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Synthesis of racemic and enantiopure building blocks for naturally occurring hydroporphyrins: chlorophyll *a* and bonellin

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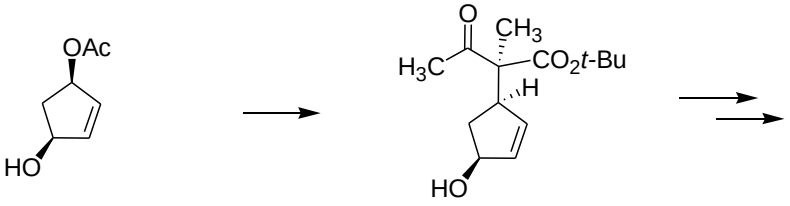
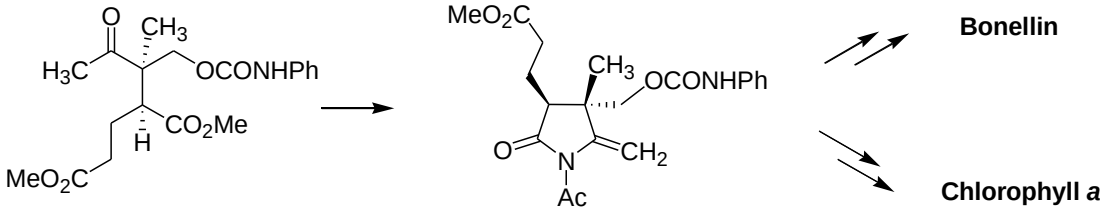
Abstract

The total syntheses of the marine pigment bonellin and photosynthesis pigment, chlorophyll *a*, require homochiral building blocks to construct their reduced ring D. The preparation of a common building block for ring D in both pigments can be achieved starting from the optical active cyclopen-2-en-1,2-diol derivative **9**. Palladium catalyzed alkylation of **9** with *t*-butyl methylacetoacetate gave intermediate **10b**. This intermediate was transformed further to the highly functionalized open-chain intermediate **6b** through reductions of the cyclopentene part and *t*-butyl carboxylate residue of **10b**. This step was followed by an oxidative cleavage of cyclopentene ring. The formation of the heterocyclic **7b** was accomplished by introducing nitrogen.



9 **10b**



6b **7b**

Keywords: Chlorins, chlorophyll *a*, bonellin, enantiopure building blocks,

Introduction

Chlorophyll *a* is the most common[1,2,3] and bonellin is a very unique[1,4,5] representative of the chlorin (dihydroporphyrin) class of porphyrinoid pigments. Chlorophyll *a*, the main pigment in photosynthesis is ubiquitously distributed. On the other hand, bonellin, found in the marine animal *Bonellia viridis* functions as remarkable sex differentiating pheromone.[4,6-9] Partial reduction in rings D of chlorophyll *a* and bonellin results in their green color (Greece: chloros) after which this class of pigments are denominated chlorins. Chlorophyll ring D possesses two adjacent stereogenic centers one substituted by a methyl group, the other one by a propionic acid side chain. Partially saturated ring D of bonellin bears as chlorophyll *a* a propionic acid residue and is geminally dimethylated at the adjacent position. Bonellin´s single centre of chirality is sensitive to bases and acids which can induce racemization. However, in chlorophyll *a,* the thermodynamically *trans*-arrangement of methyl and propionic acid groups prevents facile epimerization/racemization.

In a total synthesis[10,11] of bonellin dimethylester we utilized building block **A** for constructing ring D (Figure 1). Synthesis of this building block from (+)-camphor[12,13] was developed by R. B. Woodward in his monumental work on total synthesis of vitamin B_{12}.[14-16] As optically active camphor was the starting material, all the intermediates of bonellin synthesis were obtained in enantiomerically pure form. However, as expected, racemization happened in the final step of bonellin formation. To prevent this racemization, we aimed on the synthesis of a novel ring D building block **B**. This novel building block has a protected hydroxymethyl substituent instead of a simple methyl group. This bulky substituent creates an additional stable centre of chirality, assuring the stereochemical integrity of the adjacent propionic acid substituted centre of chirality during the course of synthesis.

After the chlorin macrocycle has been formed, the protected hydroxymethyl substituent should be converted into a methyl group by reduction, resulting in enantiopure bonellin (Figure 1). On the other hand, the novel ring D building block **C** could be of interest for the total synthesis of chlorophyll *a*. A retroaldol type fragmentation, with the loss of the hydroxymethyl group, could establish the correct substitution pattern with thermodynamically favoured *trans*-stereochemistry in ring D of chlorophyll *a* after the chlorin macrocycle has been formed.

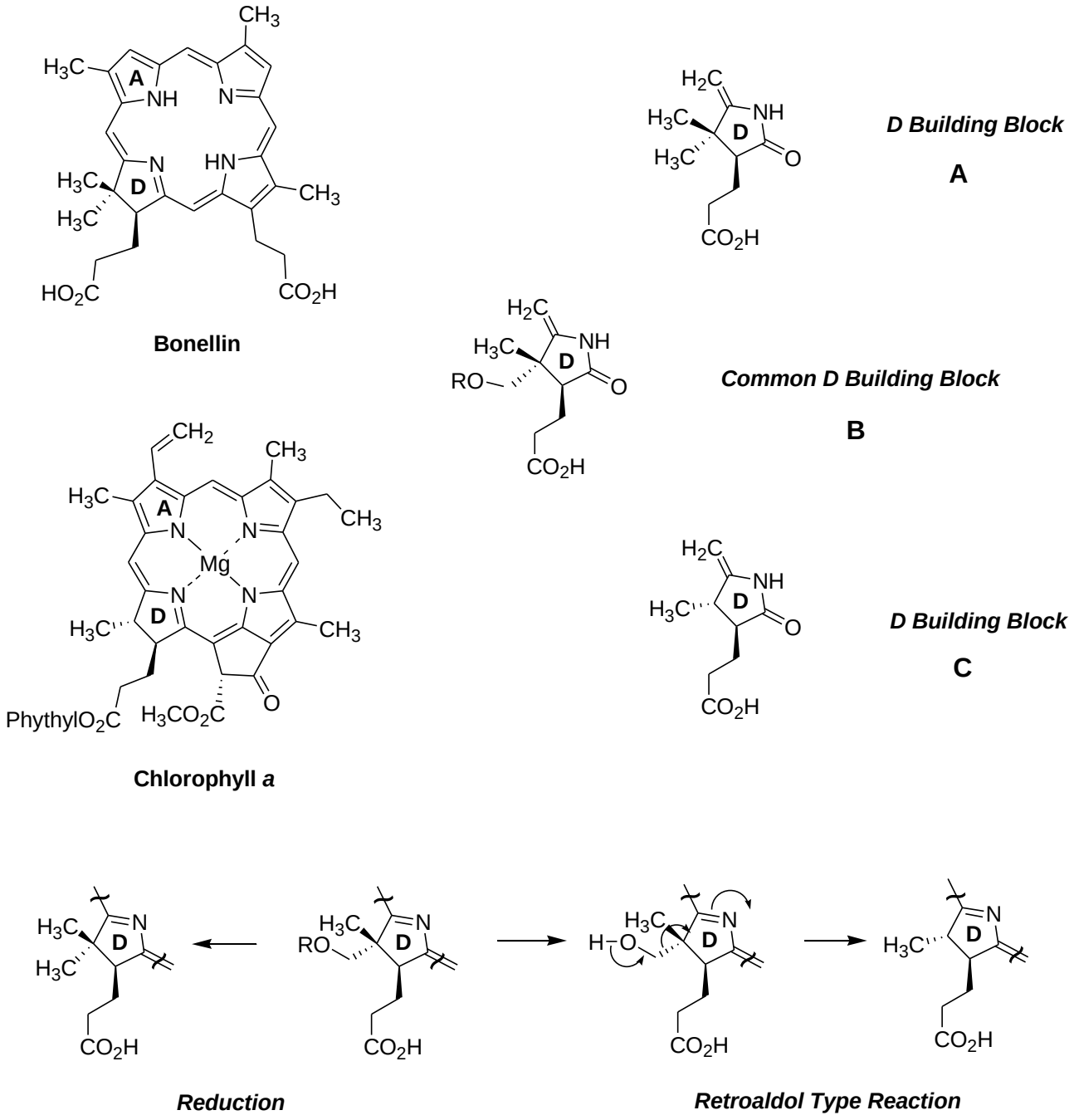


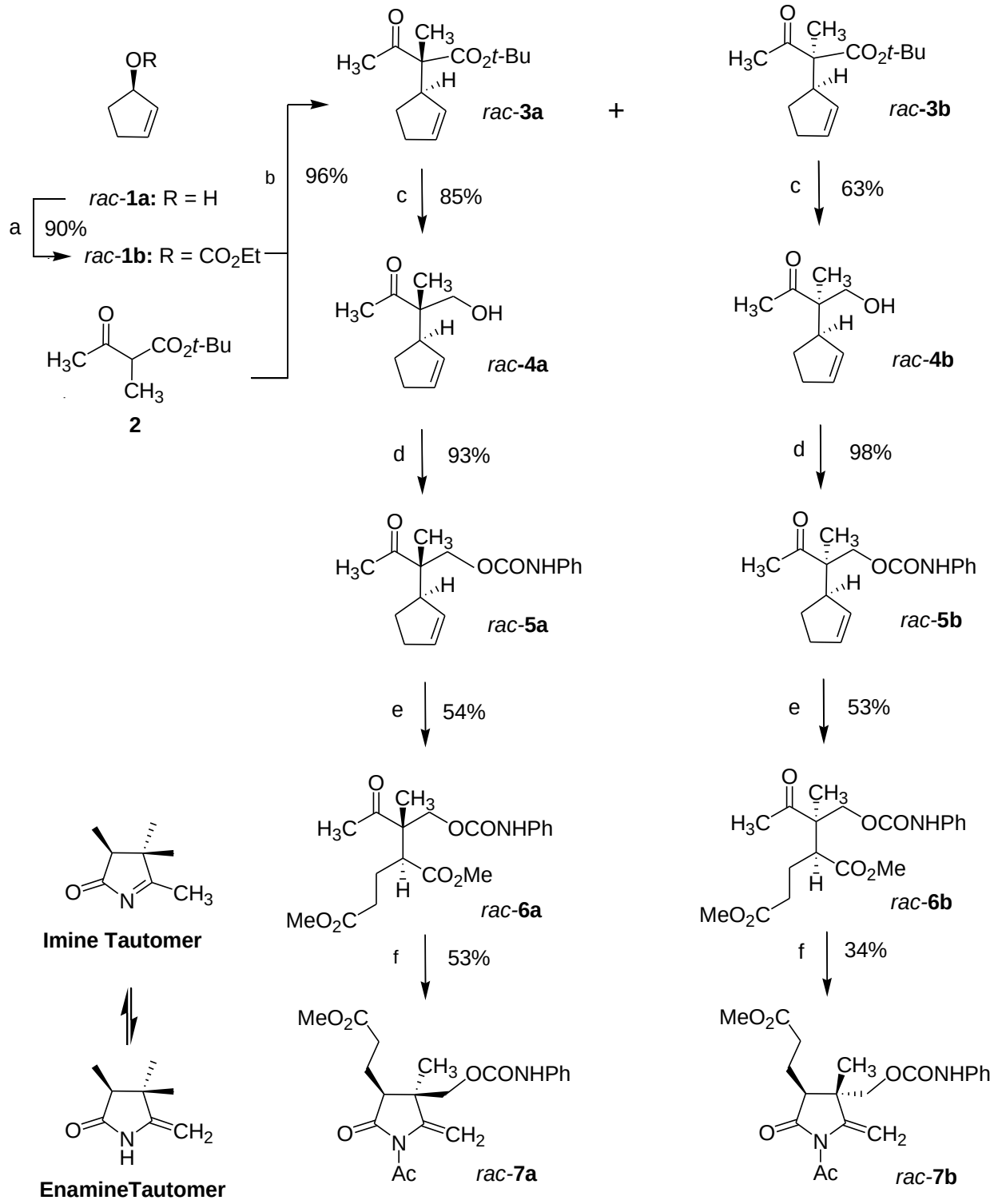
Figure 1. A common building **B** for access to the ring D for Bonellin and Chlorophyll *a.*

Results and Discussion

Cyclopent-2-yl-1-ol (*rac*-**1a**)[17,18] should form one part and *t*-butyl 2-methylacetoacetate (**2**) the other part of the carbon framework of racemic ring building blocks *rac*-**7a**,**b**. Experiences collected from this racemic route can then be applied for the synthesis of enantiomerically pure ring D targets. Therefore, optically active 4-hydroxy-cyclopent-2-en-1-yl acetate (**9**)[19-21] should be utilized as the starting material instead of *rac*-**1a**.

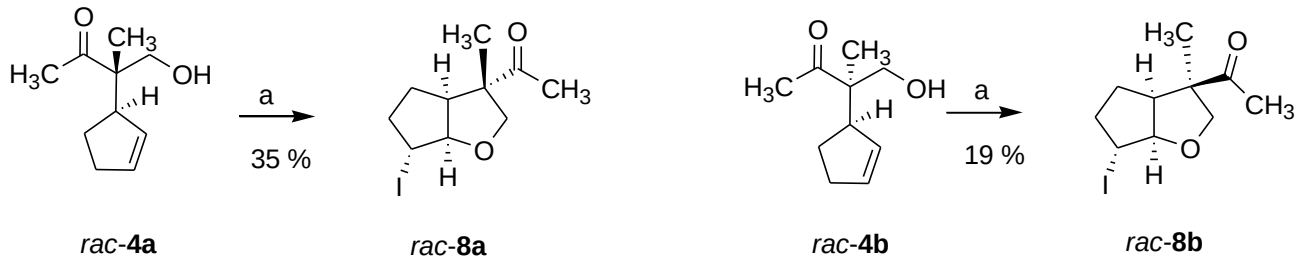
Palladium(0)-catalyzed coupling of allyl carbonate *rac*-**1b** with *t*-butyl methylacetoacetate **2**, according to Tsuji´s method[22,23] gave a mixture of diastereomers *rac*-**3a** and *rac*-**3b** in high yields (Scheme 1). The mixture of

diastereomers was separated by preparative HPLC to give *rac*-**3a** and *rac*-**3b** in about 1:2 ratio. Both diastereomers were separately transformed into the desired targets (Scheme 1).



