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Note

The Knoevenagel-Doebner reaction on 2,3-*O*-isopropylidene derivatives of D-ribo- and D-manno-furanose

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The Knoevenagel–Doebner reaction of aldehydo sugars with alkyl hydrogen malonates[1] is a highly stereoselective method for the preparation of alkyl *trans*-3-polyhydroxyalkylacrylates, in contrast to the Wittig reaction which gives *cis,trans* mixtures. These acrylate derivatives have been used for the preparation of 2-deoxyaldono-1,4-lactones[2], higher sugar derivatives[3], and polyhydroxyalkyl heterocycles[4].

The reaction[5] of 2,3:5,6-di-*O*-isopropylidene-D-mannofuranose (**1**) with the monomethyl ester of malonic acid in pyridine with piperidine as the catalyst gave, as the principal product, a compound thought to be methyl *trans*-2,3-dideoxy-4,5:7,8-di-*O*-isopropylidene-D-*manno*-oct-2-enonate (**2**). However, in a study[2] of the conversion of Knoevenagel–Doebner products into 2-deoxy-3-*O*-methylaldono-1,4-lactones, epimerisation at C-4 was observed. Consequently, the above-mentioned reaction of **1** (see Experimental) results in epimerisation at C-2 and yields the D-*gluco* product **4**. In fact, both **4** and **15** may be transformed into the same 2-deoxy-3-*O*-methyl-D-aldonolactones (**16**), instead of the corresponding L-analog that might be expected from **2**, thereby showing that both compounds **4** and **15** have the same configuration at C-4. A comparative spectroscopic study of **4**, with samples of **2** and **4** prepared by the Wittig reactions of methoxycarbonylmethylenetriphenylphosphorane with **1** and with 2,3:5,6-di-*O*-isopropylidene-*aldehydo*-D-glucose, reported by Collins *et al.*[6], gave similar conclusions.

A similar Knoevenagel-Doebner reaction of 2,3-*O*-isopropylidene-D-ribo-furanose (**7**) with methyl hydrogen malonate gave a product (**8a**) which was identical with that obtained on partial acid hydrolysis of **11**, prepared by the Knoevenagel–Doebner reaction of 2,3:4,5-di-*O*-isopropylidene-D-arabinose (**10**) with methyl hydrogen malonate. Moreover, the C-4 epimer **14** of **8a**, prepared by the Wittig reaction of **7** with methoxycarbonylmethylenetriphenylphosphorane, had properties different from those of **8a**. The product **14b** was obtained together with the *cis*-isomer **14a** and **9a**. The isolation of **14b** from traces of **7** was very difficult. More reaction time increased the proportion of **9a**.

These results suggest that the more drastic conditions required in the

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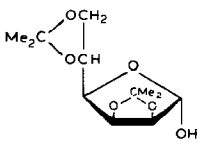

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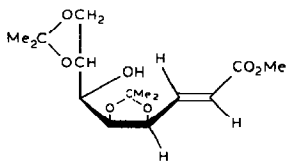

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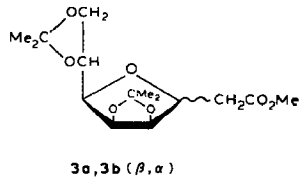
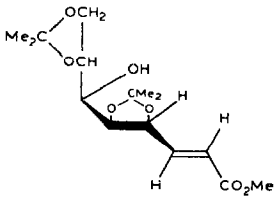


3a,3b (β,α)



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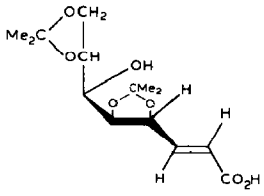

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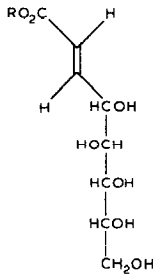


6a R = Me

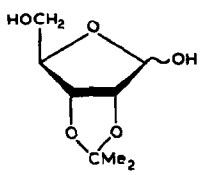
6b R = H

Knoevenagel–Doebner reactions of 2,3-*O*-isopropylidene sugars caused a C-4 isomerisation to give the, possibly more-stable, 4-epimer with a 4,5-*threo* structure.

