462. *Esters containing Phosphorus. Part XIV.* Some* tert.*-Butyl Esters and Their Reactions.*

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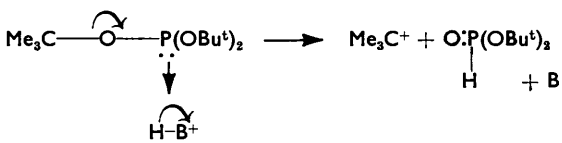
Di-*tert.*-butyl phosphorochloridate reacts in an unusual way with primary aromatic amines, yielding amine salts of mono-*tert.*-butyl *N*-arylphosphoramidates. These salts when heated *in vacuo* give *N*-arylphosphoramidic acids. The complete sequence of reactions constitutes a new method of phosphorylating these amines.

SEVERAL workers have prepared *tert.*-butyl esters containing phosphorus. Milobedzki and Sachnowski [1] and Kosolapoff [2] claimed that tri-*tert.*-butyl phosphite was produced by the reaction between 3 mols. of *tert.*-butyl alcohol and 1 mol. of phosphorus trichloride in the presence of a tertiary base, but later Young [3] and Gerrard *et al.*[4] showed that the product was di-*tert.*-butyl phosphite (I). We have confirmed the observations of these later workers and have shown, in addition, that even in the presence of a large excess of tertiary base the product is still the dialkyl phosphite.

In general, excellent yields of primary and secondary trialkyl phosphites are obtained by the reaction between alcohols and phosphorus trichloride in the presence of a tertiary base.[5] In the absence of a tertiary base, the dialkyl hydrogen phosphite is normally produced.[5,6] It is clear therefore that, in these cases, the free acid, not bound as base hydrochloride, is required for dealkylation : [7]

$$(RO)_3P + HCl \longrightarrow Cl^- + (RO)_3PH^+ \longrightarrow RCl + (RO)_2PH(\colon O)$$

It is necessary to invoke a different mechanism to account for the apparent dealkylation of tri-*tert.*-butyl phosphite (assuming this to be the initial reaction product). In this case, the dealkylation is by a base hydrochloride :



$$Me_3C^+ \longrightarrow Me_2C\colon CH_2 + H^+$$

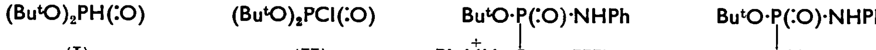
In view of this ease of dealkylation of *tert.*-butyl phosphites under mild conditions and of the known rapid hydrolysis of *tert.*-butyl esters of carboxylic acids,[8,9] it seemed that dealkylation of *tert.*-butyl esters of phosphoramidic acids might be a reasonable method for synthesising the free acids. Accordingly, a series of reactions was designed to effect this.

When di-*tert.*-butyl phosphite was treated with *N*-chlorosuccinimide,[10,11] it yielded di-*tert.*-butyl phosphorochloridate (II) which, being thermally unstable, could not be purified by distillation. The formation, however, of the phosphorochloridate in solution was definitely established by its conversion in high yield into di-*tert.*-butyl phosphoramidate

* Part XIII, *J.*, 1955, 3564.

[1] Milobedski and Sachnowski, *Chem. Polski*, 1917, **15**, 34.
[2] Kosolapoff, *J. Amer. Chem. Soc.*, 1952, **74**, 4953.
[3] Young, *ibid.*, 1953, **75**, 4620.
[4] Gerrard, Isaacs, Machell, Smith, and Wyvill, *J.*, 1953, 1920.
[5] McCombie, Saunders, and Stacey, *J.*, 1945, 380.
[6] Cook, Saunders, and Smith, *J.*, 1949, 635.
[7] Gerrard, Nechvatal, and Wilson, *J.*, 1950, 2088.
[8] Skrabal and Jugetz, *Monatsh.*, 1926, **47**, 117.
[9] Skrabal and Zahorka, *ibid.*, 1927, **48**, 459.
[10] Kenner, Todd, and Weymouth, *J.*, 1952, 3675.
[11] Goldwhite and Saunders, *J.*, 1955, 2040.

