Rearrangements of a Cation of the Neopentyl-type containing a Diphenylphosphinyl Substituent [1]

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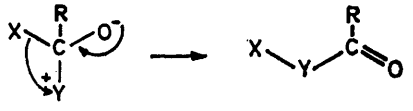
Deamination of 2-diphenylphosphinyl-2-methylpropylamine (4) and solvolysis of the 2-diphenylphosphinyl-2-methylpropyl toluene-*p*-sulphonate (9) lead to diphenylphosphinyl migration and products arising from the tertiary cation (15). The deamination also gives some of a product with a cyclopropane ring, but in no case is methyl migration observed. It is suggested that a protonated cyclopropyl intermediate is formed in the deamination. Rate studies on the tosylate suggest that the diphenylphosphinyl group participates in the rate-determining step and that it is *ca.* 70 times less effective than a methyl group at participation in this system.

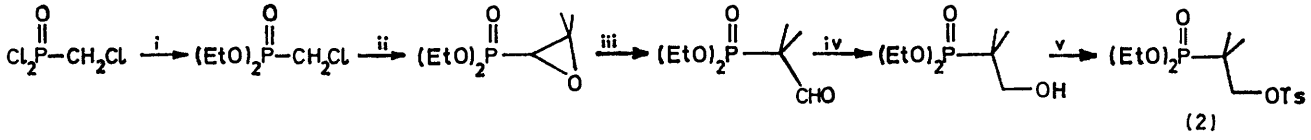
REARRANGEMENTS of phosphyl groups ($R_2P{:}O$; R = R'O, alkyl, or aryl) are well known when the migratory origin has a substituent able to stabilise the resulting cation with lone-pair electrons.[2] Little can be learnt from such rearrangements about the migratory aptitude of functional groups as bond formation between the stabilising substituent [O in (1)] and the migratory



(1)

origin [C in (1)] is well advanced in the transition state, suppressing the dependence of the stability of the pair electrons (Cl, OR) and can migrate without σ-participation, or are reluctant to migrate at all (RC=O). Phosphyl groups are known to migrate in Baeyer–Villiger,[3] Schmidt,[3] and epoxide [4] rearrangements and have the advantage of two variable substituents on the phosphorus atom as mechanistic probes.

We synthesised the diethyl phosphonate analogue (2) of 2,2-dimethylpropyl (neopentyl) tosylate from the corresponding aldehyde, itself synthesised by an epoxide rearrangement of the kind reported by Griffin [4] (Scheme 1). Solvolysis of the crystalline tosylate under a variety of conditions led to no rearrangement. Instead nucleophilic attack occurred at the phosphorus atom with the formation of diethyl phosphate and, presumably, isobutene.

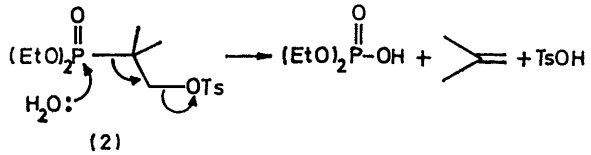


SCHEME 1

Reagents: i, EtOH–C_5H_5N; ii, Me_2CO–NaH–DMSO; iii, BF_3; iv, $NaBH_4$; v, TsCl–C_5H_5N (Ts = *p*-$MeC_6H_4{\cdot}SO_2$).

transition state on the migrating group. We have therefore studied rearrangements of phosphyl groups in molecules having carbon atoms with simple alkyl substituents at both the migratory origin and terminus with the aim of using these electronegative groups to investigate the transition state in cationic rearrangements. Other electronegative groups either have lone-

Under other conditions saponification of the ester functions occurred before P–C cleavage, and so we turned



(2)

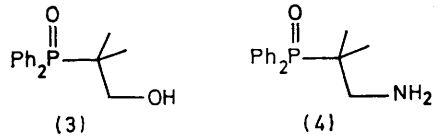
[1] Preliminary communication, P. F. Cann and S. Warren, *Chem. Comm.*, 1970, 1026.

[2] S. G. Warren, *Angew. Chem. Internat. Edn.*, 1968, **7**, 606; C. E. Griffin, in 'Chimie Organique du Phosphore,' Colloques Internationaux du Centre de la Recherche Scientifique, No. 182, Paris, 1970, p. 95.

[3] M. Sprecher and E. Nativ, *Tetrahedron Letters*, 1968, 4405; D. Kost and M. Sprecher, *ibid.*, 1970, 2535.

[4] R. H. Churi and C. E. Griffin, *J. Amer. Chem. Soc.*, 1966, **88**, 1824; M. Sprecher and D. Kost, *Tetrahedron Letters*, 1969, 703.

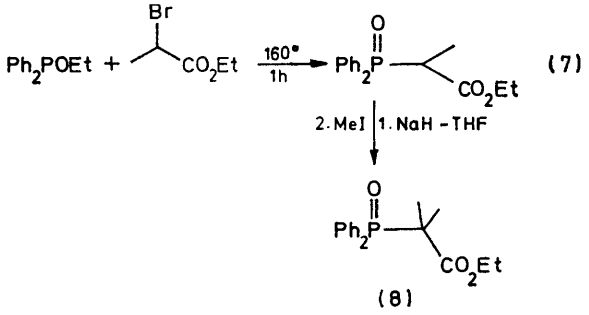
to the diphenylphosphinyl series, aiming to produce low energy cations [5] by a solvolytic pathway from the tosylate of the alcohol (3), and high energy cations [5] from the diazotisation and deamination of 2-diphenylphosphinyl-2-methylpropylamine (4).



(3) (4)

Base-catalysed addition of diphenylphosphine oxide to acetone was already known [6] and we found that addition to mesityl oxide, catalysed by sodium hydride, occurs in the Michael sense to give the ketone (5) and hence an oxime which might rearrange to a derivative of the amine (4) (Scheme 2). Although a single isomer of the oxime (sharp m.p. 214—216°, single methyl resonance at τ 8·25) was formed, rearrangement in polyphosphoric acid at 130° gave a mixture of amides. Hydrolysis of the mixture in 70% sulphuric acid gave a mixture of the required amine (4) (60%) and the carboxylic acid (6) (35% isolated). Extractions with dichloromethane from an alkaline solution gave the amine (4), purified as its crystalline picrate. The picrate was best decomposed by hot aqueous 20% lithium hydroxide: extraction with dichloromethane then gave the crystalline amine (4).

