

## Note

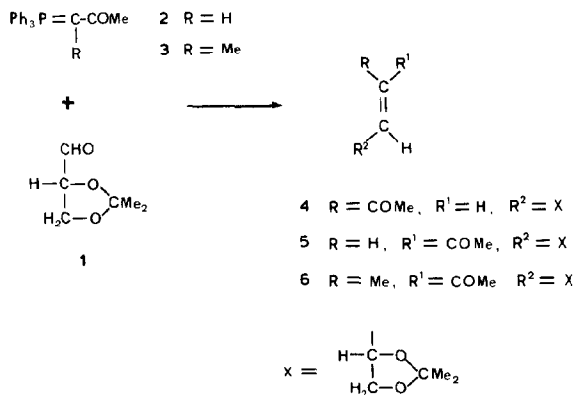
### Synthesis of enuloses and branched-chain enuloses\*

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The reaction between phosphorus ylids and *aldehyde* and *keto* sugars has been extensively studied<sup>2</sup> and the reaction of D-glyceraldehyde with various phosphoranes has been reported<sup>3</sup>. We now report on the reaction of 2,3-*O*-isopropylidene-D-glyceraldehyde (**1**) with acetylmethylenetriphenylphosphorane<sup>4</sup> (**2**) and (1-acetylethylidene)triphenylphosphorane<sup>5</sup> (**3**) to give enulose derivatives to be used as starting products for the synthesis of deoxyhexuloses and branched-chain deoxyhexuloses.



Compounds **5** and **6** have been synthesised by the Knoevenagel–Doebner condensation of **1** with acetoacetic acid<sup>6</sup> and  $\alpha$ -methylacetoacetic acid<sup>7</sup>, respectively, but the formation of only one stereoisomer together with by-products limits the scope of this reaction for the purposes mentioned above.

The reactions of **1** with **2** or **3** were monitored by t.l.c., which revealed, in the first case, the rapid formation of two products, with the minor having the higher mobility. Column chromatography of the mixture gave (*Z*)- (**4**) and (*E*)-1,3,4-

\*Branched-chain Sugars, Part XI. For Part X, see ref. 1.

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trideoxy-5,6-*O*-isopropylidene-D-glycero-hex-3-enulose (**5**, major product).

Compound **5** was known<sup>6</sup>, and the structure of **4** was established on the basis of its spectroscopic and analytical data. Thus, the i.r. carbonyl absorption of **4** occurred at a frequency higher ( $\Delta\nu$  10  $\text{cm}^{-1}$ ) than that of **5**, reflecting the poorer conjugation in the *Z* isomer. The reverse difference ( $\Delta\nu$  15  $\text{cm}^{-1}$ ) was found for the C=C absorption. The  $\epsilon$  value associated with the u.v. spectrum of **4** was less than that of **5** and indicative<sup>7</sup> of the *Z* configuration. The  $^1\text{H}$ -n.m.r. spectrum of **4** (see Experimental) confirmed the structure, the absence of coupling between H-3 and H-4 reflected the *Z* configuration, whereas the upfield ( $\Delta\delta$  0.47 p.p.m.) and downfield ( $\Delta\delta$  0.63 p.p.m.) shifts of the signals for H-4 and H-5, respectively, in **4** compared to those for **5** were also in agreement with those reported<sup>7</sup> for *E*-*Z* isomers. Likewise, in the  $^{13}\text{C}$ -n.m.r. spectra of **4** and **5**, the signals for C-1 and C-4 in **5** were shifted upfield ( $\Delta\delta$   $\sim$ 3.5 and 4.5 p.p.m., respectively) in comparison with those for **4**, and the signal for C-3 in **5** appeared at lower field ( $\Delta\delta$   $\sim$ 3.5 p.p.m.) than for **4**.

In contrast to the above results, the reaction of **1** and **3** gave (*E*)-1,3,4-trideoxy-5,6-*O*-isopropylidene-3-*C*-methyl-D-glycero-hex-3-enulose (**6**) as the sole product, the spectroscopic and analytical data for which accorded with those reported previously<sup>7</sup>.

