

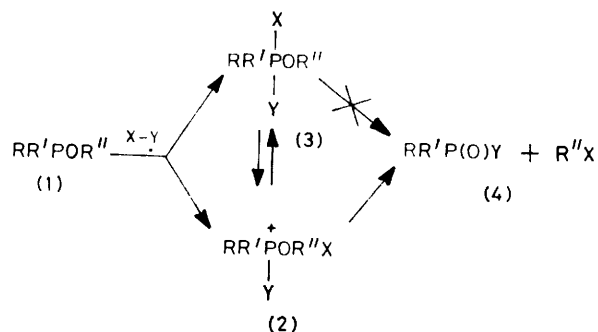
Arbuzov Reaction of Alkyl and Silyl Phosphites with Halogens involving Four- and Five-co-ordinate Intermediates

By Jan Michalski,* Marek Pakulski, and Aleksandra Skowrońska,* Centre of Molecular and Macromolecular Studies, Polish Academy of Sciences, Boczna 5, 90-362 Lodz, Poland

Low temperature ^{31}P n.m.r. spectroscopy and chemical data have been applied to elucidate the mechanism of the Arbuzov-type reaction between phosphites and halogens. Simple and substituted trialkyl, alkyl 1,2-phenylene, and trisilyl phosphites have been allowed to react with chlorine, bromine, and iodine. In some cases intermediate halogenophosphonium salts (2) and in others halogenophosphoranes (3) are observed which then decompose into the corresponding pure highly reactive phosphorhalidates (4). It was possible to prepare stable phosphonium salts from halogenophosphonium salts (2) and halogenophosphoranes (3).

THE oxidative addition of molecules $\text{X}-\text{Y}$ to three-co-ordinate phosphorus esters $\text{RR}'\text{POR}''$ is of considerable general interest. If the group R'' is alkyl, the final product is almost always $\text{RR}'\text{P}(\text{O})\text{Y}$ with the formation of an alkyl halide $\text{R}''\text{X}$. This is known as the Arbuzov reaction, the mechanism of which can be represented, according to our present knowledge, as in Scheme 1.

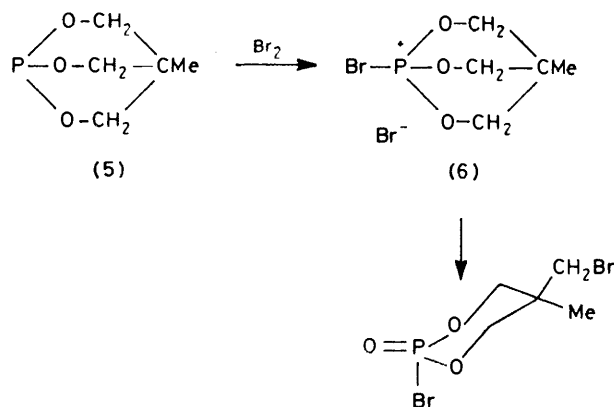
An early report on the isolation of diethyl(methoxy)-methylphosphonium iodide (2; $\text{R} = \text{R}' = \text{Et}$, $\text{R}'' = \text{Y} = \text{Me}$, $\text{X} = \text{I}$) in the reaction of methyl diethylphosphinite with methyl iodide¹ has recently been confirmed.² There is now good evidence furnished by low temperature ^{31}P n.m.r. spectroscopy for the intermediate (2; $\text{R} = \text{R}' = \text{OEt}$, $\text{Y} = \text{PhS}$, $\text{X} = \text{Cl}$) in the Arbuzov reaction between triethyl phosphite and benzenesulphenyl chloride.³ Other cases in which species of type (2) have been detected comprise of an anion of low nucleophilicity derived from trifluoromethanesulphonic acid,² fluoroboric acid,⁴ or sterically hindered alkoxy groups⁵⁻⁸ resistant to dealkylation. The phosphorane



intermediate (3; $\text{RR}' = \text{Z}$; $\text{R}'' = \text{Et}$, $\text{Y} = \text{PhS}$, $\text{X} = \text{Cl}$) has recently been detected in the reaction of ethyl 1,2-phenylene phosphite and benzenesulphenyl chloride⁹ and in the case of phosphorfluoro-organic derivatives (2; $\text{R} = \text{R}' = \text{MeO}$; $\text{R}'' = \text{Me}$, $\text{Y} = \text{perfluorocyclobut-1-enyl}$, $\text{X} = \text{F}$).^{10,11} Stereochemical studies with (3; $\text{RR}' = \text{Z}$, $\text{X} = \text{Y} = \text{Cl}$ or Br) containing a chiral alkyl substituent R'' have been reported from this laboratory; they indicate the equilibrium between (3) and (2) and the absence of the direct dealkylation path from (3) to (4).¹² However, there is little evidence available

whether phosphonium salts (2) are formed directly from (1) or *via* intermediacy of phosphoranes (3).¹³

