Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron: *Asymmetry* 19 (2008) 38–44
Tetrahedron: *Asymmetry*

Stereocontrolled oxycarbonylation of 4-benzyloxyhepta-1,6-diene-3,5-diols promoted by chiral palladium(II) complexes

Peter Kapitán and Tibor Gracza*

Department of Organic Chemistry, Institute of Organic Chemistry, Catalysis and Petrochemistry, Slovak University of Technology, Radlinského 9, SK-812 37 Bratislava, Slovakia

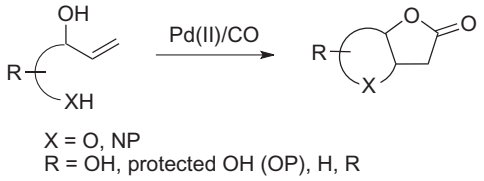
Received 2 October 2007; accepted 16 December 2007

Abstract—The synthesis of all diastereomers of 4-benzyloxyhepta-1,6-diene-3,5-diols **8**–**10** is described. The diastereo- and enantioselectivity of palladium(II)-catalysed oxycarbonylation of the symmetric compounds **8**–**10** were studied. The substrates **8**–**10** underwent Pd(II)-initiated oxycarbonylative bicyclisation to afford bicyclic lactones **11**–**14** in good yields and with excellent *threo*-diastereoselectivity. Additionally, the synthesis of enantiomerically pure lactone D-*gluco*-**12**, precursor for syntheses of goniofufurone and 7-*epi*-goniofufurone, was developed.

1. Introduction

Palladium(II)-catalysed reactions are fundamentally important in organic transformations due to the versatility, selectivity and overall synthetic usefulness of palladium.[1] Amongst the most interesting and synthetically useful reactions using palladium as a catalyst are cyclisations of unsaturated alcohols, amines and other suitable substrates accompanied by the insertion of carbon monoxide.[2] Pd-catalysed carbonylation is a very attractive method due to the effective one-carbon homologation it accomplishes. These reactions provide a simple and straightforward access to esters or amides. Intramolecular versions of these processes have proven particularly useful for construction of a range of oxygen and nitrogen-containing heterocycles.[3] Early examples of this domino reaction include Pd(II)-promoted cyclisation—intramolecular oxycarbonylations were described for 1,4- and 1,3-alkenediols, providing preferably *cis*-fused bicyclic lactones having tetrahydropyran[4] and/or tetrahydrofuran[5] structural motifs, respectively (Scheme 1).

Such transformation of enantiomerically pure substrates has found numerous applications in the total syntheses of natural compounds frenolicine,[6a,b] kalafungin,[6b] goniofufurone,[6c,d] 7-*epi*-goniofufurone,[6c,d] goniothalesdiol,[6e,f]



Scheme 1. Intramolecular Pd(II)-catalysed oxy-/amidocarbonylation of unsaturated polyols and/or aminopolyols.

erythroskyrine,[6g] kumausyne,[6h] Hagen's gland lactones,[6i] and/or plakortones[6j–l] (Fig. 1).

The Pd(II)-induced intramolecular attack of heteroatom nucleophiles on alkenes with subsequent carbonylation leads to σ-acylpalladium intermediates, which in turn can react further to carboxylic acid derivatives. This chemistry enables highly efficient domino transformations, which are of outstanding value for the synthesis of complex heterocyclic molecules. While in many cases the chemo- and regioselectivities of such reactions can be efficiently controlled by the proper choice of substrates and reaction conditions, the control of absolute configuration in the case of chirogenic reactions still remains a challenge for research and development. Recently, we have communicated the first asymmetric intramolecular oxycarbonylation of an unsaturated diol, catalysed by chiral palladium(II) complexes.[7] The kinetic resolution of racemic pent-4-ene-1,3-diol (±)-**1** in the presence of $Pd(OAc)_2$-{(*R*,*S*)-indabox}, *p*-benzoquinone in acetic acid under a carbon monoxide

* Corresponding author. Tel.: +421 2 593 25160; fax: +421 2 529 68560; e-mail: tibor.gracza@stuba.sk

0957-4166/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetasy.2007.12.003

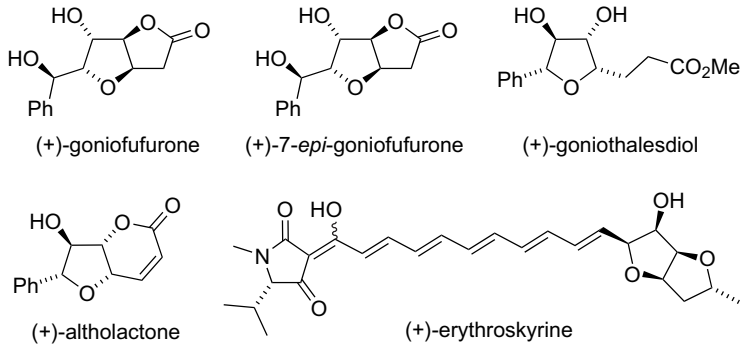
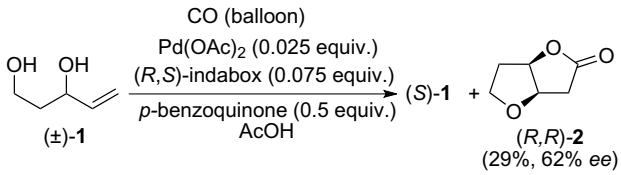


Figure 1.

atmosphere afforded enantiomerically enriched (1*R*,5*R*)-2,6-dioxabicyclo[3.3.0]octan-3-one (*R*,*R*-**2**) in 29% yield and 62% ee (Scheme 2).



Scheme 2. Kinetic resolution of (±)-**1** in an asymmetric Pd(II)-catalysed oxycarbonylation.

In this paper, we report our studies on the enantio- and diastereoselectivity of oxycarbonylative bicyclisation of 4-benzyloxyhepta-1,6-diene-3,5-diols promoted by chiral Pd(II) complexes.

2. Results and discussion

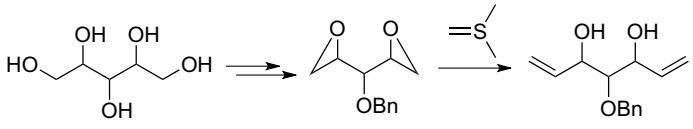
Having obtained preliminary success with the use of chiral Pd(II)-complexes in oxycarbonylative kinetic resolution of pent-4-ene-1,3-diol (Scheme 1), we now focused on the asymmetric Pd(II)-catalysed alkoxycarbonylation of symmetric substrates with full conversion. The hepta-1,6-diene-3,4,5-triols were chosen as suitable substrates for the exploration of this transformation. Moreover, *meso*-diols **8** and **10** with *xylo* and *ribo* relative configuration, respectively, serve as precursors for the syntheses of altholactone and goniothalesdiol. The *pseudo*-C_2-symmetric D-*arabino*-derivative **9** is an intermediate for the preparation of goniolactones and erythroskyrine (Fig. 1).

