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Note

A new synthesis of 2-*C*-methyl-D-erythrono-1,4-lactone*

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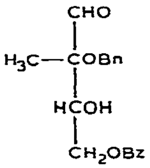
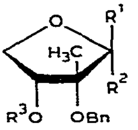
Recently, Teresa *et al.*[2] found 2-*C*-methyl-D-erythrono-1,4-lactone (**8**) in Iberian milk-vetch (*Astragalus lusitanicus* Lam., fam. Leguminosae) as the first natural aldonolactone. They compared **8** ($[\alpha]_D$ −58.6°) with a synthetic sample[3] ($[\alpha]_D$ −18°), obtained by treatment of D-xylose with calcium hydroxide, together with their 2,3-*O*-isopropylidene derivatives, and concluded that the synthetic lactone must have included partially racemized product formed during the alkaline reaction. Compound **8** was also characterized as the corresponding diacetate (**9**).

We have recently[4] synthesized 4-*O*-benzoyl-2-*O*-benzyl-2-*C*-methyl-D-erythrose (**1**), together with 3-*C*-methyl-L-erythrose and 2-*C*-methyl-L-glyceraldehyde derivatives, from 3-*O*-benzyl-1,2-*O*-isopropylidene-3-*C*-methyl-α-D-allofuranose[5] by the method of descent. In the present work, we report a new synthesis of **8** and **9** from **1**.

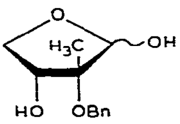


1



2 R^1 = H, R^2 = OMe, R^3 = Bz
3 R^1 = OMe, R^2 = H, R^3 = Bz
4 R^2 = OMe, R^1 = R^3 = H
5 R^1 = OMe, R^2 = R^3 = H

Bn = $PhCH_2$
Bz = PhCO



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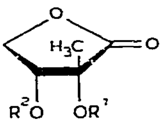

7 R^1 = Bn, R^2 = H
8 R^1 = R^2 = H
9 R^1 = R^2 = Ac

Treatment of **1** with methanol containing 1% of hydrogen chloride, and separation of the products on a column of silica gel, gave methyl 3-*O*-benzoyl-2-*O*-benzyl-2-*C*-methyl-α- (**2**) and -β-D-erythrofuranoside (**3**) and their *O*-debenzoylated products (**4** and **5**) in 10, 37, 15, and 23% yield, respectively. The anomeric configuration of

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*Branched-chain Sugars, Part XXXII. For Part XXXI, see ref. 1.

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TABLE I

COMPARISON OF PHYSICAL PROPERTIES OF **8** AND **9** WITH THOSE REPORTED[2]

Compound	*M.p.* (°C)	$[\alpha]_D$[a] *(degrees)*	*Chemical shifts (δ) and coupling constants (Hz)*[b]						ν_{max} (cm^{-1})
			H-3 ($J_{3,4}$)	*H-4* ($J_{3,4'}$)	*H-4'* ($J_{4,4'}$)	*CMe*	*OH*	*OAc*	
8[c]	syrup	−61.6		4.28–4.64m		1.60s	5.4–4.7bs		3400 (OH), 1770 (C=O)
8 (reported)	syrup	−58.6		4.1–4.6m		1.39s			3500 (OH), 1770 (C=O)
9	87–88	−7.8	5.35dd (6.2)	4.58dd (4.0)	4.29dd (10.6)	1.67s		2.08s 2.14s	1790 and 1740 (C=O)
9 (reported)	86–87	−9	5.35q (6.2)	4.5oct (4)	(10.5)	1.67s		2.07s 2.13s	

[a] Compounds **8** and **9** were measured in water and chloroform, respectively. [b] Compounds **8** and **9** were measured in pyridine-d_5 and chloroform-d, respectively. [c] Measurement of the n.m.r. spectrum in methanol-d_4 gave the following data: 4.78 (s, 2 H, DOH), 4.44 (dd, 1 H, $J_{3,4}$ 4.0, $J_{4,4'}$ 10.0 Hz, H-4), 4.13 (dd, 1 H, $J_{3,4'}$ 2.0 Hz, H-4'), 4.05 (dd, 1 H, H-3), and 1.40 (s, 3 H, CMe).

these compounds was determined by comparison of the rotational values of each pair of anomers. It is noteworthy that, in the ^{13}C-n.m.r. spectra, the 2-*C*-methyl carbon atom of **3** (16.0 p.p.m.) in *cis* orientation to the anomeric methoxyl group, resonates at higher magnetic field than that of **2** (21.1 p.p.m.). This tendency is analogous to the relationship between axial and equatorial *C*-methyl groups attached to a pyranose ring[6].

Hydrolysis of a mixture of **4** and **5** with Amberlite IR-120 (H^+) cation-exchange resin gave the corresponding erythrose derivative (**6**) as a syrup in 76% yield, and oxidation of **6** with bromine–water gave the syrupy lactone **7** in 82% yield. Hydrogenolysis of **7** in the presence of palladium-on-carbon gave, in 72% yield, the free lactone (**8**), which was characterized as the corresponding diacetate (**9**).