The anomerisation could take place in the starting sugar derivative, the resulting unsaturated ester, or in a reaction intermediate. The second possibility can be eliminated because treatment of **2** with pyridine–piperidine, even at room temperature, yielded **3a** and **3b** in almost quantitative yield but **4** was not formed. Small amounts of **3a** and **3b** were also produced in the Knoevenagel–Doebner reaction of **1** and methyl hydrogen malonate which showed that the epimerisation was not complete.

The reaction of 2,3-*O*-isopropylidene-D-ribose (**7**) with methyl hydrogen malonate for 8 h gave a mixture of the D-*arabino* unsaturated ester (**8a**) (major product) and its 7-acetate (**8b**), together with the methyl 2-(2,3-*O*-isopropylidene-D-ribofuranosyl)acetates (**9a**) and their 5-acetates (**9b**) as secondary products. After acetylation of the mixture, column chromatography gave **8c** and **9b**.

Separate hydrolysis of **4** and **8a** with aqueous 5% potassium hydroxide yielded the monohydrate of *trans*-2,3-dideoxy-4,5:7,8-di-*O*-isopropylidene-D-*gluco*-oct-2-enonic acid (**5**) and the *trans*-2,3-dideoxy-4,5-*O*-isopropylidene-D-*arabino*-hept-2-enonic acid (**12**), respectively. Hydrolysis of **4** and **5** with aqueous 20% acetic acid yielded methyl *trans*-2,3-dideoxy-D-*gluco*-oct-2-enonate (**6a**) and *trans*-2,3-dideoxy-D-*gluco*-oct-2-enonic acid (**6b**), respectively. Similarly, **8** and **9** each gave the *trans*-2,3-dideoxy-D-*arabino*-hept-2-enonate (**13**), which also confirms the structure assigned to **6**. As expected for the *trans* configuration of the 2,3-double-bond, metaperiodate oxidation of **6a** and further oxidation with silver oxide gave only fumaric acid.



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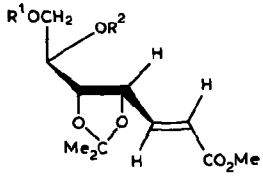

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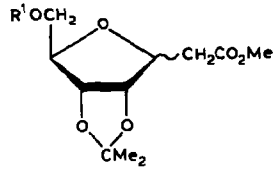

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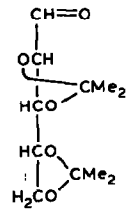
a $R^1 = R^2 = H$
b $R^1 = OAc, R^2 = H$
c $R^1 = R^2 = OAc$



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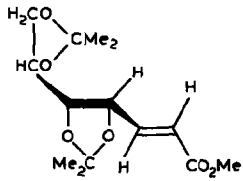

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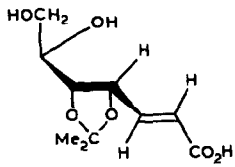

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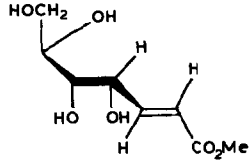

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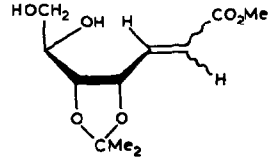
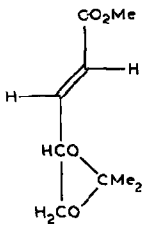


14 a *(cis)*
14 b *(trans)*



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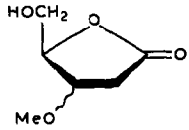