2.1. Synthesis of substrates

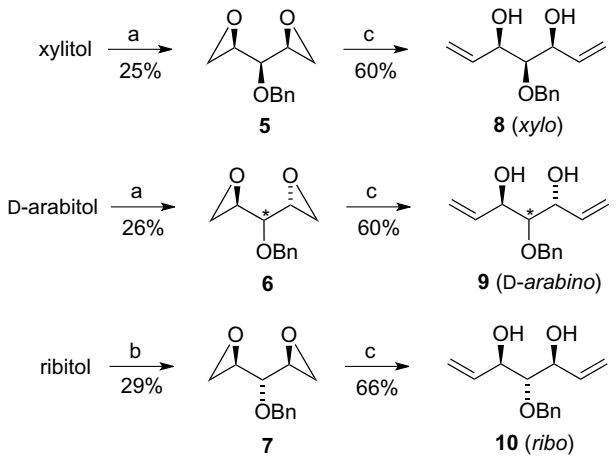
The hepta-1,6-diene-3,4,5-triols **8**–**10** were prepared from ribitol, xylitol and D-arabitol, respectively, adopting known routes to the protected 1,2:4,5-dianhydropentitols **5**–**7** (Scheme 4). These key intermediates have previously been used in the preparation of pentitol derivatives from divinyl methanol;[8] for the synthesis of 1-deoxy-4-thio-L-ribose;[9] in the preparation of a C_2-symmetric HIV protease inhibitor;[10] in the synthesis of immunosuppressive agent FK-506;[11] in the preparation of polysubstituted piperidines;[12] and in the synthesis of caribenolide I.[13] The overall strategy for our synthesis is shown in Scheme 3.

This route comprises the formation of 1,2:4,5-dianhydropentitols from the corresponding pentitols followed by introduction of both terminal C=C double bonds by treatment with an excess of dimethylsulfonium methylide. The required 1,2:4,5-dianhydropentitols were prepared from pentitols, as reported,[12,14] by a slightly modified procedure in one pot. Indeed, xylitol and D-arabitol were made to react with *p*-toluenesulfonyl chloride in pyridine, respectively, to give crude ditosylates, which were directly converted to the bis-epoxide benzyl ethers **5** and **6** in 25% and 26% overall yield, respectively, by treatment with sodium hydride and alkylation with benzyl bromide (Scheme 4).

The 3-benzyl-1,2:4,5-dianhydroribitol **7** was prepared from ribitol in 29% yield over 4 steps following Thomas's[12] synthetic sequence. Initially, protection of the terminal hydroxyl groups of ribitol as their acetonides using dimethoxypropane in acetone and a catalytic amount of *p*-toluenesulfonic acid in anhydrous DMF, followed by benzylation of the free hydroxy group at C3 with benzyl bromide furnished a fully protected ribitol. The epoxides were generated via Mitsunobu reaction on the two terminal hydroxyl groups after acidic removal of the isopropylidene protecting groups to give **7**. Finally, the carbon chain of the dianhydropentitols **5**–**7** was elongated by the reaction with dimethylsulfonium methylide to give the hepta-1,6-diene-diols **8**–**10**. Adopting the protocol for the transformation of epoxides to allylic alcohols,[15,16] diepoxides **5**–**7** were



Scheme 3. General strategy for synthesis of 4-benzyloxyhepta-1,6-diene-3,5-diols.



Scheme 4. Synthesis of 4-benzyloxyhept-1,6-diene-3,5-diols **8**–**10**. Reagents and conditions: (a) (i) TsCl (2 equiv), pyridine, −10 °C; (ii) NaH (3.3 equiv), THF, 0 °C; BnBr (1.1 equiv), 0 °C to rt, 20 h; (b) (i) dimethoxypropane, acetone, TsOH, DMF, 20 °C, 12 h (69%); (ii) NaH (1.1 equiv), BnBr (1.2 equiv), THF, −10 °C (78%); (iii) PPh_3 (2.3 equiv), DEAD (2.3 equiv), toluene, 110 °C, 12 h (53%); (c) Me_3SI (6.6 equiv), *n*-BuLi (6.0 equiv), THF, 0–25 °C.

treated with an excess of dimethylsulfonium methylide providing the corresponding key substrates **8**–**10**.

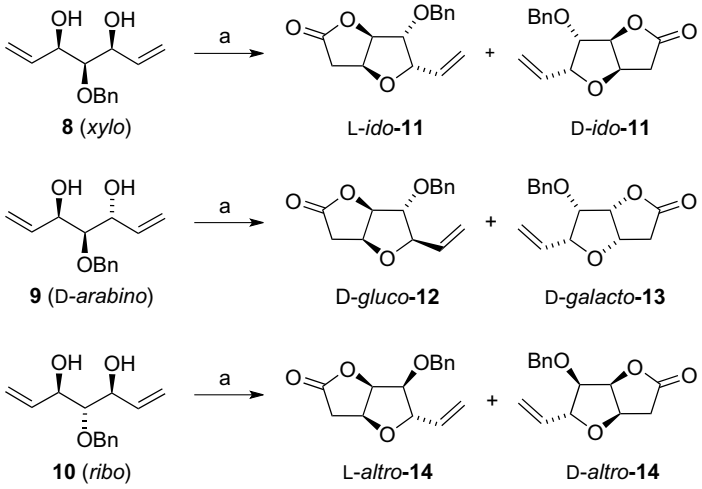
The hepta-1,6-diene-3,4,5-triols **8**–**10**, respectively, to the best of our knowledge have not yet been reported in the literature; we expect them to be highly interesting, versatile building blocks in other areas.

2.2. Palladium(II)-catalysed oxycarbonylations

With all substrates **8**–**10** in our hands, we subjected them to Pd(II)-catalysed oxycarbonylation under various reaction conditions (Scheme 5, Table 1).

