acetone was added and the solid which separated was crystallized from benzene and proved to be Va (undepressed when admixed with an authentic sample prepared by the action of tetrachloro-*o*-benzoquinone and thioxanthione. Both products have identical infrared spectra[8]).

Preparation of 9,9-(tetrabromo-o-phenylenedioxy)thiaxanthene, Vb. Thioxanthione (2.33 g.) and tetrabromo-*o*-benzoquinone (4.24 g.) were allowed to react as in the case of the chloro- analogue. Vb crystallized from ethyl acetate in colorless crystals m.p. 245° (yield about 70%).

Anal. Calcd. for $C_{19}H_8O_2Br_4S$: C, 36.77; H, 1.29; Br, 51.61; S, 5.16. Found: C, 36.87; H, 1.19; Br, 51.72; S, 4.00.

Hydrolysis of Vb. This was carried out as in the case of the chloroanalogue when thioxanthone and tetrabromocatechol (identified as the diacetate) were obtained.

Oxidation of thioxanthione in air. Tetrachloro-*o*-benzoquinone (0.5 g.) and thioxanthione (0.5 g.) in benzene (15 ml.) were refluxed on the water bath for 3 hr. while passing a stream of dry air. The reaction mixture was filtered while hot and the benzene was then driven off under reduced pressure. The residue was extracted with boiling methyl alcohol and the solid which remained was filtered and crystallized from benzene to give Va (about 0.5 g.). The alcoholic extract was concentrated and left to cool to give thioxanthone.

Reaction of tetrachloro-o-benzoquinone with thioxanthone hydrazone. A solution of tetrachloro-*o*-benzoquinone (0.5 g.) in dry ether (10 ml.) was added portionwise to a solution of the hydrazone (0.23 g.) in dry ether (15 ml.) at room temperature. A vigorous reaction with evolution of gas occurred after each addition and the color of the quinone disappeared. After all the quinone was added, a solid separated which was filtered, crystallized from benzene, and shown to be Va (melting point and mixed melting point); yield about 80%.

Reaction of tetrabromo-o-benzoquinone with thioxanthone hydrazone. The quinone (0.8 g.) and the hydrazone (0.23 g.) were allowed to react as in the case of the chloro- analogue. The solid which separated was crystallized from ethyl acetate and proved to be Vb (melting point and mixed melting point); yield about 75%.

Acknowledgment. The authors wish to express their appreciation to Professor F. G. Baddar, Faculty of Science, A' in Schams University, Cairo, for determination of infrared spectra.

DOKKI, CAIRO, U.A.R.

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[8] Samples were dried under reduced pressure at 130° before infrared determination.

[CONTRIBUTION FROM THE EDGAR C. BRITTON RESEARCH LABORATORY, THE DOW CHEMICAL CO.]

Amidation and Hydrazidation of *O*-Aryl Phosphorodichloridothioates[1]

E. H. BLAIR AND H. TOLKMITH

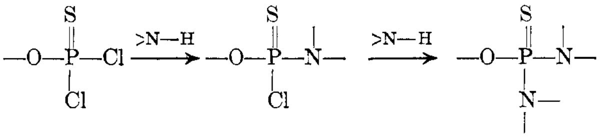
Received February 8, 1960

O-Aryl phosphorodichloridothioates on reaction with ammonia and aliphatic amines gave *O*-aryl phosphoramidochloridothioates and *O*-aryl phosphorodiamidothioates in high yields. *O*-Aryl phosphorodichloridothioates also react with substituted hydrazines to give *O*-aryl phosphorohydrazidochloridothioates and *O*-aryl phosphorodihydrazidothioates in high yields. The reactions were found to be dependent on temperature of reaction, mole ratio, and mode of addition of the reagents. Aromatic amines produced amido acid chlorides only, whereas hydrazine gave dihydrazides. *O*-Aryl phosphoramidohydrazidothioates were prepared by amidation of hydrazido acid chlorides and by hydrazidation of amido acid chlorides. A possible explanation of the difference observed in the reactions of the organophosphorus acid halides is presented.

The recent development of improved and convenient processes for the preparation of *O*-aryl phosphorodichloridothioates[2] prompted a study of the reactions of these phosphorus acid chlorides with compounds containing labile hydrogen atoms. The investigations described in this publication are concerned with the reactions of *O*-aryl phosphorodichloridothioates with ammonia, aliphatic and aromatic amines, hydrazine, and substituted hydrazines.

The first reported comprehensive study of the reactions of amines with phosphorus halides was by Michaelis.[3] *O*-Phenyl and *O*-tolyl phosphorodichloridothioates have been reported to form diamides and dihydrazides when treated with ammonia, benzylamine, hydrazine, and phenylhydrazine.[4-7] The patent literature cites examples of *O*-halophenyl phosphorodiamidothioates prepared from ammonia and amines.[8] However, no investigation has been reported on the stepwise substitution of the halogens in *O*-aryl phosphorodichloridothioates.

In the reaction I→III,



$$-O-\overset{S}{\underset{Cl}{P}}-Cl \xrightarrow{>N-H} -O-\overset{S}{\underset{Cl}{P}}-N< \xrightarrow{>N-H} -O-\overset{S}{\underset{N<}{P}}-N<$$

I II III

the logical pathway appeared to be through the partially amidated intermediate II. The remaining

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[1] Presented before the Division of Organic Chemistry, 134th Meeting of the American Chemical Society, Chicago, Illinois, September, 1958, page 102P of Abstracts.

[2] H. Tolkmith, *J. Org. Chem.* **23**, 1685 (1958).

[3] A. Michaelis, *Ann.* **326**, 129 (1903).

[4] W. Autenrieth and W. Meyer, *Ber.* **58**, 840, 848 (1925).

[5] W. Autenrieth and O. Hildebrand, *Ber.*, **31**, 1094, 1111 (1898).

[6] E. Ephraim, *Ber.*, **44**, 3414 (1911).

[7] W. Strecker and H. Heuser, *Ber.*, **57**, 1368 (1924).