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EXPERIMENTAL

General methods. — Melting points are uncorrected. Optical rotations were measured with a Perkin–Elmer 141 or 241 polarimeter, using a 1-dm cell. I.r. spectra were recorded with a Beckman Aculab IV spectrophotometer, ^{1}H-n.m.r. spectra (internal Me_4Si or 2,2-dimethyl-2-silapentane-5-sulfonate) with Perkin–Elmer Hitachi R-24B (60 MHz), Bruker WP-200 SY (200.13 MHz), and Bruker WM-250 (250 MHz) spectrometers, u.v. spectra with a Beckman DB-GT spectro-

photometer, and mass spectra with a Hewlett–Packard 5930A mass spectrometer. G.l.c. was carried out on a Hewlett–Packard 5710A flame-ionisation chromatograph with a stainless-steel column (2.00 m × 3.00 mm i.d.) packed with (*a*) 3% of diethyleneglycol succinate on Chromosorb WAW (80–100 mesh) or (*b*) 10% of UCB-982 on WAW-DMCS B-79 (80–100 mesh). The He flow-rate was 30 mL/min, the injection-port temperature was 250°, and the zone-detector temperature was 300°. T.l.c. was performed on Silica Gel G (Merck), with detection by charring with sulfuric acid. Preparative t.l.c. was performed on Silica Gel 60 F_{254} (Merck, 13895), column chromatography on Silica Gel 7734 (Merck), and flash chromatography on Silica Gel 9385 (Merck), using *A*, ethyl acetate–hexane (1:1); *B*, ethyl acetate–hexane (1:2); *C*, ethyl acetate–hexane (1:3); *D*, ethyl acetate–hexane (1:5); *E*, ether–hexane (1:1); and *F*, chloroform–methanol (10:1). Elemental analyses were carried out by the Microanalysis Services of the Universities of Granada and Santiago de Compostela.

*Reaction of 2,3:5,6-di-*O*-isopropylidene-*D*-mannofuranose* (**1**) *with methyl hydrogen malonate.* — A solution of **1**[7] (13 g, 50 mmol) and methyl hydrogen malonate[8] (10.7 g, 100 mmol) in pyridine (20 mL) and piperidine (1.4 mL) was boiled under reflux for 18 h. More ester (2 × 7.5 g, 150 mmol) was added after 4 and 10 h. The reaction was monitored by ^{1}H-n.m.r. spectroscopy. G.l.c. [column (*a*) at 180°] of the reaction mixture revealed **3a**[9] (*T* 5.6 min, 9.91%), **3b**[9] (*T* 7.1 min, 12.97%), **1** (*T* 6 min, 5.5%), and **4** (*T* 10.2 min, 71.92%). The solvent was evaporated *in vacuo* and the residue was extracted with boiling hexane (100 mL) for 30 min, and the extract was filtered and cooled to ~0° which caused the separation of an oil. The remaining solution was cooled (−40°) to give crystalline **4**. Further extraction of the oil with hexane gave more **4** (total yield, 11 g, 70%).

Alternatively, the above initial residue (5 g) was subjected to flash column chromatography (solvent *D*), to yield methyl 2-(2,3:5,6-di-*O*-isopropylidene-β-D-mannofuranosyl)acetate (**3a**; 0.180 g, 3.3%), a mixture of **3a** and **3b** (0.017 g, 0.3%), methyl 2-(2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranosyl)acetate (**3b**; 0.131 g, 2.4%), **1** (0.029 g, 0.5%), and methyl *trans*-2,3-dideoxy-4,5:7,8-di-*O*-isopropylidene-D-*gluco*-oct-2-enonate (**4**; 3.85 g, 70%), m.p. 75–76° $[\alpha]_D^{20}$ −9° (*c* 1.3, methanol); λ_{max}^{MeOH} 215 nm (ε 6000); R_F 0.2 (solvent *D*); ν_{max}^{KBr} 3500, 2950, 2940, 1720, 1665, 1460, 1440, 1385, 1375, 900, and 850 cm^{-1}. ^{1}H-N.m.r. data (200 MHz, $CDCl_3$): δ 6.85 (dd, 1 H, *J* 16 and 7 Hz, H-3), 6.05 (dd, 1 H, *J* 16 and 1.5 Hz, H-2), 4.56 (ddd, 1 H, *J* 8.7 and 1.5 Hz, H-4), 3.98 (m, 4 H, H-6,7,8,8'), 3.68 (s, 3 H, MeO), 3.4 (bd, 1 H, *J* 8 Hz, H-5), 2.34 (bs, 1 H, OH, exchangeable with D_2O), 1.36, 1.34, 1.28, and 1.24 (4 s, each 3 H, two Me_2C). Mass spectrum: *m/z* 301 (M^+ − Me), 243 (M^+ − Me − Me_2CO), 185 (M^+ − Me − 2 Me_2CO), 101 (100%).

