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STUDIES IN THE PHENOXAPHOSPHINE SERIES

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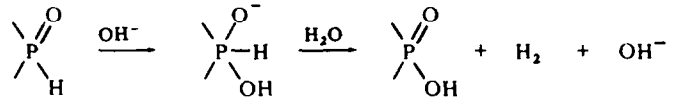
Abstract—4,4'-Difluoro- and 4,4'-dichlorodiphenyl ether give with phosphorus trichloride and aluminium chloride 2,8-dihalogenophenoxaphosphine-10-oxides (I). With alkali, the latter yield the salts of phenoxaphosphinic acids (II, R = H) with evolution of molecular hydrogen. The mechanism of this and similar reactions is discussed.

IT HAS been shown[1, 2] that di-*p*-tolyl ether can be converted, by treatment with phosphorus trichloride and aluminium chloride, into 2,8-dimethylphenoxaphosphine 10-oxide (I, R = H, R' = Me), which easily autoxidized to 2,8-dimethylphenoxaphosphinic acid (II, R = H, R' = Me). The analogous reaction of 4,4'-difluoro- and 4,4'-dichlorodiphenyl ether was expectedly slower. Surprisingly, the 2,8-dihalogenophenoxaphosphine 10-oxides (I, R = H, R' = Cl or F) did not autoxidize. On the other hand, they reacted readily with aqueous alkali or alcoholic alkoxides, the reaction rate decreasing in the order: F > Cl > Me, to give the alkali salts or the substituted phenoxaphosphinic acids (II, R = H). In all these cases, *molecular hydrogen was evolved.*

Campbell and Stevens[3] have formulated this curious oxidation reaction as follows:



This mechanism did not completely satisfy us, as methanolic methoxide, e.g., should have given the methyl ester of the phosphinic acid whilst in fact the sodium *salt* of the acid was formed. Indeed, sodium thiophenoxide[3] does give the phenylthiol ester; on the other hand, the sodium derivative of β-diethylaminoethanethiol gives again only the salt of II (R = H). We have found that a *catalytic* quantity of sodium methoxide in anhydrous methanol produces the desired methyl ester, but that this ester is transformed smoothly into the sodium salt by an excess of sodium methoxide. It is unclear how this decomposition reaction proceeds; it does not produce dimethyl ether. Equally, when the n-butyl ester of 2,8-difluorophenoxaphosphinic acid (II, R = C_4H_9, R' = F) was treated with sodium n-butoxide, the sodium salt of the acid, but no di-n-butyl ether was formed nor could butane be detected amongst the reaction products.

We have observed an equally curious oxidation process when the secondary phosphine oxide (I, R = H, R' = F) was treated with a secondary amine (2 mole): the dialkylammonium salt of the acid II (R = H, R' = F) was obtained.

Some other reactions of the phosphine oxides I(R = H) followed more closely the expected course. Treatment with elemental sulphur led to insertion of sulphur

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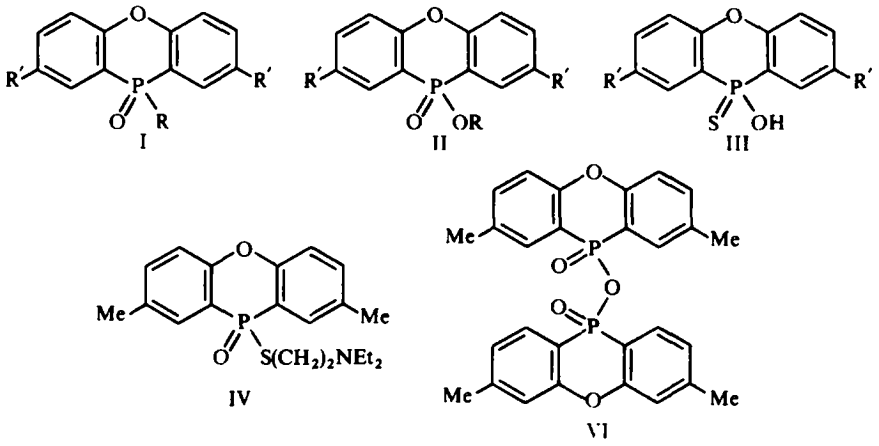
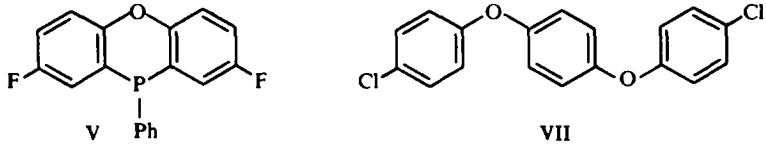


