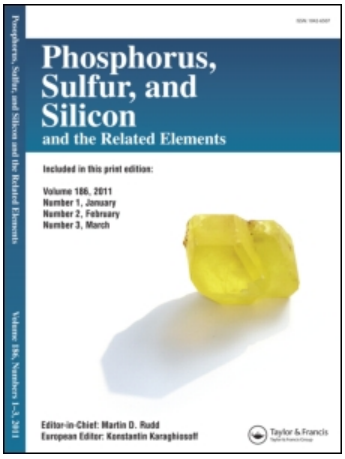



## Phosphorus, Sulfur, and Silicon and the Related Elements

Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

# Polyhalomethane Reactions with Phosphite Anions: Fluorophilic Reactivity of Phosphorus

G. Michael Blackburn[a]; Mao-Jun Guo[a]; Steven Taylor[a]
[a] Department of Chemistry, The University, Krebs Institute, Shefield, UK

**To cite this Article** Blackburn, G. Michael , Guo, Mao-Jun and Taylor, Steven(1993) 'Polyhalomethane Reactions with Phosphite Anions: Fluorophilic Reactivity of Phosphorus', Phosphorus, Sulfur, and Silicon and the Related Elements, 75: 1, 139 — 142
**To link to this Article: DOI:** 10.1080/10426509308037384
**URL:** http://dx.doi.org/10.1080/10426509308037384

*Phosphorus, Sulfur, and Silicon*, 1993, Vol. 75, pp. 139–142 
Reprints available directly from the publisher
Photocopying permitted by license only Printed in the United States of America

# POLYHALOMETHANE REACTIONS WITH PHOSPHITE ANIONS: FLUOROPHILIC REACTIVITY OF PHOSPHORUS

G. MICHAEL BLACKBURN,* MAO-JUN GUO, AND STEVEN TAYLOR
*Krebs Institute, Department of Chemistry, The University, Sheffield, UK S3 7HF*

Abstract Di-isopropyl phosphite reacts with bromotrifluoromethane under basic conditions giving a mixture of some seven products. Identification of these by high-resolution NMR and MS shows that 80% of all products are formed by displacement of fluorine from carbon. Dialkyl fluorophosphate is a minor product in these reactions and in additional examples involving other fluorocarbons and α-fluorophosphonates. In all cases, fluorine is removed from carbon in direct competition with either bromine or chlorine with relative halophilic ratios near unity. These processes are best understood in terms of fluorophilic reactions of a phosphorus anion on the C-F bond, and thereby constitute a new class of X-philic reaction.



## INTRODUCTION

Polyhalomethanes are fairly unreactive toward normal nucleophiles but are especially labile toward halophilic attack.[1] Such halophilic attack has been recognised for phosphite anions,[2] phenolate anions,[3] thiophenolate anions,[3c,4] and carbanions.[5] The transfer of positive halogen to the halophilic species is involved and there are many reports of such reactions for bromo- and chloro-philic processes. An authoritative review[1] of X-philic reactions has stated "To our knowledge, there are no examples of this *(X-philic)* reaction for X = F". This appears generally to be true, although a few other possible candidate F-philic deserve consideration.[7,8] For example, the Arbusov reaction of tributyl phosphite with 2,2-dichloro-octafluorobutane gives dibutyl fluorophosphate (59%) along with 2-chloroheptafluorobut-2-ene (87% as mixed *E*- and *Z*-isomers).[7] While this process could arguably constitute an F-philic reaction, two alternative mechanisms are viable. First, a chlorophilic process and elimination of fluoride anion would provide the observed alkene products. The subsequent displacement at phosphorus of chloride by fluoride would then afford the fluorophosphate. Secondly, dehalogenation by phosphorus biphilic attack on the halocarbon[9] would produce the alkenes directly and give a pentaco-ordinate phosphorane from which subsequent extrusion of chlorobutane would provide the fluoro-phosphate. In addition, alternative mechanisms to halophilic reactions have been proposed for nucleophilic attack on polyhalomethanes.[6]

Clearly, the reality of fluorophilic processes involving phosphorus has to be addressed by the investigation of reactions involving fluoromethanes where such alternative possibilities can be excluded. As part of an ongoing programme in the synthesis and application of phosphonates to nucleotides,[10,11] we have explored several halophilic reactions and identified the formation of products, including ones containing the P-F bond, which provide genuine evidence for fluorophilic reactions of phosphorus.

