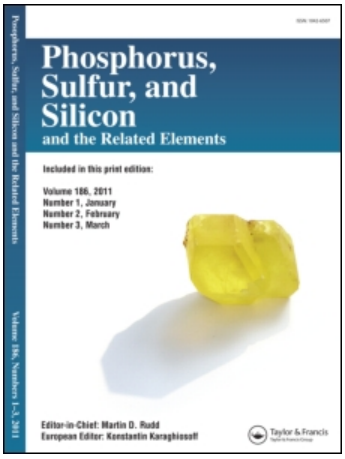


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

Synthesis of Dichloromethylphosphonates

Piotr Majewski[a]; Jacek F. Koszuk[a]
[a] Technical University of Łódź, Institute of Organic Chemistry, Łódź, Poland

To cite this Article Majewski, Piotr and Koszuk, Jacek F.(2009) 'Synthesis of Dichloromethylphosphonates', Phosphorus, Sulfur, and Silicon and the Related Elements, 184: 4, 956 — 962
To link to this Article: DOI: 10.1080/10426500902719248
URL: http://dx.doi.org/10.1080/10426500902719248

Phosphorus, Sulfur, and Silicon, 184:956–962, 2009

ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/10426500902719248

Taylor & Francis
Taylor & Francis Group

Synthesis of Dichloromethylphosphonates

Piotr Majewski and Jacek F. Koszuk
Technical University of Łódź, Institute of Organic Chemistry, Łódź, Poland

Efficient synthesis of O,O-*dialkyl,* O-*alkyl*-N,N-*dialkylamido and* N,N,N′,N′-*tetraalkyldiamido dichloromethylphosphonates via treatment of* O,O-*dialkyl,* O-*alkyl*-N,N-*dialkylamido, and* N,N,N′,N′-*tetraalkyldiamido trichloromethylphosphonates with diethyl phosphite in the presence of triethylamine in ethanol has been described.*

Keywords Dichloromethylphosphonates

INTRODUCTION

The chemistry of *O*,*O*-dialkyl, *O*-alkyl-*N*, *N*-dialkylamido, and *N,N,N*′,*N*′-tetraalkyldiamido dihalogenomethylphosphonates has been extensively investigated 30 years ago[1,2,3a] and later.[3b,c] These phosphonates have found wide application as starting materials for the synthesis of functionalized 1-halogenomethylphosphonates,[1–3] 1,1-dihalogenoalkenes,[2] and 1,2-epoxyalkanephosphonates.[1] 1,1-Dihalogenophosphonates can be also readily transformed into the corresponding carbanions, which are the goal of carbon–carbon bond forming strategy.[2]

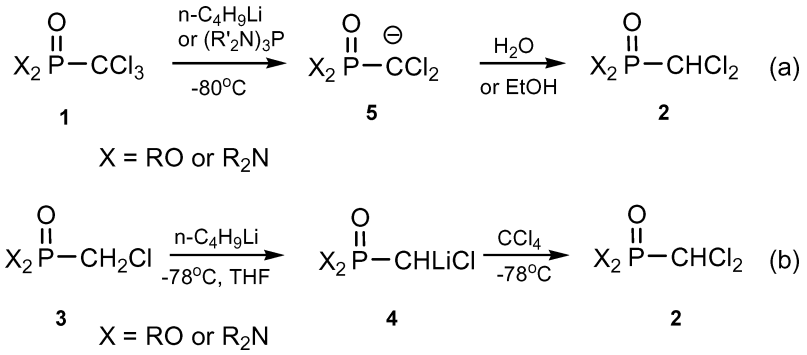
Three general methods have been commonly used for the preparation of *O*,*O*-dialkyl and *N,N,N*′,*N*′-tetraalkyldiamido dichloromethylphosphonates **2**.

The Normant's pioneering approach is based on the dechlorination of 1,1,1-trichloromethylphosphonates **1** with *n*-buthyllithium/hexamethylphosphoramidate and subsequent quenching of the resulting dichloromethylphosphonate anion **5** with water or ethanol

Received 19 December 2007; accepted 29 February 2008.

Dedicated to Professor Marian Mikołajczyk from the CBMiM PAN in Łódź, Poland, on the occasion of his 70th birthday.

