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Asymmetric Hydroboration with New Chiral Monoalkylboranes bearing a Non-Stereogenic, Chirotopic Center

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Dedicated to Professors David A. Evans and Teruaki Mukaiyama

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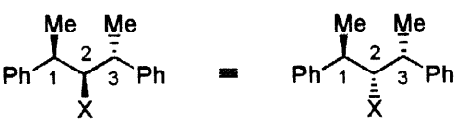
Abstract: Enantiomerically pure 2,5-diorganocyclopentanecarboxylic acids bearing a non-stereogenic, chirotopic center were prepared via stereoselective copper catalyzed carbon-carbon bond forming reactions. These compounds serve as intermediates in the synthesis of new chiral monoalkylboranes which lead to enantioselectivities of up to 64 % *ee* in the asymmetric hydroboration of cyclic olefins.

Keywords: chirotopic center; carboxylic acids; addition reactions; asymmetric hydroboration.

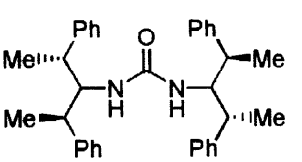
Introduction

The design of new chiral ligands for asymmetric synthesis is an active field of research [1-4]. Recently, we have introduced a new class of powerful chiral ligands [5]. The key feature of these new pseudo-C_2-symmetrical ligands of type **1** is the presence of the non-stereogenic center C(2) which can be described as a chirotopic center (center being in a chiral environment) according to the definition of K. Mislow [6].



1a **1b**

X = NH_2, PR_2, BH_2, Metal



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By design, these ligands avoid the control of the stereochemistry at C(2). In comparison with most ligands described in the literature, this represents a great synthetic advantage because there is no need for linking stereospecifically a secondary carbon center to an heteroatom (**1a** = **1b**).

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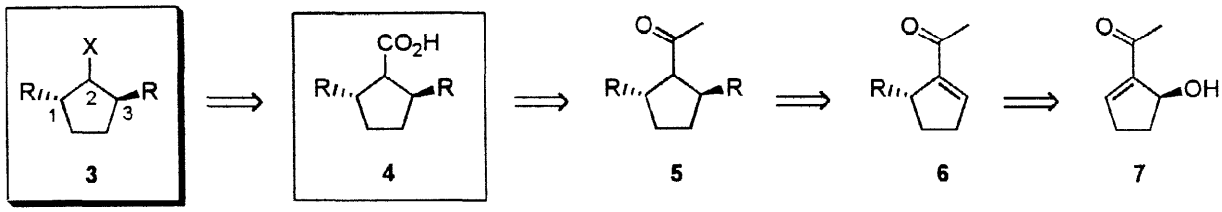
First applications of ligands of type **1** in asymmetric synthesis showed promising results [5]. For example, anions of urea **2** proved to be useful for enantioselective deprotonations of prochiral cycloalkanones (up to 88 % *ee*) as well as for enantioselective alkylations of ketones (up to 81 % *ee*). Herein, we wish to report the extension of this new concept to cyclic systems of type **3** with the emphasis on the preparation of the corresponding monoalkylboranes (**3**, X = BH_2) and their use in asymmetric hydroboration.

Results and Discussion

As key intermediates for the preparation of those compounds we chose carboxylic acids of type **4** (Scheme 1).

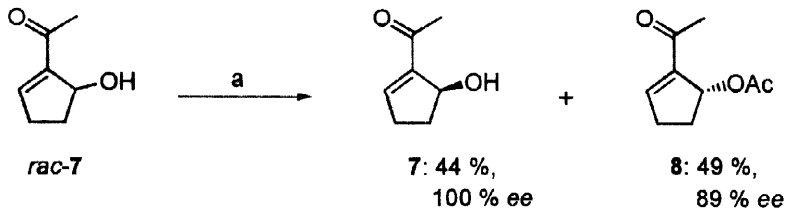


X = BH_2, NH_2, PR'_2
R = alkyl, aryl

Scheme 1

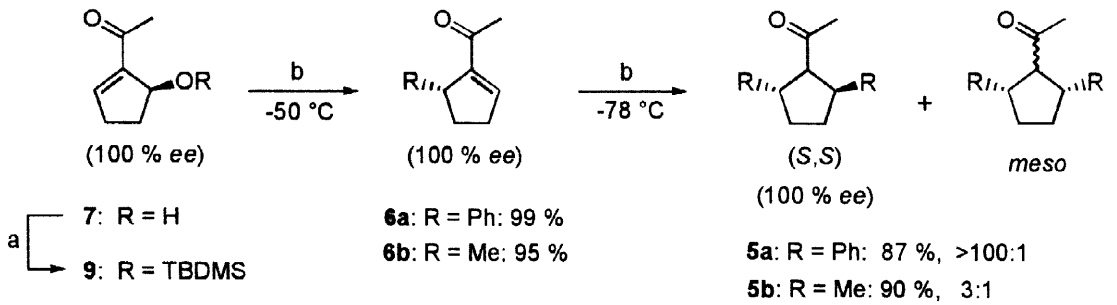
First, it was necessary to develop a flexible approach to enantiomerically pure carboxylic acids which allows a facile introduction of a wide variety of alkyl and aryl groups R in order to enable a fine-tuning of steric hindrance. As precursor of carboxylic acid **4**, we envisioned to use the ketone **5** which should be available via an *anti*-selective Michael addition of a cuprate [7] to the highly reactive enone **6** [8]. In turn, **6** should be produced stereoselectively via allylic substitution [9] of a suitable derivative of the enantiomerically pure allylic alcohol **7** with the same cuprate reagent. The alcohol **7** was already known as racemate [10].

In order to obtain the required optically pure starting material, racemic (±)-**7** was kinetically resolved via enzymatic transesterification [11] with a lipase (from *Pseudomonas* species) using vinyl acetate as acyl donor (Scheme 2). After chromatography, the allylic alcohol **7** was isolated in 44 % yield in enantiomerically pure form. The absolute configuration of **7** was predicted by the rule of Kazlauskas [12]. At a later stage of the synthesis, it was indirectly confirmed by an X-ray crystal structure analysis of a corresponding carboxylic amide (*vide infra*).



Scheme 2. a) PS-lipase "Amano", CH_2=CHOAc (2 equiv), *t*-BuOMe, 35 °C, 2.5 d.

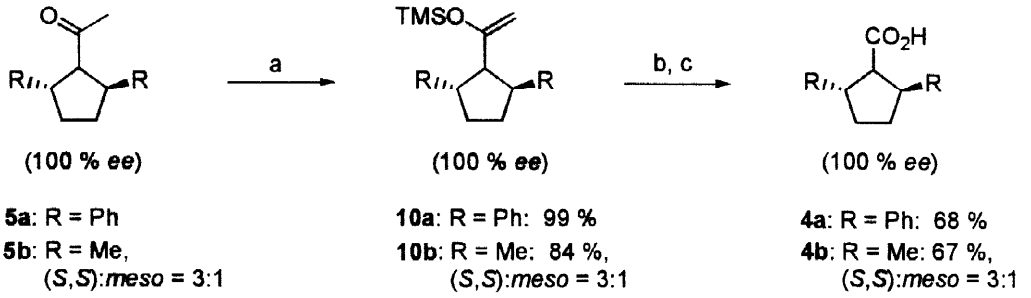
The enantiomerically pure silyl ether **9**, obtained in 80 % yield from 7 by a standard silylation procedure, was treated with an organomagnesium *bromide* (RMgBr; R = Ph, Me) in the presence of a catalytic amount of CuBr·SMe_2 and an excess of TMSCl (Scheme 3) [13]. After acidic aqueous work-up, the enantiomerically pure enones **6** (R = Ph, Me) were obtained in almost quantitative yields.



Scheme 3. a) TBDMSCl, imidazole, DMF, 80 %;
b) RMgBr (1.3 equiv), CuBr·SMe_2 (10 mol-%), TMSCl (2.5 equiv), THF/DMPU.

