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A Novel Synthesis of Methyl 4, 6-O-Benzylidene-α -D-Glucopyranoside 2, 3-Cyclic Phosphite Ethyl Ester

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Abstract: A new compound, methyl 4, 6-O-benzylidene-α -D-glucopyranoside 2, 3-cyclic phosphite ethyl ester was synthesized *via* the reaction of methyl 4, 6-O-benzylidene-α -D-glucopyranoside and ethyl dichlorophosphite. Its structure was confirmed by NMR and MS spectral methods.

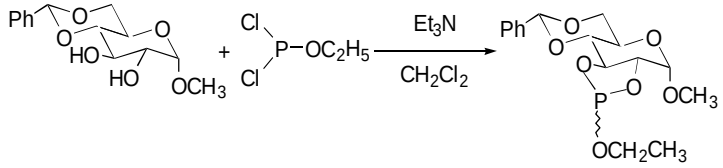
Keywords: 2, 3-Cyclic glucopyranosyl phosphite ester, synthesis, structure determination.

It is well known that nearly all the biochemical metabolic processes of carbohydrates in living organisms involve the participation of phosphorus. For example, glycosyl phosphates are of great significance for the biological activity of glycoconjugates and can serve as intermediates in biological glycosyl transfer. They are also of great importance as glycosyl donors in preparation of oligosaccharides, which are constituents of biologically important compounds such as antibiotics, glycolipids, glycoproteins, and immunodeterminants[1]. Hence the investigation of phosphorus-containing carbohydrate compounds is of particular interest. Nevertheless, up to now, the studies of phosphorous carbohydrates mainly focused on hexose phosphates, especially glycosyl-1-phosphates[1, 2]. There was no report about glucose 2, 3-phosphite. In this letter, a convenient method to synthesize tricoordinate phosphorous saccharide, methyl 4, 6-O-benzylidene-α -D-glucopyranoside 2, 3-cyclic phosphite ethyl ester **3**, is presented. Its structure was established by NMR and MS methods.

Methyl α -D-glucopyranoside was acetalized by benzaldehyde to give methyl 4, 6-O-benzylidene-α -D-glucopyranoside **1**[3]. Ethyl dichlorophosphite **2** was prepared by reaction of phosphorus trichloride with absolute ethanol in anhydrous ethyl ether[4].

2 mmol (564 mg) **1** in 5 ml dichloromethane[5] was mixed with 8 mmol (808 mg) triethyl amine. 2 mmol (294 mg) **2** was added to the mixture in ice-salt bath under nitrogen protection. The reaction proceeded for two hours at the same condition and for additional one and half-hours at room temperature. The resulting salt of triethyl amine was precipitated by addition of 10 ml anhydrous ethyl ether and removed by filtration. The filtrate was evaporated *in vacuo*, and then purified by flash column chromatography on silica gel with petroleum ether (b.p. 30-60℃) - anhydrous ethyl ether (2:1) elution to

give **3** (white product, 576 mg, yield 80.9%). The structure of **3** was confirmed by its characteristic NMR and FAB-MS spectroscopic data[6]. Two similar groups of peaks appeared in the ^{31}P, ^{13}C and ^{1}H NMR spectra, which indicated that **3** included two isomers owing to the existence of chiral phosphorous center. The attempts to separate the two isomers failed.



1 **2** **3**

Phosphite **3** is the first synthetic phosphorous glucose containing a 2, 3-cyclic ring, and it provides a convenient and novel methodology for the manufacture of hexose phosphite compounds. Due to the high instability of five-membered-ring and trans-dioxygen-containing **3**, it has the potential application as coupling reagent in oligosaccharides synthesis[5, 7]. Further studies on hydrolysis and oxaphosphorane-formation of **3** are in progress.

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References and notes

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6. Spectral data for compound **3** (two isomers: different chemical shiftes assigned to the same atom are marked with asterisk). ^{13}C NMR (125MHz, C_6D_6), δ ppm: 137.9, 129.1, 128.3, 126.7 (Ar-C), 101.3 (Ph-CH), 99.6*, 99.3* (C-1), 81.8*, 81.4* (C-4), 77.7*, 75.3* (C-2), 74.4*, 72.7* (C-3), 68.6 (C-6), 64.9*, 64.6* (C-5), 59.9*, 59.7* (CH_2), 55.4 (OCH_3), 17.3*, 16.9* (CH_3). ^{1}H NMR (500MHz, C_6D_6), δ ppm: 7.62-7.10 (m, 5H, Ar-H), 5.34*, 5.29* (s, 1H, Ph-CH), 4.86*, 4.78* (d, J=3.5Hz, 1H, H-1), 4.61*, 4.37* (dd, J=10.5Hz, J=9.5Hz, 1H, H-4), 4.10-3.40 (m, 7H, H-2, H-3, H-5, H-6ax, H-6eq, CH_2), 2.95 (s, 3H, OCH_3), 0.99*, 0.92* (t, J=7.0Hz, 3H, CH_3). ^{31}P NMR (81.0MHz, CH_2Cl_2), δ ppm: +142.2*, +139.7*. Positive-ion FAB-MS (m/z): 357 (M+1), 325, 311, 251.
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