Mechanism of the Pseudo-molecular Rearrangement of Triethyl *N*-Phenylphosphorimidate to Diethyl *N*-Ethyl-*N*-phenylphosphoramidate

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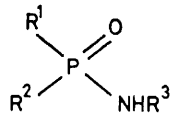
Kinetic studies are reported for the pseudo-molecular rearrangement of triethyl *N*-phenylphosphorimidate to diethyl *N*-ethyl-*N*-phenylphosphoramidate in MeCN. This transformation is shown to be readily catalysed by electrophilic reagents such as alkyl halides, zinc halides, I_2, MeCOBr, and halogen acids where Rate = k_2[Substrate]-[Catalyst]. For alkyl halides, the reaction proceeds *via* a two-step mechanism involving an ionic intermediate: formation of the intermediate by an S_N2 reaction between the substrate and alkyl halide is rate limiting. Other catalysts effect rearrangement by the intermediate formation of alkyl halides in an initial rapid reaction with the substrate. In the absence of electrophilic reagents, rearrangement proceeds in MeCN at 100 °C by a much slower thermal process which has a second order dependence on [Substrate].

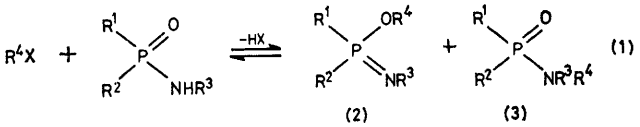
The results are compared with the related rearrangement of *N*-methylbenzimidates to tertiary amides and discussed in relation to the ambident nucleophilic properties of phosphylamidates. It is suggested that, like carboxylic acid amides, alkylation occurs most readily at the *O*-atom of neutral phosphylamidates to give a phosphylimidate (kinetic product) which then rearranges in the presence of electrophilic catalysts to an *N*-substituted phosphylamidate (thermodynamic product).

We have recently shown [1,2] that the ' ambident ' nucleophilic properties of neutral amides can be well understood in terms of the formation of a kinetic product (an *O*-substituted imidate) which, under suitable conditions, rearranges to the thermodynamic product (an *N*-substituted amide). Phosphoramidates (1a), phosphonamidates (1b), and phosphinamidates (1c) (all closely related to amides) may be expected to behave similarly in their nucleophilic reactions, giving a kinetic product (2) (*O*-substituted phosphylimidate *) and, provided conditions are appropriate for rearrangement, the thermodynamic product (3) (*N*-substituted phosphylamidate) [equation (1)]. Of the few alkylation



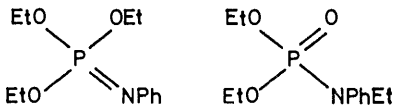
(1) a; R^1, R^2 = alkoxy or aryloxy
b; R^1 = alkyl, aryl, R^2 = alkoxy, aryloxy
c; R^1, R^2 = alkyl or aryl
(1a),(1b),(1c); R^3 = H, alkyl or aryl

reactions of phosphylamidates so far studied, those taking place under mild conditions (such as reaction of *N*-t-butylmethylphenylphosphinamidate with triethyloxonium hexafluorophosphate [3]) produce only *O*-alkylated product (2), whilst those with less reactive reagents, which require higher temperatures, produce either a mixture of *O*- and *N*-alkylated products (2), (3) (as in the reaction of diphenyl *N*-phenylphosphoramidate with trimethylsilyl chloride at *ca.* 80 °C [4]) or the *N*-alkylated product (3) only (*e.g.* in the reaction of diethyl



(2) (3) (1)

phosphoramidate with n-propyl iodide at *ca.* 100 °C [5] or of di-isopropyl *N*-benzylphosphoramidate with trimethyl-silyl, tin or germanium chlorides at *ca.* 101 °C [6]). This pattern of alkylation suggests product orientation is indeed dependent on the incidence of kinetic *versus* thermodynamic control. It is known that the transformation of (2) to (3) (R^1, R^2 = alkyl or alkoxyl, R^3 = Ph, R^4 = Et) does proceed in the presence of methyl or ethyl iodide in acetonitrile at 50 °C,[7] and that (2) and (3) ($R^1 = R^2 = R^3$ = Ph, $R^4 = Me_3Si$) are in equilibrium.[4] We have now investigated the kinetics of the conversion of triethyl *N*-phenylphosphorimidate (2a) into diethyl *N*-ethyl-*N*-phenylphosphoramidate (3a) by various electrophilic agents both to establish the



(2a) (3a)

reaction mechanism and to determine whether the rearrangement is feasible under the conditions of alkylation in which *N*-alkylated products are formed.

