## 349. *The Reaction between Acetimidates and Acid Esters of Phosphoric Acid.*

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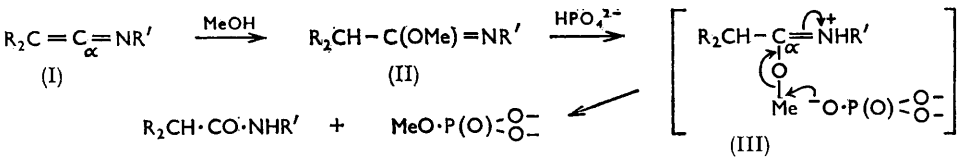
Methyl *N*-methyldi(methylsulphonyl)acetimidate and methyl trichloroacetimidate react with secondary phosphates to yield the corresponding tertiary phosphates; but ethyl *N*-methyldi(methylsulphonyl)acetimidate and methyl diphenyl-*N*-*p*-tolylacetimidate do not produce tertiary phosphates under comparable conditions.

Khorana [1] prepared a number of mixed tertiary phosphates by the action of mono- and di-esters of phosphoric acid on *O*-alkylisoureas. The latter were obtained by reaction of alcohols with diarylcarbodi-imides in the presence of the corresponding alkoxide. Dialkylcarbodi-imides were unreactive, presumably owing to the relatively high electron density at their central carbon atom, which would be the initial point of attack by alkoxide ions (cf. Hünig *et al.*[2]). By analogy, alkyl acetimidates could be useful in syntheses of tertiary

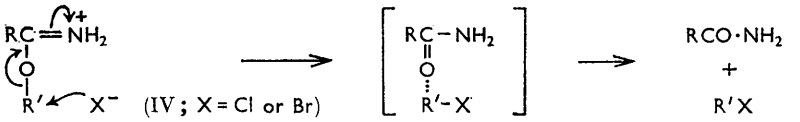



phosphates. Diphenylketen *p*-tolylimide (I; R = Ph; R' = $C_6H_4Me$) [3] and di(methylsulphonyl)keten methylimide (I; R = $SO_2Me$, R' = Me) [4] react with methanol to give high yields of the corresponding methyl acetimidates (II); the former requires the presence

[1] Khorana, *Canad. J. Chem.*, 1954, **32**, 227.
[2] Hünig, Lehmann, and Grimmer, *Annalen*, 1953, **579**, 77.
[3] Stevens and French, *J. Amer. Chem. Soc.*, 1953, **75**, 657.
[4] Backer and Dijkstra, *Rec. Trav. chim.*, 1954, **73**, 575, 695.

of sodium methoxide, but the latter will react with boiling methanol alone. Di(methylsulphonyl)keten methylimide should react more readily with alcohols than does diphenylketen *p*-tolylimide, since the two strongly electrophilic methylsulphonyl groups will increase the formal positive charge on the central carbon atom ($C_\alpha$) more readily than the weakly electron-withdrawing phenyl groups. Methyl *N*-methyldi(methylsulphonyl)acetimidate (II; R = $SO_2Me$, R′ = Me) has been treated with phosphates under various conditions. With an equimolar quantity of dibenzyl hydrogen phosphate, the optimum preparative conditions (heating in nitromethane solution at 90—110°) gave a 71% yield of dibenzyl methyl phosphate. Use of dioxan, boiling benzene, boiling aqueous acetone, or dimethylformamide at 90—100°, afforded yields of 62, 40, 6, and 6%, respectively. Substitution of dibenzyl tetramethylammonium phosphate for the free acid reduced the yield of dibenzyl methyl phosphate to 53%, but use of diphenyl hydrogen phosphate had little effect on yield. However, when phenyl dihydrogen phosphate (0·5 mole) in dioxan was substituted, the yield of dimethyl phenyl phosphate was only 25%. Ethyl *N*-methyldi(methylsulphonyl)acetimidate was similarly prepared, though the yield was only 46%; but subsequent treatment with phosphates in nitromethane and other solvents failed to produce tertiary phosphates. Numerous unsuccessful attempts have been made to prepare other alkyl *N*-methyldi(methylsulphonyl)acetimidates by reaction of the keten imide with the appropriate alcohol. Methyl diphenyl-*N*-*p*-tolylacetimidate (II; R = Ph, R′ = $C_6H_4Me$) was treated with dibenzyl or diphenyl hydrogen phosphate in hot nitromethane and dioxan, but the phosphate was largely recovered unchanged. The inertness of methyl diphenyl-*N*-*p*-tolylacetimidate is probably explained by the strong electromeric effect of the *p*-tolyl group neutralising the positive charge on the protonated nitrogen atom, and therefore preventing appreciable removal of electrons from the central carbon atom ($C_\alpha$) upon which the success of the phosphorylation ultimately depends (cf. III).

