Tetrahedron: *Asymmetry* 20 (2009) 887–891

Contents lists available at ScienceDirect

Tetrahedron: *Asymmetry*

journal homepage: www.elsevier.com/locate/tetasy

Highly regioselective primary etherification of racemic propane-1,2-diol by the tin(II) bromide-catalyzed reaction with diazo[bis(4-methoxyphenyl)] methane and the resolution of enantiomers with the help of *Pseudomonas cepacia* lipase

Sigthor Petursson *

Faculty of Business and Science, University of Akureyri, Borgum v/Nordurslod, 600 Akureyri, Iceland

ARTICLE INFO

Article history:
Received 4 February 2009
Accepted 4 March 2009
Available online 1 April 2009

This paper is dedicated to Professor George Fleet, on the occasion of his 65th birthday

ABSTRACT

The tin(II) bromide-catalyzed reaction of diazo[bis(4-methoxyphenyl)]methane with racemic propane-1,2-diol in 1,2-dimethoxymethane resulted in the highly regioselective etherification of the primary hydroxyl group. After tritylation of the minor 2-ether, 1-[bis(4-methoxyphenyl)]methoxypropane-2-ol was obtained in pure form. The enantiomeric mono-ethers were resolved by kinetic resolution by transacetylation with the help of *Pseudomonas cepacia* lipase.

1. Introduction

The protection of hydroxyl groups in carbohydrates dates back to the pioneering work of Emil Fischer in the late 19th century and his use of cyclic acetals.[1] Acetals are probably the most widely used carbohydrate protecting groups, but are limited to neutral and basic conditions. If acid stability is required, ethers give the best protection. Benzyl ethers are by far the most common ethers used in polyol chemistry, but triphenylmethyl (trityl) ethers have found a use for the selective primary protection of monosaccharides and in nucleoside chemistry.[2–5] More recently the use of diphenylmethyl (benzhydryl) ethers for the protection of carbohydrate hydroxyl groups has been explored.[6] One of the advantages of the use of the benzhydryl group is the mild reaction conditions for its introduction by the use of diazodiphenylmethane in refluxing non-protic solvents and removal by catalytic hydrogenolysis using a palladium catalyst. This has recently been demonstrated for a series of sugar lactones.[7] These reactions take place via a reactive carbene intermediate, which makes the reaction non-selective and only suitable where peretherification is desired. Methods for the mono-etherification of a vicinal diol pair were also developed using tin(II) chloride catalysis in 1,2-dimethoxyethane. Varied regioselectivities were observed for different diaryldiazomethanes in reactions with methyl 4,6-*O*-isopropylidenes-α-D-mannopyranoside containing an *ax*–*eq* vicinal diol. Interestingly, in the case of the equivalent benzylidene mannopyranoside, the equatorial 3-OH was always favoured. Instability of the catalyst is sometimes observed, especially in the case of trans *eq*–*eq* pyranose systems as, for example, the 2,3-diol pair in glucose.[8–11] The selectivity of the etherification of diol pairs in simple γ-lactones has also been demonstrated by the tin(II) chloride-catalyzed reaction of diazo[bis(4-methylphenyl)]methane with L-erythronolactone which gave a five-fold excess of the 2-ether, that is 2-*O*-(4,4′-dimethylbenzhydryl)-L-erythronolactone.[12] The considerable regioselectivity that has been observed is an important aspect of the tin(II) chloride diaryldiazomethane etherification methodology for vicinal diols. Enantiomerically pure alcohol derivatives of simple alkanes are valuable synthons. Perhaps the best known group of compounds in this category are glycerol derivatives, which includes triacylglycerols and phospholipids, both of which are of industrial and biological interest.[13–17] Propane-1,2-diol is a bulk chemical with various applications, such as an antifreeze, an emulsifier, a solvent for food colours and in deodorant sticks.[18] Its enantiomerically pure forms have interest as chiral synthons. Propane-1,2-diol is also of pharmaceutical and other industrial interest, for example, in the synthesis of optically active liquid crystals.[19–25] Selective protection of the primary hydroxyl group of racemic propane-1,2-diol would give a vicinal ether–alcohol systems similar to those resolved by transesterification by the use of lipases in organic solvents.[26,27] An earlier investigation of the mono-diarylmethylation methodology is the benzhydrylation of propane-1,2-diol, which gave a disappointing 53:47 preference for the primary hydroxyl group.[11] It has recently been shown that tin(II) bromide is also a catalyst for the monoalkylation of vicinal diols with diaryldiazomethanes.[28] Herein we report the use of tin(II) bromide to catalyze the reaction of diazo[bis(4-methoxyphenyl)]methane with racemic propane-1,2-diol to obtain the 1-ether which is then resolved with the help of the *Pseudomonas cepacia* lipase.