* In accord with recent practice ' phosphyl ' is used as a collective term to include phosphoryl, phosphonyl, and phosphinyl groups.

[1] B. C. Challis and J. A. Challis in ' The Chemistry of Amides,' ed. J. Zabicky, Interscience, London, 1970. ch. 13.
[2] B. C. Challis and A. D. Frenkel, *J.C.S. Perkin II*, 1977, 192.
[3] K. E. DeBruin and L. L. Thomas, *J.C.S. Chem. Comm.*, 1977, 33.
[4] P. K. G. Hodgson, R. Katz, and G. Zon, *J. Organometallic Chem.*, 1976, **117**, C63.
[5] J. I. G. Cadogan, R. K. Mackie, and J. A. Maynard, *J. Chem. Soc.* (*C*), 1967, 1356.
[6] C. Glidewell, *J. Organometallic Chem.*, 1976, **108**, 335.
[7] G. K. Genkina, V. A. Gilyarov, E. I. Matrosov, and M. I. Kabachnik, *J. Gen. Chem. U.S.S.R.*, 1970, **40**, 1482.

EXPERIMENTAL

Substrates and Products.—Triethyl *N*-phenylphosphorimidate (2a) was prepared from phenyl azide [8] and triethyl phosphite according to the procedure of Gilyarov and Kabachnik [9] [b.p. 84 °C/2 × 10^{-4} mmHg; n_D^{21} 1.501 4 (lit.,[7] b.p. 53—56 °C/10^{-3} mmHg; n_D^{20} 1.501 5); $\nu_{max.}$ 2 980, 1 595, 1 500, 1 370, 1 355 (P=N), 1 115, 1 030, 760, and 700 cm^{-1}; n.m.r. data are given in Table 1 (Found: C, 56.1; H, 7.7; N, 5.4. Calc. for $C_{12}H_{20}NO_3P$: C, 56.0; H, 7.8; N, 5.4%)]. Diethyl *N*-phenylphosphoramidate (4) and diethyl *N*-ethyl-*N*-phenylphosphoramidate (3a) were synthesized by the method of Atherton *et al.*[10] from diethyl phosphite and aniline or *N*-ethylaniline, respectively. [(4) gave m.p. 93—95 °C (lit.,[10] 92—94 °C), $\nu_{max.}$ 3 300—3 100 (N–H) and 1 225 (P=O) cm^{-1} and (3a) gave b.p. 135 °C/1.5 mmHg, n_D^{21} 1.487 5 (lit.,[7] b.p. 91 °C at 0.5 mmHg; n_D^{20} 1.497 2), and $\nu_{max.}$ 1 255 cm^{-1}. N.m.r. chemical shifts of both compounds are given in Table 1].

TABLE 1

^1H N.m.r. chemical shifts (δ) relative to $SiMe_4$ and coupling constants for phosphorimidate (2a) and product phosphoramidates (3a) and (4) [a]

	N-C_6H_5	N-H [b]	N-CH_2 [c]	NCH_2CH_3	OCH_2 [d]	OCH_2CH_3 [e]
(2a)	6.85m				4.1 quint 4.15d [f]	1.35tr
(3a)	7.3s		3.6m 3.55d [g]	1.25d tr	4.1m 4.1d	1.25d tr
(4)	7.05m	8.1d			4.1 quint 4.1d [f]	1.35tr

[a] *ca.* 0.2—0.8M solutions in CCl_4. [b] J_{PNH} 10 Hz. [c] J_{PNCH} 10 Hz, J_{CHCH} 7.5 Hz. [d] J_{POCH} 8 Hz, J_{CHCH} 7—7.5 Hz. [e] J_{CHCH} 7—7.5 Hz. [f] Spin decoupled at 81 Hz. [g] Spin decoupled at 74 Hz.

Reagents and Solvents.—AnalaR CCl_4 was dried over $CaCl_2$ and redistilled. Reagent Grade acetonitrile was distilled from CaH_2 and stored over molecular sieves (4A). [$^2H_3$]Acetonitrile (Merck, Sharp, and Dohme) was used without further purification other than drying by molecular sieves. AnalaR nitrobenzene was distilled under reduced pressure and dried over CaH_2. All the alkyl halides were redistilled. Acetyl bromide was distilled from *NN*-dimethylaniline. Iodine was recrystallised from benzene and sublimed. The zinc halides were heated at 200 °C for 2 h at reduced pressure and then sublimed *in vacuo*. Anhydrous hydrogen bromide was passed through acetonitrile until crystals of the conjugate acid ($MeCNH^+Br^-$) were formed. Anhydrous sodium ethoxide was prepared from ethanol and sodium.

