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Phosphaorganic Chemistry

Triphenylphosphaalkenes in Chemical Equilibria

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Abstract: Triphenylphosphaalkenes **1a**–**c** were prepared in good to excellent yields in a modified *phospha*-Peterson reaction between PhP(Li)TMS and benzophenones with different *para*-substituents at the *C*-phenyl groups (**a**: R = H, **b**: R = *O*-octyl, **c**: R = F). Owing to the low kinetic stabilization that is provided by the *P*-phenyl group, compounds **1a**–**c** engage in reversible dimerization and oligomerization reactions, some of which are not detectable by ^{31}P NMR monitoring. The dimers and oligomers are in chemical equilibria with monomeric **1a**–**c** and can be converted quantitatively to phosphinites **4a**–**c** by the irreversible addition of methanol across the P=C double bond.

Introduction

In the field of low-coordinate main group chemistry, kinetic stabilization is an often encountered strategy to prevent decomposition of the target compounds, and other side reactions such as dimerizations, oligo- and polymerization.[1] For example, several sterically bulky substituents have been developed over the years to stabilize the P=C double bond in phosphaalkenes.[2] Amongst these, the supermesityl group (2,4,6-tBu$_3$Ph, Mes*)[3] is particularly popular as it allows the purification of phosphaalkenes by column chromatography.[4] Decreasing the steric bulk of the protecting group at the phosphorus atom decreases the kinetic stabilization, and thus results in synthetic challenges, as illustrated for example by the fact that phosphaalkenes with smaller mesityl groups [2,4,6-(CH$_3$)$_3$Ph, Mes] are fewer in the literature.[5] *P*-phenyl substituted phosphaalkenes are even less stable, are often not isolable, and are reported to rapidly dimerize to the corresponding 1,2-diphosphetanes.[6] On the contrary, highly reactive phosphaalkenes are appealing if they are intermediates in downstream chemical transformations. We have recently reported such a process in which phosphaalkenes are key intermediates for the reductive cross-coupling of aldehydes to alkenes.[7] By using Mes*[8] and Mes[9] to stabilize the P=C double bonds, 1,2-disubstituted olefins can be synthesized in a one-pot reaction. *P*-phenyl substituted phosphaalkenes are most likely even more reactive and may allow an even broader substrate scope in terms of carbonyl compounds that could be used for the reductive carbonyl-to-alkene cross-coupling chemistry.

Unfortunately, the current approaches to *P*-phenyl-phosphaalkenes are somewhat unreliable, and their stability and reactivity not systematically investigated. Herein, we report an improved synthetic procedure towards *P*-phenylphosphaalkenes, strategies to prevent the formation of unwanted side products during their formation, as well as an in-depth study of their dimerization and oligomerization behavior. It is shown that the products of the latter two processes are in chemical equilibria with the monomeric phosphaalkene.

Results and Discussion

We recently reported a modified protocol[9] for the *phospha*-Peterson reaction[5,10] to synthesize *P*-Mes-phosphaalkenes. Prior to our work, the starting material MesP(Li)TMS was made in situ by treating MesP(TMS)$_2$ with one equivalent of MeLi in THF.[11] The so-formed MesP(Li)TMS was then reacted in THF with ketones to afford the corresponding *P*-Mes-phosphaalkenes.[12] In our hands, this procedure was plagued by irreproducibility and the formation of various undesirable side products. We hypothesized that small amounts of unreacted MeLi or other organolithium products thereof may be responsible for this behavior, in particular, since it is known that such species initiates the anionic polymerization of phosphaalkenes.[13] As we could show in our adjusted protocol,[9] this undesired reactivity can be overcome by using LiOEt[14] as desilylating agent instead of MeLi. Thus, MesP(Li)TMS was prepared from MesP(TMS)$_2$ by treatment with one equivalent of LiOEt to afford MesP(Li)TMS which reacts smoothly at room temperature in Et$_2$O with several aldehydes to afford Mes-phosphaalkenes as the only products.[9]

Encouraged by these results, we were interested to see whether a similar procedure would also be applicable for the preparation of *P*-phenyl-phosphaalkenes. Thus, PhP(Li)TMS was prepared by treating PhP(TMS)$_2$ with one equivalent of LiOEt in THF at room temperature. Removal of the solvent afforded a yellow solid which was dissolved in water-free Et$_2$O and used as prepared for all subsequent reactions. The reactivity of ethereal solution of PhP(Li)TMS towards benzophenone was tested.

