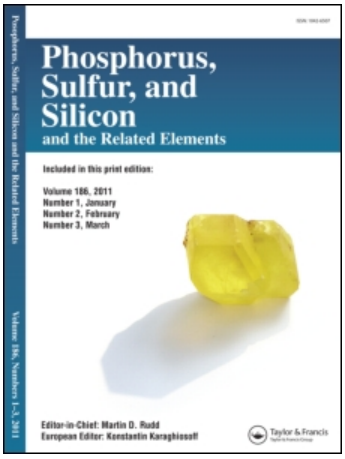

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O-Aryl,S-(ethoxycarbonyl)methyl,N^1-methyl (di)thiophosphorohydrazides (**21**) were prepared in high yield from sodium ethyl 2-mercaptoacetate and O-aryl,N^1-methyl (thio)phosphorochlorohydrazides derived from O-aryl (thio)phosphorodichloridates and methyl hydrazine. The thermal reaction of (**21**) resulted in the formation of hexahydro-1,3,4,2-thiadiazaphosphorin-2,5-dione(or 2-thion-5-ones) (**22**). The X-ray diffraction analysis of (**22a**) indicated the ring containing P atom has a boat conformation.

Key words: Phosphorohydrazide; phosphorohydrazone; hexahydro-1,3,4,2-thiadiazaphosphorin-2,5-dione(or 2-thion-5-ones); crystal structure.

INTRODUCTION

Sulfur, nitrogen and phosphorus-containing heterocyclic compounds have generally received little attention, primarily due to the difficulty of synthesis and their hydrolysis.[1,2] However, it was found that they have insecticidal,[3] fungicidal,[4] herbicidal,[5] antitumoral,[6] and fumigating[7] effects. In addition, a recent report[8] indicated that O,O,N^1,N^2-tetraalkyl phosphorohydrazides have both good insecticidal and acaricidal effects.

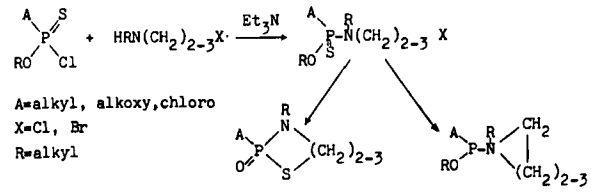
This paper describes methods developed towards the O-aryl-S-(ethoxycarbonyl) methyl, N^1-methyl phosphorohydrazides, their phosphorohydrazones (**24**) and hexahydro-1,3,4,2-thiadiazaphosphorin-2,5-dione (or-2-thion-5-ones) (**22**). The preliminary bioassays indicate that (**21a**) has 100% inhibiting effect against wheat leaf rust (puccinia triticina eriks) at 500 ppm.

RESULTS AND DISCUSSION

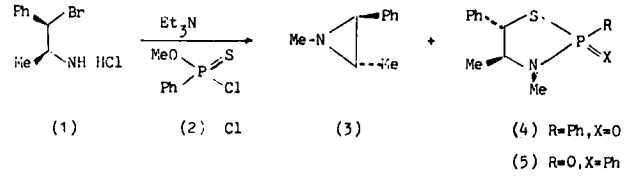
1. Synthesis

The generally applied route[2] for the preparation of 1,3,2-thiazaphospholidines and hexahydro-1,3,2-thiazaphosphorines is outlined in Scheme 1.

It involves the condensation of a halogenated amine with a thiophosphoryl chloride followed by a thermally catalyzed intramolecular reaction. It is,



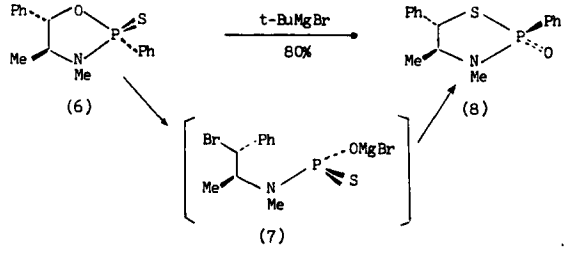
SCHEME 1



SCHEME 2

however, not an effective method because of the cyclization of halogenoamines with themselves. For example (Scheme 2), the treatment of solutions of (**1**) and (**2**) with triethylamine resulted only in (**3**). In the absence of solvent the reaction was highly exothermic and resulted in (**4**) and (**5**) (yield 17%).