Kinetics.—The rearrangement of (2a) to (3a) in acetonitrile, [$^2H_3$]acetonitrile, CCl_4, or nitrobenzene was followed by the n.m.r. method previously described.[2] Typically, kinetic measurements were carried out on a solution of the phosphorimidate (0.2M) and electrophile (10^{-2}—0.2M) in solvent (0.5 ml) contained in a sealed n.m.r. tube. Reactions in acetonitrile, [$^2H_3$]acetonitrile, and CCl_4 were monitored by following the increase in the *N*–Ph absorption (δ 7.3) of (3a) whilst those in nitrobenzene were followed by the increase in the *N*–CH_2 multiplet (δ 3.6), each spectrum being integrated at least three times to minimise errors arising from fluctuations in the n.m.r. signals.

Pseudo-first-order rate coefficients {Rate = k_0 [(2a)]} were calculated from equation (2), where x = area of either the *N*–Ph or the *N*–CH_2 signal for the product amidate at time t and a = total area of either the *N*–Ph or the *N*–CH_2 signals for both starting imidate and product amidate. Results for a typical run are shown in Figure 1. Linear plots

$$k_0 = 2.303 \log (1 - x/a)/t \qquad (2)$$

were obtained up to *ca.* 80% reaction when the insensitivity of the n.m.r. procedure introduced significant errors in the measurement of small integrals. Rate coefficients obtained by this method were reproducible to ±10%.

Product Analysis.—Products were identified from comparison of n.m.r. spectra of the reaction solutions with authentic materials. In several reactions the solvent and reagent were removed, and the products were isolated to be identified by g.l.c., m.p., and i.r. and n.m.r. spectroscopy (in CCl_4). For the thermal reaction in the absence of added electrophiles the formation of ethylene was evident from the n.m.r. spectrum (δ 5.2, d).

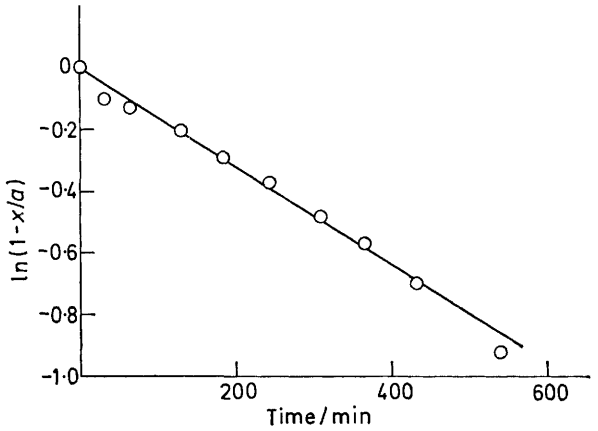


FIGURE 1 Typical first-order plot for the rearrangement of phosphorimidate (2a) catalysed by 0.062M-EtI in MeCN at 100 °C

RESULTS AND DISCUSSION

In the absence of any added electrophiles, triethyl *N*-phenylphosphorimidate (2a) rearranged very slowly ($t_{\frac{1}{2}}$ *ca.* 30 days) to diethyl *N*-ethyl-*N*-phenylphosphoramidate (3a) when heated in organic solvents at 100 °C [equation (3)]. Further, the appearance of an ethylene

$$(EtO)_3P{=}NPh \xrightarrow{Heat} (EtO)_2P(=O)NEtPh \qquad (3)$$

[8] R. O. Lindsay and C. F. H. Allen, *Org. Synth.* Coll. Vol. 3, 1955, 710.

[9] V. A. Gilyarov and M. I. Kabachnik, *Izvest. Akad. Nauk S.S.S.R., Otdel Khim. Nauk*, 1957, 790.