* Tel.: +354 460 8000; fax: +354 460 8999.
E-mail address: sigthor@unak.is.

0957-4166/$ - see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetasy.2009.03.003

2. Results and discussion

2.1. Regioselective etherification of propane-1,2-diol

The results from the tin(II) chloride-catalyzed reaction of diazodiphenylmethane with racemic propane-1,2-diol predominantly gave mono-etherification with a slight preferential selectivity for either hydroxyl group. Based on steric consideration only, one would predict a preferential reaction of the primary position, however, based on results for the tin(II) chloride-catalyzed reaction of diazo(phenyl)methane and diazomethane with glycerol obtained by Chittenden one might have predict the opposite selectivity.[29] Chittenden reacted the two diazo compounds with glycerol in a mixture of methanol and dichloromethane in the presence of tin(II) chloride and in both cases isolated only the 2-ether and unreacted starting material. Earlier work on the reaction of diaryldiazo compounds catalyzed by tin(II) chloride showed that the most reactive compound (diazo[bis(4-methoxyphenyl)]methane) gave the highest selectivity for the less sterically hindered hydroxyl group of a vicinal diol pair. Preliminary work with the tin(II) bromide catalyst has also shown that the selectivity for the primary hydroxyl group increases with increased reactivity of the diazo compound. The reaction of diazo[bis(4-methoxyphenyl)]methane with propane-1,2-diol (I) in the presence of tin(II) bromide gave mono-etherification in 68% yield. The 1:2-selectivity can be easily monitored by the integration of the proton-NMR signal for the diarylmethyl proton (Ar_2CH–) which appears around 5.55 ppm, with the signal for the 2-ether always 0.1–0.2 units further downfield. A high selectivity for the primary position was observed with the 1/2 ratio = 8.3. In addition to the use of the chemical shift for the 'benzhydryl' proton (Ar_2CH-) to distinguish between the 1- and 2-ether, the proton signal for the free hydroxyl group also shows whether the alcohol is primary or secondary. Thus, the signal for the secondary –OH of the major 1-ether (II) appears as a doublet with $J_{OH,H2}$ 2.53 Hz, whereas the signal for the primary –OH of the minor 2-ether (III) appears as a triplet with $J_{OH,H1}$ 5.56 Hz. A confirmation of these assignments was obtained by the removal of the minor 2-ether on tritylation and subsequent enantiomeric enzymatic acetylation which gave the 2-acetate as shown by the shift of the multiplet 2-C*H* signal from 3.94 ppm for the free alcohol to 5.12 ppm for the acetate. The reaction is shown in Scheme 1.

The racemic mono-ether products turned out to be chromatographically indistinguishable on silica gel and it was impossible to separate them. To obtain the pure 1-ether, it was decided to react the mixture (II and III) with triphenylmethyl chloride in the hope that an insignificant amount of the 1-ether (II) would react, but the 2-ether (III) would react to completion, making the chromatographic purification of the 1-ether possible. This reaction gave the pure unreacted 4,4′-dimethoxybenzhydryl 1-ether in 76%, yield after chromatography, based on the total amount of the 1- and 2-ether. The minor 2-(4,4′-dimethoxybenzhydryloxy)-1-triphenylmethyloxypropane formed during the reaction could not be separated from by-products and was not investigated further.

2.2. Kinetic resolution of enantiomers by lipase-catalyzed transacetylation

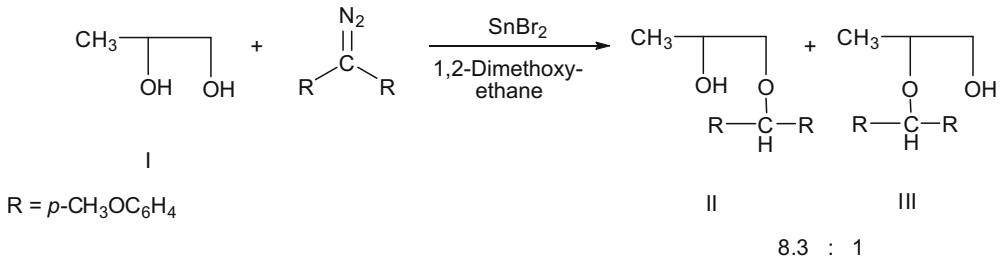
Lipases, for example, from *P. cepacia* and *Candida antarctica*, have proven very effective for the kinetic resolution of propane-1,2-diol derivatives.[26,27] The enzyme used for the resolution of the racemic 1-[bis(4-methoxyphenyl)]methoxypropane-2-ol by transacetylation from vinyl acetate was the *P. cepacia* lipase immobilized on ceramic particles. The reaction was carried out on a 0.5 mmol scale using di-isopropyl ether as a solvent and 10 mg of the immobilized enzyme. The reaction was monitored by HPLC with UV detection at 254 nm. Samples were extracted at regular intervals and were quenched in a tenfold volume of acetonitrile before injecting 0.010 mL into the HPLC instrument. The results are shown in Table 1.

