A Facile Synthesis of Diethyl 1-(Phenylthio)alkylphosphonates

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The title compounds have been obtained in moderate yields by the reaction of diethyl 1-hydroxyalkylphosphonates with thiophenol in the presence of the triphenylphosphine/diethyl azodicarboxylate system.

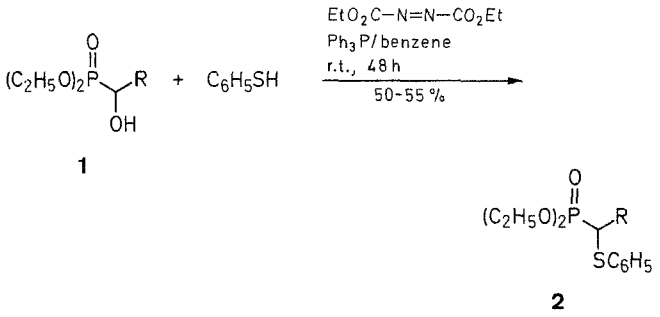
Dialkyl 1-(alkylthio)- and 1-(arylthio)alkylphosphonates are key reagents in the Horner reaction for the preparation of vinyl sulfides which, upon hydrolysis afford the desired carbonyl compounds.[1-6]

Although dialkyl 1-(alkylthio)- and 1-(arylthio)alkylphosphonates are readily available by well established methods,[4,7-13] the preparation of these compounds may still demand new synthetic solutions. So far, these phosphonates have been obtained by the following methods: addition of elemental sulfur to dialkyl alkylphosphonate carbanions and subsequent alkylation of α-phosphorylated thiols thus formed;[4] alkylation of metallated diethyl methylthiomethyl- or phenylthiomethylphosphonates with alkyl halides;[1,14] sulfenylation of metallated dialkyl alkylphosphonates by means of dialkyl or diaryl disulfides;[15] Friedel-Crafts arylation of diethyl chloro(methylthio)-methylphosphonate by aromatic compounds;[16,17] or alkylation[17] and arylation[18] of α-phosphorylated sulfides generated by Pummerer rearrangement of the corresponding sulfoxides.

No attempts have hitherto been made to use the easily accessible (from diethyl phosphite and aldehydes) diethyl 1-hydroxyalkylphosphonates **1**[19,20] as starting materials.

On the other hand, the reaction of alcohols with thiophenol using triphenylphosphine/diethyl azodicarboxylate[21,22] is known to provide alkyl aryl sulfides in good yields.

I report here the facile synthesis of diethyl 1-(phenylthio)alkylphosphonates **2** from diethyl 1-hydroxyalkylphosphonates **1** and thiophenol utilizing the triphenylphosphine/diethyl azodicarboxylate (diethyl diazenedicarboxylate) system.[21]



1 **2**

1, 2	a	b	c	d	e
R	H	CH_3	C_2H_5	n-C_3H_7	n-C_5H_{11}

The reaction proceeds at room temperature under mild and neutral conditions and affords (after column chromatography) the pure products **2a–e** in moderate (50–55%) yields.

The synthesis is limited to phosphonates **2** possessing an alkyl substituent at C-1. When R is an aromatic group, an unidentified mixture of products is formed.

The advantage of the method presented here is the possibility of direct transformation of the readily accessible 1-hydroxyalkylphosphonates **1** into the corresponding 1-phosphorylated alkyl phenyl sulfides **2**.

Diethyl 1-hydroxyalkylphosphonates **1** were prepared, according to the previously described procedure,[20] from diethyl phosphite and the appropriate aldehyde in the presence of Et_3N. Diethyl azodicarboxylate (diethyl diazenedicarboxylate) was obtained by the established procedure.[23]