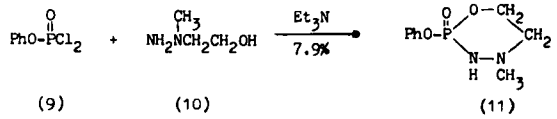
Recently, C. Richard Hall and coworker[9] found that heating of (**6**) with t-butylmagnesium bromide in boiling benzene for several hours resulted in a 80% yield of (**8**). The most likely course of this rearrangement is shown in Scheme 3. This method is also limited because intermediate (**7**) may be effectively formed only if carbon-5 of (**6**) is a reactive benzyl carbon.



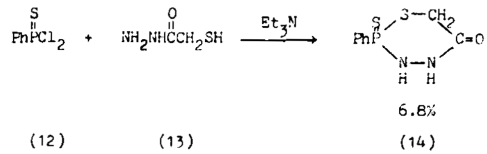
SCHEME 3

L. A. Cates[10] reported that treatment of 1-β-hydroxyethyl)-1-methylhydrazine with thiophosphoryl dichloride (**9**) resulted in (**11**) at a yield of only 7.9% (Scheme 4).

Compound (**14**) was prepared by the reaction of phenylphosphonodichlorothioate (**12**) with equivalent amounts of 2-mercaptoacethydrazide (**13**) and triethylamine in 1,4-dioxane (Scheme 5). Monitoring the reaction mixture by TLC indicated the completion of the reaction and only 6.8% of (**14**) was obtained.

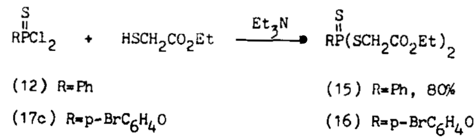


SCHEME 4

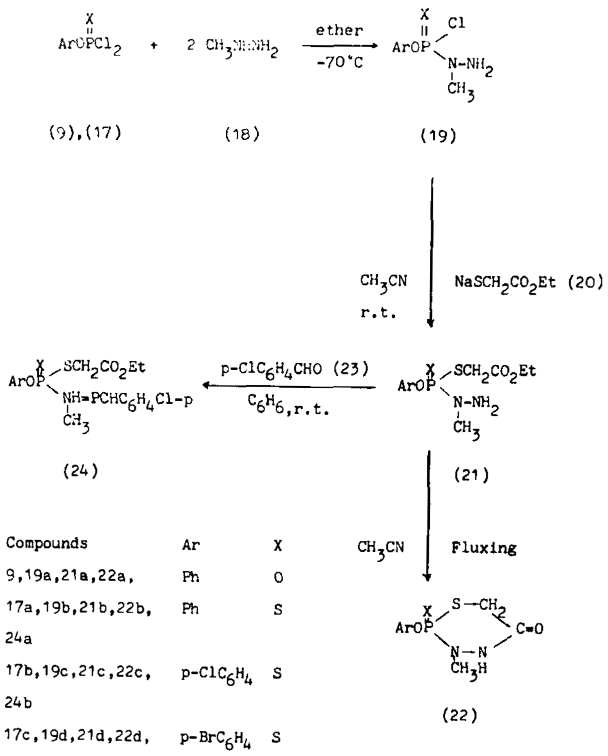


SCHEME 5

An attempt to raise the yield of (**14**) by changing the addition sequence of the reagents and reaction temperature, or increasing the amounts of Et_3N was unsuccessful. It is likely that because of the strong nucleophilicity of the mercapto group two chlorine atoms of the phenylphosphonodichloriate (**12**) were substituted by two mercapto groups in 2-mercaptoacethydrazides (**13**). In another experiment (Scheme 6), the treatment of phenylphosphonodi-chloridate (**12**) at −10 to −5°C with equivalent amounts of 2-mercaptoacetate and triethylamine or the treatment of O-(P-bromo)-phenylthiophosphoryl dichloride (**17c**) at −16°C



SCHEME 6



Compounds	Ar	X
9,19a,21a,22a,	Ph	O
17a,19b,21b,22b, 24a	Ph	S
17b,19c,21c,22c, 24b	p-ClC_6H_4	S
17c,19d,21d,22d, 24c	p-BrC_6H_4	S