Firstly, the reaction was carried out with palladium(II) chloride (catalyst, 0.1 equiv), copper(II) chloride (oxidant, 3 equiv), and sodium acetate (buffer, 3 equiv) in acetic acid under carbon monoxide at normal pressure and at room temperature. This system, used in various Pd(II)-catalysed reactions previously,[2,3] had been shown to be advantageous for intramolecular carbonylation.[3c,d,4,5] The enitols **8**–**10** (entries 1–3) on such treatment all underwent slow conversion, which could be monitored by a colour change of the reaction suspension from green to ochre. In all cases, the corresponding *cis*-fused bicyclic lactones **11**–**14** were obtained in good yields and with high *threo*-selectivity with respect to the newly formed stereogenic centre at C5, as expected. In the reaction of the *pseudo*-C_2-symmetric enitol **9**, the diastereomer D-*gluco*-**12** was isolated as the major product (65% yield, resulting from intramolecular *Si*-attack of the nucleophilic hydroxyl group to the Pd(II)-activated double bond) along with its minor diastereomer D-*galacto*-**13** (9%) (entry 2). Such a product distribution is most probably due to the *endo*-positions of two attached substituents on fused rings of the lactone D-*galacto*-**13**, an arrangement that in consequence increased the steric hindrance, and therefore the formation of **13** was slowed down. In fact, simply raising the temperature to 60 °C led to the complete consumption of enitol **9** in only 30 min to form energetically favourable diastereomer D-*gluco*-**12** as the sole product in 78% yield (entry 4).

Next, the asymmetric oxycarbonylations of *meso*-substrates **8** and **10** were examined. Based on the observed enantioselectivity (62% ee[7]) in the kinetic resolution of racemic pent-4-ene-1,3-diol (±)-**1**, the higher stereodifferentiation of the double bond in hepta-1,6-diene-diols **8** and **10** in the asymmetric alkoxycarbonylation was expected due to the bulky benzyloxy and vinyl groups of substrates. The first trial was effected with **8** in the presence of $Pd(OAc)_2$ (0.1 equiv), {(3a*R*,8a*S*)-(8,8a)-dihydro-3a*H*-indeno[1,2-*d*]oxazol-2-yl}methane **A**, [(*R*,*S*)-indabox] (0.12 equiv) and *p*-benzoquinone (1.1 equiv) in acetic acid under carbon monoxide at 25 °C (entry 5). Surprisingly, the required lactone D-*ido*-**11** was obtained in 63% yield, albeit with only poor enantiomeric purity (11% ee). Similarly, the use of ligand with opposite asymmetric induction[7] **B** [(*S*,*S*)-bis(4-isopropyloxazol-2-yl)methane] under the same reaction conditions furnished only racemic product *ido*-**11** (entry 6).

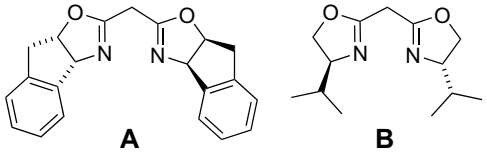


Scheme 5. Pd(II)-Catalysed oxycarbonylation of 4-benzyloxyhepta-1,6-diene-3,5-diols **8**–**10**. Reagents and conditions: (a) see Table 1.

Table 1. Pd(II)-catalysed oxycarbonylation of 4-benzyloxyhepta-1,6-diene-3,5-diols **8**–**10**

Entry	Substrate	Solvent	Catalyst and additive(s)	Conditions[a]	Product(s), yield[b]	ee[c] (%)
1	**8**	AcOH	0.1 equiv $PdCl_2$, 3 equiv $CuCl_2$, 3 equiv AcONa	25 °C, 12 h	*ido*-**11** (72%)	—
2	**9**	AcOH	0.1 equiv $PdCl_2$, 3 equiv $CuCl_2$, 3 equiv AcONa	25 °C, 20 h	D-*gluco*-**12** (65%) D-*galacto*-**13** (9%)	—
3	**10**	AcOH	0.1 equiv $PdCl_2$, 3 equiv $CuCl_2$, 3 equiv AcONa	25 °C, 12 h	*altro*-**14** (66%)	—
4	**9**	AcOH	0.1 equiv $PdCl_2$, 3 equiv $CuCl_2$, 3 equiv AcONa	65 °C, 30 min	D-*gluco*-**12** (78%)	—
5	**8**	AcOH	0.1 equiv $Pd(OAc)_2$, 0.12 equiv **A**,[e] 1.1 equiv BQ	20 °C, 24 h	D-*ido*-**11**[d] (63%)	11
6	**8**	AcOH	0.1 equiv $Pd(OAc)_2$, 0.12 equiv **B**,[e] 1.1 equiv BQ	20 °C, 24 h	*ido*-**11** (67%)	—
7	**8**	CH_2Cl_2	0.1 equiv $Pd(TFA)_2$, 0.12 equiv **A**,[e] 1.1 equiv BQ	40 °C, 24 h	D-*ido*-**11**[d] (15%)	13
8	**8**	AcOH/CH_2Cl_2 (1:8)	0.05 equiv $Pd(TFA)_2$, 0.15 equiv **A**,[e] 4 equiv BQ	20 °C, 4 d	D-*ido*-**11**[d] (63%)	11
9	**8**	AcOH/CH_2Cl_2 (1:8)	0.05 equiv $Pd(TFA)_2$, 0.15 equiv **B**,[e] 4 equiv BQ	20 °C, 4 d	L-*ido*-**11**[d] (79%)	7
10	**10**	AcOH/CH_2Cl_2 (1:8)	0.05 equiv $Pd(TFA)_2$, 0.15 equiv **A**,[e] 4 equiv BQ	20 °C, 5 d	D-*altro*-**14**[d] (61%)	12
11	**10**	AcOH/CH_2Cl_2 (1:8)	0.05 equiv $Pd(TFA)_2$, 0.15 equiv **B**,[e] 4 equiv BQ	20 °C, 4 d	L-*altro*-**14**[d] (77%)	7

[a] All runs were carried out under carbon monoxide at normal pressure (balloon).
[b] Isolated yields after flash column chromatography.
[c] Enantiomeric excesses were determined using gas chromatography with chiral stationary phase.
[d] Tentative absolute configuration based on previous results[7] with these catalysts in the oxycarbonylative kinetic resolution of pent-4-ene-1,3 diol.
[e] Chiral ligands.



We then turned our attention to a closer examination of the reaction conditions. Initially, different Pd(II)-salts and solvents were checked. Simply changing from $Pd(OAc)_2$ in AcOH to $Pd(TFA)_2$ in dichloromethane resulted in decrease of the yield of D-*ido*-**11** from 63% (entry 5) to 15% (entry 7). A significant counterion and solvent dependence was also observed in our work on the oxycarbonylative kinetic resolution of pentene–diol[7] and points to an exceedingly subtle reason for the general reactivity of intermediates in this catalytic reaction. Then we decided to investigate the relative stoichiometry of reagents used in the reaction and found that in the presence of $Pd(TFA)_2$ (0.05 equiv), chiral ligand (0.15 equiv) and *p*-benzoquinone (4 equiv) in the mixture of CH_2Cl_2–AcOH (8:1) the reaction was improved to give the corresponding products in good yields, however, with the same low enantioselectivity (entries 8–11). Interestingly, the presence of AcOH seems to be important for accomplishment of asymmetric oxycarbonylation. Unfortunately, not even the increased ratio of catalyst/ligand (1:3) effected the desired enantio differentiation of alkenes **8** and **10**.

