SYNTHETIC APPLICATIONS OF DIMETHYL ACETYLENEDICARBOXYLATE IN PHOSPHORUS
HETEROCYCLIC CHEMISTRY

Alan N. Hughes

Department of Chemistry, Lakehead University, Thunder Bay, Ontario, Canada
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Abstract: The reactions of tertiary phosphorus compounds with dimethyl acet-
ylenedicarboxylate and, on occasion, other acetylenic systems are discussed
with emphasis upon the synthesis of phosphorus heterocycles. The discussion
is divided into two sections. The first section surveys the reactions of
open-chain tertiary phosphines, bis-phosphines and vinylphosphines with acet-
ylenic systems while the second section is concerned with similar reactions
of cyclic phosphines with these alkyne derivatives. Both sections record
syntheses of novel heterocyclic systems which, for the most part, are inac-
cessible by more conventional routes.

INTRODUCTION

Dimethyl acetylenedicarboxylate is a versatile and readily available electrophile which
has played a role of considerable importance in the chemistry of nitrogen heterocyclic compounds[1,2]
Phosphorus in tertiary phosphines, like nitrogen in amines, is a reasonably good nucleophile in
many instances and one might expect reactions between dimethyl acetylenedicarboxylate and either
phosphines or phosphorus heterocycles to lead to synthetically interesting products by mechanisti-
cally interesting pathways. This is indeed the case but there are some important differences be-
tween the chemistry of nitrogen and phosphorus compounds in this context as outlined below.

For example, although phosphorus has an outer shell electronic configuration similar to
that of nitrogen, by using its normally vacant but accessible 3d orbitals, it is capable of val-
ence shell expansion and a change of oxidation state to give both four-coordinate and five-coor-
dinate, five-valent phosphorus compounds as well as a range of compound types which parallel those
of nitrogen. In addition, the chemistry of phosphorus-carbon heterocycles in general and the
phosphorus analogues of pyrrole (phosphole) and pyridine (λ^3- and λ^5-phosphorin) in particular re-
mained relatively undeveloped until very recently and systematic studies of these systems began
only about twenty years ago. Thus, much less is known about these systems than the corresponding
nitrogen systems. Furthermore, while the non-bonding electron pair of the nitrogen atom in the
various types of amine and nitrogen heterocycle is apparently almost always in the highest occu-

pied molecular orbital, this is not necessarily the case in phosphorus heterocycles such as the phosphorus analogues of pyridine.[3]

Next, there are significant hybridization and other electronic differences between three-coordinate nitrogen and phosphorus compounds. Thus, while the nitrogen atom in ammonia is close to sp^3 hybridized, with a bond angle of about 107^0, the phosphorus atom in phosphine (PH_3) behaves as if it is essentially unhybridized with a bond angle of only 93.5^0.[4] Even trialkylphosphines have bond angles at the phosphorus atom of only about 100^0 and some degree of rehybridization is therefore required when the phosphorus atom acts as a nucleophile. Also, while the lone pair in conjugated unsaturated nitrogen compounds, particularly aryl amines, is often extensively delocalized, such delocalization is usually negligible in the corresponding phosphines although there are some notable exceptions to this which will be touched upon later. Finally, simple amines normally have very low pyramidal inversion barriers while tertiary phosphines have inversion barriers which are generally over 30 kcal/mol.

It is apparent then from the differences noted above that while three-coordinate phosphorus compounds (open chain and heterocyclic) could be expected to react in many instances with dimethyl acetylenedicarboxylate, it is most unlikely that the reactions would parallel those of the corresponding nitrogen compounds.

Reactions of nitrogen heterocycles with dimethyl acetylenedicarboxylate and related acetylenic systems have been studied very thoroughly.[1,2] However, while similar reactions with phosphines and phosphorus heterocycles have received much less attention, it is already apparent that such reactions lead to a wide variety of structural types (often heterocyclic in nature) by mechanistically unusual pathways. It is the purpose of this brief review, therefore, to summarize these studies in the context of phosphorus heterocyclic chemistry. The investigations fall conveniently into two sections - i.e., reactions of phosphines with dimethyl acetylenedicarboxylate which produce phosphorus heterocycles and reactions of phosphorus heterocycles themselves with the acetylenic ester. From time to time, reactions with other acetylenic systems will be discussed to illustrate particular points. It should perhaps also be mentioned that a much more general review of early studies of the reactions of tertiary phosphorus compounds with electrophilic olefins and acetylenes appeared in 1972[5] as did a more specialized review on cyclic phosphonium ylids.[6]

Finally, while several of the papers reviewed here were published some years ago, phosphorus heterocyclic chemistry has deveoped very rapidly during recent years[7-11] and renewed activity in this area of phosphorus heterocycle-acetylenic ester reactions is to be expected in the near future. A review at this time is therefore considered to be desirable.
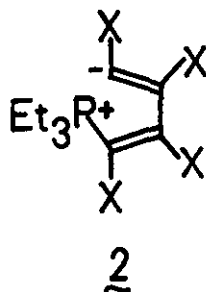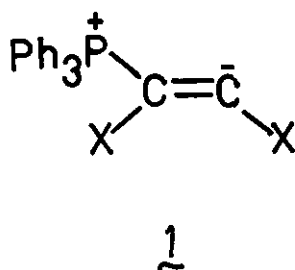
REACTIONS OF SIMPLE PHOSPHINES WITH DIMETHYL ACETYLENEDICARBOXYLATE

Several studies of the reactions of simple phosphines, such as triphenylphosphine, with

dimethyl acetylenedicarboxylate have been made - mainly by Tebby's group. The type of product obtained depends critically upon the reactant ratios and the temperature at which the reaction is carried out and, although the final product is an ylid or bis-ylid, phosphorus heterocyclic ylids are obtained only under certain conditions. It should also be noted at the outset of this discussion that several incorrect structure assignments of the products of various reactions of this type were made in the early studies in the area. Indeed, it was not until it was recognized that these reactions almost always give ylidic products or intermediates and that products containing five-coordinate phosphorus are rarities and are, at best, transient intermediates in some of the reactions that structure assignments became much less speculative. The work of Tebby's group[12] and others[13,14] on the identification and characterization of carbonyl stabilized ylids by ir[12,13] and variable temperature nmr[12-14] methods (which demonstrate the slow rotation of the carbonyl-containing function about the bond linking the carbonyl group to the ylidic carbon atom) was particularly useful in this respect.
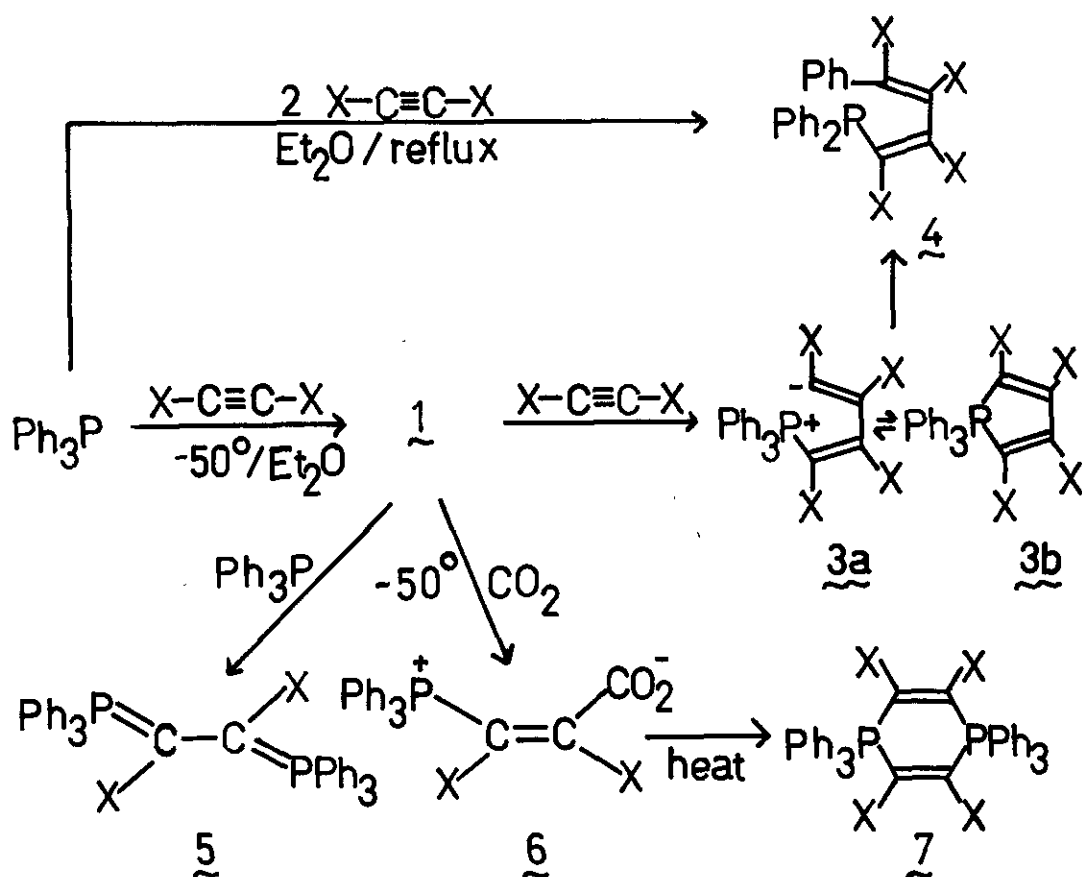
The very early work in this area will be summarized rather briefly here since it has been reviewed much earlier elsewhere[5,6] (from a somewhat different viewpoint) and because many of the reactions of this type initially studied, despite the early conclusions, do not lead to phosphorus heterocycles or involve such heterocycles as intermediates. Nevertheless, these reactions provide structural and mechanistic information which has been of great value in later work involving phosphorus heterocycles.

