Pergamon

Tetrahedron: *Asymmetry* 11 (2000) 789–796

TETRAHEDRON: *ASYMMETRY*

A highly stereoselective synthesis of D-erythrose derivatives by one-carbon homologation of 2,3-*O*-isopropylidene-D-glyceraldehyde with (*R*)-methyl *p*-tolyl sulfoxide

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Received 11 November 1999; accepted 31 December 1999

Abstract

A highly diastereoselective three-step synthesis of 2-*O*-benzyl-3,4-*O*-isopropylidene-D-erythrose **9** is described (de >98%; 50% overall yield) starting from D-glyceraldehyde acetonide and (*R*)-methyl *p*-tolyl sulfoxide. Treatment of **9** with trifluoroacetic acid gives 2-*O*-benzyl-D-erythrofuranose.

1. Introduction

The inherent chirality in monosaccharides and polyhydroxyl compounds makes them valuable starting materials for the asymmetric synthesis of other more elaborate molecules.[1] Amongst these compounds, optically active tethroses and their derivatives are especially interesting, since they are very useful C-4 building blocks for the synthesis of a large variety of biologically interesting compounds, such as acyclic fatty acids, metabolites,[2] nucleosides,[3] and other monosaccharides,[3b,4] not to mention many other molecules of biological interest.[5] This accounts for the importance of finding new methodologies enabling the synthesis of erythrose, threose and their derivatives, in high chemical yields and enantiomeric excess, so that they can be used in total synthesis.

D-Erythrose derivatives have been prepared by transforming naturally occurring chiral compounds,[2f,6] enzymatic resolution,[7] or asymmetric synthesis.[8–12] Outstanding examples of the latter methodology are: (1) the Sharpless asymmetric epoxidation of C-4 allylic alcohols[8] and/or related methods,[9] and (2) the iterative chain elongation of 2,3-*O*-isopropylidene-D-glyceraldehyde **1** by using Dondoni's method[11] (via thiazole intermediates), or our recently described method using ethyl ethylthiomethyl sulfoxide as a formyl anion equivalent.[12] These methods afford high diastereoselectivities, but all of them require chromatographic stereoisomer separations in order to obtain enantiomerically pure products.

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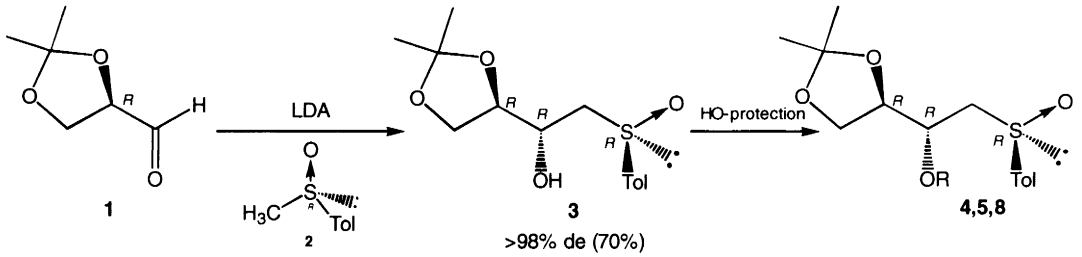
0957-4166/00/$ - see front matter
PII: S0957-4166(00)00005-7

2. Results and discussion

In this paper we report an efficient and highly stereoselective synthesis of D-erythrose derivatives by means of the one-carbon chain elongation of 2,3-*O*-isopropylidene-D-glyceraldehyde **1** by using readily available (+)-(*R*)-methyl *p*-tolyl sulfoxide **2** as the nucleophilic reagent. The addition of the lithium salt of sulfoxide **2** to aldehyde **1** gave rise to the corresponding β-hydroxysulfoxide **3**, in 70% yield, as the single diastereoisomer (only one diastereoisomer could be detected in the ^{1}H and ^{13}C NMR spectra of the crude reaction). The high diastereoselectivity of the process is attributed to the matched asymmetric induction of both the chiral aldehyde and the nucleophile (Table 1).

Table 1
Addition of sulfoxide **2** to aldehyde **1** and protection of the hydroxyl group of compound **3**

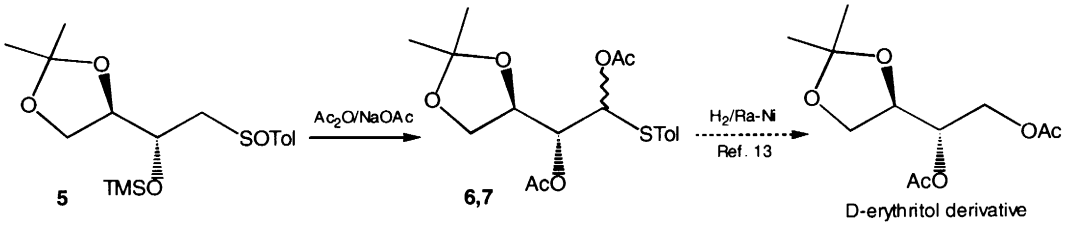


Product	R	yield (%)[a]	$[\alpha]_D$
4	TBS[b]	15[e]	+111.3
5	TMS[c]	80	+108.9
8	Bn[d]	70	+89.8

a) Isolated yield; b) TBDMSCl/DMF/Imidazole; c) TMSOTf/CH_2Cl_2/TEA; d) BnBr/NaH/tBu$_4$NI/THF; e) A 75% of the unaltered starting material was recovered.

