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Acetylenes and nitriles as unconventional reactants for aza-Wittig reactions

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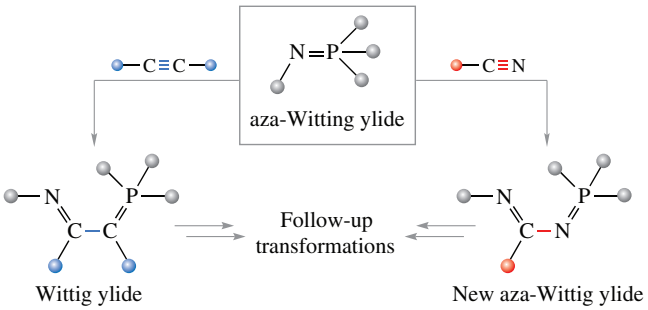
The classic version of aza-Wittig reactions, namely, reactions between phosphazenes and compounds with polar double bonds, is widely employed in organic synthesis to produce C=N bonds. However, only a limited number of aza-Wittig reactions between phosphazenes and compounds with triple bonds is known, which has a lot to do with certain structural features of the reactants, wherein additional activation is required. This review provides a guide to those rare examples of aza-Wittig reactions with acetylenes and nitriles. A unique trait of these atom-economic processes is that they afford Wittig or new aza-Wittig reagents, respectively, which offers new opportunities for employing these reactions in organic syntheses, especially those of N-heterocyclic compounds.

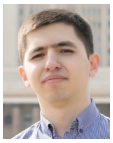


Keywords: aza-Wittig reaction, phosphazenes, acetylenes, nitriles, N-heterocyclic compounds.

1. Introduction

Even though the reactions of azaphosphonium ylides (also known as λ^5-phosphazenes, iminophosphoranes or phosphine imines) with compounds that contain carbonyl moieties or similar groups with polar multiple bonds were first attested in Staudinger's research dating back to early 20th century,[1,2] tradition dictates that those processes are treated as aza-analogues of Wittig reactions (Figure 1). This can be ascribed to the fact that phosphazene chemistry began its rapid ascent only in the second half of the 20th century which led to these compounds being widely employed to provide practical building blocks for the formation of C=N bonds, further leading to N-containing compounds of various classes. These investigations have been covered in several reviews.[3–18]

Similarly, a significant amount of research is focused on the mechanism of aza-Wittig reactions.[19–25] According to experimental and DFT data, these reactions proceed *via* a two-step mechanism that includes [2+2]-cycloaddition, resulting in



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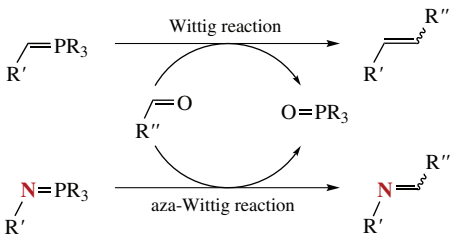


Figure 1 Analogy between Wittig and aza-Wittig reactions.

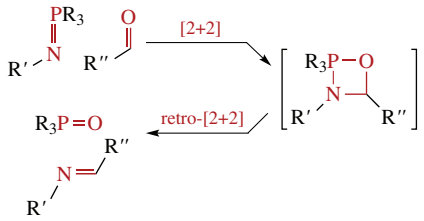


Figure 2 Suggested mechanism in aza-Wittig reactions.

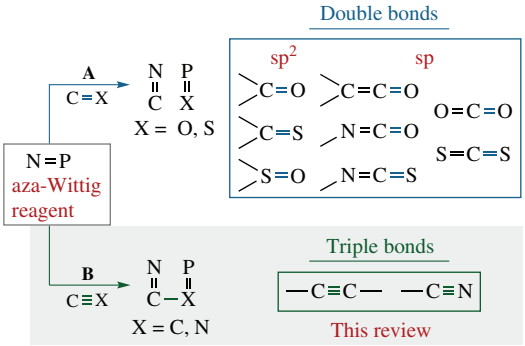


Figure 3 Scope of aza-Wittig reactions.

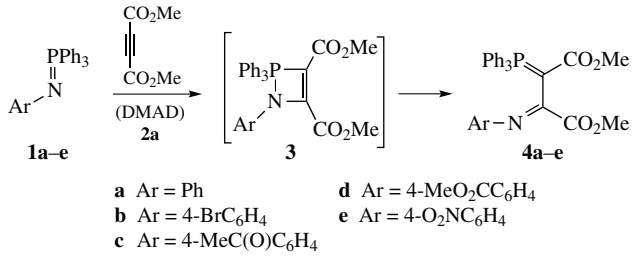
oxazaphosphazetidines as intermediates, and retro-[2+2]-cycloaddition (Figure 2).

At present, greatest insight in this area has been gained in the field of reactions between phosphazenes and compounds which contain polar double bonds with sp^2- or sp-hybridized electrophilic centers, namely, carbonyl and thiocarbonyl compounds, isocyanates and isothiocyanates, ketenes, carbon dioxide and carbon disulfide (Figure 3, path **A**). These processes are comprehensively studied and widely used by synthetic organic chemists; therefore, they overshadow any other examples in reviews focused on aza-Wittig reactions.[9–18] Meanwhile, aza-Wittig reactions with compounds that contain triple bonds have also been reported (see Figure 3, path **B**). However, these processes are a lot less widespread due to the challenges that chemists usually face in these cases. Problems primarily arise from low reactivity of the initial compounds which are driven by low electrophilicities of the carbon centers in triple bonds. Undoubtedly, tackling the problem of low reactivity for these compounds in their aza-Wittig reactions head-on could lead to this approach to new phosphazenes blossoming and providing new pathways to targeted functionalization of these intriguing molecules.

This review summarizes and analyzes scattered examples of aza-Wittig reactions between phosphazenes and compounds that contain C≡C and C≡N bonds.

2. aza-Wittig reactions with acetylenes

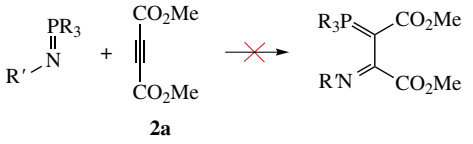
The first example of aza-Wittig reactions with compounds containing a triple C≡C bond was reported in 1964 by Brown *et al.*[26] They carried out reactions of phosphazenes **1** with dimethyl acetylenedicarboxylate (DMAD) **2a**, resulting in iminophosphonium ylides **4** (Scheme 1). Initially, the authors suggested two possible structures for the products: acyclic iminophosphonium ylide **4** and azaphosphetene **3**. Based on the X-ray crystallography data for the product containing a *para*-bromophenyl substituent, the structures of the resulting compounds were interpreted as those of iminophosphonium ylides **4**.



a Ar = Ph
b Ar = 4-BrC_6H_4
c Ar = 4-$MeC(O)C_6H_4$
d Ar = 4-$MeO_2CC_6H_4$
e Ar = 4-$O_2NC_6H_4$

Scheme 1

Subsequently, the same researchers carried out a detailed study of this reaction, wherein azaphosphetene **3** was suggested as an intermediate.[27] Phosphazenes with electron-withdrawing groups (EWGs) at the nitrogen atom as well as those with alkoxy groups at the phosphorus atom were found to be inert *vs.* DMAD **2a** under the studied conditions (Scheme 2).



