A Convenient Synthesis of Diethyl 1-Chloroalkylphosphonates

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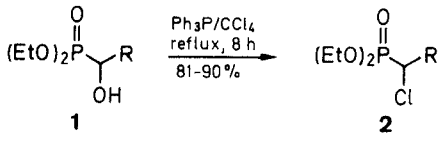
The title compounds were obtained in high yield by the reaction of diethyl 1-hydroxyalkylphosphonates with triphenylphosphine carbon tetrachloride.

Diethyl 1-chloroalkylphosphonates are key reagents for the preparation of α-chloro-α,β-unsaturated acids,[1] diethyl 1,2-epoxyalkylphosphonates,[2-5] and 1-(methylthio)methylphosphonate[6] as well as derivatives of alkylidenediphosphonates and vinylphosphonates.[7]

Despite of their wide range of synthetic applications, the synthesis of diethyl 1-chloroalkylphosphonates has received little attention. The following methods, not generally applicable, have been reported in the literature: (i) direct α-chlorination of diethyl 1-(aryl)methylphosphonates using a butyllithium/carbon tetrachloride system;[8] (ii) monodechlorination of diethyl 1,1-dichloroalkylphosphonates with butyllithium, and subsequent hydrolysis or alkylation of the thus formed diethyl 1-chloro-1-lithioalkylphosphonates;[9] (iii) alkylation of lithiated diethyl trimethylsilylchloromethylphosphonate followed by desilalation;[10] (iv) ethanolysis of the 1-chloroalkylphosphonic dichlorides;[11-13] and (v) direct chlorination of diethyl 1-hydroxyalkylphosphonates with thionyl chloride.[14,15] The last reaction usually proceeds only in moderate yield, except when diphenyl 1-hydroxy-1-(aryl)methylphosphonates are used as starting materials.[16,17]

The above results prompted the investigation of the possibility of direct hydroxyl-chloride exchange in easily accessible (from diethyl phosphite and aldehydes) diethyl 1-hydroxyalkylphosphonates **1**.[18,19] The reaction of alcohols with carbon tetrachloride in the presence of triphenylphosphine is known to provide, via oxyphosphonium intermediates, the appropriate chlorides[20-22] generally in good yield.

Reported herein is an operationally simple and convenient synthesis of diethyl 1-chloroalkylphosphonates **2**,



1 **2**

1, 2	a	b	c	d	e
R	H	Me	Et	Pr	Ph

Table. Diethyl 1-Chloroalkylphosphonates **2** Prepared

Product	Yield[a] (%)	bp (°C)/Torr and n_D^{20}	Molecular Formula or Lit. bp and n_D^{20}	IR (film)[c] ν (cm^{-1})	^{1}H-NMR ($CDCl_3$/TMS)[d] δ, J(Hz)	^{31}P-NMR ($CCl_4/H_3PO_{4\,ext}$)[e] δ
2a	86	61/0.4 1.4386	86–87/2.5[12] 1.4360[12]	1268, 1164, 1066, 968	1.37 (t, 6H, J = 7.1, $2CH_3$), 3.55 (d, 2H, J = 10.6, CH_2), 4.22 (quin, 4H, J = 7.1, $2CH_2$)	18.5
2b	90	50–52/0.1 1.4355	62/0.2[9] 1.4352[9]	1252, 1164, 1030, 960	1.36 (t, 6H, J = 7.0, $2CH_3$), 1.70 (dd, 3H, J = 7.2, 16.5, CH_3), 3.97 (dq, 1H, J = 7.2, 9.8, CH), 4.05–4.41 (m, 4H, $2CH_2$)	20.6
2c	84	60–62/0.15 1.4400	70/0.3[9] 1.4390[9]	1256, 1098, 1052, 966	1.13 (t, 3H, J = 6.9, CH_3), 1.36 (t, 6H, J = 7.1, $2CH_3$), 1.63–2.32 (m, 2H, CH_2), 3.63–3.93 (m, 1H, CH), 4.03–4.42 (m, 4H, $2CH_2$)	19.8
2d	83	64–66/0.15 1.4410	$C_8H_{18}ClO_3P$[b] (228.7)	1260, 1096, 1052, 968	0.95 (bt, 3H, J = 6.9, CH_3), 1.37 (t, 6H, J = 7.1, $2CH_3$), 1.50–2.12 (m, 4H, $2CH_2$), 3.71–4.42 (m, 5H, $2CH_2$, CH)	19.9
2e	81	118–120/0.4 1.5116	120–125/0.1[8] 1.5125[12]	1266, 1096, 1044, 972	1.17, 1.31 (2t, 6H, J = 7.1, $2CH_3$), 3.76–4.48 (m, 4H, $2CH_2$), 4.90 (d, 1H, J = 14.3, CH), 7.31–7.60 (m, $5H_{arom}$)	17.1

[a] Yield of isolated pure product, based on **1**.

[b] Elemental analyses:
calc. C 42.02 H 7.93 P 13.55
found 42.16 8.13 13.58

[c] Recorded on a Specord M 80 (C. Zeiss) spectrophotometer. Only the most characteristic bands are given.

[d] Recorded at 80 MHz with a Tesla BS 587 FT spectrometer.

[e] Recorded at 36.43 MHz with a Bruker HFX-90 spectrometer. Positive chemical shifts are downfield from H_3PO_4 (85%) as a standard.

from diethyl 1-hydroxyalkylphosphonates **1**, utilizing triphenylphosphine/carbon tetrachloride system.[20–22] The reaction proceeds smoothly in boiling carbon tetrachloride affording (after vacuum distillation) analytically pure products **2a–e** in high yield. The best results are obtained when a 50% molar excess of triphenylphosphine is used. The synthesis is limited to primary or secondary diethyl 1-hydroxyalkylphosphonates **1**.

The main advantage of the method presented is the possibility of direct transformation of the readily accessible diethyl 1-hydroxyalkylphosphonates **1** into diethyl 1-chloroalkylphosphonates **2** in high yields and purity under neutral conditions.

Diethyl 1-hydroxyalkylphosphonates **1** are prepared, according to the previously described procedure,[19] from diethyl phosphite and the appropriate aldehyde in the presence of Et_3N.

Diethyl 1-Chloroalkylphosphonates 2a–e; General Procedure:
A solution of diethyl 1-hydroxyalkylphosphonate **1** (0.02 mol) and triphenylphosphine (7.86 g, 0.03 mol) in dry CCl_4 (35 mL) is refluxed for 8 h. Then, the mixture is evaporated under reduced pressure, and the semisolid residue is extracted with hexane (3 × 50 mL). The combined extracts are filtered, and the solvent is removed *in vacuo*. The oily residue is distilled under reduced pressure to afford the analytically pure product **2**.

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