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'Phospha-variations' on the themes of Staudinger and Wittig: phosphorus analogs of Wittig reagents

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Abstract

The Wittig and Aza-Wittig reactions have undergone tremendous development over the past 50 years in light of their potential in organic synthesis to construct carbon–carbon and carbon–nitrogen double bonds. In contrast, the development of the analogous phospha-Wittig reaction has only seen progress over the last 12 years. A phospha-Wittig process is one that uses phosphaylides to convert carbonyl compounds to new materials possessing phosphorus–carbon double bonds (phosphaalkenes). The phospha-Wittig reaction has evolved from initial work involving metal-assisted phospha-Wittig reactions, to phospha-Wittig reactions of terminal phosphinidene complexes to, more recently, free phosphanylidene-σ^4-phosphoranes as phospha-Wittig reagents. The major developments in the phospha-Wittig reaction are highlighted and divided into these three methodologies. The complementary nature and the

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differences between the three approaches is also discussed. Finally, wherein applicable, comparisons between the Wittig reaction and the phospha-Wittig reaction are presented.

Keywords: Wittig; Phospha-Wittig; Phosphanylidenephosphorane; Ylide; Terminal phosphinidene complex; Phosphaalkene

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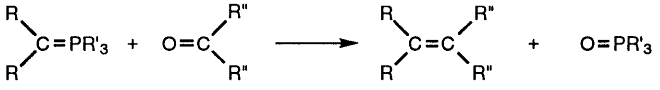
1. Introduction

The Wittig reaction, the process by which phosphorus ylides convert aldehydes and ketones to alkenes, is perhaps one of the most seminal contributions to the field of organic chemistry (Eq (1.1)).



(1.1)

The incipient development and potential applications of the Wittig reaction was brought to widespread attention by Georg Wittig and his students in the early 1950s [1,2]. Since then, the reaction has been of unparalleled significance in formation of carbon–carbon double bonds, and has influenced virtually every sphere of modern organic chemistry. The Wittig reaction has seen use in applications ranging from the synthesis of simple alkenes to the construction of complex biologically active molecules for the pharmaceutical industry. The enormous number of applications of the Wittig reaction eventually led to the conferral of the Nobel Prize in chemistry to Georg Wittig in 1979 [3,4].

Wittig reagents or alkylidenephosphoranes (**I**) belong to a broad class of compounds termed as ylides. A ylide is defined as ‘a substance in which a carbanion is attached directly to a heteroatom carrying a substantial degree of positive charge and in which the positive charge is created by the sigma bonding of substituents to the heteroatom’ [5].

Chart 1

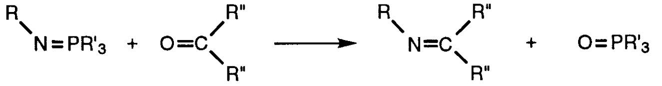
$$R_2C{=}PR_3 \longleftrightarrow R_2\overset{-}{C}{-}\overset{+}{P}R_3 \qquad RN{=}PR_3 \longleftrightarrow R\overset{-}{N}{-}\overset{+}{P}R_3$$

I

II

Different resonance structures are commonly drawn (Chart 1, left). A charge-separated canonical description is probably more befitting such compounds, rather than the double bond notation which is commonly employed for ease of representation.

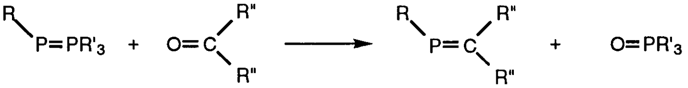
Although the chemistry of ylides received a tremendous boost after Wittig’s initial report in 1953, the first compounds of this nature were actually synthesized during the turn of the 20th century. In 1894, Michaelis and co-workers [6] had unknowingly prepared the first example of a phosphonium ylide, although it was not until almost 70 years later in 1961, that its structure was correctly described as $(C_6H_5)_3P{=}C(H)CO_2C_2H_5$ [7]. In 1919, Staudinger and Meyers prepared $PhN{=}PPh_3$, the first example of an Aza-Wittig reagent, the nitrogen analog of a Wittig reagent [8]. Aza-Wittig reagents or iminophosphoranes (**II**) can also be portrayed in a similar fashion (Chart 1, right). Strikingly, the above report by Staudinger also describes the synthesis of $Ph_2C{=}PPh_3$ and its Wittig-type reactivity with substrates such as phenylisocyanate. Similar to Wittig reagents, Aza-Wittig reagents react with organic carbonyls to effect the Aza-Wittig reaction (Eq. (1.2)).



(1.2)

Although Staudinger described the first phosphorus ylide as formulated in Chart 1, it was not till Wittig's work more than 30 years later that the reaction became accepted practice. As a consequence, Wittig's lecture describing his initial work was suitably titled 'Variations on a theme of Staudinger' [9]. A further detailed historical sketch of carbon (and nitrogen) based phosphonium ylides is much beyond this review, but the interested reader is referred to Johnson's excellent treatise on the subject [5].

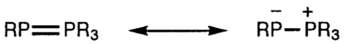
The last 30 years has seen intense efforts to unveil relationships between phosphorus and carbon chemistry, and emphasize the realistic nature of the diagonal analogy between the two elements [10]. Amongst these efforts has also been the goal to extend the Wittig and Aza-Wittig reactions to include 'phospha-Wittig' for the synthesis of phosphaalkenes (Eq. (1.3)).



(1.3)

The main obstacle to achieving this goal has been the synthesis of phosphanylidene-σ^4-phosphoranes [11], the phosphorus analogs of Wittig reagents (**III**, Chart 2), that can serve as efficient phospha-Wittig reagents in reactions with aldehydes and ketones. Such phosphanylidene-σ^4-phosphoranes are often unstable and their chemistry rather undeveloped.

Chart 2



$$RP{=}PR_3 \longleftrightarrow R\overset{-}{P}{-}\overset{+}{P}R_3$$

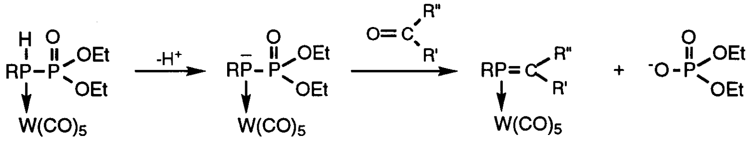
III

Examples now exist of the phospha-Wittig reaction whereby stability issues of these unusual analogues of Wittig reagents have been overcome by assistance of transition metals and complexation. More recently, the authors have serendipitously encountered stable examples of phosphanylidene-σ^4-phosphoranes which participate in reactions with aldehydes to achieve phospha-Wittig reactions and produce stable phosphaalkenes.

In this review, the authors aim to highlight efforts leading to the development of phospha-Wittig reactions, which in a historical sense, represent 'phospha-variations' on the themes of Staudinger and Wittig. Additionally, taking into account the widespread recognition of the carbon–phosphorus diagonal relationship, it seemed timely, and perhaps enlightening, to parallel the chemistry of phospha-Wittig reagents to the more popular Wittig reagents.