R = Ph; R′ = PhC(O), EtO_2C, 4-$MeC_6H_4SO_2$, 2,4-$(O_2N)_2C_6H_3$
R = EtO; R′ = Ph, PhC(O), 4-$MeC_6H_4SO_2$

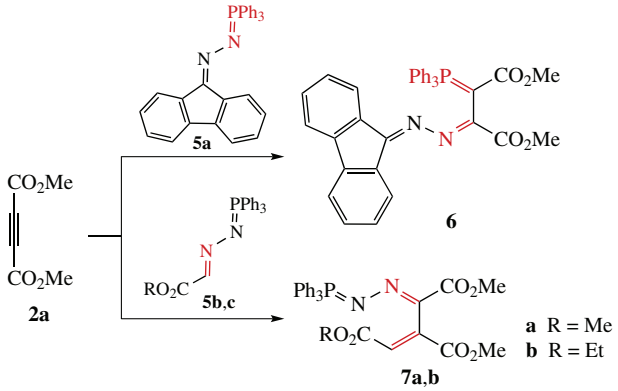
Scheme 2

Later studies of aza-Wittig reactions between phosphazenes and acetylenes demonstrated that only those acetylenes that are activated with acceptor moieties can participate in these reactions. Mostly these are 'bis-EWG-activated' acetylenes, such as DMAD **2a** or dibenzoylacetylene **2b**. Examples of such reactions with 'mono-EWG-activated' acetylenes are much scarcer (*e.g.* propynoates **2c**,**d**). Furthermore, depending on the structure of the initial phosphazenes, their aza-Wittig reactions with acetylenes can be suppressed, with other reactions of cycloaddition and electrocyclization taking place instead.

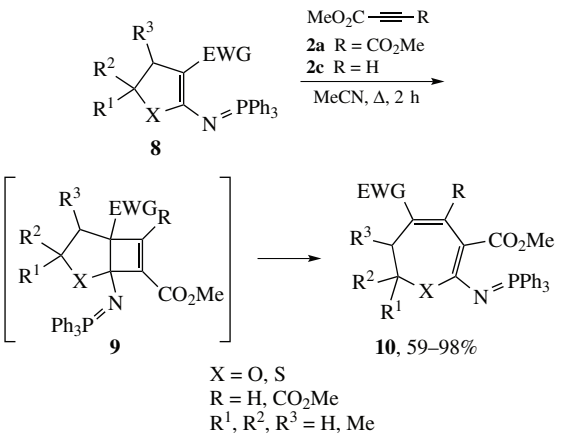
2.1. Substituent-dependent switching between aza-Wittig reactions and alternative processes

Using the hydrazone-derived phosphazenes **5** results in either the aza-Wittig reaction product **6** or products **7**, forming *via* [2+2]-cycloaddition of DMAD **2a** to the C=N double bond (Scheme 3).[27] This depends on the accepting abilities of substituents (aryl groups in **5a** *vs.* ester groups in **5b**,**c**).

Similarly, dihydrofurans and dihydrothiophenes **8**, wherein the phosphazene moiety at the C2 position of a heterocycle is conjugated to an EWG, do not participate in aza-Wittig reactions with mono- and disubstituted acetylenes **2a**,**c**.[28] In this case, [2+2]-cycloaddition of **2a**,**c** along the C=C bonds in dihydrofurans and dihydrothiophenes takes places instead, with subsequent rearrangement of the bicyclic system in intermediates **9** resulting in seven-membered heterocycles **10** (Scheme 4). The fact that the phosphazene moiety remains intact might be explained by the lower nucleophilicity of the nitrogen atom in the phosphazene group upon its conjugation with an EWG. This



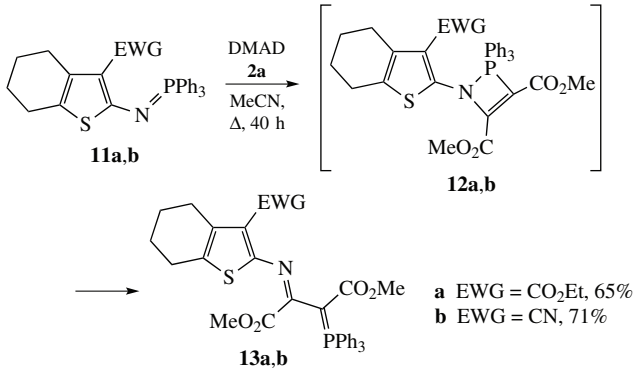
Scheme 3



Scheme 4

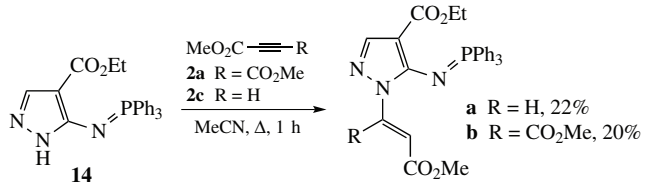
is analogous to the phosphazenes that are N-substituted with EWG groups[27] (see Scheme 2).

At the same time, the reaction of DMAD **2a** with compounds **11**, wherein the phosphazene moiety is bonded to thiophene, an aromatic hetereocycle, proceeds along the aza-Wittig reaction pathway *via* intermediates **12**, despite the phosphazene moiety being conjugated to an EWG (Scheme 5).[29] This results in thiophenes **13**, functionalized with fragments of iminophosphonium ylides.



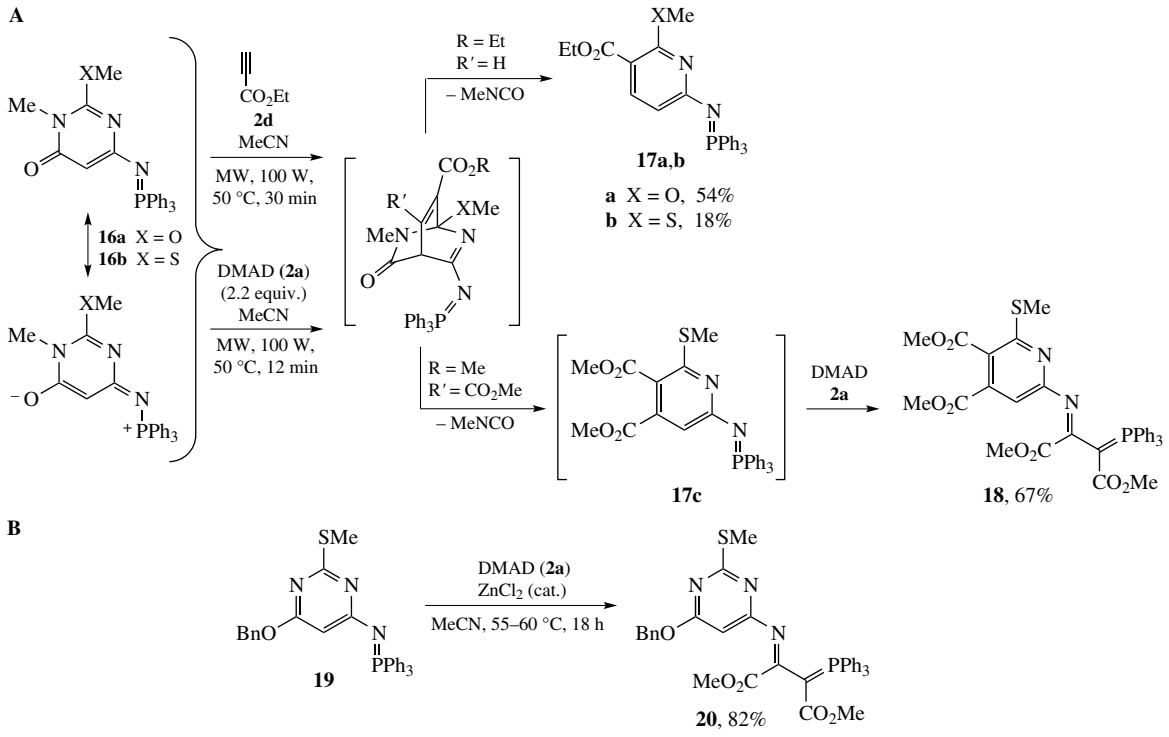
Scheme 5

As for the pyrazole-substituted phosphazene **14**, the nucleophilicity of the nitrogen atom in the pyrazole group turned out to be higher than that of the nitrogen atom in the phosphazene fragment. Thus, the reactions between **14** and **2a**,**c** proceed as nucleophilic addition of pyrazole to acetylene, yielding the derivatives of *N*-vinylpyrazole **15** (Scheme 6).