[10] F. K[illegible], H. T. Openshaw, and A. R. Todd, *J. Chem. Soc.*, 1945, [illegible].

doublet in the n.m.r. spectrum showed that dealkylation was taking place concurrently [equation (4)]. The

$$(EtO)_3P{=}NPh \xrightarrow{Heat} (EtO)_2P(=O)NHPh + CH_2{=}CH_2 \quad (4)$$
(4)

extent of dealkylation, calculated from the relative intensities of the ethylene to N–Ph signals was *ca.* 9% of the total reaction. The overall thermal reaction (k_Δ) followed second-order kinetics in accordance with equation (5) implying intermolecular pathways for both

$$\text{Rate} = k_\Delta[(2a)]^2 = k_{rearr}[(2a)]^2 + k_{dealk}[(2a)]^2 \quad (5)$$

rearrangement and dealkylation. Rate coefficients for rearrangement and dealkylation (k_{rearr} and k_{dealk}) were computed in the usual way from k_Δ and the product ratios, and their values are given in Table 2.

Conversion of (2a) into (3a) occurred much more readily in the presence of alkyl halides. These reaction rates were solvent dependent decreasing in the order MeCN > $PhNO_2$ > CCl_4 by factors of 1.21 and 46, respectively (see Table 2). This dependence suggests

TABLE 2

Second-order rate coefficients (k_2) for the reaction of triethyl *N*-phenylphosphorimidate (2a) with alkyl halides in MeCN; initial [(2a)] = 0.2M; [alkyl halide] = 10^{-2} — 0.2M

Alkyl halide	t/°C	10^6k_2/l mol^{-1} s^{-1}
MeI	34.2	39.5
EtI	34.2	4.12
EtI	50	15.7
EtI	74.5	94.3
EtI	100	400
EtI [a]	100	307
EtI [b]	100	7.15
EtBr	100	88.0
$EtNO_3$	100	4.10
EtI–$AgNO_3$	100	27.5
Pr^iI	100	60.8
Pr^iBr	100	8.52
Pr^iCl	100	1.68 [c]
None	100	1.65 [d]

[a] In $PhNO_2$ solvent. [b] In CCl_4 solvent. [c] $k_2 = k_{rearr}$; $k_{dealk} = 1.50 \times 10^{-7}$ l mol^{-1} s^{-1}. [d] $k_2 = k_{rearr}$; $k_{dealk} = 1.66 \times 10^{-7}$ l mol^{-1} s^{-1}.

that solvent polarity is important and implies the formation of an ionic intermediate. For practical reasons MeCN was most suitable and all the following results refer to this solvent. Unlike the thermal rearrangement, the rate of conversion of (2a) to (3a) in the presence of alkyl halides (with the exception of isopropyl chloride where catalysis was negligible) follows equation (6)

$$\text{Rate} = k_0[(2a)] \quad (6)$$

which has only a first-order dependence on substrate. By using an appropriate alkyl halide concentration it was possible in most cases to obtain a much faster rearrangement rate than by heating alone. The reactions then followed equation (6) closely (see Experimental section) without any evidence of significant concurrent dealkylation. The pseudo-first-order rate coefficients (k_0) varied linearly with the concentration of added alkyl halide (Figure 2). It follows that the reaction is bimolecular and the catalysed reaction rates are governed by equation (7). Values of k_2 obtained for various alkyl

$$\text{Rate} = k_2[(2a)][\text{Alkyl halide}] \quad (7)$$

halides and $EtNO_3$ in MeCN are also summarised in Table 2.

In the presence of added isopropyl halides, the plot of log $(1 - x/a)$ *versus* t was curved, becoming of steeper

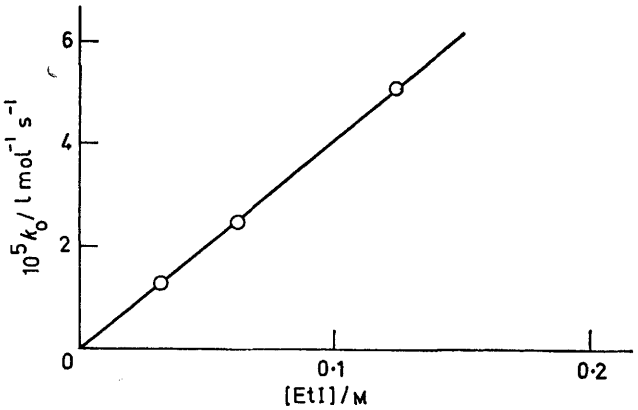


FIGURE 2 Linear dependence of k_0 on [EtI] for the rearrangement of (2a) in MeCN at 100 °C; initial [(2a)] = 0.2M