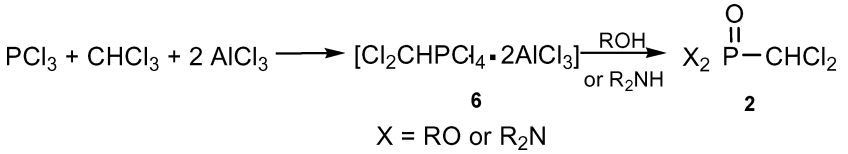
Address correspondence to Piotr Majewski, Technical University of Łódź, Institute of Organic Chemistry, Żeromskiego 116, 90-924 Łódź, Poland. E-mail: biotr.majewski@p.lodz.pl



SCHEME 1

(Scheme 1a).[5a] The second procedure relies on metallation of the chloromethylphosphonates **3** with butyllithium[4,5] followed by chlorination of the obtained lithium chloromethylphosphonate **4** with carbon tetrachloride (Scheme 1b).

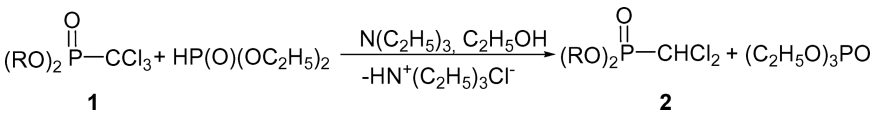
The third method involves the standard preparation of the phosphorus trichloride/aluminum chloride/chloroform complex **6** and its decomposition with the selected alcohol or secondary amine, respectively (Scheme 2).[6]



SCHEME 2

A few other additional procedures for the synthesis of *N*,*N*,*N*′,*N*′-tetraalkyldiamido methylphosphonates and *O*,*O*-dialkyl alkylphosphonates have been reported.[7–13] For example, *N*,*N*,*N*′*N*′-tetraalkyldiamido methylphosphonate has been obtained by aminolysis of chlorobis(dialkylamine)dichloromethylenephosphorane[7,8] and its precursors,[9,10] whereas *O*,*O*-dialkyl dichloromethylphosphonates have been produced from *O*,*O*-dialkyl trichloromethylphosphonates and diethyl phosphite in the presence of stoichiometric amounts of ethanol[14] (Scheme 3).

In this article, we describe an efficient and general procedure for the preparation of *O*,*O*-dialkyl, *O*-alkyl-*N*, *N*-dialkylamido, and *N*, *N*, *N*′, *N*′-tetraalkyldiamido dichloromethyl-phosphonates using mild reaction conditions and readily available starting materials.

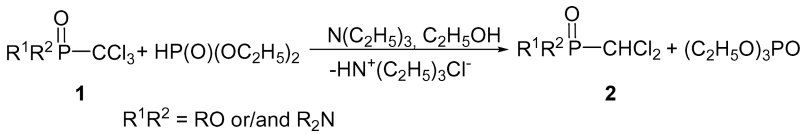


1 **2**

SCHEME 3

RESULTS AND DISCUSSION

From the synthesis of *O*,*O*-dialkyl dichloromethylphophonates, using diethyl phosphite, triethyl amine, and stoichiometric amounts of ethanol, we assumed that this method can be successfully used for the synthesis of *O*-ethyl-*N*,*N*-dialkylamido and *N*,*N*,*N*′,*N*′-tetraalkyldiamido dichloromethylphosphonates **2** according to Scheme 4.



1 **2**

1,2	a	b	c	d	e	f	g	h	i
R^1	C_2H_5O	*n*-C_3H_7O	*i*-C_3H_7O	*n*-C_4H_9O	CH_3O	C_2H_5O	C_2H_5O	$(C_2H_5)_2N$	$(n\text{-}C_3H_7)_2N$
R^2	C_2H_5O	*n*-C_3H_7O	*i*-C_3H_7O	*n*-C_4H_9O	CH_3O	$(CH_3)_2N$	$(C_2H_5)_2N$	$(C_2H_5)_2N$	$(n\text{-}C_3H_7)_2N$

SCHEME 4

When *O*-alkyl-*N*,*N*-dialkylamido and *N*,*N*,*N*′,*N*′-tetraalkyldiamido trichloromethyl-phosphonates **1f–i** were treated with dialkyl phosphite in the presence of triethylamine and stoichiometric amounts of ethanol in a neutral solvent, the corresponding dichloromethyl-phosphonates were produced in rather low yield. However, when similar reactions were carried out in ethanol at ambient temperature, the yields of the *O*-alkyl-*N*,*N*-dialkylamido and *N*,*N*,*N*′,*N*′-tetraalkyldiamido dichloromethylphosphonates **2f–i** were high to excellent.

