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Asymmetric Synthesis of Polyacetate Derived Building Blocks with α-Oxyanion Functionality. Lewis Acid Catalyzed Opening of 2,9-Dioxabicyclo[3.3.1]nonan-3-ones

Ralf Dunkel and H. M. R. Hoffmann

Department of Organic Chemistry, University of Hannover, Schneiderberg 1B, D-30167 Hannover, Germany

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Abstract. All four stereoisomeric cyclic 3,5,7-trihydroxyheptanoic acid equivalents of the polyacetate aldol type (Scheme 1) are obtainable from 8-oxabicyclo[3.2.1]oct-6-en-3-one which functions as a *meso-configurated 4-way optical switch*. Lewis acid assisted nucleophilic ring opening of anomeric [3.3.1] oxabicyclic lactones is a key step. The utility of the methodology is exemplified by a 6 step synthesis of the C17-C23 fragment of spongistatin (altohyrtin) and C-glycoside analogues. © 1999 Elsevier Science Ltd. All rights reserved.

Polyketides are widespread building blocks of natural products.[1] The asymmetric aldol reaction works almost perfectly for the *polypropionate* type,[2] where stereocontrol is not only established by the chiral auxiliary, but

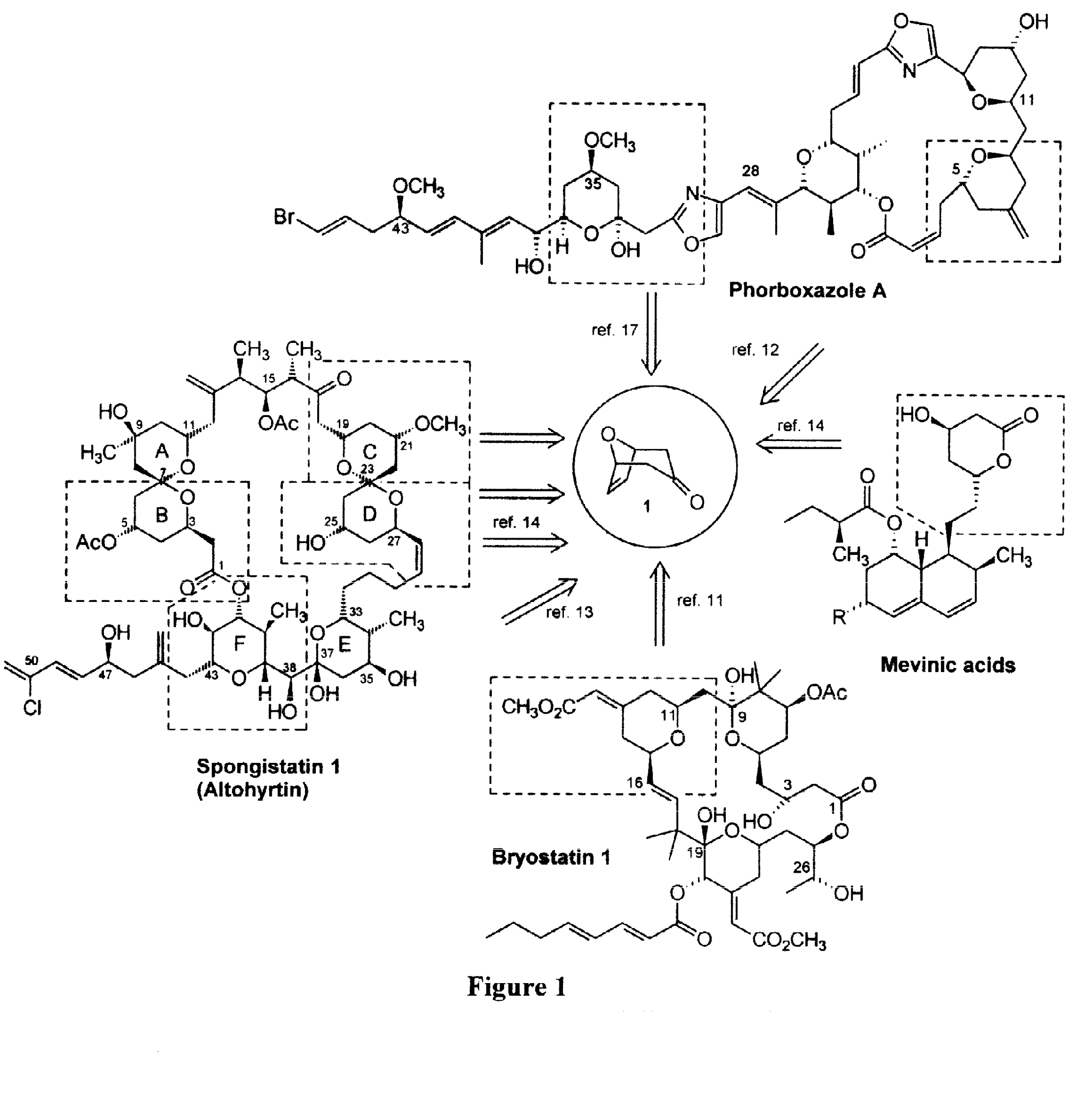
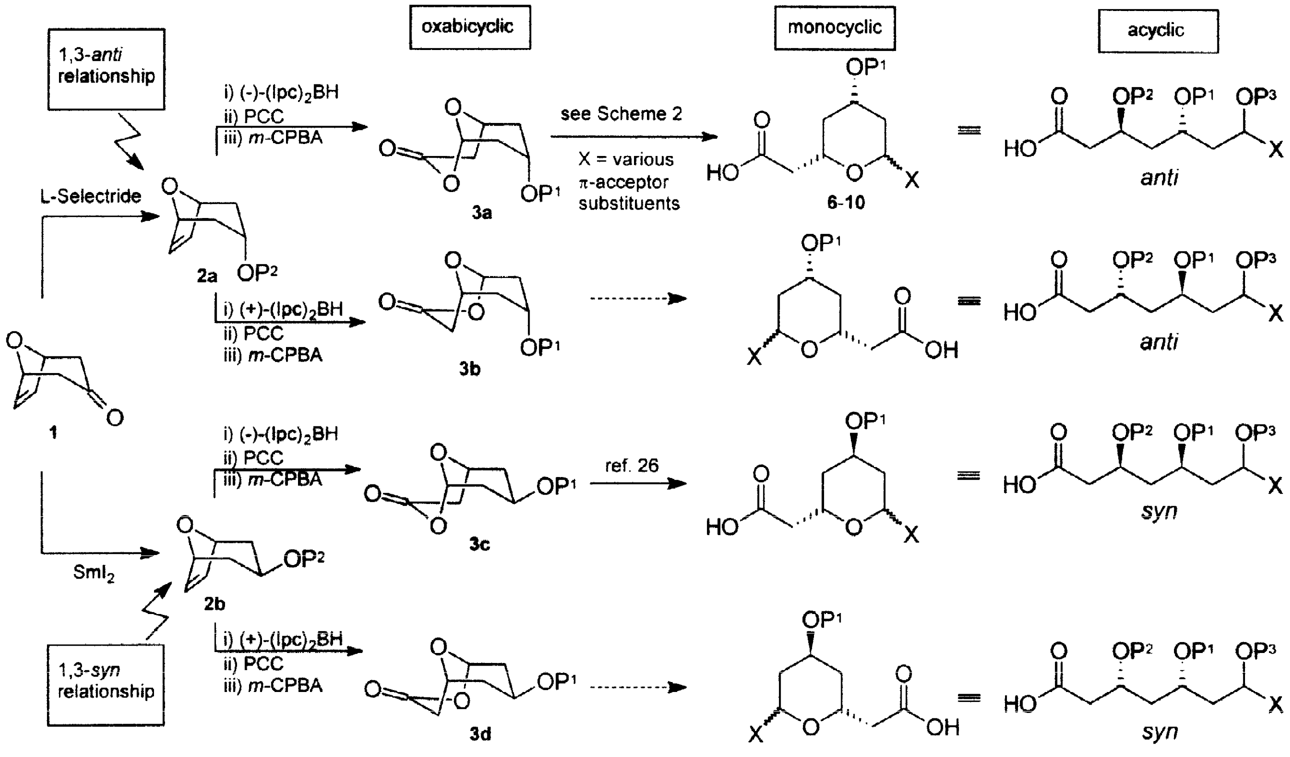