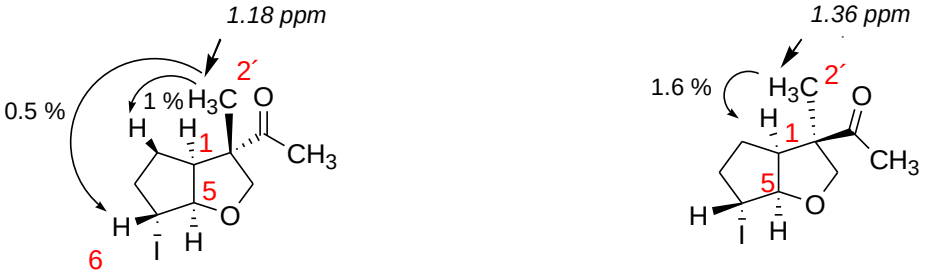
Scheme 1. Synthesis of diastereomeric racemic building blocks *rac*-**7a** and *rac*-**7b**. (a) $ClCO_2Et$, pyridine, CH_2Cl_2, Ar, rt, 12 h. (b) Pd_2dba_3 x $CHCl_3$, Ph_3P, *t*-butyl 2-methylacetoacetate (**2**), THF, Ar, rt, 5 h; prep. HPLC: 25.5% *rac*-**3a**, 49.2% *rac*-**3b**, 13.3% mixture of *rac*-**3a,b**. (c)(i) LDA, THF, Ar, -78 °C, 30 min; (ii) Me_3SiCl, THF, Ar, -60 °C, 20 min; (iii) $LiAlH_4$, THF, Ar, rt, 5 h. (d) PhNCO, DMAP, benzene, Ar, rt, 1 h. (e) $NaIO_4$, $RuCl_3$, acetone, H_2O, 0 °C, 2 h then rt, 12 h. (f) (i) NH_3, MeOH, NaOAc, rt, 13 h; (ii) Ac_2O, DMAP, CH_2Cl_2, rt, 6 h.

The *t*-butoxycarbonyl groups of *rac*-**3a**/*rac*-**3b** were reduced with lithium aluminium hydride, resulting in the desired hydroxymethyl residues of *rac*-**4a**/*rac*-**4b**. Protection of the acyl residues was achieved by deprotonation and silylation prior to reduction. Deprotection occurred during the acidic work-up of the reduction. Thus, intermediates *rac*-**4a**/*rac*-**4b** were obtained for this single step procedure with excellent yields (85% resp. 63%). Phenylisocyanate was then used to protect the hydroxyl groups of *rac*-**4a**/*rac*-**4b** through carbamate formation. Oxidative cleavage of cyclopentene rings of carbamates *rac*-**5a**/*rac*-**5b** was performed using ruthenium trichloride/sodium periodate. Dicarboxylic acid esters *rac*-**6a**/*rac*-**6b** were obtained after esterification with diazomethane. Treatment of *rac*-**6a**/*rac*-**6b** with ammonia in methanol formed ketoimines, which reacted to yield 5-membered lactam rings with the corresponding carboxylate groups. The five-membered lactam rings can exist in two tautomeric forms - an imine tautomer (see Scheme 1) with an endocyclic double bond, and an enamine tautomer with an exocyclic methylene double bond. To fix the enamine tautomer, acylation of the pyrrolidine nitrogen was performed to yield ring D-building blocks, *rac*-**7a**/*rac*-**7b**. Syntheses of both diastereomeric target ring D lactams, *rac*-**7a** and *rac*-**7b,** were achieved in six steps, with an overall yield of 20% and 10% respectively.



rac-**4a** *rac*-**8a** *rac*-**4b** *rac*-**8b**

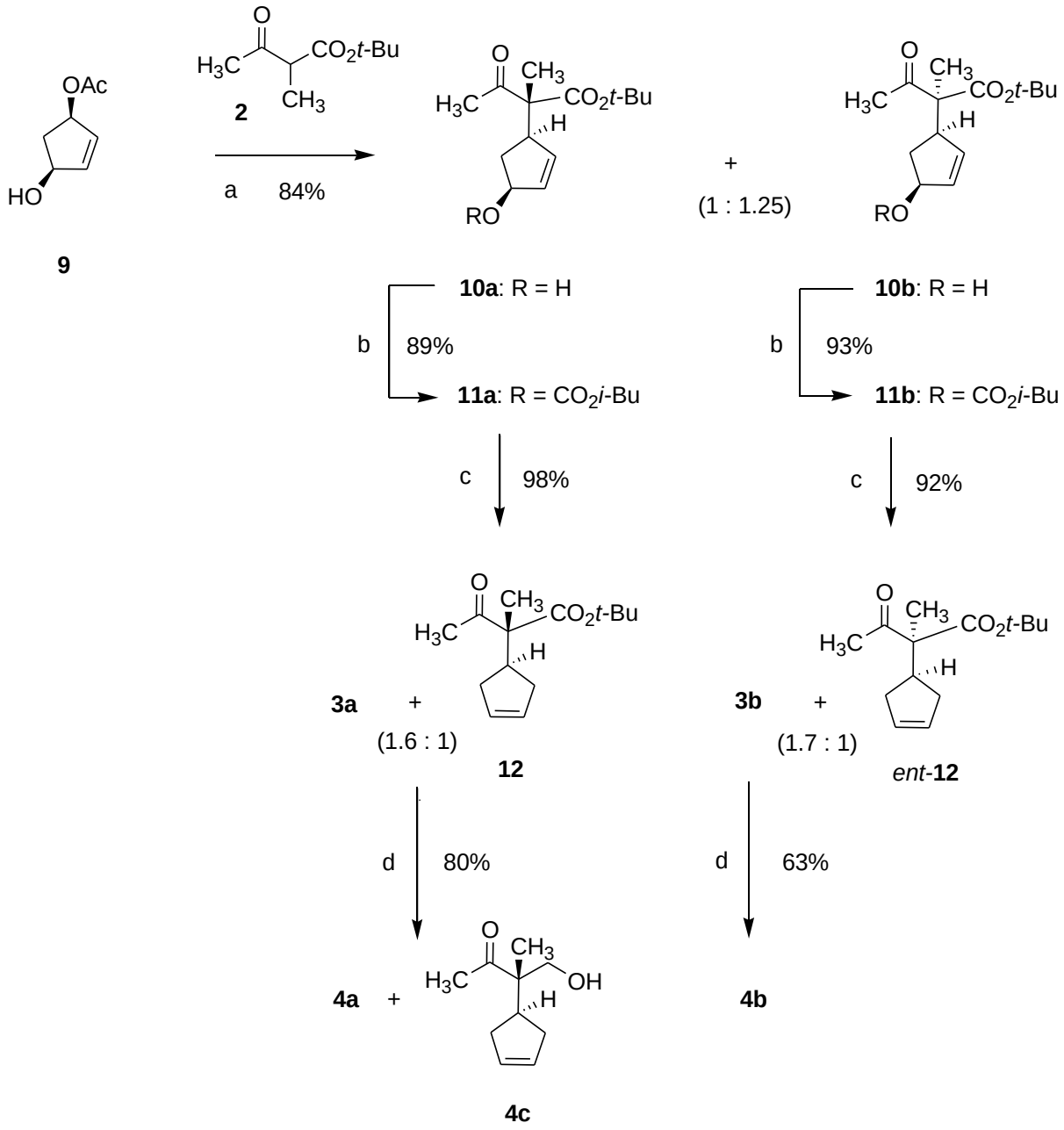
Scheme 2. Elucidation of relative configurations of *rac*-**4a** and *rac*-**4b.** (a) I_2, KI, $NaHCO_3$, H_2O, rt, 18 h.



rac-**8a** *rac*-**8b**

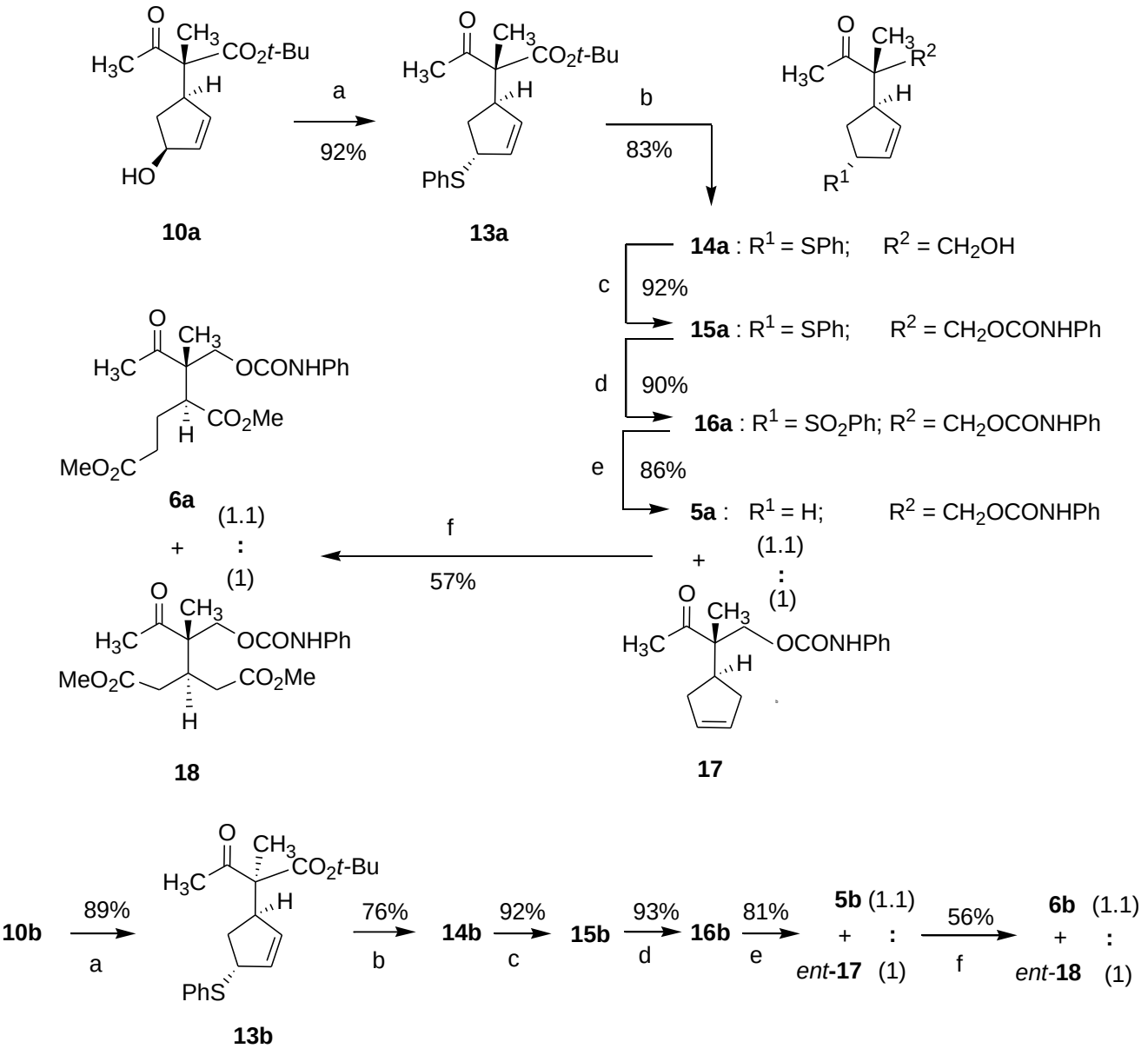
Figure 2. Determination of configurations of *rac*-**8a** and *rac*-**8b** by NOE experiments. Only main NOE correlations are depicted.

For the determination of the stereochemistry, alcohols *rac*-**4a** and *rac*-**4b** were subjected to iodoetherification to yield oxabicyclo[3.3.0]heptanes *rac*-**8a** and *rac*-**8b** (Scheme 2). Classical ^{1}H-NOE-NMR experiments on the rigid bicyclohexane structures revealed an *endo*-position of the 2-methyl group for *rac*-**8a** and an *exo*-orientation of 2-methyl group of *rac*-**8b** (Figure 2). An independent confirmation of these findings was achieved by a ^{1}H-1D-NOESY experiment on *rac*-**7a**, which demonstrated a *trans*-configuration between the 4-methyl group and the 3-propionate side chain (see Supplementary Material for *rac*-**7a**).



Scheme 3. Synthesis of enantiomerically pure building blocks **4a** and **4b**. (a)(i) **2**, NaH, cyclohexane, THF, 0 °C to rt, 30 min; (ii) addition of **9**, $Pd[P(Ph)_3]_4$, THF, Ar, rt, 90 min; prep HPLC: 28% **10a**, 44% **10b**, 2.8% mixture of **10a**,**b**. (b) $ClCO_2$-*i*Bu, pyridine, CH_2Cl_2, 0 °C, to rt, 2 h. (c) Polymethyl hydrosiloxane, Na_2HPO_4, $Pd[P(Ph)_3]_4$, THF, Ar rt, 3 h; 60% **3a**, 38% **12**; resp. prep HPLC: 38% **3b**, 20% *ent*-**12**, 11% **3b/***ent*-**12**. (d) (i) LDA, THF Ar, -78 °C, 30 min; (ii) Me_3SiCl, THF, Ar, -60 °C, 20 min; (iii) $LiAlH_4$, THF, Ar, -60 °C to rt, 5 h; prep. HPLC: 31% **4a**, 12.5% **4c**.

Optically active cyclopent-2-ene-1,4-diol monoacetate **9** was chosen as an attractive starting material to achieve homochiral building blocks **7a**,**b** along "enantiomeric" routes (Scheme 3). Monoacetate **9** is easily available[19-21] with high enantiomeric excess (ee > 98%) by enzymatic hydrolysis from its diacetate. From earlier investigations directed to natural products, such as (-)-methyljasmonate,[21] it has been shown that monoacetate **9** can be transformed into both enantiomers using enantiodivergent routes.



Scheme 4. Alternative route for synthesis of enantiomerically pure building blocks **5a** and **5b**. (a) PhSSPh, Bu_3P, pyridine, rt, 5h. (b)(i) LDA, THF, Ar, -78 °C, 2 h; (ii) Me_3SiCl, THF, -78 °C, 25 min; (iii) $LiAlH_4$, THF, Ar, -78 °C to rt, 7.5 h. (c) PhNCO, DMAP, benzene, rt, 90 min. (d) *m*-CPBA, $CHCl_3$, -20 °C, 13 h. (e) Na/Hg, MeOH, Ar, rt, 90 min. (f) $NaIO_4$, $RuCl_3$, acetone, H_2O, 0 °C to rt, 14 h; flash chromatogr. 26% **6a**, 23% **18**; prep. HPLC: 24% **6b**, 23% *ent*-**18**.