in the P—H bond, followed by hydrogen migration.[4] Thus the thiono-acids III were obtained. The characteristic P═O absorption was absent from their IR spectra. The NMR spectra of the phosphorus[5] showed $\delta_P = -46$ ppm, whilst for compound IV, which is the ester of a thiol-acid, $\delta_P = -15$ ppm has been observed. Compound IV shows, of course, the IR P═O absorption at 1180 cm^{-1}.

With thionyl chloride, the acids of type II (R = H) give the corresponding acid chlorides. The chloride I (R = Cl, R′ = Me) gives with alcohols and mercaptans the corresponding esters and thiol-esters. Thus, with β-diethylaminoethanethiol the ester IV was prepared. The chloride (I, R = Cl, R′ = F) of the acid II (R = H, R′ = F) reacted smoothly with phenylmagnesium bromide to give 2,8-difluoro-10-phenylphenoxaphosphine 10-oxide (I, R = Ph, R′ = F). In analogy to previous observations of ours,[2] this tertiary phosphine oxide is reduced by trichlorosilane to 2,8-difluoro-10-phenylphenoxaphosphine (V).

The secondary phosphine oxide (I, R′ = Me, R = H) was not reduced by trichlorosilane to the corresponding phosphine, but rather chlorinated. Thus I (R = Cl, R′ = Me) was obtained; its structure followed from its hydrolysis to a compound of



the formula $C_{28}H_{24}O_5P_2$. The synthesis of the compound from the chloride of the acid II (R = H, R′ = Me) and the theoretical amount of water in the presence of triethylamine proved that it is the anhydride VI of 2,8-dimethylphenoxaphosphinic acid. A similar compound has been recently obtained[6] from 2,4,6-triphenylphosphorin.

EXPERIMENTAL

All m.ps are uncorrected. The IR spectra were measured in KBr pellets, the UV spectra in 96% EtOH. The phosphorus NMR spectra refer to 85% phosphoric acid.

Whilst 4,4′-difluorodiphenyl ether was a commercial product, *4,4′-dichlorodiphenyl ether* was prepared as follows: *p*-Chlorophenol (128·5 g), *p*-bromochlorobenzene (132·0 g) and KOH (62·0 g) were heated, and the water formed was permitted to distil off continuously. Then *p*-bromochlorobenzene (ca. 30 ml) was distilled off, and the residue refluxed for 6 hr with 4·0 g copper bronze. After cooling, the mixture was

treated with 200 ml water and extracted with ether. Fractionation gave apart from 60·0 g *p*-bromochlorobenzene, 75·0 g (yield, 31%) of 4,4'-dichlorodiphenyl ether, b.p. 185–187° (20 mm), and 30·0 g (9%) of a product of b.p. 285° (20 mm), m.p. 92° (from EtOH) which according to the analysis was not quite pure *p-di (4-chlorophenoxy) benzene* (VII). (Found: C, 64·3; H, 3·2; Cl, 20·7; Calcd. for $C_{18}H_{12}Cl_2O_2$: C, 65·5; H, 3·6; Cl, 21·2%).

2,8-*Dichlorophenoxaphosphine* 10-*oxide* (I, R = H, R' = Cl). A mixture of 4,4'-dichlorodiphenyl ether (47·8 g), $AlCl_3$ (34·0 g) and PCl_3 (70 ml) was refluxed for 22 hr and poured onto 500 g crushed ice. The solid product was filtered off and recrystallized from benzene; m.p. 325°; yield, 28·4 g (50%); $\tilde{\nu}_{max}$ 2340 (P—H), 1450, 1385, 1265 (C—O—C), 1220, 1190 (P—O), 110, 820 cm^{-1}; λ_{max} 223 (4·39); 248 (4·31); 251 (4·32); 255[s] (4·10); 288 (3·98); 298[s] (3·60); 306 mμ (log ε 3·66). (Found: C, 50·3; H, 2·6; Cl, 24·5; P, 10·2. Calc. for $C_{12}H_7Cl_2O_2P$: C, 50·5; H, 2·5; Cl, 24·9; P, 10·9%).

