Heteroatom Chemistry
Volume 10, Number 6, 1999

Synthesis and Insecticidal Activity of O-Aryl O-(1,2,2,2-tetrachloroethyl)phosphoramidothioates and Their Thiophosphoric Hydrazides [1]

Liang-Nian He,[1] Ming-Wu Ding,[1] Sheng-Biao Li,[1] Qing-Chun Zhou,[1] Yan-Ping Luo,[1] Tian-Jie Wu,[2] Xiao-Peng Liu,[2] and Fei Cai[2]

Institute of Organic Synthesis, Central China Normal University, Wuhan 430079, People's Republic of China

Center of Analysis and Testing, Central China Normal University, Wuhan 430079, People's Republic of China

Received 4 December 1998; revised 10 April 1999

ABSTRACT: *O-Aryl O-(1,2,2,2-tetrachoroethyl)phosphoramidothioates* **3a–h** *and their thiophosphoric hydrazides* **4a–e** *were synthesized by reactions of O-aryl O-(1,2,2,2-tetrachoroethyl)thiophosphorochloridates* **2** *with amines and hydrazines, respectively. Their structures were characterized by elemental analysis IR* ^1H *NMR,* ^{31}P *NMR, and MS. The O-aryl O-(1,2,2,2-tetrachloroethyl)thiophosphoric hydrazides* **4a–d** *($R^2 = H$) can be transformed into 1,3,4,2-oxadiazaphospholanes* **5a–d** *by the reaction of triethylamine. The results of preliminary bioassays indicated that some of the title compounds have good insecticidal activities against nematodes (Meloidogyne spp.) and pea aphids.* © 1999 John Wiley & Sons, Inc. Heteroatom Chem 10: 441–445, 1999

INTRODUCTION

Several literature references [2–4] have disclosed that *O,O*-diethyl *O*-(1,2,2,2-terachloroethyl)phosphorothioate has high activity against certain insect larvae that inhabit the soil and feed on growing plants, and also has a persistent effectiveness over an extended period of time. It was also reported that phosphoryl hydrazines possess good biological activity [5,6]. The synthesis of biologically active phosphorus compounds has been of continuing interest to us for a dozen years [7–10]. We have found that *β*-(1,3-benzothiazole-2-)phosphoric hydrazides have good inhibitory effects against tobacco mosaic virus and soil insects, such as rootworms, cutworms, and wireworms [6,8,11]. In this article, we report the synthesis of new *O*-aryl *O*-(1,2,2,2-tetrachoroethyl) phosphoramidothioates **3a–h** and their thiophosphoric hydrazides **4a–e**. The results of insecticidal activity are also presented.

RESULTS AND DISCUSSION

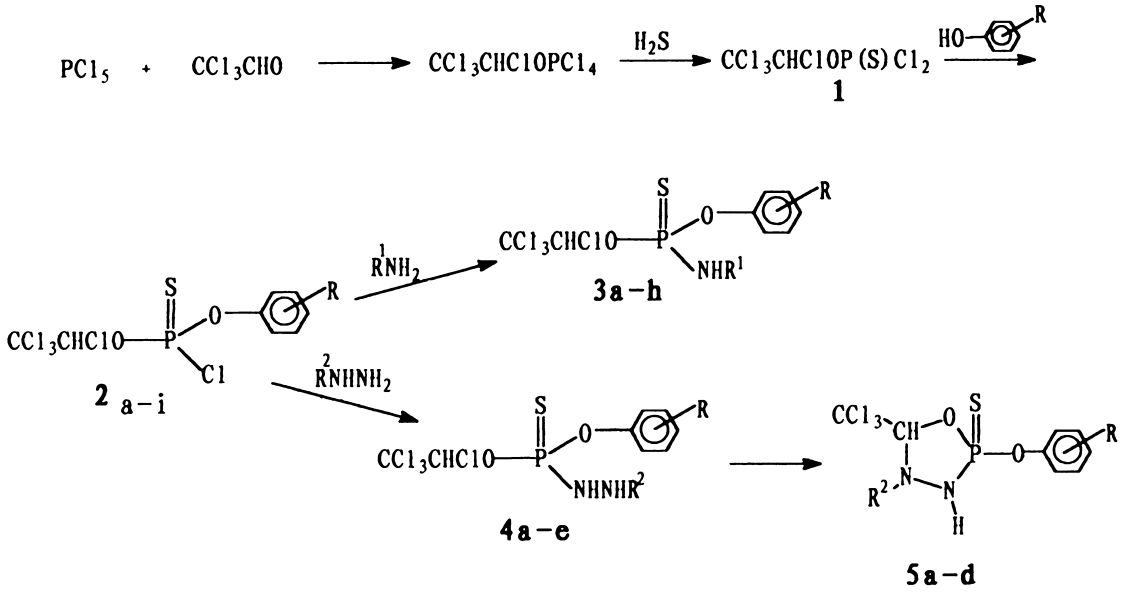
The title compounds, O-aryl O-(1,2,2,2-tetrachoroethyl)phosphoramidothioates **3a–h** and their thiophosphoric hydrazides **4a–e**, can be prepared by one of the conventional methods of preparing thiophosphorus acid ester amides and phosphoric hydrazides (Scheme 1). Chloral was treated with phosphorus pentachloride to give $CCl_3CHClOPCl_4$, which was