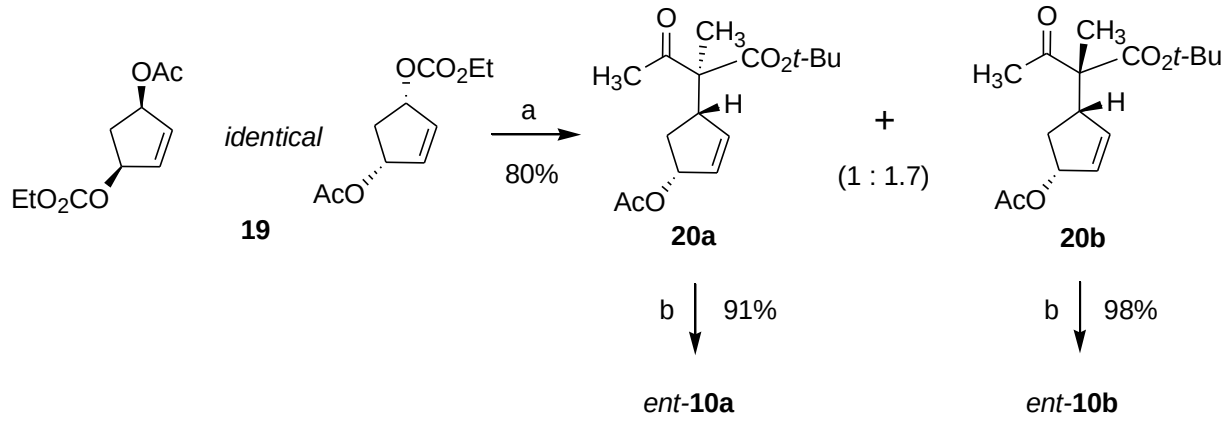
The allylic acetoxy group of **9** was substituted by *t*-butyl methyl acetoacetate **2** using a catalytic amount of tetrakis(triphenylphosphine)palladium(0) according to Trost´s and Tsuji´s method.[22-26] As expected, the substitution took place with retention of configuration due to double inversion. The initial backside attack of the palladium catalyst formed a transient π-allyl palladium intermediate followed by a further backside attack by acetoacetate **2**. In contrast to *rac*-**1b**, the stereochemical outcome of the reaction could be observed with **10**, due to the additional hydroxyl substituted stereocenter. Also, the regioselectivity of the substitution of the π-allyl palladium intermediate is unequivocally defined by the constitution of **10**. As observed for the racemic series, a mixture of diastereomers **10a** and **10b** was formed in a 1:1.25 ratio. Pure diastereomers **10a** and **10b** were separated by preparative HPLC and then were reacted separately. The hydroxyl groups of **10a** and **10b**

were removed by palladium(0) catalyzed reduction[27-31] for which their *iso*-butyl carbonates were prepared. The best results for the reduction were achieved with polymethyl hydrosiloxane[31] in the presence of disodium hydrogen phosphate. Without the disodium hydrogen phosphate additive considerable amounts of *iso*-butyl ethers were produced. Disodium hydrogen phosphate is crucial for the success of the reaction, as it protonates the initially formed *iso*-butoxylate and prevents its addition to the intermediate π-allyl palladium complex. The regioselectivity was not fully controlled during reduction, as the intermediate π-allyl palladium complex was attacked at both terminal positions. The undesired isomer *ent*-**12** was removed by chromatography directly after the reduction, and the other isomer **12** after the subsequent synthesis step. The protocol developed for the racemic sequence was used to reduce the *tert*-butoxy carbonyl groups of **3a** and **3b**. The physical and spectroscopic properties of **3a**, **3b**, **4a**, and **4b** were found to be completely identical - except for chiroptical data – when compared with the corresponding compounds of the racemic series.

The moderate regioselectivity of the reduction of **10a** and **10b** prompted us to explore a different reaction sequence (Scheme 4). The hydroxyl groups in **10a**/**10b** were converted to phenyl thioethers **13a**/**13b** through a modified Mitsunobu reaction.[32] As expected, substitution happened with an inversion of configuration. The *t*-butoxy carbonyl functions present in **13a**/**13b** were reduced and the formed hydroxy methyl groups of **14a**/**14b** were subsequently protected, leading with an excellent overall yield to phenyl carbamates **15a**/**15b**.The sulfur functionality in **15a**/**15b** were oxidized through *m*-CPBA and the produced sulfones **16a**/**16b** were reduced through sodium amalgam. Even though, the reduction with sodium amalgam gave high yields of the reduction products, the regioselectivity could not be improved. A 1:1-mixture of isomers **5a** and **17** respectively **5b** and *ent*-**17** were obtained.

For the cleavage of five-membered rings, mixtures of isomers **5a**/**17** resp. **5b**/*ent*-**17** were oxidized by using $RuCl_3/NaIO_4$, leading to open chain isomers **6a**/**18** and **6b**/*ent*-**18**. Compounds **6a** and **6b** were separated from the mixture of isomers by preparative HPLC. Enantiomerically pure **6a** and **6b** were in any respect - except for chiroptical properties - identical to *rac*-**6a** and *rac*-**6b** (Scheme 1, racemic sequence).

A comparison between alternative synthesis pathways in Schemes 3 and 4 indicates that the first variant is more efficient than the second route. According to Scheme 3, intermediates **5a**/**5b** can be obtained in five steps with an overall yield of 65% for **5a** and 53% for **5b**. The reduction shows a regioselectivity of 1.6:1. Contrastingly, the alternative route (Scheme 4) requires six steps and only an overall yield of 53% for intermediate **5a** and 47% for **5b**. Moreover, the regioselectivity of the reduction is relatively low (1.1:1).



Scheme 5. Synthesis of enantiomers of building blocks **10a** and **10b**. (a)(i) *t*-Butyl 2-methyl-acetoacetate (**2**), NaH, cyclohexane, THF, Ar, 0 °C to rt; (ii) addition of **19**, $Pd[P(Ph)_3]_4$, rt, 2 h; prep HPLC: 31% **20a** and 49% **20b**. (b) K_2CO_3, MeOH, rt, 30 min.

For physiological investigations there could be an interest in studying enantiomeric congeners of bonellin and chlorophyll. Cyclopentene-1-carbonate-4-acetate **19** (Scheme 5) provides an opportunity to prepare enantiomeric building blocks *ent*-**10a** and *ent*-**10b**. Carbonate **19**[21], derived from hydroxy-cyclopentene acetate **9** undergoes regioselective palladium(0)-catalyzed substitution of its carbonate function by *t*-butyl methyl-acetoacetate **2** according to Tsuji´s method[23], leading to formation of diastereomers **20a** and **20b** in a 1:1.7 ratio. These single diastereomers were separated on a preparative scale by HPLC. The hydrolysis of the acetate groups in **20a** and **20b** produced *ent*-**10a** and *ent*-**10b**, which correspond to their enantiomeric intermediates **10a** and **10b** (Scheme 3, 4).

Conclusions

Racemic and enantioselective synthesis pathways to access ring D building blocks, required for chlorin pigments, bonellin and chlorophyll *a* were explored. A racemic synthesis pathway, starting from cyclopent-2-ene-1-ol *rac*-**1a**, forms D building blocks *rac*-**7a** and *rac*-**7b** in six steps with an overall yield of 20% and 10% respectively.

Two different synthesis routes were explored to achieve enantiomerically pure key intermediates **5a** and **5b** for **7a**/**7b**. A comparison between both routes proved the superiority of the first alternative (Scheme 3) in terms of yield and selectivity over the second one (Scheme 4). The initial route involves five steps starting from enantiomerically pure cyclopent-2-ene-1,4-diol monoacetate **9**, yielding 65% **5a** and 53% **5b**.

An enantiodivergent access to the opposite enantiomeric series was established by employing cyclopentene carbonate **19** (Scheme 5). It was derived from enantiomerically pure cyclopentene monoacetate **9**.

Experimental Section

General. Starting materials were prepared either according to literature procedures or were purchased from Fluka, Merck-Schuchardt, Jansen or Aldrich and used without further purification. All solvents were purified and dried by standard methods. All reactions were carried out under argon atmosphere. Melting points are not corrected. TLC: Silica gel plates (Woelm, silica gel 60 F 254/366). Column chromatography: Silica gel (Woelm, 63 - 200 µm) or silica gel (ICN, 32 -63 µm, flash chromatography). Analytical HPLC: Waters 244 M6 KA system, M 440 EB UV detector and R 410 differential refractometer, nucleosil 50 - 10. Preparative HPLC: Waters Prep LC system 500, 2 cartridges PrepPak 500 silica gel Waters. For crystallization of products, samples were dissolved in minimum volumes of polar solvents (EtOAc or ether) and nonpolar *n*-hexane was then slowly added until crystallization began. Optical Rotation: Perkin-Elmer 141, 241 and 243 polarimeter, c [g/100 mL]. UV/Vis: Applied Physics Corporation, CARY 15. CD: CARY spectropolarimeter 61, c [mg/mL]. IR: Perkin-Elmer 257 spectrometer. NMR: Bruker WH 270, Bruker AM 300 and Bruker 600 AVANCE neo. All chemical shifts were referenced to TMS lock signal. MS: Finnigan MAT 8222 and MAT 95XL spectrometer [E (70 eV)]. Elemental analyses: Microanalytical Laboratories Malissa & Reuter (Engelskirchen) and Laboratory Prof. W. Ried (University Frankfurt).

[(1*RS*)-Cyclopent-2-en-1-yl]-ethyl-carbonate (*rac*-**1b**). To a solution of cyclopent-2-en-1-ol (*rac*-**1a**) (10.17 g, 121 mmol) and pyridine (12.7 mL, 157 mmol) in dichloromethane (150 mL) were added slowly ethyl chloroformate (15.0 mL, 157 mmol) at 0 °C. The mixture was stirred at rt overnight. Then the mixture was washed five times

with 1N HCl (5 x 35 mL), three times with saturated Na_2CO_3 (3 x 40 mL) and three times with saturated NaCl (3 x 40 mL). The organic layer was dried by filtration through cotton wool and evaporated. The residue was purified by column chromatography [SiO_2 (250 g), hexane/ether = 3:1] to remove excess of unreacted ethyl chloroformate. Bulb to bulb distillation of the main fraction (95 °C/18 Torr) gave *rac*-**1b** as a colorless liquid (17.1 g, 90%). TLC (silica gel, hexane/ether = 3:1): R_f 0.56. IR (film, $\tilde{\nu}_{max}$, cm^{-1}): 3060, 2980, 2930, 2850, 1740s (C=O), 1450, 1395, 1375, 1365, 1335, 1255, 1160, 1095, 1010, 935, 860, 790. ^{1}H NMR (270 MHz, $CDCl_3$): δ_H (3H, t, *J* 7.2 Hz, H_3C-C), 1,86 – 1.98 [1H, m, HC(5)], 2.21 -2.38 [2H, m, HC(5), HC(4)], 2.46 -2.61 [1H, m, HC(4)], 4.18 (2H, q, *J* = 7.2 Hz, H_2C-OC=O), 5.62 [(1H, m, HC(1)], 5.87 [1H, m, HC(2) or HC(3)], 6.15 [1H, m, HC(2) or HC(3)]. Microanalysis for $C_8H_{12}O_3$ (156.18): calcd. C 61.52, H 7.74; found C 61.55, H 7.62.

***t*-Butyl (2*RS*)-2-[(1*RS*)-cyclopent-2-en-1-yl]-2-methyl-3-oxo-butanoate** (*rac*-**3a**) and ***t*-butyl (2S*R*)-2-[(1*RS*)-cyclopent-2-en-1-yl]-2-methyl-3-oxo-butanoate** (*rac*-**3b**). Pd_2dba_3 x $CHCl_3$ (1.86 g, 1.8 mmol) and PPh_3 (3.90 g, 15.0 mmol) in THF (150 mL) were stirred under an argon atmosphere for 20 min at rt. A solution of cyclopentene carbonate *rac*-**1b** and *tert*-butyl 2-methyl-actoacetate (**2**) in THF (100 mL) were added slowly to the prepared solution of $Pd[P(Ph)_3]_4$ [tetrakis(triphenylphosphine)palladium] and stirred for 4 h at rt. The solvent was then evaporated in vacuo. The residue was purified by column chromatography [SiO_2 (220 g), hexane/EtOAc = 10: 1] to give a diastereomeric mixture of *rac*-**3a** and *rac*-**3b** (21.0 g, 96%). Separation of mixture of diastereomers by preparative HPLC [PrepPak 500 silica gel (Waters), *n*-hexane/EtOAc = 10:0.25] gave *rac*-**3a** (5.53 g, 25.5%), *rac*-**3b** (10.67 g, 49.2%) and *rac*-**3a**,**b** (mixture, 2.97 g, 13.6%). The pure fractions were further purified by bulb to bulb distillation (15 Torr/140 °C).

rac-**3a**: TLC (silica gel, hexane/ether = 3:1): R_f 0.54. IR (film, $\tilde{\nu}_{max}$, cm^{-1}): 3050, 2980, 2930, 2850, 1740s (CO ester), 1715s (CO ketone), 1460, 1395, 1370, 1355, 1340, 1250, 1215, 1150, 1110, 1055, 1020, 965, 920, 845. ^{1}H NMR (270 MHz, $CDCl_3$) δ_H 1.16 [3H, s, H_3C-C(2)], 1.44 (9H, s, *t*-Bu), 1.37 – 1.5 (1H, m, *H*HC), 1.88-2.02 (1H, m, *H*HC), 2.16 (3H, s, acyl), 2.26- 2.32 (2H, m, H_2C), 3.50 [1H, m, H(C1´)], 5.63 [1H, m, H(C2´) or H(C3´)], 5.80 [1H, m, H(C3´) or H(C2´)]. Microanalysis for $C_{14}H_{22}O_3$ (238.32): calcd. C 70.55, H 9.30; found C 70.43, H 9.22.

rac-**3b:** TLC (silica gel, hexane/ether = 3:1): R_f 0.54. IR (film, $\tilde{\nu}_{max}$, cm^{-1}): 3050, 2970, 2930,2845, 1740s (CO ester), 1710s (CO ketone), 1460, 1390, 1365, 1355, 1250, 1210, 1155, 1110, 1050, 1015, 915, 840. ^{1}H NMR (270 MHz, $CDCl_3$): δ_H 1.17 [3H, s, H_3C-C(2)], 1.45 (9H, s, *t*-Bu), 1.52 – 1.69 (1H, m, *H*HC), 1.94-2.07 (1H, m, *H*HC), 2.15 (3H, s, acyl), 2.26- 2.34 (2H, m, H_2C), 3.48 [1H, m, H(C1´)], 5.54 [1H, m, H(C2´) or H(C3´)], 5.80 [1H, m, HC3´) or H(C2´)]. Microanalysis for $C_{14}H_{22}O_3$ (238.32): calcd. C 70.55, H 9.30; found C 70.62, H 9.25.

(3*SR*)-3-[(1*RS*)-Cyclopent-2-en-1-yl]-4-hydroxy-3-methyl-butan-2-on (*rac*-**4a**). LiN(*i*-Pr)$_2$ was prepared from (*i*-Pr)$_2$NH (4.95 mL, 35.0 mmol) and *n*-BuLi (21.8 mL, 35.0 mmol, 1.6 M solution in *n*-hexane) in THF (100 mL) at -10° C. The solution was cooled to -78 °C. Ketoester *rac*-**3a** (5.53 g, 23.2 mmol) in THF (30 mL) was slowly added during 20 min and the mixture was stirred for 30 min at -78 °C. Me_3SiCl (4.50 mL, 35.0 mmol) was added and the solution stirred for 20 min. Monitoring by TLC indicated complete formation of silylenol ether. $LiAlH_4$ (3.70 g, 93.0 mmol) was added in portions and stirring was continued for 5 h during which the temperature rose up to 20 °C. Excess of $LiAlH_4$ was destroyed by cautious addition of EtOAc and then 10% sulfuric acid (75 mL). The organic layer was separated and the mixture extracted twice with ether (2 x 50 mL). The combined organic extracts were washed with 10% sulfuric acid (50 mL) and five times with saturated brine (5 x 50 mL). The solvent was dried by filtration through cotton wool and evaporated. The residue was purified by column chromatography [SiO_2 (350 g), hexane/EtOAc = 1:1] to yield after bulb to bulb distillation (0.3 Torr/120 °C) alcohol *rac*-**4a** (3.32 g, 85%).

rac-**4a**: TLC (silica gel, hexane/EtOAc = 1:1): R_f 0.37. IR (film, $\tilde{\nu}_{max}$, cm^{-1}): 3445 (OH), 3050, 2940, 2870, 2845, 1700s (C=O), 1465, 1425, 1360, 1285, 1265, 1205, 1135, 1105, 1035s (C-O), 935, 915, 740. ^{1}H NMR (270 MHz, $CDCl_3$): δ_H 1.14 [3H, s, H_3C-C(2)], 1.47-1.60 (1H, m, *H*HC), 1.87-2.0 (1H, m, *H*HC), 2.11 (1H, t, *J* = 6.4 Hz, OH,

exchangeable by D_2O), 2.19 (3H, s, acyl), 2.27-2.34 (2H, m, H_2C), 3.08 [1H, m, H(C1´)], 3.47 (1H, dd, J_{gem} = 11.3 Hz, J_{vic} = 7.0 Hz, *H*HCOH), 3.86 (1H, dd, J_{gem} = 11.3 Hz, J_{vic} = 5.7 Hz, *H*HCOH), 5.60 [1H, m, H(C2´) or H(C3´)], 5.84 [1H, m, H(C2´) or H(C3´)]. Microanalysis for $C_{10}H_{16}O_2$ (168.23): calcd. C 71.39, H 9.58; found C 71.29, H 9.60.

