

On the Synthesis of the Phosphoric Acid Esters, I.

By

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Phosphoric acid esters are interesting substances in the chemical study of alcoholic fermentation and of living cells, specially from the biochemical standpoint.¹ As to the synthesis of phosphoric acid esters with hydroaromatic alcohols, only that of the inosite was described by S. Posternak² and R. J. Anderson.³ The esters of other mono- and di-atomic alcohols of polymethylene series, however, have not yet been described. In our present article we have undertaken the preparation of the hexahydrophenol esters.

Phosphoric acid hexahydrophenol ester was prepared, in the same manner with inosite ester studied by S. Posternak,² from phosphoric acid and hexahydrophenol, phosphorpentoxide using as a catalyser; to a cold and uniform mixture of 60 grms phosphoric acid and 84 grms phosphorpentoxide were added 60 grms hexahydrophenol prepared from phenol by the catalytic hydrogenation following the Prof. P. Sabatier's directions.⁴ The mixture was left to stand at an ordinary temperature

¹ A. Harden, *Alcoholic fermentation* (1911), 38.

H. Euler, P. Lindner, *Chemie der Hefe u. den alkoholischen Gärung* (1915), 158.

F. Czapek, *Biochemie der Pflanzen* I, 764; III, 483 (1921).

W. Glikin, *Chemie der Fette Lipoide u. Wachsarten*, I, 324 (1912).

H. Maclean, *Lecithin and allied substances* (1918) 170.

E. B. Forbes and M. H. Keith, *A review of the literature of phosphorus compounds in animal metabolism* (1914). R. Rose, *A resumé of the literature on inositephosphoric acid & c.* *Biochem J.* **2**, 21 (1912).

² C. R. **168**, 1216; **169**, 79 (1919); *Hel. chim. Acta*, **4**, 150 (1921).

³ *J. Biol. Ch.*, **43**, 167 (1920).

⁴ C. R. **137**, 1025 (1903).

for a few days, and then water was added, whereupon a brown oil separated. The acid solution separated from the upper oily layer, was neutralized with barium hydroxide solution, and the excess of baryta remaining in the solution was removed by passing carbon dioxide into the solution. The filtrate separated from the insoluble barium salt, was evaporated to dryness on a water bath, and the residue was recrystallized from the water solution and a white crystalline substance was obtained which was confirmed by elementary analysis to be the barium salt of mono-hexahydrophenol phosphoric acid ester.

0.1218 grms. of the substance gave 0.1011 grms. CO₂ & 0.0419 grms. H₂O
 0.2030 grms. of the substance gave 0.1492 grms. BaSO₄
 0.1366 grms. of the substance gave 0.0464 grms. Mg₂P₂O₇

	Calc. for	$\begin{array}{c} \text{C}_6\text{H}_{11}\text{O} \\ \diagdown \quad \diagup \\ \text{Ba} \langle \text{O} \rangle \text{P}=\text{O} \\ \diagup \quad \diagdown \\ \text{O} \end{array}$	Found.
C		22.83	22.64
H		3.49	3.82
Ba		43.56	43.25
PO ₄		30.12	29.05

The oily part separated from the aqueous layer was dissolved entirely into ether, and the ethereal solution was then treated with barium hydroxide to remove phosphoric acid ester as the barium salt from hexahydrophenol unchanged. An excess of barium hydroxide in the aqueous extract was removed by means of carbon dioxide, and the water solution was evaporated to dryness on a water bath. The white residue thus obtained was extracted with anhydrous ether in Soxley's apparatus and the insoluble residue was confirmed to be the barium salt of the mono-ester by analysis.

0.1316 grms. of the substance gave 0.1106 grms. CO₂, 0.0441 grms. H₂O and 0.0950 grms. ash.

	Calc. for	$\begin{array}{c} \text{C}_6\text{H}_{11}\text{O} \\ \diagdown \quad \diagup \\ \text{Ba} \langle \text{O} \rangle \text{P}=\text{O} \\ \diagup \quad \diagdown \\ \text{O} \end{array}$	Found.
C		22.83	22.92
H		3.49	3.72
Ash		73.68	72.19

The ether extract was divided into two parts: to the one, dry ammonia gas was passed and a white precipitate was obtained which

after being converted into silver salt with silver nitrate was analysed, with the following results.

