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Asymmetric Synthesis of Seven-Carbon Segments of the Phorboxazoles and (–)-Discodermolide: Complementary Route from Racemic *trans*-2,4-Dimethyl-8-oxabicyclo[3.2.1]oct-6-en-3-one

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Abstract: The C20-C26 segment of the phorboxazoles A and B and the C1-C7 segment of (–)-discodermolide were synthesized in excellent chemical and optical yield using *trans*-2,4-dimethyl-8-oxabicyclo[3.2.1]oct-6-en-3-one ***rac*-1** with four stereogenic centres and three prostereogenic sp^2-sites as an *early racemic switch*.

The phorboxazoles A and B, first described by Molinski in 1995[1] and (+)-discodermolide, characterized by Gunasekera in 1990[2] are important marine natural products isolated from the marine sponges *Phorbas sp.* and *Discodermia dissoluta*. They exhibit extraordinary cytotoxic potential in sub-nanomolar concentrations. The phorboxazoles seem to interact in the S phase of the cell cycle,[1] whereas discodermolide causes mitotic arrest during the M phase by stabilization of the microtubules and preventing a proper assembly of the mitotic spindle.[3] Since the discovery of both natural compounds several synthetic approaches have been described including total syntheses of the phorboxazoles A[4] and (+)- and (–)-discodermolide.[5]

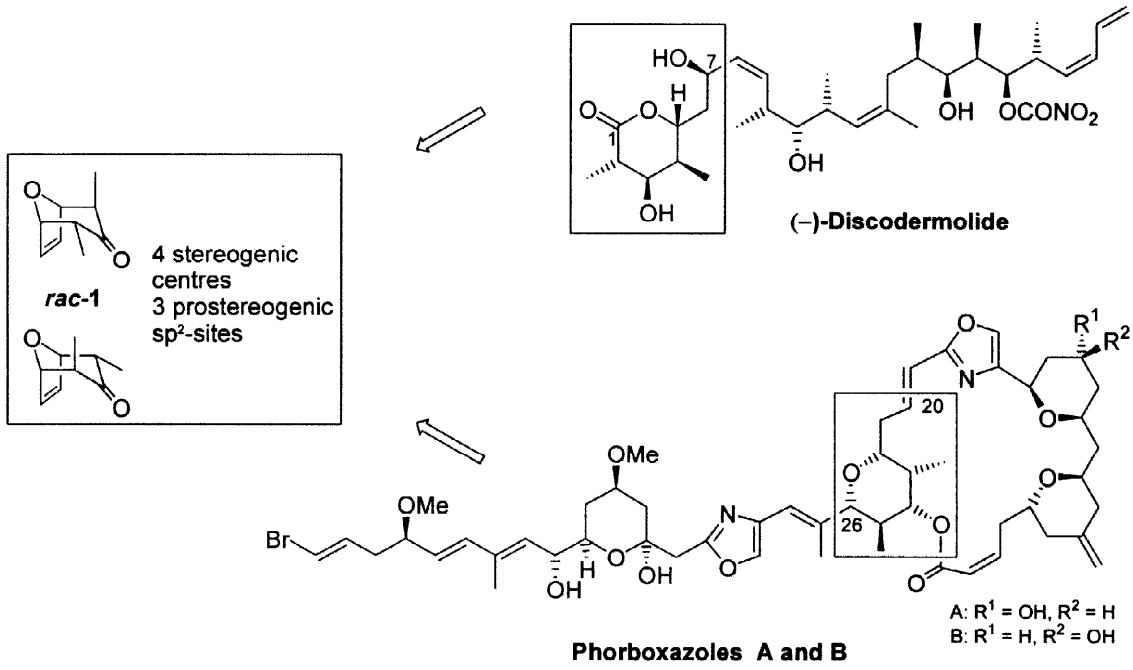


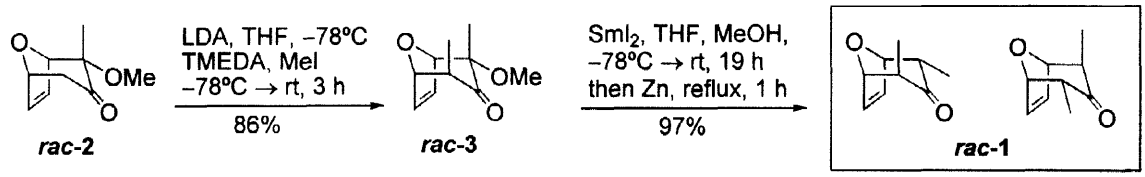
Figure 1

PII: S0040-4020(99)00127-1

We have previously published a convenient route to functionalized enantiopure tetrahydropyrans starting from 8-oxa-bicyclo[3.2.1]oct-6-en-3-one.[6a,b] The C20-C26 segment of the phorboxazoles A and B and the C1-C7 segment of (−)-discodermolide should be accessible from *trans*-2,4-dimethyl-8-oxabicyclo[3.2.1]-oct-6-en-3-one ***rac*-1** (Figure 1).

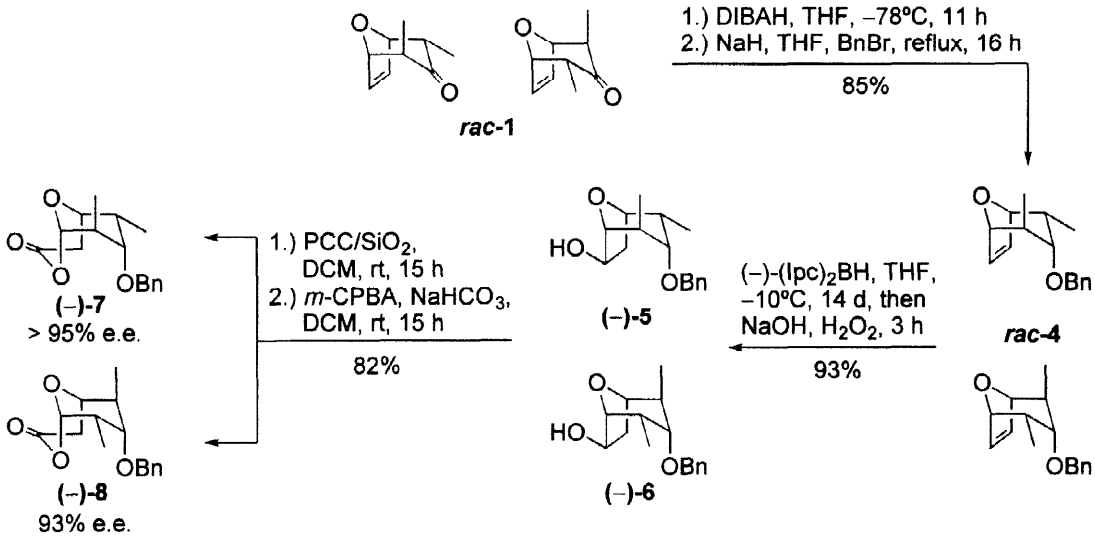
Current [4+3] cycloaddition methodology[7] provides oxabicyclic ketone ***rac*-1** only as a mixture of 2,4-epimers and in low yield.[8] We herein report a novel two step process to obtain selectively this useful module in very high yield. Furthermore an efficient synthesis of the C20-C26 segment of the phorboxazoles A and B and the C1-C7 segment of (−)-discodermolide using oxabicyclic ketone ***rac*-1** is described.