In spite of the great practical and theoretical importance of Arbuzov's reaction with halogens only one case of a phosphonium intermediate (6) of type (2) of relatively high stability has been established in the reaction of the cage-type phosphite (5) with elemental bromine⁶ (Scheme 2). The chlorophosphonium salts



(2; $\text{X} = \text{Y} = \text{Cl}$) and dichlorophosphorane (3) derived from pyrocatechol ($\text{R}, \text{R}' = \text{Z}$) have been found as Arbuzov intermediates by low temperature ^{31}P n.m.r. spectroscopy.^{3,9} Carrying forward these investigations we report here a further study of the reaction between alkyl and tris(trimethylsilyl) phosphites and halogens.

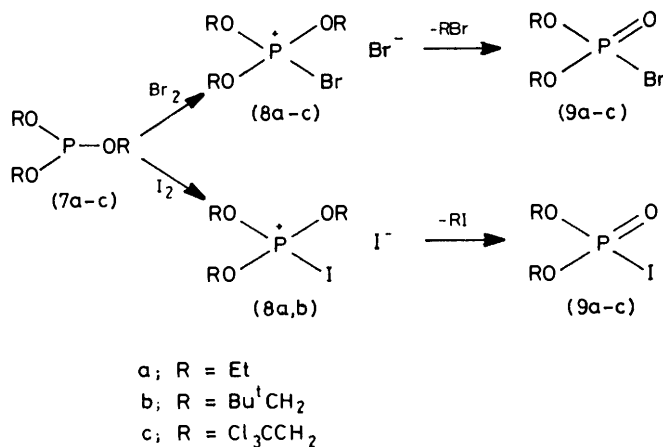
RESULTS AND DISCUSSIONS

Reaction of Halogens with Trialkyl Phosphites.—Halogens react very readily with trialkyl phosphites. The reaction is fast even at -100°C . In a typical experiment the phosphite was dissolved in ethyl chloride. The solution was cooled in liquid nitrogen and an equimolar quantity of a halogen in ethyl chloride solution was added. In liquid nitrogen no detectable reaction takes place. The temperature was then gradually raised to ambient and the reaction course was observed by Fourier transform proton decoupled ^{31}P n.m.r. spectroscopy.

In the case of triethyl (7a), trineopentyl (7b), and tris-(2,2,2-trichloroethyl) phosphites (7c), the ^{31}P n.m.r.

spectroscopy clearly indicated the formation of bromo- (8a–c) and iodo-phosphonium salts (8a and b) when the temperature was raised to -100°C (Scheme 3).

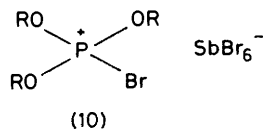
Tris-(2,2,2-trichloroethyl) phosphite (7c) is distinctly less reactive towards elemental iodine. The reaction starts at -50°C . The rate of decomposition of the intermediate phosphonium salt seems to be too high to



SCHEME 3

secure a concentration which would be noticeable by ^{31}P n.m.r. spectroscopy. The formation of phosphonium salts (8a–c; X = Y = Br) and (8a and b; X = Y = I) was quantitative according to ^{31}P n.m.r. spectroscopy and no other products were detected. However, their thermal stability was lower than that of phosphonium salts derived from the analogous reaction with elemental chlorine. Both bromo- (8a–c; X = Y = Br) and iodo-phosphonium salts (8a and b; X = Y = I) decompose into the corresponding bromidates (9a–c; X = Br) and iodidates (9a–c; X = I) at -85°C . The most surprising result is the low stability of bromo- and iodo-neopentoxyphosphonium salts (8b; X = Y = Br and X = Y = I) which dealkylate with the formation of the corresponding neopentyl halides.

