## 3.1 INTRODUCTION

During the last couple of decades, a large variety of azaphospholes has become available through several facile routes described in the previous chapter. After having the heterophospholes become accessible, investigation of their reactivity has been an active field due to the presence of several functionalities in the azaphosphole ring (Figure 3.1).

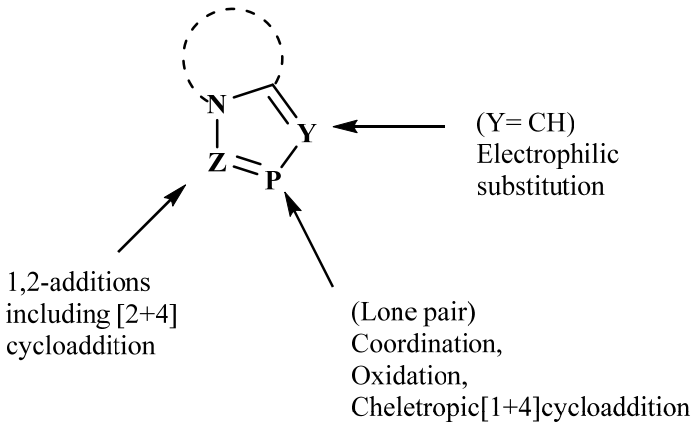
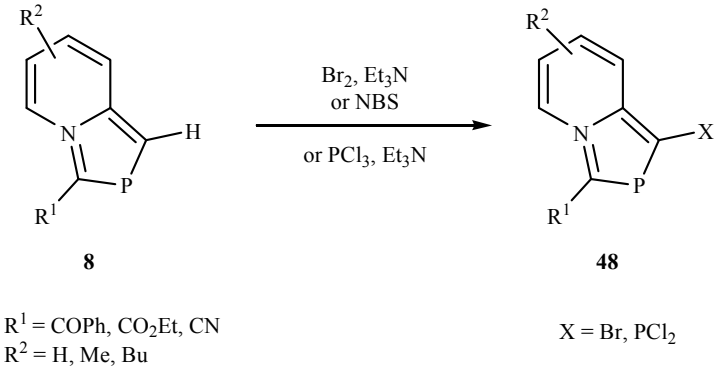



**Figure 3.1.** Different functionalities in heterophosphole.

The interesting reactions given by azaphospholes can be categorized under the following subheadings.

### 3.1.1 Electrophilic substitution

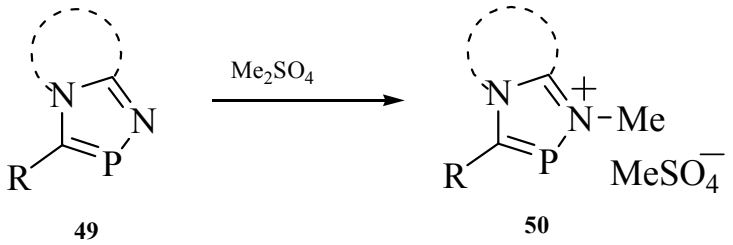
2-Phosphoindolizines without substitution on 1-position reacts with phosphorous trichloride, bromine or N- bromosuccinamide in the presence of a base to yield substituted-2- phosphaindolizines.[137,138]




**Scheme 3.1.** Electrophilic substitution on 2-Phosphoindolizines.

### 3.1.2 N-Alkylation

Methyl iodide is not reactive with 2-phosphaindolizines. However, pyrido-, thiazolo-, 5,6-dihydrothiazolodiazaphospholes undergo methylation at their $\sigma^2,\lambda^3$-N atom to yield $\sigma^3$-*N*-methylated salts on reacting with dimethyl sulphate (Scheme 3.2)[111,139]




**Scheme 3.2.** Methylation of diazaphosphole with dimethyl sulphate .

### 3.1.3 Addition reaction on >C=P functionality

In azaphospholes, two functionalities namely >C=P– or –N=P- moiety and the lone pair on the phosphorous atom are responsible for various cycloaddition reactions[103,140-143]

1,2-Addition on the >C=P– functionality leads to [2+4] and [2+3] cycloaddition reactions, whereas 1,1-addition on phosphorous results in cheletropic [1+4] cycloaddition. This differential reactivity is rationalized by Frontier Molecular Orbitals (FMO) analysis and it is concluded that the mode of cycloaddition depends upon the HOMO/LUMO combination of the two reactants.[144] It has also been found in case of cycloaddition that the nature of diene also affects the type of cycloaddition. Generally, electron-rich dienes lead to [4+2] cycloaddition while electron-deficient dienes react in [4+1] cycloaddition mode. In contrast, sometimes the –C=C–C=P– moiety of the heterophosphole ring can also behave as a diene component to produce [4+2] cycloadduct by reacting with alkynes or phosphaalkynes. Therefore, the mode of the cycloaddition reactions depends upon the electronic environment of both the azaphosphole and diene. Various possible cycloaddition modes are shown in Figure 3.2.

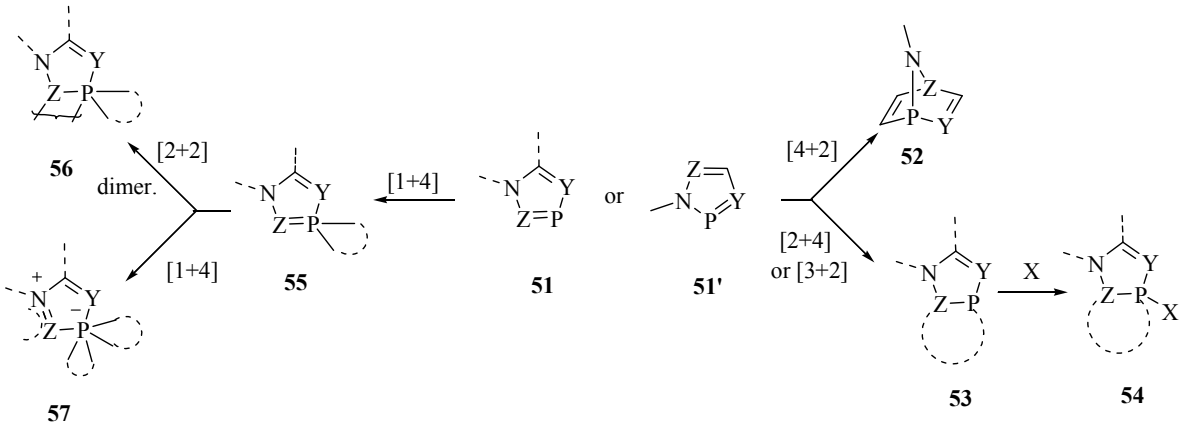
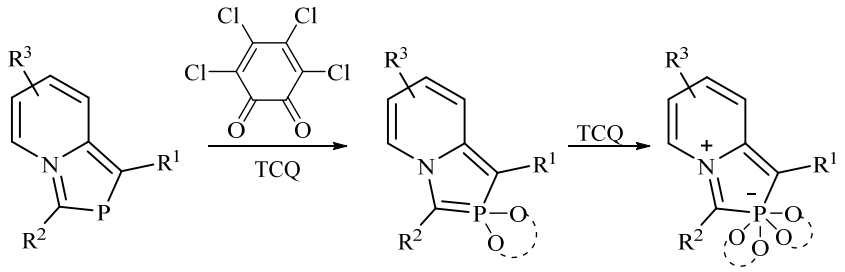



**Figure 3.2.** Possible cycloaddition modes of >C=P functionality.

The azaphospholes having strong electron releasing group in the vicinity of the >C=P– functionality undergo two successive cheletropic [1+4] additions to produce a zwitterionic product (**57**) having a six-coordinate phosphorous atom,

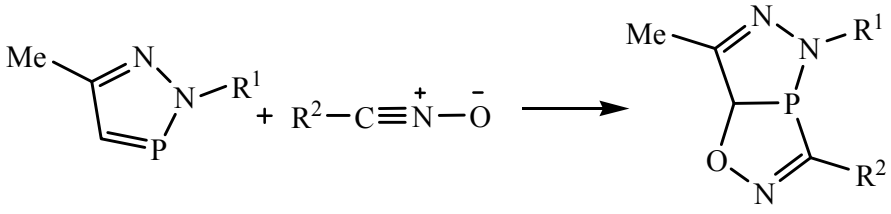
such as the cycloadduct **59** which is obtained by the reaction of 2-phospaindolizine with an electron-deficient heterodiene (Scheme 3.4)[138,145]




$\delta^{31}P = 45$ to 46 $\delta^{31}P = -134$ to -141

**Scheme 3.4.** Possible cycloaddition modes of >C=P functionality.

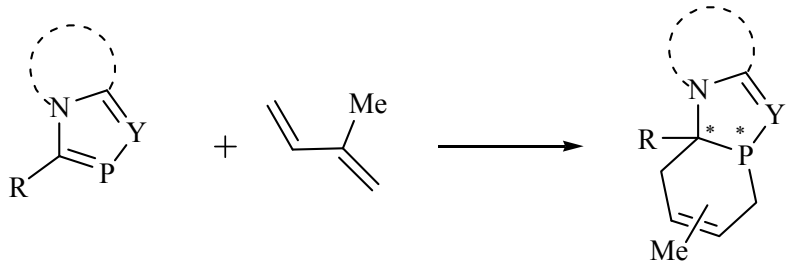
Azaphospholes undergo [2+3] cycloaddition with a variety of 1,3-dipoles, such as nitrile oxides ,nitrilimines, and nitrile ylides with regioselectivity where the carbon atom of the 1,3-dipole is bonded to the phosphorous atom of the azaphosphole ring. For example, *2H*-1,2,3-diazaphospholes undergo [2+3] cycloaddition with nitrile oxide to give corresponding cycloadduct **61** (scheme 3.5).