2,8-*Dichlorophenoxaphosphinic acid* (II, R = H, R' = Cl). The foregoing product (14·3 g) was heated with 150 ml 10% NaOH aq until a clear soln had formed (10 min). During this period H_2 was evolved. Acidification of the soln with HCl gave the *acid* in quantitative yield, m.p. above 350°. It was characterized by its *dicyclohexylammonium* salt, m.p. 267°, which was prepared in and recrystallized from DMF; $\tilde{\nu}_{max}$ 1450, 1380, 1265 (C—O—C), 1170 (P═O), 1100, 1035 cm^{-1}; λ_{max} 223 (4·41); 248 (4·32); 252 (4·34); 255 (4·22); 270 (3·22); 284 (3·28); 296 (3·56); 306 mμ (log ε 3·65). (Found: C, 59·8; H, 6·1; Cl, 15·1; P, 6·3. Calc. for $C_{24}H_{30}Cl_2NO_3P$: C, 59·8; H, 6·2; Cl, 14·7; P, 6·4%).

2,8-*Dichlorophenoxathionophosphinic acid* (III, R' = Cl). A mixture of I (R = H, R' = Cl) (2·85 g), S (0·32 g) and xylene (10 ml) was refluxed for 2 hr. The product crystallized upon cooling and was recrystallized from toluene; yield, 2·4 g (77%); m.p. 179°; $\tilde{\nu}_{max}$ 1450, 1390, 1265 (C—O—C), 1140, 925, 825 cm^{-1}; λ_{max} 225 (4·57); 239 (4·39); 244 (4·40); 249 (4·41); 255 (4·35); 261 (4·25); 269 (3·78); 388 (3·29); 309 mμ (log ε 3·66); NMR spectrum: δ_{HO} = 5·65 ppm (broad); $\delta_P = -46·0 \pm 0·5$ ppm. (Found: Cl, 21·9; S, 9·6; P, 9·7. Calc. for $C_{12}H_7Cl_2O_2PS$: Cl, 22·4; S, 10·1; P, 9·8%).

2,8-*Difluorophenoxaphosphine* 10-*oxide*. (I, R = H, R' = F). A mixture of 4,4'-difluorodiphenyl ether (61·8 g), $AlCl_3$ (51·0 g) and PCl_3 (105 ml) was refluxed for 53 hr (shorter heating periods gave lower yields) and poured onto 1 kg crushed ice. The solid product (40·8 g; 54%) was recrystallized from toluene and melted at 230°; $\tilde{\nu}_{max}$ 2340 (P—H), 1460, 1400, 1265 (C—O—C), 1200 (C—F), 1180 (P═O), 830 cm^{-1}; λ_{max} 224 (4·20); 239 (4·09); 244 (4·06); 249 (3·85); 255 (3·80); 261 (3·70); 269 (2·94); 296 (3·62); 305 mμ (log ε 3·73); NMR spectrum δ_{HP} = 8·62 ppm, J_{HP} = 525 c/s.* (Found: C, 57·7; H, 3·4. Calc. for $C_{12}H_7F_2O_2P$: C, 57·1; H, 2·8%).

2,8-*Difluorophenoxaphosphinic acid* (II, R = H, R' = F). The acid, prepared as for the corresponding dichloro compound, could not be recrystallized and was therefore synthesized by an alternative method which gave directly a pure product. To a soln of 2·52 g of the foregoing compound in a minimum of hot n-BuOH, 10 ml of a 0·01M soln of n-BuONa in BuOH was added. In an exothermic reaction, H_2 was evolved, and the Na salt of the desired acid precipitated. It was filtered off, dissolved in water and treated with HCl. The *acid* was filtered off, washed with water and ether and dried, m.p. above 350°; $\tilde{\nu}_{max}$ 2240, 1660 (P—OH), 1465, 1400, 1265 (C—O—C), 1200 (C—F), 1160 (P═O), 1130, 995, 970, 885, 825 cm^{-1}; λ_{max} 225 (4·24); 236 (4·08); 255 (2·62); 260 (2·71); 270 (2·96); 297 (3·72); 305 mμ (log ε 3·77). (Found: C, 53·9; H, 2·8; P, 11·4. Calc. for $C_{12}H_7F_2O_3P$: C, 53·7; H, 2·6; P, 11·5%).

