PHOSPHORYLATION OF HEXAFURANOSIDES WITH TRIAMIDES OF PHOSPHOROUS ACID

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As was demonstrated earlier, 1,2-alkylidene- α -D-glucofuranoses react smoothly with hexaethyltriamide of phosphorous acid (HETPA), yielding bicyclo-phosphites exhibiting specific properties (1,2). It has become possible to extend this reaction to the series of hexafuranosides which contain four alcohol hydroxyls. As has been shown, the formation of bicyclophosphites, in this case, is strictly determined by stereochemistry of the monosaccharide. For example, S-ethyl-1-thio-D-glucofuranoside (I) is converted to 3,5, 6-bicyclophosphite (II).
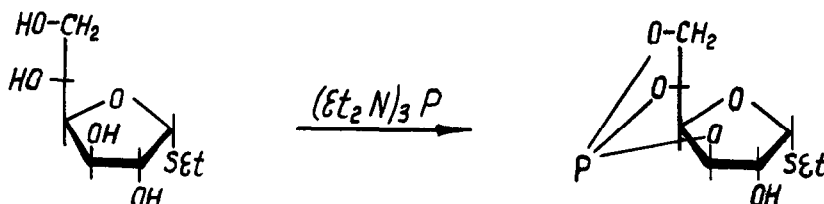
0.01 mole of (I) and 0.01 mole of HETPA are heated in pyridine (50 ml) at 90-100°C until no more diethylamine is liberated. The mixture is then eva-porated in vacuum and chromatographed on SiO_2 (eluent ethyl acetate). Yield of (II) is 0.21 g (82%), m.p. 97-98°C, $[\alpha]_D^{20}$ + 45° (C 0,1, methylene chlo-ride); TLC on SiO_2: R_f 0,81 (benzene: dioxan 3:1 - A), 0.75 (ethyl acetate - B), 0.3 (chloroform - C). Found, %: C 38.8, H 5.0, P 12.2, calculated for $C_8H_{13}O_5P$. %: C 38.2, H 5.2, P 12.5.

A mixture of α - (III) and β -ethyl-D-glucofuranosides-(IV) (0.01 mol), (3) and 0.01 mole of HETPA in pyridine (100 ml) is treated under the same conditions to afford a mixture of 3,5,6-bicyclophosphites (V) and (VI). Chromatography on SiO_2 (A) reveals 1.16 g (60%) of (V), m.p. 121-122°C,

$[\alpha]_D^{20}$ + 62° (C 0.06, tetrahydrofuran); TLC on SiO_2 : R_f 0.8 (A), 0.5 (C),

0.9 (B) (Found, %: C 40.8, H 5.5, P 13.5, calculated for $C_6H_{13}O_6P$. %: C41.1,

H 5.5, P 13.4) and 0.28 g (15%) of (VI), m.p. 127-128°C $[\alpha]_D^{20}$ - 122° (C 0.06,

tetrahydrofuran); TLC on SiO_2 : R_f 0.4 (C), 0.6 (B). Found, %: C 40.8, H 5.4,

P 13.3.

Methanolysis of separated (V) and (VI) yields 90% of pure α -and β -
ethylglucofuranosides synthesis of which was earlier very complicated (4).

α -Methyl-D-mannofuranoside (VII) differing from glucofuranosides by the

configuration at C_2 forms, together with HETPA, 3,5,6-bicyclophosphite (VIII)

(which should preferably be isolated in the form of an acetate) and a small

amount of oligomers.

0.01 mole of (VII) and 0.01 mole of HETPA are heated for 1 hour to

80-90°, the reaction mixture is cooled to 20°C, acetic anhydride (0.025

mole) is added. The resulting mixture is allowed to stay for 24 hours, eva-

porated to dry in vacuum (1 mm Hg), chromatographed on SiO_2. The yield of

2-acetyl- α -methyl-D-mannofuranoside 3,5,6-phosphite (IX) is 0.17 g (71%);

m.p. 133 to 135°C $[\alpha]_D^{20}$ + 12.4 (C 0.01, methylene chloride); TLC on

SiO_2: R_f 0.9 (B), 0.45 (C), 0.57 (butyl acetate - D). Found, %: C 41.2,

H 5.1, P 11.6, calculated for $C_9H_{13}O_7P$.%: C 40.9, H 4.9, P 11.7.