2. The first breakthrough: metal-assisted phospha-Wittig reactions

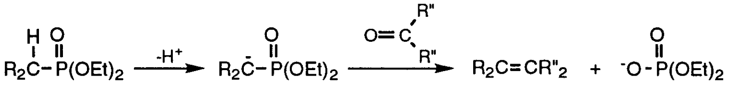
The first examples of phospha-Wittig reactions were pioneered by Mathey and Marinetti in 1988 [12]. Deprotonation of transition-metal phosphorylphosphine complexes (**1a**) led to phosphorylphosphide complexes (**2a**) that react with aldehydes and ketones to afford phosphaalkene complexes (Eq. (2.1)).



1a **2a**

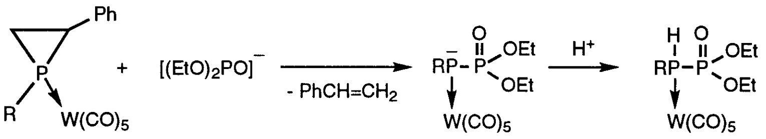
(2.1)

The reaction as delineated in Eq. (2.1) is, strictly speaking, the phosphorus analog of an extension of the Wittig reaction, the Wadworth–Emmons synthesis, whereby phosphonate carbanions react with aldehydes and ketones to furnish alkenes (Eq. (2.2)) [13–15].



$$R_2C(H)-P(O)(OEt)_2 \xrightarrow{-H^+} R_2\bar{C}-P(O)(OEt)_2 \xrightarrow{O=CR''_2} R_2C=CR''_2 + {}^-O-P(O)(OEt)_2 \quad (2.2)$$

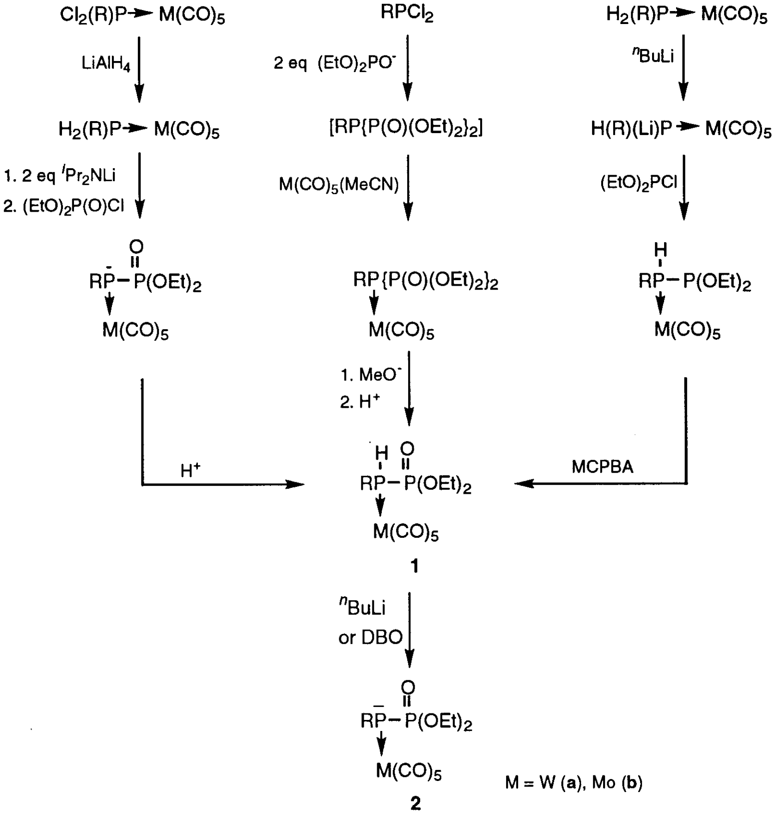
Complexes **1a** were initially prepared via the nucleophilic attack of $(EtO)_2PO^-$ upon (phosphirane)pentacarbonyltungsten complexes, followed by protonation (Eq. (2.3)) [16].



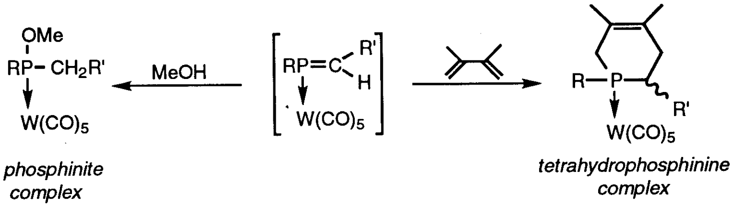
(2.3)

Although free secondary phosphorylphosphines are generally unstable [17], compounds **1a** are stable and isolable as a consequence of transition-metal complexation. Alternate synthetic routes were later devised, which involved more readily accessible precursor reagents and allowed for variation in nature of the metal center and the substituents on phosphorus (Scheme 1) [18–21].

Deprotonation of the acidic proton at phosphorus in **1** with ^{n}BuLi or a tertiary amine such as DBO generates anionic complexes **2**, which are reacted in situ with carbonyl compounds as shown in Eq. (2.1). The reactions involve mild reaction conditions and reaction times range from a few minutes to 3 h. In some reactions with aldehydes, the derived phosphaalkenes can be unstable despite transition-metal complexation. Hence, the phosphaalkene complexes were trapped in situ with reagents such as methanol and 2,3-dimethylbutadiene (Scheme 2). Table 1 lists the phospha-Wittig reactions of the anions **2** with some simple aldehydes and ketones.



Scheme 1.



Scheme 2.

Table 1
Reactions of **2a** with aldehydes and ketones

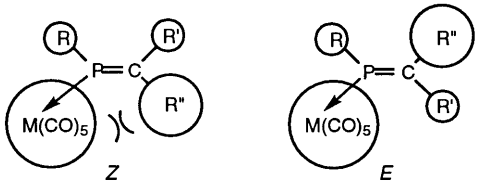
Entry	R	Aldehyde or ketone	Yield of phosphaalkene (%)	Refs.
1	Ph	Isobutyraldehyde	70 [a] *Z*:*E* 1:2 (−70°C); *Z*:*E* 9:1 (25°C)	[18]
2	Ph	Isobutyraldehyde	79 [b,c]	[12]
3	Ph	Isobutyraldehyde	56 [b,d]	[12]
4	^{t}Bu	Isobutyraldehyde	54 Only *Z* observed	[18]
5	Ph	*p*-Chlorobenzaldehyde	57 [b,e]	[12]
6	Ph	Pivaldehyde	68 *Z*:*E* 9:1 (25°C)	[18]
7	^{t}Bu	Pivaldehyde	87 Only *Z* observed	[18]
8	Me	2-Adamantylidenealdehyde	62	[18]
9	Ph	2-Adamantylidenealdehyde	66	[18]
10	Me	Acetone	73 [b,c,g]	[12]
11	Ph	Acetone	51, 56 [f]	[12,18]
12	^{t}Bu	Acetone	58	[18]
13	Ph	Cyclopentanone	40, 37 [f]	[12,18]
14	Ph	Methylethylketone	37 *Z*:*E* 1:1 (40°C)	[18]
15	Me	Benzophenone	48 [b,c]	[12]
16	Ph	Benzophenone	No rxn	[12]

[a] Two ratios of *Z*:*E* observed dependent on reaction conditions.
[b] Yield of phosphaalkene based on trapping reaction.
[c] Methanol used as trapping agent.
[d] Cyclopentadiene used as trapping agent.
[e] 2,3-Dimethylbutadiene used as trapping agent.
[f] The latter yields are for reactions with $Mo(CO)_5$ as the complexing agent.
[g] Transient phosphaalkene observed by ^{31}P-NMR (δ 159).