[8] L. R. Drake and A. J. Erbel, U. S. Patent **2,552,537** (1951); L. R. Drake and C. Moyle, U. S. Patent **2,552,538** (1951).

chlorine atom in II would then be less reactive toward further nucleophilic attack because of a decrease in the partial positive charge on the phosphorus atoms. This change in the electron density would result because of the displacement of the electronegative chlorine atom by the less electronegative amido group. As no successful preparation or isolation of an amido acid chloride (II) or a hydrazido acid chloride [—P(S)(NH—$\overset{|}{\text{N}}$—)Cl] had been reported in the literature, our main efforts were directed toward the preparation of such intermediates which would enable us to develop a scheme of reactions as outlined in Fig. 1.

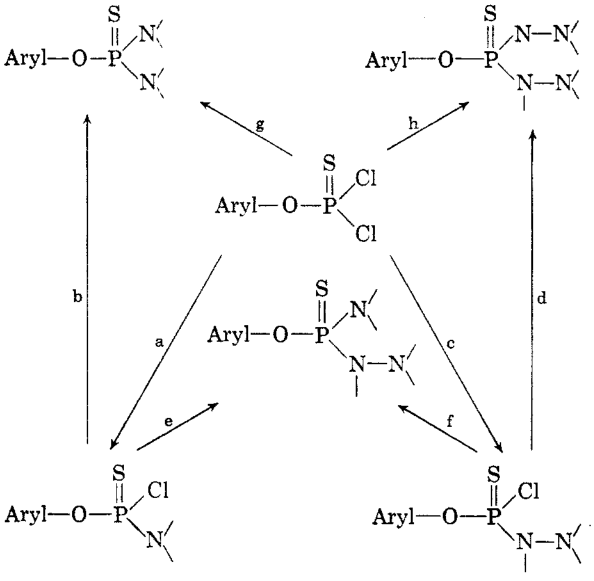

Fig. 1. Reaction scheme

Anhydrous ammonia and aliphatic amines underwent both reactions (a) and (g), Fig. 1. These reactions were determined by temperature, mole ratio and mode of addition of the reactants. The slow addition of two moles of an aliphatic amine to one mole of a well stirred solution of *O*-aryl phosphorodichloridothioate in ether or benzene at 0° to 10° gave the *O*-aryl phosphoramidochloridothioate and the amine hydrochloride, generally in high yields. Anhydrous ammonia added to *O*-(2,4,5-trichlorophenyl) phosphorodichloridothioate produced an amido acid chloride in satisfactory yield only at -20 to $-30°$. Attempts to prepare this particular amido acid chloride at higher temperatures were unsuccessful. The reverse addition, using the same amount of reactants as indicated above, always gave a mixture of diamide and unreacted acid chloride.

The amido acid chlorides were isolated by filtering from amine hydrochloride and removing solvent under reduced pressure. Amido acid chlorides could also be freed from amine hydrochlorides by a water wash. In many instances liquid products crystallized when stirred with cold low-boiling petroleum ether. The products which did not crystallize were purified by petroleum ether extraction, the amido acid chlorides being soluble whereas diamides were generally insoluble. The solid products were recrystallized from petroleum ether. Most of the amido acid chlorides prepared from aliphatic amines were white crystalline solids possessing well defined melting points. Although these acid chlorides did not decompose at their melting points, the amido acid chlorides prepared from primary amines might be expected to dehydrochlorinate at higher temperatures. No decomposition was ever encountered on storage at room temperature, however.

These phosphorus acid halides were relatively stable to hydrolysis. In many instances the crude amido acid chlorides were washed with water to free them from amine hydrochloride with no apparent decomposition. Aqueous isopropylamine was successfully employed in the preparation of *O*-(2,4,5-trichlorophenyl) isopropylphosphoramidochloridothioate (yield 80%). Evidently these phosphorus acid halides are considerably more resistant toward hydrolysis than phenylphosphonothioic dichloride, for Smith and Audrieth[9] have found the latter hydrolyzes so rapidly that aqueous amines are unsuitable for amidation.

The most interesting compound of this series was that prepared from anhydrous ammonia, for it represents the first reported phosphorus acid chloride containing the grouping [—P(S)(NH_2)Cl]. As might be expected, this amido acid chloride was not as stable as those prepared from aliphatic amines. While no decomposition was observed on taking the melting point, the compound did deteriorate in about two months on storage at room temperature.

Table I lists the physical and analytical data for an umber of *O*-aryl phosphoramidochloridothioates.

Symmetrical diamides were prepared by the reaction of *O*-aryl phosphorodichloridothioates with at least four equivalents of aqueous or anhydrous ammonia and aliphatic amines [route(g)]. A useful method for the preparation of unsymmetrical diamides was that of route (b). A definite decrease in the rate of formation of diamides was observed in going from ammonia and primary amines to the branched and bulkier amines. The unsymmetrical diamides described in this report were prepared from purified amido acid chlorides. All diamides reported herein were white crystalline solids with well defined melting points.

Further chemical evidence for the existence of the amido acid chlorides was established by the preparation of an unsymmetrical diamide from two different amido acid chlorides (Fig. 2). Preparations of the unsymmetrical diamide *O*-(2,4,5-trichlorophenyl) *N*,*N*-dimethylphosphorodiamido-

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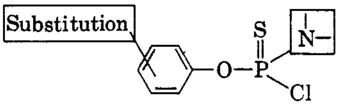
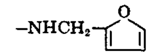
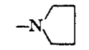
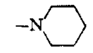
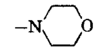
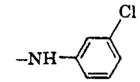
[9] W. Smith and L. F. Audrieth, *J. Org. Chem.* **22,** 265 (1957).

