A Straightforward Access to 5-Deoxy-D-arabinono-1,4-lactone, a Versatile Intermediate in the Lauraceae Lactones Syntheses

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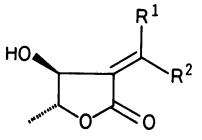
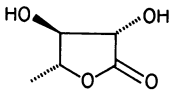
Synopsis. 5-Deoxy-D-arabinono-1,4-lactone (**2**) was synthesized by a RuO_4-catalyzed oxidative cleavage of 6-deoxyglucal diacetate (**5d**), derived from D-glucal triacetate (**3**), followed by alkaline hydrolysis and acidic work-up.

Chiral γ-lactones are versatile building blocks in natural product synthesis and their syntheses from readily available carbohydrates are currently an important area of research.[1] In connection with our programs dealing with the total synthesis of the lauraceae lactones, *i.e.*, (−)-litsenolide B_1 (**1a**) and B_2 (**1b**),[2] we sought a simple method for the preparation of optically active derivatives of β-hydroxy-γ-methyl-γ-lactone. Although 5-deoxy-L-arabino-γ-lactone [(2*R*,3*S*,4*S*)-2,3-dihydroxy-4-pentanolide] is easily accessible from L-rhamnose,[3,4] the preparation of its antipode, 5-deoxy-D-arabinono-1,4-lactone (**2**) whose chirality at the C(3) and C(4) carbons coincides with asymmetric carhons of **1**, is not explored to data due to the scant availability of 6-deoxy-D-mannose. More recently, on the other hand, derivation of (3*R*,4*R*)-pentan-4-olide from D-(+)-ribonic acid by the double



1a: R^1 = H, R^2 = $(CH_2)_9C{\equiv}CH$
1b: R^1 = $(CH_2)_9C{\equiv}CH$, R^2 = H

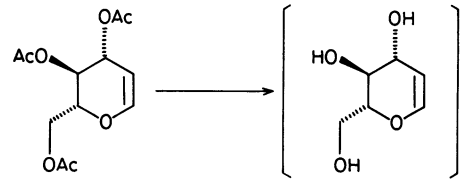


2

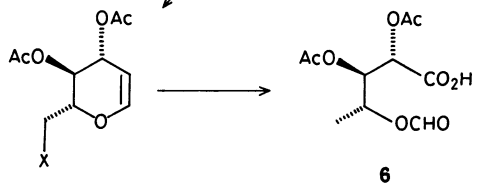
deoxygenation at the C(2) and C(5) positions and its utilization in the synthesis of (−)-litsenolide C_1 and C_2 has been reported.[2d] We describe here a facile synthesis of **2** from the commercially available D-glucal triacetate (**3**)[5] *via* the oxidative cleavage of carbon–carbon double bond of the corresponding 6-deoxyglucal diacetate (**5d**).

Deoxygenation at the C(6) position of **3** to **5d** is the initially requested task in the present synthesis. According to the procedure reported preliminarily by Fraser-Reid *et al.*,[6] we first attempted to transform **3** to the *p*-toluenesulfonate **5a** by selective sulfonylation of the primary hydroxyl group of D-glucal (**4**). After alkaline hydrolysis of **3** with aqueous potassium carbonate, the liberated triol **4** was treated successively with *p*-toluenesulfonyl chloride in pyridine at range 0—50 °C for extended period and then with excess acetic anhydride. Unfortunately, no intended tosylation was observed in this reaction and the starting **3** was recovered. However, the selective sulfonylation of **4** was successfully achieved by using more reactive methanesulfonyl chloride and the desired **5b** was obtained in 52% overall yield from **3** when the reaction was followed by acetylation with acetic anhydride after mesylation. Displacement of the mesylate **5b** with lithium iodide in 2-butanone heated at reflux produced the 6-iodo derivative **5c** which was in turn reduced to the key intermediate **5d** with tributyltin hydride in 91% yield (from **5b**).

