CH_2), 29.9 (CH_2), 37.3 (CH_2), 49.4 (CH), 50.3 (CH), 54.6 (CH_3), 82.2 (CH), 105.5 (CH).

Anal. Calcd for $C_{11}H_{20}O_2$ (184.28): C, 71.95; H, 10.94. Found: C, 71.65; H, 10.84.

rac-β-7ac

IR (film): 2957, 2870, 2833 (CH_{aliph}) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.91 (t, *J* = 7.3 Hz, 3 H), 1.21–1.81 (m, 1 H), 2.42 (m_c, 1 H), 2.56 (m_c, 1 H), 3.29 (s, 3 H), 3.65 (ddd, *J* = 4.3, 5.6, 7.8 Hz, 1 H), 4.65 (d, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1 (CH_3), 19.7 (CH_2), 25.8 (CH_2), 30.4 (CH_2), 32.9 (CH_2), 40.2 (CH_2), 48.4 (CH), 51.5 (CH), 54.5 (CH_3), 87.9 (CH), 111.9 (CH).

rac-(3*RS*,3a*SR*,6a*RS*)-3-Propylhexahydrocyclopenta[*c*]furan-1-one (*rac*-8ac)

According to GP3, a mixture of *rac*-**α**- and **α-7ac** (478 mg, 2.60 mmol) was oxidized with *m*-CPBA (704 mg, 2.86 mmol, ca 60 proc.) and $BF_3{\cdot}OEt_2$ (728 μL, 5.20 mmol). After workup, the crude products were purified by flash chromatography (petroleum ether–EtOAc, 1:2) to yield *rac*-**8ac** (311 mg, 71%) as a colourless oil; R_f 0.54 (petroleum ether–EtOAc, 1:2).

IR (film): 1776 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.92 (t, *J* = 7.2 Hz, 3 H), 1.28–2.09 (m, 10 H), 2.51 (m_c, 1 H), 2.99 (m_c, 1 H), 4.04 (ddd, ^3J = 3.8, 5.4, 7.3 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.7 (CH_3), 18.3 (CH_2), 25.4 (CH_2), 30.7 (CH_2), 33.5 (CH_2), 38.7 (CH_2), 45.0 (CH), 45.0 (CH), 86.0 (CH), 180.5 (C=O).

rac-(1*SR*,3*RS*,3a*SR*,6a*RS*)- and *rac*-(1*RS*,3*RS*,3a*SR*,6a*RS*)-1-Methoxy-3-octyl-hexahydrocyclopenta[*c*]furan (*rac*-α-7ad) and (*rac*-β-7ad)

According to GP2, *rac*-**6ad** (1.31 g, 3.56 mmol) was cyclized with $Hg(OAc)_2$ (226 mg, 0.71 mmol) and $MeSO_3H$ (684 mg, 7.10 mmol). After workup, the crude products were purified by flash chromatography (petroleum ether–Et_2O, 10:1) to yield *rac*-**α-7ad** [262 mg (29%); R_f 0.43 (petroleum ether–Et_2O, 4:1)] and *rac*-**β-7ad** [354 mg (39%); R_f 0.52 (petroleum ether–Et_2O; 4:1)] as colourless oils.

rac-α-7ad

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.86 (t, *J* = 6.9 Hz, 3 H), 1.18–1.91 (m, 20 H), 2.22 (m_c, 1 H), 2.73 (dddd, *J* = 2.9, 6.1, 9.1, 10.5 Hz, 1 H), 3.40–3.49 (m, 1 H), 4.86 (d, *J* = 6.1 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1 (CH_3), 22.7 (CH_2), 26.3 (CH_2), 26.4 (CH_2), 27.7 (CH_2), 29.3 (CH_2), 29.6 (CH_2), 29.8 (CH_2), 30.0 (CH_2), 31.9 (CH_2), 35.1 (CH_2), 49.4 (CH), 50.3 (CH), 54.6 (CH_3), 82.4 (CH), 105.5 (CH).

Anal. Calcd for $C_{16}H_{20}O_2$ (254.41): C, 75.54; H, 11.89. Found: C, 75.62; H, 12.03.

rac-β-7ad

IR (film): 2930, 2857, 2827 (CH_{aliph}) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.85 (t, *J* = 6.9 Hz, 3 H), 1.16–1.81 (m, 20 H), 2.36–2.46 (m, 1 H), 2.56 (m_c, 1 H), 3.30 (s, 3 H), 3.63 (ddd, *J* = 4.5, 5.9, 7.7 Hz, 1 H), 4.64 (d, *J* = 1.0, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1 (CH_3), 22.6 (CH_2), 25.8 (CH_2), 26.5 (CH_2), 29.3 (CH_2), 29.6 (CH_2), 30.4 (CH_2), 31.9 (CH_2), 32.9 (CH_2), 38.0 (CH_2), 48.4 (CH), 51.5 (CH), 54.5 (CH_3), 88.3 (CH), 111.9 (CH).

EI–MS [$C_{16}H_{30}O_2$ (254.41)]: *m*/*z* (%) = 254 (0.1) $[M]^+$, 223 (8) $[M - OCH_3]^+$, 194 (7), 141 (100), 112 (17), 95 (8), 81 (49), 67 (19), 55 (11).

rac-(3*RS*,3a*SR*,6a*RS*)-3-Octylhexahydrocyclopenta[*c*]furan-1-one (*rac*-8ad)

According to GP3, a mixture of *rac*-**α**- and **β-7ad** and (491 mg, 2.60 mmol) was oxidized with *m*-CPBA (523 mg, 2.12 mmol, content ca 60 proc.) and $BF_3{\cdot}OEt_2$ (540 μL, 3.86 mmol). After workup, the crude products were purified by flash chromatography (petroleum ether–EtOAc, 1:2) to yield *rac*-**8ad** (380 mg, 83%) as a colourless oil; R_f 0.53 (petroleum ether–EtOAc, 1:2).

