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A NEW PHOSPHORYLATING REAGENT. II.[1)] PREPARATION OF MIXED DIESTERS OF PHOSPHORIC ACID BY THE USE OF ALKYL 2-CHLOROMETHYL-4-NITROPHENYL HYDROGEN PHOSPHATES

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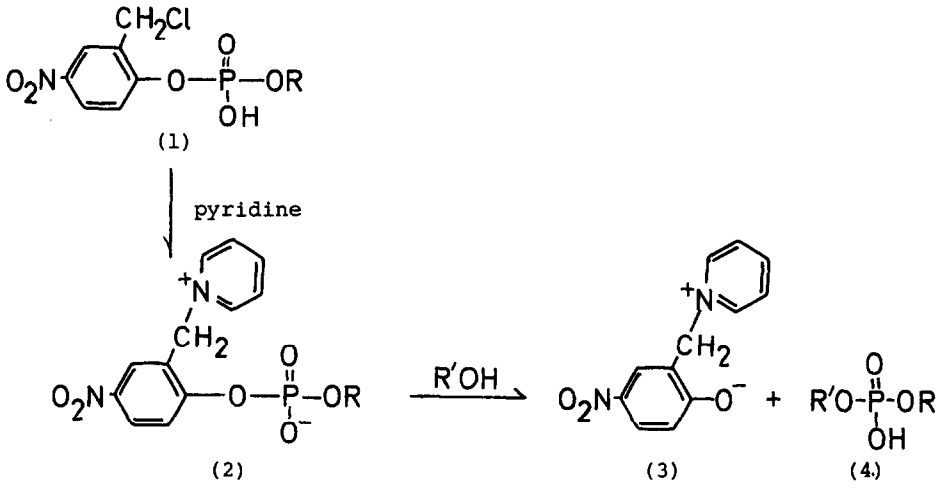
Study on "the activatable protecting group" in the phosphate chemistry has led us to a novel method for the preparation of alkyl dihydrogen phosphates.[1)] Alkyl dihydrogen phosphates were obtained in high yields along with inner salt of 1-(2'-hydroxy-5'-nitrobenzyl)pyridinium hydroxide(3) by treating alkyl 2-chloromethyl-4-nitrophenyl hydrogen phosphate(1) with aqueous pyridine.

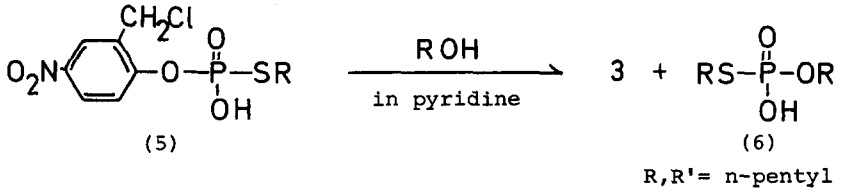
In the present study, the preparation of mixed diesters of phosphoric acid from 1[2)] and alcohols was tried with the expectation that mixed diesters of phosphoric acid would be produced by the reaction of 1 with alcohols in dry pyridine through an intermediate, inner salt of 1-(2'-alkyl hydrogen phosphoroxy-5'-nitrobenzyl)pyridinium hydroxide(2).



For example, when a mixture of one equiv of 1a and two equiv of n-pentyl alcohol in five equiv of pyridine was allowed to stand at room temperature for two days and then was further heated at 90° for 6 hours, ethyl n-pentyl hydrogen phosphate(4a) was obtained in 81% yield along with 3. The phosphate 4a was easily and completely separated from 3 by filtration after ethyl alcohol was added to the resulting reaction mixture.

In a similar manner, various mixed dialkyl esters of phosphoric acid were obtained in high yields.[3] Phenols are also phosphorylated by the same procedure with 1 to give the corresponding alkyl aryl hydrogen phosphates in good yields. These results are summerized in Table I.

On the other hand, the reaction of n-pentylmercaptan with 1a proceeded very sluggishly even when they were refluxed in pyridine. O,S-Di-n-pentyl phosphorothioate(6) could be prepared in 42% yield starting from S-n-pentyl O-2-chloromethyl-4-nitrophenyl hydrogen phosphate(5) by the treatment with n-pentyl alcohol in dry pyridine as shown in the following equation.



R,R'= n-pentyl

Table I. Preparation of Dialkyl Hydrogen Phosphates(4)

Compound	R	R'	Yield[a] (%)	Mp. (°C)	$n_D^{°C}$	Rf[b]	Formula	Calcd. C	Calcd. H	Found C	Found H
4a	ethyl	n-pentyl	81		1.4250[26]	0.83	$C_7H_{17}O_4P$	42.85	8.73	42.91	8.90
4b		n-hexadecyl	74	54-55		0.90	$C_{18}H_{39}O_4P$	61.69	11.22	62.31	11.21
4c		cyclohexyl	58		1.4552[26]	0.83	$C_8H_{17}O_4P$	46.15	8.23	46.50	8.51
4d		bornyl	69		1.4717[25]	0.87	$C_{12}H_{23}O_4P$	54.95	8.84	54.50	8.78
4e		benzyl	60		c)	0.81	$C_9H_{13}O_4P$	50.00	6.06	50.64	5.84
4f	n-pentyl	p-tolyl	57		1.4891[25]	0.91	$C_{12}H_{19}O_4P$	55.81	7.42	55.62	7.17
4g		p-chlorophenyl	61		1.4933[25]	0.91	$C_{11}H_{16}ClO_4P$	47.41	5.79	47.27	5.62
4h		p-nitrophenyl	55	61-62		0.91	$C_{11}H_{16}NO_6P$	45.68 (N= 4.84)	5.58	46.30 (N= 4.69)	5.62
4b	n-hexadecyl	ethyl	97	54-55		0.90					
4i		n-pentyl	92	45-47		0.94	$C_{21}H_{45}O_4P$	64.25	11.55	63.95	11.90
4j		cyclohexyl	87		1.4717[25]	0.92	$C_{22}H_{45}O_4P$	65.31	11.21	65.73	10.96
4k		bornyl	89		1.4782[24]	0.94	$C_{26}H_{51}O_4P$	68.09	11.21	68.37	11.60
4l		benzyl	86	58-60		0.94	$C_{23}H_{41}O_4P$	66.96	10.02	66.99	10.36
4f	p-tolyl	n-pentyl	72		1.4893[25]	0.91					

a) Yields are based on the phosphate 1. b) Paper chromatography was carried out by ascending technique using Toyo Roshi No.50 paper. Solvent system used was: isopropyl alcohol, conc.ammonium hydroxide, water (7:1:2 v./v.). c) The compound 4e is pale yellowish oil.

In conclusion, it is noted that satisfactory yields are maintained with respect to various kinds of mixed diesters of phosphoric acid and most of these phosphates were analytically pure by treating the reaction mixture with conventional organic technique.

Acknowledgement

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References

1) T.Hata, Y.Mushika and T.Mukaiyama, J.Am.Chem.Soc.,91,4532(1969).
2) The phosphates 1 were prepared in high yields by the reaction of 2-chloromethyl-4-nitrophenyl phosphorodichloridate and alcohols in the presence of tertiary amines as described in a previous paper.[1)]
3) The structures of 4 were confirmed by elemental analysis, ir and paper chromatography.