Synthesis of Enantioenriched and Diastereomerically Pure *cis*-Fused Bicyclic α-Oxy-Substituted γ-Lactones via Epoxidation of Optically Active Homoaldol Products

Seda Ünaldi, Roland Fröhlich,[1] Dieter Hoppe*

Institut für Organische Chemie, Westfälischen Wilhelms-Universität Münster, Corrensstraße 40, 48149 Münster, Germany
Fax +49(251)8336531; E-mail: dhoppe@uni-muenster.de

Received 9 March 2005; revised 11 April 2005

Abstract: By applying the (–)-sparteine-mediated asymmetric deprotonation to 1-*O*-(2-alkylcycloalk-1-enyl)methyl *N*,*N*-diisopropylcarbamates, combined with a lithium–titanium exchange followed by addition to achiral aldehydes, enantioenriched homoaldol products **6** were prepared. Hydroxyl-directed epoxidation resulted in the cleavage of the oxirane ring by the migration of the *N*,*N*-diisopropylcarbamoyloxy group to form bicyclic γ-lactols **10** via the corresponding γ-hydroxy aldehydes. After oxidation, diastereomerically pure, penta-substituted γ-lactones **11** were obtained.

Key words: carbamates, aldol reactions, sparteine, diastereoselectivity, epoxides, bicyclic compounds, lactones

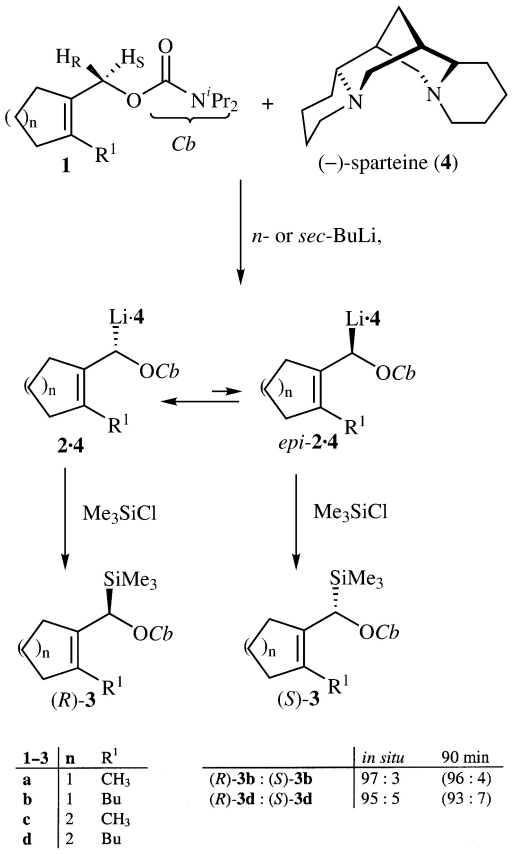
Primary 2-alkenyl *N*,*N*-diisopropylcarbamates undergo highly stereoselective α-deprotonation by means of BuLi/(–)-sparteine (**4**).[2,3] Unlike simple derivatives,[4] 1-*O*-(2-methylcycloalk-1-enyl)methyl carbamates **1a** and **1c** lead to configurationally stable lithium intermediates[5] **2a** and **2c** (Scheme 1). This was demonstrated by trapping **2** by means of chlorotrimethylsilane as silanes **3** after different standing times.[5] The same features turned out to be also true for the 1-*O*-(2-butylcycloalk-1-enyl)methyl carbamates **1b** and **1d**. The silylation proceeds with inversion of configuration.

The high configurational stability of the carbanionic intermediates allows for asymmetric hydroxyalkylation with aldehydes.[5] These 'homoaldol reactions', when carried out after lithium–titanium exchange (inversion of configuration), proceed via Zimmerman–Traxler transition states, combined with essentially complete chirality transfer to form enantioenriched homoaldol products **6** with the relative configuration (*Z*)-*anti* (Scheme 2).[6]

We recently reported the oxidative cyclization of homoaldol products with formation of bicyclic γ-lactones.[5b]

During the epoxidation of racemic homoaldol products we observed the opening of the oxirane ring, by the migrating carbamoyloxy group to form finally a lactol which was characterized by an X-ray crystal structure analysis.[7]

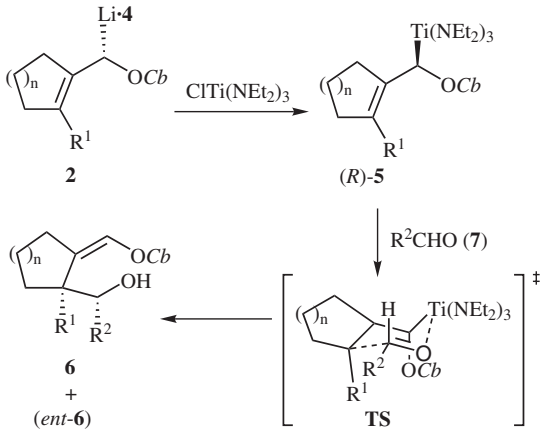
Combined with the enantioselective deprotonation and the asymmetric homoaldol reaction, the epoxidation–rear-



1–3	n	R¹
a	1	CH_3
b	1	Bu
c	2	CH_3
d	2	Bu

	in situ	90 min
(*R*)-**3b** : (*S*)-**3b**	97 : 3	(96 : 4)
(*R*)-**3d** : (*S*)-**3d**	95 : 5	(93 : 7)

Scheme 1 Silylations of substituted lithioallyl carbamates



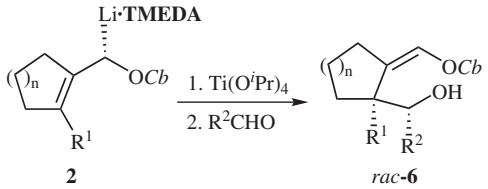
Scheme 2 Synthesis of enantioenriched homoaldol products

SYNTHESIS 2005, No. 15, pp 2507–2520
Advanced online publication: 20.07.2005
DOI: 10.1055/s-2005-872080; Art ID: T03305SS

rangement offers a versatile 'brick-box approach' towards complex α-oxy-γ-lactones.

Asymmetric Homoaldol Reaction

Whereas the 1-*O*-(2-alkylcycloalk-1-enyl)methyl carbamates **1a–c** were smoothly deprotonated by BuLi/(–)-sparteine in toluene below –78 °C,[5] the 1-*O*-(2-butylcyclohexenyl)methyl carbamate (**1d**) required the application of *sec*-BuLi/(–)-sparteine for complete deprotonation under these conditions (Scheme 1). Trapping the mixtures of epimeric ion pairs by chlorotrimethylsilane 'in situ' and also after 90 min stirring before silylation, afforded essentially the same enantiomeric ratios of (*R*)- and (*S*)-**3b** and (*R*)- and (*S*)-**3d**, respectively, which demonstrates the high configurational stability of the intermediate lithium–sparteine complexes[5] **2·4** and *epi*-**2·4** (Scheme 1). The lithium–titanium exchange in **2**/*epi*-**2·4** with chlorotris(diethylamino)titanium followed by achiral aldehydes afforded diastereomerically pure (dr ≥ 95:5) and enantiomerically enriched homoaldol products **6** with good yields (Scheme 2, Table 1). The enantiomeric ratios (er) in compounds **6** were determined by HPLC on chiral columns and by chiral ^{1}H NMR shift reagents (Table 1). When Ti(OPr-*i*)$_4$ or Ti(OPr-*i*)$_3$Cl were used, much lower yields were recorded.[8] There is some evidence that the allyltrialkoxytitanates undergo a facile homolytic cleavage at the Ti–C bond.[9] However, when BuLi–TMEDA was used, the intermediates, prepared from *rac*-**2·TMEDA** and Ti(OPr-*i*)$_4$ gave high yields of homoaldol products *rac*-**6** (Scheme 3).



Scheme 3 Synthesis of racemic homoaldol products

Epoxidation and Rearrangement of 6

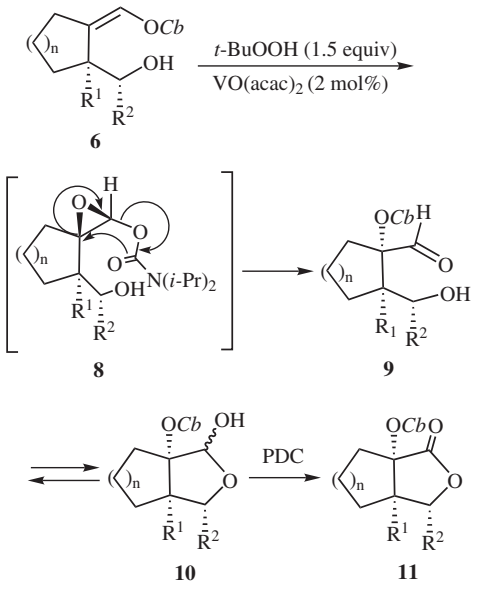
The (*Z*)-*anti*-homoaldol products **6** were treated with an excess of *tert*-butyl hydroperoxide in the presence of 2 mol% of VO(acac)$_2$ in dichloromethane[7], according to Sharpless[10] and Mihelich[11] (Scheme 4). In the first step, a highly diastereoface-differentiating attack is induced by the directing hydroxyl group to form the epoxide **8**. The epoxide is not stable under the reaction conditions and is

Table 1 New Homoaldol Products **6** Prepared

Substrates	Aldehyde	Product	n	R^1	R^2	ee (%)	Yield (%) [of *rac*-**6**][a]
5a[b]	4-BrC_6H_4CH=O (**7a**)	**6a**[d]	1	Me	4-BrC_6H_4	93	72 [81]
5a[b]	4-ClC_6H_4CH=O (**7b**)	**6b**	1	Me	4-ClC_6H_4	74	79 [74]
5a[b]	β-Naphthyl-CH=O (**7c**)	**6c**	1	Me	β-Naphthyl	81	73 [78]
5b[b]	Me_2CHCH=O (**7d**)	**6d**	1	$(CH_2)_3$Me	Me_2CH-	65	52 [54]
5b[b]	PhCH=O (**7e**)	**6e**	1	$(CH_2)_3$Me	Ph	79	53 [54]
5b[b]	4-BrC_6H_4CH=O (**7a**)	**6f**	1	$(CH_2)_3$Me	4-BrC_6H_4	72	53 [52]
5b[b]	β-Naphthyl-CH = O (**7c**)	**6g**	1	$(CH_2)_3$Me	β-Naphthyl	84	57 [55]
5b[b]	CH_2=CHCH=O (**7f**)	**6h**	1	$(CH_2)_3$Me	CH_2=CH	88	56 [58]
5c[b]	4-BrC_6H_4CH=O (**7a**)	**6i**[d]	2	Me	4-BrC_6H_4	86	58 [79]
5d[c]	α-Naphthyl-CH=O (**7g**)	**6j**	2	$(CH_2)_3$Me	α-Naphthyl	74	63 [65]
5d[c]	PhCH=O (**7e**)	**6k**	2	$(CH_2)_3$Me	Ph	78	65 [68]
5d[c]	4-BrC_6H_4CH=O (**7a**)	**6l**	2	$(CH_2)_3$Me	4-BrC_6H_4	76	58 [65]
5d[c]	β-Naphthyl-CH=O (**7c**)	**6m**	2	$(CH_2)_3$Me	β-Naphthyl	66	67 [68]
5d[c]	Me_2CHCH=O (**7d**)	**6n**	2	$(CH_2)_3$Me	Me_2CH-	72	55 [62]
5d[c]	4-MeOC_6H_4CH=O (**7h**)	**6o**	2	$(CH_2)_3$Me	4-MeOC_6H_4	74	58 [68]

[a] Yield of *rac*-**6**, prepared via deprotonation in the presence of TMEDA.
[b] Deprotonation with BuLi/(–)-sparteine.
[c] Deprotonation with *sec*-BuLi/(–)-sparteine.
[d] For the data see ref.[5]

opened with inversion of the configuration by the migrating carbamoyloxy group. The γ-hydroxy aldehydes **9** are in equilibrium with the anomeric lactols **10**, which finally are oxidized to the γ-lactones **11** (Table 2).



Scheme 4 Epoxidation, rearrangement and oxidation of compounds **6**

The lactones *rac*-**11i**, *rac*-**11k** and **11c** were subjected to X-ray crystal structure analyses (Figures 1–3),[12] which confirmed the expected relative configuration.[12] The enantiomeric ratios of the lactones **11** match well with those of the utilized homoaldol product **6**. As standard for the enantiomeric lactones **11**, the appropriate compounds *rac*-**11** were synthesised from *rac*-**6** following the same route.