The formation of the acetylated product is shown in Figure 1a as an integration area of the product peak as a percentage of the total integrated area for both starting material and product. It is clear from this plot that the reacting enantiomer is virtually exhausted after about 12 h under the reaction conditions used the first-order rate plot (ln(%REM) vs time, REM = reacting enantiomer) shows this more accurately. The reaction was, however, left to proceed for 19 h. The magnitude of the first-order rate constant (0.317 h^{-1}) is related to the amount of enzyme present. The rate is first order with respect to the reacting enantiomer; for a fixed amount of enzyme used, the reaction appears first order overall. It is pseudo first order.

Based on earlier results with lipase-catalyzed transesterification, it is the (*R*)-enantiomer which reacts according to the Kazlauskas rule.[26,27,30] It is therefore proposed that the reaction which takes place is the one shown in Scheme 2. This was confirmed by the removal of the 4,4′-dimethoxybenzhydryl ether by catalytic hydrogenation in the case of the alcohol (IV) and catalytic hydrogenation followed by Zemplen deacetylation in the case of the acetate (V), giving in both cases the free diol. The ^1H and ^{13}C NMR in D_2O were in both cases identical to authentic racemic propane-1,2-diol. The specific rotation of free diol [(*S*)-propane-1,2-

Table 1
HPLC monitoring of the lipase-catalyzed transacetylation from vinyl acetate to 1-[bis(4-methoxyphenyl)]methoxypropane-2-ol

Day	Time	Reaction time (h)	% A, reacting enantiomer (REM)	ln (% A_{REM})
1	13:30	0		
	14:45	0.75	39.2	3.67
	15:30	2	26.8	3.29
	18:00	4.5	11.3	2.42
	22:30	9	2.9	1.06
2	07:30	19	1.1	0.0517



Scheme 1. Mono-etherification of a propane-1,2-diol by the tin(II) bromide-catalyzed reaction with diazo[bis(4-methoxyphenyl)]methane.

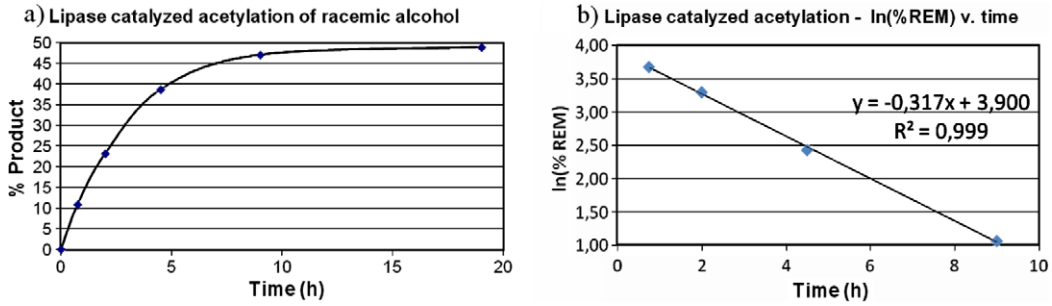
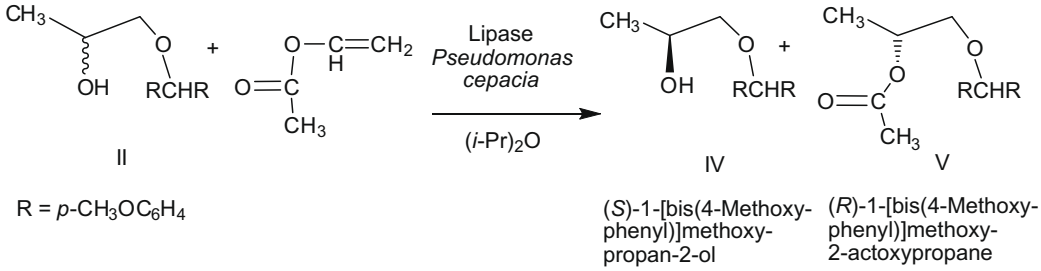


Figure 1. (a) Percentage product formed during transesterification (% product of total integration for starting material + product). (b) First order rate plot – ln(% reacting enantiomer) versus time.