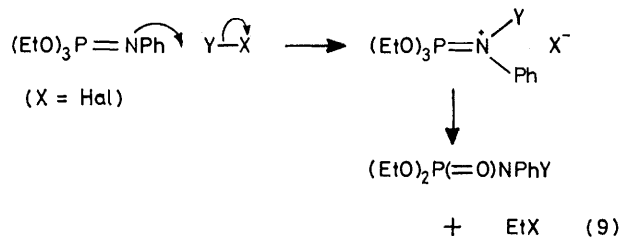
slope as the reaction proceeded. This arose from the formation of ethyl halides during reaction [equation (8)] which then acted as more effective reagents than the

$$(EtO)_3P{=}NPh + Pr^iX \rightleftharpoons (EtO)_2P(=O)NPhPr^i + EtX \quad (8)$$

corresponding isopropyl halides. Sensible rate coefficients for the isopropyl halides could be obtained, however, from the initial reaction and these values are cited in Table 2. The rate enhancement induced by isopropyl chloride was negligible, and rearrangement in this instance occurs predominantly by the thermal process.

The effect of electrophilic reagents other than alkyl halides was also examined and the second-order rate coefficients (k_2) obtained are listed in Table 3. It is significant that k_2 values for ZnI_2 and I_2 are similar to that for EtI, whilst those for $ZnBr_2$, MeCOBr, and HBr (0.1 equivalents) are similar to that for EtBr. These observations can be explained by the generation of a phosphoramidate derivative and ethyl halide following nucleophilic attack by the phosphorimidate (2a) on the electrophile (Y–X) [equation (9)]. The ensuing rearrangement of (2a) then arises from the usual reaction with ethyl halide, so the observed rates correspond to those for added ethyl halide itself. Independent evidence for this sequence of reactions was the relatively rapid appearance of absorption bands characteristic of ethyl halides in the n.m.r. spectrum of the reaction solutions after addition of the electrophilic reagent. Further, the intensity of these bands was proportional

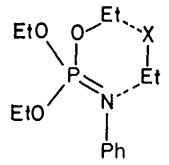
to the amount of electrophilic reagent added. Significantly, rearrangement in the presence of $ZnCl_2$ and, *inter alia*, by EtCl, is no faster than the purely thermal rate as found above for isopropyl chloride. When 1 equivalent of the electrophilic reagent X–Y (*e.g.* HBr) was added, *no* rearrangement occurred but dealkylation took place. The product [diethyl *N*-phenylphosphoramidate (4)] was characterised by comparison of spectral properties and m.p. with an authentic sample and the n.m.r. spectrum of the reaction solution indicated that the ethyl bromide co-product was formed in quantitative yield. When 0.1 equivalents of HBr was added, rearrangement took place at the rate expected for EtBr as noted above.



The effect of temperature on the rearrangement rate of (2a) in the presence of ethyl iodide was also examined. The data (Table 2) gave a linear Arrhenius plot of log k_2 *versus* $1/T$ leading to values of E_A 67 kJ mol^{-1}, $\Delta H^{\ddagger}$ 64 $\pm$ 2 kJ mol^{-1}, $\Delta S^{\ddagger}$ -140 ± 4 J K^{-1} mol^{-1}, and $\Delta G^{\ddagger}$ 116 $\pm$ 3 kJ mol^{-1}.

Examination of the results in Table 2 shows that $EtNO_3$ is *ca.* 100 times less effective than EtI in promoting the rearrangement of (2a) to (3a) at 100 °C. It follows that addition of $AgNO_3$ might inhibit the alkyl halide catalysed rearrangement as observed previously for benzimidate esters [2] and thereby lead to a new synthetic procedure for the direct *O*-alkylation of phosphoramidates with alkyl halides. When equimolar quantities of $AgNO_3$ and EtI were added to a 10-fold excess of (2a) in MeCN, precipitation of AgI was apparent, but at 100 °C the reduction in the rate of rearrangement was much smaller than the factor of 100 anticipated from the relative rate coefficients for $EtNO_3$ and EtI (Figure 3) indicating that heterogeneous catalysis by AgI was occurring. The lowest value obtained for k_2 after centrifugation was 2.75×10^{-5} l mol^{-1} s^{-1}, a reduction of *ca.* 15 times on k_2 for EtI in the absence of $AgNO_3$. These reactions were not examined exhaustively, but it was also found that 8×10^{-3}M-$AgNO_3$ accelerated the $EtNO_3$-catalysed rearrangement of (2a) to (3a) in MeCN at 100 °C by a factor of *ca.* 6.

