at 25° with 1 equiv of potassium *tert*-butoxide[18d] afforded after quenching with acetic acid and chloroform isolation[13a] a yellow oil which contained no **1a** as judged by the absence of carbonyl absorption in the ir spectrum and the absence of a uv maximum at wavelength longer than 330 nm (observed λ_{max}^{EtOH} 328 and shoulder 260 nm).

Nearly identical results were obtained from similar experiments using lithium bis(trimethylsilyl)amide[18c] as the base.

Registry No.—**1**, 36612-02-9; **2**, 869-95-4; **3**, 36612-04-1; **4**, 36612-05-2; **5**, 36612-06-3; **6**, 36612-07-4; **7**, 36612-08-5; **8**, 36635-93-5; **9**, 36612-09-6.

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Reaction of Trialkyl Phosphites with Haloamides[1]

JAMES M. DESMARCHELIER AND TETSUO R. FUKUTO*

Department of Entomology and Department of Chemistry, University of California, Riverside, California 92502

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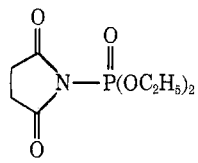
Synthetic routes to insecticidally active *O,S*-dialkyl *N*-acylphosphoramidothioates are multistep and often result in poor yields.[2] In seeking alternate routes to these compounds, the reactions between *N*-bromoacetamide (**1**) and triethyl phosphorothioite and between *N*-chlorobenzamide (**2**) and trimethyl phosphorothioite were investigated. In each case, no dialkyl *N*-acylphosphoramidothioate could be isolated although the starting materials were consumed and alkyl halides were evolved.

In an attempt to understand these reactions it was decided to investigate the reaction between *N*-haloamides and trialkyl phosphites, as the products from these reactions have not been fully elucidated.[3] *N*-Chlorosuccinimide[4] (**3**) and *N*-bromosuccinimide[5] (**4**) react with trialkyl phosphites to give the Arbuzov products. *N*-Chloro-*N*-alkylamides, on the other hand, react with trialkyl phosphites to give imidoyl chlorides and trialkyl phosphates.[6] Similarly, *N*-chloro-*N*-ethylbenzamide and triphenylphosphine react to give *N*-ethylbenzimidoyl chloride and triphenylphosphine oxide.[7] However, the action of triphenylphosphine on *N*-bromoamides results in the corresponding nitrile and triphenylphosphine oxide.[8]

This note describes the products obtained from the reaction between trialkyl phosphites and the following *N*-haloamides: *N*-bromoacetamide (**1**), *N*-chlorobenzamide (**2**), *N*-chlorosuccinimide (**3**), *N*-bromosuccinimide (**4**), *N*-bromo-2-pyrrolidinone (**5**), *N*-chloroacetamide (**6**), *N*-chloro-*N*-methylacetamide (**7**), and *N*-bromobenzamide (**8**).

The cyclic haloamides or imides (**3**–**5**) reacted with 1 equiv of triethyl phosphite to give ethyl halide and phosphoramidate **9** or **10**. The product **9**, which was



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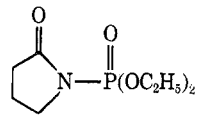

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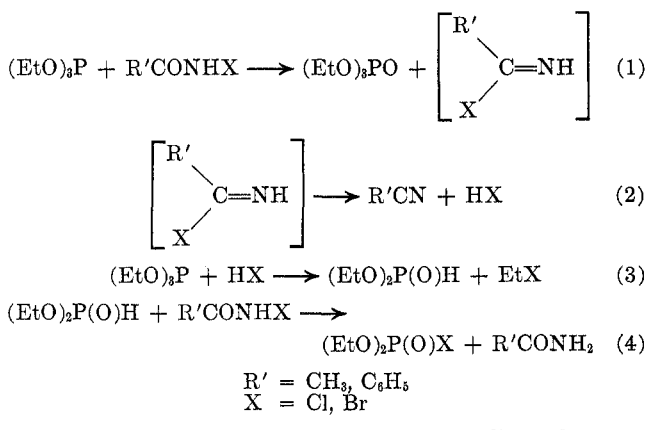
the same whether prepared from **3** or **4**, was identical with that reported previously.[5]

The acyclic primary haloamides (**1**, **2**, **6**, and **8**) did not give the expected Arbuzov products but instead reacted to give products (Table I) consistent with Scheme I.