## RESULTS and DISCUSSION

As an approach to the use of α-fluoromethylphosphonates as analogues of biological phosphates in nucleotides and elsewhere, we needed a simple and convenient route for the synthesis of $CF_3P(O)(OR)_2$ and $(RO)_2(O)PCFHP(O)(OR)_2$. The reactions of phosphites and sodiophosphites with polyhalomethanes (Arbuzov and Michaelis-Becker reactions respectively) are general methods for making halomethylphosphonates and halomethylene-bisphosphonates.[12] Normally, they involve nucleophilic attack on bromine or chlorine to form a carbanion and a phosphoryl halide which then recombine to give halomethyl-phosphonates.

In an attempted preparation of di-isopropyl trifluoromethylphosphonate, diisopropyl sodiophosphite was added to an excess (two equivalents) of $CF_3Br$ in toluene at a temperature below 20°C. After standard work-up, the crude product was seen to be a complex mixture by $^{31}P$ NMR at 32MHz. Distillation under vacuum failed to give a good separation, although different fractions gave graded compositions of the major components. From their $^{31}P$, $^{19}F$, and $^{13}C$ NMR spectra (Bruker AMX 500) and MS ($NH_3$-CI) data we identified peaks arising from seven products, as shown in Scheme 1. It is notable that products (**1**, **3**, **4**, & **5**) involve transfer of fluorine from carbon, accounting for some 80% of total products. The statistically-corrected ratio of C-F to C-Br bond cleavage in formation of the above products, *i.e.* (**3**+**4**+**5**)÷3×(**2**), is approximately 1·7:1 (this calculation presumes that (**1**) is formed as a co-product).

**Scheme 1**

$(Pr^iO)_2PONa$ + $CF_3Br$ —(0-20°C, toluene)→

| | | |
|---|---|---|
| $(Pr^iO)_2P(O)F$ | (**1**) | 16.4% |
| $(Pr^iO)_2P(O)CF_3$ | (**2**) | 12.3% |
| $(Pr^iO)_2P(O)CF_2P(O)(OPr^i)_2$ | (**3**) | 26.3% |
| $(Pr^iO)_2P(O)CF_2H$ | (**4**) | 7.4% |
| $(Pr^iO)_2P(O)CF_2Br$ | (**5**) | 29.2% |
| $(Pr^iO)_2P(O)H$ & $(Pr^iO)_3P(O)$ | (**6**,**7**) | 8.4% |

In order to ascertain whether such a fluorophilic process is restricted to perhalomethanes, we performed a Michaelis-Becker reaction between diethyl sodiophosphite and

dibromofluoromethane (Scheme 2). At least seven products were visible in the NMR of the crude reaction mixture of which six were identified by NMR and MS as above. In addition to diethyl fluorophosphate (**8**) we also observed ethyl ethanephosphonofluoridate,[13] (**13**), which together account for some 15% of products, along with a fluorine-free ester ($\delta_P$ +6.5, 11%), possibly tetraethyl dibromomethylenebisphosphonate[14] (**14**). The loss of bromine from $CHFBr_2$ clearly leads to the formation of the major products (**9**) and (**10**). However, in this reaction, it is equally clear that the removal of fluorine from carbon is also strongly competitive with loss of bromine. The statistically corrected ratio of C-F to C-Br cleavage, *i.e.* 2×(**8**+**13**)÷(**9**+**10**) is approximately 1:1·6 (assuming that **8** is a co-product of an F-philic process).