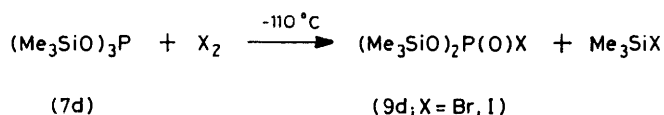
It has been possible to transform the phosphonium salt (8b; X = Y = Br) into the relatively stable hexabromoantimonate (10b; Y = Br, X = SbBr₆) in nitropropane solution. All the reactions between phosphites



SCHEME 4

Other compounds of this type like diethyl phosphoroiodidate (9a) can be used either in peptide synthesis or, like bis-(2,2,2-trichloroethyl) phosphorohalidates (9c; X = Br or I), as phosphorylating agents. Further studies on the synthetic application of bromidates and iodidates are in progress. To our knowledge, the phosphoroiodidates (9) have never been prepared before in high purity. Low temperature iodination offers a unique synthetic approach to this class of compounds since iodination of dialkyl phosphites (RO)₂P(O)H does not lead to pure iodidates as already noted earlier¹⁵ and confirmed in this study.

Reaction of Halogens with Tris(trimethylsilyl) Phosphite.—The reaction starts below -110°C but the phosphonium intermediates were too thermally unstable to be detected by ^{31}P n.m.r. spectroscopy above this temperature (Scheme 4). The silyl phosphorohalidates (4d) are formed in high purity and represent another class of potential peptide forming or phosphorylating agents.¹⁶



Reaction of Halogens with 1,2-Phenylene Phosphites.—This was performed by using experimental techniques analogous to those described above. When ethyl and neopentyl 1,2-phenylene phosphites were allowed to react with elemental chlorine and bromine in ethyl chloride at -100°C the five-co-ordinate adducts were produced. This reaction, interesting from the point of view of the Arbuzov reaction, leads quantitatively to a genuine five-co-ordinate structure which is not only supported by the characteristic ^{31}P n.m.r. upfield shift but also by its ability to be transformed into four-co-ordinate phosphonium structure as shown in Scheme 5.

It is of interest to note that in nitropropane in spite of its high polarity the phosphorane structures (12a and b) are preserved. Transformation of dichloro- and dibromo-phosphoranes (12a and b) into the phosphonium salts (13a and b) was carried out by addition of an equimolar amount of the corresponding antimony pentahalide in nitropropane solution.

The magnitude of the chemical shift indicates four-co-ordinate phosphorus structure. Interestingly, an analogous phosphonium salt (14b) is formed when dibromophosphorane (12b) is treated with an additional equivalent of elemental bromine. This demonstrates the lower nucleophilicity of Br₃[−] anion towards phosphorus in contrast to bromide anion. The salt (14b) reacts with phosphite (11b) to give back the dibromophosphorane (12b) (Scheme 6). Formation of phosphonium salts of type (13) containing a five-membered ring structure derived from pyrocatechol has recently been reported.^{17,18} The dibromophosphoranes (12a and b) decompose at -50°C into the corresponding bromidates (15) and alkyl bromides (16a and b). To our surprise, in the case

and halogens described above can readily be performed on a preparative scale. The halidates formed are of high purity provided that the reaction is carried out below -40°C . Under a moisture-free atmosphere they are stable for several hours at ambient temperature and can be stored for lengthy periods in a refrigerator.

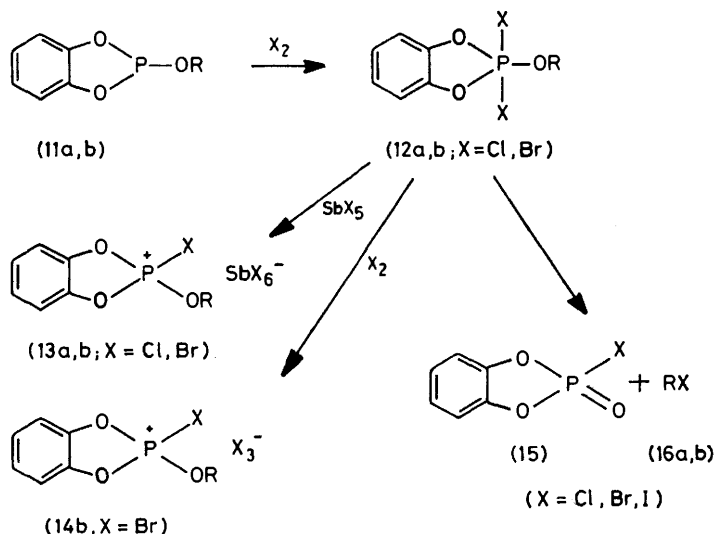
The diethyl phosphorobromidate (EtO)₂P(O)Br prepared by the 'low temperature' method has recently been applied as an efficient peptide bond forming agent.¹⁴