SCHEME I[a]



$$(EtO)_3P + R'CONHX \longrightarrow (EtO)_3PO + \left[\begin{matrix} R' \\ \diagdown \\ C{=}NH \\ \diagup \\ X \end{matrix}\right] \quad (1)$$

$$\left[\begin{matrix} R' \\ \diagdown \\ C{=}NH \\ \diagup \\ X \end{matrix}\right] \longrightarrow R'CN + HX \quad (2)$$

$$(EtO)_3P + HX \longrightarrow (EtO)_2P(O)H + EtX \quad (3)$$

$$(EtO)_2P(O)H + R'CONHX \longrightarrow (EtO)_2P(O)X + R'CONH_2 \quad (4)$$

R′ = CH_3, C_6H_5
X = Cl, Br

[a] Square brackets are used to indicate intermediates that were never isolated.

When *N*-chloro-*N*-methylacetamide (**7**) and trialkyl phosphite were allowed to react, the only products were the trialkyl phosphate and *N*-methylacetimidoyl chloride,[6] analogous to step 1 in the scheme. For the primary haloamides, Scheme I is supported by the following evidence.

(1) Reaction of 1 equiv of primary haloamide with 1 equiv of triethyl phosphite led to the formation of approximately 0.5 equiv of ethyl halide, nitrile, amide, triethyl phosphate, and diethyl halophosphate (*cf.* Table I).

(2) The reaction was exothermic until almost 2 equiv of triethyl phosphite had been added. At this point, no triethyl phosphite could be isolated when it was introduced rapidly.

(3) Addition of 2 equiv of triethyl phosphite to 1 equiv of primary haloamide gave in good yields the products indicated in eq 5 (the summation of steps 1–3). Small amounts of amide and diethyl halophosphate (the products of step 4) also were isolated.

$$2(EtO)_3P + R'CONHX \longrightarrow (EtO)_2P(O)H + (EtO)_3PO + R'CN + EtX \quad (5)$$

(1) This investigation was supported in part by a Research-Training Grant from The Rockefeller Foundation and by Research Grant No. EP-00806 from the Environmental Protection Agency, Washington, D. C.

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TABLE I

PRODUCTS OBTAINED FROM THE REACTION BETWEEN *N*-HALOAMIDES AND TRIETHYL PHOSPHITE AT 25°

Haloamide	Liquid vehicle	Moles of reagents: Haloamide	Moles of reagents: Phosphite	Moles of products: RCN	RCONH$_2$	EtX	(EtO)$_2$P(O)X	(EtO)$_2$P(O)H	(EtO)$_3$P(O)
1	Toluene	0.5	1.0	0.46	<0.04	0.45	~0	0.36	0.41
2	CCl_4	0.5	1.0	0.44	0.02	0.25	0.07	0.32	0.45
2	Ether	1.0	1.0	0.34	0.42		0.32	0.02	0.47
2	Benzene	1.0	1.0	0.41	0.48	0.48	0.36	<0.01	0.41
6	Benzene	1.0	1.0	0.47	0.48	0.50	0.42	~0	0.36
8	CCl_4	0.5	1.0	0.48	<0.02	0.50	0.03	0.36	0.36
8	CCl_4	1.0	1.0	0.48	0.44	0.50	0.37	0.05	0.46
8	Ether	1.0	1.0	0.44	0.46	0.37	0.43	0.06	0.43

(4) When 1 equiv of triethyl phosphite was treated with 1 equiv of **1** in the presence of pyridine, the ratio of acetonitrile to ethyl bromide increased and pyridinium hydrobromide was isolated (*cf.* Table II).

