71. Enantiomerically Pure 7-Oxabicyclo[2.2.1]hept-5-en-2-yl Derivatives as Synthetic Intermediates

Part III[1])

Total Synthesis of D- and L-Ribose Derivatives[2])

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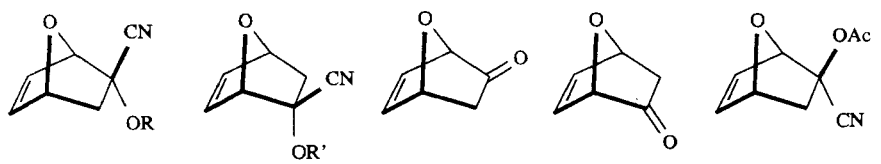
Enantiomerically pure methyl 5-bromo-5-deoxy-2,3-*O*-isopropylidene-β-D- (D-**5b**) and -β-L-ribofuranoside (L-**5b**) have been derived from (−)-(1*R*,2*S*,4*R*)-2-*exo*-cyano-7-oxabicyclo[2.2.1]hept-5-en-2-*endo*-yl (1′*S*)-camphanate (**1**) and (+)-(1*S*,2*R*,4*S*)-2-*exo*-cyano-7-oxabicyclo[2.2.1]hept-5-en-2-*endo*-yl (1′*R*)-camphanate (**2**), respectively, in 5 synthetic steps and 28% overall yield. Hydrolysis of D-**5b** and L-**5b** afforded methyl 2,3-*O*-isopropylidene-β-D-ribofuranoside (D-**5a**) and methyl 2,3-*O*-isopropylidene-β-L-ribofuranoside (L-**5a**), respectively. The intermediate (+)-(1*R*,4*R*,5*R*,6*R*)-5-*exo*,6-*exo*-(isopropylidenedioxy)-7-oxabicyclo[2.2.1]heptan-2-one ((+)-**7**) and its enantiomer (−)-**7** were also obtained enantiomerically pure by resolution of (±)-**7** by the *Johnson-Zeller* method. In both approaches, the chiral auxiliaries ((−)- and (+)-camphanic acids, or (+)-(*S*)-*N*,*S*-dimethyl-*S*-phenylsulfoximide) were recovered at an early stage of the synthesis.

Introduction. – Derivatives of 7-oxabicyclo[2.2.1]heptane have been used as starting materials in the synthesis of natural products [1–3] or of products of biological interest [4]. We have shown that diastereoisomerically pure 7-oxabicyclo[2.2.1]hept-5-en-2-yl derivative **1** can be obtained readily [5] from the commercially available (−)-camphanic acid. (+)-Camphanic acid is also commercially available and should allow one to obtain **2** as easily. Saponification of **1** furnishes enone (+)-**3** and (−)-camphanic acid which can be recycled in the synthesis of **1**. Similarly, **2** gives (−)-**3** and (+)-camphanic acid. Acetate **4** can also be obtained enantiomerically pure [2] [6].

We now present an application of **1** and **2** to the total synthesis of D- and L-ribose derivatives D- and L-**5**, respectively. The synthetic scheme exploits reactions already



1 **2** (+)-**3** (−)-**3** **4**

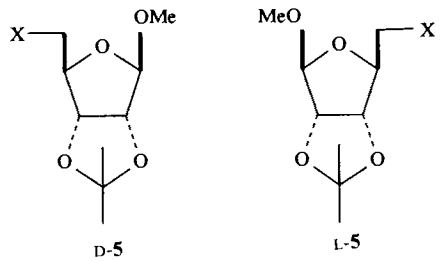
R = (1′*S*)-camphanoyl
R′ = (1′*R*)-camphanoyl

[1]) Part I, see [1]; Part II, see [2].

[2]) For a preliminary communication, see Y. Auberson, R. Bimwala, J. Wagner, P. Vogel, Société Suisse de Chimie, Berne, 16 Oct. 1987, Abstract p. 29.

[3]) Part of the planned Ph. D. thesis of *J. W.*, Ecole Polytechnique fédérale de Lausanne.

[4]) Part of the Ph. D. thesis of *E. V.*, University of Lausanne, Dec. 1986.



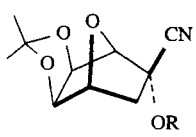
presented by *Schmidt et al.* [7a] and by *Vieira* and *Vogel* [7b] in 1982 for the preparation of racemic 2-*exo*-cyano-7-oxabicyclo[2.2.1]hept-5-en-2-*endo*-yl acetate.

The best syntheses of D-ribose (an important component of nucleic acids, polysaccharides, vitamins, coenzymes, many antibiotics, *etc.*) use natural, optically pure starting materials. *Stroh et al.* [8] on one hand and *Kiss et al.* [9] on the other hand transformed D-glucose into D-ribose in 5 steps and in 24 and 18.1% overall yield, respectively. *Yamada* and coworkers [10] transformed L-glutamic acid in 7 steps into a 2.7:1 mixture (8.5% overall yield) of methyl 5-*O*-benzyl-2,3-*O*-isopropylidene-β-D-ribofuranoside and methyl 5-*O*-benzyl-2,3-*O*-isopropylidene-α-D-lyxofuranoside. More recently, *Grignon-Dubois* and coworkers [11] have obtained D-ribose from the inexpensive D-xylose in 6 steps and 21% overall yield. Other syntheses [12–14] of D-ribose use 2,3-*O*-isopropylidene-D-glyceraldehyde [15] as starting material. Using a chemicoenzymatic approach, *Ohno et al.* [16] transformed dimethyl 7-oxabicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylate into methyl 2,3-*O*-isopropylidene-β-D-ribofuranoside (D-**5a**; 8 steps; 11.8%, 95% e.e.) and into methyl 2,3-*O*-isopropylidene-β-L-ribofuranoside (L-**5a**; 7 steps; 15.1%, 77% e.e.). To our knowledge, this constitutes the first total synthesis of these ribose derivatives with good enantioselectivity.