In the preceding article[7] we described a ruthenium tetroxide-catalyzed oxidative cleavage of enolic olefins of cyclic structure, giving the corresponding carboxylic acids in good yields. Taking into the advantage of this procedure, the conversion of **5d** into the carboxylic acid **6** was attempted. Thus, the treatment of **5d** with ruthenium tetroxide, generated *in situ* from a catalytic amount of ruthenium dioxide and a stoichiometric amount of sodium periodate (3 equiv) in a biphase solution of carbon tetrachloride and water (1:1 v/v), provided the tri-*O*-acyl-D-arabinonic acid **6** in 78% yield. Finally, the hydrolysis of **6** with aqueous potassium carbonate followed by acidic work-up with 10% hydrogen chloride furnished the desired **2** in 89% yield.



3 **4**



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5a: X = OTs
5b: X = OMs
5c: X = I
5d: X = H

Experimental

Melting points are uncorrected and boiling points are indicated by an air-bath temperature without correction. IR spectra were recorded with a JASCO IRA-1 grating spectrometer. Unless otherwise noted, ^1H NMR spectra were determined with either a Hitachi R-24 (60 MHz) or a JEOL FX-100 (100 MHz). ^{13}C NMR spectra were recorded with a JEOL FX-100 (25.05 MHz) spectrometer. Optical rotations were taken on a JASCO DIP-140 digital polarimeter. Ele-

mental analyses were performed in our laboratory.

3,4-Di-O-acetyl-6-O-methylsulfonyl-1,5-anhydro-2-deoxy-D-arabino-hex-1-enitol (5b). To a solution of D-glucal triacetate (**3**, 1.0 g, 3.67 mmol) in EtOH (10 ml) was added 2M K_2CO_3 (5.5 ml) (1 M=1 mol dm^{-3}). After stirring for 19 h at room temperature, the mixture was filtered and the filtrate was concentrated *in vacuo*. The remaining solid was dried at 50—60 °C for 24 h at diminished pressure and then dissolved in pyridine (7 ml). To this solution was added methanesulfonyl chloride (0.43 ml, 5.56 mmol) at −20 °C and the resulting solution was stirred for 6.5 h at −20 °C and allowed to warm gradually to room temperature. After recooling to 0 °C, the mixture was treated with acetic anhydride (1.4 ml, 14.7 mmol) at 0 °C and stirred for 1 h at 0 °C and additional 17 h at room temperature. The mixture was poured into saturated $NaHCO_3$ and extracted several times with AcOEt. The extracts were washed with 5% $NaHCO_3$ and saturated NaCl, dried (Na_2SO_4), and concentrated. Purification of the crude products on column chromatography (SiO_2, hexane–AcOEt 5:1) gave 590 mg (52%) of **5b**: Mp 47—51 °C (from ether); $[\alpha]_D^{17}$ +15.0 °(*c* 1.6 in EtOH); IR (Nujol) 1730 (ester C=O), 1641 (C=C),1352, 1240, 1220, 1161, 1070, 1039, 963, 929 cm^{-1}; ^{1}H NMR (60 MHz, $CDCl_3$) δ=2.07, 2.11 (s, 6, CH_3CO), 3.09 (s, 3, CH_3SO_2), 4.20—4.60 (m, 1, CH–O), 4.42 (m, 2, CH_2OSO_2), 4.91 (d, d, *J*=6, 3 Hz, 1, O–C=CH), 5.13—5.50 (m, 2, CH–O), 6.51 (d, *J*=6 Hz, 1, O–CH=C). Found: C, 42.97; H, 5.35. Calcd for $C_{11}H_{16}O_8S$: C, 42.86; H, 5.23.