3. Conclusion

In conclusion, we have developed the synthesis of all diastereomers of 4-benzyloxyhepta-1,6-diene-3,5-diols **8**–**10**, respectively. The *pseudo*-C_2-symmetric D-*arabino*-alkenitol **9** represents a useful C7-chain building block. The *meso*-enitols **8** and **10** serve excellent substrates for asymmetric transformations.

The diastereo- and enantioselectivity of palladium(II)-catalysed oxycarbonylation of dienols **8**–**10** were studied. The 4-benzyloxyhepta-1,6-diene-3,5-diols undergo Pd(II)-initiated oxycarbonylative bicyclisation to afford bicyclic lactones in good yields and with excellent *threo*-diastereoselectivity. In addition, we have demonstrated the value of this method in the synthesis of enantiomerically pure lactone D-*gluco*-**12**, precursor for syntheses of goniofufurone and 7-*epi*-goniofufurone (Fig. 1).

Although the level of asymmetric induction achieved so far is rather poor, this is the first report on the asymmetric version of this transformation in the desymmetrisation of *meso*-substrates. Further studies to improve the performance of the asymmetric catalysts for this transformation are ongoing.

4. Experimental

4.1. General

Commercial reagents were used without further purification. All solvents were distilled before use. Hexanes refer

to the fraction boiling at 60–65 °C. Flash column liquid chromatography (FLC) was performed on Silica Gel Kieselgel 60 (40–63 μm, 230–400 mesh) and analytical thin-layer chromatography (TLC) was performed on aluminium plates pre-coated with either 0.2 mm (DC-Alufolien, Merck) or 0.25 mm Silica Gel 60 F_{254} (ALUGRAM® SIL G/UV_{254}, Macherey-Nagel). The compounds were visualised by UV fluorescence and by dipping the plates in an aqueous H_2SO_4 solution of cerium sulfate/ammonium molybdate followed by charring with a heat gun. General conversion control and analyses of purified products were performed on a GC Top 8000/MS Voyager (quadropol, EI+) using a standard capillary column BGB5 (30 mP 0.32 mm ID). Enantiomeric excesses were determined by chiral-phase GC using a BGB 175 column (30 mP 0.25 mm ID, 0.25 mm film) and a BGB 173 column (30 mP 0.25 mm ID, 0.25 mm film) on a ThermoQuest Trace GC 2000 and a Thermo Focus GC. Melting points were obtained using a Kofler hot plate and are uncorrected. Optical rotations were measured with a POLAR L-μP polarimeter (IBZ Messtechnik) with a water-jacketed 10.000 cm cell at the wavelength of sodium D line ($\lambda = 589$ nm). Specific rotations are given in units of 10^{-1} deg cm^2 g^{-1} and concentrations are given in g/100 mL. Elemental analyses were run on FISONS EA1108 instrument. Infrared spectra were recorded either on a Philips Analytical PU9800 FTIR spectrometer or a Perkin–Elmer 1750 FTIR spectrophotometer as KBr discs (KBr) or as thin films on KBr plates (film). NMR spectra were recorded on a Varian VXR-300 spectrometer. Chemical shifts (δ) are quoted in ppm and are referenced to the tetramethylsilane (TMS) as internal standard. The multiplicities of carbons were assigned from a broadband decoupled analysis used in conjunction with either APT or DEPT programs.

4.2. Synthesis of dianhydroalditols 5–7

4.2.1. 3-*O*-Benzyl-1,2:4,5-dianhydroxylitol 5. Toluenesulfonyl chloride (6.3 g, 33 mmol, 2 equiv) in pyridine (12 mL) was added to a solution of xylitol (2.5 g, 16 mmol) in pyridine (10 mL) at −10 °C over 45 min. The reaction mixture was stirred at −10 °C for further 15 min and then poured onto ice (250 g). HCl (2 M, 75 mL) was then added. The aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL), dried over Na_2SO_4 and concentrated. The residue (6.2 g, 83%) was used in the next reaction without any purification. To solution of the crude ditosylate (6.2 g) in anhydrous THF (200 mL), NaH (1.72 g, 60% in paraffin, 45 mmol, 3.3 equiv) was added at 0 °C and the mixture was stirred at 0 °C for 30 min and subsequently BnBr (1.7 mL, 15 mmol) was added. The reaction mixture was stirred overnight at room temperature, quenched with water (50 mL), and extracted with CH_2Cl_2 (3 × 40 mL). The organic layers were combined, dried over Na_2SO_4 and concentrated in vacuo. The pure 3-*O*-benzyl-1,2:4,5-dianhydroxylitol **5** was obtained by flash column chromatography (50 g of silica gel, Et_2O–hexanes, 1:5); yield 860 mg (25%), as a colourless oil, R_f 0.29 (Et_2O–hexanes, 1:1); IR (film, cm^{-1}): ν 3063, 3031, 2992, 2921, 2862, 1492, 1454, 1085; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.67 (dd, 2H, $J = 2$ Hz, $J = 5$ Hz, 1-H_A, 5-H_A); 2.79–2.82 (m, 2H, 1-H_B, 5-H_B); 3.10–3.16 (m, 3H, 2-H, 3-H, 4-H); 4.76 (s, 2H, CH_2Ph); 7.28–7.40 (m, 5H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$): δ 43.2 (t, C-1, C-5), 52.0 (d, C-2, C-4), 71.9 (t, CH_2Ph), 79.4 (d, C-3), 127.7, 127.9, 128.4 (all d, Ph), 137.8 (s, Ph). HRMS for $C_{12}H_{14}O_3$ (M^+): calcd, 206.0943; found, 206.0947.