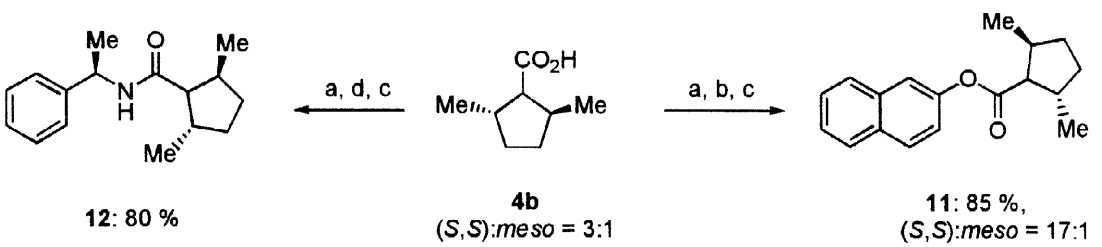
For the next step, the copper catalyzed 1,4-addition of a Grignard reagent to enones **6**, the same set of reagents as before was employed, but now at a lower reaction temperature [14] (Scheme 3). The desired saturated ketones **5** were isolated in enantiomerically pure form and in high yields. In the case of R = phenyl, the diastereoselectivity of this Michael addition was excellent (>100:1), thereby indicating that the attack of the incoming nucleophile took exclusively place from the top face of the enone **6a** as a result of the efficient shielding of the bottom face of the molecule by the bulky phenyl substituent of **6a**. In the case of R = Me, a dramatic decrease in selectivity (3:1) was observed which can be explained by the inefficient shielding of the bottom face of **6b** by the smaller methyl group. At this stage, it was not possible to separate the diastereomers of **5b**.

The conversion of the acetyl function of **5** to a carboxyl group [15] was accomplished in two steps (Scheme 4). First, the methyl ketones **5** were transformed into the corresponding silyl enol ethers **10** by deprotonation with LDA under kinetic control and quenching the in situ formed enolates with TMSCl. The resulting silyl enol ethers **10** were then subjected to ozonolysis leading to the desired carboxylic acids **4** in good yields and in enantiomerically pure form (>99.9 % *ee*).



Scheme 4. a) LDA, TMSCl, THF, -78 °C; b) O_3, CH_2Cl_2, -78 °C; c) Me_2S.

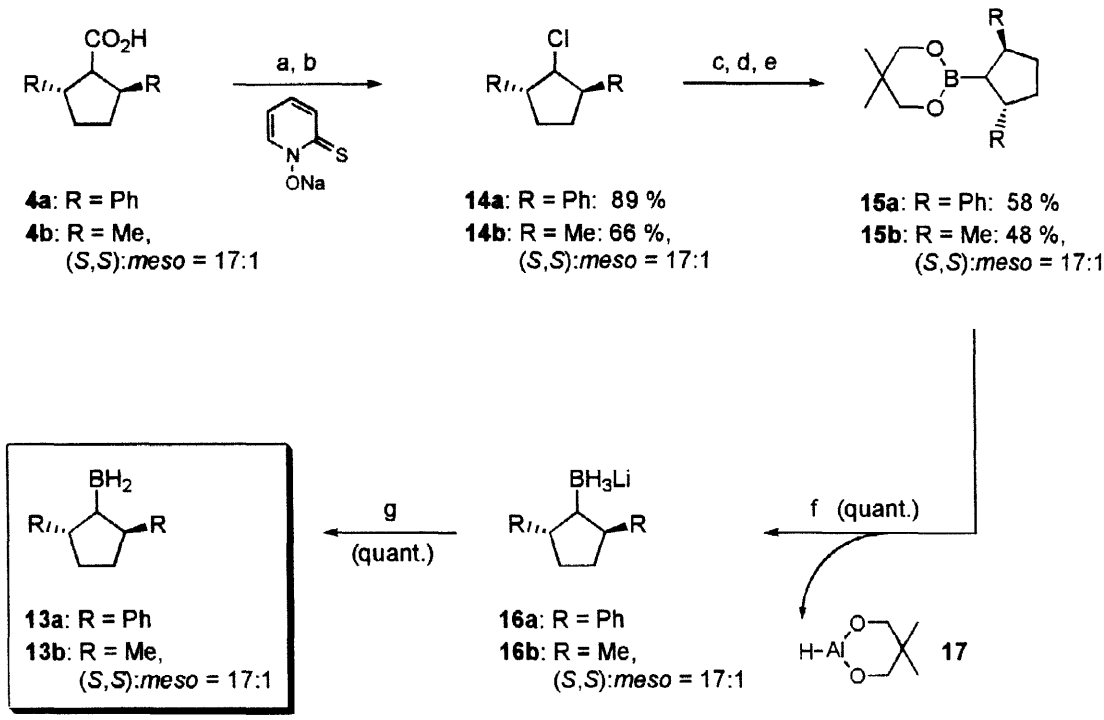
However, carboxylic acid **4b** was still contaminated with 25 % of the undesired *meso*-isomers which could not be separated chromatographically nor by fractional crystallization of the low melting acids (mp. 40 °C). After some experimentation it was found that fractional crystallization of the 2-naphthyl ester **11** improved the ratio (*S,S*) : *meso* to 17:1 (Scheme 5).



Scheme 5. a) $SOCl_2$; b) 2-naphthol, pyridine; c) recrystallization; d) (*R*)-phenylethylamine, pyridine.

In order to determine the absolute configuration of 2,5-dimethylcyclopentanecarboxylic acid **4b** the latter was converted into carboxylic amide **12** which was obtained in diastereomerically and enantiomerically pure form after simple recrystallization from toluene (Scheme 5). As expected, the absolute configuration of the cyclopentyl moiety of **12** turned out to be (2*S*,5*S*) [16].

Next, we turned our attention to the synthesis of the derived monoalkylboranes **13** with a non-stereogenic, chirotopic center (Scheme 6). The carboxylic acids **4** were readily converted into the corresponding alkyl chlorides **14** via a radical decarboxylation [17]. Thus, treatment of **4** with thionyl chloride followed by reaction with the sodium salt of 2-mercaptopyridine-*N*-oxide with simultaneous photolysis in the presence of CCl_4 or CF_3CCl_3 [18] as chlorine donor furnished the alkyl chlorides **14** in good to excellent yields. They were reductively lithiated using excess lithium powder in the presence of catalytic amounts of 4,4'-di-*t*-butylbiphenyl [19]. The in situ generated alkyllithium reagents were allowed to react with triethylborate followed by the addition of 2,2-dimethyl-1,3-propanediol providing the boronates **15** in moderate yields (48-58 %).

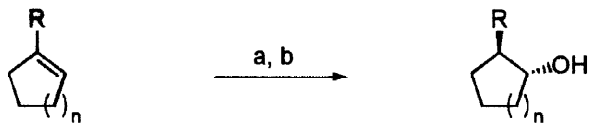


Scheme 6. a) $SOCl_2$; b) NaC_5H_4NOS, DMAP cat., CCl_4 or CF_3CCl_3, 80 °C, *hν* (300 W); c) lithium powder, 4,4'-di-*t*-butylbiphenyl (10 mol-%), THF, -78 °C; d) $B(OEt)_3$, -78 to 25 °C; e) $HOCH_2CMe_2CH_2OH$, THF, 25 °C; f) $LiAlH_4$ (1 equiv), Et_2O/pentane, 25 °C; g) HCl/Et_2O (1 equiv), 0 °C.

According to a protocol of H.C. Brown [20], the boronic esters **15** were cleanly reduced to the lithium borates **16** employing an ethereal solution of $LiAlH_4$ (1 equiv). The by-product **17** precipitated and was separated by centrifugation. The ethereal solution of borates **16** can be stored for months without decomposition. Their conversion to the monoalkylboranes **13** required for asymmetric hydroboration was accomplished by addition of ethereal HCl (1 equiv) [21,22]. The very clean reaction took instantaneously place and could be conveniently monitored by ^{11}B-NMR spectroscopy. The boranes **13** were prepared from **16** directly before use because of the known instability of monoalkylboranes. Monoalkylboranes show a high tendency for deboration and scrambling by redistribution processes [21,22].

In order to evaluate the potential of the new chiral boranes **13** in asymmetric hydroboration [23], we used cycloalkenes such as 1-phenylcyclopentene (**18**) and 1-methylcyclohexene (**19**). The hydroborations were performed in THF at -25 °C for 24 h followed by a standard oxidative work-up (Scheme 7 and Table 1). The alcohols **20** and **21** were isolated in 54-68 % yield and 29-64 % *ee* thereby indicating a moderate reactivity of the employed boranes **13**. Interestingly, higher enantioselectivities were generally observed in the hydroboration of 1-phenylcyclopentene (**18**) compared to 1-methylcyclohexene (**19**). This correlates well with the results obtained by H.C. Brown using isopinocampheylborane ($IpcBH_2$) as chiral hydroborating agent [24,25]. The

structure of the organoborane **13b** resembles the highly stereoselective 2,5-dimethylborolane [26] and led to the highest enantioselectivities despite its contamination with 6 % of the achiral *meso*-isomers.