The transformation of *O*,*O*-dialkyl trichloromethylphosphonates into *O*,*O*-dialkyl dichloromethylphosphonates **2a–d** was also very effective following the same protocol. The dechlorination reaction was readily monitored by ^{31}P NMR. The reaction products were isolated by distillation under reduced pressure. The structures of the new compounds were confirmed by IR and NMR spectroscopy. All of them have IR (film) absorption band characteristic for a P=O moiety: broad band at 1280 cm^{-1}. Their ^1H NMR spectra ($CDCl_3$) showed characteristic doublets at $\delta = 5.65$–5.75 ppm ($^2J_{PH} = 1$ Hz) for the methine proton of $CHCl_2$ moiety (see the Experimental section).

O,*O*-dialkyl, *O*-alkyl-*N*, *N*-dialkylamido, and *N*, *N*, *N*′, *N*′-tetraalkyldiamido dichloro-methylphosphonates (**2a–d, f–i,** and**1f)** gave satisfactory elemental analyses (C ± 0,3%, H ± 0,2%). Yields and physical constants are presented in Table I.

As shown in Table I, *O*,*O*-dimethyl dichloromethylphosphonate (**2e**) could not be obtained by the present method, probably due to the extensive dealkylation of the substrate **1e** as well as of the potential product **2e**. In all other cases, no traces of the dealkylation reaction of the substrates and the products were observed.

CONCLUSION

Here we have reported a general synthetic procedure providing *O*,*O*-dialkyl, *O*-alkyl-*N*, *N*-dialkylamido, and *N*, *N*, *N*′, *N*′-tetraalkyldiamido dichloromethylphosphonates under mild conditions in high to excellent yields.

EXPERIMENTAL

Organic solvents and reagents were purified by commonly used procedures.[19] IR spectra were recorded with a Specord M-80 spectrophotometer. ^{1}H NMR (250 MHz) and ^{31}P{^{1}H} NMR (101 MHz) spectra were recorded with a Bruker DPX-250 spectrometer with TMS as an internal standard for ^{1}H and 85% H_3PO_4 as an external standard for ^{31}P. ^{31}P NMR spectra were recorded using broadband proton decoupling. All chemical shifts (δ) are reported in ppm. In the case of ^{1}H, the residual solvent peak was used as the internal standard ($CHCl_3$ at 7.26 ppm). Coupling constants (J) are reported in Hz. *O*,*O*-Dialkyl trichloromethyl-phosphonates have been prepared according to literature procedures.[11,15–17]

Physical and analytical data of the phosphonates **2** are presented in Table I.

Reaction of *O,O*-Dialkyl-, *O*-Alkyl-*N,N*-dialkylamido-, *N,N,N′,N′*-Tetraalkylamido-1,1,1-trichloromethylphosphonates 1a–i with Diethylphosphite: General Procedure

To a solution of the dialkyl 1,1,1-trichloromethylphosphonate **1** (0.1 mol) and triethylamine (12.1 g, 0.12 mol) in ethanol (50 mL), diethyl phosphite (16.5 g, 0.12 mol) was added dropwise at 20°C. The mixture was kept at room temperature, and the progress of the reaction was monitored by ^{31}P NMR spectroscopy. After six days, or longer if

TABLE I Synthesis of *O*,*O*-Dialkyl, *O*-Alkyl-*N*,*N*-dialkylamido, and *N*,*N*,*N*′,*N*′-Tetraalkylamido Dichloromethylphosphonates 2a–d, f–i via the Reaction of 1,1,1-Trichloromethylphosphonates 1a–i with Diethyl Phosphite in the Presence of Triethylamine in Ethanol at Room Temperature