Scheme 6

Pyrimidone-containing phosphazenes **16a**,**b** yield pyridines **17** in their reactions with acetylene **2d** upon microwave irradiation (Scheme 7, part **A**).[30,31] Apparently, **17** are formed in a cascade process that involves a Diels–Alder reaction between pyrimidone and acetylene as well as a retro-Diels–Alder reaction involving methyl isocyanate elimination. Interestingly, the

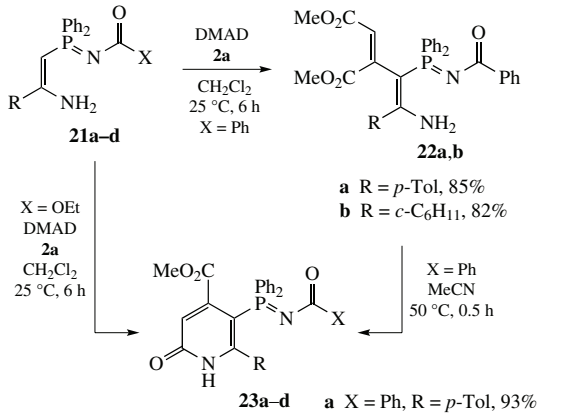


Scheme 7

phosphazene fragment does not react due to its nucleophilicity being lowered upon conjugation with the electron-withdrawing pyrimidone ring.

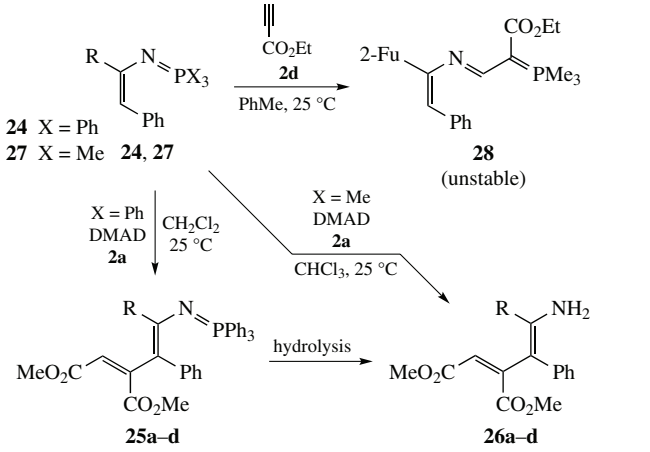
In analogous reaction of **16b** with two equivalents of the more reactive acetylene **2a**, not only the pyrimidone-to-pyridine transformation takes place, but the aza-Wittig reaction with the phosphazene fragment proceeds as well, leading to pyridinoiminophosphonium ylide **18** (see Scheme 7, part **B**). Phosphazene **19**, substituted with pyrimidine, selectively reacts along the aza-Wittig pathway with **2a**, forming pyrimidinoiminophosphonium ylide **20**; the heterocyclic fragment remains as is.[32]

The presence of a strong acceptor group at the nitrogen atom in *N*-benzoyl-substituted phosphazenes **21a**,**b** results in these compounds yielding the products of nucleophilic addition **22a**,**b** in their reactions with DMAD **2a** at room temperature (Scheme 8).[33,34] When heated to 50 °C, compounds **22a**,**b** undergo δ-lactamization into pyridones **23a**,**b** which contain intact phosphazene fragments. Notably, in a similar reaction with DMAD **2a**, carbamate derivatives **21c**,**d** form pyridones **23c**,**d** even at room temperature.



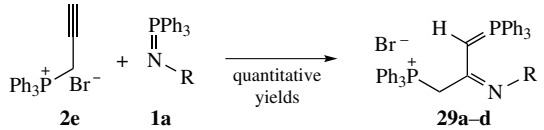
Scheme 8

The same can be said for *N*-vinylphosphazenes **24** which react with DMAD **2a** as C-nucleophiles and do not partake in aza-Wittig reactions regardless of the donor or acceptor nature of the R substituent at the α-position in relation to the nitrogen atom (Scheme 9).[35] As a result, butadienyl-substituted phosphazenes **25** are formed. When partial hydrolysis occurs, aminobutadienes **26** are yielded additionally. The reaction of the more reactive P-methylated phosphazenes **27** with DMAD **2a** proceeds along the same pathway. Curiously though, the monoactivated acetylene **2d** promotes a selective pathway for the aza-Wittig reaction with the unstable phosphonium imine **28** as the product.



Scheme 9

Another curious example of an aza-Wittig reaction involving phosphazenes **1a** and **5b**,**d**,**e** as well as the monosubstituted acetylene **2e** was reported by Schweizer *et al*. (Scheme 10).[36] Therein, the triphenylphosphonium substituent acts as an activating group. The described reaction results in quantitative yields of compounds **29**; their molecules include both phosphonium ylide fragments and the fragments of its precursor, a phosphonium salt.

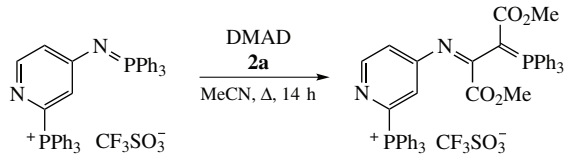


1a R = Ph
5b R = NHCO$_2$Et
5d R = N=CHC(O)Me
5e R = N=CHC(O)Ph

a R = Ph
b R = NHCO$_2$Et
c R = N=CHC(O)Me
d R = N=CHC(O)Ph

Scheme 10

Similar compounds can also be produced when a fragment of a phosphonium salt is located in the phosphazene molecule. Hence, phosphazene **30**, substituted with a triphenylphosphonium fragment, reacts with DMAD **2a** along the aza-Wittig pathway, forming the iminophosphonium ylide **31** in a 52% yield (Scheme 11).[37]

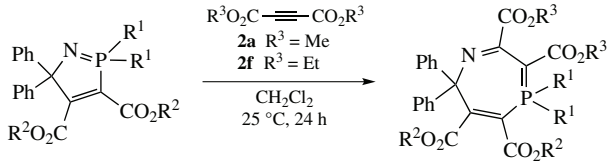


Scheme 11

2.2. Reactions with cyclic phosphazenes

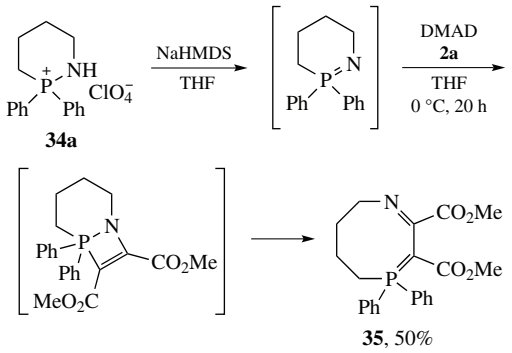
When a phosphazene fragment is placed within a cyclic structure, its reactions with acetylenes can be used to enlarge the cyclic system. Thus, the reactions between the five-membered cyclic phosphazenes **32a**–**c** and acetylenes **2a**,**f** resulted in seven-membered cyclic iminophosphonium ylides **33a**–**c** with yields of 55–65% (Scheme 12).[38]