Correspondence to: Liang-Nian He.
Contract Grant Sponsor: National Science Foundation of China.
Contract Grant Sponsor: NSF of Hubei Province.
Contract Grant Sponsor: Dawn Plan of Science and Technology for Young Scientists of Wuhan City.
 CCC 1042-7163/99/060441-05

then treated with hydrogen sulfide to give the intermediate **1**, *O*-(1,2,2,2-tetrachoroethyl) phosphorothioic dichloride. These were useful intermediates for the production of a variety of *O*-(1,2,2,2-tetrachloroethyl)thiophosphoryl compounds. The yield was about 70% when tetrabutylammonium chloride was used as a phase transfer catalyst [12]. This dichloridate was treated with phenols to form the chloridates **2a–i**, which reacted with amines or hydrazines to give the desired compounds presented here, *O*-aryl *O*-(1,2,2,2-tetrachoroethyl) phosphoramidothioates **3a–h** and their thiophosphoric hydrazides **4a–e**, respectively.

Each compound **4a–d** ($R^2 = H$) was treated with an equivalent amount of triethylamine in anhydrous chloroform at 60°C under dry nitrogen for 1 hour to give a product of intramolecular cyclization, 1,3,4,2-oxadiazaphospholane **5a–d** in a significant yield as shown in Table 2. When **4e** ($R^2 = Ph$) was reacted with triethylamine under the same conditions, a product of intramolecular cyclization was not isolated. When the reaction was carried out at higher temperature, a very complex reaction mixture was obtained, but no pure product was isolated and characterized.

The structures of the new compounds **3, 4**, and **5** were confirmed by IR, ^{1}H NMR, ^{31}P NMR, and MS spectroscopic studies, and by elemental analysis. The data are listed in Tables 2 and 3. The IR spectra of compounds **3, 4**, and **5** showed normal stretching absorption bands, indicating the existence of the N–H (3340–3400 cm^{-1}), P=S (660–690 cm^{-1}), and P–O–$CHClCCl_3$ (1190–1250 cm^{-1}) groups. In the ^{1}H NMR spectra of compounds **4a–d**, the protons of the



SCHEME 1

TABLE 1 The Experimental Data of Compounds **1**

				Elemental Analysis Found (*Calcd.*)		
No	*R*	*M.P.* (°*C*)/n_D^{20}	*Yield* (%)	*C* (%)	*H* (%)	*N* (%)
2a	H	1.6241	72	25.62(25.81)	1.42(1.61)	
2b	4-NO_2	47–49	68	23.28(23.02)	1.40(1.20)	3.67(3.36)
2c	4-OCH_3	1.6326	69	27.02(26.87)	2.04(1.99)	
2d	4-Me	1.6341	66	28.06(27.98)	2.32(2.07)	
2c	3-Me	1.6346	70	27.82(27.98)	2.26(2.07)	
2f	4-Cl	1.6249	77	23.71(23.65)	1.26(1.23)	
2g	3-Cl	1.6251	71	23.96(23.65)	1.41(1.23)	
2h	4-Br	1.6323	66	21.71(21.33)	1.26(1.11)	
2i	2,4,5-Cl_3	43–45	63	20.42(20.23)	0.89(0.65)	

TABLE 2 The Physical Data and Elemental Analysis for New Compounds **3, 4** and **5**

