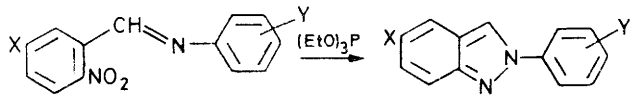
Reduction of Nitro- and Nitroso-compounds by Tervalent Phosphorus Reagents. Part XI.[1] A Kinetic Study of the Effects of varying the Reagent and the Nitro-compound in the Conversion of *o*-Nitrobenzylideneamines to 2-Substituted Indazoles

By **Margaret-Ann Armour, J. I. G. Cadogan,* and David S. B. Grace,** Department of Chemistry, University of Edinburgh, West Mains Road, Edinburgh EH9 3JJ

A kinetic study of the effects of varying the phosphorus reagent and substituents in the nitro-compound in the reductive cyclisation of *o*-nitrobenzylideneamines to 2-substituted indazoles has been made. First-order rate constants vary from 8.2 to 52.2 × 10^{-5} s^{-1} for the triethyl phosphite-induced reduction of *N*-*o*-nitrobenzylideneanilines [*o*-$NO_2C_6H_4CH{=}NC_6H_4Y$; Y = *p*-MeO, *p*-Me, H, *p*-Cl, *p*-Br, *p*-CO_2Et, *p*-CN, *p*-NO_2, or *o*-Cl] and *N*-5-chloro-2-nitrobenzylideneaniline, and vary slightly from 5 to 6 × 10^{-5} s^{-1} for *o*-nitrobenzylideneamines [*o*-$NO_2{\cdot}C_6H_4{\cdot}CH{=}NR$; R = Me, Et, Pr^i, or Bu^n]. The products of these reactions are the corresponding 2-aryl- (aryl = C_6H_4Y) and 2-alkyl- (alkyl = R)-indazoles. These results point to nucleophilic attack by phosphorus on the nitro-group *via* an intermediate $ArN(O^-)OP(OEt)_3^+$. This is confirmed by a similar kinetic study of the conversion of *N*-*o*-nitrobenzylideneaniline into 2-phenylindazole using a series of tervalent phosphorus reagents. Acyclic reagents react in the decreasing order $(Me_2N)_3P$ > $(EtO)_2PMe$ ~ $EtOPPh_2$ > $EtOP(NEt_2)_2$ ~ $EtOPNC_4H_{10}$ > $(MeO)_3P$ ~ $(EtO)_3P$ ~ $(Pr^iO)_3P$. In accord with the nucleophilic character of the attack by phosphorus, the small ring effect in 2-diethylamino- and 2-ethoxy-1,3,2-dioxaphospholan manifests itself in a rate decrease compared with acyclic analogues. 2-Ethoxy-1,3,2-diazaphospholan, on the other hand, shows much increased activity pointing to stabilisation of the transition state for deoxygenation by hydrogen bonding. These results enable a brief comment to be made on the reagent of choice for preparative reactions.

ALTHOUGH the triethyl phosphite reduction of aromatic nitro-compounds as a route to heterocycles [2] has been widely investigated,[3] little data exist on the effect of substituents in the phosphorus reagent, or in the aromatic rings, on the ease of reaction. Such data are desirable not only because it would be useful to know which is the best reagent, but also because it would give further information about the mechanism of this synthetically useful reaction.

Before this investigation Cadogan and Todd [4] had reported half-lives of 50, 17, and 50 min for the reaction of 2-nitrobiphenyl and its 4-bromo- and 4'-methyl derivatives, respectively, with triethyl phosphite at 145.5°, and had also noted that the reactivity of reagents in this reaction fell in the order $(EtO)_2PMe \gg (Et_2N)_3P \sim EtOP(NEt_2)_2 > (EtO)_3P \sim (Pr^iO)_3P \gg PCl_3$ (inactive). Their investigation was severely limited, however, by analytical difficulties. We now report circumvention of these by choice of a different system: cyclisation of *o*-nitrobenzylideneanilines (1) to 2-substituted indazoles (2).[5] This has enabled us to make a kinetic study



(1) (2)

embracing a range of substituents (Y) in the nitro-compound and also to examine the effect of changing the phosphorus-containing deoxygenating agent, including an investigation of the small ring effect,[6] which is a particularly useful mechanistic probe.

