presumed to alkylate by substitution processes (at least with primary alkyl halides).

Experimental Section

NMR spectra were obtained on Varian EM-390 and CFT-20 spectrometers and mass spectra with a Hewlett-Packard gas chromatography/mass spectroscopy system. Microanalyses were performed by Galbraith Laboratories, Inc.

Metal–Ammonia Reduction. General Procedure. Excess (1.5–2 equiv) metal (Na or Li) is added to the aromatic compound in ammonia/THF (2:1) at reflux (or −78 °C). After 10–30 min, the reaction is inverse[3] quenched into dilute ammonium chloride solution, and the product is isolated by ether extraction.

Metal–Ammonia Reductive Methylation. The metal–ammonia solution is prepared as above except that (1) methyl bromide gas is passed in (normal quench), or (2) the reaction mixture is pumped into methyl iodide in THF (inverse quench). This is followed by addition of aqueous ammonium chloride and ether extraction.

1-Methyl- and 2-methylnaphthalene were reduced with sodium according to the general procedure to produce 8-methyl- and 2-methyl-1,4-dihydronaphthalenes as indicated previously.[6] The presence of a second isomer in the latter case is discussed in the body of this paper.

Reductive Methylation of 4-Methylbiphenyl. Lithium wire (0.08 g) was added to 4-methylbiphenyl (0.5 g) in THF (15 mL) and ammonia (40 mL) at reflux. After 30 min, methyl bromide gas was passed in until the deep color was discharged. The reaction mixture was then treated with aqueous NH_4Cl followed by ether extractions. GC showed two major products (45:55) confirmed by gas chromatography/mass spectroscopy to be dimethyldihydrobiphenyls [m/e 184 (M), 169 (loss of CH_3)]. The first peak was trapped off to afford 1,4-dimethyl-1,4-dihydrobiphenyl (**16**): NMR ($CDCl_3$) δ 7.2 (m, 5 aryl), 5.6 (d, 4 vinyl), 2.75 (q, 1), 1.5 (s, 3), 1.13 (d, 3). The second peak was 1,4′-dimethyl-1,4-dihydrobiphenyl (**17**): NMR ($CDCl_3$) δ 7.06 (AB q, 4), 5.03 (s, 4), 2.69 (m, 2), 2.31 (s, 3), 1.5 (s, 3). Because of difficulties in obtaining suitable analytical samples from the GC for elemental analysis, the above reaction mixture was subjected to microdistillation (bp 140 °C) and a combined sample of **16** and **17** was analyzed.

Anal. Calcd for $C_{14}H_{16}$: C, 91.30; H, 8.70. Found: C, 91.46; H, 8.54.

Reductive Methylation of 3-Methylbiphenyl. The procedure was similar to that above. The first peak trapped (80%) was 1,3-dimethyl-1,4-dihydrobiphenyl (**13**): NMR ($CDCl_3$) δ 7.21 (m, 5 aryl), 5.66 (m, 2 vinyl), 5.33 (m, 1 vinyl), 2.59 (m, 2), 1.75 (s, 3), 1.48 (s, 3). The second (20%) was 4,3′-dimethyl-1,4-dihydrobiphenyl (**14**): NMR ($CDCl_3$) δ 7.1 (m, 4), 5.61 (s, 4), 2.63 (m, 2), 2.28 (s, 3), 1.43 (s, 3). Furthermore, ^{13}C NMR of **14** showed three upfield singlets (37.08, 34.34, 29.59 ppm) with proton decoupling that yielded a triplet, a doublet, and a triplet under off-resonance conditions, consistent with CH_3, CH_2, and CH_3.

Reductive Methylation of 2-Methylanthracene. 2-Methylanthracene (0.3 g) was dissolved in THF (20 mL) and added to ammonia (50 mL) at reflux. Sodium (0.09 g) was then added, and after 15 min, the reaction mixture was pumped into 8 mL of methyl iodide in 10 mL of THF. The major reduction product (>80%) was shown to be 2,9-dimethyl-9,10-dihydroanthracene (**18**) by comparison with an authentic sample obtained by the reduction of 2,9-dimethylanthracene:[18] mp 70–70.5 °C; NMR ($CDCl_3$) δ 7.15 (m, 7), 3.9 (m, 3), 2.3 (s, 3), 1.35 (d, 3).

Anal. Calcd for $C_{16}H_{16}$; C, 92.31; H, 7.69. Found: C, 92.31; H, 7.99.

Acknowledgment. This work was supported by the U.S. Department of Energy, Office of Basic Energy Sciences. Partial funding of the EM-390 NMR spectrometer was provided by the National Science Foundation (Grant No. CHE 79-16449). We thank Mrs. Elizabeth Solow for performing gas chromatographic/mass spectroscopic analyses.

Registry No. 2, 91-57-6; **3**, 2717-43-3; **4**, 2717-46-6; **12**, 643-93-6; **13**, 76613-02-0; **14**, 76613-03-1; **15**, 644-08-6; **16**, 76613-04-2; **17**, 76613-05-3; **18**, 76613-06-4; 2-methylanthracene, 613-12-7.

Reactions of Tris(dialkylamino)phosphines with Carbonyl Compounds

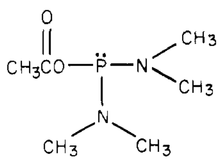
J. H. Hargis* and G. A. Mattson

Department of Chemistry, Auburn University, Alabama 36849

Received October 10, 1980

The reactions of hexamethylphosphorous triamide and some cyclic analogues with anhydrides, acid chlorides, and esters are reported. A mechanism is postulated which involves nucleophilic attack of trivalent phosphorus upon the carbonyl carbon, followed by phosphorane formation and a concerted fragmentation to products.

