Reaction of Trisdialkylaminophosphines with Aromatic Aldehydes. I. The Nitrobenzaldehydes. Formation of 2,2,2-Trisamino-1,3,2-dioxaphospholanes and Their Conversion into Epoxides

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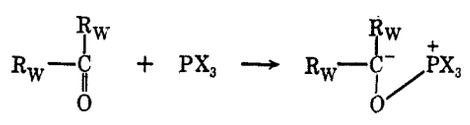
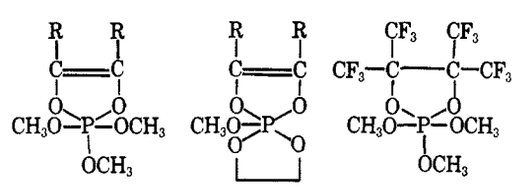
The phosphorus of trisdialkylaminophosphines attacked the carbonyl oxygen of *o*-, *m*-, and *p*-nitrobenzaldehydes. The resulting 1:1 adducts with P–O–C bonds added to a second molecule of the aldehyde and formed 2:1 adducts. The 2:1 adducts were isolated as stable 2,2,2-triamino-1,3,2-dioxaphospholanes in the case of five-membered cyclic trisdialkylaminophosphines. These phosphoranes were converted at 80° into dinitrostilbene oxides and the amidates with inversion of configuration at carbon. The 2:1 adducts derived from open-chain trisdialkylaminophosphines were unstable even below 0° and gave the dinitrostilbene oxides. The P^{31} nmr shifts are described.

Previous papers from this laboratory have dealt with the mechanism of the reactions of *trialkyl phosphites* and of *trisdialkylaminophosphines* with a variety of ketones.[2-14] In all cases the phosphorus of the trivalent phosphorus compound added to the oxygen of the carbonyl function to form 1:1 adducts with P–O–C bonds, provided that the carbonyl function was activated by electron-withdrawing substituents. The types of structures that have been obtained and corresponding values of P^{31} nmr shifts are shown in II–VI.



X = OR, NR_2
R_W = electron-withdrawing groups

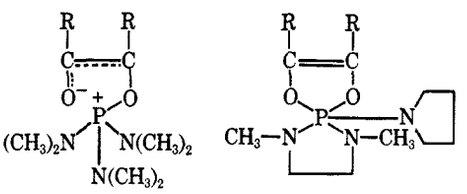
I



II, δP^{31} = +44 to +50 ppm *vs.* H_3PO_4

III, δP^{31} = +23 to +28 ppm

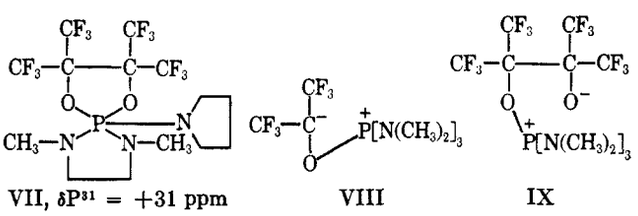
IV, δP^{31} = +50 ppm



V, δP^{31} = −39 ppm to −35 ppm

VI, δP^{31} = +35 ppm to +42 ppm

The reaction of hexafluoroacetone with a five-membered cyclic aminophosphine gave the stable 2,2,2-triamino-1,3,2-dioxaphospholane (VII). However, the reaction with an acyclic aminophosphine led to very unstable 1:1 and 2:1 adducts, VIII and IX, respectively, which underwent molecular fragmentations to several products at about 0°.

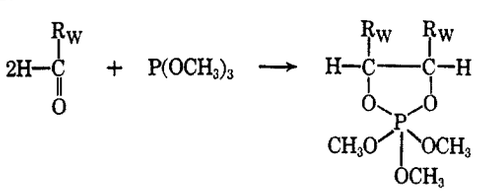


VII, δP^{31} = +31 ppm

VIII

IX

The behavior of aldehydes toward trialkyl phosphites has also been studied.[15,16] Again, the phosphite added to the carbonyl oxygen of aromatic aldehydes that had electron-withdrawing substituents. The products were 2,2,2-trialkoxy-1,3,2-dioxophospholanes, X–XII.



X, R_W = *p*-$NO_2C_6H_4$
XI, R_W = *o*-$NO_2C_6H_4$
XII, R_W = *o*-$CHOC_6H_4$
δP^{31} = *ca.* +50 ppm

The unsubstituted aliphatic monoaldehydes behaved differently toward trialkyl phosphites. Now, the phosphorus of the phosphites attacked the carbonyl

(1) This work was supported by National Science Foundation Grant, GP-3341 and by the Public Health Service Grant CA-04769-06-08 from the National Cancer Institute.

(2) F. Ramirez, C. P. Smith, A. S. Gulati, and A. V. Patwardhan, *Tetrahedron Letters*, 2151 (1966).

(3) F. Ramirez, C. P. Smith, and S. Meyerson, *ibid.*, 3651 (1966).

(4) F. Ramirez, A. S. Gulati, and C. P. Smith, *J. Am. Chem. Soc.*, **89**, 6283 (1967).

(5) For other work on the reactions of hexafluoroacetone with trialkyl phosphites, see (a) N. P. Gambaryan, Yu. A. Cheburkov, and I. L. Knunyants, *Bull. Acad. Sci., USSR*, **8**, 1433 (1964); (b) E. M. Rokhlin, Yu. V. Zeifman, Yu. A. Cheburkov, N. P. Gambaryan, and I. L. Knunyants, *Dokl. Akad. Nauk SSSR*, **161**, 1356 (1965).

(6) (a) F. Ramirez and C. P. Smith, *Chem. Commun.*, 662 (1967); (b) I. J. Borowitz and M. Anschel, *Tetrahedron Letters*, 1517 (1967).

(7) (a) F. Ramirez and N. B. Desai, *J. Am. Chem. Soc.*, **82**, 2652 (1960); (b) *ibid.*, **85**, 3252 (1963).

(8) (a) F. Ramirez, A. V. Patwardhan, H. J. Kugler, and C. P. Smith, *Tetrahedron Letters*, 3053 (1966); (b) F. Ramirez, A. V. Patwardhan, H. J. Kugler, and C. P. Smith, *Tetrahedron*, in press.

(9) For other work on the reactions of trialkyl phosphites with α-diketones, see (a) G. H. Birum and J. L. Dever, Abstracts, 135th National Meeting of the American Chemical Society, Chicago, Ill., Sept 1958, p 101P.

(10) K. M. Kirillova and V. A. Kuhktin, *Zh. Obshch. Khim.*, **35**, 544 (1965); *Chem. Abstr.*, **63**, 5236 (1965).

(11) (a) F. Ramirez, A. V. Patwardhan, and C. P. Smith, *J. Am. Chem. Soc.*, **87**, 4973 (1965); (b) F. Ramirez, A. V. Patwardhan, H. J. Kugler, and C. P. Smith, *ibid.*, **89**, 6276 (1967).

(12) (a) F. Ramirez, A. V. Patwardhan, and C. P. Smith, *J. Org. Chem.* **30**, 2575 (1965); (b) F. Ramirez, S. B. Bhatia, and C. P. Smith, *ibid.*, **31**, 4105 (1966).