of (12b), a mixture (1 : 2) of neopentyl bromide and 2-bromo-2-methylbutane is formed.

The mechanistic significance of this finding is beyond the scope of this paper and will be discussed elsewhere. We were not able to detect any intermediates in the

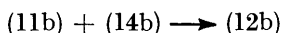
EXPERIMENTAL

Solvents were purified by conventional method. Trialkyl, tris(trimethylsilyl),¹⁹ and alkyl 1,2-phenylene phosphites²⁰ were prepared and purified by standard methods. All reactions were done in sealed tubes and standard vacuum



SCHEME 5

reaction between (11a and b) and elemental iodine in which the final products, namely, iodidates (15) analogous to bromidates (15) and ethyl iodide (16a) or a mixture



SCHEME 6

(1 : 10) of neopentyl iodide and 2-iodo-2-methylbutane (16b) are formed.

Conclusions.—Both four- and five-co-ordinate intermediates can be formed in the Arbuzov reaction of halogens with phosphites depending on the structure of

techniques were used throughout. ³¹P N.m.r. spectra were recorded at 24.3 MHz with a JEOL R-60H spectrometer operating in the pulsed Fourier transform mode. A heteronuclear spin decoupler JNM-SD-HC was used for chemical shifts determination and integration. All spectra were recorded on samples which consisted of the compound (*ca.* 0.001 mol) in solvent (2 ml).

General Preparative Procedure for Reaction of Phosphites with Halogens.—*Bis(trimethylsilyl) phosphoroiodate* (9d). Iodine (7.62 g, 0.03 mol) was added with efficient stirring to a solution of tris(trimethylsilyl) phosphite (8.43 g, 0.03 mol) in Et₂O (60 ml). The temperature of the mixture was kept at -40 to -30 °C. After the addition of iodine had

³¹P Chemical shifts for Arbuzov intermediates and the corresponding phosphorohalidates

	δ^a (p.p.m.)						
	(8a)	(8b)	(8c)	(9a)	(9b)	(9c)	(9d)
X = Cl							
X = Br	+11.5 ^b	+13 ^b	+6.5 ^b	-9.7 ^b	-8.5 ^b	-12.7 ^b	-34 ^{b,d}
X = I	-15.1 ^b	-14 ^b		-41 ^b	-40 ^b	-50 ^b	-76 ^b
	(10b)	(12a)	(12b)	(13a)	(13b)	(14b)	(15)
X = Cl		-35 ^c	-34.5 ^b	+45 ^c	+45.5 ^c		-19 ^b
X = Br	+15.1 ^c	-104.2 ^b	-104 ^b	+36.5 ^c	+37 ^c	+34 ^c	+5.1 ^b
X = I							+12 ^b

^a ³¹P Shifts are reported as positive downfield from 85% phosphoric acid as standard. ^b Solution in ethyl chloride. ^c Solution in nitropropane. The spectroscopic properties of (9d; X = Br) were identical with those of the compound obtained by silylation of dimethyl phosphorobromidate.

the latter. It is most likely that in the case of five-co-ordinate intermediates one has to do with an equilibrium involving a four-co-ordinate phosphorus intermediate¹² which is responsible for the easy conversion of bromophosphoranes into the corresponding bromophosphonium salts demonstrated in this paper. Bromidates and iodidates (9) which are the final products of the Arbuzov reaction of phosphites with halogens are interesting peptide-forming and phosphorylating reagents.

been completed stirring was continued for 30 min. The formation of (9d) in 100% yield was recorded by ³¹P n.m.r.

