## 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

By Itshak Granoth,\* Yoffi Segall, and Asher Kalir, Israel Institute for Biological Research, Ness-Ziona, Israel

Condensations of 4-chloro- and 4-fluoro-phenyl 3-bromophenyl ether (3) with phosphorus trichloride and with oxalvl chloride in the presence of aluminium chloride gave, essentially in a one-step reaction. 7-bromo-2-chlorophenoxaphosphine 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-chloridecatalysed condensation of aromatic sulphides with phosphorus trichloride,<sup>1</sup> we observed that ortho- and parabrominated 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).<sup>3</sup> 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 hydrogen<sup>4</sup> and then yielded the corresponding phosphinic acids (5) upon acidification. Standard transformations<sup>4</sup> were used to obtain the phenyl derivative (6) from (5; X = Cl). The characteristic u.v.<sup>4</sup> and mass spectra <sup>5,6</sup> were used to establish the structures of the compounds obtained. The only prominent mass spectral fragments of (5) were formed by eliminations of PO<sub>2</sub>H; those of (4) were formed by competing losses of H' and OH'.

This method represents the first preparation 7 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.

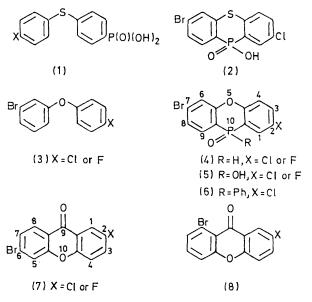
<sup>1</sup> I. Granoth, A. Kalir, Z. Pelah, and E. D. Bergmann, Tetrahedron, 1969, 25, 3919. <sup>2</sup> I. Granoth, A. Kalir, Z. Pelah, and E. D. Bergmann,

Chem. Comm., 1969, 260.

<sup>3</sup> I. Granoth, A. Kalir, Z. Pelah, and E. D. Bergmann, Israel J. Chem., 1970, 8, 613. <sup>4</sup> I. Granoth, A. Kalir, Z. Pelah, and E. D. Bergmann, Tetrahedron, 1970, 26, 813.

<sup>5</sup> I. Granoth and J. B. Levy, J. Chem. Soc. (B), 1971, 2391.

The synthetic method has been applied to the xanthen system.<sup>8,9</sup> Treatment of the ethers (3) with oxalyl chloride in the presence of aluminium chloride in carbon



disulphide gave the substituted xanthen-9-ones (7). The expected u.v.<sup>10</sup> spectra and the consecutive eliminations of two CO molecules in the mass spectrometer <sup>11</sup> 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 <sup>1</sup>H n.m.r. spectrum of (7; X = Cl), one would expect to

<sup>6</sup> I. Granoth, J. B. Levy, and C. Symmes, jun., J.C.S. Perkin

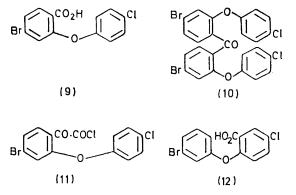
11, 1972, 697. <sup>7</sup> J. B. Levy, G. W. Whitehead, and I. Granoth, Israel J. Chem., 1972, 10, 27.

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

 I. Granoth and A. Kalir, J. Org. Chem., 1973, 38, 841.
R. A. Morton and W. T. Earlman, J. Chem. Soc., 1941, 159.
C. S. Barnes and J. L. Occolowitz, Austral. J. Chem., 1964, 17, 975.

see two proton deshielded by the carbonyl group. A two- and a four-proton multiplet centred at  $\delta 8.40$  and 7.75, respectively, were in fact observed. In structure (8) only one proton should be deshielded.

The best yields in this reaction were obtained from dilute solutions in carbon disulphide. When relatively concentrated solutions were used in the case of (3; X = Cl), two by-products, (9) and (10), were isolated.



The formation of these products suggested that the decarbonylation of the oxalyl chloride  $^{12}$  or the oxalyl intermediate (11) takes place prior to the formation of the central ring. Furthermore, the first electrophilic attack apparently occurs on the brominated ring rather than on the chlorinated ring. The latter mode would have led to structure (12), which was not detected.

Structures (9) and (10) were assigned on the basis of their mass spectra. Both spectra showed prominent ions at m/e 111 and 113, in the ratio 3:1, corresponding to the two isotopes of  $C_6H_4Cl^+$ . In the mass spectrum of structure (12) one would expect to find fragments of m/e 155 and 157 ( $C_6H_4Br^+$ ), which were not in fact observed.