Starting from the easily accessible 2α-methoxy-2β-methyl-8-oxabicyclo-[3.2.1]oct-6-en-3-one ***rac*-2**,[9] we prepared ketone ***rac*-3** by α-methylation. A SmI_2-mediated reduction of the tertiary ether afforded *trans*-2,4-dimethyl-8-oxabicyclo[3.2.1]oct-6-en-3-one ***rac*-1** in excellent yield (Scheme 1). It has been reported that reduction of similar tertiary ethers was not successful.[10] To promote this reaction we added Zn powder. Alternatively, a very slow addition of methanol (7 equivalents) was possible, but did not give the high yield of the Zn addition procedure (see experimental). Interestingly, HMPA as a cosolvent made no improvement.



Scheme 1

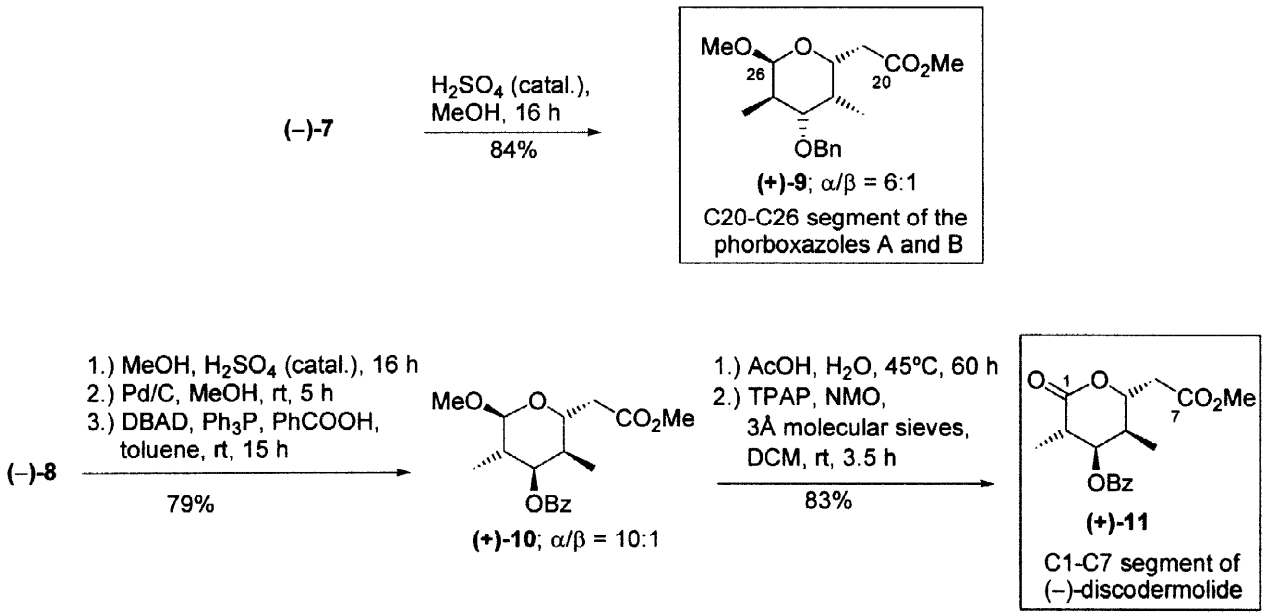
Diastereoselective DIBAH reduction of ketone ***rac*-1** and subsequent O-protection afforded benzyl ether ***rac*-4**. Asymmetric hydroboration furnished the diastereomeric alcohols **(−)-5** and **(−)-6** in high chemical and optical yield. Oxidation using PCC on silica and Baeyer-Villiger oxidation yielded the lactones **(−)-7** and **(−)-8**, which could easily be separated by column chromatography (Scheme 2).



Scheme 2

The synthesis of the C20-C26 segment of the phorboxazoles A and B was completed by acidic methanolysis of lactone (–)-**7** giving methyl acetal ester (+)-**9** in 8 steps and in excellent 25% overall yield (Scheme 3).

Acidic methanolysis of lactone (–)-**8**, catalytic hydrogenation and Mitsunobu inversion gave benzoate (+)-**10**. The acetal was cleaved to the corresponding hemi acetal. Oxidation with TPAP/NMO[11] to lactone (+)-**11** completed the synthesis of the C1-C7 segment of (–)-discodermolide in good overall yield (12 steps, 16%, Scheme 3).



Scheme 3

In conclusion, the starting material *trans*-2,4-dimethyl-8-oxabicyclo[3.2.1]oct-6-en-3-one ***rac*-1** is a versatile building block in the synthesis of enantiomerically pure *trans*-3,5-dimethylated tetrahydropyrans. These ring systems also occur in the lonomycins A-C.[12] In addition *trans*-2,4-dimethyl-8-oxabicyclo[3.2.1]oct-6-en-3-one ***rac*-1** can also be used as an early racemic switch[13] for access to *trans*-polypropionate units of several natural products including the spongistatins.[14]

Experimental

Infrared spectra were recorded on a Perkin-Elmer 1710 infrared spectrometer. - ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AM 400 spectrometer in deuterated chloroform unless otherwise stated, with tetramethylsilane as an internal standard. - Mass spectra were recorded on a Finnigan MAT 312 (70 eV) or a VG Autospec spectrometer at rt unless otherwise stated. - Preparative column chromatography was performed on J. T. Baker silica gel (particle size 30-60 μm). – Analytical TLC was carried out on aluminium-baked 0.2-mm silica gel 60 F254 plates (E. Merck). – THF was distilled over sodium and benzophenone before use. CH_2Cl_2 (DCM) was distilled over CaH_2 before use. Methanol was distilled over magnesium before

use. Methyl t-butyl ether (MTBE), ethyl acetate (EtOAc) and light petroleum (PE, bp 40-60°C) were distilled before use.