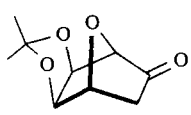
L-Ribose is quite rare, and the only practical method for its preparation is the transformation of L-arabinose by the method of *Austin* and *Humoller* [17] (4 steps; 9.5% overall yield). L-Ribose was also derived from 2,3-*O*-isopropylidene-L-glyceraldehyde (5 steps; 12%), after separation from a mixture containing L-arabinose [12][5]. As we shall see, our diastereoisomerically pure 7-oxabicyclo[2.2.1]hept-5-en-2-yl derivatives **1** and **2** can be transformed efficiently, stereospecifically, and with high enantiomeric purity into D- and L-ribose derivatives, respectively.

Results. – Stereospecific *cis*-bishydroxylation of **1** with H_2O_2 and a catalytical amount of OsO_4 [7] gave the corresponding 5-*exo*,6-*exo*-diol which was not isolated. It was transformed into the acetonide (−)-**6** (65%) on treatment with acetone, 2,2-dimethoxypropane, and TsOH. Saponification of (−)-**6** (KOH/H_2O/THF), followed by treatment with formaline (40% aq. CH_2O, used to displace the equilibrium implying the corresponding cyanohydrines) gave ketone (+)-**7** (92%) and pure (−)-camphanic acid (73%). The latter could be recycled in the preparation of starting material **1** [5]. *Baeyer-Villiger* oxidation of (+)-**7** [7a] with *m*-chloroperbenzoic acid yielded (−)-**8** (98%) which, on treatment with anh. MeOH, 2,2-dimethoxypropane, and a trace amount of MsOH, afforded the methyl uronate (−)-**9** (82%). Saponification of (−)-**9** (KOH/H_2O/THF) gave (−)-**10** (98%). The latter could also be obtained directly from (−)-**8** in a 'one-pot'

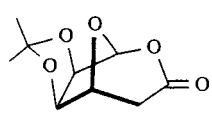
[5]) For the total synthesis of DL-sugars, see [18].



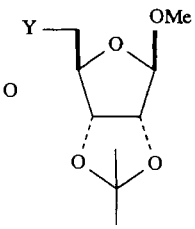
(−)-**6** R = (1′*S*)-camphanoyl



(+)-**7**



(−)-**8**

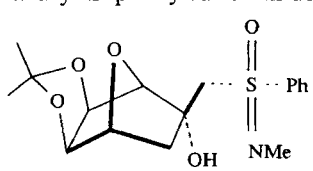


(−)-**9** Y = $COOCH_3$
(−)-**10** Y = COOH

procedure in 80% yield (see *Exper. Part*). Oxidative decarboxylation of (−)-**10** with red HgO and Br_2 gave bromide D-**5b** (60%) whose spectral data were identical with those reported by *Kiss et al.* [19]. D-**5b** has been shown to be a useful starting material for the preparation of 5-deoxy-D-ribose and derivatives, including the anticancer agent 5′-deoxy-5-fluorouridine [19].

Hydrolysis (HMPA/H_2O 17:3, $NaHCO_3$, 130°) of D-**5b** yielded the partially protected D-ribose derivative D-**5a** (75%, 21% based on **1**) [16]. Displacement of the Br-atom in DL-**5b** by treatment with AcOK in DMF afforded the corresponding acetate DL-**5c** (75%). L-Ribose derivatives L-**5b** and L-**5a** were obtained in a similar way starting with camphanate **2**.

Alternatively, the enantiomerically pure ketones (+)-**7** and (−)-**7** could be obtained by applying the resolution technique of *Johnson* and *Zeller* [20] to the racemic (±)-**7** [7]. The sulfoximides **11** (38%, > 99% d.e.) and **12** (37%, > 99% d.e., by HPLC) were derived from (±)-**7** and (+)-(*S*)-*N*,*S*-dimethyl-*S*-phenylsulfoximide and were readily separated by column chromatography on silica gel ($\Delta R_f = 0.13$). Pyrolysis of **11** and **12** (230°/15 Torr) gave (+)-**7** and (−)-**7**, respectively, in *ca.* quantitative yield, together with (+)-(*S*)-*N*,*S*-dimethyl-*S*-phenylsulfoximide.



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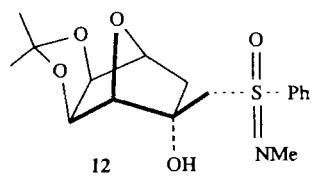

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Because of its simplicity and the use of readily available chiral auxiliaries that are recovered at an early stage of the synthesis, our stereospecific approach should be easy to scale up and be applicable to the preparation of further derivatives of D- and L-ribose[6]).

We thank *F. Hoffmann-La Roche & Co. AG*, Basel, the *Fonds Herbette*, Lausanne, and the *Swiss National Science Foundation* for financial support.