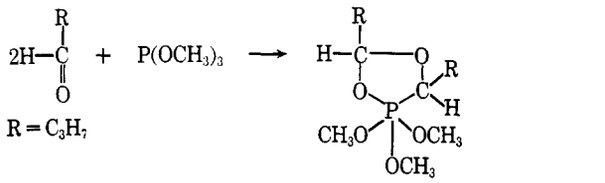
(13) F. Ramirez, N. B. Desai, and N. Ramanathan, *Tetrahedron Letters*, 323 (1963).

(14) F. Ramirez, M. Nagabhushanam, and C. P. Smith, *Tetrahedron*, in press.

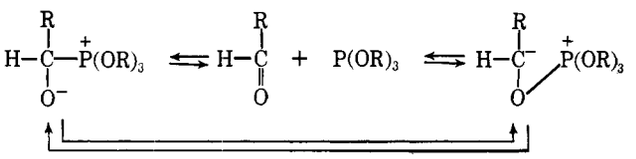
(15) F. Ramirez, S. B. Bhatia, and C. P. Smith, *ibid.*, **23**, 2067 (1967).

(16) F. Ramirez, S. B. Bhatia, A. V. Patwardhan, and C. P. Smith, *J. Org. Chem.*, **32**, 2194 (1967).

carbon of the aldehydes,[17] forming 2,2,2-trialkoxy-1,4,2-dioxaphospholanes, XIII. It is entirely possible that the reactions of phosphites with aldehydes involved in all cases two sets of equilibria, one between the reactants and the 1:1 adducts with P–C–O bonds, and the other between the reactants and the 1:1 adducts with P–O–C bonds. However, the P–O–C adducts would be sufficiently stable only in those cases in which the negative charge on carbonyl carbon is stabilized by electron-withdrawing groups. It is also possible that the two types of 1:1 adducts may be interconvertible through an intermediate or a transition state having a three-membered ring and pentavalent phosphorus. These questions have not been resolved.



XIII, R = C_3H_7; δP^{31} = +34 ppm

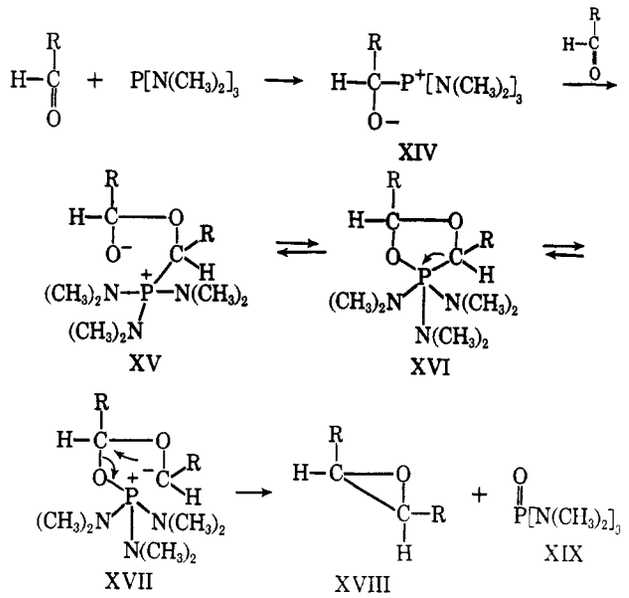


The theoretical aspects of the reactions of trivalent phosphorus compounds with carbonyl compounds have received considerable attention in the last few years.[18] To provide more information on these questions, we have now examined the behavior of aldehydes with a series of acyclic and of five-membered cyclic trisdialkylaminophosphines. The results are reported in this and in subsequent papers.

Mark[19,20] concluded recently that the reactions of trisdimethylaminophosphine with aliphatic aldehydes and with aromatic aldehydes, having electron-withdrawing and electron-releasing substituents, gave in all cases 1:1 adducts with P–C–O bonds, XIV. He reported the P^{31} nmr shifts, δP^{31} = −32 to −28 ppm *vs.* H_3PO_4, of several of these adducts. It should be noted, however, that only one of these adducts had an electron-withdrawing substituent, namely, a fluorine atom in the *para* position of the phenyl ring. In all other cases, the substituents were electron-releasing groups or simple alkyl radicals.

Mark[19] reported also the formation of several epoxides from these reactions. However, in all cases, *the epoxides were derived from benzaldehyde and from its derivatives having electron-withdrawing substituents.* Mark[19] assumed that the 1:1 P–C–O adducts, XIV, condensed, in all cases, with a second molecule of the aldehyde to form 2:1 dipolar adducts, XV. The latter were said to be in equilibrium with the cyclic 2,2,2-triamino-1,4,2-dioxaphospholanes, XVI, which reopened with the rupture of a P–C bond to the dipolar structure, XVII. This new intermediate, XVII, then gave the epoxides, XVIII, and the amidates, XIX (Scheme I).

SCHEME I



It should be emphasized that adducts of type XV, XVI, or XVII were not made from the reactions of the isolated 1:1 P–C–O adducts of type XIV.[19] There is no evidence that a 2:1 adduct with a P–C–O bond can give rise to an epoxide and an amidate.

In the present paper, we will be concerned only with the reactions of trisdialkylaminophosphines with aromatic aldehydes *having electron-withdrawing substituents.* Subsequent papers will deal with the corresponding reactions of aromatic aldehydes having electron-releasing substituents and with unsubstituted aliphatic monoaldehydes.

Results

Reaction of the Nitrobenzaldehydes with Trisdialkylaminophosphines.—*p*-Nitrobenzaldehyde was allowed to react with 2-N-pyrrolidino-1,3-dimethyl-1,3,2-diazaphospholane, XX, in methylene chloride solution at −70°. The solvent was removed after the temperature had reached 20°. The crystalline product was isolated in 90% yield and was shown to be a mixture of the two diastereomeric 2,2,2-triamino-1,3,2-dioxaphospholanes, XXIVa and XXIVb. These isomers were formed in the approximate proportion of 2.4:1. The major isomer was obtained in pure form by fractional crystallization; it was assigned the configuration having the two hydrogens on the phospholane ring in the *cis* relationship as shown in formula XXIVa. This assignment was based on the observation that the two phospholane hydrogens of the major isomer, XXIVa, gave a doublet at a lower magnetic field (τ 4.77) and with a larger H^1–P^{31} coupling constant (J_{HP} = 11.0 cps) than the corresponding doublet of the minor isomer, XXIVb (τ 5.54, J_{HP} <1 cps). A hydrogen adjacent to another hydrogen should be less

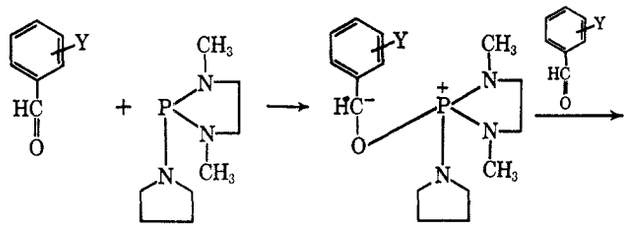
(17) F. Ramirez, A. V. Patwardhan, and S. R. Heller, *J. Am. Chem. Soc.*, **86**, 514 (1964).

