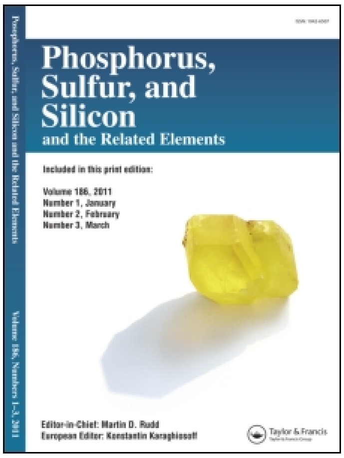

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SYNTHESIS OF THIOLS BEARING PHOSPHONATE GROUPS

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SYNTHESIS OF THIOLS BEARING PHOSPHONATE GROUPS

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Two phosphonated compounds bearing a mercaptan group have been prepared. These thiols are : $HSCH_2CO_2(CH_2)_2S(CH_2)_3PO(OEt)_2$ (I) and $HS(CH_2)_3PO(OEt)_2$ (II). Both originate from diethyl allylphosphonate, (I) with mercaptoethanol and thioglycolic acid and (II) with thioacetic acid.

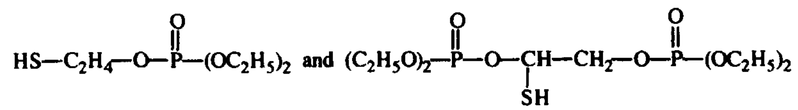
(I) is obtained in two steps, firstly by addition of mercaptoethanol on diethyl allylphosphonate and secondly by esterification of the previous compound with thioglycolic acid (total yield 70%).

In the same manner, (II) is obtained by addition of thioacetic acid followed by hydrolysis by KCN in methanol (total yield 90%).

Keywords: Thiols; mercaptoethanol; thioglycolic acid; thioacetic acid; photoaddition; phosphonates; sulfanylalkylphosphonates

INTRODUCTION

Organophosphorus compounds bearing a mercaptan group have been prepared previously. At first Clouet et al.[1] had obtained the following mono and diphosphates:



* Corresponding author

However these products exhibit poor hydrolytic stability due to the C-O-P linkage bond. On the contrary Farrington et al.[2] had prepared diethyl 1 sulfanylmethylphosphonate from polyoxymethylene by the following scheme :

$$(CH_2O)_n + CH_3-\overset{O}{\overset{\|}{C}}-SH \longrightarrow CH_3-\overset{O}{\overset{\|}{C}}-S-CH_2OH \xrightarrow{PBr_3} CH_3-\overset{O}{\overset{\|}{C}}-S-CH_2Br$$

$$\xrightarrow{P(OEt)_3} CH_3-\overset{O}{\overset{\|}{C}}-S-CH_2-PO(OEt)_2 \xrightarrow{NaOEt} HS-CH_2-PO(OEt)_2$$

Yet this product is unstable particularly concerning the oxydation and should be stored as the acetyl derivative before its use[3,4].

More recently two other teams[5,6] had prepared diethyl sulfanylalkylphosphonates as follow :

$$CH_2{=}CH-(CH_2)_n-Br \xrightarrow{P(OEt)_3} CH_2{=}CH-(CH_2)_n-PO(OEt)_2 \xrightarrow{AcSH}$$

$$AcS(CH_2)_{n+2}PO(OEt)_2 \xrightarrow{HCl} HS-(CH_2)_{n+2}PO(OEt)_2 \quad n = 6, 9$$

$$Ac = CH_3-\overset{O}{\overset{\|}{C}}-$$

As far as we are concerned, we decided to prepare two new sulfanylalkylphosphonates with a different spacer between thiol and the phosphonated groups.