## EXPERIMENTAL

M.p.s were taken with a Thomas Hoover capillary apparatus. U.v. spectra were recorded for solutions in 96%ethanol with a Bausch and Lomb Spectronic 505 instrument. N.m.r. spectra were run on a JEOL C-60 HL high resolution spectrometer. Low-resolution mass spectra were obtained with a Hitachi-Perkin-Elmer RMU 6 spectrometer at 70 eV (direct insertion probe; source temperature 150-200°). Only ions of structural significance are given; isotopic ions are excluded.\*

3-Bromophenyl-4-Chlorophenyl Ether <sup>13</sup> (3; X = Cl).—4-Chlorophenol (58 g) and potassium hydroxide (18.6 g) were heated until no more water distilled off. Then 1,3-dibromobenzene (100 g) and copper bronze (1.0 g) were added. The mixture was refluxed for 2 h, cooled, treated with 10% sodium hydroxide (200 ml), and extracted with chloroform. Fractionation gave [apart from recovered 1,3-dibromobenzene (44.0 g)] the *ether* (3; X = Cl) (30.0 g), b.p. 195— 205° at 20 mmHg (Found: C, 51.0; H, 2.7. C<sub>12</sub>H<sub>8</sub>BrClO requires C, 50.8; H, 2.8%);  $\delta$  (CDCl<sub>3</sub>) 7.21 (m, ArH), and a residue which was not examined.

\* Further mass spectral details are given in Supplementary Publication No. SUP 20749 (2 pp.). For information concerning Supplementary Publications, see Notice to Authors No. 7 in J. Chem. Soc. (A), 1970, Issue No. 20. 3-Bromophenyl 4-Fluorophenyl Ether (3; X = F).—Prepared similarly from 4-fluorophenol (26.0 g), potassium hydroxide (10.5 g), 1,3-dibromobenzene (44.0 g), and copper bronze (1.0 g), the ether (3; X = F) (16.0 g) had b.p. 220° at 25 mmHg (Found: C, 53.6; H, 2.9; Br, 30.4.  $C_{12}H_8BrFO$  requires C, 53.9; H, 3.0; Br, 30.0%);  $\delta$  (CDCl<sub>3</sub>) 7.10 (m, ArH).

7-Bromo-2-chlorophenoxaphosphine 10-Oxide (4; X = Cl). —A mixture of the ether (3; X = Cl) (8.5 g), phosphorus trichloride (20 ml), and aluminium chloride (5.1 g) was refluxed for 24 h and poured on crushed ice (300 g). The solid product was filtered off and recrystallized from benzene; m.p. 230—233°; yield 6.0 g (60%);  $\lambda_{max}$  224 (log  $\varepsilon$  4.59), 240sh (4.52), 252sh (4.32), 269sh (3.36), 293sh (3.59), and 303 nm (3.66) (Found: C, 43.5; H, 1.9. C<sub>12</sub>H<sub>7</sub>BrClO<sub>2</sub>P requires C, 43.7; H, 2.1%); *m/e* 328 (38%, *M*<sup>++</sup>), 327 (67, *M*<sup>+</sup> - H), 311 (75, *M*<sup>+</sup> - OH), 277 (35, C<sub>12</sub>H<sub>7</sub>BrOP<sup>+</sup>), 233 (56, C<sub>12</sub>H<sub>7</sub>ClOP<sup>+</sup>), and 202 (29, *M*<sup>++</sup> - Br - PO).

7-Bromo-2-chloro-10-hydroxyphenoxaphosphine 10-Oxide (5; X = Cl).—The phosphine oxide (4; X = Cl) (5.0 g) and 10% sodium hydroxide solution (200 ml) were heated until a clear solution had formed.<sup>4</sup> During this time molecular hydrogen was evolved. Acidification of the clear solution with hydrochloric acid afforded the acid in quantitative yield, m.p. 250—252°;  $\lambda_{\text{max}}$  222 (log  $\varepsilon$  4.66), 239sh (4.53), 250sh (4.32), 269 (3.33), 294 (3.64), and 303 nm (3.70),  $M^+$  344, characterized as its dicyclohexylammonium salt, m.p. 252° (prepared in and recrystallized from dimethylformamide) (Found: C, 54.7; H, 5.7; P, 5.5. C<sub>24</sub>H<sub>30</sub>-BrCINO<sub>3</sub>P requires C, 54.7; H, 5.7; P, 5.9%).