The first report of reactions between tertiary phosphines and dimethyl acetylenedicarboxylate was made by Horner and Hoffmann.[15] They stated that triphenylphosphine reacts with the acetylenic ester to give the very water-sensitive 1:1 zwitterionic adduct (1) (a result which could not be duplicated by later workers) while triethylphosphine was reported to give the 1:2 adduct (2). Few details were given in this paper but, very shortly after this, both Johnson

1

2

X = CO$_2$Me in all structures

and Tebby[16] and Hendrickson's group[17] carried out similar studies which were reported in considerably more detail. The paper by Johnson and Tebby[16], though relatively short, is of considerable interest for two reasons. First, it showed how the reaction pathway is critically dependent upon reaction conditions such as reactant ratios and temperature. Second, a number of incorrect structure assignments were made for the reasons outlined in the introduction to this review. The preliminary observations and conclusions of Johnson and Tebby[16] are summarized in the reaction scheme below:
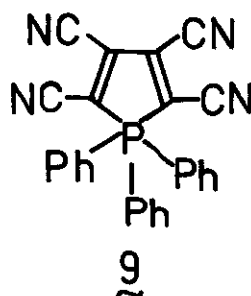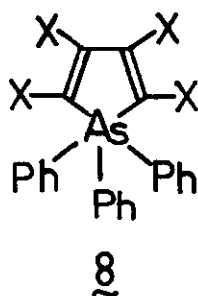

Hendrickson et al.[17a] stated shortly after this that they too had prepared the yellow, unstable phosphole (3a $\rightleftharpoons$ 3b) and the yellow, stable rearrangement product (4) by the same route. In addition, they claimed to have made the corresponding 1,1,1-triphenylarsole (8) as colourless crystals (stable at room temperature) by a similar method although the reaction only occurred at room temperature over several days. They, however, preferred the pentacovalent formulation (3b) for the unstable phosphole, mainly on the basis of its physical properties and its behaviour on

treatment with HCℓ (causing rearrangement to (4) rather than protonation of (3a). On the other hand, Johnson and Tebby[16] preferred the zwitterionic formulation (3a) on the grounds that this provided a driving force for phenyl migration to give (4) even though a 1,2 migration might be considered more reasonable than a 1,5 migration. The structure of the compound formulated as (4) was assigned mainly on the grounds that oxidation with hydrogen peroxide in acetic acid gave both diphenylphosphinic acid and benzoic acid.

Pentacovalent phospholes and arsoles and related pentacovalent phosphorus heterocycles such as (7) therefore seemed relatively readily available by this type of reaction and this conclusion was reinforced by a report by Reddy and Weis[18] in 1963 that dicyanoacetylene reacts with triphenylphosphine in acetonitrile at 25° to give an orange 2:1 adduct tentatively identified[18] as the pentacovalent phosphole (9).
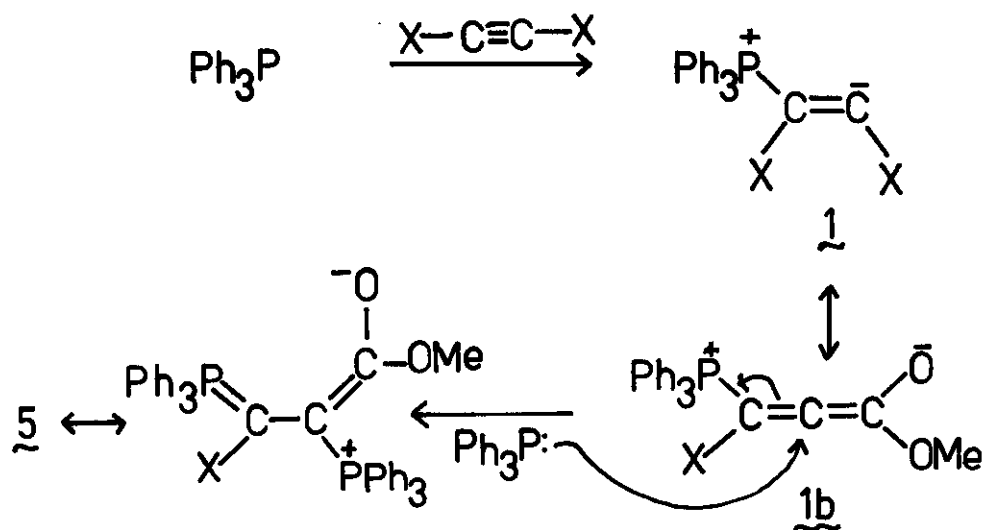
Rather interestingly, it was shown later in a series of studies spanning almost a decade that, while structures (5) and (6) are correct and (3b) is in a sense correct in that it is an intermediate in these reactions, the tentatively assigned structures (7), (8) and (9) are not, in fact, heterocyclic whereas the product formulated as the open-chain structure (4) is a

phosphorus heterocycle. Furthermore, it has also been shown that there are additional intermediates and products in the reactions of triphenylphosphine with the acetylenic ester and the mechanisms of the various reactions and transformations have been established beyond reasonable doubt.
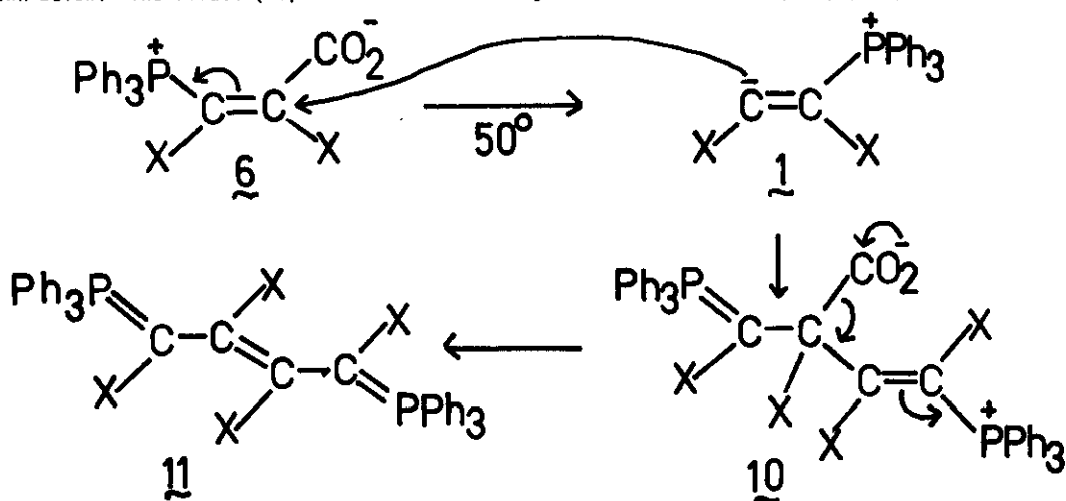
Dealing first with the triphenylphosphine-acetylenic ester reactions, Tebby et al. confirmed[19] the structure of the 2:1 adduct (5), mainly by ir and variable-temperature nmr measurements (which demonstrate the carbonyl-stabilized ylidic nature of the system) and by chemical degradation. This compound is not of particular importance in the context of the present discussion but its probable mode of formation ((1)↔(1b)→(5)) is of interest since

mechanisms of this type, which can be regarded in a sense as nucleophilic attack upon a vinyl-
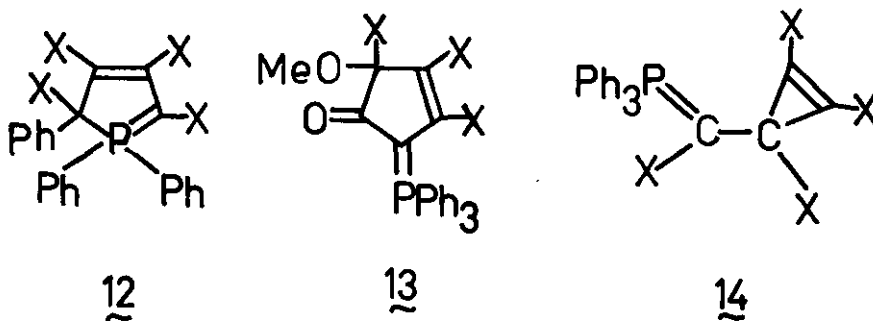

phosphonium system, are quite common in phosphine-acetylenic ester reactions. Indeed, many such reactions yield quite novel phosphorus heterocycles as will be seen later.

By similar methods and also by potentiometric titration, formation of a bis-perchlorate and ^{31}P nmr chemical shift measurements, Tebby et al. also showed[20] that the 2:2 adduct origi- nally[16] assumed to be the pentacovalent phosphorus heterocycle (7) is, in fact, the open-chain bis-ylid (11) which is probably formed by a mechanism similar to that outlined above and as shown below. The adduct (11) can also be formed by direct action of triphenylphosphine upon

the acetylenic ester under certain circumstances.