No	R	R^1	R^2	*Yield* (%)	*MP* (°C)/n_D^{20}	*Elemental Analysis Found* (*Calcd.*)			*MS* (*M*, %$^+$)
						C (%)	*H* (%)	*N* (%)	
3a	H	i-Pr		81	1.7264	40.50(40.80)	3.72(3.58)	3.53(3.55)	
3b	4-NO_2	i-Pr		75	66–68	29.92(30.00)	2.75(2.95)	6.54(6.36)	440(3.2)
3c	4-OCH_3	Et		87	1.7024	31.53(31.21)	3.10(3.31)	3.40(3.31)	
3d	4-OCH_3	H		79	1.7006	27.60(27.34)	2.26(2.53)	3.66(3.54)	
3e	4-Cl	Et		86	1.7020	28.54(28.79)	2.68(2.64)	3.67(3.36)	415(7.3)
3f	4-Cl	i-Pr		81	1.7016	30.70(30.76)	3.36(3.03)	3.50(3.26)	
3g	3-Cl	i-Pr		87	1.7926	30.52(30.76)	3.06(3.03)	3.54(3.26)	
3h	4-NO_2	Et		80	64–65	28.41(28.04)	2.56(2.34)	6.54(6.62)	
4a	H		H	67	43–45	25.93(26.08)	2.43(2.45)	7.37(7.61)	368(7.5)
4b	3-Me		H	73	50–52	28.37(28.27)	2.58(2.88)	7.52(7.33)	
4c	4-NO_2		H	68	62–64	23.50(23.24)	2.06(1.93)	10.42(10.17)	
4d	4-OCH_3		H	70	57–59	27.41(27.14)	2.91(2.76)	6.96(7.04)	
4e	4-OCH_3		Ph	79	88–90	37.81(37.97)	3.01(3.16)	6.11(5.91)	474(9.6)
5a	H		H	67	46–48	29.05(28.92)	2.39(2.41)	8.31(8.43)	
5b	3-Me		H	61	57–59	31.42(31.21)	3.06(2.89)	8.07(8.09)	346(5.3)
5c	4-NO_2		H	70	65–67	25.72(25.46)	1.89(1.86)	11.40(11.14)	
5d	4-OCH_3		H	74	61–63	30.21(29.83)	2.92(2.76)	7.71(7.73)	362(6.2)

TABLE 3 IR, ^{1}H NMR, and ^{31}P NMR Data of New Compounds **3, 4**, and **5**

No	*IR* (cm^{-1})	^{1}*H NMR* (*$CDCl_3$*, δ)	^{31}*P NMR* (*$CDCl_3$*, δ)
3a	690, 1215, 3300	7.10–7.40 (m, 5H),6.45–6.55 (dd, 1H), 3.75 (s, 1H) 2.80–3.30 (m, 1H), 1.20 (m, 6H)	69.57
3b	690, 1220, 3350	7.40–8.40 (m, 4H), 6.45–6.65 (dd, 1H), 3.80 (s, 1H) 3.55 (s, 1H), 1.20 (m, 6H)	
3c	690, 1190, 3350	6.85–7.20 (m, 4H), 6.65–6.80 (dd, 1H), 3.80 (s, 1H) 3.50 (m, 2H), 3.30 (s, 1H), 1.20 (m, 6H)	65.49
3d	700, 1210, 3340	6.8–7.20 (m, 4H), 6.45–6.65 (dd, 1H), 3.80 (m, 3H) 3.50 (s, 1H)	66.78
3e	690, 1190, 3340	7.10–7.40 (m, 4H), 6.80 (dd, 1H), 3.50 (m, 1H) 3.25 (m, 1H), 1.30 (t, 3H)	
3f	680, 1200, 3340	7.10–7.40 (m, 4H), 6.45–6.85 (dd, 1H), 3.80 (s, 1H) 3.55 (m, 1H), 1.30 (m, 6H)	
3g	690, 1210, 3340	7.20–7.40 (m, 4H), 6.45–6.65 (dd, 1H), 3.70 (s, 1H) 3.30 (m, 1H), 1.15–1.40 (m, 6H)	64.54
3h	660, 1200, 3340	7.28–7.68 (dd, 4H), 6.92 (dd, 1H), 3.52 (m, 2H) 1.21 (m, 3H)	73.97
4a	690, 1250, 3350	7.10–7.40 (m, 5H), 6.66–6.71 (dd, 1H), 3.42 (m, 3H)	
4b	670, 1230, 3350	6.70–7.10 (m, 4H), 6.65–6.68 (dd, 1H), 4.10 (s, 3H) 2.35 (s, 3H)	58.64
4c	690, 1253, 3400	7.80–8.20 (m, 4H), 6.64 (dd, 1H), 4.02 (s, 3H)	59.72
4d	685, 1240, 3400	7.20–7.40 (m, 4H), 6.65–6.73 (dd, 1H), 4.16 (s, 3H) 3.80 (s, 3H)	
4e	690, 1250, 3300	6.76–6.90 (dd, 8H), 6.50–6.58 (dd, 1H), 5.27–5.50 (s, 2H)	60.34
5a	690, 1230, 3400	7.20–7.40 (m, 5H), 6.60–6.65 (m, 1H), 3.30 (s, 1H) 2.25–2.35 (s, 3H)	
5b	680, 1240, 3450	7.00–7.20 (m, 4H), 6.50–6.55 (m, 1H), 3.05 (s, 1H) 2.30 (s, 3H), 2.10 (s, 1H)	57.58
5c	670, 1230, 3400	7.80–8.20 (m, 4H), 6.55–6.68 (m, 1H), 3.30–3.50 (s, 1H), 2.30–2.45 (s, 1H)	
5d	690, 1210, 3400	7.00–7.20 (m, 4H), 6.60–6.65 (m, 1H), 3.80 (s, 3H), 3.25 (s, 1H), 2.25 (s, 1H)	58.26