As can be discerned from the data presented in Table 1, various factors can play a potential role in determining the scope of this phospha-Wittig approach including the steric nature of the substituent R on the anionic phosphorus, the steric nature of the aldehyde and ketone, the inherent stability of the phosphaalkene complex formed [22,23], and the nature of the trapping agent.

It is difficult to draw conclusive separate arguments about each factor due to the limited information available. Nevertheless, Mathey and co-workers have commented on some general features. In reactions with aldehydes, the degree of bulk on the anionic phosphorus and/or the carbonyl carbon has influence upon the inherent stability, and thus, yields of the derived phosphaalkenes. This is well depicted by the examples in Table 1 (entries 4, 6–9). Steric factors also play an important role in the stereochemistry of the phosphaalkene complexes that are produced (Table 1, entries 1, 4, 6, 7, 14). Reactions conducted at ambient conditions or higher temperatures lead to the thermodynamically favored *Z* isomer, whereby the bulkier substituents are oriented in a *trans* fashion (Chart 3).

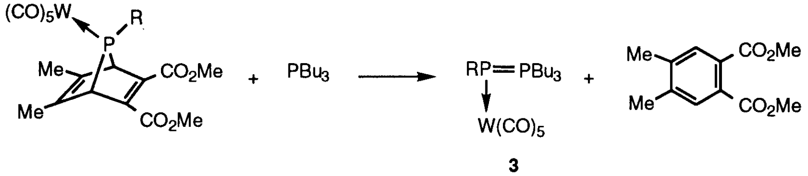
Chart 3



R" more bulky than R'

The nature of the R substituent on the anionic phosphorus may also have some bearing on the reactivity of **2**, as portrayed by entries 15–16 in Table 1; alternatively, a threshold overall balance of sterics may be necessary with respect to substituents on the anionic phosphorus and the carbonyl carbon in order for the condensation reaction to proceed. Changing the nature of the metal center employed for complexation from $W(CO)_5$ to $Mo(CO)_5$ does not have appreciable bearing on the yields observed (Table 1, entries 11 and 13). The type and efficiency of the reagent employed to trap the unstable phosphaalkene complex may also have some bearing on the eventual yield of the derived product (Table 1, entries 2–3).

In further developments, Mathey and co-workers were successful in transposing Wittig chemistry itself when they prepared neutral phosphanylidenephosphorane complexes **3** by reacting 7-phosphanorbornadiene complexes with tributylphosphine (Eq. (2.4)) [24].



(2.4)

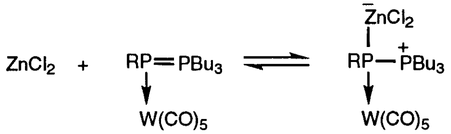
The phosphanylidenephosphorane complexes **3** are difficult to isolate and thus were utilized in situ immediately on formation from the corresponding 7-phosphanorbornadiene complexes.

A simpler synthesis for **3** was later found when dichloroalkyl- or dichloroarylphosphine complexes were reduced with zinc powder in the presence of trialkylphosphines (Eq. (2.5)) [25].

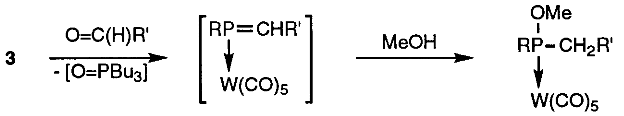
$$Cl_2(R)P\rightarrow W(CO)_5 + Zn + PBu_3 \longrightarrow \mathbf{3} + ZnCl_2 \qquad (2.5)$$

Phosphanylidenephosphorane complexes obtained via this route display longer lifetimes (for example, for complex $[(CO)_5W(PhP{=}PBu_3)]$ (**3a**), ~1 week at −20°C). These complexes delineate two characteristic doublets on ^{31}P-NMR with large $^1J_{PP}$ coupling constants of approximately 350–500 Hz. Interestingly, the ^{31}P-NMR chemical shifts for **3a** show small differences depending on the synthetic route employed and thus, an equilibrium between **3** and zinc chloride was proposed (Chart 4) to account for the enhanced stability of the phosphanylidenephosphorane complexes when prepared by the Zn/PR_3 route [26].

Chart 4



The phosphanylidenephosphorane complexes **3** also display phospha-Wittig chemistry but are less reactive than the more nucleophilic complexes **2**, as exemplified by very sluggish reactions with ketones [24]. Reactions of **3** with aldehydes proceed rapidly under mild conditions to generate reactive phosphaalkene complexes, the presence of which was established by in situ trapping with reagents such as methanol, as shown in reaction sequence (Eq. (2.6)) [24,25].



(2.6)

Table 2 lists some reactions of **3** with aldehydes and yields of the quenching experiments. As can be discerned from the table, the reaction works well for a variety of aldehydes, and the relative lesser yields observed in some cases (Table 3, entries 3 and 6) may be due to the greater instability of the phosphaalkene complexes, and may not necessarily reflect upon the efficiency of the condensation reaction. Phosphanylidenephosphorane complexes with conjugating substituents such as ethoxycarbonyl (CO_2Et) are unreactive toward aldehydes, presumably due to an excessive delocalization of the lone pair of the phosphanylidene center [24].

It can be speculated that by altering the bulk of the substituent on either the phosphanylidene or carbonyl centers, more stable phosphaalkenes, as depicted in Table 1, may be synthesized using this approach. However, in such cases, the less reactive nature of **3** as compared with **2** may result in sluggish reactions.

Table 2
Some reactions of **3** with aldehydes

Entry	R	M	Aldehyde	Yield of trapped product (%)	Refs.
1	Ph	$W(CO)_5$	Benzaldehyde	75 [a]	[24]
2	Ph	$W(CO)_5$	Benzaldehyde	80 [b]	[24]
3	Me	$W(CO)_5$	Isobutyraldehyde	58 [c,d]	[24]
4	Ph	$W(CO)_5$	Isobutyraldehyde	70 [a]	[24]
5	Allyl	$W(CO)_5$	Isobutyraldehyde	68 [a]	[24]
6	Me	$W(CO)_5$	4-Chlorobenzaldehyde	57 [c]	[24]
7	Allyl	$W(CO)_5$	4-Chlorobenzaldehyde	80 [a]	[24]
8	Ph	$Fe(CO)_4$	4-Chlorobenzaldehyde	85[a]	[25]
9	^{t}Bu	$Fe(CO)_4$	4-Chlorobenzaldehyde	73 [a]	[25]

[a] Phosphaalkene trapped with methanol.