SCHEME 7

TABLE I

The prepared data of compounds

Compounds	Molecular formula (M.W.)	Yield[a] (%)	m/e (Int.)	Elementary analysis						M.P. (°C)[b]	Eluents
				Calculated			Found				
				C	H	N	C	H	N		
14	$C_9H_9N_2OPS_2$ (244.27)	6.8	345 (M + H)	39.34	3.71	11.47	39.50	3.82	11.36	154–5	3:1[c]
15	$C_{14}H_{19}O_4PS_3$ (378.45)	81.3		44.43	5.06		44.90	5.13		31–2	1:7[c]
16	$C_{14}H_{18}BrO_5PS$ (473.34)	37.6		35.52	3.83		35.46	4.01			1:5[c]
19a	$C_7H_{10}ClN_2OP$ (220.58)	74.7	94 (100.0), 220 (27.1) 222 (8.3)							53–5	
19b	$C_7H_{10}ClN_3OPS$ (236.58)	71.2	45 (100.0), 236 (48.2) 238 (16.2)							61–2	
19c	$C_7H_9Cl_2N_2OP$ (271.08)	81.5									
19d	$C_7H_9BrClN_2OP$ (315.63)	84.4									
21a	$C_{11}H_{17}N_2O_4PS$ (304.30)	83.3	45 (100.0) 304 (207)	43.42	5.63	9.21	42.99	5.57	9.01		1.5:1–2.0:1 d
21b	$C_{11}H_{17}N_2O_3PS_2$ (320.36)	71.2	275 (100.0) 320 (19.7)	41.24	5.35	8.74	41.38	5.28	8.59		1:2 d

21c	$C_{11}H_{16}ClN_2O_3PS_2$ (354.79)	67.2	46 (100.0) 354 (8.7) 356 (3.6)	37.24	4.55	7.89	37.20	4.56	7.79		1.5:1 d
21d	$C_{11}H_{16}BrN_2O_3PS_2$ (399.24)	84.0	45 (100.0) 398 (1.0) 400 (1.0)	33.09	4.04	7.01	32.90	4.01	6.91		1:1.5 d
22a	$C_9H_{11}N_2O_3PS$ (258.23)	78.1	258 (100.0)	41.83	4.29	10.85	41.82	4.13	10.48	156–8	1:2 d
22b	$C_9H_{11}N_2O_2PS_2$ (274.29)	71.7	274 (100.0)	39.41	4.04	10.21	39.29	4.10	10.47	107–8	6:1-d 1:0
22c	$C_9H_{10}ClN_2O_2PS_2$ (308.72)	73.6	308 (100.0) 310 (402)	35.02	3.27	9.07	34.91	3.25	9.27	152–4	1.5:1 d
22d	$C_9H_{10}BrN_2O_2PS_2$ (353.27)	65.0	118 (100.0) 352 (23.5) 354 (25.0)	30.60	2.85	7.93	30.41	3.16	8.05	163–5	1:1.2-d 1.5:1
24a	$C_{18}H_{20}ClN_2O_3PS_2$ (442.90)	94.8	275 (100.0) 442 (14.9) 444 (5.9)	48.84	4.55	6.32	48.85	4.48	6.46		1:2.5 d
24b	$C_{18}H_{19}Cl_2N_2O_3PS_2$ (477.24)	94.3	309 (100.0) 476 (20.2) 478 (15.6) 480 (3.6)	45.29	4.01	5.87	45.18	4.06	5.91		1:6 d
24c	$C_{18}H_{19}BrClN_2O_3PS_2$ (521.89)	90.0	29 (100.0) 349 (3.2) 353 (8.3) 355 (88)	41.43	3.67	5.37	41.33	3.68	5.45		1:6 d

a. Yields of pure products. b. Uncorrected. c. Eluents of column chromatograph: ethylacetate: petroleum ether (60–90°C). d. Eluents of column chromatograph: ether: petroleum ether (60–90°C).