α -Methylgalactofuranoside, in which the mutual arrangement of the

substituents at C_3 and C_4 of the furanoside system is different from that in

glucosides and mannoside, reacts differently with HETPA; according to TLC

and NMR data, a mixture of compounds is formed, containing no 3,5,6-bicyclo-

phosphite.

Thus, we demonstrated that formation of bicyclophosphites is determined

by steric factors, namely, by the cis-position of the vicinal groups at the

3rd and 4th carbon atoms of the furanose ring. Reactions with HEPTA could

be useful as a stereochemical probe reacting only to a particular steric

situation in the tetraolic system.

The structure of all synthesized compounds has been assigned by the NMR data (see Table 1). The nuclei of phosphorus resonate in a region (δ =-115 to -117.2 p.p.m.) characteristic of bicyclophosphites in which 5- and 6-membered cycles combined (2,5). The signal from the phosphorus atom is not split on C_2 atom and proton at C_2 while that produced by H-2 is split on anomeric H-1 into a duplet, which is indicative of the absence of C_2 -O- P fragment. Conformationally, the synthesized esters are rigid systems corresponding to 1,2-alkylidene glucofuranose bicyclophosphites. We have arrived at this conclusion as a result of comparing their ^1H-^1H, ^1H-^{31}P, ^{13}C-^{31}P splitting constants with respective constants of 1,2-alkylidene glucofuranose bicyclophosphites (2).

The prepared glycofuranoside bicyclophosphites could be introduced into various reactions on the second free hydroxyl, which in combination with easy removal of the phosphite group by methanolysis, opens up some new possibilities for preparative chemistry of sugars.

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Table 1

$H-H_1$ $^1H-^{31}P$ and $^{13}C-^{31}P$ Chemical Shifts and Coupling Constants
with Respect to TMS or H_3PO_4

Chemical shift, ppm

Compound	H-1	H-2	H-3	H-4	H-5	H-6	H-6'	C-1	C-2	C-3	C-4	C-5	C-6	^{31}Pmd
II	5.62	4.61	4.25	4.15	4.71	4.19	3.84	88.50	79.53	73.82	77.78	72.14	67.70	-117.2
V	5.41	4.18	4.20	4.16	4.75	4.19	3.84							-115.0
IX	5.32	4.84	4.74	4.15	4.84	4.29	3.98	106.00	78.10	70.00	78.00	68.30	67.00	-115.7
X	6.07	4.51	4.57	4.09	4.82	4.28	3.91	106.00	84.30	73.80	78.10	70.00	67.48	-117.0

Coupling Constants

Compound	H1-H2	H2-H3	H3-H4	H4-H5	H4-P	H5-H6	H5-H6'	H6-H6'	H6-P	H6'-P	C1-P	C2-P	C3-P	C4-P	C5-P	C6-P
II	3.8	0.0	2.2	0.0	2.7	3.9	0.6	9.2	5.3	9.9	4.6	1.5	0.6	0.6	2.6	6.0
V	3.7	0.0	2.1	0.0	2.8	3.9	0.6	9.2	5.3	9.8	4.5	1.5				
IX	3.7	5.2	3.3	0.6	2.5	4.0	0.8	9.2	5.5	9.8	4.1	1.8	0.6	0.6	2.6	5.0
X	3.6	0.0	3.0	0.0	2.7	3.9	0.7	9.2	5.3	9.8	4.5	1.6	0.6	0.6	2.6	6.0

X – 1,2-cyclohexylidene- -D-glucofuranose 3,5,6-phosphite (2)