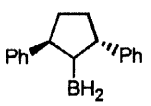
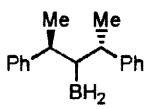
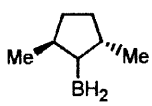


18: n = 1, R = Ph
19: n = 2, R = Me

20: n = 1, R = Ph
21: n = 2, R = Me

Scheme 7. a) R*-BH_2 (**13**), THF, -25 °C, 24 h; b) H_2O_2, NaOH.

Table 1. Asymmetric hydroboration of cycloalkenes with chiral boranes **13**.

product alcohol	 **13a**	 **13c**[a]	 **13b**[b]
20[c]	68 %; 38 % *ee*	66 %; 52 % *ee*	67 %; **64 % *ee***
21[d]	59 %; 38 % *ee*	57 %; 29 % *ee*	54 %; **55 % *ee***

[a] This borane was prepared in the same way as described for its cyclic analogues starting from the corresponding acid [5]. [b] (*S,S*) : *meso* = 17:1. [c] The enantiomeric excess was determined by HPLC. [d] The enantiomeric excess was determined by GC of the corresponding benzoate.

Conclusion

In summary, we have developed a flexible and general approach to enantiomerically pure 2,5-diorganocyclopentanecarboxylic acids **4** bearing a non-stereogenic, chirotopic center. They serve as key intermediates in the synthesis of new chiral ligands, for example, new pseudo-C_2-symmetrical monoalkylboranes **13**. These boranes could be employed successfully in the asymmetric hydroboration of cyclic olefins providing the corresponding alcohols in moderate to good enantiomeric excesses.

Experimental

General: Melting points are uncorrected. NMR spectra were recorded at rt on Bruker ARX 200 or AC 300 instruments. Signals of the *meso*-diastereomers that appear separated from the (*S,S*)-isomer are given for sake of comparison. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. IR spectra were recorded on a Nicolet 510 FT-IR spectrometer. Mass spectra were recorded on Varian CH7A. Elemental analyses were performed by the Microanalytical Service Laboratory of the Fachbereich Chemie (Marburg). Enantiomeric

excesses were determined by HPLC. Chiralcel columns OD, OB and OJ (Daicel Chemical Industries) were used at rt with *n*-heptane/2-propanol as mobile phase and detection by a diode array UV/VIS detector. Alternatively, determination of optical purity was carried out by GC on a Chirasil-DEX CB column (Chrompak) with hydrogen as carrier gas. Racemic compounds were used to choose the operating conditions for the resolution of the enantiomer and diastereomer peaks. Column chromatography was carried out on silica gel 60 (70-230 mesh ASTM). All reactions with air sensitive compounds were carried out under argon.

Materials: THF was distilled from potassium, Et_2O was distilled from sodium/benzophenone. CH_2Cl_2, DMF, DMPU and TMSCl were distilled from CaH_2. Pyridine was dried over KOH. Triethylborate was distilled from sodium and CCl_4 from P_4O_{10}. Commercial reagents were used without further purification. The following starting materials were prepared according to literature procedures: (±)-2-acetyl-2-cyclopenten-1-ol (*rac*-**7**) [10], (*S*)-3-phenyl-2-[(*S*)-phenylethyl]butanoic acid [5] and 1-phenylcyclopentene (**18**) [27].

Resolution of (±)-2-acetyl-2-cyclopenten-1-ol (*rac*-**7**): To a solution of alcohol *rac*-**7** (11.0 g, 87.2 mmol) in *t*-BuOMe (410 mL) was added vinyl acetate (15.0 g, 174 mmol) and PS-lipase ("Amano"; 870 mg). The suspension was stirred at 35 °C for 2.5 d. After filtration through a pad of Celite, the filtrate was concentrated under reduced pressure and chromatographed (pentane/acetone 8:1 to 2:1) to give the allylic acetate **8** as a colourless oil (7.20 g, 49 %; 89 % *ee*) and the allylic alcohol **7** as a colourless oil (4.80 g, 44 %; 100 % *ee*). The latter can be stored at -30 °C for months without racemization.

(*S*)-2-Acetyl-2-cyclopenten-1-ol (**7**): HPLC (OB, 10 % *i*-PrOH, 0.6 mL/min, 244 nm): t_R/min = 14.6 (*R*), 16.5 (*S*); $[\alpha]_D^{25}$ = +35.7 (c = 2.4, $CHCl_3$); IR (neat): 3433 (br), 3056 (w), 2941 (s), 2842 (m), 1667 (s), 1617 (s), 1427 (s), 1373 (s), 1290 (s), 1050 (s), 984 (m), ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 6.80 (t, *J* = 2.6 Hz, 1 H), 5.05 (m, 1 H), 3.16 (bs, 1 H), 2.70-2.56 (m, 1 H), 2.45-2.38 (m, 1 H), 2.36-2.20 (m, 1 H), 2.28 (s, 3 H), 1.84-1.70 (m, 1 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 197.8, 146.7, 146.2, 75.1, 31.5, 30.9, 26.6; MS (EI): m/z 126 (M^+, 5), 125 (70), 109 (15), 83 (18), 55 (14), 43 (100), 28 (51); HRMS calcd for $C_7H_{10}O_2$ (126.15): 126.0681; found: 126.0674.

(*R*)-5-Acetoxy-1-acetyl-1-cyclopentene (**8**): GC (CB, 100 kPa, 80 °C (1 min) to 120 °C; 4 °C/min): t_R/min = 13.5 (*S*), 13.9 (*R*); $[\alpha]_D^{25}$ = -17.4 (c = 2.0, $CHCl_3$); IR (neat): 3063 (w), 2980 (s), 2943 (s), 1732 (s), 1670 (s), 1620 (s), 1429 (s), 1371 (s), 1251 (s), 1157 (m), 1035 (s), 977 (s), 841 (s), 735 (s); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 6.98 (t, *J* = 2.6 Hz, 1 H), 5.92 (dt, *J* = 2.3 and 7.4 Hz, 1 H), 2.75-2.61 (m, 1 H), 2.53-2.40 (m, 1 H), 2.35-2.23 (m, 1 H), 2.27 (s, 3 H), 1.94 (s, 3 H), 1.88-1.77 (m, 1 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 194.5, 170.3, 149.1, 143.2, 76.7, 31.5, 30.9, 27.0, 21.0; MS (EI): m/z 125 (42), 93 (13), 83 (11), 65 (8), 43 (100); the compound could not be obtained in analytically pure form.

(*S*)-1-Acetyl-5-*tert*-butyldimethylsiloxy-1-cyclopentene (**9**): Alcohol **7** (12.6 g, 99.9 mmol; 100 % *ee*) was added at 0 °C to a solution of TBDMSCl (16.8 g, 112 mmol) in DMF (50 mL). After stirring for 5 min, imidazole (15.0 g, 220 mmol) was added in one portion. The cooling bath was removed and the reaction mixture was stirred at rt for 45 min. The yellow solution was poured into water (600 mL) and extracted with pentane (5 x 150 mL). After washing with water (2 x 100 mL) and brine (150 mL), the organic layer was dried ($MgSO_4$) and concentrated to an oil which was distilled (0.01 torr). Silyl ether **9** (19.3 g, 80 %) was obtained as a colourless oil: bp 76 °C (0.01 torr); $[\alpha]_D^{25}$ = +18.1 (c = 1.3, $CHCl_3$); IR (neat): 3055 (w), 2955 (s), 2930 (s), 2856 (s), 1676 (s), 1620 (s), 1471 (m), 1373 (s), 1253 (s), 1080 (s), 1064 (s), 869 (s), 837 (s), 777 (s); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 6.73 (t, *J* = 2.6 Hz, 1 H), 5.01 (dt, *J* = 2.3 and 7.0 Hz, 1 H), 2.70-2.56 (m, 1 H), 2.37-2.23 (m, 1 H), 2.22 (s, 3 H), 2.15-2.00 (m, 1 H), 1.80-1.65 (m, 1 H), 0.79 (s, 9 H), 0.04 (s, 3 H), 0.00 (s, 3 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 195.6, 147.4, 145.7, 75.0, 34.0, 31.1, 27.3, 25.8, 18.1, -4.9, -5.0; MS (EI): m/z 225 (M^+-CH_3, 5), 184 (13), 183 (100), 75 (71), 73 (11), 43 (11); $C_{13}H_{24}O_2Si$ (240.42): calcd C 64.94, H 10.06; found C 64.83, H 10.31.