Anal. Calc. for $C_{15}H_{24}O_7$: C, 56.95; H, 7.64. Found: C, 56.70; H, 7.56.

A solution of methyl *trans*-2,3-dideoxy-4,5:7,8-di-*O*-isopropylidene-D-*manno*-oct-2-enonate[10] (**2**; 958 mg, 3 mmol) in pyridine (1.24 mL) containing piperidine (0.03 mL) was stored at room temperature for 30 min. G.l.c. [column (*a*) at 180°] showed the complete conversion of **2** into a 1:2 mixture of **3b** and **3a**.

^{1}H-N.m.r. analysis showed the absence of vinyl protons as well as the occurrence of the corresponding H-2 signals of **3a** and **3b**: δ 2.76 and 2.65 (2 dd of **3a**), and 2.48 and 2.40 (2 dd of **3b**). When the reaction mixture was kept at room temperature for 4 days, g.l.c. revealed a 2:5 ratio for **3b** and **3a**.

Reaction of 2,3-O-isopropylidene-β-D-ribofuranose (**7**) *with methyl hydrogen malonate.* — A solution of **7**[11] (10 g, 52.6 mmol) and methyl hydrogen malonate (12.4 g, 105.2 mmol) in pyridine (17 mL) and piperidine (0.9 mL) was heated at 85°. After 4 h, more ester (4.6 g, 39 mmol) was added and the reaction was continued until the ^{1}H-n.m.r. spectrum showed that **7** had disappeared (loss of signal for H-1 at δ 5.3 in ~8 h). The pyridine was evaporated and a solution of the residue in ether (50 mL) was washed with saturated aqueous $NaHCO_3$ (50 mL) and cold water (25 mL), then dried (Na_2SO_4), filtered, and concentrated. Column chromatography (solvent *E*) of the residue on silica gel (500 g) gave **9b** (0.546 g, 3.5%; R_F 0.67, solvent *F*), **8b** (1.023 g, 7%; R_F 0.55), **9a** (0.398 g, 2.6%; R_F 0.51), **8a** (6.859 g, 54%; R_F 0.46), and mixed fractions.

Methyl *trans*-2,3-dideoxy-4,5-*O*-isopropylidene-D-*arabino*-hept-2-enonate (**8a**) had $[\alpha]_D^{20}$ +6° (*c* 0.9, chloroform); λ_{max}^{MeOH} 222 nm (ε 10800); ν_{max}^{film} 3450, 2980, 2940, 1730, 1670, 1380, and 995 cm^{-1}. ^{1}H-N.m.r. data (250 MHz, $CDCl_3$): δ 6.93 (dd, 1 H, *J* 15.5 and 4.5 Hz, H-3), 6.08 (dd, 1 H, *J* 15.5 and 1.7 Hz, H-2), 4.53 (ddd, 1 H, *J* 7, 4.5, and 1.7 Hz, H-4), 3.65 (s, MeO), 3.4 (bs, 2 H, 2 OH, exchangeable with D_2O, 1.32 and 1.36 (2 s, each 3 H, Me_2C).

Anal. Calc. for $C_{11}H_{18}O_6$: C, 53.69; H, 7.31. Found: C, 53.82; H, 7.48.

Methyl *trans*-7-*O*-acetyl-2,3-dideoxy-4,5-*O*-isopropylidene-D-*arabino*-hept-2-enonate (**8b**) had $[\alpha]_D^{20}$ +5° (*c* 1.3, chloroform); λ_{max}^{MeOH} 225 nm (ε 8200) ν_{max}^{film} 3450, 2980, 2940, 1730, 1720, 1660, 1380, and 980 cm^{-1}. ^{1}H-N.m.r. data: δ 6.9 (dd, 1 H, *J* 15.5 and 5 Hz, H-3), 6.08 (dd, 1 H, *J* 15.5 and 1.5 Hz, H-2), 4.52 (ddd, 1 H, *J* 7.5, 5, and 1.5 Hz, H-4), 4.27 (dd, 1 H, *J* 11.5 and 3 Hz, H-7), 3.87 (ddd, 1 H, *J* 7, 6, and 3 Hz, H-6), 3.68 (dd, 1 H, *J* 7.5 and 7 Hz, H-5), 3.67 (s, MeO), 2:56 (bs, OH), 2.03 (s, Ac), 1.36 and 1.34 (2 s, each 3 H, Me_2C), 4.02 (dd, 1 H, *J* 11.5 and 6 Hz, H-7′).