(18) (a) R. F. Hudson, "Structure and Mechanisms in Organo-Phosphorus Chemistry," Academic Press Inc., New York, N. Y., 1965, Chapters 4 and 5, in particular p 153. This review contains numerous references dealing in particular with the reactions of trialkyl phosphites and of tertiary phosphines with α-halo ketones. (b) F. Ramirez, O. P. Madan, and C. P. Smith, *Tetrahedron*, **22**, 567 (1966). This paper deals with the reactions of trialkyl phosphites, trisdialkylaminophosphines, and tertiary phosphines with α,β-unsaturated ketones. (c) R. G. Pearson and J. Songstad, *J. Am. Chem. Soc.*, **89**, 1827 (1967), have discussed nucleophilic substitutions by "hard" and "soft" bases.

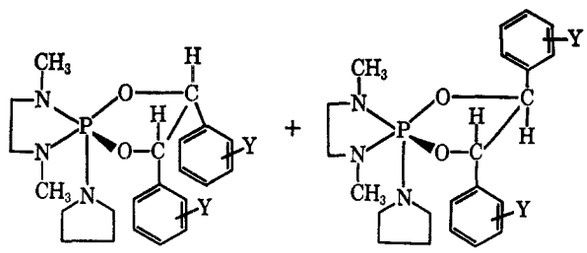
(19) V. Mark, *ibid.*, **85**, 1884 (1963).

(20) For a recent review on this subject, see R. Burgada, *Ann. Chim.*, 15 (1966).

shielded than a hydrogen adjacent to the phenyl ring in these compounds. A similar relationship has already been noted in the diastereomeric 2,2,2-trialkoxy-1,3,2-dioxaphospholanes, Xa and Xb, made from *p*-nitrobenzaldehyde and trimethyl phosphite.



Y = *p*-NO_2 XX, δP^{31} = XXI, Y = *p*-NO_2
Y = *o*-NO_2 −104.9 ppm XXII, Y = *p*-NO_2
Y = *m*-NO_2 XXIII, Y = *m*-NO_2



XXIVa, Y = *p*-NO_2, δP^{31} = +42.3 ppm XXIVb, Y = *p*-NO_2
XXVa, Y = *o*-NO_2, δP^{31} = +42.4 ppm XXVb, Y = *o*-NO_2
XXVIa, Y = *m*-NO_2, δP^{31} = +41.4 ppm XXVIb, Y = *m*-NO_2

The six protons of the two magnetically equivalent or indistinguishable methyl groups on the nitrogens gave doublets at τ 7.38 (J_{HP} = 10.0 cps) and 7.25 (J_{HP} = 10.0 cps) in the *cis* and *trans* isomers, XXIVa and XXIVb, respectively.

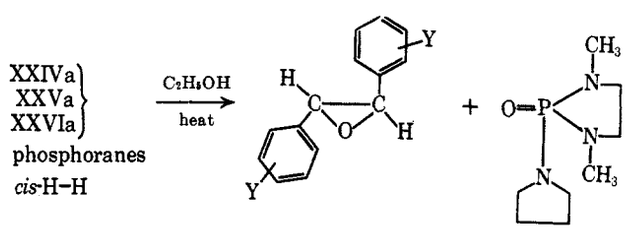
The P^{31} nmr shifts of the two diastereomers, XXIVa and XXIVb had very similar values. The positive value of this shift was one of the main reasons for assigning to the adducts the structure with pentavalent phosphorus.[4,8,11] Note the large positive values of the corresponding pentaoxyphosphoranes Xa and Xb.

It was not possible to isolate or to detect a 1:1 adduct during the formation of the 2:1 adducts XXIVa and XXIVb. However, in view of the triaminodioxyphosphorane structure of these 2:1 adducts, it is clear that P–O–C bonds must have been established at some point during the reaction. We have been able to isolate 1:1 adducts with P–O–C bonds, for example V and VI, from the reactions of trisdialkylaminophosphines with vicinal polycarbonyl compounds. Therefore, we infer that a 1:1 adduct with a P–O–C bond, namely XXI, was the precursor of the 2:1 adducts XXIVa and XXIVb. Adducts like XXI made from monocarbonyl compounds should be less stable, hence more reactive, than adducts like V and VI made from vicinal polycarbonyl compounds owing to the lower degree of negative charge delocalization.

It should be pointed out that, as in the case of the reaction of the nitrobenzaldehydes with trialkyl phosphites,[15] the reaction of the nitrobenzaldehydes with the triaminophosphines may give first a *transient* 1:1 adduct with a P–C–O bond, which then rearranged to the adduct XXI with a P–O–C bond. We found no experimental evidence to support or reject this hypothesis. It may be that the transient deep brown color which was noted during the reaction at −70° was due to the carbanion present in the 1:1 P–O–C adduct. We see no obvious reason for the appearance of color associated with a 1:1 adduct with P–C–O bond, like XIV. The color, however, may be due to a charge-transfer complex between the aminophosphine as donor and the nitrobenzaldehyde as acceptor.

When the reaction of the aminophosphine, XX, with *p*-nitrobenzaldehyde was carried out in benzene, the same oxyphosphoranes, XXIVa and XXIVb, were formed. In this case small amounts of the cyclic phosphoroamidate, XXVII, were also produced. The fate of the aldehyde could not be established for that minor portion of the reaction.

The *cis*-aminooxyphosphorane, XXIVa, was converted into *trans-p,p'*-dinitrostilbene oxide, XXVIIIa, and the cyclic phosphoroamidate, XXVII, by boiling ethanol. The formation of *trans*-epoxide from *cis*-phosphorane is reasonable since epoxide formation should involve an inversion of configuration at one of the carbons.



XXIVa, XXVa, XXVIa phosphoranes *cis*-H–H

XXVIIIa, Y = *p*-NO_2 XXVII, δP^{31} =
XXIXa, Y = *o*-NO_2 −23.1 ppm
XXXa, Y = *m*-NO_2