The next such structure revision was that of the product originally[16] assigned the open-chain phosphine structure (4) and was also carried out by Tebby's group.[21] Using methods similar to those outlined for the other adducts discussed above, Tebby *et al*. showed that the structure of the adduct is, in fact, the 2H-phosphole structure (12) - *i.e.* it is yet another ylidic structure. Clearly, ylidic products are strongly favoured in these reactions and, equally clearly, the pentacovalent phosphole structure (3b) is a probable immediate precursor of
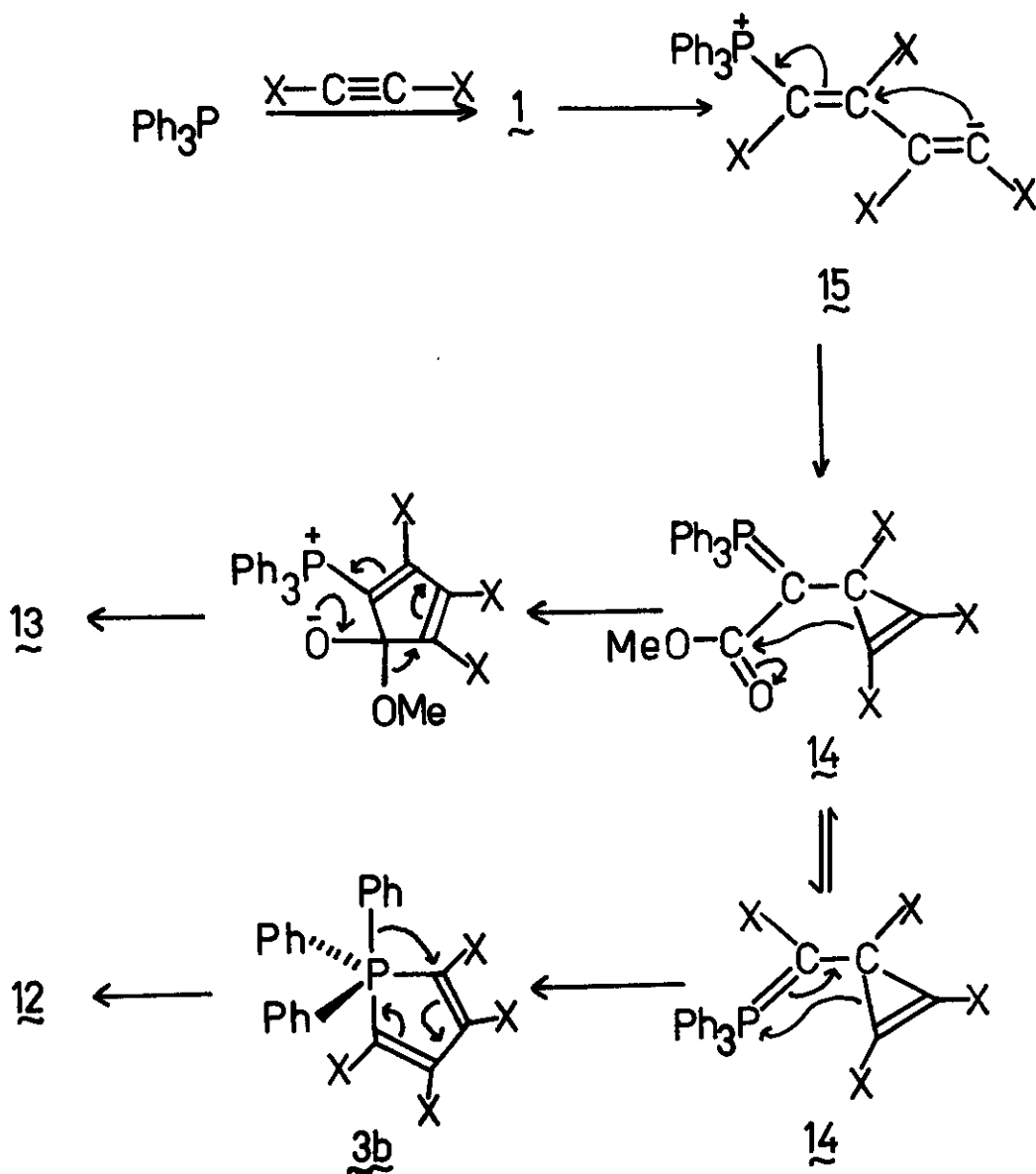

the 2H-phosphole (12) since formation of (12) from (3b) requires only a 1,2-phenyl shift. As will be seen later, this 1,2-shift in a five-coordinate, trigonal bipyramidal phosphorus structure is a common (and synthetically very useful) reaction in phosphorus heterocyclic chemistry. Thus, the original tentative assignments[16,17] of the structure (3b) to the unstable 1:2 adduct of the phosphine with the ester formed at -50° would, at this stage, appear to be reasonable.

Shortly after the structure reassignment discussed immediately above, Tebby's group[22] isolated yet another 1:2 adduct of the phosphine with the acetylenic ester (not previously isolated because of its great solubility in methanol) which is isomeric with the 2H-phosphole (12) and which, as will be seen shortly, is formed from the same precursor. The cyclic, but not heterocyclic, structure (13) was assigned to this adduct on the basis of the usual chemical and spectroscopic evidence and the structure was confirmed by an X-ray crystallographic study.[23]

In a final paper on the triphenylphosphine-dimethyl acetylenedicarboxylate system, Tebby *et al*.[24] carried out a detailed study aimed at determining the nature of the unstable 1:2 adduct of the phosphine with the ester formed at -50° which, to this point, had been assumed to be the pentacovalent 1,1,1-triphenylphosphole (3b). This study showed that, while the pentacovalent phosphole (3b) is involved as a transient intermediate in the formation of the 2H-phosphole (12), the unstable adduct which can actually be isolated at -50° has the unexpected cyclopropenyl-phosphonium ylid structure (14). The arguments leading to the assignment of this structure are outside the scope of this review and are well set out in the original paper.[24] However, it is clear that, in the reactions of triphenylphosphine with the acetylenic ester, at least five (two

stable, one unstable but isolable, and two transient) 1:2 adducts are formed. The various inter-
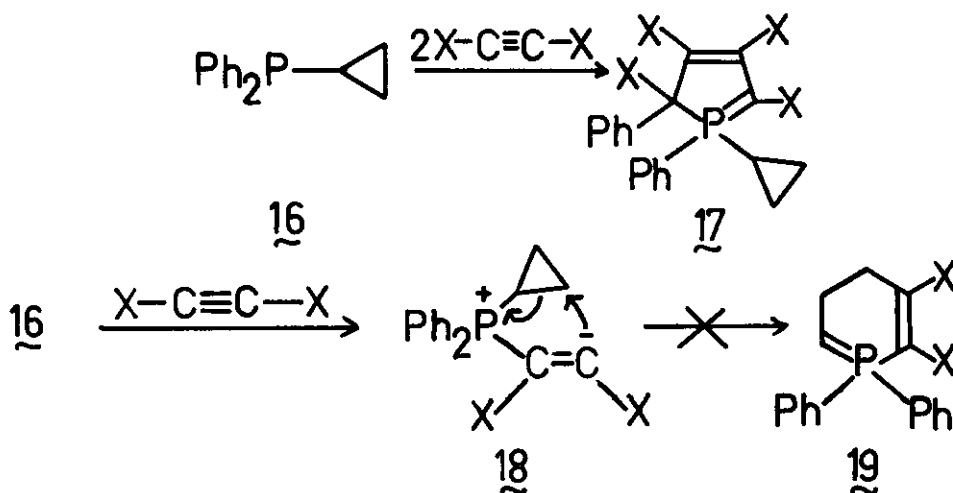conversions leading to the formation of the two stable adducts (12) and (13) are outlined below.

It should be noted that the transient intermediate (15) is merely a transoid version of
the zwitterionic structure (3a) originally proposed[16] for the unstable intermediate isolable at
-50° and now known to be (14).

This last study established a number of other important points. For example, whether
one obtains the 2H-phosphole (12) or the phosphorane (13) depends merely upon conformational

changes in (14). Furthermore, the reaction is not limited to triphenylphosphine since tri-p-tolylphosphine, diphenyl-p-chlorophosphine, diphenylanisylphosphine, and diphenyl-p-tolylphosphine all react with the ester to give 2H-phospholes. Moreover, the results obtained with the last three of the above-mentioned phosphines showed that the ease of aryl group migration is in the order p-chlorophenyl>phenyl> p-tolyl>anisyl - i.e. migration is easier for groups with better stabilization of negative charge. This is consistent with migration from an apical position of a trigonal bipyramidal phosphorus atom.

The mechanism shown earlier indicates that aryl migration in (3b) to give (12) is an intramolecular process. This was confirmed[24] by carrying out reactions using mixtures of triphenylphosphine and tri-p-tolylphosphine with the acetylenic ester. Mass spectrometric analysis of the 2H-phosphole fraction of the products showed the presence of only the triphenyl- or tri-p-tolyl- products. No mixed phenyl-p-tolyl- product was detectable. Finally, migration of the various aryl groups noted above occurs with retention of orientation - i.e. p-tolyl- remained p-tolyl- after migration. All of this information then is consistent with intramolecular migration of an aryl group from an apical position of a trigonal bipyramidal phosphorus atom of a transient intermediate, such as (3b), to an adjacent equatorial carbon atom by a process involving the development of at least a partial negative charge upon the migrating group. Presumably, much of the driving force for the rearrangement comes from the formation of the carbonyl-stabilized ylidic product (e.g. 12).

Before leaving this series of studies, it is worth noting that cyclopropyldiphenyl-phosphine (16) reacts[25] with the acetylenic ester in a manner similar to that of triphenyl-phosphine as shown in the sequence (16)→(17). It had been thought possible[25] at the time this
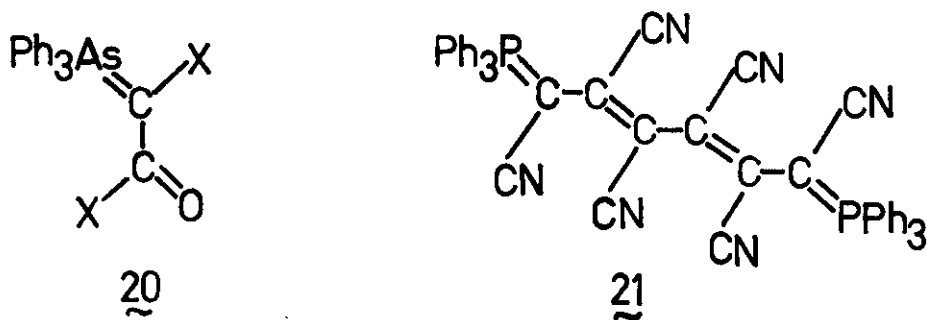

reaction was carried out that generation of the zwitterion (18) would polarize the C-C bonds of

the cyclopropyl group and formation of the six-membered but unstabilized cyclic ylid (19). It appears, however, that formation of the stabilized ylid (17) is still the favoured reaction pathway.

From the preceding discussion, it is very clear that, at least in the case of triarylphosphines and dimethyl acetylenedicarboxylate, phosphorus heterocycles are formed only under certain conditions and heterocycles containing five-coordinate phosphorus exist, at best, only as transient intermediates in these reactions. This, of course, suggests that the proposed 1,1,1-triphenylarsole and 1,1,1-triphenylphosphole structures (8) and (9) could bear reexamination. It should be borne in mind at this point that, although many of the original structure assignments in the triphenylphosphine-acetylenic ester reactions were incorrect, the actual structures are, in all cases, isomeric with those originally proposed. This is not the case with either of the adducts formulated as (8) and (9).

