HETEROCYCLES DERIVED FROM 1,3,2-DIOXAPHOSPHOLENES

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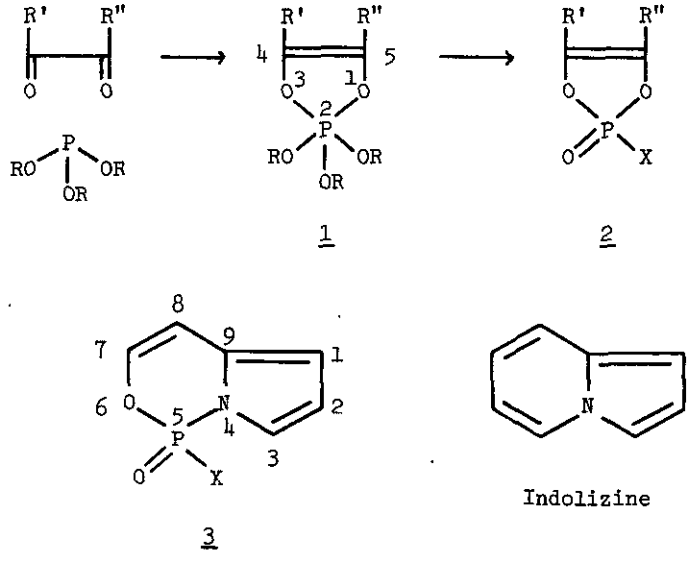
Summary

The 1,3,2-dioxaphospholene ring with pentacoordinate phosphorus is obtained from the reaction of trialkyl phosphites with α-dicarbonyl compounds. The synthetic potential of this ring system is illustrated by a series of reactions which produce 1,3,2-dioxaphospholenes with tetracoordinate phosphorus, other phosphorus-containing heterocycles, e.g., 5-phospha-6-oxa-indolizines, and a series of phosphorus-free heterocycles containing nitrogen, oxygen and sulfur.

Contents

1. Introduction

The five-membered unsaturated ring system containing pentacoordinate phosphorus connected to two oxygen atoms (1, Scheme 1) was discovered by three groups of investigators at about the same time[1-3]. The main route to this heterocycle is the reaction of trialkyl phosphites with α-dicarbonyl compounds, e.g., glyoxal, pyruvaldehyde and biacetyl, which leads to the 2,2,2-trialkoxy-2,2-dihydro-1,3,2-dioxaphospholenes (abbreviated as DOP) in nearly quantitative yield.



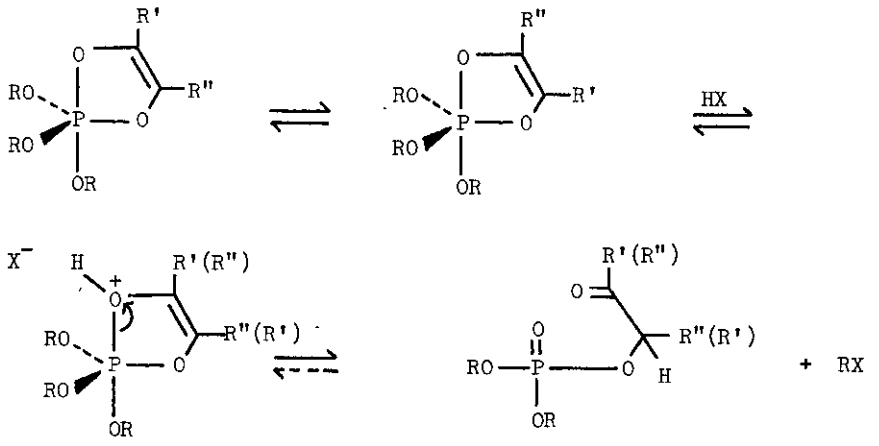
Scheme 1

We were led to the DOP compounds (1) by the discovery that tricoordinate phosphorus has a relatively high affinity for the oxygen atom, rather than the carbon atom, of certain activated carbonyl functions, e.g., those in para- and ortho-quinones[4-7]. This fundamental difference between phosphorus and nitrogen constitutes the basis of many of the synthetically useful reactions of phosphorus compounds.

The 1,3,2-dioxaphospholene ring can also be obtained with tetracoordinate phosphorus, e.g., in 2-alkoxy-2-oxo-2-hydro-1,3,2-dioxaphospholenes (2, X = OR)[8,9]; these compounds are derivatives of the cyclic enediol phosphoryl group, CEP-, and therefore will be abbreviated as CEP-X. Several review articles from this Laboratory have summarized various aspects of the chemistry of DOP[10-16] and CEP-X[17,18] systems, in particular the utilization of the latter in the synthesis of complex biological phosphodiesters, such as oligonucleotides[19] and phospholipids[20], $(R^{I}O)(R^{II}O)P(O)OH$. The present review focuses on two topics: (i) The conversion of certain CEP-X reagents (2) into a new type of phosphorus heterocycle, the 5-phospha-6-oxa-indolizine ring (3). (ii) The utilization of DOP reagents (1) in the synthesis of several of the traditional phosphorus-free heterocycles.

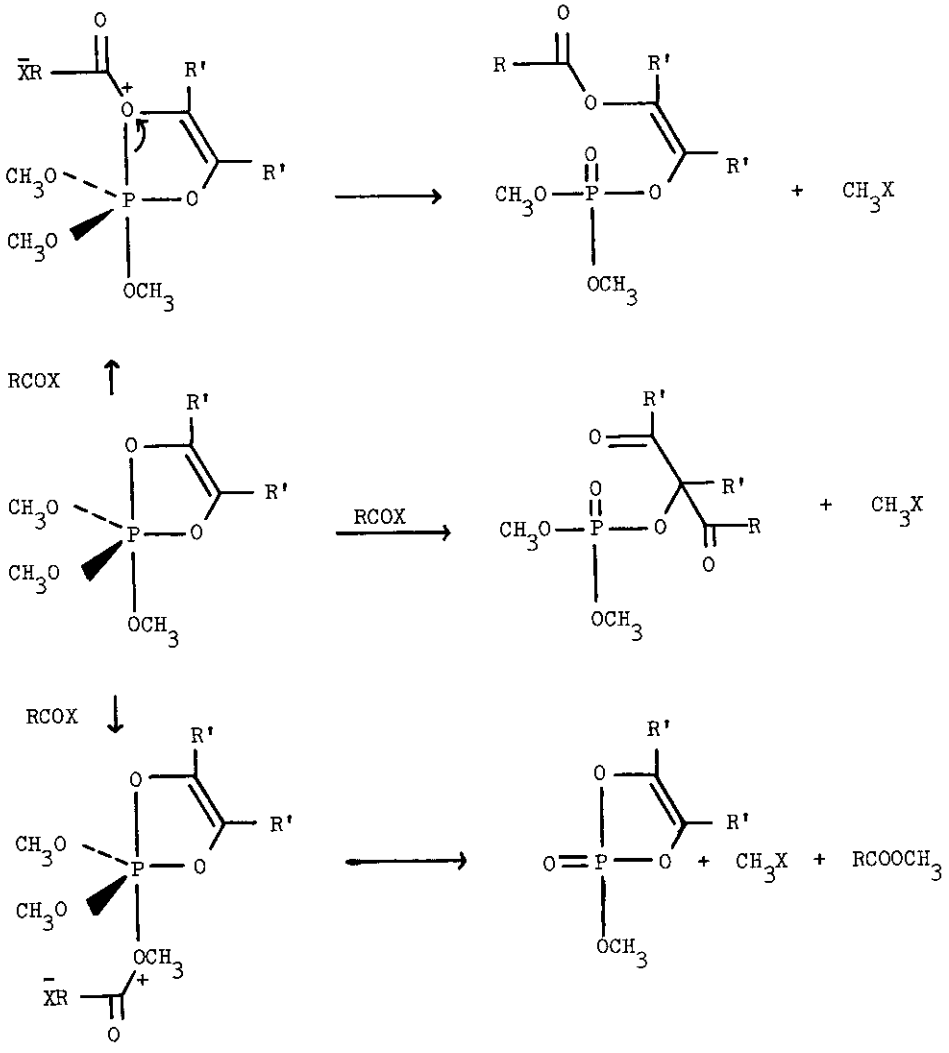
2. Structure and Mechanisms of Reaction of Pentacoordinate 1,3,2-Dioxaphospholenes (DOP).