2-Methoxy-2,4-dimethyl-8-oxabicyclo[3.2.1]oct-6-en-3-one (***rac*-3**). A solution of LDA was prepared from diisopropyl amine (8.48 g, 11.9 ml, 83.8 mmol) and *n*-BuLi (52.4 ml, 83.8 mmol, 1.6 M solution in hexane) in THF (60 ml) at –78°C. Bicyclic ketone ***rac*-2** (11.3 g, 67.0 mmol) dissolved in THF (30 ml) was added. After 0.5 h, first TMEDA (9.72 g, 12.6 ml, 83.8 mmol) was added dropwise, then MeI (47.6 g, 20.9 ml, 33.5 mmol). The solution was kept at this temperature for 1 h and slowly allowed to warm to ambient temperature over 2 h. The mixture was quenched with water (50 ml), the organic layer was washed with brine (40 ml) and the combined aqueous layers were extracted with MTBE (5 × 40 ml). The combined organic layers were dried over $MgSO_4$, filtered, concentrated *in vacuo* and purified by column chromatography (PE/EtOAc 5:1) to yield ketone ***rac*-3** (10.5 g, 57.6 mmol, 86%) as white crystals, mp 61°C. $\nu_{max}(CHCl_3)/cm^{-1}$ 2980, 2952, 2836, 1720, 1460, 1408, 1364, 1336, 1264, 1228, 1172, 1112, 1084, 1044, 996, 960, 932, 884, 860, 828; ^1H NMR (400 MHz, $CDCl_3$) δ 6.36 (ddd, J = 4.3, 1.7, 0.5 Hz, 1H), 6.29 (ddd, J = 4.3, 1.8, 0.4 Hz, 1H), 4.63 (d, J = 1.7 Hz, 1H), 4.61 (d, J = 1.8 Hz, 1H), 3.5 (s, 3H), 2.36 (dq, J = 7.5, 0.5 Hz, 1H), 1.57 (s, 3H), 1.36 (d, J = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.2 (CO), 133.3 (=CHR), 131.5 (=CHR), 82.8 ($OCHR_2$), 82.7 ($COCH_3$), 81.8 ($OCHR_2$), 51.3 (OCH_3), 48.2 (CH), 19.3 (CH_3), 16.1 (CH_3); MS (RT): M^+ = 182 (100), 167 (37.2), 152 (2.5), 139 (5.8), 125 (16.5), 114 (32.6), 107 (6.6), 95 (58.7), 91 (4.3), 86 (49.7), 79 (29.8), 71 (24.7), 67 (27.6); HRMS calcd for $C_{10}H_{14}O_3$ (M^+) 182.0943, found 182.0943.

trans-*2,4-Dimethyl-8-oxabicyclo[3.2.1]oct-6-en-3-one* (***rac*-1**). *Method A.* To samarium (17.4 g, 115 mmol) and diiodoethane (31.7 g, 113 mmol) desox. THF (220 ml) was added and the mixture stirred for 3 h at ambient temperature to afford a deep blue solution. At –78°C a solution of ketone ***rac*-3** (10.0 g, 55.0 mmol) in desox. THF (110 ml) and desox. methanol (1.76 g, 2.20 ml, 55.0 mmol) was added. Then desox. methanol (10.6 g, 13.4 ml, 330 mmol) was added dropwise over a period of 6 h. After another 3 h, the reaction was completed (GC-monitoring). The still blue reaction mixture was quenched at –78°C with 2N aqueous HCl (200 ml) and allowed to warm to ambient temperature. The aqueous layer was extracted with MTBE (5 × 60 ml), the combined organic layers were dried over $MgSO_4$, filtered, concentrated *in vacuo* and purified by column chromatography (PE/EtOAc 5:1) to yield ketone ***rac*-1** (6.85 g, 45.1 mmol, 82%) as a pale yellow solid. *Method B.* To samarium (3.80 g, 25.3 mmol) and diiodoethane (6.81 g, 24.2 mmol) desox. THF (44 ml) was added and stirred for 3 h at ambient temperature to afford a deep blue solution. At –78°C a solution of ketone ***rac*-3** (2.00 g, 11.0 mmol) in desox. THF (22 ml) and desox. methanol (11 ml) was added dropwise. After 4 h, the mixture was allowed to warm to ambient temperature and stirred for 15 h. The colour of the solution turned to dark green. A suspension of Zn powder (1.44 g, 22.0 mmol; dried in a vacuum pistol above 300°C) in THF (5 ml) was added *via* syringe and the mixture refluxed for 1 h, then diluted with a saturated aqueous solution of K_2CO_3 (80 ml). The aqueous layer was extracted with MTBE (5 × 30 ml), the combined organic layers were dried over $MgSO_4$, filtered, concentrated *in vacuo* and purified by column chromatography (PE/EtOAc 5:1) to yield ketone ***rac*-1** (1.63 g, 10.7 mmol, 97%) as a pale yellow solid, mp 37°C. $\nu_{max}(CHCl_3)/cm^{-1}$ 2972, 2876, 1708, 1456, 1376, 1340, 1228, 1176, 1108, 1084, 1056, 1020, 976, 960, 936, 908, 868, 816; ^1H NMR (400 MHz, $CDCl_3$) δ 6.33 (dd, J = 6.1, 1.7 Hz, 1H), 6.30 (dd, J = 6.1, 1.4 Hz, 1H), 4.80 (dd, J = 4.7, 1.7 Hz, 1H), 4.68 (d, J = 1.4 Hz, 1H), 2.90 (dq, J = 6.9, 4.7 Hz, 1H), 2.33 (q, J = 7.35 Hz, 1H), 1.35 (d, J = 7.35 Hz, 3H), 0.96 (d, J = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.5 (CO), 134.0 (=CHR), 131.0 (=CHR), 81.9 ($OCHR_2$), 80.9 ($OCHR_2$), 48.6 (CH), 47.6 (CH), 15.0 (CH_3), 9.0 (CH_3); MS (RT): M^+ = 152 (52.2), 137 (20.3), 129 (1.1), 123 (4.3), 109 (7.9), 101 (1.57), 96 (76.2), 91 (3.7), 85 (1.5), 81 (100), 77 (2.8), 67 (11.6); HRMS calcd for $C_9H_{12}O_2$ (M^+) 152.0837, found 152.0838.

trans-*2,4-Dimethyl-8-oxabicyclo[3.2.1]oct-6-en-3α-ol* (***rac*-4a**). To a solution of bicyclic ketone ***rac*-1** (3.20 g, 21.1 mmol) in THF (100 ml) at –78°C DIBAH (26.3 ml, 26.3 mmol, 1M solution in hexane) slowly was added *via* perfusor over a period of 6 h. The solution was left at this temperature for 5 h, then quenched at

–78°C with 2N aqueous HCl (40 ml) and allowed to warm to ambient temperature. The organic layer was washed with brine (2 × 15 ml) and the combined aqueous layers were extracted with MTBE (5 × 40 ml). The combined organic layers were dried over $MgSO_4$, filtered, concentrated *in vacuo* and purified by column chromatography (PE/EtOAc 4:1) to yield alcohol ***rac*-4a** (2.75 g, 17.9 mmol, 85%) as a colourless oil. $\nu_{max}(CHCl_3)/cm^{-1}$ 3680, 3600, 3068, 3000, 2964, 2932, 2876, 1716, 1600, 1460, 1404, 1380, 1352, 1308, 1264, 1232, 1152, 1092, 1084, 1040, 1004, 988, 968, 936, 904, 856; ^1H NMR (400 MHz, $CDCl_3$) δ 6.50 (dd, J = 6.1, 1.7 Hz, 1H), 6.44 (dd, J = 6.1, 1.7 Hz, 1H), 4.50 (br. d, J = 1.7 Hz, 1H), 4.40 (m, 1H), 3.45 (br. s, 1H), 2.32 (m, 1H), 1.91 (br. s, 1H), 1.83 (q, J = 7.4 Hz, 1H), 1.20 (d, J = 7.4 Hz, 3H), 0.92 (d, J = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.1 (=CHR), 133.2 (=CHR), 80.8 ($OCHR_2$), 80.6 ($OCHR_2$), 73.3 ($OCHR_2$), 37.5 (CH), 34.2 (CH), 16.0 (CH_3), 11.1 (CH_3); MS (RT): M^+ = 154 (4.2), 148 (1.0), 136 (8.2), 125 (2.7), 121 (16.7), 111 (2.6), 107 (6.0), 95 (17.5), 91 (100), 85 (1.2), 81 (10.9), 77 (3.3), 69 (9.4); HRMS calcd for $C_9H_{14}O_2$ (M^+) 154.0994, found 154.0995.