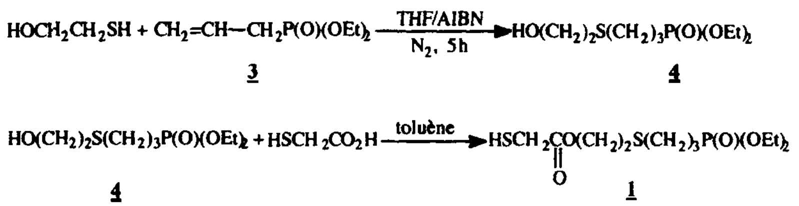
RESULTS AND DISCUSSION

The two thiols prepared are :

$$\underline{1}\ HS-CH_2-\overset{O}{\overset{\|}{C}}-O-C_2H_4-S-C_3H_6-PO(OEt)_2 \quad \text{and} \quad \underline{2}\ HS-(CH_2)_3-PO(OEt)_2$$

A) Preparationof 1

The compound **1** is prepared in two steps :



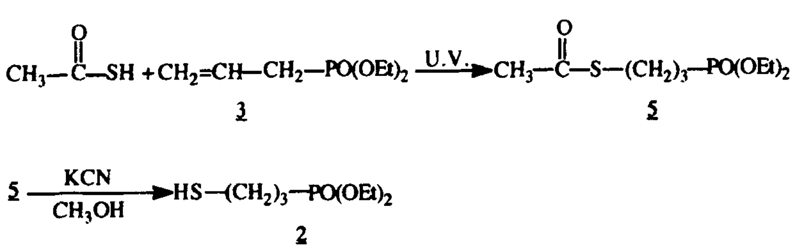
The first step addition of mercaptoethanol to diethyl allylphosphonate 3 was previously described by us[7] with a yield of 92%.

The esterification of monoalcohol 4 is performed with an excess of thioglycolic acid in toluene with azeotropic distillation of the formed water. The yield of distilled product is 75%. The structure of compound 1 was determined by ^{1}H NMR.

In conclusion the thiol 1 is obtained with an overall yield of 70%; this thiol is activated by the ester group in the β position and is useful for radical reactions as it has been described by Tadlaoui[8].

B) Preparation of 2

The synthesis of 2 is also performed in two steps :



The first step is initiated by UV at room temperature in acetonitrile using benzophenone as a photoinitiator. After purification and distillation, product 5 is obtained in 90% yield. ^{1}H NMR analysis (FIGURE 1) confirms the selectivity of the addition proved by the fact that no inverse addition is observed,contrary to addition of thiol on allyl acetate[9]. ^{31}P NMR confirms this through the only peak at 31.15 ppm whereas phosphonated allyl 3 gives a peak 27.6 ppm.