The molecular structure of DOP (1) is known from x-ray diffraction analysis[21]. The phosphorus atom is at the center of a more or less deformed trigonal bipyramid, which defines two stereoelectronically distinct skeletal sites: two apical and three equatorial positions (Scheme 2). Due to the phenomenon of permutational isomerization[22,23], apical and equatorial groups undergo positional exchange at relatively rapid rate, when the substances are present in the liquid state or in solution. Considerable interest has been aroused by this phenomenon, and two distinct mechanisms have been devised to account for it, namely, pseudorotation[24] and turnstile rotation[25]. These two mechanisms of permutational isomerization differ in the motions performed by the five groups attached to trigonal bipyramidal phosphorus during the isomerization. ^{31}P and ^{1}H NMR spectrometry have been useful tools in the study of such phenomena.



Scheme 2

The DOP derivatives are thermally stable; however, they are quite sensitive to water, and are utilized in aprotic solvents or in the pure liquid state. Anhydrous acids, XH, where the anion X^- has moderate nucleophilicity, convert the DOP ring into α-ketol phosphotriesters (Scheme 2). Theoretical studies have indicated that the lone electron pairs on atoms which occupy equatorial positions in DOP are delocalized into the d-orbitals of pentavalent phosphorus to a greater extent than those of atoms in apical positions. This preferential p-d π-bonding of equatorial ligands suggests the apical oxygen atoms as the site of the DOP protolysis. Thus, ring-opening results from an attack on the apical endocyclic oxygen. The formation of RX, and the enol-keto tautomerization implied in Scheme 2 proceed by well known mechanisms.



Scheme 3

Toward acyl halides, the DOP ring behaves as an ambident nucleophile, with the endo- or exo-cyclic apical oxygens as electron-donors. The course of the reaction is controlled, mainly by steric factors (Scheme 3); e.g., the glyoxal-trimethyl phosphite DOP (R' = H) gives exclusively the product of ring-opening resulting from apical endocyclic O-acylation[26]. However, the picture is more complicated when the apical endocyclic oxygen is shielded by alkyl groups[27]. Table 1 shows that, under certain experimental conditions, namely with a highly reactive acyl halide in a relatively polar aprotic solvent, the biacetyl-trimethyl phosphite DOP gives almost exclusively the product of ring-retention, which results from apical exocyclic O-acylation. This is synthetically useful because CEP-OCH_3 is a practical starting material for the synthesis of a variety of CEP-X reagents.

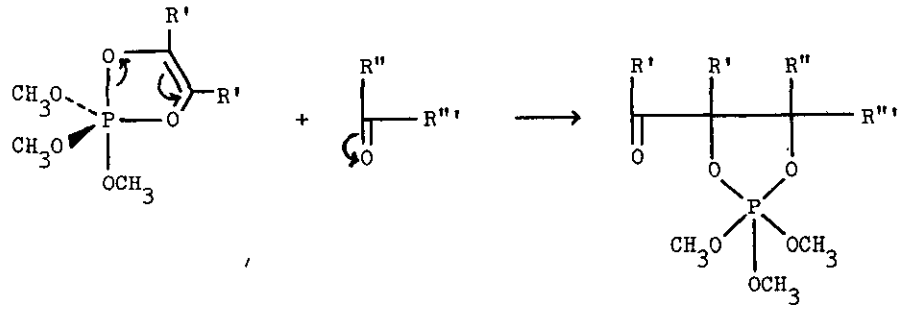
Table 1. Acylation of the Biacetyl-Trimethyl Phosphite 1,3,2-Dioxaphospholene[a]

Exocyclic O-Acylation, %	C-Acylation, %	Acyl Halide	Solvent
95	5	CH_3COBr	Acetonitrile
90	10	CH_3COBr	Dichloromethane
80	20	CH_3COCl	Dichloromethane
75	25	CH_3COBr	None
35	65	CH_3COCl	Acetonitrile
3	97	CH_3COCl	None

[a] Equimolar reagents in 2.7 M solutions, or in the absence of solvent, at 40° C.

Table 1 discloses that, in the absence of solvent, acetyl chloride converts the biacetyl-DOP into the phosphate ester of an α-hydroxy-β-diketone. The reaction mechanism which leads to this interesting result involves a nucleophilic attack by the potential enolate carbanion present in the DOP ring. This new C-acylation reaction is also synthetically useful, as will be shown in another section of this review.

A second manifestation of the carbon-nucleophilicity of DOP reagents leads to the creation of highly functionalized carbon-carbon single bonds (Scheme 4). This dioxaphospholane condensation generates α,β-dihydroxy-carbonyl compounds, e.g., aldehydes, ketones and esters[15]. Moreover, since group R"' in R"COR"' can also be an α-polycarbonyl compound, the resulting saturated 1,3,2-dioxaphospholanes can contain additional carbonyl functions. The reaction, in fact, constitutes a new route to the sugars[28].

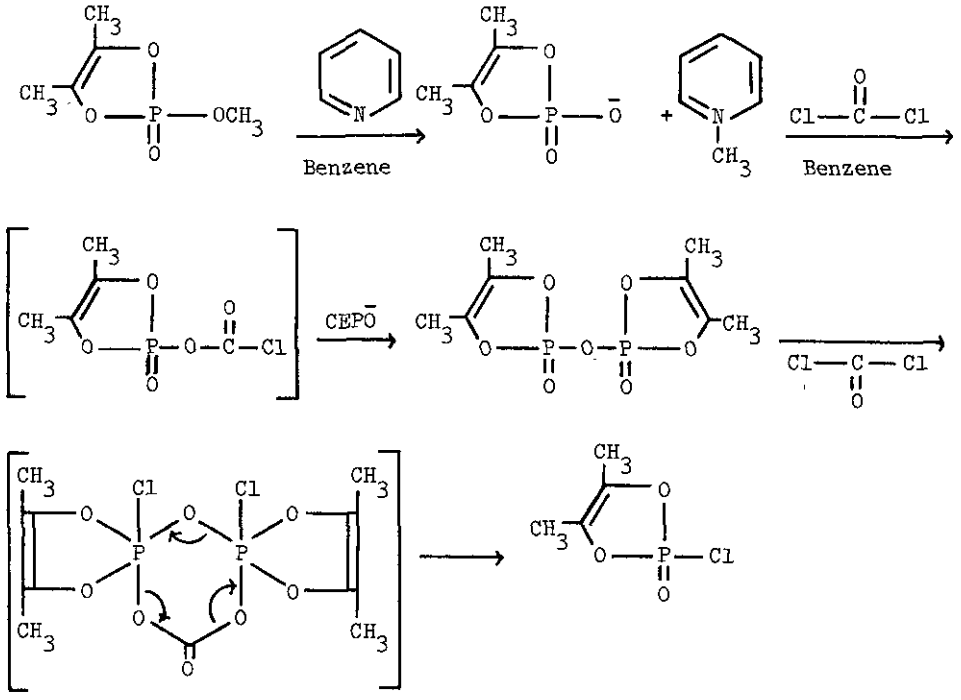


Scheme 4

3. Preparation and Reactions of Tetracoordinate 1,3,2-Dioxaphospholenes.

The CEP-OCH_3 which is readily available from the reaction given in Scheme 3 is used as starting material for the preparation of a variety of CEP-X compounds by the procedure outlined in Scheme 5[18]. Stoichiometric amounts of phosgene at lower temperatures and for limited amounts of time

