The Mechanism of the Insertion of Phenyl Isocyanate into the P–N Bond of Phosphoramidites

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ISOCYANATES react readily with compounds of the type $Ph_2P–NHR$ to give phosphino-ureas, and a common product is isolated from the following reactions:[1]

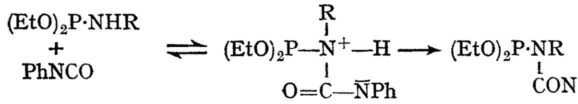
$$Ph_2P–NHR + PhNCO \rightarrow Ph_2P–NR–CO\cdot NHPh \leftarrow Ph_2P–NHPh + RNCO$$

$$R = Me, Et, Pr^n$$

The reaction of $(EtO)_2P–NHR$ however gives two isomeric products which can be assigned structures (I) and (II) on the basis of ^{31}P n.m.r. and i.r. spectra. These products are mainly unstable oils, decomposing rapidly on distillation, although analytically pure samples have been obtained from the reaction where R = Et.

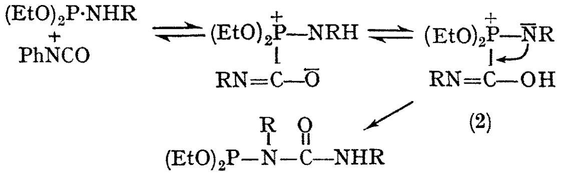
$$\text{(I)}\ (EtO)_2P\cdot NR\cdot CO\cdot NHPh \rightleftharpoons (EtO)_2P\cdot NPh\cdot CO\cdot NHR\ \text{(II)}$$

Kinetic investigations show that: (a) the compounds $R_2P–NHR^1$ are *ca.* 10^4—10^5 times more reactive than $R_2P–NR_2$; this may be attributed to proton mobility. (b) $(EtO)_2P\cdot NHR$ is much more reactive than Ph_2PNHR, *e.g.* when $R = Pr^n$ the rate ratio is 30. (*c*) R_2PNHPr is more reactive than R_2PNHPh owing to the greater basicity of nitrogen; the difference is however small, *e.g.* the relative reactivity of $(EtO)_2P–NHPr$ and $(EtO)_2P–NHPh$ is 2 : 1. (d) The temperature coefficients are very small *e.g. ca.* 1 kcal./mole for the reaction of $(EtO)_2PNHR$ with phenyl isocyanate and 3—4 kcal./mole for the corresponding reactions of Ph_2PNHR. These low values suggest that the reaction proceeds through a pre-equilibrium, and two mechanisms may be advanced to account for these observations.



$$(EtO)_2P\cdot NHR + PhNCO \rightleftharpoons (EtO)_2P–\underset{O=C–\bar{N}Ph}{\overset{R}{N^+}}–H \longrightarrow (EtO)_2P\cdot \underset{CONPh}{NR}$$

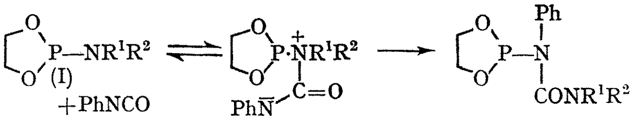
(1)



$$(EtO)_2P\cdot NHR + PhNCO \rightleftharpoons (EtO)_2\underset{RN=C–\bar{O}}{\overset{+}{P}}–NRH \rightleftharpoons (EtO)_2\underset{RN=C–OH}{\overset{+}{P}}–\bar{N}R \rightarrow (EtO)_2P–\overset{R}{N}–\overset{O}{\overset{\|}{C}}–NHR$$

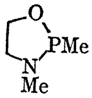
(2)

In order to decide between these two mechanisms, the rates of reaction of the corresponding cyclic phosphoramidites were followed. We have suggested[2] that the relative reactivity of cyclic and non-cyclic compounds depend on the change in ring strain, when the phosphorus acts as nucleophile or an electrophile. The cyclic *N*-dialkyl compounds are considerably more reactive than the non-cyclic analogues[2] (Table) in agreement with the suggested mechanism:



In contrast, the cyclic *N*-alkyl derivatives are less

Rates of reaction of P^{III}–N *compounds with phenyl isocyanate in toluene.* (*k in* M.$^{-1}$*sec.*$^{-1}$)

	k (40°)		k (60°)
$(EtO)_2P{\cdot}NHEt$	$1{\cdot}29 \times 10^{-2}$	(I; $R^1 = R^2 =$ Et)	$3{\cdot}63 \times 10^{-4}$
(I; $R^1 =$ H, $R^2 =$ Et	$1{\cdot}34 \times 10^{-3}$	$(EtO)_2P{\cdot}NEt_2$	$7{\cdot}69 \times 10^{-6}$
(I; $R^1 =$ H, $R^2 = Pr^n$)	$9{\cdot}24 \times 10^{-4}$		*ca.* 3×10^{-3} [44°]
$(EtO)_2P\text{-}NHPr^n$	$1{\cdot}85 \times 10^{-2}$		

reactive by factors of 10—25 than the non-cyclic analogues (Table). This appreciable rate decrease is to be expected for a process involving quaternisation on phosphorus, in view of the increase in O-P-O angle. The effect is in the same direction, but much greater than that observed in the reaction with methyl iodide.

A rate decrease of this kind is to be expected for mechanism (2) whereas mechanism (1) predicts similar reactivities for the cyclic and non-cyclic compounds. This mechanism (2) is also in agreement with the greater reactivities of the phosphoramidites compared to the phosphinous amides which may be attributed to increased p_π–d_π-bonding in the intermediate phosphinimine [*cf.* the stabilities of the adducts[3] of $(EtO)_3P$ and Ph_3P with BH_3].

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[3] M. F. Lappert and B. Prokai, *Adv. Organometallic Chem.*, 1967, **5**, 225.