EXPERIMENTAL

All compounds had the expected ^1H n.m.r. spectra.

o-Nitrobenzylideneamines.—These were prepared from *o*-nitrobenzaldehyde and the amine by standard methods. *N*-*o*-Nitrobenzylideneanilines (*o*-$NO_2C_6H_4CH{=}NC_6H_4Y$) had the following characteristics: Y = *p*-MeO, m.p. 71—72° (lit.,[5b] 79°); Y = *p*-Me, 73° (lit.,[5b] 72—73°); Y = H, 64—65° (lit.,[5a] 64—66°); Y = *p*-Cl, 92° (lit.,[7] 92.5°); Y = *o*-Cl, 115° (lit.,[7] 116.5°); Y = *p*-Br, 97° (lit.,[5b] 97—98°); Y = *p*-CO_2Et, 84—86°; Y = *p*-CN, 88—89°; Y = *p*-NO_2, 135—136°. 5-Chloro-2-nitrobenzylideneaniline had m.p. 93—94°. *o*-Nitrobenzylidenemethylamine had b.p. 92° at 0.8 mmHg (lit.,[8] 145° at 23 mmHg), the ethylamine had b.p. 110° at 0.6 mmHg, the isopropylamine had b.p. 82° at 0.2 mmHg, and the n-butylamine, b.p. 145° at 1.6 mmHg.

Tervalent Phosphorus Reagents.—Triethyl and trimethyl phosphites were dried (Na) and distilled (N_2). Tri-isopropyl phosphite, diethyl methylphosphonite, ethyl diphenylphosphinite, and ethyl *N*-tetraethylphosphorodiamidite were as described previously.[4,9]

Diethyl piperidinophosphoramidite. Diethyl phosphorochloridite (5 g, 0.032 mol) was added dropwise to a solution of piperidine (5.5 g, 0.064 mol) in light petroleum (b.p. 40—60°; 50 ml). The precipitated amine hydrochloride was removed by filtration, the solvent was evaporated and the product was obtained by distillation under reduced pressure under nitrogen, b.p. 64—66° at 1 mmHg.

2-Ethoxy-1,3,2-diazaphospholan. Ethanol (46 g, 1 mol) was added over 5 h to stirred phosphorus trichloride (137.3 g,

[1] Part X, Th. de Boer, J. I. G. Cadogan, H. M. McWilliam, and A. G. Rowley, *J.C.S. Perkin II*, 1975, 554.
[2] J. I. G. Cadogan and M. Cameron-Wood, *Proc. Chem. Soc.*, 1962, 361.
[3] J. I. G. Cadogan, *Synthesis*, 1969, **1**, 11; *Quart. Rev.*, 1968, **22**, 222; J. I. G. Cadogan and R. F. Mackie, *Chem. Soc. Rev.*, 1974, **3**, 87.
[4] J. I. G. Cadogan and M. J. Todd, *J. Chem. Soc.* (*C*), 1969, 2808.
[5] (*a*) J. I. G. Cadogan and R. K. Mackie, *Org. Synth.*, 1968, **48**, 113; (*b*) J. I. G. Cadogan, M. Cameron-Wood, R. K. Mackie, and R. J. G. Searle, *J. Chem. Soc.*, 1965, 4831.
[6] R. F. Hudson and C. Brown, *Accounts Chem. Res.*, 1972, **5**, 204.
[7] A. Senier and R. Clarke, *J. Chem. Soc.*, 1914, **105**, 1917.
[8] C. Andree, *Ber.*, 1902, **35**, 424.
[9] J. I. G. Cadogan, D. J. Sears, and D. M. Smith, *J. Chem. Soc.* (*C*), 1969, 1314.

1 mol) cooled in a CO_2–methanol bath. The resulting liquid was distilled, b.p. 28—30° at 18 mmHg. Ethyl phosphorodichloridite (50 g, 0.375 mol) was slowly added to 1,2-diaminoethane (45 g, 0.75 mol) in light petroleum (b.p. 60—80°; 200 ml) at 0°. After 3 h at the b.p. the liquid was decanted from the solid tarry material and concentrated to *ca.* 20 ml. Distillation under nitrogen gave 2-*ethoxy*-1,3,2-*diazaphospholan* (3 g, 5%), b.p. 48—50° at 1 mmHg (Found: C, 36.2; H, 8.0; N, 20.3. $C_4H_{11}N_2OP$ requires C, 35.8; H, 8.2; N, 20.9%).