In analogy to a report by Gates et al.,[6] three species were expected when benzophenone is added to an ethereal solution

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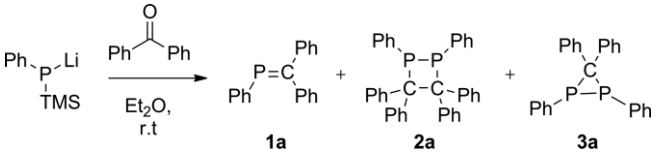
of PhP(Li)TMS (Scheme 1). The ^{31}P NMR spectrum of the reaction mixture (Figure 1a) shows these three compounds, i.e. the desired phosphaalkene **1a** (δ = +233 ppm), its head-to-head dimer **2a** (δ = +5 ppm) and the diphosphirane **3a** (δ = –118 ppm).



Scheme 1. Reaction between equimolar amounts of PhP(Li)TMS and benzophenone leading to the formation of **1a**, **2a**, and **3a**. In this example an ethereal solution of the ketone was added to a solution of PhP(Li)TMS in water-free Et_2O at room temperature.

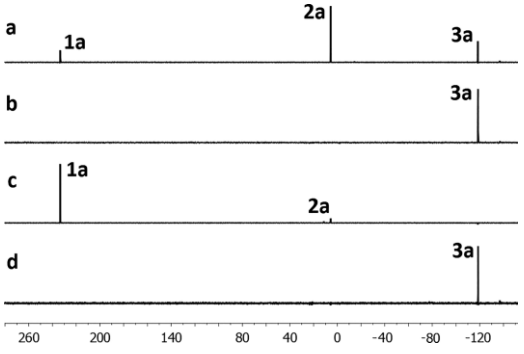
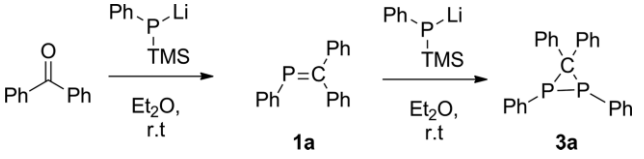


Figure 1. ^{31}P NMR spectra of the reactions depicted in Scheme 1 and Scheme 2. a) Reaction monitoring for the conditions reported in Scheme 1 showing a mixture of **1a**, **2a** and **3a**. b) Selective formation of **3a** obtained by reacting one equivalent of benzophenone and two equivalents of PhP(Li)TMS. c) Selective synthesis of **1a**, achieved by adding one equivalent of a Et_2O solution of PhP(Li)TMS to an ethereal solution of benzophenone. d) Transformation of **1a** to **3a** by addition of a second equivalent of PhP(Li)TMS to the mixture shown in Figure 1c.

While monitoring the equilibrium between **1a** and **2a**, it was noticed that the concentration of **3a** remained constant. Thus, **3a** is formed as a side product during the formation of **1a** but is not in equilibrium with either **1a** or **2a**. Mechanistically, we hypothesized that **3a** may however be formed from **1a**. As the P=C double bond is polarized[15] with the *P*-center being partially positively charged,[16] there could be the possibility of a nucleophilic attack of PhP(Li)TMS on the phosphaalkene **1a**. In order to prove this hypothesis, a test reaction between two equivalents of PhP(Li)TMS and one equivalent of benzophenone was performed, as depicted in Scheme 2.

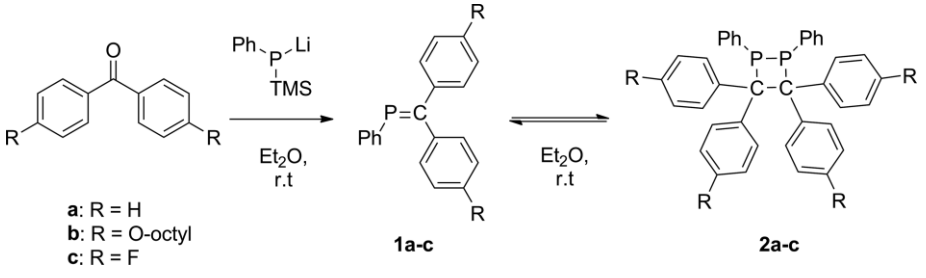


Scheme 2. Reaction between benzophenone and one equivalent of PhP(Li)TMS gives rise to phosphaalkene **1a**. The latter can be reacted further with a second equivalent of PhP(Li)TMS to form **3a**.