Scheme 2. Kinetic resolution of the racemic 1-[bis(4-methoxyphenyl)]methoxypropane-2-ol by transacetylation from vinyl acetate using *Pseudomonas cepacia* lipase as catalyst.

diol] from IV was $[\alpha]_D^{20} = +29$ (*c* 1.1, $CHCl_3$). Lit. $[\alpha]_D^{20} = +16.6$ (neat).[33] The optical rotation of the free diol from V [(*R*)-propane-1,2-diol] was $[\alpha]_D^{20} = -28$ (*c* 0.34, $CHCl_3$). Lit. $[\alpha]_D^{20} = -16.5$ (neat).[34] The –O*H* signal in the proton NMR which appears as a doublet at 2.35 ppm with a coupling constant to the single proton on the 2-carbon ($J_{OH,H2}$ 2.53 Hz) strongly indicates that the tin(II) bromide-catalyzed etherification gave the 1-ether (*rac*-1-[bis(4-methoxyphenyl)]methoxypropane-2-ol) as a major product. This was further supported by the triphenylmethylation and confirmed with the formation of the 2-acetate in the lipase-catalyzed acetylation when the 2-C*H* multiplet signal is shifted downfield from 3.94 to 5.12 ppm. Further confirmation of this was obtained when the Mosher ester of the unreacted alcohol was prepared and this signal was shifted still further downfield to 5.36 ppm. The results from the determination of the specific rotations of the fully deprotected propanediols show a complete or at least a very high degree of enantiomeric discrimination by the enzyme. Preliminary analysis of one of the enantiomers, (*S*)-1-[bis(4-methoxy-phenyl)]methoxy-propan-2-ol, by the preparation of a Mosher ester [(*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoyl ester] has confirmed a complete acetylation of the (*R*)-enantiomer. The work on the acetylated enantiomer is not complete and further results will be published later.

3. Conclusions

In conclusion it can be stated that tin(II) bromide is an effective catalyst for the monoalkylation of vicinal diol pairs. The little used and highly reactive diazo[bis(4-methoxyphenyl)]methane has proven to be a useful reagent, which gives excellent regioselectivity for the primary hydroxyl group in the sterically simple and non-crowded propane-1,2-diol system. The stereospecificity of the *P. cepacia* lipase for the (*R*)-enantiomer of propane-1,2-diol with the bulky 4,4′-dimethoxybenzhydryl ether on the primary oxygen has been shown to be excellent.

4. Experimental

4.1. General

Thin layer chromatography (TLC) was carried out on aluminium sheets coated with silica gel 60-F_{254} and detected using a spray of 0.2% w/v cerium(IV) sulfate and 5% ammonium molybdate in 2 M sulfuric acid with heating. ^1H and ^{13}C NMR spectra were run on a Bruker AV400 instrument with Me_4Si as the external standard. Diaryldiazomethanes were prepared using published methods.[8] General reagents and the catalyst were obtained from chemical suppliers and usually used without further purification. 1,2-Dimethoxyethane was distiled from and stored over sodium. Ethyl acetate and hexane were of HPLC grade and used as received. The enzyme used was Fluka *P. cepacia* lipase immobilized on ceramic particles supplied by Sigma/Aldrich. High resolution mass spectra (HRMS) were recorded on a VG Autospec mass spectrometer using chemical ionization. The HPLC instrument was Shimadzu Prominence with a reversed phase 150 × 4.6 mm SS Wakosil C18RS 3 mm column. The elution was isocratic with acetonitrile/water 4:1 and detection was done with a UV detector at 254 nm.