Figure 1

PII: S0040-4020(99)00460-3

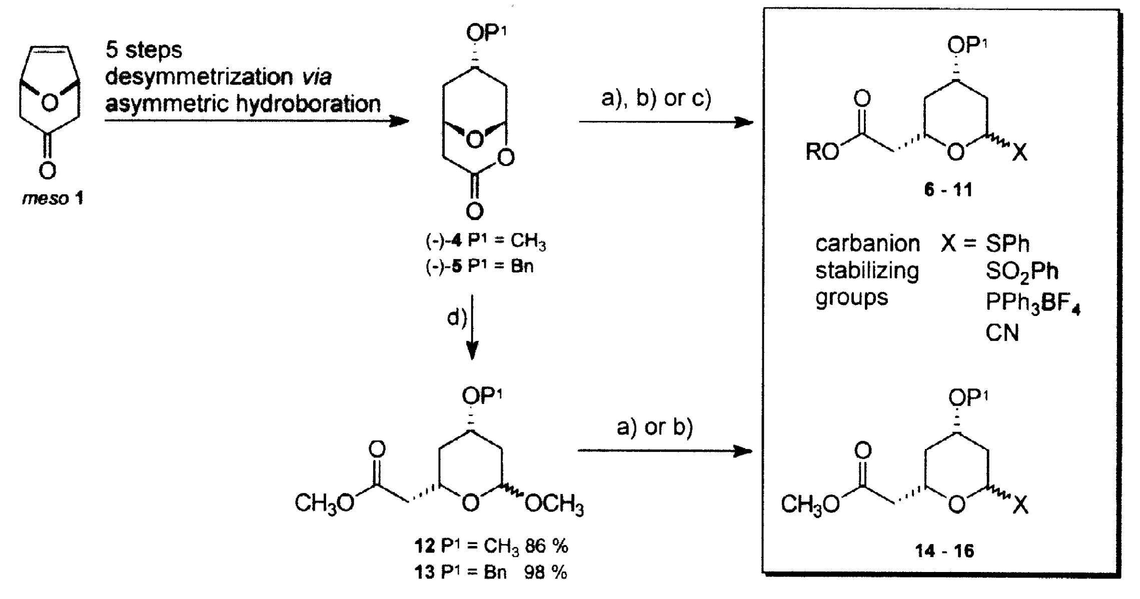
supported by a 1,2-relationship of alkyl substituent and carbonyl function in the transition state.[3] In aldol reactions of the *polyacetate* type chiral induction is necessarily weaker and enantioselectivity drops, often dramatically. Enantioselective variants of Lewis acid catalyzed additions of enol silanes to aldehydes commonly known as Mukaiyama aldol reaction are limited to specific substrates, e. g. d^2 components with phantom ligands[4] which are removed eventually or a^1 components with bulky substituents.[5] Chiral boron reagents in methyl ketone aldol reaction give only moderate levels of enantioselectivity at least for 1,3-induction.[6] Thus chirality is often transferred intramolecularly, as in hydroxy directed hydride transfer reactions to a prostereogenic carbonyl group. Recent examples for the reduction of aldols to 1,3-*anti* diols are Evans-Tishchenko[7] and Saksena-Evans[8] *internal* hydride transfer. In contrast 1,3-*syn* diols have often been obtained *via* Lewis acid complexation and *external* hydride donors.[9] Several skipped polyol chains have been prepared by two directional synthesis[10] *via meso* compounds and then desymmetrization.

We recently demonstrated high stereocontrol for the construction of polyacetate building blocks starting from *meso* 8-oxabicyclo[3.2.1]oct-6-en-3-one (**1**) as outlined in Figure 1. For example *cis* and also *trans* C-glycosides as in bryostatin ring A[11] and the C3-C9 fragment of the phorboxazoles A and B,[12] respectively, are easily accessible *via* different ring opening strategies of the five membered ring of the bicyclic starting material. Stereocontrol of all five ring carbon centres is possible as shown for spongistatin ring E.[13] High flexibility and absolute stereocontrol are demonstrated in the synthesis of the tetrahydropyran rings B, C and D[14] of the spongistatins[15, 16] and the C33-C37 fragment of the phorboxazoles A and B[17] (Figure 1). Functionalized 3,5-substituted β-alkoxy-δ-valerolactones allow coupling through nucleophilic attack. They also appear as chiral unit in the mevinic acids.[14, 18]



Scheme 1

We now report functionalization of the anomeric centre to provide C-glycoside precursors. In fact, *meso* bicyclic ketone **1** offers access to all four stereoisomers of the corresponding 3,5,7-trihydroxyheptanoic acids and their cyclic equivalents (Scheme 1). Selective reduction of the carbonyl function by reagent and substrate control gives the *syn*-aldol equivalent **2b** and *anti*-1,3-diol **2a**. The *meso* compounds **2a** and **2b** were desymmetrized *via* asymmetric hydroboration, oxidized and submitted to Baeyer-Villiger rearrangement. Thus all four enantiopure compounds **3a** - **3d** have been prepared. Oxabicyclic ketone **1** functions as an early *meso-configurated 4-way optical switch.* For umpolung of anomeric reactivity we have introduced a triphenylphosphonium group which allows Wittig olefination,[19] e. g. in natural product synthesis.[20]



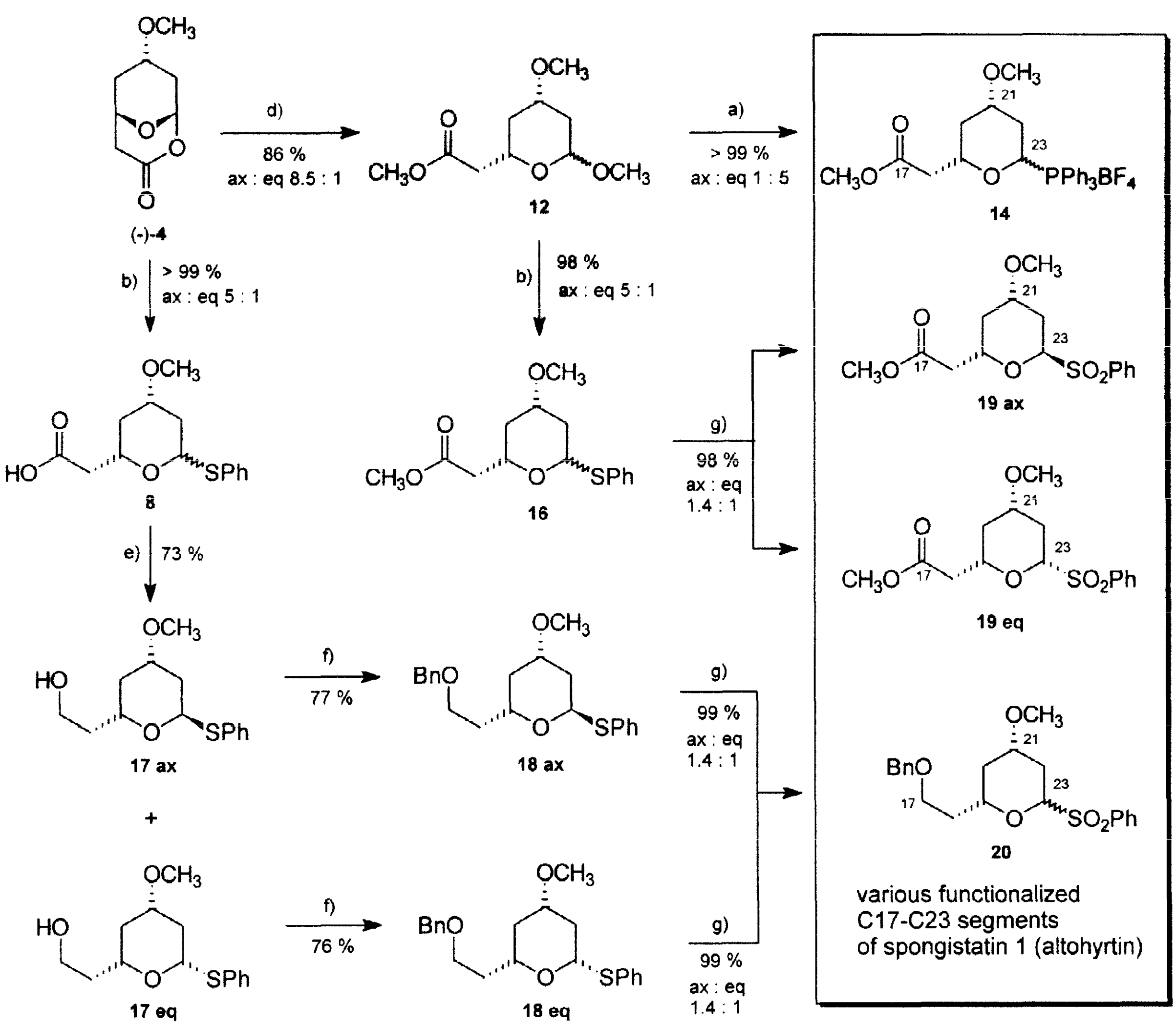
Scheme 2. a) $HPPh_3BF_4$; b) PhSH, $BF_3{\cdot}OEt_2$; c) TMSCN, TMSOTf; d) CH_3OH, catal. H_2SO_4.

Table 1. Various carbanion stabilizing groups at the anomeric centre.