With this stoichiometry of the reagents, the formation of **3a** is immediate and quantitative, as illustrated by the ^{31}P NMR spectrum in Figure 1b. During the reaction, phosphaalkene **1a** is formed, but the second equivalent of PhP(Li)TMS attacks the P=C double bond of **1a**, resulting in the formation of **3a**. Having understood how **3a** is formed, we set out to develop a procedure that would suppress its formation, and allow high yields of the desired phosphaalkene **1a**. In this procedure, precaution was taken to minimize the exposure of already formed **1a** to unreacted PhP(Li)TMS. This can be achieved easily by simply reversing the order of addition of the two reagents. Thus, one equivalent of PhP(Li)TMS was added quickly to the ethereal benzophenone solution instead (Scheme 2). The reaction mixture was monitored by ^{31}P NMR spectroscopy which showed the selective formation of **1a** (Figure 1c) without any **3a** being detected. Finally, to confirm the mechanism proposed above for the formation of **3a**, a second equivalent of PhP(Li)TMS was added to the reaction mixture from Figure 1c, resulting in the clean conversion of **1a** into **3a**, as shown in Figure 1d. Unfortunately, all attempts to isolate **3a** were unsuccessful. So were attempts to coordinate **3a** to tungsten [$W(CO)_5$CNMe] or molybdenum [$Mo(CO)_5$CNMe] fragments. Decomposition to multiple phosphorus containing products was observed in all of the cases.

The reliable and high-yielding synthetic procedure that was developed for **1a** was then used for the preparation of two other triphenylphosphaalkenes that carry either an electron-donating (**1b**) or -withdrawing (**1c**) substituent in the *para*-positions of their *C*-phenyl groups. The latter two compounds were prepared by reacting ketone **b** (R = *O*-octyl) and **c** (R = F) with PhP(Li)TMS as described above (Scheme 3). We were interested to see how these substituents effect the synthesis of the phosphaalkenes, as well as their stability and reactivity.

The main differences between the three ketones may be in their reactivity towards PhP(Li)TMS and in the stabilities of the subsequently formed phosphaalkenes **1a**–**c**. From a mechanis-



Scheme 3. Synthesis of **1a**–**c** from ketones **a**–**c** and PhP(Li)TMS, followed by the dimerization equilibrium to form **2a**–**c**.

tic viewpoint, one would expect that a ketone with electron withdrawing groups (EWG) such as **c** would be a more reactive electrophile than the electron rich analogue **b**, with unsubstituted benzophenone **a** being in between. Also, the electronic nature of the P=C double bonds in **1a**–**c** will vary, which could have a noticeable impact on the stability of these compounds. In order to get quantitative information from the ^{31}P NMR spectroscopic monitoring of the reactions, an internal standard was used. We decided to use a Mes*-phosphaalkene, more specifically [(*E*)-(4-methoxybenzylidene) (2,4,6-tri-*tert*-butylphenyl)-phosphane] as internal standard since it has been shown to have a high chemical stability[8] and a similar relaxation time as phosphaalkenes **1a**–**c**. A typical example of such a ^{31}P NMR reaction monitoring starting from ketone **a** is shown in Figure 2.

After their selective formation, phosphaalkenes **1a**–**c** slowly decrease in concentration due to their dimerization to the corresponding head-to-head dimers **2a**–**c**. This reaction is not a simple decomposition pathway, as evidenced by the fact that a steady state concentration of both compounds is reached on timescales of hours to days. **1** and **2** are thus in a chemical equilibrium. For **1**,**2a**, this equilibrium is reached after 48 hours when a ratio between **1a**:**2a** of 1:2.4 is established. The reactions of **b** and **c**, as well as the dimerizations of **1b**,**c** to **2b**,**c** were studied analogously, the results of which are summarized in Table 1 (see Supporting Information for details). In the presence of electron rich substituents, the equilibrium is shifted towards the phosphaalkene **1b**. Even after four days, the ratio between **1b**:**2b** is 3.9:1. In the opposite case with the electron poor ketone, the equilibrium is shifted toward the dimer **1c** and the ratio between **1c**:**2c** is found to be 1:2.1.