Thus, Hendrickson's group showed [17b] that the product of the slow reaction of triphenylarsine with dimethyl acetylenedicarboxylate in ether is, in fact, an adduct of triphenylarsine, one molecule of the ester and an oxygen atom apparently derived from water. On the basis of a variety of chemical and physical evidence, the highly stabilized arsonium ylid structure (20) was proposed for the adduct.
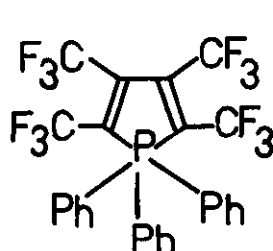

The mechanism for the formation of (20) is obscure. One piece of mechanistic evidence is that in the reaction of the arsine with the ester to give (20), dimethyl fumarate is also a major product. Thus, as one molecule of the ester is consumed to give (20), another is reduced to dimethyl fumarate thereby also consuming one molecule of water. One is tempted to invoke a zwitterionic intermediate related to (3a) or (15) which hydrates and then undergoes fragmentation to give the observed products. However, the fact that the best yields of (20) and dimethyl fumarate were obtained in the presence of benzoyl peroxide suggests that a free radical mechanism may operate here.
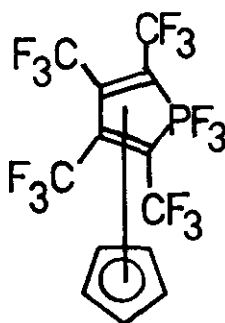
The final structure revision of a possible pentacovalent phosphole derived from

triphenylphosphine and the very powerful electrophile dicyanoacetylene was also carried out by Tebby's group.[26] Again, the product postulated by Reddy and Weis[18] as having the 1,1,1-triphenylphosphole structure (9) has an entirely different stoichiometry to that originally suggested. It is, in fact, an adduct of two molecules of the phosphine and three molecules of the alkyne to which has been assigned[26] the open-chain ylidic structure (21). As usual, the structural assignment was made on the basis of extensive chemical and spectroscopic evidence and of particular importance here is the ^{31}P nmr chemical shift. For the adduct, a downfield shift of 22.0 ppm (relative to external 85% H_3PO_4) was observed whereas most phosphorus atoms bonded to five carbon atoms have strong upfield shifts in the range 80 - 100 ppm.[27] The downfield shift observed is typical of ylidic structures.
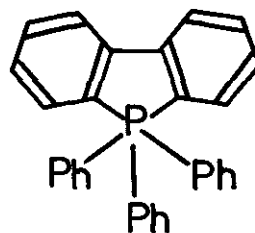
These structure corrections, together with the very transient nature of (3b), might suggest that stable phospholes containing five-coordinate phosphorus cannot exist. This is not the case since the free 1,1,1-triphenylphosphole (22)[28], the coordinated system (23)[29] and the fused-ring system (24)[30] have all been prepared. The methods of preparation are outside this discussion and it is only necessary to state here that the syntheses of (22) and (23) used phosphine-metal complexes as starting materials while the synthesis of (24) involved methods entirely different from the reactions discussed in this review.
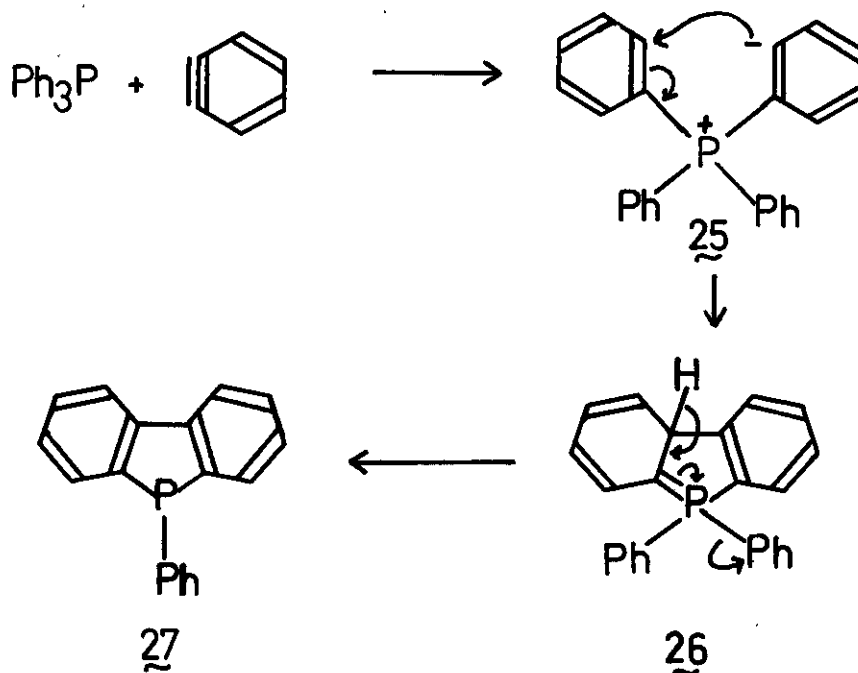

Before moving on from this discussion of the reactions of tertiary phosphines with electrophilic alkynes, there is one other type of reaction which deserves brief attention. To this point in this discussion, all of the reactions surveyed lead to acyclic or heterocyclic, carbonyl or nitrile stabilized phosphonium (or, in one case, arsonium) ylids although non-ylidic transient intermediates are involved in some of the reactions. Although this is not strictly a part of the main theme of this survey, the question of what types of products would be obtained if ylid stabilization by negative charge delocalization were not possible nevertheless arises. Most alkynes lacking strongly electron-withdrawing groups are not sufficiently active to react

with triarylphosphines but one highly active alkyne-related system which does not bear electron-withdrawing groups is benzyne.

   Both Wittig et al.[31,32] and Zbiral[33] have investigated reactions of triphenylphosphine with benzyne. In the first of these studies, carried out many years ago, Wittig's group showed[31] that the product of the reaction (obtained in low yield) is the 5-phenyl-5H-dibenzophosphole (27) which almost certainly arises from the route reactants → (25) → (26) → (27).
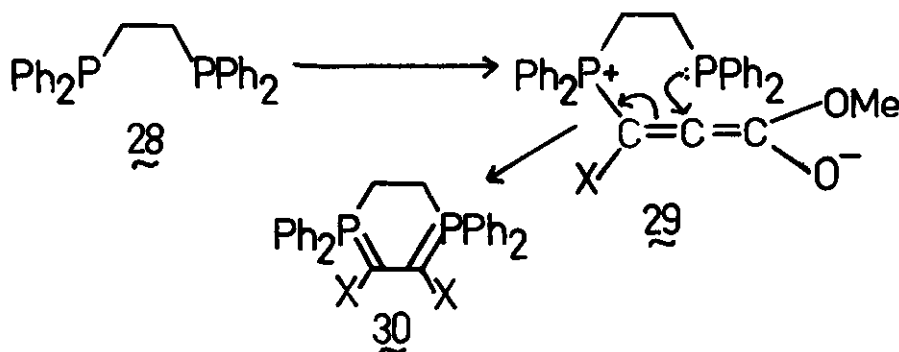

   This reaction is of interest for several reasons. First, the carbanionic portion of the zwitterion (25) is sufficiently nucleophilic to attack a benzene ring attached to a phosphonium grouping. Next, an ylid (26) is formed (transiently) even though it has little stabilization through delocalization. Furthermore, the ylid (26) decomposes by elimination of benzene to give the fully unsaturated species (27). That this is indeed the correct structure assignment for the product is irrefutable since such structures have been well known for many years.[7,34] This means, of course, that in contrast to the reactions discussed previously where phosphorus changes permanently its coordination number from three to four and its oxidation state from three to five during the reaction, these changes are temporary in the triphenylphosphine-benzyne reaction where, in the final product, phophorus reverts to a three-coordinate, three-valent state. Nonetheless, as in all other reactions of this kind discussed so far, an ylid

is formed during the reaction. It should also be noted that the zwitterion (25) can be trapped[31] as the corresponding triphenylborane adduct and that (25) is sufficiently stable at low tempera-ture in the free state to have been studied fairly extensively.[32]

Zbiral[33] has carried out similar reactions between benzyne and triphenylphosphine and was able to increase the yield of (27) to 40%. He also carried out reactions between benzyne and phosphorus heterocyclic systems.

To survey briefly developments to this point, on the one hand many interesting and rather novel reactions have been reported but, on the other hand, the initial promise of these reactions as useful tools in phosphorus heterocyclic chemistry would appear to have faded some-what because of numerous structure revisions. This however is _not_ the case and virtually all reactions of this nature investigated since these initial studies have led to phosphorus hetero-cyclic systems, some of which would be extremely difficult to prepare by more conventional methods.
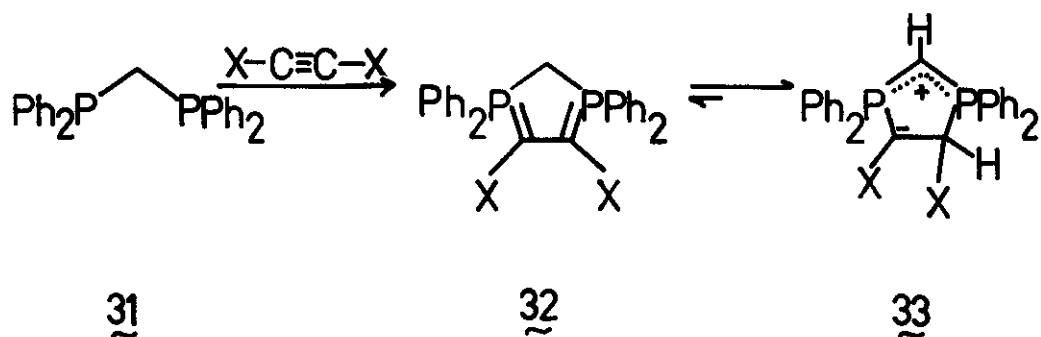
The next significant development came when two groups investigated the reactions of bis-phosphines with dimethyl acetylenedicarboxylate. The first such report[35] was of the reaction of 1,2-bis(diphenylphosphino)ethane (28) with the acetylenic ester to give the relatively stable yellow 1,4-diphosphacyclohexa-1,3-diene (30) by a cycloaddition reaction. The reaction is now

thought to follow the route (28)→(29)→(30) although a slightly different mechanism was considered (on the basis of incomplete information derived from some unpublished related reactions) to be a possibility at the time of publication. Clearly, the reaction is very closely related to that leading to the 2:1 adduct (5) of triphenylphosphine with the ester as outlined in the sequence (1)↔(1b)→(5).
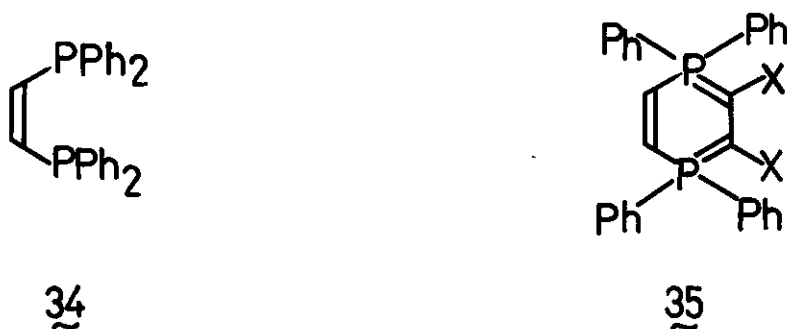
Shortly after this, Tebby et al.[36] and Hughes et al.[37] investigated the similar reaction of bis(diphenylphosphino)methane (31) with the ester and found that a reaction almost identical

to that described above occurs to give the bis-ylid (32) which, however, is in tautomeric
equilibrium with the isomer (33) with the equilibrium favouring (33). Again the product is
relatively stable under normal conditions. Structures were determined by the usual chemical and

spectroscopic methods.