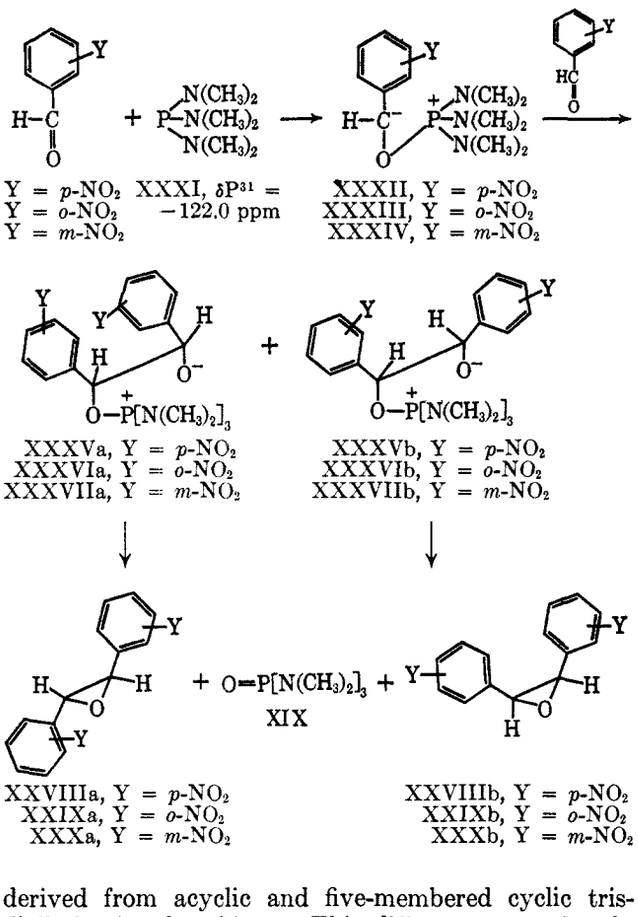
The reaction of *p*-nitrobenzaldehyde with trisdimethylaminophosphine, XXXI, occurred rapidly at −70° in both methylene chloride and benzene solutions. When the mixture was allowed to reach 20°, the products formed were the *trans*- and the *cis-p,p'*-dinitrostilbene oxides, XXVIIIa and XXVIIIb, and hexamethylphosphoroamidate, XIX. Under all conditions, the *trans*-epoxide predominated over the *cis*-epoxide; however, the proportions of isomers in both solvents differed, *i.e.*, 2.6:1.0 in methylene chloride and 3.4:1 in benzene. These values were obtained from the H^1 nmr of the epoxides in $AsCl_3$. The *trans*-epoxide, XXVIIIa, had a singlet at τ 5.95 while the *cis*-epoxide, XXVIIIb, had a singlet at 5.38. Both epoxides are known.[15,21] (See Scheme II.)

No intermediates could be detected in the formation of the epoxides from *p*-nitrobenzaldehyde and trisdimethylaminophosphine, XXXI, but the previous observations in the case of the five-membered cyclic aminophosphine, XX, leave no doubt that the epoxides are formed *via* a 1:1 adduct, XXXII, and the 2:1 adducts, XXXVa and XXXVb.

Evidently, the relationship between the open and the cyclic forms of the 2:1 adducts, XXXV and XXIV, derived from *p*-nitrobenzaldehyde and the aminophosphines, XXXI and XX, respectively, is entirely analogous to the corresponding open and cyclic forms IX and VII for the 2:1 adducts derived from the reactions of hexafluoroacetone with the same aminophosphines, XXXI and XX.[11] Again, we see the difference in the relative stabilities of quadruply and of quintuply connected phosphorus in the compounds

(21) (a) F. Barrow and E. D. Griffiths, *J. Chem. Soc.*, 212 (1921); (b) E. Bergmann and J. Harvey, *Ber.*, **62B**, 893 (1919); (c) S. Bodforss, *Ann. Chem.*, **534**, 243 (1938); (d) S. B. Hanna, Y. Iskander, and J. Riad, *J. Chem. Soc.*, 217 (1961).

SCHEME II



derived from acyclic and five-membered cyclic trisdialkylaminophosphines. This difference was already emphasized in the case of the 1:1 adducts such as V and VI made from the reaction of α-diketones with the aminophosphines,[8] XXXI and XX. *The cyclic aminophosphine tends to give adducts with pentavalent phosphorus which are considerably more stable than the adducts with tetravalent phosphorus made from the acyclic aminophosphine.* Therefore, the *trans*-epoxide, XXVIIIa, was obtained stereospecifically from the *cis*-phosphorane, XXIVa, only at relatively high temperatures.

o-Nitrobenzaldehyde reacted with the cyclic aminophosphine, XX, in methylene chloride at −70° and gave a mixture of the corresponding *cis*- and *trans*-triaminodioxyphosphoranes, XXVa and XXVb, in the proportion of 2.3:1. The 1:1 adduct, XXII, is postulated as an intermediate in this condensation. The arguments in favor of the phosphorane structures and for their configuration are similar to those given in the *p*-nitrobenzaldehyde case. The two phospholane protons of the *cis* isomer, XXVa, gave a doublet at τ 4.05, J_{HP} = 11.0 cps, while the corresponding protons of the *trans* isomer gave a doublet at a 4.82, J_{HP} = 3.0 cps.

The formation of significant amounts of the cyclic phosphoroamidate, XXVII, was observed when the reaction of *o*-nitrobenzaldehyde with the cyclic aminophosphine, XX, was carried out in benzene solution at −70°.

The *cis*-triaminodioxyphosphorane, XXVa, was converted into *trans-o,o'*-dinitrostilbene oxide, XXIXa, by boiling ethanol. The *trans*-epoxide, XXIXa, has already been reported.[15,21]

The reaction of *o*-nitrobenzaldehyde with trisdimethylaminophosphine was carried out in methylene chloride and benzene solutions at −70°. In all cases, the products were the *trans*- and the *cis-o,o'*-dinitrostilbene oxides, XXIXa, and XXIXb, and hexamethylphosphoroamidate, XIX. The proportion of these isomers seems to depend on the reaction conditions. At −70°, the epoxides were formed in the proportions of 1.1:1 in methylene chloride and 3.1:1 in benzene. At 20°, the epoxides were formed in the proportion of 1.3:1 in methylene chloride solution and 2.6:1 in benzene solution.

The protons of the *trans*-epoxide gave a singlet at τ 5.50, and those of the *cis*-epoxide gave a singlet at 4.92. The *trans*-epoxide is known,[15,21] but the *cis*-epoxide has not been reported.

It is assumed that the trisdimethylaminophosphine, XXXI, just as the five-membered cyclic triaminophosphine, XX, attacked the carbonyl oxygen of *o*-nitrobenzaldehyde and gave a 1:1 adduct, XXXIII. This adduct condensed with a second molecule of *o*-nitrobenzaldehyde and gave a mixture of *erythro* and *threo* 2:1 dipolar adducts, XXXVIa and XXXVIb. These adducts are written in the open form in accordance with the evidence so far gathered concerning the relative stabilities of the forms with quadruply and with quintuply connected phosphorus made from the acyclic aminophosphine, XXXI. If the *erythro* dipolar ion, XXXVIa, predominated over the *threo*, XXXVIb, the *trans*-epoxide, XXIXa, formed by loss of the amidate, XIX, should predominate over the *cis*-epoxide, XXIXb. Evidently, the proportions of diastereomers of the dipolar ion varied with the reaction conditions, since the proportion of the resulting epoxides were different.