IR (film): 1770 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ= 0.85 (t, *J* = 6.9 Hz, 3 H), 1.13–2.10 (m, 20 H), 2.51 (dddd, *J* = 3.8, 3.8, 8.3, 9.0 Hz, 1 H), 2.99 (m_c, 1 H), 4.04 (ddd, *J* = 3.8, 5.7, 7.2 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0 (CH_3), 22.6 (CH_2), 25.0 (CH_2), 25.5 (CH_2), 29.1 (CH_2), 29.4 (CH_2), 30.7 (CH_2), 31.8 (CH_2), 33.6 (CH_2), 36.6 (CH_2), 45.0 (CH), 45.0 (CH), 86.3 (CH), 180.5 (C=O).

Anal. Calcd for $C_{15}H_{26}O_2$ (238.37): C, 75.58; H, 10.99. Found: C, 75.43; H, 11.17.

rac-(3*RS*,3a*RS*,6a*SR*)-3-Phenylhexahydrocyclopenta[*c*]furan-1-one (*rac*-8ae)[8]

According to GP2, *rac*-**6ae** (1.19 g, 3.60 mmol), was cyclized with $Hg(OAc)_2$ (229 mg, 0.72 mmol) and $MeSO_3H$ (692 mg, 7.20 mmol). The crude mixture of anomeric lactol ethers *rac*-**7ae** [316 mg (1.45 mmol) of the crude product (609 mg)] was oxidized (GP3) with *m*-CPBA (394 mg, 1.60 mmol, content ca. 60 proc.) and $BF_3{\cdot}OEt_2$ (406 μL, 2.90 mmol). After purification by silica gel chromatography (petroleum ether–Et_2O, 2:1) lactone *rac*-**8ae** (186 mg, 63%) was isolated as a colourless oil; R_f 0.18 (petroleum ether–Et_2O. 4:1).

IR (film): 1765 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.60–2.20 (m, 6 H), 2.85 (m, 1 H), 3.15 (m, 1 H), 5.10 (d, *J* = 3.6 Hz, 1 H), 7.25 (m, 5 H).

Anal. Calcd for $C_{13}H_{14}O_2$ (202.26): C, 77.20; H, 6.98. Found: C, 77.12; H, 6.99.

(3*R*,3a*S*,6a*R*)-3-Isopropyl-3a-methylhexahydrocyclopenta[*c*]furan-1-one (8bb)

According to GP2, **6bb** (189 mg, 0.61 mmol, $[\alpha]_D^{20}$ = +29.6) was cyclized with $Hg(OAc)_2$ (20 mg, 0.06 mmol) and $MeSO_3H$ (117 mg, 1.22 mmol). The crude mixture of **7bb** was oxidized according to GP3 with *m*-CPBA (165 mg, 0.67 mmol, content ca. 60 proc.) and $BF_3{\cdot}OEt_2$ (94 μL, 0.67 mmol). After flash chromatography (petroleum ether–Et_2O, 1:2) of the crude product, **8bb** was yielded (60 mg, 54%) as a colourless oil; R_f 0.67 (petroleum ether–Et_2O, 1:2); $[\alpha]_D^{20}$ = +21.3 (*c* = 0.15, $CHCl_3$).

IR (film): 1771 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.97 (d, *J* = 6.8 Hz, 6 H), 1.16 (s, 3 H), 1.49–2.12 (m, 7 H), 2.52 (dd, *J* = 5.4, 8.9 Hz, 1 H), 3.83 (d, *J* = 6.9 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.7 (CH_3), 20.0 (CH_3), 20.4 (CH_3), 25.4 (CH_2), 29.3 (CH_2), 29.5 (CH), 40.9 (CH_2), 50.1 (C_q), 53.7 (CH), 91.8 (CH), 179.8 (C=O).

Anal. Calcd for $C_{11}H_{18}O_2$ (182.13): C, 72.49; H, 9.95. Found: C,72.16; H, 10.45.

(3*R*,3a*S*,6a*R*)-3a-Methyl-3-phenylhexahydrocyclopenta[*c*]furan-1-one (8be)

According to the GP2, **6be** (139 mg, 0.42 mmol, 70% ee) was cyclized with $Hg(OAc)_2$ (13 mg, 0.04 mmol) and $MeSO_3H$ (81 mg, 0.84 mmol). After workup, the crude mixture of **7be** was used without further purification. According to GP3, **7be** was oxidized with *m*-CPBA (242 mg, 0.84 mmol, content ca. 60 proc.) and $BF_3{\cdot}OEt_2$ (118 μL, 0.84 mmol). After workup, the crude products were purified by flash chromatography (petroleum ether–Et_2O, 4:1) to yield **8be** (51 mg, 56% based on **6be**) as a solid; R_f 0.21 (petroleum ether–Et_2O, 4:1); $[\alpha]_D^{20}$ = –6.2 (*c* = 1.34, $CHCl_3$); mp 58 °C (petroleum ether–Et_2O).

IR (KBr): 1771 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.72 (s, 3 H), 1.57–2.22 (m, 6 H), 2.66 (dd, *J* = 3.6, 9.3 Hz, 1 H), 5.21 (s, 1 H), 7.15–7.39 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.7 (CH_3), 25.1 (CH_2), 29.5 (CH_2), 41.2 (CH_2), 51.6 (C_q), 51.8 (CH), 88.5 (CH), 125.6 (CH), 128.1 (CH), 128.7 (CH), 137.6 (C_q), 180.5 (C=O).

HRMS: *m*/*z* calcd $C_{14}H_{16}O_2$ (216.28): 216.11504; found: 216.11564.