Experimental Part

1. *General.* Solvents were either reagent or technical grade and when necessary were purified and dried by distillation from an appropriate dessiccant under N_2. Solns. after reactions and extractions were evaporated at *ca.* 20 Torr. HMPA = hexamethylphosphoric triamide. M.p. and b.p. (not corrected): *Tottoli* apparatus. Optical

[6]) After submission of our manuscript, a synthesis of (+)-L-ribose *via* (*S*)-pinanediol (α*S*)-α-bromoboronic esters has been reported [21].

rotations ($[\alpha]_\lambda^T$): thermostated *Perkin-Elmer-241* polarimeter. UV/VIS spectra (λ_{max} [nm] (ε [dm^3/mol·cm])): *Philips-Pye-Unicam-SP-8-100,* or *Perkin-Elmer-Hitachi-340,* or *Hewlett-Packard-8450-A.* CD spectra (λ ($\Delta\varepsilon$) [nm]; 20°): *Roussel-Jouan (Jobin-Yvon) Dichrographe III* instrument. IR spectra ($\tilde{\nu}$[cm^{-1}]): *Beckmann-IR-4230,* or *Perkin-Elmer-1420* spectrometers. ^{1}H- and ^{13}C-NMR spectra (δ [ppm]; apparent coupling constant J [Hz]): *Bruker WP-80 CW* (^{1}H, 80 MHz) or *Bruker WH-360 FT* (^{1}H, 360 MHz; ^{13}C 90.55 MHz) equipped with *Aspect-2000* computer, 32 K memory space; deuterium signals of solvent as lock signal, tetramethylsilane (0.0 ppm) or solvent's residual signals ($CDCl_3$: δ(H) 7.24, δ(C) 77.0; C_6D_6: δ(H) 7.15, δ(C) 128.5; CD_3COCD_3: δ(H) 1.95, δ(C) 29.8; CD_3CN: δ(H) 2.05, δ(C) 1.3; CD_3COCD_3: δ(H) 2.50, δ(C) 39.5) as internal reference. Mass spectra (MS; m/z [amu] (% base peak)): electron-ionization mode (70 eV) or chemical ionization mode (CI, ionized gaz), *Finnigan 1020* or *Nermag R 10–10C.* Elementary analysis were performed by the laboratory *Ilse Beetz* in Kronach, Germany.

2. *(–)-(1*R*,2*S*,4*R*,5*R*,6*R*)-2-*exo*-*Cyano*-5-*exo*,6-*exo*-(isopropylidenedioxy)-7-oxabicyclo[2.2.1]hept-2-*endo*-yl (1'*S*)-Camphanate* ((–)-**6**). A mixture of **1** [5] (8.1 g, 25.5 mmol), acetone (100 ml), 30% aq. H_2O_2 (25 ml), and 0.02M OsO_4 in *t*-BuOH (2 ml) was stirred at 20° for 15 h. After solvent evaporation, anh. acetone (100 ml), 2,2-dimethoxypropane (4.9 g, 28 mmol), and TsOH (50 mg) were added, and the mixture was stirred at 20° for 4 days. After the addition of H_2O (200 ml), the mixture was extracted with CH_2Cl_2 (200 ml, 3 times). The org. extracts were combined and washed successively with H_2O (200 ml, 3 times), 10% aq. $NaHSO_3$ (100 ml, twice), 5% aq. $NaHCO_3$ (100 ml, twice), and H_2O (100 ml, twice). After drying ($MgSO_4$), the solvent was evaporated and the residue filtered through a short column of silica gel (AcOEt/hexane 1:1). Recrystallization from hexane/AcOEt yielded 6.46 g (65%) of colourless crystals. M.p. 191–192.5°. $[\alpha]_{589}^{25} = -27.5$, $[\alpha]_{578}^{25} = -28.5$, $[\alpha]_{546}^{25} = -32.8$, $[\alpha]_{436}^{25} = -56.6$, $[\alpha]_{365}^{25} = -92.2$ ($c = 2$, CH_2Cl_2). UV (isooctane): final absorption 200 (70). IR (KBr): 2980, 2960, 2220, 1795, 1750, 1445, 1400, 1390, 1380, 1340, 1320, 1270, 1225, 1205, 1185, 1160, 1095, 1055, 1030, 1015, 985, 970, 955, 930, 895, 865, 845, 825. ^{1}H-NMR (80 MHz, $CDCl_3$): 4.87 (*s*, H–C(1)); 4.7–4.4 (*m*, H–C(4), H–C(5)); 4.32 (*d*, $^3J = 6$, H–C(6)); 2.75 (*dd*, $^2J = 14$, $^3J = 6$, H_{exo}–C(3)); 2.6–1.5 (*m*, 4 H); 1.58 (*d*, $^2J = 14$, H_{endo}–C(3)); 1.46, 1.28 (2*s*, Me_2C); 1.10, 1.07, 0.99 (3*s*, 3 Me). MS (70 eV): 391 (0.4, M^+), 376 (100), 194 (36), 181 (8), 169 (9), 153 (14), 137 (14), 136 (16), 135 (10), 125 (30), 109 (31), 108 (15), 107 (16), 97 (32), 83 (77), 69 (32). Anal. calc. for $C_{20}H_{25}NO_7$ (391.43): C 61.37, H 6.44; found: C 61.43, H 6.41.