(*R*)-1-Acetyl-5-phenyl-1-cyclopentene (**6a**): To a solution of silyl ether **9** (15.0 g, 62.3 mmol; 100 % *ee*) in THF (250 mL) and DMPU (17.0 g, 133 mmol) was added CuBr·SMe_2 (1.10 g, 5.35 mmol). The suspension

was cooled to -50 °C and TMSCl (16.0 g, 147 mmol) was added, followed by the slow addition of PhMgBr (27.0 mL, 81.0 mmol, 3 M in Et_2O) with vigorous stirring. The heterogeneous reaction mixture was stirred further 30 min at -50 °C before aqueous HCl (15 %, 100 mL) was added. After warming to rt, the mixture was poured into water (600 mL) and extracted with pentane (5 x 100 mL). After washing with water (100 mL) and brine (100 mL), the organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. The crude product was purified by chromatography (pentane/Et_2O 2:1) yielding enone **6a** (11.5 g, 99 %; 100 % *ee*) as a viscous oil. HPLC (OJ, 30 % *i*-PrOH, 0.6 mL/min, 244 nm): t_R/min = 26.6 (*S*), 30.9 (*R*); $[\alpha]_D^{25}$ = -151.9 (c = 3.0, $CHCl_3$); IR (neat): 3021 (w), 2998 (m), 2836 (m), 1658 (s), 1616 (s), 1490 (s), 1454 (s), 1372 (s), 1285 (s), 765 (s), 705 (s); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.30-7.08 (m, 5 H), 6.90 (m, 1 H), 4.17 (m, 1 H), 2.78-2.64 (m, 1 H), 2.62-2.54 (m, 1 H), 2.52-2.40 (m, 1 H), 2.22 (s, 3 H), 1.94-1.84 (m, 1 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 195.7, 148.2, 145.0, 144.6, 128.3, 126.8, 126.0, 49.4, 33.9, 32.5, 27.2; MS (EI): m/z 186 (M^+, 82), 171 (52), 143 (78), 128 (70), 115 (44), 105 (27), 91 (22), 43 (100), 28 (36); $C_{13}H_{14}O$ (186.25): calcd C 83.83, H 7.58; found C 83.60, H 7.37.

(*S*)-1-Acetyl-5-methyl-1-cyclopentene (6b): Silyl ether **9** (34.5 g, 144 mmol; 100 % *ee*) in THF (350 mL) and DMPU (36.0 g, 281 mmol) was treated with TMSCl (39.0 g, 359 mmol) and MeMgBr (63.0 mL, 189 mmol, 3 M in Et_2O) in the presence of CuBr·SMe_2 (2.80 g, 13.6 mmol) as described for **6a**. After aqueous work-up the solvent was distilled off through a Vigreux column at atmospheric pressure. The crude product was distilled at 40 mbar yielding enone **6b** (16.9 g, 95 %; 100 % *ee*) as a volatile liquid: bp 70 °C (40 mbar); GC (CB, 100 kPa, 60 °C (1 min) to 90 °C, 4 °C/min): t_R/min = 9.3 (*S*), 9.7 (*R*); $[\alpha]_D^{25}$ = +23.5 (c = 1.7, $CHCl_3$); IR (neat): 3056 (w), 2954 (s), 2867 (s), 1668 (s), 1612 (s), 1449 (m), 1375 (s), 1364 (s), 1295 (s), 1252 (s), 918 (m), 908 (m), 733 (s); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 6.62 (m, 1 H), 2.95 (m, 1 H), 2.59-2.44 (m, 1 H), 2.42-2.27 (m, 1 H), 2.23 (s, 3 H), 2.12-1.98 (m, 1 H), 1.52-1.40 (m, 1 H), 1.01 (d, *J* = 6.9 Hz, 3 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 196.6, 150.3, 143.8, 38.1, 32.0, 31.7, 27.0, 19.6; MS (EI): m/z 124 (M^+, 33), 109 (100), 81 (94), 79 (17), 53 (31), 43 (88), 41 (31), 39 (14); $C_8H_{12}O$ (124.18): calcd C 77.38, H 9.74; found C 77.12, H 9.96.

(2*S*,5*S*)-1-Acetyl-2,5-diphenylcyclopentane (5a): To a solution of enone **6a** (11.4 g, 61.2 mmol; 100 % *ee*) in THF (250 mL) and DMPU (19.0 g, 148 mmol) was added CuBr·SMe_2 (1.20 g, 5.84 mmol). The suspension was cooled to -78 °C and TMSCl (16.0 g, 147 mmol) was added, followed by the slow addition of PhMgBr (32.0 mL, 96.0 mmol, 3 M in Et_2O) with vigorous stirring. The heterogeneous reaction mixture was stirred further 45 min at -78 °C before aqueous HCl (15 %, 100 mL) was added. After warming to rt, the mixture was poured into water (600 mL) and extracted with pentane (5 x 100 mL). Trifluoroacetic acid (80 mL) was added to the combined organic phases and the solution was stirred for 1 h at rt. After washing with sat. aq. K_2CO_3 (3 x 100 mL) and brine (100 mL), the organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. The crude product was purified by chromatography (pentane/Et_2O 10:1, then pentane/Et_2O/CH_2Cl_2 5:1:1) yielding diastereomerically pure ketone **5a** (14.1 g, 87 %; 100 % *ee*) as a colourless solid: mp 78 °C; $[\alpha]_D^{25}$ = +42.7 (c = 1.2, $CHCl_3$); IR (KBr): 3027 (m), 2958 (s), 2869 (m), 1700 (s), 1601 (m), 1493 (s), 1453 (s), 1348 (m), 760 (s), 698 (s); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.25-7.04 (m, 10 H), 3.80-3.58 (m, 2 H), 3.31 (dd, *J* = 8.2 and 10.2 Hz, 1 H), 2.32-2.21 (m, 1 H), 2.20-2.07 (m, 1 H), 2.06-1.95 (m, 1 H), 1.86-1.72 (m, 1 H), 1.42 (s, 3 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 209.5, 144.9, 141.5, 128.4, 128.3, 128.2, 127.2, 126.7, 126.1, 65.0, 49.6, 46.9, 34.3, 33.5, 31.5; MS (EI): m/z 264 (M^+, 11), 160 (100), 145 (49), 117 (40), 103 (15), 91 (52), 43 (62), 28 (15); $C_{19}H_{20}O$ (264.37): calcd C 86.32, H 7.63; found C 85.92, H 7.48.

(2*S*,5*S*)-1-Acetyl-2,5-dimethylcyclopentane (5b): Enone **6b** (16.9 g, 136 mmol; 100 % *ee*) in THF (300 mL) and DMPU (36.0 g, 281 mmol) was treated with TMSCl (30.0 g, 276 mmol) and MeMgBr (59.0 mL, 177 mmol, 3 M in Et_2O) in the presence of CuBr·SMe_2 (2.80 g, 13.6 mmol) as described for **5a**. After aqueous work-up the solvent was distilled off through a Vigreux column at atmospheric pressure. The crude product was distilled at 38 mbar yielding ketone **5b** (17.1 g, 90 %; 100 % *ee*) as an inseparable diastereomeric mixture (*S*,*S*) : *meso* = 3:1: bp 78 °C (38 mbar); GC (CB, 100 kPa, 70 °C (1 min) to 100 °C, 2 °C/min): t_R/min = 8.1 (1*r*,2*R*,5*S*), 8.2 (1*s*,2*R*,5*S*), 8.4 (2*R*,5*R*), 9.6 (2*S*,5*S*); IR (neat): 2955 (s), 2869 (s), 1707 (s), 1460 (m), 1377 (m), 1352 (m), 1167 (w); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 2.49-2.39 (m, 1 H), 2.06 (s, 3 H), 1.96-1.74 (m,

2 H), 1.34-1.16 (m, 4 H), 0.87 (d, J = 6.5 Hz, 3 H), 0.74 (d, J = 6.9 Hz, 3 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 210.2, 64.4, 39.0, 33.6, 33.5, 33.3, 31.1, 20.2, 17.0; MS (EI): m/z 140 (M^+, 8), 125 (17), 97 (41), 85 (95), 55 (100), 43 (68), 41 (22); $C_9H_{16}O$ (140.22): calcd C 77.09, H 11.50; found C 77.02, H 11.40. **(1*r*,2*R*,5*S*)-1-Acetyl-2,5-dimethylcyclopentane**: ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 2.89 (m, 1 H), 2.19-2.00 (m, 2 H), 2.03 (s, 3 H), 1.58-1.42 (m, 4 H), 0.90 (d, J = 7.0 Hz, 6 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 212.2, 60.1, 39.1, 34.6, 31.9, 16.1. **(1*s*,2*R*,5*S*)-1-Acetyl-2,5-dimethylcyclopentane**: ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 2.38-2.30 (m, 1 H), 2.08 (s, 3 H), 1.96-1.74 (m, 2 H), 1.15-1.01 (m, 4 H), 0.95 (d, J = 6.7 Hz, 6 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 211.7, 69.1, 36.7, 32.6, 29.5, 20.0.