Mechanism of the Rearrangement Reaction.—It has previously been suggested [7] that the alkyl halide-catalysed conversion of phosphorimidates into phosphoramidates proceeds by a cyclic six-membered transition state [such as (5)] of low polarity. However, our finding that the rearrangement rate is markedly dependent on solvent polarity (MeCN > $PhNO_2$ > CCl_4) implies considerable charge development in the transition state and the involvement of ionic intermediates. The observation of second-order kinetics [equation (7)], the decrease in reagent reactivity along the series



(5)

Pr^{i}I > Pr^{i}Br $\gg$ Pr^{i}Cl, and the rate reduction with increased branching (steric hindrance) of the reagent (MeI > EtI > Pr^{i}I) are also found in the analogous imidate–amide rearrangement.[2] They are best explained, as in the imidate–amide rearrangement, by an S_N2 process (Scheme 1) where rate-limiting attack by the phosphorimidate on the alkyl halide (step k_a) produces an ionic intermediate (6) followed by rapid removal of the *O*-ethyl group by halide ion to give the phosphoramidate (step k_b). Rearrangement, initiated by the addition of either metal halides, I_2, MeCOBr, or HBr proceeds similarly and is brought about, as noted above, by ethyl halide formed in a rapid initial reaction between the phosphorimidate and the added electrophile [equation (9)]. There is no evidence to show that the phosphoramidate derivative produced in this initial reaction plays a significant part in the ensuing rearrangement processes. The relatively slow rate of rearrangement obtained with $EtNO_3$, however, is inconsistent with its expected alkylating ability. The most likely explanation here is that decomposition of the ionic intermediate (6) to products (step k_b) becomes rate

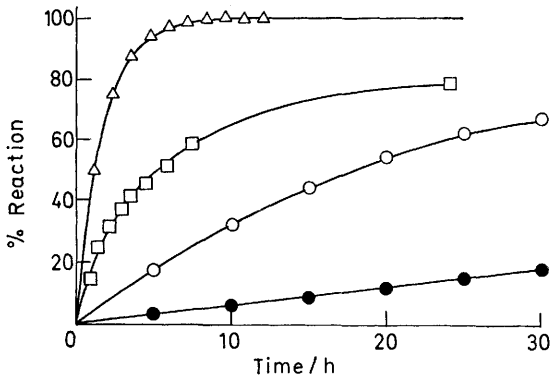
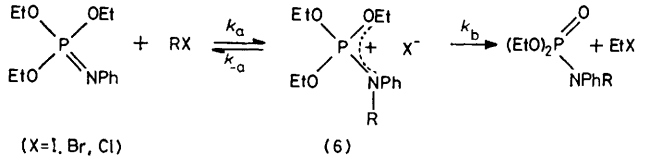


FIGURE 3 Effect of added $AgNO_3$ on the rate of the EtI-catalysed rearrangement of phosphorimidate (2a) in MeCN at 100 °C; △ 0.4M-EtI only, □ 0.43M-EtI plus 0.43M-$AgNO_3$ without centrifugation, ○ 0.39M-EtI plus 0.39M-$AgNO_3$ after centrifugation, ● 0.4M-$EtNO_3$

limiting for the reagent because of the low nucleophilic reactivity of NO_3^-. An analogous S_N2 mechanism to that described by Scheme 1 probably applies to thermal rearrangement. The second-order dependence on substrate concentration implies an intermolecular process such as alkylation of the phosphorimidate *N*-atom by a second substrate molecule to give the ionic intermediate (7), followed by transalkylation of the phosphorimidate

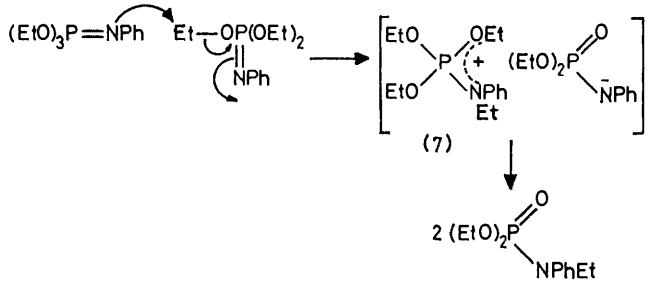
anion (Scheme 2). The results neither identify the rate-limiting step nor exclude a concerted bimolecular mechanism, but the high nucleophilicity of the phosphoramidate anion suggests that formation of (7) would



SCHEME 1 S_N2 Mechanism for the conversion of triethyl *N*-phenylphosphorimidate into diethyl *N*-ethyl-*N*-phenylphosphoramidate by alkyl halides

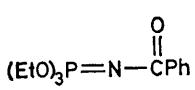
be slow for the stepwise pathway. The concurrent dealkylation under thermal conditions represents the usual competitive *E*-2 component of S_N2 processes involving proton abstraction by the substrate from either a second substrate molecule or the intermediate ion (7).