Anal. Calc. for $C_{13}H_{20}O_7$: C, 54.20; H, 6.94. Found: C, 54.20; H, 7.14.

Methyl 2-(5-*O*-acetyl-2,3-*O*-isopropylidene-D-ribofuranosyl)acetate (**9b**) had $[\alpha]_D^{20}$ −35° (*c* 1.1, methanol); λ_{max}^{MeOH} 240 nm (ε 4500); ν_{max}^{film} 2980, 2950, 1755, 1740, 1440, and 1380 cm^{-1}. ^{1}H-N.m.r. data (60 MHz, CCl_4): δ 4.45–3.70 (m, 6 H, H-1′,2′,3′,4′,6a′,6b′), 3.51 (s, MeO), 2.42 (d, 2 H, *J* 6 Hz, H-2a,2b), 1.93 (s, Ac), 1.4 and 1.2 (2 s, each 3 H, Me_2C).

The g.l.c. [column (*a*), 200°, *T* 3 min] behaviour of **9a** and its ^{1}H-n.m.r. spectrum were identical with those of authentic methyl 2-(2,3-*O*-isopropylidene-D-ribofuranosyl)acetates[9].

Methyl trans *6,7-di-*O*-acetyl-2,3-dideoxy-4,5-*O*-isopropylidene-*D-arabino-*hept-2-enonate* (**8c**). — The syrupy product of the reaction of **7** with methyl hydrogen malonate was acetylated conventionally with acetic anhydride (15 mL) in pyridine (40 mL). Flash column chromatography (solvent *C*) of the product gave **8c**

(9.11 g, 52.5%) and **9b** (1.67 g, 11%). Compound **8c** had $[\alpha]_D^{20}$ +62° (*c* 1.1, methanol); R_F 0.8 (solvent *F*); λ_{max}^{MeOH} 225 nm (ε 1700); ν_{max}^{film} 2990–2950, 1730, 1720, 1660, 1380, and 985 cm^{-1}. ^{1}H-N.m.r. data (200 MHz, $CDCl_3$): δ 7.8 (dd, *J* 16 and 6 Hz, H-3), 6.05 (dd, *J* 16 and 1.5 Hz, H-2), 5.11 (ddd, *J* 7.5, 6, and 3 Hz, H-6), 4.42 (dd, *J* 12.5 and 3 Hz, H-7), 4.40 (ddd, *J* 8, 6, and 1.5 Hz, H-4), 4.04 (dd, *J* 12.5 and 6 Hz, H-7′), 3.86 (dd, *J* 8 and 7.5 Hz, H-5), 3.69 (s, 3 H, MeO), 2.02 and 2 (2 s, each 3 H, 2 Ac), 1.43 and 1.36 (2 s, 6 H, Me_2C).

Anal. Calc. for $C_{15}H_{22}O_8$: C, 54.58; H, 6.66. Found: C, 54.40; H, 6.61.