TABLE II

The data of ^{31}PNMR and ^{1}HNMR spectra

Compounds	^{31}PNMR (ppm)	^{1}HNR (ppm) and J (Hz)
14a		3.16–3.88(septet, 3H, $PSCH_2$ and PNH, 7.36–8.24(m, 5H, C_6H_5), 9.47(s, broad, 1H, NHC═O)
14b		3.12–4.00(octet, 2H, $PSCH_2$), $_A$3.31, $_B$3.81, $^3J_{PSCH}$(A)20.10, $^3J_{PSCH}$(B)23.04, $^2J_{H-H}$11.8), 7.28–8.00(m, 5H, C_6H_5)
15		1.12–1.28(t, 6H, O—C—CH_3, $^3J_{H-H}$7.2), 3.18–3.86(d, 4H, PSCH O, $^2J_{H-H}$O), 3.98–4.21(q, 4H, O—CH_2—C, $^3J_{H-H}$7.2), 7.44–8.24(m, 5H, C_6H_5)
16		1.22–1.37(t, 6H, O—C—CH_3, $^3J_{H-H}$7.2), 3.72–3.92(d, 2H, $PSCH_2$, $^3J_{PSCH}$ O, $^2J_{H-H}$ O), 4.09–4.32(q, 2H, O—CH_2—C, $^3J_{H-H}$7.2), 7.10–7.52(m, 4H, C_6H_4)
19a		2.95–3.09(d, $PNCH_3$, $^3J_{PNCH}$12.2), 5.60(s, 2H, NH_2), 7.04–7.52(m, 5H, C_6H_5)
19b		3.04–3.20(d, 3H, $PNCH_3$, $^3J_{PNCH}$14.94), 6.05(s, 2H, NH_2), 7.13–7.30(m, 5H, C_6H_5)
19c		3.96–4.12(d, 3H, $PNCH_3$, $^3J_{PNcH}$15.12), 4.02(s, 2H, NH_2), 7.04–7.28 (m, 4H, ClC_6H_4).
19d		3.99–4.16(d, 3H, $PNCH_3$, $^3J_{PNCH}$15.12) 5.0(s, broad, 2H, NH_2), 7.02–7.56(m, 4H, BrC_6H_4)
21a	32.24	1.20–1.36(t, 3H, O—C—CH_3, $^3J_{H-H}$7.20), 2.94–3.40(d, 3H, $PMCH_3$, $^3J_{PNCH}$9.36) 3.67(s, broad, 2H, NH_2), 3.51–3.79(q, 2H, SCH_2 $^3J_{PSCH(A)}$9.72 $^3J_{PSCH(B)}$ 7.20, $^3J_{H-H}$O), 4.07–4.32 (q, 2H, O—CH_2—C, $^3J_{H-H}$7.20), 7.20–7.50(m, 5H, C_6H_5)
21b	98.27	1.23–1.38(t, 3H, O—C—CH_3, $^3J_{H-H}$7.20), 3.01–3.15(d, 3H, $PNCH_3$, $^3J_{PNCH}$12.0), 3.58–3.88(q, 2H, SCH_2, $^3J_{PSCH(A)}$10.80, $^3J_{PSCH(B)}$4.32, $^2J_{H-H}$O), 3.94(s, broad.2H, NH_2), 4.10–4.34(q, 2H, O—CH_2—C, $^3J_{H-H}$7.20), 7.20–7.48(m, 5H, C_6H_5)
21c	99.09	1.12–1.28(t, 3H, O—C—CH_3, $^3J_{H-H}$7.20), 2.92–3.05(3, 3H, $PNCH_3$, $^3J_{PNCH}$12.24), 3.48–3.78(q, 2H, $PSCH_2$, $^3J_{PSCH(A)}$9.36, $^3J_{PSCH(B)}$3.60, $^2J_{H-H}$O), 4.05 (s, 2H, NH_2), 3.99–4.23)(q, 2H, O—CH_2 C, $^3J_{H-H}$7.2), 7.04–7.42(m, 4H, ClC_6H_4)
