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Structural Effects in Reactions of Organophosphorus Compounds. I. Reactions of Phosphorus Oxychloride with Hindered Phenols

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2,6-Dialkyl-phenols exhibit little steric hindrance on reaction with phosphoryl chloride unless the alkyl substituent is bulky (*i.e.* t-butyl). Where bulky substituents are present reaction with phosphoryl chloride occurs only in the presence of Friedel–Crafts type catalysts after either a dealkylation or a rearrangement of the *ortho*-placed alkyl groups, followed by *O*-phosphorylation, has occurred.

DIALKYLANILINES react with phosphoryl chloride and phosphorus trichloride by C-phosphorylation at the *para*-position both in the presence ¹ and the absence of ² specific Friedel–Crafts type catalysts to give mixtures of products containing from one to three phosphorus–

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carbon bonds; the composition of the mixtures is largely determined by the reactant ratious used. An apparently simple typographical error in the paper by Koenigs and

¹ A. Michaelis and S. Schenk, Annalen, 1890, **260**, 1; M. Bourneuf, Bull. Soc. chim. France, 1923, (4), **33**, 1808; H. Raudnitz, Ber., 1927, **60**, 743.

² E. Koenigs and H. Friedrich, Annalen, 1934, 509, 138.

Friedrich, which described possibly the simplest route to tertiary phosphine oxides with p-dialkylaminophenyl groups, gives a completely erroneous set of reactant proportions for this reaction [*i.e.* dimethylaniline (10 g.), phosphorus oxychloride (8 g.) and pyridine (15 g.) as the acid-binding agent]. With these reactant proportions the yield of the desired product is almost nil, although a simple readjustment of the proportions to give a 3:1 molar ratio of both the amine and pyridine to phosphoryl chloride readily yields a satisfactory reaction. The erroneous proportions have been perpetuated in the review literature for over 30 years.

Since Friedel-Crafts type para-substitution in dialkylanilines is paralleled by the similar reactivity of phenolic compounds, we felt that p-phosphorylations of phenols by phosphoryl chloride (or phosphorus trichloride) in the presence of suitable catalysts was possible, provided that conventional O-phosphorylation could be suppressed. This suppression seemed likely by the presence of bulky alkyl groups in 2,6-dialkylphenols. The likelihood of such a substitution appeared to be enhanced by the known C-phosphorylation of phenolic ethers in the presence of aluminium chloride and zinc chloride catalysts.³

We found that 2,6-dialkylphenols with progressively bulkier alkyl groups exhibit steric hindrance effects in their reaction with phosphoryl chloride, but that the effect is relatively small until the bulk of the alkyl group approaches that of t-butyl. With smaller alkyl substituents the phenols show a relatively slower rate of reaction with phosphoryl chloride but not a qualitative change in the nature of the *O*-phosphorylation reaction. With *ortho*-t-butylphenol no reaction takes place in the absence of a Friedel-Crafts catalyst, while in the presence of such a catalyst the t-butyl group adjacent to the hydroxy-group is either eliminated as t-butyl chloride or undergoes rearrangement to the p-position after which the normal *O*-phosphorylation takes place.

No evidence of *para*-substitution by phosphorus could be found in the reactions of these hindered phenols regardless of conditions used. This appears to be the first report of such behaviour of so-called 'hindered' phenols with phosphorus chlorides.

EXPERIMENTAL

The n.m.r. spectra were taken on a Varian Associates spectrometer, model A60, with tetramethylsilane as the internal reference.

2,6-Dimethylphenol.—Phosphorus oxychloride (40 ml.), 2,6-dimethylphenol (17.4 g.), and iron filings (2.88 g.) were heated under reflux for 24 hr. and gave 2,6-dimethylphenyl phosphorodichloridate (32.7%), b. p. $110^{\circ}/1.5$ mm. (or 139—140°/12 mm.), which was hydrolysed in aqueous acetone to 2,6-dimethylphenyl dihydrogen phosphate, needles, m. p. 185—186.5° (Found: C, 47.65; H, 5.5; P, 15.5. $C_8H_{11}O_4P$ requires C, 47.5; H, 5.5; P, 15.3%).

This ester, heated with dilute hydrochloric acid, hydrolysed to the original 2,6-dimethylphenol, m. p. $46-47^{\circ}$.

The same reaction gave an 80.6% yield of the phosphorodichloridate when lithium chloride (134 mg.) was used as the catalyst, or 67.9% with metallic magnesium (311 mg.) as the catalyst. In the two latter cases the reaction was complete within 2-3.5 hr. Unexpectedly, phosphorus oxychloride (22 ml.), 2,6-dimethylphenol (27.8 g.), and zinc chloride (1.39 g.) catalyst, failed to yield any hydrogen chloride after 2 hr. at 186° and no evidence of reaction could be found.