As a continuation of our studies of the nucleophilic reactions of phosphorodiamidites[1,2] we undertook a study of the reactions of bis(dimethylamino)phosphinous ethanoic anhydride (1). While compounds of this general type have been reported in the literature,[3] syntheses and in particular purification of this type of compound are made difficult by the thermal lability of the product. A novel synthesis of a closely related compound was reported by Kabachnik et al. in 1963[4] (eq 1). This paper reports the



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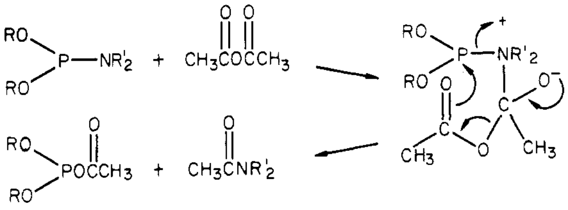
Scheme I



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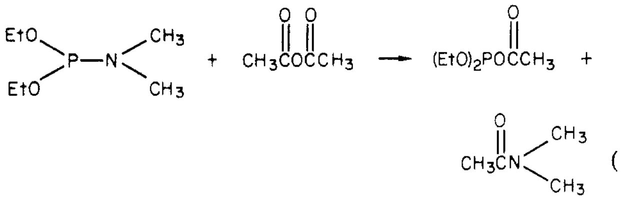
(1) J. H. Hargis and W. D. Alley, *J. Am. Chem. Soc.*, **96**, 5927 (1974).

(2) J. H. Hargis and W. D. Alley, *J. Chem. Soc., Chem. Commun.*, 612 (1975).

(3) E. E. Nifant'ev and I. V. Fursenko, *Russ. Chem. Rev.* (*Engl. Transl.*), **39**, 1050 (1970).



(1)

results of studies of this transformation and similar reactions in an attempt to determine the mechanism of this type of reaction. These reactions are unusual in that in contrast to more normal P(III) chemistry, the formation of phosphoryl bonds is not observed. The elucidation of mechanisms of this type of reaction is complicated because of the biphilic properties[5] of P(III) centers and the possibility of nucleophilic attack on the anhydride by either phosphorus or nitrogen at either carbonyl carbon or at the ether type oxygen. The anhydrides could also serve as nucleophiles via the carbonyl oxygen.[6] Mechanisms previously postulated include those shown in Schemes I[7,8] and II.[3] Scheme I has the obvious advantage of simplicity but can be objected to on the basis that in tervalent P–N compounds, phosphorus is usually observed to be much more nucleophilic than nitrogen. This has been demonstrated unequivocally in reactions with alkyl halides[9] and aldehydes[10] and is indicated in a variety of other reactions. Specifically in order to avoid this difficulty, Nifant'ev[3] postulated the mechanism of Scheme II. This, however, is also open to criticism in that while the protonation of phosphorus eliminates its nucleophilic character, it should also greatly decrease the nucleophilicity of the adjacent nitrogen.

Results

The results of preliminary studies outlined in eq 2–4

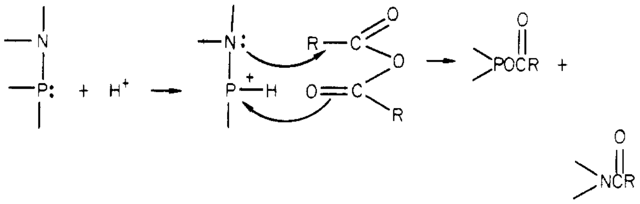
$$\underset{\mathbf{2}}{P(NMe_2)_3} + CH_3C(O)OC(O)CH_3 \rightarrow CH_3C(O)NMe_2 + \underset{\mathbf{1}}{(Me_2N)_2POC(O)CH_3} \quad (2)$$

$$\mathbf{1} + CH_3C(O)OC(O)CH_3 \rightarrow CH_3C(O)NMe_2 + \underset{\mathbf{3}}{(Me_2N)P(OC(O)CH_3)_2} \quad (3)$$

$$\mathbf{3} + CH_3C(O)OC(O)CH_3 \rightarrow CH_3C(O)NMe_2 + \underset{\mathbf{4}}{P(OC(O)CH_3)_3} \quad (4)$$

established that the addition at 0 °C of 1 molar equiv of ethanoic anhydride to hexamethylphosphorous triamide (**2**) resulted cleanly in the formation of *N,N*-dimethylethanamide and bis(dimethylamino)phosphinous ethanoic anhydride, (**1**, eq 2). These products were characterized by following the reaction with ^1H, ^{13}C, or ^{31}P NMR or by high-pressure liquid chromatography. Compound **1** was found to be thermally labile. An attempted distillation to separate **1** from the *N,N*-dimethylethanamide coproduct resulted in formation of an orange waxy solid. This was also observed when the undistilled reaction mixture was allowed to stand at room temperature overnight. The NMR spectra (^1H, ^{13}C, or ^{31}P) are characteristic, however, (see Table I). The ^{31}P chemical shift is particularly noteworthy, with the δ 129.6 (from 85% H_3PO_4 standard) chemical shift demonstrating the trivalent nature of the compound. This reaction proceeds very rapidly. No anhydride was detected by NMR even when it was injected into a solution of **2** in the probe and an immediate scan was initiated. In separate experiments with added triethylamine or ethanoic acid no change in the reaction products or significant change in the rate of reaction was noted.