21d	98.90	1.05–1.36(t, 3H, O—C—CH_3, $^3J_{H-H}$7.20), 3.04–3.21(d, 3H, $PNCH_3$, $^3J_{PNCH}$15.1), 3.56–3.86(q, 2H, $PSCH_2$, $^3J_{PSCH(A)}$9.0, $^3J_{PSCH(B)}$3.6, $^2J_{H-H}$O), 3.96(s, broad, 2H, NH_2),
21d		4.07–4.28 (q, 2H, O—CH_2—C, $^3J_{H-H}$7.20, 7.08–7.58(m, 4H, BrC_6H_4)
22a	32.84	2.88–3.92 (octet.2H, $PSCH_2$, $_A$3.17, $_B$3.82, $^3J_{PSCH(A)}$30.10, $^3J_{PSCH(B)}$7.82, $^2J_{H-H}$13.85), 3.23–3.31 (d, 3H, $PNCH_3$, $^3J_{PNCH}$7.2), 7.16–7.35(m, 5H, C_6H_5), 8.10(s, H, NHC═O)
22b	88.30	2.96–3.92(octet, 2H, $PSCH_2$, $_A$3.19, $_B$3.80, $^3J_{PSCH(A)}$26.24, $^3J_{PSCH(B)}$5.44, $^2J_{H-H}$13.68), 3.34–3.45(d, 3H, PNCH 9.36), 7.24–7.33(m, 5H, C_6H_5), 8.07(s, 1H, NHC═O)
22c	88.84	2.95–3.93 (octet, 2H, SCH_2, $_A$3.18, $_B$3.82, $^3J_{PSCH(A)}$28.15, $^3J_{PSCH(B)}$4.43, $^2J_{H-H}$13.59), 3.32–3.44(d, 3H, $PNCH_3$, $^3J_{PNCH}$10.80), 7.05–7.36(m, 4H, ClC_6H_4), 8.48(s, broad, 1H, NHC═O)
22d	88.71	2.95–3.92 (octet, 2H, $PSCH_2$, $_A$3.18, $_B$3.80, $^3J_{PSCH(A)}$27.5, $^3J_{PSCH(B)}$5.42, $^2J_{H-H}$13.35) 3.32–3.42(d, 3H, $PNCH_3$, $^3J_{PNCH}$9.72), 7.00–7.50(m, 4H, BrC_6H_4), 8.32(s, broad, 1H, NHC═O)
24a	92.30	1.11–1.27(t, 3H, O—C—CH_3, $^3J_{H-H}$7.20), 3.26–3.38(d, 3H, $PNCH_3$, $^3J_{PNCH}$10.80), 3.70–3.71(d, 1H, PSCH(A), $^3J_{PSCH(A)}$1.08), 3.91(s, 1H, PSCH(B), $^3J_{PSCH(B)}$O, $^2J_{H-H}$O), 3.97–4.20(q, 2H, O—CH_2—C, $^3J_{H-H}$7.2), 7.11–7.66(m, 10H, C_6H_5 and N═CHC_6H_4Cl—(p))
24b	93.29	1.14–1.30(t, 3H, O—C—CH_3, $^3J_{H-H}$7.20), 3.28–3.40(d, 3H, $PNCH_3$, $^3J_{PNCH}$10.80), 3.70–3.71(d, 1H, PSCH(A), $^3J_{PSCH(A)}$1.44), 3.92(s, 1H, PSCH(B), $^3J_{PSCH(B)}$O, $^2J_{H-H}$O), 4.00–4.24(q, 2H, O—CH_2—C, $^3J_{H-H}$7.2), 7.12–7.68(m, 9H, ClC_6H_4 and N═CHC_6H_4Cl—(p))
24c	93.15	1.12–1.36(t, 3H, O—C—CH_3, $^3J_{H-H}$7.20), 3.26–3.38(d, 3H, $PNCH_3$, $^3J_{PNCH}$10.80), 3.70(s, 1H, PSCH(A), $^3J_{PSCH(A)}$O, $^2J_{H-H}$O), 3.95(s, 1H, PSCH(B), $^3J_{PSCH(B)}$O, $^2J_{H-H}$O)