The corresponding alcohol (3) could not be made by a Baeyer–Villiger rearrangement of the ketone (5), which was recovered even after treatment for 100 h with perbenzoic acid in chloroform. However, the ester (7), readily prepared by an Arbuzov reaction between ethoxydiphenylphosphine and ethyl bromopropionate, could be methylated with sodium hydride and methyl iodide to give the ester (8). Reduction of

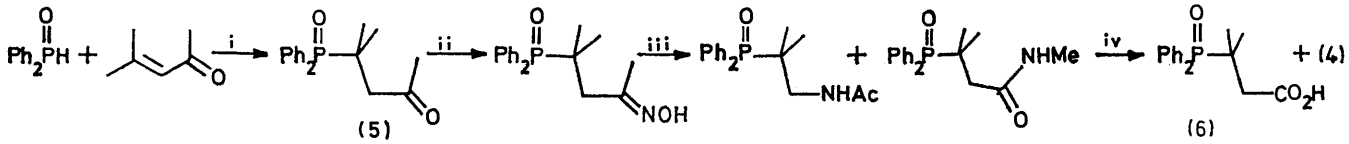


(7) (8)

the ester (8) with lithium aluminium hydride gave considerable amounts of phosphines, but treatment with sodium borohydride in refluxing methanol gave the crystalline alcohol, though only in 50% yield, and this was converted into the tosylate (9).

Solvolysis of the tosylate at 120° in 98% formic acid gave a single product isolated in 84% yield. This product had a strong i.r. absorption at 1630 cm^{-1} (conjugated C=C) and a single olefinic proton signal at τ 4·11 split into a doublet by the phosphorus atom (J_{PH} 26 Hz), with further allylic coupling (J_{PH} 2 Hz). There were two distinct methyl signals in the n.m.r. spectrum: a doublet at τ 7·97 (J_{HH} 2 Hz) and a singlet at 8·06. The molecular ion in the mass spectrum was at *m/e* 256, and the compound is clearly the vinylphosphine oxide (10).

The amine (4) was diazotised in aqueous nitrous acid and in anhydrous acetonitrile with 3-methylbutyl nitrite. In both cases, removal of starting amine by

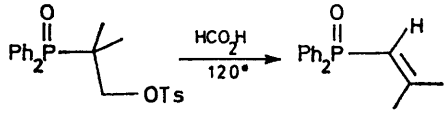


(5) (6)

SCHEME 2

Reagents: i, NaH–THF; ii, $\overset{+}{N}H_3OHCl^-$–Et_3N–EtOH; iii, polyphosphoric acid–130°; iv, 70% H_2SO_4–140°–3 days.

acid extraction left five products which were separated by repeated preparative t.l.c. on silica gel with chloroform as eluant. Yields and R_F values are given in



(9) (10)

the Table. Compound C was the vinyl phosphine oxide (10). Compound E, the major product in anhydrous conditions, was an isomer of the vinylphosphine

Products from the diazotisation of the amine (4)

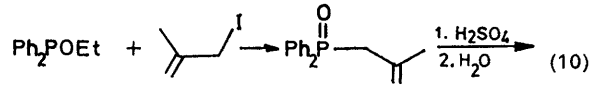
Compound	R_F [a]	Yield (%) Aqueous solution	Yield (%) Anhydrous acetonitrile solution
A	0·50	5	10
B	0·55	40	10
C	0·60 [b]	10	10
D	0·65 [b]	15	5
E	0·70	25	50

[a] 3% Methanol in chloroform on silica gel GF_{254}. [b] Compounds C and D were not separated by the first elution (see Experimental section).

oxide (10) with a weak i.r. band at 1640 cm^{-1} (unconjugated C=C). It had two olefinic proton resonances in the n.m.r. spectrum along with signals for one methyl group and a methylene group next to the phosphorus atom. It also, unlike the vinyl compound (10), readily

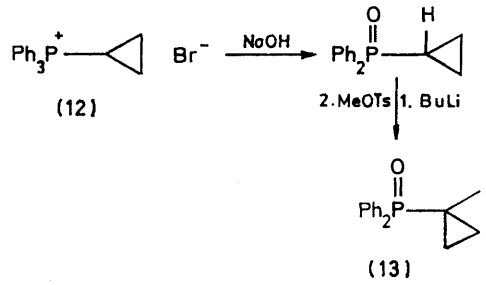
[5] M. S. Silver, *J. Amer. Chem. Soc.*, 1961, **83**, 3482.
[6] L. Horner, H. Hoffmann, H. G. Wippel, and G. Klahre, *Chem. Ber.*, 1959, **92**, 2499.

lost the methylallyl group in the mass spectrum (M — 55; 100%), and is assigned the methylallylphosphine oxide structure (11). It was synthesised from ethoxydiphenylphosphine and methylallyl iodide. Synthesis of the vinyl isomer (10) from the methylallyl compound (11) was easily accomplished by dissolving the methylallyl compound in conc. sulphuric acid and quenching the solution with water.



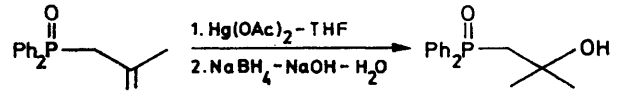
(11)

Compound D (m/e 256) was another isomer of the phosphine oxide (10) but with no olefinic i.r. absorptions nor olefinic proton resonances in the n.m.r. spectrum. Instead it showed two very high field methylene resonances [τ 8·84 (2H, d, J_{PH} 12 Hz) and 9·38 (2H, d, J_{PH} 10 Hz) each with further fine splitting] suggestive of a cyclopropane ring. Synthesis from cyclopropyltriphenylphosphonium bromide (12) confirmed that it was the methylcyclopropylphosphine oxide (13).



(12) (13)

Compounds A and B were isomeric alcohols (i.r. absorptions at 3150 and 3340 cm^{-1}). Compound A was the alcohol (3) but the n.m.r. spectrum of compound B showed the six-proton resonance for the two methyl groups no longer split by the phosphorus atom and this compound is clearly the rearranged alcohol (14). It was synthesised from the methylallylphosphine oxide (11) by mercuration with mercury(II) acetate and reduction with sodium borohydride.