TABLE II

EFFECT OF HBr ON THE REACTION BETWEEN *N*-BROMOACETAMIDE AND TRIETHYL PHOSPHITE IN BENZENE

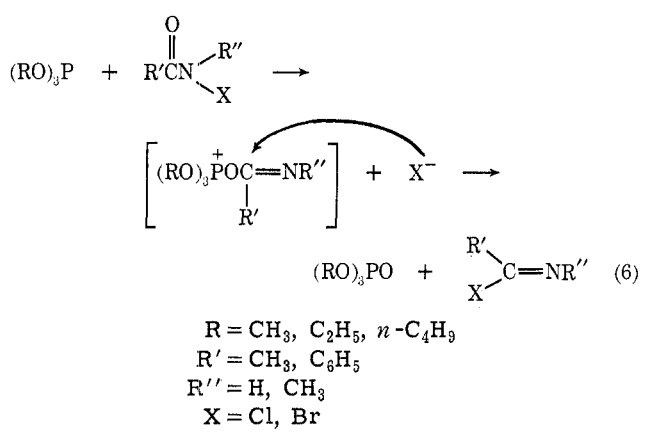
Moles of reagents: Haloamide	Phosphite	Other	Moles of volatile products: EtBr	CH_3CN
1.0	1.0		0.37	0.48
1.0	1.0	HBr 1.0	0.74	0.08
1.0	1.0	Pyridine 1.0	0.26	0.68

Pyridine, by acting as a scavenger for HBr formed in step 2, decreased the availability of HBr to react with triethyl phosphite (step 3).

(5) When 1 equiv of triethyl phosphite was treated with 1 equiv of **1** in the presence of 1 equiv of HBr, the ratio of ethyl bromide to acetonitrile increased, indicating that HBr can compete with **1** for triethyl phosphite under the conditions of the reaction (*cf.* Table II).

(6) The reactions given in steps 2,[7,9] 3,[10,11] and 4[12] are known to occur readily.

The first step in the reaction sequence (eq 1) for acyclic *N*-haloamides probably occurs through the imidoyl phosphonium halide as shown below.



$R = CH_3,\ C_2H_5,\ n\text{-}C_4H_9$
$R' = CH_3,\ C_6H_5$
$R'' = H,\ CH_3$
$X = Cl,\ Br$

The formation of the imidoyl phosphonium halide is required by the isolation of *N*-methylacetimidoyl chloride from **7**[6] and the isolation of the respective nitriles from **1**, **2**, **6**, and **8**. The structure of the reactive phosphonium intermediate has been discussed for **3** and **4**.[4,5] The presence of a phosphonium intermediate in the reaction between **4** and trialkyl phosphites has been argued from the products obtained by carrying out the reaction in the presence of excess nucleophile.[5] A similar procedure was used in this work for **1–3** and **5–8** and the products obtained were consistent with the formation of a reactive phosphonium intermediate (*cf.* Table III). Nucleophiles used were alcohols and water, resulting in the formation of phosphates and dialkyl phosphoric acids, respectively.

TABLE III

PRODUCTS FROM THE REACTIONS BETWEEN *N*-HALOAMIDES AND (RO)$_3$P IN THE PRESENCE OF WATER, METHANOL, OR ETHANOL

Reagents: Haloamide	R	Nucleophile	Liquid vehicle	Product, % yield: Amide	(RO)$_3$PO	(RO)$_2$P(O)OH
1	Et	EtOH	C_6H_6	100[a]	100[a]	
2	Et	H_2O	Ether	95		78
2	Et	EtOH	Ether	100[a]	100[a]	
3	Et	H_2O	Ether	96		57
5	Et	H_2O	Ether			58
5	Me	MeOH	Ether	93	96	
6	Et	EtOH	C_6H_6	84	66	
7	Et	EtOH	C_6H_6	93	71	
8	Me	MeOH	C_6H_6	82	84	
8	Et	H_2O	C_6H_6	88		48

[a] Based on tlc analysis.

The reaction between trimethyl phosphorothioite and **2** was reinvestigated in the light of this knowledge. One equivalent of trimethyl phosphorothioite reacted with 1 equiv of **2** to give approximately 0.3 equiv each of benzamide, benzonitrile, and methyl chloride together with other products that were not identified. These products in large part explain the failure to isolate any dimethyl *N*-benzoylphosphoramidothioate from this reaction.

The probable initial reaction (Scheme I, step 1) between acyclic *N*-haloamides and trialkyl phosphites and phosphorothioites thus resembles the reaction between *N*-haloamides and phosphines[7,8] leading to the formation of tertiary phosphorus oxides rather than to the formation of the Arbuzov products.