TABLE I

PHYSICAL AND ANALYTICAL DATA OF *O*-ARYL PHOSPHORAMIDOCHLORIDOTHIOATES



Substitution	—N<[a,b]	Reaction[c] Temp.	Yield,[d] %	M.P.[e]	Nitrogen, % Calcd.	Nitrogen, % Found	Chlorine, % Calcd.	Chlorine, % Found
H	—NHCH$_3$[f]	15 ± 5	92.5	22–22.5[g]	6.32	6.14	16.45	16.05
H[h]	—NHC$_6$H$_5$	40	85.8	[i]	4.93	4.82	12.49	12.10
2,4-Cl$_2$	—NHCH(CH$_3$)$_2$	0 ± 5	83	50.5–51	4.39	4.63	33.39	33.09
2,4,5-Cl$_3$[h]	—NH$_2$[f]	−25 ± 5	92	55–56	4.50	4.39	45.60	44.48
2,4,5-Cl$_3$	—NHCH$_3$[f]	−5	99.5	61–62	4.31	4.27	43.64	43.56
2,4,5-Cl$_3$	—N(CH$_3$)$_2$[f]	5 ± 10[j]	54.6[k]	49–50	4.13	4.13	41.60	41.77
2,4,5-Cl$_3$	—NHCH(CH$_3$)$_2$	−5 ± 5	83[k]	51.5–52.5	3.97	3.75	40.17	40.13
2,4,5-Cl$_3$	—NHC$_6$H$_{11}$	0 ± 5	93.5	88–89	3.56	3.46	36.07	35.90
2,4,5-Cl$_3$	—NHCH$_2$C$_6$H$_5$[l]	−5 ± 5	80[k]	73–73.5	3.49	3.46	35.36	35.10
2,4,5-Cl$_3$		25 ± 5	48	[m]	3.58	3.15	36.28	36.54
2,4,5-Cl$_3$		25 ± 5	76	66–68	3.84	3.56	38.85	38.65
2,4,5-Cl$_3$		25 ± 5	80	40–43	3.68	3.58	37.42	37.40
2,4,5-Cl$_3$		25 ± 5	77	93–95	3.58	3.24	37.22	37.80
2,4,5-Cl$_3$	—NHC$_6$H$_5$[l]	33 ± 8[j]	70	[n]	3.62	3.60	36.64	36.20
2,4,5-Cl$_3$		82 ± 2[j]	56.5	[o]	3.33	3.28	42.20	42.50
2,4,6-Cl$_3$	—NHCH$_3$[f]	5	91.4	80–81	4.31	4.36	43.64	43.41
2-Cl,4-C(CH$_3$)$_3$	—NHCH$_3$[f]	23 ± 1	90.5	[p]	4.50	4.48	22.71	21.25
3-Cl,4-NO$_2$	—NHCH$_3$[f]	0 ± 5	74	[q]	9.35	9.15	23.55	23.41

[a] Prepared by addition of amine dissolved in ether or benzene to *O*-aryl phosphorodichloroidothioate dissolved in same solvent. [b] Amine hydrochloride removed by filtration. [c] Reaction time 1–4 hr. [d] Yield of technical grade material. [e] Recrystallized from petroleum ether (b.p. 60–70°). [f] Gaseous amine passed into the reaction mixture. [g] Recrystallized from petroleum ether (b.p. 30–60°); d_4^{25} 1.3195, n_D^{25} 1.5767. [h] Described in detail in Experimental section. [i] d_4^{25} 1.3091, n_D^{25} 1.6242. [j] Reaction time 6–8 hr. [k] Yield of purified product. [l] Amine hydrochloride removed by water wash. [m] n_D^{25} 1.606. [n] d_4^{25} 1.5140, n_D^{25} 1.6386. [o] d_4^{25} 1.5470, n_D^{25} 1.6318. [p] d_4^{25} 1.2547, n_D^{25} 1.5602. [q] n_D^{25} 1.6100.

thioate by the two routes differed in melting point by one degree (119–120° *vs.* 118–120°). A mixed melting point of 118–120° was obtained. Combustion analysis and infrared spectra substantiated the identity of the two diamides. Table II lists the physical properties and analytical data of a number of *O*-aryl phosphorodiamidothioates.

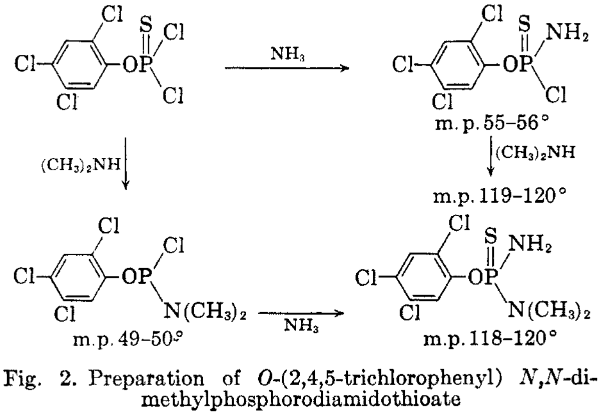


Fig. 2. Preparation of *O*-(2,4,5-trichlorophenyl) *N*,*N*-dimethylphosphorodiamidothioate

Amines containing an aromatic or heterocyclic group, linked through a methylene bridge such as benzylamine and furfurylamine, underwent reactions (a), (g), and (b) as expected. Secondary heterocyclic amines such as piperidine and morpholine likewise reacted exothermically along these routes.

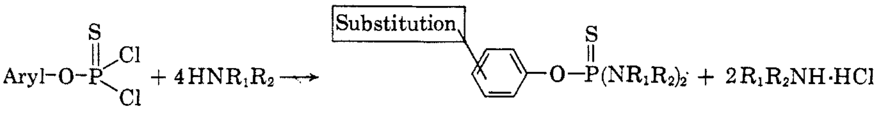
Amidation of *O*-aryl phosphorodichlorodothioates with aniline and *m*-chloroaniline in the absence of a separate hydrogen chloride acceptor reacted differently and unexpectedly, proceeding only to the extent of reaction (a), Fig. 1. This reaction required several hours of refluxing. Furthermore, it was not clear-cut and side reactions resulted—a marked contrast to the other amine reactions discussed.