Reaction of (9d) with aniline. *Bis(trimethylsilyl) phosphoroanilidate*.—Aniline (8.4 g, 0.09 mol) was added dropwise at -20 °C to a solution of (9d) (9.6 g, 0.03 mol) in Et₂O (60 ml) with vigorous stirring. The mixture was then allowed to warm slowly to ambient temperature and the precipitate was filtered off. The ethereal solution was evaporated *in vacuo* to afford the crude product which on recrystallization from benzene-hexane (1 : 1) gives bis-

(trimethylsilyl)phosphoroanilidate as needles (7.35 g, 77%), m.p. 140–142° (Found: C, 45.9; H, 7.7; N, 4.8; P, 10.2. $C_{12}H_{24}O_3NPSi_2$ requires C, 45.4; H, 7.62; N, 4.41; P, 9.75%), δ_P –15.8 p.p.m. (J^2_{P-N-H} 10 ± 0.3 Hz).

This work was supported by the Polish Academy of Sciences.

[9/643 Received, 24th April, 1979]

REFERENCES

- ¹ N. N. Bankovskaya and A. I. Razumov, *J. Gen. Chem. U.S.S.R.*, 1964, **34**, 1871.
- ² K. S. Colle and E. S. Lewis, *J. Org. Chem.*, 1978, **43**, 571.
- ³ J. Michalski, J. Mikołajczak, and A. Skowrońska, *J. Amer. Chem. Soc.*, 1978, **100**, 5386.
- ⁴ K. Dimroth and A. Nurrenbach, *Angew. Chem.*, 1958, **70**, 26.
- ⁵ H. R. Hudson, R. G. Rees, and J. E. Weeks, *Chem. Comm.*, 1971, 1297; H. R. Hudson, R. G. Rees, and J. E. Weeks, *J.C.S. Perkin I*, 1974, 982.
- ⁶ G. K. McEwen and J. G. Verkade, *Chem. Comm.*, 1971, 668.
- ⁷ A. I. Razumov, B. G. Liorber, and Z. M. Khammatova, *J. Gen. Chem. U.S.S.R.*, 1967, **37**, 1825.
- ⁸ A. I. Razumov, B. G. Liorber, Z. V. Khammatova, and I. V. Beresovskaya, *J. Gen. Chem. U.S.S.R.*, 1964, **34**, 163.
- ⁹ A. Skowrońska, J. Mikołajczak, and J. Michalski, *J.C.S. Chem. Comm.*, 1975, 791.
- ¹⁰ I. I. Knunyants, V. V. Tynleneva, E. V. Perrova, and R. N. Sterlin, *Izvest. Akad. Nauk S.S.S.R.*, 1964, **10**, 1797.
- ¹¹ G. Bauer and G. Hägele, *Angew. Chem. Internat. Edn.*, 1977, **7**, 493.
- ¹² J. Michalski, J. Mikołajczak, M. Pakulski, and A. Skowrońska, *Phosphorus and Sulfur*, 1978, **4**, 233.
- ¹³ C. L. Bodkin and P. Simpson, *J.C.S. Perkin II*, 1972, 2050.
- ¹⁴ A. Górecka, M. Leplawy, J. Zabrocki, and A. Zwierzak, *Synthesis*, 1978, 474.
- ¹⁵ H. McCombie, B. C. Saunders, and G. J. Stacey, *J. Chem. Soc.*, 1945, 921; W. Gerrard and G. J. Jeacocke, *ibid.*, 1954, 3647.
- ¹⁶ J. Chojnowski, M. Cypryk, and J. Michalski, *Synthesis*, 1978, 777.
- ¹⁷ D. B. Denney, D. Z. Denney, and G. Dimiele, *Phosphorus and Sulfur*, 1978, **4**, 125.
- ¹⁸ J. Gloede and M. Gross, *J. prakt. Chem.*, 1978, **320**, 140.
- ¹⁹ N. F. Orlov, N. A. Jelokrinskyj, J. W. Sudakova, and B. L. Kaufman, *Zhur. obshchei Khim.*, 1968, **38**, 1656.
- ²⁰ P. C. Crofts, J. H. H. Markes, and H. N. Rydon, *J. Chem. Soc.*, 1958, 4250; B. Denney and D. H. Jones, *J. Amer. Chem. Soc.*, 1969, **91**, 5821.