The aryl phosphorodichloridate and an excess of benzylamine in benzene gave 2,6-dimethylphenyl NN'-dibenzylphosphorodiamidate, m. p. 95–97.5° (from chloroformhexane) (Found: N, 7.0; P, 8.1. $C_{22}H_{25}N_2O_2P$ requires N, 7.35; P, 8.1%).

The distillation residue left after the isolation of the phosphorodichloridate could not be distilled under reduced pressure and, treated with aqueous acetone gave, after acidification bis-2,6-dimethylphenyl hydrogen phosphate, leaflets (13.1 g. 37.75%), m. p. 141-142° (chloroform-hexane) (Found: C, 62.55; H, 6.45; P, 10.1. $C_{16}H_{19}O_4P$ requires C, 62.75; H, 6.25; P, 10.1%). This ester (1.444 g.) and dicyclohexylcarbodi-imide (0.55 g.), kept 1 day in tetrahydrofuran gave, after the removal of the precipitated substituted urea, tetra-2,6-dimethylphenyl pyrophosphate, m. p. 152.5-153.5° (chloroform-hexane) (Found: C, 64.45; H, 5.7; P, 10.45. $C_{32}H_{36}O_7P_2$ requires C, 64.65; H, 6.1; P, 10.4%).

A portion of the crude distillation residue from the isolation of the above aryl phosphorodichloridate was kept overnight with benzylamine in benzene and yielded a small amount of the above pyrophosphate and *bis-2,6-dimethyl-phenyl* N-benzylphosphoramidate, m. p. 120—121.5° (chloroform-hexane), formed evidently from the unisolated (ArO)₂POCl (Found: N, 3.65; P, 7.95; C₂₃H₂₆NO₃P requires N, 3.55; P, 7.85%).

No reaction was observed when 2,6-dimethylphenol was heated with phosphorus oxychloride in the presence of small amounts of zinc chloride; with equimolar amount of the catalyst (relative to phosphorus oxychloride) the reaction proceeded as indicated above and was complete after heating under reflux for 2-3 hr.

Upon mixing equimolar amounts of 2,6-dimethylphenol (25.04 g.) and phosphorus trichloride (19.5 ml.) a rapid and spontaneous reaction resulted with the copious evolution of hydrogen chloride; this was complete in 1 hr. after the mixture had been finally heated to 75°. Distillation gave 2,6-dimethylphenyl phosphorodichloridite (46%), b. p. 100°/5 mm. Attempts to characterise this substance by reactions with benzaldehyde or methyl vinyl ketone gave only glassy products. Oxidation of the distilled dichloride with sulphuryl chloride in carbon tetrachloride at 0° for 1.5 hr., followed by quenching in ice, gave the 2,6-dimethylphenyl dihydrogen phosphate (>91%) described above. Similar treatment of the distillation residue, left after the removal of the aryl phosphorodichloridite, gave bis-2.6dimethylphenyl hydrogen phosphate (50%), identical with that described above.

2,6-Di-isopropylphenol.—Upon heating 2,6-di-isopropylphenol (25 ml.), and phosphoryl chloride (40 ml.) with

³ A. Michaelis, Annalen, 1896, **293**, 193; 1897, **294**, 1; G. Kamai, Zhur. obshchei Khim., 1934, **4**, 192; M. P. Viout and P. Rumpf, Bull. Soc. chim. France, 1957, 768; I. S. Protopopov and M. Ya. Kraft, Zhur. obshchei Khim., 1963, **33**, 3050; 1964, **34**, 1446.

lithium chloride (124 mg.) as catalyst for 24 hr. under reflux 2,6-di-isopropylphenyl phosphorodichloridate (15.6 g., 40.3%) was obtained, b. p. 138—140°/0·1 mm. With a reaction period of 72 hr. the yield rose to 82%. Hydrolysis of the distilled product with aqueous acetone gave 2,6-di-isopropylphenyl dihydrogen phosphate, plates, m. p. 175— 176.5° (chloroform-hexane) (Found: C, 55.4; H, 7.3; P, 12.1. $C_{12}H_{19}O_4P$ requires C, 55.8; H, 7.4; P, 12.0%).

The aryl phosphorodichloridate and benzylamine, in benzene, gave 2,6-di-isopropylphenyl NN'-dibenzylphosphorodiamidate, m. p. 119—121° (aqueous ethanol) (Found: N, $6\cdot55$; P, $7\cdot15$. C₂₆H₃₃N₂O₂P requires N, $6\cdot40$; P, $7\cdot10\%$).

