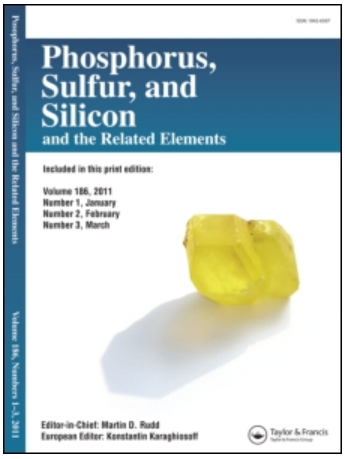

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THE ISOMERIZATION/CHLORINATION OF O,O-DIALKYL PHENYLTHIOPHOSPHONATES WITH PHOSPHORUS OXYCHLORIDE—A NEW CONVENIENT SYNTHESIS OF S-ALKYL PHENYLTHIOPHOSPHONIC ACID DERIVATIVES

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THE ISOMERIZATION/CHLORINATION OF O,O-DIALKYL PHENYLTHIOPHOSPHONATES WITH PHOSPHORUS OXYCHLORIDE—A NEW CONVENIENT SYNTHESIS OF S-ALKYL PHENYLTHIOPHOSPHONIC ACID DERIVATIVES

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A new method for the synthesis of S-alkyl phenylthiophosphonic acid derivatives is reported. The chlorination of O,O-dialkyl phenylthiophosphonates with phosphorus oxychloride proceeds with isomerization to give S-alkyl phenylthiophosphonochloridates, which react further with various nucleophiles in the presence of triethylamine to give the title compounds.

Key words: Phosphonothionate; phosphonothiolate; phosphonodithiolate; phosphonamidothiolate; isomerization; chlorination.

INTRODUCTION

As is well known, S-alkyl thiophosphoric acid derivatives possess extensive biological, especially insecticidal activity. In the synthetic methods reported for these compounds, mercaptans or their derivatives were generally used as starting materials[1–7] or they were prepared by reacting salts of thiophosphoric acid with an alkyl bromide.[8–11]

In the previous paper,[12–15] we reported that when O,O-dialkyl thiophosphoric acid derivatives 1 are chlorinated with phosphorus oxychloride, the isomerization of P=S to P—S bond occurs at the same time. This isomerization/chlorination can convert an achiral phosphorus atom into a chiral phosphorus atom to give S-alkyl thiophosphorochloridate 2, which reacts further with various nucleophiles, NuH 4, in the presence of a base to obtain a varied S-alkyl thiophosphoric acid derivative 5. Thus, this constitutes a new convenient method for the synthesis of this type of compound possessing extensive biological activity.

Recently, we have found that the isomerization/chlorination of O,O-dialkyl phenylthiophosphonates 6 with phosphorus oxychloride can also give the desired products, S-alkyl phenylthiophosphono chloridates 7 and O-alkyl phosphorodichloridates 3. In this paper, we report that the isomerization/chlorination is used for the synthesis of S-alkyl phenylthiophosphonic acid derivatives 8.

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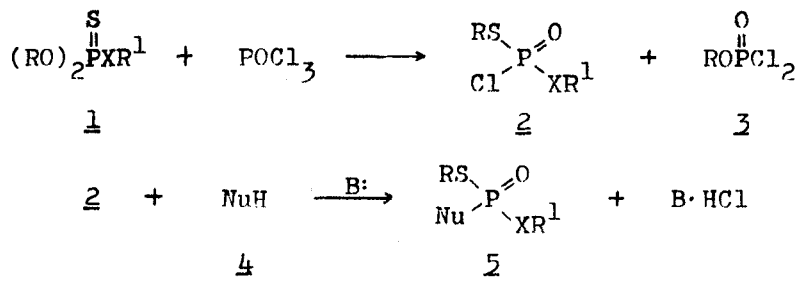


R = C_{1-4} Alkyl
X = O, S, NR^1
R^1 = Alkyl, Aryl
Nu = Alkoxy, Aryloxy, Alkylthio, Arylthio, Amino