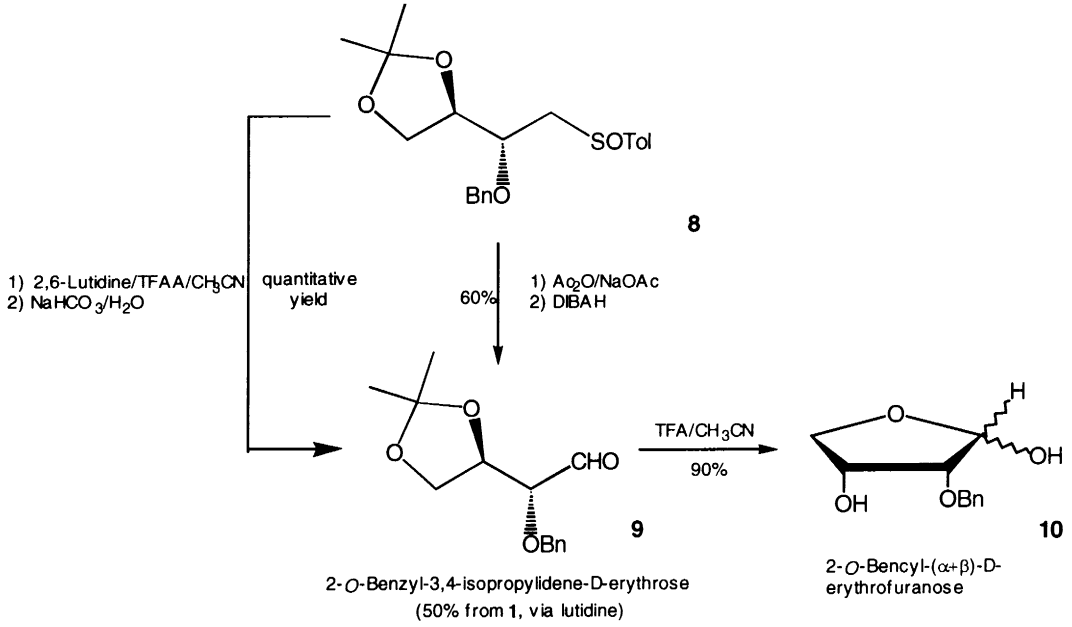
The protection of alcohol **3** as the corresponding TBS-ether was not successful. The reaction of **3** with *t*-butyldimethylsilyl chloride in DMF–imidazole gave rise, after three days at 70°C, to the desired product **4** in only 15% yield. Alternatively, the employment of a more reactive silylation reagent, such as trimethylsilyl trifluoromethanesulfonate in Et_3N, gave rise to the TMS-ether **5** in 80% yield (Table 1). Pummerer rearrangement of compound **5** using acetic anhydride and sodium acetate yielded the corresponding *S*-ketals **6** and **7**, epimers at C-1 (Scheme 1). Under these conditions hydrolysis of the TMS group and further transformation of the intermediate carbinol into its corresponding *O*-acetyl derivative took place. Both epimers **6** and **7** are stable compounds which, after desulfurisation with Ra–Ni according to the method described by Solladié,[13] can be transformed into erythritol, bearing differentially protected hydroxyl groups.

β-Hydroxysulfoxide **3** has also been transformed into its *O*-benzyl derivative by treatment with BnBr/NaH/tBu$_4$NI, yielding the benzylic ether **8** in a good yield. Compound **8** was submitted to a Pummerer rearrangement with Ac_2O/NaOAc, and the resulting product was treated with DIBAH in dichloromethane, at −78°C, to give 2-*O*-benzyl-3,4-*O*-isopropylidene-D-erythrose **9** in a 60% yield (Scheme 2). Alternatively the *O*-benzyl derivative **8** was submitted to a Pummerer rearrangement with



Scheme 1.

trifluoroacetic anhydride/lutidine combination at 0°C. Subsequent treatment of the Pummerer product with saturated aqueous sodium hydrogen carbonate[14] is enough to afford aldehyde **9** in quantitative yield (Scheme 2). It should be noted that the Pummerer rearrangement of sulfoxide **6** and subsequent hydrolysis, following the last procedure, occurs under exceptionally mild conditions. This is an especially interesting result since it allows the synthesis of D-erythrose derivative **9**, with the hydroxyl groups differently protected, in only three steps from aldehyde **1**. The overall yield of **9** starting from **1** is 50%. The configuration of compound **9** could be assigned unequivocally since specific rotation and spectroscopic data coincide with those described in the literature.[11b] Hence, this confirmed the *R* absolute configuration at C-2 assigned to β-hydroxysulfoxide **3**, obtained by reaction of aldehyde **1** with the anion of **2** (Table 1).



Scheme 2.

Aldehyde **9** was treated with trifluoroacetic acid,[15] to give the corresponding 2-*O*-benzyl-D-erythrofuranose **10**, as a mixture of α and β anomers. Configurations of both anomers have been established from Demuynck's results[5b,16] for analogous derivatives; the C-1 signal of the β anomer resonates downfield of the C-1 signal of its anomeric partner α anomer (Scheme 2). Compound **10** is a versatile four-carbon unit which has been used for the synthesis of both enantiomers of *epi*-muricatacin.[17]

In summary, 2-*O*-benzyl-3,4-*O*-isopropylidene-D-erythrose **9** has been prepared from 2,3-*O*-isopropylidene-D-glyceraldehyde and (*R*)-methyl *p*-tolyl sulfoxide by a three-step procedure with a high diastereoselectivity (>98%) and in 50% overall yield. The aldehyde group was obtained directly from

the Pummerer reaction after work-up with saturated aqueous solution of $NaHCO_3$. Acetonide hydrolysis of **9** with TFA gave 2-*O*-benzyl-D-erythrofuranose **10**. Following a parallel chemistry, L-erythrose derivatives could be obtained from L-glyceraldehyde and (*S*)-methyl *p*-tolyl sulfoxide.

