Reaction of Acyclic Phosphine Oxides with Toluene-*p*-sulphonyl Isocyanate and Related Reactions

By **C. Richard Hall** and **David J. H. Smith**,* Department of Chemistry, The University, Leicester LE1 7RH
Peter Watts, Chemical Defence Establishment, Porton Down, Salisbury, Wiltshire SP4 0JQ

Acyclic phosphine oxides (1) form the corresponding imides (2) when treated with toluene-*p*-sulphonyl isocyanate (TsNCO) in aprotic solvents. Optically active phosphine oxides are racemised faster than imides are formed. The kinetics and mechanism of the racemisation process are discussed. The addition of TsNCO to methylphenyl-t-butylphosphine formed a 1 :1 adduct. whereas addition to trimethyl phosphite gave dimethyl methylphosphonate together with trimethyl phosphate.

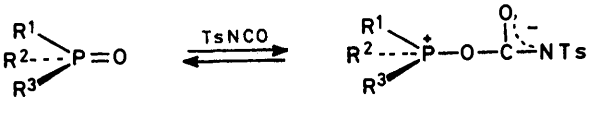
We have shown that some cyclic phosphine oxides and phosphines react with sulphonyl isocyanates to form the corresponding imines.[1] We now describe an investigation of reactions of toluene-*p*-sulphonyl isocyanate (TsNCO) with a series of acyclic phosphine oxides (1). In general the rate of phosphine imide (2) formation is very low in comparison with that of phosphetan imides. However reaction does occur in a range of aprotic solvents. Preliminary results indicated that the reaction was much faster in the more polar media, acetonitrile being the solvent of choice. Variation of the substituents on phosphorus did not appear to have much effect upon the rate of reaction, except when either two phenyl or two t-butyl groups were attached. In these cases there was no observed reaction.

$$\underset{(1)}{R^1R^2R^3P{=}O} + TsNCO \longrightarrow \underset{(2)}{R^1R^2R^3P{=}NTs} + CO_2$$

a; $R^1 = PhCH_2, R^2 = Ph, R^3 = Me$
b; $R^1 = PhCH_2, R^2 = Ph, R^3 = Et$
c; $R^1 = Et, R^2 = Ph, R^3 = Me$
d; $R^1 = Bu^t, R^2 = Ph, R^3 = Me$

(+)-(*R*)-Benzylmethylphenylphosphine oxide (1a)[2] was used to determine the stereochemistry of the reaction. When the reaction was monitored polarimetically in acetonitrile the rotation dropped rapidly to zero. A quantitative yield of racemic phosphine oxide could be recovered if the reaction was quenched at this point. For a molar ratio of phosphine oxide (1a) (0.020 g ml^{-1}) to TsNCO of 1 : 4 in acetonitrile at 25 °C the half-life of racemisation is 40 min, while that of phosphine imide formation is 36 h.

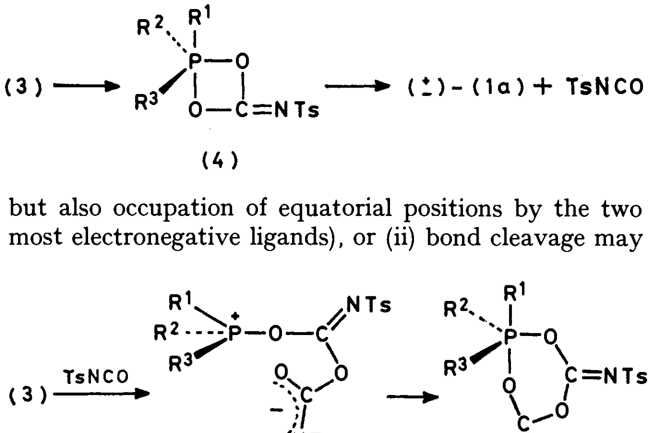
The first step in these reactions can be assumed to be the reversible formation of the zwitterions (3) by nucleophilic attack of the phosphoryl oxygen at the isocyanate[1] carbon. These species do not have the benefit of any relief of ring-strain upon ring closure to a pentacoordinate phosphorane and presumably are longer lived than the corresponding zwitterions generated from phosphetan oxides.[1]



