

Friedel–Crafts Acylation–Cyclisation Reactions of 3-Bromophenyl Ethers with Phosphorus Trichloride and Oxalyl Chloride to give the Corresponding Phenoxaphosphine and Xanthen-9-one Derivatives

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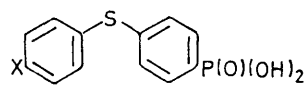
Condensations of 4-chloro- and 4-fluoro-phenyl 3-bromophenyl ether (3) with phosphorus trichloride and with oxalyl chloride in the presence of aluminium chloride gave, essentially in a one-step reaction, 7-bromo-2-chloro-phenoxaphosphine 10-oxide (4) and 6-bromo-2-fluoroxanthen-9-one (7), respectively. Best yields were obtained in dilute solutions.

DURING an investigation of the aluminium-chloride-catalysed condensation of aromatic sulphides with phosphorus trichloride,¹ we observed that *ortho*- and *para*-brominated diphenyl sulphides underwent 'debrominative phosphorylation,'² producing eventually phosphonic acids [e.g. (1)]. Under similar conditions, 3-bromophenyl 4-chlorophenyl sulphide yielded the heterocyclic phosphinic acid (2).³ We now report that a *meta*-bromo-substituent in an activated aromatic compound, such as diphenyl ether, can serve as an efficient *para*-protecting group.

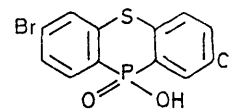
Friedel–Crafts acylation–cyclisation of the ethers (3) with phosphorus trichloride in the presence of aluminium chloride and subsequent hydrolysis gave the phenoxaphosphines (4) in good yields. These secondary phosphine oxides (4), when treated with sodium hydroxide, evolved molecular hydrogen⁴ and then yielded the corresponding phosphinic acids (5) upon acidification. Standard transformations⁴ were used to obtain the phenyl derivative (6) from (5; X = Cl). The characteristic u.v.⁴ and mass spectra^{5,6} were used to establish the structures of the compounds obtained. The only prominent mass spectral fragments of (5) were formed by eliminations of PO₂H; those of (4) were formed by competing losses of H⁺ and OH⁻.

This method represents the first preparation⁷ of brominated phenoxaphosphinic acids (5) which is achieved essentially in a one-step process from easily accessible acyclic ethers. Removal of the bromine atom from the aromatic nucleus by hydrogenolysis may offer an attractive route to monosubstituted derivatives of phenoxaphosphine.

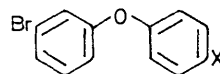
The synthetic method has been applied to the xanthen system.^{8,9} Treatment of the ethers (3) with oxalyl chloride in the presence of aluminium chloride in carbon



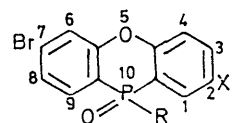
(1)



(2)



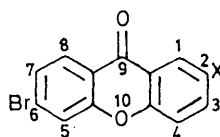
(3) X = Cl or F



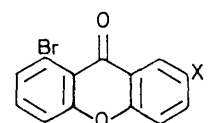
(4) R = H, X = Cl or F

(5) R = OH, X = Cl or F

(6) R = Ph, X = Cl



(7) X = Cl or F



(8)

disulphide gave the substituted xanthen-9-ones (7). The expected u.v.¹⁰ spectra and the consecutive eliminations of two CO molecules in the mass spectrometer¹¹ confirmed the structures. Structures such as (8) were excluded on grounds of steric hindrance to electrophilic attack on one *ortho*-position when another, considerably less hindered, position is available. Furthermore, in the ¹H n.m.r. spectrum of (7; X = Cl), one would expect to

⁶ I. Granoth, J. B. Levy, and C. Symmes, jun., *J.C.S. Perkin II*, 1972, 697.

⁷ J. B. Levy, G. W. Whitehead, and I. Granoth, *Israel J. Chem.*, 1972, **10**, 27.

⁸ J. W. Cusic and R. A. Robinson, U.S.P. 2,776,299 (*Chem. Abs.*, 1957, **51**, 8146).

⁹ I. Granoth and A. Kalir, *J. Org. Chem.*, 1973, **38**, 841.

¹⁰ R. A. Morton and W. T. Earلمان, *J. Chem. Soc.*, 1941, 159.

¹¹ C. S. Barnes and J. L. Occolowitz, *Austral. J. Chem.*, 1964, **17**, 975.

¹ I. Granoth, A. Kalir, Z. Pelah, and E. D. Bergmann, *Tetrahedron*, 1969, **25**, 3919.

² I. Granoth, A. Kalir, Z. Pelah, and E. D. Bergmann, *Chem. Comm.*, 1969, 260.