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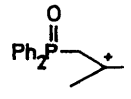
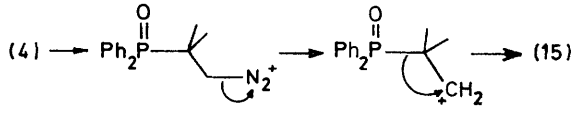


(15)

The rearranged products (10), (11), and (14) most reasonably come from the tertiary cation (15), which is presumably also an intermediate in the acid-catalysed isomerisation of the olefins [(10) ⟶ (11)]. However, the cation (15) leads to a single product, the vinylphosphine oxide (11), in the solvolysis of the tosylate and in the isomerisation of the olefins, but to a whole range of products in the deamination.

The cation (15) is then produced in the deamination as an energetic species, the unstable primary cation (16) being an intermediate. The formation of unrearranged alcohol (3) represents the capture of this cation by solvent. This type of route is well known from other deaminations.[7]

No products of complete methyl migration were formed in these reactions. This is clearly an unfavourable pathway as it would generate the very unstable α-phosphyl cation (17). The formation of a cyclopropane product, presumably from the non-classical ion (18), without the appearance of any products of methyl migration is unique. In other cases where cyclopropanes are formed in such reactions, they are not products of the major pathway which is methyl migration.[8] That such a pathway can be wholly



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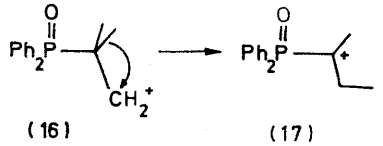
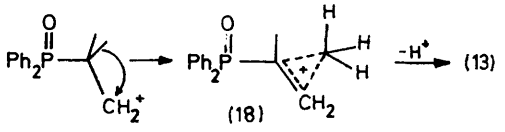


(16) (17)



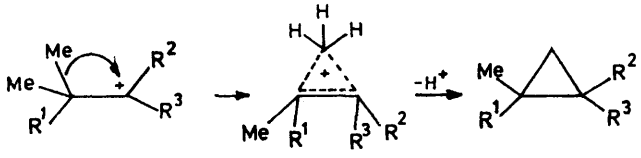
(18)

diverted to give cyclopropane derivatives suggests that the non-classical ion (18), which is a protonated cyclopropane, is an intermediate and not a transition state.

It has been suggested[9] that the life-time of a protonated cyclopropane intermediate, and hence the amount of cyclopropane product formed from it, is related to its symmetry. Thus the 2,2-dimethylpropyl cation (19; R^1 = Me, R^2 = R^3 = H) gives a maximum of 0·3% cyclopropyl product,[10] the 2 methylpropyl cation (19; R^1 = R^2 = R^3 = H) gives 4%, but the 1,2-dimethylpropyl cation gives, *via* the symmetrical protonated cyclopropane (20; R^3 = Me, R^1 = R^2 = H), 15% cyclopropane.[11] What then of the cation (18) which gives up to 15% of the cyclopropane derivative? Perhaps

[7] D. V. Banthorpe in 'The Chemistry of the Amino Group,' ed. S. Patai, Interscience London, 1968, p. 587.
[8] G. M. Fraser and H. M. R. Hoffman, *Chem. Comm.*, 1967, 561.
[9] M. S. Silver, *J. Org. Chem.*, 1963, **28**, 1686.
[10] G. J. Karabatsos, N. Hsi, and S. Meyerson, *J. Amer. Chem. Soc.*, 1966, **88**, 5649; G. J. Karabatsos, R. A. Mount, D. O. Rickter, and S. Meyerson, *ibid.*, p. 5651.
[11] M. S. Silver, *J. Amer. Chem. Soc.*, 1960, **82**, 2971; *J. Org. Chem.*, 1963, **28**, 1686.

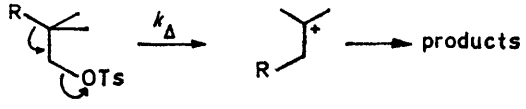
the kind of symmetry which produces the highest yield of cyclopropane derivative is not steric symmetry but rather a balance of electron-donating and -withdrawing substitutents about the bond along which migration takes place. In cation (18), one end of this bond carries two hydrogen atoms while at the other, the electron-donating methyl group and the electron-withdrawing diphenylphosphinyl group cancel each other out. The cation (18) is therefore electronically symmetrical in the sense that neither end of the bond is well able to support a localised cation. Thus formation of the cyclopropane derivative here is a case of arrested



(19) (20)

development in methyl migration, ring opening of the intermediate (18) in either direction is unfavourable [cations (16) and (17) are both unstable] and loss of a proton is the only reasonable pathway. It is of course still a high energy one as it is entirely absent in the solvolysis reaction. Protonated cyclopropane intermediates are now well established in a variety of reactions.[12]

The less energetic pathway to the tertiary cation (15) from the solvolysis of the tosylate (9), giving only the vinylphosphine oxide (10) may not involve the primary cation (16) at all, but may lead in a single step, that is by diphenylphosphinyl participation in the rate-determining step, to the tertiary cation (15). All 2,2-dimethylpropyl-derived systems can be solvolysed directly to a tertiary cation by a participation process (rate constant k_Δ) or to a derivative of the primary cation by a solvent-assisted process (rate constant k_s) which does not normally lead to rearranged products.[13] For (21; R = H or Me) the k_Δ route is followed to a very large extent in most solvents, and the formation of only rearranged product (10) suggests that it is followed exclusively for (21; R = $Ph_2P{:}O$), but this can be checked by an estimate of the maximum possible value of k_s, and a measurement of the actual rate of solvolysis of the tosylate (9).



(21)

In formic acid, all simple primary alkyl tosylates are solvolysed at about the same rate, ethyl tosylate entirely by the k_s route, 2,2-dimethylpropyl tosylate entirely by the k_Δ route, and for n-propyl and isobutyl increasing β-methyl substitution leads to an increasing k_Δ just compensating for decreasing k_s from the steric hindrance of the methyl groups.[13] Whether the tosylate (9) reacts by the k_Δ or the k_s route, we would expect a decrease in rate. If the reaction is by the k_Δ route, the decrease occurs because the diphenylphosphinyl group is less able than the methyl group to participate in the solvolysis step, and this is what we hoped to measure, if by the k_s route, because steric hindrance and inductive effect should lower k_s even below the (unobserved) k_s for 2,2-dimethylpropyl tosylate in this solvent. In fact, k_s is measurable for 2,2-dimethylpropyl tosylate only in ethanol, where it contributes 7·3% of the rate.[13] However, a plot of log k_s for n-propyl tosylate against log k_s for ethyl tosylate in various solvents gives a straight line with slope 0·925.[13] A similar plot for isobutyl against n-propyl tosylate is also linear, with slope 0·93. Thus each methyl group introduces a factor of *ca.* 0·93 in sensitivity to the nucleophilicity of the solvent. Assuming the same factor between isobutyl and 2,2-dimethylpropyl tosylate we estimate[14] k_s for 2,2-dimethylpropyl tosylate in formic acid as 8×10^{-9} s^{-1} at 75°, or $2{\cdot}4 \times 10^3$ slower than the observed rate (actually k_Δ) in these conditions.