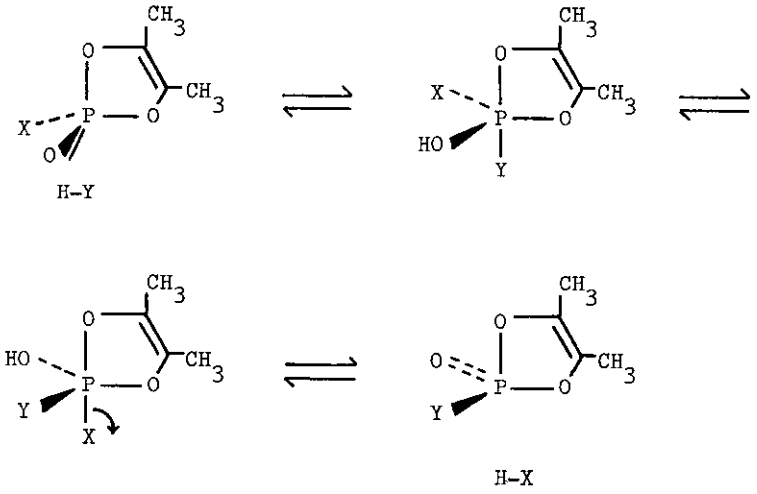
convert the salts of CEPO into the crystalline pyrophosphate, CEP-OCEP, in about 90% yield. Excess of phosgene at 25° for longer periods of time convert the same salts of $CEPO^-$ into the liquid phosphorochloridate, CEP-Cl, in about 90% yield. The phosphorochloridate results from reaction of the pyrophosphate with phosgene.



Scheme 5

CEP-OCEP and CEP-Cl are the prototypes of a family of very high energy phosphates endowed with an extraordinarily high electrophilic reactivity. The kinetic and thermodynamic reasons for the occurrence of rapid nucleophilic displacements with ring-retention at the phosphorus atom of certain CEP-X compounds are now fairly well understood (Scheme 6)[18,29]. The first step of the reaction is the addition of the nucleophile YH to CEP-X to yield an oxyphosphorane intermediate. This step involves relatively small additional

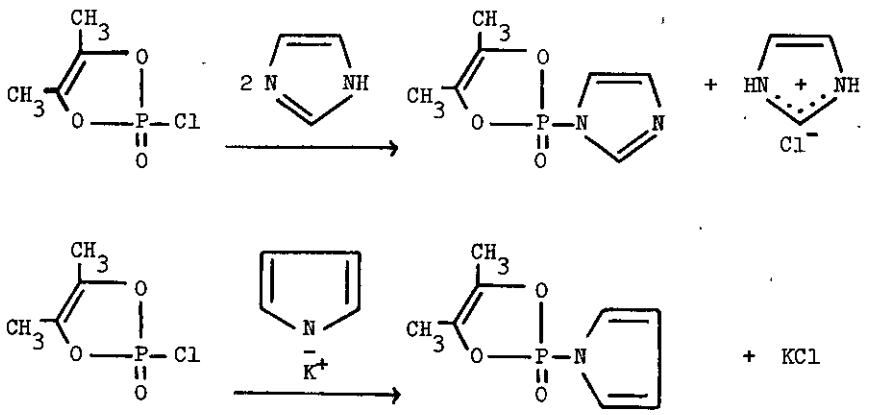
bond angle deformations beyond those already present in the cyclic phosphate. In general, cyclic phosphates are less stable than the corresponding acyclic compounds, mainly because they have more ring-strain[30]. However, the opposite is true among oxyphosphoranes[12-14,31]. Oxyphosphoranes with small and medium size relatively planar rings are more stable than the corresponding acyclic compounds, because trigonal bipyramidal phosphorus is subject to significant intramolecular crowding among its five ligands. The decrease in crowding which results from the introduction of the rings usually outweighs any ring strain associated with bond angle deformations in the cyclic vs the acyclic oxyphosphorane. The extraordinary reactivity of the CEP-X compound is due to these two combined effects: an increase in ground state energy, and a decrease in the energy of the transition state that leads to the oxyphosphorane intermediate, both effects relative to those in the acyclic analogs.



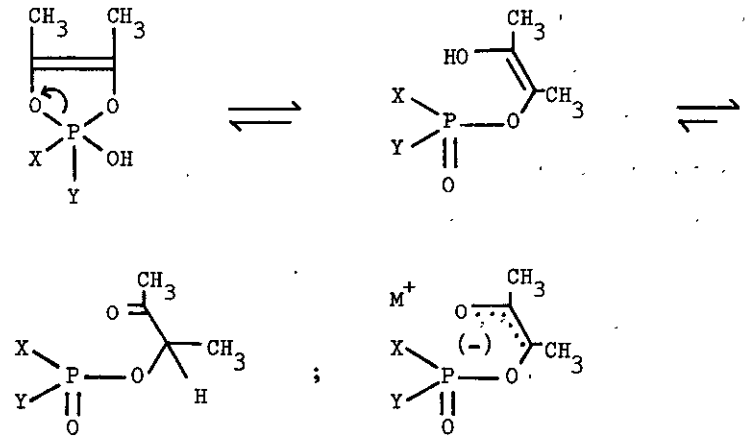
Scheme 6

Permutational isomerization allows for the rapid equilibration among isomers, the equilibrium position being regulated by the relative apicophilicities of groups X vs Y. Apical departure of group X leads to the product of ring-retention, CEP-Y. The rate of elimination of ligand X depends on its nucleofugicity which is related to the usual considerations of stability of X^- as reflected in the pKa of the dissociation equilibrium, $XH \rightleftharpoons X^- + H^+$. The position of the equilibrium: CEP-X + YH $\rightleftharpoons$ CEP-Y + XH depends on the relative energy contents of CEP-X vs CEP-Y and YH vs XH. Control of the equilibrium can be achieved by the addition of bases, B, as a function of the relative acidities of XH vs YH; thus, $XH + B \rightleftharpoons \overset{+}{B}HX^-$ shifts the equilibrium to the right. A variation of this approach consists of the use of a metal salt, such as M^+Y^- as nucleophile. Illustrations of these procedures is given in Scheme 7 which shows the preparation of the N-phosphorylimidazole[18], CEP-imidazole, and the N-phosphorylpyrrole[32], CEP-pyrrole. The structure of these compounds, as well as that of the pyrophosphate, CEP-OCEP, are known from x-ray diffraction analysis[29,33].

In principle, formation of the product of ring-retention in the displacement reaction, CEP-X + YH $\longrightarrow$ CEP-Y + XH, implies that the product of ring-opening (Scheme 8) has a higher energy content than the combination of products, CEP-Y + XH, provided that the various intermediates are in thermodynamic equilibrium. The ring-opening product is indeed a high energy phosphate, as a result of the particular electronic structure of the α-ketol group, as well as of the X and Y groups. Moreover, the formation of CEP-Y can be favored by the shift in equilibrium, $XH + B \longrightarrow \overset{+}{B}HX^-$, mentioned above. The ring-opening product is disfavored by the instability of its enolate metal salt (Scheme 8), relative to M^+X^-, when the nucleophilic reagent employed is the metal salt M^+Y^- (cf. the preparation of CEP-pyrrole).