(3*R*,3a*S*,6a*R*)-3-(4-Bromophenyl)-3a-methylhexahydrocyclopenta[*c*]furan-1-one (8bi)

According to GP2, **6bi** (158 mg, 0.372 mmol, 79% ee) was cyclized with $Hg(OAc)_2$ (13 mg, 0.04 mmol) and $MeSO_3H$ (81 mg, 0.84 mmol). After workup, **7bi** was used without further purification. According to GP3, the crude mixture of **7bi** was oxidized with *m*-CPBA (213 mg, 0.74 mmol, content ca. 60 proc.) and $BF_3{\cdot}OEt_2$ (103 μL, 0.74 mmol) to yield **8bi** (53 mg, 49%, based on **6bi**) as colourless crystals; mp 118 °C (petroleum ether–Et_2O); R_f 0.20 (petroleum ether–Et_2O, 4:1); $[\alpha]_D^{20}$ = –3.0 (*c* = 0.50, $CHCl_3$).

IR (KBr): 1766 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.73 (s, 3 H), 1.58–2.22 (m, 6 H), 2.63 (dd, *J* = 3.6, 9.3 Hz, 1 H), 5.16 (s, 1 H), 7.07 (m_c, 2 H), 7.48 (m_c, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.7 (CH_3), 25.2 (CH_2), 29.6 (CH_2), 41.1 (CH_2), 51.5 (C_q), 51.8 (CH), 87.7 (CH), 122.1 (C_q), 127.3 (CH), 131.6 (CH), 136.7 (C_q), 179.7 (C=O).

HRMS: *m*/*z* calcd $C_{14}H_{15}BrO_2$ (295.17): 294.02554; found (for $C_{14}H_{15}{}^{79}BrO_2$): 294.02394.

X-ray crystal structure analysis (Figure 1):[12] formula $C_{14}H_{15}BrO_2$, *M* = 295.17, colourless crystal 0.50 × 0.10 × 0.10 mm, *a* = 7.342 (2), *b* = 9.829 (2), *c* = 17.829 (5) Å, *V* = 1286.6 (6) Å^3, ρ_{calcd} = 1.524 g cm^{-3}, μ = 42.52 cm^{-1}, empirical absorption correction via ψ scan data (0.225 ≤ *T* ≤ 0.676), *Z* = 4, orthorhombic, space group $P2_12_12_1$ (No. 19), λ = 1.54178 Å, *T* = 223 K, ω/2θ scans, 2966 reflections collected (–*h*, +*k*, ±*l*), [(sinθ)/λ] = 0.62 Å^{-1}, 2612 independent (R_{int} = 0.027) and 2481 observed reflections [$I \geq 2\sigma(I)$], 156 refined parameters, *R*1 = 0.030, *wR*2 = 0.078, Flack parameter –0.01(2), max. residual electron density 0.60 (–0.47) e Å^{-3}, hydrogens calculated and refined as riding atoms.

***rac*-(3*RS*,3a*SR*,7a*RS*)-3a-Methyl-3-propylhexahydrobenzo[*c*]furan-1-one (*rac*-8dc)**

According to GP2, *rac*-**6dc** (511 mg, 1.57 mmol) was cyclized with $Hg(OAc)_2$ (25 mg, 0.08 mmol) and $MeSO_3H$ (226 mg, 2.36 mmol). After workup, the crude mixture of products was used without further purification. The crude mixture *rac*-**7dc** was oxidized according GP3 with *m*-CPBA (515 mg, 2.09 mmol, content ca. 60 proc.) and $BF_3{\cdot}OEt_2$ (220 μL, 1.57 mmol). Purification by flash chromatography (petroleum ether–Et_2O, 4:1) yielded *rac*-**8dc** (232 mg, 75%) as a colourless oil; R_f 0.29 (petroleum ether–Et_2O, 4:1).

IR (film): 1772 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.92 (t, *J* = 7.3 Hz, 3 H), 1.05 (s, 3 H), 1.20–1.96 (2 × m, 12 H), 2.29 (t, *J* = 5.0 Hz, 1 H), 3.99 (t, *J* = 6.4 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.8 (CH_3), 19.5 (CH_2), 19.8 (CH_3), 21.3 (CH_2), 21.7 (CH_2), 22.9 (CH_2), 31.5 (CH_2), 34.4 (CH_2), 40.1 (C_q), 45.0 (CH), 86.4 (CH), 178.3 (C=O).

Anal. Calcd for $C_{12}H_{20}O_2$ (196.29): C, 73.43; H, 10.27. Found: C, 73.33; H, 10.28.

(3*R*,3a*S*,7a*R*)-3a-Methyl-3-octylhexahydro-benzo[*c*]furan-1-one (8dd)

According to GP2, **6dd** (104 mg, 0.26 mmol, ($[\alpha]_D^{20}$ = +45.4) was cyclized with $Hg(OAc)_2$ (10 mg, 0.03 mmol) and $MeSO_3H$ (50 mg, 0.52 mmol). The crude mixture of **7dd** was oxidized according to GP3 with *m*-CPBA (96 mg, 0.34 mmol, content ca. 60 proc.) and $BF_3{\cdot}OEt_2$ (48 μL, 0.34 mmol). Purification by flash chromatography (petroleum ether–Et_2O, 4:1) yielded **8dd** (54 mg, 78%) as a colourless oil; R_f 0.38 (petroleum ether–Et_2O, 4:1); $[\alpha]_D^{20}$ = +25.4 (*c* = 0.34, $CHCl_3$).

