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NUCLEOPHILIC SUBSTITUTION AT PHOSPHORYL PHOSPHORUS

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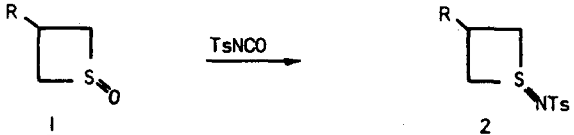
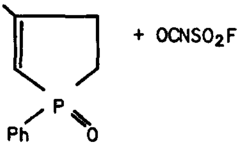
Informative stereochemical features have been observed in nucleophilic substitution at phosphorus when phosphorus is constrained in a ring.[1] There has been much interest recently in nucleophilic substitution at sulphoxide sulphur[2] and it is possible that such features would be observable in the nucleophilic substitution of sulphoxides with p-tosyl isocyanate (TsNCO). Preliminary results indicated that the reaction of thietane-1-oxides (1) in a variety of solvents gave the corresponding sulphimide (2) with inversion of configuration.[3] We therefore decided to investigate the corresponding reaction in which there was no complication from the lone-pair on the hetero-atom, namely the reaction of isocyanates with phosphetan oxides.



1   2

R = Ph, Me

The formation of carbodiimides from isocyanates by the catalytic action of phosphine oxides is a well characterised reaction which is thought to proceed via the corresponding phosphinimine.[4] The best catalyst was shown to be the compound now known to be (3). Hoffmann[5] more recently described the reaction of (3) with N-fluorosulphonyl isocyanate. No carbodiimide is obtained because the reaction does not proceed beyond the intermediate N-fluorosulphonylphospholene imine (4).



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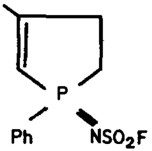

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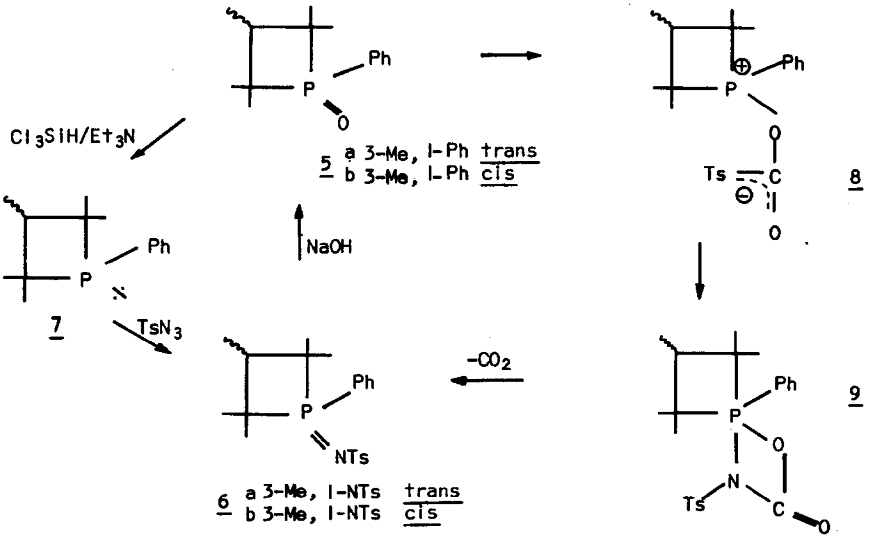
We have found that phosphetan oxides (5) react with TsNCO remarkably smoothly. Addition of the isocyanate to a cooled solution of the phosphetan oxide in benzene gave the phosphinimine stereospecifically, (6a, 97%), m.p. 144°C ($CHCl_3$, light petroleum)[6], τ ($CDCl_3$) 1.75 - 2.84 (9H, m), 7.45 - 8.06 (1H, m), 7.68 (3H, s), 8.64 (6H, d, J_{PH} 19 Hz), 8.81 (6H, d, J_{PH} 19 Hz), 9.02 (3H, dd, J 1 and 6 Hz), and (6b, 94%), m.p. 179 - 180°C ($CHCl_3$, light petroleum) τ ($CDCl_3$) 2.24 - 3.10 (9H, m), 7.10 - 7.65 (1H, m), 7.76 (3H, s), 8.45 (6H, d, J_{PH} 19 Hz), 8.75 (6H, d, J_{PH} 19 Hz), 9.04 (3H, dd, J 1 and 7.5 Hz). Chlorosulphonyl isocyanate also gave the corresponding imines as unstable clear oils in high yield. The reaction could also be carried out in acetonitrile, dichloromethane and pyridine as solvents.

Alkaline hydrolysis of 6a or 6b in aqueous methanol gave the starting phosphine oxide 5a or 5b respectively, again essentially quantitatively. It is somewhat surprising that this hydrolysis occurs with no stereochemical crossover, in view of the fact that loss of stereospecificity has been observed in the alkaline hydrolysis of some phosphetan salts.[7]

Phosphetan oxides (5) are reduced by trichlorosilane and triethylamine with retention of configuration.[8] Reaction of the phosphetans (7) with *p*-tosyl azide in benzene gave the *same* phosphinimine as the corresponding phosphine oxide and TsNCO. Since the reaction of the phosphetan only involves oxidation of the phosphorus lone-pair, a reaction that almost certainly proceeds with retention of configuration, all of the reactions in the cycle must proceed with retention of configuration.