Scheme 7



Scheme 8

For synthetic purposes, it is convenient to speak of CEPylating reagents, whenever the structure of the CEP-X compound is such that its reactions with nucleophiles, YH, proceed with virtually complete ring-retention. CEPylating reagents transfer the cyclic enediol phosphoryl ring, intact, to the nucleophile YH; thus, CEP-Cl, CEP-OCEP, and CEP-imidazole are reagents of this type since their reactions with most nucleophiles proceed with virtually complete ring-retention:

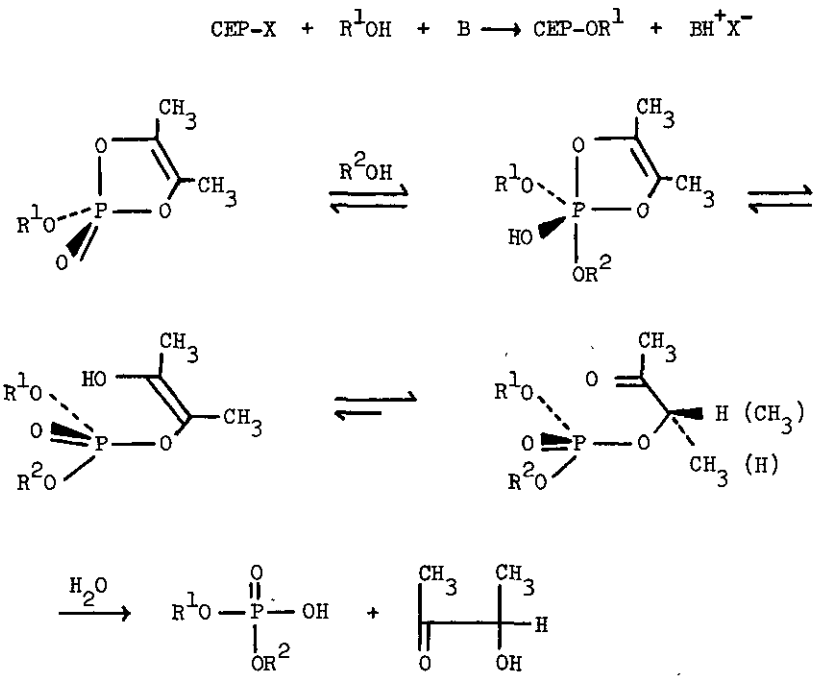
$$\text{CEP-Cl} + \text{ROH} + \text{B} \longrightarrow \text{CEP-OR} + \text{BH}^{+}\text{Cl}^{-}$$

$$\text{CEP-OCEP} + \text{ROH} + \text{B} \longrightarrow \text{CEP-OR} + \text{CEPO}^{-}\text{BH}^{+}$$

$$\text{CEM-IM} + \text{ROH} \longrightarrow \text{CEP-OR} + \text{IMH}$$

In contrast, CEP-PYR is not a CEPylating reagent because its reactions with most nucleophiles proceed with ring-opening, exclusively or predominantly, as will be discussed in a subsequent Section.

The non-CEPylating CEP-X compounds also have a synthetic function. For example, to develop a practical synthesis of unsymmetrical dialkyl phosphates, it is necessary to carry out a nucleophilic displacement on a CEP-OR^1 compound by alcohols, R^2OH, with complete, or nearly complete, ring-opening (Scheme 9). This question has been approached within the mechanistic framework outlined in the preceeding paragraphs, and reasonably satisfactory results have been achieved in this respect with the assistance of catalytic effects by certain tertiary amines, e.g., triethyl amine. The catalysis achieve three highly desirable effects: (i) an increase in the rate of the phosphorylative coupling reaction (Scheme 9); (ii) an increase in the proportion of ring-opening to ring-retention in the coupling; and (iii) an ability to phosphorylate a primary alcohol function in the presence of an unprotected secondary alcohol group. These aspects of 1,3,2-dioxaphospholene chemistry will not be pursued further in the present Review[18].

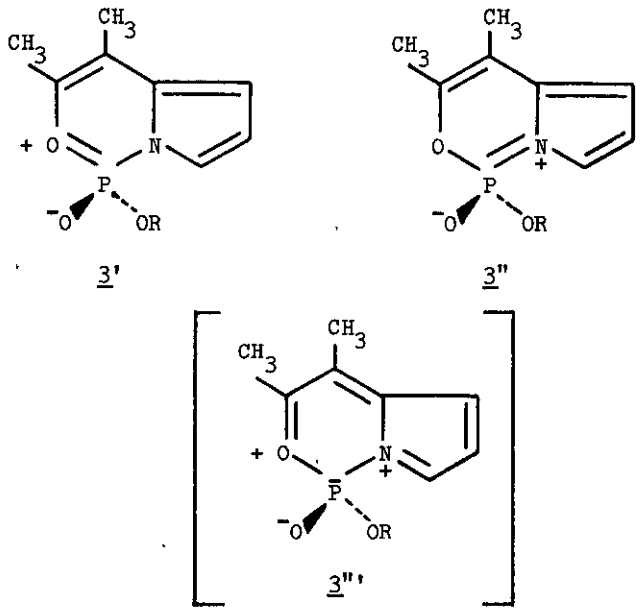


Scheme 9

4. Synthesis and Structure of 5-Phospha-6-oxa-indolizines.

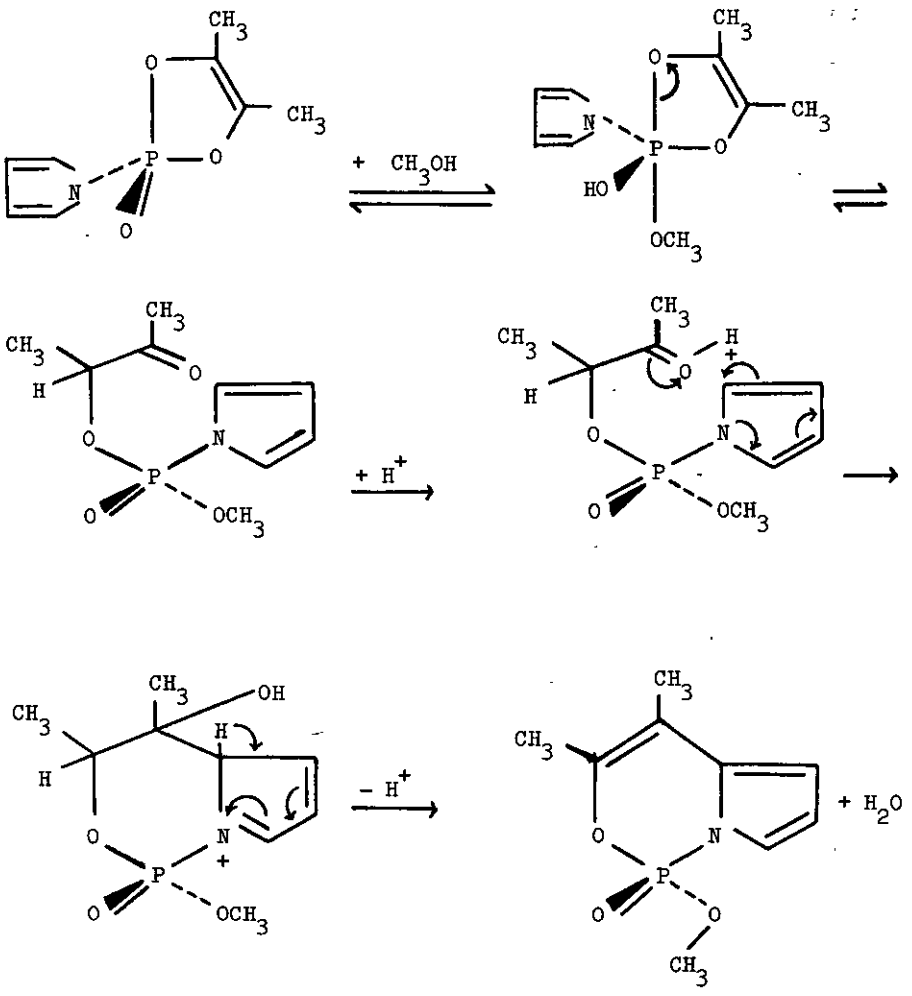
N-(1,2-dimethylethenylenedioxyphosphoryl)pyrrole (CEP-PYR), obtained by the procedure outlined in Scheme 7, provides a route to a new type of phosphorus heterocycle, the 5-phospha-6-oxa-indolizine ring[34,35] (3; abbreviated as POI). This heterocycle arises from the replacement of one of the pairs of sp^2-carbons of indolizine by the -OP- group present in the phosphoramidate function, -OP(O)(OR)N<. The POI ring provides an opportunity to explore the ability of the -O-P=O unit to transmit electronic effects of the type depicted in Scheme 10. Remarkable progress has been made within the last few years in the field of phosphorus heterocycles, in particular in