(3*RS*)-3-[(1*RS*)-Cyclopent-2-en-1-yl]-4-hydroxy-3-methyl-butan-2-on (*rac*-**4b**). Ketoester *rac*-**3b (**10.67 g, 44.7 mmol) was reacted as described for *rac*-**3a** to *rac*-**4a.** Yield of alcohol *rac*-**4b** (4.77 g, 63%).

rac-**4b**: TLC (silica gel, hexane/EtOAc = 1:1): R_f 0.37. IR (film, $\tilde{\nu}_{max}$, cm^{-1}): 3430 (OH), 3045, 2930, 2870, 2840, 1695s (C=O), 1495, 1425, 1360, 1150, 1100, 1040s (C-O), 910, 730. ^{1}H NMR (270 MHz, $CDCl_3$): δ_H 1.19 [3H, s, H_3C-C(2)], 1.51-1.64 (1H, m, *H*HC), 1.83-1.96 (1H, m, *H*HC), 2.19 (3H, s, acyl), 2.24-2.45 (3H, m, H_2C and OH, exchangeable by D_2O), 3.12 [1H, m, H(C-1´)], 3.41 (1H, dd, J_{gem} = 11.4 Hz, J_{vic} 7.0 Hz, *H*HCOH), 3.82 (1H, dd, J_{gem} = 11.4 Hz, J_{vic} = 5.8 Hz, *H*HCOH), 5.58 [1H, m, H(C2´) or H(C3´)], 5.85 [1H, m, H(C2´) or H(C3´)]. Microanalysis for $C_{10}H_{16}O_2$ (168.23): calcd. C 71.39, H 9.58; found C 71.36, H 9.48.

(3*SR*)-3-[(1*RS*)-Cyclopent-2-en-1-yl]-3-methyl-4-phenyl-carbamoyloxy-butan-2-on (*rac*-**5a**). To alcohol *rac*-**4a** (2.09 g, 12.04 mmol) and 4-*N,N*-dimethyaminopyridine (DMAP) (1.52 g, 12.4 mmol) in benzene (65 mL) was added slowly phenyl isocyanate (1.37 mL, 12.45 mmol) in benzene (10 mL). The reaction mixture stirred at rt for 3 h. The solvent was evaporated in vacuo and the residue purified by column chromatography [SiO_2 (340 g), CH_2Cl_2/hexane/EtOAc = 10:6:1] to yield carbamate *rac*-**5a** as a viscous colorless oil which became crystalline on standing (3.31 g, 93%). For recording analytical data a sample was recrystallized from ether/*n*-hexane.

rac-**5a**: M.p. 94-95 °C. TLC (silica gel, CH_2Cl_2/hexane/EtOAc = 10:6:1): R_f 0.44. UV [MeOH, λ_{max}, nm (ε, $Lmol^{-1}cm^{-1}$)]: 234 (18163), 272 (842), 280 (629). IR (film, $\tilde{\nu}_{max}$, cm^{-1}): 3260, 3130 (NH), 3045, 2980, 2930, 2890, 2840, 1740s (C=O carbamate), 1700s (C=O ketone), 1605, 1540, 1505, 1445, 1390, 1365, 1315, 1220s (C-O), 1145,1110, 1050, 1030, 900, 855, 750, 690. ^{1}H NMR (270 MHz, $CDCl_3$): δ_H 1.09 [3H, s, H_3C-C(2)], 1.49-1.61 (1H, m, *H*HC), 1.84-1.97 (1H, m, *H*HC), 2.21 (3H, s, acyl), 2.28-2.35 (2H, m, H_2C), 3.13 [1H, m, H(C-1´)], 4.25 (1H, d, *J* = 10.9 Hz, *H*HCOR), 4.41 (1H, d, *J* = 10.9 Hz, *H*HCOR), 5.61 [1H, m, H(C2´) or H(C3´)], 5.88 [1H, m, H(C2´) or H(C3´)], 6.61 (1H, s, br, NH), 7.07 (1H, m, *p*-H), 7.26-7.40 (4H, m, phenyl ring). Microanalysis for $C_{17}H_{21}NO_3$ (287.36): calcd. C 71.05, H 7.36, N 4.87; found C 71.13, H 7.43, N 4.70.

(3*RS*)-3-[(1*RS*)-Cyclopent-2-en-1-yl]-3-methyl-4-phenyl-carbamoyloxy-butan-2-on (*rac*-**5b**). Alcohol *rac*-**4b (**1.40 g, 8.3 mmol) was reacted as described for *rac*-**4a** to *rac*-**5a.** Yield of alcohol *rac*-**5b** (2.34 g, 98%).

rac-**5b**: M.p. 88-90 °C. TLC (silica gel, CH_2Cl_2/hexane/EtOAc = 10:6:1): R_f 0.44. UV [MeOH, λ_{max}, nm (ε, $Lmol^{-1}cm^{-1}$)]: 234 (18113), 272 (842), 279 (618). IR (film, $\tilde{\nu}_{max}$, cm^{-1}): 3330, 3200, 3120 (NH), 3090, 3040, 2990, 2930, 2835, 1735s (C=O carbamate), 1700s (C=O ketone), 1605, 1545, 1495, 1445, 1385, 1360, 1315, 1230s (C-O), 1210, 1150, 1105, 1080, 1055, 1025, 900, 845, 755, 730. ^{1}H NMR (270 MHz, $CDCl_3$): δ_H 1.12 [3H, s, H_3C-C(2)], 1.57-1.72 (1H, m, *H*HC), 1.88-2.01 (1H, m, *H*HC), 2.21 (3H, s, acyl), 2.29-2.36 (2H, m, H_2C), 3.13 [1H, m, H(C-1´)], 4.22 (1H, d, *J* = 10.9 Hz, *H*HCOR), 4.39 (1H, d, *J* = 10.9 Hz, *H*HCOR), 5.49 [1H, m, H(C2´) or H(C3´)], 5.86 [1H, m, H(C2´) or H(C3´)], 6.67 (1H, s, br, NH), 7.06 (1H, m, *p*-H), 7.26-7.38 (4H, m, phenyl ring). Microanalysis for $C_{17}H_{21}NO_3$ (287.36): calcd. C 71.05, H 7.36, N 4.87; found C 71.30, H 7.54, N 5.00.

Methyl (4*SR*,5*SR*)-4-methoxycarbonyl-5-methyl-5-(phenylcarbamoyloxy-methyl)-6-oxo-heptanoate (*rac*-**6a**). To carbamate *rac*-**5a** (1.21 g, 4.2 mmol) in acetone (25 mL) was added a solution of $NaIO_4$ (3.59 g, 16.8 mmol) in H_2O (25 mL). The solution was cooled to 0 °C, $RuCl_3$ (46 mg, 0.21 mmol) was added and the mixture was stirred at 0 °C for 2 h and at rt for 24 h. The reaction mixture was filtered through a layer of Celite and thoroughly washed with ether. The aqueous layer of the filtrate was extracted four times with ether (4 x 40 mL). The combined organic layers were extracted four times with saturated aqueous Na_2CO_3 (4 x 40 mL). The alkaline extracts were acidified with concentrated hydrochloric acid, saturated with NaCl and extracted five times with ether (5 x 50 mL). The combined ether extracts were washed three times with saturated brine, dried over $MgSO_4$ and the solvent was evaporated. The residue was dissolved in ether (ca. 15 mL) and CH_2N_2 in ether (25 mL) was

added. After evaporation of the solvent the residue was purified by column chromatography [SiO_2 (90 g), hexane/EtOAc = 2:1]. After removal of the eluent in vacuo *rac*-**6a** was obtained as a colorless oil which became crystalline on standing (860 mg, 54%). For recording analytical data a sample was recrystallized from EtOAc/*n*-hexane.

rac-**6a**: M.p. 109-110 °C. TLC (silica gel, hexane/EtOAc = 2:1): R_f 0.18. UV [MeOH, λ_{max}, nm (ε, $Lmol^{-1}cm^{-1}$)]: 234 (17440), 272 (820), 280 (595). IR (KBr, $\tilde{\nu}_{max}$, cm^{-1}): 3330, 3130 (NH), 3050, 2975, 2940, 2840, 1715s (C=O), 1600, 1540, 1510, 1440, 1420, 1380, 1370, 1320, 1280, 1260, 1215s (C-O), 1170, 1060, 1020, 990, 980, 900, 895, 825, 795, 750, 695. ^{1}H NMR (270 MHz, $CDCl_3$): δ_H 1.28 [3H, s, H_3C-C(5)], 1.55-1.67 [1H, m, *H*HC(3)], 1.90-2.05 [1H, m, *H*HC(3)], 2.17-2.42 [2H, m, H_2C(2)], 2.26 [3H, s, H3C(7)], 3.03 [1H, m, HC(4)], 3.67 (3H, s, H_3C-O), 3.70 (3H, s, H_3C-O), 4.19 (1H, d, *J* = 11.3 Hz, *H*HC-OCO), 4.32 (1H, d, *J* = 11.3 Hz, H*H*C-OCO), 6.66 (1H, s, br, NH), 7.07 (1H, m, *p*-H), 7.26-7.37 (4H, m, phenyl ring). Microanalysis for $C_{19}H_{25}NO_7$ (379.41): calcd. C 60.14, H 6.64, N 3.69; found C 60.11, H 6.45, N 3.89.

Methyl (4*SR*,5*RS*)-4-methoxycarbonyl-5-methyl-5-(phenylcarbamoyloxy-methyl)-6-oxo-heptanoate (*rac*-**6b**). Carbamate *rac*-**5b (**990 mg, 3.4 mmol) was reacted as described for *rac*-**5a** to *rac*-**6a**. Yield of methyl heptanoate *rac*-**6b** (678 mg, 53%).

rac-**6b**: M.p. 89-91 °C. TLC (silica gel, hexane/EtOAc = 2:1): R_f 0.18. UV [MeOH, λ_{max}, nm (ε, $Lmol^{-1}cm^{-1}$)]: 235 (17700), 272 (823), 280 (600). IR (KBr, $\tilde{\nu}_{max}$, cm^{-1}): 3340, 3190, 3140 (NH), 3080, 3060, 3030, 2980, 2910, 1730s (C=O, ester, carbamate), 1705s (CO, ketone), 1605, 1550, 1505, 1490, 1440, 1360, 1320, 1230s (C-O), 1170, 1115, 1085, 1060, 1030, 1010, 905, 845, 825, 790, 755, 695. ^{1}H NMR (270 MHz, $CDCl_3$): δ_H 1.30 [3H, s, H_3C-C(5)], 1.84-1.92 [2H, m, H_2C(3)], 2.24-2.51 [2H, m, H_2C(2)], 2.24 [3H, s, H_3C(7)], 2.97 [1H, m, HC(4)], 3.67 (3H, s, H_3C-O), 3.68 (3H, s, H_3C-O), 4.30 (1H, d, *J* = 11.4 Hz, *H*HC-OCO), 4.37 (1H, d, *J* = 11.4 Hz, H*H*C-OCO), 6.82 (1H, s, br, NH), 7.07 (1H, m, *p*-H), 7.26-7.37 (4H, m, phenyl ring). Microanalysis for $C_{19}H_{25}NO_7$ (379.41): calcd. C 60.14, H 6.64, N 3.69; found C 59.93, H 6.48, N 3.61.

Methyl 3-[(3*SR,*4*RS*)-1-acetyl-4-methyl-5-methylene-2-oxo-4-(phenylcarbamoyloxy-methyl)-pyrrolidin-3-yl]-propionate (*rac*-**7a**). Ester *rac*-**6a** (129 mg, 0.34 mmol) and NaOAc (197 mg, 2.4 mmol) were dissolved in MeOH saturated with NH_3 (5.9 mL) and stirred in a sealed tube at rt for 14 h. MeOH was evaporated, saturated brine (10 mL) was added to the residue and the mixture was extracted seven times with CH_2Cl_2 (7 x 10 mL). The combined organic extracts were washed with saturated brine (15 mL) and dried with $MgSO_4$. After evaporation of the solvent the crude product was dissolved in CH_2Cl_2 (5 mL). 4-*N,N*-Dimethylamino-pyridine (DMAP) (62 mg, 0.5 mmol) and Ac_2O (0.18 mL, 2.0 mmol) were added and the mixture stirred at rt for 22 h. The reaction mixture was washed three times with saturated aqueous Na_2CO_3 (3 x 5 mL), saturated brine (10 mL) and, dried by filtration through cotton wool. After evaporation of the solvent, the residue was purified by column chromatography [SiO_2 (10 g), CH_2Cl_2/hexane/EtOAc = 10:3:2]. Crystallization of the main fraction from ether/*n*-hexane gave *rac*-**7a** as colorless needles (70 mg, 53%).

rac-**7a**: M.p. 118-120 °C. TLC (silica gel, CH_2Cl_2/hexane/EtOAc = 10:3:2): R_f 0.37. IR (KBr, $\tilde{\nu}_{max}$, cm^{-1}): 3520, 3390, 3320, 3210, 3150, 3105 (NH), 3040, 2980, 2970, 2930, 2890, 2860, 1755s (C=O), 1750s (C=O), 1695s (C=O), 1645, 1600, 1545, 1535, 1505, 1495, 1470, 1445, 1375, 1310, 1285, 1255, 1215, 1165, 1115, 1095, 1085, 1065, 1040, 995, 985, 950, 935, 915, 880, 860, 845, 820, 765, 690, 665, 650. ^{1}H NMR (270 MHz, CD_2Cl_2): δ_H 1.32 [3H, s, H_3C-C(4)], 1.83-2.06 [2H, m, H_2C(3´)], 2.44-2.84 [3H, m, H_2C(3´´), HC(3)], 2.50 [3H, s, H_3CCON(1)], 3.67 (3H, s, H_3CO), 4.09 [2H, "dd", 4´-H_2CO], 4.83 [1H, s, *H*HC=C(5)], 5.93 [1H, s, H*HC*=C(5)], 6.70 (1H, s, br, NH), 7.07 [1H, m, *p*-H(phenyl)], 7.26-7.38 [4H, m, *o,o´-*, *m,m´*-H (phenyl)]. ^{1}H NMR (600 MHz, $CDCl_3$): δ_H 1.34 [3H, s, H_3C-C(4)], 1.83-2.06 [2H, m, H_2C(3´)], 2.50 [1H, m, HC(3)], 2.55 [3H, s, H_3CCON(1´)], 2.66-2.84 [2H, m, H_2C-C(3´´)], 3.74 (3H, s, H_3CO), 4.12 [2H, "dd", 4´-H_2CO), 4.84 [1H, s, *H*HC=C(5)], 6.00 [1H, s, H*HC*=C(5)], 6.55 [1H, s, br, NH], 7.09 [1H, m, *p*-H(phenyl)], 7.26-7.38 (4H, m, *o,o´-, m,m´*- (phenyl ring)]. ^{13}C NMR ($CDCl_3$, 600 MHz): δ_C 19.9 [H_2C(3´)], 20.76

[4-CH_3], 27.23 [*C*H_3CON(1)], 32.02 [H_2C(3´´)], 44.51 [C(4)], 49.44 [C(3)], 51.93 [H_3CO], 69.37 [H_2C(4´)O], 97.93 [H_2*C*=C(5)], 124.04, 129.25 [*o,o´,m,m´´,p*-C -5x (phenyl)], 137.33 [phenyl-C], 146.85 [C(5)], 170.91, 173.63, 177.15, 177.18 [CO x 4]. EI-MS (70 eV, 150° C): *m/z* (%) 388 (29, M^+), 346 (32, M^+ - C_2H_2O), 315 (9, M^+ - $CH_2CO_2CH_3$), 238 (7, M^+ - CH_2OCONHPh), 197 (33), 196 (100, 346 – CH_2OCONHPh), 178 (23), 165 (31), 164 (63), 150 (16), 136 (12), 123 (20), 120 (16), 119 (17), 110 (40), 93 (23), 91 (11), 77 (17), 43 (32). Microanalysis for $C_{20}H_{24}N_2O_6$ (388.42): calcd. C 61.84, H 6.22, N 7.21; found C 61.76, H 6.45, N 7.32.