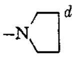
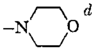
The preparation of *O*-phenyl phenylphosphoramidochloridothioate from *O*-phenyl phosphorodichloridothioate and aniline in the presence of 10% sodium hydroxide has been described.[4] The reported melting point of 153° is abnormally high for such a compound. As it was isolated as a benzene insoluble material and only a sulfur analysis

TABLE II

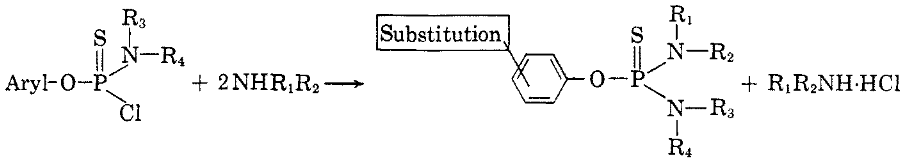
PHYSICAL AND ANALYTICAL DATA OF *O*-ARYL PHOSPHORODIAMIDOTHIOATES

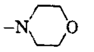
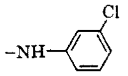
Symmetrical



Substitution	$-NR_1R_2$	Yield,[a] %	Crystallization Solvent	M.P.	Nitrogen, % Calcd.	Nitrogen, % Found	Chlorine, % Calcd.	Chlorine, % Found
2,4,5-Cl_3	$-NH_2$[b]	95.9	Ethanol[c]	143.5–144.5	9.61	9.39	36.48	36.29
2,4,5-Cl_3	$-NHCH_3$[b]	95	Ethanol	116.5–117.5	8.76	8.73	33.28	32.91
2,4,5-Cl_3	$-NHC_2H_5$[b]	84	Cyclohexane	79–80	8.05	8.03	30.59	30.26
2,4,5-Cl_3	$-NHCH(CH_3)_2$[d]	93.5	Ethanol	90–91	7.46	7.45	27.99	28.31
2,4,5-Cl_3	$-NHC_6H_{11}$[d]	100	Propanol	124–124.5	6.15	6.28	23.33	23.12
2,4,5-Cl_3	$-N(CH_3)_2$[b]	97.8	Methanol	62.5–63	8.05	8.03	30.59	30.26
2,4,5-Cl_3[e]	 [d]	39	Cyclohexane	99–101	7.03	7.06	26.61	26.80
2,4,5-Cl_3[e]	 [d]	86.7	Propanol	156–157	6.49	6.71	24.64	24.40

Unsymmetrical[f]



Substitution	$-NR_1R_2$	$-NR_3R_4$	Yield,[a] %	Crystallization Solvent	M.P.	Nitrogen, % Calcd.	Nitrogen, % Found	Chlorine, % Calcd.	Chlorine, % Found
H[e]	$-NHCH(CH_3)_2$	$-NHC_6H_5$	89	Methyl cyclohexane	96–97	9.14	8.99	10.11[g]	10.38
2,4,5-Cl_3	$-NH_2$	$-NHCH_3$	82	Ethanol	113–114	9.17	9.23	34.81	34.81
2,4,5-Cl_3	$-N(CH_3)_2$	$-NHCH_3$	85.9	Methanol	106–107.5	8.40	8.40	31.88	31.31
2,4,5-Cl_3	$-NHC_2H_5$	$-NHCH_3$	85.9	Methyl cyclohexane	91–92.5	8.40	8.41	31.88	32.00
2,4,5-Cl_3	$-NHCH(CH_3)_2$	$-NHCH_3$	85.5	Petroleum ether (60–70°)	88–89	8.05	8.00	30.59	31.15
2,4,5-Cl_3[h]		$-NHCH_3$	44	Cyclohexane	149–150	7.47	7.17	28.40	28.77
2,4,5-Cl_3[h]	$-NHCH_3$		46.5	Cyclohexane	132–133	6.73	6.69	34.10	33.76
2,4,5-Cl_3	$-N(CH_3)_2$	$-NH_2$	69.5	Methanol[c]	119–120	8.76	8.72	33.28	33.21
2,4,5-Cl_3	$-NH_2$	$-N(CH_3)_2$	92.8	Methanol	118–120	8.76	9.02	33.28	33.80
2,4,5-Cl_3	$-N(C_6H_{11})_2$	$-NHC_2H_5$	70	Methylene dichloride	144–145	5.79	5.70	21.98	22.10
2,4,6-Cl_3	$-NHCH_3$	$-NHC_2H_5$	86	Cyclohexane	106–107	8.40	8.30	31.88	31.47
2-Cl,4-NO_2[e]	$-NHCH_3$	$-NHC_2H_5$	80	Methyl cyclohexane	75–77	13.56	12.50	11.45	11.84

[a] Yield of technical grade material. [b] Gaseous amine passed into the dichloridothioate dissolved in methylene dichloride. [c] Described in detail in Experimental section. [d] Liquid amine added at room temperature, reaction mixture heated at 40° for 3–4 hr. and allowed to stand at room temperature overnight. [e] Benzene solvent. [f] Prepared by addition of gaseous or liquid amine at 25° to the amido acid chloride dissolved in methylene dichloride; reaction mixture then heated at 40° for 0.5–3.0 hr. [g] Phosphorus analysis. [h] Ether solvent.

was presented, there is some doubt as to the identity of the product. We prepared this compound, which was a dark brown oil. The infrared spectrum was in accord with the assigned structure. This amido acid chloride was further amidated with isopropylamine to give the unsymmetrical diamide *O*-phenyl *N*-isopropyl-*N'*-phenylphosphorodiamidothioate, m.p. 96–97°, in high yield.

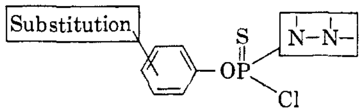
In order to allow the aromatic amines to react through route (g) to the dianilide, it was necessary to carry out a Schotten-Baumann reaction as suggested by Autenrieth and Hildebrand.[5]

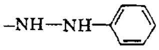
In view of the results obtained from amidation studies, hydrazides offered an interesting challenge. Previous workers restricted themselves to the preparation of symmetrical dihydrazides and apparently made no attempt to isolate or identify intermediates such as a hydrazido acid chloride.[4–6] We approached the problem in a manner similar to that described for the amides, *i.e.* along routes (c), (d), and (h), Fig. 1.