An analogous enlargement of a six-membered ring afforded an eight-membered ring.[39] The initial six-membered cyclic phosphazene was produced *in situ* by mixing NaHMDS with salt **34a**. Then, the mixture was kept with DMAD **2a** at 0 °C for 20 h.



a $R^1 = R^2 = R^3$ = Me, 63%
b R^1 = Ph, $R^2 = R^3$ = Me, 55%
c R^1 = Me, $R^2 = R^3$ = Et, 65%

Scheme 12



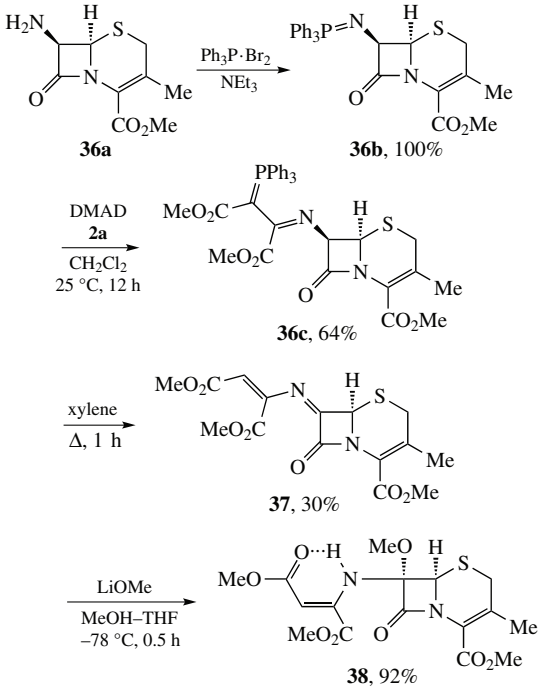
Scheme 13

This resulted in the eight-membered cyclic phosphorus ylide **35** with the yield of 50% (Scheme 13).

2.3. Follow-up transformations

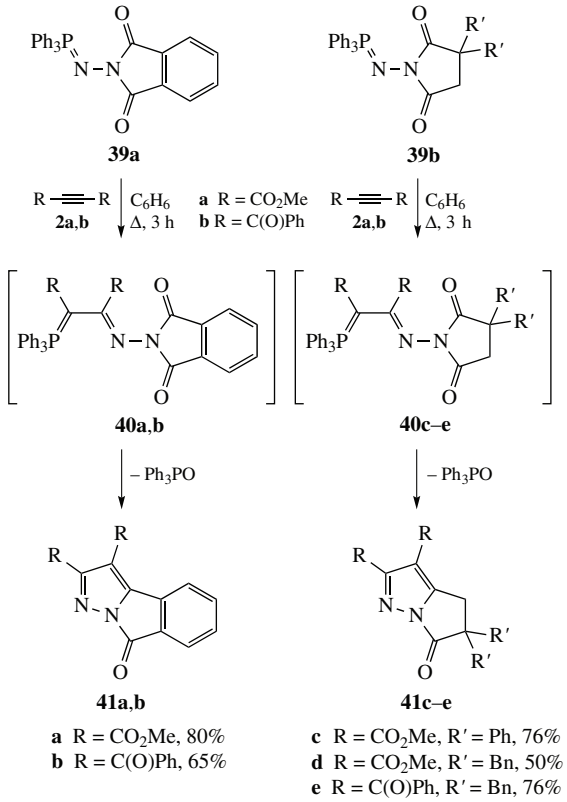
Due to the presence of the newly installed functional groups, the products of aza-Wittig reactions can be easily transformed into N-containing acyclic and cyclic compounds.

Phosphazenes and acetylenes reacting along the aza-Wittig pathway were successfully employed to produce compounds of type **38**: namely, the methoxylated derivatives of 7-amino-cephalosporanic acid **36a** (7-ACA). These compounds are valuable since they exhibit antibacterial activity towards gram-negative bacteria.[40] At the first step, phosphazene **36b** was synthesized from **36a** (Scheme 14). Then, it was introduced into an aza-Wittig reaction with **2a**. Further thermal transformation of the resulting ylide **36c** into **37** and the following methoxylation led to the target structure **38**.



Scheme 14

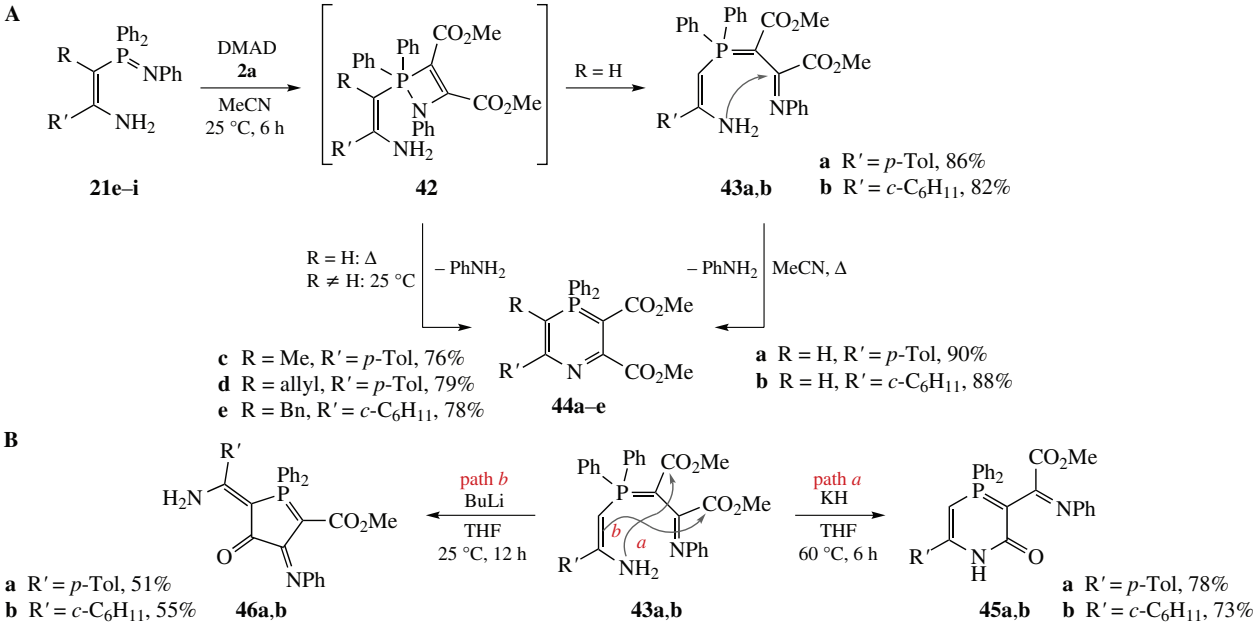
Owing to a new phosphonium ylide produced in the aza-Wittig reaction with acetylenes, further transformations of the synthesized molecules that involve this species are possible. Specifically, Foucaud *et al*. used a two-step aza-Wittig/Wittig reaction sequence to produce functionalized derivatives of pyrazole **41** from phosphazenes **39** and disubstituted acetylenes **2** (Scheme 15).[41] The intermediate iminophosphonium ylides **40**, formed at the first step, undergo cyclization to form pyrazoles **41** upon the reaction between the phosphorus ylide fragment and one of the carbonyl groups. When the carbonyl groups are non-equivalent, as in some succinimide fragments (**40c–e**), the phosphorus ylide selectively reacts with a less hindered carbonyl group, exclusively yielding the products **41c–e**.