The *dicyclohexylammonium salt*, prepared in DMF, melted at 261°. The same salt was obtained (m.p. and mixed m.p. 261°) when I (R = H, R' = F) was heated in MeOH with dicyclohexylamine (2 mole) for 1 hr. (Found: C, 63·8; H, 6·4; P, 6·8. Calc. for $C_{24}H_{30}F_2NO_3P$: C, 64·1; H, 6·7; P, 6·9%).

In the same way the *piperidinium salt* was obtained, m.p. 136° (from toluene). (Found: C, 57·1; H, 5·3; P, 8·8. Calcd. for $C_{17}H_{18}F_2NO_3P$: C, 57·8; H, 5·1; P, 8·8.)

2,8-*Difluorophenoxathionophosphinic acid* (III, R' = F). Prepared in the same way as the dichloro compound, in 85% yield, the acid melted at 252° (toluene); $\tilde{\nu}_{max}$ 1460, 1400, 1260 (C—O—C), 1200 (C—F), 930, 835 cm^{-1}; λ_{max} 224 (4·31); 238 (4·09); 244 (4·06); 249 (3·97); 255 (3·89); 261 (3·78); 269[s] (3·39); 306 mμ (log ε 3·80); NMR spectrum: $\delta_P = -46·0 \pm 0·5$ ppm; δ_{HO} = 6·98 ppm. (Found: C, 50·8; H, 2·4; P, 10·9. Calc. for $C_{12}H_7F_2O_2PS$: C, 50·7; H, 2·5; P, 10·9%).

2,8-*Difluoro*-10-*phenylphenoxaphosphine* 10-*oxide* (I, R = Ph, R' = F). The acid chloride of II (R = H, R' = F) was treated with $PhMgBr^2$ and the product (yield, 70%), recrystallized from cyclohexane. It melted at 168°; $\tilde{\nu}_{max}$ 1460, 1400, 1265 (C—O—C), 1200 (C—F, P═O), 1190 cm^{-1}; λ_{max} 226 (4·44), 248 (3·97); 254[s] (3·66); 261 (3·44); 268 (3·18); 275 (3·25); 304[s] (3·29); 312 mμ (log ε 3·85). (Found: C, 66·1; H, 3·4; P, 9·0. Calc. for $C_{18}H_{11}F_2O_2P$: C, 65·9; H, 3·4; P, 9·5%).

2,8-*Difluoro*-10-*phenylphenoxaphosphine* (VI). The foregoing compound was treated with trichlorosilane

as described in a previous paper[2], yield, 96%; m.p. 57° (EtOH); $\bar{\nu}_{max}$ 1460, 1390, 1260 (C—O—C), 1240, 1190 (C—F), 825, 816, 750 cm^{-1}; λ_{max} 227 (4·99); 243^s (4·16); 248^s (4·01); 255 (3·77); 261 (3·62); 268^s (3·39); 274 (3·32); 305 mμ (log ε 3·75). (Found: C, 69·9; H, 3·6; P, 9·8. Calc. for $C_{16}H_{11}F_2OP$: (C, 69·2; H, 3·5; P, 9·9%).

Methiodide, prepared in EtOH, m.p. 275° (from EtOH–ether); λ_{max} 227 (4·50); 243^s (4·20); 249 (4·04); 255 (3·87); 261 (3·73); 271 (3·31); 278 (3·40); 295^s (3·66); 308^s (3·80); 316 mμ (log ε 3·89). (Found: P, 6·6. Calc. for $C_{19}H_{14}F_2IOP$: P, 6·8%).

Methyl 2,8-difluorophenoxaphosphinate (II, R = Me, R′ = F). The methylation of II (R = H, R′ = F) was carried out as described.[7] The *ester* (yield 80%) melted at 153° (EtOH). (Found: C, 55·6; H, 3·4; P, 10·9. Calc. for $C_{13}H_9F_2O_3P$: C, 55·3; H, 3·2; P, 11·0%).