(2*S*,5*S*)-2,5-Diphenyl-1-(1'-trimethylsiloxy-1'-ethenyl)cyclopentane (10a): At -78 °C, n-BuLi (45.0 mL, 65.3 mmol, 1.4 M in n-hexane) was added to a solution of i-Pr_2NH (8.00 g, 79.1 mmol) in THF (100 mL). The cooling bath was removed and the solution was stirred for 20 min at 0 °C. After cooling back to -78 °C, TMSCl (29.0 g, 267 mmol) was added, followed by a solution of ketone **5a** (14.0 g, 53.0 mmol; 100 % *ee*) in THF (20 mL). The reaction mixture was stirred for 1 h at -60 °C. It was cooled back to -78 °C before the reaction was quenched by addition of Et_3N (80 mL), followed by sat. aq. $NaHCO_3$ (80 mL). After warming to rt, the mixture was poured into water (500 mL) and extracted with pentane (5 x 100 mL). After washing with water (100 mL) and brine (100 mL), the organic layer was dried (Na_2SO_4) and concentrated under reduced pressure. The crude product was purified by bulb-to-bulb distillation yielding the silyl enol ether **10a** (17.8 g, 99 %; 100 % *ee*) as a yellowish viscous oil: bp 220 °C (0.7 torr); $[\alpha]_D^{25}$ = +56.5 (c = 2.3, $CHCl_3$); IR (neat): 3061 (m), 3028 (s), 2955 (s), 2870 (m), 1651 (m), 1602 (s), 1496 (m), 1452 (m), 1327 (s), 1251 (s), 1022 (s), 846 (s), 754 (s), 698 (s); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.38-7.18 (m, 10 H), 3.83 (d, J = 1.2 Hz, 1 H), 3.72 (d, J = 1.1 Hz, 1 H), 3.62-3.52 (m, 1 H), 3.51-3.41 (m, 1 H), 3.00 (dd, J = 8.6 and 9.5 Hz, 1 H), 2.44-2.33 (m, 1 H), 2.30-2.20 (m, 2 H), 2.02-1.86 (m, 1 H), 0.00 (s, 9 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 158.3, 145.7, 143.0, 128.6, 128.3, 127.5, 127.3, 125.9, 125.6, 90.1, 58.2, 48.9, 48.3, 34.4, 31.6, -0.4; MS (EI): m/z 336 (M^+, 29), 245 (33), 232 (61), 219 (44), 91 (34), 75 (50), 73 (100), 45 (22), 28 (64); HRMS calcd for $C_{22}H_{28}OSi$ (336.55): 336.1909; found: 336.1908.

(2*S*,5*S*)-2,5-Dimethyl-1-(1'-trimethylsiloxy-1'-ethenyl)cyclopentane (10b): Ketone **5b** (17.0 g, 121 mmol; (*S*,*S*) : *meso* = 3:1; 100 % *ee*) was treated with LDA, prepared from n-BuLi (103 mL, 144 mmol, 1.4 M in n-hexane) and i-Pr_2NH (18.3 g, 181 mmol) in THF (220 mL), and TMSCl (66.2 g, 610 mmol) as described for **10a**. After aqueous work-up, the solution was concentrated under reduced pressure. The crude product was distilled yielding the silyl enol ether **10b** (21.6 g, 84 %; 100 % *ee*) as an inseparable diastereomeric mixture (*S*,*S*) : *meso* = 3:1: bp 55 °C (0.7 torr); IR (neat): 3111 (w), 2955 (s), 2870 (s), 1651 (m), 1458 (w), 1375 (w), 1253 (s), 1020 (s), 844 (s), 756 (m); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 4.00 (bs, 1 H), 3.91 (bs, 1 H), 2.18-2.06 (m, 1 H), 1.96-1.66 (m, 2 H), 1.32-1.01 (m, 4 H), 0.92 (d, J = 6.1 Hz, 3 H), 0.87 (d, J = 6.5 Hz, 3 H), 0.14 (s, 9 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 159.9, 89.6, 57.7, 36.6, 35.3, 33.6, 33.5, 20.0, 16.9, 0.2; MS (EI): m/z 212 (M^+, 3), 197 (22), 157 (100), 75 (29), 73 (87); HRMS calcd for $C_{12}H_{24}OSi$ (212.41): 212.1596; found: 212.1578. **(1*r*,2*R*,5*S*)-2,5-Dimethyl-1-(1'-trimethylsiloxy-1'-ethenyl)cyclopentane**: ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 159.6, 90.0, 63.3, 37.7, 32.8, 19.4, 0.2. **(1*s*,2*R*,5*S*)-2,5-Dimethyl-1-(1'-trimethylsiloxy-1'-ethenyl)cyclopentane**: ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 159.7, 90.2, 55.7, 38.4, 32.9, 16.4, 0.1.

(2*S*,5*S*)-2,5-Diphenylcyclopentanecarboxylic acid (4a): Ozone was passed into a well stirred solution of silyl enol ether **10a** (17.8 g, 52.9 mmol; 100 % *ee*) in CH_2Cl_2 (60 mL) at -78 °C until a blue colour persisted. After purging with argon, Me_2S (16.0 g, 258 mmol) was added at -78 °C and the solution stirred for further 45 min at this temperature. After stirring for 2 h at 40 °C, the solution was diluted with $CHCl_3$ (300 mL), washed successively with aqueous HCl (10 %, 100 mL) and brine (80 mL) and dried ($MgSO_4$). The solvent was evaporated under reduced pressure and the product purified by chromatography (pentane/EtOAc 4:1, 0.5 % AcOH added). Recrystallization from pentane/Et_2O (4 °C) gave the acid **4a** (9.60 g, 68 %; 100 % *ee*) as colourless needles: mp 84-86 °C; $[\alpha]_D^{25}$ = +72.0 (c = 1.1, $CHCl_3$); IR (KBr): 3028 (m), 2945 (m), 2859 (m), 2600 (br), 1692 (s), 1601 (m), 1493 (s), 1434 (s), 1265 (s), 1218 (m), 946 (m), 751 (s), 699 (s); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 10.19 (br, 1 H), 7.34-7.08 (m, 10 H), 3.72-3.54 (m, 2 H), 3.18 (dd, J = 8.8 and 9.8 Hz, 1 H), 2.43-2.09 (m, 3 H), 1.95-1.79 (m, 1 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 179.3, 144.0, 141.0, 128.5,

128.1, 128.0, 127.2, 126.6, 126.4, 57.4, 49.1, 47.8, 34.4, 32.4; MS (EI): m/z 266 (M^+, 28), 162 (100), 144 (33), 131 (27), 117 (43), 104 (56), 91 (43), 77 (14), 28 (49); $C_{18}H_{18}O_2$ (266.34): calcd C 81.17, H 6.81; found C 81.25, H 6.94.