**Scheme 3.5.** [2+3] cycloaddition of *2H*-1,2,3-diazaphospholes with nitric oxide.

4-Aminodiazaphospholes, 1,3,4-thiazahospholes, 1,2,3,4-triazaphospholes have been reported to undergo [2+3] cycloaddition to afford the corresponding cycloadducts.[146-149]

[2+4] Cycloaddition, i.e. the Diels-Alder reaction of azaphospholes has significant feature that it develops as two chiral centres in single step (Scheme 3.6). Azaphospholes act as dienophile and undergo DA reaction with a wide range of symmetrical as well as unsymmetrical dienes with high degree of stereo- and regiochemical aspects.[132] The DA reaction with cyclic dienes shows topographical selectivity and leads to *endo*-isomer at low temperature due to kinetic preference.




**Scheme 3.6.** Diels-Alder reaction of heterophospholes.

DA reactions of heterophospholes[140] has been categorised here under two subheadings, namely [2+4] cycloadditions which involves >C=P– functionality as dienophile and [4+2] cycloadditions where the phosphadiene component present in the heterophosphole ring behaves as diene. The versatility and importance of DA reactions of azaphospholes are further increased by the accompanying high stereo- and regioselectivity.[103,141-144]

**[2+4] Cycloadditions**

It has been observed that the [2+4] cycloaddition of >C=P– moiety in heterophospholes is much more facile than the corresponding carbocyclic analogues. Theoretical calculations have also rationalised this fact and it was concluded that there is lowering of the activation energy barrier due to weaker

>C=P– π bond as compared to the >C=C< π bond in the presence of the P-atom.[150,151] In fact, the >C=P– π bond is only 60-70% as strong as >C=C< π bond due to weak 2*p*-3*p* overlapping in the former.[152] It may be noted that $HOMO_{diene}$-$LUMO_{phosphaethene}$ gap (4.55 eV) is much smaller than the one between $HOMO_{diene}$-$LUMO_{diene}$ (6.32 eV) which indicates that the reaction of phosphaethene may be expected to be much faster with lower activation barrier than that of ethene, according to FMO theory (Figure 3.3). Almost similar pattern is observed when the >C=P- functionality is integrated in the aromatic sextet, except that more vigorous conditions (catalyst or high temperature ) may be required for completion of the DA reaction and the activation energy barrier may get raised .

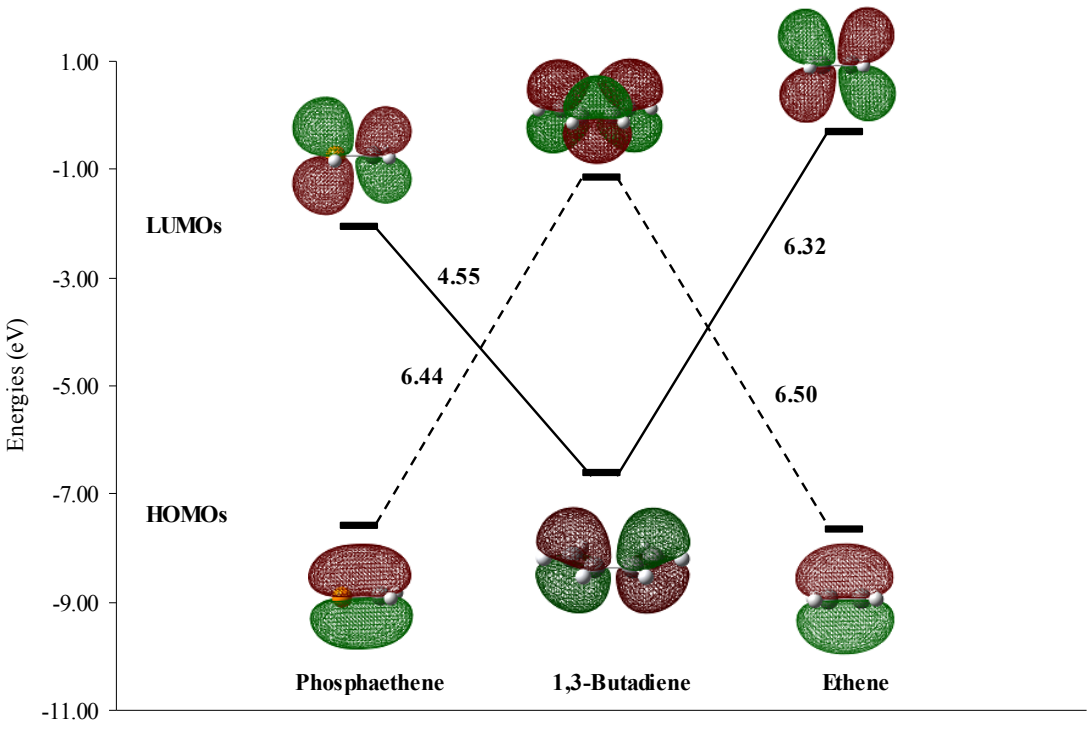
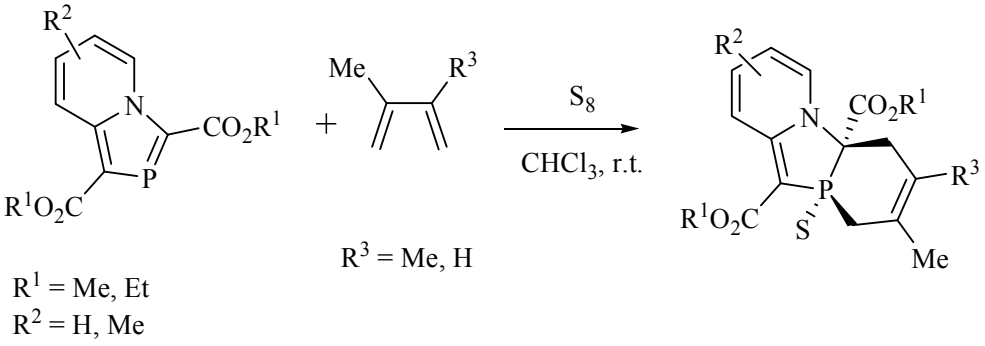



**Figure 3.3.** Frontier molecular orbitals of phosphaethene, 1,3-butadiene and ethene at B3LYP/6-311+G**.[23a]

Where DA reaction is not accomplished with indolizines , DA reaction of 1,3-bis(alkoxycarbonyl)-2-phosphaindolozine (**39**)[109] having EWG at 1- and 3-positions, synthesised from disproportination followed by 1,5- electrocyclization of the pyridinium dichlorophosphinomethylides,[107,131] with 2,3-dimethylbutadiene (DMB) and with isoprene was reported successfully with complete diastereo- and regioselectivity (Scheme 3.6).[133,136a] Reaction is done in presence of sulphur to jostle the reversible DA reaction in forward direction by oxidizing $\sigma^3,\lambda^3$-phosphorous atom of the initially formed cycloadduct, otherwise the reaction is slow at room temperature.




$R^1$ = Me, Et
$R^2$ = H, Me

$R^3$ = Me, H

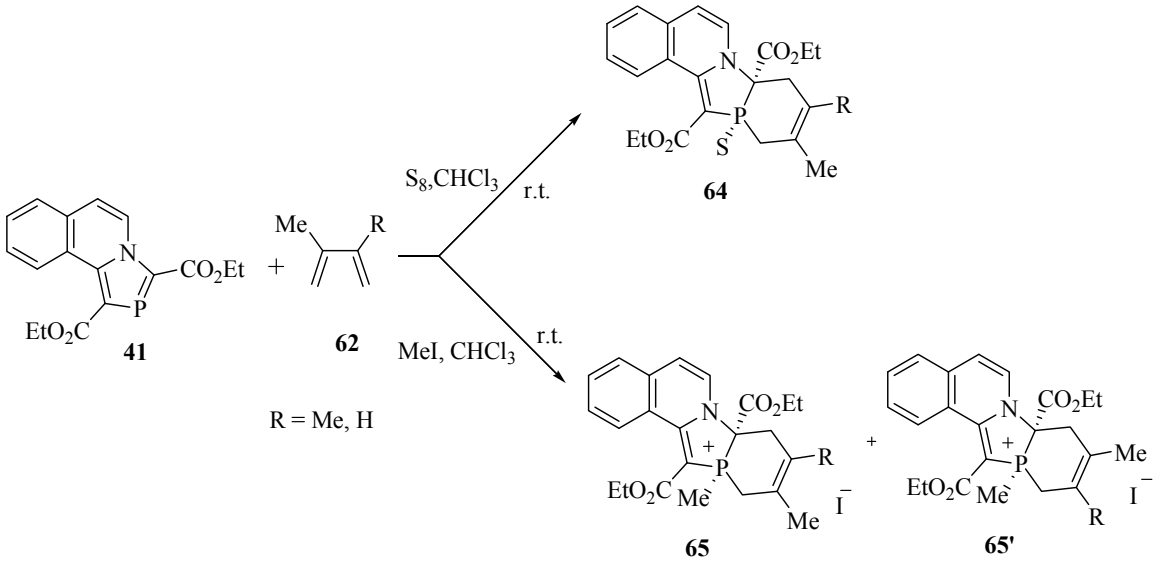
**39** **62** **63**

**Scheme 3.6.** DA reaction of 1,3-bis(alkoxycarbonyl)-2-phosphaindolozine with dienes.

The noticed stereo- and regioselectivity of the above reaction have been justified theoretically at the DFT level.[153]