NH-NH_2 moiety appeared as a broad peak in the range of δ 3.40–4.40. Compound **4e** showed signals at δ = 5.27 and 5.50 (PhNH–NH). The protons in NH–NH of each compound **5** showed broad peaks at δ 2.2 and δ 3.4. The peaks of the mobile protons of the N–H compounds **3, 4**, and **5** disappeared when deuterated. The proton in CCl_3CHClO of each compound **3** or **4** appeared as two doublet peaks with $^3J_{POCH}$ = 11–15 Hz in the range of δ 6.45–6.80. Compounds **3, 4**, and **5** gave ^{31}P NMR chemical shifts in the range of δ 57.58–73.97, which were in accordance with other compounds containing the -NH-P(S)-NH- moiety [13].

The EI-MS spectra of compounds **3, 4**, and **5** demonstrated the existence of the weak molecular ion peaks (M^+). The fragmentation ions were consistent with their structures and can be clearly assigned. For example, compound **4a**, under electron

impact, gave the molecular ion peak *m/z* (%): 368(1.50), and the other conspicuous peaks: 277(3.80), 243(19.0), 207(11.50), 111(93.10), 95(39.00), 83(100.00). Compound **5b**, *m/z* (%): 346(M^+, 1.32), 311(2.50), 228(60.74), 254(22.48), 137(87.39), 117(18.79), 57(100.00).

The insecticidal activities of the title compounds **3a–h** and **4a–c** were tested as done previously [2,3]. The results are given in Table 4. The effectiveness against nematodes was expressed in terms of an ABC system wherein A = 0–20% infestation, B = 21–50%, and C = 51–100% infestation. The preliminary bioassays showed that some of the title compounds **3** and **4** display good activities against pea aphids and nematodes (*Meloidogyne* spp.).

EXPERIMENTAL

Melting points were uncorrected, and ^{1}H NMR and ^{31}P-NMR spectra were recorded on a Varian XL-200 MHz spectrometer. Tetramethylsilicon (TMS) was used as an internal standard for ^{1}H NMR, and 85% H_3PO_4 was used as an external standard for the ^{31}P NMR. Mass spectra were measured on a HP 5988A spectrometer. The IR spectra were measured by using a SHIMADZU-408 instrument. Elemental analysis was performed with a PE-2400 elementary analyzer. Column chromatography was performed on a silica gel II (10–40 μ, Hai Yang Chemical Factory of Qingdao). All solvents and materials were reagent grade and purified as required. *O*-(1,2,2,2-Tetrachoroethyl)phosphorothioic dichloride **1** was synthesized as described in the literature [12,14].