1,1-Dimethylhydrazine reacted analogously to aliphatic amines. The slow addition of two moles of this hydrazine to one mole of dichloridothioate

TABLE III

PHYSICAL AND ANALYTICAL DATA OF *O*-ARYL PHOSPHOROHYDRAZIDOCHLORIDOTHIOATES



Substitution[a]	$-\overset{\vert}{N}-\overset{\vert}{N}-$	Yield,[b] %	M.P.	n_D^{25}	d_4^{25}	Nitrogen, % Calcd.	Nitrogen, % Found	Chlorine, % Calcd.	Chlorine, % Found
H	$-NHN(CH_3)_2$	97.1[c]		1.5663	1.2464	11.18	11.73	14.10	14.52
2-Cl	$-NHN(CH_3)_2$	95.8[c]		1.5701	1.3237	9.82	9.56	24.87	23.85
2,4-Cl_2[d]	$-NHN(CH_3)_2$	99.0	74–75			8.77	8.72	33.28	33.90
3,4-Cl_2	$-NHN(CH_3)_2$	84.0[c]		1.5794	1.4111	8.77	8.72	33.28	33.36
2,4,5-Cl_3	$-NHN(CH_3)_2$	100	76–78[e]			7.91	7.32	40.01	38.78
2,4,5-Cl_3[d]		79	120–122	—		6.97	7.01	35.27	34.73

[a] Reactions carried out at 20–25° in ether or benzene unless otherwise noted. [b] Yield of technical grade material. [c] Product isolated by filtering 1,1-dimethylhydrazine hydrochloride and removing solvent under reduced pressure. [d] Described in detail in Experimental section. [e] *Recrystallized from petroleum ether (b.p. 60–70°) then from methylcyclohexane.*

in ether at 0° to 10° produced the hydrazido acid chlorides (route c) in nearly quantitative yields, again demonstrating a degree of difference in the ease of displacement of the phosphoryl halogen of $-OP(S)Cl_2$ and $-OP(S)(\overset{|}{N}-\overset{|}{N}-)Cl$ by the nucleophilic reagent. Crystalline hydrazido acid chlorides were recrystallized from petroleum ethers and liquid products purified by extraction with petroleum ether. These acid chlorides were as stable as the amido acid chlorides toward hydrolysis and on storage. No decomposition was observed on melting.

Phenylhydrazine differed from 1,1-dimethylhydrazine only in that lower temperatures, −20 to −30°, were required to prepare the hydrazido acid chloride. As no solvent suitable for crystallization could be found, this hydrazido acid chloride was purified by dissolving in ether, precipitating insoluble material by the addition of petroleum ether (b.p. 30–60°), and removing the solvents under reduced pressure. This acid chloride was considerably less stable than the previously described acid chlorides. On standing at room temperature for a few weeks the sample deteriorated with sublimation of 2,4,5-trichlorophenol.

Attempts to prepare hydrazido acid chlorides from anhydrous hydrazine were unsuccessful. Failure to find nonreactive solvents compatible with anhydrous hydrazine and *O*-aryl phosphorodichloridothioates was a contributing factor. We were interested in the synthesis of amidohydrazides as additional proof for the existence of the disclosed amido and hydrazido acid chlorides. The reaction of *O*-(2,4,5-trichlorophenyl) 2,2-dimethylphosphorohydrazidochloridothioate with methylamine [route (f)] gave the same amidohydrazide (Fig. 3) as that obtained by hydrazidation of *O*-(2,4,5-trichlorophenyl) methylphosphoramidochloridothioate with 1,1-dimethylhydrazine [route (e)]. Physical properties and analytical data for *O*-aryl phosphorohydrazidochloridothioates are given in Table III.

Table IV lists the properties of *O*-aryl phosphoramidohydrazidothioates. The amidohydrazides were crystalline solids, recrystallizable from lower alcohols. All but one had melting points below those of the corresponding diamides and dihydrazides.

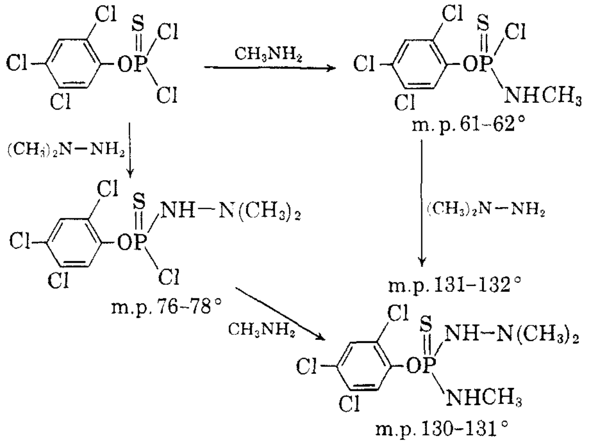


Fig. 3. Synthesis of *O*-aryl phosphorohydrazidochloridothioates

Dihydrazides were prepared, in high yields, from hydrazine hydrate, phenylhydrazine, and 1,1-dimethylhydrazine [route (h)], using four moles of hydrazine per mole of dichloridothioate. All were crystalline solids, insoluble in water and difficultly soluble in many organic solvents. These products were recrystallized from lower alcohols. The dihydrazides were higher melting than the diamides. Substitution of alkyl groups for hydrogens on the hydrazido groups lowered the melting points in much the same manner as alkyl substitution lowered the melting points of the diamides. Smith, Gher, and Audrieth[10] obtained phenylphosphonothioic

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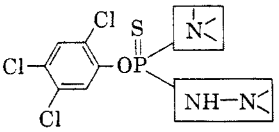
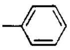
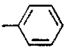
(10) W. C. Smith, R. Gher, Jr., and L. F. Audrieth, *J. Org. Chem.* 21, 113 (1956).