The reaction of 1,3-bis(ethoxycarbonyl)-1,3-azaphospholo[5,1-*a*]isoquinoline with 2,3-dimethylbutadiene in presence of sulphur or methyl iodide yielded cycloadduct **64** and **65**, respectively. Reaction of isoprene in presence of sulphur took place

with full diastereo- and regioselectivities, but the presence of methyl iodide, lowered the regioselectivity and two regioisomers **65** and **65′** were obtained (Scheme 3.7). The structure of the compound **64** was confirmed by X-ray diffraction studies.[133,136a]




**Scheme 3.7.** DA reaction of 1,3-bis(ethoxycarbonyl)-1,3-azaphospholo[5,1-*a*]isoquinoline with dienes.

It is observed that the $HOMO_{diene} - LUMO_{dienophile}$ gap decreases significantly for 1,3-bis(ethoxycarbonyl) derivative of isoquinoline (**41**) as compared to monosubstituted derivative to make the DA reaction feasible and the reaction could also be possible in the absence of oxidizing agent by refluxing in chloroform at room temperature.[135]

Microwave irradiation has also been found to be helpful in the faster completion of the DA reaction of 1,3- azaphospholo[5,1-*a*]isoquinoline with 2,3-dimethylbutadiene and isoprene in presence of sulfur without affecting the yields, stereo- and regioselectivities.[136b]

In contrast to these results, 3-alkoxycarbonyl-2- phosphaindolizines , obtained through [4+1] cyclocondensation and having an electron withdrawing group at position -3, was unable to undergo DA reaction even on heating under reflux in toluene with or without sulfur.[136b] This unusual effect of substituent (in spite of $CO_2Et$ being bonded directly to the dienophilic moiety) has been studied theoretically at the DFT (B3LYP/6-31G**) level., wherein NBO interactions unveils that the bridgehead nitrogen atom acting as an electron donor lowers the dienophilic activity of **8** ($R^1$ = Me) remarkably, but, in **39**, this electron-donating effect of nitrogen is counterbalanced by the another $CO_2Et$ group, making it receptable to undergo DA reaction (Figure 3.4).

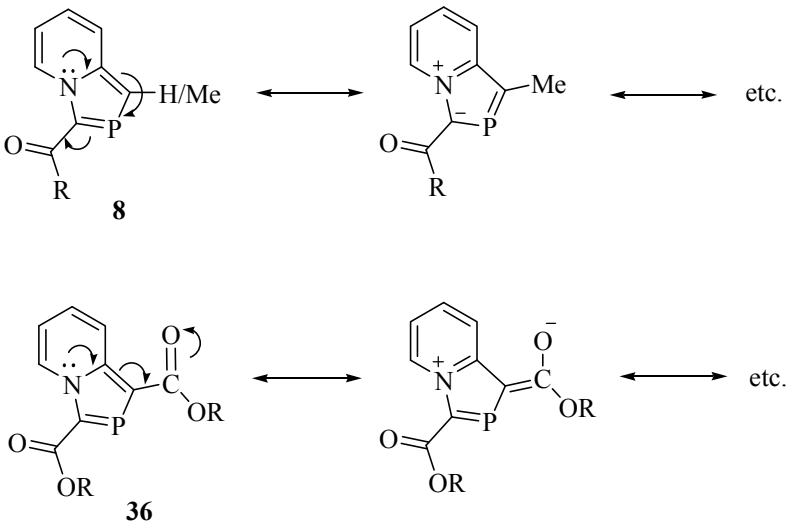
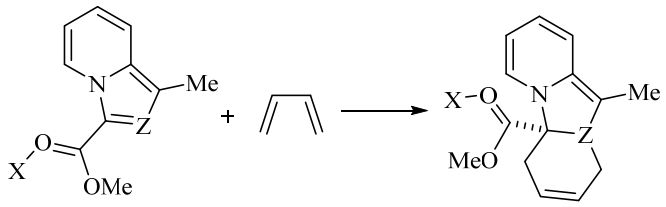



**Figure 3.4.** Effect of substituents on reactivity of 2-Phospaindolizine.

Theoretical calculations enabled us to rationalize the difference in the dienophilic reactivities of **36** and **8**.[135,136a]

The effect of organo-alumunium chloride catalysts on the dienophilic reactivity of indolozine and 2-phospaindolizines towards DA reaction with 1,3-butadiene has been further investigated theoretically at the DFT level (B3LYP/6-31+G**). On co-ordination of organo-alumunium catalyst (i. e. Lewis acid) with oxygen atom of the carbonyl group of indolizine or 2-phospaindolizine, the activation energy barrier is enhanced instead of being lowered juxtaposed to the activation energy barrier of for the DA reaction with the non-complexed compound (Scheme 3.8).[154]



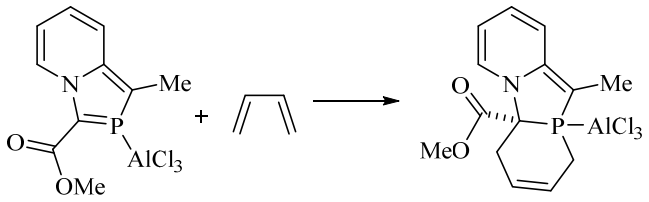

**66** **67**

| X | Z | $E_a$ (kcal $mol^{-1}$) in $CH_2Cl_2$ |
|---|---|---|
| - | CH | 45.68 |
| $AlCl_3$ | CH | 46.77 |
| - | P | 30.80 |
| $AlCl_3$ | P | 32.43 |

**Scheme 3.8.** Effect of organo-aluminium chloride catalyst on the reactivity of 2-phosphaindolizines towards DA reaction.

The co-ordination of Lewis acid with oxygen atom of the carbonyl group in 2-phosphaindolizine makes a facile transfer of the lone-pairs from the bridgehead nitrogen atom making the dienophilic moiety, (>C=P-) more electron rich in contrast to that in the uncomplexed indolizine or 2-phospaindolizine. It explains the non-reactivity of the compounds of type **8** towards DA reactions even in presence of Lewis acid catalyst.

$\sigma^2,\lambda^3$-phosphorous atom is, however, another site to co-ordinate with the Lewis acid, in 2-Phosphaindolizine . Theoretical studies of the DA reaction of 2-phosphaindolizine complexed to $AlCl_3$ at the $\sigma^2,\lambda^3$-phosphorous atom with 1,3-butadiene, revealed that the activation energy barrier was lowered significantly.[135,154] Guided by these results, DA reactions of 2-phosphaindolizines (**8**) were accomplished successfully with 2,3-dimethylbutadiene (DMB) in the presence of ethylaluminium dichloride as catalyst (Scheme 3.9).[155]

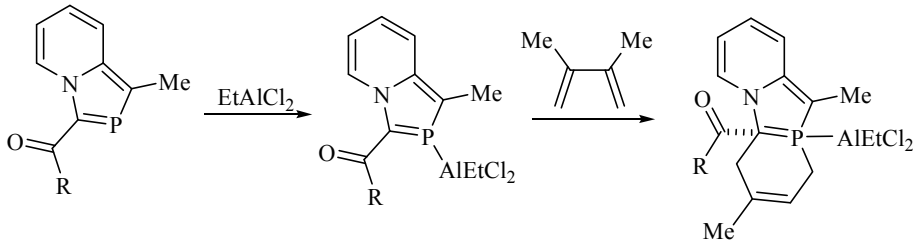



**68** **69**

$\mathbf{E_a\ (kcal\ mol^{-1})} = 22.57$
in $CH_2Cl_2$

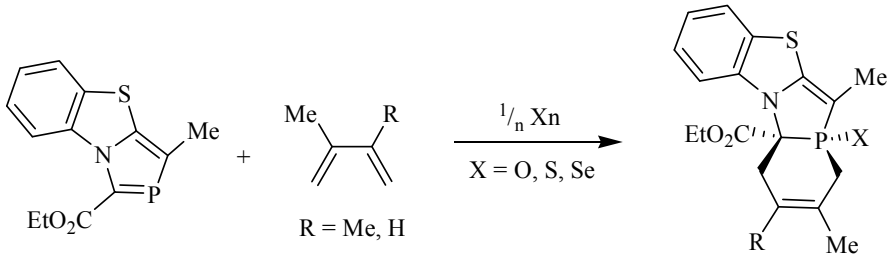
**Scheme 3.9.** Catalytic DA reaction of 2- phosphaindolizine.