matters related to electron-delocalization in unsaturated ring systems[36-39]. Thus, it appeared desirable to include analogs of indolizine in such studies.



Scheme 10

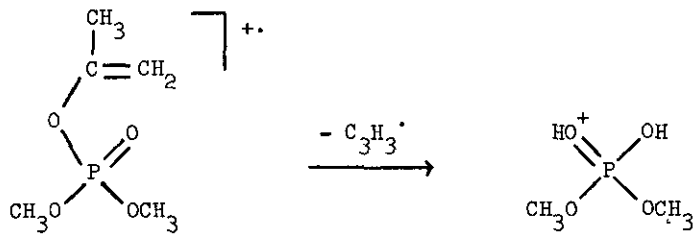
The synthesis of 7,8-dimethyl-5-methoxy-5-oxo-λ^5-5-phospha-6-oxa-indolizine is shown in Scheme 11. CEP-PYR reacts with methanol to produce the two possible diastereomers of N-[methoxy(3-oxo-2-butoxy)phosphoryl]pyrrole in high yield. Both diastereomers of the acyclic phosphoramide are transformed into the POI-derivative under catalysis by hydrogen chloride.



Scheme 11

This procedure rests on the tendency of CEP-PYR to undergo displacements at phosphorus with ring-opening, rather than with ring-retention. In terms of the mechanisms discussed in the previous Section, these results mean that the reaction of CEP-PYR with alcohols follows the pathway in Scheme 8 rather than the pathway in Scheme 6. This surprising difference between CEP-pyrrole and CEP-imidazole (which is a CEPylating reagent) may be the result of one of the following effects, or a combination of both of them: (a) the N-pyrrolyl group has little or no tendency to move from the equatorial to the apical position of the oxyphosphorane intermediate, relative to the methoxy-group; (b) the acyclic phosphoramide is more stable than the products of displacement with ring-retention, i.e., CEP-OCH_3 + pyrrole. It is of interest that this latter reaction does not take place at all, but this may be traced to kinetic rather than thermodynamic considerations, i.e., to a combination of the very poor nucleophilicity of pyrrole, and the moderate electrophilicity of CEP-OCH_3.

Methoxy-POI is a crystalline substance with considerable thermal stability in the liquid and vapor phases, and can be recovered unchanged after distillation in vacuum. The heterocycle, in fact, preserves its integrity under electron-impact, and the most intense peak in its mass spectrum corresponds to m/e 213, i.e., to the molecular ion $[C_9H_{12}O_3NP]^{+\cdot}$. Most of the ion current is carried by this species and by a fragment of it which results from the loss of a methyl radical, m/e 198, $[C_8H_9O_3NP]^{+}$. This spectrum contrasts sharply with that of the acyclic functional analog dimethyl(2-propenyl) phosphate, whose molecular ion undergoes fragmentation as shown in Scheme 12, i.e., with loss of the elements of the methylacetylene radical and formation of protonated dimethyl phosphate.



Scheme 12

The base peak in the mass spectrum of indolizine is also the molecular ion, m/e 117, and its fragmentation occurs by loss of hydrogen cyanide or of acetylene. The mass spectra of polycyclic aromatic and heterocyclic compounds with a methoxy group are characterized by strong parent and parent-CH_3 peaks, without evidence of extensive fragmentation. By these analogies we do not imply that the POI ring possesses "aromatic character", but simply that the ring is preserved as a unit in the vapor phase under electron impact.

Methoxy-POI has strong UV absorption at 269 nm (ε = 30,000, in acetonitrile solution). This is presumably the triene chromophore, and should be compared with the medium intensity band of indolizine in the region of 270-310 nm; however, the latter has also a broad, medium intensity band at 330-360 nm, and an intense band at 225-240 nm, which are absent in methoxy-POI.

The molecular structure of methoxy-POI has been established by x-ray crystallographic techniques[35]. The molecule can be adequately described as being a six-membered cyclic enol phosphoramidate in which the nitrogen function is part of a pyrrole ring. The best least-squares plane in the molecule contains the pyrrole atoms. Good planes are also obtained by inclusion of the phosphorus atom, or the vinyl group atoms C(7) and C(8), in the plane of the pyrrole. However, the endocyclic oxygen atom, O(6),

protrudes from the molecular plane. The six-membered ring is quite irregular, with a relatively small (102°) O-P-N angle, and two larger angles, P-N-C (123°) and P-O-C (125°). On the other hand, the five-membered ring is regular and has all its angles close to 109°.

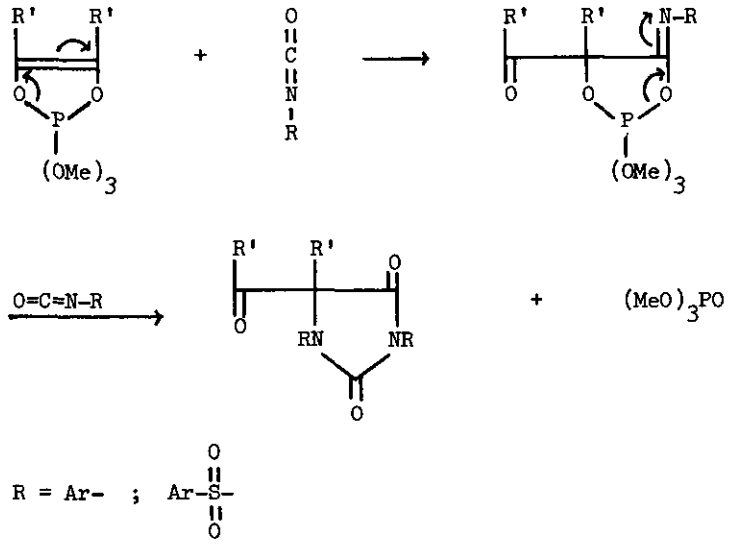
The triene system of methoxy-POI has alternating C-C bond distances of 1.33 and 1.45 Å. Hence, the electron-delocalizations that may exist in the ground state of this molecule, do not appear to extend to this unsaturated system. In other words, formula 3"' is not justified by the x-ray crystallographic analysis. The latter, however, suggests the existence of a modest degree of p-d π-bonding, i.e., delocalization of unshared electron-pairs on oxygen and nitrogen into phosphorus d-orbitals. The observed phosphorus-oxygen bond distances are 1.44 Å (P=O), and 1.57 Å (exo- and endo-cyclic P-O), which are shorter than the estimated pure single P-O distance of 1.76 Å; the phosphorus-nitrogen bond distance of 1.65 Å is also somewhat shorter than the estimated pure P-N value of 1.78 Å. It would appear, then, that formulas 3' and 3" in Scheme 10 are meaningful descriptions of some of the electron-delocalizations which occur in the ground state of the POI ring.