RESULTS AND DISCUSSION

Compounds 6 react with equivalent amounts of phosphorus oxychloride at 55–90°C. It takes 1.5–17 h for 6 to disappear (TLC control). The reaction time and temperature increases with increasing number of carbon atoms in the R group. Compared with the relative thiophosphate, the reaction of the thiophosphonate 6 with phosphorus oxychloride occurs easily, thus, when the R group equals a long chain alkyl over C_4 and 2-chloroethyl, the desired product 7 can also be obtained, but in the thiophosphate case, this is not possible, the R group only equals a alkyl with C_{1-4}. However, with phenylthiophosphonate or thiophosphate, when the R

TABLE I
Compounds 8 prepared

8	n_D^{25} or mp (°C)	Yield (%)[a]	Molecular Formula or Lit. Data	Elemental analyses C% Calc.	C% Found	H% Calc.	H% Found
a	1.5435	54.3	bp 145–6/5 mm Lit. 16				
b	1.6029	55.2	$C_{13}H_{12}ClO_2PS$ (298.7)	52.27	52.25	4.05	3.93
c	1.5430	53.2	$C_{13}H_{22}NOPS$ (271.4)	57.54	57.84	8.17	8.37
d	1.5923	50.5	$C_{16}H_{16}Cl_3O_2PS$ (409.7)	46.91	46.97	3.94	3.85
e	1.5815	45.6	$C_{17}H_{21}OPS_2$ (336.5)	60.69	60.88	6.29	6.21
f	1.5279	42.5	$C_{12}H_{19}O_2PS$ (258.3)	55.80	55.52	7.41	7.38
g	1.5503	46.1	$C_{10}H_{14}ClO_2PS$ (264.7)	45.37	45.29	5.33	5.37
h	1.5098	47.8	$C_{14}H_{23}O_2PS$ (286.4)	58.72	58.96	8.10	8.32
i	33–35	57.6	$C_{13}H_{10}Cl_3O_2PS$ (367.6)	42.47	42.56	2.74	2.73
j	1.6068	44.0	$C_{14}H_{12}Cl_3O_2PS$ (381.6)	44.02	43.82	3.17	3.05
k	1.6061	62.0	$C_{14}H_{12}Cl_3O_2PS$ (381.6)	44.02	44.16	3.17	3.27
l	55–56	50.0	$C_{14}H_{10}Cl_5O_2PS$ (450.5)	37.32	37.29	2.24	2.24
m	1.5985	50.2	$C_{15}H_{14}Cl_3O_2PS$ (395.7)	45.53	45.39	3.57	3.48
n	1.6121	45.3	$C_{14}H_{11}Cl_4O_2PS$ (416.1)	40.41	40.72	2.66	2.79

[a]Total yield of two-step reactions based on 6.

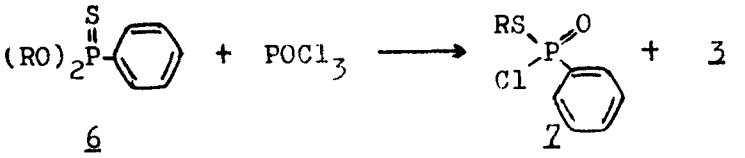
TABLE II
IR and ^{1}H-NMR data of compounds 8