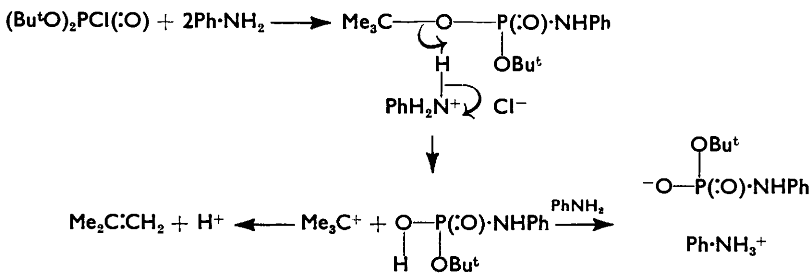
and di-*tert.*-butyl *N*-benzylphosphoramidate by the action of ammonia and of benzylamine respectively.



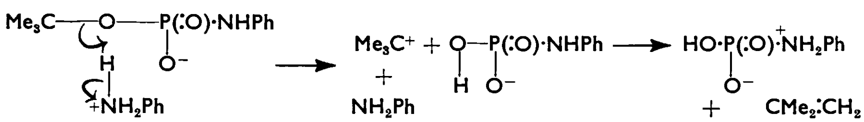
(I) (II) (III) (IV)

When the phosphorochloridate was allowed to react with aniline, the sole isolable product containing phosphorus was the anilinium salt of mono-*tert.*-butyl *N*-phenylphosphoramidate (III). The structure of (III) was confirmed by analysis, the infrared spectrum, and by conversion into *tert.*-butyl hydrogen *N*-phenylphosphoramidate (IV) on treatment with acids or the hydrogen form of a cation-exchange resin.

The formation of the anilinium salt can be rationalised by assuming that di-*tert.*-butyl *N*-phenylphosphoramidate is first formed and then suffers dealkylation by the aniline hydrochloride produced. The relative stability of the *tert.*-butyl carbonium ion may explain the ease of this dealkylation which occurs under very mild conditions, as shown :



When the anilinium salt was heated *in vacuo* it was converted quantitatively into *N*-phenylphosphoramidic acid. This further dealkylation can be pictured as following a course similar to the first stage :



The identity of the *N*-phenylphosphoramidic acid has been confirmed by analysis, by electrometric titration, and by comparison with the compound prepared by the hydrogenolysis of dibenzyl *N*-phenylphosphoramidate.[12] The acid is formulated as a zwitterion because of its high melting point [13] and the absence of N–H stretching bands in its infrared spectrum.

By similar methods *N*-*p*-chlorophenyl-, *N*-*p*-bromophenyl-, and *N*-*p*-tolyl-phosphoramidic acids have been prepared from the corresponding amines. The *p*-bromophenyl and *p*-tolyl acids have not previously been recorded since the compounds prepared by Otto [14] and Michaelis [15] by hydrolysing *N*-arylphosphoramidic dichlorides have been shown to be *N*-arylphosphorodiamidic acids.[16, 17]

It is interesting that the reaction between di-*tert.*-butyl phosphite, carbon tetrabromide, and benzylamine gave in very good yield a compound identical with di-*tert.*-butyl *N*-benzyl phosphoramidate obtained by the action of the phosphorochloridate on benzylamine. This indirectly confirms Steinberg's suggestion [18] that the first step of this type of reaction

[12] Cook, Ilett, Saunders, Stacey, Watson, Wilding, and Woodcock, *J.*, 1949, 2921.
[13] Clark and Todd, *J.*, 1950, 2030.
[14] Otto, *Ber.*, 1895, **28**, 616.
[15] Michaelis, *Annalen*, 1903, **326**, 129.
[16] Caven, *J.*, 1902, 1367.
[17] Rorig, *J. Amer. Chem. Soc.*, 1949, **71**, 3561.
[18] Steinberg, *J. Org. Chem.*, 1950, **15**, 637.