Compound	R	P^1	X	Yield [%]	ax : eq
6	H	CH_3	PPh_3BF_4	>99	1 : 1
7	H	Bn	PPh_3BF_4	>99	1 : 1
8	H	CH_3	SPh	>99	5 : 1
9	H	Bn	SPh	93	1 : 1
10	H	Bn	CN	98	5 : 1
11	Bu^t	Bn	CN	53[a)]	5 : 1
14		CH_3	PPh_3BF_4	>99	1 : 5
15		Bn	PPh_3BF_4	>99	1 : 1
16		CH_3	SPh	98	5 : 1

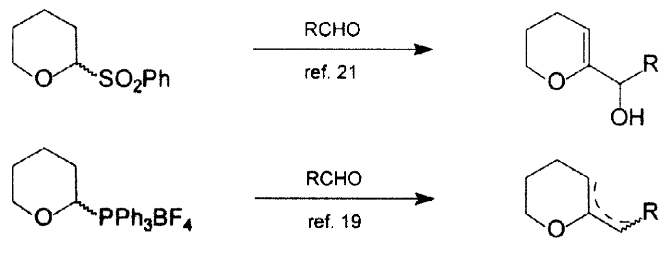
[a)] small scale esterfication of **10** *via* Bu^tOH, DCC, DMAP

Introduction of a sulfone group for which α-oxyanion stabilization is also known (Scheme 4 below),[21] was considered. However, attempts to convert simplified glycosidic methyl acetals, e. g. **12**, **13** with benzenesulphinic acid[22] into the sulfones and with dipyridyl disulphide and tributylphosphine[23] into the corresponding sulfides were not successful. The soft-hard combination of thiophenol and boron trifluoride etherate was more promising. The reaction proceeded directly and under even milder conditions with anomeric lactones, i. e. 2,9-dioxabicyclo[3.3.1]nonan-3-ones (–)-**4**, (–)-**5**. Introduction of the phosphonium group was tolerated by the protecting groups present in the lactones (–)-**4**, (–)-**5** and in the acetals **12** and **13**. The high reactivity of anomeric oxabicyclic lactones is obvious from the reaction of thiophenol with boron trifluoride etherate. Thus, lactones (–)-**4** and (–)-**5** were converted without deprotection at 0 °C and even at room temperature into the corresponding O,S-acetals **8** and **9** (Scheme 2). In contrast monocyclic acetals **12**, **13**, containing a terminal ester functionality required longer reaction times at ambient temperature for complete conversion. With stable protecting groups such as methyl protected acetal **12** conversion occurs without any side reactions, but the benzyl protecting group as in acetal **13** was partly removed during conversion into the corresponding O,S-acetal.[24] Ring opening of the 2,9-dioxabicyclo[3.3.1]nonan-3-ones was extended to other Lewis acid/nucleophile combinations, such as the opening of lactone (–)-**5** with trimethylsilyl cyanide and trimethylsilyl triflate, giving cyano acid **10**. Reaction was almost quantitative although characterization was easier with the derived *t*-butyl ester **11**.



Scheme 3. a) $HPPh_3BF_4$; b) PhSH, $BF_3{\cdot}OEt_2$; c) TMSCN, TMSOTf; d) CH_3OH, catal. H_2SO_4; e) $BH_3{\cdot}DMS$, $B(OEt)_3$; f) NaH, BnBr, Bu_4NI; g) *m*-CPBA, $NaHCO_3$.

For anomeric sulfides **8** the sequence was completed by borane reduction to the corresponding alcohols **17ax** and **17eq** which were separated by column chromatography (Scheme 3). Protection to the benzyl ethers **18ax** and **18eq** and oxidation to the anomeric sulfones **20** afforded the spongistatin C17-C23 fragment, correctly functionalized for α-oxyanion coupling. Sulfones **19ax** and the epimeric **19eq** were obtained by a shorter sequence *via* oxidation of anomeric sulfides **16**. They are equivalent building blocks and contain an ester functionality at C17 (Figure 1), ready for C16-C17 coupling by established methodology.[25]



Scheme 4

In summary all four bicyclic anomeric lactones **3a** - **3d** and their monocyclic deoxygenated heptopyranuronic acids are accessible from *meso* 8-oxabicyclo[3.2.1]oct-6-en-3-one (**1**), which is a highly versatile building block (Scheme 1). Polyacetate based oxacycles **6** - **10** were obtained enantiopure in only 6 steps and 50% yield overall. Stereoselectivity is induced by substrate and reagent control only, without recourse to a chiral auxiliary. Beyond Figure 1 we have extended the utility of title bicyclic compound to building blocks containing a variety of carbanion stabilizing π-acceptors (Scheme 2, 3). Umpolung of anomeric reactivity was established by straightforward Lewis acid catalyzed ring opening of 2,9-dioxabicyclo[3.3.1]nonan-3-ones. The utility of our single-isomer, anomeric [3.3.1] oxabicyclic lactones has also been illustrated by the synthesis of the spongistatin ring C and E segment.[26]

Experimental

General. 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 internal standard. – Mass spectra were recorded on a Finnigan MAT 312 (70 eV) or a VG Autospec spectrometer at room temperature 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-backed 0.2-mm silica gel 60 F_{254} plates (E. Merck). – Diethyl ether (E) and THF were distilled over sodium and benzophenone before use. CH_2Cl_2 (DCM) was distilled over CaH_2 before use. DMF was dried over BaO and distilled over CaH_2 before use. Methyl *t*-butyl ether (MTBE), ethyl acetate (EA), cyclohexane (CH) and light petroleum (PE, bp 40-60 °C) were distilled before use.

8-Oxabicyclo[3.2.1]oct-6-en-3-one (**1**) was prepared from furan and tetrabromoacetone by our optimized procedure[27] on a 1 molar scale. Selective reduction to the axial **2a** or equatorial alcohol **2b** was performed *via* L-Selectride at –78 °C or SmI_2 reduction in refluxing THF, respectively.[14] Desymmetrization of the protected alcohols *via* asymmetric hydroboration with (–)-$(Ipc)_2BH$ or (+)-$(Ipc)_2BH$ afforded the enantiopure alcohols **3a** - **3d**.[14] PCC and Baeyer-Villiger oxidation gave the 2,9-dioxabicyclo[3.3.1]nonan-3-ones, e. g. (–)-**4** and (–)-**5** which were cleaved as described below, or by acidic methanolysis to give methylacetals **12** and **13**.[11, 14]

General procedure for the conversion of lactones and acetals into the corresponding triphenylphosphonium tetrafluoroborates. The substrate was heated (0.1 M in acetonitrile) with an equimolar amount of triphenylphosphonium tetrafluoroborate under reflux for 1 h. The mixture was concentrated *in vacuo* and recrystallized from ethyl ether/chloroform (50/1).

Triphenylphosphonium tetrafluoroborate salt **6**. According to the general procedure lactone (–)-**4** was converted into **6**, white solid (ax/eq = 1/1) in >99% yield. Spectroscopic data was determined from the anomeric mixture. ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 7.85 - 7.62 (m, 30 H, PPh_3), 5.71 (m, 2 H, H-6/H-6'), 4.64 (m, 1 H, H-2), 4.36 (m, 1 H, H-2'), 3.93 (m, 1 H, H-4), 3.79 (bd, *J* = 3.1 Hz, 1 H, H-4'), 3.32 (s, 3 H, OCH_3), 3.27 (s, 3 H, OCH_3), 2.69 (dd, *J* = 16.4 Hz, *J* = 4.3 Hz, 1 H, H-7a), 2.55 (m, 2 H, H-7b/H-7a'), 2.48 (dd, *J* = 16.2 Hz, *J* = 8.3 Hz, 1 H, H-7b'), 2.36 (m, 1H, H-3_{eq}), 2.09 (m, 3 H, H-3_{eq}', H-5_{eq}/H-5_{eq}'), 1.92 (bd, *J* = 15.7 Hz, 1 H, H-3_{ax}), 1.45 (ddd, *J* = 11.6 Hz, *J* = 11.6 Hz, *J* = 10.7 Hz, 1 H, H-3_{ax}'), 1.23 (m, 2 H, H-5_{ax}/H-5_{ax}'); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 173.85 (C, C-8), 135.75/135.72/135.55/135.52 (CH, *p*-C_{Ph}), 134.36/134.32/134.26/ 134.22 (CH, *o*-C_{Ph}), 130.73/130.60/130.57/130.45 (CH, *m*-C_{Ph}), 116.28/115.90/115.43/115.06 (C, C_{Ph}), 75.48/74.27 (CH, C-2), 71.73/70.81 (CH, C-4), 70.51/65.22 (CH, C-6), 56.36/55.92 (CH_3, OCH_3), 40.50/37.75 (CH_2, C-7), 36.63/31.26 (CH_2, C-3), 30.51/29.13 (CH_2, C-5); ν_{max} ($CHCl_3$)/cm^{-1} 3300, 3040, 2932, 1716, 1484, 1440, 1388, 1372, 1340, 1284, 1228, 1188, 1152, 1112, 1072, 996; FAB: 435 (M^+–87 (BF_4), 100), 263 (54), 183 (15), 141 (17).