2,6-Di-isopropylphenol (40.3 g.) phosphoryl chloride (22 ml.) and magnesium shavings (0.45 g.) were heated for 3.5 hr. (final temperature was 163.5°) when the reaction was completed (hydrogen chloride evolution had ceased). The residue of magnesium was filtered off and the filtrate gave the above aryl phosphorodichloridate (47 g., 70.4%), while the distillation residue from this gave, after hydrolysis in aqueous acetone, a low yield of bis-2,6-di-isopropylphenyl hydrogen phosphate, m. p. 155—159° (benzene-chloroform) (Found: C, 68.7; H, 8.3. $C_{24}H_{35}O_4P$ requires C, 68.9; H, 8.45%).

When 2,6-di-isopropylphenol (15 ml.) was heated with phosphoryl chloride (8 ml.) and zinc chloride (5.354 g., 0.499 mole) for 4.5 hr. (final mixture temperature 177—179°) the evolution of hydrogen chloride was complete after 3 hr. The mixture was extracted with benzene and the extract treated with water to yield the 2,6-di-isopropylphenyl dihydrogen phosphate (1.468 g., 7.22%) described above. No bis-aryl ester was detected.

2,6-Di-isopropylphenol and phosphorus trichloride were heated for 3 hr. and the crude product was oxidised with sulphuryl chloride at 0°, as described above. After heating the crude reaction product under reflux with aqueous acetone for 0.5 hr. the above aryl dihydrogen phosphate was obtained (54.3%). The same product (46.6%) was obtained when di-isopropylphenol (30 g.) and phosphorus trichloride (15 ml.) were kept with zinc chloride (1.44 g.) for 6 hr. at room temperature and 2 hr. at 137° (final temperature), and the product was oxidised with sulphuryl chloride and heated with aqueous acetone. The best yield (65%) of 2,6-di-isopropylphenyl dihydrogen phosphate was obtained from the reaction of the phenol (10 ml.) with phosphoryl chloride (24 ml. 5.04 moles) and lithium chloride (0.114 g.) after being heated under reflux (final temperature 140-145°) for 3 days. Magnesium shavings as the catalyst gave the same result as did zinc chloride.

2,6-Di-t-butylphenol.—Heating 2,6-di-t-butylphenol (10 g. with phosphoryl chloride (24 ml.) and lithium chloride (0·138 g.) for 7 days at reflux resulted in a negligible evolution of hydrogen chloride and the recovery of 98% of starting materials. When the initial dialkyl phenol also contained some 2% of 2,4-di-t-butylphenol, the above reaction gave, following the hydrolysis of the crude mixture with aqueous acetone, some 1·46% of 2,4-di-t-butylphenyl dihydrogen phosphate, m. p. 172—176·5° (chloroformhexane); this was also prepared conventionally from the corresponding phenol and phosphorus oxychloride. Both aryl dihydrogen phosphate specimens gave the n.m.r. proton signals at τ 8·57 (from the t-butyl group in the *para*position) and τ 8·57 (from t-butyl group in the *ortho*position).

The same result was obtained by heating the reaction mixture for 2 hr. using a magnesium catalyst, and starting

with crude di-t-butylphenol containing some 2% of the 2,4-isomers.

Upon heating pure 2,6-di-t-butylphenol (10 g.) for 5 min. at 50° with a few drops of conc. sulphuric acid a moderate yield of the 2,4-isomer was obtained, which, treated as above, gave, with phosphoryl chloride, 2,4-di-t-butylphenyl dihydrogen phosphate (50%), after hydrolysis. The pure ester, m. p. 176–177.5° (Found: C, 58.95; H, 8.25; P, 10.9. $C_{14}H_{23}O_4P$ requires C, 58.75; H, 8.1; P, 10.8%).

Upon heating pure 2,6-di-t-butylphenol (35.645 g.) with phosphoryl chloride (18 ml.) and zinc chloride (1.79 g.) for 3.5 hr. (final temperature 155°) 4-t-butylphenyl phosphorodichloridate (23.2 g., 50.1%) was obtained, b. p. $130^{\circ}/4$ mm. The same product (24.5%) was obtained from 4-t-butylphenol (30 g.) and phosphoryl chloride (35 ml.) with lithium chloride (0.294 g.) after being heated for 22.5 hr. under reflux. Hydrolysis of this ester with dilute hydrochloric acid gave *p*-t-butylphenol. The aryl phosphorodichloridate treated with aqueous acetone gave 4-t-butylphenyl dihydrogen phosphate, m. p. 185—186° (acetone-hexane), the ¹H n.m.r. spectrum of which gave a signal at τ 8.71 (Found: C, 52.15; H, 6.7; P, 13.3. $C_{10}H_{15}O_4P$ requires C, 52.15; H, 6.55; P, 13.45%).