(2*S*,5*S*)-2,5-Dimethylcyclopentanecarboxylic acid (4b) [28]: a) Silyl enol ether **10b** (29.3 g, 138 mmol; (*S*,*S*) : *meso* = 3:1; 100 % *ee*) was ozonized as described for **10a**. The crude product obtained after work-up was dissolved in Et_2O (100 mL), cooled in an ice bath and mixed carefully with aqueous NaOH (40 %, 100 mL). The aqueous phase was extracted with Et_2O (3 x 30 mL), separated and cooled back to 0 °C. After acidifying with conc. HCl, the resulting emulsion was extracted with $CHCl_3$ (6 x 80 mL), the combined organic phases were washed with brine (80 mL) and dried ($MgSO_4$). After evaporation of the solvent under reduced pressure, the carboxylic acid **4b** (13.1 g, 67 %; (*S*,*S*) : *meso* = 3:1; 100 % *ee*) was obtained as a yellowish oil which solidified slowly upon standing. The diastereomeric mixture could only be separated via fractional crystallization of the ester **11** (*vide infra*).
b) The ester **11** (10.1 g, 37.6 mmol; (*S*,*S*) : *meso* = 17:1; 100 % *ee*) was dissolved in a saturated solution of KOH in methanol (35 mL) and refluxed for 1 h. After cooling to rt, the viscous solution was poured into water (100 mL). The aqueous phase was extracted with Et_2O (3 x 40 mL), separated and cooled back to 0 °C. After acidifying with conc. HCl, the resulting emulsion was extracted with $CHCl_3$ (5 x 80 mL), the combined organic phases were washed with brine (80 mL) and dried ($MgSO_4$). After evaporation of the solvent under reduced pressure, the solid residue was redissolved in Et_2O (30 mL). It was cooled to 0 °C before *i*-Pr_2NH (3.80 g, 37.6 mmol) was carefully added in portions. After stirring for 1 h at rt, the heterogeneous reaction mixture was diluted with water (100 mL) and Et_2O (30 mL) and extracted with Et_2O (3 x 20 mL). The aqueous phase was separated and cooled back to 0 °C. After acidifying with conc. HCl, the resulting emulsion was extracted with $CHCl_3$ (6 x 60 mL), the combined organic phases were washed with brine (60 mL) and dried ($MgSO_4$). After evaporation of the solvent under reduced pressure, the carboxylic acid **4b** (5.1 g, 95 %; (*S*,*S*) : *meso* = 17:1; 100 % *ee*) was obtained as a colourless oil which solidified slowly upon standing: mp 40 °C; $[\alpha]_D^{25}$ = +59.0 (c = 1.2, acetone); IR (KBr): 3100 (br), 2961 (s), 2871 (s), 1705 (s), 1460 (m), 1380 (m), 1261 (m); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 11.53 (bs, 1 H), 2.46-2.17 (m, 3 H), 1.96-1.72 (m, 2 H), 1.37-1.20 (m, 1 H), 1.18-1.02 (m, 1 H), 0.97 (d, *J* = 6.3 Hz, 3 H), 0.90 (d, *J* = 6.8 Hz, 3 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 181.4, 56.3, 36.8, 35.9, 33.8, 33.4, 20.1, 17.0; MS (EI): m/z 142 (M^+, 1), 127 (26), 100 (29), 87 (100), 82 (25), 55 (27), 41 (45); $C_8H_{14}O_2$ (142.20): calcd C 67.57, H 9.92; found C 67.65, H 10.14. **(1*r*,2*R*,5*S*)-2,5-Dimethylcyclopentanecarboxylic acid**: ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 182.7, 60.5, 39.7, 33.2, 19.9. **(1*s*,2*R*,5*S*)-2,5-Dimethylcyclopentanecarboxylic acid**: ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 180.7, 55.1, 38.6, 31.8, 16.2.

2-Naphthyl-(2*S*,5*S*)-2,5-dimethylcyclopentanoate (11): Carboxylic acid **4b** (11.4 g, 80.1 mmol; (*S*,*S*) : *meso* = 3:1; 100 % *ee*) was converted into the corresponding acid chloride by refluxing with thionyl chloride (40.0 g, 336 mmol) for 3 h. Excess reagent was evaporated in vacuo and the oily residue dissolved in CH_2Cl_2 (8 mL). At 0 °C, this solution was slowly added to a mixture of 2-naphthol (12.5 g, 86.7 mmol), DMAP (900 mg, 7.37 mmol) and pyridine (20.0 g, 253 mmol) in CH_2Cl_2 (20 mL). After stirring for 3 h at rt, the reaction mixture was diluted with Et_2O (200 mL) and washed successively with aqueous HCl (10 %, 4 x 70 mL), aqueous NaOH (10 %, 100 mL) and brine (80 mL). The organic phase was dried ($MgSO_4$) and the solution concentrated under reduced pressure. The crude product was purified by chromatography (pentane/Et_2O 15:1 to 10:1) yielding the ester **11** (18.3 g, 85 %; (*S*,*S*) : *meso* = 3:1; 100 % *ee*) as a viscous oil. This diastereomeric mixture was recrystallized four times from ethanol/water (3:1) at rt yielding ester **11** (10.3 g; (*S*,*S*) : *meso* = 17:1; 100 % *ee*) as fine needles. From the mother liquors ester **11** (7.10 g; (*S*,*S*) : *meso* = 1:1; 100 % *ee*) could be recovered as an equimolar mixture of (*S*,*S*)- and *meso*-forms.
Mp 58 °C; IR (KBr): 3060 (w), 2954 (s), 2869 (m), 1744 (s), 1599 (m), 1465 (m), 1376 (s), 1244 (m), 1160 (s), 1132 (s), 901 (s), 744 (s); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.88-7.70 (m, 3 H), 7.54 (m, 1 H), 7.51-7.37 (m, 2 H), 7.26-7.18 (m, 1 H), 2.72-2.44 (m, 3 H), 2.09-1.90 (m, 2 H), 1.50-1.36 (m, 1 H), 1.29-1.15 (m, 1 H), 1.14 (d, *J* = 1.7 Hz, 3 H), 1.11 (d, *J* = 1.4 Hz, 3 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 174.5 (*meso*), 173.3, 148.5, 133.8, 131.4, 129.2, 127.7, 127.5, 126.4, 125.5, 121.3, 118.5, 60.6 (*meso*), 56.3, 39.9 (*meso*), 37.1, 36.2, 33.9, 33.4, 33.2 (*meso*), 20.1, 20.0 (*meso*), 17.4; MS (EI): m/z 268 (M^+, 7), 144 (100), 125 (11), 97 (60), 55 (45); HRMS calcd for $C_{18}H_{20}O_2$ (268.35): 268.1463; found: 268.1463.

***N*-[(*R*)-Phenylethyl]-(2*S*,5*S*)-2,5-dimethylcyclopentanecarboxylic amide (12)**: Carboxylic acid **4b** (350 mg, 2.46 mmol; (*S*,*S*) : *meso* = 17:1; 100 % *ee*) was converted into the corresponding acid chloride by refluxing with thionyl chloride (2.00 g, 16.8 mmol) for 3 h. Excess reagent was evaporated in vacuo and the oily residue dissolved in CH_2Cl_2 (1 mL). At 0 °C, this solution was slowly added to a solution of (*R*)-phenylethylamine (390 mg, 3.22 mmol) in pyridine (2 mL). After stirring for 3 h at rt, the reaction mixture was diluted with Et_2O (80 mL) and washed successively with aqueous HCl (10 %, 2 x 30 mL) and brine (40 mL). The organic phase was dried ($MgSO_4$) and the solution concentrated under reduced pressure. The crude product was purified by chromatography (pentane/EtOAc/CH_2Cl_2 8:2:1) affording the desired product as a diastereomeric mixture. Recrystallization from pentane/Et_2O gave diastereomerically pure carboxylic amide **12** (485 mg, 80 %; 100 % *ee*) as fine needles. In order to obtain crystals suitable for X-ray crystal structure analysis, a part of the material was recrystallized from toluene at rt: mp 112 °C; $[\alpha]_D^{25}$ = +125.6 (c = 1.2, $CHCl_3$); IR (KBr): 3309 (s), 3029 (w), 2959 (s), 2869 (m), 1644 (s), 1539 (s), 1451 (m), 1373 (m), 1231 (m), 1135 (m), 762 (s), 702 (s); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.27-7.12 (m, 5 H), 5.81 (m, 1 H), 5.08 (quint, *J* = 7.0 Hz, 1 H), 2.39-2.25 (m, 1 H), 2.22-2.12 (m, 1 H), 2.02 (t, *J* = 8.7 Hz, 1 H), 1.91-1.69 (m, 2 H), 1.41 (d, *J* = 6.9 Hz, 3 H), 1.32-1.20 (m, 1 H), 1.11-0.98 (m, 1 H), 0.93 (d, *J* = 6.7 Hz, 3 H), 0.72 (d, *J* = 7.0 Hz, 3 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 172.9, 143.6, 128.5, 127.1, 126.2, 58.0, 48.4, 37.1, 36.0, 34.0, 33.4, 21.8, 20.1, 16.9; MS (EI): m/z 245 (M^+, 52), 190 (46), 120 (22), 105 (100), 97 (40), 86 (29), 55 (93), 28 (19); HRMS calcd for $C_{16}H_{23}NO$ (245.37): 245.1780; found: 245.1774.