Triphenylphosphonium tetrafluoroborate salt **7**. According to the general procedure lactone (–)-**5** was converted into **7**, white solid (ax/eq = 1/1) in >99% yield. Spectroscopic data was determined from the anomeric mixture. Further assignment was possible through CH-COSY (400 MHz, TMS). ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 7.88 - 7.62 (m, 30 H, PPh_3), 7.29 - 7.15 (m, 10 H, Bn), 5.71 (m, 1H, H-6$^\alpha$), 5.69 (dd, *J* = 11.0 Hz, *J* = 3.7 Hz, 1 H, H-6$^\beta$), 4.64 (m, 1H, H-2$^\alpha$), 4.58/4.51 (d, *J* = 11.2 Hz, 1 H, CH_2Ph), 4.52/4.44 (d, *J* = 12.1 Hz, 1 H, CH_2Ph), 4.38 (m, 1 H, H-2$^\beta$), 4.20 (ddd, *J* = 10.8 Hz, *J* = 6.1 Hz, *J* = 4.4 Hz, H-4$^\alpha$), 4.00 (m, 1H, H-4$^\beta$), 3.32 (dd, *J* = 16.4 Hz, *J* = 9.9 Hz, 1 H, H-7a$^\beta$), 2.74 (dd, *J* = 16.4 Hz, *J* = 4.2 Hz, 1 H, H-7b$^\beta$), 2.56 (dd, *J* = 16.1 Hz, *J* = 3.6 Hz, 1 H, H-7a$^\alpha$), 2.48 (dd, *J* = 16.1 Hz, *J* = 8.4 Hz, 1 H, H-7b$^\alpha$), 2.35 (m, 1H, H-5_{ax}^α), 2.22 (m, 1H, H-3_{eq}^β), 2.12 (m, 2 H, H-3_{eq}^α/H-5_{eq}^α), 2.06 (m, 1H, H-5_{ax}^β), 1.93 (bd, *J* = 13.2 Hz, 1 H, H-5_{eq}^β), 1.54 (ddd, *J* = 11.6 Hz, *J* = 11.5 Hz, *J* = 10.7 Hz, H-3_{ax}^β), 1.34 (ddd, *J* = 12.0 Hz, *J* = 11.8 Hz, *J* = 11.7 Hz, H-3_{ax}^α); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 174.44/174.26 (C, C-8), 138.20/137.83 (C, C_{Bn}), 135.75/135.72/135.53/135.50 (CH, *p*-C_{Ph}), 134.32/134.27/134.23/134.18 (CH, *m*-C_{Ph}), 130.71/130.58/130.54/130.42 (CH, *o*-C_{Ph}), 128.53/ 128.35 (CH, *m*-C_{Bn}), 127.94/127.69 (CH, *o*-C_{Bn}), 127.81/127.64 (CH, *p*-C_{Bn}), 116.20/115.80/115.36/114.96 (C, C_{Ph}), 75.38/75.24 (CH, C-2), 73.31/73.14 (CH, C-4), 71.08/70.89 (CH, C-6), 40.40/37.90 (CH_2, C-7), 37.12/31.85 (CH_2, C-3), 31.39/29.48 (CH_2, C-5); ν_{max} ($CHCl_3$)/cm^{-1} 3336, 3012, 2952, 2924, 2872, 2848, 1716, 1652, 1616, 1600, 1588, 1508, 1484, 1440, 1396, 1360, 1112, 1072, 996, 912, 864, 620, 568, 520; MS (200 °C): 565 (M^+–33, 3.2), 424 (3.0), 310 (3.2), 277 (3.1), 263 (21.0), 262 (100.0), 261 (15.8), 184 (17.5), 183 (75.4), 157 (6.7), 152 (11.2), 108 (36.8), 107 (16.3), 91 (14.9), 81 (10.1), 79 (14.8), 77 (15.6); FAB: 511 (M^+–87 (BF_4), 100), 403 (5), 263 (46), 183 (14), 141 (8).

(2S,4S)-(4-Methoxy-6-phenylsulfanyl-tetrahydro-pyran-2-yl)-acetic acid (**8**). At 0 °C 72.0 μl (0.7 mmol) of thiophenol and 88.0 μl (0.7 mmol) of boron trifluoride etherate were added to a solution of 120.7 mg (0.7 mmol) of lactone (–)-**4** in 2 ml of abs. DCM. The solution was stirred 2 h at 0 °C and quenched with 0.5 ml of water, stirred for 1.5 h at rt, dried over Na_2SO_4 and concentrated *in vacuo*. Recrystallization of the crude product (PE/E = 15/1) afforded **8** (197.0 mg, 0.7 mmol, >99%) as an anomeric mixture α/β = 5/1 (determined by ^{1}H NMR). Spectroscopic data for the predominating α-anomer were determined from the anomeric mixture. ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 7.51 - 7.41 (m, 2 H, *o*-Ph), 7.33 - 7.18 (m, 3 H, *m*-, *p*-Ph), 5.68 (bd, *J* = 5.3 Hz, 1 H, H-6), 4.76 (dd, *J* = 12.0 Hz, *J* = 1.8 Hz, 1 H, H-2), 4.70 (dddd, *J* = 11.7 Hz, *J* = 11.4 Hz, *J* = 5.5 Hz, *J* = 5.3 Hz, 1 H, H-4), 3.38 (s, 3 H, OCH_3), 2.59 (dd, *J* = 15.4 Hz, *J* = 7.5 Hz, 1 H, H-7a), 2.52 (dd, *J* = 15.4 Hz, *J* = 7.4 Hz, 1 H, H-7b), 2.20 (ddd, *J* = 12.0 Hz, *J* = 5.3 Hz, *J* = 1.8 Hz, 1 H, H-3_{eq}), 2.09 (m, 1H, H-5_{eq}), 1.86 (m, 1H, H-5_{ax}), 1.52 (ddd, *J* = 12.0 Hz, *J* = 11.9 Hz, *J* = 11.2 Hz, 1 H, H-3_{ax}); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 176.39 (C, C-8), 134.89 (C, C_{Ph}), 131.31 (CH, *m*-C_{Ph}), 128.90 (CH, *o*-C_{Ph}), 127.08 (CH, *p*-C_{Ph}), 84.79 (CH, C-6), 72.12 (CH, C-2), 65.55 (CH, C-4), 55.55 (CH_3, OCH_3), 40.52 (CH_2, C-7), 37.34 (CH_2, C-5), 36.74 (CH_2, C-3); ν_{max} ($CHCl_3$)/cm^{-1} 3512, 3064, 3000, 2928, 1712, 1584, 1480, 1440, 1380, 1296, 1264, 1228, 1188, 1152, 1080, 1024, 984, 956, 908; FAB: 282 (M^+, 27), 281 (36), 218 (46), 173 (100), 163 (57); HR-MS calcd. for $C_{14}H_{18}O_4S$ (M^+) 282.0926, found 282.0928.

(2S,4S)-(4-Benzyloxy-6-phenylsulfanyl-tetrahydro-pyran-2-yl)-acetic acid (**9**). At 0 °C 23.0 μl (0.2 mmol) of thiophenol and 28.0 μl (0.2 mmol) of boron trifluoride etherate were added to a solution of 55.7 mg (0.2 mmol) of lactone (–)-**5** in 1 ml of abs. DCM. The solution was stirred 15 min at 0 °C and 45 min at rt, quenched with 30 μl of water, dried over Na_2SO_4 and concentrated *in vacuo*. Recrystallization of the crude product (PE/E = 15/1) afforded **9** (74.2 mg, 0.2 mmol, 93%) as an anomeric mixture α/β = 1/1 (determined by ^{1}H NMR). Spectroscopic data were determined from the anomeric mixture. ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 7.45 - 7.39 (m, 4 H, *o*-SPh), 7.34 - 7.14 (m, 16 H, *p*-, *m*- SPh/Bn), 5.68 (d, *J* = 5.1 Hz, H-6^{α}), 4.73 (dd, *J* = 11.8 Hz, *J* = 1.9 Hz, 1 H, H-6^{β}), 4.68 (m, 1H, H-2), 4.57 (d, *J* = 12.0 Hz, 1 H, CH_2Ph), 4.53 (d, *J* = 12.0 Hz, 1 H, CH_2Ph), 4.55 (d, *J* = 12.5 Hz, 1 H, CH_2Ph), 4.52 (d, *J* = 12.5 Hz, 1 H, CH_2Ph), 3.90 (m, 1H, H-4^{α}), 3.86 (m, 1H, H-2), 3.62 (ddd, *J* = 11.7 Hz, *J* = 10.8 Hz, *J* = 4.6 Hz, 1 H, H-4^{β}), 2.73 (dd, *J* = 16.4 Hz, *J* = 8.5 Hz, 1 H, H-7a), 2.73 (dd, *J* = 15.4 Hz, *J* = 8.1 Hz, 1 H, H-7a), 2.53 (dd, *J* = 15.4 Hz, *J* = 4.4 Hz, 1 H, H-7b), 2.52 (dd, *J* = 16.4 Hz, *J* = 5.0 Hz, 1 H, H-7b), 2.45 (ddd, *J* = 12.9 Hz, *J* = 4.4 Hz, *J* = 1.7 Hz, 1 H, H-5_{eq}^{α}), 2.39 (ddd, *J* = 12.9 Hz, *J* = 4.6 Hz, *J* = 1.9 Hz, 1 H, H-5_{eq}^{β}), 2.20 (ddd, *J* = 11.8 Hz, *J* = 4.4 Hz, *J* = 2.2 Hz, 1 H, H-3_{eq}), 2.09 (ddd, *J* = 11.8 Hz, *J* = 4.4 Hz, *J* = 2.2 Hz, 1 H, H-3_{eq}), 1.95 (ddd, *J* = 12.9 Hz, *J* = 11.8 Hz, *J* = 5.1 Hz, 1 H, H-5_{ax}^{α}), 1.62 (ddd, *J* = 12.9 Hz, *J* = 11.8 Hz, *J* = 11.8 Hz, 1 H, H-5_{ax}^{β}), 1.39 (ddd, *J* = 11.8 Hz, *J* = 11.7 Hz, *J* = 11.6 Hz, 1 H, H-3_{ax}), 1.36 (ddd, *J* = 11.8 Hz, *J* = 11.7 Hz, *J* = 11.4 Hz, 1 H, H-3_{ax}); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 176.61/176.54 (C, C-8), 138.16/138.02 (C, C_{Bn}), 134.87/134.38 (C, C_{SPh}), 132.77/132.44/131.38/130.66/128.96 /128.81/128.78/128.51/128.48/128.47/127.96/127.89/127.76/127.73/127.70/127.64/127.60/127.10/127.09 (CH, C_{Bn}/C_{SPh}), 84.83/82.53 (CH, C-2), 74.40/73.88 (CH, C-4), 72.12/70.92 (CH, C-6), 70.09/69.91 (CH_2, CH_2Ph), 40.70/40.52 (CH_2, C-7), 37.87/37.24/37.16/36.68 (CH_2, C-5/C-3); ν_{max} ($CHCl_3$)/cm^{-1} 3400, 3064, 3028, 2948, 2924, 1712, 1584, 1480, 1440, 1412, 1360, 1296, 1256, 1192, 1152, 1112, 1068, 1024, 984, 960, 932, 908; MS (130 °C): 250 (M^+–108, 1.4), 249 (7.7), 218 (3.8), 200 (2.4), 199 (9.9), 155 (2.3), 143 (5.3), 141 (31.3), 118 (8.6), 109 (20.5), 91 (100.0), 81 (10.4), 70 (8.1), 65 (11.2); HR-MS calcd. for $C_{14}H_{17}O_4$ (M^+–SPh) 249.1126, found 249.1124.