7-Bromo-2-fluoro-10-hydroxyphenoxaphosphine 10-Oxide (5; X = F). The secondary phosphine oxide (4; X = F) was prepared as for (4; X = Cl) from (3; X = F) (14 g), phosphorus trichloride (40 ml), and aluminium chloride (17.0 g). The oily product was extracted with chloroform and converted into the phosphinic acid (5; X = F) (10.1 g, 51%) as described for (5; X = Cl); m.p. 237°;  $\lambda_{max}$  220 (log  $\varepsilon$  4.52), 238sh (4.32), 246sh (4.09), 268 (3.30), 278sh (3.37), 292 (3.61), and 300 nm (3.67) (Found: C, 47.5; H, 2.4; P, 9.4. C<sub>12</sub>H<sub>7</sub>BrFO<sub>3</sub>P requires C, 47.4; H, 2.1; P, 9.4%); m/e 328 (100%, M<sup>++</sup>), 264 (55, M<sup>++</sup> - PO<sub>2</sub>H), and 186 (31, M<sup>++</sup> - PO<sub>2</sub>Br).

7-Bromo-2-chloro-10-phenylphenoxaphosphine 10-Oxide (6). -A mixture of the acid (5; X = Cl) (7.5 g) and thionyl chloride (40 ml) was stirred and refluxed for 2 h, then evaporated under reduced pressure, ultimately after addition of toluene (10 ml). To a suspension of the residue in dry ether (100 ml), phenylmagnesium bromide [from bromobenzene (11.8 g) and magnesium (1.85 g) in ether (100 ml)was added. The mixture was refluxed for 2 h and decomposed with ice-cold 10% hydrochloric acid (100 ml). The organic layer yielded the phenyl derivative (6) (3.1 g, 35%), m.p. 182° (cyclohexane);  $\lambda_{max}$  235 (log  $\epsilon$  4.56), 247sh (4.49), 268 (3.45), 276 (3.47), 290sh (3.52), 301 (3.67), and 310 nm (3.68) (Found: C, 53.1; H, 2.9; P, 7.8.  $C_{18}H_{11}$ -BrClO<sub>2</sub>P requires C, 53·3; H, 2·7; P, 7·6%); m/e 404 (77%,  $M^{+*}$ ), 327 (47,  $M^{+} - C_{6}H_{5}$ ), 311 (20,  $M^{+} - C_{6}H_{5}O$ ), 280 (10,  $M^{+*} - C_6H_5PO$ ), 277 (12,  $C_{12}H_7BrOP^+$ ), and 233 (28, C<sub>12</sub>H<sub>7</sub>ClOP<sup>+</sup>).

7-Bromo-2-chloro-10-phenylphenoxaphosphine.— The foregoing phosphine oxide (6) (1.5 g), trichlorosilane (3 ml), and dry benzene (20 ml) were boiled for 2 h, cooled, and

<sup>12</sup> P. E. Sokol, Org. Synth., 1964, 44, 69.

<sup>13</sup> Monsanto Co., Neth. P. Appl. 6,512,286 (Chem. Abs., 1966, 65, 7104).

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);  $\lambda_{max}$  239 (log  $\varepsilon$  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. C<sub>18</sub>H<sub>11</sub>BrClOP requires C, 55·5; H, 2·8; P, 8·0%); *m/e* 388 (67%, *M*<sup>+</sup>·), 311 (71, *M* - C<sub>6</sub>H<sub>5</sub>), 309 (19, *M*<sup>+</sup> - Br), 232 (*M*<sup>++</sup> - C<sub>6</sub>H<sub>5</sub> - Br), 197 (33, *M*<sup>+</sup> - C<sub>6</sub>H<sub>5</sub> - Br - Cl), and 108 (27, C<sub>6</sub>H<sub>5</sub>P<sup>+</sup>·).

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);  $\lambda_{max}$  228 (log  $\varepsilon$  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. C<sub>13</sub>H<sub>6</sub>-BrFO<sub>2</sub> requires C, 53·3; H, 2·1; F, 6·4%); m/e 292 (100%,  $M^{+*}$ ), 264 (15,  $M^{+*}$  – CO), 236 (2,  $M^{+*}$  – 2CO), 213 (9,  $M^{+*}$  – Br), 185 (17,  $M^{+}$  – Br – CO), and 157 (84,  $M^{+}$  – Br – 2CO).

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);  $\lambda_{max}$  243 (log  $\varepsilon$ 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. C<sub>13</sub>H<sub>6</sub>BrClO<sub>2</sub> requires C, 50·4; H, 1·9%); *m/e* 308 (75%, *M*<sup>+</sup>), 280 (11, *M*<sup>+</sup> - CO), 229 (4. *M*<sup>+</sup> - Br), 201 (9, *M*<sup>+</sup> - Br - CO), and 173 (30, *M*<sup>+</sup> - Br - 2CO).

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. C<sub>13</sub>H<sub>8</sub>BrClO<sub>3</sub> 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. C<sub>25</sub>H<sub>14</sub>Br<sub>2</sub>Cl<sub>2</sub>O<sub>3</sub> 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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