The reaction of *m*-nitrobenzaldehyde with the cyclic triaminophosphine, XX, was significantly different from the reaction of the *p*-nitro- and the *o*-nitrobenzaldehydes with the same aminophosphine. When the reaction was carried out in methylene chloride solution at −70°, a dark reddish brown solution resulted. The *cis*-triaminodioxyphosphorane, XXVIa, was isolated in approximately 20% yield. The two protons on the phospholane ring gave an nmr doublet at τ 4.80, J_{HP} = 11.5 cps. No evidence could be obtained for the formation of the *trans*-phosphorane, XXVIb, and no other crystalline materials could be isolated from this rather complex reaction. Examination of the P^{31} nmr spectrum of the crude reaction mixture revealed the presence of four nuclei in the approximate proportions of 1.0:1.2:0.5:1.5. The signals were at −24.3, −19.1, −16.1, and +41.9 ppm, respectively. The nucleus with the positive shift was due to the *cis*-phosphorane, XXVIa. Of the nuclei with negative shifts, the major one was due to the cyclic amidate, XXVII, but the other two were of unknown origin. Possibly, one of them could be due to a 1:1 adduct with P–C–O bonds analogous to the adduct which was reported by Mark[19] as the *only* type of adduct formed from the reactions of aldehydes with trisdimethylaminophosphine, XXXI. This point, however, could not be confirmed.

In another experiment, which was carried out in benzene solution at −70°, the proportion of amidate to phospholane had increased considerably, as had been

the case in the reactions of the cyclic aminophosphine with *p*-nitro- and *o*-nitrobenzaldehydes.

Ethanolysis of the *cis-m*-nitrobenzaldehydephosphorane, XXVIa, gave *trans-m,m'*-dinitrostilbene oxide, XXXa. This isomer has been mentioned in the preliminary communication by Mark.[19]

The reaction of *m*-nitrobenzaldehyde with trisdimethylamino phosphine, XXXI, was carried out in methylene chloride and benzene solutions at −70°. The products were the *trans*- and *cis-m,m'*-dinitrostilbene oxides, XXXa and XXXb. As in the case of the isomeric nitrobenzaldehydes, the *trans*-epoxide always predominated over the *cis* isomer, but the proportion depended on reaction conditions, *i.e.*, 1.3:1.0 in methylene chloride and 1.5:1 in benzene. Mark[19] had reported the *trans*- and the *cis*-epoxides in the proportion of 2.8:1, but experimental conditions were not specified. Mark[19] assumed that the epoxides resulted from an initial attack by phosphorus on carbonyl carbon. The present work shows that this interpretation of the course of the formation of epoxides is incorrect.

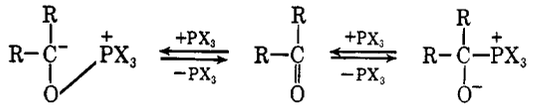
Discussion

Our investigations[4,8,11] showed conclusively that the phosphorus of trisdialkylaminophosphines tends to add to the oxygen atom of carbonyl functions, when the latter are activated by substituents which are capable of stabilizing a negative charge on carbon. The fate of the 1:1 adducts with P–O–C bonds thus formed, XXI–XXIII and XXXII–XXXIV, depend a great deal on the structures of the trisdialkylaminophosphines and of the carbonyl compounds. These 1:1 adducts can decompose by the loss of phosphoroamidate with formation of carbenoid fragments whose fate is not well-understood at this time. The 1:1 adducts with P–O–C bonds can, when generated at sufficiently low temperatures, condense with a second molecule of the carbonyl compound to form 2:1 adducts with a new C–C bond. These 2:1 adducts can be isolated and have proved to be relatively stable if the structure of the trisdialkylaminophosphine permits the formation of a cyclic phosphorane with pentavalent phosphorus, for example, VII and XXIV–XXVI. If stabilization by phosphorane formation is difficult or impossible, then, the 2:1 adduct will lose phosphoroamidate and will form epoxides even at relatively low temperatures, for example, in the cases of adducts XXXV–XXXVII.

The results described in this paper show that epoxides are readily formed from isolated 2:1 adducts having the structure of cyclic triaminodioxyphosphoranes. We infer that the mechanism of epoxide formation is analogous in those cases in which 2:1 adducts cannot be isolated, as in the case of trisdimethylaminophosphine. This inference is strengthened by the stereochemical observations which were made during the formation of the epoxides using cyclic and noncyclic aminophosphines.

The structure of the 1:1 adduct derived from the reaction of trisdialkylaminophosphines with aliphatic aldehydes, with benzaldehydes, and with derivatives of benzaldehyde having electron-releasing substituents will be the subject of a separate communication.

The factors that determine whether the phosphorus or the nitrogen of a trisdialkylaminophosphine will attack the oxygen or the carbon of a carbonyl function are not known. Also, the relationship between the structure of a trivalent phosphorus compound, PX_3, and the nucleophilicity toward the oxygen and the carbon of a carbonyl function is obscure.[18,22,23]



Pearson[18c] and his coworkers have correlated data on relative nucleophilicity of a series of nucleophiles toward various electrophiles of different structures. They have advanced the generalization that "soft bases" tend to react with "soft acids," while "hard bases" tend to react with "hard acids." Hudson[18a] has applied some of these ideas to the reactions of trivalent phosphorus compounds. The results of this and previous investigations from this laboratory could be fitted into Pearson's scheme provided that (1) the phosphorus of trisdialkylaminophosphines is a softer base than the phosphorus of trialkyl phosphites,[24] and (2) the oxygen of a carbonyl function is a softer acid than the carbon in the carbonyl function, *since the phosphorus of trisdialkylaminophosphines exhibits a greater tendency to attack the carbonyl oxygen than the phosphorus of trialkyl phosphites.*

Finally, certain correlations can be made between the structure of trisdialkylaminophosphines on the one hand and the stereospecificity of the reactions with the nitrobenzaldehydes on the other hand. In the case of *p*-nitrobenzaldehyde, the relative proportions (2.4:1) of the oxyphosphoranes, XXIVa and XXIVb, having the *cis*- and *trans*-H–H relationship, respectively, was very similar to the relative proportion (2.6:1) of the open dipolar structures, XXXVa and XXXVb, having the *erythro* and *threo* configurations, under comparable experimental conditions.

On the other hand, in the *o*-nitrobenzaldehyde case, the proportion of *cis*- to *trans*-phosphoranes (2.3:1, XXVa:XXVb), was different from the proportion of the *erythro* and the *threo* dipolar structures (1.1:1, XXXVIa:XXXVIb). In other words, the tendency for the formation of the *threo* dipolar ion, XXXVIb, appeared to be relatively high.[25]

These differences are undoubtedly related to the stereoelectronic properties of the transition states of the condensation of the nitrobenzaldehydes with the 1:1 dipolar adducts, XXI–XXIII and XXXII–XXXIV derived from the cyclic and acyclic triaminophosphines. In fact, changes in the nature of the solvent appeared to affect significantly the stereo-

(22) E. H. Amonoo-Neizer, S. K. Ray, R. A. Shaw, and B. C. Smith, *J. Chem. Soc.*, 4296 (1965).

(23) For recent reviews of possible modes of reactions of trialkyl phosphites with α-halo ketones, see (a) ref 18a; (b) P. A. Chopard, V. M. Clark, R. F. Hudson, and A. J. Kirby, *Tetrahedron*, **21**, 1961 (1965); (c) I. J. Borowitz, M. Anschel, and S. Firstenberg, *J. Org. Chem.*, **32**, 1723 (1967).