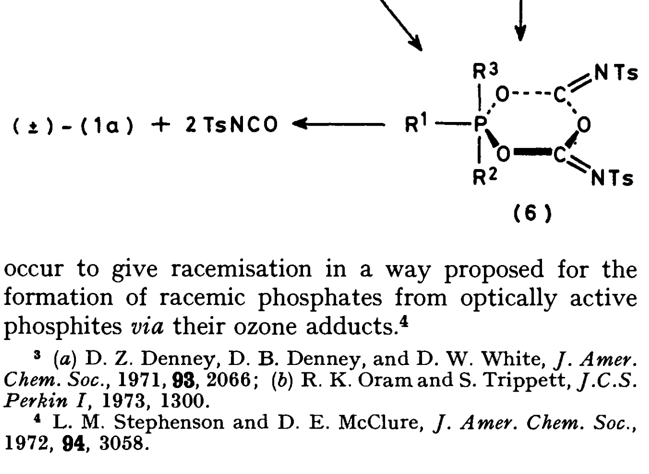
(+)-(1a) (3)

Three alternative reactions of the zwitterion (3) resulting in racemisation can be considered, as follows.

(*A*) Ring closure by nucleophilic apical attack of oxygen at phosphorus, to give the phosphorane (4). In order for this intermediate to lead to racemisation, either (i) it must pseudorotate through an intermediate in which the four-membered ring spans two equatorial positions (this is a very unlikely process because it involves not only a considerable degree of ring strain,[3] but also occupation of equatorial positions by the two most electronegative ligands), or (ii) bond cleavage may occur to give racemisation in a way proposed for the formation of racemic phosphates from optically active phosphites *via* their ozone adducts.[4]



(4)



(6)

---

[1] C. R. Hall and D. J. H. Smith, preceding paper.

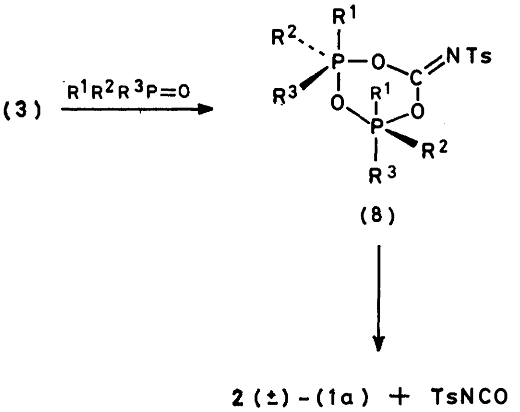
[2] O. Korpium, R. A. Lewis, J. Chickos, and K. Mislow, *J. Amer. Chem. Soc.*, 1968, **90**, 4842.

[3] (*a*) D. Z. Denney, D. B. Denney, and D. W. White, *J. Amer. Chem. Soc.*, 1971, **93**, 2066; (*b*) R. K. Oram and S. Trippett, *J.C.S. Perkin I*, 1973, 1300.

[4] L. M. Stephenson and D. E. McClure, *J. Amer. Chem. Soc.*, 1972, **94**, 3058.

(*B*) The zwitterion (**3**) can react with a second molecule of TsNCO to give the extended system (**5**) which can undergo ring closure by attack of oxygen at phosphorus. The racemisation process is assumed to occur by formation of the symmetrical phosphorane (**6**), in one of two ways: (i) by direct equatorial attack, or (ii) by apical attack to give the phosphorane (**7**) followed by permutational isomerisation to place the ring diequatorial. Although equatorial attack–equatorial loss mechanisms have been proposed for substitution reactions at sulphinyl sulphur,[5] such mechanisms have not yet been demonstrated in phosphorus chemistry. Indeed calculations[6] suggest that apical attack at tetrahedral phosphorus involves less energy than the corresponding equatorial attack. It seems reasonable that if racemisation proceeds by incorporation of a second molecule of TsNCO it will do so *via* the route (5) ⟶ (7) ⟶ (6), not by formation of (6) directly from (5).

(*C*) The zwitterion (**3**) can react with a second molecule of phosphine oxide, and ring closure will then give an intermediate such as (**8**). Permutational isomerisation and fragmentation would lead to racemisation.