3,4-Di-O-acetyl-6-iodo-1,5-anhydro-2,6-dideoxy-D-arabino-hex-1-enitol (5c). A mixture of **5b** (667 mg, 2.17 mmol) and LiI (487 mg, 3.26 mmol) in 2-butanone (15 ml) was heated at reflux for 29 h. After cooling, the mixture was filtered and the filtrate was concentrated *in vacuo*. The residue was purified on column chromatography (SiO_2, hexane–AcOEt 5:1) to give 676 mg (92%) of **5c**: Bp 119—120 °C/2.5 Torr (1 Torr=133.3 Pa); $[\alpha]_D^{13}$ −3.43° (*c* 1.76 in EtOH); IR (neat) 3040, 3000, 1740, 1725 (ester C=O), 1640 (C=C), 1420, 1363, 1220, 1130, 1078, 1037, 945, 809, 745 cm^{-1}; ^{1}H NMR (60 MHz, $CDCl_3$) δ=2.06, 2.10 (s, 6, CH_3CO), 3.35 (d, *J*=1.5 Hz, 1, CH_2I), 3.44 (s, 1, CH_2I), 3.90—4.30 (m, 1, CH–O), 4.38 (m, 1, O–C=CH), 5.17—5.88 (m, 2, CH–O), 6.50 (d, *J*=6 Hz, 1, O–CH=C); ^{13}C NMR ($CDCl_3$) δ=2.0 (t), 20.8 (q), 21.0 (q), 66.6 (d), 69.7 (d), 74.8 (d), 98.8 (d), 145.3 (d), 169.3 (s), 170.1 (s). Found: C, 35.19; H, 3.73. Calcd for $C_{10}H_{13}IO_5$: C, 35.32; H, 3.86.

3,4-Di-O-acetyl-1,5-anhydro-2,6-dideoxy-D-arabino-hex-1-enitol (5d). A solution of **5c** (357 mg, 1.05 mmol) and *n*-Bu_3SnH (920 mg, 3.16 mmol) in toluene (7 ml) was stirred at room temperature for 4.5 d under nitrogen atmosphere. Evaporation of the solvent followed by column chromatography (SiO_2, hexane–AcOEt 15:1) of the residue gave 222 mg (99%) of **5d**: Bp 87—88 °C/2 Torr; $[\alpha]_D^{15}$ −47.7° (*c* 1.36 in EtOH); IR (neat) 3040, 1735 (ester C=O), 1644 (C=C), 1375, 1220, 1109, 1045, 1022, 910 cm^{-1}; ^{1}H NMR (100 MHz, $CDCl_3$) δ=1.31 (d, *J*=7 Hz, 3, CH_3), 2.04, 2.09 (s, 6, CH_3CO), 4.09 (d, q, *J*=7, 6.5 Hz, 1, CH–O), 4.75 (d, d, *J*=6.5, 3.3 Hz, 1, O–C=CH), 4.99 (d, d, *J*=8, 6 Hz, 1, CH–O), 5.32 (d, d, d, *J*=8, 3.3, 1.5 Hz, 1, CH–O), 6.40 (d, d, *J*=6.5, 1.5 Hz, O–CH=C); ^{13}C NMR ($CDCl_3$) δ=16.6 (q), 20.9 (q), 21.1 (q), 68.3 (d), 71.9 (d), 72.5 (d), 98.8 (d), 146.0 (d), 169.9 (s), 170.6 (s). Found: C, 56.23; H, 6.75. Calcd for $C_{10}H_{14}O_5$: C, 56.07; H, 6.59.

2,3-Di-O-acetyl-4-O-formyl-5-deoxy-D-arabinonic Acid (6). A solution of **5d** (71 mg, 0.33 mmol) in CCl_4 (5 ml) was mixed with a solution of $NaIO_4$ (211 mg, 0.99 mmol) in H_2O (5 ml) and to this mixture was added $RuO_2 \cdot 2H_2O$ (3 mg, 0.02 mmol). After vigorous stirring for 1 h at room temperature, the reaction was quenched with a small amount of 2-propanol. The CCl_4 layer was separated and the aqueous layer was acidified with aqueous 5% HCl and extracted several times with AcOEt. The combined extracts were filtered and the filtrate was dried (Na_2SO_4) and concentrated to give 67 mg (78%) of **6**: $[\alpha]_D^{16}$ +37° (*c* 0.75 in EtOH); IR($CHCl_3$) 3600—2400 (COOH), 1740, 1720 (C=O), 1365, 1205, 1160, 1120, 1040, 840, 930 cm^{-1}; ^{1}H NMR (60 MHz, $CDCl_3$) δ=1.30 (d, *J*=6 Hz, 3, CH_3), 2.11, 2.17 (s, 6, CH_3CO), 4.90—5.70 (m, 3, CH–O), 8.02 (s, 1, CHO), 8.50 (br, 1, COOH). Satisfactory elemental analysis for the methyl ester of **6**; Found: C, 47.70; H, 5.95. Calcd for $C_{11}H_{16}O_8$: C, 47.83; H, 5.84.