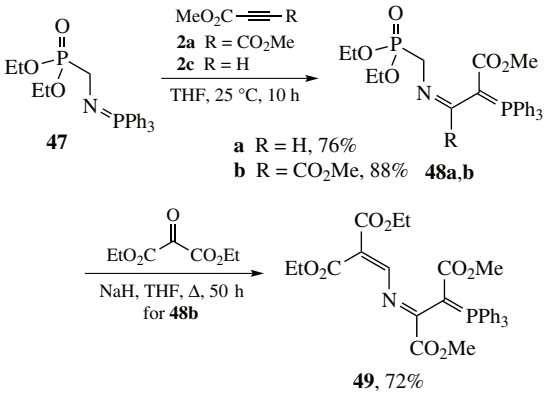
Scheme 15

Barluenga, Palacios *et al*. synthesized unusual compounds **44** wherein the iminophosphazene fragment is a part of the six-membered aromatic system.[33,42] Upon introducing phosphazenes **21e**,**f** (R = H) into a reaction with DMAD **2a**, acyclic iminophosphonium ylides **43** are formed at room temperature within 6 h (Scheme 16, part **A**). They only undergo cyclization at reflux in acetonitrile, eliminating aniline and yielding compounds **44a**,**b**. The authors demonstrated that this process can be switched to a one-pot mode if the reaction between **2a** and **21e**,**f** is immediately carried out at reflux in acetonitrile. For phosphazenes **21g–i** (where R ≠ H), heterocyclic ring closure in **44c–e** proceeds spontaneously even at room temperature. The enamine fragment acts as an ambident nucleophile in reactions of **43a**,**b** with bases (see Scheme 16, part **B**). Upon treating **43a**,**b** with potassium hydride (path *a*), the intermediate amide anion initiates δ-lactamization which results in six-membered cyclic structures **45a**,**b**. However, upon introducing *n*-butyl lithium to the reaction with **43a**,**b** (path *b*), a regular C-nucleophilic attack on the carbonyl group occurs, yielding curious five-membered cyclic compounds **46a**,**b**.

A different example of successfully involving the monosubstituted acetylene **2d** in an aza-Wittig reaction with phosphazene **47** was reported by the Palacios group.[35] This phosphazene contains a phosphonate group, making subsequent olefination possible (Scheme 17). Upon the aza-Wittig reaction of **47** with **2c** as well as DMAD **2a**, iminophosphonium ylides **48a,b** were produced in high yields. A further reaction of **48b** with dimethyl oxomalonate proceeds selectively, introducing the phosphonate fragment into Horner–Wadsworth–Emmons olefination and yielding compound **49**. Meanwhile, the phosphonium ylide fragment in **48b**, conjugated with EWG,



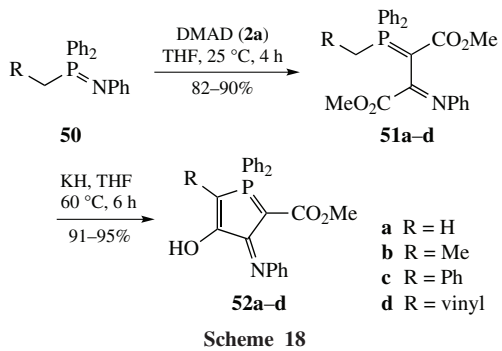
Scheme 16



Scheme 17

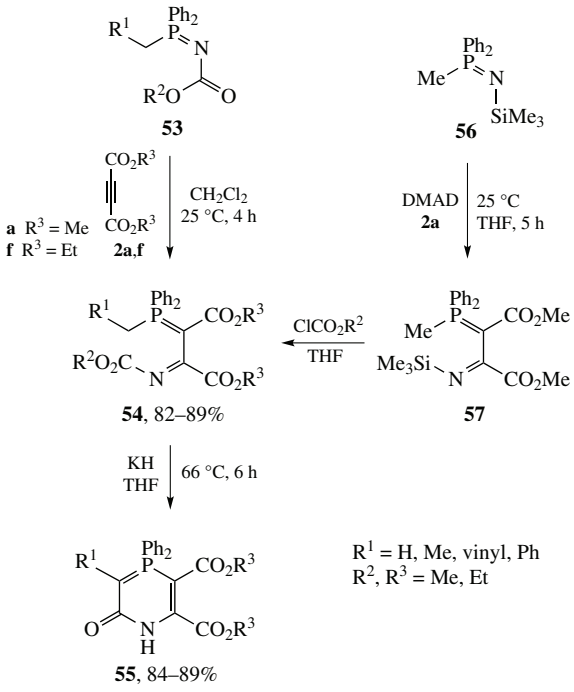
does not react with dimethyl oxomalonate along the Wittig pathway.

The Barluenga group meticulously investigated the reactions between DMAD **2a** and phosphazenes **50**, containing benzyl, allyl or alkyl substituents at the phosphorus atom (Scheme 18).[43] The aza-Wittig reactions taking place result in products **51**. Upon treating these products with potassium hydride, they undergo cyclization into λ5-phosphates **52**.



Scheme 18

Further investigation of this process with variations in the substituents at the nitrogen and phosphorus atoms showed that *N*-alkoxycarbonylphosphazenes **53**, previously considered non-reactive towards DMAD **2a** (see Schemes 2 and 8),[27,33,34] could actually be introduced into this reaction.[44] Supposedly, this can be associated with higher reactivities of phosphazenes **53**, wherein one phenyl group at the phosphorus atom is replaced with an alkyl group. As a result, a representative series of iminophosphonium ylides **54** was synthesized (Scheme 19). Upon treatment with potassium hydride, ylides **54** undergo cyclization into six-membered heterocycles **55**. To produce ylides **54**, an alternative approach was devised. It involved an aza-Wittig reaction between DMAD **2a** and phosphazene **56** which contains a trimethyl silyl (TMS) group at the nitrogen atom. Subsequent treatment of the formed *N*-TMS-substituted ylide **57** with chloroformates results in ylides **54**.

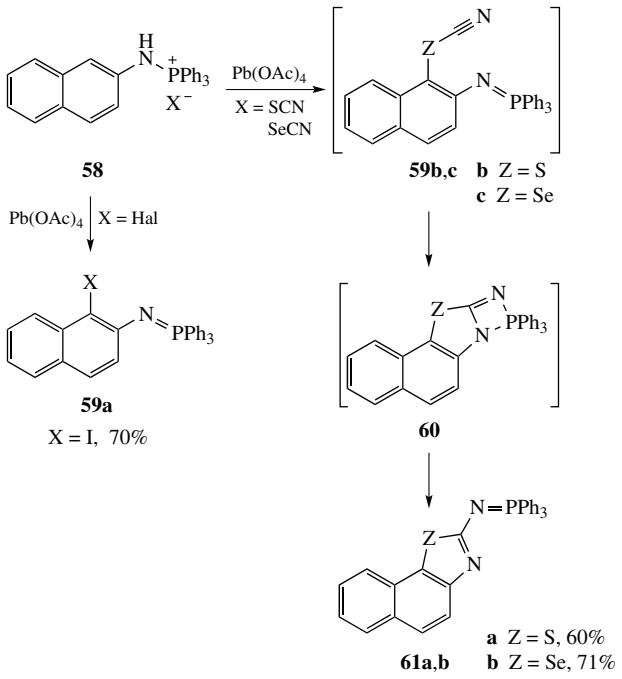


Scheme 19

3. aza-Wittig reactions with nitriles

In 1966, Zbiral discovered the very first example of an aza-Wittig reaction between phosphazenes and nitriles.[45] Upon the oxidation of *N*-(2-naphthyl)aminotriphenylphosphonium salts