**Scheme 2**

$(EtO)_2PONa$ + $CHFBr_2$ —6-10°C→

| | | |
|---|---|---|
| $(EtO)_2P(O)F$ | (**8**) | 8% |
| $(EtO)_2P(O)CHFP(O)(OEt)_2$ | (**9**) | 18% |
| $(EtO)_2P(O)CH_2F$ | (**10**) | 31% |
| $(EtO)_3P(O)$ | (**11**) | 12% |
| $(EtO)_2P(O)Et$ | (**12**) | 13% |
| $(EtO)EtP(O)F$ | (**13**) | 7% |
| $(EtO)_2P(O)CBr_2P(O)(OEt)_2$ | (**14**) | 11% |

Finally, in order better to understand the formation of the bisphosphonates (**3**, **9**, & **13**), we re-examined[10] the reaction between diethyl dichlorofluoromethylphosphonate (**15**) and diethyl sodiophosphite. On $^{31}P$ NMR analysis, the crude reaction product was seen to be a mixture of some nine components (Scheme 3) (yields are relative and based on NMR peak integration) along with a small amount of diethyl ethanephosphonate (**12**), present as an impurity in the initial sample of (**15**) as obtained from a high pressure Arbusov reaction between triethyl phosphite and fluorotrichloromethane. The products (**8**, **16**, **17**, & **18**) (nett 14%) clearly result from C-F cleavage processes, in each case in competition with C-Cl cleavage. By contrast, the major products (**9** and **10**) (38%) arise

**Scheme 3**

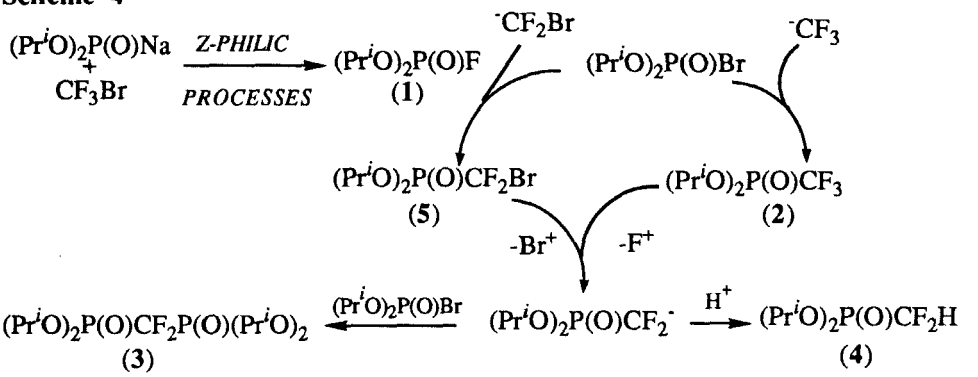
$(EtO)_2PONa$ + $(EtO)_2P(O)CFCl_2$ (**15**) —< 30 °C→

| | | |
|---|---|---|
| $(EtO)_2P(O)F$ | (**8**) | 5% |
| $(EtO)_2PCHFP(O)(OEt)_2$ | (**9**) | 18% |
| $(EtO)_2P(O)CH_2F$ | (**10**) | 20% |
| $(EtO)_3PO$ | (**11**) | 26% |
| $(EtO)_2P(O)Et$ | (**12**) | 7% |
| $(EtO)_2P(O)CFCl_2$ | (**15**) | 13% |
| $(EtO)_2PCHClP(O)(OEt)_2$ | (**16**) | 3% |
| $(EtO)_2PCCl_2P(O)(OEt)_2$ | (**17**) | 3% |
| $(EtO)_2PCH_2P(O)(OEt)_2$ | (**18**) | 3% |
| $(EtO)_2P(O)OP(O)(OEt)_2$ | (**19**) | 13% |

from C-Cl cleavage of (**15**) followed by further reactions. The statistically corrected ratio of C-F to C-Cl cleavage, *i.e.* 2×(**16**+**17**+**18**)÷(**9**+**10**) is thus approximately 1:2.