5-Deoxy-D-arabinono-1,4-lactone (2). To a solution of **6** (207 mg, 0.79 mmol) in MeOH (10 ml) was added 2 M K_2CO_3 (2 ml) at 3—5 °C. After stirring for 20 h at room temperature, the mixture was acidified to pH 2—3 with 10% HCl and concentrated *in vacuo*. The remaining solids were washed several times with hot AcOEt and the washings were filtered, dried (Na_2SO_4), and concentrated. The crude product was purified on column chromatography (SiO_2, hexane–AcOEt 2:1) to give 92.3 mg (89%) of **2**: Mp 124.5—125.5 °C (from methanol) (lit, data of L-enantiomer[3] 125 °C); $[\alpha]_D^{13}$ +37.3 °(*c* 1.01 in EtOH) (lit, data of L-enantiomer[3] −34—−39°); IR (KBr) 3400 (OH), 1758 (lactone C=O), 1390, 1363, 1330, 1230, 1195, 1144, 1095, 1055, 1019, 945, 870 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD)[8] δ=1.41 (d, *J*=6.3 Hz, 3, CH_3), 3.76 (d, d, *J*=8.8, 8.3 Hz, 1, CH–O), 4.15 (d, q, *J*=8.3, 6.3 Hz, 1, CH–O), 4.28 (d, *J*=8.8 Hz, 1, CH–O), 4.84 (s, OH); ^{13}C NMR (CD_3OD) δ=18.0 (q), 75.1 (d), 78.2 (d), 80.1 (d), 176.0 (s). Found: C, 45.32; H, 5.95. Calcd for $C_5H_8O_4$: C, 45.46; H, 6.10.

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References

1) S. Hanessian, "Total Synthesis of Natural Products: The 'Chiron' Approach," Pergamon Press, Oxford (1983); T. D. Inch, *Tetrahedron*, **40**, 3161 (1984).

2) Isolation a) K. Takeda, K. Sakurai, and H. Ishii, *Tetrahedron*, **28**, 3757 (1972); b) M. Niwa, M. Iguchi, and S. Yamamura, *Chem. Lett.*, **1975**, 655; c) J. C. V. Martinez, M. Yoshida, and O. R. Gottlieb, *Tetrahedron Lett.*, **1979**, 1021: *Phytochemistry*, **20**, 459 (1981); Chiral Synthesis d) S. -Y. Chen and M. M. Joullié, *J. Org. Chem.*, **49**, 2168 (1984); Racemic synthesis e) R. H. Wollenberg, *Tetrahedron Lett.*, **21**, 3139 (1980); f) P. Barbier and C. Benezra, *ibid.*, **23**, 3513 (1982); g) K. Tanaka, M. Terauchi, and A. Kaji, *Bull. Chem. Soc. Jpn.*, **55**, 3935 (1982); h) A. S. Kende and B. H. Toder, *J. Org. Chem.*, **47**, 163 (1982).

3) P. Andrews, L. Hough, and J. K. N. Jones, *J. Am. Chem. Soc.*, **77**, 125 (1955). Synthesis of *dl*-**2**; J. Jary and K. Kefurt, *Collect. Czech. Chem. Commun.*, **27**, 2561 (1962).

4) T. Ohgi, S. M. Hecht, *J. Org. Chem.*, **46**, 1232 (1981).

5) Obtainable from Pfanstiehl Laboratories, Waukegan, IL 60085; W. Roth and W. Pigman, "Methods in Carbohydr. Chem., ed by R. L. Whistler, M. L. Wolfrom, and J. N. BeMiller, Academic Press, New York (1963), Vol. 2 pp. 405—408.

6) D. B. Tulshian and B. Fraser-Reid, *J. Am. Chem. Soc.*, **103**, 474 (1981).

7) S. Torii, T. Inokuchi, and K. Kondo, *J. Org. Chem.*, December issue (1985).

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