The reaction of CEP-pyrrole with alcohols is quite general, but the reaction rate decreases as the size of the alcohol increases. This effect can be overcome with the aid of imidazole catalysis. This type of catalysis makes it possible to add phenol to CEP-pyrrole and to make the phenoxy-POI derivative. Without imidazole, the reaction does not proceed at a practical rate.

The closest analogy we have found for our synthesis of POI derivatives is the acid-catalyzed cyclization of N-(3-cyanoalkyl)pyrrole[40].

5. Phosphorus-Free Heterocycles From Pentacoordinate 1,3,2-Dioxaphospholenes.

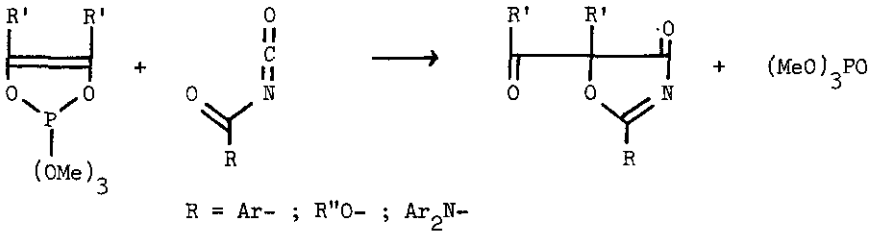
The DOP reagents (1) can be used as starting materials for the synthesis of several of the traditional phosphorus-free heterocycles containing nitrogen, oxygen and sulfur in various combinations[41-46]. The preparation of 5-acylhydantoins from DOP and aryl isocyanates or arylsulfonyl isocyanates is illustrated in Scheme 13. The reaction proceeds in two distinct steps, and the intermediate 4-imino-5-acyl-1,3,2-dioxaphospholene is detectable, but need not be isolated. Yields in these reactions usually exceed 80% of the theoretical value. Isothiocyanates, unlike isocyanates, exhibit little reactivity toward DOP reagents.

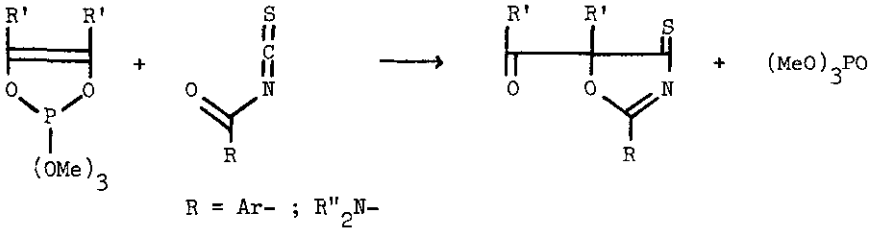


Scheme 13

The reactions of DOP reagents with acylisocyanates, carboalkoxyisocyanates or carbamylisocyanates have a 1:1 stoichiometry and yield the respective 2-substituted 5-acyl-2-oxazolin-4-one ring system (Scheme 14). An analogous reaction with acylisothiocyanates or carbamylisothiocyanates results in the

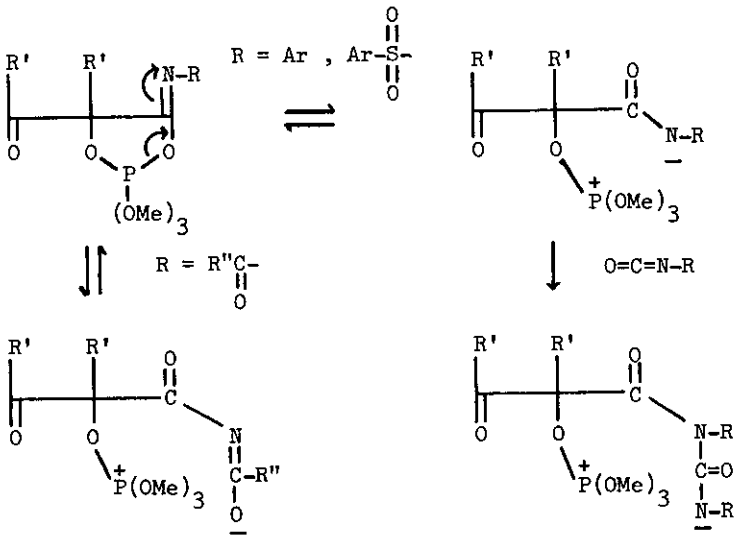
corresponding 5-acyl-2-oxazolin-4-thione ring. These reactions proceed smoothly and in respectable yields. The by-product in all cases is a trialkyl phosphate.



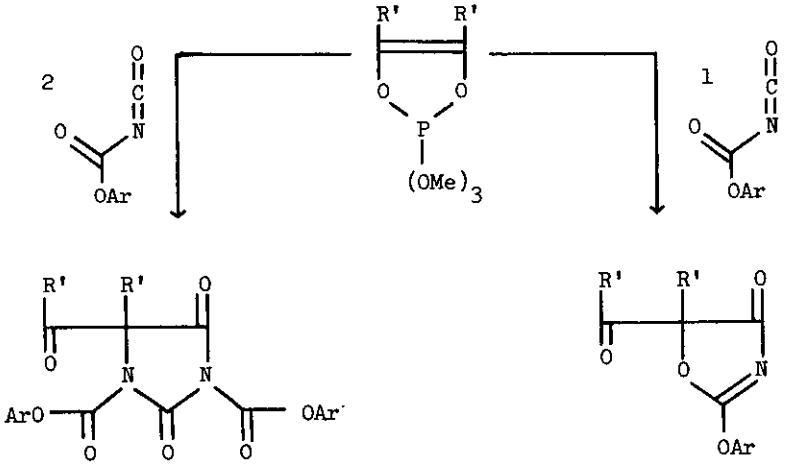


Scheme 14

The key intermediate in the DOP-isocyanate condensation is the iminophospholane (Scheme 15), which can generate a dipolar ambident anion by rupture of a P-O bond. The dipolar anion from a simple arylisocyanate reacts with a second isocyanate molecule by virtue of the nucleophilicity of nitrogen; the resulting 1:2 adduct cyclizes to hydantoin also as a result of a nucleophilic attack by nitrogen. The dipolar anion from an acylisocyanate or related compounds undergoes intramolecular nucleophilic attack by oxygen to give the oxazolone. In both cases, the driving force is the ejection of trialkyl phosphate.



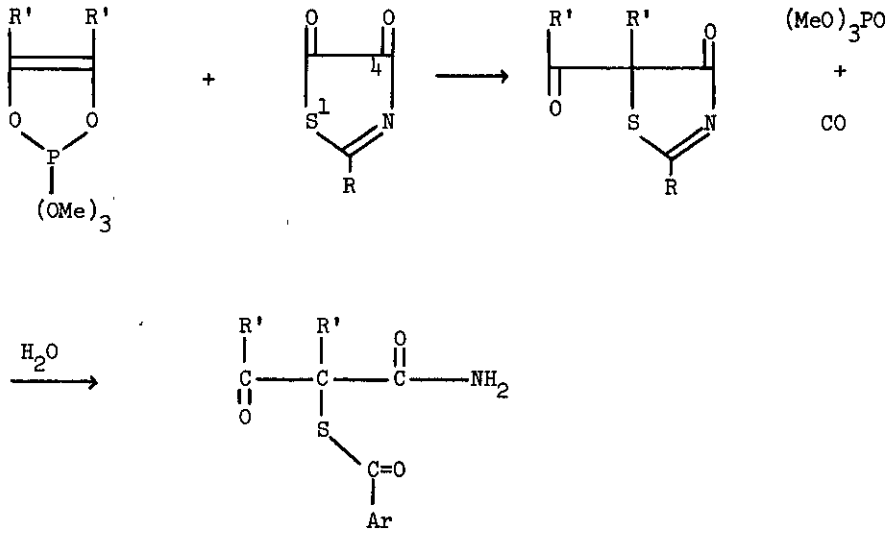
Scheme 15



Scheme 16

The energetics of the two pathways shown in Scheme 15 are quite comparable, as can be shown by suitable alterations in the heterocumulene, e.g., carbophenoxyisocyanate allows the formation of over 50% of hydantoin, or of over 50% of oxazolone, depending on experimental conditions (Scheme 16).

