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SYNTHESIS OF NEW ANALOGS OF PHOSPHOENOL PYRUVATE

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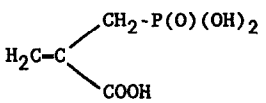
Summary : Some new phospho-, phosphono- and phosphinicoenol pyruvate, phosphodi- and tri(enol pyruvate) have been synthesized by Perkow reaction.

In a previous paper [1], we described the synthesis of new thio-analogs of the important biochemical intermediate phosphoenol pyruvate (PEP).

Some phosphono-analogs of PEP have already been synthesized, in particular the α-(phosphonomethyl) acrylic acid [2] 1, but phosphono- or phosphinicoenol pyruvates which possess one or two P-C bonds are still unknown. Furthermore, amino- or diaminophosphoenol pyruvate and aminophosphonoenolpyruvate as well as phosphodi- or tri(enol pyruvate) have never been prepared. We have tried to synthesize some of these new compounds 3.



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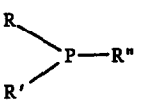

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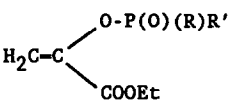


3

The dialcoxymethyl or phenyl phosphines 2a and 2b react with ethyl bromopyruvate, leading by a Perkow reaction to the phosphonoenol pyruvate, respectively 3a (δ ^{31}P = 15.0 ppm) and 3b (δ ^{31}P = 27.1 ppm). The ethoxydiphenylphosphine 2c gives a similar reaction and we obtain the phosphinicoenol pyruvate 3c (δ ^{31}P = 29.5 ppm).

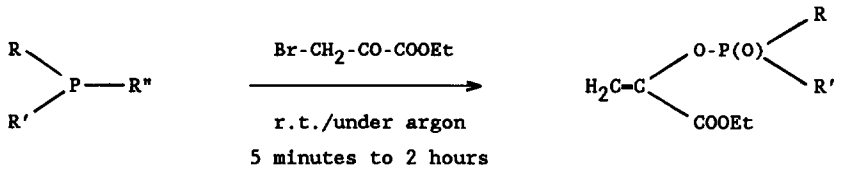
When the Perkow reaction is carried out with the (dimethylamino)methylpropyloxyphosphine 2d, the eliminated molecule is propyl bromide and we obtain the compound 3d (δ ^{31}P = 32.3 ppm).

In the Perkow reaction of ethyl bromopyruvate with the alcoxybis(dimethylamino)phosphines 2e and 2f, the eliminated molecule is always the alkyl bromide (propyl bromide or i-propyl bromide) and we obtain in both cases the dimethylaminophosphoenol pyru-

vate 3e (δ ^{31}P = 15.4 ppm). If the reaction is carried out with the dialcoxy(dimethylamino)phosphines 2g, 2h, 2i and 2j, the corresponding alkyl bromide is formed together with the alkyl(dimethylamino)phosphoenol pyruvate, respectively 3f (δ ^{31}P = 5.9 ppm), 3g (δ ^{31}P = 5.9 ppm), 3h (δ ^{31}P = 4.8 ppm) and 3i (δ ^{31}P = 5.8 ppm).

In a previous paper[1], we described the synthesis of the phosphinoenol pyruvate 2k (δ ^{31}P = 134 ppm). Chlorodiethylphosphine and dichloroethylphosphine react with methyl pyruvate to give the phosphites, respectively 2l (δ ^{31}P = 132 ppm) and 2m (δ ^{31}P = 126.3 ppm). These phosphites 2k, 2l and 2m react with ethyl bromopyruvate in a Perkow reaction to give the phosphodi- or tri(enolpyruvate), respectively 3j (δ ^{31}P = -13.4 ppm), 3k (δ ^{31}P = -12.4 ppm) and 3l (δ ^{31}P = -18.9 ppm). The eliminated molecule is always ethyl bromide rather than the ethyl or methyl 2,3-dibromo or 2-bromo acrylate.

For compounds 3a and 3c, distillation is not necessary. 3g and 3h have been purified by thin layer chromatography. 3e, 3j and 3k have been obtained with good degree of purity but still now not isolated pure. These compounds have been characterized by ^{1}H, ^{13}C NMR and microanalysis or mass spectrometry.



		Yields (%)	Eb °C (mm Hg)
2a, R = Ph, R' = R" = OEt	3a, R = Ph, R' = OEt	100	
2b, R = Me, R' = R" = OPr	3b, R = Me, R' = OPr	80	70 (0.05)
2c, R = R' = Ph, R" = OEt	3c, R = R' = Ph	100	
2d, R = Me, R' = NMe_2, R" = OPr	3d, R = Me, R' = NMe_2	80	90 (0.05)
2e, R = R' = NMe_2, R" = OPr	3e, R = R' = NMe_2		
2f, R = R' = NMe_2, R" = OiPr			
2g, R = NMe_2, R' = R" = OEt	3f, R = NMe_2, R' = OEt	80	79 (0.05)
2h, R = NMe_2, R' = R" = OPr	3g, R = NMe_2, R' = OPr	80	
2i, R = NMe_2, R' = R" = OiPr	3h, R = NMe_2, R' = OiPr	80	
2j, R = NMe_2, R' = R" = $OCH_2C(CH_3)_3$	3i, R = NMe_2, R' = $OCH_2C(CH_3)_3$	80	100 (0.01)
2k, R = OC(COOEt)=CHBr, R' = R" = OEt	3j, R = OC(COOEt)=CHBr, R' = OEt	70	120 (0.01)
2l, R = OC(COOMe)=CH_2, R' = R" = OEt	3k, R = OC(COOMe)=CH_2, R' = OEt	90	90 (0.001)
2m, R = R' = OC(COOMe)=CH_2, R" = OEt	3l, R = R' = OC(COOMe)=CH_2	90	

References

1 C. Despax and J. Navech, Tetrahedron Letters, in press.

2 J.A. Stubbe and G.L. Kenyon, Biochemistry, 11, 338 (1972).

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