Methyl 3-[(3*SR*,4*SR*)-1-acetyl-4-methyl-5-methylene-2-oxo-4-(phenylcarbamoyloxy-methyl)-pyrrolidin-3-yl]-propionate (*rac*-**7b**). Ester *rac*-**6b** (127 mg, 0.33 mmol) was reacted as described for *rac*-**6a** to *rac*-**7a.** Yield of pyrrolidine *rac*-**7b** as crystalline solid (44 mg, 34%).

rac-**7b**: M.p. not determined. TLC (silica gel, CH_2Cl_2/hexane/EtOAc = 10:3:2): R_f 0.46. IR (Film, $\tilde{\nu}_{max}$, cm^{-1}): 3550, 3210, 3155 (NH), 3075, 3055, 3105, 2980, 2960, 1720s (C=O), 1750s (C=O), 1650, 1600, 1530, 1505, 1445, 1415, 1380, 1305, 1210, 1175, 1145, 1060, 1025, 995, 950, 895, 845, 755, 690. ^{1}H NMR (270 MHz, CD_2Cl_2): δ_H 1.18 [3H, s, H_3C-C(4)], 1.83-1.98 [2H, m, H_2C(3´)], 2.52 [3H, s, H_3CCON(1)], 2.52-2.78 [3H, m, H_2C(3´´), HC(3)], 3.65 (3H, s, H_3CO), 4.19 [2H, "dd", 4´-H_2CO], 4.79 [1H, s, *H*HC=C(5)], 5.92 [1H, s, H*HC*=C(5)], 6.93 [1H, s, br, NH], 7.07 [1H, m, *p*-H(phenyl)], 7.28-7.40 (4H, m, *o,o´*-, *m,m´*- (phenyl)]. EI-MS (70 eV, 200° C): *m/z* (%) 388 (29, M^+), 346 (30, M^+ - C_2H_2O, 315 (16, M^+ - $CH_2CO_2CH_3$), 238 (8, M^+ - CH_2OCONHPh), 197 (28), 196 (100, 346 – CH_2OCONHPh), 178 (19), 165 (31), 164 (54), 150 (14), 136 (17), 120 (11), 119 (50), 110 (53), 93 (11), 91 (18), 77 (11), 64 (8). Microanalysis for $C_{20}H_{24}N_2O_6$ (388.42): calcd. C 61.84, H 6.22, N 7.21; found C 61.78, H 6.34, N 7.09.

***t*-Butyl (2*R*)-2-[(1*R,*4*S*)-4-hydroxy-cyclopent-2-en-1-yl]-2-methyl-3-oxo-butanoate** (**10a**) and ***t*-butyl (2*S*)-2-[(1*R,*4*S*)-4-hydroxy-cyclopent-2-en-1-yl]-2-methyl-3-oxo-butanoate** (**10b**). To a suspension of NaH (1.26 g, 42 mmol) in THF (20 mL) was added dropwise at 0 °C a solution of *t*-butyl 2-methylacetoacetate **2** (7.23 g, 42 mmol) in THF (50 mL). After complete addition of **2**, the mixture was stirred at rt for 30 min. In a separate flask a solution of [(1*R,4S*)-4-hydroxy-cylopent-2-en-1-yl]-acetate (**9**) (4.97 g, 35.0 mmol; $[\alpha]_D^{20}$ +68.8, *c* = 1.3 in $CHCl_3$, ee > 99%) and $Pd[P(Ph)_3]_4$ (680 mg, 0,68 mmol) in THF (80 mL) was prepared. To this solution was added all at once the solution of deprotonated acetoacetate. The reaction mixture was stirred at rt for 90 min. An aqueous HCl (1N, 50 mL) was added to the reaction mixture and extracted twice with ether (75 mL and 25 mL). The combined organic extracts were washed with 1N aqueous HCl (50 mL) and saturated brine (50 mL). The extracts were dried over $MgSO_4$ and the solvent was evaporated. Flash chromatography [SiO_2 (250 g), hexane/EtOAc = 2:1] gave after removal of the eluent a mixture of diastereomers **10a**/**10b** (7.45 g, 84%). The ratio of diastereomers **10a**/**10b** was determined as 1:1.25 by HPLC (Nucleosil 50-10, *iso*-hexane/EtOAc = 10:6.6, 2 mL/min, RI detection). The mixture of diastereomers was separated by preparative HPLC [PrepPak 500, silica gel (Waters), *n*-hexane/EtOAc = 10:6.6] to give after bulb to bulb distillation (0.05 Torr/140 °C) single fractions of **10a** (2.49 g, 28%), **10b** (3.92 g, 44%) and **10a**,**b** (mixture 250 mg, 2.8%).

10a: $[\alpha]_D^{20}$ + 47.9, *c* = 1.567 in $CHCl_3$. CD: Θ (λ) - 612 (294 nm), (c 2.69 mg/mL, MeOH). UV [MeOH, λ_{max}, nm (ε, $Lmol^{-1}cm^{-1}$)]: 261sh (61.3), 286.4 (72.3). IR (Film, $\tilde{\nu}_{max}$, cm^{-1}): 3415 br (OH), 3050, 2970, 2930, 2865, 1710s (C=O), 1460, 1395, 1370, 1250 and 1155s (C-O), 1125, 1070, 1045, 1015, 905, 775, 750. ^{1}H NMR (270 MHz, $CDCl_3$): δ_H 1.26 [3H, s, H_3C-C(2)], 1.26-1.38 [1H, m, *H*HC(5´)], 1.45 (9H, s, *t*-Bu), 1.81 (1H, s, OH, exchangeable by D_2O), 2.16 [3H, s, H_3C(4), acyl], 2.43 [1H, "dt", J_{gem} = 14.0 Hz, J_{vic} = 8.1 Hz, *H*HC(5´)], 3.30 [1H, m, HC(1`)], 4.80 [1H, m, HC(4´)], 5.84 [2H, m, HC(2´) and HC(3´)]. Microanalysis for $C_{14}H_{22}O_4$ (254.32): calcd. C 66.11, H 8.71; found C 66.21, H 8.63.

10b: $[\alpha]_D^{20}$ - 45.6, c = 1.846 in $CHCl_3$. CD: Θ (λ) - 3449 (291 nm), (c 2.69 mg/mL, MeOH). UV [MeOH, λ_{max}, nm (ε, $Lmol^{-1}cm^{-1}$)]: 262sh (60.3), 288 (60.0). IR (Film, $\tilde{\nu}_{max}$, cm^{-1}): 3415 br (OH), 3050, 2970, 2925, 2865, 1710s (C=O), 1460, 1395, 1370, 1250s (C-O), 1215, 1160s (C-O), 1110, 1065, 1040, 1015, 960, 900, 870, 840, 780, 745. ^{1}H NMR (270 MHz, $CDCl_3$): δ_H 1.25 [3H, s, H_3C-C(2)], 1.40-1.49 [1H, m, *H*HC(5´)], 1.46 (9H, s, *t*-Bu), 1.98 (1H, s, OH,

exchangeable by D_2O), 2.16 [3H, s, H_3C(4), acyl], 2.45 [1H, "dt", J_{gem} = 13.9 Hz, J_{vic} = 8.2 Hz, *H*HC(5´)], 3.30 [1H, m, HC(1´)], 4.80 [1H, m, HC(4´)], 5.78, 5.87 [2H, 2 m, HC(2´) and HC(3´)]. Microanalysis for $C_{14}H_{22}O_4$ (254.32): calcd. C 66.11, H 8.71; found C 65.99, H 8.56.

***t*-Butyl (2*R*)-2-[(1*R,4S*)-4-*iso*-butyloxycarbonyloxy-cyclopent-2-en-1-yl]-2-methyl-3-oxo-butanoate** (**11a**). To a solution of butanoate **10a** (520 mg, 2.0 mmol) and pyridine (0.22 mL, 2.6 mmol) in CH_2Cl_2 (10 mL) was added dropwise a solution of *iso*-butyl chloroformate (0.34 mL, 2.6 mmol) in CH_2Cl_2 (5 mL) at 0 °C. The reaction mixture was stirred at rt for 2.5 h and then washed with 1N HCl (10 mL), saturated aqueous Na_2CO_3 (10 mL) and saturated brine (10 mL). The organic layer was dried over Na_2SO_4 and the solvent evaporated. The residue was purified by flash chromatography [SiO_2 (80 g), hexane/ether = 2:1] and bulb to bulb distillation (0.5 Torr/150 °C) to yield *rac*-**11a** (630 mg, 89%).

11a: TLC (silica gel, hexane/ether = 3:1): R_f 0.38. $[\alpha]_D^{20}$ + 26.6, *c* = 1.240 in $CHCl_3$. IR (Film, $\tilde{\nu}_{max}$, cm^{-1}): 3060, 2955, 2925, 2865, 1740s (C=O, ester), 1710s (C=O, ketone), 1460, 1395, 1380, 1365, 1345, 1300, 1250s (C-O), 1155, 1125, 1110, 1090, 1065, 1045, 970, 945, 905, 865, 845, 790, 755. ^{1}H NMR (270 MHz, $CDCl_3$): δ_H 0.94 (6H, d, *J* = 6 Hz, H_3C, *i*-Bu), 1.20 [3H, s, H_3C-C(2)], 1.39-1.48 [1H, m, *H*HC(5´)], 1.45 (9H, s, *t*-Bu), 1.89-2.03 (1H, m, HC, *i*-Bu), 2.15 [3H, s, H_3C(4), acyl], 2.53 [1H, "dt", J_{gem} = 14.5 Hz, J_{vic} = 8.2 Hz, *H*HC(5´)], 3.41 [1H, m, HC(1`)], 3.89 (1H, d, *J* = 6.7 Hz, H_2CO-, *i*-Bu), 5.55 [1H, m, HC(4´)], 5.88, 5.98 [2H, m, HC(2´) and HC(3´)]. Microanalysis for $C_{19}H_{30}O_6$ (354.44): calcd. C 64.38, H 8.53; found C 64.20, H 8.56.

***t*-Butyl (*2S*)-2-[(1*R,4S*)-4-*iso*-butyloxycarbonyloxy-cyclopent-2-en-1-yl]-2-methyl-3-oxo-butanoate** (**11b**). Butanoate **11b** (765 mg, 3.0 mmol) was reacted as described for **10a** to **11a.** Yield of carbonate **11b** after bulb to bulb distillation (0.45 Torr/140 °C) (990 mg, 93%).

11b: TLC (silica gel, hexane/ether = 3:1): R_f 0.38. $[\alpha]_D^{20}$ - 62.2, *c* = 1.362 in $CHCl_3$. IR (Film, $\tilde{\nu}_{max}$, cm^{-1}): 3060, 2955, 2915, 2865, 1740s (C=O, ester), 1710s (C=O, ketone), 1460, 1395, 1380, 1365, 1345, 1300, 1250s (C-O), 1215, 1160, 1110, 1045, 970, 945, 905, 870, 840, 790, 750. ^{1}H NMR (270 MHz, $CDCl_3$): δ_H 0.94 (6H, d, *J* = 6.8 Hz, H_3C, *i*-Bu), 1.20 [3H, s, H_3C-C(2)], 1.45 (9H, s, *t*-Bu), 1.52-1.61 [1H, m, *H*HC(5´)], 1.89-2.04 (1H, m, HC, *i*-Bu), 2.15 [3H, s, H_3C(4), acyl], 2.53 [1H, "dt", J_{gem} = 14.6 Hz, J_{vic} = 8.3 Hz, *H*HC(5´)], 3.42 [1H, m, HC(1`)], 3.90 (1H, d, *J* = 6.6 Hz, H_2CO-, *i*-Bu), 5.56 [1H, m, HC(4´)], 5.86, 5.95 [2H, m, HC(2´) and HC(3´)]. Microanalysis for $C_{19}H_{30}O_6$ (354.44): calcd. C 64.38, H 8.53; found C 64.29, H 8.41.

***t*-Butyl (2*R*)-2-[(1*R*)-cyclopent-2-en-1-yl]-2-methyl-3-oxo-butanoate** (**3a**) and ***t*-butyl (2*R*)-2-(cyclopent-3-en-1-yl)-2-methyl-3-oxo-butanoate** (**12**). Disodium hydrogen phosphate (1.80 g, 12.8 mmol) was suspended in a solution of carbonate **11a** (1.14 g, 3.2 mmol) and polymethyl hydrosiloxane (450 mg) in THF (25 mL). $Pd[P(Ph)_3]_4$ (74 mg, 0.064 mmol) was added and the mixture was stirred at rt for 3.5 h. After filtration of the reaction mixture, the solvent was evaporated and the residue filtered with CH_2Cl_2 over silica gel (55 g) for removal of polymethyl hydrosiloxane. After evaporation of CH_2Cl_2 the residue was purified by column chromatography [SiO_2 (80 g), hexane/ether = 3:1] to yield a mixture of isomers **3a** and **12** (755 mg, 98%). The ratio of isomers was determined by ^{1}H NMR as **3a**/**12** = 1.6:1 (2 s at 1.16 and 1.23). Separation of the isomers was performed in the next step.