We compared the rates of solvolysis of the tosylate (9) and 2,2-dimethylpropyl tosylate in formic acid at 99° by separating the reaction mixture on t.l.c. This method does not pretend to $> \pm 10\%$ accuracy but this is adequate for these very slow reactions. We found that tosylate (9) reacted 220 times slower than 2,2-dimethylpropyl tosylate. Since k_s for 2,2-dimethylpropyl tosylate is about 2400 times less than the observed rate, and k_s for the tosylate (9) would be even less than this, the observed rate for the tosylate (9) must be k_Δ, and the factor of 220, divided by the statistical factor of 3 to give ~70, is the relative participating ability of methyl to diphenylphosphinyl per participating group. This is a surprisingly small ratio considering the large difference in electronegativity between the two groups, but it must be remembered that there is a very large driving force for this rearrangement in the stability of the developing tertiary cation (15). We have also shown that diphenylphosphinyl migration takes place from secondary to tertiary cations and even between tertiary cations of the same energy.[15]

EXPERIMENTAL

I.r. spectra were taken on Pye–Unicam SP 1000 and Perkin-Elmer 257 machines; n.m.r. spectra were run on Varian HA100, 100XL, and Perkin-Elmer R-12 machines. Mass spectra were taken with A.E.I. MS9, MS902, and MS12 spectrometers. T.l.c. was run on silica gel GF254 and column chromatography with Malinckrodt ' SilicAR CC-7 ' (100—120 mesh).

[12] C. J. Collins, *Chem. Rev.*, 1969, **69**, 543; G. J. Karabatsos, C. Zioudrou, and S. Meyerson, *J. Amer. Chem. Soc.*, 1970, **92**, 5996; C. C. Lee and D. J. Woodcock, *ibid.*, p. 5992; G. M. Kramer, *ibid.*, 1969, **91**, 4819, 1970, **92**, 4344; N. C. Deno and W. E. Billups, *Chem. Comm.*, 1970, 1387.

[13] I. L. Reich and S. Winstein, *J. Amer. Chem. Soc.*, 1969, **91**, 5635.

[14] Data from S. Winstein and H. Marshall, *J. Amer. Chem. Soc.*, 1952, **74**, 1120.

[15] P. F. Cann, D. Howells, and S. Warren, *Chem. Comm.*, 1971, 1148.

Diethyl Chloromethylphosphonate.[16]—Chloromethylphosphonic dichloride [17] (300 g, 1·8 mol) was added slowly and with stirring to absolute ethanol (800 ml) kept at 5° with an ice–salt bath. The mixture was left overnight and the excess of ethanol and HCl were removed at 50° under vacuum. The residue was neutralised (sodium carbonate) and extracted with ether. Evaporation of the ether and distillation gave chloromethyldiethylphosphonate (264·5 g 79%), b.p. 75—79° at 0·75 mmHg (lit.,[18] 86—87° at 2·5 mmHg).

Diethyl 1,2-*Epoxy*-2-*methylpropylphosphonate*.—Diethyl chloromethylphosphonate (279 g, 1·5 mol), dry acetone (87 g, 1·5 mol) (AnalaR), and redistilled dimethyl sulphoxide (300 ml) were stirred under nitrogen while sodium hydride–oil emulsion (72 g, 1·5 mol) was added in small portions at 25°. The mixture was left overnight, the precipitated sodium chloride was centrifuged off, and the solution was washed with benzene and centrifuged again [sodium chloride (90 g, 100%) was collected]. Dimethyl sulphoxide (250 ml) was removed at 15 mmHg and the residue was dissolved in water and extracted with benzene. Distillation gave the *epoxyphosphonate* (188 g, 61%), b.p. 78—82° at 0·75 mmHg (Found: C, 46·4; H, 7·7; P, 14·0. $C_8H_{17}O_4P$ requires C, 46·2; H, 8·2; P, 14·9%), $\nu_{max.}$ (film) 1265 (P=O), 1165 (P–OEt), 1030 (P–OEt), and 850 cm^{-1} (epoxide), τ 5·93 and 5·95 (double quintet, 4H, $J_{HH} = J_{PH} = 7$ Hz, P·O·CH_2), 6·45 (d, 1H, J_{PH} 26 Hz, PCH), 8·50 and 8·66 (two s, 6H, Me_2), and 8·69 (t, 6H, J_{HH} 7 Hz, P·O·CH_2·CH_3).

Diethyl 1-*Formyl*-1-*methylethylphosphonate*.—Boron trifluoride–ether complex (30 ml, 0·24 mol) was added to a solution of diethyl 1,2-epoxy-2-methylpropylphosphonate (80·4 g, 0·4 mol) in benzene (800 ml). The mixture was swirled and left at room temperature for 50 min. Ether (200 ml) was added and the solution was washed with water. The washings were neutralised (sodium carbonate), saturated with sodium chloride, and extracted with ether. The combined organic layers were dried ($MgSO_4$) and distilled to give the *aldehyde*, b.p. 74—78° at 0·2 mmHg, $\nu_{max.}$ (film) 2730 (aldehyde C–H), 1725 (CHO), 1250 (P=O), 1165 (P–OEt), and 1030 cm^{-1} (P–O–R), τ 0·50 (d, 1H, J_{PH} 0·8 Hz, CH=O), 5·94 (quintet, 4H, $J_{HH} = J_{PH} = 7$ Hz, P·O·CH_2), 8·71 (t, 6H, J_{HH} 7 Hz, P·O·CH_2·CH_3), and 8·74 (d, 6H, J_{HP} 16 Hz, P·CMe_2).

The 2,4-*dinitrophenylhydrazone* had m.p. 176—177° (from ethanol) (Found: C, 42·7; H, 5·6; N, 14·4; P, 8·1. $C_{14}H_{21}N_4O_7P$ requires C, 43·3; H, 5·4; N, 14·4; P, 8·0%).