It should in principle be possible to distinguish amongst these three proposed racemisation schemes by considering the kinetics of the reaction. The data (*e.g.* Table 1) indicate the initial rapid reversible formation of an intermediate, followed by its slow breakdown. This intermediate must either have a lower rotation than the original phosphine oxide or its rotation must be different in sign. Plots of the logarithm of the rotation against time showed that, subsequent to its initial rapid fall, the decrease in rotation is first order over the majority of the reaction. The rate coefficients are given in Table 2. This rapid reversible reaction followed by a process involving first-order dependence upon phosphine oxide indicates that scheme (*C*) does not contribute significantly to the observed reaction, and also that the TsNCO concentration remains effectively constant throughout the reaction. The latter is to be expected if the concentrations of any intermediates are small, since TsNCO is regenerated. A plot of the logarithm of the observed reaction rate constant against the logarithm of the TsNCO concentration has a gradient of two, demonstrating a second-order dependence upon TsNCO and indicating that scheme (*B*) rather than (*A*) is predominant.

TABLE 1

Decrease in the normalised rotation as a function of time for the reaction of (+)-(*R*)-benzylmethylphosphine oxide with toluene-*p*-sulphonyl isocyanate in acetonitrile at 26 °C

Run 1 [TsNCO]/[phosphine oxide] = 1

		Calc. rotation (°)	
Time (min)	Obs. rotation (°)	Scheme (*B*1)	Scheme (*B*2)
0	100	100	100
2	95	96	96
6	91	92	92.5
10	89	89.5	90
20	85	85.5	86
29	82	82.5	82.5
38	79	79	79
50	74	75	75
65	69	70.5	70
80	65	66.5	65.5
95	61	62	61.5
110	58	58.5	57.5
140	51	51.5	50
170	45	45.5	44
200	39	40	38.5
245	32	33	31.5
290	26	27	25.5
335	21	22.5	20.5
380	17	18.5	17

TABLE 2

Observed rate constants for the reaction of (+)-(*R*)-benzylmethylphenylphosphine oxide with toluene-*p*-sulphonyl isocyanate in acetonitrile at 26 °C

Run	[TsNCO]/M	[TsNCO]/[phosphine oxide]	k_{obs}/s^{-1}
1	0.089	1	3.20×10^{-5}
2	0.044	0.5	8.75×10^{-6}
3	0.176	2	9.82×10^{-5}
4	0.266	3	3.25×10^{-4}

Two alternative versions of scheme (*B*) were then considered [(*B*1) and (*B*2), where P is the phosphine oxide and I the intermediate], and the associated differential equations were solved by using an analogue computer.

(*B*1) An inversion scheme:

$$(+)\text{-p} \underset{k_2}{\overset{k_1}{\rightleftharpoons}} (+)\text{-I} \xrightarrow{k_3} (-)\text{-P} \underset{k_2}{\overset{k_1}{\rightleftharpoons}} (-)\text{-I} \xrightarrow{k_3} (+)\text{-P}$$

(*B*2) A racemisation scheme:

$$(+)\text{-P} \underset{k_2}{\overset{k_1}{\rightleftharpoons}} (+)\text{-I} \xrightarrow{k_3} (+)\text{-P} + (-)\text{-P}$$

Two major assumptions were made in the computer simulation: (i) that the specific rotation of the intermediate is such that it does not contribute to the observed rotation and (ii) that the concentration of TsNCO remains constant throughout the reaction. Since considerable quantities of intermediate may be formed during the reaction, this introduces an error, but even in run 4 where one might expect 30% concentration

---

[5] F. G. Yamagishi, D. R. Rayner, E. T. Zwicker, and D. J. Cram, *J. Amer. Chem. Soc.*, 1973, **95**, 1916.

[6] D. B. Boyd, *J. Amer. Chem. Soc.*, 1969, **91**, 1200.

of intermediate this only involves a 10% change in the concentration of TsNCO in the initial stages of the reaction (see Table 3).

TABLE 3

Computer simulation of kinetic data *

		Scheme ($B1$)			Scheme ($B2$)		
Run	A_0/B_0	k_1	k_3	%I	k_1	k_3	%I
1	1	3.8	4.4	8	3.8	10	7
2	0.5	3.4	5.0	4	3.4	12.4	4
3	2	3.8	3.8	15	5.0	7.5	14
4	3	6.8	4	30	7.7	11.3	28

* A_0 = initial concentration of TsNCO; B_0 = initial concentration of (+)-(1a); k_1 and k_3 are the second-order rate constants (l mol^{-1} s^{-1}) derived from the computation. The values of the actual rate coefficients used are equal to the rate constants multiplied by A_0/B_0. The first-order rate constant k_2 was fixed at 38 × 10^{-4} s^{-1}. %I refers to the percentage of the phosphine oxide bound up in the intermediate.