*(+)-(1*R*,4*R*,5*R*,6*R*)-5-*exo*-6-*exo*-(Isopropylidenedioxy)-7-oxabicyclo[2.2.1]heptan-2-one* ((+)-**7**). A mixture of (–)-**6** (5.8 g, 14.8 mmol), THF (75 ml), H_2O (65 ml), and 3N KOH in H_2O (10 ml) was allowed to stand at 20° for 30 min. After the addition of 40% aq. CH_2O (120 ml, 148 mmol), the soln. was poured into a vigourously stirred mixture of CH_2Cl_2 (200 ml), H_2O (100 ml), and ice (50 g). The aq. layer was extracted with CH_2Cl_2 (200 ml, twice). The org. phases were combined and washed with brine (200 ml, 3 times). After drying ($MgSO_4$), the solvent was evaporated and the residue recrystallized from hexane, yielding 2.7 g (92%), colourless crystals. M.p. 128–128.5°. $[\alpha]_{589}^{25} = +129$, $[\alpha]_{578}^{25} = +136$, $[\alpha]_{546}^{25} = +160$, $[\alpha]_{436}^{25} = +340$, $[\alpha]_{365}^{25} = +835$ ($c = 0.72$, $CHCl_3$). UV (dioxane): 290 (sh), 303 (32), 313 (33), 325 (sh, 20). UV (95% aq. EtOH): 290 (sh), 303 (32), 313 (33), 325 (sh, 20). CD (isooctane): 312 (+1.1). CD (95% aq. EtOH): 310 (+0.36). IR (KBr): 3050, 3005, 2970, 2955, 1778, 1380, 1215, 1160, 1015. ^{1}H-NMR (80 MHz, $CDCl_3$): 4.8 (*d*, $^3J = 6$, H–C(4)); 4.6–4.4 (*m*, H–C(5), H–C(6)); 4.25 (*s*, H–C(1)); 2.4 (*dd*, $^2J = 18$, $^3J = 6$, H_{exo}–C(3)); 1.84 (*d*, $^2J = 18$, H_{endo}–C(3)); 1.51, 1.32 (2*s*, Me_2C). ^{13}C-NMR (90.55 MHz, $CDCl_3$): 207.8, 113.7 (2*s*); 83.5 (*d*, $^1J(C,H) = 170$); 82.0 (*d*, $^1J(C,H) = 158$); 79.6 (*d*, $^1J(C,H) = 166$); 78.2 (*d*, $^1J(C,H) = 158$); 38.0 (*t*, $^1J(C,H) = 136$); 25.6, 25.0 (2*q*, $^1J(C,H) = 126$). MS (70 eV): 184 (2, M^+), 169 (100). Anal. calc. for $C_9H_{12}O_4$ (184.19): C 58.69, H 6.57; found: C 58.83, H 6.59.

Recovery of (–)-camphanic acid: the aq. phases were united, acidified with conc. HCl, and extracted with CH_2Cl_2 (100 ml, 4 times). The org. extract was washed with brine (100 ml, twice). After drying ($MgSO_4$), the solvent was evaporated and the residue recrystallized from AcOEt/hexane, yielding 2.14 g (73%) of pure (–)-camphanic acid, m.p. 198–199°.

3. *Optical Resolution of (±)-***7** via *the Separation of (+)-(*S*)-*S-{[(1*R*,2*R*,4*R*,5*R*,6*R*)-2-*endo*-Hydroxy-5-*exo*,6-*exo*-(isopropylidenedioxy)-7-oxabicyclo[2.2.1]hept-2-yl]methyl}-*N*-methyl-*S*-phenylsulfoximide* (**11**) *and (+)-(*S*)-*S-{[(1*S*,2*S*,4*S*,5*S*,6*S*)-2-*endo*-Hydroxy-5-*exo*,6-*exo*-(isopropylidenedioxy)-7-oxabicyclo[2.2.1]hept-2-yl]methyl}-*N*-methyl-*S*-phenylsulfoximide* (**12**). At –25°, 1.6M BuLi in hexane (12 ml, 19.2 mmol) was added dropwise to a stirred soln. of (+)-(*S*)-*N*,*S*-dimethyl-*S*-phenylsulfoximide [20] (2.6 g, 15.38 mmol) in anh. THF (40 ml) under Ar. The mixture was stirred at 0° for 10 min and then cooled to –65°. Then (±)-**7** (2.7 g, 14.7 mmol) in anh. THF (10 ml) was added dropwise. After disappearance of (±)-**7** (TLC control (silica gel, AcOEt/petroleum ether 2:1): R_f of **11**, 0.48; R_f of **12**, 0.35; *ca.* 30 min), the mixture was poured in a sat. aq. NH_4Cl soln. (100 ml) stirred at 0°. The mixture was extracted with Et_2O (35 ml, 5 times). After drying ($MgSO_4$), the solvent was evaporated and the residue purified by CC on silica gel (*Lichroprep Si60,* 40–63 μm, *Lobar,* AcOEt/petroleum ether 2:1). The first fraction afforded 1.955 g (38%) of **11**, colourless crystals. M.p. 112–112.5°, after recrystallization from Et_2O/petroleum ether 1:10. The second fraction gave 1.804 g (37%) of **12**, colourless crystals. M.p. 144–145°,

after recrystallization from AcOEt/petroleum ether 2:1. Anal. HPLC (*Du Pont, Spherisorb*, 5 μm, 500 × 6.2 mm, AcOEt/petroleum ether 1:1, 3.5 ml/min) confirmed d.e. > 99%.

Data of **11**. $[\alpha]_{589}^{25} = +21.5$, $[\alpha]_{578}^{25} = +22.8$, $[\alpha]_{546}^{25} = +26.7$, $[\alpha]_{436}^{25} = +52.3$, $[\alpha]_{365}^{25} = +99.7$ ($c = 1.435$, acetone). UV (95% aq. EtOH): 273 (920), 266 (1190), 259 (1090), 217 (9200). UV (isooctane): 272 (1040), 265 (1280), 259 (1120), 216 (9900). IR (KBr): 3150, 3040, 2980, 2925, 2875, 2800, 1440, 1375, 1365, 1220, 1152, 1075, 1052, 855, 743. ^{1}H-NMR (360 MHz, $CDCl_3$): 7.88, 7.63 (2*m*, Ph); 7.2 (*s*, OH); 5.07 (*d*, $^3J = 5.7$, H–C(6)); 4.42 (*d*, $^3J = 6.1$, H–C(4)); 4.40 (*d*, $^3J = 5.7$, H–C(5)); 3.87 (*s*, H–C(1)); 3.51, 3.29 (2*d*, $^3J = 14$, CH_2–C(2)); 2.74 (*dd*, $^2J = 13.2$, $^3J = 6.4$, H_{exo}–C(3)); 2.62 (*s*, MeN); 1.50 (*d*, $^2J = 13.2$, H_{endo}–C(3)); 1.44, 1.30 (2*s*, Me_2C). ^{13}C-NMR (90.55 MHz, $CDCl_3$): 138.5 (*s*); 133.5, 129.8, 129.0 (3*d*, $^1J(C,H) \approx 164$); 110.8 (*s*); 84.6 (*d*, $^1J(C,H) = 159$, C(1)); 81.7 (*d*, $^1J(C,H) = 162$, C(4)); 81.2 (*d*, $^1J(C,H) = 162$, C(6)); 77.9 (*d*, $^1J(C,H) = 164$, C(5)); 63.5 (*t* $^1J(C,H) = 139$, CH_2–C(2)); 38.3 (*t*, $^1J(C,H) = 135$, C(3)); 28.8 (*q*, $^1J(C,H) = 138$, MeN); 25.8, 24.9 (2*q*, $^1J(C,H) = 127$, 2 Me). CI-MS (NH_3): 354 (13, $M^{+\cdot}$ + H), 218 (38), 201 (18), 185 (10), 173 (31), 156 (100), 140 (6), 125 (21), 107 (25), 94 (4), 78 (15). Anal. calc. for $C_{17}H_{23}NO_5S$ (353.44): C 57.77, H 6.56; found: C 57.80, H 6.58.