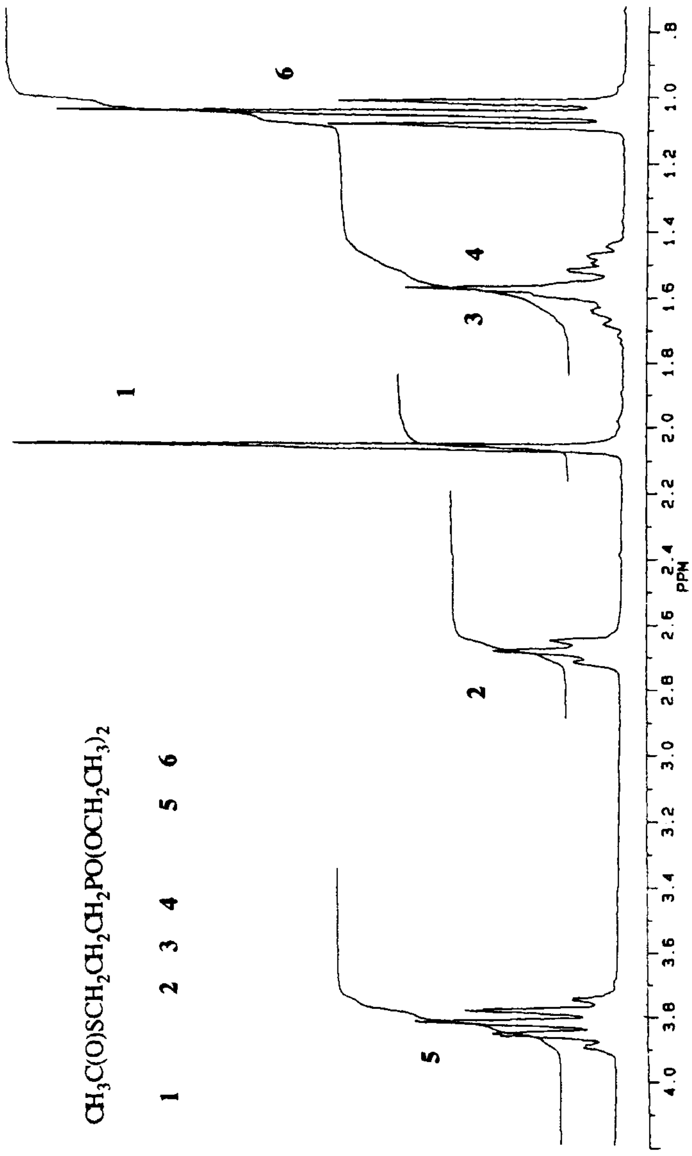


FIGURE 1 ^1H-NMR ($CDCl_3$) spectrum of diethyl 3-acetylsulfanylpropylphosphonate

We have realized the optimization of this reaction by GC and ^{31}P NMR. For instance we give the relation between yield and time in FIGURE 2. As it can be seen the higher yield is obtained in four hours, showing the very good reactivity of this addition as opposed to the higher unsaturated phosphonates (n = 6,9)[5,6].

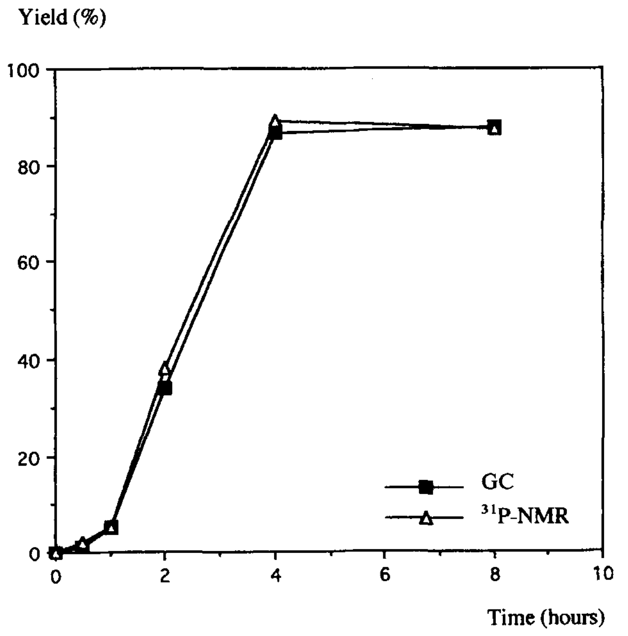
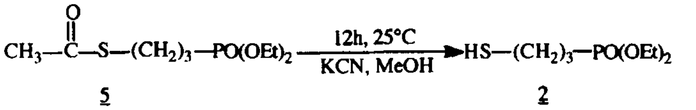


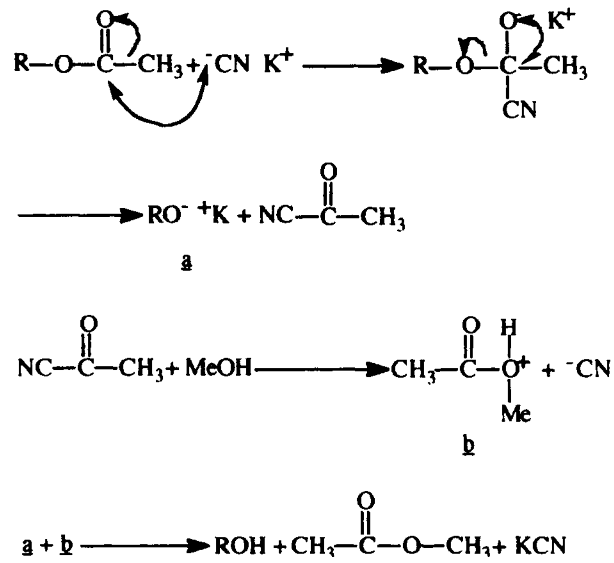
FIGURE 2 Yield (GC and ^{31}P-NMR) versus time

The second step of this synthesis is the hydrolysis of the acetyl group. Contrary to Randall[6] and Putvinski[5] who have used HCl, we have performed this hydrolysis by a catalytic amount of KCN in methanol as recommanded by Herzig[10].