The groups of Tebby[36] and of Hughes[38] also briefly studied the reaction of the
unsaturated bis-phosphine cis-1,2-bis(diphenylphosphino)ethylene (34) with the acetylenic ester.
Both groups isolated a highly water sensitive adduct which they characterized as the fully
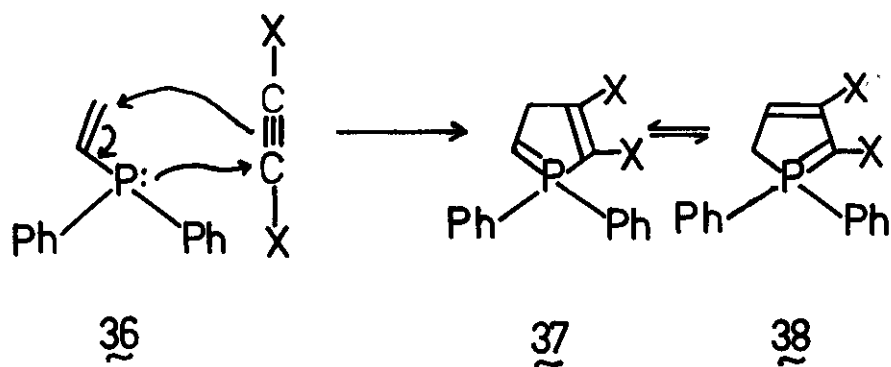unsaturated phosphorus heterocycle (35). The characterization by Tebby's group[36] rested mainly

upon ir and mass spectral data while the other workers were able (with difficulty) to obtain
reproducible analyses, nmr data in $CDCl_3$ and acid solution, and a stable, crystalline bis-
perchlorate.

The adduct (35) is of interest for two reasons. First, it is a potentially aromatic
phosphorus heterocycle. Whether it is aromatic in the conventional sense or not is debatable but
what may be significant here is the infrared spectrum. This shows that the main carbonyl
stretching frequency in (35) occurs at 1640 cm^{-1} with lesser peaks nearby on either side. By
itself, this observation is not startling since it indicates a certain amount of ylidic negative

charge delocalization into the ester groups. However, in the similar system (30), where an aromatic phosphorus-containing ring is not possible, the main carbonyl stretching frequency is at 1585 cm^{-1}. This indicates that negative charge delocalization into the carbonyl groups is much less in (35) than in (30) and this, in turn, may indicate a greater degree of electron delocalization into the phosphorus-containing ring of (35) to give something like an aromatic system. The other point of interest is the extreme sensitivity of the adduct (35) towards hydrolysis compared with the adduct (30) which is easily isolated and characterized and which can be stored for quite long periods without serious deterioration. Clearly, there are considerable electronic differences between (30) and (35) but whether these differences arise from some degree of aromaticity in (35) is not yet clear.

Reactions between the _trans_ isomer of the bis-phosphine (34) and the acetylenic ester have also been investigated[38] but, since the reactions do not parallel those outlined above for other bis-phosphines and for mechanistic reasons, discussion of this will be deferred until a little later.

Yet another approach to phosphorus heterocycles from reactions of simple phosphines with dimethyl acetylenedicarboxylate involves treatment of vinylphosphines with this ester.[38,39] Addition reactions occur but, as with triphenylphosphine, the nature of the product depends upon the conditions of the reaction - particularly the ratios of the reactants and the nature of the vinylphosphine used. The 1:1 cycloaddition which would be expected from diphenylvinylphosphine is outlined in the sequence (36)→(37) but, although this occurs when the ester (1 mole) is added
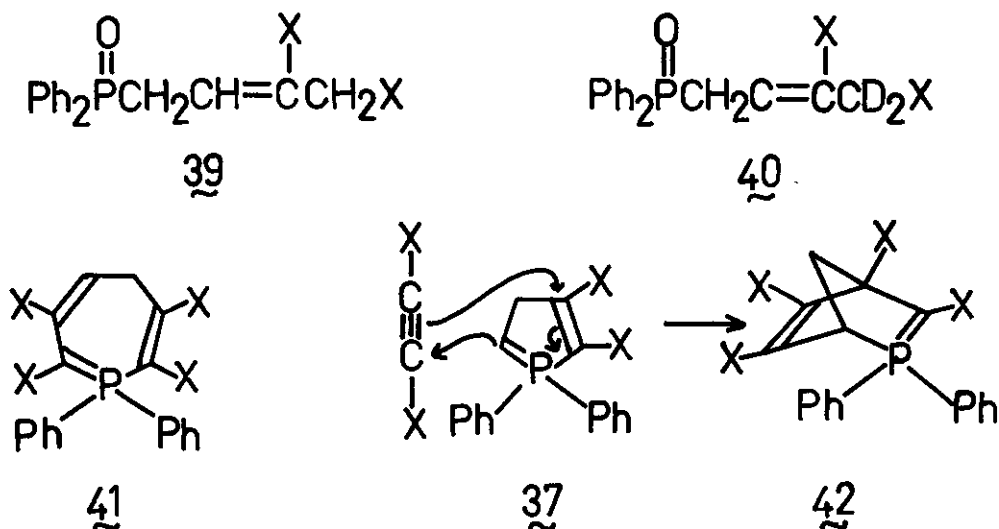

to the phosphine (1 mole) in ether, tautomerization of (37) to the carbonyl stabilized isomer (38) also occurs. As can be seen, (37) is a 3H-phosphole while (38) is a 2H-phosphole and these products are therefore closely related to the 2H-phosphole (12) which was obtained by an entirely different route mechanistically.

In fact, both (37) and (38) are highly reactive and water sensitive and neither can be
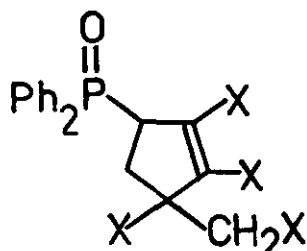
isolated in the free state. However, (37) can be trapped[38] (as it is formed and before tautomerization can occur) by p-nitrobenzaldehyde in a Wittig reaction and in another reaction which will be discussed shortly while (38) has been characterized as its hydrolysis and deuterolysis products (39) and (40). The fact that both deuterium atoms are introduced at the site indicated confirms the nature of the cyclic precursor (38) and the mechanism of hydrolysis. The structures of the Wittig reaction product mentioned above and of (39) and (40) were established by highly detailed nmr and mass spectral examination.

It was mentioned in the above discussion that the 1:1 cycloaddition product (37) can be trapped in two reactions, one of which was the Wittig reaction already referred to. If one mole of the vinylphosphine (36) is added to two moles of the acetylenic ester in ether, the initially formed cyclic ylid (37) is generated in the presence of an excess of the ester. Phosphonium ylids with relatively littlecarbanion stabilization are known[40] to react very readily with dimethyl acetylenedicarboxylate (as would be expected from the strongly nucleophilic nature of the ylidic carbon atom) and, at the time this research was in progress, all such reactions known[40] resulted in the insertion of a two-carbon unit directly into the ylidic P-C link by a cycloaddition followed by ring opening of the resulting four-membered ring. If this were to occur with the adduct (37) the product would be the seven-membered ring (41). However, the product actually formed[38,39] is the phosphabicycloheptadiene (42) which presumably arises by the route shown in the sequence (37)→(42). Superficially, this reaction resembles a Diels-Alder cycloaddition but, in view of the highly polar nature of the ylidic link in (37) and the strongly
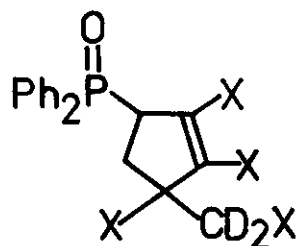

nucleophilic nature of the ylidic carbon atom, it is unlikely that (42) arises from a (4+2) cyclo-addition governed by the rules for the conservation of orbital symmetry.

As with (37) and (38), the bicyclic adduct (42) is much too water sensitive to allow
its isolation. It has, however, been characterized (by detailed spectroscopic examination) as
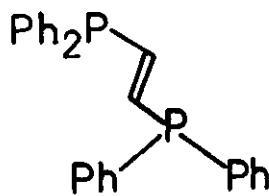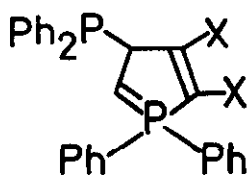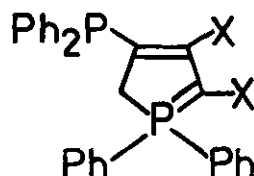the hydrolysis and deuterolysis products (43) and (44).