3α-Benzyloxy-trans-*2,4-dimethyl-8-oxabicyclo[3.2.1]oct-6-ene* (***rac*-4**). To NaH (1.20 g, 36.4 mmol, 70% in paraffine) a solution of ***rac*-4a** (2.75 g, 17.9 mmol) in THF (50 ml) was added at ambient temperature and then refluxed. After 0.5 h, BnBr was added and continued to reflux for 15 h. The mixture was cooled to 0°C and quenched with water (15 ml). The organic layer was washed with brine (10 ml) and the combined aqueous layers were extracted with MTBE (4 × 20 ml). The combined organic layers were dried over $MgSO_4$, filtered, concentrated *in vacuo* and purified by column chromatography (first PE, then PE/EtOAc 10:1) to yield benzyl ether ***rac*-4** (4.35 g, 17.8 mmol, 99%) as a colourless oil. $\nu_{max}(CHCl_3)/cm^{-1}$ 3088, 3064, 2988, 2936, 2876, 2832, 1496, 1452, 1380, 1320, 1292, 1264, 1236, 1176, 1148, 1108, 1088, 1064, 1028, 1012, 992, 960, 916, 892, 852; ^1H NMR (400 MHz, $CDCl_3$) δ 7.29 (m, 5H), 6.3 (dd, J = 6.1, 1.4 Hz, 1H), 6.24 (dd, J = 6.1, 1.7 Hz, 1H), 4.51 (d, J = 12.2 Hz, 1H), 4.46 (d, J = 1.4 Hz, 1H) 4.36 (m, 1H), 4.28 (d, J = 12.2 Hz, 1H), 3.22 (d, J = 5.3 Hz, 1H), 1.81 (q, J = 7.5 Hz, 1H), 1.16 (d, J = 7.5 Hz, 3H), 0.88 (d, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.2 (ArC), 133.5 (=CHR), 131.4 (=CHR), 127.1 (*m*-ArC), 126.3 (*p*-ArC), 126.2 (*o*-ArC), 81.3 ($OCHR_2$), 80.3 ($OCHR_2$), 70.9 (OCH_2Ar), 34.7 (CH), 33.0 (CH), 17.0 (CH_3), 11.8 (CH_3); MS (RT): M^+ = 244 (2.3), 215 (1.8), 191 (2.9), 179 (8.3), 169 (11.0), 153 (35.8), 145 (1.3), 136 (7.1), 121 (10.1), 105 (7.7), 91 (100), 81 (10.9), 69 (12.0); HRMS calcd for $C_{16}H_{20}O_2$ (M^+) 244.1463, found 244.1265.

(1R,2R,3S,4R,5R,6R)-3-Benzyloxy-2,4-dimethyl-8-oxabicyclo[3.2.1]octan-6-ol (**(–)-5**), *(1R,2S,3S,4S,5R,6R)-3-Benzyloxy-2,4-dimethyl-8-oxabicyclo[3.2.1]octan-6-ol* (**(–)-6**). To a solution of (+)-α-pinene (9.11 g, 10.6 ml, 66.9 mmol) in THF (8 ml) slowly was added without stirring BH_3·DMS (2.03 g, 2.54 ml, 26.7 mmol) at ambient temperature. After 24 h, large crystals of (–)-$(Ipc)_2BH$ had been precipitated. The solvent was taken off *via* syringe, the remaining solid was washed twice with diethyl ether, powdered under nitrogen atmosphere and dried *in vacuo*. At –78°C, a solution of alkene ***rac*-4** (4.35 g, 17.8 mmol) in THF (18 ml) was added and the mixture slowly warmed up to –20°C, then stored in a freezer at –10°C for 14 d. Aqueous solutions of NaOH (3N, 40.0 ml,120 mmol) and H_2O_2 (30%, 12.4 ml, 120 mmol) were carefully added at 0°C. After 3 h the mixture was acidified with aqueous 6N HCl (25 ml), the clear layers were separated and the aqueous layer was extracted with MTBE (8 × 30 ml). The combined organic layers were dried over $MgSO_4$, filtered, concentrated *in vacuo* and purified by column chromatography (PE/EtOAc 3:1) to yield a mixture of alcohols **(–)-5** and **(–)-6** (4.36 g, 16.7 mmol, 93%) as a colourless oil. $\nu_{max}(CHCl_3)/cm^{-1}$ 3592, 3516, 3428, 3408, 3088, 3064, 2960, 2936, 2908, 2876, 1712, 1600, 1496, 1452, 1380, 1340, 1312, 1276, 1236, 1172, 1096, 1068, 1044, 964, 940, 908, 884, 860, 824; ^1H NMR (400 MHz, $CDCl_3$) δ 7.29 (m, 10H), 4.67 (dd, J = 7.2, 2.1 Hz, 1H), 4.59 (d, J = 3.6 Hz, 1H), 4.56 (d, J = 3.6 Hz, 1H), 4.57 (dd, J = 7.2, 2.1 Hz, 1H), 4.28 (d, J = 7.2 Hz, 1H), 4.25 (d, J = 7.2 Hz, 1H), 4.21 (d, J = 7.9 Hz, 1H), 4.14 (dd, J = 8.1, 3.8 Hz, 1H) 3.86 (s, 1H), 3.83 (d, J = 3.9 Hz, 1H), 3.14 (d, J = 3.7 Hz, 1H), 3.11 (d, J = 3.7 Hz, 1H), 2.83 (dd, J = 13.4, 7.2 Hz, 1H), 2.73 (dd, J = 13.1, 7.2 Hz, 1H), 2.15 (m, 2H), 2.04 (q, J = 7.4 Hz, 1H), 1.86 (q, J = 7.4 Hz, 1H), 1.75 (ddd, J = 13.1, 7.2, 2.1 Hz, 1H), 1.52 (ddd, J = 13.4, 7.9, 2.1 Hz, 1H), 1.10 (d, J = 7.4 Hz, 3H), 1.07 (d, J = 7.4 Hz, 3H), 0.99 (d, J = 7.4 Hz, 3H), 0.86 (d, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.7 (ArC), 127.3, 127.2 (*m*-ArC), 126.3

(*p*-ArC), 126.2 (*o*-ArC), 126.1 (*o*-ArC), 86.5 ($OCHR_2$), 86.0 ($OCHR_2$), 79.8 ($OCHR_2$), 79.7 ($OCHR_2$), 78.6 ($OCHR_2$), 77.9 ($OCHR_2$), 74.7 ($OCHR_2$), 70.8 (OCH_2Ar), 70.6 ($OCHR_2$), 70.5 (OCH_2Ar), 40.8 (CH_2), 36.2 (CH_2), 34.9 (CH), 33.5 (CH), 33.3 (CH), 33.2 (CH), 16.3 (CH_3), 12.1 (CH_3), 12.0 (CH_3); MS (RT): M^+ = 262 (0.8), 199 (0.9), 193 (7.6), 187 (1.2), 171 (4.6), 155 (5.7), 138 (2.7), 122 (5.7), 105 (10.8), 91 (100), 85 (8.1), 77 (7.5), 6.9 (10.7); HRMS calcd for $C_{16}H_{22}O_3$ (M^+) 262.1569, found 262.1570.