produces a phosphorohalidate rather than a trihalogenomethylphosphonate. An examination of this particular example using Courtauld space-filling models [19] strongly suggests that di-*tert.*-butyl tribromomethylphosphonate (VI) would be very highly strained, if indeed it could exist at all, whereas di-*tert.*-butyl phosphorobromidate (V) is not strained. The ease of the reaction and the high yield point to the latter (V) as the more likely intermediate.

$$(Bu^tO)_2POH \xrightarrow{CBr_4 + Base} (Bu^tO)_2P(:O){\cdot}Br \longrightarrow (Bu^tO)_2P(:O){\cdot}NH{\cdot}CH_2Ph$$

(V)

$$(Bu^tO)_2P(:O){\cdot}CBr_3 \quad (VI)$$

Experimental

Di-tert.-*butyl Phosphite.*—Phosphorus trichloride (45·75 g., 0·33 mole) in ether (60 ml.) was dropped during 2 hr. into a well-stirred solution of *tert.*-butyl alcohol (74 g., 1 mole) and pyridine (1 mole) in ether (400 ml.) cooled in ice–salt. The mixture was stirred for 1 hr. after the addition and then filtered. The filtrate was warmed under reduced pressure to remove low-boiling liquids, and the residue was distilled rapidly to yield di-*tert.*-butyl phosphite, b. p. 66—68°/0·5 mm. (50 g., 77%) (Found: C, 49·6; H, 9·6; P, 15·7. Calc. for $C_8H_{19}O_3P$: C, 49·5; H, 9·8; P, 16·0%). The principal absorption bands * in the infrared spectrum occur at 2976 (aliphatic C–H); 2410 (P–H); 1479, 1395, and 1370 (–CMe_3); 1263 (P=O); 1172, 1071, 1042, 967 (P–O–C); 920, 825, and 700 cm.$^{-1}$.

Reaction between tert.-*Butyl Alcohol and Phosphorus Trichloride in the Presence of a Large Excess of Pyridine.*—Phosphorus trichloride (22·9 g., 0·167 mole) and pyridine (39·5 g., 0·5 mole) in ether (60 ml.) were dropped during 2 hr. into a well-stirred solution of *tert.*-butyl alcohol (37 g., 0·5 mole) and pyridine (0·5 mole) in ether (400 ml.) cooled in ice–salt. The mixture was stirred for 1 hr. after the addition and then filtered. Ether was evaporated from the filtrate by warming under reduced pressure. The infrared spectrum of the undistilled residue contained no absorption bands which were not attributable either to di-*tert.*-butyl phosphite or to pyridine. When the liquid was distilled it gave pyridine and then pure di-*tert.*-butyl phosphite, b. p. 72—74°/1 mm.

Di-tert.-*butyl Phosphorochloridate.*—*N*-Chlorosuccinimide (6·67 g., 0·05 mole) was added in portions to a solution of di-*tert.*-butyl phosphite (9·7 g., 0·05 mole) in carbon tetrachloride (50 ml.) at *ca.* 65°. The mixture was cooled and filtered and the solvent was removed by warming under reduced pressure. The residual liquid decomposed on attempted distillation, but before distillation was a reasonably pure sample of *di*-tert.-*butyl phosphorochloridate* (Found: Cl, 15·3. $C_8H_{18}O_3ClP$ requires Cl, 15·5%).

Di-tert.-*butyl Phosphoramidate.*—A solution of di-*tert.*-butyl phosphorochloridate (0·0215 mole) in ether (30 ml.) was saturated with ammonia. The mixture was filtered and the filtrate evaporated to a crystalline residue, which recrystallised from light petroleum (b. p. 40—60°) as needles of *di*-tert.-*butyl phosphoramidate* sintering at 75—90°, m. p. 122—125° (decomp.) (4·1 g., 91%) (Found: C, 45·8; H, 9·1; N, 7·1. $C_8H_{20}O_3NP$ requires C, 45·9; H, 9·5; N, 6·7%).