Scheme II



Upon addition of a second equivalent of ethanoic anhydride to **1** (eq 3), the diacetoxyphosphorus derivative, **3**, and a second equivalent of *N,N*-dimethylethanamide were formed. Continued addition of ethanoic anhydride resulted in formation of a white precipitate (from benzene, chloroform, or neat reaction mixture) as well as a third equivalent of the amide. Presumably this is the triacetoxy derivative, **4** (eq 4).

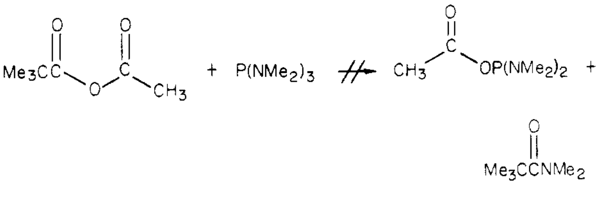
In order to elucidate the mechanism of this reaction, we found it of interest to determine whether the anhydride moiety undergoing attack (or attacking) was becoming part of the amide product or of the mixed phosphorous–carboxylic anhydride. To this end the reaction of 2,2-dimethylpropanoic ethanoic anhydride (**5**) with **2** was studied. Initially it was demonstrated that 2,2-dimethylpropanoic anhydride reacted with **2** analogously to ethanoic anhydride (eq 5). *N,N*,2,2-tetramethylpropanamide

$$Me_3CC(O)OC(O)CMe_3 + P(NMe_2)_3 \rightarrow Me_3CC(O)OP(NMe_2)_2 + Me_3CC(O)NMe_2 \quad (5)$$

was formed cleanly and quantitatively. The NMR spectra and retention time on high-pressure LC were compared with those of an independently synthesized sample. It was also demonstrated that the reaction of 2,2-dimethylpropanoic anhydride with **2** was much slower than that of ethanoic anhydride by a competitive experiment. When a limited amount of **2** was added to an equimolar mixture of ethanoic and 2,2-dimethylpropanoic anhydrides, products corresponding to those described in eq 2–4 were observed. After the ethanoic anhydride had been consumed, the formation of the products shown in eq 5 was observed. It is clear, therefore, that the less hindered ethanoic moiety is more reactive by a large factor.

The reaction of **2** with the mixed anhydride **5** resulted in the formation of **6** and *N,N*-dimethylethanamide (eq 6). The other possible set of products (eq 7) could not be detected by either NMR or high-pressure LC.

$$\underset{\mathbf{5}}{Me_3CC(O)OC(O)CH_3} + P(NMe_2)_3 \rightarrow \underset{\mathbf{6}}{Me_3CC(O)OP(NMe_2)_2} + CH_3C(O)NMe_2 \quad (6)$$



(7)

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(4) M. I. Kabachnik, T. A. Mastryukova, and A. E. Shipoo, *Zh. Obshch. Khim.*, **33**, 320 (1963).

(5) A. J. Kirby and S. G. Warren, "The Organic Chemistry of Phosphorus", Elsevier, Amsterdam, 1967, p 20.

(6) F. Ramirez, A. S. Gulati, and C. P. Smith, *J. Org. Chem.*, **33**, 13 (1968).

(7) V. P. Eudakov and E. K. Shlenkova, *Zh. Obshch. Khim.*, **35**, 739 (1965).

(8) C. Brown, R. F. Hudson, and R. J. G. Searle, *Phosphorous Relat. Group V Elem.*, **2**, 287 (1973).

(9) R. F. Hudson and C. Brown, *Acc. Chem. Res.* **5**, 204 (1972).

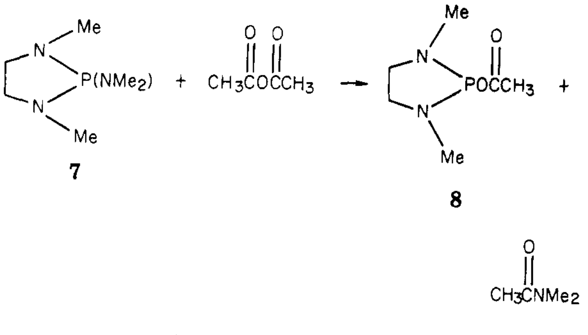
(10) V. Mark, *J. Am. Chem. Soc.*, **85**, 1884 (1963).

Table I. ^{31}P, ^{1}H, and ^{13}C Chemical Shifts and Coupling Constants

compd	exo- or acyclic NCH_3			endo-NCH_3		ring NCH_2		$CH_3C(O)OP$	
	$\delta_{^{31}P}$ [a,e]	$\delta_{^{1}H}$ ($^3J_{PCN}$) [a]	$\delta_{^{13}C}$ ($^2J_{PCN}$) [f]	$\delta_{^{1}H}$ ($^2J_{PNCH}$)	$\delta_{^{13}C}$ ($^2J_{PNC}$) [f]	$\delta_{^{1}H}$ ($^3J_{PNCH}$)	$\delta_{^{13}C}$ ($^2J_{PNC}$) [f]	$\delta_{^{1}H}$ ($^4J_{POCCH}$)	$\delta_{^{13}C}$ ($^3J_{POCC}$) [f]
1	129.6	2.56 (9.7)	37.27 (18.9)					1.99 (1.0)	21.79 (3.1)
3	129.3	2.62 (10.5)	37.90 (19.2)					2.05 (1.5)	
7	114.7	2.58 (11.2) [b,d]	37.67 (16.8)	2.60 (14.8) [b,d]	35.07 (21.6)	5.5–7.0 (m) [b]	53.6 (−8.8)[16]		
8	129.0			2.71 (13.3)	34.51 (21.3)	3.07 (3.18)	52.85 (9.7)	1.88 (~0)	22.8 (3.9)
10	138.1 [b]	2.48 (9.0) [b]						3.31 (12.5) [c]	
11	143.4 [b]	2.55 (9.5) [b]						1.98 (1.2) [b] 3.41 (12.5) [c]	
12				2.64 (12.0)		2.96 (3.36)		3.18 (8.5) [c]	
13	158.7	2.39 (12.3)							
14	165.6	2.26 (13.2)							
15	165.0			2.65 (15.0)		3.23 (7.2)			
16	133.9	2.43 (9.4)							
17	138.4	2.47 (9.6)							