(1R,2R,3S,4R,5R)-3-Benzyloxy-2,4-dimethyl-8-oxabicyclo[3.2.1]octan-6-one **((–)-7a)**, *(1R,2S,3S,4S,5R)-3-Benzyloxy-2,4-dimethyl-8-oxabicyclo[3.2.1]octan-6-one* **((–)-8a)**. To a suspension of PCC (1.05 g, 4.87 mmol) and silica gel (1 g) in DCM (30 ml) was added dropwise a solution of the diastereomeric alcohols **(–)-5/(–)-6** (0.85 g, 3.24 mmol) in DCM (30 ml) at ambient temperature. After 15 h, the mixture was filtered through silica, concentrated *in vacuo* and purified by column chromatography (PE/EtOAc 5:1) to yield ketone **(–)-7a/(-)-8a** (811 mg, 3.12 mmol, 96%) as a white solid, mp 68°C. $\nu_{max}(CHCl_3)/cm^{-1}$ 3088, 3064, 3000, 2964, 2932, 2908, 2876, 1756, 1496, 1452, 1404, 1380, 1356, 1320, 1272, 1240, 1168, 1144, 1092, 1068, 1028, 996, 964, 932, 900, 880; ^1H NMR (400 MHz, $CDCl_3$) δ 7.25 (m, 10H), 4.64 (d, J = 12.2 Hz, 1H), 4.60 (d, J = 11.6 Hz, 1H), 4.43 (m, 2H), 4.40 (d, J = 12.2 Hz, 1H), 4.14 (d, J = 11.6 Hz, 1H), 3.73 (s, 1H), 3.37 (d, J = 4.2 Hz, 1H), 3.32 (m, 1H), 3.32 (m, 1H), 2.72 (d, J = 17.9 Hz, 1H), 2.68 (d, J = 16.5 Hz, 1H), 2.53 (ddd, J = 17.9, 8.2, 1.4 Hz, 1H), 2.40 (m, 3H), 2.32 (q, J = 7.4 Hz, 1 H), 2.10 (q, J = 7.4 Hz, 1H), 1.22 (d, J = 7.4 Hz, 3H), 1.16 (d, J = 7.4 Hz, 3H), 1.05 (d, J = 7.2 Hz, 3H), 0.89 (d, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 214.0 (CO), 212.3 (CO), 137.2 (ArC), 137.0 (ArC), 127.3 (*m*-ArC), 127.2 (*m*-ArC), 126.6 (*p*-ArC), 126.5 (*p*-ArC), 126.3 (*o*-ArC), 125.9 (*o*-ArC), 79.5 ($OCHR_2$), 79.2 ($OCHR_2$), 78.4 ($OCHR_2$), 78.3 ($OCHR_2$), 77.6 ($OCHR_2$), 77.0 ($OCHR_2$), 70.5 (OCH_2Ar), 70.1 (OCH_2Ar), 41.1 (CH_2), 37.8 (CH_2), 35.5 (CH), 34.5 (CH), 34.0 (CH), 32.7 (CH), 15.5 (CH_3), 14.5 (CH_3), 12.2 (CH_3), 11.1 (CH_3); MS (RT): M^+ = 260 (1.7), 169 (49.9), 151 (2.5), 141 (2.7), 124 (6.3), 109 (10.4), 96 (4.6), 91 (100), 83 (11.9), 65 (7.7); HRMS calcd for $C_{16}H_{20}O_3$ (M^+) 260.1412, found 260.1414.

(1S,5R,6R,7R,8S)-7-Benzyloxy-6,8-dimethyl-2,9-dioxabicyclo[3.3.1]nonan-3-one **((–)-7)**, *(1S,5R,6S,7S,8S)-7-Benzyloxy-6,8-dimethyl-2,9-dioxabicyclo[3.3.1]nonan-3-one* **((–)-8)**. To a suspension of $NaHCO_3$ (3.52 g, 41.9 mmol) and *m*-CPBA (70%, 5.17 g, 21.0 mmol) in DCM (25 ml) was added a solution of the diastereomeric ketones **(–)-7a/(–)-8a** (3.63 g, 14.0 mmol) in DCM (25 ml) at ambient temperature. After 15h the mixture was washed with a saturated aqueous solution of $NaHCO_3$ (3 × 15 ml), the combined aqueous layers were extracted with MTBE (8 × 30 ml). The organic layers were dried over $MgSO_4$, filtered, concentrated *in vacuo* and purified by column chromatography (PE/EtOAc 5:1) to yield the lactones **(–)-7** (1.86 g, 6.74 mmol, 47%) and **(-)-8** (1.44 g, 5.21 mmol, 38%) as white solids, mp 56°C (**(-)-7**) and mp 77°C (**(-)-8**). Data for **(–)-7**: $[\alpha]_D^{20}$ = -66.2° (c = 0.8, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3064, 3000, 2968, 2936, 2912, 2880, 1740, 1496, 1452, 1392, 1352, 1324, 1296, 1264, 1228, 1168, 1120, 1068, 1028, 980, 904, 880, 836, 552, 536; ^1H NMR (400 MHz, $CDCl_3$) δ 7.30 (m, 5H), 5.45 (d, J = 1.3 Hz, 1H), 4.74 (d, J = 12.3 Hz, 1H), 4.28 (d, J = 12.3 Hz, 1H), 4.11 (ddd, J = 4.4, 4.4, 4.3 Hz, 1H), 3.37 (d, J = 2.9 Hz, 1H), 2.75 (d, J = 4.4 Hz, 2H), 2.53 (q, J = 7.5 Hz, 1H), 2.40 (ddq, J = 7.1, 4.3, 2.9 Hz, 1H), 1.05 (d, J = 7.5 Hz, 3H), 0.97 (d, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2 (CO), 136.5 (ArC), 127.3 (*m*-ArC), 127.0 (*o*-ArC), 126.6 (*p*-ArC), 99.4 ($CH(OR)_2$), 76.9 ($OCHR_2$), 69.7($OCHR_2$), 69.4 (OCH_2Ar), 32.4 (CH), 30.9 (CH), 30.5 (CH_2), 13.9 (CH_3), 12.5 (CH_3); MS (80°C): M^+ = 276 (3.7), 258 (4.1), 229 (1.6), 199 (4.7), 185 (38.0), 170 (100), 155 (23.3), 139 (17.0), 120 (94.3), 105 (3.3); HRMS calcd for $C_{16}H_{20}O_4$ (M^+) 276.1362, found 276.1363. Anal. Calcd for $C_{16}H_{20}O_4$: C, 69.55; H, 7.30. Found C, 69.37; H, 7.10. Data for **(–)-8**: $[\alpha]_D^{20}$ = -38.0° (c = 1.5, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3064, 3032, 2972, 2940, 2880, 1740, 1496, 1452, 1396, 1348, 1312, 1288, 1264, 1232, 1172, 1104, 1072, 1036, 1000, 980, 828; ^1H NMR (400 MHz, $CDCl_3$) δ 7.30 (m, 5H), 5.41 (d, J = 2.9 Hz, 1H), 4.68 (d, J = 12.3 Hz, 1H), 4.42 (d, J = 12.3 Hz, 1H), 4.10 (d, J = 8.6 Hz, 1H), 3.36 (dd, J = 2.4, 1.3 Hz, 1H), 2.96 (dd, J = 17.8, 8.6 Hz, 1H), 2.54 (d, J = 17.8 Hz, 1H), 2.16 (m, 2H), 1.15 (d, J = 7.4 Hz, 3H), 1.10 (d, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3 (CO), 136.5 (ArC), 127.3 (*m*-ArC), 126.7 (*o*-ArC), 126.6 (*p*-ArC), 99.0 ($CH(OR)_2$), 77.4 ($OCHR_2$), 71.1 (OCH_2Ar), 69.3 ($OCHR_2$), 34.8 (CH_2), 33.9 (CH),