A general method for the preparation of imidate hydrochlorides (IV; X = Cl) is treatment of a nitrile with an alcohol in the presence of dry hydrogen chloride.[5] These compounds, when heated in various solvents, decompose into the amide and the alkyl chloride,[6] the rate of decomposition being dependent on the solvent and the nature of the anion.[7] In chloroform and t-butyl alcohol pyrolysis proceeds by the $S_N2$ mechanism:[8]




This suggested that pyrolysis of alkyl acetimidate phosphates (IV; X = $H_2PO_4^-$) might afford a useful synthesis of mixed tertiary phosphates. The presence of electrophilic atoms or groups attached to the carbon atom of the cyanide group, increases both the ease of formation of the imidate hydrochloride and also its subsequent decomposition when warmed. Thus methyl trichloroacetimidate hydrochloride decomposes at room temperature into trichloroacetamide and methyl chloride[9] and cannot be prepared by the normal Pinner reaction. However, Steinkopf and Semmig[10] discovered that this compound can be obtained by treatment of trichloroacetonitrile with boiling methanol containing a little acetone. Direct treatment of this mixture with dibenzyl or diphenyl hydrogen phosphate in hot nitromethane gave the corresponding methyl tertiary phosphates in approximately 45% yield. Unsuccessful attempts were made to obtain other

[5] Pinner, *Ber.*, 1883, **16**, 352, 1643 *et seq.*
[6] Lengfeld and Stieglitz, *Amer. Chem. J.*, 1894, **16**, 70; Stieglitz, *ibid.*, 1899, **21**, 101.
[7] McElvain and Tate, *J. Amer. Chem. Soc.*, 1951, **73**, 2233.
[8] Stevens, Morrow, and Lawson, *J. Amer. Chem. Soc.*, 1955, **77**, 2341.
[9] Steinkopf, *Ber.*, 1907, **40**, 1643.
[10] Steinkopf and Semmig, *Ber.* 1920 **53**, 1149.

trichloroacetimidates from the appropriate alcohol and trichloroacetonitrile. Recently, however, several of these imidates have been prepared by Cramer,[11] who showed that reaction could be promoted by the presence of weakly alkaline catalysts; and their subsequent phosphorolysis in boiling acetonitrile solution gave the corresponding mixed tertiary phosphates in 30—90% yield.[12]

## Experimental

*Methyl Diphenyl*-N-p-*tolylacetimidate*.—Diphenylketen *p*-tolylimide (0·297 g.) in dry ether (3 c.c.) was treated with boiling methanol (6 c.c.) and sodium methoxide (0·035 g.), as described by Stevens and French.[3] The methyl ester formed needles (0·285 g.; m. p. 95—97°) on recrystallisation from light petroleum (b. p. 60—80°)–chloroform.

The corresponding *ethyl ester* was prepared similarly; it recrystallised from ethanol as prisms, m. p. 103—105° (73%) (Found: C, 83·7; H, 7·1; N, 4·5. $C_{23}H_{23}NO$ requires C, 83·9; H, 7·0; N, 4·3%).

*Methyl* N-*Methyldi(methylsulphonyl)acetimidate*.—Di(methylsulphonyl)keten *N*-methylimide (0·211 g.) was boiled under reflux with excess of methanol (15 c.c.) for 3 hr. Removal of the methanol and recrystallisation from benzene–chloroform afforded the methyl ester (211 mg.), m. p. 137—140° (lit.,[3] m. p. 143—144°) (Found: C, 29·6; H, 5·2; N, 6·0. Calc. for $C_6H_{13}NO_5S_2$: C, 29·6; H, 5·3; N, 5·8%).

The *ethyl ester*, similarly prepared, crystallised from light petroleum (b. p. 60—80°)–chloroform in prisms, m. p. 104—106° (46%) (Found: C, 32·5; H, 6·0; N, 5·7. $C_7H_{15}NO_5S_2$ requires C, 32·7; H, 5·8; N, 5·5%).