The derived rate constants and the total percentages of phosphine oxide in the form of an intermediate are given in Table 3. The reaction schemes ($B1$) and ($B2$) were simulated for one set of concentrations and the values of k_1, k_2, and k_3 were calculated. The concentration of TsNCO was allowed to vary. It was observed that both k_1 and k_3 varied but k_2 remained constant. A value of 38 × 10^{-4} s^{-1} for k_2 was established and used throughout subsequent computations.

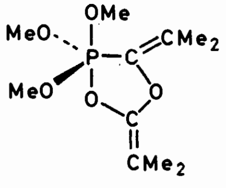
The observed kinetic data are consistent with those calculated for both the inversion and the racemisation schemes (see Table 1). The individual rate constants vary somewhat, as does the percentage of intermediate, but no distinction between ($B1$) and ($B2$) could be made. The computer simulation suggests that the reaction proceeds with the reversible formation of an optically active intermediate from one molecule of phosphine oxide and one molecule of TsNCO. This can react irreversibly with a further molecule of TsNCO to regenerate either inverted or racemised phosphine oxide. The model produced does not require the formation of an intermediate containing one molecule of phosphine oxide and two of TsNCO; if one is formed then its breakdown is much faster than its formation.

A surprising result from the simulation studies was the large amount of phosphine oxide apparently bound-up as an intermediate, as much as 30% if the reaction proceeds *via* scheme ($B1$). We have made considerable efforts to find this, but no intermediate was detected in reaction mixtures monitored by u.v., i.r., or n.m.r. spectroscopy. In reactions monitored by ^1H n.m.r. there was a gradual build-up of absorption due to product (imide) formation. The phosphine oxide completely disappears after about 4 days at room temperature in typical experiments, but no other absorptions were seen. The ^{31}P n.m.r. signal of a mixture of (1a) and TsNCO (3 mol. equiv.) in acetonitrile rapidly shifted from an initial 32.02 p.p.m. downfield from phosphoric acid to 31.20 p.p.m. This is consistent with the reversible build-up of an intermediate containing a more shielded phosphorus atom. Cooling this solution down to −56 °C did not prevent rapid equilibration between starting material and the intermediate. There was a chemical shift change (to 30.20 p.p.m.) but the signal remained sharp, with no indication of broadening.

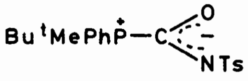
Electron-withdrawing groups are known to stabilise phosphoranes.[7] Replacement of the alkyl groups on phosphorus with alkoxy-groups might therefore be expected to stabilise any intermediate phosphoranes. Attempted reactions of TsNCO with trimethyl phosphate and dimethyl methylphosphonate led to quantitative recovery of starting material. The same factors which stabilise phosphoranes will make the starting phosphoryl oxygen less nucleophilic.

Bentrude [8] has isolated oxyphosphoranes such as (9) from reactions of trivalent phosphorus compounds with dimethylketen. The structural similarities suggested to us that oxyphosphoranes might be formed from the reaction of P^{III} compounds with TsNCO.

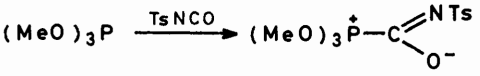
A white crystalline unstable material (80%) was obtained from the addition of TsNCO to a degassed solution of methylphenyl-t-butylphosphine in dichloromethane or benzene. That this material was not a phosphorane was indicated by the low-field ^{31}P n.m.r. signal (−23.6 p.p.m. relative to phosphoric acid). The adduct, by analogy with the work of Hoffmann [9] and the reaction of tertiary amines with TsNCO,[10] probably has the zwitterionic structure (10).



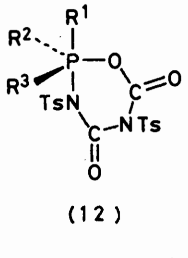
(9)



(10)



(11)



(12)

A small amount of the phosphine oxide (1d) could also be obtained from this reaction, although control experiments showed that the phosphine was stable under the reaction conditions in the absence of TsNCO.