8	IR (film or KBr) (cm^{-1}) P—S—C	P=O	P—Ph	^{1}H-NMR ($CDCl_3$/TMS) (ppm), J_{PH} (Hz)
a	569	1224	1437	1.08 (t, 3H, CH_3), 1.19 (t, 3H, CH_3), 2.53 (dq, 2H, J = 14.0, CH_2S), 3.99 (dq, 2H, J = 9.0, CH_2O), 7.00–7.73 (m, $5H_{arom}$)
b	565	1231	1437	2.00 (d, 3H, J = 13.5, CH_3S), 7.00–7.90 (m, $9H_{arom}$)
c	565	1210	1432	0.81 (t, 3H, CH_3), 0.92 (t, 6H, $2CH_3$), 1.50 (m, 2H, CH_2), 2.47 (m, 2H, CH_2S), 2.90 (dq, 4H, J = 19, $2CH_2N$), 7.13–7.83 (m, $5H_{arom}$)
d	580	1236	1439	0.72 (t, 3H, CH_3), 0.97–1.66 (m, 4H, CH_2—CH_2), 2.70 (dt, 2H, J = 13.2, CH_2S), 6.87–8.06 (m, $7H_{arom}$)
e	564	1201	1435	0.68 (t, 3H, CH_3), 0.90–1.70 (m, 4H, CH_2CH_2), 2.69 (dt, 2H, J = 13.2, CH_2S), 3.75 (d, 2H, J = 11.6, CH_2S), 6.80–7.82 (m, $5H_{arom}$)
f	570	1232	1434	0.78 (d, 6H, $2CH_3$), 1.10–1.67 (m, 3H, CH_2CH), 2.58 (dt, 2H, J = 13.0, CH_2S), 3.65 (d, 3H, J = 12.0, CH_3O), 7.10–7.80 (m, $5H_{arom}$)
g	563	1226	1434	1.44 (t, 3H, CH_3), 3.08 (dt, 2H, J = 14.4, CH_2S), 3.56 (t, 2H, CH_2Cl), 4.28 (dq, 2H, J = 9.0, CH_2O), 7.32–8.04 (m, $5H_{arom}$)
h	567	1223	1435	0.86 (t, 3H, CH_3), 1.18–1.68 (m, 8H, $(CH_2)_4$), 1.42 (t, 3H, CH_3), 2.74 (m, 2H, CH_2S), 4.28 (dq, 2H, J = 9.0, CH_2O), 7.33–8.10 (m, $5H_{arom}$)
i	580	1235	1451	2.20 (d, 3H, J = 15.3, CH_3S), 7.52–8.16 (m, $7H_{arom}$)
j	580	1233	1448	1.16 (t, 3H, CH_3), 2.80 (dq, 2H, J = 14.4, CH_2S), 7.50–8.16 (m, $7H_{arom}$)
k	580	1235	1451	1.16 (t, 3H, CH_3), 2.76 (dq, 2H, J = 14.4, CH_2S), 7.36–8.04 (m, $7H_{arom}$)
l	576	1227	1434	1.24 (t, 3H, CH_3), 2.86 (dq, 2H, J = 15.1, CH_2S), 7.06–8.24 (m, $5H_{arom}$)
m	581	1234	1449	0.80 (t, 3H, CH_3), 1.40 (m, 2H, CH_2), 2.67 (dt, 2H, J = 13.7, CH_2S), 7.44–8.04 (m, $7H_{arom}$)
n	578	1235	1453	3.14 (dt, 2H, J = 14.8, CH_2S), 3.50 (t, 2H, CH_2Cl), 7.46–8.08 (m, $7H_{arom}$)

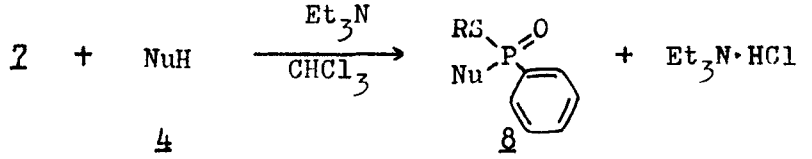
group equals a bulky group, e.g., isopropyl or t-butyl, the desired product 7 or 2 can not be always formed.