Thus DA reaction of 2-phosphaindolizine-$\eta^1$-P=aluminium(O-menthoxy)dichloride complex was carried out with DMB, when complete diastereoselectivity was observed (Scheme 3.10). The results of the computational calculations at the DFT level (B3LYP/6-31+G*) unveils that the O-menthoxy moiety blocks the *Re* face of the >C=P- functionality so that only *Si* face is available for the attack of the diene.[134]




**Scheme 3.10.** Lewis acid-catalyzed DA reaction of 2-phosphaindolizine.

1,3-Azaphospholo[5,1-*b*]benzothiazole (**72**) , prepared through a [4+1] cyclocondensation method,[21] undergoes DA reaction with 1,3-dienes in the presence of an oxidizing agent with with complete stereo- and region-selectivity. When the reaction was carried out with isoprene, complete regioselectivity was observed and products **73d,e** were formed in the reaction (Scheme 3.11).[156]

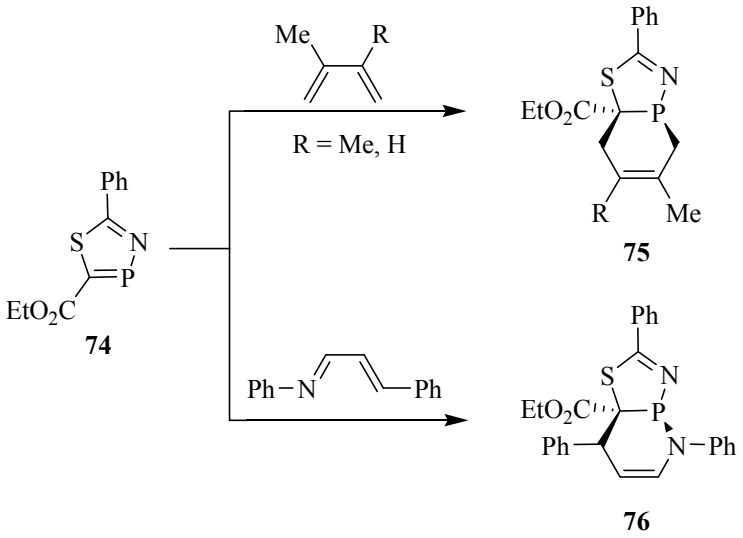



| | R | X |
|---|---|---|
| **a** | Me | O |
| **b** | Me | S |
| **c** | Me | Se |
| **d** | H | S |
| **e** | H | Se |

**Scheme 3.11.** DA reaction of 1,3-Azaphospholo[5,1-*b*]benzothiazole with 1,3-dienes.

An identical pattern of reactivity was shown by 5-ethoxycarbonyl-2-phenyl-1,3,4-thiazaphosphole (**74**), which accomplished DA reactions with 1,3-dienes and

phenyl-1-azabutadiene.[7] On carrying out reaction with 1,4-diphenyl-1-azabutadiene, compound **76** was formed with complete regioselectivity.[157]

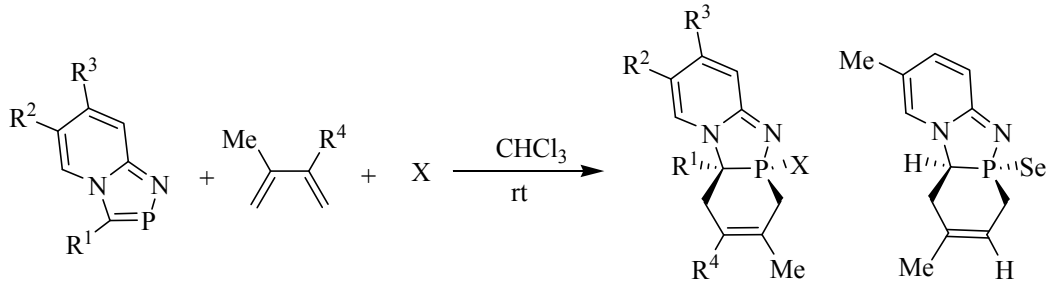



**Scheme 3.12.** DA reactions of 5-ethoxycarbonyl-2-phenyl-1,3,4-thiazaphosphole with differently substituted 1,3-dienes.

Introduction of additional $\sigma^2,\lambda^3$-nitrogen atom in 1,3-azaphosphole ring constitutes diazaphosphole ring and this extra nitrogen enhances the reactivity of the >C=P- moiety towards DA reaction. The DA reaction of annelated diazaphospholes are possible even in the absence of an oxidizing agent. However, due to greater reactivity of the three- coordinated phosphorous, the resulting cycloadducts are very sensitive towards air oxidation. Pure products are obtained only when the reaction is carried out in presence of an oxidizing agent.

[1,4,2]Diazaphospholo[4,5-*a*]pyridines (**77**)[115,158] undergo DA reaction with 2,3-dimethylbutadiene and with isoprene in the presence of sulfur or selenium as oxidizing agent at room temperature to yield [2+4] cycloadducts diastereo- and regioselectively. The reaction of **77b** ($R^1$, $R^3$ = H, $R^2$ = Me) with isoprene in the

presence of selenium yielded **78g** and **78g′** in an approximate 4:1 ratio (as determined by $^{31}$P NMR) (Scheme 3.13).[159]




**77** **78a-g** **78g'**

$R^1$ = H, $CO_2Et$
$R^2$, $R^3$ = H, Me

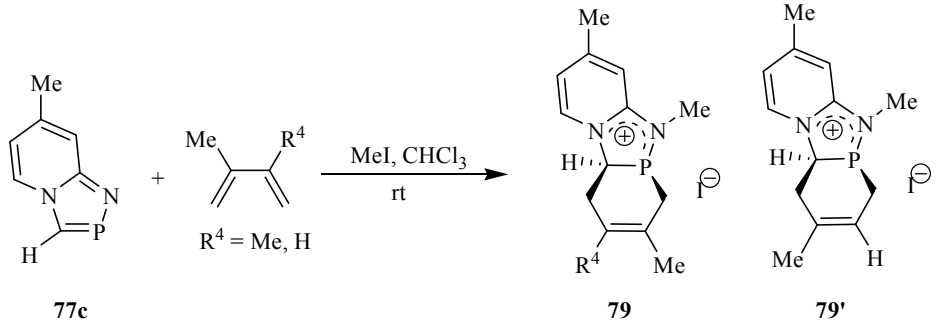
$R^4$ = Me, H
X = S, Se

| **63** | $R^1$ | $R^2$ | $R^3$ | $R^4$ | X |
|---|---|---|---|---|---|
| **a** | H | H | H | Me | S |
| **b** | H | Me | H | Me | S |
| **c** | H | H | Me | Me | S |
| **d** | H | H | Me | Me | Se |
| **e** | $CO_2Et$ | H | H | Me | S |
| **f** | $CO_2Et$ | H | H | Me | Se |
| **g** | H | Me | H | H | Se |

**Scheme 3.13.** Regioselective DA reaction of [1,4,2]Diazaphospholo[4,5-*a*]pyridines with substituted dienes.

In contrast to it, in the absence of an oxidising agent, reaction of **77b** with 2,3-dimethylbutadiene was very slow and was found to be completed only after refluxing in chloroform for 24 days ($\delta^{31}$P = 66.0 ppm). These results again confirmed the fact that oxidizing agents are required in DA reactions to apply a thrust to these reversible processes in forward direction by oxidizing the $\sigma^3$-phosphorous atom of initially formed [2+4] cycloadduct. This fact was further supported by the reaction of **77c** with 2,3-dimethylbutadiene and methyl iodide under similar conditions to give **79** ($R^4$ = Me). Here, methylation occurred at the $\sigma^2,\lambda^3$-nitrogen atom of the cycloadduct. Likewise, the reaction with isoprene under these conditions afforded $\sigma^2,\lambda^3$-nitrogen methylated cycloadducts regioselectively,

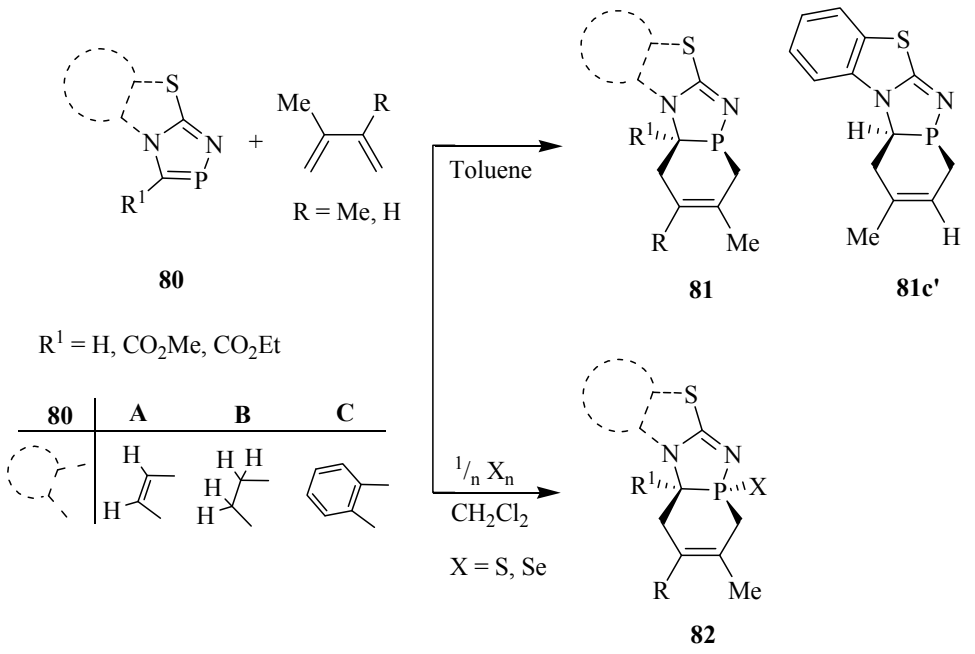
where both the regioisomers **79** ($R^4$ = H) and **79′** were produced where the former product was the predominant one (70%) (Scheme 3.14).[159]




**Scheme 3.14.** Regioselective DA reaction of [1,4,2]diazaphospholo[4,5-*a*]pyridines with dienes in the presence of methyl iodide.