2-*Diethylamino*-1,3,2-*dioxaphospholan*. This was prepared from 2-chloro-1,3,2-dioxaphospholan, b.p. 43—44° at 10 mmHg (lit.,[10] 46—47° at 15 mmHg), by reaction with diethylamine as described by Hudson.[11] The product had b.p. 65—66.5° at 10 mmHg (lit.,[11] 50° at 2 mmHg) and had the expected ^{1}H n.m.r. spectrum, ^{31}P n.m.r. δ ($CHCl_3$) −143.6 p.p.m. (external standard 85% H_3PO_4) (lit.,[11] −144 p.p.m.).

2-*Ethoxy*-1,3,2-*dioxaphospholan*. This had b.p. 47.5—48.5° at 10 mmHg (lit.,[12] 50—51° at 15 mmHg) and the expected ^{1}H n.m.r. spectrum, ^{31}P n.m.r. δ −134.1 p.p.m. (ext. 85% H_3PO_4) (lit.,[13] δ = −134 p.p.m.).

2-*Alkylindazoles*.—These were characterised by n.m.r. and m.s. 2-Methylindazole had τ 5.91 (s, CH_3) and 2.2—*m/e* 132 (M^+), 117 ($M - CH_3$), 104, 90, and 76, b.p. 134—136°. 2-Ethylindazole had τ 8.81 (t, CH_2CH_3), 5.68 ($ArCH_2CH_3$), and 2.12—3.22 (m, aromatic H_5), *m/e* 146 (M^+), 117, 104, 90, and 76, b.p. 141° at 15 mmHg. 2-Isopropylindazole had τ 8.52 [d, $CH(CH_3)_2$], 5.39 [septet, $CH(CH_3)_2$], and 2.21—3.25 (m, aromatic H_5), b.p. 142° at 15 mmHg. 2-n-Butylindazole had τ 9.07 (t, CH_3CH_2), 8.72 (sextet, $CH_3CH_2CH_2$), 8.01 (quintet, $CH_3CH_2CH_2CH_2$), 5.62 (t, CH_2CH_2N), and 2.08—3.20 (m, aromatic H_5), b.p. 153° at 13 mmHg.

2-*Arylindazoles*.—The yields and characteristics of these compounds obtained by phosphite reduction are given in Table 1.

TABLE 1

2-Arylindazoles

Aryl substituent	Yield (%)	M.p. (°C) (lit)	Ref.
H	77	82 (81—82)	*5a*
p-MeO	91	130 (130—131)	*5b*
p-Me	96	98—99 (99—100)	*5b*
p-Cl	80	133 (134)	*a*
p-Br	93	147—148 (147—148)	*5b*
p-CO_2Et	85	126—127	
p-NO_2	43	223—225	*b*
p-CN	60	107	
o-Cl	60	119	

[a] B. Busch and L. Vokening, *J. prakt. Chem.*, 1895, **52**, 380. [b] L. Krbchek and H. Takimoto, *J. Org. Chem.*, 1964, **29**, 1150.

Reactions of o-*Nitrobenzylideneanilines and* o-*Nitrobenzylideneamines with Triethyl Phosphite.—Benzylideneanilines*. All of the anilines studied cyclised under the reaction conditions (see later) to yield the corresponding indazoles. The yields of product, determined by g.l.c. analysis of the reaction mixture after 10 half-lives are included in Table 1 as are the m.p. of isolated specimens. When the mixture from the reaction of *p*-nitro-*N*-*o*-nitrobenzylideneaniline with triethyl phosphite after heating at 105° for 3 h was cooled to room temperature, crystals were formed. After recrystallisation from ethanol–water, the product was shown by i.r. and n.m.r. spectroscopy and mass spectrometry to be 2-(*p*-nitrophenyl)indazole. When this compound was heated at 105° with triethyl phosphite, g.l.c. analysis indicated that further reaction occurred and a mixture of products which were not identified was formed. The half-life of the latter reaction was *ca.* 4 h.

Benzylidineamines. When the Schiff's bases prepared from *o*-nitrobenzaldehyde and methylamine, ethylamine, isopropylamine, or n-butylamine were allowed to react with an excess of triethyl phosphite, the product was shown by i.r. and n.m.r. spectroscopy and mass spectrometry to be the corresponding 2-alkylindazole. These indazoles were not so stable as those formed using aromatic bases, and tended to darken on storage. The rates of reaction of the nitrobenzalimines with triethyl phosphite were followed by g.l.c. analysis and were shown to be the same within the experimental error (Table 2).