4.2.2. 3-*O*-Benzyl-1,2:4,5-dianhydro-D-arabitol 6. Prepared as described for **5** from D-arabitol (5.0 g, 33 mmol). The crude product was purified by flash column chromatography (50 g of silica gel, Et_2O–hexanes; 1:4); yield 1.73 g (26%), as a colourless oil, R_f 0.30 (Et_2O–hexanes, 1:1); $[\alpha]_D^{25} = +31$ (*c* 0.65, $CHCl_3$); {lit.[14]: $[\alpha]_D^{22} = +29.8$ (*c* 1.0, $CHCl_3$)}; HRMS for $C_{12}H_{14}O_3$ (M^+): calcd 206.0943, found 206.0940. The spectral data are in good agreement with those reported in the lit.[14]

4.2.3. 3-*O*-Benzyl-1,2:4,5-dianhydroribitol 7. Prepared from 3-*O*-benzyl-ribitol,[17] modifying the procedures of Thomas.[12] To a suspension of 3-*O*-benzyl-ribitol (1.0 g, 4.1 mmol) and PPh_3 (2.79 g, 2.6 equiv) in anhydrous toluene at rt was added DEAD (1.7 mL, 2.6 equiv) dropwise and stirring was continued at rt for 30 min. The yellow solution was then heated at 110 °C for 12 h. The solvent was removed in vacuo, Et_2O (100 mL) was added and precipitated triphenylphosphine oxide was filtered off and washed with Et_2O (2 × 20 mL). After drying over $MgSO_4$ and evaporation a yellow oil was obtained, which was purified by flash chromatography (40 g silica gel, AcOEt–hexanes, 1:6). Yield 450 mg (53%), as a colourless oil, R_f 0.67 (AcOEt–hexanes, 1:2); IR (film, cm^{-1}): ν 3065, 3031, 2994, 2930, 1493, 1454; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.75–2.81 (m, 4H, 1-H, 5-H); 3.09–3.13 (m, 2H, 2-H, 4-H); 3.36 (t, 1H, $J = 5$ Hz, 3-H); 4.64 (s, 2H, CH_2Ph); 7.31–7.36 (m, 5H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$): δ 44.6 (t, C-1, C-5), 51.1 (d, C-2, C-4), 72.7 (t, CH_2Ph), 76.8 (d, C-3), 127.7, 127.9, 128.4 (all d, Ph), 137.9 (s, Ph). HRMS for $C_{12}H_{14}O_3$ (M^+): calcd, 206.0943; found, 206.0940.

4.3. Synthesis of the symmetric dienes 8–10

4.3.1. (*xylo*)-4-Benzyloxyhepta-1,6-diene-3,5-diol 8. According to the literature,[16] to a stirred mixture of trimethylsulfonium iodide (9.83 g, 48 mmol, 6.6 equiv) in anhydrous THF (100 mL) was added butyllithium (20 mL, 2.0 M in hexane, 6 equiv) at − 10 °C. The resulting mixture was stirred at −10 °C for 30 min and a solution of diepoxide **5** (1.5 g, 7.3 mmol) in dry THF (50 mL) was added. The reaction mixture was stirred at room temperature for 2 h, hydrolysed with water (60 mL), extracted with CH_2Cl_2 (3 × 30 mL), dried over $MgSO_4$ and concentrated. The crude product was purified by Kugelrohr distillation under reduced pressure (175 °C/0.02 Torr) to yield compound **8** (1.06 g, 60% yield), as a colourless oil, R_f 0.24 (AcOEt–hexanes, 1:2); IR (film, cm^{-1}): ν 3399, 3082, 3024, 2921, 1725, 1454; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.38 (br s, 2H, OH); 3.38 (t, 1H, $J_{3,4} = J_{4,5} = 5$ Hz, 4-H); 4.29–4.32 (m, 2H, 3-H, 5-H); 4.69 (s, 2H, CH_2Ph); 5.25 (ddd, 2H, $J_{1A,2} = 10$ Hz, $J_{1A,1B} = J_{1A,3} = 1$ Hz, 1-H_A, 7-H_A); 5.41 (ddd, 2H, $J_{1B,2} = 17$ Hz, $J_{1A,1B} = J_{1B,3} = 1$ Hz, 1-H_B, 7-H_B); 5.89–6.00 (m, 2H, 2-H, 6-H); 7.29–7.36 (m, 5H, Ph); ^{13}C NMR

(75 MHz, $CDCl_3$): δ 72.7 (d, C-3, C-5), 75.5 (t, *C*H_2Ph), 84.3 (d, C-4), 116.9 (t, C-1, C-7), 128.1, 128.2, 128.6 (all d, Ph), 137.5 (s, Ph), 137.7 (d, C-2, C-6). Anal. Calcd for $C_{14}H_{18}O_3$ (234.3): C 71.77; H 7.74. Found: C 71.37; H 7.80.

4.3.2. (D-*arabino*)-4-Benzyloxyhepta-1,6-diene-3,5-diol 9. Prepared as described for **8**, from **6** (1.5 g, 7.3 mmol). Analytically pure product **9** was obtained after Kugelrohr distillation (175 °C/0.02 Torr) and recrystallisation from hexane. Yield 1.03 g (60%), colourless crystals, mp 50–52 °C, R_f 0.27 (AcOEt–hexanes, 1:2); $[\alpha]_D^{20} = +45$ (*c* 0.50, $CHCl_3$); IR (film, cm^{-1}): *v* 3380, 3089, 3031, 2875, 1725, 1641, 1454; ^1H NMR (300 MHz, $CDCl_3$): δ 2.38 (br s, 2H, OH); 3.38 (t, 1H, $J_{3,4} = J_{4,5} = 5$ Hz, 4-H); 4.29–4.32 (m, 2H, 3-H, 5-H); 4.69 (s, 2H, C*H*$_2$Ph); 5.25 (ddd, 2H, $J_{1A,2} = 10$ Hz, $J_{1A,1B} = J_{1A,3} = 1$ Hz, 1-H_A, 7-H_A); 5.41 (ddd, 2H, $J_{1B,2} = 17$ Hz, $J_{1A,1B} = J_{1B,3} = 1$Hz, 1-H_B, 7-H_B); 5.89–6.00 (m, 2H, 2-H, 6-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 72.2, 72.8 (all d, C-3, C-5), 73.6 (t, *C*H_2Ph), 82.7 (d, C-4), 116.3, 116.7 (all t, C-1, C-7), 128.1, 128.2, 128.6 (all d, Ph), 137.3, 137.6 (all d, C-2, C-6), 137.7 (s, Ph). Anal. Calcd for $C_{14}H_{18}O_3$ (234.3): C 71.77; H 7.74. Found: C 71.86; H 7.91.