Returning now briefly to bis-phosphines, the _trans_ isomer (45) of the unsaturated bis-
phosphine (34) reacts[38] with dimethyl acetylenedicarboxylate more as a vinylphosphine than as a
bis-phosphine. However, in this case several quite unexpected reactions occur. Thus, when one
mole of the acetylenic ester is added to one mole of the phosphine (45) in benzene-pentane, a
1:1 adduct is obtained[38] as a pale yellow precipitate which can be isolated, analyzed and
spectroscopically examined without hydrolytic decomposition if reasonable precautions are taken.
By analogy with the behaviour of diphenylvinylphosphine (36) the expected product or products
would be one or more of the cyclic ylids (46), (47) or (48) with, perhaps, (47) as the most
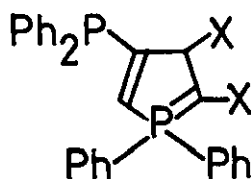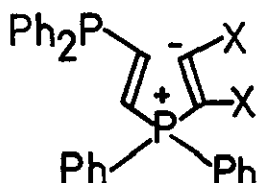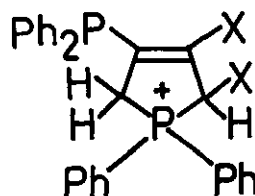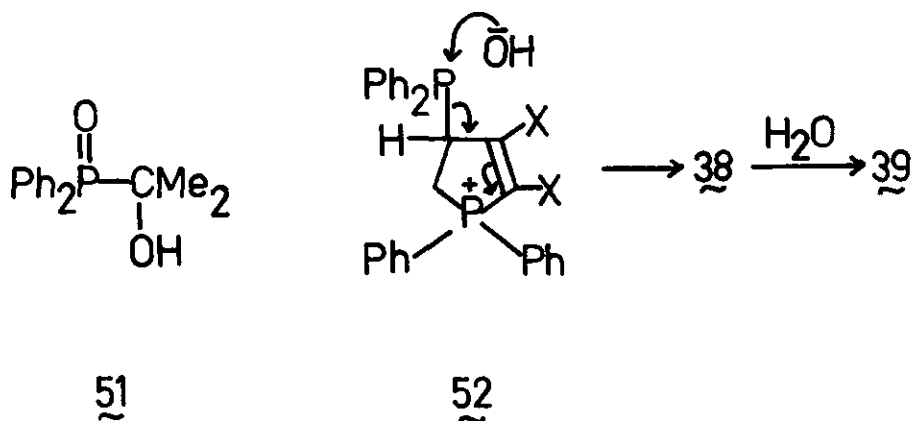
likely structure.

While the infrared spectrum is consistent with a carbonyl-stabilized ylidic structure in that it shows one normal ester carbonyl stretching frequency at 1712 cm^{-1} and apparently ylidiccarbonyl group stretching frequencies at 1601 and 1585 cm^{-1} (suggesting (47) or (48) for the structure, the ^{1}H nmr spectrum of the adduct is not consistent with any of the three proposed structures. For example, the ^{1}H spectrum (at -2^0 to slow hydrolytic decomposition) shows only 20 aromatic, 2 olefinic and 6 methoxy protons. This appears to rule out all three of the structures suggested above since (46) should show one ylidic proton, one tertiary proton and no olefinic protons, (47) should show two methylene protons and no olefinic protons and (48) should show a tertiary proton and only one olefinic proton. Variable temperature ^{1}H nmr studies (down to -50^0) showed that while one of the ester groups appears as a singlet the other splits into a doublet (with the two peaks of unequal area) thereby exhibiting the conformational preference shown[12] by ester carbonyl stabilized ylids. However, if one remembers that this behaviour really only shows that the ester group is adjacent to a negatively charged carbon atom, other possible structures for the adduct can be envisaged.

It was therefore suggested[38] that the 1:1 adduct isolated exists, in solution at least, mainly in the zwitterionic form (49). This structure would be compatible with all of the spectroscopic evidence in that it would show the low frequency carbonyl stretch in the ir spectrum and it contains only aromatic, olefinic and methoxy protons with one ester group adjacent to a negatively charged carbon atom.
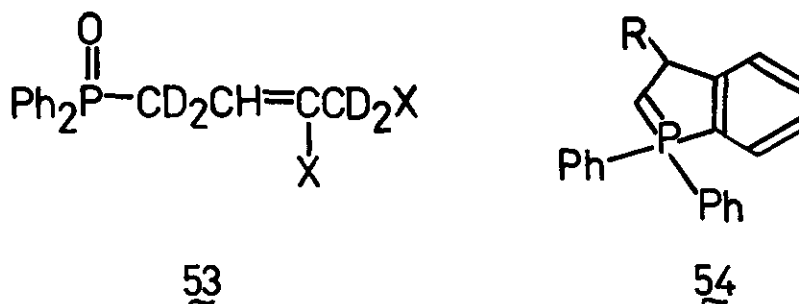
The nmr spectra of the adduct in acid (CF$_3$CO$_2$H) solution under various conditions are of interest. A freshly prepared solution shows a very complex ^{1}H nmr spectrum which suggests that it is a mixture of protonated forms of the zwitterion (49) and some or all of the isomeric structures (46)-(48). However, over a period of several days, the mixture equilibrates and the solution then shows a spectrum entirely consistent with structure (50) which is presumably derived from (47).

The behaviour of the adduct forumulated as (49) upon hydrolysis is even more surprising. Cyclic ylids such as (38) and (42) (possibly also derived from zwitterionic precursors related to (49)) have been characterized as the hydrolytically ring opened phosphine oxide products (39) and (43) respectively. One would therefore expect that the 1:1 adduct (49) (which may also react with water as one or more of the isomeric forms (46)-(48)) might behave similarly. Instead, the product of the hydrolysis[38] of the 1:1 adduct (49) is the phosphine oxide (39) - i.e. the product is the same as that obtained from (38)! Clearly, one of the diphenylphosphino groups has been removed during the hydrolysis. Indeed, it appears to be liberated as diphenylphosphine oxide since the acetone-diphenylphosphine oxide adduct (51) can

also be isolated from the reaction.[38] The reaction is thought to follow the unusual course

51   **52**

$(49) \rightleftharpoons (46)+H_2O \rightarrow (52) \rightarrow (38)+H_2O \rightarrow (39)$ as shown above. This proposed mechanism is suggested both by the isolation of (51) and by deuterolysis experiments which produce the tetradeuterated phosphine oxide (53).

53   **54**

        Before leaving reactions of vinylphosphines and also this section of the review, we will consider very briefly reactions of vinylphosphines with benzyne since, as mentioned earlier in the context of triphenylphosphine, such reactions cannot lead to carbonyl-stabilized ylids but may lead to heterocyclic systems. Moreover, one of these reactions gives a most unexpected result. Thus, preliminary studies[38] of the thermal decomposition of o-benzenediazonium carboxylate in the presence of diphenylvinylphosphine (36) show that the reaction leads not to the expected heterocycle (54,R=H) but to the saturated bis-phosphine 1,2-bis(diphenylphosphino)-ethane (28) in moderate yield. This quite extraordinary reaction has not yet been explained. On the other hand, the unsaturated bis-phosphine trans-1,2-bis(diphenylphosphino)ethylene (45) apparently reacts[38] quite normally to give the expected heterocycle (54,R=PPh$_2$) which was, as is usual in these reactions, trapped and isolated as its hydrolysis product.

REACTIONS OF PHOSPHORUS HETEROCYCLES WITH ACETYLENIC ESTERS

Although relatively few papers have been published in this area, the results obtained
are very significant. Thus, several mechanistically unusual and synthetically very useful
reactions have been investigated and there is clearly very great potential in reactions of this
type. The ring systems which have received attention are simple, four-membered, saturated,
phosphorus-containing rings (phosphetans); simple, fully unsaturated five-membered phosphorus
heterocycles (phospholes);benzophospholes (phosphindoles) and dibenzophospholes. Reactions have
also been attempted, without success, with six-membered, fully unsaturated phosphorus hetero-
cycles (λ^3-phosphorins) and further comment on this will be made later.

Considering first the four-membered ring systems, Trippett's group has examined[41] the
reactions of both 2,2,3,3-tetramethyl-1-phenylphosphetan (55,R=Me) and 2,2,3-trimethyl-1-
phenylphosphetan (55,R=H) with dimethyl acetylenedicarboxylate and also with ethyl propiolate.
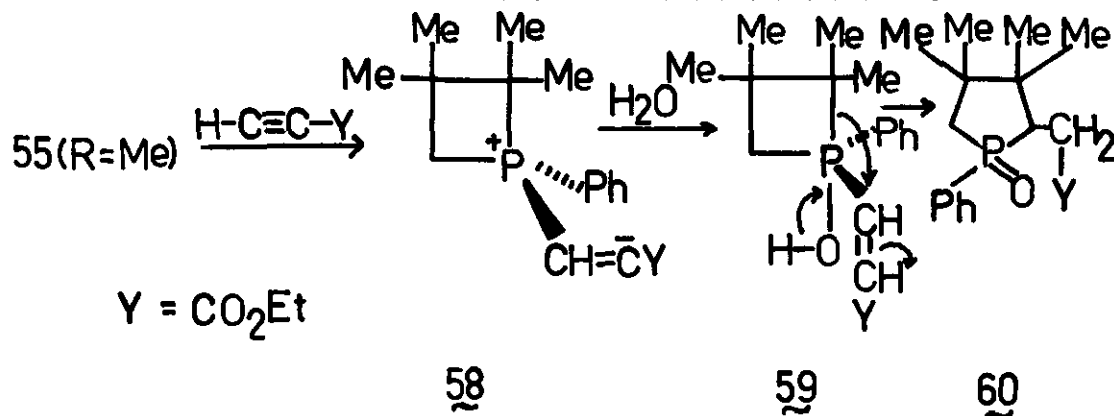In all four reactions, one-carbon ring expansions of the four-membered ring occur.

55   56   57

For example, the tetramethyl compound (55,R=Me) reacts smoothly to give, in moderate
yield, the ring expanded product (57) (with no trace of the isomer which would be formed by -CH$_2$-
migration), probably by the mechanism shown in the sequence (55)→(56)→(57) although the authors[41]
suggested a mechanism involving electron flow in the opposite direction. This suggestion was
made on the grounds that one might expect the CH$_2$ group of the ring to be more likely than the
CMe$_2$ group to occupy the apical position in the intermediate (56) (because of its better accommo-
dation of nagative charge) and to migrate more easily than the CMe$_2$ group by any mechanism
involving the development of negative charge upon the apical migrating group. These authors
therefore attributed the apparent apical nature of CMe$_2$ in the probably intermediate (56) as
being due to steric reasons[41] and invoked a mechanism involving development of positive charge

upon the apical migrating group. While Trippett et al.[41] are probably correct in assigning the

CMe_2 group to the apical position for steric reasons, the driving force for rearrangement of

trigonal bipyramidal intermediates to carbonyl stabilized ylids is so great compared with the

minor electronic differences between the CH_2 and CMe_2 groups that this author prefers the

mechanism shown. The evidence for developing negative charge on the migrating group in these

reactions is also reasonably convincing (see earlier discussion of triarylphosphine-acetylenic

ester 1:2 adducts). Further discussion of similar reactions will be made later. It is quite

possible, incidentally, that cyclopropenyl intermediates related to (14) may also be involved

but, since the reaction was carried out at 0°-room temperature, no evidence for such an inter-

mediate was obtained.