TABLE 2

Rates of deoxygenation of *o*-nitrobenzylideneamines (*o*-$NO_2C_6H_4CH{:}NR$) in triethyl phosphite at 105 ± 0.1°

R	$10^5k_1/s^{-1}$	$t_{\frac{1}{2}}$/min
p-$MeOC_6H_4$	8.2	143
p-MeC_6H_4	9.8	118
Ph	13.1	89
p-ClC_6H_4	14.8	78
o-ClC_6H_4	17.8	65
p-BrC_6H_4	18.3	63
p-$CO_2EtC_6H_4$	20.6	56
p-CNC_6H_4	27.0	43
p-$NO_2C_6H_4$	52.2	23
Me	5.3	219
Et	6.0	193
Pr^i	5.0	232
Bu^n	5.5	208

Kinetics of the Reactions of o-*Nitrobenzylideneanilines and* o-*Nitrobenzylideneamines with Tervalent Phosphorus Compounds*.—Substrate (*ca.* 0.001 mol), tervalent phosphorus compound (0.02 mol), and *trans*-stilbene (0.001 mol), or, in the case of ethyl diphenylphosphinite, 2-bromocarbazole, or, in the case of 2-ethoxy-1,3,2-dioxaphospholan, anthracene, were placed in the reaction vessel which had been flushed with nitrogen. A positive pressure of nitrogen was maintained throughout the reaction. The vessel was suspended in a constant temperature bath at 105 ± 0.1, 91.5 ± 0.3, 40 ± 0.1, or 30 ± 0.1°, and the contents allowed to equilibrate. Samples were withdrawn through a Suba Seal cap using a leak-proof microlitre syringe and were either directly analysed or stored at −70° and later analysed for disappearance of starting nitro-compound by g.l.c. using an Aerograph model 1520B, or a Pye model 104 equipped with columns packed with 5% SE30. The temperature of the column was between 150 and 250° depending on the substrate being analysed. The peaks of the chromatogram were integrated by a Kent Chromalog 2

[10] H. J. Lucas, F. W. Mitchell, jun., and C. N. Scully, *J. Amer. Chem. Soc.*, 1950, **72**, 5491.
[11] R. F. Hudson, personal communication.
[12] G. M. Kosolapoff, 'Organophosphorus Compounds,' Wiley, New York, 1950.
[13] M. M. Crutchfield, C. H. Dungan, J. H. Lekber, V. Mark, and R. J. Van Wazer, *Topics Phosphorus Chem.*, 1967, **5**, 1.
[14] J. Elguero, A. Fruchier, and R. Jacquier, *Bull. Soc. chim. France*, 1966, 2075.

integrator. The ratio of the substrate to marker was used to calculate the first-order rate constant, using the procedure of Cadogan and Sadler.[15] Good first-order plots were obtained in all cases. An error of 5% is associated with the pseudo-first-order rate constants, which are shown in Table 3. A satisfactory Hammett correlation was obtained

TABLE 3

Rates of deoxygenation of *o*-nitrobenzylideneaniline in various tervalent phosphorus reagents

Reagent	Temp. (°C)	$10^5 k_1/s^{-1}$	t/min
$(Pr^iO)_3P$	105	9.7	120
$(MeO)_3P$	105	10.0	116
$(MeO)_3P$	91.5	2.3	505
$(MeO)_3P$ *	91.5	2.65	630
$(EtO)_3P$	105	13.1	89
$(EtO)_3P$	91.5	3.4	337
$(EtO)_3P$ *	91.5	3.4	338
$(EtO)_2PNC_5H_{10}$	105	41.2	28
$EtOP(NEt_2)_2$	105	80	20
	40	7.6	153
$EtOPPh_2$	30	6.2	188
$(EtO)_2PMe$	40	14.0	83
HN–P–NH (7) OEt	40	46.5	25
O–P–O (5) * OEt	91.5	0.5	2 224
O–P–O NEt$_2$	91.5	3.1	378
O–P–O * NEt$_2$	91.5	2.9	396
$(Me_2N)_3P$	91.5	Reaction complete in <20 min	

* Rate of appearance of 2-phenylindazole.

using σ values rather than σ^+ values and yielded a ρ value of 0.74. The rate of deoxygenation of an *o*-nitrobenzylideneaniline which carried a substituent *para* to the nitro-group was also measured. At 105°, and in a 10-fold excess of triethyl phosphite, 5-chloro-2-nitrobenzylideneaniline cyclised to form 5-chloro-2-phenylindazole with a pseudo-first-order rate constant of 25.8×10^{-5} s^{-1}.