3. Experimental

3.1. General methods

Dry solvents and liquid reagents were distilled under argon just prior to use: THF and diethyl ether were distilled from sodium and benzophenone ketyl; $CF_3SO_3SiMe_3$ was distilled at reduced pressure. NaH (60% mineral oil) was activated by repeated treatments with hexane, and further removal of the residual solvent at reduced pressure. All reaction vessels were flame-dried and flushed with argon. Organic solutions were dried over anhydrous sodium or magnesium sulfate, and the solvent was evaporated at reduced pressure below 40°C.

TLC was performed on glass plates coated with silica gel G (Merck) or SI-F-254 (Scharlau), spots being developed either with sulfuric acid in ethanol (10%) or with phosphomolybdic acid in ethanol. Silica gel Merck 60 (230–400 mesh) was used for flash chromatography.

Optical rotations were measured with a 141 Perkin–Elmer polarimeter. Specific rotations are given in units of 10^{-1} deg cm^2 g^{-1}.

^1H NMR (300 MHz, $CDCl_3$) and ^{13}C NMR (80 MHz, $CDCl_3$) spectra were performed with a Bruker AC-300 spectrometer. Chemical shifts are given in ppm (δ), relative to $SiMe_4$ as the internal reference; signal multiplicities are quoted as s, singlet; d, doublet; dd, double doublet; ddd, doubled double doublet; dddd, double double doublet; dq, double quartet; t, triplet; q, quartet; and m, multiplet. J-Values are given in hertz. Diastereoisomeric ratios were determined by integration of well-separated signals of the ^1H NMR spectra. IR spectra were measured by using a Nicolet FTIR-20-SX spectrometer. Mass spectra were recorded by the direct insertion technique by electronic impact (EI), by using an HP-588-A spectrometer at 230 eV with a source temperature of 200°C. Elemental analyses were determined with a Carlo Erba Elemental Analyzer 1106.

2,3-*O*-Isopropylidene-D-glyceraldehyde **1** was synthesised from 1,2:5,6-di-*O*-isopropylidene-D-mannitol by oxidation with sodium periodate.[18] (*S*)-Menthyl *p*-toluenesulfinate and (*R*)-methyl *p*-tolyl sulfoxide **2** were prepared as described previously.[19,20]

3.2. Addition of (R)-(+)-methyl p-tolyl sulfoxide **2** to 2,3-O-isopropylidene-D-glyceraldehyde **1**

A solution of sulfoxide **2** (1 g, 6.5 mmol) in THF (25 ml) was slowly added to a solution of LDA[21] (6.5 mmol) in THF (19 ml) at −78°C and the resulting mixture was stirred for 1 h. Then, a solution of aldehyde **1** (840 mg, 6.5 mmol) in THF (25 ml) was slowly added at the same temperature, the reaction mixture was stirred for an additional hour and was allowed to reach room temperature (about 2 h). The reaction mixture was quenched with saturated NH_4Cl aqueous solution and extracted with dichloromethane (3×20 ml). The combined organic layers were dried (Na_2SO_4), the solvent was removed under reduced pressure, and the residue was purified by flash chromatography (hexane:ethyl acetate, 3:2) to give compound **3** (1.27 g, 4.55 mmol, 70%) as a white solid.

*3.2.1. S(*R*)-1-Deoxy-1-(*p*-tolylsulfinyl)-3,4-*O*-isopropylidene-*D*-erythritol **3***

Mp 66–68°C (hexane:Et_2O); R_f=0.47 (hexane:AcOEt, 9:1); $[\alpha]_D^{20}$=+162.0 (c 0.5, $CHCl_3$); ^{1}H NMR δ 1.31 and 1.41 (2 s, each 3H, C(CH_3)$_2$), 2.43 (s, 3H, CH_3-Ar), 2.90 (dd, 1H, $J_{1,2}$ 9.9, J_{gem} 13.2, H-C1), 3.10 (dd, 1H, $J_{1',2}$ 1.4, J_{gem} 13.2, H′-C1), 3.90 (ddd, 1H, $J_{3,2}$ 7.6, $J_{3,4}$ 5.0, $J_{3,4'}$ 6.5, H-C3), 4.02 (dd, 1H, $J_{4,3}$ 5.0, J_{gem} 8.7, H-C4), 4.12 (dd, 1H, $J_{4',3}$ 6.5, J_{gem} 8.7, H′-C4), 4.15 (d, 1H, $J_{OH,2}$ 2.9, OH-C2), 4.23 (dddd, 1H, $J_{2,1}$ 9.9, $J_{2,1'}$ 1.4, $J_{2,OH}$ 2.9, $J_{2,3}$ 7.6, H-C2), 7.35 and 7.56 (AA′BB′ system, 4H, C_6H_4); ^{13}C NMR δ 21.4 (CH_3-Ar), 25.1 and 26.7 (C(*C*H_3)$_2$), 59.0 (C-1), 66.8 (C-4), 71.0 and 77.7 (C-2, C-3), 109.7 (*C*(CH$_3$)$_2$), 123.9 and 130.2 (*C*H-arom.), 140.4 and 142.2 (*C*-arom.); IR (KBr, liquid film): 3500, 3000, 1600, 1500, 1465, 1420, 1390, 1375, 1250, 1215, 1155, 1070, 845, 815, 730 cm^{-1}; MS (m/e) (relative intensity): 284 (0.1, M^+), 269 (5, M^+-CH_3), 139 (72, $C_7H_7OS^+$), 127 (50, $C_7H_{11}O_2^+$), 101 (46, $C_5H_9O_2^+$), 91 (29, $C_7H_7^+$), 73 (26, $C_3H_5O_2^+$), 43 (100, $C_2H_3O^+$). Anal. calcd for $C_{14}H_{20}O_4S$: C, 59.13; H, 7.09. Found: C, 59.26; H, 7.06.