4.3.3. (*ribo*)-4-Benzyloxyhepta-1,6-diene-3,5-diol 10. Prepared as above from **7** (800 mg, 3.9 mmol). The product **10** was obtained after Kugelrohr distillation (175 °C/0.02 Torr) Yield 600 mg (66% yield), colourless oil, R_f 0.22 (AcOEt–hexanes, 1:2); IR (film, cm^{-1}): *v* 3404, 3087, 3031, 2889, 1454, 1102; ^1H NMR (300 MHz, $CDCl_3$): δ 2.58 (br s, 2H, OH); 3.41 (t, 1H, $J_{3,4} = J_{4,5} = 6$ Hz, 4-H); 4.35 (dddd, 2H, $J_{2,3} = J_{3,4} = 6$ Hz, $J_{1A,3} = J_{1B,3} = 1$ Hz, 3-H, 5-H); 4.63 (s, 2H, C*H*$_2$Ph); 5.24 (ddd, 2H, $J_{1A,2} = 10$ Hz, $J_{1A,1B} = J_{1A,3} = 2$ Hz, 1-H_A, 7-H_A), 5.37 (ddd, 2H, $J_{1B,2} = 17$ Hz, $J_{1A,1B} = J_{1B,3} = 1$Hz, 1-H_B, 7-H_B); 5.93–6.14 (m, 2H, 2-H, 6-H); 7.29–7.36 (m, 5H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$): δ 73.6 (d, C-3, C-5), 73.8 (t, *C*H_2Ph), 83.9 (d, C-4), 116.5 (t, C-1, C-7), 127.9, 128.5 (all d, Ph), 137.4 (d, C-2, C-6), 137.8 (s, Ph). Anal. Calcd for $C_{14}H_{18}O_3$ (234.3): C 71.77; H 7.74. Found: C 72.03; H 7.92.

4.4. Pd(II)-catalysed oxycarbonylation of diols 8–10

4.4.1. Typical procedure for $PdCl_2$-catalysed oxycarbonylation of diols 8–10. A 25 mL-flask with stopcock equipped with side inlet was charged with AcONa (0.25 g, 3 equiv), $CuCl_2$ (41 mg, 3 equiv) and $PdCl_2$ (18 mg, 0.1 equiv). 4-Benzyloxyhepta-1,6-diene-3,5-diols **8–10** (234 mg, 1.0 mmol) in glacial AcOH (5 mL) were added and the flask was purged with CO from balloon (residual air was removed through side inlet with water aspirator). The mixture was vigorously stirred at room temperature until the colour of the mixture changed from green to pale brown. The mixture was filtered through a bed of Celite and the filtrate was concentrated in vacuo. The crude product was purified by flash column chromatography (20 g of silica gel, AcOEt–hexanes, 1:6) to afford lactones **11–14**.

4.4.2. Data for (±)-(1*S*,5*R*,7*R*,8*S*)-8-benzyloxy-7-vinyl-2,6-dioxabicyclo[3.3.0]octan-3-one *ido*-11. Yield 187 mg (72%), colourless oil, R_f 0.36 (AcOEt–hexanes, 1:2); IR (film, cm^{-1}): *v* 3032, 2934, 1789, 1062; ^1H NMR (300 MHz, $CDCl_3$): δ 2.69 (dd, A of ABX, 1H, $J_{4A,4B} = 18$ Hz, $J_{4A,5} = 1$ Hz, 4-H_A); 2.76 (dd, B of ABX, 1H, $J_{4A,4B} = 18$ Hz, $J_{4B,5} = 5$ Hz, 4-H_B); 4.14 (d, 1H, $J_{7,8} = 4$ Hz, 8-H); 4.51 (dd, 1H, $J_{7,1'} = 7$ Hz, $J_{7,8} = 4$ Hz, 7-H); 4.64 (s, 2H, C*H*$_2$Ph); 4.95 (d, 1H, $J_{1,5} = 4$ Hz, 1-H); 4.98 (ddd, dX of ABX, 1H, $J_{4B,5} = 5$ Hz, $J_{1,5} = 4$ Hz, $J_{4A,5} = 1$ Hz, 5-H); 5.36 (dd, 1H, $J_{1',2'A} = 10$ Hz, $J_{2'A,2'B} = 1$ Hz, 2′-H_A); 5.43 (dd, 1H, $J_{1',2'B} = 18$ Hz, $J_{2'A,2'B} = 1$ Hz, 2′-H_B); 6.01 (ddd, 1H, $J_{1',2'B} = 18$ Hz, $J_{1',2'B} = 10$ Hz, $J_{7,1'} = 7$ Hz, 1′-H); 7.32–7.38 (m, 5H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$): δ 36.0 (t, C-4); 72.8 (t, *C*H_2Ph); 76.5, 82.0, 82.6, 85.9 (all d, C-1, C-5, C-7, C-8); 119.6 (t, C-2′); 127.7, 128.1, 128.5 (all d, Ph); 132.0 (d, C-1′); 137.0 (s, Ph); 175.5 (s, C-3). Anal. Calcd for $C_{15}H_{16}O_4$ (260.3): C 69.22; H 6.20. Found: C 70.02; H 6.51.

4.4.3. Data for (1*R*,5*S*,7*R*,8*R*)-8-benzyloxy-7-vinyl-2,6-dioxabicyclo[3.3.0]octan-3-one D-*gluco*-12. Yield 203 mg (78%), colourless oil, R_f 0.35 (AcOEt–hexanes, 1:2); $[\alpha]_D^{20} = -29$ (*c* 1.46, $CHCl_3$); IR (film, cm^{-1}): *v* 3065, 3032, 2929, 2871, 1789; ^1H NMR (300 MHz, $CDCl_3$): δ 2.72 (d, 2H, $J_{4,5} = 3$ Hz, 4-H); 3.95 (dd, 1H, $J_{7,8} = 8$ Hz, 8-H); 4.32 (dd, 1H, $J_{7,8} = 8$ Hz, $J_{7,1'} = 6$ Hz, 7-H); 4.59 (d, 1H, $J = 12$Hz, C*H*$_2$Ph); 4.67 (d, 1H, $J = 12$ Hz, C*H*$_2$Ph); 4.79 (dd, 1H, $J_{1,5} = 4$ Hz, $J_{4,5} = 3$ Hz, 5-H); 4.89 (d, 1H, $J_{1,5} = 4$ Hz, 1-H); 5.24 (d, 1H, $J_{1',2'A} = 10$ Hz, 2′-H_A); 5.36 (d, 1H, $J_{1',2'B} = 17$ Hz, 2′-H_B); 5.85 (ddd, 1H, $J_{1',2'B} = 17$ Hz, $J_{1',2'A} = 10$ Hz, $J_{7,1'} = 6$ Hz, 1′-H); 7.31–7.39 (m, 5H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$): δ 35.9 (t, C-4); 72.7 (t, *C*H_2Ph); 77.3, 85.1, 87.0, 87.7 (all d, C-1, C-5, C-7, C-8); 118.3 (t, C-2′); 127.9, 128.2, 128.6 (all d, Ph); 134.8 (d, C-1′); 136.7 (s, Ph); 175.0 (s, C-3). Anal. Calcd for $C_{15}H_{16}O_4$ (260.3): C 69.22; H 6.20. Found: C 70.15; H 6.43.