4.2. *rac*-1-[Bis(4-methoxyphenyl)]methoxypropane-2-ol (major) and *rac*-2-[bis(4-methoxyphenyl)]methoxypropane-1-ol (minor)

Racemic propane-1,2-diol (304 mg, 4,00 mmol) and diazo[bis(4-methoxyphenyl)]methane (2,05 g, 8,00 mmol) were dissolved in 1,2-dimethoxyethane (DME) (25 mL) and cooled on ice. Tin(II) bromide (20 mg, 0.072 mmol) was dissolved in DME (5 mL) and added to the reaction mixture. The purple colour of the diazo compound had disappeared after about 20 min. TLC (hexane/EtOAc 1:1) showed a complete reaction of the diol (R_f 0.7) and the product as a deep red spot with the cerium molybdate spray (R_f 0.43). The product was purified on a column of silica gel (Hex/EtOAc 4:1–3:2) to give a non-crystalline oily mixture. This is a

8.3:1 inseparable mixture of the title compounds (823 mg, 68%); ^{1}H NMR (400 MHz, $CDCl_3$). δ_H 1.057 (3H d, $J_{H3,H2}$ 6.32 Hz, CH_3 for 1-ether), 1.057 (3H d, $J_{H3,H2}$ 6.06 Hz, CH_3 for 2-ether), 1,84 (1H t, $J_{OH,H1}$ 5.56 Hz (O*H* for 2-ether), 2.351 (1H d, $J_{OH,H2}$ 2.53 Hz (O*H* for 1-ether) 3.178 (1H, dd, J_{AB} 9.60 Hz, $J_{H1,H2}$ 7.83 Hz, H-1_A), 3.349 (1H, dd, J_{BA} 9.35 Hz, $J_{H1,H2}$ 3.03 Hz, H-1_B for 1-ether), 3.44, 3.52, 3.60 (3 × 1H multiplets, geminal H1's and H-2 for 2-ether), 3.71 (7H s, 2 × OCH_3 for 1 and 2 ethers), 3.94 (1H m, H-2 for 1-ether), 5.24 (1H s, Ar_2CH for 1-ether, relative integration 10,0), 5.39 (1H s, Ar_2CH for 2-ether, relative integration 1.2), 6.79 (4H m, 2 × aromatic *meta* H), 7.17 (4H m, 2 × aromatic *ortho* H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 16.17, 18.7 (C-3 2-ether, C-3 1-ether), 55.29 (OCH_3 1- and 2-ether), 66.56, 66.77 (C-2 2-ether, C-2 1-ether), 73.23, 74.61 (C-1 2-ether, C-1 1-ether), 80.67, 83.42 (Ar_2CH 2-ether, Ar_2CH 1-ether), 100, 113 (aromatic C-2 and 6 2-ether, aromatic C-2 and 6 1-ether), 128 (aromatic C-3 and 5), 134 (aromatic C-1), 159 (aromatic C-4). Anal. Calcd for $C_{18}H_{22}O_4$: C, 71.50; H, 7.33; O, 21.17. Found: C, 71.10; H, 7.61. HRMS, $C_{18}H_{22}NaO_4$ requires: 325.1410. Found 325.1408 (M^+Na^+).

4.3. Triphenylmethylation of *rac*-1-[bis(4-Methoxyphenyl)]methoxypropane-2-ol (major) and *rac*-2-[bis(4-methoxyphenyl)]-methoxypropane-1-ol (minor) mixture and the isolation of *rac*-1-[bis(4-methoxyphenyl)]methoxypropane-2-ol

The title mixture (703 mg, 2.32 mmol) was dissolved in dichloromethane (10 mL) after which triethylamine (71 mg, 0.098 mL, 0.70 mmol) and dimethylaminopyridine (2.3 mg, 0.019 mmol) were added followed by triphenylmethyl chloride (144 mg, 0.52 mmol). The reaction was left at RT overnight when TLC (Hex/EtOAc, 4:1) showed a new ether product at R_f 0.63 with yellow by-products and the main unreacted *rac*-1-[bis(4-methoxyphenyl)]methoxypropane-2-ol (R_f 0.63, 0.21). The reaction was quenched by washing with 20 mL of 5% ammonium chloride solution. The layers were separated and the aqueous layer was extracted with more dichloromethane (20 mL). The mixture was purified on a column of silica gel eluting with Hex/EtOAc 9:1–3:2. The faster ether component could not be separated from by-products but the compound of interest, *rac*-1-[bis(4-methoxyphenyl)]methoxypropane-2-ol, was isolated as a pure oil, 536 mg, 76%. ^{1}H NMR (400 MHz, $CDCl_3$). δ_H 1.057 (3H d, $J_{H3,H2}$ 6.32 Hz, CH_3), 2.351 (1H d, $J_{OH,H2}$ 2.53 Hz (O*H*), 3.178 (1H, dd, J_{AB} 9.60 Hz, $J_{H1,H2}$ 7.83 Hz, H-1_A), 3.349 (1H, dd, J_{BA} 9.35 Hz, $J_{H1,H2}$ 3.03 Hz, H-1_B), 3.71 (6H s, 2 × OCH_3), 3.94 (1H m, H-2), 5.24 (1H s, Ar_2CH), 6.79 (4H m, 2 × aromatic *meta* H), 7.17 (4H m, 2 × aromatic *ortho* H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C, 18.7 (C-3), 55.29 (OCH_3), 66.77 (C-2), 74.61 (C-1), 83.42 (Ar_2CH), 113 (aromatic C-2 and 6), 128 (aromatic C-3 and 5), 134 (aromatic C-1), 159 (aromatic C-4).