---

[7] F. H. Westheimer, *Accounts Chem. Res.*, 1968, **1**, 70.

[8] W. G. Bentrude, W. D. Johnson, and W. A. Khan, *J. Amer. Chem. Soc.*, 1972, **94**, 3058.

[9] H. Hoffmann, H. Forster, and G. T. Poghossian, *Monatsh.*, 1969, **100**, 311.

[10] M. Seefelder, *Chem. Ber.*, 1963, **96**, 3243.

The main products identified from the addition of TsNCO to a solution of trimethyl phosphite were trimethyl phosphate (30%) and dimethyl methylphosphonate (55%). However no phosphorus–nitrogen-containing compounds were obtained. The dimethyl methylphosphonate is probably formed by an Arbusov reaction from the zwitterion (11). This process regenerates TsNCO and therefore only catalytic amounts of isocyanate should be required. This is not the case, probably because the phosphate-forming reaction, either by direct oxidation [11] or *via* (11), consumes TsNCO.

Phosphine imide (2) formation presumably occurs *via* (5) by nucleophilic attack of nitrogen at phosphorus to give the intermediates or transition states (12) analogous to (7). The relative rates of racemisation and phosphine imide formation can be correlated to the relative nucleophilicites of oxygen and nitrogen in the zwitterion at phosphorus.

EXPERIMENTAL

For general procedures see the preceding paper.[1]

Reaction of Acyclic Phosphine Oxides with Toluene-p-*sulphonyl Isocyanate.—General procedure.* Toluene-*p*-sulphonyl isocyanate (1.3 mmol) was slowly added to a stirred solution of the phosphine oxide (0.9 mmol) in acetonitrile, benzene, dichloromethane, or chloroform (5 ml). The reaction was monitored by ^{1}H n.m.r. spectrometry and was complete in *ca.* 4 days, at room temperature. The excess of isocyanate was then hydrolysed with water and the solvent was removed under reduced pressure to give a clear oil. Chromatography on silica (elution with ethyl acetate) gave *benzylmethylphenylphosphine* N-(p-*tolylsulphonyl*)*imide* (2a) (95%), m.p. 130—131° (from chloroform–light petroleum), $\nu_{max.}$ ($CHCl_3$) 1 495, 1 440, 1 250, 1 140br, 1 085s, and 900 cm^{-1}, τ 2.00—3.10 (14 H, m), 6.38 (2 H, dd, J_{PH} 16, J_{PH} 3 Hz), 7.63 (3 H, s), and 8.10 (3 H, d, J_{PH} 14 Hz), ^{31}P δ 40.92 p.p.m. (downfield from H_3PO_4), *m/e* 383, 349, 306, 293, 292, 276, 229, 228, 214, and 91 (Found: C, 66.05; H, 5.85; N, 3.75; P, 7.9. $C_{21}H_{22}NO_2PS$ requires C, 65.8; H, 5.75; N, 3.65; P, 8.1%).

Benzylethylphenylphosphine N-(p-*tolylsulphonyl*)*imide* (2b) (98%) had m.p. 106—107° (from chloroform–light petroleum), $\nu_{max.}$ ($CHCl_3$) 1 440, 1 260, 1 140br, and 1 087 s cm^{-1}, τ 2.05—3.13 (14 H, m), 6.28 (2 H, d, J_{PH} 16 Hz), 7.62 (3 H, s), 7.28—8.08 (2 H, m), and 8.60—9.38 (3 H, m), *m/e* 397, 368, 333, 332, 306, 242, 175, 160, 144, 142, and 112 (Found: C, 66.45; H, 5.95; N, 3.5. $C_{22}H_{24}NO_2PS$ requires C, 66.5; H, 6.05; N, 3.5%).