Data of **12**. $[\alpha]_{589}^{25} = +49$, $[\alpha]_{578}^{25} = +51$, $[\alpha]_{546}^{25} = +58.5$, $[\alpha]_{436}^{25} = +103$, $[\alpha]_{365}^{25} = +170$ ($c = 1.51$, acetone). UV (95% aq. EtOH): 273 (1000), 266 (1280), 259 (1180), 217 (9700). UV (isooctane): 272 (1000), 265 (1250), 259 (1080), 216 (9400). IR (KBr): 3260, 3050, 2975, 2930, 2845, 2785, 1442, 1375, 1225, 1140, 1060, 1035, 1000, 875, 740. ^{1}H-NMR (360 MHz, $CDCl_3$): 7.86, 7.61 (2*m*, Ph); 7.20 (*s*, OH); 5.08 (*d*, $^3J = 5.9$, H–C(6)); 4.96 (*s*, H–C(1)); 4.35 (*d*, $^3J = 5.9$, H–C(5)); 4.28 (*d*, $^3J = 6.5$, H–C(4)); 3.40, 3.31 (2*d*, $^3J = 14$, CH_2–C(2)); 2.60 (*s*, MeN); 1.60 (*dd*, $^2J = 13.5$, $^3J = 6.5$, H_{exo}–C(3)); 1.47, 1.32 (2*s*, Me_2C); 1.34 (*d*, $^2J = 13.5$, H_{endo}–C(3)). ^{13}C-NMR (90.55 MHz, $CDCl_3$): 138.5 (*s*); 133.5, 129.7, 129.1 (3*d*, $^1J(C,H) \approx 164$); 111.1 (*s*); 82.8 (*d*, $^1J(C,H) = 163$, C(1)); 81.9 (*d*, $^1J(C,H) = 158$, C(4)); 79.7 (*d*, $^1J(C,H) = 163$, C(6)); 78.8 (*d*, $^1J(C,H) = 161$, C(5)); 62.3 (*t*, $^1J(C,H) = 140$, CH_2–C(2)); 41.5 (*t*, $^1J(C,H) = 134$, C(3)); 28.7 (*q*, $^1J(C,H) = 138$, MeN); 25.9, 25.1 (2*q*, $^1J(C,H) = 127$, 2 Me). CI-MS (NH_3): 354 (50, $M^{+\cdot}$ + H), 218 (77), 201 (19), 185 (8), 173 (67), 156 (100), 140 (5), 125 (15), 107 (19), 94 (3), 78 (8). Anal. calc. for $C_{17}H_{23}NO_5S$ (353.44): C 57.77, H 6.56; found: C 57.72, H 6.58.

On heating **11** (214 mg, 0.6 mmol) in a *Büchi* 'Kugelrohr' oven to 230°/15 Torr, a mixture of (+)-**7** and (+)-(*S*)-*N*,*S*-dimethyl-*S*-phenylsulfoximide was obtained in the receiver cooled with dry ice. These two products were readily separated by percolation of the mixture through a short bed of silica gel (sulfoximinide retained), giving 105 mg (94%) of (+)-**7**. $[\alpha]_{589}^{25} = +129$ ($c = 0.72$) (e.e. > 99%). The sulfoximide was recovered by extracting the silica gel with AcOEt, giving 90 mg (90%). Similarly, pyrolysis of **12** (406 mg, 1.15 mmol) gave 173 mg (89%) of (+)-(*S*)-*N*,*S*-dimethyl-*S*-phenylsulfoximide and 197 mg (93%) of (−)-**7**, colourless crystals. M.p. 128–128.5°. $[\alpha]_{589}^{25} = -133$, $[\alpha]_{578}^{25} = -139$, $[\alpha]_{546}^{25} = -165$, $[\alpha]_{436}^{25} = -350$, $[\alpha]_{365}^{25} = -862$ ($c = 0.79$, $CHCl_3$).