4.4. Enantiospecific acetylation of *rac*-1-[bis(4-methoxyphenyl)]-methoxypropane-2-ol

The racemic title compound (428 mg, 1.42 mmol) was dissolved in di-isopropyl ether (10 mL). Vinyl acetate (147 mg, 0.155 mL, 1.70 mmol) was added, followed by the immobilized enzyme (40 mg). The mixture was stirred gently at rt using a magnetic stirrer. The reaction was monitored by periodically stopping the stirring and extracting 20 μL of the clear reaction solution and injecting into 180 μL of acetonitrile. Ten microlitres of this diluted solution were then injected into the HPLC instrument (see discussion). The reaction was stopped after 19 h by removing the enzyme by filtration and rinsing the reaction vessel and filtered by dichloromethane. Two components were visible on TLC (Hex/EtOAc 4:1). The faster acetylated enantiomer is (*R*)-1-[bis(4-methoxyphenyl)]methoxy-2-acetoxypropane, R_f 0.3, and the unreacted alcohol is (*S*)-1-[bis(4-methoxyphenyl)]methoxypropan-2-ol, R_f 0.1. The two compounds were separated on a column of silica gel using Hex/EtOAc 4:1–3:2 as eluent. Fractions 6–10 gave the acetate as an oil, 180 mg, 37% yield or 74% based on the reacting enantiomer. Fractions 18–19 gave the unreacted alcohol, 140 mg, 33% or 66% based on the non-reacting enantiomer. NMR for (*R*)-1-[bis(4-methoxyphenyl)]methoxy-2-acetoxypropane ^{1}H NMR (400 MHz, $CDCl_3$). δ_H 1.25 (3H d, $J_{H3,H2}$ 6.57 Hz, CH_3), 2.03 (3H s, acetate CH_3), 3.44 (2H ABM octet, J_{AB} 10.36, $J_{A,H2}$ 4.55, J_{BA} 10.10, $J_{B,H2}$ 6.06 Hz, *gem* H1's), 3.78 (6H s, 2 × OCH_3), 5.12 (1H m, H2), 5.29 (1H s, Ar_2CH), 6.84 (4H d, $J_{m,o}$ 8.84 Hz, 2 × aromatic *meta* H), 7.22 (4H d, $J_{o,m}$ 8.84 Hz, 2 × aromatic *ortho* H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 16.90, (C-3), 21.34, (C-3), 55.27 (OCH_3), 69.63, (C-2), 71.01 (C-1), 82.91 (Ar_2CH), 113.7 (aromatic C-2 and 6), 128.2 (aromatic C-3 and 5), 134.5 (aromatic C-1), 158.9 (aromatic C-4), 170.6 (C=O). NMR for (*S*)-1-[bis(4-methoxyphenyl)]methoxypropan-2-ol ^{1}H NMR (400 MHz, $CDCl_3$). δ_H 1.06 (3H d, $J_{H3,H2}$ 6.57 Hz, CH_3), 2.44 (1H s, –OH), 3.35 (2H ABX octet, J_{AB} 9.35, $J_{A,H2}$ 8.08, J_{BA} 9.35, $J_{B,H2}$ 3.28 Hz, *gem* H1's), 3.80 (6H s, 2 × OCH_3), 4.03 (1H m, H2), 5.33 (1H s, Ar_2CH), 6.87 (4H d, $J_{m,o}$ 8.59 Hz, 2 × aromatic *meta* H), 7.25 (4H d, $J_{o,m}$ 9.35 Hz, 2 × aromatic *ortho* H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 18.70, (C-3), 55.28 (OCH_3), 66.71, (C-2), 74.57 (C-1), 83.28 (Ar_2CH), 113.8 (aromatic C-2 and 6), 128.2 (aromatic C-3 and 5), 134.4 (aromatic C-1), 159.0 (aromatic C-4).