*3.3. S(*R*)-1-Deoxy-1-(*p*-tolylsulfinyl)-2-*O*-(*t*-butyldimethylsilyl)-3,4-*O*-isopropylidene-*D*-erythritol **4***

To a solution of alcohol **3** (100 mg, 0.35 mmol) in DMF (0.2 ml), imidazole (47 mg, 0.70 mmol) and *t*-BuMe_2SiCl[11b] (106 mg, 0.70 mmol) were added. The solution was stirred for 36 h at 70°C, cooled to rt, poured into water (15 ml), and extracted with ether (2×5 ml). The combined ethereal layers were dried over Na_2SO_4, the solvent was removed under reduced pressure, and the residue was purified by column chromatography (hexane:Et_2O, 3:1) to give compound **4** (20 mg, 0.052 mmol, 15%) as a colourless oil. R_f=0.11 (hexane:Et_2O, 3:1); $[\alpha]_D^{20}$=+111.3 (c 0.2, $CHCl_3$); ^{1}H NMR δ 0.11 and 0.12 (2 s, each 3H, (CH_3)$_2$Si-), 0.90 (s, 9H, (CH_3)$_3$CSi-), 1.34 and 1.36 (2 s, each 3H, C(CH_3)$_2$), 2.41 (s, 3H, CH_3-Ar), 2.90 (dd, 1H, $J_{1,2}$ 6.6, J_{gem} 13.5, H-C1), 3.13 (dd, 1H, $J_{1',2}$ 3.5, J_{gem} 13.5, H′-C1), 3.87 (dd, 1H, $J_{4,3}$ 5.4, J_{gem} 8.4, H-C4), 4.00 (ddd, 1H, $J_{2,1}$ 6.6, $J_{2,1'}$ 3.5, $J_{2,3}$ 6.7, H-C2), 4.05 (dd, 1H, $J_{4',3}$ 6.4, J_{gem} 8.4, H′-C4), 4.31 (ddd, 1H, $J_{3,2}$ 6.7, $J_{3,4}$ 5.4, $J_{3,4'}$ 6.4, H-C3), 7.32 and 7.54 (AA′BB′ system, 4H, C_6H_4); ^{13}C NMR δ −4.0 and −4.6 ((CH_3)$_2$Si-), 18.0 ((CH_3)$_3$*C*Si-), 21.4 (CH_3-Ar), 25.2 and 26.6 (C(*C*H_3)$_2$), 25.7 ((*C*H_3)$_3$CSi-), 63.5 and 66.4 (C-1, C-4), 69.1 and 78.0 (C-2, C-3), 109.5 (*C*(CH$_3$)$_2$), 124.2 and 130.0 (*C*H-arom.), 141.5 and 141.6 (*C*-arom.).

*3.4. S(*R*)-1-Deoxy-1-(*p*-tolylsulfinyl)-2-*O*-(trimethylsilyl)-3,4-*O*-isopropylidene-*D*-erythritol **5***

To a solution of alcohol **3** (100 mg, 0.35 mmol) in CH_2Cl_2 (2 ml), triethylamine (0.085 ml, 0.61 mmol) and trimethylsilyl trifluoromethanesulfonate[22] (0.1 ml, 0.54 mmol) were added. The solution was stirred at 0°C for 30 min, poured into ice, and extracted with ether (2×5 ml). The combined ethereal layers were dried over Na_2SO_4, the solvent was removed under reduced pressure, and the residue was purified by column chromatography (CH_2Cl_2:acetone, 10:1) to give compound **5** (100 mg, 0.28 mmol, 80%) as a white solid. Mp 77–79°C (hexane:Et_2O); R_f=0.80 (CH_2Cl_2:acetone, 10:1); $[\alpha]_D^{20}$=+109.9 (c 1.0, $CHCl_3$); ^{1}H NMR δ 0.14 (s, 9H, (CH_3)$_3$Si-), 1.32 and 1.36 (2 s, each 3H, C(CH_3)$_2$), 2.41 (s, 3H, CH_3-Ar), 2.97 (dd, 1H, $J_{1,2}$ 5.8, J_{gem} 13.6, H-C1), 3.12 (dd, 1H, $J_{1',2}$ 4.5, J_{gem} 13.6, H′-C1), 3.83 (dd, 1H, $J_{4,3}$ 5.2, J_{gem} 8.5, H-C4), 3.95 (ddd, 1H, $J_{2,1}$ 5.8, $J_{2,1'}$ 4.5, $J_{2,3}$ 11.3, H-C2), 4.03 (dd, 1H, $J_{4',3}$ 6.3, J_{gem} 8.5, H′-C4), 4.21 (ddd, 1H, $J_{3,2}$ 11.3, $J_{3,4}$ 5.2, $J_{3,4'}$ 6.3, H-C3), 7.30 and 7.54 (AA′BB′ system, 4H, C_6H_4); ^{13}C NMR δ 0.0 ((CH_3)$_3$Si-), 21.0 (CH_3-Ar), 25.8 and 26.2 (C(*C*H_3)$_2$), 62.6 and 65.9 (C-1, C-4), 68.5 and 77.7 (C-2, C-3), 109.3 (*C*(CH$_3$)$_2$), 123.9 and 129.6 (*C*H-arom.), 141.1 and 141.2 (*C*-arom.); IR (KBr, liquid film): 2953, 1600, 1500, 1465, 1420, 1357, 1211, 1150, 1075, 1025, 958, 891, 845, 805, 710 cm^{-1}; MS (m/e) (relative intensity): 341 (7, $M^+-[O]$), 139 (46, $C_7H_7OS^+$), 127 (100, $C_7H_{11}O_2^+$), 101 (94, $C_5H_9O_2^+$), 91 (29, $C_7H_7^+$), 73 (71, $C_3H_9Si^+$), 43 (71, $C_2H_3O^+$).