Diethyl 2-*Hydroxy*-1,1-*dimethylethylphosphonate*.—A solution of sodium borohydride (3 g, 0·083 mol) in aqueous sodium hydroxide (3 ml 2M-NaOH and 25 ml water) was added dropwise to a stirred solution of the aldehyde (41·6 g, 0·2 mol) in ethanol (120 ml) below 25°. The addition was stopped when a drop of the reaction mixture liberated hydrogen when acidified. The ethanol was removed under reduced pressure and the residue was dissolved in ether (100 ml). The solution was washed with dilute sulphuric acid until no more hydrogen was evolved, then with dilute (10%) sodium carbonate, and finally with water. The aqueous washings were combined, neutralised, salted out (NaCl), and extracted with ether (20 × 25 ml). The combined ether layers were dried ($MgSO_4$) and distilled giving the *alcohol* (36·5 g, 86%), redistillation giving a fraction with b.p. 71·5—72·5° at 0·15 mmHg, $\nu_{max.}$ (film) 3400 (OH), 1240 (P=O), 1165 (P–OEt), and 1030 cm^{-1} (POR), τ 5·99 (quintet, 4H, $J_{HH} = J_{PH} = 7$ Hz, P·O·CH_2), 6·07 (s, 1H, OH, exchanges with D_2O), 6·62 (d, 2H, J_{PH} 18 Hz, PC·CH_2·OH), 8·73 (t, 6H, J_{HH} 7 Hz, P·O·CH_2·CH_3), and 8·94 (d, 6H, J_{PH} 16 Hz, P·CMe_2).

The 3,5-*dinitrobenzoate* had m.p. 69—70° (from light petroleum) (Found: C, 44·2; H, 5·0; N, 6·7; P, 8·9. $C_{15}H_{21}N_2O_9P$ requires C, 44·5; H, 5·2; N, 7·1; P, 7·7%).

Diethyl 1,1-*Dimethyl*-2-p-*tolylsulphonyloxyethylphosphonate* (2).—Toluene-*p*-sulphonyl chloride (7·6 g, 0·04 mol) was added in portions with stirring to a solution of the alcohol (4·2 g, 0·02 mol) in dry pyridine (20 ml) at −5°. The solution was stirred for 2 h and kept overnight at 0°. Water (40 ml) was added, and the mixture extracted with ether (2 × 25 ml). The extracts were washed [HCl (2 × 25 ml), water (10 ml) aqueous sodium carbonate (10 ml)], dried ($MgSO_4$), and evaporated. The resulting oil solidified on trituration with petroleum at −10° to give the *toluene*-p-*sulphonate*, m.p. 16°, $\nu_{max.}$ (film) 1600 (C=C, Ar), 1260 (SO_2–O–), 1240 (P=O), 1180 (SO_2–O–), and 1030 cm^{-1} (POR), τ 2·1 and 2·65 (AB quartet, J_{AB} 8 Hz, ArH), 5·90 (quintet, 4H, $J_{HH} = J_{PH} = 7$ Hz, P·O·CH_2), 6·01 (d, 2H, J_{PH} 10 Hz, CH_2·OTs), 7·50 (s, 3H, $ArCH_3$), 8·70 (t, 6H, J_{HH} 7 Hz, PO·CH_2·CH_3), and 8·83 (d, 6H, J_{PH} 16 Hz, P·CMe_2).

Solvolysis of the Toluene-p-*sulphonate* (2).—The toluene-*p*-sulphonate (1 g, 0·005 mol) and re-fused sodium acetate (0·42 g, slightly >0·005 mol) were dissolved in acetic acid (5 ml) containing a few drops of acetic anhydride. The mixture was heated under reflux and inspected at intervals by t.l.c. It was then dissolved in aqueous sodium carbonate and extracted with ether. The ether contained only the toluene-*p*-sulphonate (2). Acidification of the sodium carbonate solution gave diethyl phosphate.

2-*Diphenylphosphinyl*-2-*methylpropyl Methyl Ketone* (5).—Diphenylphosphine oxide, prepared by the method of Hunt and Saunders,[19] (101 g, 0·5 mol) and re-distilled mesityl oxide (49 g, 0·5 mol) were dissolved in tetrahydrofuran (400 ml) and sodium hydride–oil emulsion (2·5 g, 0·05 mol) was added. The mixture was stirred at room temperature for 3 h and conc. hydrochloric acid (5 ml) was added. The solution was filtered and evaporated. Steam distillation removed a small amount of mesityl oxide, and the remaining aqueous solution was extracted with chloroform (100 ml). The extract was dried ($MgSO_4$) and evaporated to give the *ketone* (146 g, 98·5%), m.p. 76·5—77·5°, $\nu_{max.}$ 1705 (C=O), 1440 (P–Ph), and 1175 cm^{-1} (P=O), M^+ 300, τ 1·8—2·6 (m, 10H, Ph_2PO), 7·30 (d, 2H, J_{PH} 7·5 Hz, CH_2·CO), 7·97 (s, 3H, COMe), and 8·64 (d, 6H, J_{PH} 16 Hz, P·CMe_2).

Treatment with hydroxylamine hydrochloride and triethylamine in ethanol gave the *oxime*, m.p. 214—216° (from aqueous ethanol), $\nu_{max.}$ 3160 (OH), 1650 (C=N), 1439 (PPh), and 1175 cm^{-1} (P=O), M^+ 315, τ 1·8—2·6 (m, 10H, Ph_2PO), 7·56 (d, 2H, J_{PH} 8 Hz, CH_2·C=N·OH), 8·25 (s, 3H, CH_3·C=N·OH), and 8·80 (d, 6H, J_{PH} 16 Hz, P·CMe_2) (Found: C, 68·6; H, 6·9; N, 4·3; P, 10·0. $C_{18}H_{22}NO_2P$ requires C, 68·6; H, 7·0; N, 4·4; P, 9·8%).