(2S,4S)-(4-Benzyloxy-6-cyano-tetrahydro-pyran-2-yl)-acetic acid (**10**). At 0 °C 140.0 μl (1.0 mmol) of trimethylsilyl cyanide and 40.0 μl (0.2 mmol) of trimethylsilyl triflate were added successively to a solution of 52.0 mg (0.2 mmol) of lactone (–)-**5** in 2 ml of abs. acetonitrile. The reaction mixture was stirred for 30 min at rt, then poured into sodium hydrogen carbonate solution. After neutralization with ammonium chloride the aqueous layer was extracted with DCM, dried over Na_2SO_4 and concentrated *in vacuo* to afford a yellow solid which was recrystallized from PE/E = 10/1. Yield 41.2 mg (0.15 mmol, 71%) of **10** (ax/eq = 5/1). Spectroscopic data were determined from the anomeric mixture. ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 9.20 (bs, 1 H, OH), 7.38 - 7.30 (m, 5 H, Ph), 4.94 (dd, *J* = 5.5 Hz, *J* = 1.3 Hz, 1 H, H-6), 4.61 (d, *J* = 11.4 Hz, 1 H, CH_2Ph), 4.56 (d, *J* = 11.4 Hz, 1 H, CH_2Ph), 4.25 (m, 1H, H-2), 3.93 (dddd, *J* = 11.4 Hz, *J* = 11.3 Hz, *J* = 4.4 Hz, *J* = 4.2 Hz, 1 H, H-4), 2.66 (dd, *J* = 16.0 Hz, *J* = 7.5 Hz, 1 H, H-7a), 2.56 (dd, *J* = 16.0 Hz, *J* = 5.2 Hz, 1 H, H-7b), 2.25 (ddd, *J* = 13.6 Hz, *J* = 4.2 Hz, *J* = 1.3 Hz, 1 H, H-5_{eq}), 2.24 (bd, *J* = 12.5 Hz, 1 H, H-3_{eq}), 1.81 (ddd, *J* = 13.6 Hz, *J* = 11.3 Hz, *J* = 5.5 Hz, 1 H, H-5_{ax}), 1.40 (ddd, *J* = 12.5 Hz, *J* = 11.6 Hz, *J* = 11.4 Hz, 1 H, H-3_{ax}); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 175.60 (C, C-8), 137.70 (C, C_{Ph}), 128.54 (CH, *m*-C_{Ph}), 127.92 (CH, *o*-C_{Ph}), 127.64 (CH, *p*-C_{Ph}), 116.93 (C, CN), 70.97/70.44 (CH, C-2/C-6), 63.72 (CH, C-4), 40.33 (CH_2, C-7), 37.01 (CH_2, C-5), 29.65 (CH_2, C-3); ν_{max} ($CHCl_3$)/cm^{-1} 3040, 2924, 2868 , 2680, 2584, 1716, 1452, 1432, 1364, 1312, 1264, 1228, 1164, 1120, 1076, 1028, 976, 912, 864, 840; MS (50 °C): 279 (M^++4, 2.5), 168 (2.8), 167 (4.0), 149 (12.8), 139 (2.3), 111 (3.8), 107 (6.8), 91 (12.7), 87 (12.1), 85 (69.3), 84 (10.6), 83 (100.0), 80 (9.8), 69 (6.6).

(2S,4S)-(4-Benzyloxy-6-cyano-tetrahydro-pyran-2-yl)-acetic acid tert*-butyl ester* (**11**). A solution of 30.0 mg (0.1 mmol) of acid **10**, 26.5 mg (0.1 mmol) of N,N'-dicyclohexylcarbodiimide, 96.2 mg (1.3 mmol) of *t*-butanol and a catalytic amount of 4-dimethylaminopyridine in 1 ml of abs. DCM was stirred overnight at rt. The reaction mixture was poured into sodium hydrogen carbonate solution, extracted with DCM, dried over Na_2SO_4 and concentrated *in vacuo*. Purification by column chromatography (CH/EA = 5/1) yielded 19.2 mg (0.06 mmol, 53%) of ester **11** (ax/eq = 5/1). Spectroscopic data were determined from the anomeric mixture. ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 7.36 - 7.32 (m, 5 H, Ph), 4.93 (dd, *J* = 5.9 Hz, *J* = 1.7 Hz, 1 H, H-6), 4.60 (d, *J* = 11.6 Hz, CH_2Ph), 4.56 (d, *J* = 11.6 Hz, 1 H, CH_2Ph), 4.21 (m, 1H, H-2), 3.90 (dddd, *J* = 11.2 Hz, *J* = 8.8 Hz, *J* = 6.7 Hz, *J* = 4.4 Hz, 1 H, H-4), 2.49 (dd, *J* = 15.3 Hz, *J* = 7.5 Hz, 1 H, H-7a), 2.43 (dd, *J* = 15.3 Hz, *J* = 5.4 Hz,

1 H, H-7b), 2.23 (ddd, J = 13.1 Hz, J = 4.4 Hz, J = 1.7 Hz, 1 H, H-5_{eq}), 2.21 (m, 1H, H-3_{eq}), 1.79 (ddd, J = 13.1 Hz, J = 11.2 Hz, J = 5.9 Hz, 1 H, H-5_{ax}), 1.47 (s, 9 H, $C(CH_3)_3$), 0.97 (m, 1H, H-3_{ax}); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 169.12 (C, C-8), 137.88 (C, C_{Ph}), 128.55 (CH, m-C_{Ph}), 127.90 (CH, p-C_{Ph}), 127.64 (CH, o-C_{Ph}), 117.15 (C, *C*N), 81.19 (C, $\textit{C}(CH_3)_3$), 73.77 (CH, C-6), 70.91 (CH, C-2), 70.43 (CH_2, CH_2Ph), 63.75 (CH, C-4), 42.06 (CH_2, C-7), 37.18 (CH_2, C-5), 34.49 (CH_2, C-3), 28.07 (CH_3, $C(\textit{C}H_3)_3$); ν_{max} ($CHCl_3$)/cm^{-1} 3008, 2980, 2932, 2868, 1724, 1496, 1452, 1392, 1368, 1312, 1260, 1232, 1152, 1076, 1028, 976, 840; MS (80 °C): 276 (M^+–55, 1.4), 275 (7.4), 274 (18.4), 258 (2.5), 240 (1.8), 184 (1.5), 167 (5.1), 150 (3.7), 141 (12.7), 107 (51.6), 105 (6.3), 92 (18.6), 91 (100.0), 80 (3.7), 65 (4.7); HR-MS calcd. for $C_{15}H_{16}NO_4$ (M^+–Bu^t) 274.1079, found 274.1076.

Triphenylphosphonium tetrafluoroborate salt **14**. According to the general procedure acetal **12** was converted into **14**. Yield 129.0 mg (0.24 mmol, >99%) of white crystals, mp 153 - 156 °C. The product was obtained as an anomeric mixture (ax : eq = 1 : 5 (^1H NMR)). Spectroscopic data for the major anomer were determined from the anomeric mixture. ^1H NMR (400 MHz, $CDCl_3$, TMS) δ 7.90 - 7.65 (m, 15 H, PPh_3), 5.78 (dd, J = 12.3 Hz, J = 2.6 Hz, 1 H, H-6), 4.38 (m, 1H, H-2), 3.94 (m, 1H, H-4), 3.54 (s, 3 H, OCH_3), 3.34 (s, 3 H, OCH_3), 2.52 - 2.47 (m, 2 H, H-3_{eq}/H-5_{eq}), 2.41 (bd, J = 12.9 Hz, 1 H, H-7a), 2.18 (bd, J = 12.9 Hz, 1 H H-7b), 1.42 (ddd, J = 11.4 Hz, J = 11.0 Hz, J = 10.8 Hz, 1 H, H-3_{ax}), 1.21 (ddd, J = 12.9 Hz, J = 11.8 Hz, J = 11.8 Hz, 1 H, H-5_{ax}); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 170.29 (C, C-8), 135.40/135.37 (CH, p-C_{Ph}), 134.37/134.27 (CH, o-C_{Ph}), 130.52/130.40 (CH, m-C_{Ph}), 116.35/115.51 (C, C_{Ph}), 75.53 (CH, C-2), 74.11 (CH, C-4), 70.51 (CH, C-6), 55.97 (CH_3, OCH_3), 51.73 (CH_3, OCH_3), 40.68 (CH_2, C-7), 36.80 (CH_2, C-3), 31.21 (CH_2, C-5); ν_{max} ($CHCl_3$)/cm^{-1} 3040, 2952, 2932, 1736, 1588, 1440, 1228, 1112, 1076; FAB: 449 (M^+–87 (BF_4), 80), 263 (100), 183 (70), 155 (47), 133 (50).