TLC (silica gel, hexane/ether = 3:1): R_f 0.54. ^{1}H NMR (270 MHz, $CDCl_3$) δ_H 1.16 [3H, s, H_3C-C(2), **3a**], 1.23 [3H, s, H_3C-C(2), **12**], 1.44 (9H, s, *t*-Bu, **3a, 12**), 1.37-1.50]1H, m, *H*HC(5´), **3a**], 1.88-2.02 [1H, m, *H*HC(5´) **3a**], 1.99 -2.12 [2H, m, *H*HC(2´), **12**], 2.15 (3H, s, acyl, **3a**, **12**), 2.15 - 2.32 (2H, m, H_2C, **3a**,**12**), 2.39 – 2.58 [2H, m, *H*HC(2´), **12**], 3.00 [1H, m, H(C1´), **12**], 3.50 [1H, m, H(C1´), **3a**], 5.63 [3H, m, H(C2´) or H(C3´), **3a**, H(C2´) and H(C3´), **12**], 5.80 [1H, m, H(C3´) or H(C2´), **3a**].

***t*-Butyl (2*S*)-2-[(1*R*)-cyclopent-2-en-1-yl]-2-methyl-3-oxo-butanoate** (**3b**) and ***t*-butyl (2S)-2-(cyclopent-3-en-1-yl)-2-methyl-3-oxo-butanoate** (*ent*-**12**). Disodium hydrogen phosphate (1.47 g, 10.4 mmol) was suspended in a solution of carbonate **11b** (922 mg, 2.6 mmol) and polymethyl hydrosiloxane (440 mg) in THF (20 mL).

$Pd[P(Ph)_3]_4$ (60 mg, 0.052 mmol) was added and the mixture was stirred at rt for 3 h. After filtration of the reaction mixture, the solvent was evaporated and the residue dissolved in CH_2Cl_2 was filtered over silica gel (50 g) for removal of polymethyl hydrosiloxane. After evaporation of CH_2Cl_2 the residue was purified by column chromatography [SiO_2 (50 g), hexane/ether = 3:1] to yield a mixture of isomers **3b** and *ent*-**12** (570 mg, 92%). The ratio of isomers was determined by ^{1}H NMR as **3b**/*ent*-**12** = 1.7:1 (2 s at 1.17 and 1.23). Separation of the isomers 570 mg (plus 450 mg from another batch) was performed by preparative HPLC [PrepPak 500 silica gel (Waters), *n*-hexane/EtOAc = 10:0.25] to give after bulb to bulb distillation pure fractions (15 Torr/140 °C) of **3b** (427 mg), of *ent*-**12** (224 mg) and **3b**/**12** (mixture, 120 mg).

3b: for TLC, IR- and ^{1}H NMR spectra see *rac*-**3b**. $[\alpha]_D^{20}$ +30.4, *c* = 2.731 in $CHCl_3$. Microanalysis of $C_{14}H_{22}O_3$ (238.32): calcd. C 70.55, H 9.30; found C 70.68, H 9.22.

ent-**12**: TLC (silica gel, hexane/ether = 3:1): R_f 0.54. $[\alpha]_D^{20}$ -24.1, *c* = 1.641 in $CHCl_3$. IR (Film, $\tilde{\nu}_{max}$, cm^{-1}): 3030, 2970, 2930, 2850, 1740s (C=O, ester), 1715s (C=O), 1625, 1455, 1370, 1255s (C-O), 1155s (C-O), 1110, 1110, 895, 845, 690. ^{1}H NMR (270 MHz, $CDCl_3$): δ_H 1.23 [3H, s, H_3C-C(2)], 1.44 (9H, s, *t*-Bu), 1.99 - 2.12 [2H, m, *H*HC(2´) and C(5´)], 2.15 [3H, s, H_3C(4), acyl], 2.15 – 2.29 [2H, *H*HC(2´)and C(5´)], 3.00 [1H, m, HC(1´)], 5.63 [2H, m, HC(3´) and HC(4´)]. Microanalysis of $C_{19}H_{30}O_6$ (238.2): calcd. C 70.55, H 9.30; found C 70.71, H 9.19.

(3*S*)-3-[(1*R*)-Cyclopent-2-en-1-yl]-4-hydroxy-3-methyl-butan-2-on (**4a**) and **(3*S*)-3-[Cyclopent-3-en-1-yl]-4-hydroxy-3-methyl-butan-2-on** (**4c**). A mixture of **3a** and **12** (1.6:1, 1.06 g, 4.4 mmol) was reacted and worked up as described for *rac*-**3a** to *rac*-**4a.** A mixture of **4a** and **4c** was obtained (590 mg, 80%). Separation of the mixture of isomers 590 mg was performed by preparative HPLC [PrepPak 500 silica gel (Waters), *iso*-hexane/EtOAc = 10:6.66] and gave after bulb to bulb distillation pure fractions (0.1 Torr/145 °C) of **4a** (229 mg, 31%), of **4c** (93 mg, 12.5%).

4a: for TLC, IR- and ^{1}H NMR spectra see *rac*-**4a**. $[\alpha]_D^{20}$ +52.3, *c* = 1.350 in $CHCl_3$. Microanalysis of $C_{10}H_{16}O_2$ (168.23): calcd. C 71.39, H 9.58; found C 71.25, H 9.46.

4c: TLC (silica gel, hexane/EtOAc = 1:1): R_f 0.37. $[\alpha]_D^{20}$ - 15.2, *c* = 0.721 in $CHCl_3$. IR (Film, $\tilde{\nu}_{max}$, cm^{-1}): 3400br (OH), 3020, 2910, 2845, 1690s (C=O), 1620, 1455, 1355, 1265, 1220, 1185, 1150, 1100, 1035, 965, 935 835, 695. ^{1}H NMR (270 MHz, $CDCl_3$): δ_H 1.16 [3H, s, H_3C-C(2)], 2.01 - 2.23 [3H, m, *H*HC(2´, 5´) and OH exchangeable by D_2O], 2.19 [3H, s, H_3C(4), acyl], 2.26 – 2.43 [2H, m, *H*HC(2´, 5´)], 2.67 [1H, m, HC(1´)], 3.46 [1H, d, *J* = 11.3 Hz, *H*HCOH), 3.82 [1H, d, *J* = 11.3 Hz, H*H*COH), 5.66 [2H, m, HC(3´) and HC(4´)]. Microanalysis for $C_{10}H_{16}O_2$ (168.23): calcd. C 71.39, H 9.58; found C 71.26, H 9.57.

(3*R*)-3-[(1*R*)-Cyclopent-2-en-1-yl]-4-hydroxy-3-methyl-butan-2-on (**4b**). Ketoester **3b** (348 mg, 1.46 mmol) was reacted as described for *rac*-**3a** to *rac*-**4a.** Yield of alcohol **4b** (156 mg, 63%).

4b: for TLC, IR- and ^{1}H NMR spectra see *rac*-**4b**. $[\alpha]_D^{20}$ +113.3, *c* = 1.236 in $CHCl_3$. Microanalysis for $C_{10}H_{16}O_2$ (168.23): calcd. C 71.39, H 9.58; found C 71.21, H 9.47.

***t*-Butyl (2*R*)-2-methyl-3-oxo-2-[(1*R,*4*R*)-4-phenylsufanyl-cyclopent-2-en-1-yl]-butanoate** (**13a**). To a solution of alcohol **10a** (2.93 g, 6.3 mmol) and diphenyl disulfide (2.93 g, 13.3 mmol) was added tributyl phosphine (3.38 mL, 13.3 mmol) at rt. After stirring the mixture at rt for 5 h, ether (70 mL) was added and the solution was washed three times with 2N NaOH (3 x 25 mL), three times with 2N HCl (3 x 25 mL) and saturated brine (35 mL). The organic layer was dried over $MgSO_4$ and the solvent was evaporated under reduced pressure. Flash chromatography [SiO_2 (250 g), hexane/EtOAc = 10:1] gave phenyl thioether **13a** (2.01 g, 92%).

13a: TLC (silica gel, hexane/EtOAc = 10:1): R_f 0.32. $[\alpha]_D^{20}$ + 180.1, *c* = 1.479 in $CHCl_3$. CD: Θ (λ) - 2628 (246.5), + 4608 (263 nm), (c 0.07782 mg/mL, MeOH). UV [MeOH, λ_{max}, nm (ε, $Lmol^{-1}cm^{-1}$)]: 255 (5971). IR (Film, $\tilde{\nu}_{max}$, cm^{-1}): 3055, 2970, 2930, 2865, 1740s (C=O, ester), 1710s (C=O, ketone), 1590, 1485, 1460, 1440, 1395, 1370, 1325, 1255s (C-O), 1210, 1155, 1115, 1065, 1025, 975, 960, 945, 900, 840, 770, 735, 690. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.15 [3H, s, H_3C-C(2)], 1.43 (9H, s, *t*-Bu), 1.91 – 2.18 [2H, m, H_2C(5´)], 2.12 [3H, s, H_3C(4), acyl], 3.53 [1H, m,

HC(1´)], 4.23 [1H, m, HC(4´)], 5.82 [2H, m, HC(2´) and HC(3´)], 7.19 – 7.31 [3H, m, *p*- and *m*-phenyl] 7.35 – 7.39 [2H, m, *o*-phenyl]. Microanalysis for $C_{20}H_{26}O_3S$ (346.48): calcd. C 69.33, H 7.56, S 9.25; found C 69.28, H 7.53, S 9.43.

***t*-Butyl (2*S*)-2-methyl-3-oxo-2-[(1*R,4R*)-4-phenylsulfanyl-cyclopent-2-en-1-yl]-butanoate** (**13b**). Alcohol **10b** (2.85 g, 11.2 mmol) was reacted as described for **10a** to **13a.** Yield of phenyl thioether **13b** (3.46 g, 89%).

13b: TLC (silica gel, hexane/EtOAc = 10:1): R_f 0.32. $[\alpha]_D^{20}$ + 147.4, *c* = 1.377 in $CHCl_3$. CD: Θ (λ) - 2374 (285), -2724 (292), 2078 (300 nm), (c 0.19334 mg/mL, MeOH). UV [MeOH, λ_{max}, nm (ε, $Lmol^{-1}cm^{-1}$)]: 219sh (10873), 256 (5740). IR (Film, $\tilde{\nu}_{max}$, cm^{-1}): 3060, 2985, 2935, 2870, 1740s (C=O, ester), 1715s (C=O, ketone), 1590, 1485, 1460, 1430, 1395, 1370, 1255s (C-O), 1215, 1160, 1115, 1065, 1025, 950, 840, 775, 740, 690. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.15 [3H, s, H_3C-C(2)], 1.43 (9H, s, *t*-Bu), 2.08 – 2.15 [2H, m, H_2C(5´)], 2.12 [3H, s, H_3C(4), acyl], 3.50 [1H, m, HC(1´)], 4.24 [1H, m, HC(4´)], 5.71 [1H, m, HC(2´) or HC(3´)], 5.84 [1H, m, HC(2´) or HC(3´)], 7.19 – 7.31 [3H, m, *p*- and *m*-phenyl] 7.36 – 7.40 [2H, m, *o*-phenyl]. Microanalysis for $C_{20}H_{26}O_3S$ (346.48): calcd. C 69.33, H 7.56, S 9.25; found C 69.40, H 7.57, S 9.37.

(3*S*)-4-Hydroxy-3-methyl-3-[(1*R,4R*)-4-phenylsulfanyl-cyclopent-2-en-1-yl]-butan-2-on (**14a**). Ketoester **13a (**1.95 g, 5.6 mmol) was reacted as described for *rac*-**3a** to *rac*-**4a.** Flash chromatography [SiO_2 (150 g), hexane/EtOAc = 1.5:1] gave alcohol **14a** (1.28 g, 83%).

14a: TLC (silica gel, hexane/EtOAc = 1.5:1): R_f 0.25. $[\alpha]_D^{20}$ + 169.7, *c* = 1.499 in $CHCl_3$. CD: Θ (λ) - 2842 (243.0), + 4297 (263.4 nm), (c 0.06303 mg/mL, MeOH). UV [MeOH, λ_{max}, nm (ε, $Lmol^{-1}cm^{-1}$)]: 256 (6181). IR (Film, $\tilde{\nu}_{max}$, cm^{-1}): 3445 (OH), 3055, 2970, 2930, 2875, 1695s (C=O), 1585, 1480, 1440, 1355, 1240, 1210, 1090, 1040, 960, 935, 780, 735, 685. ^{1}H NMR (270 MHz, $CDCl_3$): δ_H 1.11 [3H, s, H_3C-C(3)], 1.97 (1H, s br, HO, exchangeable with D_2O), 2.05 [2H, m, H_2C(5´)], 2.14 [3H, s, H_3C(1), acyl], 3.15 [1H, m, HC(1´)], 3.48 [1H, d, *J* = 11.3 Hz, *H*HCOH], 3.80 [1H, d, *J* = 11.3 Hz, H*H*COH], 4.26 [1H, m, HC(4´)], 5.77, 5.82 [2H, 2 m, HC(2´) and HC(3´)], 7.20 – 7.32 [3H, m, *p*- and *m*-phenyl] 7.35 – 7.40 [2H, m, *o*-phenyl]. Microanalysis for $C_{16}H_{20}O_2S$ (276.39): calcd. C 69.53, H 7.29, S 11.60; found C 69.30, H 7.33, S 11.75.

(3*R*)-4-Hydroxy-3-methyl-3-[(1*R,4R*)-4-phenylsulfanyl-cyclopent-2-en-1-yl]-butan-2-on (**14b**). Ketoester **13b** (3.81 g, 10.9 mmol) was reacted as described for *rac*-**3a** to *rac*-**4a.** Flash chromatography [SiO_2 (250 g), hexane/EtOAc = 1.5:1] gave alcohol **14b** (2.28 g, 76%).

14b: TLC (silica gel, hexane/EtOAc = 1.5:1): R_f 0.25. $[\alpha]_D^{20}$ + 214.1, *c* = 1.054 in $CHCl_3$. CD: Θ (λ) - 3594 (243.6), + 2034 (257.5 nm), - 2154 (292 nm), (c 0.06303 mg/mL, MeOH). UV [MeOH, λ_{max}, nm (ε, $Lmol^{-1}cm^{-1}$)]: 256 (6347). IR (Film, $\tilde{\nu}_{max}$, cm^{-1}): 3455 (OH), 3065, 2975, 2940, 2885, 1695s (C=O), 1590, 1485, 1445, 1360, 1250, 1215, 1095, 1045, 1030, 890, 785, 740, 695. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.15 [3H, s, H_3C-C(3)], 1.94 – 2.19 [3H, m, H_2C(5´) and HO, exchangeable with D_2O], 2.16 [3H, s, H_3C(1), acyl], 3.21 [1H, m, HC(1´)], 3.42 [1H, dd, J_{gem} = 11.3 Hz, J_{vic} = 6.3 Hz, *H*HCOH], 3.74 [1H, dd, J_{gem} = 11.3 Hz, J_{vic} = 6.3 Hz, *H*HCOH], 4.29 [1H, m, HC(4´)], 5.73, 5.89 [2H, 2 m, HC(2´) and HC(3´)], 7.20 – 7.31 [3H, m, *p*- and *m*-phenyl] 7.32 – 7.39 [2H, m, *o*-phenyl]. Microanalysis for $C_{16}H_{20}O_2S$ (276.39): calcd. C 69.53, H 7.29, S 11.60; found C 69.47, H 7.19, S 11.67.