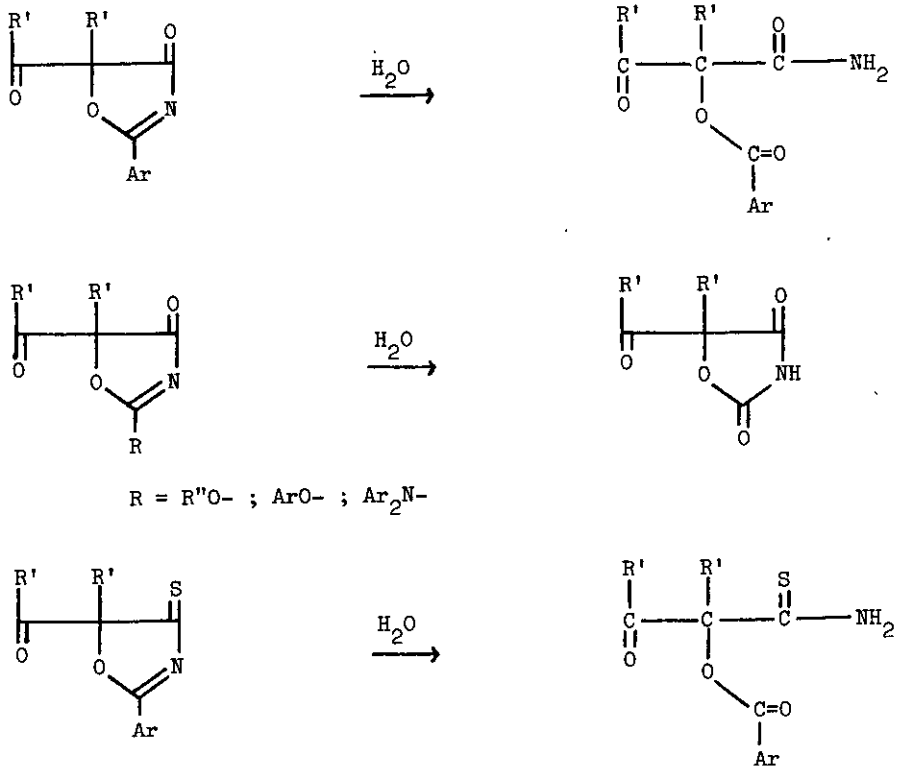
Thioacylisocyanates are extremely unstable compounds, but their precursors, the 2-thiazolin-4,5-diones, are quite stable and easy to make. DOP reagents have the ability to react with the 4-carbonyl group of these diones to produce the 2-substituted 5-acyl-2-thiazolin-4-one ring system (Scheme 17). The hydrolysis of the thiazolone can be controlled to yield the thioester of β-keto-α-mercapto amides.



R = Ar- ; Ar_2N- ; RS-

Scheme 17

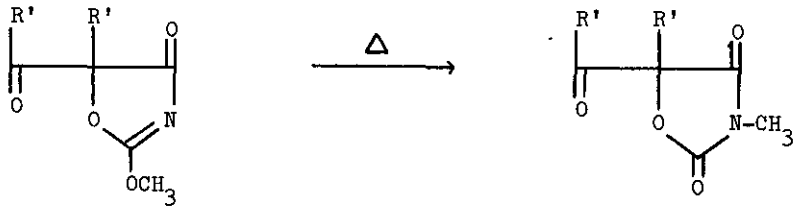
Scheme 18 depicts other types of compounds that can be obtained from the DOP reagents via phosphorus-free heterocycles, e.g., α-hydroxy-β-keto amides, 5-acyl-2,4-oxazolidindiones, and β-keto-α-hydroxy thioamides.



R = R"O- ; ArO- ; Ar_2N-

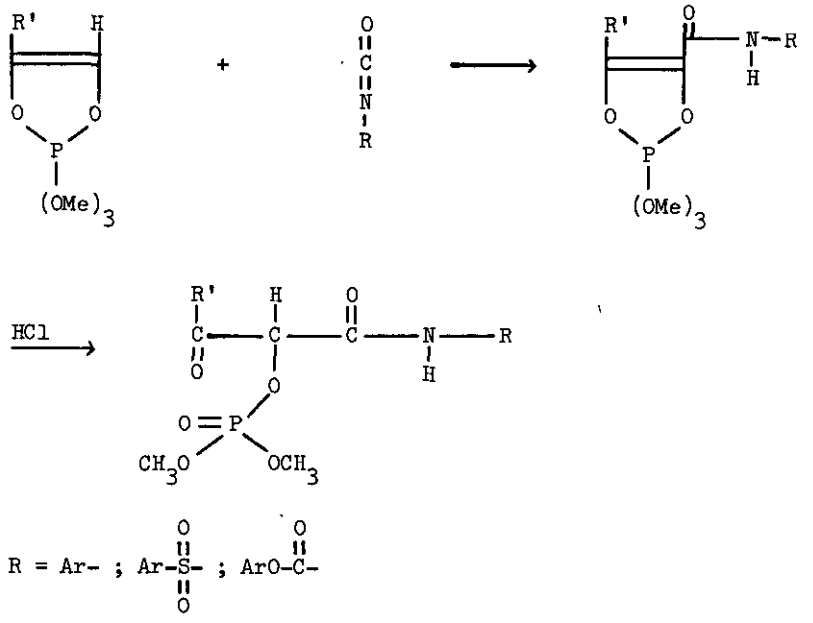
Scheme 18

2-Methoxy-2-oxazolin-4-one undergoes a facile thermal O → N alkyl migration, to give 3-methyl-oxazolidin-2,4-dione (Scheme 19). This reaction is related to the Chapman rearrangement of O-alkyl imino carboxylates to N,N-disubstituted amides.



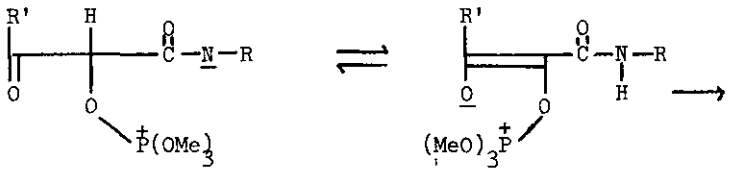
Scheme 19

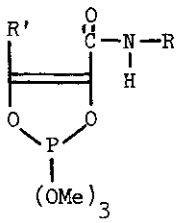
An interesting variation of the DOP-isocyanate condensation is observed when the DOP reagent carries a hydrogen atom on the ring-carbon (Scheme 20). The pyruvaldehyde-DOP ($R^1 = CH_3$) reacts with various types of isocyanates to give 4-carbamyl-1,3,2-dioxaphospholenes. This reaction amounts to the intercalation of the isocyanate molecule at the C-H bond. The carbamyl-DOP compounds are useful reagents in their own right; e.g., they yield phosphate esters of β-keto-α-hydroxyamides.