*Reaction of 2,3:4,5-di-O-isopropylidene-*D*-arabinose* (**10**) *with methyl hydrogen malonate.* — A mixture of **10**[12] (10.6 g, 39.5 mmol), methyl hydrogen malonate (5.3 g, 45 mmol), pyridine (3.5 mL), and piperidine (0.17 mL) was heated for 6 h at 50–55° and then concentrated, and a solution of the residue in ether (150 mL) was washed with saturated aqueous $NaHCO_3$ (2 × 50 mL) and cold water, dried (Na_2SO_4), filtered, and concentrated. The residue was distilled to give **11** (9.32 g, 70.7%), b.p. 110°/0.2 Torr, $[\alpha]_D^{20}$ +1.5° (*c* 1, ethanol); ν_{max}^{film} 3020, 2980, 2920, 1745, 1675, 1392, 1380, 995, 935, and 855 cm^{-1}. ^{1}H-N.m.r. data (200 MHz, $CDCl_3$): δ 6.86 (dd, *J* 15.7 and 4.4 Hz, H-3), 5.97 (dd, *J* 15.7 and 1.6 Hz, H-2), 4.34 (ddd, *J* 7.7, 4.4, and 1.6 Hz, H-4), 3.48 (t, *J* 7.7 Hz, H-5), 4–3.4 (m, 3 H), 3.55 (s, OMe), 1.22, 1.21, and 1.15 (3 s, 3, 6, and 3 H, 2 Me_2C).

Anal. Calc. for $C_{14}H_{22}O_6$: C, 58.73; H, 7.74. Found: C, 58.78; H, 7.82.

Compound **11**, which we have described[2], was also obtained by Horton *et al.*[13], together with the *cis*-isomer, by reaction of **10** with methoxycarbonylmethylenetriphenylphosphorane but in lower yield.

Partial acid hydrolysis of methyl trans*-2,3-dideoxy-4,5:6,7-di-*O*-isopropylidene-*D*-*arabino*-hept-2-enonate* (**11**). — A mixture of **11** (3 g, 0.001 mol), ethanol (250 mL), and aqueous 1.2% sulphuric acid (250 mL) was heated for 30 min at 50°, then neutralised with $CaCO_3$, filtered, and concentrated to yield **8a** (2.6 g, 94.5%). The product was purified by flash chromatography (solvent *A*) to give a product that was identical (^{1}H-n.m.r. data) to that described above.

trans*-2,3-Dideoxy-4,5:7,8-di-*O*-isopropylidene-*D*-gluco-oct-2-enonic acid* (**5**). — Methyl *trans*-2,3-dideoxy-4,5:7,8-di-*O*-isopropylidene-D-*gluco*-oct-2-enonate (**4**; 2 g, 6.4 mmol) was treated with aqueous 5% potassium hydroxide (20 mL) at room temperature overnight. The solution was extracted with ether (20 mL), and the aqueous layer was acidified with 2M hydrochloric acid (Congo Red) and extracted with ether (3 × 10 mL). The combined extracts were dried (Na_2SO_4) and concentrated to give **5** (1.2 g, 63%), m.p. 117–118° (from hexane–ether), $[\alpha]_D^{20}$ −19° (*c* 1, ethanol); ν_{max}^{film} 3450, 3400, 3200, 2970, 1695, 1650, 1635, 1450, and 990 cm^{-1}. ^{1}H-N.m.r. data (60 MHz, $CDCl_3$): δ 6.90 (dd, 1 H, *J* 16 and 6 Hz, H-3), 6.07 (dd, 1 H, *J* 16 and 1.5 Hz, H-2), 4.55 (m, 1 H, H-4), 4.2–3.3 (2 m, 5 H), 1.45 (s, 6 H, Me_2C), 1.35 and 1.3 (2 s, each 3 H, Me_2C). Acid equivalent, 306 (calc. 302). Mass spectrum: *m/z* 287 (M^+ − Me), 229 (M^+ − Me − Me_2C).

Anal. Calc. for $C_{14}H_{24}O_8 \cdot H_2O$: C, 52.53; H, 7.49. Found: C, 52.54; H, 7.00.

Methyl trans*-2,3-dideoxy-*D*-gluco-oct-2-enonate* (**6a**). — A solution of **4** (2 g,

6.4 mmol) in aqueous 20% acetic acid (40 mL) was boiled under reflux for 30 min and then concentrated to dryness. The residue was recrystallised from ethanol to give **6a** (0.95 g, 63.6%), m.p. 119–120°, $[\alpha]_D^{20}$ −28° (*c* 1, ethanol); ν_{max}^{film} 3400–3200, 2900, 1730, 1650, 1380, 1200, 1117, and 880 cm^{-1}. ^{1}H-N.m.r. data (200 MHz, D_2O): δ 7.02 (dd, 1 H, *J* 15 and 5.5 Hz, H-3), 6.20 (dd, 1 H, *J* 15 and 1.5 Hz, H-2), 3.78 (s, 3 H, MeO). Mass spectrum: *m/z* 237 (M^+ + 1), 205 (M^+ − MeO), 187 (M^+ − MeO − H_2O).