(3*S*)-3-Methyl-4-phenyl-carbamoyloxy-3-[(1*R,4R*)-4-phenylsulfanyl-cyclopent-2-en-1-yl]-butan-2-on (**15a**). Butanon **14a** (1.48 g, 5.3 mmol) was reacted as described for *rac*-**4a** to *rac*-**5a.** Column chromatography [SiO_2 (100 g), CH_2Cl_2/EtOAc = 20:1] gave carbamate as a yellow oil which after crystallization from EtOAc/*n*-hexane yielded **15a** (1.95 g, 92%).

15a: M.p. 123-124 °C. TLC (silica gel, hexane/EtOAc = 2:1): R_f 0.43. $[\alpha]_D^{20}$ + 148.5, *c* = 1.007 in $CHCl_3$. CD: Θ (λ) + 3706 (263.5 nm), (c 0.1174 mg/mL, MeOH). UV [MeOH, λ_{max}, nm (ε, $Lmol^{-1}cm^{-1}$)]: 232 (22212), 255 (6333). IR (Film, $\tilde{\nu}_{max}$, cm^{-1}): 3755 (NH), 3055, 3005, 2950, 2920, 2890, 1700s (C=O), 1600, 1530, 1480, 1445, 1385, 1325, 1315, 1310, 1230, 1205, 1155, 1110, 1080, 1065, 1025, 940, 895, 785, 775, 765, 740, 690. ^{1}H NMR (270 MHz, $CDCl_3$): δ_H 1.06 [3H, s, H_3C-C(3)], 2.00 – 2.09 [2H, m, H_2C(5´)], 2.16 [3H, s, H_3C(1), acyl], 3.17 [1H, m, HC(1´)], 4.23

[1H, d, *J* = 11.0 Hz, *H*HCOR], 4.25 [1H, m, HC(4´)], 4.35 [1H, d, *J* = 11.0 Hz, H*H*COR], 5.76, 5.91 [2H, 2 m, HC(2´) and HC(3´)], 7.07 [1H, m, *p*-phenyl carbamate] 7.21 – 7.39 [9H, m, *o-, m-, p*-phenyl carbamate and thioether]. Microanalysis for $C_{23}H_{25}NO_3S$ (395.51): calcd. C 69.84, H 6.37, N 3.54, S 8.10; found C 69.88, H 6.36, N 3.47, S 7.96.

(3*R*)-3-Methyl-4-phenyl-carbamoyloxy-3-[(1*R,4R*)-4-phenylsulfanyl-cyclopent-2-en-1-yl]-butan-2-on (**15b**). Butanon **14b** 1.84 g, 6.6 mmol) was reacted as described for *rac*-**4a** to *rac*-**5a.** Column chromatography [SiO_2 (260 g), CH_2Cl_2/EtOAc = 20:1] gave carbamate as a pale yellow oil **15b** (1.95 g, 92%).

15b: TLC (silica gel, hexane/EtOAc = 2:1): R_f 0.43. $[\alpha]_D^{20}$ + 130.4, *c* = 0.7333 in $CHCl_3$. CD: Θ (λ) - 1206 (286.5), - 1338 (292.3), - 1023 ((303), (c 0.25278 mg/mL, MeOH). UV [MeOH, λ_{max}, nm (ε, $Lmol^{-1}cm^{-1}$)]: 232 (23489), 255 (6765). IR (Film, $\tilde{\nu}_{max}$, cm^{-1}): 3315 (NH), 3295, 3235, 3055, 2970, 2940, 1705s (C=O), 1600, 1525, 1505, 1480, 1445, 1360, 1315, 1215s (C-O), 1175, 1155, 1105, 1070, 1055, 1025, 995, 910, 895, 850, 750, 690. ^{1}H NMR (270 MHz, $CDCl_3$): δ_H 1.09 [3H, s, H_3C-C(3)], 2.04 – 2.14 [2H, m, H_2C(5´)], 2.17 [3H, s, H_3C(1), acyl], 3.19 [1H, m, HC(1´)], 4.19 [1H, d, *J* = 11.0 Hz, *H*HCOR], 4.26 [1H, m, HC(4´)], 4.29 [1H, d, *J* = 11.0 Hz, H*H*COR], 5.68, 5.89 [2H, 2 m, HC(2´) and HC(3´)], 6.60 (1H s br, NH), 7.07 [1H, m, *p*-phenyl carbamate] 7.20 – 7.40 [9H, m, *o-, m-, p*-phenyl carbamate and thioether]. Microanalysis for $C_{23}H_{25}NO_3S$ (395.51): calcd. C 69.84, H 6.37, N 3.54, S 8.10; found C 69.72, H 6.35, N 3.51, S 7.92.

(3*S*)-3-Methyl-4-phenyl-carbamoyloxy-3-[(1*R,4R*)-4-phenylsulfonyl-cyclopent-2-en-1-yl]-butan-2-on (**16a**). To carbamate **15a** (1.69 g, 4.2 mmol) in $CHCl_3$ (55 mL) was added dropwise during 70 min at – 20 °C a solution of *m*-chlorobenzoic acid (3.04 g, 9.6 mmol) in $CHCl_3$ (25 mL). The mixture was stored overnight at – 17 °C in a freezer. An aqueous solution of sodium bisulfite (20%, 8 mL) was added. The organic layer was separated and washed three times with saturated aqueous sodium carbonate (3 x 20 mL). The combined aqueous phases were extracted twice with $CHCl_3$ (2 x 10 mL), the combined organic extracts were dried over $MgSO_4$ and the solvent was evaporated. The residue was purified by column chromatography [SiO_2 (170 g), hexane/EtOAc = 1.25: 1] to yield sulfone **16a** as an oil (1.70 g, 95%). Crystallization from EtOAc/*n*-hexane gave **16a** as colorless needles (1.62 g, 90%).

16a: M.p. 133.5 -135 °C. TLC (silica gel, hexane/EtOAc = 1.25:1): R_f 0.43. $[\alpha]_D^{20}$ + 175.0, *c* = 0.6194 in $CHCl_3$. CD: Θ (λ) – 1614 (259), - 2888 (265.5), -2233 (272.3 nm), (c 0.1732 mg/mL, MeOH + trace $CHCl_3$). UV [MeOH + trace $CHCl_3$, λ_{max}, nm (ε, $Lmol^{-1}cm^{-1}$)]: 233 (20309), 258 (1430), 265 (1813), 272 (1765), 279 (662 sh). IR (KBr, $\tilde{\nu}_{max}$, cm^{-1}): 3385 (NH), 3070, 2995, 2980, 2925, 2915, 1715s, 1705s (C=O), 1605, 1530, 1480, 1450, 1390, 1370, 1315, 1230, 1210, 1180, 1145, 1115, 1085, 1065, 1030, 990, 945, 895, 845, 790, 780, 745, 715, 685, 660. ^{1}H NMR (270 MHz, $CDCl_3$): δ_H 1.03 [3H, s, H_3C-C(3)], 1.89 – 1.93 [1H, m, *H*HC(5´)], 2.15 [3H, s, H_3C(1), acyl], 2.35 – 2.45 [1H, m, H*H*C(5´)], 3.16 [1H, m, HC(1´)], 4.20 [1H, d, *J* = 11.2 Hz, *H*HCOR], 4.24 [1H, m, HC(4´)], 4.30 [1H, d, *J* = 11.2 Hz, H*H*COR], 5.77, 6.05 [2H, 2 m, HC(2´) and HC(3´)], 6.61 [1H, s br, NH], 7.08 [1H, m, *p*-phenyl carbamate] 7.26 – 7.38 [4H, m, *o-, m*-phenyl carbamate], 7.52 – 7.68 [3H, m, *m-, p*-phenyl sulfone], 7.85 – 7.89 [2H, m, *o*-phenyl sulfone]. Microanalysis for $C_{23}H_{25}NO_5S$ (427.51): calcd. C 64.62, H 5.89, N 3.27, S 7.49; found C 64.55, H 5.83, N 3.21, S 7.39.

(3*R*)-3-Methyl-4-phenyl-carbamoyloxy-3-[(1*R,4R*)-4-phenylsulfonyl-cyclopent-2-en-1-yl]-butan-2-on (**16b**). Carbamate **15b (**2.11 g, 5.3 mmol) was reacted as described for **15a** to **16a**. Flash chromatography [SiO_2 (210 g), hexane/EtOAc = 1.25:1] gave sulfone **16b** as a pale yellow oil (2.11 g, 93%).

16b: TLC (silica gel, hexane/EtOAc = 1.25:1): R_f 0.28. $[\alpha]_D^{20}$ + 174.1, *c* = 1.0043 in $CHCl_3$. CD: Θ (λ) – 1189 (259.2), - 2321 (265.2), -2224 (272 nm), (c 0.1776 mg/mL, MeOH). UV [MeOH, λ_{max}, nm (ε, $Lmol^{-1}cm^{-1}$)]: 222 (17484), 233 (19154), 258 (1361), 264 (1738), 272 (1656), 280 (605 sh). IR (KBr, $\tilde{\nu}_{max}$, cm^{-1}): 3555, 3360, 3325 (NH), 3165, 3095, 2995, 2985, 1745s, 1720s (C=O), 1620, 1545, 1465, 1450, 1375, 1325, 1235, 1195, 1155, 1095, 1075, 1045, 1010, 945, 915, 860, 770, 755, 735, 705. ^{1}H NMR (270 MHz, $CDCl_3$): δ_H 1.05 [3H, s, H_3C-C(3)], 1.92 – 2.04 [1H, m,

*H*HC(5´)], 2.16 [3H, s, H_3C(1), acyl], 2.38 – 2.48 [1H, m, H*H*C(5´)], 3.17 [1H, m, HC(1´)], 4.18 [1H, d, *J* = 11.2 Hz, *H*HCOR], 4.23 [1H, d, *J* = 11.2 Hz, H*H*COR], 4.28 [1H, m, HC(4´)], 5.73, 5.97 [2H, 2 m, HC(2´) and HC(3´)], 6.78 [1H, s br, NH], 7.08 [1H, m, *p*-phenyl carbamate] 7.26 – 7.38 [4H, m, *o-, m*-phenyl carbamate], 7.53 [2H, m, *m*-phenyl sulfone], 7.65 [1H, m, *p*-phenyl sulfone], 7.86 [2H, m, *o*-phenyl sulfone]. Microanalysis for $C_{23}H_{25}NO_5S$ (427.51): calcd. C 64.62, H 5.89, N 3.27, S 7.49. found: though correct structure and "purity" of **17b** could be confirmed by spectroscopic analysis and HPLC (Nucleosil 50-10, *iso*-hexane/EtOAc = 10:6.7), elemental analysis did not give a correct C value.

Methyl (4*S*,5*S*)-4-methoxycarbonyl-5-methyl-5-(phenylcarbamoyloxy-methyl)-6-oxo-heptanoate (**6a**) and **methyl (*S*)-3-(methoxycarbonyl-methyl)-4-methyl-5-oxo-4-(phenylcarbamoyloxy-methyl)-hexanoate** (**18**). To a solution of sulfone **16a** (2.05 g, 4.8 mmol) in MeOH (125 mL) was added Na/Hg (20.5 g, 5% Na) over 10 min and the mixture was stirred at rt for 2 h. The reaction mixture was poured into saturated brine (80 mL), 1N hydrochloric acid was added and the mixture was extracted four times with ether (4 x 80 mL). The combined organic extracts were washed with saturated brine (100 mL), dried over $MgSO_4$ and the solvent evaporated. Column chromatography [SiO_2 (130 g), hexane/EtOAc = 2:1] gave a mixture of (3*S*)-3-[(1*R*)-cyclopent-2-en-1-yl]-3-methyl-4-phenyl-carbamoyloxy-butan-2-on (**5a**) and (3*S*)-3-[cyclopent-3-en-1-yl]-3-methyl-4-phenyl-carbamoyloxy-butan-2-on (**17**) (1.19 g, 86%). TLC (silica gel, CH_2Cl_2/hexane/EtOAc = 10:6:1): R_f 0.44. The ratio of **5a**/**17** was determined by ^{1}H NMR as 1.1:1. The mixture of **5a**/**17** (1.19 g, 4.1 mmol) was reacted in the next reaction step without further separation and characterization as described for *rac*-**5a** to *rac*-**6a.** Flash chromatography [SiO_2 (95 g), hexane/EtOAc = 2:1] gave a mixture (880 mg, 57%) of the isomers **6a** and **18** in a ratio of 1.2:1. The ratio was determined by HPLC (Nucleosil 50-10, *iso*-hexane/EtOAc = 10:5.5, 2 mL/min, RI detection). Preparative HPLC [PrepPak 500 silica gel (Waters), *iso*-hexane/EtOAc = 10:0.25] gave **6a** (401 mg, 26%) and **18** (356 mg, 23%).

6a: TLC (silica gel, hexane/EtOAc = 2:1): R_f 0.18. $[\alpha]_D^{20}$ + 30.0, *c* = 0.6826 in $CHCl_3$. Analytical, physical and spectroscopic data were identical with those of *rac*- **6a**.

18: Analytical, physical and spectroscopic data were identical to those reported for *ent*-**18** (see subsequent procedure).

Methyl (4*S*,5*R*)-4-methoxycarbonyl-5-methyl-5-(phenylcarbamoyloxy-methyl)-6-oxo-heptanoate (**6b**) and **methyl (*S*)-3-(methoxycarbonyl-methyl)-4-methyl-5-oxo-4-(phenylcarbamoyloxy-methyl)-hexanoate** (*ent*-**18**). Sulfone **16b** (1.36 g, 3.1 mmol) was reacted as described for **16a** to **6a**/**18**. Column chromatography [SiO_2 (90 g), hexane/EtOAc = 2: 1] gave a mixture of isomers (3*R*)-3-[(1*R*)-cyclopent-2-en-1-yl]-4-phenyl-carbamoyloxy-3-methyl-butan-2-on (**5b**) and (3*R*)-3-[cyclopent-3-en-1-yl]-3-methyl-4-phenyl-carbamoyloxy-butan-2-on (*ent*-**17**) (719 mg, 81%). TLC (silica gel, CH_2Cl_2/hexane/EtOAc = 10:6:1): R_f 0.44. The ratio of **5b**/*ent*-**17** was determined by ^{1}H NMR as 1.1:1. The mixture of **5a**/*ent*-**17** (719 mg, 2.5 mmol) was involved in the next reaction step without further separation and characterization as described for *rac*-**5a** to *rac*-**6a.** Flash chromatography [SiO_2 (50 g), hexane/EtOAc = 2 :1] gave a mixture (530 mg, 56%) of isomers **6b** and *ent*-**18** in a ratio of 1.1:1. The ratio was determined by HPLC (Nucleosil 50-10, *i*-hexane/EtOAc = 10:5.5, 2 mL/min, RI detection). Preparative HPLC [PrepPak 500 silica gel (Waters), *iso*-hexane/EtOAc = 10:5.5] gave **6b** (229 mg, 24%), *ent*-**18** (217 mg, 23%) and **6b**/*ent*-**18** (13 mg, 1.4%).