Diethyl 1-(Phenylthio)alkylphosphonates 2a–e; General Procedure:
A solution of diethyl azodicarboxylate (2.09 g, 0.012 mol) in benzene (5 mL) is added dropwise to a stirred mixture of the diethyl 1-hydroxyalkyl phosphonate **1** (0.01 mol), triphenylphosphine (3.14 g, 0.012 mol), and benzene (25 mL) at room temperature. Stirring is continued for 5 min, and a solution of thiophenol (1.32 g, 0.012 mol) in benzene (5 mL) is slowly added over a period of 30 min. A slightly exothermic reaction occurs, the mixture becomes pale yellow, and a white precipitate of diethyl hydrazine-*N,N'*-dicarboxylate is formed. After the addition is completed, the mixture is stirred for 2 days at room temperature, and then the precipitate is filtered off. The filtrate is carefully washed with 5% K_2CO_3/H_2O (2 × 5 mL) and H_2O (3 × 5 mL). The organic layer is separated, dried ($MgSO_4$), and evaporated under reduced pressure. Hexane (80 mL) is added to the semisolid residue. The resultant solution is filtered and the solvent is removed in vacuo.

Table. Diethyl 1-(Phenylthio)alkylphosphonates **2** Prepared

Product	Yield[a] (%)	n_D^{20}	Molecular Formula[b] or Lit. n_D^{20}	IR (film)[c] ν (cm^{-1})	^{1}H-NMR (CCl_4/TMS)[d] δ, J (Hz)	^{31}P-NMR (CCl_4/H_3PO_{4ext})[e]/δ
2a	50	1.5336	1.5326[24]	1260, 1070, 1040, 980	1.25 (t, 6H, J = 7, $2CH_3$); 3.03 (d, 2H, J = 14, CH_2); 4.00 (dq, 4H, J = 7, $2CH_2$); 6.98–7.47 (m, $5H_{arom}$)	22.2
2b	51	1.5215	1.5189[15]	1255, 1070, 1040, 975	1.27 (t, 6H, J = 7, $2CH_3$); 1.43 (dd, 3H, J = 7.5, 17, CH_3); 3.18 (dq, 1H, J = 7.5, 16.3, CH); 4.07 (dq, 4H, J = 7, $2CH_2$); 7.10–7.59 (m, $5H_{arom}$)	25.4
2c	55	1.5205	$C_{13}H_{21}O_3PS$ (288.3)	1245, 1050, 1020, 960	1.09 (t, 3H, J = 7.2, CH_3); 1.26 (t, 6H, J = 7, $2CH_3$); 1.43–2.10 (m, 2H, CH_2); 2.86 (m, 1H, J_{PH} = 16.8, CH); 4.06 (d quin, 4H, J = 7, $2CH_2O$); 7.10–7.56 (m, $5H_{arom}$)	24.7
2d	50	1.5145	$C_{14}H_{23}O_3PS$ (302.4)	1245, 1060, 1020, 960	0.84 (t, 3H, J = 7, CH_3); 1.21 (t, 6H, J = 7, $2CH_3$); 1.40–1.96 (m, 4H, $2CH_2$); 2.99 (m, J_{PH} = 16, CH); 4.06 (d quin, 4H, J = 7, $2CH_2O$); 7.10–7.62 (m, $5H_{arom}$)	24.9
2e	53	1.5204	$C_{16}H_{27}O_3PS$ (330.4)	1250, 1160, 1030, 965	0.83 (br t, 3H, J = 6, CH_3); 1.24 (t, 6H, J = 7, $2CH_3$); 1.19–2.01 (m, 8H, $4CH_2$); 2.89 (m, 1H, J_{PH} = 16, CH); 4.06 (d quin, 4H, J = 7, $2CH_2O$); 7.08–7.59 (m, $5H_{arom}$)	25.0

[a] Yield of isolated pure product, based on **1**.
[b] Satisfactory microanalyses obtained: C ±0.15, H ±0.20, P ±0.30.
[c] Recorded on a Specord 71 IR (C. Zeiss) spectrophotometer. Only the most characteristic absorption bands are given.
[d] Recorded at 80 MHz with a Tesla BS 487C spectrometer.
[e] Recorded at 24.3 MHz with a Jeol JNM-FX60 spectrometer. Positive chemical shifts are downfield from H_3PO_4 (85%) as standard.

The oily residue is chromatographed on silica gel 60 G (Merck; 100 g) using benzene/acetone (4:1 v/v) as eluent to afford the analytically pure product **2**.

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