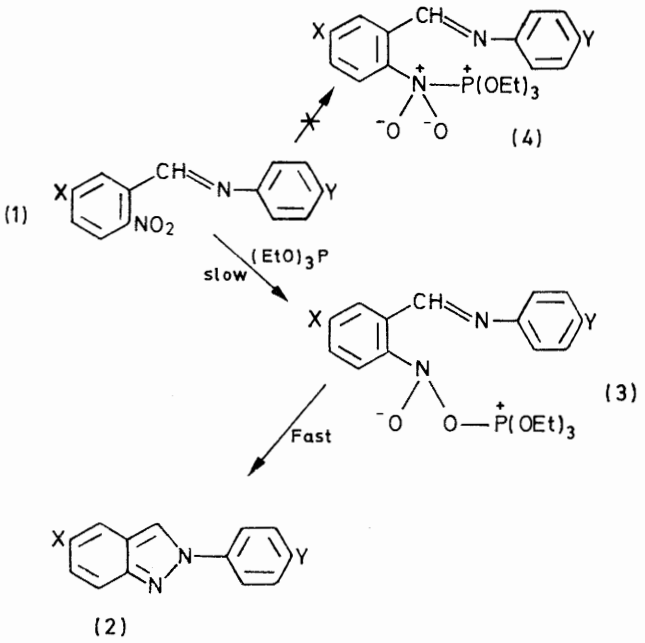
In four cases the rates of appearance of 2-phenylindazole were also measured and good correlations were obtained.

DISCUSSION

Effect of Changing the Nitro-compound.—In the present study we have measured the effect of changing the substituent in the ring remote from the nitro-group on the rate of triethyl phosphite deoxygenation of the *o*-nitro-group in *o*-nitrobenzylideneanilines (1). The results are summarised in Table 2. The reactions all proceeded in good yield to give the corresponding 2-arylindazoles. In all cases the reactions were cleanly first order in the nitro-compound, as shown by measurement of its rate of disappearance. As a check, the rate of formation of 2-phenylindazole was also measured in some cases with satisfactory results. A good Hammett ρ–σ plot was obtained (ρ 0.75), and the reaction proceeded faster with electron-withdrawing substituents, despite the fact that these are in the remote ring. The results support the formation in the rate determining step of a zwitterionic intermediate (3) resulting from nucleophilic attack of phosphorus on one of the oxygen atoms of the nitro-group (Scheme 1). Initial attack of phosphorus on the nitrogen atom would lead to structure (4) which would be expected to be less stable than (3).

There is no significant difference in the rate of reactions of compounds having chloro-substituents *ortho* or *para* to the site of attachment of the amino nitrogen. This result is to be expected if the site of attack in the rate-determining step is the nitro-group, which is sufficiently far removed from the substituent to make steric effects unimportant.

The rates of deoxygenation of triethyl phosphite of the nitro-groups in *p*-nitro-*o*-nitrobenzylideneaniline (1; X = H, Y = NO_2) differ by a factor of *ca.* 10. The



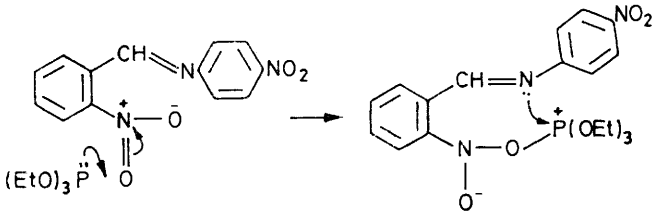
SCHEME 1

o-nitro-group which leads to the formation of the indazole (2; X = H, Y = NO_2) reacts more rapidly, allowing the isolation of 2-(*p*-nitrophenyl)indazole (2; X = H, Y = NO_2). The electronic factors influencing attack on each nitro-group would be expected to be similar, if not the same, and steric factors would be expected to *deter* attack on the *o*-nitro group, rather than give rise to the observed increase in rate. It seems reasonable to ascribe the preferential reaction at the *o*-nitro-group, therefore, to stabilisation of the transition state by interaction between the electrophilic phosphorus atom and nucleophilic nitrogen atom (Scheme 2). A similar explanation has been advanced by Suschitzky [16] to account for the preferential reaction at the *ortho*-group followed by cyclisation of *N*-2,4-dinitrophenylpiperidine to the corresponding nitrodihydrobenzimidazole.