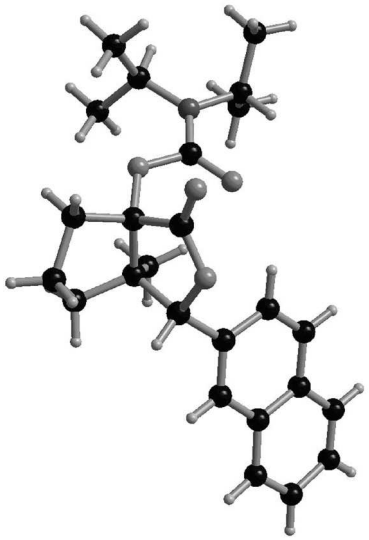


Figure 1 Solid-state structure of **11c**[12]

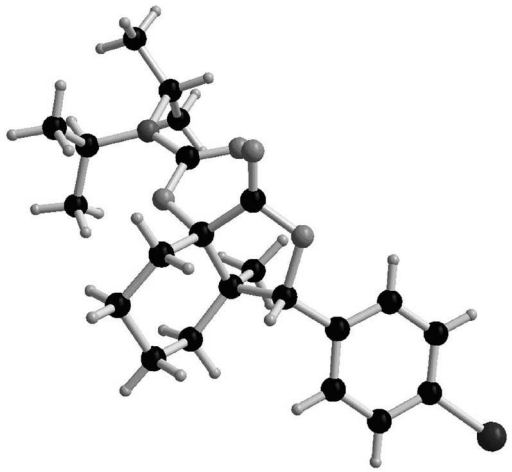


Figure 2 Solid-state structure of **11i**[12]

Table 2 Prepared Bicyclic α-Oxy-Substituted γ-Lactones **11**

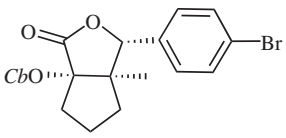
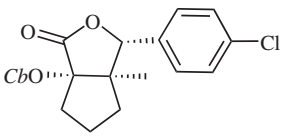
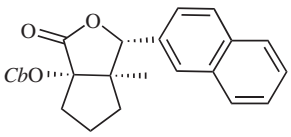
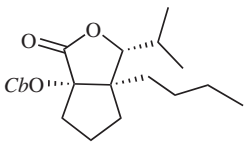
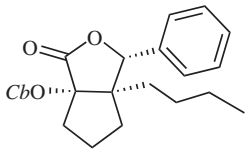
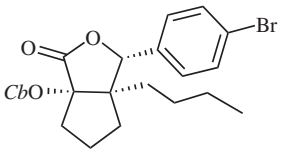
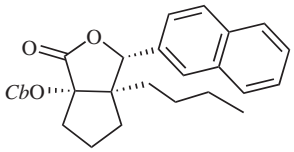
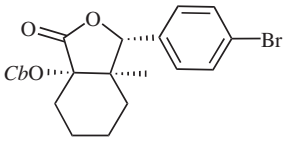
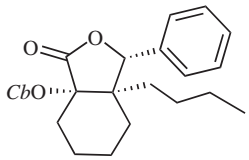
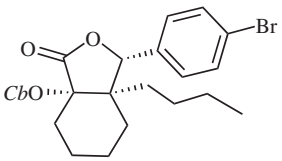
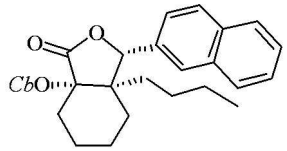
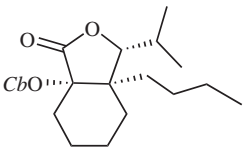
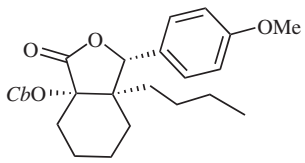
Product	Yield[a] (%) [of *rac*-**11**][b]	ee (%)	Product	Yield[a] (%) [of *rac*-**11**][b]	ee (%)
11a	58 [58]	93	**11b**	62 [49]	74
					
11c	44 [47]	83	**11d**	66 [65]	65
					

Table 2 Prepared Bicyclic α-Oxy-Substituted γ-Lactones **11** (continued)

Product	Yield[a] (%) [of *rac*-**11**][b]	ee (%)	Product	Yield[a] (%) [of *rac*-**11**][b]	ee (%)
11e 	66 [69]	78	**11f** 	68 [72]	72
11g 	72 [72]	82	**11i** 	70 [74]	86
11k 	69 [72]	78	**11l** 	70 [70]	76
11m 	73 [71]	66	**11n** 	76 [79]	72
11o 	68 [70]	73			

[a] Yields are based on homoaldol products **6**.
[b] Yields are based on homoaldol products *rac*-**6**.

All together, the combination of asymmetric homoaldol reaction, epoxidation with rearrangement, and oxidation of the formed γ-lactol offers a versatile access to highly substituted bicyclic γ-lactones.

BuLi (1.6 M in hexane) and *sec*-BuLi [1.18 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, CH_2Cl_2) 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 HPLC was carried out with a chiral column: chiragrom-2, 250 × 2; and chiragrom-1, 60 × 2 mm purchased from GROM ANALYTIC and HPLC GmbH, Herrenberg. The solvent systems used for the measurement were hexane–*i*-PrOH (100:1), (200:1) and (500:1). ^{1}H and ^{13}C NMR spectra were recorded on ARX 300, AMX 400, Bruker. 2D NMR experiments were carried out by Varian Unity Plus 600. $CDCl_3$ was used as solvent for normal NMR measurements, C_6D_6 was used for ^{1}H NMR shift experiments. Chemical shifts are reported in ppm (δ); ^{1}H shifts are related to TMS $\delta_H = 0$ and ^{13}C shifts $CDCl_3$ to $\delta_C = 77.0$. The NMR resonances of the diastereomers were listed in brackets as far as observable. IR absorption spectra were recorded using a IFS 28 purchased from Bruker and a PE 298 purchased from Perkin–Elmer & Co GmbH, Überlingen. The mps were measured on an SMP3 mp apparatus purchased from Stuart Scientific, UK. The optical rotations were measured in a 10 cm cuvette on a polarimeter 241 purchased from Perkin–Elmer &

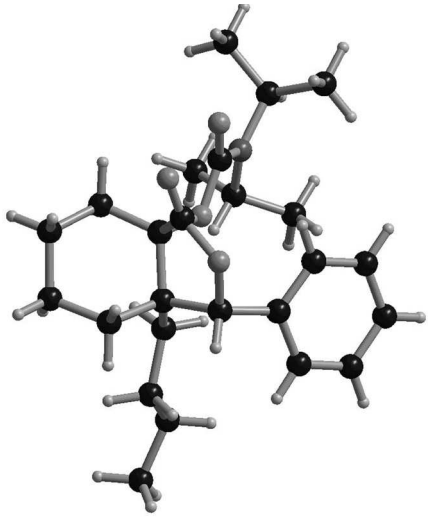


Figure 3 Solid-state structure of **11k**[12]

Co GmbH, Überlingen. Elemental analysis were performed at the microanalytical section of the Organisch-Chemisches Institut, WWU Münster on a Vario El III, purchased from Elementar-Analysen-Systeme GmbH. The mass spectral measurements were carried out by electron spray ionization method (ESI) on Quatro LCZ (Waters-Micromass; Manchester, UK) with a nanospray inlet and exact mass measurements were carried out on Micro Tof (Bruer Daltronics, Bremen), calibrations were done directly before the measurements of samples with sodium formate clusters. Petroleum ether refers to the fraction with bp 35–60 °C.

Deprotonation of Allyl Carbamates; General Procedure (GP1)

BuLi (1.6 M, 0.17 mL, 0.27 mmol, 1.1 equiv) or *sec*-BuLi (1.18 M, 0.23 mL, 0.27 mmol, 1.1 equiv) was added dropwise with vigorous stirring to a solution of allyl carbamates **1b** (70 mg, 0.25 mmol) or **1d** (73 mg, 0.25 mmol) and (–)-sparteine (63 mg, 0.27 mmol, 1.1 equiv) in toluene (3 mL) at –78 °C. After the reaction mixture had been stirred for 0–180 min at the same temperature, the electrophile TMSCl (44 mg, 0.37 mmol, 1.5 equiv) was added. The mixture was stirred for 1 h at –78 °C, after which it was allowed to warm to r.t. and quenched with aq HCl (2 N; 1 mL), the mixture was poured into an ice-cooled mixture of Et_2O (10 mL) and aq HCl (2 N; 10 mL). The aq layer was extracted with Et_2O (3 × 15 mL). The combined organic layer was dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by flash column chromatography (silica gel; petroleum ether–EtOAc, 10:1).

In Situ Silylation of Carbamates

BuLi (1.6 M, 0.17 mL, 0.27 mmol, 1.1 equiv) or *sec*-BuLi (1.18 M, 0.23 mL, 0.27 mmol, 1.1 equiv) was added over a period of 10 min to a solution of **1b** (70 mg, 0.25 mmol) or **1d** (73 mg, 0.25 mmol) and (–)-sparteine (63 mg, 0.27 mmol, 1.1 equiv) in the presence of TMSCl (44 mg, 0.37 mmol, 1.5 equiv) in toluene (5 mL) at –78 °C. Stirring was continued for 30 min and the mixture was quenched with MeOH (1 mL) at –78 °C. After usual workup, the crude product was purified by flash column chromatography (silica gel; petroleum ether–EtOAc, 10:1).

(*R*)-1-(2-Butyl-1-cyclopentenyl)-1-(trimethylsilyl)methyl *N*,*N*-Diisopropylcarbamate (3b)

According to GP1, **3b** (yield: 54 mg, 62%) was obtained from **1b** (60 mg, 0.25 mmol) with 30 min deprotonation time with BuLi; colourless oil; R_f = 0.31 (petroleum ether–EtOAc, 10:1); $[\alpha]_D^{20}$ +7.2 (*c* 0.9, $CHCl_3$); ^{1}H NMR shift experiment: er 96:4 (92% ee); 6.3 mg + 30 mol% Eu(hfc)$_3$ in C_6D_6, Δδ (1 H at δ 5.82) = 0.11, signal of major enantiomer appears at lower field.

90 min deprotonotation time: yield: 70%; 92% ee; $[\alpha]_D^{20}$ +7.2 (*c* 0.9, $CHCl_3$).

In situ experiment: yield: 35%; 94% ee; $[\alpha]_D^{20}$ +7.3 (*c* 0.9, $CHCl_3$).

rac-**3b** (yield: 66 mg, 75%) was prepared by applying the analogous procedure with *sec*-BuLi–TMEDA (1.1 equiv) with 90 min deprotonation time.

IR (film): 2965, 2940, 2854, 2856, 1700 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = –0.04 (s, 9 H), 0.86 (t, 3 H), 1.21 (d, *J* = 6.4 Hz, 12 H), 1.15–2.42 (m, 12 H), 3.97 (br s, 2 H), 5.82 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = –3.4 [$Si(CH_3)_3$], 16.3 (CH_3), 21.7 (CH_3), 23.4 (CH_2), 24.4 (CH_2), 25.3 (CH_2), 26.1 (CH_2), 30.1 (CH_2), 31.3 (CH_2), 48.0 (CH), 70.2 (CH), 130.5 (C_q), 131.3 (C_q), 158.3 (C=O).

Anal. Calcd for $C_{20}H_{39}NO_2Si$ (353.61): C, 67.93; H, 11.12; N, 3.96. Found: C, 67.75; H, 11.25; N, 3.91.

(*R*)-1-(2-Butyl-1-cyclohexenyl)-1-(trimethylsilyl)methyl *N*,*N*-Diisopropylcarbamate (3d)

According to GP1, **3d** (yield: 58 mg, 63%) was obtained from **1d** (63 mg, 0.25 mmol) with 30 min deprotonation time with *sec*-BuLi as a colourless oil; R_f = 0.33 (petroleum ether–EtOAc, 10:1); $[\alpha]_D^{20}$ –85.0 (*c* 0.64, $CHCl_3$); ^{1}H NMR shift experiment: er 93:7 (86% *ee*); 6.3 mg + 30 mol% Eu(hfc)$_3$ in C_6D_6, Δδ (1 H at δ 5.72) = 0.28, signal of major enantiomer appears at lower field.

90 min deprotonotation time: yield: 81%; 86% ee; $[\alpha]_D^{20}$ –85.2 (*c* 0.65, $CHCl_3$).

120 min deprotonotation time: yield: 82%; 84% ee; $[\alpha]_D^{20}$ –82.9 (*c* 0.70, $CHCl_3$).

In situ experiment: yield: 42%; 90% ee; $[\alpha]_D^{20}$ –88.8 (*c* 0.68, $CHCl_3$).

rac-**3d** (yield: 73 mg, 80%) was prepared by applying the analogous procedure with *sec*-BuLi–TMEDA (1.1 equiv) with 90 min deprotonation time.

IR (film): 2969, 2942, 2856, 2858, 1698 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = –0.04 (s, 9 H), 0.87 (t, 3 H), 1.25 (d, *J* = 6.7 Hz, 12 H), 1.05–2.50 (m, 14 H), 3.94 (br s, 2 H), 5.72 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = –2.5 [$Si(CH_3)_3$], 13.2 (CH_3), 19.8 (CH_3), 22.2 (CH_2), 24.6 (CH_2), 25.9 (CH_2), 28.7 (CH_2), 30.6 (CH_2), 31.1 (CH_2), 32.0 (CH_2), 46.3 (CH), 75.2 (CH), 128.5 (C_q), 129.5 (C_q), 150.9 (C=O).

Anal. Calcd for $C_{21}H_{41}NO_2Si$ (367.64): C, 68.61; H, 11.24; N, 3.81. Found: C, 68.55; H, 11.35; N, 3.91.

Homoaldol Reactions of Allyl Carbamates for Enantioenriched Compounds; General Procedure (GP2)

To a solution of allyl carbamate **1a–c** (1.0 mmol) and (–)-sparteine (257 mg, 1.1 mmol) in toluene (3–10 mL) at –78 °C, BuLi (1.6 M, 0.68 mL, 1.1 mmol) was added dropwise under vigorous stirring. For **1d**, *sec*-BuLi (1.18 M, 0.93 mL, 1.1 mmol) was used. The reaction mixture was stirred at –78 °C for 10 min for the synthesis of **6i**, and 1.5 h for the synthesis of **6a–h** and **6j–o**. Then a precooled (–78 °C) solution of chlorotris(diethylamino)titanium [$ClTi(NEt_2)_3$, 897 mg, 3 mmol] in toluene (1 mL) was added. The reaction mixture was stirred for 2 h at –78 °C and subsequently the aldehyde (3 mmol), 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 an ice-cooled mixture of Et_2O (15 mL) and aq HCl (2 N; 15 mL). The aq layer was extracted with Et_2O

(3 × 15 mL). The combined organic phases were dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by flash column chromatography (silica gel; petroleum ether–EtOAc, 10:1).

Homoaldol Reactions of Allyl Carbamates for Racemic Compound; General Procedure (GP3)

To a solution of allyl carbamate **1a–d** (1.0 mmol) and TMEDA (131 mg, 1.1 mmol) in toluene (3–10 mL) at –78 °C, *sec*-BuLi (1.18 M, 0.92 mL, 1.1 mmol) was added dropwise under vigorous stirring. The reaction mixture was stirred at –78 °C for 1 h and then a precooled (–78 °C) solution of tetraisopropoxytitanium (TiPT, 852 mg, 3 mmol) in toluene (1 mL) was added. The reaction mixture was stirred for 30 min at –78 °C and subsequently the aldehyde (3 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 an ice-cooled mixture of Et_2O (15 mL) and aq HCl (2 N; 15 mL). The aq layer was extracted with Et_2O (3 × 15 mL). The combined organic phases were dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by flash column chromatography (silica gel; petroleum ether–EtOAc, 10:1).