TABLE IV

PHYSICAL AND ANALYTICAL DATA OF *O*-ARYL PHOSPHORAMIDOHYDRAZIDOTHIOATES



—N<[a]	—NH—N<[b]	Yield, %[c]	M.P.[d]	Nitrogen, %		Chlorine, %	
				Calcd.	Found	Calcd.	Found
$—NH_2$[e]	$—NH—NH_2$	75	86–87[f]	13.71	13.35	34.53	33.87
$—NH_2$	—NH—NH— 	87	137–139[g]	10.99	10.71	27.39	27.79
$—NHCH_3$	$—NH—NH_2$[h]	90.5	104–105	13.13	14.79	33.10	33.10
$—NHCH_3$[i]	$—NH—N(CH_3)_2$	100	130–131	12.04	11.48	30.51	30.39
$—NHCH_3$	$NH—N(CH_3)_2$	70.5	131–132	12.04	11.45	30.51	30.50
$—NHCH_3$[j]	—NH—NH— 	44[k]	112–113	10.61	11.04	26.82	26.91

[a] Reactions carried out at 25–35° for 1 to 3 hr. [b] Prepared by addition of hydrazine reagent to the amido acid chloride unless otherwise noted. [c] Yield of technical grade material. [d] Recrystallized from ethanol or methanol. [e] Amido acid chloride in ether added to anhydrous hydrazine. [f] Purified by ether extraction and precipitation with petroleum ether (b.p. 30–60°). [g] Recrystallization from benzene prior to alcohol recrystallization. [h] Reaction carried out in methylene chloride with hydrazine hydrate. [i] Prepared by addition of a gaseous amine to hydrazido acid chloride in methylene chloride solvent described in detail in the Experimental. [j] Reaction carried out in benzene at 25–50° for 3 hr. [k] Yield of purified product.

dihydrazide by a similar type of reaction. Table V lists the analytical and physical properties of the *O*-aryl phosphorodihydrazidothioates.

The formation of the many products resulting from amidation and hydrazidation of *O*-aryl phosphorodichloridates can be related to electronic effects, steric effects, and base strength of the nucleophilic reagents as well as to reaction temperatures, mole ratios, and mode of addition of reagents.

In general diamide formation, (g) Fig. 1, results *via* two bimolecular reactions—(a) and (b). The phosphorus atom of the dichlorothioate is more susceptible to nucleophilic attack than the phosphorus atom of the amido acid chloride. When ammonia or an amine was added to a dichloridothioate, an amido acid chloride was generally obtained in high yields with little or no diamide. The amido nitrogen, following displacement of one of the two chlorine atoms attached to the phosphorus atom, decreases the positive charge on phosphorus *via* an inductive effect. This increase in electron density about the phosphorus atom causes the remaining chlorine atom to be less susceptible to further nucleophilic attack.

All of the nitrogen bases studied (except hydrazine) with *p*Ka values substantially higher than 5 gave a constant pattern of reaction; products *via* routes (a), (b), (g), (c), (d), and (h) in Fig. I were obtained in high yields.

Dostrovsky and Holmann,[11] in their kinetics studies on the amidation of dialkyl phosphorochloridates, showed that secondary amines, though stronger nucleophiles, reacted much more slowly than corresponding primary amines, indicating the operation of steric factors. These steric effects are also operative in the rate of formation of diamide *vs.* amidochloride. When ammonia gas was used to prepare the amidochloride, it was necesary to go to temperatures of −20° to −30° to obtain an amidochloride free of diamide, whereas isopropylamine gave the diamide only at temperatures above 30°.

Hydrazine gave the expected dihydrazide but failed to give a hydrazidochloride of sufficient purity and yield for identification, even at temperatues of −30° and −40°. Being a bifunctional material, hydrazine may behave anomalously on partial hydrazidation. The substituted hydrazines, having less bifunctional character and offering more steric interaction, did give the expected hydrazidochloride. Tolkmith and Britton[12] have found that the bifunctionality of amines such as ethylenediamine makes the isolation of an intermediate amido acid chloride improbable, for only the heterocyclic product resulting from complete dehydrochlorination was obtained.

Of the group of weak organic bases, aniline, *m*-chloroaniline, and phenylhydrazine reacted quite differently and unexpectedly. Independent of mole ratio of reactants and reaction conditions, the anilines did not react beyond the formation of aryl-OP(S)(Cl)NHC_6H_5, while phenylhydrazine readily produced aryl-OP(S)$(NH—NH—C_6H_5)_2$, and it was necessary to perform the reaction at −30° to obtain the product aryl-OP(S)(Cl)-$NH—NH—C_6H_5$. The lack of reactivity of aniline to form the diamido product was probably due more to its low basicity, *p*Ka = 4.58, than to steric

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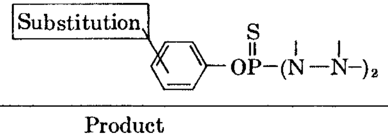
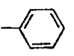
[11] I. Drostovsky and M. Holmann, *J. Chem. Soc.* 511 (1953).

[12] H. Tolkmith and E. C. Britton, *J. Org. Chem.* **24,** 705 (1959).