[a] In benzene solution except when noted otherwise. [b] Determined neat. [c] Methoxy signal. [d] These assignments are tentative and may have to be reversed. [e] In parts per million from 85% H_3PO_4. [f] Determined in $CDCl_3$ with Me_4Si as internal standard.

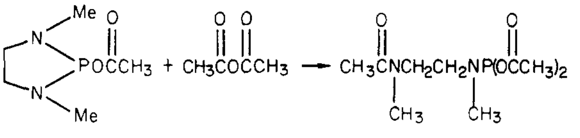
The addition of 1 equiv of ethanoic anhydride to 1,3-dimethyl-2-(dimethylamino)-1,3,2-diazaphospholane (**7**) resulted in the formation of *N,N*-dimethylethanamide and 2-acetoxy-1,3-dimethyl-1,3,2-diazaphospholane (**8**, eq 8).



7 **8**

(8)

No ring-opened product was observed. The addition of a second equivalent of ethanoic anhydride to this reaction mixture resulted in the formation of a product whose ^1H NMR spectrum was consistent with ring-opened compound **9** shown in eq 9. This reaction is much slower than



(9)

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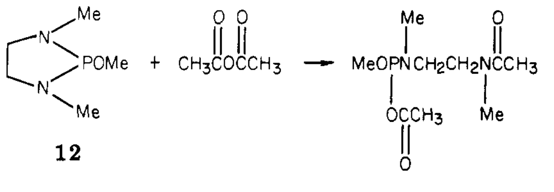
that of either the initial reaction (eq 8) or of that of the acyclic analogue (eq 3). Unlike those reactions in which the ethanoic anhydride is consumed immediately upon addition at 0 °C, this reaction goes to completion only over a period of approximately 1 h at 37 °C (NMR probe temperature).

We have also determined the relative rates of reaction of **2** and **7** with ethanoic anhydride. When 0.14 molar equiv of ethanoic anhydride was added at 0 °C to an equimolar mixture of **2** and **7**, the ratio of **2** to **7** remaining was found to be 0.92 ± 0.03 (from intergration of the appropriate NMe signals in the proton NMR for four different samples). Assumption of the initial rate approximation allows a calculated relative reactivity of **2**/**7** ratio of 1.7.

The reactions with ethanoic anhydride have also been investigated with phosphorodiamidites **10** and **12** (eq 10 and 11). In a competitive experiment no reaction of **12** was observed until all **10** had been consumed.

$$\underset{\mathbf{10}}{MeOP(NMe_2)_2} + CH_3C(O)OC(O)CH_3 \rightarrow \underset{\mathbf{11}}{MeOP(NMe_2)OC(O)CH_3} + CH_3C(O)NMe_2 \quad (10)$$



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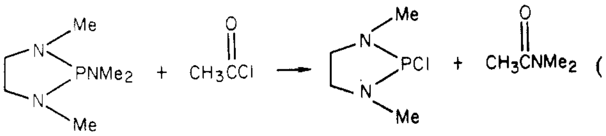
We have also examined the analogous reactions with ethanoyl chloride. Compound **2** reacted with 1 equiv of ethanoyl chloride to produce *N,N*-dimethylethanamide and bis(dimethylamino)chlorophosphine (**13**, eq 12). The

$$P(NMe_2)_3 + CH_3C(O)Cl \rightarrow \underset{\mathbf{13}}{ClP(NMe_2)_2} + CH_3C(O)NMe_2 \quad (12)$$

$$\mathbf{13} + CH_3C(O)Cl \rightarrow \underset{\mathbf{14}}{Cl_2P(NMe_2)} + CH_3C(O)NMe_2 \quad (13)$$

$$14 + CH_3C(O)Cl \rightarrow PCl_3 + CH_3C(O)NMe_2 \quad (14)$$

structure of this compound was verified by comparison of ^1H and ^{31}P NMR spectra with those of this compound produced by an alternate synthetic method.[11] Upon addition of a second equivalent of ethanoyl chloride the dichloro compound **14** was produced, and the addition of a third equivalent of ethanoyl chloride resulted in formation of PCl_3 which was detected by observation of the ^{31}P NMR spectrum. An analogous reaction was observed (eq 15) between **7** and ethanoyl chloride to yield *N,N*-dimethylethanamide and 1,3-dimethyl-2-chloro-1,3,2-diazaphospholane (**15**).



(15)

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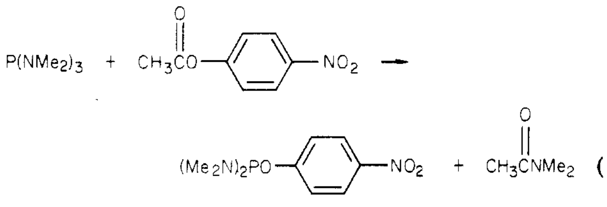
Although no reaction of **2** was noted with ethyl ethanoate at room temperature, *p*-nitrophenyl ethanoate was found to react rapidly, yielding products (eq 16 and 17) corresponding to those from the anhydrides and acid chloride. NMR data of the compounds discussed above are tabulated in Table I.