{1*Z*,1[2*S*,2(1*R*)]}-{2-[1-(4-Bromophenyl)-1-hydroxymethyl]-2-methylcyclopentylidene}methyl *N*,*N*-Diisopropylcarbamate (6a)

According to GP2, **6a** (yield: 305 mg, 72%) was obtained from allyl carbamate **1a** (239 mg, 1.0 mmol) and *p*-bromobenzaldehyde (**7a**, 556 mg, 3 mmol) as a colourless solid; R_f = 0.27 (petroleum ether–EtOAc, 10:1); $[\alpha]_D^{20}$ +113.3 (*c* 0.50, $CHCl_3$); ^{1}H NMR shift experiment: er 96:3 (93% ee); {ref: [5] $[\alpha]_D^{20}$ +112.5 (*c* 0.20, $CHCl_3$); 92% *ee*}.

According to GP3, *rac*-**6a** (yield: 343 mg, 81%) was obtained from allyl carbamate **1a** (239 mg, 1.0 mmol).

IR (KBr): 3496 (OH), 1691 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.12 (s, 3 H), 1.22 (d, *J* = 6.6 Hz, 12 H), 1.38 (m, 2 H),1.56 (m, 2 H), 1.80 (m, 2 H), 3.62/4.16 (br s, 2 H), 4.88 (s, 1 H), 6.89 (br s, 1 H), 7.17 (m_c, 2 H), 7.34 (m_c, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.3 (CH_3), 23.8 (CH_3), 26.9 (CH_2), 31.6 (CH_2), 36.9 (CH_2), 49.2 (CH), 50.4 (C_q), 76.5 (CH), 120.9 (C_q), 122.3 (C_q), 129.5 (CH), 130.1 (CH), 133.6 (CH), 140.7 (C_q), 151.7 (C=O).

HRMS: *m*/*z* calcd: 446.1301; found: 446.1310 [M + Na]$^+$.

Anal. Calcd for $C_{21}H_{30}BrNO_3$ (424.37): C, 59.43; H, 7.13; N, 3.30. Found: C, 59.36; H, 6.81; N, 3.04.

{1*Z*,1[2*S*,2(1*R*)]}-{2-[1-(4-Chlorophenyl)-1-hydroxymethyl]-2-methylcyclopentylidene}methyl *N*,*N*-Diisopropylcarbamate (6b)

According to GP2, **6b** (yield: 302 mg, 79%) was obtained from allyl carbamate **1a** (239 mg, 1.0 mmol) and *p*-chlorobenzaldehyde (**7b**, 420 mg, 3 mmol) as a colourless solid; mp 118.7 °C (petroleum ether–Et_2O, 4:1); R_f = 0.22 (petroleum ether–EtOAc, 10:1); $[\alpha]_D^{20}$ +46.35 (*c* 0.85, $CHCl_3$); ^{1}H NMR shift experiment: er 87:13 (74% ee); 5.2 mg + 10.6 mol% Eu(hfc)$_3$ in C_6D_6, Δδ (1 H at δ 4.89) = 0.14, signal of major enantiomer appears at lower field.

According to GP3, *rac*-**6b** (yield: 280 mg, 74%) was obtained from allyl carbamate **1a** (239 mg, 1.0 mmol).

IR (KBr): 3413 (OH), 1691 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.04 (s, 3 H), 1.22 (d, *J* = 6.4 Hz, 12 H), 1.51 (m, 2 H), 1.59 (m, 2 H), 1.76 (m, 2 H), 3.70/4.21 (br s, 2 H), 4.89 (s, 1 H), 6.88 (br s, 1 H), 7.13 (m_c, 2 H), 7.27 (m_c, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.5 (CH_3), 21.2 (CH_3), 24.4 (CH_2), 32.7 (CH_2), 36.2 (CH_2), 46.5 (CH), 51.0 (C_q), 76.9 (CH), 120.3 (C_q), 122.6 (C_q), 129.6 (CH), 131.2 (CH), 133.3 (CH), 140.6 (C_q), 152.2 (C=O).

HRMS: *m*/*z* calcd: 402.1806; found: 402.1812 [M + Na]$^+$.

Anal. Calcd for $C_{21}H_{30}ClNO_3$ (379.92): C, 66.39; H, 7.96; N, 3.69. Found: C, 66.03; H, 7.67; N, 3.51.

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

According to GP2, **6c** (yield: 287 mg, 73%) was obtained from allyl carbamate **1a** (239 mg, 1.0 mmol) and β-naphthaldehyde (**7c**, 468 mg, 3 mmol) as a colourless solid; mp 109.3 °C (petroleum ether: Et_2O, 4:1); R_f = 0.21 (petroleum ether–EtOAc, 10:1); $[\alpha]_D^{20}$ +118.5 (*c* 0.95, $CHCl_3$); ^{1}H NMR shift experiment: er 90:9 (81% ee); 4.8 mg + 10.2 mol% Eu(hfc)$_3$ in C_6D_6, Δδ (1 H at δ = 5.09) = 0.12, signal of major enantiomer appears at lower field.

According to GP3, *rac*-**6c** (yield: 308 mg, 78%) was obtained from allyl carbamate **1a** (239 mg, 1.0 mmol).

IR (KBr): 3452 (OH), 1713 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.11 (s, 3 H), 1.16 (d, *J* = 6.7 Hz, 12 H), 1.51 (m, 2 H), 1.66 (m, 2 H), 1.75 (m, 2 H), 3.68 (br s, 2 H), 5.09 (s, 1 H), 6.92 (t, *J* = 1.6 Hz, 1 H), 7.14–7.25 (m, 7 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.8 (CH_3), 22.2 (CH_3), 23.5 (CH_2), 27.5 (CH_2), 36.2 (CH_2), 49.8 (CH), 51.2 (C_q), 78.3 (CH), 123.3 (C_q), 133.2 (CH), 126.1/127.4/127.8/128.1/128.8/129.7/130.0/130.6/133.2/132.6 (CH and C_q), 152.3 (C=O).

Anal. Calcd for $C_{25}H_{33}NO_3$ (395.53): C, 75.91; H, 8.41; N, 3.54. Found: C, 75.73; H, 8.42; N, 3.76.

{1*Z*,1[2*S*,2(1*R*)]}-[2-Butyl-2-(1-hydroxy-2-methylethyl)cyclopentylidene]methyl *N*,*N*-Diisopropylcarbamate (6d)

According to GP2, **6d** (yield: 92 mg, 52%) was obtained from allyl carbamate **1b** (140 mg, 0.50 mmol) and 2-methylpropanal (**7d**, 108 mg, 1.5 mmol) as a yellow oil; R_f = 0.26 (petroleum ether–EtOAc, 10:1); $[\alpha]_D^{20}$ –17.9 (*c* 0.85, $CHCl_3$); chiral HPLC (chiragrom-1; hexane–*i*-PrOH, 500:1), 65% ee, major enantiomer appears at lower retention time.

According to GP3, *rac*-**6d** (yield: 95 mg, 54%) was obtained from allyl carbamate **1b** (140 mg, 0.50 mmol).

IR (film): 3482 (OH), 1721 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.99 (t, 3 H), 0.97/0.96 (2 d, 6 H), 1.07 (m, 2 H), 1.25–1.52 (m, 14 H), 1.52 (m, 2 H), 1.66 (m, 2 H), 1.78 (m, 2 H), 2.19 (m, 2 H), 3.24 (m, 1 H), 3.27 (m, 1 H), 3.86/4.25 (br s, 2 H), 7.13 (br s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.5 (CH_3), 19.9 (CH_3), 21.4 (CH_3), 21.8 (CH_3), 22.2 (CH_2), 24.4 (CH_2), 25.6 (CH_2), 27.2 (CH_2), 31.3 (CH_2), 32.4 (CH), 32.8 (CH_2), 46.3 (CH), 49.4 (C_q), 73.7 (CH), 123.9 (C_q), 131.1 (CH), 149.4 (C=O).

HRMS: *m*/*z* calcd: 376.2827; found: 376.2820 [M + Na]$^+$.

Anal. Calcd for $C_{21}H_{39}NO_3$ (353.54): C, 71.34; H, 11.12; N, 3.96. Found: C, 71.25; H, 11.15; N, 3.71.

{1*Z*,1[2*S*,2(1*R*)]}-[2-Butyl-2-(1-hydroxy-1-phenylmethyl)cyclopentylidene]methyl *N*,*N*-Diisopropylcarbamate (6e)

According to GP2, **6e** (yield: 102 mg, 53%) was obtained from allyl carbamate **1b** (140 mg, 0.50 mmol) and benzaldehyde (**7e**, 160 mg, 1.5 mmol) as a yellow oil; R_f = 0.25 (petroleum ether–EtOAc, 10:1); $[\alpha]_D^{20}$ –45.1 (*c* 1.05, $CHCl_3$); ^{1}H NMR shift experiment: er 89:10 (79% ee); 5.1 mg + 26.3 mol% Eu(hfc)$_3$ in C_6D_6, Δδ (1 H at δ 5.01) = 0.23, signal of major enantiomer appears at lower field.

According to GP3, *rac*-**6e** (yield: 104 mg, 54%) was obtained from allyl carbamate **1b** (140 mg, 0.50 mmol).

IR (film): 3429 (OH), 1704 (C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.83 (t, 3 H), 0.97 (m, 2 H), 1.27–1.54 (m, 14 H), 1.57 (m, 2 H), 1.64 (m, 2 H), 1.73 (m, 2 H), 2.18 (m, 2 H), 3.93/4.25 (br s, 2 H), 5.01 (s, 1 H), 6.89 (br s, 1 H), 7.15–7.35 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.5 (CH_3), 19.9 (CH_3), 22.6 (CH_2), 24.8 (CH_2), 25.3 (CH_2), 27.8 (CH_2), 31.4 (CH_2), 32.6 (CH_2), 44.3 (CH), 46.6 (C_q), 75.7 (CH), 125.3 (CH), 128.9 (C_q), 130.6 (CH), 131.7 (CH), 133.7 (CH), 138.4 (C_q), 150.8 (C=O).

Anal. Calcd for $C_{24}H_{37}NO_3$ (387.56): C, 74.38; H, 9.62; N, 3.61. Found: C, 74.82; H, 9.60; N, 3.41.

{1*Z*,1[2*S*,2(1*R*)]}-{2-[1-(4-Bromophenyl)-1-hydroxymethyl]-2-butylcyclopentylidene}methyl *N*,*N*-Diisopropylcarbamate (6f)

According to GP2, **6f** (yield: 123 mg, 53%) was obtained from allyl carbamate **1b** (140 mg, 0.50 mmol) and *p*-bromobenzaldehyde (**7a**, 277 mg, 1.5 mmol) as a yellow oil; R_f = 0.24 (petroleum ether–EtOAc, 10:1); $[\alpha]_D^{20}$ +35.7 (*c* 1.05, $CHCl_3$); ^1H NMR shift experiment: er 86:14 (72% ee); 9.8 mg + 11 mol% $Eu(hfc)_3$ in C_6D_6, Δδ (1 H at δ 4.91) = 0.13, signal of major enantiomer appears at higher field.

According to GP3, *rac*-**6f** (yield: 121 mg, 52%) was obtained from allyl carbamate **1b** (140 mg, 0.50 mmol).

IR (film): 3426 (OH), 1691 (C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.89 (t, 3 H), 0.98 (m, 2 H), 1.29–1.48 (m, 14 H), 1.54 (m, 2 H), 1.62 (m, 2 H), 1.74 (m, 2 H), 2.15 (m, 2 H), 3.98/4.26 (br s, 2 H), 4.91 (s, 1 H), 6.86 (br s, 1 H), 7.11 (m_c, 2 H), 7.32 (m_c, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.2 (CH_3), 19.6 (CH_3), 22.4 (CH_2), 24.5 (CH_2), 25.4 (CH_2), 27.6 (CH_2), 30.6 (CH_2), 32.2 (CH_2), 44.9 (CH), 46.6 (C_q), 75.6 (CH), 125.2 (C_q), 129.9 (C_q), 130.2 (CH), 131.1 (CH), 133.2 (CH), 138.1 (C_q), 150.9 (C=O).

HRMS: *m*/*z* calcd: 490.1776; found: 488.1784 $[M + Na]^+$.

Anal. Calcd for $C_{24}H_{36}NO_3Br$ (466.45): C, 61.80; H, 7.78; N, 3.00. Found: C, 61.22; H, 7.90; N, 3.09.

{1*Z*,1[2*S*,2(1*R*)]}-{2-Butyl-2-[1-hydroxy-1-(naphth-2-yl)methyl]cyclopentylidene}methyl *N*,*N*-Diisopropylcarbamate (6g)

According to GP2, **6g** (yield: 124 mg, 57%) was obtained from allyl carbamate **1b** (140 mg, 0.50 mmol) and β-naphthaldehyde (**7c**, 234 mg, 1.5 mmol) as an amorphous solid; R_f = 0.27 (petroleum ether–EtOAc, 10:1); $[\alpha]_D^{20}$ +96.7 (*c* 0.45, $CHCl_3$); ^1H NMR shift experiment: er 92:8 (84% ee); 7.2 mg + 31.2 mol% $Eu(hfc)_3$ in C_6D_6, Δδ (1 H at δ 5.12) = 0.18, signal of major enantiomer appears at lower field.

According to GP3, *rac*-**6g** (yield: 120 mg, 55%) was obtained from allyl carbamate **1b** (140 mg, 0.50 mmol).

IR (KBr): 3430 (OH), 1691 (C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.80 (s, 3 H), 0.95 (m, 2 H), 1.26–1.43 (m, 14 H), 1.58 (m, 2 H), 1.68 (m, 2 H), 1.70 (m, 2 H), 2.18 (m, 2 H), 3.92/4.23 (br s, 2 H), 5.12 (s, 1 H), 6.83 (br s, 1 H), 7.35–7.81 (m, 7 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.3 (CH_3), 20.6 (CH_3), 22.5 (CH_2), 24.8 (CH_2), 26.2 (CH_2), 27.3 (CH_2), 30.4 (CH_2), 32.7 (CH_2), 44.5 (CH), 48.5 (C_q), 75.3 (CH), 128.9 (C_q), 133.4 (CH), 126.9/127.2/127.9/128.4/129.6/130.3/131.2/132.3/132.9/132.6 (CH and C_q), 151.3 (C=O).

Anal. Calcd for $C_{28}H_{39}NO_3$ (437.61): C, 76.85; H, 8.98; N, 3.20. Found: C, 76.95; H, 8.95; N, 73.37.