3.5. *S(*R*)-1-Deoxy-1-(*p*-tolylsulfinyl)-2-*O*-(benzyl)-3,4-*O*-isopropylidene-*D*-erythritol* ***8***

To a solution of compound **3** (500 mg, 1.76 mmol) in THF (40 ml), a suspension of NaH (46 mg, 1.94 mmol) in THF was added at rt. The mixture was stirred at reflux for 30 min, cooled at rt, and then *t*Bu_4NI (65 mg, 0.01 mmol) and benzyl bromide[11b] (0.21 ml, 1.76 mmol) were successively added. The solution was stirred for 20 h at rt, the solvent was removed under reduced pressure, and the residue was treated with saturated aqueous $NaHCO_3$ (20 ml) and extracted with CH_2Cl_2 (2×10 ml). The combined organic extracts were dried (Na_2SO_4), the solvent was removed under reduced pressure, and the residue was purified by flash chromatography (hexane:Ac_2OEt, 2:1) to yield **8** (461 mg, 1.23 mmol, 70%) as a colourless oil. R_f=0.67 (hexane:Ac_2OEt, 9:1); $[\alpha]_D^{20}$=+89.8 (c 1.0, $CHCl_3$); ^{1}H NMR δ 1.33 and 1.38 (2 s, each 3H, $C(CH_3)_2$), 2.40 (s, 3H, CH_3-Ar), 3.10 (dd, 1H, $J_{1,2}$ 4.8, J_{gem} 13.8, H-C1), 3.19 (dd, 1H, $J_{1',2}$ 5.5, J_{gem} 13.8, H′-C1), 3.73 (ddd, 1H, $J_{2,1}$ 4.8, $J_{2,1'}$ 5.5, $J_{2,3}$ 6.2, H-C2), 3.82 (dd, 1H, $J_{4,3}$ 5.3, J_{gem} 8.6, H-C4), 4.05 (dd, 1H, $J_{4',3}$ 6.6, J_{gem} 8.6, H′-C4), 4.24 (ddd, 1H, $J_{3,2}$ 6.2, $J_{3,4}$ 5.3, $J_{3,4'}$ 6.6, H-C3), 4.53 and 4.56 (AB system, 2H, J 11.5, $PhCH_2$), 7.24–7.34 (m, 5H, C_6H_5), 7.33 and 7.49 (AA′BB′ system, 4H, C_6H_4); ^{13}C NMR δ 21.42 (CH_3-Ar), 25.0 and 26.5 ($C(CH_3)_2$), 59.8 (C-1), 66.3 (C-4), 74.2 ($PhCH_2$), 75.6 and 77.0 (C-2, C-3), 109.8 ($C(CH_3)_2$), 124.3 and 130.0 (*C*H-arom.), 127.7, 127.9 and 128.4 (C_6H_5), 137.4 (C_{Ph}-CH_2), 140.7 and 140.8 (*C*-arom.); IR (KBr, liquid film): 2925, 1618, 1460, 1385, 1250, 1050, 845, 750 cm^{-1}; MS (m/e) (relative intensity): 359 (4%, M^+-Me), 139 (13, $C_7H_7OS^+$), 127 (32, $C_7H_{11}O_2^+$), 101 (21, $C_5H_9O_2^+$), 91 (100, $C_7H_7^+$), 43 (30, $C_2H_3O^+$). Anal. calcd for $C_{21}H_{26}O_4S$: C, 67.35; H, 7.00. Found: C, 67.41; H, 6.96.

3.6. *Pummerer-type rearrangement of compound* ***5****, with NaAcO/*Ac_2O[13a,b]

To a solution of compound **5** (107 mg, 0.30 mmol) in Ac_2O (3 ml), NaOAc (28 mg, 0.35 mmol) was added. The solution was refluxed for 2.5 h, cooled at rt, diluted with benzene (7 ml), and filtered through a Celite pad. The solvent was removed under reduced pressure and the residue was purified by flash chromatography (hexane:AcOEt, 6:1) affording pure **6** (24 mg, 0.07 mmol, 19%) and **7** (33 mg, 0.09 mmol, 26%) as colourless oils.