The choice of liquid vehicle did not affect the product ratios significantly (*cf.* Table I). The reactions described above occurred with carbon tetrachloride as liquid vehicle, even though this solvent itself is known to react with trialkyl phosphites to form Arbuzov products.[13]

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Experimental Section

Compounds **3** and **4** were purchased from Matheson Coleman and Bell. Compounds **1**,[14] **2**,[15] **5**,[16] **6**,[17] **7**,[6] and **8**[17] were prepared by known procedures. All starting materials were purified by distillation or recrystallization prior to use. Melting points were taken on a Fisher-Johns melting point apparatus and all melting and boiling points are uncorrected. Pmr spectra were taken on a Varian T-60 spectrometer using TMS as an internal standard. Ir spectra were determined in a Perkin-Elmer Model 21 spectrophotometer; mass spectra in a Finnegan 1015 mass spectrometer. In most cases, product verification and quantitation was accomplished by gas–liquid chromatography using an F & M Model 402 gas chromatograph equipped with columns made from 5% Carbowax 20 n on Gas-Chrom Q, 1800 mesh (system A), and 1.5% OV-3 on Gas-Chrom Q, 80/100 mesh (system B), at a flow rate of 60 ml of carrier gas (nitrogen) per minute. Retention times of the products from the reaction between the various *N*-haloamides and phosphates are given in Table IV.

TABLE IV
RETENTION TIMES (MIN) AT FLOW RATE OF 60 ML/MIN

Compd	Column	Temp, °C	Retention time
$(EtO)_2P(O)Cl$	A[a]	108	2.20
	A	116	1.62
	B[b]	115	0.50
$(EtO)_2P(O)H$	A	108	2.75
	A	116	1.75
	B	115	0.68
$(EtO)_2P(O)Br$	A	108	2.45
	B	116	0.60
C_6H_5CN	A	116	2.40
$(EtO)_3PO$	A	116	2.88
	B	115	1.12
$(EtO)_2P(O)NHPr$	B	115	5.49
	B	171	0.51

[a] Column A, 5% Carbowax 20 n on Gas-Chrom Q, 1800 mesh. [b] Column B, 1.5% OV-3, on Gas-Chrom Q, 80/100 mesh.

All organophosphorus compounds were detectable at the nanogram level. Diethyl halophosphates also were identified and quantitated by converting them to *O,O*-diethyl *N*-propylphosphoramidates by reaction with excess propylamine and subsequent analysis by glc. This reaction was shown to be quantitative in control experiments. Benzonitrile also was quantitated from the nitrile absorption peak at 2250 cm^{-1}. Tlc systems used were silica/ether–petroleum ether (bp 30–60°) (1:1), silica/chloroform, alumina/chloroform, alumina/ether, and cellulose/benzene.

Reaction of Triethyl Phosphite and *N*-Bromoacetamide.—To a vigorously stirred suspension of 6.9 g (0.05 mol) of *N*-bromoacetamide in 30 ml of toluene at room temperature was added rapidly 16.6 g (0.1 mol) of triethyl phosphite. The reaction was exothermic and, after cooling, the mixture was distilled through a Vigreux column at atmospheric pressure to give 4.88 g (90%) of ethyl bromide, bp 40–41°, and 1.90 g (93%) of acetonitrile, bp 82–84°. Toluene was removed under reduced pressure and distillation of the residue gave 5.05 g (73%) of diethyl hydrogen phosphite, bp 66–74° (8.0–8.5 mm), $n^{25}D$ 1.4068 [lit.[18] bp 75° (15 mm), $n^{26}D$ 1.4080], and 7.6 g (83%) of triethyl phosphate, bp 94–96° (8.0 mm), $n^{25}D$ 1.4040 [lit.[19] bp 90° (10 mm), $n^{25}D$ 1.4039]. Products also were verified by tlc and ir.

Reaction of Triethyl Phosphite and *N*-Chlorobenzamide.—*N*-Chlorobenzamide (1.55 g, 0.01 mol) was added in small portions over 15 min to a stirred suspension of 3.32 g (0.02 mol) of triethyl phosphite in 10 ml of carbon tetrachloride under a nitrogen atmosphere. Ethyl chloride was removed under reduced pressure and identified by pmr. The reaction mixture was cooled and benzamide, mp 128–130°, was collected. Diethyl phosphorochloridate, diethyl hydrogen phosphite, benzonitrile, and triethyl phosphate were identified and quantitated by glc.