(a) Solvent: DMSO, (b) Solvent: DMSO + D_2O.

with equivalent amounts of 2-mercaptoacetate and triethylamine resulted mainly in disubstituted (**15**) and (**16**) instead of the monosubstituted products.

In view of the above facts, we designed a new route shown in Scheme 7. At first, the reaction of 1:2 molecular ratio of O-arylthiophosphoryl dichloride and methylhydrazine at −70°C resulted in a high yield (**19**), which was then treated with sodium ethyl 2-mercaptoacetate in acetonitrile giving a high yield of phosphorohydrazides (**21**). Compound (**21**) underwent selfcyclization at 100°C to form (22). The rate of cyclization was reduced at 100°C and the reaction mixture decomposed at a temperature above 110°C. The yield of (**22d**) was low (<70) probably due to some decomposition caused by the elevated temperature.

2. *The structure of products*

The molecular structures of (**14**), (**19**), (**21**), (**22**) and (**24**) were confirmed by elemental analysis or/and MS, ^{31}P-NMR and ^{1}H-nMR spectra. These results are summarized in Tables I and II.

The interesting fact revealed by the proton NMR spectra is that the chemical shifts of the two protons of the methylene group near the phosphorus atom in compounds (**14**), (**21**), (**22**) and (**24**) are different. This is because the methylene groups in these compounds are prochiral which cause different environments for each proton of this group. The chemical shift δ(A) is between 3.55 and 3.72 ppm and δ(B) is between 3.75 and 3.95 ppm for the open-chain compounds (**21**) and (**24**). The pattern of the methylene protons for cyclic compounds (**14**) and (**24**) appear as typical octet peaks of the AB part of a ABX system (X is phosphorus) since the ring restricts the rotation around the C—S single bond. For (**22a–d**) the chemical shifts δ(A) 3.17–3.19 ppm and δ(B) is 3.80–3.82 ppm, $^{2}J_{H-H}$ is between 13.35–13.85 Hz, $^{3}J_{PSCH(B)}$ and $^{3}J_{PSCH(B)}$ equal respectively 26.24–30.10 and 4.43–7.82 Hz. It is expected that proton A which has a large value of $^{3}J_{PSCH}$ corresponds to the pseudo-equatorial proton of the boat conformation and proton

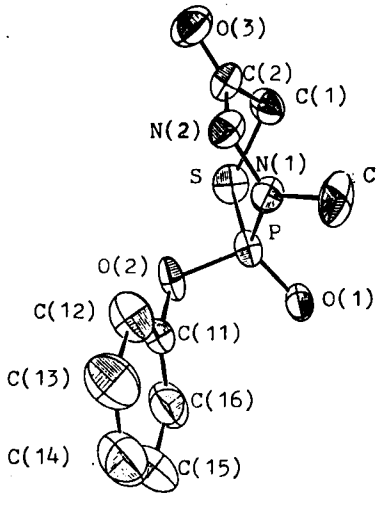


FIGURE 1 The molecular structure of compound **22a**.

TABLE III

The bond distances (A) of compound **22a**

P	S	2.059 (1)	C (1)	C (2)	1.515 (5)
P	O (1)	1.467 (2)	C (11)	C (12)	1.378 (6)
P	O (2)	1.583 (2)	C (11)	C (16)	1.343 (6)
P	N (1)	1.651 (3)	C (12)	C (13)	1.414 (6)
S	C (1)	1.816 (5)	C (13)	C (14)	1.365 (7)
O (2)	C (11)	1.419 (4)	C (14)	C (15)	1.358 (8)
N (1)	C	1.438 (4)	C (15)	C (16)	1.440 (8)
N (1)	N (2)	1.382 (4)	C (21)	C (22)	1.40 (1)
O (3)	C (2)	1.199 (4)	C (22)	O (23)	1.39 (1)
N (2)	C (2)	1.361 (5)	C (22)	O (24)	1.26 (2)

TABLE IV

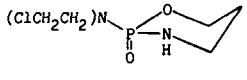
The bond angles (deg.) of compound **22a**

S	P	O (1)	118.2 (1)	O (2)	C (11)	C (16)	119.6 (4)
S	P	O (2)	99.6 (2)	C (12)	C (11)	C (16)	123.2 (4)
S	P	N (1)	105.0 (1)	C (11)	C (12)	C (13)	117.9 (5)
O (1)	P	O (2)	114.7 (1)	C (12)	C (13)	C (14)	119.7 (6)
O (1)	P	N (1)	110.9 (1)	C (13)	C (14)	C (15)	121.8 (5)
O (2)	P	N (1)	107.5 (1)	C (14)	C (15)	C (16)	119.2 (5)
P	S	C (1)	96.1 (1)	C (11)	C (16)	C (15)	118.2 (5)
P	O (2)	C (11)	118.2 (2)	O (3)	C (2)	N (2)	122.8 (4)
P	N (1)	C	124.5 (3)	O (3)	C (2)	C (1)	123.2 (4)
P	N (1)	N (2)	117.5 (2)	N (2)	C (2)	C (1)	114.0 (3)
C	N (1)	N (2)	116.6 (3)	C (21)	C (22)	O (23)	110.3 (8)
N (1)	N (2)	C (2)	122.0 (3)	C (21)	C (22)	O (24)	122 (2)
S	C (1)	C (2)	109.8 (2)	O (23)	C (22)	O (24)	127 (2)
O (2)	C (11)	C (12)	117.2 (4)				

Numbers in parentheses are estimated standard deviations in the least significant digits.

B which has a small value of $^3J_{PSCH}$ corresponds to the pseudo-axial proton of the boat conformation (Fig. 1) according to the relation of the values of coupling constants $^3J_{P-H}$ with the values of dihedral angles. $^3J_{PSCH(A)}$ (20.10 Hz) and $^3J_{PSCH(B)}$ (23.04 Hz) for (**14**) are almost equally large, this may be the result of the equilibrium of two or more conformations in solution.