(2*R*,5*R*)-1-Chloro-2,5-diphenylcyclopentane (14a): Carboxylic acid **4a** (4.00 g, 15.0 mmol; 100 % *ee*) was converted into the corresponding acid chloride by refluxing with thionyl chloride (8.00 g, 67.2 mmol) for 3 h. Excess reagent was evaporated in vacuo and the solid residue dissolved in CCl_4 (20 mL). This solution was dropwise added (syringe pump) to a refluxing suspension of the sodium salt of 2-mercaptopyridine-*N*-oxide (2.80 g, 17.8 mmol) and DMAP (200 mg, 1.64 mmol) in CCl_4 (15 mL) *under argon* whilst being irradiated with a photo lamp (300 W). After the addition of the acid chloride the lamp was switched off. After further 45 min at reflux, the brown reaction mixture was cooled, diluted with pentane (250 mL) and poured into aqueous HCl (10 %, 100 mL). The aqueous phase was extracted with pentane (4 x 60 mL), the combined organic phases were washed with water (90 mL) and brine (90 mL) and dried ($MgSO_4$). After evaporation of the solvent under reduced pressure the crude product was purified by chromatography (pentane/Et_2O 40:1 to 10:1) yielding the alkyl chloride **14a** (3.45 g, 89 %; 100 % *ee*) as a viscous oil. $[\alpha]_D^{25}$ = +56.0 (c = 1.9, $CHCl_3$); IR (neat): 3028 (s), 2960 (s), 2874 (m), 1602 (m), 1494 (s), 1450 (s), 754 (s), 696 (s); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.40-7.18 (m, 10 H), 4.46 (m, 1 H), 3.71-3.53 (m, 2 H), 2.58-2.20 (m, 3 H), 2.07-1.91 (m, 1 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 143.2, 140.0, 128.6, 128.5, 127.9, 127.2, 126.7, 126.6, 71.4, 55.3, 49.7, 30.6, 28.3; MS (EI): m/z 256 (M^+, 8), 220 (100), 143 (60), 129 (23), 117 (86), 104 (95), 91 (65), 77 (31), 28 (25); $C_{17}H_{17}Cl$ (256.77): calcd C 79.52, H 6.67; found C 79.36, H 6.68.

(2*S*,5*S*)-1-Chloro-2,5-dimethylcyclopentane (14b): Carboxylic acid **4b** (2.60 g, 18.3 mmol; (*S*,*S*) : *meso* = 17:1; 100 % *ee*) was converted into the corresponding acid chloride with thionyl chloride (10.0 g, 84.1 mmol). The acid chloride was treated with the sodium salt of 2-mercaptopyridine-*N*-oxide (3.20 g, 21.5 mmol) and DMAP (200 mg, 1.64 mmol) in refluxing CF_3CCl_3 under irradiation as described for **14a** (CCl_4 was replaced by CF_3CCl_3). After aqueous work-up the solvent was distilled off through a Vigreux column at atmospheric pressure. The crude product was distilled at 34 mbar. The alkyl chloride **14b** (1.60 g, 66 %; (*S*,*S*) : *meso* = 17:1; 100 % *ee*) was obtained as a colourless, volatile liquid: bp 50 °C (34 mbar); $[\alpha]_D^{25}$ = +39.8 (c = 1.2, $CHCl_3$); IR (neat): 2960 (s), 2872 (s), 1457 (s), 1378 (s), 1246 (m), 721 (m); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 3.84 (d, *J* = 5.4 Hz, 1 H), 2.36-2.19 (m, 2 H), 2.12-1.97 (m, 1 H), 1.88-1.75 (m, 1 H), 1.52-1.40 (m, 1 H), 1.26-1.11 (m, 1 H), 1.07 (d, *J* = 4.3 Hz, 3 H), 1.04 (d, *J* = 4.4 Hz, 3 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 73.0, 43.0, 37.9, 30.6, 30.5, 19.9, 16.3; MS (EI): m/z 132 (M^+, 1), 96 (33), 81 (58), 76 (100), 56 (80), 41 (80); $C_7H_{13}Cl$ (132.63): calcd C 63.39, H 9.88; found C 63.50, H 10.02.

(2*R*,4*R*)-3-Chloro-2,4-diphenylpentane (14c): (*S*)-3-Phenyl-2-[(*S*)-phenylethyl]butanoic acid (8.10 g, 30.2 mmol; 100 % *ee*) [5] was converted into the corresponding acid chloride with thionyl chloride (18.0 g, 151 mmol). The acid chloride was treated with the sodium salt of 2-mercaptopyridine-*N*-oxide (5.70 g,

36.3 mmol) and DMAP (380 mg, 3.11 mmol) in refluxing CCl_4 under irradiation as described for **14a**. After aqueous work-up the solvent was evaporated under reduced pressure and the crude product purified by chromatography (pentane/Et_2O 40:1 to 10:1) yielding the alkyl chloride **14c** (6.60 g, 84 %; 100 % *ee*) as a colourless, waxy solid: mp 46-48 °C; $[\alpha]_D^{25}$ = +17.3 (c = 1.9, $CHCl_3$); IR (KBr): 2970 (m), 2880 (w), 1600 (w), 1450 (s), 1380 (m), 760 (m), 700 (s), 600 (m); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.28-7.04 (m, 10 H), 4.20 (dd, *J* = 5.7 and 7.5 Hz, 1 H), 2.99-2.85 (m, 2 H), 1.31 (d, *J* = 7.1 Hz, 3 H), 1.29 (d, *J* = 6.9 Hz, 3 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 144.4, 142.4, 128.7, 128.5, 127.9, 127.7, 126.7, 126.6, 74.2, 43.5, 43.4, 20.7, 18.5; MS (EI): m/z 258 (M^+, 7), 105 (100), 91 (6), 77 (7); $C_{17}H_{19}Cl$ (258.79): calcd C 78.90, H 7.40; found C 79.00, H 7.50.

2-[(2'*S*,5'*S*)-2',5'-Diphenylcyclopent-1'-yl]-5,5-dimethyl-1,3-dioxa-2-borinane (15a): Lithium powder (550 mg, 79.3 mmol) was added at rt to a solution of 4,4'-di-*t*-butylbiphenyl (210 mg, 0.79 mmol) in THF (15 mL). The mixture was stirred vigorously. After 1 min, a dark blue colour appeared, the suspension was cooled to -78 °C and a solution of alkyl chloride **14a** (2.00 g, 7.79 mmol; 100 % *ee*) in THF (4 mL) was dropwise added. The blue colour disappeared and the reaction mixture was stirred for further 50 min. The blue colour reappeared and this cold solution was added via cannula at -70 °C to a vigorously stirred solution of triethylborate (6.00 g, 41.1 mmol) in THF (8 mL). The reaction mixture was warmed to rt overnight, cooled to 0 °C and slightly acidified (pH 6) by carefully adding aqueous HCl (10 %). After dilution with water (50 mL) and Et_2O (50 mL), the aqueous phase was separated and extracted with Et_2O (4 x 30 mL). The combined organic phases were washed with brine (50 mL) and dried ($MgSO_4$). After evaporation of the solvent under reduced pressure, the residue was dissolved in THF (4 mL) under argon. Solid 2,2-dimethyl-1,3-propanediol (730 mg, 7.01 mmol) was added and the homogeneous solution was stirred for 12 h at rt. After evaporation of the solvent under reduced pressure, the residue was crystallized from pentane at -30 °C yielding the boronate **15a** (1.50 g, 58 %) as colourless crystals: mp 74-76 °C; $[\alpha]_D^{25}$ = +66.5 (c = 1.2, $CHCl_3$); IR (nujol): 3023 (w), 2923 (s), 2853 (s), 1600 (m), 1491 (m), 1462 (s), 1415 (s), 1376 (m), 1254 (m), 757 (s), 699 (s); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.36-7.10 (m, 10 H), 3.66-3.56 (m, 1 H), 3.50-3.38 (m, 1 H), 3.17 (s, 4 H), 2.38-2.20 (m, 2 H), 2.09-1.94 (m, 1 H), 1.90-1.74 (m, 2 H), 0.58 (s, 6 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 146.7, 146.6, 128.1, 127.9, 127.3, 125.6, 125.5, 71.6, 48.1, 47.4, 43.0 (br), 36.2, 34.6, 31.1, 21.6; ^{11}B-NMR ($CDCl_3$, 96 MHz): δ = 29.7 (s); MS (EI): m/z 334 (M^+, 37), 256 (47), 230 (100), 202 (47), 144 (39), 130 (44), 117 (59), 104 (44), 91 (95), 69 (43), 56 (30), 41 (57), 28 (24); $C_{22}H_{27}BO_2$ (334.26): calcd C 79.05, H 8.14; found C 78.90, H 8.38.

