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NEW THIO-ANALOGS OF PHOSPHOENOL PYRUVATE

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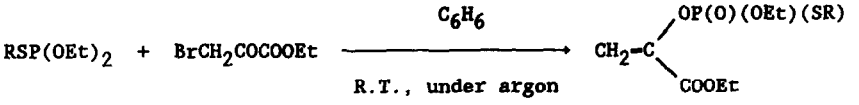
Summary : Some new thio-analogs of phosphoenol pyruvate have been synthesized from thiophosphites by Perkov reaction.

Phosphoenol pyruvate (PEP) is a substrate for many enzymes (pyruvate kinase, PEP carboxylase, enolase, ..). Many analogs of PEP have already been synthesized [1-6]. However, the thio-analogs with a P-S bond not directly linked to the enol pyruvate 3 are still unknown. These compounds can be obtained by the Perkov reaction using thiophosphites 1 and ethyl bromopyruvate 2.



1 2 3

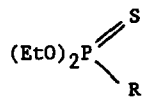
We have isolated the three new thiophosphoenolpyruvate derivatives 3 (see table 1). These compounds have been characterized by microanalysis, mass spectrometry and ^{1}H, ^{13}C, ^{31}P NMR.

Table 1

R	Compound obtained	$\delta^{31}P$ (C_6H_6)	$\delta^{1}H$ (C_6D_6) $H_2C=C<$	$\nu_{P=O}$ (cm^{-1})	$Eb_{10^{-2}}$ mmHg
$CH_3-(CH_2)_3-$	3a	23.6	5.7 and 5.85	1260	106-110 °C
$(CH_3)_2CH-$	3b	22.9	5.7 and 5.84	1266	110-120 °C
C_6H_5-	3c	17.9		1265	

The synthesis of these phosphoenolpyruvates 3 is difficult for different reasons.

1/ The phenylthiophosphite 1 (R = phenyl) is stable and can be distilled but the alkylthiophosphites 1 (R = alkyl) isomerize more or less quickly, leading to thiophosphonates 4. This isomerization is very fast when R = t-butyl and the corresponding thiophosphoenolpyruvate cannot be obtained.



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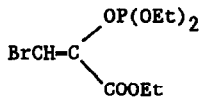

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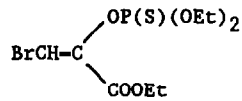

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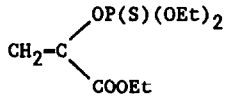
2/ If ethyl bromopyruvate 2 is added before all the diethylchlorophosphite used for the preparation of thiophosphites 1 has been consumed, it reacts preferentially on chlorophosphite, leading to the phosphitoenolpyruvate 5 ($\delta^{31}P$ = 134 ppm) which has also been prepared by the direct action of ethyl bromopyruvate on the same chlorophosphite in presence of triethylamine and characterized by sulfuration giving the thiophosphate 6 ($\delta^{31}P$ = 61.2 ppm).

3/ No reaction occurs when R = pyridino group.

For these reasons, the thiol is added quickly, in benzene, to diethylchlorophosphite in the presence of triethylamine [7] and in the dark to avoid radical reactions. Ten minutes later, the ethyl bromopyruvate is added without purification and without filtration of the formed tetraethyammonium chloride. The Perkov reaction is very fast. After filtration of the tetraethylammonium chloride, the obtained thiophosphoenolpyruvate is distilled.

The Perkov reaction on phosphite 1 gives only the phosphoenolpyruvate derivative 3. We never observe a reaction on the thiolo group with formation of compound 7. Indeed, the ^{31}P chemical shift of this thiophosphate 7 must be near 60-70 ppm by comparison with the $\delta^{31}P$ of triethyl thiophosphate (68 ppm) and of compound 6 and we do not observe any signal in this part of the ^{31}P NMR spectrum.



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