Substrate[a]	R^1	R^2	Products, Yield (%)[b]	B.p.[°C]/Torr (Mp) [°C]	^{31}P NMR δ (ppm)	Lit. or or Molecular Formula (Mol. Weight)
1a	C_2H_5O	C_2H_5O	**2a** (84)	80–82/0.5 120/12[6a]	9.8	[6a,14]
1b	*n*-C_3H_7O	*n*-C_3H_7O	**2b** (81)	100–101/0.8	10.0	$C_7H_{15}Cl_2O_3P$ (249.07)
1c	*i*-C_3H_7O	*i*-C_3H_7O	**2c** (82)	82–84/0.3 72/1[18]	8.0	[4,18]
1d	*n*-C_4H_9O	*n*-C_4H_9O	**2d** (79)	110–112/0.7 110/66 Pa[14]	9.5	[14]
1e	CH_3O	CH_3O	**2e** (0)[c]			
1f	C_2H_5O	$(CH_3)_2N$	**2f** (72)	92–93/0.5	17.0	$C_5H_{12}Cl_2NO_2P$ (220.03)
1g	C_2H_5O	$(C_2H_5)_2N$	**2g** (62)	100/0.6	18.2	$C_7H_{16}Cl_2NO_2P$ (248.09)
1h	$(C_2H_5)_2N$	$(C_2H_5)_2N$	**2h** (58)	115/0.6 157–160/8[11]	24.8 24.4[11]	[11]
1i	$(C_3H_7)_2N$	$(C_3H_7)_2N$	**2i** (64)	(107–108) petroleum ether (107–109)[7]	23.2 23.7[7]	[7]

[a]Molar ratio $(RO)_2P(O)CCl_3$, $HP(O)(OC_2H_5)_2$, $N(C_2H_5)_3$ 1:1,2:1,2 was used.
[b]Yields refer to isolated products.
[c]Compound **2e** cannot be obtained due to extensive dealkylation.

necessary, the solvent from the reaction mixture was evaporated under reduced pressure, and the residue was diluted with chloroform (100 mL). The solution was washed with water (2 × 50 mL), dried over sodium sulfate, and the solvent was removed in vacuo. The residue was purified by distillation under reduced pressure after separating triethylphosphate at 60°C/0.8 mm Hg.

O,O-Di-*n*-propyl-1,1-dichloromethylphosphonate (2b)

20.5 g (81%); b.p. 100–101°C/0.8 mm Hg. ^{1}H NMR ($CDCl_3$): $\delta = 1.0$ (t, $^3J_{HH} = 7$ Hz, 6H), 1.75 (sextet, $^3J_{HH} = 7$ Hz, 4H), 4.20 (m, $^3J_{HH} = 7$, $^3J_{PH} = 7$ Hz, 4H), 5.70 (d, $^2J_{PH} = 1$ Hz, 1H). ^{31}P{^{1}H} NMR ($CDCl_3$): $\delta =$ 10.0. IR ($CC1_4$): ν(P=O) 1280 cm^{-1}.

O-Ethyl-*N,N*-dimethyl-1,1-dichloromethylphosphonate (2f)

15.8 g (72%); b.p. 92–93°C/0.5 mm Hg. ^{1}H NMR ($CDCl_3$): $\delta = 1.35$ (t, $^3J_{HH} = 7$ Hz, 3H), 2.78 (d, $^3J_{PH} = 8.7$ Hz, 6H), 4.25 (m, $^3J_{HH} = 7$, $^3J_{PH} =$ 7 Hz, 2H), 5.75 (d, $^2J_{PH} = 1$ Hz, 1H). ^{31}P{^{1}H} NMR (CDCl3): $\delta = 17.0$. Anal. Calcd. for $C_5H_{12}Cl_2NOP$: C 27.29, H 5.49. Found: C 27.10, H 5.30%.

O-Ethyl-*N,N*-diethyl-1,1-dichloromethylphosphonate (2g)

1.2 g (62%); b.p. 100°C/0.6 mm Hg. ^{1}H NMR ($CDCl_3$): $\delta = 1.10$ (t, $^3J_{HH} =$ 7 Hz, 6H), 1.28 (t, $^3J_{HH} = 7$ Hz, 3H), 3.05 (m, 4H), 3.96 (q, $^3J_{HH} = 7$, $^3J_{PH} = 7$ Hz, 2H), 5.65 (d, $^2J_{PH} = 1$ Hz, 1H). ^{31}P{^{1}H} NMR ($CDCl_3$): 18.2. Anal. Calcd. for $C_7H_{16}Cl_2NO_2P$: C 33.89, H 6.50. Found C 33.62, H 6.32%.