3.6.1. *1,2-Di-O-acetyl-1-(p-tolylthio)-3,4-O-isopropylidene-D-erythritol*

Minor epimer ***6***. R_f=0.85 (hexane:AcOEt, 6:1); $[\alpha]_D^{20}$=+29.8 (c 0.3, $CHCl_3$); ^{1}H NMR δ 1.37 and 1.43 (2 s, each 3H, $C(CH_3)_2$), 2.04 and 2.08 (2 s, each 3H, $OCOCH_3$), 2.33 (s, 3H, CH_3-Ar), 3.87 (dd, 1H, $J_{4,3}$ 5.5, J_{gem} 8.6, H-C4), 4.07 (dd, 1H, $J_{4',3}$ 6.4, J_{gem} 8.6, H′-C4), 4.44 (ddd, 1H, $J_{3,2}$ 7.6,=$J_{3,4'}$ 6.4, $J_{3,4}$ 5.5, H-C3), 5.32 (dd, 1H, $J_{2,1}$ 3.1, $J_{2,3}$ 6.4, H-C2), 6.31 (d, 1H, $J_{1,2}$ 3.1, H-C1), 7.12 and 7.37 (AA′BB′ system, 4H, C_6H_4); ^{13}C NMR δ 20.8 and 20.9 ($OCOCH_3$), 21.2 (CH_3-Ar), 25.3 and 26.5 ($C(CH_3)_2$), 66.8 (C-4), 73.4, 74.1 and 81.5 (C-1, C-2, C-3), 109.8 ($C(CH_3)_2$), 129.9 and 133.4 (*C*H-arom.), 138.7 and 139.4 (*C*-arom.); IR (KBr, liquid film): 3000, 2950, 1750, 1600, 1500, 1495, 1365, 1210, 950, 805 cm^{-1}; MS (m/e) (relative intensity): 368 (2, M^+), 245 (4), 187 (7), 124 (40), 85 (15), 43 (100, $C_2H_3O^+$).
Major epimer ***7***. R_f=0.68 (hexane:AcOEt, 6:1); $[\alpha]_D^{20}$=−15.4 (c 0.3, $CHCl_3$); ^{1}H NMR δ 1.30 and 1.31 (2 s, each 3H, $C(CH_3)_2$), 2.09 and 2.10 (2 s, each 3H, $OCOCH_3$), 2.34 (s, 3H, CH_3-Ar), 3.89 (dd, 1H, $J_{4,3}$ 6.1, J_{gem} 8.4, H-C4), 4.06 (dd, 1H, $J_{4',3}$ 6.3, J_{gem} 8.4, H′-C4), 4.27 (ddd, 1H, $J_{3,2}$ 5.6, $J_{3,4}$ 6.1, $J_{3,4'}$ 6.3, H-C3), 5.39 (dd, 1H, $J_{2,1}$ 4.4, $J_{2,3}$ 5.6, H-C2), 6.11 (d, 1H, $J_{1,2}$ 4.4, H-C1), 7.14 and 7.42 (AA′BB′ system, 4H, C_6H_4); ^{13}C NMR δ 20.7 and 20.9 ($OCOCH_3$), 21.2 (CH_3-Ar), 25.3 and 26.4 ($C(CH_3)_2$), 65.3 (C-4), 72.8, 74.2 and 79.3 (C-1, C-2, C-3), 109.5 ($C(CH_3)_2$), 127.1 and 130.0 (*C*H-arom.), 134.4 and 139.1 (*C*-arom.); IR (KBr, liquid film): 3000, 2950, 1750, 1600, 1500, 1495, 1365, 1210, 950, 805

cm^{-1}; MS (m/e) (relative intensity): 368 (1, M^+), 245 (3, $C_{11}H_{17}O_6^+$), 187 (4), 124 (24), 85 (15), 43 (100, $C_2H_3O^+$). HRMS calcd for $C_{18}H_{24}O_6S$: 368.1294; found: 368.1295.

3.7. 2-O-*Benzyl-3,4*-O-*isopropylidene*-D-*erythrose* **9**

3.7.1. *Method A*[13a,b]

To a solution of compound **8** (47 mg, 0.13 mmol) in Ac_2O (1.5 ml), NaOAc (12 mg, 0.15 mmol) was added. The solution was refluxed for 2.5 h, cooled at rt, diluted with benzene (4 ml), and filtered through a Celite pad. The solvent was removed under reduced pressure. The residue was diluted with dry CH_2Cl_2 (10 ml) and treated with DIBAH (0.28 ml, 0.28 mmol, 1 M in dichloromethane) at −78°C. The mixture was stirred for 30 min, then saturated aqueous sodium tartrate (0.5 ml) was added, and the reaction mixture was allowed to reach room temperature. The organic layer was dried ($MgSO_4$), the solvent was removed under reduced pressure, and the residue was purified by TLC (hexane:Et_2O, 1:2) affording pure **9** (20 mg, 0.08 mmol, 60%), as a colourless oil. R_f=0.40 (hexane:Et_2O, 1:2); $[\alpha]_D^{20}$=+28.7 (c 1.2, $CHCl_3$). Spectroscopic data of **9** coincide with those reported previously:[11b] ^{1}H NMR δ 1.34 and 1.43 (2 s, each 3H, $C(CH_3)_2$), 3.82 (dd, 1H, $J_{1,2}$ 2.0, $J_{2,3}$ 6.1, H-C2), 3.92 (dd, 1H, $J_{4,3}$ 5.5, J_{gem} 8.6, H-C4), 4.07 (dd, 1H, $J_{4',3}$ 6.3, J_{gem} 8.6, H′-C4), 4.35 (ddd, 1H, $J_{3,2}$ 6.1, $J_{3,4}$ 5.5, $J_{3,4'}$ 6.3, H-C3), 4.71 and 4.59 (AB system, 2H, J_{gem} 11.6, $PhCH_2$), 7.35 (m, 5H, C_6H_5), 9.70 (d, 1H, $J_{1,2}$ 2.0, H-C1).