4. *(−)-(1S,5R,6R,7R)-6-*exo*,7-*exo*-(Isopropylidenedioxy)-2,8-dioxabicyclo[3.2.1]octan-3-one* ((−)-**8**). A mixture of (+)-**7** (327 mg, 1.78 mmol), *m*-$ClC_6H_4CO_3H$ (0.4 g, 1.85 mmol, 80%; *Aldrich*) and $NaHCO_3$ (355 mg, 3.55 mmol) in $CHCl_3$ (15 ml) was stirred at 20° overnight. After the end of the reaction (TLC control, silica gel, Et_2O/petroleum ether 2:1, vanillin as revelator), the soln. was washed with H_2O (20 ml), then with 5% aq. $NaHCO_3$ soln. The aq. phases were extracted with $CHCl_3$ (20 ml, twice). The org. phases were combined and dried ($MgSO_4$). Solvent evaporation gave 365 mg (98%), colourless crystals. M.p. 145.5–146° (recrystallization from Et_2O/petroleum ether 3:1). $[\alpha]_{589}^{25} = -52.5$, $[\alpha]_{578}^{25} = -55$, $[\alpha]_{546}^{25} = -63$, $[\alpha]_{436}^{25} = -111$, $[\alpha]_{365}^{25} = -189$ ($c = 0.6$, acetone). UV (isooctane): final absorption 220 (100). UV (95% aq. EtOH): final absorption 210 (95). IR (KBr): 2990, 2950, 1735, 1380, 1205, 1075, 980. ^{1}H-NMR (360 MHz, $CDCl_3$): 5.72 (*s*, H–C(1)); 4.84, 4.68 (2*d*, $^3J = 5.5$, H–C(6), H–C(7)); 4.63 (*d*, $^3J = 6$, H–C(5)); 3.09 (*dd*, $^2J = 13$, $^3J = 6$, H_{exo}–C(4)); 2.52 (*d*, $^2J = 13$, H_{endo}–C(4)); 1.49, 1.33 (2*s*, Me_2C). ^{13}C-NMR (90.55 MHz, $CDCl_3$): 164.1 (*s*); 113.5 (*s*); 103.3 (*d*, $^1J(C,H) = 186$, C(1)); 84.0 (*d*, $^1J(C,H) = 156$, C(6)); 81.9 (*d*, $^1J(C,H) = 156$, C(7)); 78.6 (*d*, $^1J(C,H) = 161$, C(5)); 35.2 (*t*, $^1J(C,H) = 132$, C(4)); 25.9, 24.9 (2*q*, $^1J(C,H) = 127$, Me_2C). MS (70 eV): 200 (3, M^+), 185 (49), 127 (14), 100 (25), 69 (40), 59 (53), 43 (100). Anal. calc. for $C_9H_{12}O_5$ (200.19): C 54.00, H 6.04; found: C 54.19, H 6.23.

Following the same procedure using (−)-**7**, (+)-**8** was obtained. Racemic (±)-**8** (m.p. 101–103°) was prepared in the same way using (±)-**7** [7a].

*Methyl (Methyl 5-Deoxy-2,3-*O*-isopropylidene-β-*D*-*ribo*-hexofuranosid)uronate* ((−)-**9**). A mixture of (−)-**8** (200 mg, 1 mmol), 2,2-dimethoxypropane (1.5 ml) and MsOH (65 μl) in anh. MeOH (10 ml) was allowed to stand at 20° overnight under Ar. After the addition of AcONa (100 mg), the solvent was evaporated. The residue was taken with Et_2O (30 ml) and the precipitate (MsONa) filtered off. Solvent evaporation yielded 200 mg (82%), colourless oil. $[\alpha]_{589}^{25} = -68$, $[\alpha]_{578}^{25} = -71$, $[\alpha]_{546}^{25} = -80$, $[\alpha]_{436}^{25} = -132$, $[\alpha]_{365}^{25} = -199$ ($c = 1.22$ acetone). UV (isooctane): 205 (220). UV (95% aq. EtOH): 205 (210). IR ($CHCl_3$): 2985, 2940, 2830, 1730, 1435, 1375, 1100, 862. ^{1}H-NMR (360 MHz, $CDCl_3$): 4.97 (*s*, H–C(1)); 4.64 (*m*, H–C(2), H–C(3), H–C(4)); 3.74 (*s*, COOMe); 3.34 (*s*, MeO); 2.71, 2.62 (2*dd*, $^2J = 16$, $^3J = 8$, CH_2(5)); 1.50, 1.33 (2*s*, Me_2C). ^{13}C-NMR (90.55 MHz, $CDCl_3$): 170.9,

112.5 (2*s*); 109.7 (*d*, ^1J(C,H) = 174, C(1)); 85.4 (*d*, ^1J(C,H) = 160, C(4)); 83.8 (*d*, ^1J(C,H) = 157, C(2)); 83.2 (*d*, ^1J(C,H) = 157, C(3)); 54.8 (*q*, ^1J(C,H) = 143, MeO); 51.7 (*q*, ^1J(C,H) = 148, *Me*OOC); 39.8 (*t*, ^1J(C,H) = 130, C(5)); 26.4, 25.0 (2*q*, ^1J(C,H) = 127, Me_2C). CI-MS (NH_3): 264 (100, $[M + NH_4]^+$), 247 (9, $M^+ + H$), 232 (51), 215 (56), 186 (6), 157 (4), 119 (4), 100 (12), 85 (4), 71 (3). Anal. calc. for $C_{11}H_{18}O_6$ (246.26): C 53.65, H 7.37; found: C 54.05, H 7.38.

The same procedure applied to (+)-**8** gave (+)-**9**.