5 2

The mechanism proposed by the author is the following :



The yield of this hydrolysis is 97%, and the structure is confirmed by ^{1}H NMR by the disappearance of acetyl group at 2.05 ppm. The ^{31}P NMR exhibits an only peak at 31.6 ppm.

This second synthesis was performed with an overall yield higher than 90% and provided a short mercaptan bearing a phosphonate group.

CONCLUSION

We have proposed two methods of synthesis of thiols bearing a phosphonate group with two different spacers. The first one is activated by an ester group in the β position.

The second one is shorter than the former and more stable to hydrolysis. In both cases the yield is very high although each synthesis needs two steps. These two thiols can be used as transfert agents in telomerization and to modify polymers bearing unsaturated groups as SBS and SB copolymers.

EXPERIMENTAL

Solvents and commercially available substrates were provided by Aldrich and Fluka.

Elementary analyses of the products concerning the determination of percentage of carbon (C), hydrogen (H), oxygen (O) sulfur (S) and phosphorus (P) were realized by Central Department of Analysis of CNRS of Vernaison.

IR spectra were recorded on a IRTF Nicolet 510 P spectrometer.

NMR spectra were recorded at room temperature on a Brucker AC 250 (or 200) spectrometer for solution in $CDCl_3$, and the chemical shifts values are given relative to $SiMe_4$ (1H) and phosphoric acid (^{31}P).

Vapor phase chromatograph (VPC) was realised by DELSI apparatus with a ionization flame detector, a temperature programator (heating rate 15°C/mn) and connected to a Shimadzu C-R6A integrator. Column was OV1 type (3% silicon greace on chromasorb G) 1 m long and 1/8 inch of diameter.

Reactions under UV radiations were carried out with a Philips HPK 125 W 4A lamp (λ = 360 nm).

Synthesis of phosphonated thiol $\underline{1}$

Addition of 2-sulfanylethanol to diethyl allylphosphonate $\underline{3}$

A solution of 2-sulfanylethanol (96.40 g, 1.24 moles) in dry THF (liter) was heated to reflux under nitrogen. Then a mixture of diethyl allylphosphonate (200 g, 1.12 moles) and AIBN (2.04 g, 0.0124 moles) was added dropwise to the solution. The reaction was carried on for 5 hours. Solvent and substrates which had not reacted, were removed by distillation. 255 g of the product $\underline{4}$ was obtained (90% yield).

NMR ^1H δ : 1.3 (6H,t,POCH2C$\underline{H}_3$); 1.8 (4H,m,C$\underline{H}_2$C$\underline{H}_2$P); 2.6 (4H,2t,C$\underline{H}_2$S); 3.2 (1H,s,O$\underline{H}$); 3.6 (2H,t,C$\underline{H}_2$OH); 4.0 (4H,qd,POC$\underline{H}_2$).

Analysis : $C_9H_{21}O_4PS$ (256) $\underline{4}$

% Calc. : C 42.19 H 8.20 O 25.0 P 12.11 S 12.50

% Found : 41.55 8.57 25.09 13.96 10.83

Esterification by thioglycolic acid

From a mixture of 1 l of toluene, phosphonated alcohol 4 (200 g, 0.781 mole) and thioglycolic acid (143.75 g, 1.563 moles), the formed water was removed by azeotropic distillation with an appropriate device (Dean-Stark).

When the reaction was finished, solvent was distilled off. The product was washed with water saturated with $NaHCO_3$, to eliminate thioglycolic acid in excess. Then an extraction with ether was realised (75% yield).