4.5. Deprotection of *S*-1-[bis(4-methoxyphenyl)]methoxypropan-2-ol

The title compound (186 mg, 0.62 mmol) was dissolved in methanol (8 mL) after which 10% palladium on charcoal (20 mg) and a magnetic stirring bar were added. The flask was fitted via a three-way tap containing a hydrogen balloon on the closed arm. The system was evacuated before opening the reaction flask to the hydrogen. The reaction mixture was then magnetically stirred. After about 2 h, TLC (EtOAc) showed a complete reaction of the starting material (R_f 0.78) and the free alcohol product (R_f 0.26). The bis(4-methoxyphenyl)methane byproduct was also visible at R_f 0.82 but was not investigated further. The product was purified on a column of silica gel eluting with ether/methanol 9:1. After evaporation of the solvent from the product containing fraction the yield of (*S*)-propane-1,2-diol was 6.0 mg, 13%. ^{1}H NMR (400 MHz, D_2O). δ_H 1.05 (3H d, $J_{H3,H2}$ 6.57 Hz, CH_3), 3.35 (1H dd, J_{AB} 11.62, $J_{H1A,H2}$ 6.57 Hz, A part of H1 ABX octet), 3.45 (1H dd, J_{BA} 11.37, $J_{H1B,H2}$ 4.30 Hz, B part of H1 ABX octet), 3.79 (1H ten peak m, $J_{H2,H3}$ and $J_{H2,H1A}$ 6.57, $J_{H2,H1B}$ 4.04 Hz, H2; ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 17.93, (C-3), 66.56, (C-2), 67.89 (C-1). $[\alpha]_D^{20} = +29$ (*c* 1.1, $CHCl_3$). Lit.[31] $[\alpha]_D^{20} = +22$ ($CHCl_3$). Lit.[33] $[\alpha]_D^{20} = +16.6$ (neat)

4.6. Deprotection of (*R*)-1-[bis(4-methoxyphenyl)]methoxy-2-acetoxypropane

The title compound (200 mg, 0.58 mmol) was dissolved in dry methanol (6 mL) after which 10% palladium on charcoal (20 mg) and a magnetic stirring bar were added. The hydrogen was introduced as described above and the reaction stirred magnetically. The reaction was monitored by TLC and went to completion after 24 h. Sodium methoxide (3 mg, 0.06 mmol) in dry methanol (1 mL) was added and the reaction left for 2 h after which TLC showed the reaction to be complete. The base was neutralized with a strong cation exchange resin and purified as described above, to give the (*R*)-propane-1,2-diol, 8.5 mg, 19%. This compound had identical ^{1}H and ^{13}C NMR to the (*S*)-enantiomer. $[\alpha]_D^{20} = -28$ (*c* 0.34, $CHCl_3$). Lit.[32] $[\alpha]_D^{24.4} = -28.6$ ($CHCl_3$). Lit.[34] $[\alpha]_D^{20} = -16.5$ (neat).

4.7. NMR spectra of *rac*-propane-1,2-diol

An authentic sample of *rac*-propane-1,2-diol further purified by distillation under reduced pressure was submitted for ^{1}H and ^{13}C NMR. This sample had identical spectra to the two enantiomers reported above.

Acknowledgments

The University of Akureyri is thanked for financial support. Professor George Fleet and Dr. Sarah F. Jenkinson at the Organic Chemistry Laboratory, University of Oxford, are thanked for elemental and mass spectral analysis. Dr. Sigríður Jónsdóttir, Professor Guðmundur G. Haraldsson and Rakel Sæmundsdóttir at the Science Institute, University of Iceland, are thanked for helpful discussions and NMR and optical rotation analysis.