A similar reaction occurs with the trimethylphosphetan (55,R=H) (using a 19:1 mixture

of stereoisomers) to give (57,R=H) which is presumably formed by a mechanism similar to that

involved in the formation of (57,R=Me). Thus, it seems that the type of reaction initially found

to lead to the formation of the 2H-phosphole (12) by the route (1)→(15)→(14)→(3b)→(12) is much

more general and the transient formation of five-coordinate phosphorus intermediates (e.g. 3b and

56) followed by apical migration of some grouping from the phosphorus to a neighbouring

unsaturated equatorial carbon atom to give a carbonyl-stabilized ylid seems particularly favoured.

As will be seen later, this conclusion, in general terms, is correct but there are notable

exceptions and these exceptions are not easily predictable.

Mechanistically related one-carbon ring expansions also occur when the two phosphetans

(55, R=H or Me) are treated with ethyl propiolate. For example, (55, R= Me) reacts smoothly with

the propiolic ester in moist ether, probably by the route (55)→(58)→(59)→(60), to give the
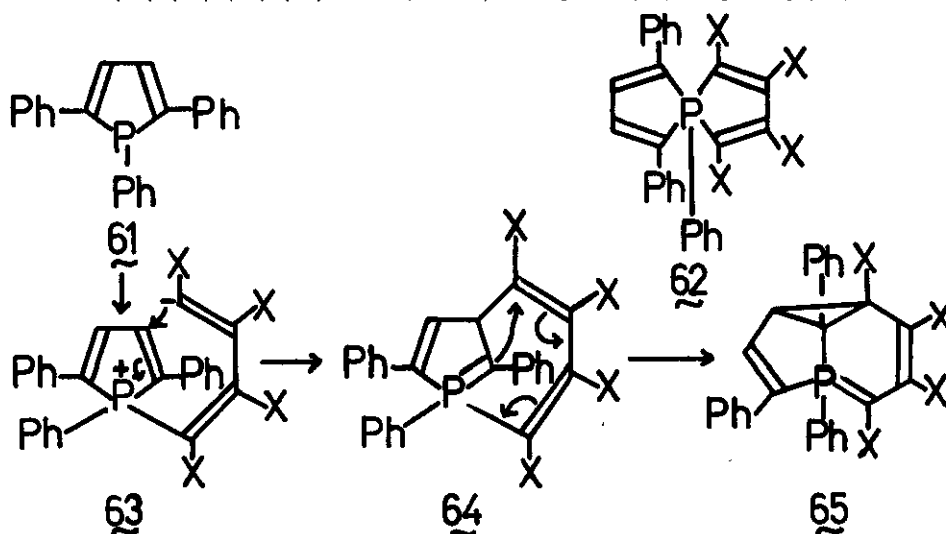

phospholane oxide (60) in very good yield (72%) with only traces of the phospholane oxide formed

by -CH_2- instead of -CMe_2- migration. A similar reaction occurs with a 19:1 isomer mixture of

the trimethylphosphetan (55, R=H) except that both -CMe_2- and -CH_2- migration occur in this

instance.

Turning now to simple unsaturated five-membered rings, there have been three studies[42], [43],[44] of the reactions of phospholes (the phosphorus analogues ofpyrroles) with dimethyl acetyle-nedicarboxylate. The first study[42] arrived at erroneous conclusions for the general reasons outlined at the beginning of this review while the other two showed that predicting mechanistic pathways and products for these reactions is very difficult.
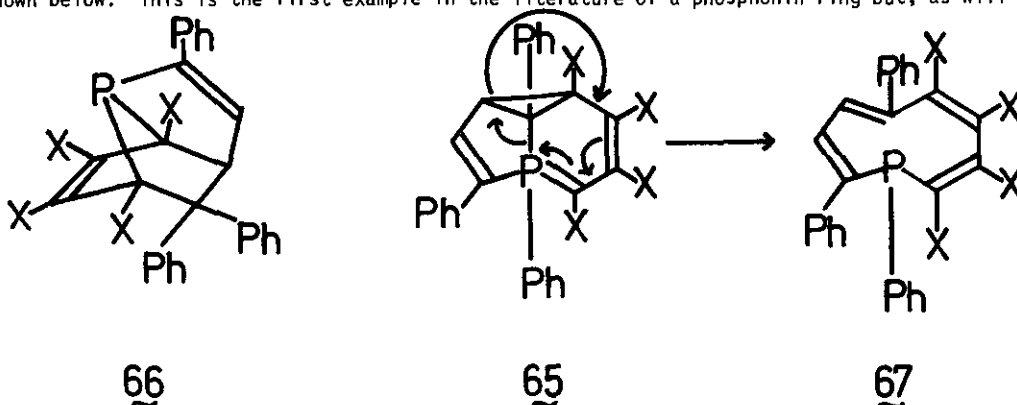
The first phosphole to be investigated in this manner was 1,2,5-triphenylphosphole (61) which was chosen because it was one of the very few phospholes readily available[45] at that time. The purpose of the study was to probe the availability of the phosphorus lone-pair for chemical reactions in the context of the possible aromatic character[9],[11] of the phosphole system. It was found that this phosphole does not react with the ester in benzene under reflux and this is in contrast to the behaviour of triphenylphosphine which reacts very readily at -50°. Clearly, in this phosphole, the lone-pair is not very readily available for reaction and this might be taken to indicate some degree of lone pair-diene interaction in the phosphole ring.

Reaction does, however, occur over a period of two days in the absence of solvent and a yellow 1:2 adduct of the phosphole with the ester is formed in good yield. The product was, on the basis of a certain amount of spectroscopic and chemical evidence and by analogy with other (incorrect) five-coordinate phosphole structures in the literature already discussed, erroneously assigned the structure (62). However, in light of various phosphine-acetylenic ester product structure revisions which were published at about the same time, Tebby reinvestigated[43] this proposed structure and showed by the usual methods already referred to that the yellow 1:2 adduct is, in fact, the complex tricyclic ylidic structure (65) apparently formed by the route (61)→(63)→(64)→(65). Thus, the spiran system (62) originally proposed[42] does

not even occur as an intermediate (unless (63) is regarded as a zwitterionic version of (62)) as
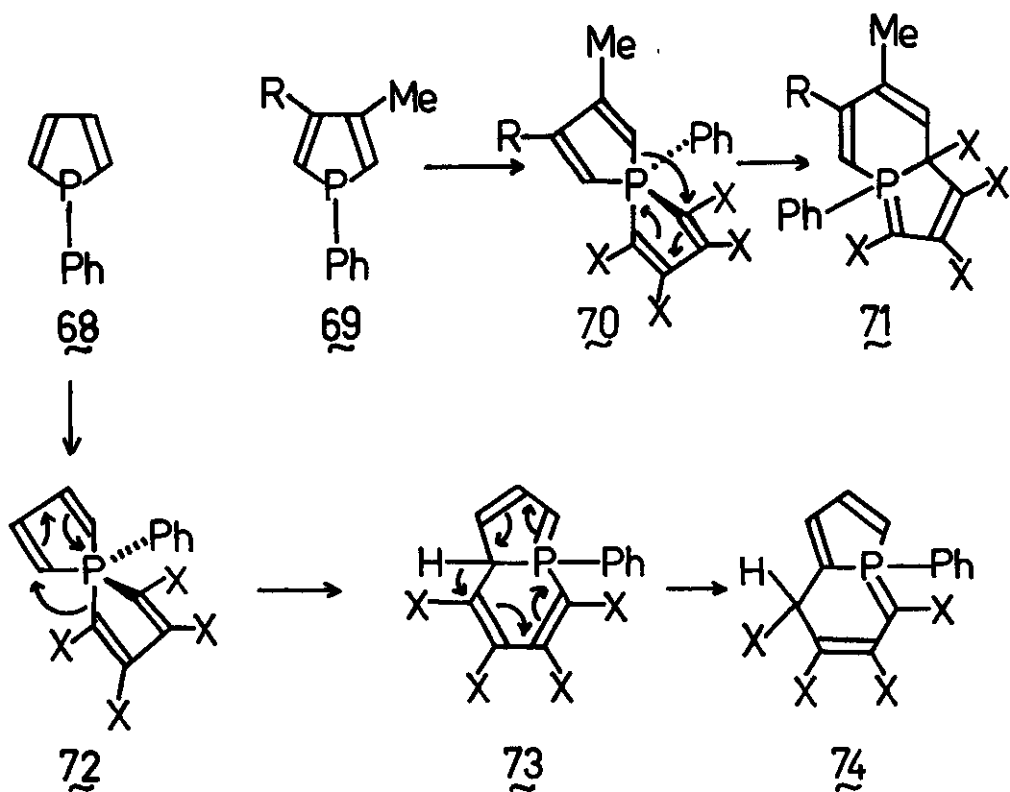might have been expected by analogy with such structures as (3b) and (56) already discussed.

Both groups of workers also found that the initially-formed adduct (65) rearranges
rapidly on boiling in chloroform to give what is clearly a tertiary phosphine to which the first
group assigned[42] the incorrect structure (66). This was later corrected[43] to the novel
phosphonin structure (67) which is thought to be formed by the interesting rearrangement (65)→(67)
shown below. This is the first example in the literature of a phosphonin ring but, as will be

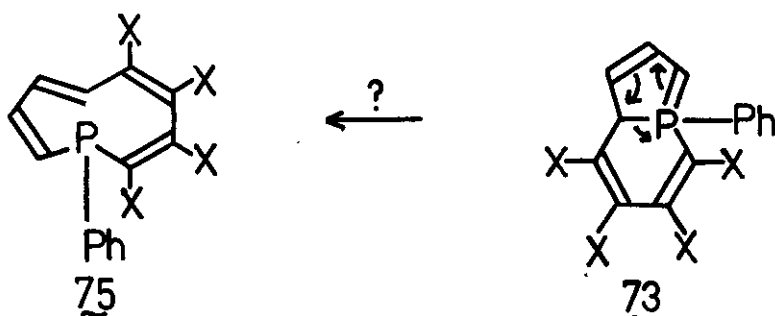$$\underset{\sim}{66} \qquad \underset{\sim}{65} \qquad \underset{\sim}{67}$$

seen shortly, there are at least two other examples of four-carbon ring expansions of this type
now known.