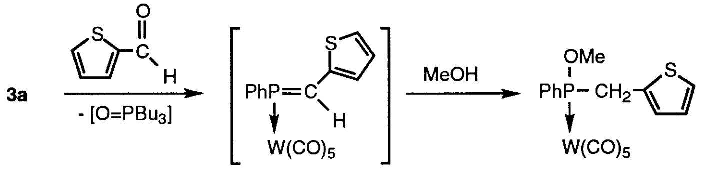
[b] Phosphaalkene trapped with benzoic acid.

[c] Phosphaalkene trapped with 2,3-dimethylbutadiene.

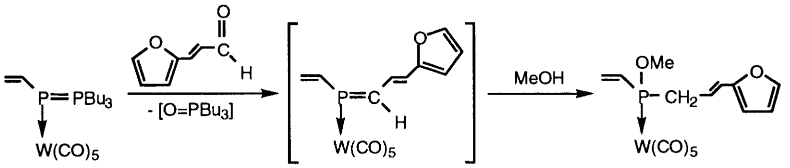
[d] Transient phosphaalkene (both isomers) observed on ^{31}P-NMR (δ 195.6, 188.3).

It is apparent that the two phospha-Wittig approaches employing **2** and **3** as the reactive species complement each other in that the former reacts with both aldehydes and ketones, whereas the latter allows for a more simplified route towards the incorporation of a variety of substituents on the phosphanylidene center. A variety of techniques are available to introduce different R groups on the phosphanylidene center in **3** via both the 7-phosphanorbornadiene complexes [27,28] and the PR_3/Zn routes.

In a set of further elegant studies, Mathey and co-workers were able to employ the phospha-Wittig synthesis in a variety of applications [18,24,25,29–34]. Reactions of **3** could be extended to substrates such as thiophene-2-carbaldehyde, and β-(2-furyl)acrolein (Eqs. 2.7 and 2.8) [24].

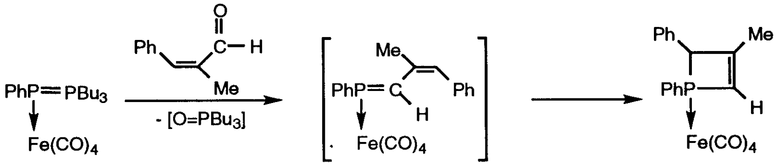


(2.7)



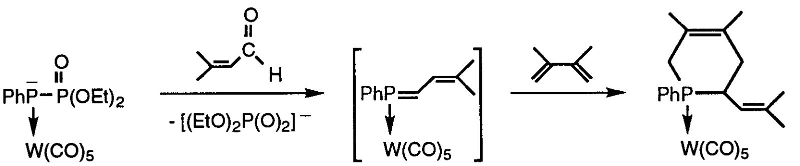
(2.8)

In reactions with free α,β-unsaturated aldehydes, reactive 1-phosphadienes were formed which cyclized to give the corresponding 1,2-dihydrophosphete complexes (Eq. (2.9)) [25].



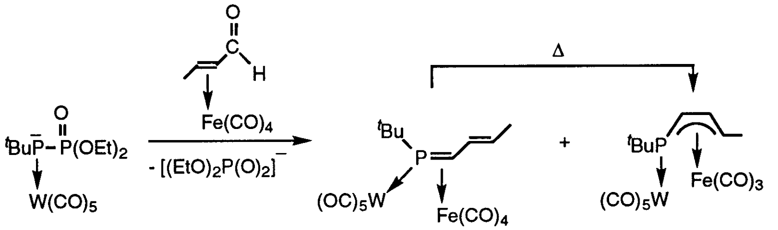
(2.9)

If a reagent such as 2,3-dimethylbutadiene was employed to trap the reactive 1-phosphadiene, the corresponding [2 + 4] cycloaddition products were afforded (Eq. (2.10)) [29].

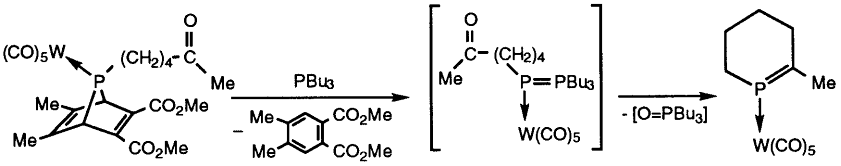


(2.10)

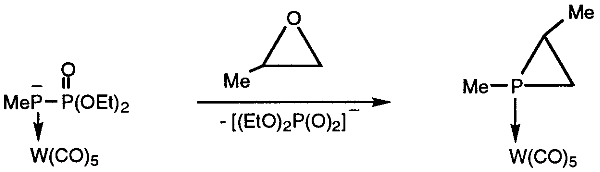
Later, Mathey and co-workers were able to isolate and crystallographically characterize 1-phosphadiene complexes by employing metal complexed α,β-unsaturated aldehydes (Eq. (2.11)) which can undergo rearrangement upon heating to 1-phosphaallyl complexes [29,30].


(2.11)

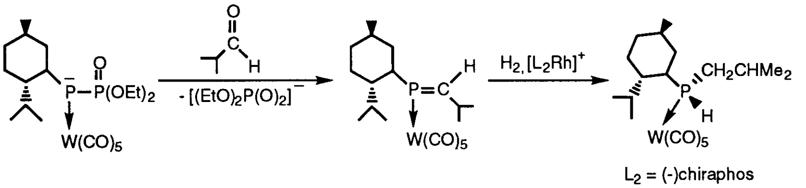
In some cases, when a carbonyl functionality is introduced in the phospha-Wittig reagent itself, cyclization is observed to give phosphacycloalkenes (Eq. (2.12)) [32].


(2.12)

Phosphirane complexes have been synthesized in reactions with oxiranes (Eq. (2.13)) therby demonstrating the reaction of **2** with other oxygen-containing substrates other than carbonyl compounds [31].


(2.13)

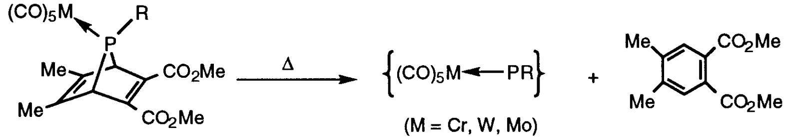
Mathey and co-workers have also used the phospha-Wittig synthesis to prepare prochiral phosphaalkene complexes that can undergo catalytic hydrogenation to yield optically active phosphines (Eq. (2.14)) [33].