(24) For recent discussions of deoxygenation reactions of aromatic nitro compounds by trialkyl phosphites, see (a) R. J. Sundberg, *J. Org. Chem.*, **30**, 3604 (1965); (b) R. J. Sundberg, *J. Am. Chem. Soc.*, **88**, 3781 (1966); (c) R. J. Sundberg, *Tetrahedron Letters*, 477 (1966); (d) J. I. Cadogan, M. Cameron-Wood, R. K. Mackie, and R. J. G. Serale, *J. Chem. Soc.*, 4831 (1965); (e) J. I. Cadogan, D. J. Sears, and D. M. Smith, *Chem. Commun.*, 491 (1966).

(25) The figures for the relative proportions of the open dipolar ions, XXXVa:XXXVb and XXXVIa:XXXVIb, are assumed to correspond to the figures for the observed *trans*- and the *cis*-epoxides, XXVIIIa:XXVIIIb and XXIXa:XXIXb. The *erythro* adduct should give rise to the *trans*-epoxide, while the *threo* adduct should give rise to the *cis*-epoxide.

chemistry of these reactions. Thus, in all cases, the reaction of the acyclic aminophosphine, XXXI, with a given nitrobenzaldehyde in benzene solution gave a higher proportion of the *erythro* dipolar ions, XXXVa–XXXVIIa, than of the corresponding *threo* dipolar ions, XXXVb–XXXVIIb, as compared with the reaction carried out in methylene chloride.[25] Small variations in the stereochemistry of the reactions were noted also with temperature in a given solvent.

Experimental Section

The analyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y. All P^{31} nmr are given in parts per million from 85% H_3PO_4 as zero; they were determined at 40.5 cps. All H^1 nmr are given in parts per million *vs.* TMS as 10 (τ values); they were determined at 60 Mcs.

Reaction of *p*-Nitrobenzaldehyde with 2-N-Pyrrolidino-1,3-dimethyl-1,3,2-diazaphospholane, XX. A. In Methylene Chloride Solution.—The aminophosphine, XX (1.23 g, 6.6 mmoles) was added dropwise under nitrogen to a solution of *p*-nitrobenzaldehyde (2.0 g, 13.2 mmoles) in 14 ml of methylene chloride at −70°. There was evidence of reaction at this low temperature. The mixture was allowed to reach 20°, and the yellow solution was evaporated under vacuum. The residue was kept for 2 days in a mixture of benzene and hexane (10 ml and 30 ml) at −20°. The crystalline mixture of diastereomers, XXIVa and XXIVb, was recrystallized from 6 ml of benzene to give the *cis*-H–H diastereomer, XXIVa, of the adduct (1.9 g, 60%), mp 121–123°. An additional crystallization from benzene gave pure *cis* adduct, XXIVa, 1.5 g, mp 122–123°, δP^{31} = +42.3 ppm (CH_2Cl_2).

The H^1 nmr spectrum in $CDCl_3$ had eight aromatic protons at τ 2.1 and 2.7, a 2 H^1 doublet at 4.77, J_{HP} = 11.0 cps (H on phospholane), a 6 H^1 doublet at 7.38, J_{HP} = 10.0 cps (CH_3–N), multiplets at 6.5, 6.9, 7.1, and 8.2 due to α- and β-CH_2.

The infrared spectrum in CH_2Cl_2 had bands at (μ) 6.60 (s), 7.47 (s), 9.30 (s), 9.85 (m) and 10.5 (m), among others.

The benzene mother liquids obtained after removal of approximately 60% of the *cis*-H–H adduct, XXIVa, were combined. The solvent was removed under vacuum, and the residue was analyzed by H^1 and P^{31} nmr spectroscopy in $CDCl_3$. Signals attributed to the *cis*-H–H and the *trans*-H–H isomers, XXIVa and XXIVb, were observed in a 1:1 proportion. *cis* isomer XXIVa had τ 4.77, J_{HP} = 11 cps, and τ 7.38, J_{HP} = 10 cps. *trans* isomer XXIVb had τ 5.54, J_{HP} = 1 cps, and τ 7.25, J_{HP} = 10 cps. The P^{31} nmr signals of the two isomers could not be resolved.

Anal. Calcd for $C_{22}H_{28}O_6N_3P$: C, 53.9; H, 5.7; N, 14.3; P, 6.3. Found: C, 53.8; H, 5.7; N, 14.0; P, 6.2.

B. In Benzene.—One mole of aminophosphine, XX, was added to 2 moles of *p*-nitrobenzaldehyde in benzene (0.4 *M*) at −70°. An orange color was noted at −70°. The mixture was allowed to reach 20°, the solvent was concentrated to a small volume, *ca.* 3 ml, under vacuum, and the solution was analyzed by P^{31} nmr spectroscopy. Four nuclei were observed in the approximate proportions of 1.0:4.0:1.6:8. The major signal was at δP^{31} = +42.3 ppm (adduct XXIVa). The three minor nuclei were in the region from −30 to −20 ppm; the most abundant was the cyclic phosphoroamidate, XXVII, δP^{31} = −23.1 ppm.

Reaction of the *cis*-*p*-Nitrobenzaldehyde–Aminophosphine Adduct, XXIV, with Ethanol.—A solution of adduct XXIV (400 mg) in 4 ml of ethanol was kept for 12 hr at reflux. The crystals thus obtained (100 mg) were identified as *trans*-*p*,*p*′-dinitrostilbene oxide, XXVIIIa, by comparison[15,21] of the melting point (202–203°) and of the H^1 nmr spectrum (singlet at τ 5.95 in $AsCl_3$) with those of an authentic sample. No evidence for the formation of the *cis*-epoxide, XXVIIIb, which is known[15,21] to have a singlet at τ 5.38 was obtained. The P^{31} nmr of the original reaction mixture had the signal due to the phosphoroamidate, XXVII.

Reaction of *p*-Nitrobenzaldehyde with Trisdimethylaminophosphine, XXXI. A. In Methylene Chloride.—The aminophosphine, XXXI, (2.49 g, 15.3 mmoles) in 5 ml of methylene chloride was added to a solution of *p*-nitrobenzaldehyde (4.62 g, 2 mole equiv) in 20 ml of methylene chloride at −70°. The addition took 2 min. The original pale yellow mixture became deep yellow at −70°. The mixture was allowed to reach 20° (*ca.* 30 min), the solvent was evaporated in vacuum, and the residue was dissolved in $AsCl_3$. The H^1 nmr spectrum had signals at τ 5.95 and 5.38 due to the *trans*- and the *cis*-epoxides, XXVIIIa and XXVIIIb, in the proportion of 2.6:1.0.

B. In Benzene.—A solution of trisdimethylaminophosphine, XXXI, (6.8 g) in 15 ml of benzene was added to a solution of *p*-nitrobenzaldehyde (12.8 g, 2 mole equiv) in 100 ml of benzene at −70°. The reaction was exothermic. The mixture was allowed to reach 20° and was kept for 15 hr at that temperature. The mixture of yellow solution and of colorless solid was evaporated under vacuum, and the residue was dissolved in $AsCl_3$ for H^1 nmr spectrometry. The signals due to *trans*- and *cis*-*p*,*p*′-dinitrostilbene oxides, XXVIIIa and XXVIIIb, were seen at τ 5.95 and 5.38 in the proportion of 3.4:1.0. The protons of hexamethylphosphoroamidate, XIX, gave a doublet at τ 7.34 (J_{HP} = 10 cps). The identity of the amidate was confirmed by P^{31} nmr, δP^{31} = −23.2 ppm.