***N*-(Diethylphosphinyl)-2-pyrrolidinone.**—To a stirred suspension of *N*-bromo-2-pyrrolidinone (6.6 g) in 10 ml of benzene was added over 30 min triethyl phosphite (6.65 g) in 6 ml of benzene. The ratio of ethyl bromide to total ethoxy protons was shown to be 1:2 by pmr spectroscopy. Rapid chromatography (alumina/$CHCl_3$) gave 8.4 g (94%) of *N*-(diethylphosphinyl)-2-pyrrolidinone, *m/e* 221, unstable to distillation: pmr (CCl_4) τ 8.87–8.49 (m, 6), 8.24–7.55 (m, 4), 7.14–6.52 (m, 2), 6.31–5.47 (m, 4).

Reaction of Triethyl Phosphite with *N*-Chlorosuccinimide in the Presence of Water.—To a stirred suspension of 6.65 g of *N*-chlorosuccinimide in a mixture of 10 ml of ether, 2 ml of acetone, and 2 ml of water was added 8.4 g of triethyl phosphite over 20 min at room temperature. The solvent was removed under reduced pressure and the residue was washed with cold ether and filtered to give 4.75 g (96%) of succinimide, mp 118.5–119.5°. The etheral filtrate was distilled to yield 4.33 g (57%) of diethylphosphoric acid, bp 130–135° (0.025 mm), $n^{25}D$ 1.4143 (lit.[20] $n^{25}D$ 1.4148).

Reaction of Trimethyl Phosphite with *N*-Bromobenzamide in the Presence of Methanol.—To a stirred suspension of 10 g of *N*-bromobenzamide in 10 ml of benzene and 5 ml of methanol was added 6.2 g of trimethyl phosphite over 30 min. The resulting solution was concentrated under reduced pressure and diluted with petroleum ether. Benzamide (4.95 g, 82%), mp 127–129°, was removed by filtration and the filtrate was distilled to give 5.9 g (84%) of trimethyl phosphate, bp 73–75° (10 mm), $n^{25}D$ 1.3954 [lit.[19] bp 73° (10 mm), $n^{25}D$ 1.3950].

Reaction of *N*-Chlorobenzamide and Trimethyl Phosphorothioite.—To a stirred suspension of *N*-chlorobenzamide (0.77 g) in benzene (10 ml) was added at room temperature trimethyl phosphorothioite (0.70 g) in benzene (5 ml). Methyl chloride (1.5×10^{-3} mol) was removed in a stream of nitrogen and identified by pmr. The reaction mixture was concentrated and filtered to give benzamide (0.21 g, 1.7×10^{-3} mol). Benzonitrile (1.6×10^{-3} mol) was identified by ir.

Registry No.—**1**, 79-15-2; **2**, 1821-34-7; **3**, 128-09-6; **4**, 128-08-5; **5**, 2401-40-3; **6**, 598-49-2; **7**, 5014-39-1; **8**, 19964-97-7; triethyl phosphite, 122-52-1; ethyl bromide, 74-96-4; acetonitrile, 75-05-8; *N*-(diethylphosphinyl)-2-pyrrolidinone, 36614-67-2; diethyl phosphoric acid, 598-02-7; trimethyl phosphite, 121-45-9; trimethyl phosphorothioite, 36614-68-3.

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Reaction of *N*-Iodosuccinimide with Tertiary Alcohols

THOMAS R. BEEBE,* MARY ADKINS, PETER KWOK, AND ROGER ROEHM

Department of Chemistry, Berea College, Berea, Kentucky 40403

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The reaction of secondary alcohols with *N*-iodosuccinimide (NIS) has been shown to produce ketones or cyclic ethers. Secondary alcohols in steroid systems with the hydroxy group in the axial position on carbon 6 produce the cyclic ethers,[1] while oxidation of 1-phenylethanol with NIS gives the ketone.[2] The formation of a cyclic ether from an alcohol and NIS indicates that

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