References

1. Kunz, H. *Angew. Chem.* **2002**, *114*, 4619–4632; . *Angew. Chem., Int. Ed.* **2002**(42), 4439–4451.
2. Greene, T. W.; Wutz, P. G. M. *Protective Groups in Organic Synthesis*, 3rd ed.; Wiley: NY, 1999. ether protection.
3. Kocieński, P. J. *Protecting Groups*, 3rd ed.; Georg Thieme: Stuttgart, NY, 2004.
4. Helferich, B.; Becker, J. *Justus Liebigs Ann. Chem.* **1924**, *440*, 1–18.
5. Smith, M.; Rammler, D. H.; Goldberg, I. H.; Khorana, H. G. *J. Am. Chem. Soc.* **1962**, *84*, 430–440.
6. Jackson, G.; Jones, H. F.; Petursson, S.; Webber, J. M. *Carbohydr. Res.* **1982**, *102*, 147–157.
7. Best, D.; Jenkinson, S. F.; Rule, S. D.; Higham, R.; Mercer, T. B.; Newell, R. J.; Weymouth-Wilson, A. C.; Fleet, G. W. J.; Petursson, S. *Tetrahedron Lett.* **2008**, *49*, 2196–2199.
8. Petursson, S.; Webber, J. W. *Carbohydr. Res.* **1982**, *103*, 41–52.
9. Petursson, S. *Carbohydr. Res.* **2001**, *331/3*, 239–245.
10. Petursson, S. *Carbohydr. Res.* **2003**, *338/9*, 963–968.
11. Petursson, S. Ethers as Protecting Groups Product Class 8, in Science of Synthesis, Houben–Weyl Methods of Molecular Transformations. In *Ethers*; Forsyth, C. J. Ed.; Stuttgart, 2008; Vol. 37.
12. Petursson, S.; Jenkinson, S. F.; Booth, K. V.; Weymouth-Wilson, A. C.; Watkin, D. J.; Fleet, G. W. J.; Best, D. *Acta Crystallogr., Sect. E* **2007**, *63*, o4121.
13. Halldorsson, A.; Thordarson, B.; Magnusson, C. D.; Haraldsson, G. G. *Tetrahedron: Asymmetry* **2004**, *15*, 2893–2899.
14. Haraldsson, G. G.; Hjaltason, B. Fish Oils as Sources of Important Polyunsaturated Fatty Acids. In *Structured and Modified Lipids*; Gunstone, F. D., Ed.; Marcel Dekker: NY and Base, 2001.
15. Urata, K.; Takaishi, N. *J. Am. Oil Chem. Soc.* **1996**, *73*, 819–830.
16. Bittman, R. *Chem. Phys. Lipids* **2004**, *129*, 111–131.
17. Guivisdalsky, P. N.; Bittman, R. *J. Org. Chem.* **1989**, *54*, 4637–4642.
18. Wikipedia, http://en.wikipedia.org/wiki/1%2C2-propanediol.
19. Abushanab, E.; Sarma, M. S. P. *J. Med. Chem.* **1989**, *32*, 76–79.
20. Yu, K.-L.; Bronson, J. J.; Yang, H.; Patick, A.; Alam, M.; Brankova, V.; Datema, R.; Hitchcock, M. J. M.; Martin, J. C. *J. Med. Chem.* **1992**, *35*, 2958–2969.
21. Theodore, L. J.; Nelson, W. L. *J. Org. Chem.* **1987**, *52*, 1309–1315.
22. Kometani, T.; Toide, H.; Daikaiji, Y.; Goto, M. *J. Biosci. Bioeng.* **2001**, *91*, 525–527.
23. Gaunt, M. J.; Yu, J.; Spencer, J. B. *J. Org. Chem.* **1998**, *63*, 4172–4173.
24. Hoff, B. H.; Waagen, V.; Antonsen, T. *Tetrahedron: Asymmetry* **1996**, *7*, 3181–3186.
25. Manzocchi, A.; Fiecchi, A.; Santaniello, E. *Synthesis* **1987**, 1007–1009.
26. Theil, F.; Lemke, K.; Ballschuh, S.; Kunath, A.; Schick, H. *Tetrahedron: Asymmetry* **1995**, *6*, 1323–1344.
27. Anthonsen, T.; Hoff, B. H. *Chem. Phys. Lipids* **1998**, *93*, 199–207.
28. Petursson, S., Tin(II) Bromide, A New Catalyst for the Petursson Monodiarylmethylation of Vicinal Diols. In *Poster Presentation at the XXIII Int. Conf. Organomet. Chem.*, Rennes, July 13–18; 2008.
29. Chittenden, G. J. F. *Carbohydr. Res.* **1981**, *91*, 85–88.
30. Kazlauskas, R. J.; Weissfloch, A. N. E.; Rappaport, A. T.; Cuccia, L. A. *J. Org. Chem.* **1991**, *56*, 2656–2665.
31. Lewis, D. *J. Chem. Soc., Perkin Trans. 2* **1991**, 197–200.
32. Shieh, N.; Price, C. C. *J. Org. Chem.* **1959**, *24*, 1169.
33. http://www.sigmaaldrich.com/catalog/ProductDetail.do?N4=237779|ALDRICH/N5=SEARCH_CONCAT_PNO|BRAND_KEY/F=SPEC.
34. http://www.sigmaaldrich.com/catalog/ProductDetail.do?N4=82284|FLUKA/N5=SEARCH_CONCAT_PNO|BRAND_KEY/F=SPEC.