(2.14)

As has been delineated by the examples above, precedence for the potential widespread applications of the phospha-Wittig synthesis towards organophosphorus compounds has been well established by Mathey and co-workers. The innovative concept of conducting the reactions in the coordination sphere of transition metals has enabled the use of relatively unhindered substituents on the reactive phosphorus center. The trapping experiments also show applications in the synthesis of new P–C single bonds and P-containing heterocycles. Methods have been described which detail the removal of the transition metal, thus enhancing the significance and the scope of this approach [18,35,36].

3. Phospha-Wittig reactions of terminal phosphinidene complexes

Critical to the success of Mathey's pioneering work in developing the phospha-Wittig reaction was the previous discovery by the same group that transient electrophilic terminal phosphinidene complexes could be generated by thermolysis (Eq. (3.1)) [27].



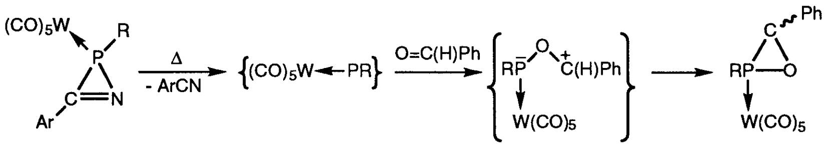
(3.1)

In particular, species **3** can be visualized as the adducts of the highly reactive electrophilic terminal phosphinidene complex and tributylphosphine (see Eq. (2.4)).

The wide-ranging applications of transition-metal carbene $[L_nM=CRR']$ complexes [37] has spawned much interest in their phosphorus analogs. Pertinent to the current review, both isolable and transient carbene complexes have been employed to effect olefinations of aldehydes and ketones (Eq. (3.2)). Noteworthy examples include complexes bearing Schrock-type alkylidene ligands [38] and other complexes such as the well known Tebbe reagent [39]. Such complexes exhibit substantial nucleophilic behavior for the multiply bonded carbon atom.

$$[L_nM{=}CR_2] + O{=}CR'_2 \longrightarrow R_2C{=}CR'_2 + [L_nM{=}O] \qquad (3.2)$$

Although there has long been evidence to suggest the presence of terminal transition-metal phosphinidenes as reactive intermediates, few isolated complexes have been reported to date [40–42]. The transient electrophilic terminal phosphinidenes discussed above undergo a different reactivity with aldehydes and ketones [43–45]. For example, Streubel describes the cycloaddition of a transient phosphinidene with the carbonyl group of benzaldehyde to yield an oxaphosphirane complex (Eq. (3.3)) [43].



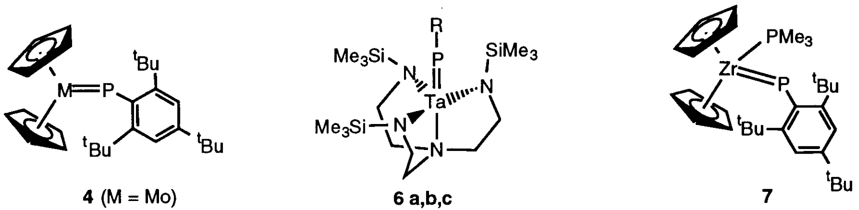
(3.3)

Consequently, for the successful extension of Eq. (3.2) to a phospha-olefination reaction (Eq. (3.4)), the presence of nucleophilic behavior for the phosphinidene is requisite.

$$[L_nM{=}PR] + O{=}CR'_2 \rightarrow RP{=}CR'_2 + [L_nM{=}O] \qquad (3.4)$$

In 1987, Lappert and co-workers reported on the synthesis and isolation of the first terminal transition-metal phosphinidene complexes $[Cp_2M{=}PR]$ (see Chart 5, **4** and **5**) [46,47].

Chart 5

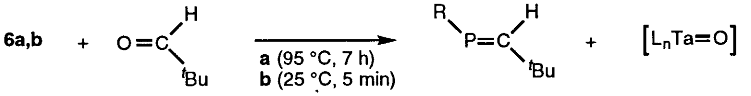


4 (M = Mo)
5 (M = W)

6 a,b,c
R = ᵗBu (**a**), R = Ph (**b**), R = Cy (**c**)

7

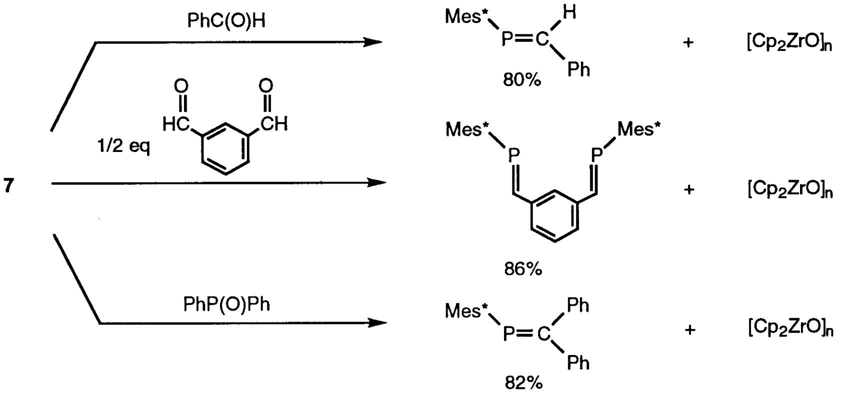
Such complexes possess a formal M=P double bond and are distinguished by high valent metal centers and π-donating ancillary ligands. Due to the higher electronegativity of phosphorus, a polarized $M^{\delta+}{=}P^{\delta-}$ bond is expected. Consequently, the phosphinidene moiety in these complexes exhibits nucleophilic behavior, akin to Schrock carbenes. Soon after the discovery of Lappert, Schrock and co-workers reported on the first phospha-Wittig reactions of terminal phosphinidene complexes [48,49]. The phosphinidene complexes $[(N_3N)Ta{=}PR]$ (**6**) (see Chart 5) react with aldehydes to furnish the corresponding phosphaalkenes. The reaction of **6b** with pivaldehyde proceeds within a few minutes at ambient conditions, whereas the reaction of **6a** with the same substrate requires relatively harsh conditions and longer times. (Eq. (3.5)).



(3.5)

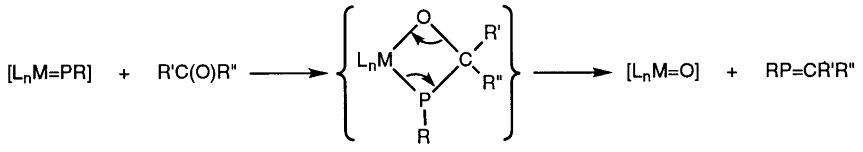
Reactions of **6a** and **6b** with ferrocenealdehyde results in formation of reactive phosphaalkenes, the presence for which was evinced by formation of dimerization products (1,3-diphosphetane) or by trapping with cyclopentadiene. The rate and efficiency of the reactions appear to be governed by the sterics at the phosphinidene, the sterics on the aldehyde, and the inherent stability of the derived phosphaalkene. In subsequent studies, Schrock and co-workers synthesized further examples of terminal phosphinidene complexes **6** bearing other R groups (Me, ⁿBu, $SiMe_3$, and $SiMe_2Ph$). These phosphinidene complexes also reacted with pivaldehyde, to give the corresponding *E*-phosphaalkenes [50].