The internal standard that was used in the reaction monitoring in Figure 2 allowed us to reveal another interesting aspect of the reactivity of **1**. During the time that was needed for **1** to equilibrate with **2**, it was noticed that the total amount of phosphorus species that could be detected by ^{31}P NMR spectroscopy decreased markedly. ^{1}H NMR spectroscopic monitoring gives a similar result and shows that the total amount of **1a** and **2a** decreases on these timescales, while the total number of aromatic protons stays unchanged (see Supporting Information). These observations can only be explained by the assumption of a second process that consumes some of the phosphaalkene. As this process does not produce any defined phosphorus species that could be identified by ^{31}P spectroscopy, we suggest this process to be the formation of higher oligomers/polymers of **1** (Scheme 4). Interestingly, the formation of such species does not deplete the solution of **1** and **2** completely, as one would expect from an irreversible process. In fact, we propose that also the oligomers are in chemical equilibrium

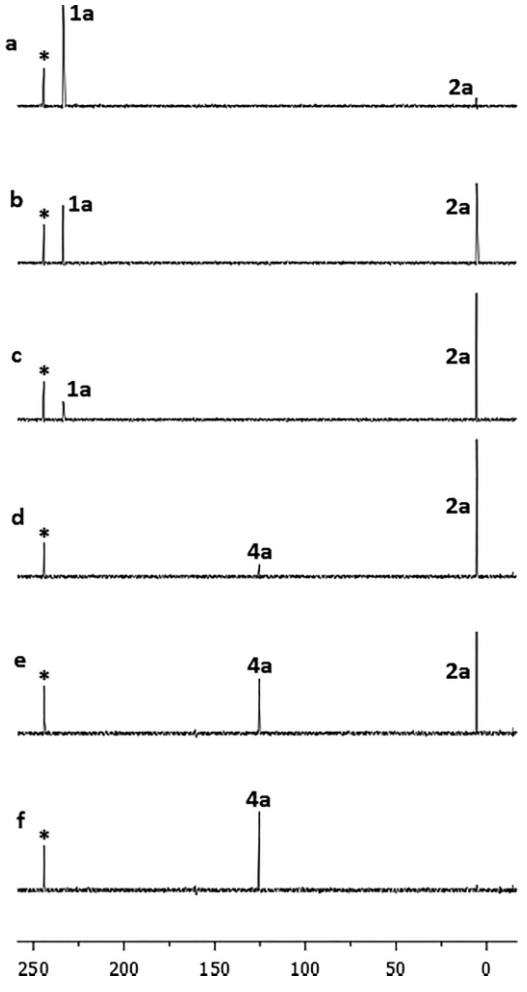


Figure 2. ^{31}P NMR investigation of the equilibrium between **1a** and **2a** (conditions as in Scheme 3) with an internal standard (*) and after MeOH addition with formation of **4a** (conditions as in Scheme 4). a) First measurement of the reaction after 14 min. The mmol of **1a** (δ = +233 [ppm]) and **2a** (δ = +5 [ppm]) can be obtained from the ratio of the integrals of their signals and the internal standard * (δ = +244 [ppm]) (see Supporting Information for details). b) after 2 hours. c) after 48 hours. d) First measurement (several minutes) after MeOH addition, showing formation of **4a** (δ = +125 [ppm]) from **1a**, with **2a** being still present in the reaction mixture. e) The second measurement after MeOH addition was performed after 30 hours, f) 7 days after MeOH addition.

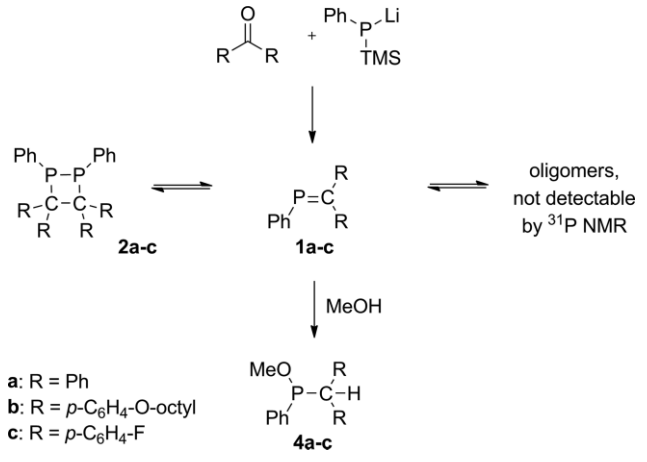
with **1** and **2**. In the example of the triphenylphosphaalkene **1a** in Figure 2, all chemical equilibria are established after 48 hours (Figure 2c), and no further changes are observed. If this hypothesis is correct, it should be possible to recover all phosphorus species by an irreversible quenching experiment that would remove **1** from all equilibria. Following Le Châtelier's principle,

Table 1. Investigation of equilibria between **1a**–**c**, **2a**–**c** and higher oligomers.