Ethylmethylphenylphosphine N-(p-*tolylsulphonyl*)*imide* (2c) (80%) had m.p. *ca.* room temp. $\nu_{max.}$ ($CHCl_3$), 1 440, 1 260, 1 140br, and 1 090s cm^{-1}; τ 1.98—2.87 (9 H, m), 7.65 (3 H, s), 7.50—8.17 (2 H, m), 8.08 (3 H, d, J_{PH} 13.5 Hz), and 8.63—9.30 (3 H, m), *m/e* 321, 293, 275, 268, 265, 257, 230, 228, 214, 139, and 71 (Found: C, 57.7; H, 6.1; N, 4.15; P, 9.4. $C_{13}H_{20}NO_2PS$ requires C, 59.8; H, 6.25; N, 4.35; P, 9.65%).

Methylphenyl-t-butylphosphine *N*-(*p*-tolylsulphonyl)-imide (2d) (75%) was a clear oil, $\nu_{max.}$ (CH_2Cl_2) 1 465, 1 350, 1 170br, 1 135br, and 1 082 cm^{-1}, τ 2.22—2.90 (9 H, m), 7.63 (3 H, s), 7.95 (3 H, d, J_{PH} 13 Hz), and 8.88 (9 H, d, J_{PH} 16.5 Hz), *m/e* 349, 334, 293, 292, 276, 258, 244, 149, 139, 138, and 91. No analysis was obtained owing to complete decomposition on attempted distillation.

Reaction of Methylphenyl-t-butylphosphine with Toluene-p-*sulphonyl Isocyanate.*—The isocyanate (0.37 g, 1.9 mmol) was slowly added to a solution of the phosphine (0.34 g, 1.9 mmol) in degassed dichloromethane (12 ml) at −78 °C. The n.m.r. spectrum of the solution, which did not change on warming to room temperature, showed the presence of phosphine oxide (5%), phosphine imide (5%), and a 1 : 1 adduct (90%). Removal of the solvent under reduced pressure and crystallisation from degassed benzene gave the adduct as sticky crystals (0.57 g, 80%), $\nu_{max.}$ (C_6H_6) 1 675s, 1 640, 1 600s, 1 440, 1 400, 1 350br, and 1 150br cm^{-1}, τ 1.73—2.83 (9 H, m), 7.53 (3 H, s), 8.72 (3 H, d, J_{PH} 16 Hz), and 8.90 (9 H, d, J_{PH} 14 Hz), *m/e* (no molecular ion) 222, 197, 180, 155, 140, 123, 91, 78, 77, and 57, ^{31}P δ −23.6 p.p.m. (rel. H_3PO_4). No analysis was obtained owing to instability. The same product was obtained when degassed benzene or chloroform was used as solvent, and when a 100% excess of the isocyanate was used.

Reaction of Trimethyl Phosphite with Toluene-p-*sulphonyl Isocyanate.*—The isocyanate (0.21 g, 1.1 mmol) was added slowly to a solution of trimethyl phosphite (0.07 g, 0.54 mmol) in deuteriochloroform (2 ml). The reaction was constantly monitored by n.m.r. and was complete after 60 min. The products, trimethyl phosphate (30%) and dimethyl methylphosphonate (55%), were characterised by comparison (g.l.c. and n.m.r.) with authentic samples and by heteronuclear decoupling experiments.

Kinetic Measurements.—Rate data were obtained by using a Perkin-Elmer 141 polarimeter operating at 589 nm. The required amount (5.2 ml) of a stock solution of the phosphine oxide (0.088M; $[\alpha]_D$ +66.3°) in acetonitrile was kept at 26 ± 0.5 °C in a 1 dm path-length quartz cell. The isocyanate was added neat with a previously standardised micro-syringe and the solution was shaken rapidly. The reactions were followed to greater than 85% loss in rotation.

The phosphine oxide was found to be optically stable for at least 6 days in acetonitrile or chloroform solution. When the reaction was quenched with water or methanol as soon as the rotation reached zero a quantitative yield of racemic phosphine oxide could be recovered. The corresponding phosphine imide was stable in a solution containing water, methanol, and toluene-*p*-sulphonamide.

We thank the S.R.C. for a Research Studentship. We also thank the Chemical Defence Establishment for the use of their analogue computer facilities, and Dr. J. M. Harrison (Porton Down) and Dr. C. Brown (University of Kent) for obtaining the ^{31}P n.m.r. spectra and for discussions.

[7/108 *Received, 24th January,* 1977]

---

[11] R. Greenhalgh and R. F. Hudson, *Phosphorus*, 1972, **2**, 1.