The terminal phosphinidene complex $[Cp_2Zr({=}PMes^*)(PMe_3)]$ (Mes* = 2,4,6-tri-*tert*-butylphenyl) (**7**) synthesized by Stephan also displays phospha-Wittig reactivity in reactions with carbonyl compounds (Scheme 3) [51,52]. As with **6**, the reactions proceed under mild conditions and excellent yields of phosphaalkenes are obtained, as ascertained by ^{1}H-NMR. The derived phosphaalkenes are readily isolable or stable, as would be anticipated due to the voluminous bulk afforded by the Mes* group.



Scheme 3.

It is noteworthy that, in relevant cases, both terminal phosphinidene complexes **6** and **7** yield the *E* isomer of the phosphaalkene, which is probably a consequence of the sterics and/or the mechanism involved in the transformation. The mechanism of the reactions of terminal phosphinidene complexes and carbonyl compounds has not been studied in detail, but a 4-center metallacycle has been proposed (Scheme 4) [48,51].

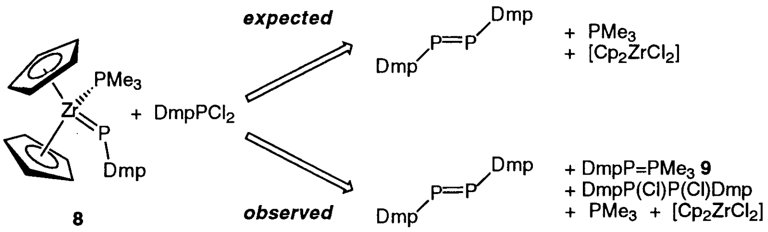


Scheme 4.

Similar 4-member metallacycles have also been invoked in mechanisms for transition-metal mediated olefin metathesis [37] and Wittig reactions (oxophosphetane intermediates) [5].

Another example of a transition metal system exhibiting potential phospha-Wittig chemistry has recently appeared. Gibson and co-workers have discovered an unusual tungsten-based system that catalyzes the metathesis of phosphinidene groups between symmetrical diphosphenes [53]. For example, a mixture of Mes*P=PMes* and Ar′P=PAr′ (Ar′ = 2,4,6-trifluoromethylphenyl), subjected to a preformed solution of [W(PMe$_3$)$_6$] and ArPCl$_2$ yields dynamic mixtures of the symmetric as well as the asymmetrical diphosphene Mes*P=PAr′. The mechanism for the metathesis was proposed to involve a W=P terminal phosphinidene complex. Addition of benzaldehyde to the active metathesis system extinguished catalytic activity and produces the two phosphaalkenes Mes*P=C(H)Ph and Ar′P=C(H)Ph, implicating a species that effects the phospha-Wittig reaction.

The isolable nucleophilic terminal transition-metal phosphinidene complexes, and corresponding free phosphaalkenes derived from reactions with aldehydes, contrast with Mathey's studies whereby the phosphanylidene source tends to be unstable at ambient conditions, and low-valent metal complexation is necessitated at the



Scheme 5.

phosphaalkenes. However, the complementary nature between the two with respect to the phospha-Wittig synthesis is also self-evident, and the discovery of terminal transition-metal phosphinidene complexes has undoubtedly broadened the scope of the approach.

4. Free phosphanylidene-σ^4-phosphoranes as phospha-Wittig reagents

During efforts to explore the reactivity of $[Cp_2Zr{=}PDmp(PMe_3)]$ (Dmp = 2,6-dimesitylphenyl) (**8**), a close analog of Stephan's terminal phosphinidene complex **7**, reactions with dichloroarylphosphines proved to be particularly enigmatic [54]. From literature precedence [55,56], as well as the ability of $[Cp_2Zr{=}PMes^*(PMe_3)]$ to effect the phospha-Wittig reaction, it was anticipated that **8** would react with the aryldichlorophosphine $DmpPCl_2$ to produce the diphosphene DmpP=PDmp (Scheme 5) and $[Cp_2ZrCl_2]$ due to the high chlorophilicity of the zirconium center [57]. Indeed, the reaction does generate the targeted diphosphene, but the appearance of another product plagued the reaction. The new species was readily discerned by a characteristic pair of doublets in the $^{31}P\{^1H\}$-NMR spectra having a large PP coupling constant (δ − 3, − 115; $J_{PP} = 582$ Hz). The spectral signatures, in fact, were remarkably similar to those reported earlier by Mathey for the phosphanylidenephospharane complexes **3**. The new species was thus tentatively identified as the free phosphanylidenephosphorane $DmpP{=}PMe_3$ (**9**), and later rigorously characterized by X-ray crystallography [58].

By taking advantage of Mathey's work [25], **9** and $Mes^*P{=}PMe_3$ (10) were found to be more readily prepared and isolable in almost quantitative yield as stable species by reduction with zinc dust in the presence of excess trimethylphosphine (Eq. (4.1)) [59].

$$ArPCl_2 + Zn + 6eqPMe_3 \rightarrow \underset{\substack{\mathbf{9}\ (Ar = Dmp)\\ \mathbf{10}\ (Ar = Mes^*)}}{ArP = PMe_3} + ZnCl_2 + xs\ PMe_3 \qquad (4.1)$$

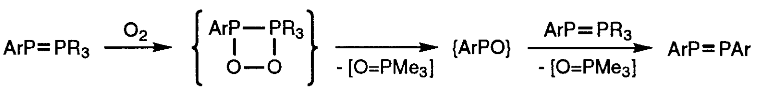
Zinc and PR_3 seem to act synergistically to aid in clean formation of $ArP{=}PR_3$. Reaction of $DmpPCl_2$ with zinc powder is slow (days) and produces only Dmp-P(Cl)P(Cl)Dmp and DmpP=PDmp. Reaction of $DmpPCl_2$ with excess PMe_3 alone produces **9** in moderate yields (in conjunction with Me_3PCl_2), but again the reaction is very sluggish (days) and not clean. Trialkylphosphines such as PEt_3 and PBu_3 can also be employed in the above sequence but reaction times are longer (~ 12 h) and final mixtures are difficult to workup due to the decreased volatility of the excess phosphine.