Triphenylphosphonium tetrafluoroborate salt **15**. According to the general procedure acetal **13** was converted into **17**. Yield 301.6 mg (0.5 mmol, >99%) of white crystals. The product was obtained as an anomeric mixture (ax : eq = 1 : 1 (^1H NMR)). Spectroscopic data were determined from the anomeric mixture. ^1H NMR (400 MHz, $CDCl_3$, TMS) δ 7.87 - 7.64 (m, 30 H, PPh_3), 7.38 - 7.21 (m, 10 H, Bn), 5.78 (dd, J = 9.9 Hz, J = 4.4 Hz, 1 H, H-2), 5.62 (m, 1H, H-2), 4.63 (m, 1H, H-4), 4.59/4.53 (d, J = 11.2 Hz, CH_2Ph), 4.54/4.45 (d, J = 12.0 Hz, 1 H, CH_2Ph), 4.38 (m, 1H, H-4), 4.20 (dd, J = 10.1 Hz, J = 4.4 Hz, 1 H, H-6^{β}), 4.04 (dd, J = 6.6 Hz, J = 3.3 Hz, 1 H, H-6^{α}), 3.59 (s, 3 H, OCH_3), 3.53 (s, 3 H, OCH_3), 3.25 (dd, J = 16.0 Hz, J = 9.9 Hz, 1 H, H-7a), 2.70 (dd, J = 16.0 Hz, J = 4.4 Hz, 1 H, H-7b), 2.50 (dd, J = 15.5 Hz, J = 4.2 Hz, 1 H, H-7a), 2.44 (dd, J = 15.5 Hz, J = 8.1 Hz, 1 H, H-7b), 2.38 (m, 1H, H-5_{eq}), 2.19 (m, 3 H, H-$5_{ax}{}^{\alpha}$, H-$5_{ax}{}^{\beta}$/H-3_{eq}), 1.92 (m, 1H, H-5_{eq}), 1.52 (ddd, J = 12.1 Hz, J = 12.1 Hz, J = 10.1 Hz, 1 H, H-3_{ax}), 1.32 (ddd, J = 12.3 Hz, J = 11.6 Hz, J = 11.4 Hz, 1 H, H-3_{ax}); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 171.20/170.34 (C, C-8), 135.72/135.69/135.38/135.35 (CH, p-C_{Ph}), 134.39/134.35/134.30/134.26 (CH, o-C_{Ph}), 130.72/130.62/130.51, 130.39 (CH, m-C_{Ph}), 128.53/128.35/127.94/127.65 (C, C_{Ph}), 75.57/73.27 (CH, C-2), 71.55/70.58 (CH, C-4), 71.21/70.96 (CH_2, CH_2Ph), 68.95/65.76 (CH, C-6), 51.88/51.74 (CH_3, OCH_3), 40.67/38.05 (CH_2, C-7), 37.32/31.82 (CH_2, C-3), 31.44/29.50 (CH_2, C-5); ν_{max} ($CHCl_3$)/cm^{-1} 3030, 2954, 1736, 1602, 1485, 1439, 1230, 1111, 1062, 998, 909, 522; FAB: 525 (M^+–87 (BF_4), 100), 417 (15), 263 (27).

(2S,4S)-(4-Methoxy-6-phenylsulfanyl-tetrahydro-pyran-2-yl)-acetic acid methyl ester (**16**). At 0 °C 47.0 µl (0.45 mmol) of thiophenol and 58.0 µl (0.45 mmol) of boron trifluoride etherate were added successively to a solution of 100.0 mg (0.45 mmol) of acetal **12** in 3 ml of abs. DCM. After 5 min. the reaction mixture was warmed to ambient temperature, stirred for 3 h, poured into sat. sodium hydrogen carbonate solution, extracted with DCM, dried over Na_2SO_4 and concentrated *in vacuo*. Column chromatography (CH/EA = 5/1 to 2/1) yielded 133.4 mg (0.45 mmol, 98%) of **16** as an anomeric mixture (ax/eq = 0.8/1 (^1H NMR)). Spectroscopic data for the major anomer were determined from the anomeric mixture. ^1H NMR (400 MHz, $CDCl_3$, TMS) δ 7.46 (m, 2 H, o-Ar), 7.25 (m, 3 H, p-/m-Ar), 5.70 (bd, J = 5.5 Hz, 1 H, H-6), 4.68 (dddd, J = 11.0 Hz, J = 8.3 Hz, J = 5.0 Hz, J = 2.2 Hz, 1 H, H-2), 3.88 (m, 1H, H-4), 3.56 (s, 3 H, OCH_3), 3.37 (s, 3 H, OCH_3), 2.57 (dd, J = 15.0 Hz, J = 8.3 Hz, 1 H, H-7a), 2.49 (dd, J = 15.0 Hz, J = 5.0 Hz, 1 H, H-7b), 2.18 (ddd, J = 12.9 Hz, J = 4.5 Hz, J = 2.2 Hz, 1 H, H-5_{eq}), 2.08 (ddd, J = 12.0 Hz, J = 4.1 Hz, J = 2.2 Hz, 1 H, H-3_{eq}), 1.85 (ddd, J = 12.9 Hz, J = 11.5 Hz, J = 5.5 Hz, 1 H, H-5_{ax}), 1.50 (ddd, J = 12.0 Hz, J = 12.0 Hz, J = 11.0 Hz, 1 H, H-3_{ax}); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 171.22 (C, C-8), 135. 20 (C, C_{Ar}), 131.06 (CH, m-C_{Ar}), 128.79 (CH, o-C_{Ar}), 126.90 (CH, p-C_{Ar}), 84.46 (CH, C-6), 72.59 (CH, C-2), 65.92 (CH, C-4), 55.57 (CH_3, OCH_3), 51.74 (CH_3, OCH_3),

40.92 (CH_2, C-7), 37.49 (CH_2, C-5), 36.73 (CH_2, C-3); ν_{max} ($CHCl_3$)/cm^{-1} 3060, 3000, 2952, 2928, 2856, 2828, 1736, 1584, 1480, 1440, 1380, 1328, 1296, 1260, 1228, 1148, 1112, 1080, 1224, 988, 956; MS (70 °C): 296 (M^+, 0.9), 233 (2.5), 219 (38.7), 210 (8.5), 199 (24.1), 187 (19.1), 155 (98.0), 143 (22.3), 124 (28.2), 109 (17.2), 106 (12.2), 105 (14.6), 101 (23.9), 95 (6.6), 87 (31.6), 85 (13.6), 81 (100.0), 77 (9.4), 65 (8.5); HR-MS calcd. for $C_{15}H_{20}O_4S$ (M^+) 296.1082, found 296.1078.

(2R,4S,6R)-2-(4-Methoxy-6-phenylsulfanyl-tetrahydro-pyran-2-yl)-ethanol (**17ax**). At 0 °C 100.0 µl (1.0 mmol) of the borane dimethyl sulphide complex (10 M) were added to a solution of 197.0 mg (0.7 mmol) of acid **8** and 237.0 µl (1.4 mmol) of triethyl borate in 1 ml of abs. THF. The solution was stirred for 1 h at 0 °C and overnight at rt. For work-up 1 ml of methanol was added and the mixture was concentrated *in vacuo*. This procedure was repeated twice. The anomers could be separated by column chromatography (CH/EA = 2/1) to afford (136.7 mg, 0.5 mmol, 73% overall) of alcohol **17ax/17eq** = 5/1. **17ax**, $[\alpha]_D^{25}$ = + 209.8 (c = 1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 7.49 (m, 2 H, *o*-Ar), 7.33 (m, 3 H, *m*-Ar u. *p*-Ar), 5.80 (d, *J* = 5.5 Hz, 1 H, H-6), 4.42 (dddd, *J* = 12.5 Hz, *J* = 8.7 Hz, *J* = 3.9 Hz, *J* = 2.2 Hz, 1 H, H-2), 3.71 (dddd, *J* = 11.4 Hz, *J* = 11.2 Hz, *J* = 5.7 Hz, *J* = 4.2 Hz, 1 H, H-4), 3.62 (ddd, *J* = 11.4 Hz, *J* = 5.3 Hz, *J* = 1.5 Hz, 2 H, H-8), 3.41 (s, 3 H, OCH_3), 2.41 (ddd, *J* = 13.2 Hz, *J* = 5.7 Hz, *J* = 1.2 Hz, 1 H, H-5_{eq}), 2.12 (ddd, *J* = 12.5 Hz, *J* = 4.2 Hz, *J* = 2.2 Hz, 1 H, H-3_{eq}), 1.89 (ddd, *J* = 13.2 Hz, *J* = 11.4 Hz, *J* = 5.5 Hz, 1 H, H-5_{ax}), 1.77 m (m, 2 H, H-7), 1.32 (ddd, *J* = 12.5 Hz, *J* = 12.5 Hz, *J* = 11.2 Hz, 1 H, H-3_{ax}); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 134.71 (C, C_{Ar}), 131.25 (CH, *m*-C_{Ar}), 129.06 (CH, *o*-C_{Ar}), 127.26 (CH, *p*-C_{Ar}), 84.10 (CH, C-6), 72.71 (CH, C-2), 67.80 (CH, C-4), 60.28 (CH_2, C-8), 55.49 (CH_3, OCH_3), 37.98 (CH_2, C-7), 36.55 (CH_2, C-5), 26.91 (CH_2, C-3); ν_{max} ($CHCl_3$)/cm^{-1} 3624, 3532, 2988, 2948, 2928, 2884, 1480, 1440, 1372, 1296, 1236, 1156, 1132, 1084, 1000, 976, 948, 908; MS (120 °C): 268 (M^+, 1.1), 237 (1.8), 219 (3.0), 179 (10.7), 163 (14.1), 159 (32.6), 149 (16.1), 135 (22.4), 127 (100.0), 115 (15.6), 110 (28.7), 109 (32.1), 101 (78.5), 91 (13.7), 87 (19.8), 75 (40.1); HR-MS calcd. for $C_{14}H_{20}O_3S$ (M^+) 268.1133, found 268.1131.