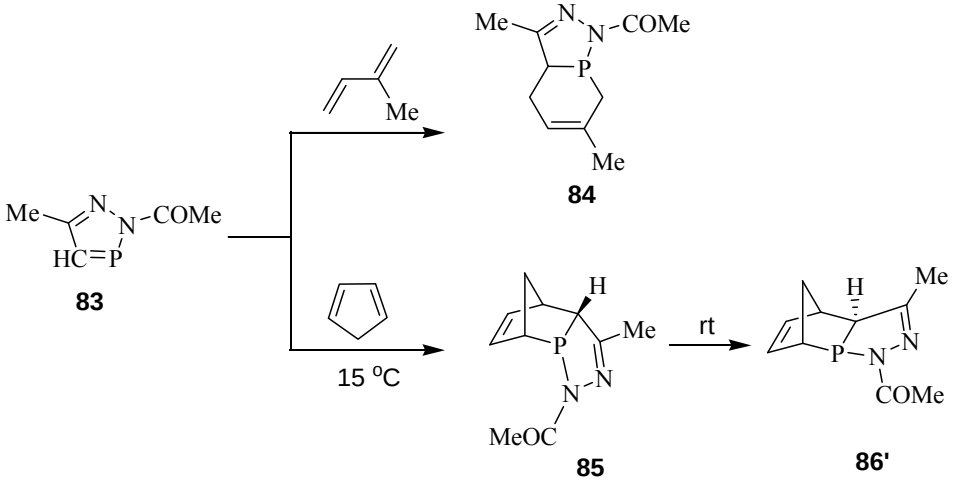
Considering the observed non-reactivity of **77** ($R^1 = R^2 = R^3$ = H) with methyl iodide,[139] it was concluded that methylation occurred after the formation of [2+4] cycloadduct and the +M effect of the junction nitrogen atom makes $\sigma^2,\lambda^3$-N more nucleophilic than $\sigma^3$-P. DFT calculations successfully explained the observed regioselectivities.[139]

Similarly, [2+4] cycloaddition reaction of thiazolo[3,2-*d*][1,4,2]diazaphospholes and their 5,6-dihydro- and benzo- derivatives (**80**), achievable through a [4+1] cyclocondensation method,[112] reacted with 2,3-dimethylbutadiene and with isoprene to give [2+4] cycloadducts stereoselectively. Moreover, the reactions with isoprene occurred with complete regioselectivity, except when the dienophilic moiety is unsubstituted, as in the case of **80C** ($R^1$ = H), when two regioisomers **81c** and **81c′** were formed in a 2:1 ratio (Scheme 3.15).[154,155]




**Scheme 3.15.** DA reaction of thiazolo[3,2-*d*][1,4,2]diazaphospholes with dienes.

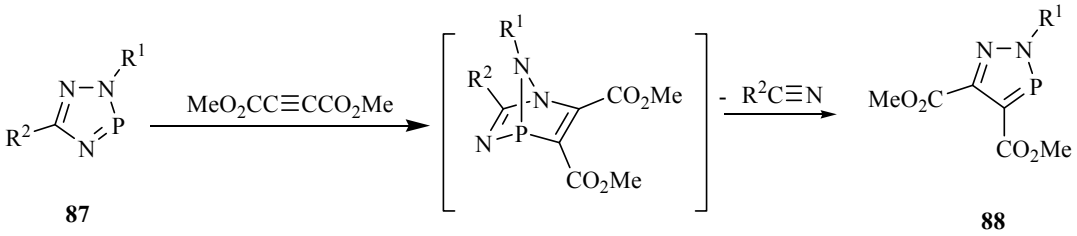
The DA reactions of 2-acetyl-[1,2,3]diazaphosphole (**83**) with isoprene[160] and with cyclopentadiene[161] took place with complete regio- and stereooselectivities to form **84** and **85** respectively (Scheme 3.16). The *endo*-product **86** was formed at lower temperature (15°C), which changed into the *exo*-product **86′** which is thermodynamically more stable through cycloreversion on keeping in solution for 3 days at room temperature.[161]




**Scheme 3.16.** DA reactions of 2-acetyl-[1,2,3]diazaphosphole with dienes.

## [4+2] Cycloaddition

It has been observed that in some cases, the azaphosphole ring can participate in cycloaddition reactions as the diene component leading to [4+2] cycloadducts. Azaphospholes, incorporating $\sigma^2,\lambda^3$- nitrogen atom adjacent to the two-coordinate phosphorus atom act as heterodiene and combine with an electron-deficient dienophile such as an acetylene, alkene or phosphaacetylene to form a [4+2] cycloadduct. The cycloaddition of azaphospholes with acetylene derivatives is usually followed by cycloreversion followed by extrusion of a nitrile or similar molecule to generate a new azaphosphole. This kind of behaviour was first reported for [1,2,4,3]triazaphosphole (87) as 1,3-heterodiene during its reaction with DMAD which led to a [4+2] cycloadduct as an unstable intermediate. This cycloadduct converted into [1,2,3]diazaphosphole (**88**) by loss of alkyl nitrile (Scheme 3.17).[162] The regioselectivity could also be observed on using monoalkyl esters of acetylenedicarboxylic acid.



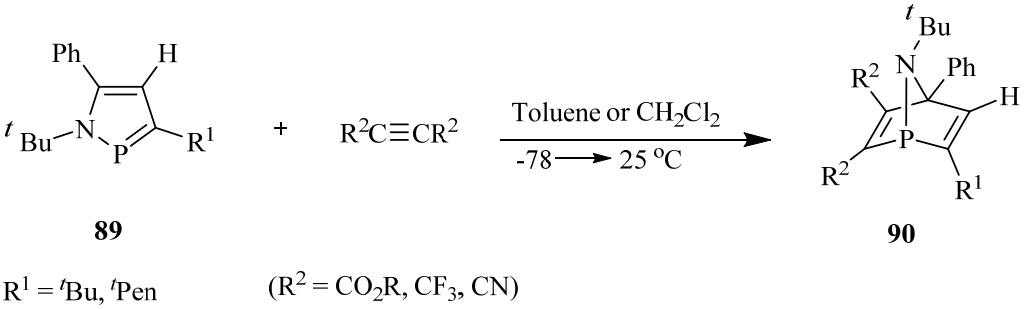

**87** **88**

$R^1/R^2$ = Me/Ph; $SiMe_3/Me_2N$

**Scheme 3.17.** [4+2] Cyloaddition of [1,2,4,3]triazaphosphole with DMAD.

Similarly, [1,3,2]diazaphosphole-4,5-dicarbonitrile (**89**) reacts with electron-deficient acetylene derivatives to afford *1H*-1,2-azaphosphole-5-carbonitriles (**90**) through [4+2] cycloaddition/reversion.[163] However, in the reaction of *1H*-1,2-

azaphospholes with electron-deficient acetylene, stable [4+2] cycloadducts was formed (Scheme 3.18).[164] The structure of the cycloadduct ($R^1$ = $^t$Bu, $R^2$ = $CF_3$) was confirmed by an X-ray crystallographic analysis.[164]



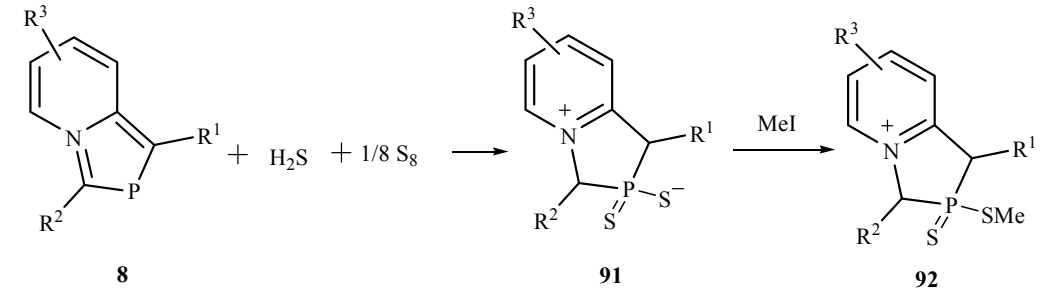

**89** **90**

$R^1$ = $^t$Bu, $^t$Pen ($R^2$ = $CO_2R$, $CF_3$, CN)

**Scheme 3.18.** [4+2] Cycloaddition of [1,3,2]diazaphosphole-4,5-dicarbonitrile with acetylene derivatives.

### 3.1.4 Other 1, 2-Addition Reactions on C=P or N=P bond:

2-Phospaindolizines (**8**) react with $H_2S$ in the presence of sulfur to give zwitterionic pyridinium dithiophosphinates (**91**) through simultaneous 1,2-addition of $H_2S$ on the >C=P– moiety and oxidation of the phosphorous atom followed by 1,3-prtotropic shift. The resulting product can be *S*-methylated with methyl iodide to yield (**92**) (Scheme3.15).[111,165] A selenium analogue was also obtained.