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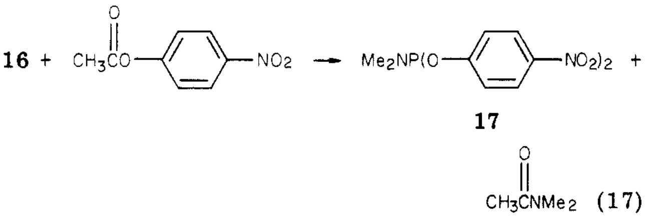

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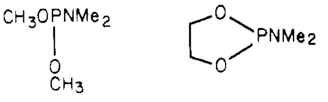
(17)

Discussion

The large difference in reactivity noted for reaction of **2** with ethanoic anhydride and 2,2-dimethylpropanoic anhydride argues against a rate-determining attack of anhydride carbonyl oxygen upon the phosphorus species whether it is protonated or unprotonated since both electronically and sterically the carbonyl oxygen portions of the anhydrides would be expected to be similar. Indeed the magnitude of the effect almost demands that the rate-determining step of the reaction must be a nucleophilic attack of **2** via either phosphorus or nitrogen upon the most sterically accessible carbonyl carbon (i.e., the ethanoic moiety). Furthermore, the experiments with the mixed anhydride **5** demonstrate that the moiety being attacked becomes bonded to nitrogen in the product. This result is in accord with the mechanisms in both Schemes I and II. While the experiment with added triethylamine is not definitive, it seems likely that a reaction proceeding through the protonated species (Scheme II) would be retarded in the presence of a large quantity of base.[12] Given this, and the argument presented earlier that protonation of the phosphorus should greatly detract from the nucleophilicity of the adjacent nitrogen, one is led to the conclusion that the mechanism postulated in Scheme II is untenable.

The relative reactivities of compounds **2** and **7** (**2**/**7** reactivity ratio of 1.7) toward ethanoic anhydride are significant. Hudson and Brown[9] have convincingly demonstrated that reactions in which P(III) in a five-membered ring functions as a nucleophile show decreased reactivity as compared to their acyclic analogues, whereas in those in which P(III) compounds are attacked by a nucleophile at phosphorus (as in step 2 of Scheme I), the cyclic compounds show dramatically enhanced reactivity when compared to the corresponding acyclic compounds. While the reduced reactivity of the cyclic compound is small in this system, it is comparable to the relative reactivity of 3.2:1 noted for the reaction of methyl iodide with dimethyl *N,N*-dimethylphosphoroamidite (**18**) as compared to the



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cyclic analogue 2-(dimethylamino)-1,3,2-dioxaphospholane, respectively, in which nucleophilic attack by phosphorus upon methyl iodide is unequivocal.[9] This reduced reactivity of the cyclic compound is *not*, however, in accord with the rate enhancements[9] of 10^2 or 10^3 for cyclic compounds in which the trivalent phosphorus is attacked by a nucleophile as is required in step 2 of Scheme I.

The formation of product only from the exocyclic nitrogen migration when **7** reacts with ethanoic anhydride (eq 8) also argues against attack upon the carbonyl carbon (Scheme I), since the nucleophilicity of cyclic nitrogen is normally greater than that of a acyclic analogue.[13]

In addition, the very similar behavior of anhydrides, acyl halides, and esters containing a good leaving group, while not demanding a common mechanism, would lead one to suspect a common mechanism is operative. The relatively great differences in nucleophilicity between chloride, acetoxy, and *p*-nitrophenoxide would make the similarities between these reactants surprising, if the reaction were dependent upon this nucleophilicity. It seems more likely that the predominant function of these groups is their leaving group ability.

Scheme III presents a mechanism which is consistent with our observations. The initial attack is postulated to occur by the trivalent phosphorus nucleophile which is intuitively attractive as well as in agreement with the relative reactivities of **2** and **7**. The stepwise nature of the reactions in transferring each R_2N group in turn also fits nicely into this Scheme (i.e., $P(NR_2)_3 > XP(NR_2)_2 > X_2P(NR_2)$ in reactivity) since replacement of each NR_2 group by the more electronegative X group would be expected to lower the nucleophilic reactivity of phosphorus. The decomposition of **19** may be regarded as an orbital symmetry allowed extrusion of the P(III) moiety.[14] Hoffmann et al.[15] have examined the theory of extrusions of this type and have shown that concerted extrusion would be orbital symmetry allowed, with both groups departing from equatorial positions or from apical positions. This formulation is also intriguing in that it allows

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[11] H. Noth and H. J. Vetter, *Chem. Ber.*, **94**, 1505 (1961).

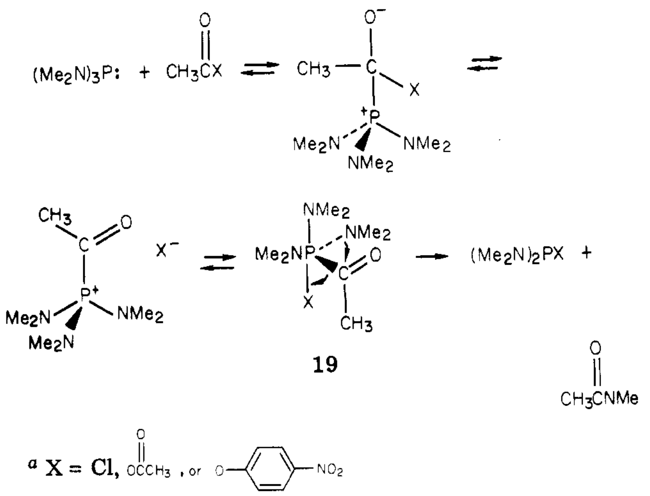
[12] Triethylamine has been reported to be more basic than **2**. J. Duncan and A. Brodsky, *J. Organomet. Chem.*, **59**, 83 (1979).