{1*Z*,1[2*S*,2(1*R*)]}-[2-Butyl-2-(1-hydroxy-2-propenyl)cyclopentylidene]methyl *N*,*N*-Diisopropylcarbamate (6h)

According to GP2, **6h** (yield: 132 mg, 56%) was obtained from allyl carbamate **1b** (196 mg, 0.70 mmol) and 2-propenal (**7f**, 117 mg, 2.1 mmol) as a yellow oil; R_f = 0.25 (petroleum ether–EtOAc, 10:1); $[\alpha]_D^{20}$ +16.5.1 (*c* 1.05, $CHCl_3$); chiral HPLC (chiragrom-2: hexane–*i*-PrOH, 200:1), 88% ee, major enantiomer appears at lower retention time.

According to GP3, *rac*-**6h** (yield: 136 mg, 58%) was obtained from allyl carbamate **1b** (140 mg, 0.50 mmol).

IR (film): 3460 (OH), 1695 (C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.84 (t, 3 H), 0.95 (m, 2 H), 1.22–1.44 (m, 14 H), 1.53 (m, 2 H), 1.65 (m, 2 H), 1.73 (m, 2 H), 2.18 (m, 2 H), 3.85 (br s, 2 H), 5.03 (d, *J* = 6.7 Hz, 1 H), 5.07 (dd, *J* = 10.6, 1.6 Hz, 1 H), 5.18 (dd, *J* = 17.4, 1.6 Hz, 1 H), 5.74 (ddd, *J* = 6.7, 10.6, 17.4 Hz, 1 H), 6.85 (br s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.4 (CH_3), 20.6 (CH_3), 22.8 (CH_2), 24.9 (CH_2), 25.4 (CH_2), 27.7 (CH_2), 30.8 (CH_2), 32.5 (CH_2), 45.9 (CH), 46.6 (C_q), 75.7 (CH), 114.6 (CH_2), 129.9 (C_q), 132.2 (CH), 138.2 (CH), 153.8 (C=O).

HRMS: *m*/*z* calcd: 360.2509; found: 360.2530 $[M + Na]^+$.

Anal. Calcd for $C_{20}H_{35}NO_3$ (337.50): C, 71.18; H, 10.45; N, 4.15. Found: C, 71.02; H, 10.60; N, 4.11.

{1*Z*,1[2*S*,2(1*R*)]}-{2-[1-(4-Bromophenyl)-1-hydroxymethyl]-methylcyclohexylidene}methyl *N*,*N*-Diisopropylcarbamate (6i)

According to GP2, **6i** (yield: 177 mg, 58%) was obtained from allyl carbamate **1c** (177 mg, 0.70 mmol) and *p*-bromobenzaldehyde (**7a**, 389 mg, 2.1 mmol) as a colourless solid; R_f = 0.26 (petroleum ether–EtOAc, 10:1); mp 119 °C (petroleum ether–Et_2O, 4:1); $[\alpha]_D^{20}$ –45.7 (*c* 0.43, $CHCl_3$); ^1H NMR shift experiment: er 93:7 (86% ee) {Lit. $[\alpha]_D^{20}$ –46.3 (*c* 0.44, $CHCl_3$), 87% ee[5]}.

According to GP3, *rac*-**6i** (yield: 240 mg, 79%) was obtained from allyl carbamate **1c** (177 mg, 0.70 mmol).

IR (KBr): 3453 (OH), 1680 (C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.08 (s, 3 H), 1.12 (d, *J* = 6.4 Hz, 12 H), 1.42 (m, 2 H), 1.56 (m, 2 H), 1.72 (m, 2 H), 2.12 (m, 2 H), 3.66/4.17 (br s, 2 H), 5.02 (s, 1 H), 6.95 (br s, 1 H), 7.25 (m, 2 H), 7.44 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.8 (CH_3), 21.6 (CH_3), 21.9 (CH_2), 26.9 (CH_2), 29.3 (CH_2), 36.9 (CH_2), 44.6 (CH), 45.9 (C_q), 74.2 (CH), 121.1 (C_q), 124.9 (C_q), 129.6 (CH), 130.5 (CH), 133.2 (CH), 139.1 (C_q), 152.4 (C=O).

HRMS: *m*/*z* calcd: 462.1440; found: 461.1461 $[M + Na]^+$.

Anal. Calcd for $C_{22}H_{32}BrNO_3$ (438.40): C, 60.27; H, 7.36; N, 3.19. Found: C, 60.86; H, 7.22; N, 2.87.

{1*Z*,1[2*S*,2(1*R*)]}-{2-Butyl-2-[1-hydroxy-1-(naphth-1-yl)methyl]cyclohexylidene}methyl *N*,*N*-Diisopropylcarbamate (6j)

According to GP2, **6j** (yield: 142 mg, 63%) was obtained from allyl carbamate **1d** (147 mg, 0.50 mmol) and α-naphthaldehyde (**7g**, 234 mg, 1.5 mmol) as a colourless oil; R_f = 0.25 (petroleum ether–EtOAc, 10:1); $[\alpha]_D^{20}$ +70.3 (*c* 0.55, $CHCl_3$); ^1H NMR shift experiment: er 87:13 (74% ee); 4.3 mg + 23 mol% $Eu(hfc)_3$ in C_6D_6, Δδ (1 H at δ 5.14) = 0.23, signal of major enantiomer appears at lower field.

According to GP3, *rac*-**6j** (yield: 146 mg, 65%) was obtained from allyl carbamate **1d** (147 mg, 0.50 mmol).

IR (film): 3451 (OH), 1691 (C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.86 (t, 3 H), 1.08 (m, 2 H), 1.22–1.49 (m, 14 H), 1.54 (m, 2 H), 1.61 (m, 2 H), 1.76 (m, 2 H), 2.12 (m,

2 H), 2.27 (m, 2 H), 3.89/4.11 (br s, 2 H), 5.14 (s, 1 H), 6.88 (t, *J* = 1.9 Hz, 1 H), 7.43–7.86 (m, 7 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.2 (CH_3), 20.8 (CH_3), 23.4 (CH_2), 24.8 (CH_2), 25.4 (CH_2), 27.7 (CH_2), 28.7 (CH_2), 31.6 (CH_2), 32.6 (CH_2), 45.8 (CH), 48.3 (C_q), 75.5 (CH), 128.9 (C_q), 125.6/126.7/127.4/128.3/128.5/129.7/130.5/131.9/132.4/132.7 (CH and C_q), 131.3 (CH), 153.3 (C=O).

HRMS: *m*/*z* calcd: 474.2984; found: 474.2995 $[M + Na]^+$.

Anal. Calcd for $C_{29}H_{41}NO_3$ (451.64): C, 77.12; H, 9.15; N, 3.10. Found: C, 77.08; H, 9.19; N, 3.20.

{1*Z*,1[2*S*,2(1*R*)]}-[2-Butyl-2-(1-hydroxy-1-phenylmethyl)cyclohexylidene]methyl *N*,*N*-Diisopropylcarbamate (6k)

According to GP2, **6k** (yield: 130 mg, 65%) was obtained from allyl carbamate **1d** (147 mg, 0.50 mmol) and benzaldehyde (**7e**, 160 mg, 1.5 mmol) as a yellow oil; R_f = 0.25 (petroleum ether–EtOAc, 10:1); $[\alpha]_D^{20}$ +96.2 (*c* 1.05, $CHCl_3$); ^{1}H NMR shift experiment: er 89:11 (78% ee), 4.6 mg + 10 mol% Eu(hfc)$_3$ in C_6D_6, Δδ (1 H at δ 4.98) = 0.21, signal of major enantiomer appears at lower field.

According to GP3, *rac*-**6k** (yield: 136 mg, 68%) was obtained from allyl carbamate **1d** (147 mg, 0.50 mmol).

IR (film): 3429 (OH), 1704 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.86 (t, 3 H), 1.07 (m, 2 H), 1.18–1.42 (m, 14 H), 1.55 (m, 2 H), 1.67 (m, 2 H), 1.78 (m, 2 H), 2.11 (m, 2 H), 2.25 (m, 2 H), 3.99/4.15 (br s, 2 H), 4.98 (s, 1 H), 6.87 (t, *J* = 1.9 Hz, 1 H), 7.15–7.35 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.4 (CH_3), 19.8 (CH_3), 23.5 (CH_2), 24.6 (CH_2), 25.2 (CH_2), 27.7 (CH_2), 28.2 (CH_2), 30.8 (CH_2), 31.6 (CH_2), 44.7 (CH), 46.9 (C_q), 75.8 (CH), 125.4 (C_q), 126.2 (C_q), 128.0 (CH), 129.2 (CH), 131.6 (CH), 138.5 (CH), 151.1 (C=O).

HRMS: *m*/*z* calcd: 424.2822; found: 424.2821 $[M + Na]^+$.

Anal. Calcd for $C_{25}H_{39}NO_3$ (401.58): C, 74.77; H, 9.79; N, 3.49. Found: C, 74.80; H, 9.80; N, 3.43.

{1*Z*,1[2*S*,2(1*R*)]}-{2-[1-(4-Bromophenyl)-1-hydroxymethyl]-2-butylcyclohexylidene}methyl *N*,*N*-Diisopropylcarbamate (6l)

According to GP2, **6l** (yield: 139 mg, 58%) was obtained from allyl carbamate **1d** (147 mg, 0.50 mmol) and *p*-bromobenzaldehyde (**7a**, 277 mg, 1.5 mmol) as a colourless oil; R_f = 0.25 (petroleum ether–EtOAc, 10:1); $[\alpha]_D^{20}$ –23.3 (*c* 1.05, $CHCl_3$); ^{1}H NMR shift experiment: er 88:12 (76% *ee*), 9.8 mg + 45 mol% Eu(hfc)$_3$ in C_6D_6, Δδ (1 H at δ = 4.93) = 0.41, signal of major enantiomer appears at lower field.

According to GP3, *rac*-**6l** (yield: 156 mg, 65%) was obtained from allyl carbamate **1d** (147 mg, 0.50 mmol).

IR (KBr): 3429 (OH), 1704 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.87 (t, 3 H), 0.98 (m, 2 H), 1.25–1.43 (m, 14 H), 1.52 (m, 2 H), 1.63 (m, 2 H), 1.78 (m, 2 H), 2.10 (m, 2 H), 2.22 (m, 2 H), 3.94/4.22 (br s, 2 H), 4.93 (s, 1 H), 6.83 (t, *J* = 1.9 Hz, 1 H), 7.08 (m_c, 2 H), 7.36 (m_c, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.2 (CH_3), 19.8 (CH_3), 22.9 (CH_2), 24.2 (CH_2), 25.9 (CH_2), 27.4 (CH_2), 28.7 (CH_2), 30.6 (CH_2), 32.0 (CH_2), 44.6 (CH), 46.3 (C_q), 75.2 (CH), 125.2 (C_q), 129.9 (C_q), 130.2 (CH), 131.1 (CH), 133.2 (CH), 138.1 (C_q), 150.9 (C=O).

HRMS: *m*/*z* calcd: 502.1927; found: 502.1959 $[M + Na]^+$.

Anal. Calcd for $C_{25}H_{38}NO_3Br$ (480.48): C, 62.49; H, 7.97; N, 2.92. Found: C, 62.42; H, 7.70; N, 2.81.

{1*Z*,1[2*S*,2(1*R*)]}-{2-Butyl-2-[1-hydroxy-1-(naphth-2-yl)methyl]cyclohexylidene}methyl *N*,*N*-Diisopropylcarbamate (6m)

According to GP2, **6m** (yield: 151 mg, 67%) was obtained from allyl carbamate **1d** (147 mg, 0.50 mmol) and β-naphthaldehyde (**7c**, 234 mg, 1.5 mmol) as a yellow oil; R_f = 0.25 (petroleum ether–EtOAc, 10:1); $[\alpha]_D^{20}$ –47 (*c* 0.55, $CHCl_3$); ^{1}H NMR shift experiment: er 83:17 (66% ee); 4.3 mg + 36 mol% Eu(hfc)$_3$ in C_6D_6, Δδ (1 H at δ 5.11) = 0.11, signal of major enantiomer appears at higher field.

According to GP3, *rac*-**6m** (yield: 153 mg, 68%) was obtained from allyl carbamate **1d** (147 mg, 0.50 mmol).

IR (film): 3451 (OH), 1691 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.87 (t, 3 H), 1.03 (m, 2 H), 1.24–1.49 (m, 14 H), 1.56 (m, 2 H), 1.66 (m, 2 H), 1.77 (m, 2 H), 2.13 (m, 2 H), 2.24 (m, 2 H), 3.90/4.10 (br s, 2 H), 5.16 (s, 1 H), 6.93 (t, *J* = 1.9 Hz, 1 H), 7.45–7.89 (m, 7 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.3 (CH_3), 20.4 (CH_3), 23.7 (CH_2), 24.5 (CH_2), 25.6 (CH_2), 27.3 (CH_2), 28.7 (CH_2), 31.7 (CH_2), 32.9 (CH_2), 45.8 (CH), 48.6 (C_q), 75.6 (CH), 128.2 (C_q), 127.3/125.4/126.2/127.4/128.9/129.6/130.2/131.2/132.5/132.8 (CH and C_q), 131.9 (CH), 154.1 (C=O).

HRMS: *m*/*z* calcd: 474.2984; found: 474.2977 $[M + Na]^+$.

Anal. Calcd for $C_{29}H_{41}NO_3$ (451.64): C, 77.12; H, 9.15; N, 3.10. Found: C, 77.15; H, 8.95; N, 3.07.

{1*Z*,1[2*S*,2(1*R*)]}-{2-Butyl-2-[1-hydroxy-1-(2-methylethyl)]cyclohexylidene}methyl *N*,*N*-Diisopropylcarbamate (6n)

According to GP2, **6n** (yield: 100 mg, 55%) was obtained from allyl carbamate **1d** (147 mg, 0.50 mmol) and 2-methylpropanal (**7d**, 108 mg, 1.5 mmol) as a yellow oil; R_f = 0.30 (petroleum ether–EtOAc, 10:1); $[\alpha]_D^{20}$ +2.52 (*c* 1.15, $CHCl_3$); chiral HPLC (chiragrom-2; hexane–*i*-PrOH, 200:1), 72% *ee*, major enantiomer appears at higher retention time.

According to GP3, *rac*-**6n** (yield: 113 mg, 62%) was obtained from allyl carbamate **1d** (147 mg, 0.50 mmol).