0.1205 grms. of the substance gave 0.0830 grms. CO₂ and 0.0306 grms. H₂O.

	Calc. for	$\begin{array}{c} \text{C}_6\text{H}_{11}\text{O} \\ \text{AgO} \diagdown \quad \diagup \\ \text{P}=\text{O} \\ \text{AgO} \diagup \quad \diagdown \end{array}$	Found.
C	18.28		18.79
H	2.79		2.82

The other part of the ethereal extract was evaporated carefully on a water bath almost to dryness, and allowed to stand for three weeks in a calcium chloride-paraffin desiccator. Thus a free monoester was obtained, consisting of colorless crystals melting at 77-78°.

0.1094 grms. of the substance gave 0.1555 grms. CO₂ and 0.0724 grms. H₂O.

	Calc. for	$\begin{array}{c} \text{C}_6\text{H}_{11}\text{O} \\ \text{HO} \diagdown \quad \diagup \\ \text{P}=\text{O} \\ \text{HO} \diagup \quad \diagdown \end{array}$	Found.
C	40.00		39.01
H	7.22		7.35

The free ester was soluble in water, alcohol and ether, and its barium and ammonium salts were soluble easily in water, but its silver salt was insoluble in water. When heated, the free ester and also the barium salt were observed to decompose into phosphoric acid and tetrahydrobenzene.

In order to prepare the tri- and di-esters, 50 grms. hexahydrophenol and 35 grms. phosphoroychloride were mixed and the mixture was left to stand at an ordinary temperature for a few weeks. When the generation of hydrogenchloride gas had ceased, the reaction product was treated with water, caustic soda solution successively and the insoluble oily residue was subjected to steam distillation. The residue in a flask was distilled and collected the distillate boiling at 230-280°. The distillate was again fractionated under 6-7 mm. pressure and the following two fractions were obtained:

- I. First fract. Bp. 100-125°; yield, 2.5 grms.
- II. Second fract. Bp. 126-127°; yield, 2.5 grms.

The first fraction was a colorless and the second was a light-yellowish-orange liquid and possessed a perfume like an orange. Density and chemical composition of both fractions were determined, and the following results were obtained.

I. $d_4^{25} = 0.9903$; $n_D^{25} = 1.5028$.

1.	0.1090 grms. of subst. gave	0.3092 grms. CO ₂ &	0.0986 grms. H ₂ O.
2.	0.1220 grms. „	0.3472 „	0.1087 „
3.	0.1196 grms. „	0.3402 „	0.1065 „
	I	2	3
	Mean		
C	77.36	77.62	77.58
H	10.05	9.90	9.89

II. $d_4^{25} = 0.9938$; $n_D^{25} = 1.5026$.

1.	0.1050 grms. of subst. gave	0.3026 grms. CO ₂ &	0.0862 grms. H ₂ O.
2.	0.1444 grms. „	0.4168 „	0.1176 „
3.	0.1260 grms. „	0.3646 „	0.1081 „
	I	2	3
	Mean		
C	78.60	78.72	78.92
H	9.12	9.05	9.53

The chemical and physical properties of the second fraction agree with those of the di-hexahydrophenyl ether requiring C=79.12; H=12.09, which was obtained by W. Ipatiew and O. Philipow¹ from phenyl ether by catalytic hydrogenation in the presence of nickel oxide under high pressure.

It is a note-worthy fact to mention here that aromatic alcohol such as phenol easily yields with phosphoric acid, mono-, di- and tri-esters² and hexahydrophenol, on the contrary, only one mono-ester.

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¹ Ber. D. Chem. Gesell., **41**, 1001 (1908).

² Williamson and Serugam, Lieb. Ann., **92**, 31 (1854).
R. Hein, Ber. D. Chem. Gesell., **16**, 1763 (1883).