[13] S. R. Hartshorn, "Aliphatic Nucleophilic Substitution, Cambridge University Press, New York, 1973, p 49.

[14] An alternative two-step mechanism which would achieve the same result cannot be excluded.

[15] R. Hoffmann, J. M. Howell, and E. L. Mutterties, *J. Am. Chem. Soc.*, **94**, 3047 (1972).

Scheme III[a]



an attractive rationalization of the retarded rates of reactions of compounds in which ring opening must occur. An examination of molecular models leads to the conclusion that the bicyclic transition state which must form during the extrusion of an endocyclic nitrogen leads to much more severe ring strain than one in which exocyclic nitrogen is involved. Consequently when the endocyclic nitrogen must be extruded (eq 11) the reaction is slow.

Experimental Section

General Methods. ^{1}H NMR spectra were obtained on Varian EM 390 spectrometer. A Varian CFT-20 was used for measuring ^{13}C and ^{31}P spectra. ^{1}H and ^{13}C chemical shifts are reported downfield from internal Me_4Si. ^{31}P shifts are reported relative to a capillary of 85% phosphoric acid with the standard convention of positive shifts corresponding to downfield. High-pressure liquid chromatography product analyses were performed on a Waters Associates high-pressure liquid chromatograph equipped with a μ-Bondpak, C-18, reverse-phase column with 60:40 acetonitrile–water as the eluent. Mass spectra and gas chromatographic analyses were performed on a Du Pont 21-491B mass spectrometer interfaced with a Varian Aerograph 2700 gas chromatograph equipped with a 5 ft, 3% SE-30 on Variport 30 (100–125-mesh) column. All melting points reported are uncorrected and were taken in a Mel-Temp melting point apparatus.

Hexamethylphosphorous triamide was obtained from Aldrich Chemical Co. and was purified by filtration through charcoal followed by distillation. Compound **7** (1,3-dimethyl-2-(dimethylamino)-1,3,2-diazaphospholane) was prepared by methods previously reported,[16] as were **10** (methyl *N,N,N′,N′*-tetramethylphosphorodiamidite[1]), **12** (2-methoxy-1,3-dimethyl-1,3,2-diazaphospholane[17]), and **15** (1,3-dimethyl-2-chloro-1,3,2-diazaphospholane).[16]

2,2-Dimethylpropanoic anhydride and ethanoic 2,2-dimethylpropanoic anhydride were prepared by carefully distilling a mixture of ethanoic anhydride (9.0 g, 8.8 mmol) and 2,2-dimethylpropanoic acid (5 g, 4.9 mmol) through a glass-helices-packed column until the temperature exceeded 120 °C, at which time the ethanoic acid and excess ethanoic anhydride are gone from the pot residue. The residue fraction (2.9 g) distilling at 56–57 °C (15 mm) is primarily the mixed anhydride [NMR 1.22 ($(CH_3)_3C$, s), 2 ppm ($CH_3C(O)$, s)], and the fraction (1.51 g) distilling at 73–75 °C (15 mm) is the symmetrical anhydride [NMR 1.23 ppm ($(CH_3)_3C$, s)].

Competitive Reaction of Methyl *N,N,N′,N′*-Tetramethylphosphorodiamidite (10) and 1,3-Dimethyl-2-methoxy-1,3,2-diazaphospholane (12). Equal volumes of **10** (150 mg, 1 mmol) and **12** (170 mg, 1.1 mmol) were mixed in an NMR tube, the mixture was cooled in an ice bath, and 25-μL (0.3 mg, 0.26 mmol) increments of ethanoic anhydride were added dropwise. An NMR spectrum was run after each incremental addition. No reaction of **12** was observed.

Reactions. General Procedure A for NMR-Scale Reactions. The tervalent phosphorus compound (and solvent where necessary) was measured into a dry, nitrogen-flushed NMR tube and cooled to ice-bath temperature. The nonphosphorus reactant was added dropwise through a serum cap by using a microsyringe. Intermittent removal of the NMR tube from the ice bath was done to shake the tube or take a spectrum.

General procedure B was the same as procedure A except that the other reactant was placed in the NMR tube and the trivalent phosphorus compound added dropwise to it.

Reaction of Hexamethylphosphorous Triamide (2) with Ethanoic Anhydride. Method A. Compound **2** (450 mg, 2.75 mmol) and ethanoic anhydride (2.60 mmol) were mixed in an NMR tube. The doublet for **2** decreased, and new absorptions appeared at 1.96 ppm (s) and at 2.82 and 2.97 ppm (two singlets) which were verified to be those of *N,N*-dimethylethanamide by addition of authentic sample. New absorptions at 2.10 ppm (d, J = 1 Hz) and 2.57 ppm (d, J = 8 Hz) were assigned to acetyl *N,N,N′,N′*-tetramethylphosphorodiamidite (**1**). During the addition of a second equivalent ethanoic anhydride, the absorptions for **1** decreased, and new absorptions appeared at 2.06 ppm (d, J = 1.5 Hz) and 2.70 ppm (d, J = 10.5 Hz). These absorptions were assigned to diacetyl *N,N*-dimethylphosphoroamidite (**3**). Toward the end of the addition of the second equivalent of anhydride, an absorption at 2.10 ppm was observed and assigned to triacetyl phosphite (**4**). Addition of the third equivalent of anhydride, however, was accompanied by the formation of a precipitate. Attempts at separation of **1** and **3** from the amide coproduct proved unsuccessful because of the thermal instability of these compounds. This precluded characterization of these compounds by elemental analysis.