*Dibenzyl Methyl Phosphate*.—Methyl *N*-methyldi(methylsulphonyl)acetimidate (0·243 g., 1 mmole) was heated at 90—110° with dibenzyl hydrogen phosphate (0·278 g., 1 mmole) in nitromethane (10 c.c.) for 36 hr. The solution was evaporated under reduced pressure (bath temp. 30—40°), cooled, and shaken with anhydrous benzene (10 c.c.); *N*-methyldi(methylsulphonyl)acetamide, m. p. 210—212° (0·192 g., 84%), was deposited. The filtrate was diluted with benzene (50 c.c.), and washed successively with 50% aqueous sodium hydrogen carbonate, water, 1N-hydrochloric acid, and water, dried (anhydrous sodium sulphate), and evaporated under reduced pressure. The resulting dibenzyl methyl phosphate was a pale yellow oil (0·206 g., 71%), $n_D^{21}$ 1·5342 (Found: C, 61·5; H, 6·0. Calc. for $C_{15}H_{17}O_4P$: C, 61·6; H, 5·8%).

*Methyl Diphenyl Phosphate*.—Similarly prepared, but by use of diphenyl hydrogen phosphate, this ester [13] was obtained as an oil (0·179 g., 68%), $n_D^{21}$ 1·5320 (Found: C, 58·9; H, 5·2. Calc. for $C_{13}H_{13}O_4P$: C, 59·1; H, 4·9%).

*Dimethyl Phenyl Phosphate*.—Methyl *N*-methyldi(methylsulphonyl)acetimidate (0·080 g., 0·33 mmole) was heated at 80° with phenyl dihydrogen phosphate (0·030 g., 0·17 mmole) in dioxan (10 c.c.) for 40 hr. After concentration under reduced pressure, cooling, and addition of benzene (5 c.c.), *N*-methyldi(methylsulphonyl)acetamide (0·074 g., 82%), m. p. 210—212° separated. The liquor gave a pale yellow oil (0·023 g.; 25%) shown to be dimethyl phenyl phosphate, by treatment with calcium iodide in boiling ethyl methyl ketone.[13] This afforded calcium methyl phenyl phosphate (0·020 g.), m. p. >300° (Found: C, 39·8; H, 3·9; P, 14·7. Calc. for $C_{14}H_{16}O_8P_2Ca$: C, 40·4; H, 3·9; P, 14·9%).

*Dibenzyl Methyl Phosphate*.—Trichloroacetonitrile (0·435 g., 3 mmoles) was boiled with anhydrous methanol (10 c.c.) containing 10 drops of acetone for 8 hr. (cf. Steinkopf and Semmig [10]); the pungent odour of the nitrile had then largely disappeared, and the methanol was removed under reduced pressure. The residual oil was heated with dibenzyl hydrogen phosphate (0·834 g., 3 mmoles) in nitromethane (10 c.c.) at 90—100° during 48 hr. The solvent was removed under reduced pressure, and the product dissolved in benzene (200 c.c.) and washed successively with 2N-hydrochloric acid, water, aqueous sodium hydrogen carbonate, and water, dried ($Na_2SO_4$), and evaporated. The oil (0·476 g.), on treatment with calcium iodide in boiling ethyl methyl ketone,[13] furnished a white solid (0·168 g.), m. p. >300°. Paper chromatography (n-butanol–water, 86 : 14) revealed two phosphorus-containing spots ($R_F$ values 0·40, 0·80), identical with those obtained from authentic dibenzyl methyl phosphate

[11] Cramer, Pawelzik, and Baldauf, *Ber.*, 1958, **91**, 1049.
[12] Cramer, Pawelzik, and Lichtenthaler, *Ber.*, 1958, **91**, 1555.
[13] Cremlyn, Kenner, Mather, and Todd, *J.*, 1958, 528.

under similar conditions. The weight of mixed calcium salts indicated a 50% yield of this phosphate.

*Methyl Diphenyl Phosphate.*—Methyl trichloroacetimidate, prepared *in situ* as above, gave on treatment with one mole of diphenyl hydrogen phosphate in nitromethane under similar conditions, an estimated 40% yield of methyl diphenyl phosphate.

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