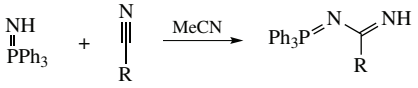
58 (with X as counterions) with lead(IV) acetate, α-halogeno-substituted β-naphthylphosphazenes **59** (X = Hal) were produced as expected, but naphthothiazole **61a** and naphthoselenazole **61b** (X = SCN, SeCN) were surprisingly afforded as well (Scheme 20). According to the author's proposition, analogous phosphazenes **59** are formed at the first step, subsequently reacting with the nitrile group in the α-substituents in naphthalene which results in new phosphazenes **61** *via* intermediate diazaphosphetenes **60**.



Scheme 20

3.1. Intermolecular reactions

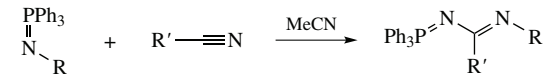
Intermolecular reactions between phosphazenes and nitriles were first reported by Shtepanek *et al.*[46] It was established that only EWG-substituted nitriles **63** could react with triphenyl-phosphazinyl hydride **62** (Scheme 21). This allows for employing acetonitrile as a solvent. The authors suggested the addition of an imine to the nitrile group as a mechanism for the formation of iminophosphazenes **64** – as opposed to the intermediate formation of diazaphosphetenes along the aza-Wittig pathway, even though both processes should lead to the same outcomes.



a R = CF_3, 76% **c** R = CCl_2Me, 35%
b R = CCl_3, 60% **d** R = $CCl_2C(Ph)(Me)CN$, 50%

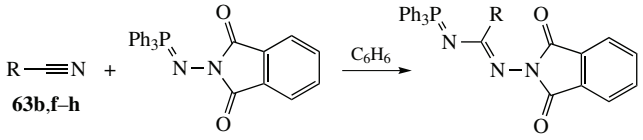
Scheme 21

A more detailed study of the Wittig and aza-Wittig reactions involving nitriles was carried out by Ciganek.[47] Specifically, it was pointed out that an aza-Wittig reaction was only initiated when there was an EWG at the nitrile group. Hence, phosphazenes **1a** and **65a**,**b** react with nitriles **63a**,**e** which contain trifluoro-methyl or cyano moieties as activating acceptors, producing iminophosphazenes **66** (Scheme 22). The reactions mostly proceed under mild conditions with high yields of the final products **66**. Curiously, phosphazene **1a** does not react with acetonitrile even upon extended exposure of the reaction mixture to higher temperatures (150 °C, 72 h).



1a R = Ph **63a** R′ = CF_3 R = Ph, Bu^t, N=CPh_2
65a R = Bu^t **63e** R′ = CN R′ = CF_3, CN
65b R = N=CPh_2

Scheme 22



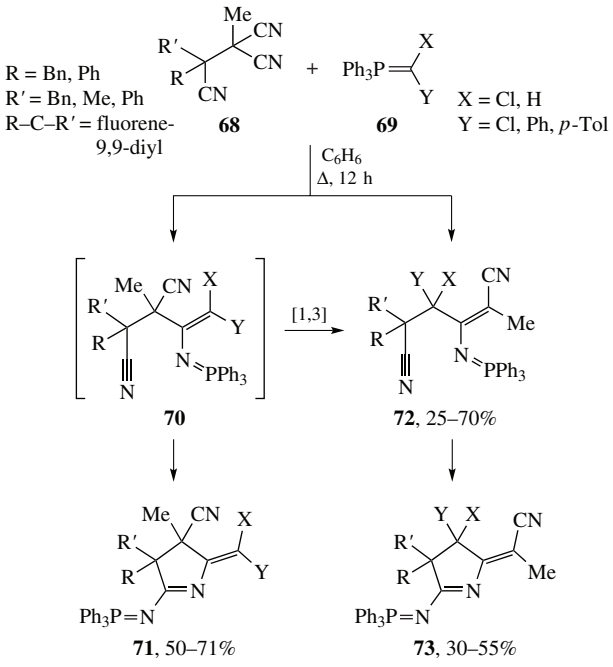
63b, **67a** R = CCl_3, 90% **63g**, **67c** R = CBr_2CN, 75%
63f, **67b** R = CCl_2CN, 53% **63h**, **67d** R =  , 76%

Scheme 23

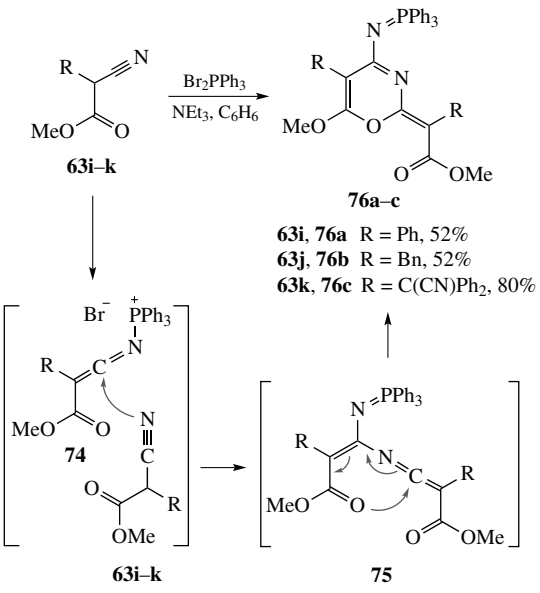
Phosphazene **39a** which contains a phthalimide substituent at the nitrogen atom reacts with EWG-substituted nitriles **63b**,**f–h** under mild conditions, yielding iminophosphazenes **67** (Scheme 23).[41]

3.2. Intramolecular and cascade reactions

Gadreau and Foucaud reported an intriguing cascade of transformations for tricarbonitriles **68** and phosphonium ylides **69**, producing cyclic iminophosphazenes **71** and **73** (Scheme 24).[48] The authors suggest that a Wittig reaction occurs at the first step, when ylide **69** reacts with one of the geminal nitrile groups in **68** and yields the intermediate vinylphosphazene **70**. Then, an intramolecular aza-Wittig reaction takes place wherein the produced phosphazene fragment in **70** reacts with the nitrile moiety therein, leading to five-membered cyclic iminophosphazenes **71**. Depending on the substituents in the initial compounds **68** and **69**, the reaction may be accompanied by the formation of phosphazenes **72** and **73**. The authors interpret this by accounting for the 1,3-shift of the $R^1R^2(CN)C$ group in intermediate **70**.