Separation of product 7 by column chromatography on silica gel was attempted and was unsuccessful because of decomposition of 7 on silica gel, but in the thiophosphate case, the product 2 (X = NR^1) was successfully separated and identified.[14]

After removal of the by-products 3 under reduced pressure, products 7, which were not purified, were reacted directly with various nucleophiles 4, e.g., alcohols, phenols, mercaptans, amines, in the presence of triethylamine to give S-alkyl O-alkyl(aryl)phenylphosphonothiolates 8a,b,d,f–n, S-alkyl S-alkyl phenylphosphonodithiolate 8e and S-alkyl N,N-diethyl phenylphosphonamidothiolate 8c, respectively. Crude products 8 can be purified by column chromatography on silica gel. Using the above reactions, fourteen compounds 8 have been prepared (Tables I and II), only 8a has been previously reported in the literature.[16]



6	R	t (°C)	Time (h)	6	R	t (°C)	Time (h)
a	Me	55	1.5	e	i-Amyl	90	10.5
b	Et	70	6	g	Hexyl	90	6
c	Pr	80	7.5	f	$ClCH_2CH_2$	85	17
d	Bu	90	7				



8	R	Nu	8	R	Nu
a	Et	EtO	h	Hexyl	EtO
b	Me	4-ClC_6H_4O	i	Me	2,4,5-$Cl_3C_6H_2O$
c	Pr	Et_2N	j	Et	2,4,5-$Cl_3C_6H_2O$
d	Bu	2,4,5-$Cl_3C_6H_2O$	k	Et	2,3,5-$Cl_3C_6H_2O$
e	Bu	$PhCH_2S$	l	Et	C_6Cl_5O
f	i-Amyl	MeO	m	Pr	2,4,5-$Cl_3C_6H_2O$
g	$ClCH_2CH_2$	EtO	n	$ClCH_2CH_2$	2,4,5-$Cl_3C_6H_2O$

The main advantage of this synthetic method is that 0,0-dialkyl phenylthiophosphonates 6 obtained by using cheap low molecular weight alcohols, are used as starting materials, it avoids the use of expensive and foul smelling mercaptans or alkyl bromides.

EXPERIMENTAL

All temperatures were uncorrected. Melting points were determined with Yanaco MP-500 apparatus. IR spectra were recorded on Shimadzu IR-435 spectrophotometer as thin films or KBr tablet. ^{1}H-NMR spectra were measured on a JEOL FX-90Q instrument at 90 MHZ, using TMS as an internal standard and $CDCl_3$ as the solvent. Column chromatography was performed on silica gel (200–300 mesh) using petroleum ether (bp 60–90°C)/EtOAc (5:1 or 3:1) as the eluent.

1. O,O-Dialkyl phenylthiophosphonates 6: Compounds 6 are synthesized according to a general procedure, by reacting phenylthiophosphonodichloride with a suitable alcohol in the presence of triethylamine at 20–60°C for 2–4 h, or with a sodium alkoxide at 15–40°C for 2–3 h. The crude products 6 are purified by distillation at reduced pressure or column chromatography on silica gel (Table III).

TABLE III
Data of compounds 6 prepared

6	R	bp (°C/mm)	n_D^{25}	Yield %
a	Me	87–88/0.3	1.5570	69.3
b	Et	90–93/0.2	1.5353	87.4
c	Pr	109–112/0.15	1.5250	77.0
d	Bu	133–136/0.3	1.5177	85.3
e	i-Amyl		1.5105	82.8
f	Hexyl		1.5028	62.4
g	$ClCH_2CH_2$		1.5370	64.2

2. S-Ethyl O-ethyl phenylphosphonothiolate 8a: Typical procedure: A mixture of O,O-diethyl phenylthiophosphonate 6b (4.60 g, 20 mmol) and $POCl_3$ (3.07 g, 20 mmol) is heated at 70°C for 6 h with stirring until 6b has disappeared from the reaction mixture (TLC control, solvent system: petroleum ether (bp 60–90°C/Et_2O, 10:1). After removal of the by-product, O-ethyl phosphorodichloride 3 (R=Et) under vacuum (1 mm) at 70°C (oil bath), the residue is dissolved in $CHCl_3$ (15 mL). To the chloroform solution a mixture of EtOH (5 mL) and Et_3N (3.50 g, 35 mmol) is added dropwise at 20°C. The reaction mixture is stirred at 45–50°C for 5h, then cooled to r.t. and poured into cold water (25 mL). The organic layer is separated, washed with water (15 mL) and dried ($MgSO_4$). After removal of the solvent the crude product 8a is purified by using column chromatography on silica gel; yield: 2.50 g (54.3%, based on 6b), n_D^{25} 1.5435 (Lit.[16]: bp 145–146°C/5 mm) (Tables I and II).