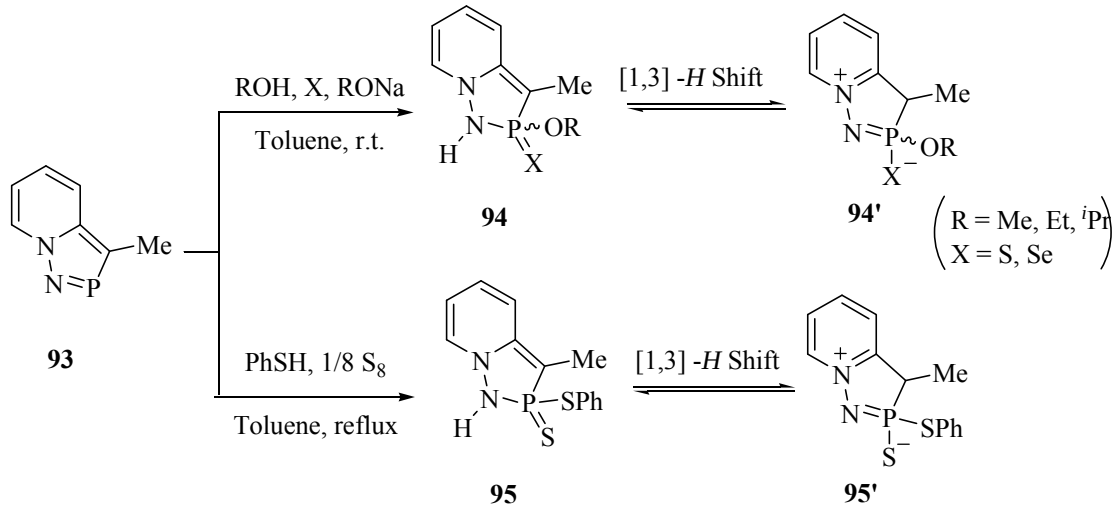



**8** **91** **92**

$R^1$ = H, Me
$R^2$ = COPh,$COCMe_3$, $CO_2Me$, $CO_2Et$, CN, $C_6H_4NO_2$-*p*
$R^2$ = H, Me, Bu

**Scheme 3.19.** 1,2-Addition of $H_2S$ on 2-Phospaindolizines in presence of sulfur.

[1,2,3]Diazaphospholo[1,5-*a*]pyridine (**73**) react with alcohols or thiophenol only in presence of sulphur or selenium to afford the corresponding 1,2-addition products (Scheme 3.20)[166]



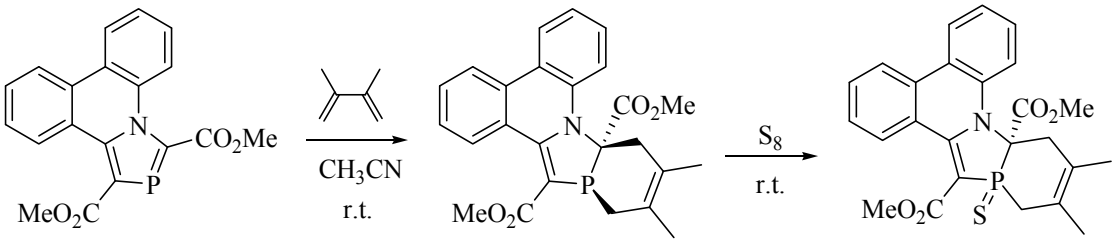

**Scheme 3.20.** 1,2- Addition of alcohols or thiophenol on [1,2,3]diazaphospholo[1,5-*a*]pyridine.

Considering all these reactions, we further extended the library of DA reaction of 1,3-azaphospholophenanthridine with 2,3-dimethylbutadiene following the methodology reported earlier for the DA reaction of isoquinolinium analogues (**41**).

## 3.2 Results and Discussion

### 3.2.1 Experimental

1,3-Bis(methoxycarbonyl)-1,3-azaphospholo[1,5-*f*]phenanthridine (**47a**) on reaction with 2,3-dimethylbutadiene (DMB) in presence of sulphur using acetonitrile as solvent at ambient temperature undergoes [2+4] cycloaddition to afford the cycloadduct **82.**[105]




**36a** **81** **82**

**d$^{31}$P 175.5 ppm** **d$^{31}$P 59.5 ppm** **d$^{31}$P 72.5 ppm**

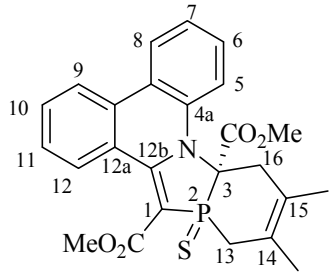
(M. P.= 104-106 $^0$C)

**Scheme 3.21.** The DA reaction of 1,3-Bis(methoxycarbonyl)-1,3-azaphospholo[1,5-*f*]phenanthridine with DMB.

Initially **36a** was reacted with DMB when a $^{31}$P NMR signal at δ 59.5 ppm confirmed the formation of the product **81**. Sulphur was thereafter added to the solution of **81** which gave cycloadduct **82**. A signal at δ 72.5 ppm in $^{31}$P NMR was observed for **82** . The compound **82** was obtained as a crystalline solid soluble in polar solvents such as chloroform, methylene chloride but sparingly soluble in non-polar solvents like hexane, benzene and diethyl ether. Its structure has been further determined on the basis of $^1$H and $^{13}$C NMR studies.

### 3.2.1 Structural elucidation of [2+4] cycloadduct

The cycloadduct of 1,3-bis(methoxycarbonyl)-1,3-azaphospholo[1,5-*f*]phenanthridine with DMB was obtained in good yield (74%). Structural elucidation was done on the basis of $^1$H, $^{31}$P and $^{13}$C NMR spectroscopic data (Table 3.1).




**82**

**Table 3.1.** $^{1}$H and $^{13}$C NMR spectral data of the cycloadduct **82**

| **$^{1}$H NMR , δ(ppm), J(Hz)** | **$^{13}$C NMR, δ(ppm), J(Hz)** |
|---|---|
| 1.33 (d, 3H, $^{5}J_{PH}$= 7.6, 15- $CH_3$), 1.37 (d, 3H, 14- $CH_3$), 3.06 (dd, 1H, $^{2}J_{HaHb}$ = 14.8, $^{3}J_{PH}$= 16.8, $H_b$-16), 3.07 (dd, 1H, $^{2}J_{HaHb}$ = 14.4, $^{2}J_{PH}$= 16.8, $H_b$-13), 3.08 (dd, 1H, $^{2}J_{HaHb}$ = 14.4, $^{3}J_{PH}$= 16.8, $H_a$-13), 3.09 (dd, 1H, $^{3}J_{HaHb}$ = 14.8, $^{3}J_{PH}$= 22.0, $H_a$-16), 3.80 (s, 3H, 1-O*CH*$_3$), 3.81 (s, 3H, 3-O*CH*$_3$)7.71 (dd, 1H, $^{3}J_{HH}$ = 8.8, H-11), 7.93- 8.25 (m, 3H, H-6, H-7, H-10), 8.27 (d, 1H, $^{3}J_{HH}$ = 8.8, H-9), 8.50 (d, 1H, $^{3}J_{HH}$ = 9.6, H-8), 8.78(d, 1H, $^{3}J_{HH}$ = 8.8, H-12), 8.83 (d, 1H, $^{3}J_{HH}$ = 9.6, H-5) | 19.9 (14-$\underline{C}H_3$), 20.0 (15-$\underline{C}H_3$), 46.0 (C-13), 46.0 (C-16), 53.8 (3-O$\underline{C}H_3$), 57.7 (1-O$\underline{C}H_3$), 76.8 (C-3), 77.4 (C-1) 118.6, 122.6, 122.9, 123.9, 124.8, 126.1, 129.8, 130.6, 132.6, 133.8, 134.4, 135.4, 139.0 (aromatic carbon), 157.9 (12b), 166.0 (3-CO), 166.1 (1-CO), |

**$^{31}$P NMR**

The Diels-Alder reaction across the >C=P- moiety of 1,3-bis(methoxycarbonyl)-1,3-azaphospholo[1,5-*f*]phenanthridine leads to an increase in the coordination number of the phosphorous atom accompanied by an upfield shift in the $^{31}$P NMR chemical shift. In the case of **81**, a $^{31}$P NMR signal at δ 59.5 ppm confirms the three co-ordinated phosphorous atom. After the addition of sulphur, the $^{31}$P NMR signal is shifted to δ 72.5 ppm (in **82**) which confirms four co-ordinated nature of

the phosphorous atom. The $^{31}P$ NMR spectra of the compounds **81** and **82** are reproduced in Figures 3.5 and 3.6 respectively.