NMR ^1H δ : 1.9(1H,t,S$\underline{H}$); 3.1(2H,d,C$\underline{H}_2$SH); 4.1(2H,t,C(O)OC$\underline{H}_2$); 2.4-2.7(4H,2t,C$\underline{H}_2$S); 1.7(4H,m,C$\underline{H}_2$C$\underline{H}_2$P); 3.9(4H,qd,POC$\underline{H}_2$); 1.2(6H,t,POCH$_2$C$\underline{H}_3$).

Analysis : $C_{11}H_{23}O_5PS_2$ (330) 1

% Calc. : C 40.00 H 6.97 O 24.24 P 9.40 S19.39

% Found : 41.59 7.58 24.27 18.93

Synthesis of diethyl 3-acetylsulfanylpropyl phosphonate 5

The reaction mixture of thioacetic acid (47.22 g, 0.620 mole), diethyl allylphosphonate (132.00 g, 0.741 mole), benzophenone (1.31 g) and acetonitrile (520 ml) was placed in a flask and irradiated with a UV-lamp at a distance of 5 cm from it, and rapidly stirred at room temperature and under nitrogen.

After reaction, the mixture was vacuum distilled and the product was purified by distillation (90–91°C / 5.10^{-3} mbar). VPC purity 97.4%.

NMR $^1H(CDCl_3)$ δ : 1.0(6H,t,OCH$_2$C$\underline{H}_3$, $^3J_{HH}$ = 7Hz); 1.5–1.7 (4H,m,C$\underline{H}_2$C$\underline{H}_2$P); 2.1 (3H,s,C$\underline{H}_3$CO); 2.7 (2H,t,C$\underline{H}_2$S. $^3J_{HH}$ = 7Hz); 3.8-3.9 (4H,m,OC$\underline{H}_2$CH$_3$)

NMR ^{31}P $(CDCl_3)$ δ : 31.1 (1P,s)

IR(KBr) : (cm^{-1}) : 2953(υ_{C-H}), 1691($\upsilon_{C=O}$), 1448(δ_{P-C}), 1240(υ_{P-O}), 1190(δ_{P-O-C}), 1030($\upsilon_{(P)-O-C}$), 819($\upsilon_{P-O-(C)}$)

Analysis : $C_9H_{19}O_4PS$ (254) 5

% Calc. : C 42.51 H 7.53 O 25.17 P 12.18 S 12.61

% Found : 42.59 7.77 25.86 – 12.40

Synthesis of diethyl 3-sulfanylpropyl phosphonate 2

To a solution of KCN (0.5 g) in methanol (60 ml), 5 (9.89 g, 0.0389 mole) was added. The mixture was stirred for 12 hours at room temperature under nitrogen. After reaction 200 ml of water was added to the mixture and the product was extracted with dichloromethane. After drying of the organic phase with magnesium sulfate, filtration and vacuum distillation, 8.5 g of a yellow oily liquid was obtained. VPC purity 97.3%.

NMR ^1H ($CDCl_3$) δ : 1.1 (6H,t,$OCH_2C\underline{H}_3$, $^3J_{HH}$ = 7Hz); 1.5–1.7 (4H,m,$C\underline{H}_2C\underline{H}_2P$); 2.37 (2H,t,$C\underline{H}_2S$, $^3J_{HH}$ = 7Hz); 3.4–3.9 (4H,m,$OC\underline{H}_2CH_3$)

NMR ^{31}P ($CDCl_3$) δ : 31.6 (s,1P)

IR(KBr)(cm^{-1}) : 2951(υ_{C-H}), 2527(υ_{S-H}), 1446(δ_{P-C}), 1238($\upsilon_{P=O}$), 1182(δ_{P-O-C}), 1030($\upsilon_{(P)-O-C}$), 818($\upsilon_{P-O-(C)}$)

Analysis : $C_7H_{17}O_3PS$ (212)

% Calc. : C 39.61 H 8.07 O 22.61 P 14.59 S 15.11

% Found : 39.19 8.38 23.54 – 14.35

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