(2R,4S,6S)-2-(4-Methoxy-6-phenylsulfanyl-tetrahydro-pyran-2-yl)-ethanol (**17eq**). $[\alpha]_D^{25}$ = −38.2° (c = 1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 7.49 - 7.47 (m, 2 H, *o*-Ar), 7.31 - 7.26 (m, 3 H, *m*-Ar/*p*-Ar), 4.73 (dd, *J* = 12.0 Hz, *J* = 2.0 Hz, 1 H, H-6), 3.72 (ddd, *J* = 14.3 Hz, *J* = 4.6 Hz, *J* = 2.4 Hz, 2 H, H-8), 3.59 (dddd, *J* = 12.0 Hz, *J* = 9.0 Hz, *J* = 5.7 Hz, *J* = 1.8 Hz, 1 H, H-2), 3.40 (dddd, *J* = 12.0 Hz, *J* = 11.3 Hz, *J* = 4.2 Hz, *J* = 2.0 Hz, 1 H, H-4), 3.35 (s, 3 H, OCH_3), 2.36 (ddd, *J* = 12.0 Hz, *J* = 4.2 Hz, *J* = 2.0 Hz, 1 H, H-5_{eq}), 1.98 (ddd, *J* = 12.0 Hz, *J* = 4.2 Hz, *J* = 1.8 Hz, 1 H, H-3_{eq}), 1.86 (m, 1H, H-7a), 1.73 (m, 1 H, H-7b), 1.47 (ddd, *J* = 12.0 Hz, *J* = 12.0 Hz, *J* = 12.0 Hz, 1 H, H-5_{ax}), 1.26 (ddd, *J* = 12.0 Hz, *J* = 12.0 Hz, *J* = 11.3 Hz, 1 H, H-3_{ax}); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 133.49 (C, C_{Ar}), 131.76 (CH, *m*-C_{Ar}), 128.88 (CH, *o*-C_{Ar}), 127.54 (CH, *p*-C_{Ar}), 82.41 (CH, C-6), 76.11 (CH, C-2), 75.23 (CH, C-4), 60.26 (CH_2, C-8), 55.47 CH_3, (OCH_3), 37.90 (CH_2, C-7), 37.01, 36.93 (CH_2, C-3/C-5); ν_{max} ($CHCl_3$)/cm^{-1} 3624, 3532, 2988, 2948, 2928, 2884, 1480, 1440, 1372, 1296, 1236, 1156, 1132, 1084, 1000, 976, 948, 908; MS (120 °C): 268 (M^+, 1.1), 237 (1.8), 219 (3.0), 179 (10.7), 163 (14.1), 159 (32.6), 149 (16.1), 135 (22.4), 127 (100.0), 115 (15.6), 110 (28.7), 109 (32.1), 101 (78.5), 91 (13.7), 87 (19.8), 75 (40.1); HR-MS calcd. for $C_{14}H_{20}O_3S$ (M^+) 268.1133, found 268.1131.

(2R,4S,6R)-2-(2-Benzyloxy-ethyl)-4-methoxy-6-phenylsulfanyl-tetrahydro-pyran (**18eq**). A suspension of 59.0 mg (0.2 mmol) of **17eq** and 18.0 mg (0.5 mmol) of sodium hydride (60%) in 1 ml of abs. THF was refluxed for 15 min. At 0 °C a catalytic amount of tetra-*n*-butylammonium iodide and 56.0 µl (0.5 mmol) of benzyl bromide were added. The mixture was heated under reflux for 10 h, poured into sat. sodium hydrogen carbonate solution, extracted with MTBE, dried over $MgSO_4$ and concentrated *in vacuo*. Column chromatography (CH/EA = 5/1) afforded 60.6 mg (0.17 mmol, 77%) of **18eq**, $[\alpha]_D^{27}$ = −14.2 (c = 1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 7.47 (m, 2 H, *o*-SPh), 7.36 - 7.20 (m, 8 H, *m*-, *p*-SPh/Ph), 4.74 (dd, *J* = 11.9 Hz, *J* = 1.9 Hz, 1 H, H-6), 4.46 (d, *J* = 11.8 Hz, 1 H, CH_2Ph), 4.41 (d, *J* = 11.8 Hz, 1 H, CH_2Ph), 3.65 - 3.53 (m, 3 H, H-8/H-2), 3.41 (dddd, *J* = 11.3 Hz, *J* = 10.9 Hz, *J* = 4.2 Hz, *J* = 4.0 Hz, 1 H, H-4), 3.34 (s, 3 H, OCH_3), 3.41 (s, 3 H, OCH_3), 2.36 (ddd, *J* = 12.3 Hz, *J* = 4.0 Hz, *J* = 1.9 Hz, 1 H, H-5_{eq}), 2.00 (ddd, *J* = 12.5 Hz, *J* = 4.2 Hz, *J* = 2.2 Hz, 1 H, H-3_{eq}), 1.84 (m, 2 H, H-7), 1.51 (ddd, *J* = 12.3 Hz, *J* = 11.9 Hz, *J* = 10.9 Hz, 1 H, H-5_{ax}), 1.22 (m, 1H, H-3_{ax}); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 138.45 (C, C_{Ph}), 134.66 (C, C_{SPh}), 130.94 (CH, C_{Ar}), 128.76 (CH, C_{Ar}), 128.40 (CH, C_{Ar}), 127.59 (CH, C_{Ar}), 127.06 (CH, C_{Ar}), 82.33 (CH, C-6), 76.44 (CH, C-2), 73.13 (CH_2, CH_2Ph), 72.88 (CH, C-4), 66.48 (CH_2, C-8), 55.54 (CH_3, OCH_3), 37.52 (CH_2, C-7), 37.07 (CH_2, C-5), 36.09 (CH_2, C-3); ν_{max} ($CHCl_3$)/cm^{-1} 3064, 3000, 2948, 2924, 2860, 1584, 1480, 1452, 1360, 1296, 1260,

1228, 1164, 1136, 1096, 1024, 948; MS (120 °C): 268 (M^+–90, 1.1), 237 (1.8), 219 (3.0), 179 (10.7), 163 (14.1), 159 (32.6), 149 (16.1), 135 (22.4), 127 (100.0), 115 (15.6), 110 (28.7), 109 (32.1), 101 (78.5), 91 (13.7), 87 (19.8), 75 (40.1); HR-MS calcd. for $C_{14}H_{20}O_3S$ (M^+–90) 268.1133, found 268.1129.

(2R,4S,6S)-2-(2-Benzyloxy-ethyl)-4-methoxy-6-phenylsulfanyl-tetrahydro-pyran (**18ax**). Following the procedure described for **18eq** alcohol **17ax** was converted into **18ax** in 76% yield, $[\alpha]_D^{27}$ = +182.3 (c = 1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 7.50 - 7.19 (m, 10 H, Ar), 5.76 (d, J = 5.5 Hz, 1 H, H-6), 4.36 (d, J = 11.8 Hz, 1 H, CH_2Ph), 4.34 (m, 1H, H-2), 4.32 (d, J = 11.8 Hz, 1 H, CH_2Ph), 3.65 (dddd, J = 11.6 Hz, J = 11.6 Hz, J = 4.6 Hz, J = 4.4 Hz, 1 H, H-4), 3.44 (m, 2 H, H-8), 3.36 (s, 3 H, OCH_3), 2.36 (ddd, J = 13.1 Hz, J = 4.4 Hz, J = 1.1 Hz, 1 H, H-5_{eq}), 2.10 (ddd, J = 12.0 Hz, J = 4.6 Hz, J = 2.2 Hz, 1 H, H-3_{eq}), 1.89 - 1.81 (m, 2 H, H-7), 1.84 (ddd, J = 13.1 Hz, J = 11.6 Hz, J = 5.5 Hz, 1 H, H-5_{ax}), 1.23 (ddd, J = 12.0 Hz, J = 11.6 Hz, J = 11.6 Hz, 1 H, H-3_{ax}); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 138.46 (C, C_{Ph}), 135.56 (C, C_{SPh}), 130.74 (CH, C_{Ar}), 129.02 (CH, C_{Ar}), 128.82 (CH, C_{Ar}), 128.79 (CH, C_{Ar}), 128.31 (CH, C_{Ar}), 127.64 (CH, C_{Ar}), 127.49 (CH, C_{Ar}), 126.69 (CH, C_{Ar}), 84.08 (CH, C-6), 73.03 (CH_2, CH_2Ph), 73.00 (CH, C-2), 66.69 (CH_2, C-8), 65.99 (CH, C-4), 55.47 (CH_3, OCH_3), 38.07 (CH_2, C-7), 36.93/36.05 (CH_2, C-3/C-5); ν_{max} ($CHCl_3$)/cm^{-1} 3064, 3000, 2948, 2924, 2860, 1584, 1480, 1452, 1360, 1296, 1260, 1228, 1164, 1136, 1096, 1024, 948; MS (120 °C): 268 (M^+–90, 1.1), 237 (1.8), 219 (3.0), 17.9 (10.7), 163 (14.1), 159 (32.6), 149 (16.1), 135 (22.4), 127 (100.0), 115 (15.6), 110 (28.7), 109 (32.1), 101 (78.3), 91 (13.7), 87 (19.8), 75 (40.1); HR-MS calcd. for $C_{14}H_{20}O_3S$ (M^+–90) 268.1133, found 268.1129.