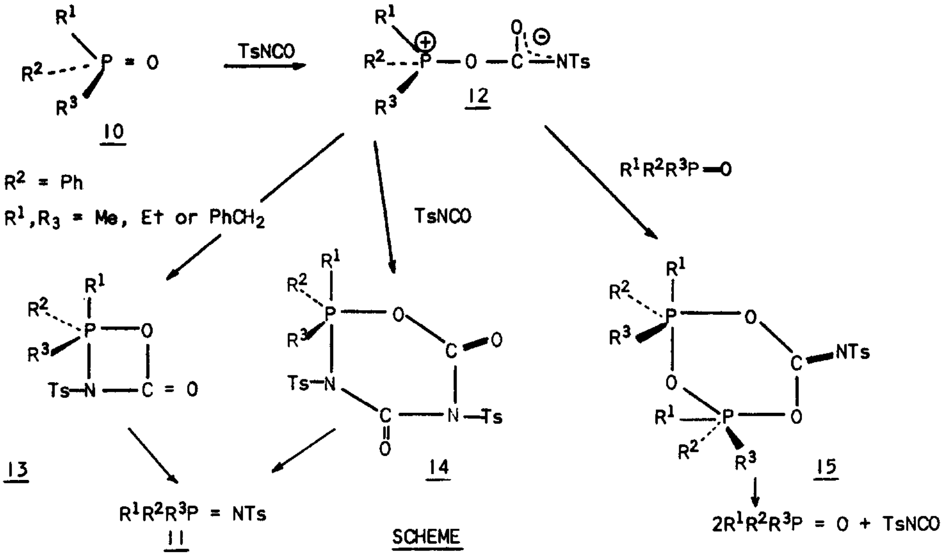


It is probable that the reaction of phosphetan oxides with TsNCO proceeds by rapid formation of a zwitterion (8) which rapidly closes to an intermediate (9) with relief of ring strain, giving products with retention of configuration. This is substantiated by the fact that the reaction shows good second order kinetics with a rate constant of 3.09×10^{-4} sec^{-1} M^{-1} at -48°C in $CDCl_3$.

However, the situation with the acyclic phosphine oxides (10) is more complex. They react with TsNCO in benzene or acetonitrile to give phosphinimines (11) e.g. R^1 = Me, R^2 = Ph, R^3 = CH_2Ph (95%) m.p. 130 - 131°C ($CHCl_3$ - light petroleum), τ ($CDCl_3$), 2.00 - 3.10 (14H, m), 6.38 (2H, dd, J_{HH} 3 Hz, J_{PH} 16 Hz), 7.63 (3H, s), 8.10 (3H, d, J_{PH} 14 Hz), at least three orders of magnitude more slowly than the cyclic oxides. Racemic product was obtained when (+)-(R)-benzylmethylphenylphosphine oxide was treated with TsNCO in acetonitrile. Furthermore we observed that the half-life of racemisation is about 15 minutes whereas the half-life for phosphinimine formation is about 50 hours at room temperature under the same conditions.

The first-formed zwitterion in these reactions could ring close to (13) as above, but as there is now no relief of ring strain, the reaction is slower and other reaction pathways are able to compete. These are outlined in the Scheme. Reaction of the zwitterion with another molecule of isocyanate followed by ring closure would give an intermediate (14), or a similar intermediate with the ring diequatorial, arising from equatorial-attack, equatorial-loss at phosphorus,[2] a process which is unprecedented and unlikely in phosphorus chemistry. Evidently phosphinimine formation whether it be via 13 or 14 is slower than racemisation.

Racemisation (oxygen exchange) could proceed via intermediates similar to 13 or 14, where oxygen and not nitrogen of the zwitterion has acted as a nucleophile at phosphorus or by an intermediate such as 15 involving another molecule of phosphine oxide. Pseudorotation which interchanges the R groups or places the ring diequatorial would lead to racemisation. Since racemisation proceeds much more quickly than product formation obviously the oxygen of the zwitterionic intermediates is more nucleophilic than the nitrogen. This exchange reaction is not observable for the phosphetan oxides, because it would give back starting material with retention of configuration. However, the reaction of the corresponding trans phosphetan sulphide with an equimolar amount of TsNCO gave-the imine 6a (50%)and *p*-tosyl isothiocyanate (50%),[9] indicating that such a process does indeed occur.



SCHEME

Kinetic studies of the racemisation process show that a complex reaction is occurring. They indicate that an intermediate is formed which probably decomposes by a number of pathways.

We thank the S.R.C. for a Research Studentship.

References and Footnotes

1. See J.R. Corfield, R.K. Oram, D.J.H. Smith, and S. Trippett, *J. Chem. Soc., Perkin I*, 1972, 713.
2. F.G. Yamagishi, D.R. Rayner, E.T. Zwicker, and D.J. Cram, *J. Amer. Chem. Soc.*, 1973, **95**, 1916, and references therein.
3. C.R. Hall and D.J.H. Smith unpublished observations. The rate of epimerisation of the sulphoxides is faster than product formation. For a discussion of this point see ref.2.
4. J.J. Monagle, T.W. Campbell, and H.F. McShane, *J. Amer. Chem. Soc.*, 1962, **84**, 4288.
5. H. Hoffmann, H. Forster, and G.T. Poghossian, *Monatsh*, 1969, **180**, 311.
6. All new compounds gave satisfactory spectroscopic data and all except the unstable chlorosulphonyl imines gave satisfactory elemental analysis results.
7. For a general discussion of this point see D.J.H. Smith in Organophosphorus Chemistry, (Specialist Periodical Report), ed. S. Trippett, The Chemical Society, 1972, Vol.3, p.20.
8. K.E. DeBruin, G. Zon, K. Naumann, and K. Mislow, *J. Amer. Chem. Soc.*, 1969, **91**, 7027.
9. The i.r. spectrum of the crude reaction product showed strong absorption at 1900cm^{-1} (NCS) and none at 2240cm^{-1} (NCO).