	NMR yield of **1a–c**[a] [%]	NMR yield of **4a–c**[a] [%]	**1a–c** at equilibrium [%]	**2a–c** at equilibrium [%]	oligomers at equilibrium [%]
a: R = Ph	97	87	18	45	37
b: R = *p*-C$_6$H$_4$-*O*-octyl	65	73	64	17	19
c: R = *p*-C$_6$H$_4$-F	40	54	14	31	55

[a] Determined with Mes*-phosphaalkene as internal standard, see Supporting Information for details.

even the species that are not detectable by ^{31}P NMR spectroscopy could thereby be recovered and possible to quantify. We decided on the addition of methanol across the P=C double bond of the phosphaalkenes as a suitable trapping reaction. Thus, methanol was added to the reaction mixtures that had reached equilibrium (Scheme 4).



Scheme 4. Proposed equilibria between **1**, **2** and higher oligomers and their reaction with MeOH.

As expected, methanol reacts fast with the P=C double bond in **1a**–**c** to generate the corresponding phosphinites **4a**–**c**,[17] while dimers **2a**–**c** are not directly affected (Figure 2d). On a timescale of hours, however, also **2a**–**c** are converted to phosphinites **4a**–**c** through their equilibrium reaction with **1a**–**c** (Figure 2e). The concentration of phosphinites **4a**–**c** increases even after all **2a**–**c** is converted and reaches a final maximum concentration within a few days (Figure 2f).

Since the addition of MeOH to the P=C bond can be expected to be quantitative, the final concentration of **4a**–**c** corresponds to the total yield of the initial *phospha*-Peterson reaction, which is otherwise difficult to determine as some product **1a**–**c** may have already reacted further to oligomers that are not visible by ^{31}P NMR spectroscopy.

With this analysis, it turns out that the yield of phosphaalkene formation in case of **1a** and **1b** is remarkably high (87 and 73%, respectively). Somewhat lower yields were found for **1c** (54%) which we attribute to the generally high reactivity of electron deficient ketone such as **c** towards nucleophiles in general. Interestingly, the yields for **1** that were obtained by the indirect method from quantification of **4** are very similar to those obtained by ^{31}P NMR analysis shortly after completion of the *phospha*-Peterson reaction. Dimerization and oligomerization are thus comparably slow processes relative to formation of **1**, which is an important finding if **1** is envisaged as an intermediate in other chemical transformations.

The combined knowledge of all analyses above allows the quantification of all species that are in equilibrium, i.e. the phosphaalkenes **1**, their dimers **2**, as well as their oligomers that are invisible by ^{31}P NMR spectroscopy (Table 1). Phosphaalkene **1c** is most prone to oligomerization with 55% residing in the oligomeric state. This reactivity is less severe for **1a** and **1b** where oligomerization occurs only in 37% and 19%, respectively. There is thus a clear correlation in that the more electron-deficient the phosphaalkene, the more it is engaged in oligomerization. In contrast, the electron rich phosphaalkene **1b** prevails largely as the monomeric species.

Conclusions

In summary, we were able to modify previously reported *phospha*-Peterson reactions and adopt them for the synthesis of *P*-phenyl-phosphaalkenes. The new protocol relies on the clean formation of lithium phenyl(trimethylsilyl)phosphanide PhP(Li)TMS which is obtained from PhP(TMS)$_2$ by cleavage of one TMS group through lithium ethanolate. PhP(Li)TMS that is obtained in this way reacts smoothly with benzophenone (**a**) as well as electron-rich (**b**) and –deficient (**c**) analogues to produce phosphaalkenes **1a**–**c** in 87, 73 and 54% yield, respectively. It is shown that the phosphaalkene can be reacted further with a second equivalent of PhP(Li)TMS under the formation of diphosphirane **3**, a compound whose origin has been unclear prior to this work. Phosphaalkenes **1a**–**c** engage in various chemical equilibria, most pronounced in a head-to-head dimerization to **2a**–**c** that can be observed by ^{31}P NMR spectroscopy. In general, it emerges that the equilibrium lies more on the monomer side for electron-rich phosphaalkene **1b**. In addition to the dimerization, quantitative quenching experiments show that phosphaalkenes **1a**–**c** engage in another chemical equilibrium reaction that we assign to a reversible oligomerization. This process does not form a defined monodisperse species and has previously escaped detection as it is not visible by ^{31}P NMR spectroscopy. Oligomerization is most pronounced for phosphaalkene **1c** with 55% of all phosphorus containing species being in the oligomer form, with less oligomers being detected for **1a** and **1b** (37% and 19%, respectively). The mixtures of phosphaalkenes, their dimers and oligomers showed a surprisingly high stability over timescales of days with negligible levels of irreversible decomposition. All species that are derived from phosphaalkenes **1a**–**c** can be channeled into one compound by an irreversible quenching step, in this case the addition of methanol across the P=C double bond of **1a**–**c** to afford phosphinites **4a**–**c**. This behavior presents a new possibility in the field of low valent phosphorus chemistry, as it shows that *P*-phenyl phosphaalkenes with poor kinetic stabilization can nevertheless be prepared in high yields and used as intermediates in subsequent chemical transformations.