4.4.4. Data for (1*R*,5*S*,7*R*,8*S*)-8-benzyloxy-7-vinyl-2,6-dioxabicyclo[3.3.0]octan-3-one D-*galacto*-13. Yield 23 mg (9%), colourless oil, R_f 0.13 (AcOEt–hexanes, 1:2); $[\alpha]_D^{20} = -74$ (*c* 0.15, $CHCl_3$); IR (film, cm^{-1}): *v* 3065, 3032, 2936, 2875, 1789, 1732; ^1H NMR (300 MHz, $CDCl_3$): δ 2.76 (d, 2H, $J_{4,5} = 5$ Hz, 4-H); 4.10 (dd, 1H, $J_{1,8} = J_{7,8} = 5$ Hz, 8-H); 4.38 (dd, 1H, $J_{7,8} = J_{7,1'} = 5$ Hz, 7-H); 4.55 (d, 1H, $J = 12$ Hz, C*H*$_2$Ph); 4.70–4.76 (m, 1H, 5-H); 4.78 (d, 1H, $J = 12$ Hz, C*H*$_2$Ph); 5,02 (dd, 1H, $J_{1,5} = 6$ Hz, $J_{1,8} = 5$ Hz, 1-H); 5.30 (dd, 1H, $J_{1',2'A} = 10$ Hz, $J_{2'A,2'B} = 2$ Hz, 2′-H_A); 5.35 (dd, 1H, $J_{1',2'B} = 17$ Hz, $J_{2'A,2'B} = 2$ Hz, 2′-H_B); 6.05 (ddd, 1H, $J_{1',2'B} = 17$ Hz, $J_{1',2'A} = 10$ Hz, $J_{7,1'} = 5$ Hz, 1′-H); 7.31–738 (m, 5H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$): δ 36.7 (t, C-4); 73.2. (t, *C*H_2Ph); 75.9, 78.7, 82.1, 82.2 (all d, C-1, C-5, C-7, C-8); 118.9 (t, C-2′); 128.0, 128.1, 128.4 (all d, Ph); 133.4 (d, C-1′); 137.2 (s, Ph); 175.3 (s, C-3). Anal. Calcd for $C_{15}H_{16}O_4$ (260.3): C 69.22; H 6.20. Found: C 69.12; H 6.28.

4.4.5. Data for (±)-(1*S*,5*R*,7*R*,8*R*)-8-benzyloxy-7-vinyl-2,6-dioxabicyclo[3.3.0]octan-3-one (*altro*-14). Yield 172 mg (66%), colourless crystals, mp 94–96 °C, R_f 0.23 (AcOEt–hexanes, 1:2); IR (film, cm^{-1}): *v* 3065, 3032, 2969, 2873, 1767; ^1H NMR (300 MHz, $CDCl_3$): δ 2.68 (dd, A of ABX, 1H, $J_{4A,4B} = 19$ Hz, $J_{4A,5} = 1$ Hz, 4-H_A); 2.79 (dd, B of ABX, 1H, $J_{4A,4B} = 19$ Hz, $J_{4B,5} = 7$ Hz, 4-H_B); 3.75

(dd, 1H, $J_{7,8} = 8$ Hz, $J_{1,8} = 4$ Hz, 8-H); 4.33 (dd, 1H, $J_{7,1'} = J_{7,8} = 8$ Hz, 7-H); 4.61 (d, 1H, $J = 12$ Hz, CH_2Ph); 4.74 (d, 1H, $J = 12$ Hz, CH_2Ph); 4.84 (ddd, dX of ABX, 1H, $J_{4B,5} = 7$ Hz, $J_{1,5} = 4$ Hz, $J_{4A,5} = 1$ Hz, 5-H); 4.93 (dd, 1H, $J_{1,5} = J_{1,8} = 4$ Hz, 1-H); 5.27 (d, 1H, $J_{1',2'} = 11$ Hz, 2′-H_A); 5.43 (d, 1H, $J_{1',2'} = 17$ Hz, 2′-H_B); 5.80 (ddd, 1H, $J_{1',2'} = 17$ Hz, $J_{1',2'} = 11$ Hz, $J_{7,1'} = 8$ Hz, 1′-H); 7.31–7.37 (m, 5H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$): δ 36.8 (t, C-4); 72.5 (t, CH_2Ph); 76.0, 80.2, 80.7, 82.1 (all d, C-1, C-5, C-7, C-8); 118.9 (t, C-2′); 127.9, 128.1, 128.5 (all d, Ph); 134.6 (d, C-1′); 137.2 (s, Ph); 175.4 (s, C-3). Anal. Calcd for $C_{15}H_{16}O_4$ (260.3): C 69.22; H 6.20. Found: C 69.44; H 6.39.

4.5. Typical procedure for the asymmetric oxycarbonylation of diols 8 and 10 with (L*)Pd(OAc)$_2$, (L*)Pd(OCOCF$_3$)$_2$

Chiral ligand (0.15 mmol) in CH_2Cl_2 (1 mL) was added to the solution of $Pd(OCOCF_3)_2$, (0.05 mmol, 0.05 equiv) in CH_2Cl_2 (1 mL). The mixture was stirred for 15 min to give a clear solution. Substrate (1.0 mmol) in CH_2Cl_2 (1 mL), *p*-benzoquinone (4.0 equiv) in CH_2Cl_2 (1 mL) and glacial AcOH (0.5 mL) were added. The flask was purged with CO from a balloon and the reaction mixture was vigorously stirred until the deposition of black palladium was observed. The solvent was evaporated and the crude product purified by flash column chromatography.

Acknowledgements

This work was supported by Slovak Grant Agencies (VEGA, Slovak Academy of Sciences and Ministry of Education, Bratislava, Project No. 1/3549/06, and APVV, Bratislava, Project No. APVV-20-000305). The authors are grateful to Professor Marko D. Mihovilovic (Vienna University of Technology) for his help with the determination of enantiomeric purity.