The distilled 4-t-butylphenyl phosphorodichloridate and benzylamine gave 4-t-butylphenyl NN'-dibenzylphosphorodiamidate, m. p. $46\cdot5-50^{\circ}$ (aqueous alcohol) (Found: N, $6\cdot6$; P, $7\cdot5$. $C_{24}H_{29}N_2O_2P$ requires N, $6\cdot85$; P, $7\cdot65\%$).

Upon heating 2-t-butylphenol (30 g.) with phosphoryl chloride (19 ml.) and magnesium shavings (0.38 g.) for 2 hr. (final temperature 150°) 2-t-butylphenyl phosphorodichloridate (40.12 g., 79.1%) was obtained, b. p. 102— 104°/0·1 mm. which, with aqueous acetone, gave 2-tbutylphenyl dihydrogen phosphate, m. p. 180—180.5° (sharply depressed mixed m. p. with the 4-t-butyl isomer). The 2-isomer gave the ¹H n.m.r. signal at τ 8.6, typical of the ortho-t-butyl group.

No reaction was detected when 2,6-di-t-butylphenol was heated with phosphoryl chloride ($0\cdot3$ — $1\cdot0$ mole) in the presence of small amounts of lithium chloride or zinc chloride for several hours.

Upon heating 2,6-di-t-butylphenol (103 g., 0.5 mole) and phosphoryl chloride (25.6 g., 0.17 mole) with zinc chloride (22.7 g., 0.17 mole) a vigorous reaction resulted; t-butyl chloride (0.15 mole) was collected in a cooled trap, and hydrogen chloride (0.27 mole) was absorbed in alkali. No other volatile products were found. The elimination of one t-butyl group as the chloride was complete within 1 hr. and proceeded rapidly at *ca.*, 140–145°. The reaction mixture gave 4-t-butylphenyl dihydrogen phosphate after the treatment described above.

Upon heating 2,6-di-t-butylphenol (10 g.) for 4 days with phosphorus trichloride (4 ml.), oxidation of the crude product with sulphuryl chloride at 0°, as described above, and hydrolysis of the resulting crude phosphorodichloridate with aqueous acetone, resulted in a low yield of 2,4-di-tbutylphenyl dihydrogen phosphate. Magnesium as the catalyst gave the same result. However, upon heating the above mixture for 7 hr. in the presence of zinc chloride (0.465 g.) (final temperature 156°) oxidation of the crude product with sulphuryl chloride (3.7 ml.) and hydrolysis of this product with aqueous acetone, a mixture (3.26 g., m. p. 141—146°) of 58% di-t-butylphenyl dihydrogen phosphate and 42% mono-t-butylphenyl dihydrogen phosphate was obtained. The ¹H n.m.r. spectrum of this mixture showed signals at τ 8.72 (typical of p-Bu^t) and 8.62 (typical of o-Bu^t). A mixture of these proportions of 2,4-di-t-butylphenyl and 2-t-butylphenyl dihydrogen phosphates (m. p. $142.5-144^{\circ}$) gave no depression of m. p. with the above material. The same mixture was formed from a reaction run at reflux for 6.5 hr. or at room temperature for 12 hr.

2-Methyl-6-t-butylphenol.— 6-t-Butyl-2-methylphenol (38·2 g.) was heated with phosphoryl chloride (23 ml.) and magnesium shavings (0·46 g.) for 8·75 hr. (final temp. 168°), to give 2-methyl-6-t-butylphenyl phosphorodichloridate (30-42%), b. p. 136-137°/7 mm., which was hydrolysed with aqueous acetone to 2-methyl-6-t-butylphenyl dihydrogen phosphate, m. p. 174-175° (chloroform-hexane); ¹H n.m.r. signals at τ 8·57 (from o-Bu^t) and 7·6 (from o-Me) group (Found: C, 53·8; H, 7·0; P, 12·9. C₁₁H₁₇PO₄ requires C, 54·1; H, 7·0; P, 12·7%).