*(Methyl 5-Deoxy-2,3-*O*-isopropylidene-methyl-β-*D*-ribo-hexofuranoside)uronic Acid* ((−)-**10**). A mixture of (−)-**9** (242 mg, 1 mmol), H_2O (5 ml), THF (2 ml), and 1N KOH in H_2O (2 ml) was allowed to stand at 20° for 5 h (TLC control, silica gel, AcOEt/petroleum ether 1:1, vanillin or bromocresol green as revelator). After addition of H_2O (20 ml) and acidification with 3% aq. HCl until pH 1, the mixture was immediately extracted with Et_2O (15 ml, 3 times). After drying ($MgSO_4$), the solvent was evaporated, yielding 227 mg (98%) of a colourless oil. $[\alpha]^{25}_{589} = -57$, $[\alpha]^{25}_{578} = -59$, $[\alpha]^{25}_{546} = -67$, $[\alpha]^{25}_{436} = -110$, $[\alpha]^{25}_{365} = -166$ (*c* = 1.26, $CHCl_3$). UV (95% aq. EtOH): 215 (40). IR (KBr, (±)-**10**, see below): 3030, 2980, 2920, 1695, 1430, 1375, 1271, 1192, 1082, 955, 862. ^{1}H-NMR (360 MHz, CD_3OD): 5.08 (br. *s*, COOH); 4.99 (*s*, H–C(1)); 4.76, 4.72 (2*d*, ^3J = 6, H–C(2), H–C(3)); 4.63 (*t*, ^3J = 8, H–C(4)); 3.40 (*s*, MeO); 2.70 (*d*, ^3J = 8, CH_2(5)); 1.53, 1.39 (2*s*, Me_2C). ^{13}C-NMR (90.55 MHz, $CDCl_3$): 176.4 (*s*, C(6)); 112.6 (*s*); 109.7 (*d*, ^1J(C,H) = 172, C(1)); 85.3 (*d*, ^1J(C,H) = 158, C(4)); 83.7 (*d*, ^1J(C,H) = 155, C(2)); 82.9 (*d*, ^1J(C,H) = 153, C(3)); 54.9 (*q*, ^1J(C,H) = 142, MeO); 39.6 (*t*, ^1J(C,H) = 129, C(5)); 26.4, 25.0 (2*q*, ^1J(C,H) = 127, Me_2C). CI-MS (NH_3): 267 (18), 250 (100, $[M + NH_4]^+$), 233 (12, $M^+ + H$), 218 (65), 201 (12), 185 (7), 172 (8), 157 (6), 143 (7), 103 (6), 85 (10). Anal. calc. for $C_{10}H_{16}O_6$ (232.24): C 51.72, H 6.94; found: C 51.79, H 6.97.

The same procedure applied to (+)- and (±)-**9** gave (+)- and (±)-**10**, respectively. (±)-**10**: colourless crystals, m.p. 65.5–66° (recrystallization from $CHCl_3$/pentane 1:5).

5. *One-Pot Transformation of (−)-***8** *into (−)-***10**. MsOH (325 µl, 5 mmol) was added slowly to a stirred soln. of (−)-**8** (1 g, 5 mmol) in anh. MeOH (30 ml) and 2,2-dimethoxypropane (7.5 ml, 61.2 mmol). After stirring at 20° for 6 h, the solvent was evaporated and the residue taken up in H_2O (25 ml) and dissolved with a minimum amount of THF (*ca.* 4 ml). The soln. was neutralized (pH 6) with 1N aq. KOH, and then 1N aq. KOH (10 ml) was added and the mixture stirred at 20° overnight. After acidification with 3.6% aq. HCl (pH 1), the mixture was extracted with Et_2O (30 ml, 3 times). The org. extract was dried ($MgSO_4$) and the solvent evaporated, yielding 950 mg (80%), colourless oil.

6. *Methyl 5-Bromo-5-deoxy-2,3-*O*-isopropylidene-β-*L*-ribofuranoside* (L-**5b**). A soln. of (+)-**10** (345 mg, 1.56 mmol) in anh. CCl_4 (15 ml) was added to red HgO (513 mg, 2.34 mmol). Br_2 (0.12 ml, 2.34 mmol) was added and the mixture heated under reflux for 1 h in the dark. After discolouration (TLC control, silica gel, Et_2O/petroleum ether 1:1, vanillin as revelator), the mixture was filtered through *Celite* and washed with 5% aq. $NaHSO_3$ soln. (15 ml) and sat. aq. $NaHCO_3$ soln. (15 ml). The layers were extracted with $CHCl_3$ (15 ml). The org. layers were combined, dried ($MgSO_4$), and the solvent eliminated by distillation (*Vigreux* column). The residue was purified by filtration on a short column of *Florisil* (Et_2O/petroleum ether 1:5), yielding 200 mg (60%), colourless liquid. $[\alpha]^{25}_{589} = +65$, $[\alpha]^{25}_{578} = +68$, $[\alpha]^{25}_{546} = +77$, $[\alpha]^{25}_{436} = +128$, $[\alpha]^{25}_{365} = +196$ (*c* = 1.09, $CHCl_3$). UV (isooctane): 206 (345). UV (95% aq. EtOH): 207 (335). IR (film): 2980, 2930, 2825, 1375, 1208, 1100, 865. ^{1}H-NMR (360 MHz, $CDCl_3$): 5.02 (*s*, H–C(1)); 4.78 (*dd*, ^3J = 6, 1, H–C(3)); 4.63 (*d*, ^3J = 6, H–C(2)); 4.40 (*ddd*, ^3J = 10.5, 6, 1, H–C(4)); 3.43 (*dd*, ^2J = 10.5, ^3J = 6, H–C(5)); 3.34 (*s*, MeO); 3.32 (*dd*, ^2J = 10.5, ^3J = 10.5, H–C(5)); 1.49, 1.32 (2*s*, Me_2C). ^{13}C-NMR (90.55 MHz, $CDCl_3$): 112.7 (*s*); 109.6 (*d*, ^1J(C,H) = 170, C(1)); 86.7 (*d*, ^1J(C,H) = 156, C(4)); 85.2 (*d*, ^1J(C,H) = 158, C(2)); 82.7 (*d*, ^1J(C,H) = 158, C(3)); 55.1 (*q*, ^1J(C,H) = 145, MeO); 32.4 (*t*, ^1J(C,H) = 152, C(5)); 26.4, 25.0 (2*q*, ^1J(C,H) = 128, Me_2C). CI-MS (NH_3): 286 (100, $[M + NH_4]^+$), 284 (92), 269 (10, $M^+ + H$), 267 (9), 253 (16), 251 (15), 193 (2), 177 (1), 127 (17), 85 (5), 75 (6). Anal. calc. for $C_9H_{15}BrO_4$ (267.13): C 40.46, H 5.66, Br 29.91; found: C 40.52, H 5.66, Br 29.95.