32.7 (CH), 15.6 (CH_3), 11.8 (CH_3); MS (RT): M^+ = 276 (2.4), 258 (5.6), 230 (3.0), 199 (2.6), **187 (48.6)**, 170 (34.7), **158** (32.4), 139 (30.9), 120 (100), 105 (34.9); HRMS calcd for $C_{16}H_{20}O_4$ (M^+) 276.1362, found 276.1361.

(2S,3R,4S,5R)-(4-Benzyloxy-6-methoxy-3,5-dimethyltetrahydropyran-2-yl) acetic acid methyl ester **((+)-9)**. To a solution of lactone **(–)-7** (0.54 g, 1.96 mmol) in methanol (25 ml) was added dropwise a catalytic amount of conc. H_2SO_4 at ambient temperature. After 16 h a saturated aqueous solution of $NaHCO_3$ (20 ml) was added and the aqueous layer extracted with MTBE (4 × 20 ml). The combined organic layers were dried over $MgSO_4$, filtered, concentrated *in vacuo* and purified by column chromatography (PE/EtOAc 10:1) to yield methyl ester **(+)-9** (0.53 g, 1.64 mmol, 84%) as a colourless oil, α:β = 6:1. Analytical data for the predominating α-anomer: $[\alpha]_D^{20}$ = +153.2° (c = 1.7, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3064, 2972, 2932, 2892, 2836, 1736, 1496, 1452, 1436, 1384, 1352, 1300, 1264, 1196, 1176, 1148, 1120, 1072, 1028, 988, 964, 932; ^1H NMR (400 MHz, $CDCl_3$) δ 7.30 (m ,5H), 4.59 (d, *J* = 11.4 Hz, 1H), 4.50 (d, *J* = 3.9 Hz, 1H), 4.37 (d, *J* = 11.4 Hz, 1H), 4.33 (ddd, *J* = 9.8, 4.0, 2.4 Hz, 1H), 3.70 (s, 3H), 3.60 (dd, *J* = 11.2, 4.8 Hz, 1H), 3.31 (s, 3H), 2.63 (dd, *J* = 15.3, 9.8 Hz), 2.37 (dd, *J* = 15.3, 4.0 Hz, 1H), 2.12 (m, 1H), 1.94 (m, 1H), 0.99 (d, *J* = 6.8 Hz, 3H), 0.94 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 170.9 (CO), 137.6 (ArC), 127.3 (*m*-ArC), 126.6 (*o*-ArC), 126.5 (*p*-ArC), 101.3 ($CH(OR)_2$), 77.7 ($OCHR_2$), 69.3 (OCH_2Ar), 65.7 ($OCHR_2$), 53.9 (OCH_3), 50.6 (OCH_3), 36.9 (CH_2), 33.7 (CH), 33.3 (CH), 11.7 (CH_3), 4.3 (CH_3); MS (RT): M^+ = 322 (2.1), 292 (7.8), 263 (2.4), 253 (7.2), 231 (5.9), 214 (2.7), 199 (100), 183 (95.7), 171 (19.3), 148 (90.6), 139 (14.0), 114 (41.4); HRMS calcd for $C_{18}H_{26}O_5$ (M^+) 322.1780, found 322.1778. Anal. Calcd for $C_{18}H_{26}O_5$: C, 67.06; H, 8.13. Found C, 66.92; H, 8.01.

(2R,3S,4S,5S)-(4-Benzyloxy-6-methoxy-3,5-dimethyltetrahydropyran-2-yl) acetic acid methyl ester **((+)-10a)**. To a solution of lactone **(–)-8** (320 mg, 1.16 mmol) in methanol (15 ml) was added dropwise a catalytic amount of conc. H_2SO_4 at ambient temperature. After 16 h a saturated aqueous solution of $NaHCO_3$ (10 ml) was added and the aqueous layer extracted with MTBE (4 × 10 ml). The combined organic layers were dried over $MgSO_4$, filtered, concentrated *in vacuo* and purified by column chromatography (PE/EtOAc 10:1) to yield methyl ester **(+)-10a** (355 mg, 1.10 mmol, 95%) as a white solid, mp 50°C, α:β = 10:1. Analytical data for the predominating α-anomer: $[\alpha]_D^{20}$ = +14.7° (c = 2.0, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3064, 2988, 2968, 2936, 2912, 2836, 1736, 1496, 1452, 1436, 1384, 1364, 1316, 1292, 1272, 1236, 1192, 1176, 1140, 1084, 1028, 1000, 964; ^1H NMR (400 MHz, $CDCl_3$) δ 7.31 (m, 5H), 4.59 (d, *J* = 11.2 Hz, 1H), 4.57 (s, 1H), 4.32 (d, *J* = 11.2 Hz, 1H), 3.88 (ddd, *J* = 10.2, 10.2, 2.7 Hz, 1H), 3.70 (s, 3H), 2.55 (dd, *J* = 10.5, 5.0 Hz, 1H), 3.34 (s, 3H), 2.66 (dd, *J* = 15.1, 2.7 Hz, 1H), 2.43 (dd, *J* = 15.1, 10.2 Hz, 1H) 2.32 (m 1H), 1.71 (m 1H), 1.01 (d, *J* = 7.2 Hz, 3H), 0.96 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 171.1 (CO), 137.5 (ArC), 127.3 (*m*-ArC), 126.7 (*o*-ArC), 126.5 (*p*-ArC), 102.5 ($CH(OR)_2$), 77.4 ($OCHR_2$), 69.6 ($OCHR_2$), 69.4 (OCH_2Ar), 53.7 (OCH_3), 50.6 (OCH_3), 37.5 (CH_2), 34.5 (CH), 33.8 (CH), 12.3 (CH_3), 9.6 (CH_3); MS (70°C): M^+ = 322 (0.3), 292 (2.6), 262 (1.6), 231 (1.2), 214 (1.4), 199 (7.8), 185 (4.7), 171 (3.8), 148 (14.4), 119 (6.3), 99 (4.4), 91 (100), 83 (3.4), 72 (7.3); HRMS calcd for $C_{18}H_{26}O_5$ (M^+) 322.1780, found 322.1780. Anal. Calcd for $C_{18}H_{26}O_5$: C, 67.06; H, 8.13. Found C, 66.75; H, 8.00.