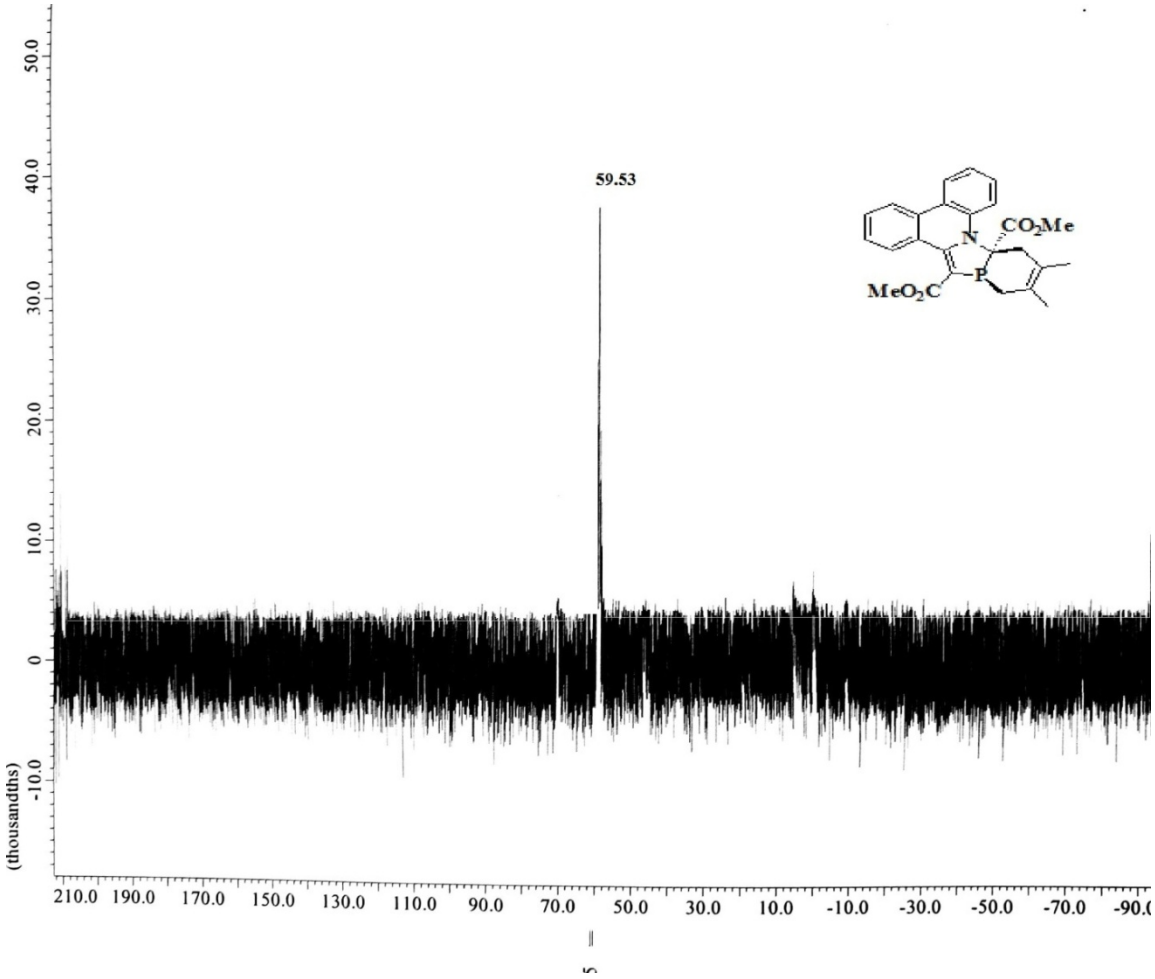



**Figure 3.5.** $^{31}P$ NMR spectrum of cycloadduct 81.

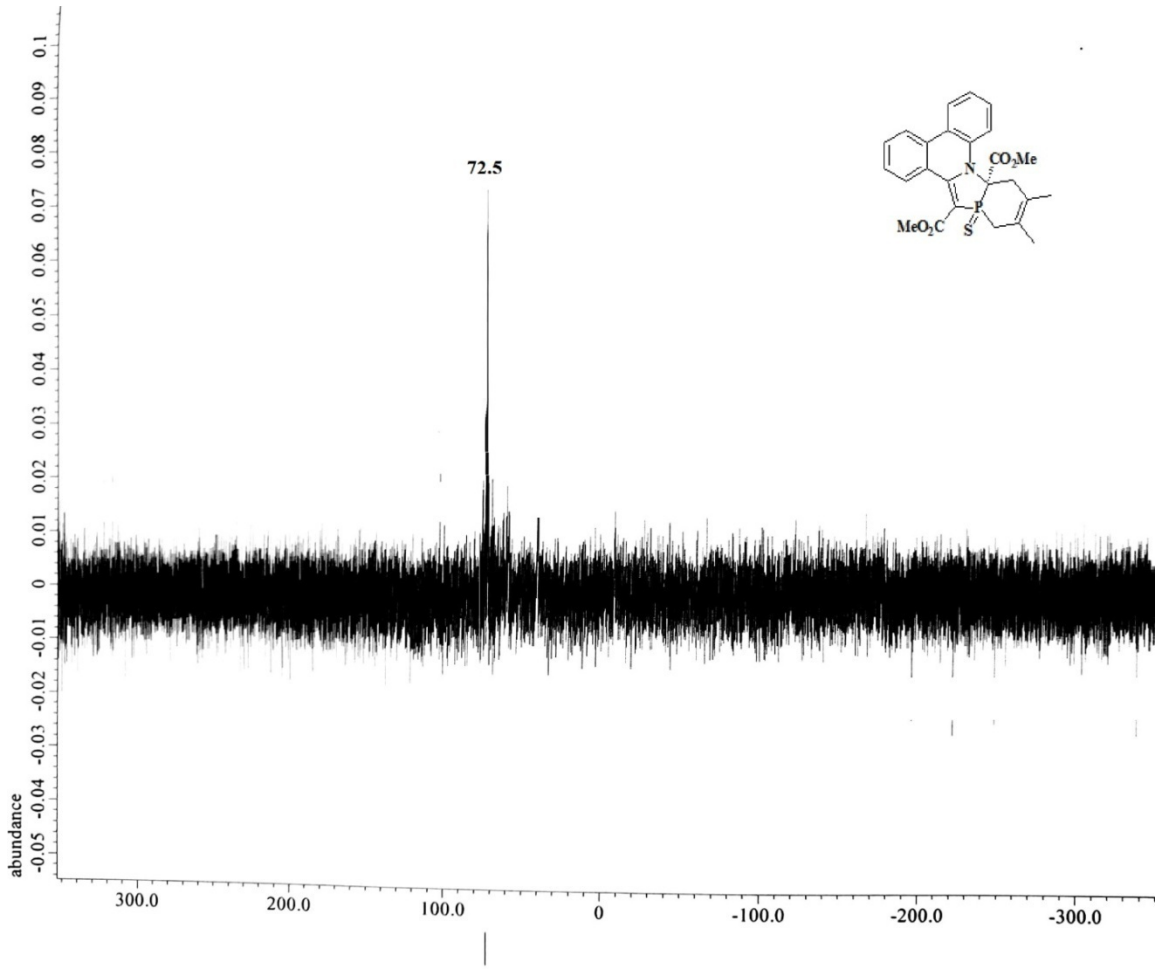



**Figure 3.6.** $^{31}$P NMR spectrum of cycloadduct 82.

## $^{1}$H NMR

The most deshielded signal in the $^{1}$H NMR spectrum of **82** is a doublet of H-5 at δ 8.8 ppm showing three bond coupling of δ 9.6 Hz with H-6. Next to the H-5, H-12 gives a doublet at δ 8.7 ppm showing three bond coupling of 8.8 Hz. Further, H-8 and H-9 also give doublets at δ 8.5 ppm and δ 8.3 ppm respectively. H-11 proton gives a doubledoublet (dd) at δ 7.7 ppm showing three bond coupling of 8.8 Hz with H-10 and H-12. The methyl protons of methoxycarbonyl are found at δ ~3.8 ppm as singlets. The diastereotopic behaviour can be seen for methylene protons at C-13 and C-16 in $^{1}$H NMR spectrum. Each of these protons absorbs separately

and shows germinal and vicinal couplings as defined in Table 3.1. Ha and Hb of C-16 show three bond coupling with phosphorous ($^3J_{PH}$= 16.8 Hz and $^3J_{PH}$= 22.0 Hz respectively) while Ha and Hb of C-13 show two bond coupling with phosphorous ($^2J_{PH}$= 16.8 Hz for both). The $^1$H NMR spectrum of the cycloadduct **82** is reproduced below in Figure 3.7.