IR (film): 1777 (C=O) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.85 (t, *J* = 7.0 Hz, 3 H), 1.05 (s, 3 H), 1.18–1.96 (2 × m, 22 H), 2.29 (t, *J* = 5.1 Hz, 1 H), 3.98 (dd, *J* = 4.2, 9.3 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0 (CH_3), 19.8 (CH_3), 21.4 (CH_2), 21.7 (CH_2), 22.6 (CH_2), 22.9 (CH_2), 26.3 (CH_2), 29.2 (CH_2), 29.4 (CH_2), 29.5 (CH_2), 29.5 (CH_2), 31.8 (CH_2), 34.4 (CH_2), 40.2 (C_q), 45.1 (CH), 86.7 (CH), 178.2 (C=O).

HRMS: *m*/*z* calcd $C_{17}H_{30}O_2$ (266.42): 266.22458; found: 266.22421.

(3*R*,3a*S*,7a*R*)-3a-Methyl-3-(1-naphthyl)hexahydrobenzo[*c*]furan-1-one (8dg)

According to GP2, **8dg** (116 mg, 0.28 mmol, 76% ee) was cyclized with $Hg(OAc)_2$ (10 mg, 0.03 mmol) and $MeSO_3H$ (54 mg, 0.56 mmol). The crude mixture of **7dg** was oxidized according to GP3 with *m*-CPBA (148 mg, 0.60 mmol, content ca 60 proc.) and $BF_3{\cdot}OEt_2$ (84 μL, 0.60 mmol). Purification by flash chromatography (petroleum ether–EtOAc, 5:1) yielded **8dg** (63 mg, 80%) as a colourless oil; R_f = 0.44 (petroleum ether–Et_2O, 4:1); $[\alpha]_D^{20}$ = –85.5 (*c* = 0.40, $CHCl_3$); mp 189 °C (petroleum ether–EtOAc).

IR (KBr): 1778 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.72 (s, 3 H), 1.22–2.23 (m, 8 H), 2.56 (br s, 1 H), 5.97 (s, 1 H), 7.28–7.96 (3 × m, 7 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.4 (CH_3), 21.1 (CH_2), 21.5 (CH_2), 22.7 (CH_2), 36.1 (CH_2), 42.6 (C_q), 43.2 (CH), 84.7 (CH), 122.8 (CH), 123.0 (CH), 125.2 (CH), 125.8 (CH), 126.2 (CH), 128.6 (CH), 129.1 (CH), 131.0 (C_q), 132.3 (C_q), 133.4 (C_q), 178.6 (C=O).

Anal. Calcd for $C_{19}H_{20}O_2$ (280.36): C, 81.40; H, 7.19. Found: C, 81.09; H, 7.09.

(3*R*,3a*S*,7a*R*)-3-(4-Bromophenyl)-3a-methylhexahydrobenzo[*c*]furan-1-one (8di)

According to GP2, **6di** (60 mg, 0.137 mmol, 87% *ee*) was cyclized with $Hg(OAc)_2$ (4.5 mg, 0.014 mmol) and $MeSO_3H$ (26 mg, 0.27 mmol). The crude mixture of **7di** was oxidized according to GP3 with *m*-CPBA (118 mg, 0.41 mmol, content ca. 60 proc.) and $BF_3{\cdot}OEt_2$ (51 μL, 0.36 mmol). After purification by flash chromatography (petroleum ether–Et_2O, 1:2) **8di** was yielded (31 mg, 73%) as a colourless solid; R_f 0.22 (petroleum ether–Et_2O, 4:1); $[\alpha]_D^{20}$ = –15.8 (*c* = 0.10, $CHCl_3$).

IR (KBr): 1781 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.74 (s, 3 H), 1.35–2.05 (m, 8 H), 2.37 (m_c, 1 H), 5.06 (s, 1 H), 7.03 (m_c, 2 H), 7.47 (m_c, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.4 (CH_3), 21.5 (CH_2), 21.9 (CH_2), 22.8 (CH_2), 34.8 (CH_2), 42.0 (C_q), 44.4 (CH), 86.4 (CH), 122.2 (C_q), 127.6 (CH), 131.5 (CH), 135.3 (C_q), 178.1 (C=O).

Anal. Calcd for $C_{15}H_{17}BrO_2$ (309.20): C, 58.27; H, 5.54. Found: C, 58.08; H, 5.80.

X-ray crystal structure analysis (Figure 2):[12] formula $C_{15}H_{17}BrO_2$, *M* = 309.20, colourless crystal 0.30 × 0.20 × 0.20 mm, *a* = 13.749 (2), *b* = 7.353 (1), *c* = 13.993(2) Å, = 101.12(1), *V* = 1388.1 (3) Å^3, ρ_{calcd} = 1.480 g cm^{-3}, μ = 39.67 cm^{-1}, empirical absorption correction via ψ scan data (0.382 ≤ *T* ≤ 0.504), *Z* = 4, monoclinic, space group $P2_1$ (No. 4), λ = 1.54178 Å, *T* = 223 K, ω/2θ scans, 3190 re-

flections collected (±*h*, –*k*, +*l*), [(sinθ)/λ] = 0.62 Å^{-1}, 3065 independent (R_{int} = 0.025) and 2873 observed reflections [$I \geq 2\sigma(I)$], 328 refined parameters, *R*1 = 0.039, *wR*2 = 0.121, Flack parameter 0.03(3), max. residual electron density 0.49 (–0.63) e Å^{-3}, two almost identical molecules in the asymmetric unit, hydrogens calculated and refined as riding atoms.

rac-(3*RS*,3a*SR*,8a*RS*)- and _rac_-(3*RS*,3a*SR*,8a*SR*)-3-(4-Bromophenyl)-3a-methyloctahydrocyclohepta[*c*]furan-1-one [*rac*-8ei(c)] and [*rac*-8ei(t)]