The molecular structure of (**22a**) was confirmed by X-ray diffraction analysis. Unlike the cyclophosphamide (**25**) for which the ring containing the P atom has a chair conformation, the ring containing the P atom for (**22a**) has a boat conformation where the P atom is in the boat bottom and N(1) and C(1) are at tops of the boat (Fig. 1). N(1) and C(1) are 0.497 and 0.848 Å above best least-square plane formed by P–S–C(1)–C(2)–N(2)–N(1). The dihedral angle between the least-square plane through P,S,N(2) and C(2) and the plane defined by P, N(1),N(2) is 41.73°, the corresponding dihedral angle with the plane of S,C(1), C(2) is 119.26°. The bond distances and angles of **22(a)** are shown in Tables III and IV.



(25)

EXPERIMENTAL

Instruments: Elemental analyses were obtained with a CHN CORDERD MT-3 elementary analyser. Mass spectra were recorded with a VG-ZAB-HS spectrometer at 70 ev ionization energy, but the mass spectrum of (**14**) was recorded with a VG-7O7OE spectrometer using FAB method. ^{1}HNMR and ^{31}PNMR spectra were recorded with a JEOL-FX-90 Q spectrometer. TMS was used as an internal standard for ^{1}HNMR and 85% H_3PO_4 was used as an external standard for ^{31}PNMR. The low field was used as positive direction of chemical shifts. The molecular structure of (**22a**) was recorded with an ENRAF-NONIUS CAD_4 diffractometer.

Solvents: 1,4-dioxane was dried with potassium hydroxide. benzene was dried with calcium hydride. Ether and acetonitrile were dried respectively with sodium or phosphorus pentaoxide.

Reagents: PCl_3, $P(S)Cl_3$ and Et_3N were distilled freshly before being used. Methylhydrazine,[12] 2-mercaptoacethydrazide[13] (**13**), phenylphosphonodichlorothioate[14] (**12**), O-phenyl phosphoryl dichloride[15] (**9**) and O-aryl thiophosphoryl dichlorides (**17a–c**)[16] were prepared according to the literatures.

Hexahydro-2-phenyl-1,3,4,2-thiadiazaphosphorin-2-thion-5-one (**14**). To a stirred solution of 2-mercaptoacethydrazide (**13**) (2.12 g, 0.020 mol.) and triethylamine (4.04 g, 0.04 mol.) in 1,4-dioxane (35 ml) is added dropwise a solution of phenylphosphonodichloridate (**12**) (3.80 g, 0.020 mol.) in 1,4-dioxane (20 ml) at 15–20°C during 30 min. The mixture is stirred continuously for 1.5 hr at this temperature and for 36 hr at about 45°C. Triethylamine hydrochloride is filtered off. The filtrate is evaporated under vacuum to remove the solvent and the residue is chromatographed on a silica gel flash column (10–40μ) using ethyl acetate/petroleum ether (60–90°C) (3:1) as the eluent. Light yellow solid with Rf 0.60 is recrystallized from benzene and petroleum ether (60°–90°C). The white crystal (0.33 g, yield 6.8%) is obtained, m.p. 154–5°C. The analytical data are listed in Table I and II.

S,S'-Bis (Ethoxy carbonyl) methyl, phenyl-phosphonotrithioate (**15**). To a stirred solution of phenylphosphonodichlorothioate (**12**) (14.9 g, 0.070 mol.) in ether (20 ml) is added dropwise a solution of 2-ethyl mercaptoacetate (8.5 g, 0.070 mol.) in ether (20 ml) at −10 to −5°C during 1 hr. and 50 min. The mixture is stirred continuously for 1 hr. at this temperature and for 6.5 hr. at room temperature. The solid is filtered off. The filtrate is evaporated under vacuum to remove the solvent, and the residue is chromatographed in a silica gel flash column (10–40μ) using ethyl acetate/petroleum ether (60–90°C) (1:7) as the eluent. The colorless oil with Rf 0.36 is obtained (10.8 g, yield 81.3%). The oil is solidified after standing several days, m.p. 31–2°C.

Compound (**16**) is prepared by a similar method, petroleum ether (60–90°C) as the solvent and the reaction temperature, −16 to −15°. The analytical data of (**15**) and (**16**) are listed in Table I and II.