TABLE 4 Insecticidal Activity for New Compounds **3, 4**, and **5**

No.	*Concn* ($10^6 \times$ *C/mol* $\cdot$ L^{-1})	*Mortality* (%) *against pea Aphids*	*Effectiveness against Meloidogyne spp.*
3a	100	26.5	C
3b	100	40.0	C
3c	100	33.3	B
3d	100	16.7	C
3e	100	36.4	C
3f	100	25.6	C
3g	100	80.1	B
3h	100	10.5	C
4a	100	55.1	B
4b	100	78.5	B
4c	100	52.9	B
4d	100	63.4	B
4e	100	75.3	A

*Preparation of O-Aryl O-(1,2,2,2-Tetrachoroethyl)*phosphorothioic Chlorides **2a–i**

A solution of each phenol (5.0 mmol) in 5 ml of chloroform and 5.0 mmol of triethylamine was added dropwise to a mixture of each compound **1** and 10 ml of chloroform at −10°C with stirring. The reactants were stirred at room temperature for 3 hours. After filtration, the filtrate was washed with ice water and the organic phase was dried over anhydrous magnesium sulfate. It was then evaporated under reduced pressure, followed by purifying the residue on a silica gel column using a dry ethyl ether/petroleum ether mixture (1:1) to yield each **2**. The physical data and elemental analysis for compounds **2** are listed in Table 1.

General Procedure for Synthesis of Compounds **3a–h**

To a solution of each compound **2** (5.0 mmol) in 15 ml of chloroform, each amine was added dropwise (10 mmol) at room temperature. The reaction mixture was stirred for 2 hours, filtered, and the filtrate was washed with ice water. The separated organic phase was dried, evaporated, and the residue was purified on a silica gel column using a petroleum ether/dry ethyl ether mixture (1:2) as an eluent. The results and spectral data for compounds **3** are tabulated in Tables 2 and 3.

General Procedure for Synthesis of Compounds **4a–e**

To a mixture of 5.0 mmol of each compound **2**, 5.0 mmol of each hydrazine, and 5 ml of chloroform, 5.0 mmol of triethylamine was added dropwise. The reactants were stirred at 30°C for 2 hours. After filtration, the mixture was washed with ice water. The organic layer was dried with anhydrous magnesium sulfate. The solvent was removed, and the residue was passed through a short silica gel column with petroleum ether/dry ethyl ether (1:2) as an eluent to give each **4**.

Procedure for Intramolecular Cyclizations of **4a–d** *and Preparation of 1,3,4,2-Oxadiazaphospholanes* **5a–d**

Triethylamine (2.0 mmol) was added dropwise to a solution of each compound **4** in 15 ml of chloroform at −5 to 0°C with stirring. After 30 minutes, the reaction mixture was warmed slowly and filtered. The filtrate was washed with ice water, and the organic phase was dried with anhydrous magnesium sulfate.

After the solvent was removed, the residue was separated with petroleum ether/ethyl ether (1:1) by being passed through a short silica gel column. After the solvent had been removed, each **5** was obtained.

REFERENCES

[1] This work is considered as part 30 of the series on Studies on Biologically Active Phosphorus Compounds.
[2] Watkinson, I. A. U.S. Patent 4,753,931 1988.
[3] Tieman, C. H.; Eur. Patent 0160344 1985.
[4] Schnell, M.; Erfurt, G.; Zinner, H. J Prakt Chem 1977, 319, 723.
[5] Brown, M. J.; Batch, J. J.; Hawkin, A. F. US Patent 4203932 1980.
[6] Cao, Z. S.; Zhang, J. L. J of Central China Normal University Patent (Nat. Sci.) 1984, 18, 69.
[7] He, L. N.; Li, S. B.; Zhang, J. L. Youji Huaxue 1994, 14, 210.
[8] He, L. N.; Zhang, J. L.; Luo, G. F. J of Central China Normal University (Nat Sci), Monog 1992, 1, 137.
[9] He, L. N.; Zhuo, R. X.; Chen, R. Y.; Zhou, J. Synth Commun 1997, 27, 2853.
[10] He, L. N.; Cai, F.; Chen, R. Y.; Zhou, J.; Phosphorus, Sulfur and Silicon 1997, 130, 65.
[11] He, L. N.; Feng, B.; Huang, T. B.; Zhou, Q. C.; Zhang, J. L.; Phosphorus, Sulfur and Silicon 1999, 148, 156.
[12] He, L. N.; Cai, F.; Zhang, J. L.; Fine Chemicals 1997, 14, 60.
[13] Clausen, K.; El-Barary, A. A.; Lawesson, S. O.; Tetrahedron 1981, 37, 1019.
[14] Czerwon, L.; Erfurt, G.; Kochmann, W. Ger (East) Patent 12,096, 1976.