IR (film): 3451 (OH), 1691 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.96 (t, 3 H), 0.98 (d, 3 H), 0.97 (d, 3 H), 1.07 (m, 2 H), 1.22–1.49 (m, 14 H), 1.51 (m, 2 H), 1.68 (m, 2 H), 1.73 (m, 2 H), 2.19 (m, 2 H), 2.22 (m, 2 H), 3.12 (d, *J* = 2.9 Hz, 1 H), 3.26 (m, 1 H), 3.85/4.15 (br s, 2 H), 7.09 (t, *J* = 1.8 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.9 (CH_3), 18.8 (CH_3), 21.2 (CH_3), 21.5 (CH_3), 23.6 (CH_2), 24.3 (CH_2), 25.7 (CH_2), 27.6 (CH_2), 28.4 (CH_2), 30.2 (CH), 30.8 (CH_2), 34.6 (CH_2), 46.7 (CH), 50.9 (C_q), 73.8 (CH), 126.2 (C_q), 129.2 (CH), 154.1 (C=O).

Anal. Calcd for $C_{22}H_{41}NO_3$ (367.57): C, 71.89; H, 11.24: N, 3.81. Found: C, 71.25; H, 11.55; N, 3.71.

{1*Z*,1[2*S*,2(1*R*)]}-{2-Butyl-2-[1-hydroxy-1-(4-methoxyphenyl)methyl]cyclohexylidene}methyl *N*,*N*-Diisopropylcarbamate (6o)

According to GP2, **6o** (yield: 125 mg, 58%) was obtained from allyl carbamate **1d** (147 mg, 0.50 mmol) and *p*-methoxybenzaldehyde (**7h**, 204 mg, 1.5 mmol) as a yellow oil; R_f = 0.25 (petroleum ether–EtOAc, 10:1); $[\alpha]_D^{20}$ –45.5 (*c* 0.43, $CHCl_3$); $[\alpha]_D^{20}$ –74.4 (*c* 0.45, $CHCl_3$); shift experiment: er 87:13 (74% ee); 9.8 mg + 45 mol% Eu(hfc)$_3$ in C_6D_6, Δδ (1 H at δ 4.92) = 0.15, signal of major enantiomer appears at higher field.

According to GP3, *rac*-**6o** (yield: 146 mg, 68%) was obtained from allyl carbamate **1d** (147 mg, 0.50 mmol).

IR (film): 3469 (OH), 1695 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.84 (t, 3 H), 0.92 (m, 2 H), 1.29–1.45 (m, 14 H), 1.54 (m, 2 H), 1.61 (m, 2 H), 1.75 (m, 2 H), 2.09 (m, 2 H), 2.21 (m, 2 H), 3.90/4.21 (br s, 2 H), 3.86 (s, 3 H), 4.92 (s, 1 H), 6.73 (t, *J* = 1.9 Hz, 1 H), 7.01 (m_c, 2 H), 7.32 (m_c, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.0 (CH_3), 19.7 (CH_3), 21.8 (CH_2), 23.2 (CH_2), 25.4 (CH_2), 26.7 (CH_2), 28.1 (CH_2), 30.3 (CH_2), 32.5 (CH_2), 43.2 (CH), 46.5 (C_q), 55.1 (OCH_3), 72.2 (CH), 125.6 (C_q), 128.3 (C_q), 131.2 (CH), 131.9 (CH), 133.3 (CH), 138.7 (C_q), 158.9 (C=O).

HRMS: *m*/*z* calcd: 454.2933; found: 454.2926 $[M + Na]^+$.

Anal. Calcd for $C_{26}H_{41}NO_4$ (431.61): C, 72.35; H, 9.57; N, 3.25. Found: C, 72.67; H, 9.05; N, 3.81.

Lactols 10; General Procedure (GP4)

A solution of enol carbamate **6** (0.25 mmol) and $VO(acac)_2$ (1.3 mg, 2 mol%) in anhyd CH_2Cl_2 (5 mL) was stirred at 20 °C for 12 h with *tert*-butyl hydroperoxide (42 µl, 0.37 mmol), dissolved in CH_2Cl_2 (1 mL). Subsequently, dimethyl sulfide (13 µl, 2.4 mmol) was added and stirring was continued for a further 30 min. For workup, the mixture was extracted by sat. aq $NaHCO_3$ (2 × 20 mL), sat. aq KCl (15 mL), and dried ($MgSO_4$). Evaporation of the solvent under reduced pressure, followed by chromatography (silica gel; petroleum ether–Et_2O, 4:1) afforded products **10** and minor epimer. Characterization by elemental analysis and enantiometric excesses were performed at the stage of lactones **11**.

(1*S*,2*RS*,4*R*,5*R*)-4-(4-Bromophenyl)-1-(*N*,*N*-diisopropylaminocarbonyloxy)-5-methyl-3-oxabicyclo[3.3.0]octan-2-ol (10a)

According to GP4, **10a** and minor epimer (yield: 83 mg, 76%) was synthesized as a colourless oil with the diastereomeric ratio 2.1:1.0 from **6a** (105 mg, 0.25 mmol); R_f = 0.23 (petroleum ether–Et_2O, 4:1).

rac-**10a** was obtained from *rac*-**6a**, yield: 71%.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.67 (s, 3 H), 1.14 (d, 12 H), 1.47 (m, 2 H), 1.53–1.85 (m, 2 H), 2.42 (m, 2 H), 3.86 (br s, 2 H), 4.90 [4.69] (s, 1 H), 5.62 [5.74] (s, 1 H), 7.20 (m_c, 2 H), 7.37 (m_c, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.6 (CH_3), 19.3 [21.1] (CH_3), 27.2 [28.4] (CH_2), 34.7 [37.5] (CH_2), 36.6 [38.3] (CH_2), 46.6 (C_q), 56.3 [58.8] (CH), 84.5 [86.2] (CH), 95.3 [99.7] (C_q), 100.5 [102.2] (CH), 121.6 (C_q), 131.1 (CH), 131.4 (CH), 139.6 (C_q), 155.6 (C=O).

(1*S*,2*RS*,4*R*,5*R*)-4-(4-Chlorophenyl)-1-(*N*,*N*-diisopropylaminocarbonyloxy)-5-methyl-3-oxabicyclo[3.3.0]octan-2-ol (10b)

According to GP4, **10b** and minor epimer (yield: 88 mg, 83%) was synthesized as a colourless oil with a diastereomeric ratio of 1.9:1.0 from **6b** (100 mg, 0.27 mmol); R_f = 0.23 (petroleum ether–Et_2O, 4:1).

rac-**10b** was obtained from *rac*-**6b**, yield: 66%.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.69 (s, 3 H), 1.15 (d, 12 H), 1.42 (m, 2 H), 1.50–1.89 (m, 2 H), 2.47 (m, 2 H), 3.78 (br s, 2 H), 4.92 [4.71] (s, 1 H), 5.62 [5.74] (s, 1 H), 7.16–7.25 (m, 4 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.6 (CH_3), 19.5 [21.1] (CH_3), 26.8 [27.1] (CH_2), 28.9 [29.1] (CH_2), 29.9 [30.3] (CH_2), 46.9 (C_q), 49.9 (CH), 84.2 [86.7] (CH), 95.6 [99.8] (C_q), 100.2 [102.6] (CH), 121.5 (C_q), 131.4 (CH), 131.6 (CH), 139.9 (C_q), 155.2 (C=O).

(1*S*,2*RS*,4*R*,5*R*)-1-(*N*,*N*-Diisopropylaminocarbonyloxy)-5-methyl-4-(naphth-2-yl)-3-oxabicyclo[3.3.0]octan-2-ol (10c)

According to GP4, **10c** and minor epimer (yield: 80 mg, 75%) were synthesized as a colourless oil with the diastereomeric ratio 2.3:1.0 from **6c** (102 mg, 0.26 mmol); R_f = 0.23 (petroleum ether–Et_2O, 4:1).

rac-**10c** was obtained from *rac*-**6c**, yield: 69%.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.72 (s, 3 H), 1.16 (d, 12 H), 1.49 (m, 2 H), 1.43–1.85 (m, 2 H), 2.47 (m, 2 H), 3.78 (br s, 2 H), 5.12 [5.19] (s, 1 H), 5.72 [5.81] (s, 1 H), 7.36–7.77 (m, 7 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1 [14.5] (CH_3), 22.1 [20.6] (CH_3), 25.3 [26.2] (CH_2), 27.2 [28.3] (CH_2), 29.3 [30.2] (CH_2), 47.2 (C_q), 49.1 [50.6] (CH), 77.3 (CH), 92.4 (C_q), 101.6 (CH), 122.4/123.9/124.9/125.3/126.8/130.3/131.6/132.3/133.4/139.9 (CH and C_q), 154.3 (C=O).

(1*S*,2*RS*,4*R*,5*R*)-5-Butyl-1-(*N*,*N*-diisopropylaminocarbonyloxy)-4-(2-methylethyl)-3-oxabicyclo[3.3.0]octan-2-ol (10d)

According to GP4, **10d** and minor epimer (yield: 77 mg, 85%) was synthesized as a colourless oil with the diastereomeric ratio 3.2:1.0 from **6d** (87 mg, 0.25 mmol); R_f = 0.23 (petroleum ether–Et_2O, 4:1).

rac-**10d** was obtained from *rac*-**6d**, yield: 86%.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.78 (t, 3 H), 1.13 (m, 2 H), 1.22 (m, 14 H), 1.43 (m, 2 H), 1.45 (m, 2 H), 1.73–1.81 (m, 2 H), 2.30 (m, 2 H), 2.34 (m, 6 H), 3.27 (m, 1 H), 3.60 (br s, 2 H), 3.82 [3.94] (d, 1 H), 6.21 [6.25] (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.5 [13.9] (CH_3), 20.5 [19.2] (CH_3), 20.6 [20.2] (CH_3), 20.6 [20.3] (CH_2), 21.0 [21.5] (CH_2), 22.1 [22.6] (CH_2), 23.5 [23.4] (CH_2), 26.4 [26.6] (CH_2), 29.8 [30.1] (CH_2), 30.4 (CH), 44.6 (C_q), 48.5 (CH), 78.8 (CH), 93.8 (C_q), 101.3 (CH), 151.2 (C=O).

(1*S*,2*RS*,4*R*,5*R*)-5-Butyl-1-(*N*,*N*-diisopropylaminocarbonyloxy)-4-phenyl-3-oxabicyclo[3.3.0]octan-2-ol (10e)

According to GP4, **10e** and minor epimer (yield: 116 mg, 83%) was synthesized as a colourless oil with the diastereomeric ratio 1.1:1.0 from **6e** (135 mg, 0.35 mmol); R_f = 0.25 (petroleum ether–Et_2O, 4:1).

rac-**10e** was obtained from *rac*-**6e**, yield: 85%.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.77 (t, 3 H), 1.13 (m, 2 H), 1.21 (m, 14 H), 1.43 (m, 2 H), 1.58 (m, 2 H), 1.78–1.92 (m, 2 H), 2.48 (m, 2 H), 3.65 (br s, 2 H), 4.96 [4.95] (s, 1 H), 5.56 [5.37] (s, 1 H), 7.15–7.23 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.2 [14.6] (CH_3), 20.7 [21.7] (CH_3), 21.6 [21.8] (CH_2), 23.9 [24.7] (CH_2), 24.4 [25.3] (CH_2), 26.6 [27.6] (CH_2), 28.3 [29.6] (CH_2), 29.5 [30.3] (CH_2), 47.7 (C_q), 49.6 [50.8] (CH), 78.5 (CH), 93.5 (C_q), 101.4 (CH), 121.3 [122.4]/123.9 [124.5]/126.2 [127.6]/137.4 [138.9] (CH and C_q), 154.9 (C=O).

(1*S*,2*RS*,4*R*,5*R*)-4-(4-Bromophenyl)-5-butyl-1-(*N*,*N*-diisopropylaminocarbonyloxy)-3-oxabicyclo[3.3.0]octan-2-ol (10f)

According to GP4, **10f** and minor epimer (yield: 126 mg, 82%) was synthesized as a colourless oil with the diastereomeric ratio 4.6:1.0 from **6f** (148 mg, 0.32 mmol); R_f = 0.23 (petroleum ether–Et_2O, 4:1).

rac-**10f** was obtained from *rac*-**6f**, yield: 89%.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.77 (t, 3 H), 1.11 (m, 2 H), 1.23 (m, 14 H), 1.45 (m, 2 H), 1.58 (m, 2 H), 1.78–1.82 (m, 2 H), 2.34 (m, 2 H), 3.64 (br s, 2 H), 4.95 [4.98] (s, 1 H), 5.53 [5.36] (s, 1 H), 7.15 (m_c, 2 H), 7.24 (m_c, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.7 [14.9] (CH_3), 21.3 [19.8] (CH_3), 21.7 [21.9] (CH_2), 23.2 [22.4] (CH_2), 25.3 [24.2] (CH_2), 26.1 [27.1] (CH_2), 28.8 [29.5] (CH_2), 31.0 [32.1] (CH_2), 47.6 (C_q), 49.8 [50.3] (CH), 79.6 (CH), 93.6 (C_q), 101.4 (CH), 121.6 [122.9] (C_q), 131.1 (CH), 132.9 (CH), 139.7 (C_q), 153.4 (C=O).

(1*S*,2*RS*,4*R*,5*R*)-5-Butyl-1-(*N*,*N*-diisopropylaminocarbonyloxy)-4-(naphth-2-yl)-3-oxabicyclo[3.3.0]octan-2-ol (10g)
According to GP4, **10g** and minor epimer (yield: 104 mg, 86%) were synthesized as a colourless oil with the diastereomeric ratio 3.2:1.0 from **6g** (117 mg, 0.27 mmol); R_f = 0.22 (petroleum ether–Et_2O, 4:1).

rac-**10g** was obtained from *rac*-**6g**, yield: 87%.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.78 (t, 3 H), 1.12 (m, 2 H), 1.25 (m, 14 H), 1.43 (m, 2 H), 1.45 (m, 2 H), 1.78–1.91 (m, 2 H), 2.30 (m, 2 H), 3.64 (br s, 2 H), 4.96 [4.93] (s, 1 H), 5.54 [5.37] (s, 1 H), 7.17–7.25 (m, 7 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.3 [14.7] (CH_3), 21.3 [19.6] (CH_3), 21.8 [21.3] (CH_2), 23.8 [24.6] (CH_2), 25.4 [24.9] (CH_2), 26.3 [27.4] (CH_2), 28.5 [29.7] (CH_2), 29.7 [30.7] (CH_2), 47.9 (C_q), 49.3 [50.4] (CH), 77.2 (CH), 93.2 (C_q), 101.4 (CH), 122.5/123.4/125.3/125.8/126.4/130.9/131.1/132.4/132.4/139.6 (CH and C_q), 154.9 (C=O).