According to GP2, *rac*-**6ei** (179 mg, 0.40 mmol) was cyclized with $Hg(OAc)_2$ (6.4 mg, 0.02 mmol) and $MeSO_3H$ (58 mg, 0.60 mmol). The crude mixture of **7ei** was oxidized according to GP3 with *m*-CPBA (515 mg, 2.09 mmol, content ca. 60 proc.) and $BF_3{\cdot}OEt_2$ (400 μL, 3.10 mmol). Purification by flash chromatography (petroleum ether–EtOAc, 20:1) yielded the *cis*-isomer *rac*-**8ei(c)** [(58 mg, 44%); R_f 0.19 (petroleum ether–EtOAc, 20:1), mp 109 °C (petroleum ether–EtOAc)] and the *trans* isomer *rac*-**8ei(t)** [(29 mg, 23%); R_f 0.25 (petroleum ether–EtOAc, 20:1); mp 161 °C (petroleum ether–EtOAc)]; NOE between 3a-CH_3 and 8a-H.

***rac*-8ei(c)**

IR (film): 1770 (C=O) cm^{-1}.

^{1}H NMR (400 MHz, C_6D_6): δ = 0.26 (s, 3 H), 0.75–0.84 (m, 1 H), 0.89–0.98 (m, 2 H), 0.99–1.07 (m, 2 H), 1.19–1.26 (m, 1 H), 1.33 (m_c, 1 H), 1.48 (br s, 1 H), 1.65 (br s, 1 H), 1.79 (dd, *J* = 6.1, 14.1 Hz, 1 H), 2.03 (d, *J* = 12.1 Hz, 1 H), 4.55 (s, 1 H), 6.70 (m_c, 2 H), 7.22 (m_c, 2 H).

^{13}C NMR (100 MHz, C_6D_6): δ = 22.8 (CH_3), 23.2 (CH_2), 27.3 (CH_2), 30.4 (CH_2), 31.3 (CH_2), 37.0 (CH_2), 46.4 (C_q), 55.2 (CH), 87.3 (CH), 122.1 (C_q), 127.7 (CH), 131.5 (CH), 135.3 (C_q), 177.7 (C=O).

HR-MS: *m*/*z* calcd for $C_{16}H_{19}BrO_2$ (323.22): 322.05685; found [for $C_{16}H_{19}{}^{79}BrO_2$]: 322.05491.

***rac*-8ei(t)**

IR (KBr): 1767 (C=O) cm^{-1}.

^{1}H NMR (400 MHz, C_6D_6): δ = 0.21 (s, 3 H), 0.69–1.58 (m, 9 H), 2.00–2.14 (m, 2 H), 4.24 (s, 1 H), 6.73 (m_c, 2 H), 7.23 (m_c, 2 H).

^{13}C NMR (100 MHz, C_6D_6): δ = 14.1 (CH_3), 22.3 (CH_2), 25.2 (CH_2), 26.2 (CH_2), 26.6 (CH_2), 38.0 (CH_2), 48.1 (C_q), 49.1 (CH), 87.3 (CH), 122.2 (C_q), 128.2 (CH), 131.5 (CH), 134.8 (C_q), 176.5 (C=O).

HRMS: calcd $C_{16}H_{19}BrO_2$ (323.22): 322.05685; found [for $C_{16}H_{19}{}^{79}BrO_2$]: 322.05495.

rac-(3*RS*,3a*SR*,9a*RS*)- and _rac_-(3*RS*,3a*SR*,9a*SR*)-3-(4-Bromophenyl)-3a-methyloctahydro-cycloocta[*c*]furan-1-one [*rac*-8fi(c)] and [*rac*-8fi(t)]

According to GP2, *rac*-**6fi** (233 mg, 0.48 mmol) was cyclized with $Hg(OAc)_2$ (7.6 mg, 0.024 mmol) and $MeSO_3H$ (69 mg, 0.72 mmol). According to GP3 the crude diastereomeric *rac*-**7fi** was oxidized with *m*-CPBA (515 mg, 2.09 mmol, content ca. 60 proc.) and $BF_3{\cdot}OEt_2$ (400 μL, 3.10 mmol). Purification by flash chromatography (petroleum ether–EtOAc, 20:1) yielded a inseparable mixture of diastereomers *rac*-**8fi(c)** and *rac*-**fi(t)** (103 mg, 62%); R_f 0.12 (petroleum ether–EtOAc, 20:1); ratio 25:75, as a colourless solid; chemical shift of minor diastereomer in parenthesis.

^{1}H NMR (400 MHz, C_6D_6): δ = 0.25 [0.31] (s, 3 H), 0.59–2.24 (m, 13 H), 4.31 [4.46] (s, 1 H), 6.70–6.79 (m, 2 H), 7.19–7.27 (m, 2 H).

^{13}C NMR (100 MHz, C_6D_6): δ = 16.0 [19.7] (CH_3), 22.7 (CH_2), 24.3 (CH_2), 24.5 (CH_2), 24.6 (CH_2), 25.3 (CH_2), 26.2 (CH_2), 26.9 (CH_2), 27.0 (CH_2), 27.8 (CH_2), 30.5 (CH_2), 31.8 (CH_2), 36.3 (CH_2), 46.3 [45.2] (C_q), 54.4 [48.0] (CH), 85.5 [86.6] (CH), 122.5 [122.4] (C_q), 129.0 [128.8] (CH), 131.4 [131.3] (CH), 134.2 [134.4] (C_q), 177.1 [179.4] (C=O).

ESI–MS: *m*/*z* calcd for $C_{17}H_{21}BrO_2$ (337.25): 359, 361 [M + Na]$^+$.

