

HIGH STEREOSELECTIVE SYNTHESIS OF  
DIETHYL (2,3-ISOPROPYLIDENE-5-TRITYL- $\alpha$ -D-RIBOFURANOSYL)-METHANEPHOSPHONATE,  
A PRECURSOR TO THE PHOSPHONO ANALOG OF  $\alpha$ -D-RIBOSE 1-PHOSPHATE

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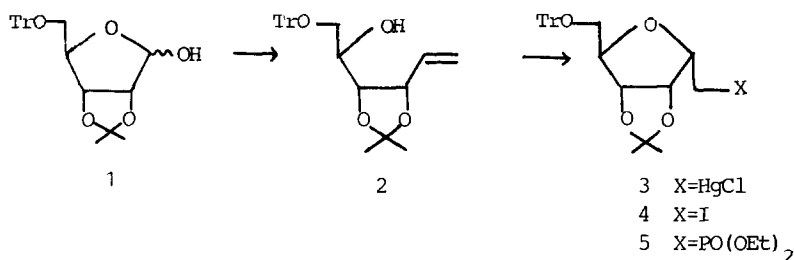
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Summary: The reaction of 2,3-isopropylidene-5-trityl-D-ribofuranose with methylenetriphenylphosphorane and the subsequent mercuriocyclusation, iodomercuriation and Arbuzov reaction, allow a highly stereoselective entry to the phosphono analog of  $\alpha$ -D-ribose 1-phosphate.

Phosphono analogs of naturally occurring phosphates have reached interest<sup>1</sup> as potential inhibitors or regulators of biological processes. In the carbohydrate field, many efforts have been made towards the synthesis of these compounds, but until recently<sup>2-4</sup>, the anomeric position of the sugar has never been involved. On the other hand, the phosphono analogs of sugars phosphorylated at that position are of predominant biological interest.

We wish now to report a highly stereoselective and high-yield route to the phosphono analog of  $\alpha$ -D-ribose 1-phosphate.<sup>5</sup> The synthetic scheme lies on our recent finding<sup>6</sup> that the mercuriocyclusation of the product obtained by reaction of different carbohydrates with methylenetriphenylphosphorane, affords consistently 1,2-cis C-glycosides with good to excellent stereoselection.

In this case, 2,3-isopropylidene-5-trityl-D-ribose<sup>7</sup> **1** was reacted with methylenetriphenylphosphorane (THF-HMPA, 4:1) and the obtained product **2**<sup>8</sup> (96% yield) was submitted to mercuriocyclusation (1. Hg(OAc)<sub>2</sub>, THF, rt 1h; 2. KCl, H<sub>2</sub>O). The mercurioderivatives were isolated in 82% overall yield and the  $\alpha$ -product **3**<sup>9</sup>, which was largely predominant ( $\alpha/\beta$  95:5), was easily isolated by chromatography. Its anomeric configuration was attributed on the light



of the <sup>13</sup>C-NMR chemical shifts of the isopropylidene methyl groups (24.66 and 26.69 ppm) which fall into an established region for α anomers<sup>10</sup> (24.9±0.3 -26.69±0.2) and the <sup>1</sup>H-NMR coupling constant between H-4 and H-5 which is characteristic for 2,3-isopropylidene-5-trityl-α-D-ribofuranosides.<sup>10</sup> Treatment of 3 with iodine in CCl<sub>4</sub> afforded the iododerivative 4<sup>11</sup> (80% yield) which was then submitted to Arbuzov reaction (P(OEt)<sub>3</sub>, rfx 4h) so affording diethyl (2,3-isopropylidene-5-trityl-α-D-ribofuranosyl)-methanephosphonate 5 in 70% yield.

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#### References and notes

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5. Recently a synthesis of the phosphono analogues of D-ribose 1-phosphate has been reported by R.W. McClard, *Tetrahedron Lett.*, 2631 (1983), but it has the disadvantage of affording predominantly the β-product (80:20) whereas the α is that of biological interest.
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8. m.p. 93-94°C (from Et<sub>2</sub>O-Hexane);  $[\alpha]_D^{20}$  0 (c=1.5 in CHCl<sub>3</sub>). All new compounds gave satisfactory elemental analysis, <sup>1</sup>H and <sup>13</sup>C - NMR spectra.
9. m.p. 138-139°C (from Et<sub>2</sub>O);  $[\alpha]_D^{20}$  +1.2 (c=1.2 in CHCl<sub>3</sub>).
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11. m.p. 105-106°C (from methanol);  $[\alpha]_D^{20}$  +9.54 (c=2.4 in CHCl<sub>3</sub>).
12. oil,  $[\alpha]_D^{20}$  +1.0 (c=1.7 in CHCl<sub>3</sub>), <sup>31</sup>P(CDCl<sub>3</sub>) 28.106ppm.

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