A survey of other dichlorophosphines in reaction 4.1 proved that isolation of materials such as **9** and **10** requires sterically demanding ligands such as Dmp and Mes*. With less hindered dichlorophosphines $RPCl_2$ (R=Trip (Trip = 2,4,6-$^{i}Pr_3C_6H_2$), Mes, or ^{t}Bu), attempts to isolate phosphanylidenephosphoranes instead resulted in formation of mixtures of cyclooligomers of the form $(RP)_n$, regardless of the tertiary phosphine used. Reduction of dichlorophosphines by tertiary phosphines has long been known to produce similar mixtures of cyclopolyphosphines and trialkylphosphonium salts [60–62]. Thus, there appears to be a limited window of synthetic viability towards isolation of free phosphanylidenephosphoranes, particularly with respect to simple alkyl and aryl substituents on the phosphorus atoms.

Phosphanylidenephosphoranes **9** and **10**, which represent direct and isolable structural phosphorus analogs of simple classical Wittig reagents, are stable yellow crystalline solids and can be stored for extended periods in the solid state in air and moisture free conditions. In solution, $ArP{=}PR_3$ slowly decompose (days to weeks) with elimination of PR_3 to give the corresponding diphosphenes (Eq. (4.2)).

$$ArP{=}PR_3 \rightarrow ArP{=}PAr + PR_3 \qquad (4.2)$$

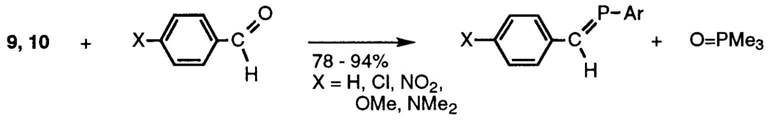
In the cases of $PR_3 = PEt_3$ and PBu_3, the decomposition is extremely sluggish. Preliminary studies have indicated that diphosphene formation is seemingly 'promoted' by dioxygen as proposed in reaction sequence (Eq. (4.3)).



(4.3)

Similar autoxidation processes have been invoked with Wittig reagents [5,63] and further studies by the authors are currently underway in order to probe the details of this interesting process.

Bearing such a close kinship to Wittig reactions, it was of immediate interest to determine the potential of **9** and **10** at effecting phospha-Wittig reactions. Indeed, reactions of **9** and **10** with a wide variety of aldehydes have been surveyed and shown to provide access to phosphaalkenes (Eq. (4.4)) [59].



(4.4)

The reactions proceed rapidly under ambient conditions and ^{31}P-NMR indicates clean formation of the phosphaalkene and phosphine oxide (Fig. 1). In general, the efficiency of phosphaalkene formation is dependent on the electronic nature of the aldehyde. The presence of electron-withdrawing groups on the aldehyde permits faster reaction times and higher yields. Parallel trends are found with Wittig reactions. The resulting phosphaalkenes are stable due to the presence of the bulky Dmp or Mes* ligands. Additionally, in virtually all cases, the *E* isomer of the phosphaalkene was formed exclusively, indicating the high stereoselectivity of the reaction.

The phospha-Wittig chemistry of **9** and **10** seems to be limited to aldehydes, however. No phosphaalkenes are detected, for example, from the reactions of **9** and

10 with ketones such as benzophenone, acetophenone, and cyclohexanone. This result suggests that a similar mechanism entailing a 4-member metallacycle, as proposed for reactions of terminal transition-metal phosphinidene complexes or Wittig reagents with aldehydes, may prevail in these reactions. Thus far, no ^{31}P-NMR resonances suggesting presence of betaine-like or oxophosphetane-like intermediates in reactions of the **9** and **10** with aldehydes have been detected. It is noteworthy that Stephan's terminal phosphinidene complex **7** shows reactivity with benzophenone, and this fact probably reflects the relative thermodynamic strengths of M=O over P=O bonds in the transition-metal oxo complex and trialkylphosphine oxide, respectively.

It should also be noted that although **9** and **10** represent the first examples of reagents effecting phospha-Wittig reactivity without the assistance of transition metals, they are clearly not the first types of phosphanylidene-σ^4-phosphoranes to be reported. The first evidence for a phosphanylidenephosphorane, $F_3CP{=}PMe_3$, was obtained by Burg and Mahler in 1961 by the reaction of cyclopolyphosphines $(PCF_3)_3$ and $(PCF_3)_4$ with trimethylphosphine [64]. This particular species is rather unstable, and undergoes a facile equilibrium with its constituents [65]. A variety of other phosphanylidenephosphoranes have appeared since and have been reviewed by Schmidpeter [17]. However, no phospha-Wittig reactivity has been described for these phosphanylidenephosphoranes. This inhibition of potential phospha-Wittig chemistry may be a consequence of the presence of either functionalized or conjugating substituents used to stabilize these compounds. In other cases, the limited thermal stability of such species may have prevented careful examination of their reactions with aldehydes and ketones. The phosphino-functionalized derivatives ^{t}Bu$_2$PP=PR′R$_2$ extensively studied by Fritz, show appreciable thermal stability and have been used successfully as sources of the phosphinophosphinidene '^{t}Bu$_2$PP' [66–73]. One such derivative ^{t}Bu$_2$PP=P(Me)^{t}Bu$_2$ was reported to show no reactivity

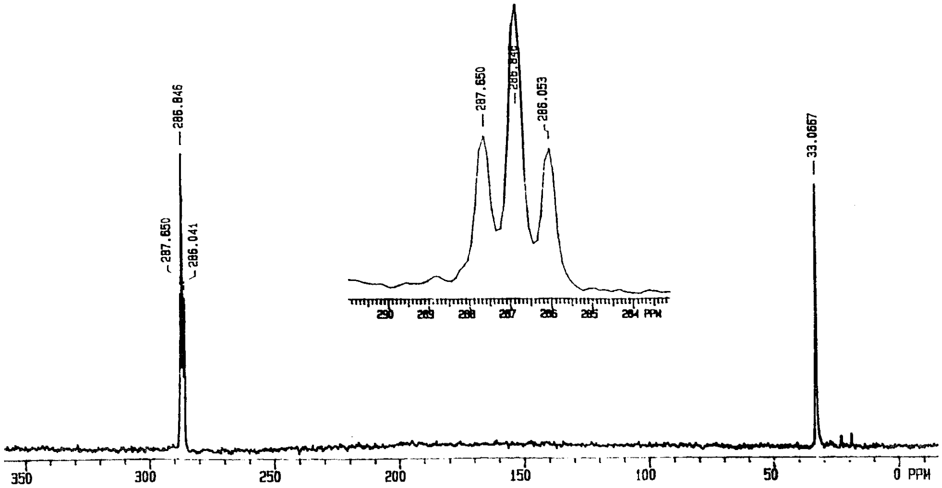
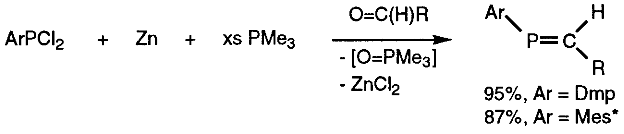