(3*R*,3a*S*,7a*R*)-3a-Methyl-3-vinylhexahydro-benzo[*c*]furan-1-one (8df) from 6df via Vinyllithiation and Methanesulfenylation

To enol carbamate **6df** (82% ee, 327 mg, 1.06 mmol), Et_3N (192 mg, 1.90 mmol) in CH_2Cl_2, chlorotrimethylsilane (172 mg, 1.59 mmol) was added at 0 °C. The mixture was stirred at 25 °C for 15 h and subsequently poured to a mixture of Et_2O (10 mL) and sat. aq NH_4Cl (10 mL). The Et_2O solution was separated and the aqueous phase extracted with Et_2O (3 × 10 mL). The combined organic solutions were neutralised with aq $NaHCO_3$ solution (20 mL) and dried (solid $MgSO_4$). The solvents were removed in vacuo and the crude silyl ether **9** dissolved in toluene (10 mL). After renewed removal of the solvent in vacuo, the residue was dissolved in anhyd THF (5 mL) under Ar, TMEDA (148 mg, 1.25 mmol) was added, and at –78 °C *n*-BuLi in hexane (1.51 mmol) was slowly introduced through the septum with a syringe. Stirring was continued for 2 h before dimethyl disulfide (150 mg, 1.59 mmol) was added at –78 °C within 5 min. After having stirred at –78 °C for 3 h, the reaction mixture was allowed to warm to 0 °C. The solution was extracted with sat. aq NH_4Cl, and the aqueous phase extracted with Et_2O (3 × 10 mL). The solvent of the combined organic solutions was evaporated in vacuo. The remaining crude ketene monothio acetal **10**, dissolved in MeOH (5 mL), and methane sulfonic acid (152 mg, 1.59 mmol) were heated to 50 °C for 15 h. The reaction mixture was allowed to cool to r.t., poured to a mixture of Et_2O (10 mL) and 1 N aq HCl. Separation of the Et_2O phase, extraction of the aq phase with Et_2O (3 × 10 mL each), extraction of the combined ethereal solutions with sat. $NaHCO_3$ solution, drying over $MgSO_4$, and evaporation led to crude γ-lacton **8df**. Chromatographic purification on silica gel (petroleum ether–Et_2O, 4:1) afforded **8df** (106 mg, 56%) as a colourless oil; R_f 0.16 (petroleum ether–Et_2O, 4:1); $[\alpha]_D{}^{20}$ = +33.6 (*c* = 0.14, $CHCl_3$); GC: Supelco β-Dex© 120 (82% *ee*), major enantiomer appears at lower retention time.

IR (film): 1778 (C=O) cm^{-1}.

^{1}H NMR (360 MHz, $CDCl_3$): δ = 1.04 (s, 3 H), 1.19–2.01 (2 × m, 8 H), 2.28 (dd, *J* = 4.4, 5.4 Hz, 1 H), 4.42 (dΨt, *J* = 1.3, 6.3 Hz, 1 H), 5.26 (dΨt, *J* = 1.3, 10.6 Hz, 1 H), 5.30 (dΨt, *J* = 1.3, 17.0 Hz, 1 H), 5.80 (ddd, *J* = 6.3, 10.6, 17.0 Hz, 1 H).

^{13}C NMR (90 MHz, $CDCl_3$): δ = 20.2 (CH_3), 21.3 (CH_2), 21.4 (CH_2), 22.7 (CH_2), 34.2 (CH_2), 41.0 (C_q), 44.3 (CH), 86.4 (CH), 118.2 (CH_2), 132.1 (CH), 178.1 (C=O).

Anal. Calcd for $C_{11}H_{16}O_2$ (180.24): C, 73.30; H, 8.95; found: C, 72.97; H, 8.66.

Alkylation of Bicyclic Lactones; General Procedure (GP4)

1,1,1,3,3,3-Hexamethyldisilazane (1.05–2.10 mmol) was added dropwise to 1.6 M *n*-BuLi (1.0–2.0 equiv) in hexane at 0 °C. The cooling bath was removed and the reaction mixture was stirred for 15 min. Then, the solvent was removed at reduced pressure with exclusion of moisture; the residue was dissolved in THF (5 mL) and cooled to –78 °C. The lactone **8** (1.0 mmol), dissolved in THF (5 mL), was added and the mixture was stirred for 1 h at –78 °C before the 2-naphthylmethyl bromide (1.05–2.10 mmol), dissolved in THF (3 mL), was added. The reaction mixture was allowed to attain r.t. for a period of 15 h and then was poured in a mixture of sat. NH_4Cl solution (10 mL/mmol) and Et_2O (20 mL). The aqueous layer was extracted with Et_2O (3 × 15 mL). The combined organic extracts were dried over anhyd $MgSO_4$ and concentrated in vacuo. The residue was purified by silica gel flash column chromatography.

***rac*-(3*RS*,3a*SR*,6a*SR*)-3-Methyl-6a-(2-naphthylmethyl)hexahydrocyclopenta[*c*]furan-1-one (*rac*-12a)**

According to GP4, 1,1,1,3,3,3-hexamethyldisilazane (163 mg, 1.01 mmol) was deprotonated with *n*-BuLi (0.60 mL, 0.96 mmol). Compound *rac*-**8aa** (90 mg, 0.64 mmol) was added and the enolate was quenched with 2-bromomethyl-naphthalene (170 mg, 0.77 mmol). After purification by flash chromatography (petroleum ether–EtOAc, 5:1) *rac*-**12a** (80 mg, 45%) was obtained as a colourless solid; R_f 0.56 (petroleum ether–EtOAc, 5:1); mp 93 °C (petroleum ether–EtOAc).