With zinc chloride (1.92 g.) the reaction gave after 2.75 hr., 2-methyl-4-t-butylphenyl phosphorodichloridate (32%), b. p. 126—128°/3 mm. The same product was formed from 4,6-di-t-butyl-2-methylphenol, phosphoryl chloride, and zinc chloride, after they had been heated for 4 hr. Hydrolysis of both products with aqueous acetone gave 2-methyl-4-t-butylphenyl dihydrogen phosphate, m. p. 143.5—145.5° (chloroform-hexane); ¹H n.m.r. signals at $\tau 8.7$ (from p-Bu^t) and 7.71 (from o-Me). A molar quantity of t-butyl chloride was collected and the expected amount of hydrogen chloride from 2-methyl-4-t-butylphenol and phosphoryl chloride, followed by mild hydrolysis (Found: C, 53.45; H, 7.0; P, 12.65. C₁₁H₁₇O₄P requires C, 54.10; H, 7.0; P, 12.7%).

6-t-Butyl-2-methylphenol (10 g.) and phosphorus trichloride (5.6 ml.) was heated under reflux for 18 hr. (final temp. 150°); the reaction mixture was then oxidised with sulphuryl chloride (4.7 ml.) in carbon tetrachloride at 0°. Hydrolysis of the reaction product with aqueous acetone, gave 2-methyl-6-t-butylphenyl dihydrogen phosphate, m. p. 174.5—175.5°. In the presence of zinc chloride (0.5 g./10 g. of the phenol) the reaction gave (heated 6 hr.) mixed aryl dihydrogen phosphates (19.8%), m. p. 174— 175°, which contained 2-methyl-6-t-butylphenyl dihydrogen phosphate and 2-methyl-4-t-butylphenyl dihydrogen phosphates (40%); ¹H n.m.r. signals at τ 8.57 (o-Bu^t) and 8.72 (p-Bu^t).

⁴ W. Autenrieth and E. Bölli, Ber., 1925, 58, 2146; E. Rapp, Annalen, 1884, 224, 169. 2,6-Di-t-butyl-4-methylphenol.—This phenol (38.27 g.) was heated under reflux for 3 hr. with phosphoryl chloride (18 ml.) and zinc chloride (1.9 g.) (final temp. 142°) to give *p*-tolyl phosphorodichloridate (53%), b. p. $118-120^{\circ}/6$ mm. The same product was obtained from 4-methyl-2-t-butylphenol in 3 hr. (identical with the product from *p*-cresol and phosphoryl chloride). Mild hydrolysis with aqueous acetone gave *p*-tolyl dihydrogen phosphate, m. p. 115-116.5°,⁴ ¹H n.m.r. signal at τ 7.72 (*p*-Me).

This aryl phosphorodichloridate and benzylamine gave p-tolyl NN'-di-benzylphosphorodiamidate, m. p. $93\cdot5-94^{\circ}$ (acetone-hexane) (Found: N, 7.8; P, 8.45. $C_{21}H_{23}N_2O_2P$ requires N, 7.65; P, 8.45%).

o-Cresol and phosphoryl chloride, with lithium chloride catalyst, gave o-tolyl phosphorodichloridate, b. p. $80^{\circ}/0.8$ mm (b. p. $118^{\circ}/8$ mm.).⁵ This was hydrolysed to o-tolyl dihydrogen phosphate, m. p. 97—98° (chloroform-hexane); ¹H n.m.r. signal at τ 7.72 (o-Me) (Found: C, 44.25; H, 5.0; P, 16.45. C₇H₉O₄P requires C, 44.45; H, 4.80; P, 16.4%).

2-t-Butyl-4-methylphenol.—Upon heating this phenol (40 g.) with phosphoryl chloride (24.5 ml.) and magnesium shavings (0.482 g.) for 2 hr. (final temp. 165°) 2-t-butyl-4methylphenyl phosphorodichloridate (53.8 g., 78.4%), was obtained, b. p. 140°/6—7 mm., which with aqueous acetone gave 2-t-butyl-4-methyl dihydrogen phosphate, m. p. 131.5— 133° (chloroform-hexane); ¹H n.m.r. signal at τ 8.62 (o-Bu^t) and (p-Me) (Found: C, 54.35; H, 6.95; P, 12.5. C₁₁H₁₇O₄P requires C, 54.1; H, 7.0; P, 12.7%). After treatment with water the distillation residues gave a further quantity of ester (8%) to bring the total yield to 86%.

Note added in proof: Reactions of ortho-substituted t-butylphenols with phosphoryl chloride in the presence of much zinc chloride invariably gave appreciable amounts of polyphenolic products similar to those reported by Yu. M. Paushkin, O. Yu. Omarov, S. A. Nisova and E. A. Selezneva (Abstracts of Internat. Symposium on Macromolecular Chemistry, Tokyo, 1966, p. 43) formed from substituted phenols and zinc chloride at elevated temperatures.

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⁵ V. V. Katyshkina and M. Ya. Kraft, *Zhur. obshchei Khim.*, 1956, **26**, 3060.