Di-tert.-*butyl* N-*Benzylphosphoramidate.*—(1) Benzylamine (4·28 g., 0·04 mole) was slowly added to a cooled solution of di-*tert.*-butyl phosphorochloridate (0·02 mol.) in ether (20 ml.). After 1 hr. the mixture was shaken with water (100 ml.) and ether (50 ml.), and the ethereal layer was separated and dried ($MgSO_4$). On evaporation the residue crystallised, and was twice recrystallised from aqueous ethanol, giving needles of *di*-tert.-*butyl* N-*benzylphosphoramidate*, m. p. 97—98° (5·1 g., 85%) (Found: C, 59·9; H, 8·95; N, 4·7. $C_{15}H_{26}O_3NP$ requires C, 60·2; H, 8·7; N, 4·7%).

(2) *Synthesis using carbon tetrabromide.* Carbon tetrabromide (8·3 g., 0·025 mole) and benzylamine (10·7 g., 0·1 mole) were added to di-*tert.*-butyl phosphite (9·7 g., 0·05 mole) in ether (60 ml.). After a few minutes the mixture became warm and a precipitate separated, and after 4 hr. at room temperature the whole was shaken with ether (40 ml.) and water (100 ml.). The aqueous layer was discarded and the ethereal layer washed with 3N-hydrochloric acid

* The infrared spectra of other phosphorus compounds recorded in this paper were determined and the results confirmed chemical conclusions.

[19] Hartley and Robinson, *Trans. Faraday Soc.*, 1952, **48**, 847.

(3 × 50 ml.) and water (50 ml.) and dried ($MgSO_4$). The ether was evaporated and the residue recrystallised from aqueous methanol as needles (9·3 g., 62%) of di-*tert*.-butyl *N*-benzylphosphoramidate, m. p. 96—98°, alone and mixed with sample prepared as in (1).

Anilinium tert.-*Butyl* N-*Phenylphosphoramidate*.—(1) Di-*tert*.-butyl phosphorochloridate (0·01 mol.) was added to aniline (2·8 g., 0·03 mole). After 2 hr. the solid mass was extracted with boiling benzene (50 ml.) and filtered. The filtrate deposited needles which recrystallised from *cyclo*hexane–ethanol to yield *anilinium* tert.-*butyl* N-*phenylphosphoramidate*, m. p. 140—141° with effervescence followed by resolidification and remelting at 264—270° (decomp.) (Found: C, 59·4; H, 7·8; N, 8·8; P, 9·6. $C_{16}H_{23}O_3N_2P$ requires C, 59·6; H, 7·2; N, 8·7; P, 9·6%).

(2) *Synthesis using carbon tetrabromide*. Carbon tetrabromide (3·32 g., 0·01 mole) and aniline (3·72 g., 0·04 mole) were added to di-*tert*.-butyl phosphite (3·88 g., 0·02 mol.) in ether (40 ml.). The solution became bright orange and the precipitate of aniline hydrobromide that was slowly formed was filtered off. The filtrate was washed with water (4 × 50 ml.) and dried ($MgSO_4$). After removal of the solvent, the residue was dissolved in hot ethanol (20 ml.) and cooled to 5°. The slightly coloured crystals obtained (1·05 g.) had m. p. 142—145°, resolidified, and remelted at 250—260° (decomp.). The infrared spectrum was identical with that of the anilinium *tert*.-butyl *N*-phenylphosphoramidate obtained by method (1).

tert.-*Butyl Hydrogen* N-*Phenylphosphoramidate*.—The anilinium salt (0·2 g., 0·62 mmole) was dissolved in a minimum of water (*ca*. 40 ml.), and concentrated hydrochloric acid (4 ml.) was added. Colourless needles separated and were rapidly filtered off and proved to be tert.-*butyl hydrogen* N-*phenylphosphoramidate* (0·083 g., 58%) which blackened at 240° and had m. p. 253—256° (decomp.) (Found: C, 51·9; H, 7·2; N, 6·3%; Equiv., by electrometric titration, 225 ± 10. $C_{10}H_{16}O_3NP$ requires C, 52·3; H, 7·0; N, 6·1%; Equiv., 229).