Beckmann Rearrangement of the Oxime.—The oxime (21 g) was added to polyphosphoric acid (120 g) at about

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130°. The mixture was stirred until homogeneous (*ca.* 1 h) and then for a further 2 h. The hot solution was poured into water (1 l) and extracted with dichloromethane (3 × 100 ml). The extracts were dried ($MgSO_4$) and evaporated to give a mixture of amides (20 g, 95%). The mixture was normally hydrolysed without purification, but a sample (1 g) chromatographed on a column of SilicAR (20 g) and eluted with chloroform gave N-(2-*diphenylphosphinyl*-2-*methylpropyl*)*acetamide* (0·6 g), $\nu_{max.}$ (Nujol) 3280 (NH), 1670 and 1560 (amide I and II), 1440 (PPh), and 1160 cm^{-1} (P=O), M^+ 315, τ 1·9—2·6 (m, 10H, Ph_2PO), 2·35br (1H, NH·CO), 6·66 (dd, 2H, J_{PH} 19, J_{HH} 7 Hz, CH_2·NH), 8·07 (s, 3H, NAc), and 8·83 (d, 6H, J_{PH} 14·5 Hz, P·CMe_2).

2-*Diphenylphosphinyl*-2-*methylpropylamine* (4).—The mixture of amides from the Beckmann rearrangement (20 g) was heated under reflux with 70% sulphuric acid (200 ml) for 3 days. The mixture was cooled, dichloromethane (100 ml) and water (200 ml) were added, and the phases were separated. The aqueous layer was again extracted with dichloromethane (2 × 50 ml), basified with aqueous 40% sodium hydroxide, and extracted with dichloromethane (4 × 50 ml). These latter extracts were dried ($MgSO_4$) and evaporated to give the amine (7·7 g, 42%). Picric acid was added to a hot ethanolic solution of the amine to give the *picrate*, m.p. 180—181·5° (from ethanol) (Found: C, 53·2; H, 4·7; N, 10·7; P, 6·3. $C_{22}H_{23}N_4O_8P$ requires C, 52·6; H, 4·6; N, 11·1; P, 6·2%). The picrate (10 g) was dissolved in hot aqueous 20% lithium hydroxide (500 ml) and the solution was cooled and extracted with dichloromethane (2 × 25 ml). The extracts were in turn extracted with dil. hydrochloric acid (2 × 50, 1 × 25 ml) and the aqueous solution of the amine hydrochloride was basified with aqueous 40% sodium hydroxide and extracted with dichloromethane (2 × 50 ml). The extracts were dried ($MgSO_4$) and evaporated to give the *amine*, which was recrystallised from di-isopropyl ether to give platelets, m.p. 106—107·5°, $\nu_{max.}$ (Nujol) 3380 and 3300 (NH), 1580 (δ NH), 1440 (PPh), and 1165 cm^{-1} (P=O), M^+ 273, τ 1·9—2·6 (m, 10H, Ph_2PO), 7·19 (d, 2H, J_{PH} 14 Hz, CH_2·N), 8·59 (s, 2H, NH_2), and 8·84 (d, 6H, J_{PH} 15 Hz, P·CMe_2).

3-*Diphenylphosphinyl*-3-*methylbutyric Acid* (6).—The dichloromethane extracts from the acidic solution from the hydrolysis of the amide mixture were combined and extracted with aqueous 10% sodium hydroxide. Acidification of the alkaline extract gave an oil which solidified and was crystallised from aqueous ethanol to give the *acid* (6) (7 g, 35%), m.p. 152·5—154°, $\nu_{max.}$ (Nujol) 2700—2400 (CO_2H), 1708 (CO), 1440 (PPh), and 1130 cm^{-1} (P=O), τ (MeOD) 1·8—2·5 (m, 10H, Ph_2PO), 7·51 (d, 2H, J_{PH} 10 Hz, CH_2·CO_2H), and 8·66 (d, 6H, J_{PH} 16 Hz, P·CMe_2).

Deamination of the Amine (4).—(a) *In aqueous solution.* The amine (246 g, 2 mmol) and sulphuric acid (AnalaR; 250 mg) were dissolved in water (1 ml) and cooled to 5°. Sodium nitrite (138 mg, 2 mmol) was added over 30 min at 5°. The mixture was stirred for 4 h and extracted with dichloromethane (3 × 2 ml). The aqueous layer, on basification and extraction, produced 155 mg (28%) of the starting amine. The organic extracts were washed with aqueous 10% sodium carbonate solution (2 × 1 ml) and water (1 ml), dried ($MgSO_4$), and evaporated. The resulting gum was subjected to p.l.c. (several elutions with chloroform). The four bands were scraped off and extracted with acetone.

Bands 1, 2, and 4 proved to be single compounds but repeated p.l.c. of band 3 in ether–benzene (1 : 1) separated it into two compounds which were extracted as above. The yields are given in the Table.

(b) *Anhydrous conditions.* A solution of the amine (4) (546 mg, 2 mmol) and 3-methylbutyl nitrite (290 mg, 2·5 mmol) in anhydrous acetonitrile (2 ml) was heated under reflux for 5 h. A further 117 mg (1 mmol) of 3-methylbutyl nitrite was added, and heating was continued for 5 h. Evaporation of the solvent gave a gum which was dissolved in dichloromethane (3 ml), washed with dil. hydrochloric acid (2 × 2 ml, 82 mg; 15% of the starting amine was removed in this way), aqueous 10% sodium carbonate solution (2 × 2 ml), and water (2 ml). The solution was dried ($MgSO_4$) and evaporated (finally at 100° and 0·1 mmHg to remove as much 3-methylbutanol as possible) to give a gum which was separated as under (a). The yields are again given in the Table.

The compounds were identified by spectroscopic properties and independent syntheses.

Methylallyldiphenylphosphine Oxide (11).—Freshly distilled ethoxydiphenylphosphine [20] (11·5 g, 0·05 mol) and methylallyl iodide (9·1 g, 0·05 mol) were mixed at room temperature in a wide-mouthed flask fitted with an air condenser. As soon as the exothermic reaction started, the flask was cooled in running water. When the reaction had subsided, the mixture was cooled, dissolved in dichloromethane, washed with dilute aqueous sodium thiosulphate solution and water, dried ($MgSO_4$), and evaporated. The product (12·5 g, 99%) was recrystallised from chloroform–di-isopropyl ether to give white cubes, m.p. 144—145° (lit.,[21] 137—138°), $\nu_{max.}$ (Nujol) 3095 (olefinic CH), 1644 (C=C), 1440 (PPh), and 1186 cm^{-1} (P=O), M^+ 256, τ 2·1—2·7 (m, 10H, Ph_2PO), 5·19 (m, 1H, C=CH), 5·35br (d, 1H, C=CH), 6·94 (d, 2H, J_{PH} 14 Hz, P–CH_2), and 8·23br (s, 3H, C=C–CH_3).