Anal. Calc. for $C_9H_{16}O_7$: C, 45.76; H, 6.77. Found: C, 45.65; H, 6.72.

A mixture of **6a** (500 mg, 1.58 mmol) and water (25 mL) containing sodium metaperiodate (2.4 g) was kept for 1 h at room temperature and then cooled, and the insoluble material was collected and washed with cold water (10 mL). The combined filtrate and washings were stirred with Ag_2O (2.5 g) at 90° for 2 h, neutralised with 12M hydrochloric acid (25 mL), filtered hot, partially concentrated, and cooled to give fumaric acid (120 mg, 65%), m.p. 300°.

trans-*2,3-Dideoxy*-D-gluco-*oct-2-enonic acid* (**6b**). — *trans*-2,3-Dideoxy-4,5:7,8-di-*O*-isopropylidene-D-*gluco*-oct-2-enonic acid (**5**; 1 g, 3.2 mmol) was treated with boiling aqueous 20% acetic acid (20 mL) for 30 min. Work-up described above gave **6b** (244 mg, 64%), m.p. 139–141°, $[\alpha]_D^{20}$ −24.5° (*c* 1, water); ν_{max}^{film} 3400–2500, 1640, 1385, 1300, 1260, 1220, 1190, 1080, 1020, 960, 890, and 775 cm^{-1}. ^{1}H-N.m.r. data (200 MHz, D_2O): δ 6.99 (dd, 1 H, *J* 15.7 and 5.9 Hz, H-3), 6.12 (dd, 1 H, *J* 15.7 and 1.5 Hz, H-2), 4.47 (ddd, 1 H, *J* 6.8, 5.9, and 1.5 Hz, H-4), 3.86–3.70 (m, 3 H, H-5,6,7), 3.65–3.55 (m, 2 H, H-8,8′). Acid equivalent, 225 (calc. 222). Mass spectrum: *m/z* 173 (M^+ − CH_2OH − H_2O), 143 (173 − CHOH).

Anal. Calc. for $C_8H_{14}O_7 \cdot 0.5\ H_2O$: C, 41.55; H, 6.53. Found: C, 40.96; H, 6.17.

trans-*2,3-Dideoxy-4,5*-O-*isopropylidene*-D-arabino-*hept-2-enonic acid* (**12**). — Compound **8** (2.4 g, 9.7 mmol) was treated with aqueous 5% potassium hydroxide (14 mL) at room temperature overnight. The solution was extracted with ether (2 × 10 mL), and the aqueous layer was neutralised with Amberlite IR-120 (H^+) resin, and concentrated to give **12** (970 mg, 43%), m.p. 118–120° (from ethanol), $[\alpha]_D^{20}$ +28° (*c* 0.8, methanol); λ_{max}^{MeOH} 227 nm (ε 11900); ν_{max}^{film} 3380, 3200, 3000, 2930, 2910, 1700, 1645, 1385, 1230, 1110, 1065, 1040, and 985 cm^{-1}. ^{1}H-N.m.r. data (200 MHz, D_2O): δ 7.10 (dd, 1 H, *J* 16 and 5 Hz, H-3), 6.3 (dd, 1 H, *J* 16 and 1.2 Hz, H-2), 5–4.7 (m, H-4 and OH), 4.1–3.6 (m, 4 H, H-5,6,7,7′), 1.5 and 1.52 (2 s, 6 H, Me_2C).

Anal. Calc. for $C_{10}H_{16}O_6 \cdot 0.5\ H_2O$: C, 49.78; H, 7.10. Found: C, 49.19; H, 6.75.