Reaction of 2 with 2,2-Dimethyl Propanoic Anhydride. Method A. Compound **2** (270 mg, 1.65 mmol) and dimethylpropanoic anhydride (310 mg, 1.69 mmol) were mixed in a NMR tube. As the doublet for **2** decreased, new absorptions appeared at 1.21 (s) and 2.97 ppm, which were verified by the addition of authentic samples to be due to 2,2,*N,N*-tetramethylpropanamide, and at 1.18 (s) and 2.56 ppm (d, J = 9.5 Hz), which were assigned to 2,2-dimethylpropanoyl *N,N,N′,N′*-tetramethylphosphorodiamidite (**6**). This compound was also found to be thermally labile, precluding isolation and further characterization.

Reaction of 2 with Ethanoic Anhydride and 2,2-Dimethylpropanoic Anhydride by General Procedure B. Ethanoic anhydride (90 mg, 0.87 mmol), 2,2-dimethylpropanoic anhydride (140 mg 0.74 mmol), and **2** (70 mg, 0.41 mmol) were mixed in an NMR tube. The NCH_3 absorption at 2.79 ppm was not apparent, indicating negligible formation of 2,2,*N,N*-tetramethylpropanamide.

Reaction of 2 with Ethanoic 2,2-Dimethylpropanoic Anhydride (5). Method B. Compounds **5** (300 mg, 2.08 mmol) and **2** (70 mg, 0.41 mmol) were mixed in an NMR tube. The NCH_3 absorption at 2.97 ppm was not apparent, indicating negligible 2,2,*N,N*-tetramethylpropanamide formation.

Reaction of 1,3-Dimethyl-2-(dimethylamino)-1,3,2-diazaphospholane (7) with Ethanoic Anhydride by General Procedure A. Compound **7** (280 mg, 1.74 mmol) and ethanoic anhydride (160 mg, 1.59 mmol) were mixed in an NMR tube. As the absorptions for **7** decreased, new absorptions appeared which were assigned to *N,N*-dimethylethanamide (singlets at 1.96, 2.82, and 2.97 ppm) and to 1,3-dimethyl-2-acetoxy-1,3,2-diazaphospholane (**8**) [1.88 ($CH_3C(O)$, s), 2.71 (NCH_3, d, J = 13.3 Hz), 3.72–3.18 ppm (NCH_2, m)]. The addition of a second equivalent of anhydride produced a diacetoxy absorption at 2.07 ppm (d, J = 1.3 Hz). In a separate trial, 1.58 mmol of **7** and 1.50 mmol of ethanoic anhydride were mixed. Liquid chromatographic analysis of the reaction mixture indicated formation of 1.42 mmol (95% of *N,N*-dimethylethanamide). Compound **8** also proved to be nonisolable because of its thermal degradation at room temperature.

Reaction of Methyl *N,N,N′,N′*-Tetramethylphosphorodiamidite (10) with Ethanoic Anhydride by General Procedure A. Compound **10** (350 mg, 2.34 mmol) and ethanoic

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(16) J. H. Hargis, W. B. Jennings, S. D. Worley, and M. S. Tolley, *J. Am. Chem. Soc.*, **102**, 13 (1980).

(17) F. Ramirez, A. U. Patwardhan, H. J. Kugler, and C. P. Smith, *J. Am. Chem. Soc.* **89**, 6276 (1967).

anhydride (220 mg, 2.10 mmol) were mixed in an NMR tube. As the absorptions for **10** decreased, new absorptions appeared for *N*,*N*-dimethylacetamide (singlets at 1.91, 2.76 and 7.92 ppm) and acetyl methyl *N*,*N*-dimethylphosphoroamidite (**11**) [1.98 ($CH_3C(O)$, d, $J = 1.0$ Hz), 2.55 (NCH_3, d, $J = 9$ Hz), 3.41 ppm (CH_3O, d, $J = 12.7$ Hz)]. The addition of a second equivalent of anhydride resulted in a decrease in all the absorptions and the appearance of new absorptions assigned to diacetyl methyl phosphite [2.15 ($CH_3C(O)$, d, $J = 1.3$ Hz), 3.63 ppm (CH_3O, d, $J = 9$ Hz). These compounds were also found to be thermally labile.

Reaction of 2 and *p*-Nitrophenyl Ethanoate. A 27-mg (0.165 mmol) sample of **2** was placed in each of five NMR tubes. The tubes were capped with a rubber septum and cooled in an ice bath. A 0.2575-g (1.42 mmol) sample of *p*-nitrophenyl ethanoate was dissolved in 500 μL of C_6D_6 plus a few drops of Me_4Si, and the total volume of ester solution was measured to be 661 μL, yielding a concentration of 0.00214 mmol/μL. Increments of ester solution varying by multiples of 31 μL [(1) 0.0663, (2) 0.133, (3) 0.199, (4) 0.265, and (5) 0.398 mmol] were added dropwise to each of the NMR tubes and the solutions in the tubes diluted to approximately the same volume with C_6D_6. The NMR spectra after increments 1–3 indicated the presence of *N*,*N*-dimethylacetamide: 1.68 (CH_3-$C(O)$, s), 2.23 and 2.62 (NCH_3, 2 s), and a doublet absorption at 2.43 ppm ($J = 9.4$ Hz) assigned to *p*-nitrophenyl *N*,*N*,*N'*,*N'*-tetramethylphosphorodiamidite (**16**). Continued addition of ester solution (increments 4 and 5) indicated a greater concentration of *N*,*N*-dimethylethanamide (concentration increases noted from relative peak heights as well as a downfield shift solvent effect in benzene) and produced a new doublet at 2.47 ppm ($J = 9.6$ Hz) assigned to bis(*p*-nitrophenyl) *N*,*N*-dimethylphosphoroamidite (**17**).