Comparison of the physical properties of **8** and **9** thus obtained with those reported[2], shown in Table I, supported the conclusion of Teresa *et al.*[2] as to its identity.

EXPERIMENTAL

General methods. — Melting points were determined with a Mel-Temp hot-plate and are uncorrected. Evaporations were conducted under diminished pressure. Optical rotations were measured with a Carl Zeiss LEP-A1 or a JASCO DIP-4 polarimeter, using chloroform as the solvent unless stated otherwise. Infrared spectra were recorded with a Hitachi EPI-G2 grating spectrometer. ^{1}H-N.m.r. spectra were recorded with a JEOL PS-100 spectrometer for solutions in chloroform-*d* containing tetramethylsilane as the internal reference, unless stated otherwise. ^{13}C-N.m.r. data were obtained at 25.16 MHz with a JEOL FX-100 spectrometer for solutions in chloroform-*d*, using 8 k data points, with proton-noise decoupling.

*Treatment of 4-*O*-benzoyl-2-*O*-benzyl-2-*C*-methyl-*D*-erythrose* (**1**) *with methanolic hydrogen chloride.* — A solution of **1** (1.42 g, 4.32 mmol) in 1% methanolic hydrogen chloride (15 mL) was boiled under reflux for 1 h, made neutral with aqueous sodium hydrogencarbonate, and evaporated to a syrup which was fractionated in a column of silica gel with 8:1:18 benzene–acetone–hexane. The initial fractions gave methyl 3-*O*-benzoyl-2-*O*-benzyl-2-*C*-methyl-β-D-erythrofuranoside (**3**) as a syrup (550 mg) in 37.1% yield; $[\alpha]_D^{22}$ −72.6° (*c* 2.8); ν_{max}^{film} 1725 cm^{-1} (OBz); n.m.r.: δ 8.1–7.9 and 7.6–7.2 (m, 10 H, 2 Ph), 5.39 (dd, 1 H, $J_{3,4'}$ 4.4, $J_{3,4}$ 6.2 Hz, H-3), 4.96 (s, 1 H, H-1), 4.65 (s, 2 H, CH_2Ph), 4.36 (dd, 1 H, $J_{4,4'}$ 9.8 Hz, H-4), 4.01 (dd, 1 H, H-4'), 3.47 (s, 3 H, OMe), and 1.52 (s, 3 H, CMe); ^{13}C-n.m.r.: 166.1 (C=O), 138.8–126.9 (2 Ph), 107.5 (C-1, $^1J_{C,H}$ 107.0 Hz), 82.9 (C-2), 77.8 (C-3), 69.4 (CH_2Ph), 66.1 (C-4), 55.8 (OMe), and 16.0 (CMe) p.p.m. The second fractions gave the α anomer (**2**) of **3** as crystals (145 mg) in 9.8% yield; m.p. 76–77°, $[\alpha]_D^{22}$ −8.8° (*c* 0.85); ν_{max}^{KBr} 1725 cm^{-1} (OBz); n.m.r.: δ 8.15–7.95 and 7.6–7.0 (m, 10 H, 2 Ph), 5.25 (dd, 1 H, $J_{3,4'}$ 2.6, $J_{3,4}$ 6.0 Hz, H-3), 4.68 (s, 1 H, H-1), 4.54 (s, 2 H, CH_2Ph), 4.34 (dd, 1 H, $J_{4,4'}$ 10.0 Hz, H-4), 4.05 (dd, 1 H, H-4'), 3.45 (s, 3 H, OMe), and 1.43 (s, 3 H, CMe); ^{13}C-n.m.r.: 166.3 (C=O), 138.6–127.9 (2 Ph), 106.6 (C-1, $^1J_{C,H}$ 108.4 Hz), 81.6

(C-2), 74.9 (C-3), 71.3 (CH_2Ph), 66.6 (C-4), 55.1 (OMe), and 21.1 (CMe) p.p.m.

Anal. Calc. for $C_{20}H_{22}O_5$: C, 70.16; H, 6.48. Found for **3**: C, 69.86; H, 6.61, and for **2**: C, 70.19; H, 6.48.

The third fractions gave methyl 2-*O*-benzyl-2-*C*-methyl-β-D-erythrofuranoside (**5**) as a syrup (234 mg) in 22.7% yield; $[\alpha]_D^{22}$ −86.9° (*c* 1.7); ν_{max}^{film} 3500 cm^{-1} (OH); n.m.r.: δ 7.4–7.2 (m, 5 H, Ph), 4.90 (s, 1 H, H-1), 4.56 (s, 2 H, CH_2Ph), 4.2–3.6 (m, 3 H, H-3,4,4′), 3.38 (s, 3 H, OMe), 2.92 (d, 1 H, $J_{3,OH}$ 8.4 Hz, OH), and 1.43 (s, 3 H, CMe). The last fractions gave the α anomer (**4**) of **5** as a syrup (156 mg) in 15.1% yield; $[\alpha]_D^{22}$ +29.3° (*c* 1.6); ν_{max}^{film} 3500 cm^{-1} (OH); n.m.r.: δ 7.5–7.3 (m, 5 H, Ph), 4.63 (s, 1 H, H-1), 4.57 and 4.64 (ABq, 2 H, *J* 10.2 Hz, CH_2Ph), 4.2–3.8 (m, 3 H, H-3,4,4′), 3.40 (bs, 1 H, OH), 3.40 (s, 3 H, OMe), and 1.31 (s, 3 H, CMe).