³ I. Granoth, A. Kalir, Z. Pelah, and E. D. Bergmann, *Israel J. Chem.*, 1970, **8**, 613.

⁴ I. Granoth, A. Kalir, Z. Pelah, and E. D. Bergmann, *Tetrahedron*, 1970, **26**, 813.

⁵ I. Granoth and J. B. Levy, *J. Chem. Soc. (B)*, 1971, 2391.

treated dropwise with 30% sodium hydroxide solution (50 ml). The aqueous layer was extracted with benzene. The combined organic layers gave, after the usual work-up, the *phosphine* (1.0 g, 71%), m.p. 90° (ethanol); λ_{max} 239 (log ϵ 4.26), 247sh (4.23), 268 (3.26), 275 (3.33), 289sh (3.43), 301 (3.61), and 309 nm (3.64) (Found: C, 55.3; H, 2.9; P, 7.8. $\text{C}_{18}\text{H}_{11}\text{BrClOP}$ requires C, 55.5; H, 2.8; P, 8.0%); m/e 388 (67%, $M^{+\cdot}$), 311 (71, $M - \text{C}_6\text{H}_5$), 309 (19, $M^+ - \text{Br}$), 232 ($M^{+\cdot} - \text{C}_6\text{H}_5 - \text{Br}$), 197 (33, $M^+ - \text{C}_6\text{H}_5 - \text{Br} - \text{Cl}$), and 108 (27, $\text{C}_6\text{H}_5\text{P}^{+\cdot}$).

6-Bromo-2-fluoroxanthen-9-one (7; X = F).—Oxalyl chloride (4.0 g), the ether (3; X = F) (4.0 g), aluminium chloride (3.0 g), and carbon disulphide (200 ml) were refluxed for 4 h, cooled, and treated with ice-water. The organic layer yielded (after work-up) the *xanthenone* (7; X = F) (3.8 g, 83%), m.p. 214° (ethanol); λ_{max} 228 (log ϵ 4.52), 234 (4.49), 267 (4.26), 286sh (3.93), 295 (4.15), and 345 nm (3.98) (Found: C, 53.4; H, 2.3; F, 6.5. $\text{C}_{18}\text{H}_6\text{BrFO}_2$ requires C, 53.3; H, 2.1; F, 6.4%); m/e 292 (100%, $M^{+\cdot}$), 264 (15, $M^{+\cdot} - \text{CO}$), 236 (2, $M^{+\cdot} - 2\text{CO}$), 213 (9, $M^{+\cdot} - \text{Br}$), 185 (17, $M^+ - \text{Br} - \text{CO}$), and 157 (84, $M^+ - \text{Br} - 2\text{CO}$).

6-Bromo-2-chloroxanthen-9-one (7; X = Cl).—This *ketone*,

prepared (65%) as described for the fluorinated analogue, had m.p. 237—238° (dimethylformamide); λ_{max} 243 (log ϵ 4.49), 248sh (4.48), 267 (4.11), 288sh (3.79), 296 (3.95), and 344 nm (3.75) (Found: C, 50.9; H, 2.4. $\text{C}_{18}\text{H}_6\text{BrClO}_2$ requires C, 50.4; H, 1.9%); m/e 308 (75%, $M^{+\cdot}$), 280 (11, $M^{+\cdot} - \text{CO}$), 229 (4, $M^+ - \text{Br}$), 201 (9, $M^+ - \text{Br} - \text{CO}$), and 173 (30, $M^+ - \text{Br} - 2\text{CO}$).

When this reaction was carried out with (3; X = Cl) (12.0 g), oxalyl chloride (7.0 g), aluminium chloride (7.8 g), and carbon disulphide (200 ml) a mixture of three products was obtained, separated as follows. Extraction with 10% sodium hydroxide solution followed by acidification of the aqueous layer gave **4-bromo-2-(4-chlorophenoxy)benzoic acid** (9) (1.0 g), m.p. 238—240° (ethanol) (Found: C, 48.0; H, 2.8. $\text{C}_{13}\text{H}_8\text{BrClO}_3$ requires C, 47.6; H, 2.4%), M^+ 326. The base-insoluble residue was extracted with petroleum giving **bis-[4-bromo-2-(4-chlorophenoxy)phenyl] ketone** (10) (3.5 g), m.p. 131° (ethanol) (Found: C, 50.9; H, 2.3. $\text{C}_{25}\text{H}_{14}\text{Br}_2\text{Cl}_2\text{O}_3$ requires C, 50.6; H, 2.4%), M^+ 590. The residue (4.1 g), m.p. 237—238° (dimethylformamide) was the xanthenone (7; X = Cl).

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