2-[(2'*S*,5'*S*)-2',5'-Dimethylcyclopent-1'-yl]-5,5-dimethyl-1,3-dioxa-2-borinane (15b): Alkyl chloride **14b** (600 mg, 4.52 mmol; (*S,S*) : *meso* = 17:1; 100 % *ee*) was treated with lithium powder (320 mg, 46.1 mmol), 4,4'-di-*t*-butylbiphenyl (120 mg, 0.45 mmol) and triethylborate (3.30 g, 22.6 mmol) as described for **15a**. After esterification with 2,2-dimethyl-1,3-propanediol (360 mg, 3.46 mmol), the resulting yellowish oil was purified by bulb-to-bulb distillation yielding the boronate **15b** (457 mg, 48 %; (*S,S*) : *meso* = 17:1) as a colourless liquid: bp 130 °C (0.7 torr); $[\alpha]_D^{25}$ = +57.1 (c = 1.6, $CHCl_3$); IR (neat): 2949 (s), 2868 (s), 1475 (s), 1411 (s), 1377 (m), 1352 (m), 1302 (m), 1251 (s); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 3.60 (s, 4 H), 2.36-2.24 (m, 1 H), 2.11-1.98 (m, 1 H), 1.90-1.77 (m, 2 H), 1.26-1.13 (m, 1 H), 1.09-1.00 (m, 1 H), 0.97 (d, *J* = 6.6 Hz, 3 H), 0.96 (s, 6 H), 0.91 (d, *J* = 7.1 Hz, 3 H), 0.84 (dd, *J* = 8.3 and 10.2 Hz, 1 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 71.8, 42.0 (br), 36.3, 35.4, 35.1, 31.5, 22.0, 21.3, 20.3; ^{11}B-NMR ($CDCl_3$, 96 MHz): δ = 31.4 (s); MS (EI): m/z 210 (M^+, 8), 195 (15), 182 (100), 168 (52), 125 (48), 109 (20), 96 (49), 81 (68), 69 (66), 56 (54), 41 (66), 29 (29); HRMS calcd for $C_{12}H_{23}BO_2$ (210.12): 210.1791; found: 210.1783.

2-{(2'*S*)-Phenyl-1'-[(*S*)-phenylethyl]propyl}-5,5-dimethyl-1,3-dioxa-2-borinane (15c): Alkyl chloride **14c** (3.00 g, 11.6 mmol; 100 % *ee*) was treated with lithium powder (840 mg, 121 mmol), 4,4'-di-*t*-butylbiphenyl (300 mg, 1.13 mmol) and triethylborate (10.0 g, 68.5 mmol) as described for **15a**. After esterification with 2,2-dimethyl-1,3-propanediol (1.80 g, 17.3 mmol), the product was purified by chromatography (pentane/Et_2O 40:1 to 10:1) yielding the boronate **15c** (2.55 g, 65 %) as colourless crystals: mp 82-84 °C; $[\alpha]_D^{25}$ = -6.9 (c = 1.9, $CHCl_3$); IR (nujol): 3025 (w), 2922 (s), 2854 (s), 1461 (s), 1377 (m), 1287 (w), 1078 (w), 753 (w), 699 (s); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.25-6.96 (m, 10 H), 3.22 (d, *J* = 11.0 Hz, 2 H), 3.15 (d, *J* = 11.0 Hz,

2 H), 2.88 (quint, J = 7.0 Hz, 1 H), 2.71 (quint, J = 7.1 Hz, 1 H), 1.42 (t, J = 8.3 Hz, 1 H), 1.21 (d, J = 7.0 Hz, 3 H), 1.14 (d, J = 7.0 Hz, 3 H), 0.56 (s, 6 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 148.4, 147.6, 128.2, 127.9, 127.7, 127.3, 125.6, 125.5, 71.5, 43.7 (br), 39.9, 39.4, 31.1, 21.9, 21.8, 19.9; ^{11}B-NMR ($CDCl_3$, 96 MHz): δ = 29.7 (s); MS (EI): m/z 336 (M^+, 4), 231 (92), 131 (25), 117 (35), 105 (100), 91 (63), 69 (28), 41 (22); $C_{22}H_{29}BO_2$ (336.28): calcd C 78.58, H 8.69; found C 78.65, H 8.77.

General procedure for the preparation of borates 16: A solution of $LiAlH_4$ (6.75 mL, 6.75 mmol, 1 M in Et_2O) was dropwise added at 0 °C to a vigorously stirred solution of boronate **15** (6.75 mmol) in pentane (7 mL) under argon. A voluminous precipitate of alane **17** separated. The cooling bath was removed and the suspension stirred for further 50 min at rt. ^{11}B-NMR indicated the clean formation of lithium borate **16** (δ = -28.1, m). The solvent was evaporated in vacuo and the residue suspended in pentane (10 mL). The suspension was centrifuged and the clear supernatant liquid transferred via a double-ended needle to another flask. The deposit was washed with pentane (8 mL) and the washing was combined with the supernatant solution. The solvent was evaporated under reduced pressure and the solid lithium borate **16** redissolved in Et_2O (0.8 M). This stock solution could be stored for months without decomposition.

General procedure for the asymmetric hydroboration using in situ generated boranes 13: Ethereal HCl (0.8 mL, 0.8 mmol, 1 M in Et_2O) was dropwise added at 0 °C to a well stirred solution of lithium borate **16** (1.0 mL, 0.8 mmol, 0.8 M in Et_2O) under argon. Evolution of hydrogen immediately occured and the reaction mixture was stirred further 15 min. ^{11}B-NMR indicated the clean formation of monoalkylborane **13** (δ = 23.2, s). After evaporation of the solvent in vacuo, the residue was redissolved in THF (1.5 mL), cooled to -25 °C and a solution of the alkene (0.8 mmol) in THF (0.4 mL) was added. After stirring further 24 h, the reaction mixture was quenched by addition of aqueous NaOH (10 %, 3 mL), followed by H_2O_2 (30 %, 3 mL). The cooling bath was removed and the mixture stirred at rt for further 1.5 h before dilution with Et_2O (80 mL). The aqueous phase was separated, extracted with Et_2O (2 x 30 mL) and the combined organic phases were washed with brine (30 mL) and dried ($MgSO_4$). The solvent was evaporated under reduced pressure and the crude alcohol purified by chromatography (pentane/Et_2O).

***trans*-2-Phenylcyclopentanol (20)** [25]: HPLC (OD, 5 % *i*-PrOH, 0.6 mL/min, 215 nm): t_R/min = 12.9 (1*S*,2*R*), 14.3 (1*R*,2*S*); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.36-7.14 (m, 5 H), 4.14 (q, J = 7.2 Hz, 1 H), 2.86 (m, 1 H), 2.23-2.02 (m, 2 H), 1.94-1.58 (m, 5 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 143.4, 128.4, 127.3, 126.3, 80.3, 54.3, 33.9, 31.8, 21.7.

***trans*-2-Methylcyclohexanol (21)** [25]: ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 3.16-3.00 (m, 1 H), 2.25 (bs, 1 H), 1.98-1.88 (m, 1 H), 1.80-1.55 (m, 3 H), 1.37-1.09 (m, 4 H), 1.05-0.87 (m, 1 H), 1.00 (d, J = 6.4 Hz, 3 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 76.3, 40.1, 35.4, 33.6, 25.6, 25.1, 18.4.
In order to determine the enantiomeric excess, **21** was converted into the corresponding benzoate (benzoyl chloride/pyridine): GC (CB, 100 kPa, 100 °C (1 min) to 160 °C, 2 °C/min): t_R/min = 24.4 (1*S*,2*S*), 24.7 (1*R*,2*R*); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.09-8.01 (m, 2 H), 7.56-7.47 (m, 1 H), 7.46-7.37 (m, 2 H), 4.67 (dt, J = 4.3 and 9.9 Hz, 1 H), 2.16-2.03 (m, 1 H), 1.86-1.61 (m, 4 H), 1.47-1.05 (m, 4 H), 0.96 (d, J = 6.5 Hz, 3 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 166.2, 132.6, 130.9, 129.4, 128.2, 78.9, 37.3, 33.4, 31.7, 25.3, 24.7, 18.4.

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