Anal. Calc. for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found for **5**: C, 65.06; H, 7.77, and for **4**: C, 65.23; H, 7.80.

*2-O-Benzyl-2-C-methyl-*D*-erythrofuranose* (**6**). — A suspension of a mixture of **4** and **5** (1.6 g, 6.72 mmol) and Amberlite IR-120 (H^+) cation-exchange resin in water (20 mL) and 1,4-dioxane (10 mL) was boiled under reflux for 6 h, filtered, and evaporated to a syrup. Purification thereof in a column of silica gel with 8:1 benzene–acetone gave **6** (1.15 g) in 76.4% yield, as a syrup that showed no significant value of optical rotation.

Anal. Calc. for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 63.98; H, 7.42.

*2-O-Benzyl-2-C-methyl-*D*-erythrono-1,4-lactone* (**7**). — To a suspension of **6** (980 mg, 4.37 mmol) and basic lead carbonate (3.40 g, 4.37 mmol) in 1,4-dioxane was added bromine (1.4 g, 8.47 mmol) in water (45 mL), and the mixture was stirred in the dark for 3 h at room temperature, bubbled with air to remove the excess of bromine, and filtered. The residue was washed several times with acetone, and the filtrate was extracted five times with chloroform. The washings and extracts were combined, and evaporated, and the residual syrup was purified in a column of silica gel with 1:2 ethyl acetate–hexane, to give **7** as a syrup (805 mg) in 82.9% yield; $[\alpha]_D^{22}$ −21.8° (*c* 1.2); ν_{max}^{film} 3470 (OH) and 1780 cm^{-1} (γ-lactone); n.m.r.: δ 7.3 (m, 5 H, Ph), 4.88 and 4.70 (ABq, 2 H, *J* 11.2 Hz, CH_2Ph), 4.5–4.0 (m, 3 H, H-3,4,4′), 2.05 (bs, 1 H, OH), and 1.56 (s, 3 H, CMe).

Anal. Calc. for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35. Found: C, 64.52; H, 6.51.

*2-C-Methyl-*D*-erythrono-1,4-lactone* (**8**). — A solution of **7** (267 mg, 1.2 mmol) in ethanol (20 mL) and acetic acid (1 mL) was catalytically hydrogenolyzed in the presence of 10% palladium-on-carbon (35 mg) under a hydrogen atmosphere for 8 h, the suspension filtered, and the filtrate evaporated to a pale-brown syrup which was purified in a column of silica gel with 1:9 ethanol–chloroform, to give syrupy **8** (115 mg) in 72% yield; its physical properties are given in Table I.

Anal. Calc. for $C_5H_8O_4$: C, 45.45; H, 6.10. Found: C, 45.38; H, 6.06.

*2,3-Di-O-acetyl-2-C-methyl-*D*-erythrono-1,4-lactone* (**9**). — To a solution of **8** (41 mg, 0.31 mmol) in pyridine (1 mL) were added acetic anhydride (95 mg, 0.93 mmol) and a catalytic amount (10 mg) of 4-(dimethylamino)pyridine; the mixture was stirred for 3 h at room temperature, and evaporated. The resulting syrup crystallized on standing overnight, and was recrystallized from ethanol–hexane, to give colorless prisms (57 mg) in 85% yield; its physical properties are given in Table I.

Anal. Calc. for $C_9H_{12}O_4$: C, 50.00; H, 5.60. Found: C, 49.67; H, 5.34.

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REFERENCES

1 K. Sato and J. Yoshimura, *Carbohydr. Res.*, in press.

2 J. de P. Teresa, J. C. H. Aubanell, A. S. Feliciano, and J. M. M. del Corral, *Tetrahedron Lett.*, (1980) 1359–1360.

3 A. Ishizu, B. Lindberg, and O. Theander, *Acta Chem. Scand.*, 21 (1967) 424–432.

4 J. Yoshimura, K. Hara, M. Yamaura, K. Mikami, and H. Hashimoto, *Bull. Chem. Soc. Jpn.*, in press.

5 M. Funabashi, S. Yamazaki, and J. Yoshimura, *Carbohydr. Res.*, 44 (1975) 275–283.

6 M. Miljković, M. Gligorijević, T. Satoh, D. Glisin, and R. D. Pitcher, *J. Org. Chem.*, 39 (1974) 3847–3850; K. Sato, M. Matsuzawa, K. Ajisaka, and J. Yoshimura, *Bull. Chem. Soc. Jpn.*, 53 (1980) 189–191.