Scheme 24

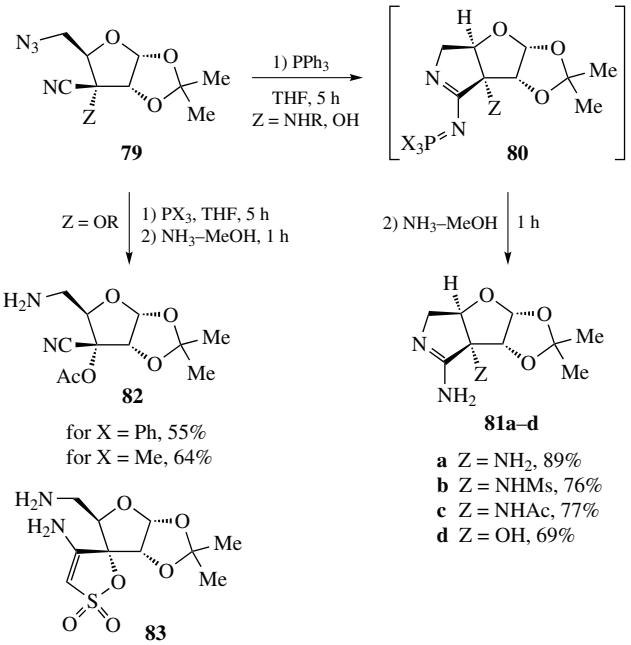


Scheme 25

Similar six-membered cyclic iminophosphazenes **76** were synthesized by Foucaud *et al*. *via* a reaction between EWG-substituted nitriles **63i–k** with triphenylphosphine dibromide (Scheme 25).[49] However, in this case iminophosphonium substituents in intermediates **74** do not partake in this reaction: the attack of the nitrile group is focused on the carbon electrophilic center. The resulting intermediates **75** undergo cyclization to form the final heterocyclic products **76**.

In another paper by Foucaud *et al*., the following cascade process was described: phosphazene **39a** reacted with tricarbonitrile **68e**, leading to a five-membered cyclic iminophosphazene **78** (Scheme 26).[41] The authors suggested that the reaction proceeded *via* an intermediate vinylphosphazene **77**, whose further cyclization followed the intramolecular aza-Wittig pathway that involved the phosphazene and nitrile fragments reacting to form product **78**. However, the outcome of this process may be interpreted in terms of an alternative mechanism that includes a sequence of intermolecular and intramolecular aza-Wittig reactions.

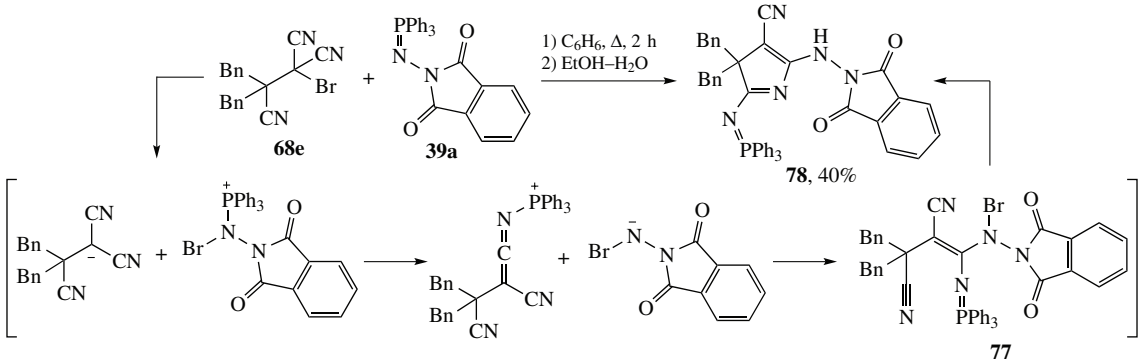
The Postel group proposed to employ intramolecular aza-Wittig reactions to synthesize iminopyrrolidine derivatives of sugars **81** starting from β-azido-glyco-α-aminonitriles **79** (Scheme 27).[50] At the first step, a phosphazene fragment is afforded upon treating **79** with trimethyl- or triphenylphosphine (*via* a Staudinger reaction). This fragment participates in an aza-Wittig reaction with a nitrile substituent, yielding cyclic iminophosphazene **80** as an intermediate. For the amino-substituted derivative, the formation of intermediate **80a** (Z = NH_2, X = Me) together with the target diamine **81a** under Staudinger conditions was detected by means of ^{13}C NMR



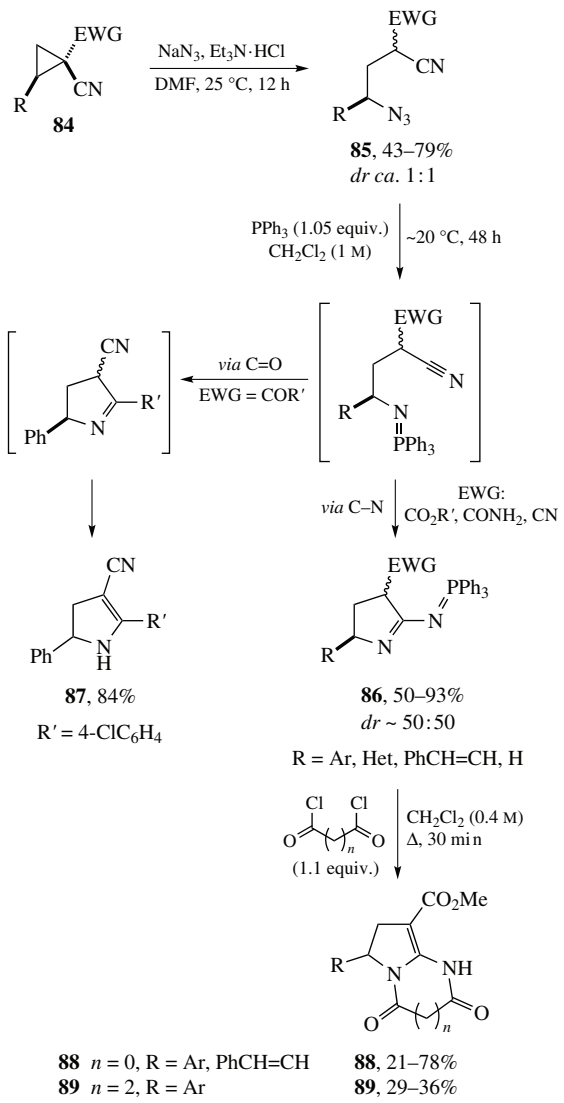
Scheme 27

spectroscopy and mass spectrometry. However, compounds **80** were not isolated individually and the subsequent treatment of reaction mixtures with the ammonia–methanol system led to products **81**. Studying the influence of the substituents at the α-position relative to the nitrile group demonstrated that amino and hydroxy groups (Z = NHMs, NHAc, OH) steered the reaction towards cyclization and products **81**. When acyloxy and sulfoxy substituents were introduced (Z = OAc, OMs), azides **79** were reduced to amines **82**. Using trimethylphosphine in a reaction with mesyl-substituted compound **79f** afforded the spirocyclic species **83**.

Our group developed an intramolecular variant of the aza-Wittig process for γ-azidobutyronitriles **85**, easily produced from donor–acceptor cyclopropanes **84** *via* nucleophilic ring opening with the azide ion (Scheme 28).[51] Triphenylphosphine induces a transformation of **85** into pyrrole-derived iminophosphazenes **86**. The EWG at the α-position in relation to the CN group in **85** defines chemoselectivity in this process. Such acceptors as ester, amide or nitrile groups activate the CN moiety toward the intramolecular aza-Wittig processes, affording **86**. Meanwhile, the ketone moiety with its highly polarized double bond competes with the CN moiety in the aza-Wittig reaction, producing pyrroline **87** exclusively in this case. Iminophosphazenes **86**, acting as N,N-binucleophiles, were transformed into polycyclic pyrrole-fused systems: pyrrolo[1,2-*a*]imidazoles **88** and pyrrolo[1,2-*a*][1,3]diazepines **89**.