IR (KBr):1755 (C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.67 (d, *J* = 6.4 Hz, 3 H), 1.44–2.32 (2 × m, 6 H), 2.36 (dd, *J* = 4.6, 6.7 Hz, 1 H), 2.79 (d, *J* = 13.6 Hz, 1 H), 3.50 (d, *J* = 13.6 Hz, 1 H), 3.95 (qd, *J* = 4.6, 6.4 Hz, 1 H), 7.32 (dd, *J* = 1.7, 8.2 Hz, 1 H), 7.43 (m_c, 2 H), 7.64 (br s, 1 H), 7.74–7.81 (m, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.2 (CH_3), 25.2 (CH_2), 33.7 (CH_2), 39.9 (CH_2), 42.7 (CH_2), 48.9 (CH), 58.8 (C_q), 81.8 (CH), 125.7 (CH), 126.1 (CH), 127.6 (CH), 127.7 (CH), 128.1 (CH), 128.3 (CH), 128.8 (CH), 132.4 (C_q), 133.4 (C_q), 135.4 (C_q), 182.0 (C=O).

Anal. Calcd for $C_{19}H_{20}O_2$ (280.36): C, 81.40; H, 7.19. Found: C, 81.21; H, 6.95.

***rac*-(3*RS*,3a*SR*,6a*SR*)-3-Isopropyl-6a-(2-naphthylmethyl)hexahydrocyclopenta[*c*]furan-1-one (*rac*-12b)**

According to GP4, 1,1,1,3,3,3-hexamethyldisilazane (144 mg, 0.89 mmol) was deprotonated with *n*-BuLi (0.53 mL, 0.85 mmol). Compound *rac*-**8ab** (142 mg, 0.85 mmol) was added and the enolate was quenched with 2-bromomethyl-naphthalene (208 mg, 0.94 mmol). After purification by flash chromatography (petroleum ether–EtOAc, 20:1) *rac*-**12b** (110 mg, 42%) was obtained as a colourless solid; R_f 0.12 (petroleum ether–EtOAc, 20:1); mp 79 °C (petroleum ether–EtOAc).

IR (KBr): 1763 (C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.57 (d, *J* = 6.7 Hz, 3 H), 0.62 (d, *J* = 6.7 Hz, 3 H), 0.96 (sept, *J* = 6.7 Hz, 1 H), 1.47–2.30 (3 × m, 6 H), 2.49 (m_c, 1 H), 2.80 (d, *J* = 13.6 Hz, 1 H), 3.44 (d, *J* = 13.6 Hz, 1 H), 3.48 (m_c, 1 H), 7.31 (dd, *J* = 1.8, 8.5 Hz, 1 H), 7.43 (m_c, 2 H), 7.63 (br s, 1 H), 7.67–7.83 (m, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.4 (CH_3), 18.0 (CH_3), 25.1 (CH_2), 32.7 (CH), 33.8 (CH_2), 39.2 (CH_2), 42.5 (CH_2), 45.4 (CH), 58.1 (C_q), 90.2 (CH), 125.6 (CH), 126.0 (CH), 127.5 (CH), 127.6 (CH), 128.0 (CH), 128.3 (CH), 128.8 (CH), 132.4 (C_q), 133.4 (C_q), 135.4 (C_q), 181.9 (C=O).

HRMS: *m*/*z* calcd for $C_{21}H_{24}O_2$ (308.41): 308.17764; found: 308.17700.

***rac*-(3*RS*,3a*SR*,6a*SR*)-6a-(2-Naphthylmethyl)-3-propylhexahydrocyclopenta[*c*]furan-1-one (*rac*-12c)**

According to GP4, 1,1,1,3,3,3-hexamethyldisilazane (202 mg, 1.25 mmol) was deprotonated with *n*-BuLi (0.74 mL, 1.19 mmol). Compound *rac*-**8ac** (200 mg, 1.19 mmol) was added and the enolate was quenched with 2-bromomethyl-naphthalene (290 mg, 1.31 mmol). After workup, the crude products were purified by flash chromatography (petroleum ether–EtOAc, 5:1) to yield *rac*-**12c** (167 mg, 46%) as a colourless solid; R_f 0.57 (petroleum ether–EtOAc, 5:1); mp 72 °C (petroleum ether–EtOAc).

IR (KBr): 1755 (C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.53 (t, *J* = 7.4 Hz, 3 H), 0.59–0.85 (m, 2 H), 0.92–1.18 (m, 2 H), 1.44–2.30 (3 × m, 6 H), 2.34–2.42 (m, 1 H), 2.78 (d, *J* = 13.6 Hz, 1 H), 3.48 (d, *J* = 13.6 Hz, 1 H), 3.79 (ddd, *J* =4.5, 6.2, 7.6 Hz, 1 H), 7.31 (dd, *J* = 1.8, 8.5 Hz, 1 H), 7.43 (m_c, 2 H), 7.62 (br s, 1 H), 7.74–7.81 (m, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.4 (CH_3), 18.2 (CH_2), 25.3 (CH_2), 34.0 (CH_2), 37.6 (CH_2), 39.5 (CH_2), 42.7 (CH_2), 47.3 (CH), 58.4 (C_q), 85.4 (CH), 125.7 (CH), 126.1 (CH), 127.5 (CH), 127.6 (CH), 128.1 (CH), 128.3 (CH), 128.8 (CH), 132.5 (C_q), 133.4 (C_q), 135.4 (C_q), 182.1 (C=O).

Anal. Calcd for $C_{21}H_{24}O_2$ (308.41): C, 81.78; H, 7.84. Found: C, 81.64; H, 8.12.