TABLE V

Physical and Analytical Data of O-Aryl Phosphorodihydrazidothioates



Substitution	—N—N[a]	Solvent	Product Isolation Method[b]	Yield,[c] %	M.P.[d]	Nitrogen, % Calcd.	Nitrogen, % Found	Chlorine, % Calcd.	Chlorine, % Found
2-Cl	—NH—NH₂[e]	Methylene dichloride	A	93.7	145-147	22.17	22.02	14.03	13.25
2,4,5-Cl₃	—NH—NH₂[e]	Benzene	A	93.5	152-153	17.42	17.14	33.07	32.64
2,4-Cl₂	–NH—NH– 	Methylene dichloride	A	96.7	156-157	12.76	12.92	16.14	15.47
2,4,5-Cl₃		Ether	B	73[f]	158-159	11.83	11.76	22.45	22.54
2-Cl, 4-C(CH₃)₃		Ether	B	92.3	151-153	12.15	12.10	7.61	7.66
2,4,5-Cl₃	NH—N(CH₃)₂	Methylene dichloride	C	93.5	123-125[g]	14.84	14.21	28.19	27.87

[a] Prepared by addition of acid chloride to excess hydrazine reagent at 5-15°, then heated to 35-40° for 1-2 hr. [b] A, product being insoluble in reaction solvent was isolated by adding water to reaction mixture, product filtered, and recrystallized; B, product being soluble in reaction solvent was isolated by filtering off the phenylhydrazine hydrochloride, removing solvent under reduced pressure, dissolving resulting solids in boiling ethanol or acetone, pouring into ice water, and recrystallizing filtered product; C, product being soluble in reaction solvent was isolated by washing with water to remove the 1,1-dimethylhydrazine hydrochloride, then proceeding as described under B. [c] Yield of technical grade material unless otherwise noted. [d] All recrystallizations from ethanol or methanol. [e] Hydrazine hydrate slurried in the solvent. [f] Yield of purified product described in detail in the Experimental. [g] Final recrystallization from methylcyclohexane.

interference of the bulky reagent for such behavior was not observed when cyclohexylamine was used.

The ease of reaction of phenylhydrazine, as evidenced by ready formation of aryl-OPS(Cl)-(NHNHC$_6$H$_5$) as well as of aryl-OPS(NHNHC$_6$H$_5$)$_2$, may be related to the fact that phenylhydrazine has a somewhat higher *p*Ka value (5.2) and a much more favorable steric factor than aniline.

EXPERIMENTAL[13]

Starting materials and procedures. All *O*-aryl phosphorodichloridothioates used have been previously described.[7] The liquid organic amines employed were freshly redistilled commercial products. Gaseous amines were volatilized into a chilled flask, then used. All hydrazines were used as commercial materials, except phenylhydrazine which was redistilled. The synthetic procedures for the preparation of the various amides and hydrazides are illustrated by the following examples.

1. *O-Aryl phosphoramidochloridothioates. O-(2,4,5-Trichlorophenyl) phosphoramidochloridothioate.* Two liters of ether containing 0.5 mole (165.2 g.) of O-(2,4,5-trichlorophenyl) phosphorodichloridothioate was cooled to −20° by means of an acetone-Dry Ice bath. Over a period of 3 hr., 1.0 mole (17.0 g.) of gaseous anhydrous ammonia was passed through a large-bore dip-pipe into the rapidly stirred reaction mixture which was maintained at −20° to −30°. After warming the mixture to room temperature the ammonium chloride was filtered and the ether removed under reduced pressure to give 138.0 g. (92% yield) of an oily product. The product solidified when stirred with 100 ml. of petroleum ether (b.p. 30-60°), m.p. 52-53°. The amidochloride after two recrystallizations from ethylcyclohexane melted at 55-56°.

O-(2,4,5-Trichlorophenyl) isopropylphosphoramidochloridothioate. To 0.15 mole (49.5 g.) of *O*-(2,4,5-trichlorophenyl) phosphorodichloridothioate dissolved in 300 ml. of methylene chloride was added a 50% aqueous solution containing 0.30 mole (17.7 g.) of isopropylamine. The addition was carried out at 0° and required 30 min. The mixture was stirred at 0° for 30 min. and allowed to come to room temperature. The aqueous phase was separated and the methylene chloride solution washed three times with water. The solvent was removed under reduced pressure leaving 44.5 g. (83% yield) of a liquid product. The liquid was dissolved in 70 cc. of petroleum ether (b.p. 30-60°) and cooled in an ice bath. A few seed crystals, obtained by freezing such a mixture in a Dry Ice-acetone bath, were added to induce crystallization. More petroleum ether was added and the amido acid chloride filtered, m.p. 51-53°, yield 60.4%. A sample when recrystallized from petroleum ether (b.p. 60-70°) melted at 51.5-52.5°.

O-Phenyl phenylphosphoramidochloridothioate. One mole (93.1 g.) of aniline was added at room temperature to 0.25 mole (56.7 g.) of *O*-phenyl phosphorodichloridothioate dissolved in 300 ml. of benzene. It was necessary to heat the solution at 40° for 24 hr. in order to obtain aniline hydrochloride equivalent to that required for monoamidation. The benzene solution was washed with 200 ml. of water, then with 200 ml. of 2.5*N* hydrochloric acid and twice with 100-ml. portions of 2.5*N* hydrochloric acid to remove excess aniline. The benzene solution was next washed twice with 100-ml. portions of aqueous 5% sodium carbonate to remove acidic materials. After four 250-ml. water washes the benzene solution was dried over Drierite. The benzene was distilled under reduced pressure, leaving 60 g. (85.8% yield) of clear light brown liquid, d_4^{25} 1.3091, n_D^{25} 1.6242.

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[13] All melting points were determined on a Fisher-Johns block and are uncorrected.

This amido acid chloride on reaction with isopropylamine gave a solid diamide, *O*-phenyl *N*-isopropyl-*N'*-phenylphosphorodiamidothioate, in 89% yield, m.p. 96–97°.

2. *O-Aryl phosphorodiamidothioates. O-(2,4,5-Trichlorophenyl) phosphorodiamidothioate.* To 0.25 mole (82.6 g.) of *O*-(2,4,5-trichlorophenyl) phosphorodichloridothioate in 500 ml. of methylene dichloride was added, with stirring, an excess of gaseous anhydrous ammonia. The ammonia was passed into the reaction mixture through a large-bore dip-pipe. The exothermic reaction was kept at 15–25° by means of an ice bath. The product and ammonium chloride separated from the reaction mixture immediately upon formation. Following the addition of ammonia (0.5 hr.) the reaction mixture was stirred at room temperature for 1 hr. Water was added to dissolve the ammonium chloride and the product collected and air dried; m.p. 134–136°, yield 70.0 g. (95.9%). An analytical sample was obtained by recrystallizing from ethanol, m.p. 143.5–144.5°.