(1*R*,6*S*,7*RS*,9*R*)-9-(4-Bromophenyl)-6-(*N*,*N*-diisopropylaminocarbonyloxy)-1-methyl-8-oxabicyclo[4.3.0]nonan-7-ol (10i)
According to GP4, **10i** and minor epimer (yield: 136 mg, 86%) were synthesized as a colourless oil with the diastereomeric ratio 1.6:1.0 from **6i** (153, 0.35 mmol); R_f = 0.22 (petroleum ether–Et_2O, 4:1).

rac-**10i** was obtained from *rac*-**6i**, yield: 88%.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.87 (s, 3 H), 1.14 (d, *J* = 6.4 Hz, 12 H), 1.57 (m, 2 H), 1.63–1.82 (m, 2 H), 2.14 (m, 2 H), 2.46 (m, 2 H), 3.13 (br s, 2 H), 4.95 [5.29] (s, 1 H), 5.50 [5.68] (s, 1 H), 7.07 (m_c, 2 H), 7.39 (m_c, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1 [14.3] (CH_3), 19.8 [21.3] (CH_3), 26.1 [27.1] (CH_2), 28.8 [29.5] (CH_2), 30.6 [29.2] (CH_2), 31.0 [32.1] (CH_2), 47.0 (C_q), 48.5 [47.9] (CH), 81.0 [81.7] (CH), 86.1 [86.1] (C_q), 101.0 [101.7] (CH), 121.6 [122.5] (C_q), 128.5 [128.9] (CH), 131.2 (CH), 137.7 (C_q), 155.4 [155.2] (C=O).

(1*R*,6*S*,7*RS*,9*R*)-1-Butyl-6-(*N*,*N*-diisopropylaminocarbonyloxy)-9-phenyl-8-oxabicyclo[4.3.0]nonan-7-ol (10k)
According to GP4, **120** and minor epimer (yield: 103 mg, 82%) was synthesized as a colourless oil with the diastereomeric ratio 1.1:1.0 from **6k** (120 mg, 0.30 mmol); R_f = 0.25 (petroleum ether–Et_2O, 4:1).

rac-**120** was obtained from *rac*-**60**, yield: 85%.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.77 (t, 3 H), 1.13 (m, 2 H), 1.21 (m, 14 H), 1.43 (m, 2 H), 1.58 (m, 2 H), 1.78–1.92 (m, 2 H), 2.13 (m, 2 H), 2.48 (m, 2 H), 3.65 (br s, 2 H), 4.96 [4.95] (s, 1 H), 5.56 [5.37] (s, 1 H), 7.17–7.28 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.2 [14.6] (CH_3), 20.7 [21.7] (CH_3), 21.6 [21.8] (CH_2), 23.9 [24.7] (CH_2), 24.4 [25.3] (CH_2), 26.6 [27.6] (CH_2), 28.3 [29.6] (CH_2), 30.4 [30.7] (CH_2), 31.4 [32.5] (CH_2), 47.8 (C_q), 49.6 [50.8] (CH), 78.5 (CH), 93.5 (C_q), 101.4 (CH), 121.3/126.2/129.4/138.9 (CH and C_q), 154.9 (C=O).

(1*R*,6*S*,7*RS*,9*R*)-9-(4-Bromophenyl)-1-butyl-6-(*N*,*N*-diisopropylaminocarbonyloxy)-8-oxabicyclo[4.3.0]nonan-7-ol (10l)
According to GP4, **10l** and minor epimer (yield: 108 mg, 87%) were synthesized as a colourless oil with the diastereomeric ratio 1.6:1.0 from **6l** (120 mg, 0.25 mmol); R_f = 0.22 (petroleum ether–Et_2O, 4:1).

rac-**10l** was obtained from *rac*-**6l**, yield: 87%.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.81 (t, 3 H), 1.14 (m, 2 H), 1.19 (m, 14 H), 1.43 (m, 2 H), 1.63 (m, 2 H), 1.75–1.88 (m, 2 H), 2.04 (m, 2 H), 2.49 (m, 2 H), 3.63 (br s, 2 H), 4.93 [4.97] (s, 1 H), 5.50 [5.32] (s, 1 H), 7.15 (m_c, 2 H), 7.24 (m_c, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1 [14.3] (CH_3), 21.3 [19.8] (CH_3), 20.7 [20.9] (CH_2), 24.2 [23.4] (CH_2), 25.9 [24.7] (CH_2), 26.1 [27.1] (CH_2), 28.8 [29.5] (CH_2), 30.6 [29.2] (CH_2), 31.0 [32.1] (CH_2), 47.0 (C_q), 49.8 [50.1] (CH), 76.8 (CH), 93.4 (C_q), 101.9 (CH), 121.5 [122.9] (C_q), 131.2 (CH), 137.7 (CH), 139.9 (C_q), 153.9 (C=O).

(1*R*,6*S*,7*RS*,9*R*)-1-Butyl-6-(*N*,*N*-diisopropylaminocarbonyloxy)-9-(naphth-2-yl)-8-oxabicyclo[4.3.0]nonan-7-ol (10m)
According to GP4, **10m** and minor epimer (yield: 127 mg, 90%) were synthesized as a colourless oil with the diastereomeric ratio 2.0:1.0 from **6m** (135 mg, 0.30 mmol); R_f = 0.22 (petroleum ether–Et_2O, 4:1).

rac-**10m** was obtained from *rac*-**6m**, yield: 90%.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.77 (t, 3 H), 1.14 (m, 2 H), 1.23 (m, 14 H), 1.42 (m, 2 H), 1.57 (m, 2 H), 1.79–1.93 (m, 2 H), 2.11 (m, 2 H), 2.56 (m, 2 H), 3.67 (br s, 2 H), 4.96 [4.94] (s, 1 H), 5.51 [5.34] (s, 1 H), 7.15–7.33 (m, 7 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.5 [14.6] (CH_3), 21.2 [21.7] (CH_3), 21.3 [21.9] (CH_2), 23.6 [24.4] (CH_2), 24.8 [25.6] (CH_2), 26.3 [27.4] (CH_2), 28.5 [29.7] (CH_2), 30.5 [30.7] (CH_2), 31.8 [32.1] (CH_2), 47.7 (C_q), 49.5 [50.6] (CH), 77.7 (CH), 93.4 (C_q), 101.5 (CH), 121.5/123.6/125.7/126.8/127.4/130.4/132.6/139.9/131.1/132.9 (CH and C_q), 154.9 (C=O).

(1*R*,6*S*,7*RS*,9*R*)-1-Butyl-6-(*N*,*N*-diisopropylaminocarbonyloxy)-9-(2-methylethyl)-8-oxabicyclo[4.3.0]nonan-7-ol (10n)
According to GP4, **10n** and minor epimer (yield: 86 mg, 90%) were synthesized as a colourless oil with the diastereomeric ratio 1.0:1.0 from **6n** (91 mg, 0.25 mmol); R_f = 0.23 (petroleum ether–Et_2O, 4:1).

rac-**10n** was obtained from *rac*-**6n**, yield: 93%.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.75 (t, 3 H), 1.12 (m, 2 H), 1.15 (m, 14 H), 1.43 (m, 2 H), 1.56 (m, 2 H), 1.76–1.91 (m, 2 H), 2.06 (m, 2 H), 2.34 (m, 2 H), 2.39 (m, 6 H), 2.41 (m, 6 H), 3.66, (d, 1 H), 3.84 [3.93] (br s, 2 H), 6.19 [6.23] (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.3 [13.8] (CH_3), 20.3 [19.2] (CH_3), 20.6 [19.9] (CH_3), 20.6 [20.9] (CH_2), 21.0 [21.2] (CH_2), 22.1 [22.3] (CH_2), 23.5 [23.9] (CH_2), 26.4 [26.2] (CH_2), 29.8 [30.2] (CH_2), 38.6 [39.2] (CH_2), 30.5 (CH), 44.4 (C_q), 48.4 (CH), 76.4 (CH), 93.4 (C_q), 101.9 (CH), 153.7 (C=O).

(1*R*,6*S*,7*RS*,9*R*)-1-Butyl-6-(*N*,*N*-diisopropylaminocarbonyloxy)-9-(4-methoxyphenyl)-8-oxabicyclo[4.3.0]nonan-7-ol (10o)
According to GP4, **10o** and minor epimer (yield: 114 mg, 85%) were synthesized as a colourless oil with the diastereomeric ratio 1.6:1.0 from **6o** (129 mg, 0.30 mmol); R_f = 0.22 (petroleum ether–Et_2O, 4:1).

rac-**10o** was obtained from *rac*-**6o**, yield: 85%.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.83 (t, 3 H), 1.15 (m, 2 H), 1.21 (d, 14 H), 1.47 (m, 2 H), 1.58 (m, 2 H), 1.78–1.92 (m, 2 H), 2.04 (m, 2 H), 2.49 (m, 2 H), 3.68 (br s, 2 H), 3.88 (s, 3 H), 4.98 [4.97] (s, 1 H), 5.55 [5.34] (s, 1 H), 7.19–7.27 (m, 4 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.3 [14.4] (CH_3), 21.4 [19.7] (CH_3), 20.9 [20.9] (CH_2), 24.5 [23.7] (CH_2), 25.3 [24.6] (CH_2), 26.3 [27.6] (CH_2), 28.5 [29.7] (CH_2), 30.5 [29.7] (CH_2), 31.5 [32.6] (CH_2), 47.3 (C_q), 49.9 [50.4] (CH), 54.6 (CH_3), 78.4 (CH), 93.5 (C_q), 101.7 (CH), 121.4 [122.5] (C_q), 131.6 (CH), 137.4 (CH), 139.5 (C_q), 153.1 (C=O).

Lactones 11; General Procedure (GP5)
A solution of **10** (0.25–0.50 mmol) in anhyd CH_2Cl_2 (5–10 mL) was oxidized with PDC (376–752 mg, 0.50–1.00 mmol) at r.t. for 15 h. After dilution with H_2O (10 mL) and extraction with Et_2O (3 × 10

mL) the mixture was dried ($MgSO_4$). Evaporation of the solvent under reduced pressure, followed by chromatography (silica gel; petroleum ether–Et_2O, 4:1) afforded products **11**.

(1*S*,4*R*,5*R*)-4-(4-Bromophenyl)-1-(*N*,*N*-diisopropylaminocarbonyloxy)-5-methyl-3-oxabicyclo[3.3.0]octan-2-one (11a)
According to GP5, **11a** (yield: 63 mg, 76%) was synthesized as a colourless solid; mp 146.1 °C (petroleum ether–Et_2O, 4:1); from **10a** (83 mg, 0.19 mmol); R_f = 0.22 (petroleum ether–Et_2O, 4:1); $[\alpha]_D^{20}$ –24.3 (*c* 0.85, $CHCl_3$); chiral HPLC (chiragrom-1; hexane–*i*-PrOH, 100:1), 93% ee, major enantiomer appears at lower retention time.

rac-**11a** was obtained from *rac*-**10a**, yield: 81%.

IR (KBr): 1782 (C=O), 1700 (C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.77 (s, 3 H), 1.11 (d, *J* = 6.3 Hz, 12 H), 1.61 (m, 2 H), 1.61–1.92 (m, 2 H), 2.34 (m, 2 H), 3.69/3.90 (br s, 2 H), 4.97 (s, 1 H), 7.28 (m_c, 2 H), 7.43 (m_c, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.2 (CH_3), 19.4 (CH_3), 20.4 (CH_2), 20.5 (CH_2), 28.7 (CH_2), 45.8 (C_q), 50.9 (CH), 87.2 (CH), 88.9 (C_q), 121.0 (C_q), 127.6 (CH), 130.1 (CH), 135.3 (C_q), 152.4 (C=O), 175.1 (C=O).

HRMS: *m*/*z* calcd: 460.1094; found: 460.1093 $[M + Na]^+$.

Anal. Calcd for $C_{21}H_{28}NO_4Br$ (438.36): C, 57.54; H, 6.44; N, 3.20. Found: C, 57.62; H, 6.80; N, 3.20.

(1*S*,4*R*,5*R*)-4-(4-Chlorophenyl)-1-(*N*,*N*-diisopropylaminocarbonyloxy)-5-methyl-3-oxabicyclo[4.3.0]octan-2-one (11b)
According to GP5, **11b** (yield: 65 mg, 75%) was synthesized as an amorphous solid from **10b** (88 mg, 0.22 mmol); R_f = 0.24 (petroleum ether–Et_2O, 4:1); $[\alpha]_D^{20}$ –12.8 (*c* 0.90, $CHCl_3$); chiral HPLC (chiragrom-2; hexane–*i*-PrOH, 200:1), 74% ee, major enantiomer appears at higher retention time.

rac-**11b** was obtained from *rac*-**10b**, yield: 74%.

IR (KBr): 1778 (C=O), 1695 (C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.76 (s, 3 H), 1.14 (d, *J* = 6.3 Hz, 12 H), 1.51 (m, 2 H), 1.62–1.92 (m, 2 H), 2.31 (m, 2 H), 3.68/3.91 (br s, 2 H), 4.99 (s, 1 H), 7.25 (m_c, 2 H), 7.36 (m_c, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.2 (CH_3), 19.9 (CH_3), 21.1 (CH_2), 22.2 (CH_2), 30.3 (CH_2), 47.5 (C_q), 52.6 (CH), 88.5 (CH), 88.9 (C_q), 122.7 (C_q), 131.8 (CH), 132.2 (CH), 136.9 (C_q), 154.1 (C=O), 176.8 (C=O).

HRMS: *m*/*z* calcd: 416.1599; found: 416.1619 $[M + Na]^+$.

Anal. Calcd for $C_{21}H_{28}NO_4Cl$ (393.90): C, 64.03; H, 7.16; N, 3.56. Found: C, 64.32; H, 7.19; N, 3.82.