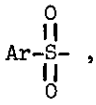
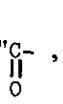


Scheme 20

The behavior of the pyruvaldehyde-DOP is reasonable in the light of the previous discussion. Scheme 21 shows that the postulated dipolar ambident anion obtained from the observed iminophospholane should undergo a proton-shift from the activated α-carbon to the basic anion. The resulting enolate anion cyclizes to the observed iminophospholane.



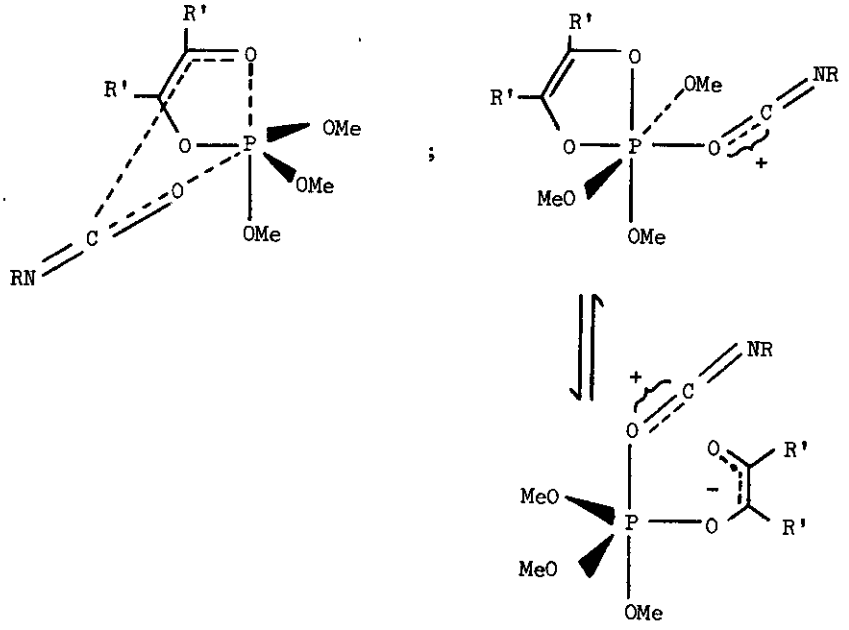


Scheme 21 R = Ar ,  ,  , ...

These C-C condensations of the DOP heterocycle are not simple 1,3-dipolar additions. There is no evidence that, in the liquid state or in solutions, the DOP reagents exist in equilibrium with dipolar structures under the conditions of the condensation reactions (Scheme 22). The physical properties of the DOP reagents are clearly those of compounds with pentacoordinate phosphorus. The reactions proceed best in aprotic solvents of relatively low polarity. Additions of the carbon of DOP to α,β-unsaturated carbonyl compounds, e.g., acrolein and p-benzoquinone are of the 1,2-type and not of the 1,4-conjugate addition type. Carbanion addition to structure $C_6H_5CO.COCH_3$ is at the benzoyl and not the acetyl carbonyl-carbon. It is, of

course, possible that the reaction proceeds via undetectably small amounts of the dipolar form of the DOP (Scheme 22). However, more subtle mechanisms, made possible by the nature of pentacoordinate phosphorus, are probably involved.

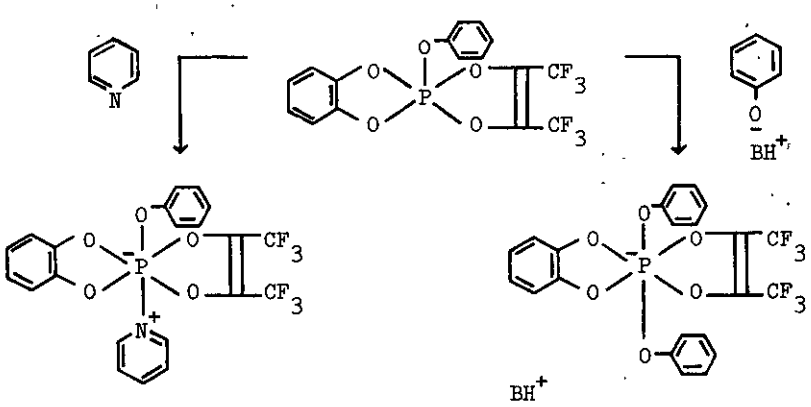
Scheme 22



Scheme 23

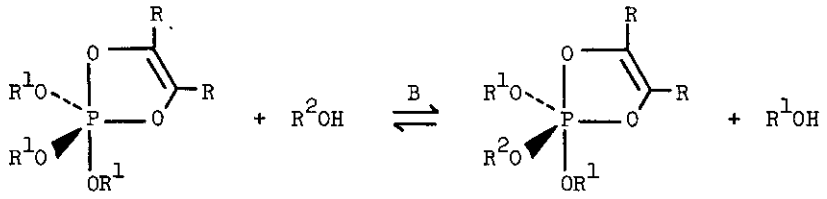
Two alternate ways of bringing together the DOP reagent and the carbonyl compound, i.e., aldehyde, ketone, isocyanate, acyl halide, etc., are illustrated in Scheme 23, with the isocyanate as an example. One formula represents a concerted one-step mechanism. The other two formulas correspond to a non-concerted mechanism, which involves hexacoordinate phosphorus. These alternatives differ, essentially, in the sequence by which the new C-C and P-O bonds of the first observable intermediate are created. It is conceivable that both mechanisms may be operative in different types of DOP-reagents. Evidently, the concerted mechanism may vary in degrees of bond-ruptures and bond-formations, as has been assumed for years in organic reaction mechanisms in general.

The possible intervention of hexacoordinate phosphorus in condensation reactions of DOP-reagents must be considered, in view of the observed interactions of oxyphosphoranes with nucleophiles (Scheme 24)[47]. Oxyphosphoranes are, indeed, electrophilic at phosphorus, and complexes with pyridine and phenoxide ions have been isolated and fully characterized by various techniques including x-ray crystallographic analysis[48].



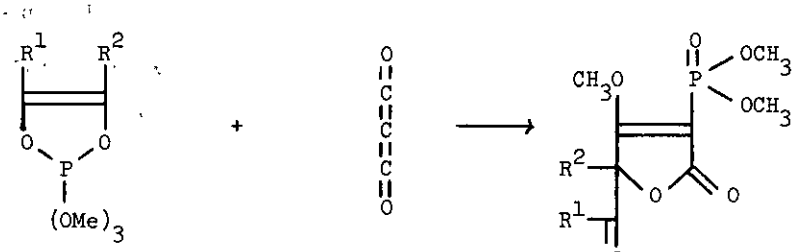
Scheme 24

The facile base-catalyzed exchange of alkoxy ligands in DOP (Scheme 25) has been attributed to phosphorus electrophilicity and the formation of intermediates with hexacoordinate phosphorus[49].



Scheme 25

A final example of the formation of heterocycles from DOP reagents is shown in Scheme 26. DOP reagents of both types, with and without hydrogen atoms on the ring react with the heterocumulene carbon suboxide to give a furan derivative[50]. A mechanism for the formation of the γ-acyl-$\Delta^{\alpha,\beta}$-butenolide has been proposed.



$R^1 = R^2 = Alkyl$

$R^1 = Alkyl$; $R^2 = H$

Scheme 26

Acknowledgments. This article is dedicated to Professor Tetsuo Nozoe on his 77th birthday. The research summarized here has been supported by Grants from the U.S.A. National Science Foundation and National Institutes of Health. Acknowledgment is also made to the Donors of the Petroleum Research Fund administered by the American Chemical Society.

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