In these three reactions, the ratio of C-F to C-X cleavage (X.=.Br, Cl) varies from 1·7:1 to 1:2 and is thus very much lower than that normally seen in $S_N2$ processes, where ratios of ≥1:10 are normal.[9] Moreover, it is well-established that chlorofluorocarbons are rather inert in nucleophilic reactions.[3b,9] Notwithstanding the possibilities of SET, carbene, or radical mechanisms,[1] we believe that the evidence provided for the three processes described above identifies them as genuine examples of fluorophilic reactions involving the phosphorus anion. Scheme 4 gives viable mechanisms for the formation of the major products in the first of these reactions (*cf.* Scheme 1). Similar mechanisms account for the products produced in the second and third reactions (Schemes 2 & 3).

**Scheme 4**




ACKNOWLEDGMENT

We thank the SERC for financial support (to M-J.G.) and a CASE studentship (to S.T.)

REFERENCES

1. N.S.Zefirov, D.I.Makhon'kov, *Chem. Rev.*, 1982, **82**, 615.
2. (a). I.J.Borowitz, G.B.Borowitz, J.V.D.Veen, G.Young, P.W.R.Corfield, *Phosphorus, Sulfur, Silicon*, 1991, **63**, 223; (b). R.R.Bard, J.F.Bunnett, R.P.Traber, *J.Org. Chem.*, 1979, **44**, 4918; (c). R.M.Magid, B.G.Talley, S.K.Souther, *J. Org. Chem.*, 1981, **46**, 824.
3. (a). X-Y.Li, H-Q.Pan, X-K.Jiang, *Tetrahedron Lett.*, 1984, **25**, 4937; (b). X-Y.Li, H-Q.Pan, X-K.Jiang, Z.Y.Zhan, *Angew. Chem. Int. Ed.*, 1985, **24**, 871; (c). I.Richo, C.Wakselman, *Tetrahedron Lett.*, 1981, **22**, 323.
4. I.Rico, C.Wakselman, *Tetrahedron*, 1981, **37**, 4209
5. I.Rico, D.Cantacuzene, C.Wakselman, *J.Chem.Soc.Perkin.Trans.1.*, 1982, 1063.
6. I.Rico, D.Cantacuzene, C.Wakselman, *Tetrahedron Lett.*, 1981, **22**, 3405; N.Kornblum, *Angew. Chem. Int. Ed. Engl.*, 1975, **14**, 734; J.F.Bunnett, *Acc.Chem.Res.*, 1978, **11**, 413.
7. A.W.Frank, C.F.Baranauckas, *J.Org.Chem.*, 1965, **30**, 3970.
8. B.L.Dyatkin, E.P.Mochalina, Y.S.Konstantinov, S.R.Sterlin, I.L.Knunyants, *Izv.Akad.Nauk.SSR., Ser.Khim.*, 1967, 227; *eng.trans.*, 2200.
9. M.Hudlicky, "Chemistry of Fluorine Compounds", Ellis Horwood, 2nd ed., p481 *et seq.*, 1992.
10. G.M.Blackburn, G.E.Taylor, *J.Organometal.Chem.*, 1988, **348**, 55.
11. M-J.Guo, G.M.Blackburn, 33rd IUPAC Congress Abstr., Budapest, 1991.
12. K-H.Worms, M.Schmidt-Dunker, in "Organic Phosphorus Compounds", eds G.M.Kosolapoff, L.Maier, John Wiley, 1976, Vol 7, Ch.18, p1 *et seq.*
13. V.V.Sheluchenko, M.A.Landau, *Doklady Akad.Nauk SSSR*, 1967, **177**, 376; V.R.Mark, C.H.Dugan, M.M.Crutchfield, J.R.Van Wazer, *Topics in Phosphorus Chemistry*, 1968, **5**, 227.
14. O.T.Quimby, J.D.Curry, D.A.Nicholson, J.Prentice, C.Roy, *J.Organometal.Chem.*,1968,13,199.