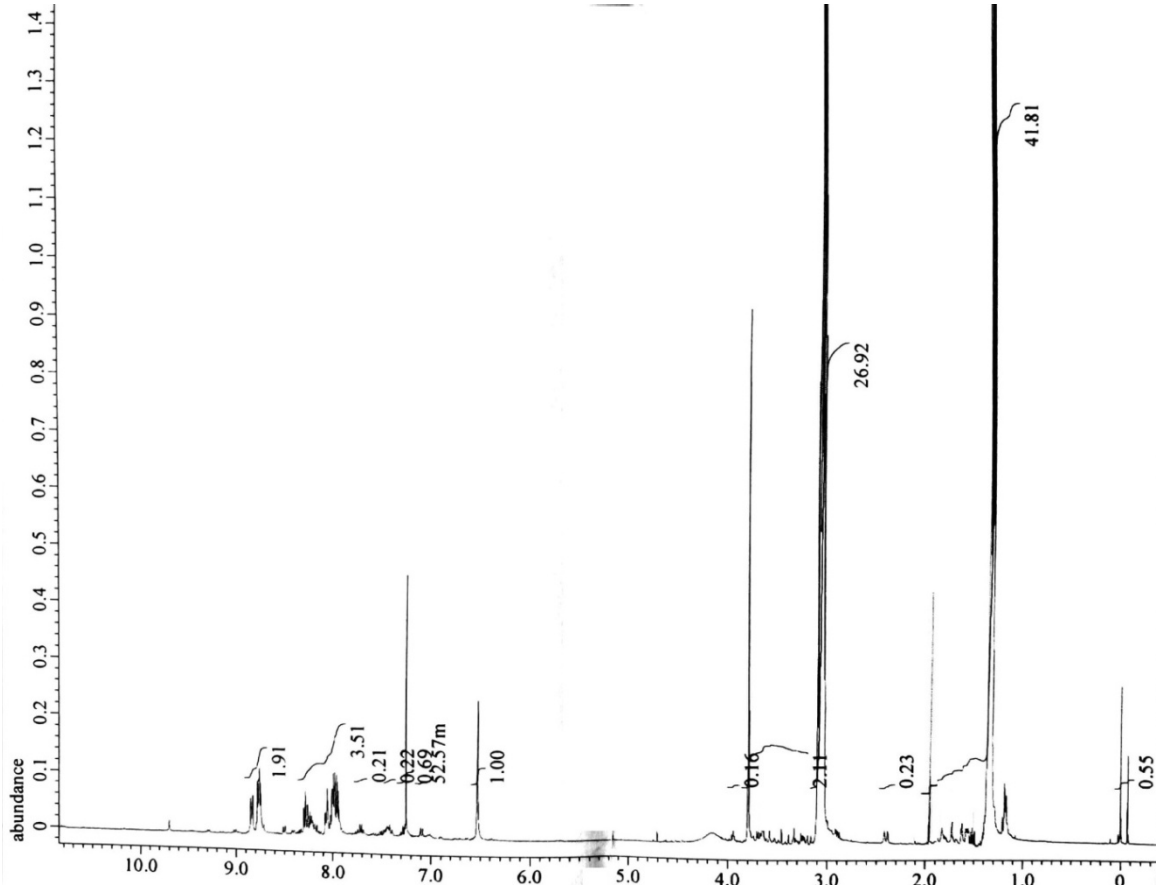



**Figure 3.7.** $^1$H NMR spectrum of the cycloadduct 82 in $CDCl_3$

## $^{13}$C NMR

The structure of the [2+4] cycloadduct **82** was further confirmed by $^{13}$C NMR spectrum. The $^{13}$C NMR chemical shifts are assigned in Table 3.1. As expected, the signal of C-3 is remarkably shielded as compared to that in the parent azaphospholopheneanthridine due to change in its hybridization to $sp^3$ and now being a part of the non-aromatic ring. Dearomatization of the azaphosphole ring

casues an upfield shift in the signal of C-1 also. The carbonyl carbon atoms are found most deshielded and show signals at ~ δ 166.0 ppm. C-12b particularly gives low intensity singlet at δ 157.9 ppm. Signals of the aromatic carbon atoms appear in characteristic region. Signals of the methyl carbon atom of the methoxy group appears at δ 53.8 ppm (3-O*CH*$_3$) and δ 57.7 ppm (1-O*CH*$_3$). Carbon atoms of the methyl substituents at C-14 and C-15 appear at ~ δ 20 ppm. C-13 and C-16 also show signals at ~ δ 46.0 ppm.

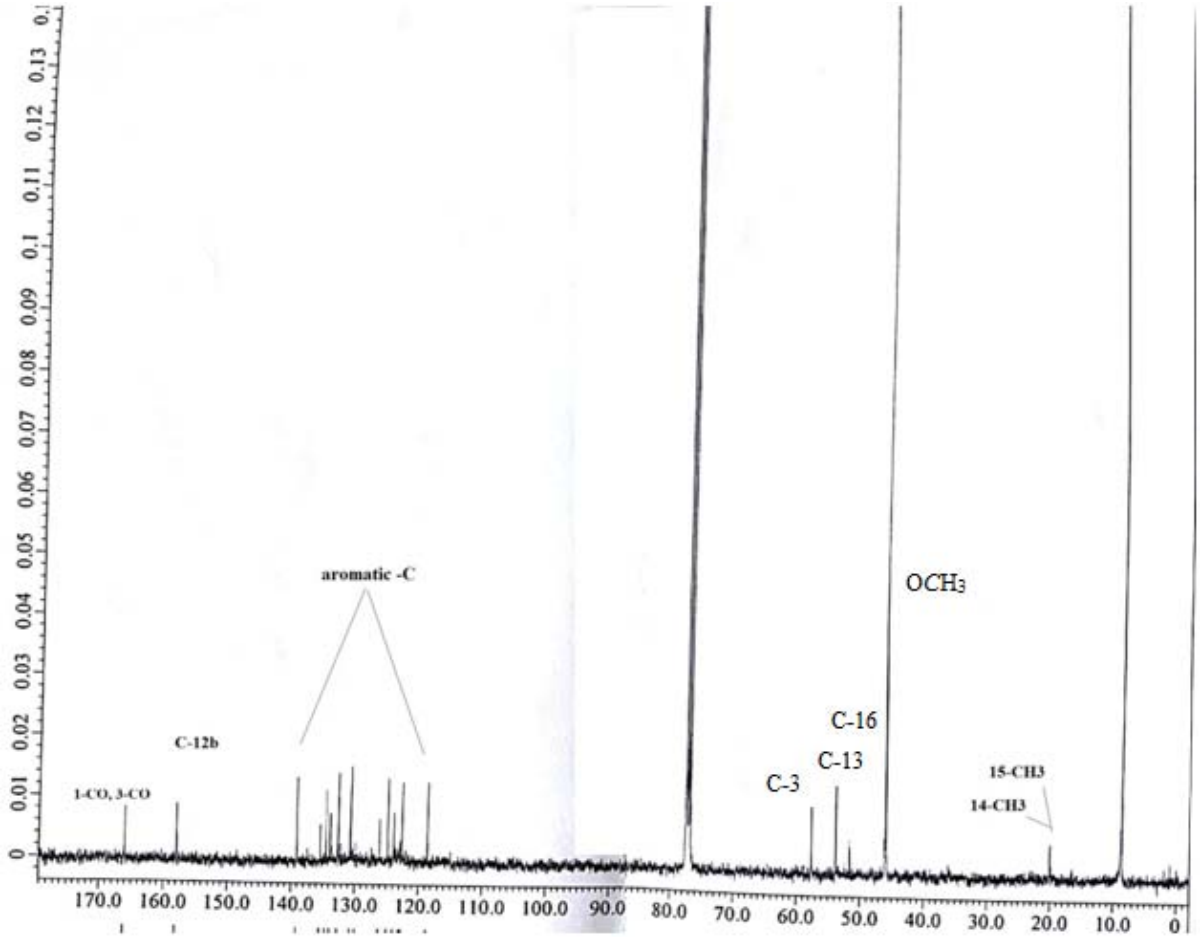



**Figure 3.8.** $^{13}$C NMR spectrum of the cycloadduct 82 in $CDCl_3$

### 3.2.3 Experimental Details

In view of the sensitivity of various reactants and products towards moisture and hygroscopic nature of the organophosphorous compounds, all possible precautions were taken to remove moisture from the apparatus. Glassware was dried for 2-3 hrs at high temperature in oven before use. All the reactions were carried out under dry oxygen-free nitrogen using Schlenk technique. Sythesized products were also stored under nitrogen atmosphere. Melting points were determined by capillary method on an electric Tempo instrument and are uncorrected.

#### 3.2.3.1Materials

In the preparation of the starting materials, the reagents and solvents were distilled and thoroughly dried. Acetonitrile and chloroform were dried over $P_2O_5$ followed by distillation. The distilled solvent was stored over molecular sieve. Hexane was dried by keeping over potassium hydroxide pallets for 24 hrs followed by refluxing over sodium wire in presence of benzophenone and distillation. 2,3-Dimethylbutadiene and sulphur were available commercially and were used as such.

#### 3.2.3.2Instrumentation

$^{31}P$ Nuclear magnetic resonance spectra were recorded on JOEL RESONANCE - 400 MHz spectrometer at frequency 161.83 MHz using 85% $H_3PO_4$ as external standard. $^{31}P$-NMR spectra, both of the reaction mixture as well as those of isolated products were scanned in 5 mm tube in $CDCl_3$.

$^{1}$H-Nuclear magnetic resonance spectra were recorded on JOEL RESONANCE-400MHz at observed frequency 399.78 MHz and Bruker-DPX-300 at frequency 300.13 MHz` spectrometer in $CDCl_3$ using Tetramethyl silane (TMS) as an internal standard in 5mm tube.

$^{13}$C-Nuclear magnetic resonance spectra were recorded on JOEL RESONANCE-400 spectrometer at observed frequency 100.52 MHz in $CDCl_3$ using TMS as an internal standard in 5mm tube.

### 3.2.3.3 General procedure

To a clear solution of 1,3-bis(methoxycarbonyl)-1,3-azaphospholo[1,5-*f*]phenanthridine (**36a**) (0.3 g, 1 mmol) in $CH_3CN$ (10 mL), an excess amount (three-fold) of DMB (0.24 g, 0.33 mL) was added dropwise and the resulting solution was stirred for 5 hrs at room temperature. Progress of the reaction was monitored by $^{31}$P NMR when a signal appeared at δ 59.5 ppm indicating completion of the cycloaddition. Thereafter, there was addition of sulfur powder (1 mmol, 0.03 g,) with stirring .Stirring was continued for another 10-12 hrs. A $^{31}$P NMR signal at δ 72.5 ppm confirmed complete oxidation of the initially formed cycloadduct. The solvent was removed under vacuum whereupon a dark yellow solid was obtained. After washing with hexane and recrystallisation was done with chloroform.

### 3.2.4 Conclusion

The >C=P- functionality in the annelated azaphospholes is more reactive than the >C=C< functionality in its non-phosphorous analogue and it undergoes Diels-Alder reaction with dienophile such as 2,3-dimethylbutadiene. The resulting [2+4] cycloadduct can be oxidized with sulphur.