(2R,3S,4S,5S)-4-Hydroxy-6-methoxy-3,5-dimethyltetrahydropyran-2-yl acetic acid methyl ester **((+)-10b)**. To a suspension of Pd/C (10%) (30 mg, 0.028 mmol) in methanol (3 ml) was added a solution of benzyl ether **(+)-10a** (180 mg, 0.559 mmol) in methanol (3 ml) at ambient temperature and the flask was set under hydrogen atmosphere. After 5 h, the mixture was filtered through a short silica gel column (MTBE) and concentrated *in vacuo* to afford alcohol **(+)-10b** (129 mg, 0.557 mmol, 100%) as a colourless oil, α:β = 10:1. Analytical data for the predominating α-anomer: $[\alpha]_D^{20}$ = +87.2° (c = 1.5, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3620, 2972, 2936, 2912, 2836, 1736, 1456, 1436, 1384, 1320, 1276, 1228, 1172, 1136, 1084, 1024, 996, 960; ^1H NMR (400 MHz, $CDCl_3$) δ 4.52 (d, *J* = 1.0 Hz, 1H), 3.85 (ddd, *J* = 10.2, 10.0, 2.9 Hz, 1H), 3.77 (dd, *J* = 10.1, 5.0 Hz, 1H), 3.71 (s, 3H), 3.3 (s, 3H), 2.67 (dd, *J* = 15.1, 2.9 Hz, 1H), 2.45 (dd, *J* = 15.1, 10.0 Hz, 1H), 2.07 (ddq, *J* = 5.0, 7.2, 1.0 Hz, 1H), 1.90 (br. s, 1H), 1.60 (ddq, *J* = 10.2, 10.1, 6.4 Hz, 1H), 1.02 (d, *J* = 7.2 Hz,

3H), 0.97 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 171.0 (CO), 102.5 ($CH(OR)_2$), 70.0 ($OCHR_2$), 69.4 ($OCHR_2$), 53.6 (OCH_3), 50.6 (OCH_3), 37.7 (CH), 37.4 (CH_2), 35.9 (CH), 12.1 (CH_3), 9.3 (CH_3); MS (RT): $M^+ - OCH_3$ = 201 (8.7), 182 (7.6), 169 (5.2), 154 (10.4), 143 (20.2), 127 (4.8), 115 (97.4), 103 (18.9), 95 (11.8), 83 (22.3), 77 (1.3), 72 (100); HRMS calcd for $C_{10}H_{17}O_4$ (M^+ - OCH_3) 201.1127, found 201.1126.

(3S,4S,5R,6R)-Benzoic acid-2-methoxy-6-methoxycarbonylmethyl-3,5-dimethyltetrahydropyran-4-yl-ester ((+)-**10**). At ambient temperature a solution of PPh_3 (1.62 g, 6.20 mmol) and DBAD (1.43 g, 6.20 mmol) in toluene (6 ml) was prepared. After 0.5 h a solution of alcohol (+)-**10b** (720 mg, 3.10 mmol) in toluene (6 ml) and 15 min later benzoic acid (760 mg, 6.20 mmol) were added. The mixture was stirred for 15 h, quenched with water (10 ml) and the aqueous layer extracted with MTBE (3 × 10 ml). The combined organic layers were dried over $MgSO_4$, filtered, concentrated *in vacuo* and purified by column chromatography (PE/EtOAc 10:1) to yield benzoic ester (+)-**10** (863 mg, 2.57 mmol, 83%) as a colourless oil, α:β = 10:1. Analytical data for the predominating α-anomer: $[\alpha]_D^{20}$ = +44.0° (c = 0.7, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 2928, 2852, 1736, 1712, 1452, 1392, 1372, 1348, 1316, 1280, 1264, 1164, 1140, 1108, 1052, 1024, 996, 968, 908; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (m, 2H), 7.41-7.62 (m, 3H), 4.98 (dd, J = 3.0, 3.0 Hz, 1H), 4.46 (s, 1H), 4.42 (ddd, J = 10.2, 10.0, 3.2 Hz, 1H), 3.74 (s, 3H), 3.36 (s, 3H), 2.69 (dd, J = 14.9, 3.2 Hz, 1H),2.47 (dd, J = 14.9, 10.0 Hz, 1H), 2.23 (ddq, J = 7.5, 3.0 Hz, 1.1 Hz, 1H), 2.05 (m, 1H), 1.16 (d, J = 7.5 Hz, 3H), 0.91 (d, J = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 171.1 (CO), 165.2 (CO), 131.8 (*p*-ArC), 129.7 (ArC), 128.9 (*m*-ArC), 127.3 (*o*-ArC), 101.4 ($CH(OR)_2$), 74.0 ($OCHR_2$), 65.8 ($OCHR_2$), 54.1 (OCH_3), 50.7 (OCH_3), 37.5 (CH_2), 35.5 (CH), 32.1 (CH), 26.0, 14.4 (CH_3), 12.3 (CH_3); MS (80°C): $M^+ - OCH_3$ = 305 (0.6), 214 (5.2), 183 (5.7), 167 (2.1), 154 (26.2), 140 (1.1), 114 (2.4), 105 (100), 95 (7.4), 72 (14); HRMS calcd for $C_{18}H_{24}O_6$ (M^+) 336.1573, found 336.1574.