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Keywords: Chemical equilibria · Phosphaalkenes · Reversibility · Cross-coupling · Synthesis design

[1] T. C. Klebach, R. Lourens, F. Bickelhaupt, *J. Am. Chem. Soc.* **1978**, *100*, 4886–4888.
[2] M. Yoshifuji, *J. Organomet. Chem.* **2000**, *611*, 210–216.

[3] a) M. Yoshifuji, I. Shima, N. Inamoto, K. Hirotsu, T. Higuchi, *J. Am. Chem. Soc.* **1981**, *103*, 4587–4589; b) R. Appel, C. Casser, M. Immenkeppel, F. Knoch, *Angew. Chem. Int. Ed. Engl.* **1984**, *23*, 895–896; *Angew. Chem.* **1984**, *96*, 905.
[4] K. Esfandiarfard, A. I. Arkhypchuk, A. Orthaber, S. Ott, *Dalton Trans.* **2016**, *45*, 2201–2207.
[5] M. Yam, J. H. Chong, C.-W. Tsang, B. O. Patrick, A. E. Lam, D. P. Gates, *Inorg. Chem.* **2006**, *45*, 5225–5234.
[6] S. Wang, K. Samedov, S. C. Serin, D. P. Gates, *Eur. J. Inorg. Chem.* **2016**, *2016*, 4144–4151.
[7] K. Esfandiarfard, J. Mai, S. Ott, *J. Am. Chem. Soc.* **2017**, *139*, 2940–2943.
[8] J. Mai, A. I. Arkhypchuk, A. K. Gupta, S. Ott, *Chem. Commun.* **2018**, *54*, 7163–7166.
[9] A. I. Arkhypchuk, N. D'Imperio, S. Ott, *Org. Lett.* **2018**, *20*, 5086–5089.
[10] H. Kawanami, K. Toyota, M. Yoshifuji, *J. Organomet. Chem.* **1997**, *535*, 1–5.
[11] S. C. Serin, F. S. Pick, G. R. Dake, D. P. Gates, *Inorg. Chem.* **2016**, *55*, 6670–6678.
[12] B. W. Rawe, C. M. Brown, M. R. MacKinnon, B. O. Patrick, G. J. Bodwell, D. P. Gates, *Organometallics* **2017**, *36*, 2520–2526.
[13] C.-W. Tsang, M. Yam, D. P. Gates, *J. Am. Chem. Soc.* **2003**, *125*, 1480–1481.
[14] F. Uhlig, R. Hummeltenberg, *J. Organomet. Chem.* **1993**, *452*, C9–C10.
[15] M. François, *Angew. Chem. Int. Ed.* **2003**, *42*, 1578–1604; *Angew. Chem.* **2003**, *115*, 1616.
[16] W. W. Schoeller, *J. Chem. Soc., Chem. Commun.* **1985**, 334–335.
[17] T. A. Van der Knaap, T. C. Klebach, R. Lourens, M. Vos, F. Bickelhaupt, *J. Am. Chem. Soc.* **1983**, *105*, 4026–4032.

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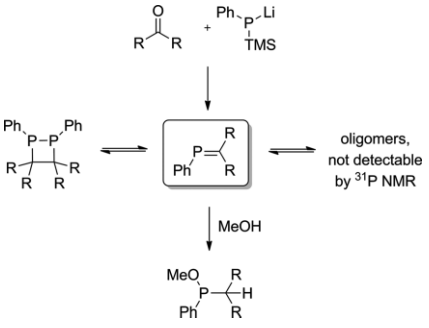

Triphenylphosphaalkenes were prepared in good to excellent yields in a modified *phospha*-Peterson reaction between PhP(Li)TMS and different benzophenones. Depending on the electronics of the *C*-substituents, the title compounds engage in reversible dimerization and oligomerization reactions, some of which are not detectable by ^{31}P NMR monitoring but can be quantified by quenching experiments.

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