Reaction of 2-Methoxy-1,3-dimethyl-1,3,2-diazaphospholane (12) with Ethanoic Anhydride by General Procedure A. Compound **12** (0.34 g, 2.3 mmol) and ethanoic anhydride (0.24 g, 2.4 mmol) were mixed in an NMR tube. As the absorptions for starting materials decreased, the new absorptions appeared typical of $CH_3C(O)N$ (1.92 ppm, s), $C(O)NCH_3$ (2.77, s, and 2.91 ppm s), $POC(O)CH_3$ (1.96 ppm, d, $J = 1.0$ Hz), and $POCH_3$ (3.39 ppm, d, $J = 10.0$ Hz).

Reaction of 2 with Ethanoyl Chloride by General Procedure A. Compound **2** (2.7 mg, 0.16 mmol) in 250 μL of benzene and ethanoyl chloride (1.1 mg, 0.14 mmol) were mixed in an NMR tube. As the absorptions for **2** decreased, new absorptions (verified by peak enhancement with authentic samples[18]) appeared for *N*,*N*-dimethylacetamide and bis(dimethylamino)phosphine chloride (**13**) [2.39 ppm (NCH_3, d, $J = 12.3$ Hz)]. The same amount of **2** in benzene was mixed with 2.2 mg (0.23 mmol) and 3.3 mg (0.42 mmol) of ethanoyl chloride to give, respectively, bis(methylamino)phosphine chloride (**14**) [2.26 ppm (d, $J = 13.2$ Hz)] and phosphorus trichloride ($\delta_{^{31}P}$ 219 ppm].

Reaction of 1,3-(Dimethylamino)-1,3,2-diazaphospholane (7) and Ethanoyl Chloride by General Procedure A. Compound **7** (164 mg, 10.2 mmol) diluted with benzene and ethanoyl chloride (7.15 mg, 0.92 nmol) were mixed in an NMR tube. As the ^{31}P absorption for **7** decreased, a new absorption at 165.02 ppm appeared which was assigned to 1,3-dimethyl-2-chloro-1,3,2-diazaphospholane (**15**).

Relative Rate Determination of 2 vs. 7 with Ethanoic Anhydride. Equimolar mixtures of **2** and **7** were prepared in quadruplicate by measuring 32 μL of **2** and 29 μL **7** into NMR tubes and accurately measuring the weight after each addition. These mixtures were diluted to approximately 0.4 mL with C_6D_6 containing Me_4Si standard. An NMR spectrum of each solution was obtained on the CFT-20, and the ratio of **2** to **7** was obtained by summation of peak heights. Ethanoic anhydride (5 μL, 0.14 equiv) was added to each tube while it was cooling in an ice bath. The average ratio of **2** to **7** remaining was measured by NMR and was found to be 0.92 ± 0.03.

Reaction of Hexamethylphosphorous Triamide (2) with Ethanoic Anhydride, Ethanoic 2,2-Dimethylpropanoic Anhydride (5), and 2,2-Dimethylpropanoic Anhydride by General Procedure A. Compound **2** (368 mg, 2.26 mmol), ethanoic anhydride (67 mg, 0.66 mmol), **5** (202 mg, 1.4 mmol), and 2,2-dimethylpropanoic anhydride (66 mg, 0.70 mmol) were mixed in an NMR tube. Liquid chromatographic analysis of the reaction mixture indicated the formation of *N*,*N*-dimethylacetamide as the only amide product.

Attempted Reaction of Hexamethylphosphorous Triamide and Ethyl Ethanoate by General Procedure A. Stoichiometric amounts of **2** and ethyl ethanoate were mixed in an NMR tube. The spectrum after mixing and after 72 h indicated only peaks for starting material.

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Registry No. 1, 76328-88-6; **2**, 1608-26-0; **3**, 76467-52-2; **4**, 32468-85-2; **5**, 7137-32-8; **6**, 76467-53-3; **7**, 6069-38-1; **8**, 76467-54-4; **9**, 76467-55-5; **10**, 17166-16-4; **11**, 76467-56-6; **12**, 7137-86-2; **13**, 3348-44-5; **14**, 683-85-2; **15**, 6069-36-9; **16**, 76467-57-7; **17**, 76467-58-8; $MeOP(OC(O)CH_3)N(Me)CH_2CH_2N(Me)C(O)CH_3$, 76467-59-9; $Me_3CC(O)NMe_2$, 24331-71-3; $CH_3C(O)NMe_2$, 127-19-5; $MeOP(OC(O)CH_3)_2$, 76467-60-2; PCl_3, 7719-12-2; $Me_3CC(O)OC(O)CMe_3$, 1538-75-6; $CH_3C(O)OC(O)CH_3$, 108-24-7; *p*-nitrophenyl ethanoate, 830-03-5; $CH_3C(O)Cl$, 75-36-5; 2,2-dimethylpropanoic acid, 75-98-9.

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[18] Authentic $(NMe_2)_2PCl$ and $(NMe_2)PCl_2$ were made by mixing PCl_3 and **2** in ratios of 1:2 and 2:1, respectively.