O-(2,4,5-Trichlorophenyl) N,N-dimethylphosphorodiamidothioate. An excess of dimethylamine was added as a gas through a wide-bore dip-pipe to 150 ml. of a stirred methylene dichloride solution containing 0.032 mole (10.0 g.) of *O* - (2,4,5 - trichlorophenyl) phosphoramidochloridothioate. Addition was complete in 0.5 hr. The temperature of the reaction mixture increased from 25° to 29°. The reaction was heated with stirring at 50° for 20 min. and then cooled to room temperature. The reaction mixture was washed twice with 150-ml. portions of water. On distilling the solvent, 8.0 g. (69.5%) of product was obtained, m.p. 112–116°. An analytical sample was prepared by extracting the product with petroleum ether (b.p. 60–70°), evaporating the ether, and recrystallizing from methanol; m.p. 119–120°. The synthesis of the same chemical by the amidation of *O* - (2,4,5 - trichlorophenyl) *N*,*N* - dimethylphosphoramido chloridothioate is recorded below.

O-(2,4,5-Trichlorophenyl) dimethylphosphoramidochloridothioate, 0.061 mole (20.0 g.), was treated with gaseous ammonia by the method described above and the product worked up in a similar manner yielding 18.0 g. (92.8%) of the desired product, m.p. 115–118°. An analytical sample crystallized from methanol melted at 118–120°. Mixed melting points with the previously prepared product gave no depression in melting point. Infrared analysis and combustion data gave added proof to the identity of the unsymmetrical diamide prepared from two different amidochlorides.

3. *O-Aryl phosphorohydrazidochloridothioates. O-(2,4-Dichlorophenyl) 2,2-dimethylphosphorohydrazidochloridothioate.* A solution of 0.6 mole (36.0 g.) of 1,1-dimethylhydrazine in 1.0 l. of ether was added dropwise over a period of 2 hr. to an agitated solution of 0.3 mole (89 g.) of O-(2,4-dichlorophenyl) phosphorodichloridothioate in 3.0 l. of ether cooled to a temperature of −20°. The reaction mixture was stirred at room temperature for 3 hr., filtered, and the solvent removed under reduced pressure. The solid product obtained as a residue was recrystallized from petroleum ether (b.p. 60–70°) to give 95.0 g. of colorless crystalline hydrazidochloridate, m.p. 74–75°, yield 99%.

This reaction was carried out at a temperature of −20° only to insure a hydrazidochloride of high purity. Other preparations of hydrazido acid chlorides prepared from 1,1-dimethylhydrazine were conducted at 0° to 10°. Infrared spectra of the 2,2-dimethyl phosphorohydrazidochloridothioates prepared at 0° to 10° compared favorably with those prepared at −20°.

O-(2,4,5-Trichlorophenyl) 2-phenylphosphorohydrazidochloridothioate. Freshly distilled phenylhydrazine (0.62 mole, 67.0 g.) in 1.0 l. of ether was added dropwise over a period of 12 hr. to a well stirred solution of 0.3 mole (102.3 g.) of *O*-(2,4,5-trichlorophenyl) phosphorodichloridothioate in 1.0 l. of ether cooled to −30° to −40°. The reaction mixture was stirred for an additional 8 hr. at −30°, allowed to warm gradually to room temperature, filtered to remove the phenylhydrazine hydrochloride, and the ether removed under reduced pressure, to give 93.4 g. of light brown crystals, m.p. 116–118°, yield 79.0%. An analytical sample was prepared by extracting with ether and filtering to remove insoluble material. Petroleum ether (b.p. 30–60°) was added to the ether solution to precipitate any dihydrazide formed. A small amount was formed; m.p. 152–154°. On evaporation of the ether solutions the desired product was obtained as a light gray solid, m.p. 120–122°.

4. *O-Aryl phosphorodihydrazidothioates. O-(2,4,5-Trichlorophenyl) 2,2 -diphenylphosphorodihydrazidothioate.* O-(2,4,5-Trichlorophenyl) phosphorodichloridothioate (0.2 mole, 66.0 g.) in 200 ml. of ether was added to 0.8 mole (86.5 g.) of phenylhydrazine in 1.0 l. of ether at room temperature. The reaction mixture was heated to 35° for 0.5 hr., allowed to cool to room temperature, and stirred for an additional 1.5 hr. Phenylhydrazine hydrochloride was filtered and the solvent evaporated. The resulting solid was dissolved in acetone and poured into water. The brown solid which separated was filtered, dried (m.p. 149–152°), and recrystallized from 1.5 l. of ethanol to give a colorless crystalline solid, m.p. 158–159°, yield 73.0%.

5. *O-Aryl phosphoramidohydrazidothioates. O-(2,4,5-Trichlorophenyl) N,2,2 - trimethylphosphoramidohydrazidothioate.* A slight excess of gaseous methylamine was passed into a stirred solution containing 0.05 mole (17.7 g.) of O-(2,4,5-trichlorophenyl) 2,2 - dimethylphosphorohydrazidochloridothiolate in 150 ml. of methylene chloride. Addition was complete in 0.5 hr. The temperature of the reaction mixture increased to 42° during the addition. The mixture was stirred for 1 hr. and washed two times with 100-ml. portions of water. Evaporation of solvent left 18.0 g. of colorless solid product, m.p. 122–125°, yield 100%. The amidohydrazide after two recrystallizations from ethanol melted at 130–131°.

The same product was obtained by the hydrazidation of O-(2,4,5-trichlorophenyl) methylphosphoramidochloridothioate with 1,1-dimethylhydrazine. This reaction was carried out in ether at 35°. After two recrystallizations from ethanol the product melted at 131–132°, yield 70.5%. The mixed melting point obtained on these two products was 130–132°. A comparison of infrared spectra of the two samples showed them to be identical.

MIDLAND, MICH.