3.7.2. *Method B*[14]

To a solution of compound **8** (73 mg, 0.19 mmol), at 0°C, in CH_3CN (0.5 ml), 2,6-lutidine (0.05 ml, 0.42 mmol) and trifluoroacetic anhydride (0.055 ml, 0.39 mmol) in CH_3CN (0.35 ml) were added. The mixture was stirred at rt for 3 h, treated with saturated aqueous $NaHCO_3$ (1 ml), and extracted with AcOEt (3×0.5 ml). The organic layer was dried (Na_2SO_4) and the solvent was removed under reduced pressure, to give aldehyde **9** (47 mg, 0.19 mmol, quantitative yield) as a colourless oil.

3.8. 2-O-*Benzyl*-D-*erythrofuranose* ***10***

To a solution of compound **9** (100 mg, 0.31 mmol) in CH_3CN (1 ml), trifluoroacetic acid (0.02 ml, 0.31 mmol) was added at rt. The mixture was stirred for 90 min, treated with saturated aqueous $NaHCO_3$ (2 ml), and extracted with AcOEt (3×1 ml). The organic layer was dried (Na_2SO_4) and the solvent was removed under reduced pressure, to give compound **10** (58 mg, 0.28 mmol, 89%) as a 63:37 mixture of α,β anomers. β Anomer: R_f=0.24 (hexane:Et_2O, 1:2); ^{1}H NMR δ 3.85 (dd, 1H, $J_{4,3}$ 3.2, J_{gem} 9.8, H-C4), 3.88 (dd, 1H, $J_{2,1}$ 2.1, $J_{2,3}$ 5.2, H-C2), 4.14 (dd, 1H, $J_{4',3}$ 4.6, J_{gem} 9.8, H′-C4), 4.38 (ddd, 1H, $J_{3,2}$ 5.2, $J_{3,4}$ 3.2, $J_{3,4'}$ 4.6, H-C3), 4.66 and 4.76 (AB system, 2H, J_{gem} 11.6, $PhCH_2$), 5.42 (d, 1H, $J_{1,2}$ 2.1, H-C1), 7.20–7.50 (m, 5H, C_6H_5); ^{13}C NMR δ 70.3 (C-3), 72.9 (Ph*C*H_2 and C-4), 83.6 (C-2), 100.4 (C-1), 128.0, 128.4 and 128.6 (*C*H-arom.), 136.8 (*C*-arom.). α Anomer: R_f=0.24 (hexane:Et_2O, 1:2); ^{1}H NMR δ 3.81 (dd, 1H, $J_{1,2}$ 4.3, $J_{2,3}$ 4.5, H-C2), 3.95 (dd, 1H, $J_{4,3}$ 4.6, J_{gem} 10.0, H-C4), 4.05 (dd, 1H, $J_{4',3}$ 1.5, J_{gem} 10.0, H′-C4), 4.26 (ddd, 1H, $J_{3,2}$ 4.5, $J_{3,4}$ 1.5, $J_{3,4'}$ 4.6, H-C3), 4.63 and 4.66 (AB system, 2H, J_{gem} 11.5, $PhCH_2$), 5.28 (d, 1H, $J_{1,2}$ 4.3, H-C1), 7.20–7.50 (m, 5H, C_6H_5); ^{13}C NMR δ 69.6 (C-3), 72.1 and 72.6 (Ph*C*H_2 and C-4), 78.2 (C-2), 95.2 (C-1), 128.0, 128.2, and 128.7 (*C*H-arom.), 136.8 (*C*-arom.). MS (m/e, CI) (relative intensity): 211 (100, M^++1), 193 (57, M^++1−H_2O), 137 (91, $C_9H_{12}O^+$), 119 (7, M^+−Bn), 103 (28, M^+−OBn), 91 (2, $C_7H_7^+$).

Acknowledgements

We thank Junta de Castilla y León for financial support and Ana Mª Martín Castro for the English translation.