Fig. 1. ^{31}P{^{1}H}-NMR spectrum of an aliquot taken after 0.5 h after mixing DmpP=PMe$_3$ (**9**) and pentafluorobenzaldehyde showing the clean formation of the phosphaalkene DmpP=C(H)C$_6$F$_5$ (δ + 286.8 ppm, t, (J_{PF} = 98 Hz)) and Me$_3$P=O (δ 33.1 ppm).

with benzophenone [70]. In this regard, compounds **9** and **10** also show no reactivity with benzophenone. Examples of isolable phosphino-phosphaalkenes, the expected products of condensation reactions between phosphino-phosphanylidenephosphoranes and aldehydes or ketones, have been described in the literature [74]. However, to the best of our knowledge, none of these examples have been prepared by a phospha-Wittig type reaction. Nevertheless, it should also be noted that the phosphino-substituted ylides $R_2P(Me)C{=}PPh_3$, (R = Et or ^{n}Pr) the carbon parallels of phosphino-phosphanylidenephosphoranes, do react with benzaldehyde to form the corresponding phosphino-substituted olefins [75].

The protocol described in (Eq. (4.4)) has been extended to a one-pot procedure, whereby the precursor dichloroarylphosphine is reacted with zinc and aldehyde in the presence of excess trialkylphosphine. Indeed, both $DmpPCl_2$ and Mes^*PCl_2 react in such a fashion without an appreciable loss in yield (Eq. (4.5)) [59].



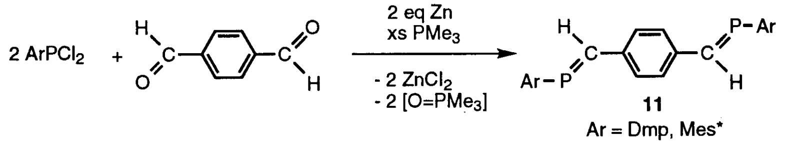
(4.5)

This discovery presents a more facile synthetic route to phosphaalkenes stabilized by bulky substituents such as Dmp and Mes*. Other synthetic techniques involve more steps, and hence a greater subsequent loss in yield with respect to the precursor dichloroarylphosphines [76,77]. One-pot Wittig reactions have also been established by Shen and co-workers for the generation of select carbon–carbon double bonds from reactions of α-bromo carboxylic derivatives (esters, amides, and nitriles) and aldehydes. The one-pot Wittig reactions employ trialkylphosphines or trialkylarsines as reagents in the presence of an appropriate catalyst (typically Zn, Pd, or Cd) [78–85].

As already mentioned, reduction of less bulky dichlorophosphines with mixtures of zinc and trialkylphosphines led not to phosphanylidenephosphoranes but to cyclooligomers. Phosphanylidenephosphoranes may lie upon the route to cyclooligomeration, however. If such transient species could be trapped by aldehydes, the scope of the phospha-Wittig reactions would be increased. Attempts to expand the one-pot procedure described above to include less bulky dichlorophosphines bearing ligands such as ^{t}Bu, Mes, or Trip were partially successful. Under a variety of conditions, such reactions resulted in competitive formation of the desired phosphaalkene accompanied by cyclophosphine oligomers (Eq. (4.6)). More work will be required to develop an effective phospha-Wittig process that utilizes the presumed transient phosphanylidenephosphoranes bearing less steric bulk.

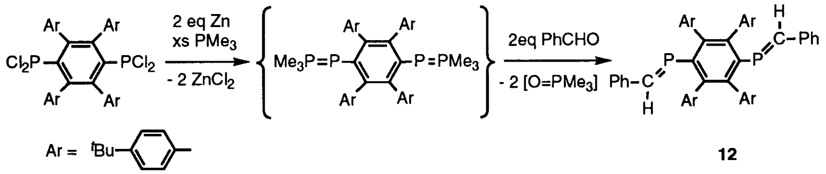
(4.6)

Ongoing efforts are currently being directed to develop the one-pot phospha-Wittig procedure described above to produce materials having a multiple number of phosphaalkene units. For example, the reaction of $ArPCl_2$ with 1,4-terepthaldehyde, zinc and PMe_3 affords the bis-phosphaalkenes **11** via a double phospha-Wittig reaction (Eq. (4.7)) [86].



(4.7)

Extension of this procedure for the formation of materials having greater than two P=C units would be made flexible by the availability of suitably designed hindered bis-dichlorophosphines. Hence, the synthesis of 1,4-$(Cl_2P)_2C_6Ar_4$ has been examined. One such species ($Ar = p\text{-}^tBuC_6H_4$) undergoes a ready one-pot double phospha-Wittig reaction to produce the bis-phosphaalkenes **12** (Eq. (4.8)) [87]. Attempts to isolate the presumed intermediate phospha-Wittig reagent have been unsuccessful, however.



(4.8)

The above approach is another example of the phosphorus carbon analogy. Bis-ylides are known [88], and are actively being used as building blocks for the systematic synthesis of oligo- and polyphenylvinylenes (PPVs) and related conjugated π-systems [89]. Clearly, bis-phosphanylidenephosphoranes have the potential to serve as analogous building blocks towards exciting analogs of PPV containing redox active P=C units.

It is apparent that the free neutral phosphoranylidenephosphoranes serve as versatile reagents in reactions with aldehydes to produce phosphaalkenes. The behavior of these efficient phospha-Wittig reagents is similar to Mathey's transition-metal complexed species (**3**). However, due to the stability afforded by the bulky Dmp or Mes* groups on the phosphinidene phosphorus, both the free phosphanylidene-σ^4-phosphoranes and the free phosphaalkenes are stable and amenable to isolation and full characterization. The free neutral phosphoranylidenephosphoranes also complement the more esoteric terminal transition-metal phosphinidene complexes in their ability to serve as carriers of the phosphinidene moiety. Hence, they can be alternatively viewed as main group phosphinidene complexes.

5. Conclusions

The past 12 or so years have seen substantial progress in the development of the phospha-Wittig reaction. As detailed above, each of the three general approaches complement one another and each has its own special merits. Clearly the systems utilizing the $[(CO)_nM]$ complexes to tame the behavior of the phospha-Wittig reagent and stabilize the resulting phosphaalkene make this approach the most general for materials without regard to sterically demanding groups. Phospha-Wittig reactions based on early transition-metal terminal phosphinidene complexes enjoy the added thermodynamic driving force that accompanies formation of M=O bonds as compared with P=O bonds. Such systems are thus able to react with less reactive ketones. Phosphanylidene-σ^4-phosphoranes can also be isolated and used for phospha-Wittig syntheses when sufficient steric protection exists. These systems allow rapid construction of stable phosphaalkenes and obviate the necessity of transition metals, and also offer what appears to be the closest direct examples of the phospha-Wittig reaction (Eq. (1.3)) in its true essence. It is anticipated that chemists armed with this array of methodologies will challenge themselves to scale new heights and claim many new exciting molecules and materials [90].

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