***rac*-(3*RS*,3a*SR*,6a*SR*)-6a-(2-Naphthylmethyl)-3-octylhexahydrocyclopenta[*c*]furan-1-one (*rac*-12d)**

According to GP4, 1,1,1,3,3,3-hexamethyldisilazane (204 mg, 1.26 mmol) was deprotonated with *n*-BuLi (0.75 mL, 1.20 mmol). Compound *rac*-**8ad** (286 mg, 1.20 mmol) was added and the enolate was quenched with 2-bromomethyl-naphthalene (292 mg, 1.32 mmol). After purification by flash chromatography (petroleum ether–EtOAc, 10:1) *rac*-**12d** (218 mg, 48%) was obtained as a colourless solid; R_f 0.27 (petroleum ether–EtOAc, 10:1); mp 71 °C (petroleum ether–EtOAc).

IR (KBr): 1749 (C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.58–2.31 (3 × m, 20 H), 0.86 (t, *J* = 7.0 Hz, 3 H), 2.38 (dd, *J* = 4.4, 7.2 Hz, 1 H), 2.76 (d, *J* = 13.5 Hz, 1 H), 3.49 (d, *J* = 13.5 Hz, 1 H), 3.76 (ddd, *J* = 4.4, 6.3, 7.3 Hz, 1 H), 7.31 (dd, *J* = 1.9, 8.6 Hz, 1 H), 7.42 (m_c, 2 H), 7.62 (br s, 1 H), 7.70–7.82 (m, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0 (CH_3), 22.6 (CH_2), 24.7 (CH_2), 25.2 (CH_2), 29.0 (CH_2), 31.7 (CH_2), 34.1 (CH_2), 35.3 (CH_2), 39.7 (CH_2), 42.7 (CH_2), 47.1 (CH), 58.4 (C_q), 85.7 (CH), 125.7 (CH), 126.0 (CH), 127.5 (CH), 127.6 (CH), 128.1 (CH), 128.3 (CH), 128.7 (CH), 132.4 (C_q), 133.4 (C_q), 135.4 (C_q), 182.0 (C=O).

Anal. Calcd for $C_{26}H_{34}O_2$ (378.55): C, 82.49; H, 9.05. Found: C, 82.47; H, 9.17.

***rac*-(3*RS*,3a*SR*,6a*SR*)-6a-(2-Naphthylmethyl)-3-phenylhexahydrocyclopenta[*c*]furan-1-one (*rac*-12e)**

According to GP4, 1,1,1,3,3,3-hexamethyldisilazane (163 mg, 1.01 mmol) was deprotonated with *n*-BuLi (0.60 mL, 0.96 mmol). Compound *rac*-**8ae** (127 mg, 0.63 mmol) was added and the enolate was quenched with 2-bromomethyl-naphthalene (170 mg, 0.77 mmol). Purification by flash chromatography (petroleum ether–EtOAc, 5:1) yielded *rac*-**12e** (160 mg, 46%) as a colourless solid; R_f 0.35 (petroleum ether–EtOAc, 5:1); mp 123 °C (petroleum ether–EtOAc).

IR (KBr): 1754 (C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.53–2.49 (2 × m, 6 H), 2.65–2.87 (m, 2 H), 3.49 (d, *J* = 13.4 Hz, 1 H), 4.77 (d, *J* = 5.3 Hz, 1 H), 6.36–7.87 (6 × m, 12 H).

^{13}C NMR (75MHz, $CDCl_3$): δ = 25.0 (CH_2), 33.3 (CH_2), 39.4 (CH_2), 42.6 (CH_2), 51.0 (CH), 58.5 (C_q), 85.6 (CH), 124,7 (CH), 125.6 (CH), 126.0 (CH), 127.4 (CH), 127.6 (CH), 127.7 (CH), 128.1 (CH), 128.2 (CH), 128.4 (CH), 128.9 (CH), 132.5 (C_q), 133.4 (C_q), 134.9 (C_q), 140.1 (C_q), 181.8 (C=O).

HRMS: *m*/*z* calcd for $C_{21}H_{22}O_2$ (342.43): 342.16199; found: 342.16239.

***rac*-(3*RS*,3a*SR*,7a*SR*)-3a-Methyl-7a-(2-naphthylmethyl)-3-propylhexahydro[c]benzofuran-1-one (*rac*-12f)**

According to GP4, 1,1,1,3,3,3-hexamethyldisilazane (282 mg, 1.75 mmol) was deprotonated with *n*-BuLi (1.04 mL, 1.66 mmol). Compound *rac*-**8bc** (162 mg, 0.83 mmol) was added and the enolate was quenched with 2-bromomethyl-naphthalene (275 mg, 1.25 mmol). After purification by flash chromatography (petroleum ether–

EtOAc, 20:1) *rac*-**12e** was yielded (145 mg, 52%) as a colourless solid; R_f 0.24 (petroleum ether–EtOAc, 20:1); mp 129 °C (petroleum ether–EtOAc).

IR (KBr): 1759 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.89–1.12 (m, 6 H), 1.16–1.80 (m, 12 H), 2.81 (d, *J* = 14.2 Hz, 1 H), 3.20 (d, *J* = 14.2 Hz, 1 H), 4.53 (dd, *J* = 9.7, 1.8 Hz, 1 H), 7.32–7.95 (2 × m, 7 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0 (CH_3), 18.6 (CH_3), 20.4 (CH_2), 20.8 (CH_2), 21.2 (CH_2), 27.0 (CH_2), 30.5 (CH_2), 31.5 (CH_2), 36.2 (CH_2), 44.5 (C_q), 49.5 (C_q), 81.7 (CH), 125.4 (CH), 125.4 (CH), 127.4 (CH), 127.5 (CH), 127.7 (CH), 129.7 (CH), 129.8 (CH), 132.3 (C_q), 133.3 (C_q), 135.0 (C_q), 180.5 (C=O).

Anal. Calcd for $C_{23}H_{28}O_2$ (336.47): C, 82.10; H, 8.39. Found: C, 81.91; H, 8.11.

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