(1*S*,4*R*,5*R*)-1-(*N*,*N*-Diisopropylaminocarbonyloxy)-5-methyl-4-(naphth-2-yl)-3-oxabicyclo[3.3.0]octan-2-one (11c)
According to GP5, **11c** (yield: 47 mg, 59%) was synthesized as colourless crystal (mp 118.2 °C, petroleum ether–Et_2O, 4:1) from **10c** (80 mg, 0.19 mmol); R_f = 0.22 (petroleum ether–Et_2O, 4:1); $[\alpha]_D^{20}$ –28.1 (*c* 0.85, CHCl3); chiral HPLC (chiragrom-2; hexane–*i*-PrOH, 500:1), 83% ee, major enantiomer appears at lower retention time.

rac-**11c** was obtained from *rac*-**10c**, yield: 68%.

IR (KBr): 1780 (C=O), 1698 (C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.79 (s, 3 H), 1.16 (d, *J* = 6.4 Hz, 12 H), 1.56 (m, 2 H), 1.65–1.89 (m, 2 H), 2.28 (m, 2 H), 3.70/3.90 (br s, 2 H), 5.19 (s, 1 H), 7.13–7.36 (m, 7 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.3 (CH_3), 19.2 (CH_3), 22.8 (CH_2), 27.9 (CH_2), 29.4, (CH_2), 45. 8 (C_q), 51.9 (CH), 86.9 (CH), 87.2 (C_q), 127.2/127.3/129.3/129.8/130.1/131.5/131.9/132.8/134.7/134.3 (CH and C_q), 152.4 (C=O), 166.7 (C=O).

HRMS: *m*/*z* calcd: 432.2145; found: 432.2163 $[M + Na]^+$.

Anal. Calcd for $C_{25}H_{31}NO_4$ (409.52): C, 73.32; H, 7.63; N, 3.42. Found: C, 73.41; H, 7.69; N, 3.48.

X-ray crystal structure analysis for HOP3117: formula $C_{25}H_{31}NO_4$, M = 409.51, colourless crystal 0.20 × 0.10 × 0.06 mm, a = 10.910(1), b = 12.345(1), c = 16.977(1) Å, V = 2286.5(3) $Å^3$, ρ_{calc} = 1.190 $g \cdot cm^{-3}$, 6.40 cm^{-1}, no absorption correction (0.883 ≤ T ≤ 0.963), Z = 4, orthorhombic, space group $P2_12_12_1$ (No. 19), λ = 1.54178 Å, T = 223 K, ω and φ scans, 11009 reflections collected (±*h*, ±*k*, ±*l*), [(sinθ)/γ] = 0.58 $Å^{-1}$, 3636 independent and 3333 observed reflections [$I \geq \sigma(I)$], 276 refined parameters, $R1$ = 0.042, $wR2$ = 0.101, Flack parameter 0.0(2), max. residual electron density 0.12 (–0131) $e \cdot Å^{-3}$, hydrogens calculated and refined as riding atoms.

(1*S*,4*R*,5*R*)-5-Butyl-1-(*N*,*N*-diisopropylaminocarbonyloxy)-4-(2-methylethyl)-3-oxabicyclo[3.3.0]octan-2-one (11d)
According to GP5, **11d** (yield: 54 mg, 78%) was synthesized as a colourless oil from **10d** (70 mg, 0.19 mmol); R_f = 0.22 (petroleum ether–Et_2O, 4:1); $[\alpha]_D^{20}$ –10.6 (*c* 0.85, $CHCl_3$); chiral HPLC (chiragrom-1; hexane–*i*-PrOH, 200:1), 65% ee, major enantiomer appears at lower retention time.

rac-**11d** was obtained from *rac*-**10d**, yield: 76%.

IR (film): 1770 (C=O), 1701 (C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.84 (t, 3 H), 1.21 (m, 2 H), 1.28 (m, 14 H), 1.50 (m, 2 H), 1.58 (m, 2 H), 1.69–1.86 (m, 2 H), 2.22 (m, 2 H), 2.37 (m, 6 H), 3.14 (m, 1 H), 3.68 (d, 1 H), 3.89/4.09 (br s, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.8 (CH_3), 20.8 (CH_3), 21.6 (CH_3), 21.5 (CH_3), 20.6 (CH_2), 21.7 (CH_2), 22.6 (CH_2), 23.4 (CH_2), 26.6 (CH_2), 29.1 (CH_2), 30.2 (CH), 44.5 (C_q), 48.7 (CH), 86.4 (CH), 98.7 (C_q), 154.6 (C=O), 173.5 (C=O).

Anal. Calcd for $C_{21}H_{37}NO_4$ (367.52): C, 68.63; H, 10.15; N, 3.81. Found: C, 68.80; H, 10.25; N, 3.76.

HRMS: *m*/*z* calcd: 390.2620; found: 390.2634 $[M + Na]^+$.

(1*S*,4*R*,5*R*)-5-Butyl-1-(*N*,*N*-diisopropylaminocarbonyloxy)-4-phenyl-3-oxabicyclo[3.3.0]octan-2-one (11e)
According to GP5, **11e** (yield: 80 mg, 80%) was synthesized as an amorphous solid from **10e** (101 mg, 0.25 mmol); R_f = 0.22 (petroleum ether–Et_2O, 4:1); $[\alpha]_D^{20}$ +9.8 (*c* 1.05, $CHCl_3$); ^1H NMR shift experiment: er 89:11 (78% ee); 5.3 mg + 24 mol% $Eu(hfc)_3$ in C_6D_6, Δδ (1 H at δ 5.15) = 0.14, signal of major enantiomer appears at lower field.

rac-**11e** was obtained from *rac*-**10e**, yield: 81%.

IR (KBr): 1767 (C=O), 1700 (C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.88 (t, 3 H), 1.24 (m, 2 H), 1.29 (m, 14 H), 1.58 (m, 2 H), 1.61 (m, 2 H), 1.78–1.94 (m, 2 H), 2.48 (m, 2 H), 3.65/3.89 (br s, 2 H), 5.15 (s, 1 H), 7.15–7.23 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.7 (CH_3), 21.1 (CH_3), 21.6 (CH_2), 24.4 (CH_2), 25.4 (CH_2), 26.7 (CH_2), 28.2 (CH_2), 30.4 (CH_2), 47.1 (C_q), 49.4 (CH), 86.2 (CH), 99.4 (C_q), 121.3/126.4/132.6/134.1 (CH and C_q), 154.9 (C=O), 174.9 (C=O).

HRMS: *m*/*z* calcd: 424.2463; found: 424.2469 $[M + Na]^+$.

Anal. Calcd for $C_{24}H_{35}NO_4$ (401.54): C, 71.79; H, 8.79; N, 3.49. Found: C, 71.62; H, 8.69; N, 3.34.

(1*S*,4*R*,5*R*)-4-(4-Bromophenyl)-5-butyl-1-(*N*,*N*-diisopropylaminocarbonyloxy)-3-oxabicyclo[3.3.0]octan-2-one (11f)

According to GP5, **11f** (yield: 100 mg, 83%) was synthesized as an amorphous solid from **10f** (120 mg, 0.25 mmol); R_f = 0.22 (petroleum ether–Et_2O, 4:1); $[\alpha]_D^{20}$ –50.9 (*c* 0.50, $CHCl_3$); ^{1}H NMR shift experiment: er 86:14 (72% ee); 4.8 mg + 45 mol% Eu(hfc)$_3$ in C_6D_6, Δδ (1 H at δ = 5.26) = 0.21, signal of major enantiomer appears at lower field.

rac-**11f** was obtained from *rac*-**10f**, yield: 81%.

IR (KBr): 1769 (C=O), 1693 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.82 (t, 3 H), 1.15 (m, 2 H), 1.24 (m, 14 H), 1.58 (m, 2 H), 1.64 (m, 2 H), 1.74–1.96 (m, 2 H), 2.32 (m, 2 H), 3.65/3.92 (br s, 2 H), 5.26 (s, 1 H), 7.25 (m_c, 2 H), 7.40 (m_c, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.2 (CH_3), 21.8 (CH_3), 21.9 (CH_2), 23.4 (CH_2), 25.2 (CH_2), 26.2 (CH_2), 28.2 (CH_2), 30.5 (CH_2), 47.8 (C_q), 49.8 (CH), 86.3 (CH), 98.9 (C_q), 121.3 (C_q), 131.4 (CH), 132.5 (CH), 133.5 (C_q), 153.1 (C=O), 174.2 (C=O).

HRMS: *m*/*z* calcd: 480.1749; found: 480.1754 [M + H]$^+$.

Anal. Calcd for $C_{24}H_{34}NO_4Br$ (480.44): C, 60.00; H, 7.13; N, 2.92. Found: C, 60.03; H, 7.09; N, 2.83.

(1*S*,4*R*,5*R*)-5-Butyl-1-(*N*,*N*-diisopropylaminocarbonyloxy)-4-(naphth-2-yl)-3-oxabicyclo[3.3.0]octan-2-one (11g)

According to GP5, **11g** (yield: 80 mg, 84%) was synthesized as a colourless oil from **10g** (95 mg, 0.21 mmol); R_f = 0.22 (petroleum ether–Et_2O, 4:1); $[\alpha]_D^{20}$ –28.1 (*c* 0.45, $CHCl_3$); ^{1}H NMR shift experiment: er 90:8 (82% ee); 5.1 mg + 29 mol% Eu(hfc)$_3$ in C_6D_6, Δδ (1 H at δ 5.15) = 0.15, signal of major enantiomer appears at lower field.

rac-**11g** was obtained from *rac*-**10g**, yield: 83%.

IR (film): 1771 (C=O), 1693 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.82 (t, 3 H), 1.23 (m, 2 H), 1.26 (m, 14 H), 1.55 (m, 2 H), 1.63 (m, 2 H), 1.76–1.96 (m, 2 H), 2.42 (m, 2 H), 3.63/3.90 (br s, 2 H), 5.15 (s, 1 H), 7.17–7.25 (m, 7 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.7 (CH_3), 21.6 (CH_3), 21.3 (CH_2), 24.8 (CH_2), 25.9 (CH_2), 26.4 (CH_2), 28.7 (CH_2), 30.7 (CH_2), 47.6 (C_q), 49.4 (CH), 86.2 (CH), 98.6 (C_q), 122.4/123.7/125.2/125.5/126.8/130.3/131.4/132.5/132.6/139.7 (CH and C_q), 154.1 (C=O), 174.3 (C=O).

HRMS: *m*/*z* calcd: 474.2620; found: 474.2626 [M + Na]$^+$.

Anal. Calcd for $C_{28}H_{37}NO_4$ (451.60): C, 74.47; H, 8.26; N, 3.10. Found: C, 74.32; H, 8.38; N, 3.11.

(1*R*,6*S*,9*R*)-9-(4-Bromophenyl)-6-(*N*,*N*-diisopropylaminocarbonyloxy)-1-methyl-8-oxabicyclo[4.3.0]nonan-7-one (11i)

According to GP5, **11i** (yield: 99 mg, 82%) was synthesized as colourless crystals from **10i** (123 mg, 0.27 mmol); R_f = 0.27 (petroleum ether–Et_2O, 4:1); mp 127.5 °C (petroleum ether–Et_2O, 4:1); $[\alpha]_D^{20}$ +50 (*c* 0.50, $CHCl_3$); chiral HPLC (chiragrom-1; hexane–*i*-PrOH, 200:1), 86% ee, major enantiomer appears at lower retention time.

rac-**11i** was obtained from *rac*-**10i**, yield: 84%.

IR (KBr): 1773 (C=O), 1702 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.67 (t, 3 H), 1.11 (d, 12 H), 1.61 (m, 2 H), 1.61–1.92 (m, 2 H), 2.04 (m, 2 H), 2.43 (m, 2 H), 3.13/3.45 (br s, 2 H), 5.19 (s, 1 H), 7.09 (m_c, 2 H), 7.42 (m_c, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 14.2 (CH_3), 21.3 (CH_3), 20.4 (CH_2), 25.4 (CH_2), 27.8 (CH_2), 31.2 (CH_2), 47.2 (C_q), 49.4 (CH), 86.4 (CH), 99.4 (C_q), 121.5 (C_q), 131.2 (CH), 132.3 (CH), 134.9 (C_q), 153.2 (C=O), 174.1 (C=O).

HRMS: *m*/*z* calcd: 452.1436; found: 452.1429 [M + H]$^+$.

Anal. Calcd for $C_{22}H_{30}BrNO_4$ (451.38): C, 58.41; H, 6.68; N, 3.10. Found: C, 58.82; H, 6.81; N, 2.81.

X-ray crystal structure analysis for HOP3061: formula $C_{22}H_{30}BrNO_4$, M = 452.38, colourless crystal 0.25 × 0.15 × 0.10 mm, a = 7.485(1), b = 20.720(1), c = 14.092(1) Å, β = 98.50(1)°, V = 2161.5(3) Å^3, ρ_{calc} = 1.390 g cm^{-3}, 19.29 cm^{-1}, empirical absorption correction (0.644 ≤ T ≤ 0.831), Z = 4, monoclinic, space group $P2_1/c$ (No. 14), λ = 0.71073 Å, T = 198 K, ω and φ scans, 13084 reflections collected (±h, ±k, ±l), [(sinθ)/λ] = 0.66 Å^{-1}, 5126 independent and 3326 observed reflections [$I \geq 2\ \sigma(I)$], 258 refined parameters, R = 0.047, wR^2 = 0.096, max. residual electron density 0.32 (–0.46) e Å^{-3}, hydrogens calculated and refined as riding atoms.

(1*R*,6*S*,9*R*)-1-Butyl-6-(*N*,*N*-diisopropylaminocarbonyloxy)-9-phenyl-8-oxabicyclo[4.3.0]nonan-7-one (11k)

According to GP5, **11k** (yield: 79 mg, 84%) was synthesized as colourless crystals from **10k** (95 mg, 0.23 mmol); R_f = 0.22 (petroleum ether–Et_2O, 4:1); $[\alpha]_D^{20}$ –42 (*c* 0.50, $CHCl_3$); ^{1}H NMR shift experiment: er 89:11 (78% ee); 4.8 mg + 45 mol% Eu(hfc)$_3$ in C_6D_6, Δδ (1 H at δ = 5.14) = 0.31, signal of major enantiomer appears at lower field.

rac-**11k** was obtained from *rac*-**10k**, yield: 85%.