(2S,4S,6R)-(6-Benzenesulfonyl-4-methoxy-tetrahydropyran-2-yl)-acetic acid methyl ester (**19ax**). At 0 °C 150.0 mg (0.6 mmol) of *m*-chloroperoxybenzoic acid (ca. 70%) was added to a suspension of 60.0 mg (0.2 mmol) of **16** and 120.2 mg (1.4 mmol) of sodium hydrogen carbonate in 6 ml of DCM. After 1 h the reaction mixture was poured into sat. sodium hydrogen carbonate solution, washed with 2 N sodium hydroxide, extracted with DCM, dried over Na_2SO_4 and concentrated *in vacuo*. The anomers could be separated by column chromatography (**19ax/19eq** = 1.4/1). Overall yield 59.0 mg (0.2 mmol, 89%). **19ax** $[\alpha]_D^{20}$ = +5.0° (c = 0.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 7.93 (m, 2 H, *o*-Ar), 7.66 (m, 1H, *p*-Ar), 7.57 (m, 2 H, *m*-Ar), 4.96 (dddd, J = 10.8 Hz, J = 7.7 Hz, J = 5.0 Hz, J = 2.6 Hz, 1 H, H-2), 4.85 (dd, J = 7.0 Hz, J = 2.0 Hz, 1 H, H-6), 4.08 (dddd, J = 11.0 Hz, J = 7.2 Hz, J = 4.4 Hz, J = 4.2 Hz, 1 H, H-4), 3.60 (s, 3 H, OCH_3), 3.42 (s, 3 H, OCH_3), 2.95 (ddd, J = 14.2 Hz, J = 4.2 Hz, J = 2.6 Hz, 1 H, H-3_{eq}), 2.45 (dd, J = 11.0 Hz, J = 7.7 Hz, 1 H, H-7a), 2.44 (dd, J = 11.0 Hz, J = 5.0 Hz, 1 H, H-7b), 2.18 (ddd, J = 12.6 Hz, J = 4.4 Hz, J = 2.0 Hz, 1 H, H-5_{eq}), 1.75 (ddd, J = 14.2 Hz, J = 10.8 Hz, J = 7.2 Hz, 1 H, H-3_{ax}), 1.27 (ddd, J = 12.6 Hz, J = 11.0 Hz, J = 5.2 Hz, 1 H, H-5_{ax}); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 170.73 (C, C-8), 136.97 (C, C_{Ar}), 133.88 (CH, *p*-C_{Ar}), 129.26 (CH, *m*-C_{Ar}), 129.02 (CH, *o*-C_{Ar}), 89.65 (CH, C-6), 71.16 (CH, C-2), 70.08 (CH, C-4), 55.88 (CH_3, OCH_3), 51.75 (CH_3, OCH_3), 41.17 (CH_2, H-7), 36.25 (CH_2, C-5), 27.67 (CH_2, C-3); ν_{max} ($CHCl_3$)/cm^{-1} 3040, 2952, 2936, 1736, 1600, 1448, 1392, 1352, 1308, 1232, 1148, 1084, 1044, 1000, 944; FAB: 351 (M^++23 (Na), 27), 297 (18), 176 (27), 165 (34), 155 (79), 133 (100).

(2S,4S,6S)-(6-Benzenesulfonyl-4-methoxy-tetrahydro-pyran-2-yl)-acetic acid methyl ester (**19eq**). $[\alpha]_D^{20}$ = +5.0° (c = 0.3, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ 7.90 (m, 2 H, *o*-Ar), 7.59 (m, 3 H, *p*- u. *m*-Ar), 4.36 (dd, J = 12.0 Hz, J = 2.2 Hz, 1 H, H-6), 3.78 (m, 1H, H-2), 3.54 (s, 3 H, OCH_3), 3.46 (dddd, J = 11.1 Hz, J = 11.0 Hz, J = 6.5 Hz, J = 4.6 Hz, 1 H, H-4), 3.38 (s, 3 H, OCH_3), 2.61 (dd, J = 15.5 Hz, J = 7.7 Hz, 1 H, H-7a), 2.43 (dd, J = 15.5 Hz, J = 5.3 Hz, 1 H, H-7b), 2.09 (m, 1 H, H-3_{eq}), 2.03 (ddd, J = 12.2 Hz, J = 4.6 Hz, J = 2.2 Hz, 1 H, H-5_{eq}), 1.51 (ddd, J = 12.2 Hz, J = 12.0 Hz, J = 11.0 Hz, 1 H, H-5_{ax}), 1.24 (ddd, J = 12.3 Hz, J = 11.1 Hz, J = 9.8 Hz, 1 H, H-3_{ax}); ν_{max} ($CHCl_3$)/cm^{-1} 3068, 3012, 2952, 2932, 2856, 2832, 1736, 1448, 1372, 1328, 1260, 1232, 1180, 1148, 1048, 992, 968, 908, 868, 808; MS (70 °C): 156 (M^+–172, 2.2), 155 (2.9), 120 (3.8), 118 (4.8), 115 (4.1), 97 (3.9), 87 (12.2), 85 (72.0), 83 (100.0), 82 (4.5), 71 (3.7); FAB: 351 (M^++ 23 (Na), 36), 209 (17), 187 (33), 155 (100), 135 (35), 123 (43), 109 (47); HR-MS calcd. for $C_8H_{12}O_3$ (M^+–CH_3OSO_2Ph) 156.0786, found 156.0782.

(2R,4S)-2-Benzenesulfonyl-6-(2-benzyloxy-ethyl)-4-methoxy-tetrahydro-pyran (**20**). At 0 °C 315.0 mg (1.3 mmol) of *m*-chloroperoxybenzoic acid (ca. 70%) were added to a suspension of 252.0 mg (3.0 mmol) of sodium hydrogen carbonate and 114.0 mg (0.3 mmol) of **18ax** in abs. DCM (8 ml). After 1 h the reaction mixture was poured into sat. sodium hydrogen carbonate solution. The organic layer was washed with 2 N sodium hydroxide solution, the combined aqueous layers were extracted with DCM, dried over Na_2SO_4 and concentrated *in vacuo*.

Column chromatography afforded 123.2 mg (0.3 mmol, 99%, white solid) of sulfone **20** as an anomeric mixture (ax/eq = 2.5/1 (^{1}H NMR)). Spectroscopic data for the axial anomer was determined from the anomeric mixture. ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 7.92 (m, 2 H, *o*-SPh), 7.65 (m, 1H, *p*-SPh), 7.52 (m, 2 H, *m*-SPh), 7.35 - 7.19 (m, 5 H, Ph), 4.33 (dd, J = 11.8 Hz, J = 2.0 Hz, 1 H, H-6), 4.27 (d, J = 12.0 Hz, 1 H, CH_2Ph), 4.22 (d, J = 12.0 Hz, 1 H, CH_2Ph), 3.52 (m, 1H, H-4), 3.41 (m, 2 H, H-8), 3.36 (s, 3 H, OCH_3), 3.31 (dddd, J = 9.2 Hz, J = 8.6 Hz, J = 5.3 Hz, J = 5.1 Hz, 1 H, H-2), 2.63 (dddd, J = 12.0 Hz, J = 3.3 Hz, J = 3.1 Hz, J = 2.0 Hz, 1 H, H-5_{eq}), 1.96 (dddd, J = 12.7 Hz, J = 3.2 Hz, J = 3.1 Hz, J = 1.8 Hz, H-3_{eq}), 1.78 (m, 2 H, H-7), 1.50 (ddd, J = 12.0 Hz, J = 11.8 Hz, J = 11.0 Hz, 1 H, H-5_{ax}), 1.25 (m, 1H, H-3_{ax}); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 138.19 (C, C_{SPh}), 136.27 (C, C_{Ph}), 133.95 (CH, *p*-C_{SPh}), 129.65/128.83/128.41 (CH, *o*-, *m*-C_{Ph}/*o*-C_{SPh}), 127.67 (CH, *p*-C_{Ph}), 127.56 (CH, *m*-C_{SPh}), 89.73 (CH, C-6), 75.43 (CH, C-2), 74.28 (CH, C-4), 73.03 (CH_2, CH_2Ph), 65.99 (CH_2, C-8), 55.75 (CH_3, OCH_3), 37.17 (CH_2, C-7), 35.62 (CH_2, C-5), 29.38 (CH_2, C-3); ν_{max} ($CHCl_3$)/cm^{-1} 3068, 3000, 2940, 2928, 2860, 1600, 1448, 1368, 1320, 1264, 1228, 1148, 1084, 1028, 984, 932, 888, 816, 600; MS (150 °C): 264 (M^+–126, 1.4), 250 (1.4), 248 (8.4), 231 (1.0), 217 (13.4), 173 (4.3), 159 (33.0), 146 (7.4), 125 (7.8), 111 (5.8), 105 (5.7), 91 (100.0), 87 (13.9), 77 (10.4); HR-MS calcd. for $C_{15}H_{20}O_3$ (M^+–HSO_2Ph) 248.1413, found 248.1413.

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