*Methyl 5-Bromo-5-deoxy-2,3-*O*-isopropylidene-β-*D*-ribofuranoside* (D-**5b**). Same procedure as above, starting with (−)-**10** yielded D-**5b** whose data were identical to those reported by *Kiss et al.* [19].

*Methyl 2,3-*O*-Isopropylidene-β-*L*-ribofuranoside* (L-**5a**). A mixture of L-**5b** (100 mg, 0.37 mmol), $NaHCO_3$ (32 mg, 0.37 mmol), and H_2O/HMPA 3:17 (2 ml) was heated to 130° for 2 days (TLC control, silica gel, CH_2Cl_2/acetone 95:5, vanillin as revelator). After cooling to 20°, Et_2O (20 ml) was added, and the soln. was washed with H_2O (10 ml, twice). The aq. layers were extracted with Et_2O (20 ml, twice). The Et_2O extracts were dried ($MgSO_4$) and evaporated. The residue was purified by filtration on a short column of silica gel (AcOEt/petroleum ether 1:3), yielding 56.6 mg (75%) of colourless liquid. UV (isooctane): 222 (sh, 28). UV (95% aq. EtOH): 220 (40). IR (film): 3440, 2980, 2930, 2830, 1375, 1090, 865. ^{1}H-NMR (360 MHz, $CDCl_3$): 4.97 (*s*, H–C(1)); 4.83, 4.58 (2*d*, ^3J = 6, H–C(2), H–C(3)); 4.43 (*dd*, ^3J = 3.5, 2.2, H–C(4)); 3.70 (*dd*, ^2J = 12.5, ^3J = 2.2); 3.61 (*dd*, ^2J = 12.5, ^3J = 3.5, CH_2(5)); 3.43 (*s*, MeO); 3.10 (br. *s*, OH); 1.48, 1.31 (2*s*, Me_2C). ^{13}C-NMR (90.55 MHz, $CDCl_3$): 112.1 (*s*); 110.1 (*d*, ^1J(C,H) = 176, C(1)); 88.4 (*d*, ^1J(C,H) = 152, C(4)); 85.9 (*d*, ^1J(C,H) = 158, C(2)); 81.5 (*d*, ^1J(C,H) = 156, C(3));

64.0 (*t*, ^1J(C,H) = 154, C(5)); 55.5 (*q*, ^1J(C,H) = 144, MeO); 26.4, 24.7 (2*q*, ^1J(C,H) = 127, Me_2C). CI-MS (NH_3): 222 (10, $[M + NH_4]^+$), 205 (1, $M^+ + H$), 191 (2), 100 (4), 86 (2), 75 (100). Anal. calc. for $C_9H_{16}O_5$ (204.22): C 52.93, H 7.90; found: C 52.81, H 7.79. Other spectral data were identical to those reported in [16].

*Methyl 2,3-*O*-Isopropylidene-β-*D*-ribofuranoside* (D-**5a**). Same procedure as above, using D-**5b**.

*Methyl 5-*O*-Acetyl-2,3-*O*-isopropylidene-β-*DL*-ribofuranoside* (DL-**5c**). A mixture of AcOK (240 mg, 1 mmol) [18]crown-6 (75 mg, 0.12 mmol), DL-**5b** (122 mg, 0.46 mmol), and DMF (1 ml) was heated to 90° for 4 h. After cooling to 20°, the mixture was purified by column chromatography on silica gel (AcOEt/petroleum ether 1:3), yielding 80 mg (75%), colourless oil. UV (isooctane): final absorption 200 (130). UV (95% aq. EtOH): 205 (150). IR (film): 2980, 2935, 2830, 1740, 1370, 1235, 1090, 1040, 865. ^{1}H-NMR (360 MHz, $CDCl_3$): 4.99 (*s*, H–C(1)); 4.69 (*dd*, ^3J = 6.5, 0.5, H–C(3)); 4.62 (*d*, ^3J = 6.5, H–C(2)); 4.37 (*ddd*, ^3J = 7.5, 6.5, 0.5, H–C(4)); 4.15 (*dd*, ^2J = 11, ^3J = 7.5); 4.10 (*dd*, ^2J = 11, ^3J = 6.5, CH_2(5)); 3.33 (*s*, MeO); 2.10 (*s*, AcO); 1.50, 1.35 (2*s*, Me_2C). ^{13}C-NMR (90.55 MHz, $CDCl_3$): 170.6 (*s*); 112.6 (*s*); 109.4 (*d*, ^1J(C,H) = 173, C(1)); 85.2 (*d*, ^1J(C,H) = 158, C(4)); 84.2 (*d*, ^1J(C,H) = 152, C(2)); 81.9 (*d*, ^1J(C,H) = 155, C(3)); 64.6 (*t*, ^1J(C,H) = 147, C(5)); 54.9 (*q*, ^1J(C,H) = 141, MeO); 26.4, 25.0, 20.8 (3*q*, ^1J(C,H) ≈ 128, 3 Me). CI-MS (NH_3): 264 (100, $[M + NH_4]^+$), 247 (11, $M^+ + H$), 232 (16), 215 (15), 128 (6), 111 (2), 85 (5), 75 (3). Anal. calc. for $C_{11}H_{18}O_6$ (246.26): C 53.65, H 7.37; found: C 53.70, H 7.14.

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