IR (KBr): 1767 (C=O), 1700 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.86 (t, 3 H), 1.18 (m, 2 H), 1.23 (m, 14 H), 1.53 (m, 2 H), 1.68 (m, 2 H), 1.74–1.96 (m, 2 H), 2.12 (m, 2 H), 2.54 (m, 2 H), 3.55/3.88 (br s, 2 H), 5.14 (s, 1 H), 7.03–7.20 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.6 (CH_3), 21.7 (CH_3), 21.6 (CH_2), 24.9 (CH_2), 25.4 (CH_2), 26.6 (CH_2), 28.6 (CH_2), 30.5 (CH_2), 31.7 (CH_2), 47.3 (C_q), 49.2 (CH), 86.5 (CH), 99.5 (C_q), 121.2/126.5/129.1/138.2 (CH and C_q), 155.1 (C=O), 174.7 (C=O).

HRMS: *m*/*z* calcd: 438.2615; found: 438.2621 [M + Na]$^+$.

Anal. Calcd for $C_{25}H_{37}NO_4$ (415.27): C, 72.26; H, 8.97; N, 3.37. Found: C, 72.32; H, 8.90; N, 3.34.

X-ray crystal structure analysis for HOP2926: formula $C_{25}H_{37}NO_4$, M = 415.56, colourless crystal 0.50 × 0.10 × 0.05 mm, a = 9.784(1), b = 15.337(1), c = 16.151(1) Å, β = 92.96(1)°, V = 2420.3(3) Å^3, ρ_{calc} = 1.140 g·cm^{-3}, 6.05 cm^{-1}, empirical absorption correction (0.752 ≤ T ≤ 0.970), Z = 4, monoclinic, space group $P2_1/c$ (No. 14), λ = 1.54178 Å, T = 223 K, ω and φ scans, 11513 reflections collected (±h, ±k, ±l), [(sin θ)/λ] = 0.58 Å^{-1}, 3200 independent and 1686 observed reflections [I 2 σ(I)], 276 refined parameters, $R1$ = 0.050, $wR2$ = 0.131, due to shape and quality poorly diffracting crystal, max. residual electron density 0.23 (–0.18) e·Å^{-3}, hydrogens calculated and refined as riding atoms.

(1*R*,6*S*,9*R*)-9-(4-Bromophenyl)-1-butyl-6-(*N*,*N*-diisopropylaminocarbonyloxy)-8-oxabicyclo[4.3.0]nonan-7-one (11l)

According to GP5, **11l** (yield: 80 mg, 80%) was synthesized as an amorphous solid from **10l** (100 mg, 0.20 mmol); R_f 0.27 (petroleum ether–Et_2O, 4:1); $[\alpha]_D^{20}$ –56.1 (*c* 0.50, $CHCl_3$); ^{1}H NMR shift experiment: er 88:12 (76% ee); 4.8 mg + 33 mol% Eu(hfc)$_3$ in C_6D_6, Δδ (1 H at δ 5.18) = 0.31, signal of major enantiomer appears at lower field.

rac-**11l** was obtained from *rac*-**10**, yield: 81%.

IR (KBr): 1770 (C=O), 1700 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.79 (t, 3 H), 1.12 (m, 2 H), 1.18 (m, 14 H), 1.45 (m, 2 H), 1.61 (m, 2 H), 1.75–1.91 (m, 2 H), 2.01 (m, 2 H), 2.46 (m, 2 H), 3.53/3.86 (br s, 2 H), 5.18 (s, 1 H), 7.15 (m_c, 2 H), 7.23 (m_c, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.2 (CH_3), 21.3 (CH_3), 20.4 (CH_2), 24.5 (CH_2), 25.4 (CH_2), 26.5 (CH_2), 27.8 (CH_2), 31.2 (CH_2), 33.2 (CH_2), 47.2 (C_q), 49.4 (CH), 86.4 (CH), 99.4 (C_q), 121.5 (C_q), 131.2 (CH), 132.3 (CH), 134.9 (C_q), 153.2 (C=O), 174.1 (C=O).

Anal. Calcd for $C_{25}H_{36}BrNO_4$ (493.46): C, 60.73; H, 7.34; N, 2.83. Found: C, 60.96; H, 7.48; N, 3.07.

(1*R*,6*S*,9*R*)-1-Butyl-6-(*N*,*N*-diisopropylaminocarbonyloxy)-9-(naphth-2-yl)-8-oxabicyclo[4.3.0]nonan-7-one (11m)

According to GP5, **11m** (yield: 94 mg, 81%) was synthesized as an amorphous solid from **10m** (116 mg, 0.25 mmol); R_f = 0.22 (petroleum ether–Et_2O, 4:1); $[\alpha]_D^{20}$ –30.0 (*c* 0.55, $CHCl_3$); ^{1}H NMR shift experiment: er 83:17 (66% ee); 4.6 mg + 48 mol% Eu(hfc)$_3$ in C_6D_6, Δδ (1 H at δ 5.15) = 0.14, signal of major enantiomer appears at lower field.

rac-**11m** was obtained from *rac*-**10m**, yield: 79%.

IR (KBr): 1769 (C=O), 1693 (C=O) cm^{-1}.

^{1}H NMR (76 MHz, $CDCl_3$): δ = 0.83 (t, 3 H), 1.15 (m, 2 H), 1.18 (m, 14 H), 1.43 (m, 2 H), 1.58 (m, 2 H), 1.78–1.94 (m, 2 H), 2.13 (m, 2 H), 2.49 (m, 2 H), 3.65/3.97 (br s, 2 H), 5.15 (s, 1 H), 7.15–7.25 (m, 7 H).

^{13}C NMR (300 MHz, $CDCl_3$): δ = 14.6 (CH_3), 21.4 (CH_3), 21.3 (CH_2), 24.3 (CH_2), 25.8 (CH_2), 26.7 (CH_2), 28.9 (CH_2), 30.9 (CH_2), 31.2 (CH_2), 47.7 (C_q), 49.0 (CH), 85.4 (CH), 99.0 (C_q), 121.3/123.5/125.6/126.7/127.0/130.7/132.0/132.4/133.3/134.7 (CH and C_q), 154.9 (C=O), 174.1 (C=O).

HRMS: *m*/*z* calcd: 488.2776; found: 488.2783 $[M + Na]^+$.

Anal. Calcd for $C_{29}H_{39}NO_4$ (465.62). C, 74.81; H, 8.44; N, 3.01. Found C, 75.36; H, 8.58; N, 3.61.

(1*R*,6*S*,9*R*)-1-Butyl-6-(*N*,*N*-diisopropylaminocarbonyloxy)-9-(2-methylethyl)-8-oxabicyclo[4.3.0]nonan-7-one (11n)

According to GP5, **11n** (yield: 67 mg, 84%) was synthesized as a colourless oil from **10n** (80 mg, 0.21 mmol); R_f = 0.22 (petroleum ether–Et_2O, 4:1); $[\alpha]_D^{20}$ –17.9 (*c* 1.15, $CHCl_3$); chiral HPLC (chiragrom-1; hexane–*i*-PrOH, 200:1), 72% ee, major enantiomer appears at higher retention time.

rac-**11n** was obtained from *rac*-**10n**, yield: 85%.

IR (film): 1771 (C=O), 1702 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.93 (t, 3 H), 1.24 (m, 2 H), 1.35 (m, 14 H), 1.56 (m, 2 H), 1.62 (m, 2 H), 1.84–1.94 (m, 2 H), 2.11 (m, 2 H), 2.35 (m, 6 H), 2.55 (m, 2 H), 2.63 (m, 6 H), 3.79 (d, 1 H), 3.85/4.18 (br s, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.1 (CH_3), 21.3 (CH_3), 21.6 (CH_3), 21.9 (CH_2), 22.6 (CH_2), 23.1 (CH_2), 23.9 (CH_2), 26.2 (CH_2), 29.3 (CH_2), 29.5 (CH), 37.7 (CH_2), 43.4 (CH), 47.5 (C_q), 83.8 (CH), 97.5 (C_q), 154.8 (C=O), 174.5 (C=O).

Anal. Calcd for $C_{22}H_{39}NO_4$ (381.55): C, 69.25; H, 10.30; N, 3.67. Found: C, 69.18; H, 10.15; N, 3.59.

(1*R*,6*S*,9*R*)-1-Butyl-6-(*N*,*N*-diisopropylaminocarbonyloxy)-9-(4-methoxyphenyl)-8-oxabicyclo[4.3.0]nonan-7-one (11o)

According to GP5, **11o** (yield: 89 mg, 80%) was synthesized as a colourless oil from **10o** (111 mg, 0.25 mmol); R_f = 0.22 (petroleum ether–Et_2O, 4:1); $[\alpha]_D^{20}$ +40.2 (*c* 0.50, $CHCl_3$); ^{1}H NMR shift experiment: er 86:13 (73% ee), 5.3 mg + 25 mol% Eu(hfc)$_3$ in C_6D_6, Δδ (1 H at δ 5.04) = 0.14, signal of major enantiomer appears at higher field.

rac-**11o** was obtained from *rac*-**10o**, yield: 82%.

IR (film): 1771 (C=O), 1700 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.89 (t, 3 H), 1.17 (m, 2 H), 1.13 (m, 14 H), 1.48 (m, 2 H), 1.64 (m, 2 H), 1.73–1.96 (m, 2 H), 2.03 (m, 2 H), 2.42 (m, 2 H), 3.64/3.98 (br s, 2 H), 3.85 (s, 3 H), 5.05 (s, 1 H), 7.17 (m_c, 2 H), 7.25 (m_c, 2 H).

^{13}C NMR (300 MHz, $CDCl_3$): δ = 14.5 (CH_3), 21.2 (CH_3), 20.9 (CH_2), 24.1 (CH_2), 25.4 (CH_2), 26.4 (CH_2), 28.8 (CH_2), 30.5 (CH_2), 31.4 (CH_2), 47.2 (C_q), 49.5 (CH), 53.6 (OCH_3), 85.6 (CH), 99.5 (C_q), 121.2 (C_q), 133.1 (CH), 132.5 (CH), 135.5 (C_q), 154.2 (C=O), 174.5 (C=O).

Anal. Calcd for $C_{26}H_{39}NO_5$ (445.50): C, 70.08; H, 8.82; N, 3.14. Found: C, 69.98; H, 8.75; N, 3.11.

Acknowledgement

The work was supported by the Deutsche Forschunggemeinschaft, (SFB 424) and the Fonds der Chemischen Industrie.

References

(1) Responsible for X-ray structure data.
(2) Review: Hoppe, D.; Hense, T. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2282; *Angew. Chem.* **1997**, *109*, 2376.
(3) Reviews: (a) Hoppe, D.; Marr, F.; Brüggemann, M. *Organolithiums in Enantioselective Synthesis, Topics in Organometallic Chemistry*, Vol 5; Hodgson, D. M., Ed.; Springer-Verlag: Berlin, **2003**, 61–138. (b) Hoppe, D.; Christoph, G. *The Chemistry of Organolithium Compounds*, Vol 2; Rappoport, Z.; Marek, I., Eds.; Wiley: Chichester, **2004**, 1055–1164.
(4) (a) Hoppe, D.; Zschage, O. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 69; *Angew. Chem.* **1989**, *101*, 67. (b) Paulsen, H.; Graeve, C.; Hoppe, D. *Synthesis* **1996**, 141. (c) Deiters, A.; Hoppe, D. *J. Org. Chem.* **2001**, *66*, 2842. (d) Beckmann, E.; Hoppe, D. *Synthesis* **2005**, 217. (e) Zeng, W.; Fröhlich, R.; Hoppe, D. *Tetrahedron* **2005**, *61*, 3281.
(5) (a) Özlügedik, M.; Kristensen, J.; Wibbeling, B.; Fröhlich, R.; Hoppe, D. *Eur. J. Org. Chem.* **2002**, 414.
(b) Özlügedik, M.; Kristensen, J.; Reuber, J.; Fröhlich, R.; Hoppe, D. *Synthesis* **2004**, 2303.
(6) Zhu, Y.; Manske, K. J.; Shi, Y. *J. Am. Chem. Soc.* **1999**, *121*, 4080.
(7) (a) Hoppe, D.; Lüßmann, J.; Jones, P. G.; Schmidt, D.; Sheldrick, G. M. *Tetrahedron Lett.* **1986**, *27*, 3591.
(b) Lüßmann, J.; Hoppe, D.; Jones, P. G.; Fittschen, C.; Sheldrick, G. M. *Tetrahedron Lett.* **1986**, *31*, 3595.
(8) Reuber, J.; Fröhlich, R.; Hoppe, D. *Org. Lett.* **2004**, *6*, 783.
(9) Reuber, J. *Dissertation*; University of Münster: Germany, **2005**, see also ref. 5a and 8.
(10) Sharpless, K. B.; Verhoeven, T. R. *Aldrichimica Acta* **1979**, *12*, 63.
(11) Mihelich, E. D.; Daniels, D.; Eickhoff, D. J. *J. Am. Chem. Soc.* **1981**, *103*, 7690.

(12) Data sets were collected with Nonius Kappa CCD diffractometers, in case of Mo-radiation equipped with a rotating anode generator. Programs used: (a) Data collection: Nonius, B. V. *COLLECT* **1998**. (b) Data reduction Denzo-SMN: Otwinowski, Z.; Minor, W. *Methods in Enzymology* **1997**, *276*, 307. Absorption correction SORTAV: (c) Blessing, R. H. *Acta Cryst.* **1995**, *A51*, 33. (d) Blessing, R. H. *J. Appl. Cryst.* **1997**, *30*, 421; Denzo: Otwinowski Z., Borek D., Majewski W., Minor W.; *Acta Cryst*.; **2003**, A59: 228;. (e) Structure solution SHELXS-97: Sheldrick, G. M. *Acta Cryst.* **1990**, *A46*, 467. (f) Structure refinement SHELXL-97: Sheldrick, G. M. *Universität Göttingen* **1997**. (g) Graphics Diamond: Brandenburg, K. *Universität Bonn* **1997**. (h) CCDC-264379, 264380, and 264831 contain the supplementary crystallographic data for this paper. This data can be obtained free of charge at www.cam.ac.uk/conts/retrieving.html [or from Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (internat.) +44 (1223)336-033; E-mail: deposit@ccdc.cam.ac.uk].