O-(p-Bromo) phenyl, N^1-methylthiophosphorochlorohydrazide (**19d**). To a solution of O-(p-bromo)phenylthiophosphoryl dichloride (17C) (9.18g, 0.030 mol.) in ether (150 ml) at −75 to −65°C, a solution of methylhydrazine (2.76 g, 0.060 mol.) in ether (50 ml) is added dropwise with stirring during 30 min. The mixture is stirred continuously for 3 hr. at this temperature and for 2 hr. at −50 to −40°C. The mixture is warmed to room temperature. Methylhydrazine hydrochloride is filtered off. The filtrate is evaporated to remove the solvent. 8 ml of ether and 16 ml of petroleum ether are added to the oily residue to remove small amount of methylhydrazine hydrochloride. The solid is filtered off and the filtrate is evaporated under vacuum to get a residue which is identified by TLC and ^{1}HNMR spectrum to be (**19d**) as an oily liquid (7.89g, yield 84.4%).

Compound (**19c**) is prepared with a similar method. (**19a**) and (**19b**) are prepared according to the literature.[17] Their analytical data are listed in Table I and II.

Sodium ethyl 2-mercaptoacetate (20): 0.46 G (0.02 mol.) of Sodium is dissolved in 15 ml of anhydrous ethanol under nitrogen atmosphere. Then ethyl 2-mercaptoacetate (2.40 g, 0.020 mol.) is added. The solution mixture is evaporated in a rotating evaporator below 50°C. 2.62 G of white powder is obtained, m.p. 142–4°C.

O-Phenyl-S-(ethoxycarbonyl)-methyl N^1-methylthiophosphorohydrazide (**21a**). To a solution of O-phenyl, N^1-methyl thiophosphorochloro hydrazide (**19a**) (1.98g, 0.009 mol.) in acetonitrile (100 ml) is added sodium ethyl 2-mercaptoacetate (**10**) (1.29 g, 0.009 mol.). By the monitoring with TLC a new product with Rf. 0.08 (ether: petroleum ether (60–90°) = 1.5:1) appears after the mixture is stirred for 24 hr. at room temperature under nitrogen atmosphere. Sodium Chloride is filtered off, the filtrate is evaporated under vacuum below 30°C and the residue is chromatographed on a silica gel column (100–140 mesh) using either/petroleum ether (60–90°C) (from 1.5:1 to 12.0:1) as the eluent. 2.28G of colorless oily substance is obtained (yield 83.3%).

(21b–d) are prepared by a similar method. Their analytical data are listed in Table I and II.

Hexahydro-2-phenyloxy, N[1]-methyl-1,3,4,2-thiadiaza-phosphorin-2-thion-5-one (**22b**). A solution of O-phenyl, S-(ethoxycarbonyl) methyl, N[1]-methyl dithiophosphorohydrazide (21b) (0.495g, 0.00154 mol.) in acetonitrile (40 ml) is stirred for 20 hr. at room temperature and for 20 hr. at 50–60°. By monitoring with TLC a new component with Rf 0.13 (ether: petroleum ether = 3:10) appears. The solvent of the mixture is evaporated off and the residue is chromatographed in a silica gel column (100–140 mesh) using ether/petroleum ether (60–90°C (1:2) as the eluent. Only 30 mg (yield 7.1%) of (**22b**) is obtained and 0.45 g of the uncyclized reactant (**21b**) is recovered. The solution of uncyclized reactant (**21b**) in acetonitrile (40 ml) is refluxed slowly in an oil bath of 105°C for 36 hr. Then the solvent is evaporated under vacuum and the residue is chromatographed. 0.30 G of white solid is obtained (yield 71.1%, total yield 78.2%), m.p. 156–8°C.

(**22a,c,d**) are prepared with a similar method. The reaction temperature are: oil bath temperature is kept at 105°C for (**22a**) and (**22c**), at 120°·C for (**22d**). Their analytical data are listed in Table I and II.

O-phenyl-S-(ethoxycarbonyl)-methyl, N[1]-methyl dithiophosphorohydrazone (**24a**): A solution of O-phenyl, S-(ethoxycarbonyl)methyl, N[1]-methyl dithiophosphorohydrazide (**21b**) (0.80 g, 0.0025 mol.) and p-chlorobenxaldehyde (**23**) (0.42 g, 0.0030 mol.) in benzene (15 ml) is stirred for 20 hr. at room temperature. The solvent is evaporated under vacuum and the residue is chromatographed in a silica get column (100–140 mesh) using ether/petroleum ether (60–90°C) (1:2.5) as an eluent. An oily liquid (1.05 g) is obtained (yield 94.8%). (**24b**) and (**24c**) are prepared with a similar method. Their analytical data are listed in Table I and II.

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