[15] J. I. G. Cadogan and I. H. Sadler, *J. Chem. Soc.* (*B*), 1966, 1191.

[16] R. Garner, G. V. Garner, and H. Suschitzky, *J. Chem. Soc.* (*C*), 1970, 825.

The above conclusions concerning mechanism are supported by the results obtained with *o*-nitrobenzylideneamines in which the amino nitrogen atom carries an

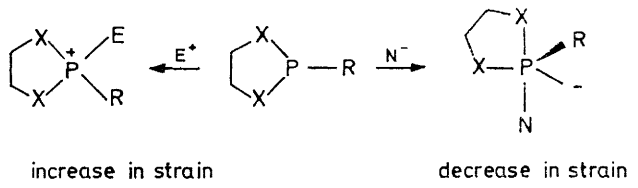


SCHEME 2

aliphatic group (Table 2). These all react at approximately the same rate, which is about half as fast as that of *o*-nitrobenzylideneaniline. Since it has been shown that the rate of disappearance of the substrate is increased by electron-withdrawing substituents in the aromatic ring, the replacement of the aromatic ring itself by electron-donating aliphatic groups would be expected to decrease the rate, as observed. The inductive effect of the aliphatic groups will be very small at the site of the reaction and hence there is no significant difference between their rates of reaction. Also in accord with the foregoing is the observation that the rate of reaction of 5-chloro-2-nitrobenzylideneaniline (1; X = Cl, Y = H) is greater by a factor of 1.7 than that of the isomeric *p*-chloro-*o*-nitrobenzylideneaniline (1; X = H, Y = Cl). The substituent in the former compound is in the same ring as the nitro-group. A Hammett correlation of substituents in this ring would therefore lead to a value of $\rho > 0.75$. Using the result from 5-chloro-2-nitrobenzylideneaniline a ρ value of *ca.* 1.3 was obtained. This is in accord with the 5-chloro-substituent being closer to the site of reaction in the rate determining step than is the chloro-substituent in *p*-chloro-*o*-nitrobenzylideneaniline. Further, there is a good correlation between the relative rate factor of 2 for reaction of 5-chloro-2-nitrobenzylideneaniline compared with 2-nitrobenzylideneaniline and that of 3 previously noted for the corresponding reactions of 4-bromo-2-nitrobiphenyl and 2-nitrobiphenyl.[4]

These results are in accord with previous suggestions [2,3,17] concerning the first step of the reaction and particularly with Lang and Sundberg's kinetic investigation [18] of the triethyl phosphite deoxygenation of simple aromatic nitro-compounds, where the substituent and nitro-group are in the same ring. Although the latter group of compounds are incapable of cyclisation, considerable correlation with our cyclising system is apparent: thus, similar electronic effects were observed while the higher value of $\rho = 1.75$ reported by Lang and Sundberg can be reconciled with our value of 0.75 on the basis of greater proximity of the substituent to the site of the reaction in the former case, as discussed above in connection with the deoxygenation of 5-chloro-2-nitrobenzylideneaniline.

Effect of Changing the Phosphorus Reagent.—The rates of deoxygenation of *o*-nitrobenzylideneaniline (1; X = Y = H) by a series of tervalent phosphorus reagents are summarised in Table 3. In each case the reaction gave 2-phenylindazole. The reagents used can be conveniently divided into two categories *viz.* acyclic phosphorus reagents and those in which phosphorus forms part of a five-membered ring. Table 3 shows that the rate of deoxygenation is very much more sensitive towards the nature of the phosphorus reagent than towards substituents in the aromatic nitro-compound (Table 2). Taking the acyclic phosphorus compounds first, the observed descending order of reactivity $(Me_2N)_3P > (EtO)_2PMe \sim EtOPPh_2 > (EtO)P(NEt_2)_2 \sim EtOPNC_5H_{10} > (MeO)_3P \sim (EtO)_3P \sim (Pr^iO)_3P$ emphasises initial nucleophilic attack by phosphorus on the nitro-group. The more electron rich the phosphorus atom the faster is the reaction.[19] This is confirmed when the results of reactions with cyclic phosphorus reagents are considered. The small ring effect enunciated by Westheimer, Hudson, and Aksnes and their co-workers,[6,20] requires that ring strain in cyclic five-membered tervalent phosphorus reagents increases on reaction with electrophiles and decreases on reaction with nucleophiles (Scheme 3), hence for a nucleophilic attack by phosphorus, five-membered cyclic tervalent phosphorus compounds should react more slowly than the corresponding acyclic phosphorus reagents (*i.e.* $k_a/k_c > 1$).