In the early 1970's much simpler phospholes became fairly readily available[11] and
further investigations of phosphole-acetylenic ester reactions were therefore undertaken.[44]
However, for the most part, these reactions are entirely different from that described for (61)
above. For example, 1-phenylphosphole (68), 3-methyl-1-phenylphosphole (69, R=H) and 3,4-dimethyl-
1-phenylphosphole (69, R=Me) all react very rapidly with dimethyl acetylenedicarboxylate in
dilute benzene solution at room temperature - i.e. these phospholes are better nucleophiles than
(61) which is also the case[46] (with one or two notable exceptions[11,47]) in reactions with transi-
tion metal ions.

Furthermore, the reactions with simple phospholes follow entirely different reaction
pathways to that followed by (61) and the three simple phospholes mentioned above do not even
react in precisely the same manner. Thus, the phospholes (69, R=H and R=Me) react with the
acetylenic ester by the sequence (69)→(70)→(71) to give the one-carbon ring expanded adduct (71).
On the other hand, although the phosphole (68) also reacts with the ester to give a one-carbon
ring expansion product, the reaction follows a slightly different sequence as outlined in (68→(72)→
(73)→(74). In addition, with the phosphole (68), a minor reaction pathway produces what has been
tentatively assigned the structure (75). This presumably arises by a mechanism similar to that

suggested[43] for the formation of (67) although the possibility that both (74) and (75) arise from the same intermediate (73) cannot be dismissed.

Similar studies have been carried out with the phosphindole (benzophosphole) system.[48] As with the early studies on phospholes the preliminary investigations with phosphindoles were carried out with the only phosphindole (the heavily substituted derivative (76)) which was readily available[49] at that time and it may be that less heavily substituted phosphindoles may react by different pathways. Even though it is very heavily substituted, the phosphindole (76) reacts smoothly with dimethyl acetylenedicarboxylate in benzene to give two products, both of which have

structures of a kind which had not been encountered in phosphine-acetylenic ester reactions
before. The first of these products is an adduct of one molecule of the phosphindole and two
molecules of the ester less one oxygen atom. On the basis of the usual chemical and spectroscopic
studies outlined earlier in this review, this adduct was assigned the phosphindolium cyclopenta-
dienylide structure (80) and it was suggested that it is formed by the sequence (76)→(77)→(78)→
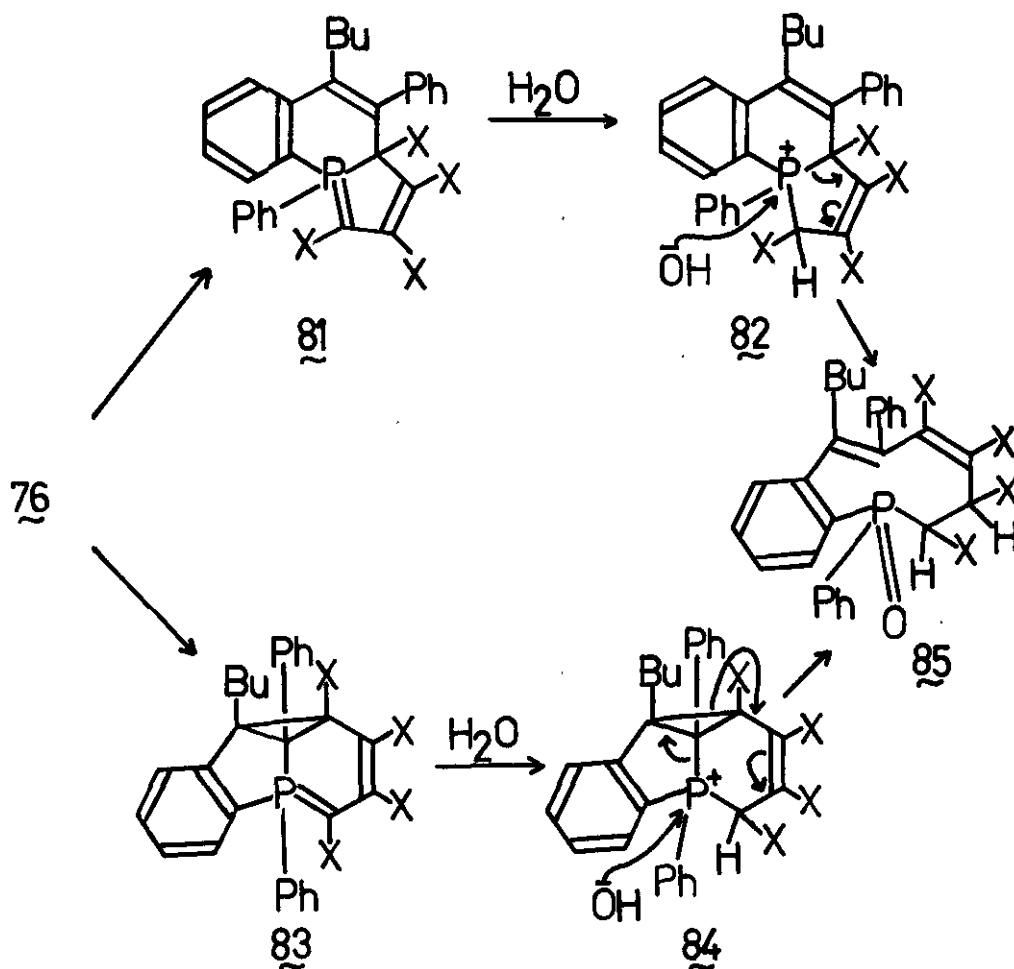(79)→(80).

There is precedent in the literature for the steps leading to (78) since the related
triphenylphosphine adduct (13) is formed by a similar route. However, in the case of the phosphin-
dole, (78) reacts further by oxirane formation rather than methoxy-migration as occurs in the
formation of (13). Presumably, the driving force for the steps (78)→(79)→(80) is provided by the
formation of the aromatic cyclopentadienylide ring with deoxygenation of the oxirane (79) occurring
by reaction with unreacted phosphindole. Evidence was presented[48] to support this.

The second product of this reaction is an adduct of one molecule of the phosphindole,
two molecules of the ester and one molecule of water. This is the four-carbon, ring-expansion
product (85) but this is a dihydrophosphonin oxide structure rather than a phosphonin of the type
encountered in similar reactions with both heavily substituted and simple phospholes.

The compound (85) is thought to arise from either of the two sequences (76)→(81)→(82)→
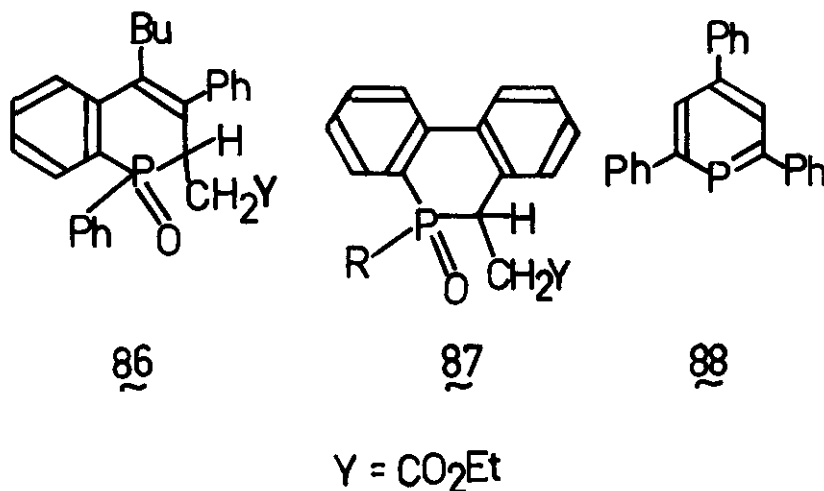
(85) or (76)→(83)→(84)→(85). Evidence was presented which suggested that the second route is the

more likely.

Other ring-expansion and ring-opening reactions of the phosphindole (76) have been carried out.[50] Among these reactions is treatment of (76) with ethyl propiolate in the presence of water which leads to the formation of the one-carbon, ring-expanded product (86). There is nothing remarkable in this reaction since, mechanistically, it is closely related to the reaction which leads to the formation of (60) discussed earlier in this section. It is, however, of interest since reactions which lead to phosphanaphthalene derivatives have received relatively little attention.[9]

Turning now very briefly to dibenzophospholes, no reactions of these systems with dimethyl acetylenedicarboxylate appear to have been recorded but 5-phenyl-5H-dibenzophosphole (27), and other dibenzophospholes with different substituents upon the phosphorus atom, have

$$Y = CO_2Et$$

been treated[51] with ethyl propiolate to give the ring-expanded products (87) by a mechanism of the type discussed above for the phosphindole system.

The only other report[52] of treatment of phosphorus heterocycle with an acetylenic ester in the literature concerns the attempted reaction of 2,4,6-triphenyl-λ^3-phosphorin (88) with dimethyl acetylenedicarboxylate. No reaction, in fact, occurs and this is because λ^3-phosphorins have a most unusual electronic structure[3] in which the phosphorus lone-pair orbital is not the highest occupied molecular orbital.

In conclusion, it can be seen that reactions between phosphines or phosphorus hetero-cycles and acetylenic esters lead to a very wide variety of structural types. Most (though not all) of the products formed are carbonyl-stabilized ylids and the majority of these products recorded in the literature are heterocyclic in nature. Reaction pathways for these reactions are difficult to predict and a large number of possible mechanistic sequences have now been identified.

Now that phosphorus heterocyclic chemistry has become firmly established, renewed interest in reactions of the type outlined in this review can be expected.

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