Our mechanism for the catalysed rearrangement



SCHEME 2 S_N2 Mechanism for the thermal rearrangement of triethyl *N*-phenylphosphorimidate to diethyl *N*-ethyl-*N*-phenylphosphoramidate

appears to have wider applicability. Thus previous qualitative work [7] suggests that the rearrangement rate for various phosphylimidates decreases in the order R = Et > Me > Ph > EtO for $R_2P(OEt)$=NPh, which is consistent with the expected substituent inductive effects on the nucleophilicity of the *N*-atom. Also we have briefly re-examined the behaviour of triethyl *N*-benzoylphosphorimidate (8) reported recently by Glidewell [6] not to form *N*-alkyl-*N*-benzoylphosphoramidate on treatment with either HBr or MeI. We have confirmed that (8) reacts rapidly with an excess of HBr to give quantitative yields of diethyl *N*-benzoylphosphoramidate and EtBr. This reaction is the same as that observed for triethyl *N*-phenylphosphorimi date(2a). Unlike Glidewell,[6] however, we have found that (8) does react, albeit slowly, with equimolar MeI in CD_3CN when heated in a sealed n.m.r. tube at 100 °C. The rate of



(8)

formation of the diethyl *N*-benzoyl-*N*-methylphosphoramidate product gives $k_2 = 1.3 \times 10^{-5}$ l mol^{-1} s^{-1}. Allowing for the temperature difference, this is *ca.* 300 times less than the comparable coefficient for (2a), reflecting the reduced nucleophilicity of the benzoylated *N*-atom.

Ambident Nucleophilic Properties of Phosphoramidates.—The ready conversion of (2a) into (3a) suggests that

TABLE 3

Second-order rate coefficients (k_2) for the rearrangement of phosphorimidate (2a) to phosphoramidate (3a) with electrophilic catalysis in MeCN at 100 °C.

Catalyst	$10^6 k_2$/l mol^{-1} s^{-1}
ZnI_2	380
$ZnBr_2$	91.6
$ZnCl_2$	1.34
I_2	378
MeCOBr	77.1
HBr (0.1 equiv.) [a]	89.9
HI (1 equiv.)	[b]

[a] When HBr (1 equiv.) was used, quantitative formation of $(EtO)_2PONHPh$ occurred after 10 min at 23 °C. [b] No rearrangement but quantitative formation of $(EtO)_2PONHPh$ and EtI immediately which remained unchanged even after heating for 24 h at 100 °C.

our recent explanation [1,2] for the apparent ambident nucleophilic properties of neutral amides can be extended to related phosphyl compounds. This requires that electrophilic substitution (*e.g.* by alkyl halides) of neutral phosphylamidates proceeds most readily at the *O*-atom, with *N*-substitution arising from subsequent rearrangement. Thus *O*-alkylphosphylimidates are kinetic products and *N*-alkylphosphylamidates are thermodynamically stable ones. Significantly, direct formation of phosphylimidates by *O*-alkylation has been reported only for $Et_3O^+PF_6^-$ at low temperature.[3] With alkyl halides, *N*-substituted compounds but not *O*-alkylphosphylimidates are obtained [5] presumably be-