The stereoselectivity of the Wittig reaction with stabilised phosphoranes has been discussed elsewhere<sup>8</sup>, but the present results demonstrate, as in other examples<sup>7</sup>, that the introduction of a methyl group at C-1 of the ylid increases the stereoselectivity, and only the *E* isomer is produced.

#### EXPERIMENTAL

*General methods.* — Solutions were concentrated under diminished pressure.  $^1\text{H}$ -N.m.r. (80 MHz) and  $^{13}\text{C}$ -n.m.r. (20 MHz) spectra were recorded with a Bruker WP-80 SY spectrometer for solutions in  $\text{CDCl}_3$  (internal  $\text{Me}_4\text{Si}$ ). I.r. spectra were recorded with a Pye Unicam SP 1000 spectrophotometer. Optical rotations were measured for solutions in  $\text{CHCl}_3$  (1-dm tube), using a Perkin-Elmer 141 polarimeter. T.l.c. was performed on Silica Gel G (Merck), with detection by charring with sulfuric acid. Column chromatography was performed on silica gel (Merck, 7734).

*Reaction of 2,3-O-isopropylidene-D-glyceraldehyde (1) with acetylmethylene-triphenylphosphorane (2).* — To a stirred solution of **1** (14.3 g, 0.11 mol) in dry dichloromethane (100 mL) at room temperature was added, dropwise, a solution of the ylid<sup>4</sup> **2** (35 g, 0.11 mol) in the same solvent (100 mL). During addition, some heat was evolved. T.l.c. (hexane-ether, 1:2) then revealed two new compounds,  $R_F$  0.61 and 0.40. The mixture was left at room temperature for 3 h and then concentrated, and the solid residue was extracted with hexane ( $4 \times 50$  mL). The combined extracts were cooled at  $5^\circ$  for 1 h, filtered to remove triphenylphosphine oxide, and concentrated to give a residue (19 g) that was subjected to column

chromatography (hexane–ether, 5:1→2:1) to yield, first, (*Z*)-1,3,4-trideoxy-5,6-*O*-isopropylidene-D-glycero-hex-3-enulose (**4**; 4.7 g, 25%) as a mobile oil,  $[\alpha]_D +222.4^\circ$  (*c* 1.26);  $\nu_{\max}^{\text{film}}$  1695 (ketone, C=O), 1620 (C=C), 1380 and 1370 (CMe<sub>2</sub>), 1265, 1215, 1180, 1150, 1060, 970 (=C-H), 855 (1,3-dioxolane ring), and 735 cm<sup>-1</sup>;  $\lambda_{\max}^{\text{MeOH}}$  224 nm ( $\epsilon$  10,100). N.m.r. data: <sup>1</sup>H,  $\delta$  6.25 (s, 1 H, H-3), 6.25 (d, 1 H, *J*<sub>4,5</sub> 2 Hz, H-4), 5.31 (sex, 1 H, *J*<sub>5,6</sub> = *J*<sub>5,6'</sub> = 7 Hz, H-5), 4.41 (dd, 1 H, *J*<sub>6,6'</sub> 8 Hz, H-6), 3.44 (dd, 1 H, H-6'), 2.23 (s, 3 H, 3 H-1), 1.43 and 1.38 (2 s, 6 H, CMe<sub>2</sub>); <sup>13</sup>C,  $\delta$  198.02 (s, C-2), 147.62 (d, C-4), 127.29 (d, C-3), 107.67 (s, 1,3-dioxolane acetal C), 74.24 (d, C-5), 69.49 (t, C-6), 30.87 (q, C-1), 26.61 and 25.42 (2 q, CMe<sub>2</sub>).

*Anal.* Calc. for C<sub>9</sub>H<sub>14</sub>O<sub>3</sub>: C, 63.51; H, 8.29. Found: C, 63.55; H, 8.27.