In another analogous experiment, the major *trans*-epoxide, XXVIIIa, was isolated and characterized by comparison with an authentic sample.[15,21]

Reaction of *o*-Nitrobenzaldehyde with 2-N-Pyrrolidino-1,3-dimethyl-1,3,2-diazaphospholane, XX. A. In Methylene Chloride.—A solution of the aminophosphine, XX (3.08 g, 16.5 mmoles) in 15 ml of methylene chloride was added over a 2-min period to a solution of *o*-nitrobenzaldehyde (4.98 g, 3,3 mmoles) in 40 ml of methylene chloride at −70°. A transient deep brown color was noted when the aminophosphine came in contact with the *o*-nitrobenzaldehyde; this color was rapidly discharged, and within 2 min the solution was deep yellow. The solvent was evaporated in vacuum after the solution had stood 30 min at −70° and 3 hr at 20°. The P^{31} nmr spectrum of the residue in CH_2Cl_2 disclosed only one nucleus at +42.4 ppm. The H^1 nmr of a $CDCl_3$ solution of the residue showed a doublet at τ 4.05 (J_{HP} = 11.0 cps) and a doublet at 4.82 (J_{HP} = 3.0 cps) in the proportion of 2.3:1 (protons on phospholane ring of *cis* and *trans* adducts, XXVa and XXVb), a doublet at τ 7.41 (J_{HP} = 10.0 cps) and a doublet at 7.30 (J_{HP} = 10.0 cps, CH_3–N of isomers), a multiplet at 2.7 (aromatic protons), and multiplets at *ca.* 7.0 and 8.2 (α- and β-CH_2).

Three recrystallizations from benzene–hexane gave the pure *cis* isomer, XXVa, mp 136–137°, δP^{31} = +42.4 ppm ($CDCl_3$).

The H^1 nmr ($CDCl_3$) showed only a 2 H^1 doublet at τ 4.08 (J_{HP} = 11.0 cps) and a 6 H^1 doublet at τ 7.45 (J_{HP} = 10.0 cps) in addition to the multiplets mentioned above.

The infrared spectrum in CH_2Cl_2 had bands at (μ) 6.65 (s), 7.48 (ms), 8.6 (m), 9.25 (m), 9.40 (m), 9.60 (m), 9.90 (m), and 10.50 (m).

Anal. Calcd for $C_{22}H_{28}O_6N_3P$: C, 54.0; H, 5.7; N, 14.3; P, 6.3. Found: C, 54.1; H, 6.0; N, 14.0; P, 6.0.

B. In Benzene.—The aminophosphine, XX, (8.8 mmoles) was added to a solution of *o*-nitrobenzaldehyde (17.7 mmoles) in 6 ml of benzene at −70°. The mixture was allowed to reach 20°, when a crystalline solid separated. The solid was a mixture of the *cis* and the *trans* isomers, XXVa and XXVb (85% yield). Three recrystallizations from benzene–hexane gave the pure *cis* isomer, XXVa, in 70% yield. The P^{31} nmr spectrum of the combined mother liquids revealed the presence of significant amounts of the cyclic phosphoroamidate, XXVII.

Reaction of the *o*-Nitrobenzaldehyde–Cyclic Aminophosphine Adduct, XXV, with Ethanol.—A solution of the *cis* adduct, XXVa, (100 mg) in 1 ml of ethanol was kept 6 hr at reflux. The colorless *trans*-*o*,*o*′-dinitrostilbene oxide, XXIXa (60 mg, 86%), mp 162–165°, was collected by filtration. The H^1 nmr had a singlet at τ 5.53 (in $CDCl_3$) and 5.50 in $AsCl_3$. The material was compared with an authentic sample.[15,21]

The *cis*-*o*,*o*′-dinitrostilbene oxide, XXIXb, is known to have a singlet at τ 4.92 in $CDCl_3$ (*vide infra*).

Reaction of *o*-Nitrobenzaldehyde with Trisdimethylaminophosphine, XXXI. A. In Methylene Chloride at −70°.—The aminophosphine, XXXI (3.28 g, 20.1 mmoles), in 10 ml of CH_2Cl_2 was added over a 2-min period to a solution of *o*-nitrobenzaldehyde (6.07 g, 2 mole equiv) in 20 ml of CH_2Cl_2 at −70°. The pale yellow mixture became deep yellow at −70°. The mixture was allowed to reach 20° (30 min) and was then evaporated under vacuum. The residue was thoroughly mixed with $CDCl_3$, and an aliquot of this homogenized mixture of finely suspended solid and solution was transferred to a H^1 nmr sample tube. More $CDCl_3$ was added, and the clear homogeneous solution was then analyzed by H^1 nmr. The singlets for the *trans*-

and the *cis-o,o'*-dinitrostilbene oxides, XXIXa and XXIXb, were observed at τ 5.50 and 4.90 in the proportion of 1.1:1.

B. In Methylene Chloride at 20°.—The aminophosphine, XXXI (4.64 g, 28.5 mmoles), was added rapidly to a solution of *o*-nitrobenzaldehyde (8.61 g, 2 mole equiv) in 28.5 ml of CH_2Cl_2 at 20°. The pale yellow solution became deep yellow and began to reflux vigorously. A brown solution resulted which soon turned yellow and deposited a solid. The mixture was allowed to cool to 20° and was then evaporated under vacuum. An aliquot was prepared for H^1 nmr analysis in $CDCl_3$ as in the previous experiment. The signals due to the *trans*- and *cis*-epoxides, XXIXa and XXIXb, were observed in the proportion of 1.3:1.0.

C. In Benzene at −70°.—The aminophosphine, XXXI (3.55 g, 21.8 mmoles) in 10 ml of benzene was added to a solution of *o*-nitrobenzaldehyde (6.58 g, 2 mole equiv) in 25 ml of benzene at −70°. The initial yellow color changed to orange and returned to pale yellow at −70°. The mixture was allowed to reach 20° (30 min) and was then evaporated under vacuum. An aliquot was prepared for H^1 nmr analysis in $CDCl_3$ as in the previous experiment. The signals due to the *trans*- and *cis*-epoxides, XXIXa and XXIXb, were observed in the proportion of 3:1.

D. In Benzene at 20°.—The aminophosphine, XXXI (3.44 g, 21.1 mmoles), in 5 ml of benzene was added rapidly to a solution of *o*-nitrobenzaldehyde (6.37 g, 2 mole equiv) in 20 ml of benzene at 20°. A very exothermic reaction occurred, and the initial pale yellow solution became orange. After about 5 min, a pale yellow solid deposited. The mixture was allowed to cool to 20° and was then evaporated under vacuum. An aliquot was prepared for H^1 nmr analysis in $CDCl_3$ as in the previous experiment. The signals due to the *trans*- and *cis*-epoxides, XXIXa and XXIXb, were observed in the proportion of 2.6:1.0.