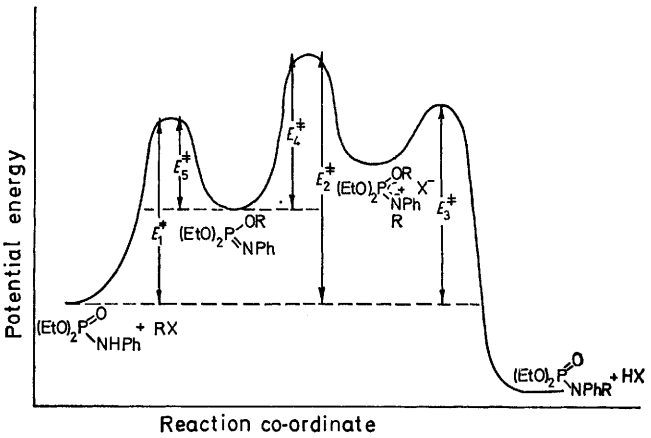


FIGURE 4 Potential-energy diagram for the alkylation of phosphoramidates with alkyl halides

cause of the higher reaction temperatures employed. The observation [5] of *O*-alkyl exchange concurrent with *N*-propylation in the reaction of diethyl phosphoramidate with an excess of Pr^nI at 100 °C implies, however, the formation of a phosphorimidate intermediate. Our results show that under the reaction conditions this

intermediate would quickly rearrange to an *N*-substituted product, so failure to isolate it is not unexpected.

These conclusions are reinforced by consideration of the potential energy profile (Figure 4) for the *O*- and *N*-alkylation of phosphoramidates by alkyl halides. The inequality $E_1^{\ddagger} < E_2^{\ddagger}$ stems directly from the assumption of kinetic and thermodynamic product control and $E_3^{\ddagger} < E_2^{\ddagger}$ from deductions that step k_a is rate limiting for alkyl halides in Scheme 1. The requirement that $E_5^{\ddagger} < E_4^{\ddagger} < E_1^{\ddagger}$ is less obvious, but it stems directly from the rapid and quantitative dealkylation of (2a) on addition of equimolar HBr or HI [equation (10)] without

$$(EtO)_3P{=}NPh + HX \rightleftharpoons (EtO)_2PONHPh + EtX \quad (10)$$

X = Br, I

significant concurrent or ensuing rearrangement to (3a). This shows that dealkylation is faster than rearrangement of (2a), *i.e.* $E_5^{\ddagger} < E_4^{\ddagger}$ and that neither EtBr nor EtI alkylates diethyl *N*-phenylphosphoramidate under conditions where their catalysed rearrangement of (2a) proceeds readily (*i.e.*, $E_4^{\ddagger} < E_1^{\ddagger}$). Unfortunately, $E_1^{\ddagger}$ cannot be ascertained experimentally, but its lowest limit is given by the enthalpy difference (E_1^0) for equation (10), which can be estimated from the relevant molar bond enthalpies.* The value calculated for HI ($E_1^0 = 110$ kJ mol^{-1}) is substantially higher than the experimental enthalpy of activation ($\Delta H^{\ddagger} = 64$ kJ mol^{-1}) for the EtI-catalysed rearrangement of (2a). It follows that $E_4^{\ddagger} < E_1^{\ddagger}$ since $E_1^{\ddagger} > E_1^0$ and $\Delta H^{\ddagger} \simeq E_4^{\ddagger}$.

The mechanism cited in Scheme 1 for the rearrangement of (2a) to (3a) requires formation of product by nucleophilic decomposition (step k_b) of the ionic intermediate (6). Apart from the low reaction temperatures, a salient feature in the successful synthesis of phosphinimidates with $Et_3O^+PF_6^-$[3] may be the low nucleophilicity of the PF_6^- counter ion. Nonetheless, our attempts to prepare phosphorimidates by direct alkylation of diethyl *N*-phenylphosphoramidate with other reagents in the absence of strongly nucleophilic anions were singularly unsuccessful. For example, in CD_3CN at 100 °C, $EtNO_3$, Me_2SO_4, and MeI in the presence of either $AgNO_3$ or AgI, all gave products whose n.m.r. spectra indicated P–N bond cleavage. With equimolar MeI and Ag_2O in CD_3CN at 34 °C, however, diethyl *N*-methyl-*N*-phenylphosphoramidate was formed in accordance with Rate = 1.7×10^{-5} l mol^{-1} s^{-1} [Substrate][MeI]. The direct *N*-alkylation apparent here may reflect either reaction *via* the phosphoramidate anion or rapid Ag^+-catalysed *O*- to *N*-rearrangement as noted earlier for (2a). Our immediate conclusion is that Ag salts are not useful catalysts for promoting the *O*-alkylation of phosphoramidates.

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* For X = I, $E_1^0 = D$(C–O) + D(P–O) + D(P=N) + D(H–I) – D(P=O) – D(P–N) – D(N–H) – D(C–I) where D refers to the relevant molar bond enthalpy. Calculation of E_1^0 was made from D values in ref. 6.