Eluted second was (*E*)-1,3,4-trideoxy-5,6-*O*-isopropylidene-D-glycero-hex-3-enulose (**5**; 12 g, 64.2%) as a mobile oil,  $[\alpha]_D +43.7^\circ$  (*c* 1.7) {lit.<sup>6</sup>  $[\alpha]_D +22.7^\circ$  (*c* 2.1, methanol)};  $\nu_{\max}^{\text{film}}$  1685 (ketone, C=O), 1635 (C=C), 1380 and 1370 (CMe<sub>2</sub>), 1255, 1220, 1150, 1060, 970 (=C-H), 850 (1,3-dioxolane ring), 820, and 780 cm<sup>-1</sup>;  $\lambda_{\max}^{\text{MeOH}}$  221 nm ( $\epsilon$  14,200). N.m.r. data: <sup>1</sup>H,  $\delta$  6.70 (dd, 1 H, *J*<sub>3,4</sub> 16, *J*<sub>4,5</sub> 6 Hz, H-4), 6.29 (d, 1 H, H-3), 4.68 (bq, 1 H, H-5), 4.18 (dd, 1 H, *J*<sub>5,6</sub> 6.5, *J*<sub>6,6'</sub> 8 Hz, H-6), 3.68 (dd, 1 H, *J*<sub>5,6'</sub> 7 Hz, H-6'), 2.28 (s, 3 H, 3 H-1), 1.46 and 1.41 (2 s, 6 H, CMe<sub>2</sub>); <sup>13</sup>C,  $\delta$  197.60 (s, C-2), 143.16 (d, C-4), 130.93 (d, C-3), 110.06 (s, 1,3-dioxolane acetal C), 74.99 (d, C-5), 68.75 (t, C-6), 27.17 (q, C-1), 26.35 and 25.53 (2 q, CMe<sub>2</sub>).

*Anal.* Calc. for C<sub>9</sub>H<sub>14</sub>O<sub>3</sub>: C, 63.51; H, 8.29. Found: C, 63.62; H, 8.16.

*Reaction of 1 with (1-acetylethylidene)triphenylphosphorane (3).* — To a stirred solution of **1** (14.3 g, 0.11 mol) in dry dichloromethane (100 mL) at room temperature was added, dropwise, a solution of the ylid<sup>5</sup> **3** (37 g, 0.11 mol) in the same solvent (100 mL). Some heat was evolved during the addition, and t.l.c. (hexane–ether, 1:2) revealed one product, *R*<sub>F</sub> 0.58. The mixture was left at room temperature for 3 h, and work-up, as described above, then gave a residue (18 g) that was subjected to column chromatography (hexane–ether, 7:1→3:1) to afford (*E*)-1,3,4-trideoxy-5,6-*O*-isopropylidene-3-*C*-methyl-D-glycero-hex-3-enulose (**6**; 15 g, 74%) as a mobile oil,  $[\alpha]_D +38.8^\circ$  (*c* 1.7) {lit.<sup>7</sup>  $[\alpha]_D +36^\circ$  (*c* 1.12)};  $\nu_{\max}^{\text{film}}$  1680 (ketone, C=O), 1380 and 1370 (CMe<sub>2</sub>), 1250, 1220, 1150, 1055, 990, 855 (1,3-dioxolane ring), 840, and 780 cm<sup>-1</sup>;  $\lambda_{\max}^{\text{MeOH}}$  228 nm ( $\epsilon$  13,000). N.m.r. data: <sup>1</sup>H,  $\delta$  6.58 (dq, 1 H, *J*<sub>4,Me-3</sub> 1, *J*<sub>4,5</sub> 7 Hz, H-4), 4.94 (bq, 1 H, H-5), 4.23 (dd, 1 H, *J*<sub>5,6</sub> 7, *J*<sub>6,6'</sub> 8 Hz, H-6), 3.64 (t, 1 H, *J*<sub>5,6'</sub> 8 Hz, H-6'), 2.35 (s, 3 H, 3 H-1), 1.47 and 1.42 (2 s, 6 H, CMe<sub>2</sub>); <sup>13</sup>C,  $\delta$  199.00 (s, C-2), 139.67 (d, C-4), 139.45 (s, C-3), 109.91 (s, 1,3-dioxolane acetal C), 73.29 (d, C-5), 68.91 (t, C-6), 26.79 and 25.81 (2 q, CMe<sub>2</sub>), 25.52 (q, C-1), and 11.82 (q, Me-3).

*Anal.* Calc. for C<sub>10</sub>H<sub>16</sub>O<sub>3</sub>: C, 65.22; H, 8.70. Found: C, 64.98; H, 8.75.

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