3. S-Butyl S-benzyl phenylphosphonodithiolate 8e: Similarly, a mixture of 6d (4.29 g, 15 mmol) and $POCl_3$ (2.30 g, 15 mmol) is heated at 90°C for 7 h. After removal of the by-product 3 (R=Bu) in vacuo, the residue is reacted with benzyl mercaptan (1.86 g, 15 mmol) in the presence of Et_3N (2.50 g, 25 mmol) at 50°C for 5 h. The crude product 8e is purified by column chromatography on silica gel; yield: 2.30 g (45.6%, based on 6d), n_D^{25} 1.5815 (Tables I and II).

4. S-Propyl N,N-diethyl phenylphosphonamidothiolate 8c: Similarly, a mixture of 6c (6.71 g, 2 mmol) and $POCl_3$ (3.99 g, 26 mmol) is heated at 80°C for 7.5 h. After removal of the by-product 3 (R=Pr), the residue is treated with excess diethylamine in chloroform. The crude product 8c is purified by column chromatography on silica gel; yield: 3.91 g (55.4%, based on 6c), n_D^{25} 1.5430 (Tables I and II).

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REFERENCES

1. K. Kobayashi, M. Eto, Y. Oshima, T. Hirano, T. Hisoi and S. Wakamori, *Bochu-Kagaku*, **34,** 165 (1969); *C.A.*, **72,** 100196 (1970).
2. S. Kishino, A. Shimomatsu and K. Shinokawa, Japan Patent, 7620506 (1976); *C.A.*, **86,** 16418 (1977).
3. Sumitomo Chemical Co., Ltd., Japan Patent, 8561586 (1985); *C.A.*, **103,** 123707 (1985).
4. K. A. Petrov, G. A. Sokolskii and B. M. Polees, *Zh. Obshch. Khim.*, **26,** 3381 (1956); *C.A.*, **51,** 9473 (1957).
5. H. Bayer and W. S. Hurt, German Patent, 2635931 (1977); *C.A.*, **87,** 52755 (1977).
6. Japan Specialty Agric. Chemicals Mfg. Co., Ltd., Japan Patent, 80139394 (1980); *C.A.*, **94,** 120852 (1981).
7. J. Saito, A. Kudamatsu, T. Kumi and S. Tsuboi, German Patent, 2732930 (1978); *C.A.*, **88,** 136133 (1978).
8. A. A. Oswald and P. L. Valint, U.S. Patent, 4075332 (1978); *C.A.*, **89,** 42423 (1978).
9. S. Kishino, A. Shimomatsu and K. Shiokawa, Japan Patent, 78111042 (1978); *C.A.*, **90,** 87005 (1979).
10. R. Buerstinghaus, W. Seufert and K. Kiehs, German Patent, 3316180 (1984); *C.A.*, **102,** 185271 (1985).

11. Sumitomo Chemical Co., Ltd., Japan Patent, 8558995 (1985); *C.A.*, **103,** 88086 (1985).
12. C. C. Tang, G. P. Wu and G. Z. Zhang, *Synthesis*, 454 (1991).
13. C. C. Tang, G. P. Wu, G. Z. Zhang, X. R. Chen, F. C. Bi, W. L. Wang and L. H. Zhu, *Chem. J. Chinese Univs.*, **12,** 1478 (1991).
14. C. C. Tang and G. P. Wu, *Chinese Chem. Lett.*, **3,** 593 (1992).
15. C. C. Tang and G. P. Wu, *ibid.*, **3,** 783 (1992).
16. R. S. Edmundson (Ed.), "Dictionary of Organophosphorus Compounds," (Chapman and Hall, London, 1988), P. 686.