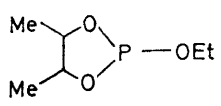
SCHEME 3

In accord with this is our observed rate deceleration $k_a/k_c = 7$ on replacing triethyl phosphite with the cyclic phosphite (5) (Table 3). This compares well with the corresponding deceleration of $k_a/k_c = 7$ obtained for the Arbusov reactions of ethyl iodide with the cyclic phosphite (6) and triethyl phosphite.[21] In our case it was necessary to replace the ethoxy-group in (5) by the more powerfully donating diethylamino-group to counteract the small ring effect and hence to restore the reactivity to that of triethyl phosphite.

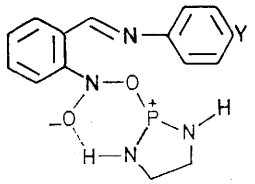
In view of the foregoing, although direct comparisons are not possible, the very high reactivity of the cyclic diamidite (7) (Table 3) is therefore surprising. The closest acyclic analogue which we were able to in-

[17] J. I. G. Cadogan and A. Cooper, *J. Chem. Soc.* (*B*), 1969, 883.
[18] C.-C. Lang and R. J. Sundberg, *J. Org. Chem.*, 1971, **36**, 300.
[19] G. Aksnes and D. Aksnes, *Acta Chem. Scand.*, 1964, **18**, 38.
[20] (*a*) R. F. Hudson and R. Greenhalgh, *Chem. Comm.*, 1968, 1300; (*b*) F. H. Westheimer, *Accounts Chem. Res.*, 1968, **1**, 70; (*c*) G. Aksnes and K. Bergesen, *Acta Chem. Scand.*, 1965, **19**, 931.
[21] G. Aksnes and R. Eriksen, *Acta Chem. Scand.*, 1966, **20**, 2463.

vestigate was *NNN'N'*-tetraethylphosphorodiamidite [$EtOP(NEt_2)_2$] and even if a very considerable, and



(6)



(8)

unlikely, steric effect at phosphorus of the diethylamino-groups is assumed, the high rate of reaction of the cyclic amidite (7), $k_a/k_c = 1/6$ is incompatible with the operation of a small ring effect, only. It is suggested that in this case hydrogen bonding in the transition state (8) for deoxygenation leads to a much enhanced rate of reaction.

It should be noted that these results do not enable us to trace in detail the conversion of the intermediate (3) (Scheme 1) into the resulting indazole. This may proceed *via* fast steps involving the formation and deoxygenation of the corresponding nitroso-compound,[17] which may or may not involve a nitrene, or by direct ring closure of (3) followed by subsequent fast deoxygenation. We have no evidence concerning these subsequent steps in this case.

Preparative Significance of the Results.—This survey of the reactivity of tervalent phosphorus reagents, in addition to being useful with regard to mechanism, enables us to define a reagent of choice. The most reactive phosphorus compounds given in Table 3 are $(Me_2N)_3P$, $EtOPPh_2$, $(EtO)_2PMe$, and the amidites. Of these only the first is readily available, although the second is easily synthesised from readily available materials. Against the first reagent is its noxious character and against the second is the additional preparative difficulty of separating the resulting ethyl diphenylphosphonate from the desired heterocyclic product. The results suggest that ethyl *NN'*-diethylphosphorodiamidite [$EtOP(NHEt)_2$] would be a particularly reactive reagent. The cyclic phosphites offer little in terms of reactivity and are not readily prepared in a pure state. Of the acyclic phosphites, triethyl phosphite is less noxious and more hydrolytically stable than trimethyl phosphite and the resulting triethyl phosphate is more easily removed by distillation than tri-isopropyl phosphate. These factors, combined with availability and cheapness, are in favour of triethyl phosphite as a general reagent for the deoxygenation of aromatic nitro-compounds.

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