Methyl trans-*2,3-dideoxy*-D-arabino-*hept-2-enonate* (**13**). — A solution of **8a** (895 mg, 3.64 mmol) in aqueous 20% acetic acid (18 mL) was boiled under reflux for 45 min, and then worked-up as described for **6a** to give **13** (714.7 mg, 95%), m.p. 159–161° (from ethanol–water), $[\alpha]_D^{20}$ +12° (*c* 1, water); ν_{max}^{film} 3400–3200, 2980, 2940, 1720, 1670, 1440, 1380, 1285, 875, and 850 cm^{-1}. ^{1}H-N.m.r. data (200 MHz, D_2O): δ 7.06 (dd, 1 H, *J* 20 and 6 Hz, H-3), 6.15 (dd, 1 H, *J* 20 and 2 Hz, H-2), 4.6 (m, 1 H, H-4), 3.9–3.56 (m, 4 H, H-5,6,7,7′), 3.75 (s, 3 H, MeO).

Anal. Calc. for $C_8H_{14}O_6$: C, 46.64; H, 6.79. Found: C, 47.02; H, 7.06.

In a similar way, **11** (1 g, 3.8 mmol) was converted into **13** (700 mg, 90%).

Wittig reaction of 2,3-O-isopropylidene-D-ribose (**7**) *with methoxycarbonylmethylenetriphenylphosphorane.* — A solution of **7** (2 g, 10.5 mmol) and the Wittig reagent (5 g, 66.8 mmol) in benzene (35 mL) was heated under reflux (28 h) until g.l.c. [column (*b*), 150°] showed, *inter alia*, the absence of **7** (*T* 1.2 min) and **8a** (*T* 6 min) and the formation of **14a** and **14b** (*T* 2 and 2.9 min). Benzene was removed *in vacuo*, the residue was extracted with cold ether (200 mL), and the extract was cooled, filtered (to remove Ph_3PO), and concentrated *in vacuo* to a syrup (2.5 g). ^{1}H-N.m.r. showed the signals of **14a** (major product), **14b, 9a**, and a trace of **7**. Part (100 mg) of this syrup was purified by preparative t.l.c. (solvent *F*, 4 developments) to give **14a** (40 mg, 39%), **14b** (25 mg) contaminated by **7**, and mixed fractions.

Methyl *cis*-2,3-dideoxy-4,5-*O*-isopropylidene-D-*ribo*-hept-2-enonate (**14a**) had $[\alpha]_D^{20}$ −93° (*c* 0.2, methanol), R_F 0.44. ^{1}H-N.m.r. data (200 MHz, $CDCl_3$): δ 6.27 (dd, 1 H, *J* 11.5 and 8.3 Hz, H-3), 6.02 (dd, 1 H, *J* 11.5 and 1.5 Hz, H-2), 5.50 (ddd, 1 H, *J* 8.3, 6.4, and 1.5 Hz, H-4), 4.32 (dd, 1 H, *J* 8.2 and 6.4 Hz, H-5), 3.75–3.5 (m, 3 H, H-6,7,7′), 3.74 (s, 3 H, MeO), 1.49 and 1.37 (2 s, 6 H, Me_2C). Mass spectrum: *m/z* 231 (M^+ − Me), 215 (M^+ − MeO), 186 (M^+ − MeOH − CO).

Methyl *trans*-2,3-dideoxy-4,5-*O*-isopropylidene-D-*ribo*-hept-2-enonate (**14b**), after further purification, had $[\alpha]_D^{20}$ −80° (*c* 0.03, methanol), R_F 0.42. ^{1}H-N.m.r. data (200 MHz, $CDCl_3$): δ 7.10 (dd, 1 H, *J* 15.5 and 5 Hz, H-3), 6.16 (dd, 1 H, *J* 15.5 and 1.7 Hz, H-2), 4.86 (ddd, 1 H, *J* 6.4, 5, and 1.7 Hz, H-4), 4.17 (m, 1 H, H-5), 3.9–3.5 (m, 3 H, H-6,7,7′), 3.75 (s, 3 H, MeO), 1.47 and 1.36 (2 s, 6 H, Me_2C). Mass spectrum: *m/z* 247 (M^+ + 1), 215 (M^+ − MeO).

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