2,2-*Dimethylvinyldiphenylphosphine Oxide* (10).—The allyl compound (11) (1·28 g) was dissolved in conc. sulphuric acid (5 ml) and the solution was added dropwise, with stirring, to water (30 ml). The mixture (containing some white solid) was extracted with chloroform (20 ml). The extract was dried ($MgSO_4$), evaporated, and the residue was recrystallised from light petroleum (100—120°) to give the *vinylphosphine oxide* (10) (1·22 g, 95%), m.p. 149—150°, $\nu_{max.}$ (Nujol) 3095 (olefinic C–H) 1630 (C=C), 1440 (PPh), and 1190 cm^{-1} (P=O), M^+ 256; τ 2·1—2·7 (m, 10H, Ph_2PO), 4·11 (d, 2H, J_{PH} 26 Hz and fine splitting, C=CH), 7·97 (d, 3H, J_{HH} 2 Hz, C=C–CH_3), and 8·06 (s, 3H, C=C–CH_3) (Found: C, 74·4; H, 6·6; P, 12·1. $C_{16}H_{17}OP$ requires C, 75·0; H, 6·7; P, 12·1%).

2-*Hydroxy*-2-*methylpropyldiphenylphosphine Oxide* [22] (14).—Mercury(II) acetate (6·5 g, 0·02 mol) was suspended in a mixture of water (20 ml) and tetrahydrofuran (20 ml), and the methylallylphosphine oxide (11) (5·12 g, 0·02 mol) was added. The mixture was stirred for 10 min and aqueous 2·5M-sodium hydroxide (20 ml) was added. Sodium borohydride (0·4 g, 0·021 mol) in aqueous 2·5M-sodium hydroxide (20 ml) was added dropwise, and the solution was stirred until the deposited mercury had coagulated (*ca.* 3 h), and then extracted with benzene

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(2 × 20 ml). The organic layers were washed with dil. acetic acid and water and dried ($MgSO_4$). Evaporation and recrystallisation from light petroleum–ethyl acetate gave the *alcohol* (14) (5·5 g, 100%), m.p. 106—108°, $\nu_{max.}$ (Nujol) 3335 (OH), 1440 (PPh), and 1170 cm^{-1} (P=O), M^+ 274, τ 2·1—2·6 (m, 10H, Ph_2PO), 4·97br (s, 1H, OH), 7·42 (d, 2H, J_{PH} 10 Hz, P–CH_2), and 8·77 (s, 6H, CMe_2).

Cyclopropyltriphenylphosphonium Bromide.[23]—2-Butyrolactonyltriphenylphosphonium bromide [24] (80 g, 0·19 mol) was heated at 0·5 mmHg at 174—180° in a drying pistol until no more gas was evolved (*ca.* 20 min). Tan-coloured crystals were obtained on cooling which were recrystallised from methanol–ethyl acetate to give cyclopropyltriphenylphosphonium bromide (62 g, 87%), m.p. 186—187° (lit.,[25] 189—190°).

Cyclopropyldiphenylphosphine Oxide.[23]—The phosphonium bromide (39 g) was gently heated with an excess of aqueous 50% sodium hydroxide solution (400 ml) for 30 min. The solution was neutralised with sulphuric acid and extracted with chloroform (3 × 100 ml). The chloroform layers were dried ($MgSO_4$) and evaporated to give the crystalline phosphine oxide (14 g, 58%), which was recrystallised from ethyl acetate–light petroleum (100—120°), m.p. 128—129° (lit.,[25] 132—133°).

1-*Methylcyclopropyldiphenylphosphine Oxide* (13).—Cyclopropyldiphenylphosphine oxide (4·2 g, 0·017 mol) was dissolved in dry tetrahydrofuran (50 ml) and treated with n-butyl-lithium (1·5M in hexane; 11·5 ml, 0·017 mol) under nitrogen at room temperature. The deep red solution which developed was left for 1 h and then methyl toluene-*p*-sulphonate (3·5 g, 0·017 mol) in tetrahydrofuran (20 ml) was added over 10 min, the red colour being completely discharged. The solvent was removed under reduced pressure, water (100 ml) was added, and the mixture was extracted with chloroform (3 × 100 ml). The chloroform layers were dried ($MgSO_4$) and evaporated to give a crystalline solid, which was recrystallised from ethyl acetate–light petroleum (100—120°) to give the *phosphine oxide* (13) (2·4 g) m.p. 95—96°, $\nu_{max.}$ ($CHCl_3$ film) 3070 (cyclopropyl C–H), 1440 (PPh), and 1175 cm^{-1} (P=O), τ 2·0—2·9 (m, 10H, Ph_2PO), 8·80 (d, 3H, J_{PH} 13 Hz, P·CMe), 8·86 (d with fine splitting, 2H, J_{PH} 10 Hz, cyclopropyl H), and 9·36 (d with fine splitting, 2H, J_{PH} 10 Hz, cyclopropyl H), M^+ 256 (88%), M − 1 255 (72), M − CH_3 241 (24), M − C_4H_7 201 (100) (Found: C, 75·0; H, 6·8; P, 12·0. Calc. for $C_{16}H_{17}OP$: C, 75·0; H, 6·7; P, 12·1%).

Ethoxydiphenylphosphine.—A solution of chlorodiphenylphosphine (100 g, 0·46 mol) in dry ether (250 ml) was added dropwise with stirring to absolute ethanol (46 g, 1·0 mol) (AnalaR) and anhydrous pyridine (54 g, 0·69 mol) at 0°. The mixture was left overnight at room temperature and filtered. The filter cake was thoroughly washed with ether (*ca.* 500 ml) and most of the solvent was removed from the combined filtrate at reduced pressure. Distillation gave ethoxydiphenylphosphine, b.p. 108—116° at 0·5 mmHg (lit.,[26] 161·2° at 10 mmHg).