(3S,4S,5R,6R)-Benzoic acid 2-hydroxy-6-methoxycarbonylmethyl-3,5-dimethyltetrahydropyran-4-yl-ester ((+)-**11a**). Benzoic ester (+)-**10** (240 mg, 0.714 mmol) was dissolved in acetic acid (9.5 ml) and water (4.8 ml) and heated for 60 h to 50-55°C. The mixture was then diluted with MTBE (50 ml) and washed with a saturated aqueous solution of $NaHCO_3$ until all acid had been neutralized. The combined aqueous layers were extracted with MTBE (6 × 50 ml). The combined organic layers were dried over $MgSO_4$, filtered, concentrated *in vacuo* and purified by column chromatography (PE/EtOAc 3:1) to yield lactol (+)-**11a** (194 mg, 0.602 mmol, 85%, α:β-anomer = 3:2) as a colourless oil. $\nu_{max}(CHCl_3)/cm^{-1}$ 3592, 2976, 2952, 2884, 1716, 1600, 1454, 1436, 1420, 1388, 1344, 1312, 1272, 1176, 1156, 1096, 1068, 1024, 996, 964, 944, 928; ^{1}H NMR (400 MHz, $CDCl_3$) α-anomer δ 8.07 (m, 2H), 7.59 (m, 1H), 7.47 (m, 2H), 5.26 (d, J = 2.4 Hz, 1H), 5.20 (dd, J = 3.0, 3.0 Hz, 1H), 4.18 (ddd, J = 10.3, 9.2, 3.4 Hz, 1H), 3.71 (s, 3H), 2.67 (dd, J = 15.5, 3.4 Hz, 1H), 2.56 (dd, J = 15.5, 9.2 Hz, 1H), 2.21 (m, 1H), 2.03 (m, 1H), 1.11 (d, J = 7.2 Hz, 3H), 0.90 (d, J = 6.9 Hz, 3H); β-anomer δ 8.07 (m, 2H), 7.59 (m, 1H), 7.47 (m, 2H), 5.11 (dd, J = 3.0, 3.0 Hz, 1H), 4.98 (s, 1H), 4.57 (ddd, J = 10.3, 9.2, 3.6 Hz, 1H), 3.74 (s, 3H), 2.69 (dd, J = 15.1, 3.6 Hz, 1H), 2.52 (dd, J = 15.1, 9.2 Hz, 1H), 2.21 (m, 1H), 2.11 (m, 1H), 1.15 (d, J = 7.4 Hz, 3H), 0.94 (d, J = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) α-anomer δ 172.0 (CO), 165.7 (CO), 133.1 (ArC), 130.1 (*m*-ArC), 129.6 (*p*-ArC), 128.5 (*o*-ArC), 94.0 (CHOH), 77.6 ($OCHR_2$), 73.7 ($OCHR_2$), 51.8 (OCH_3), 38.5 (CH_2), 37.0 (CH), 33.0 (CH), 13.3 (CH_3), 8.8 (CH_3); β-anomer δ 172.0 (CO), 165.9 (CO), 133.2(ArC), 130.1(*m*-ArC), 129.6 (*p*-ArC), 128.5 (*o*-ArC), 95.8 (CHOH), 75.6 ($OCHR_2$), 66.9 ($OCHR_2$), 51.8 (OCH_3), 38.5 (CH_2), 38.2 (CH), 32.8 (CH), 15.2 (CH_3), 8.8 (CH_3); HRMS calcd for $C_{16}H_{19}O_5$ (M^+) 291.1232, found 291.1235.

(3S,4S,5R,R6)-Benzoic acid 2-methoxycarbonylmethyl-3,5-dimethyl-6-oxotetrahydropyran-4-yl ester ((+)-**11**). To *N*-morpholino-*N*-oxide (18 mg, 0.21 mmol) and activated molecular sieves (3Å) a solution of lactol (+)-**11a** (45 mg, 0.14 mmol) in DCM (1 ml) and then TPAP (2.5 mg, 6.9×10^{-3} mmol) were added at ambient temperature. After 3.5 h, the mixture was filtered through a short silica gel column (MTBE) and concentrated in vacuo to afford lactone (+)-**11** (44 mg, 0.14 mmol, 98%) as a white solid, mp 70°C. $[\alpha]_D^{20}$ = +11.6° (c = 1.4, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3040, 2980, 2952, 1736, 1600, 1452, 1384, 1360, 1336, 1316, 1272, 1228, 1176, 1156, 1108, 1068, 1024, 992, 952, 932, 908; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01-8.04 (m, 2H), 7.59-7.64 (m,

1H), 7.46-7.50 (m, 2H), 4.18-4.20 (dd, J = 3.5, 3.5 Hz, 1H), 4.88-4.94 (ddd, J = 10.7, 7.3, 3.9 Hz, 1H), 3.75 (s, 3H), 2.92-2.99 (dq, J = 7.5, 3.5 Hz, 1H), 2.80-2.86 (dd, J = 16.2, 3.9 Hz, 1H), 2.66-2.72 (dd, J = 16.2, 7.3 Hz, 1H), 2.41-2.50 (ddq, J = 10.7, 6.8, 3.5 Hz, 1H), 1.43-1.45 (d, J = 7.5 Hz, 3H), 1.07-1.09 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 171.8 (CO), 170.2 (CO), 165.7 (ArCO), 133.6 (ArC), 129.6 (*m*-ArC), 129.2 (*p*-ArC), 128.6 (*o*-ArC), 77.5 ($OCHR_2$), 75.1 ($OCHR_2$), 52.0 (OCH_3), 40.5 (CH), 37.9 (CH_2), 32.8 (CH), 15.9 (CH_3), 12.8 (CH_3); MS (90°C): $M^+ - OCH_3$ = 289 (0.6), 247 (1.1), 215 (0.6), 198 (16.2), 170 (9.5), 154 (2.6), 137 (2.2), 125 (21.5), 114 (1.5), 105 (100), 96 (8.9), 77 (17.2); HRMS calcd for $C_{17}H_{20}O_6$ (M^+) 320.1260, found 320.1258. Anal. Calcd for $C_{17}H_{20}O_6$: C, 63.74; H, 6.29. Found C, 63.59; H, 6.15.

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References and Notes

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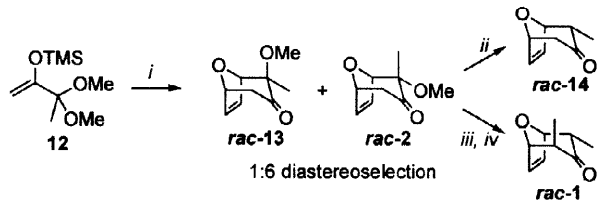
8. Basic equilibration (DBU, DCM or MeOH, MeONa) of 2α,4α-dimethyl-8-oxabicyclo[3.2.1]oct-6-en-3-one gave the epimers in a ratio of 2α,4α:2α,4β = 1.6:1 These were not separable by conventional means.
9. The Lewis acid catalyzed addition of furan to 2-trimethylsilyloxy-3,3-dimethoxy-1-butene gives 2α-methoxy-2β-methyl-8-oxabicyclo[3.2.1]oct-6-en-3-one ***rac*-2** in good yield. The diastereoselectivity of the [4+3] cycloaddition increases at lower temperature. Interestingly, the methylation of the oxabicyclic ketone ***rac*-13** did not lead to satisfactory yields. The SmI_2-promoted reduction of oxabicyclic ketone ***rac*-2** furnishes 2α-methyl-8-oxabicyclo[3.2.1]oct-6-en-3-one ***rac*-14**, a precursor of tetrahydropyran units of spongistatin and lasonolide.



i) furan (1 eq., 68 mmol), TMSOTf (5 mol%, 3.4 mmol), DCM (150 ml), -90°C (77%); *ii*) SmI_2, THF, MeOH, -78°C→rt, 16 h, then Zn, reflux, 1 h (94%); *iii*) LDA, THF, -78°C, TMEDA, MeI, -78°C→rt, 3 h (86%); *iv*) SmI_2, THF, MeOH, -78°C→rt, 19 h, then Zn, reflux, 1 h (97%)

For the [4+3] cycloaddition of α,α-dimethoxysilyl enol ethers to dienes see also: Pierau, S.; Hoffmann, H. M. R. *Synlett*, **1999**, 213.

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