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SYNTHESIS OF O,S-THIOACETALS OF FORMYLPHOSPHONATES

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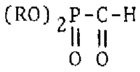
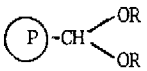
In contrast to the practically unknown formylphosphonates (1)[1] their derivatives with the modified aldehyde group are stable and can be readily prepared.



$$(RO)_2\underset{\displaystyle O}{\underset{\|}{P}}-\underset{\displaystyle O}{\underset{\|}{C}}-H$$

(1)

Until now the following compounds of this type have been described in the literature :



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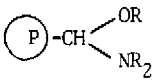

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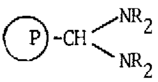

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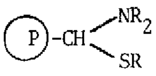

(5)[4]

Ⓟ = $(RO)_2P(O)$-

In connection with our studies on the chemistry of α-phosphorylsulphoxides[5] the various Pummerer-type reactions were investigated. Here we wish to report the reaction of sulphoxides (6) with alcohols in the presence of iodine which results in the formation of a new class of compounds - O,S-thioacetals of formylphosphonates (7).

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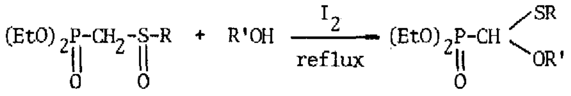


$$(EtO)_2\overset{O}{\overset{\|}{P}}-CH_2-\overset{O}{\overset{\|}{S}}-R + R'OH \xrightarrow[\text{reflux}]{I_2} (EtO)_2\overset{O}{\overset{\|}{P}}-CH\begin{matrix}SR\\OR'\end{matrix}$$

(6) (7)

(7a), R=Ph, R'=Et
(7b), R=Me, R'=Me
(7c), R=Me, R'=Et

The reaction was carried out under reflux in an excess of alcohol using equimolar amounts of iodine. After the reaction was complete an alcohol was removed and chloroform was added. The organic solution was washed with the thiosulphate solution and water, dried and evaporated. The residue was fractionated to afford pure thioacetal (7). Some experimental data and physical and spectroscopic properties of (7) obtained are summarized in Table.

TABLE

Compounds [a]	Reaction time (h)	Yield of (7) (%)	B.p. (°C/Torr); n_D(at °C)	^{31}P-n.m.r[b] δ(ppm)	^{1}H-n.m.r[c] δ(ppm); J(Hz)
7a	7	47	138-142/0.05 1.5270 (20)	- 16.0	1.20 (3H,t -CH-O-CH$_2$CH$_3$); 1.31 (3H,t -P-OCH$_2$CH$_3$); 3.67 (2H,m -CH-O-CH$_2$CH$_3$); 4.00 (2H,dq -P-OCH$_2$CH$_3$); 4.85 (1H,d, J=10.4 -P-CH); 7.37 (5H,m -C$_6$H$_5$)
7b	20	28	142-143/12 1.4622 (24)	- 16.5	1.34 (3H,t -P-OCH$_2$CH$_3$); 2.18 (3H,s -SCH$_3$); 3.46 (3H,s -OCH$_3$); 4.16 (2H,dq -P-OCH$_2$CH$_3$); 4.33 (1H,d, J=11.8 -P-CH)[d]
7c	5	33	103-105/1.5 1.4570 (24)	- 16.1	1.23 (3H,t -CH-OCH$_2$CH$_3$); 1.31 (3H,t -P-OCH$_2$CH$_3$); 2.17 (3H,s -SCH$_3$); 3.57 (2H,m -CH-OCH$_2$CH$_3$); 4.15 (2H,dq -P-OCH$_2$CH$_3$); 4.43 (1H,d, J=11.6 -P-CH)[d]

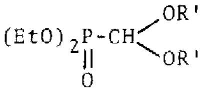
[a] Satisfactory elemental analyses have been obtained for (7).

[b] In chloroform solution with 85% phosphoric acid as external standard.

[c] In carbon tetrachloride with tetramethyl silane as internal standard.

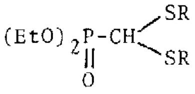
[d] Addition of pyridin results in a low-field shift of this signal.

The relatively low yields of (7) are due to the by-products formation. As it was shown by the ^{31}P-n.m.r spectra the reaction mixtures contained always in addition to (7) triethyl phosphate and disulphide, R_2S_2. In the case of the reaction of (6b) and (6c) diethyl alkoxycarbonylphosphonates as well as a small amounts of the transesterification products (8) and (9)[6] were also observed.



$(EtO)_2P(O)\text{-}CH(OR')_2$

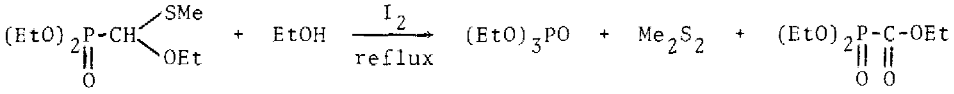
(8)



$(EtO)_2P(O)\text{-}CH(SR)_2$

(9)[6]

All the by-products undoubtedly arise from the further transformations of (7) formed under the reaction conditions. For instance, thioacetal (7c) has been found to give triethyl phosphate, dimethyl disulphide and diethyl ethoxycarbonylphosphonate (10)[7] when refluxed with ethanol in the presence of iodine.

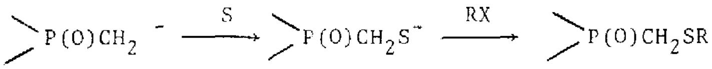


$$(EtO)_2P(O)\text{-}CH(SMe)(OEt) + EtOH \xrightarrow[\text{reflux}]{I_2} (EtO)_3PO + Me_2S_2 + (EtO)_2P(O)\text{-}C(O)\text{-}OEt$$

(7c)

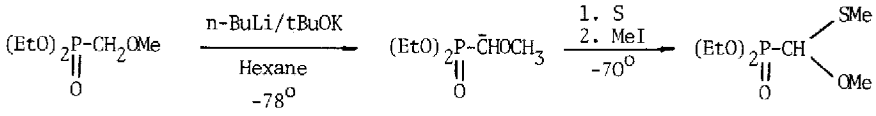
(10), $\delta_{^{31}P}$ +5.1

Very recently we have found a new route to α-phosphorylmethyl alkyl sulphides which consists in the addition of sulphur to the phosphonate carbanion and the subsequent alkylation of the mercapto-compound formed[8].



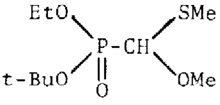
$$>P(O)CH_2^- \xrightarrow{S} >P(O)CH_2S^- \xrightarrow{RX} >P(O)CH_2SR$$

This prompted us to investigate an alternative synthesis of thioacetals (7) based on this approach from diethyl methoxymethylphosphonate (11) as a starting material. However, some difficulties in generating of the carbanion derived from (11) have been encountered[9]. For this reason more effective base has been used in the present study. Thus, the ester (11) was added to the freshly prepared mixture of potassium tert-butoxide and n-butyl lithium[10] in hexane at -78°. After 30 min sulphur was added at low temperature and then methyl iodide. After the usual work-up thioacetal (7b) was isolated by column chromatography in 53 % yield.

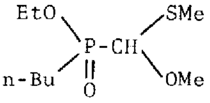


(11) (7b)

The reaction is, however, very sensitive to the experimental conditions. For example, the reverse addition of the reagents afforded the mixture of (7b) and (12). Similarly, when n-butyl lithium was used for the anion generation the mixture of (7b) and (13) was produced.



(12)



(13)

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