E. Isolation of *cis-o,o'*-Dinitrostilbene Oxide, XXIXb.—The analytical sample of the *cis-o*-nitroepoxide, XXIXb, was isolated by the following procedure. Benzene was added to a reaction mixture in which the proportion of *trans/cis*-epoxide was 1.2:1.0 and filtered. The filtrate, enriched in the *cis* isomer, was then passed through a column of neutral alumina, to remove the amidate, XIX. The column was eluted with CH_2Cl_2 and the first pale yellow fraction was collected. This fraction was evaporated to dryness and extracted with boiling *n*-hexane to remove the last traces of the amidate. The pure *cis* isomer was obtained after recrystallization from ethyl acetate as a pale yellow solid with mp 147–155°.

The infrared spectrum (in CH_2Cl_2) had the following bands (μ): 6.21 (m), 6.35 (m), 6.58 (s), 7.45 (s), 7.70 (w), 8.45 (m), 9.24 (w), 9.65 (w), 10.38 (w), 11.01 (m), 11.48 (m), 11.61 (ms), 11.82 (m), 12.63 (m).

The H^1 nmr in $CDCl_3$ had the aromatic signals centered at τ 2.18 and at 2.64, and a sharp singlet at 4.90.

Anal. Calcd for $C_{14}H_{10}O_5N_2$: C, 58.7; H, 3.5. Found: C, 58.1; H, 3.5.

Reaction of *m*-Nitrobenzaldehyde with 2-N-Pyrrolidino-1,3-dimethyl-1,3,2-diazaphospholane, XX. A. In Methylene Chloride.—The aminophosphine, XX (1.65 g, 8.8 mmoles) was added to a solution of *m*-nitrobenzaldehyde (2.67, 17.7 mmoles) in 12 ml of CH_2Cl_2 at −70° under N_2. A dark red color was noted even at −70°. The mixture was allowed to reach 20°, and the dark solution was evaporated. The noncrystalline residue was dissolved in benzene (6 ml) and hexane (a few drops). Crystals appeared at 5°; these were recrystallized from benzene (5 ml) giving the *cis* adduct, XXVIa, of mp 147–148° (25% yield). Further crystallizations from benzene did not raise the melting point, δP^{31} = +41.4 ppm ($CDCl_3$).

The H^1 nmr in $CDCl_3$ had eight aromatic protons at τ 2.0 and 2.9, a 2 H^1 doublet at 4.80, J_{HP} = 11.5 cps (H on phospholane), and a 6 H^1 doublet at 7.35, J_{HP} = 10.0 cps (CH_3–N), and multiplets at 6.9, 7.2, and 8.1 due to α- and β-CH_2.

Anal. Calcd for $C_{22}H_{28}O_6N_3P$: C, 54.0; H, 5.7; N, 14.3; P, 6.3. Found: C, 54.2; H, 6.0; N, 14.3; P, 6.1.

The benzene mother liquid, from which about 25% of the *cis* adduct, XXVIa, had been removed, did not afford any crystallizable material.

In another experiment in which a solution of 24 mmoles of the aminophosphine, XX, in 10 ml of CH_2Cl_2 was added to 48 mmoles of *m*-nitrobenzaldehyde in 70 ml of CH_2Cl_2 at −70°, an analogous red solution was obtained. Evaporation gave a deep red oil.

The P^{31} nmr spectrum in $CDCl_3$ had four nuclei in the following proportions (from low to high magnetic field): 1.0:1.2:0.5:1.5 at −24.3, −19.1, −16.1, and +41.9 ppm.

B. In Benzene.—The aminophosphine, XX (2.7 mmoles), was added to the solution of *m*-nitrobenzaldehyde (5.5 mmoles) in benzene (2 ml) at −70° under N_2. The mixture was allowed to reach 20°. The P^{31} nmr had four signals in approximately equal intensities. Three of them were in the region of −30 to −20 ppm. One of these corresponded to the cyclic amidate, XXVII. The signal of the adduct, XXVI, was also present.

Reaction of *m*-Nitrobenzaldehyde–Cyclic Phosphine Adduct, XXVI, with Ethanol.—A solution of the *cis* adduct, XXVIa (400 mg), in ethanol (5 ml) was kept 1 hr at reflux temperature, affording *trans-m,m'*-dinitrostilbene oxide, XXXa, mp 156–157°, τ 5.93. The *cis*-epoxide is known to give a singlet at τ 5.43.

Reaction of *m*-Nitrobenzaldehyde with Trisdimethylaminophosphine, XXXI. A. In Methylene Chloride.—A solution of the phosphine, XXXI, (3.7 g, 23 mmoles) in 10 ml of CH_2Cl_2 was added to a solution of *m*-nitrobenzaldehyde (7.0 g, 2 mole equiv) in 25 ml of CH_2Cl_2 at −70°. The deep red solution was kept 1 hr at −70° and 30 min at 20°. The solvent was evaporated, and the residue was dissolved in $CDCl_3$. The H^1 nmr spectrum of the solution had singlets at τ 5.93 and 5.43 in the proportion of 1.3:1 due to the *trans*- and *cis-m,m'*-dinitrostilbene oxides, XXXa and XXXb.

B. Isolation of *trans-m,m'*-Dinitrostilbene Oxide, XXXa.—The analytical sample of the *trans-m*-nitroepoxide, XXXa, was isolated by the following procedure. The concentrated reaction mixture in which the proportion of *trans/cis*-epoxide was 1.3:1.0 was passed through a column of neutral alumina to remove the amidate, XIX. The column was eluted with CH_2Cl_2, and the first, orange-brown fraction was collected. This fraction was evaporated to dryness and extracted with boiling *n*-hexane to remove the last traces of the amidate. The pure *trans* isomer was obtained after recrystallizing first from benzene–hexane and then from ethanol as tan needles, mp 156–158°.

The H^1 nmr in $CDCl_3$ had the aromatic signals centered at τ 1.82 and 2.39, and a sharp singlet at 5.93.

Anal. Calcd for $C_{14}H_{10}O_5N_2$: C, 58.7; H, 3.5. Found: C, 57.9; H, 3.4.

C. In Benzene.—The aminophosphine, XXXI (2.78 g, 17.6 mmoles), in 5 ml of benzene was added to *m*-nitrobenzaldehyde (5.32 g, 35.2 mmoles) in 20 ml of benzene at −70°. The mixture was worked and analyzed as in the previous experiment. The H^1 nmr signals due to the *trans*- and the *cis*-epoxides, XXXa and XXXb, were observed in the proportion of 1.5:1.0.

Registry No.—XXIVa, 14805-40-4; XXIVb, 14805-43-7; XXVa, 14805-41-5; XXVb, 14932-16-2; XXVIa, 14805-42-6; XXVIIIa, 14764-49-9; XXVIIIb, 14688-37-0; XXIXb, 14688-38-1; XXXa, 13528-37-5; XXXb, 13528-36-4.