Scheme 26

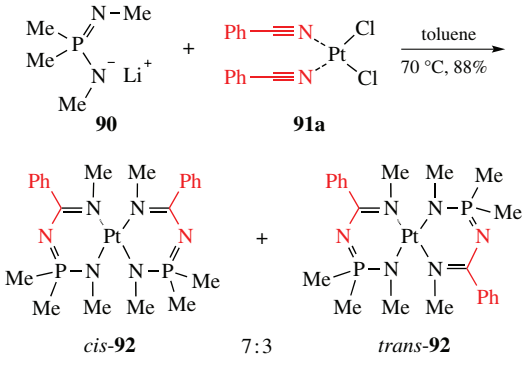


Scheme 28

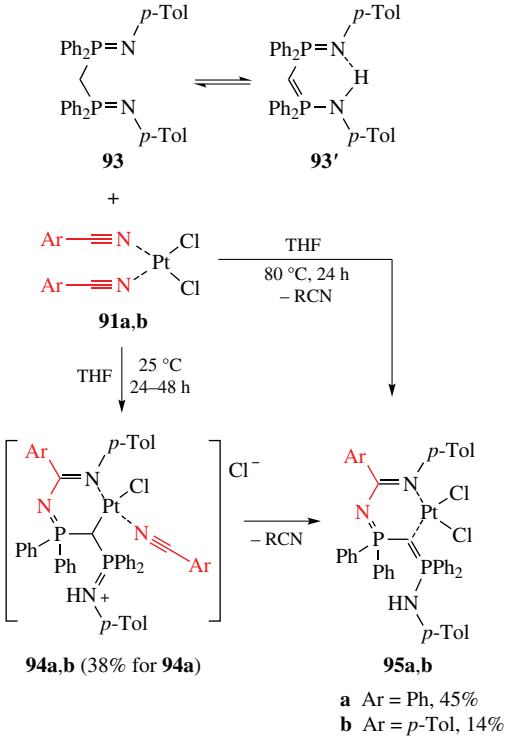
3.3. Nitrile activation *via* complexation with Pt^{II}

A curious aza-Wittig reaction involving complex platinum(II) compounds with nitrile ligands was reported by Scherer and Nahrstedt.[52] The authors posited that the reaction between phosphazenylamide **90** and *cis*-[Pt(PhCN)$_2$Cl$_2$] **91a** resulted in a new complex **92** as a 7 : 3 mixture of *cis*- and *trans*-isomers with a yield of 88% (Scheme 29). Therefore, the formation of complexes with platinum(II) activates the nitrile group towards aza-Wittig reactions.

Almost two decades later, the Elsevier group described analogous aza-Wittig reactions between complexes **91a**,**b** and compound **93** which contains two phosphazene groups.[53] As opposed to the former example (see Scheme 29), in these



Scheme 29



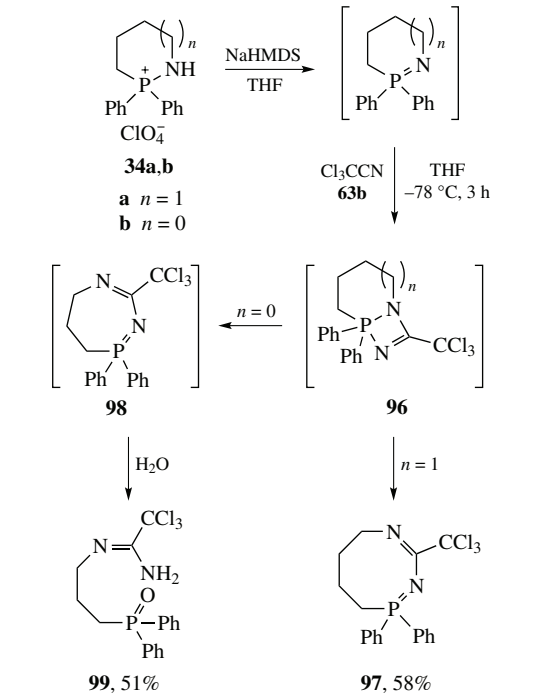
Scheme 30

processes (Scheme 30), phosphazenes **93** only react with one nitrile group in **91a**,**b**, yielding **94**. Upon heating, the latter produce the more stable complexes **95** after the elimination of the nitrile ligand. It was also established that replacing the aryl substituent with the methyl group in the nitrile ligand inhibits the aza-Wittig reaction. Besides, neither the related palladium(II) complexes nor free nitriles afford aza-Wittig products with phosphazene **93**. The authors associate these outcomes with successful aza-Wittig reactions requiring the activation of the nitrile and phosphazene moieties by means of substantial polarization of their multiple bonds when the reaction pathway adheres to the [2+2]-cycloaddition mechanism. The activation of the nitrile moiety is facilitated by the formation of a complex with platinum(II), with the presence of an easily polarizable aromatic substituent in the nitrile group playing a significant role as well. The authors propose that additional activation of phosphazene **93** has to do with tautomerization affording aminovinylphosphazene **93′**. This also explains why this reaction only involves one nitrile group.

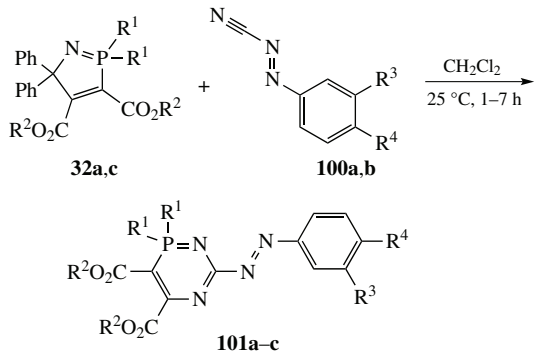
3.4. Reactions with cyclic phosphazenes

As with the aforementioned examples of aza-Wittig reactions with alkynes (see Scheme 13), a similar reaction with nitriles can be used to enlarge the rings of five- and six-membered phosphazenes **34** (Scheme 31).[39] Hence, the eight-membered cyclic iminophosphazene **97** was produced in the aza-Wittig reaction between six-membered phosphazene **34a** and nitrile **63b** presumably proceeding *via* intermediate **96**. However, the seven-membered cyclic iminophosphazene **98**, produced from five-membered phosphazene **34b**, easily undergoes hydrolysis to form acyclic phosphine oxide **99**.

The five-membered cyclic phosphazenes **32** also undergo ring enlargement upon the action of nitriles **100** (Scheme 32).[38] Unlike the aforementioned reaction between **32** with acetylenes **2**, producing seven-membered cyclic aza-Wittig products **33** (see Scheme 12), the reaction with nitriles **100** only affords six-membered aromatic iminophosphazenes **101** which do not contain diphenylmethyl fragments.



Scheme 31



a $R^1 = R^2 = Me$, $R^3 = NO_2$, $R^4 = H$, 45%
b $R^1 = Me$, $R^2 = Et$, $R^3 = NO_2$, $R^4 = H$, 48%
c $R^1 = R^2 = Me$, $R^3 = H$, $R^4 = Br$, 26%

Scheme 32

4. Conclusion

In summary, as of now, only a limited number of aza-Wittig reactions with compounds containing C≡C and C≡N bonds is known. This can be ascribed to limitations placed on substrates in those reactions: these have to be activated by means of significant polarization in multiple bonds. These limitations can be alleviated by introducing activating substituents with certain electronic properties into the reactants or, alternatively, by carrying out the aza-Wittig reactions in their intramolecular variant.

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