References

1. (a) Tsuji, J. *Palladium Reagents and Catalysts*; John Wiley & Sons: Chichester, UK, 1995; (b) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. In *Principles and Applications of Organotransition Metal Chemistry*, 2nd ed.; University Science Books, 1987; (c) Hegedus, L. S. In *Transition Metals in the Synthesis of Complex Organic Molecules*; University Science Books, 1994; (d) Tsuji, J. In *Palladium Reagents and Catalysts: New Perspective for the 21st Century*; John Wiley & Sons: Chichester, 2004; (e) Malleron, J.-L.; Fiaud, J.-C.; Legros, J.-Y. In *Handbook of Palladium Catalysed Organic Reactions*; Academic Press: London, 1997; for recent reviews, see: (f) Muzart, J. *Tetrahedron* **2003**, *59*, 5789–5816; (g) Muzart, J. *Tetrahedron* **2005**, *61*, 4179–4214.
2. (a) Colquhoun, H. M.; Thompson, D. J.; Twigg, M. V. *Carbonylation*; Plenum Press: New York, 1991; (b) Schmalz, H. G.; Geis, O. In *Handbook of Organopalladium Chemistry for Organic Syntheses*; Negishi, E.-i., Ed.; John Wiley & Sons: New York, 2002; Vol. 2, p 2397; (c) Farina, V.; Eriksson, M. In *Handbook of Organopalladium Chemistry for Organic Syntheses*; Negishi, E.-i., Ed.; John Wiley & Sons: New York, 2002; Vol. 2, pp 2351–2375; for reviews see: (d) Muzart, J. *Tetrahedron* **2005**, *61*, 5955–6008; (e) Muzart, J. *Tetrahedron* **2005**, *61*, 9423–9463.
3. (a) Orena, M. In *Cycloetherification*; Helmchen, G., Hoffmann, R., Mulzer, J., Eds., 4th ed.; Houben Weyl; Georg Thieme: Stuttgart, New York, 1995; Vol. E21c, pp 4760–4817; (b) Elbracht, D. In *Addition to Olefinic Double Bonds Catalysed by Transition Metals*; Helmchen, G., Hoffmann, R., Mulzer, J., Eds., 4th ed.; Houben Weyl; Georg Thieme: Stuttgart, New York, 1995; Vol. E21c, pp 2488–2734; (c) Gracza, T.; Hasenöhrl, T.; Stahl, U.; Jäger, V. *Synthesis* **1991**, 1108–1118; (d) Jäger, V.; Gracza, T.; Dubois, E.; Hasenöhrl, T.; Hümmer, W.; Kautz, U.; Kirschbaum, B.; Lieberknecht, A.; Remen, L.; Shaw, D.; Stahl, U.; Stephan, O. In *Pd(II)-catalyzed Carbonylation of Unsaturated Polyols and Aminopolyols*; Helmchen, G., Dibo, J., Flubacher, D., Wiese, B., Eds.; Organic Synthesis via Organometallics OSM 5; Vieweg: Braunschweig, 1997; pp 331–360; (e) Wolfe, J. P. *Eur. J. Org. Chem.* **2007**, 571–582.
4. Semmelhack, M. F.; Bodurow, Ch.; Baum, M. *Tetrahedron Lett.* **1984**, *25*, 3171–3174.
5. Tamaru, Y.; Kobayashi, T.; Kawamura, S.-i.; Ochiai, H.; Hojo, M.; Yoshida, Z.-i. *Tetrahedron Lett.* **1985**, *26*, 3207–3210.
6. (a) Kraus, G. A.; Li, J. *J. Am. Chem. Soc.* **1993**, *115*, 5859–5860; (b) Kraus, G. A.; Li, J.; Gordon, M. S.; Jensen, J. H. *J. Org. Chem.* **1995**, *60*, 1154–1159; (c) Gracza, T.; Jäger, V. *Synlett* **1992**, 191–193; (d) Gracza, T.; Jäger, V. *Synthesis* **1994**, 1359–1368; (e) Babjak, M.; Kapitán, P.; Gracza, T. *Tetrahedron Lett.* **2002**, *43*, 6983–6985; (f) Babjak, M.; Kapitán, P.; Gracza, T. *Tetrahedron* **2005**, *61*, 2471–2479; (g) Dixon, D. J.; Ley, S. V.; Gracza, T.; Szolcsányi, P. *J. Chem. Soc., Perkin Trans. 1* **1999**, 839–841; (h) Boukouvalas, J.; Fortier, G.; Radu, I.-I. *J. Org. Chem.* **1998**, *63*, 916–917; (i) Paddon-Jones, G. C.; McErlean, S. P.; Hayes, P.; Moore, C. J.; Konig, W. A.; Kitching, W. *J. Org. Chem.* **2001**, *66*, 7487–7495; (j) Hayes, P. Y.; Kitching, W. *J. Am. Chem. Soc.* **2002**, *124*, 9718–9719; (k) Semmelhack, M. F.; Shanmugam, P. *Tetrahedron Lett.* **2000**, *41*, 3567–3571; (l) Semmelhack, M. F.; Hooley, R. J.; Kraml, Ch. M. *Org. Lett.* **2006**, *8*, 5203–5206.
7. Kapitán, P.; Gracza, T. *Arkivoc* **2008**, *viii*, 8–17.
8. Holland, D.; Stoddart, J. F. *Carbohydr. Res.* **1982**, *100*, 207–220.
9. Altenbach, H. J.; Merhof, G. F. *Tetrahedron: Asymmetry* **1996**, *7*, 3087–3090.
10. Chenera, B.; Boehm, J. C.; Dreyer, G. B. *Bioorg. Med. Chem. Lett.* **1991**, *1*, 219–222.
11. Schreiber, S. L.; Sammakia, T.; Uehling, D. E. *J. Org. Chem.* **1989**, *54*, 15–16.
12. Smith, R. D.; Thomas, N. R. *Synlett* **2000**, 193–196.
13. Jalce, G.; Franck, X.; Seon-Meniel, B.; Hoequemiller, R.; Figadere, B. *Tetrahedron Lett.* **2006**, *47*, 5905–5908.
14. Leung, L. M. H.; Gibson, V.; Linclau, B. *Tetrahedron: Asymmetry* **2005**, *16*, 2449–2453.
15. Alcaraz, L.; Harnett, J. J.; Mioskowski, C.; Martel, J. P.; Gall, T.; Shin, D.-S.; Falck, J. R. *Tetrahedron Lett.* **1994**, *35*, 5449–5452.
16. Baylon, C.; Heck, M. P.; Mioskowski, C. *J. Org. Chem.* **1999**, *64*, 3354–3360.
17. Downham, R.; Edwards, P. J.; Entwistle, D. A.; Hughes, A. B.; Kim, K. S.; Ley, S. V. *Tetrahedron: Asymmetry* **1995**, *10*, 2403–2440.