References

1. Bols, M. *Carbohydrate Building Blocks*; John Wiley & Sons: New York, 1996.
2. (a) Cohen, N.; Banner, B. L.; Lopresti, R. J. *Tetrahedron Lett.* **1980**, *21*, 4163. (b) Green, R. H.; Lambeth, P. F. *Tetrahedron* **1983**, *39*, 1687. (c) Nicolau, K. C.; Ramphal, J. Y.; Palazon, J. M.; Spanevello, A. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 587. (d) Gigou, A.; Lellouche, J.-P.; Beacourt, J.-P.; Toupet, L.; Grée, R. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 755. (e) Sanière, M.; Le Merrer, Y.; Barbe, B.; Koscielniak, T.; Dumas, J.; Micas-Languin, D.; Depezay, J.-C. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 614. (f) Gravier-Pelletier, Ch.; Dumas, J.; Le Merrer, Y.; Depezay, J.-C. *J. Carbohydr. Chem.* **1992**, 969.
3. (a) Dyatkina, N. D.; Krayevsky, A. A.; Azhayev, A. V. *Synthesis* **1985**, 410. (b) Mukaiyama, T.; Suzuki, K.; Yamada, T.; Tabusa, F. *Tetrahedron* **1990**, *46*, 265.
4. (a) Dondoni, A.; Marna, A.; Merino, P. *J. Org. Chem.* **1994**, *116*, 3324. (b) Petter, R. C.; Kumaravel, G.; Powers, D. G.; Chang, Ch.-T. *Tetrahedron Lett.* **1991**, *32*, 449. (c) Carreaux, F.; Duréault, A.; Depezay, J. C. *Synlett* **1992**, 527.
5. Marshall, J. A.; Seletsky, B. M.; Luke, G. P. *J. Org. Chem.* **1994**, *59*, 3413. (b) Marshall, J. A.; Hinkle, K. W. *J. Org. Chem.* **1996**, *61*, 105.
6. (a) From D-arabinopyranose derivative: Inanaga, J.; Sugimoto, Y.; Yokoyama, Y.; Haramoto, T. *Tetrahedron Lett.* **1992**, *33*, 8109. (b) From D-isoascorbic acid: André, C.; Bolte, J.; Demuynck, C. *Tetrahedron* **1998**, *9*, 1359.
7. (a) From *meso*-erythritol: Pottie, M.; Lathuwer, G. De.; Vandewalle, M. *Bull. Soc. Chim.* **1994**, *103*, 285. (b) From *meso*-tartaric acid: Bestmann, H. J.; Bauriegel, L. *Tetrahedron Lett.* **1995**, *36*, 853.
8. (a) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5975. (b) Ko, S. Y.; Lee, A. W. M.; Masamune, S.; Reed III, L. A.; Sharpless, K. B.; Walker, F. J. *Science* **1983**, *949*, 220. (c) Lee, A. W. M.; Masamune, S.; Martin, V. S.; Sharpless, K. B.; Walker, F. J. *J. Am. Chem. Soc.* **1982**, *104*, 3515. (d) Ko, S. Y.; Lee, A. W. M.; Masamune, S.; Reed III, L. A.; Sharpless, K. B.; Walker, F. J. *Tetrahedron* **1990**, *46*, 245.
9. Achmatowicz, B.; Raubo, P. Wicha, J. *J. Org. Chem.* **1992**, *57*, 6593.
10. Asymmetric dihydroxylation: Ko, S. Y.; Malik, M. *Tetrahedron Lett.* **1993**, *34*, 4675.
11. (a) Dondoni, A.; Merino, P. *Synthesis* **1992**, 196. (b) Dondoni, A.; Orduna, J.; Merino, P. *Synthesis* **1992**, 201. (c) Dondoni, A.; Merino, P.; Franco, S.; Junquera, F.; Merchán, F. L.; Tejero, T.; Vertolasi, V. *Chem. Eur.* **1995**, *1*, 505. (d) Dondoni, A. *Synthesis* **1998**, 1681 and references cited therein.
12. (a) Báñez, J. M.; Galisteo, D.; Molina, J.; López, J. A.; Rodríguez, J. F.; Romero-Avila, M. C.; Sanz, M. A. *J. Carbohydr. Chem.* **1993**, *12*, 291. (b) Galisteo, D.; López, J. A.; Martínez, H.; Rodríguez, J. F.; Sanz, M. A. *An. Quim.* **1994**, *90*, 221. (c) Arroyo-Gómez, Y.; López-Sastre, J. A.; Rodríguez-Amo, J. F.; Sanz-Tejedor, M.A. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2933. (d) Arroyo-Gómez, Y.; López-Sastre, J. A.; Rodríguez-Amo, J. F.; Santos-García, M.; Sanz-Tejedor, M. A. *Tetrahedron: Asymmetry* **1999**, *10*, 973.
13. (a) Solladié, G.; Hutt, J.; Fréchou, C. *Tetrahedron Lett.* **1987**, *28*, 61. (b) Solladié, G. *Pure Appl. Chem.* **1988**, *60*, 1699. (c) Solladié, G.; Almario, A. *Tetrahedron: Asymmetry* **1994**, *5*, 1717.
14. Sugihara, H.; Tanikaga, R.; Kaji, A. *Synthesis* **1978**, 881.
15. Kocienski, P. J. *Protecting Groups;* Thieme Foundations of Organic Chemistry Series; Thieme: Stuttgart, New York, 1994.
16. Serianni, A.; Snyder, J. R. *Carbohydr. Res.* **1991**, *210*, 21.
17. Gypser, A.; Petereck, M.; Sharf, H. D. *J. Chem. Soc., Perkin Trans. 1* **1997**, 1013.
18. Schmid, C. R.; Bryant, J. D.; Dowlatzedah, M.; Phillips, J. L.; Prather, D. E.; Schantz, R. D.; Sear, N. L.; Vianco, C. S. *J. Org. Chem.* **1991**, *56*, 4056.
19. Solladié, G. *Synthesis* **1981**, 185.
20. Solladié, G.; Hutt, J.; Girardin, A. *Synthesis* **1987**, 173.
21. Trécourt, F.; Mallet, M.; Marsais, G.; Quéguiner, G. *J. Org. Chem.* **1988**, *53*, 1370.
22. García-Ruano, J. L.; Maestro, M. C.; Sánchez-Sancho, F. *Tetrahedron: Asymmetry* **1995**, *6*, 2299.