The compound prepared by passing a solution of the anilinium salt through a Dowex-50 cation-exchange resin in the hydrogen form was identical with that produced by this acid treatment.

N-*Phenylphosphoramidic Acid*.—Anilinium *tert*.-butyl *N*-phenylphosphoramidate (2·4 g., 7·5 mmoles) was maintained at 80°/0·5 mm. for 18 hr. The product was N-*phenylphosphoramidic acid*, m. p. 267—271° (decomp.) (1·29 g., quantitative) (Found: C, 41·2; H, 4·7; N, 8·3%; Equiv., 85 ± 5, 170 ± 10. Calc. for $C_6H_8O_3NP$: C, 41·6; H, 4·6; N, 8·1%; Equiv., 86·5, 173). A sample prepared by the method of Saunders *et al.*[12] was identical with this compound.

By similar methods the following compounds were prepared: p-*Toluidinium* tert.-*butyl* N-p-*tolylphosphoramidate*, recrystallised from *cyclo*hexane–ethanol as colourless needles, m. p. with bubbling, 147—150°, resetting, and remelting at 250—254° (decomp.) (Found: C, 61·6; H, 7·6; N, 8·2. $C_{18}H_{27}O_3N_2P$ requires C, 61·8; H, 7·7; N, 8·0%).

N-p-*Tolylphosphoramidic acid*, prepared by heating the salt at 80°/0·5 mm. for 20 hr.; m. p. 270—272° (decomp.) (Found: C, 45·0; H, 5·3; N, 7·6%; Equiv., 96 ± 5, 190 ± 10. $C_7H_{10}O_3NP$ requires C, 45·0; H, 5·3; N, 7·5%; Equiv., 93·5, 187).

p-*Chloroanilinium* tert.-*butyl* N-p-*chlorophenylphosphoramidate* recrystallised from *cyclo*hexane as cubes softening at 150°, resetting, and remelting at 250—255° (decomp.) (Found: C, 49·1; H, 5·7; N, 7·4. $C_{16}H_{21}O_3N_2Cl_2P$ requires C, 49·1; H, 5·4; N, 7·2%).

N-p-Chlorophenylphosphoramidic acid, prepared by heating the salt at 80°/1 mm. for 24 hr., blackens at 250° and decomposes at 268—270° (this compound is recorded [20] as blackening at 260° and decomposing at 290°) (Found: C, 34·3; H, 3·7; N, 6·4%; Equiv., 106 ± 5, 212 ± 10. Calc. for $C_6H_7O_3NClP$: C, 34·7; H, 3·4; N, 6·7%; Equiv., 104, 208).

p-*Bromoanilinium* tert.-*butyl* N-p-*bromophenylphosphoramidate* recrystallised from chloroform as needles sintering at 150°, m. p. 260° (decomp.) (Found: C, 40·0; H, 4·7; N, 5·9. $C_{16}H_{21}O_3N_2Br_2P$ requires C, 40·0; H, 4·4; N, 5·8%).

N-p-*Bromophenylphosphoramidic acid*, prepared by heating the salt at 80°/1 mm. for 14 hr., blackens at 255°, melts at 272—274° (decomp.) (Found: C, 28·3; H, 2·8; N, 5·5%; Equiv., 123 ± 5, 250 ± 10. $C_6H_7O_3NBrP$ requires C, 28·5; H, 2·8; N, 5·5%; Equiv., 126, 252).

We are indebted to the D.S.I.R. for a maintenance grant (to H. G.).

University Chemical Laboratory, Cambridge. [*Received, January 28th*, 1957.]

[20] Si-Oh Li, *Acta Chem. Scand.*, 1950, **4**, 610.