When 2·8 g of the ester was dissolved in a minimum of MeOH at 0° and treated with 5 ml of 2M NaOMe for 10 min at that temp, addition of 2 ml glacial AcOH and 100 ml water precipitated a small quantity of starting material. Acidification of the mother liquor with HCl gave 2·0 g of 2,8-difluorophenoxaphosphinic acid, identified by UV and IR spectrum.

2,8-Dimethylphenoxathionophosphinic acid (III, R′ = Me). As described for III (R′ = F), the acid was prepared from 2,8-dimethylphenoxaphosphine 10-oxide;[2] yield, 94%; m.p. 179° (benzene); $\bar{\nu}_{max}$ 1580, 1470, 1380, 1325, 1270 (C—O—C), 1220, 1200, 1140, 1020, 914, 890, 820, 720 cm^{-1}; λ_{max} 220 (4·66) 243 (4.26); 272 (3·48); 284 (3·42); 302^s (3·77); 310 mμ (log ε 3·81); NMR spectrum: δ_{HO} = 6·63 ppm; δ_{HCH_3} = 2·34 ppm: δ_P = −46·1 ± 0·5 ppm. (Found: C, 61·3; H, 4·7; P, 10·7. Calc. for $C_{14}H_{13}O_2PS$: C, 60·9; H, 4·7; P, 11·2%).

β-Diethylaminoethanethiol 2,8-dimethylphenoxaphosphinate (IV) *hydrochloride*. The chloride I (R = Cl, R′ = Me) of II (R = H, R′ = Me) was obtained from 2·6 g of the acid and 30 ml $SOCl_2$, which were refluxed for 2 hr. The soln was brought to dryness and the residue treated with 10 ml toluene and evaporated again. Then 80 ml benzene and 1·33 g β-diethylaminoethanethiol in 20 ml benzene were added successively, and the mixture was refluxed for 1 hr. After cooling, the hydrochloride of IV (1·9 g) was filtered off and recrystallized from acetone–EtOH, m.p. 206°; $\bar{\nu}_{max}$ 1470, 1380, 1270 (C—O—C), 1180 (P=O), 1130, 815 cm^{-1}; λ_{max} 222 (4·60); 245 (4·38); 278 (3·36); 290^s (3·53); 308^s mμ (log ε 3·72); NMR spectrum: δ_P = −15·2 ± 0·5 ppm. (Found: C, 58·6; H, 6·6; Cl, 8·9; P, 7·1. Calc. for $C_{20}H_{27}ClNO_2PS$: C, 58·3; H, 6·4; Cl, 8·6; P, 7·5%).

Anhydride V. (a) Trichlorosilane (3 ml) was added gradually at 40° to a mixture of I (R = H, R′ = Me; 2·4 g) and benzene (30 ml), and the mixture was refluxed for 2 hr. Then, 80 ml of 30% NaOH aq was added gradually and with good cooling. From the organic layer, 1·0 g (40%) of V was isolated; it melted at 252° after recrystallization from benzene.

(b) The chloride of 2,8-dimethylphenoxaphosphinic acid, prepared from 1·4 g of the acid and 10 ml $SOCl_2$, was suspended in toluene; a mixture of 48·6 mg water and 550 mg Et_3N was added and the mass refluxed for 2 hr. After filtration and evaporation of the solvent, the residue was recrystallized from benzene; m.p. and mixed m.p. 252°; yield, 0·5 g (35%); $\bar{\nu}_{max}$ 1470, 1390, 1270, 1225, 915, 826 cm^{-1}; λ_{max} 222 (4·82); 244 (4·50); 277^s (3·54); 288^s (3·73); 303 (3·93); 311 mμ (log ε 3·90); NMR spectrum: δ_{HCH_3} = 2·30 ppm. (Found: C, 66·7; H, 5·0; P, 11·9; mol. wt. (mass spectrum), 502. Calc. for $C_{28}H_{24}O_5P_2$: C, 66·9; H, 4·8; P, 12·3%; mol. wt. 502).

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* The same type of NMR spectrum has been observed for 2,8-dimethylphenoxaphosphine 10-oxide (I, R = H, R′ = Me).[2]