Ethyl 2-Diphenylphosphinylpropionate (7).—Ethoxydiphenylphosphine (23 g, 0·1 mol) and ethyl α-bromopropionate (18·1 g, 0·1 mol) were heated at 160° for 1 h while a stream of nitrogen was passed through the solution. The crystalline mass which separated on cooling was dissolved in the minimum of hot chloroform, and di-isopropyl ether was added until turbidity was observed. Cooling gave the product (24 g); more (3 g) was obtained by evaporation of the mother liquors (90% in all). Recrystallisation from di-isopropyl ether gave the *ester* (7), m.p. 145—146°, $\nu_{max.}$ (Nujol) 1726 (ester C=O), 1440 (P–Ph), and 1184 cm^{-1} (P=O), τ 2·0—2·6 (m, 10H, Ph_2PO), 6·14 (q, 2H, J_{HH} 7 Hz, O·CH_2Me), 6·45 (double q, 1H, J_{HH} 7, J_{HP} 14 Hz, P·CHMe), 8·57 (dd, J_{HH} 7, J_{HP} 15·5 Hz, P·CH*Me*), and 9·14 (t, 3H, J_{HH} 7 Hz, O·CH_2*Me*), M^+ 302 (10%), Ph_2PO^+ 201 (100).

Ethyl 2-Diphenylphosphinyl-2-methylpropionate (8).—The ester (7) (15 g, 0·05 mol) in dry tetrahydrofuran (20 ml) was gradually added to a stirred suspension of sodium hydride [1·3 g, 0·054 mol (from 2·6 g of 50% suspension in oil, washed with petroleum, 3 × 10 ml)] in tetrahydrofuran (5 ml) under reflux. Hydrogen was evolved. Methyl iodide (14·2 g, 0·1 mol) was added dropwise to the stirred solution and the mixture was refluxed for 3 h. Water (50 ml) and dichloromethane (50 ml) were added, the layers were separated, and the aqueous layer was extracted with dichloromethane (50 ml). The extracts were dried ($MgSO_4$) and evaporated to give an oil which subsequently crystallised as white prisms of the methylated *ester* (8), m.p. 72·5—75° (used in the next step without further purification), $\nu_{max.}$ 1704 (ester C=O), 1440 (P–Ph), and 1185 cm^{-1} (P=O), τ 1·9—2·6 (m, 10H, Ph_2PO), 6·06 (q, 2H, J_{HH} 7 Hz, O·CH_2Me), 8·50 (d, 6H, J_{PH} 14 Hz, P·CMe_2), 9·05 (t, 3H, J_{HH} 7 Hz, O·CH_2*Me*), M^+ 316 (19%), Ph_2POH^+ 202 (100).

2-Diphenylphosphinyl-2-methylpropan-1-ol (3).—To the ester (8) (6·3 g, 0·02 mol) in refluxing anhydrous methanol (50 ml) was added sodium borohydride (2 g, 0·04 mol) in 0·2 g portions over 1 h. The mixture was refluxed for a further 1 h, poured into dil. sulphuric acid (100 ml) and extracted with dichloromethane (3 × 25 ml). The extracts were washed with 10% sodium carbonate solution (2 × 20 ml) and water, dried, and evaporated; the residue was recrystallised from light petroleum (100—120°) to give needles of the *alcohol* (3) (2·7 g, 50%), m.p. 135—137°, $\nu_{max.}$ 3180 (O–H), 1440 (P–Ph), and 1140 cm^{-1} (P=O), τ 1·9—2·6 (m, 10H, Ph_2PO), 4·92 (s, 1H, OH), 6·41 (d, 2H, J_{PH} 17 Hz, CH_2·OH), and 8·85 (d, 6H, J_{PH} 15 Hz, P·CMe_2), M^+ 274 (0·5%), M − CH_2O 244 (100%).

2-Diphenylphosphinyl-2-methylpropyl Toluene-p-sulphonate (9).—The alcohol (3) (2·74 g, 0·01 mol) was dissolved in anhydrous pyridine (10 ml) and cooled to 0°. Toluene-*p*-sulphonyl chloride (3·8 g, 0·02 mol) was added with stirring and the mixture was left at 0° overnight. It was then poured into a mixture of conc. HCl (20 ml) and ice-water (100 ml). Dichloromethane (20 ml) was added, the layers were separated, and the aqueous layer was extracted with dichloromethane (10 ml). The extracts were washed with dil. HCl (2 × 20 ml), water (20 ml), and 10% sodium carbonate solution (20 ml), and dried ($MgSO_4$). Evaporation under reduced pressure gave an oil (4 g) which was chromatographed on a column of SilicAR (40 g), eluting with chloroform. Evaporation of the main fraction gave the *tosylate* (9), (3·6 g, 84%), as needles, m.p. 132—133° [from light petroleum (100—120°)] $\nu_{max.}$ 1440 (P–Ph), 1380 and 1180 (–SO_2O–), and 1190

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cm^{-1} (P=O), τ 1·9—2·6 (m, 10H, Ph_2PO), 2·33 and 2·70 (ABq, 4H, J_{AB} 8 Hz, tosyl ArH), 5·87 (d, 2H, J_{PH} 9 Hz, CH_2·OH), 7·61 (s, 3H, Ar*Me*), and 8·81 (d, 6H, J_{PH} 14 Hz, P·CMe_2) (Found: C, 64·6; H, 6·0. $C_{23}H_{25}O_4PS$ requires C, 64·5; H, 5·9%). A satisfactory phosphorus analysis could not be obtained for this compound.

Formolysis of the Tosylate (9).—The tosylate (9) (428 mg, 1 mmol) was dissolved in 98% AnalaR formic acid (5 ml) and heated in a sealed tube at 120° for 50 h. The contents of the tube were evaporated and the residue was dissolved in dichloromethane (10 ml). The solution was washed with 10% sodium carbonate solution (10 ml) and water (10 ml), dried ($MgSO_4$), and evaporated to give a solid (255 mg). P.l.c. separated this into starting material (21 mg) and 2,2-dimethylvinyldiphenylphosphine oxide (10) (230 mg, 84%).

Rate Determination.—The tosylate (9) (214 mg, 0·5 mol) was dissolved in 98% AnalaR formic acid (5 ml) and 0·5 ml samples were placed in sealed tubes. 2,2-Dimethylpropyl tosylate (121 mg, 0·5 mmol) was dissolved in formic acid (5 ml) and was sealed in the same way. The tubes were kept at 99 ± 1° and opened at intervals, and the contents were compared by t.l.c. with synthetic half-life mixtures [the tosylate (9) (21 mg), the phosphine oxide (10) (31 mg), and toluene-*p*-sulphonic acid (9·5 mg) in formic acid (1 ml); also 2,2-dimethylpropyl tosylate (12 mg) and toluene-*p*-sulphonic acid (9·5) in formic acid (1 ml)], to give an approximate determination of the half-lives of the two reactions.

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