6b: TLC (silica gel, hexane/EtOAc = 2:11): R_f 0.18. $[\alpha]_D^{20}$ - 12.4, *c* = 1.3035 in $CHCl_3$. Analytical, physical and spectroscopic data were identical to those reported for *rac*- **6b**. CD: Θ (λ) + 659 (287.7 sh), + 725 (296 nm), (c 0.6672 mg/mL, MeOH). Microanalysis for $C_{19}H_{25}NO_7$ (379.41): calcd. C 60.14, H 6.64, N 3.69; found C 60.09, H 6.67, N 3.77.

Ent-**18**: TLC (silica gel, hexane/EtOAc = 2:1): R_f 0.16. $[\alpha]_D^{20}$ - 13.5, *c* = 1.3618 in $CHCl_3$. CD: Θ (λ) – 1420 (286), -2233 (292.6 nm), (c 0.3152 mg/mL, MeOH). UV [MeOH, λ_{max}, nm (ε, $Lmol^{-1}cm^{-1}$)]: 234 (17186), 272 (795), 297

(587). IR (Film, $\tilde{\nu}_{max}$, cm^{-1}): 3315, 3295, 3135 (NH), 2975, 2950, 2845, 1705s (C=O), 1600, 1525, 1500, 1435, 1355, 1305, 1210, 1050, 885, 830, 790, 745, 690. ^{1}H NMR (270 MHz, $CDCl_3$): δ_H 1.14 [3H, s, H_3C-C(4)], 2.25 [3H, s, H_3C(6), acyl], 2.23 – 2.38 [4H, m, H_2C(2) and H_2C(3´)], 2.47 [1H, m, HC(3)], 3.66, 3.67 [6H, 2s, 2 H_3CO], 4.25 [1H, d, *J* = 11.2 Hz, (4´)-C*H*HO], 4.31 [1H, d, *J* = 11.2 Hz, (4´)-CH*H*O], 6.67 [1H, s br, NH], 7.07 [1H, m, *p*-phenyl carbamate] 7.26 – 7.38 [4H, m, *o-, m*-phenyl carbamate]. Microanalysis for $C_{19}H_{25}NO_7$ (379.41): calcd. C 60.14, H 6.64, N 3.69; found C 60.03, H 6.61, N 3.76.

***t*-Butyl (2*S*)-2-[(1*S,4R*)-4-acetoxy-cyclopent-2-en-1-yl]-2-methyl-3-oxo-butanoate** (**20a**) and ***t*-Butyl (2*R*)-2-[(1*S,4R*)-4-acetoxy-cyclopent-2-en-1-yl]-2-methyl-3-oxo-butanoate** (**20b**). To a suspension of NaH (156 mg, 5.2 mmol) in THF (5 mL) was added dropwise at 0 °C a solution of *t*-butyl 2-methylacetoacetate **2 (**895 mg, 5.2 mmol) in THF (10 mL). After complete addition of **2** the mixture was stirred at rt for 30 min. A solution of [(1*S,4R*)-4-acetoxy-cylopent-2-en-1-yl]-ethyl-carbonate (**19**)[21] (560 mg, 2.6 mmol; $[\alpha]_D^{20}$ - 9.9, *c* = 1.331 in $CHCl_3$, ee > 98%) and $Pd[P(Ph)_3]_4$ (72 mg, 0,065 mmol) in THF (20 mL) was prepared in a separate flask. To this solution was added all at once the solution of deprotonated acetoacetate. The reaction mixture was stirred at rt for 2 h. An aqueous HCl solution (1N, 30 mL) was added to the reaction mixture and extracted with ether (30 mL). The ether extract was washed with 1N aqueous HCl solution (30 mL), saturated brine (30 mL), dried over $MgSO_4$ and the solvent was evaporated. Column chromatography [SiO_2 (90 g), hexane/EtOAc = 3: 1] gave after removal of eluent a mixture of diastereomers **20a**/**20b** and *t*-butyl-acetoacetate. Bulb to bulb distillation gave a first fraction of acetoacetate **2** and then **20a**/**20b** (740 mg, 96%), (0.04 Torr, 140 °C) as a second fraction. The ratio of diastereomers **20a**/**20b** was determined as 1:1.7 by HPLC (Nucleosil 50-10, *iso*-hexane/EtOAc = 2:1, 2 mL/min, RI detection). The mixture of diastereomers was separated by preparative HPLC [PrepPak 500, silica gel (Waters), *n*-hexane/ether = 10: 3] to give after bulb to bulb distillation (0.2 Torr/145 °C) single fractions, **20a** (242 mg, 31%) and **20b** (380 mg, 49%).

20a: $[\alpha]_D^{20}$ - 26.9, *c* = 0.884 in $CHCl_3$. CD: Θ (λ) - 612 (294 nm), (c 2.69 mg/mL, MeOH). IR (Film, $\tilde{\nu}_{max}$, cm^{-1}): 3080, 2970, 2930, 1730s (CO, ester), 1710s (C=O, ketone), 1455, 1365, 1330, 1240 (C-O), 1155, 1125, 1105, 1050, 1015, 975, 905, 840, 795, 780, 750. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.20 [3H, s, H_3C-C(2)], 1.31-1.41 [1H, m, *H*HC(5´)], 1.45 (9H, s, *t*-Bu), 2.01 [3H, s, H_3C-CO_2, acetate], 2.16 [3H, s, H_3C(4), acyl], 2.48 [1H, "dt", J_{gem} = 14.5 Hz, J_{vic} = 8.3 Hz, *H*HC(5´)], 3.40 [1H, m, HC(1´)], 5.62 [1H, m, HC(4´)], 5.84, 5.95 [2H, 2 m, HC(2´) and HC(3´)]. Microanalysis for $C_{16}H_{24}O_5$ (296.36): calcd. C 64.84, H 8.16; found C 64.68, H 8.11.

20b: $[\alpha]_D^{20}$ + 76.4, *c* = 1.352 in $CHCl_3$. IR (Film, $\tilde{\nu}_{max}$, cm^{-1}): 3080, 2970, 2930, 1730s (CO, ester), 1710s (C=O, ketone), 1450, 1365, 1240s (C-O), 1160, 1110, 1045, 1015, 970, 905, 840, 770, 745. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.19 [3H, s, H_3C-C(2)], 1.43-1.51 [1H, m, *H*HC(5´)], 1.45 (9H, s, *t*-Bu), 2.03 [3H, s, H_3C-CO_2, acetate], 2.15 [3H, s, H_3C(4), acyl], 2.49 [1H, "dt", J_{gem} = 14.5 Hz, J_{vic} = 8.3 Hz, *H*HC(5´)], 3.42 [1H, m, HC(1´)], 5.63 [1H, m, HC(4´)], 5.83, 5.91 [2H, 2 m, HC(2´) and HC(3´)]. Microanalysis for $C_{16}H_{24}O_5$ (296.36): calcd. C 64.84, H 8.16; found C 64.73, H 8.08.

***t*-Butyl (2*S*)-2-[(1*S,4R*)-4-hydroxy-cyclopent-2-en-1-yl]-2-methyl-3-oxo-butanoate** (*ent*-**10a**). Acetate **20a** (180 mg, 0.61 mmol) and K_2CO_3 (72 mg, 0.72 mmol) were dissolved in MeOH (2mL) and stirred at rt for 30 min. To the mixture was added a saturated aqueous NaH_2PO_4 solution (15 mL) and was extracted three times with ether (3 x 10 mL). The combined organic extracts were washed with saturated brine (15 mL), dried by filtration through cotton wool and evaporated. Flash chromatography [SiO_2 (15 g), hexane/EtOAc = 2:1] and subsequent bulb to bulb distillation (0.05 Torr/140 °C) gave alcohol *ent*-**10a** (139 mg, 91%).

Ent-**10a**: TLC (silica gel, hexane/EtOAc = 2:1): R_f 0.26. $[\alpha]_D^{20}$ - 48.2, *c* = 0.790 in $CHCl_3$. CD: Θ (λ) + 630 (293.5 nm), (c 1.5058 mg/mL, MeOH). UV [MeOH, λ_{max}, nm (ε, $Lmol^{-1}cm^{-1}$)]: 281 (68.3). IR (Film, $\tilde{\nu}_{max}$, cm^{-1}): 3415 br (OH), 3050, 2970, 2930, 2865, 1710s (C=O), 1460, 1395, 1370, 1250 and 1155s (C-O), 1125, 1070, 1045, 1015, 905, 775, 750. ^{1}H NMR (270 MHz, $CDCl_3$): δ_H 1.26 [3H, s, H_3C-C(2)], 1.26-1.38 [1H, m, *H*HC(5´)], 1.45 (9H, s, *t*-Bu), 1.74

(1H, d, *J* = 7.7 Hz, OH, exchangeable by D_2O), 2.16 [3H, s, H_3C(4), acyl], 2.43 [1H, m, *H*HC(5´)], 3.30 [1H, m, HC(1´)], 4.80 [1H, m, HC(4´)], 5.84 [2H, m, HC(2´) and HC(3´)]. Microanalysis for $C_{14}H_{22}O_4$ (254.32): calcd. C 66.11, H 8.71; found C 65.97, H 8.60.

***t*-Butyl (2*S*)-2-[(1*S*,4*R*)-4-hydroxy-cyclopent-2-en-1-yl]-2-methyl-3-oxo-butanoate** (*ent*-**10b**). Acetate **20b (**300 mg, 1.01 mmol) was reacted as described for **20a** to *ent*-**10a**. Flash chromatography [SiO_2 (20 g), hexane/EtOAc = 2:1] and bulb to bulb distillation gave *ent*-**10b** (251 mg, 98%).

10b: TLC (silica gel, hexane/EtOAc = 2:1): R_f 0.26. $[\alpha]_D^{20}$ + 44.5, *c* = 1.297 in $CHCl_3$. CD: Θ (λ) + 3417 (292 nm), (c 1.2102 mg/mL, MeOH). UV [MeOH, λ_{max}, nm (ε, $Lmol^{-1}cm^{-1}$)]: 285 (48). IR (Film, $\tilde{\nu}_{max}$, cm^{-1}): 3410 br (OH), 3050, 2970, 2925, 2865, 1710s (C=O), 1460, 1395, 1370, 1250s (C-O), 1215, 1160s (C-O), 1110, 1065, 1040, 1015, 960, 900, 870, 840, 780, 745. ^{1}H NMR (270 MHz, $CDCl_3$): δ_H 1.25 [3H, s, H_3C-C(2)], 1.40-1.49 [1H, m, *H*HC(5´)], 1.46 (9H, s, *t*-Bu), 1.88 (1H, d, *J* = 7.3 Hz, OH, exchangeable by D_2O), 2.16 [3H, s, H_3C(4), acyl], 2.45 [1H, m, *H*HC(5´)], 3.30 [1H, m, HC(1´)], 4.80 [1H, m, HC(4´)], 5.78, 5.87 [2H, 2 m, HC(2´) and HC(3´)]. Microanalysis for $C_{14}H_{22}O_4$ (254.32): calcd. C 66.11, H 8.71; found C 66.07, H 8.62.

{(1*SR*,2*SR*,5*RS*,6*RS*)-6-Iodo-2-methyl-4-oxabicyclo[3.3.0]hept-2-yl}-ethanon (*rac*-**8a**). To a solution of alcohol *rac*-**4a** (252 mg, 1.5 mmol) in ether (5 mL) was added first $NaHCO_3$ (1.38 g, 16.5 mmol) in H_2O (10 mL) and then at rt during 6.5 h a solution of KI (398 mg, 2.4 mmol) and I_2 (420 mg, 1.65 mmol) in H_2O (3.5 mL). After addition of I_2/KI was completed, the mixture was stirred overnight. Ether (10 mL) was added, the organic layer was separated and was washed twice with 20% aqueous $NaHSO_3$ (2 x 5 mL) and saturated aqueous brine (10 mL). The ether layer was dried by filtration through cotton wool and the solvent was evaporated. Column chromatography [SiO_2 (25 g), CH_2Cl_2/hexane/EtOAc = 10:3:1] of the residue gave analytically pure viscous bicyclic ether *rac*-**8a** (155 mg, 35%).

Rac-**8a**: TLC (silica gel, CH_2Cl_2/hexane/EtOAc = 10:3:1): R_f 0.47. IR (Film, $\tilde{\nu}_{max}$, cm^{-1}): 2965, 2935, 2860, 1710s (C=O), 1450, 1440, 1380, 1355, 1295, 1270, 1240, 1190, 1170, 1120, 1100, 1055, 1035, 1005, 965, 945, 905, 880, 845, 815, 765. ^{1}H NMR (270 MHz, $CDCl_3$): δ_H 1.18 [3H, s, H_3C-C(2´)], 1.60 -1.70 [1H, m, β-*H*HC(8´)], 1.99-2.21 [3H, m, α-H*H*C(8´), H_2C(7´)], 2.20 [3H, s, H_3C(1), acyl], 3.14 [1H, m, HC(1´)], 3.42 [1H, d, *J* = 9.2 Hz, *H*HC(3´)], 4.22 [1H, m, HIC(6´)], 4.23 [1H, d, *J* = 9.2 Hz, H*H*C(3´)], 4.71 [1H, m, HC(5´)]. Microanalysis for $C_{14}H_{22}O_4$ (294.13): calcd. C 40.83, H 5.14, I 43.14; found C 40.70, H 5.00, I 43.34.

{(1*SR*,2*RS*,5*RS*,6*RS*)-6-Iodo-2-methyl-4-oxabicyclo[3.3.0]hept-2-yl}-ethanon (*rac*-**8b**). Alcohol *rac*-**4b (**252 mg, 1.5 mmol) was reacted as described for *rac*-**4a** to *rac*-**8a**. Column chromatography [SiO_2 (25 g), CH_2Cl_2/hexane/EtOAc = 10:3:1] gave *rac*-**8b** as an analytically pure viscous oil (82 mg, 19%).

Rac-**8b**: TLC (silica gel, CH_2Cl_2/hexane/EtOAc = 10:3:1): R_f 0.47. IR (Film, $\tilde{\nu}_{max}$, cm^{-1}): 2960, 2930, 2870, 1705s (C=O), 1485, 1455, 1380, 1360, 1295, 1275, 1255, 1230, 1175, 1160, 1110, 1065, 1030, 975, 950, 905, 885, 805. ^{1}H NMR (270 MHz, $CDCl_3$): δ_H 1..25 [1H, m, β-*H*HC(8´)], 1.36 [3H, s, H_3C-C(2´)], 1.96 - 2.29 [3H, m, α-H*H*C(8´), H_2C(7´)], 2.19 [3H, s, H_3C(1), acyl], 2.87 [1H, m, HC(1´)], 3.78 [1H, d, *J* = 9.0 Hz, *H*HC(3´)], 4.02 [1H, d, *J* = 9.0 Hz, HC(3´)], 4.33 [1H, m, HIC(6´)], 4.93 [1H,"d", J = 5.0 Hz, HC(5´)]. Microanalysis for $C_{14}H_{22}O_4$ (294.13): calcd. C 40.83, H 5.14, I 43.14; found C 40.96, H 5.05, I 43.41.

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Supplementary Material

Supplementary data associated with this article is available in the Supplementary Material.

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