REFERENCES

[1] P. Perriot, J. Villeras, and J. F. Normant, *Synthesis*, 33 (1978).
[2] (a) J. Villeras, A. Religuet, and J. F. Normant, *Synthesis*, 27 (1978); (b) P. Savignac and P. Coutrot, *Synthesis*, 197 (1976).
[3] (a) P. Coutrot, C. Laurenco, J. F. Normant, P. Perriot, P. Savignac, and J. Villeras, *Synthesis*, 615 (1977); (b) X. Zhang, W. Qiu, and D. J. Burton, *J. Fluorine Chem*., **89,** 39 (1998); (c) X. Zhang, W. Qiu, and D. J. Burton, *Tetrahedron Lett.*, **40,** 2681 (1999).
[4] P. Savignac, M. Dreux, and P. Coutrot, *Tetrahedron Lett*., **16,** 609 (1975).
[5] (a) G. Sturtz, G. Lavielle, and G. H. Normant, *Chem. Ztg.*, **96,** 503 (1972); (b) D. Seyferth and R. S. Marmor, *J. Organomet. Chem*., **59,** 237 (1973).
[6] (a) A. M. Kinnear and E. A. Perren, *J. Chem. Soc*., 3437 (1952); (b) J.-C. Elkaim and J. G. Riess, *Tetrahedron Lett*., **16,** 4409 (1975).

[7] A. P. Marchenko, I. S. Zal'tsman, and A. M. Pinchuk, *Zh. Obshch. Khim.*, **56,** 1910 (1986).
[8] G. M. Koidan, A. P. Marchenko, V. A. Oleinik, and A. M. Pinchuk, *Zh.Obshch.Khim.*, **58,** 1461 (1988).
[9] O. I. Kolodyazhnyi, *Zh. Obshch. Khim.*, **59,** 330 (1989).
[10] A. P. Marchenko, V. A. Oleinik, G. N. Koidan, and A. M. Pinchuk, *Zh. Obshch. Khim.*, **59,** 959 (1989).
[11] V. S. Abramov and N. S. Il'ina, *Zh. Obshch. Khim*., **41,** 100 (1971).
[12] R. Khazanchi and N. K. Roy, *Agric. Biol. Chem*., **47,** 331 (1983).
[13] L. P. Filonenko, G. K. Bespal'ko, A. P. Marchenko, and A. M. Pinchuk, *Zh. Obshch. Khim*., **57,** 2320 (1987).
[14] S. Albrecht and E. Hermann, *Z. Anorg. Allg. Chem*., **538,** 207 (1986).
[15] F. M. Kharrasova, T. V. Zykova, R. A. Salakhutdinov, E. V. Efimowa, and R. D. Shafigullina, *Zh. Obshch. Khim.*, **44,** 2419 (1974).
[16] *O*-Ethyl-*N*, *N*-dimethyl trichloromethylphosphonoamidate (**1f**) was obtained by refluxing $(C_2H_5O)_2PN(CH_3)_2$ in carbon tetrachloride. Yield: 72%, b.p. 130°C/10 mm Hg. ^{1}H NMR ($CDCl_3$): $\delta = 1.31$ (t, $^3J_{HH} = 7$ Hz, 3H), 2.88 (d, $^3J_{PH} = 8.5$ Hz, 6H), 4.25 (m, $^3J_{HH} = 7$ Hz, $^3J_{PH} = 7$ Hz, 2H). $^{31}P\{^1H\}$ NMR ($CDCl_3$): $\delta = 12.3$. Anal. Calcd. for $C_5H_{11}Cl_3NOP$: C 23.60, H 4.35. Found C 23.41, H 4.21%.
[17] E. S. Kozlov, L. G. Dubenko, and A. P. Marchenko, *Zh. Obshch. Khim*., **50,** 2672 (1980).
[18] A. A. Prishchenko, A. V. Gromov, M. I. Kadyko, and I. P. Lutsenko, *Zh. Obshch. Khim*., **54,** 2517 (1984).
[19] D. D. Perrin, W. L. F. Armarego, and D. R. Perrin, *Purification of Laboratory Chemicals* (Pergamon Press, Oxford, 1966).