Check for updates

EurJIC
European Journal of Inorganic Chemistry

Review
doi.org/10.1002/ejic.202300444

Chemistry Europe
European Chemical Societies Publishing

www.eurjic.org

Hydrophosphorylation of C=O/N Bonds Using Organophosphine Oxides or Sulfides

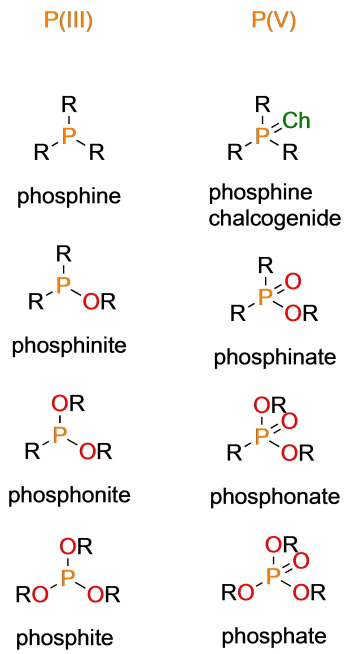
Jan-Willem Lamberink-Ilupeju,[a] Paul J. Ragogna,*[a, b] and Johanna M. Blacquiere*[a]

α-Functionalized phosphorus compounds are an important class of biologically relevant molecules. The synthesis of these compounds often proceeds through the hydrophosphorylation of a C=E bond, with the most well-known transformation being the Kabachnik-Fields reaction. The nature of the phosphorus reagent is an important aspect of the hydrophosphorylation reaction. The Kabachnik-Fields reaction uses H-phosphonates $(RO)_2P(O)H$, and similarities are often applied to 2° phosphine chalcogenides ($R_2P(Ch)H$). However, the reactivities of the P–C and P–OR molecules differ quite dramatically, which changes the operative mechanism as well as subsequent downstream chemistry. We provide an in-depth analysis of hydrophosphorylation of C=E (E=O, N) bonds with organophosphine chalcogenides. Additional discussion and a critical appraisal are provided on the similarities and differences between the H-phosphonate and phosphine chalcogenide chemistry.

1. Introduction

Phosphorus nucleophiles are ubiquitous reagents throughout synthetic chemistry. With a diverse array of substituents available, coupled with a large swath of potential electrophiles, the variety of products generated are seemingly endless. The most common structural motifs of P(III) molecules vary based on the substituents of oxygen or carbon atoms, and range from phosphines (PR_3), phosphinites ($P(OR)R_2$), phosphonites ($P(OR)_2R$), and phosphites ($P(OR)_3$) (Scheme 1, left column). The corresponding P(V) counterpart of phosphines are generally named phosphine chalcogenides ($(Ch)PR_3$). The rest of the P(V) compound types follow specific naming for Ch=O that consist of: phosphinates ($(O)P(OR)R_2$), phosphonates ($(O)P(OR)_2R$), and phosphates ($(O)P(OR)_3$; Scheme 1, right column), and are common naming conventions encountered in the literature instead of the formal IUPAC names. We have elected to use the conventional naming system to ensure both consistency with current literature and accessibility of this Review. Among these P(III) and P(V) reagents, the phosphines and phosphine chalcogenides are distinct since they do not contain any P–OR bonds.

Hydrophosphorylation, or addition of a P(V)–H bond across an unsaturated moiety, is one of the more impactful reactions that employs a phosphorus nucleophile. The most common form of this reaction involves the addition of a secondary phosphonate (*i.e.* $(O)P(OR)_2H$) to an imine, which generates an α-aminophosphonate.[1,2] This two-component version is named the Pudovik reaction.[3] *In situ* imine formation from a carbonyl and an amine occurs in the corresponding three-component reaction that is named the Kabachnik-Fields reaction (Scheme 2a). The true potential of these reactions was not realized until a few years after their discoveries when the hydrolysis product, the α-aminophosphonic acid, was determined to be a bio-isostere of α-amino acids (Scheme 2b).[4] From this revelation came a renewed interest in the wide variety of α-functionalized P(V) products, typically generated from a C=E electrophile and H–P nucleophile (Scheme 2c). The nature of the electrophile and nucleophile are important variables that, depending on the desired product, can be tuned to generate valuable P-containing products. Addition reactions using secondary phosphonate or phosphinate P(V) reagents, which contain P–OR moieties, have



Scheme 1. Left Column: P(III) Nomenclature for tertiary phosphorus reagents. Right Column: P(V) Nomenclature for tertiary phosphorus reagents.

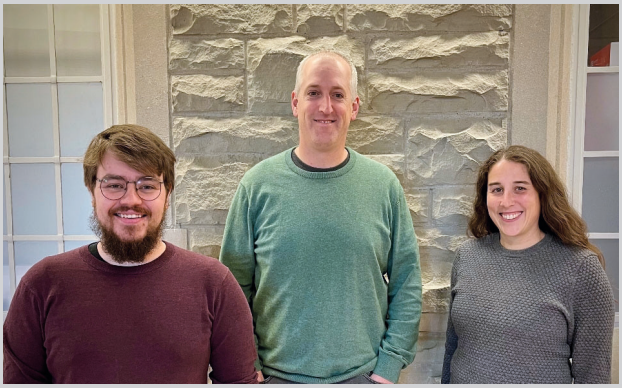
[a] *Dr. J.-W. Lamberink-Ilupeju, Prof. Dr. P. J. Ragogna, Prof. Dr. J. M. Blacquiere*
Department of Chemistry
The University of Western Ontario
London, Ontario, N6A 587 (Canada)
E-mail: pragogna@uwo.ca
johanna.blacquiere@uwo.ca

[b] *Prof. Dr. P. J. Ragogna*
Surface Science Western
The University of Western Ontario
London, Ontario, N6G 0J3 (Canada)

© 2023 Wiley-VCH GmbH

dominated the field. These contributions have already been reviewed extensively[5–7] and, as such, will not be covered in this Review.

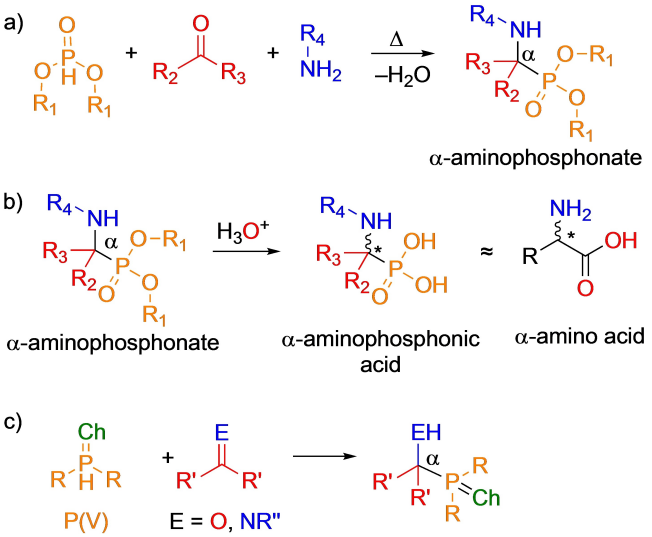
Hydrophosphorylation with carbon-substituted phosphorus reagents (*i.e.* primary or secondary phosphine chalcogenides) have received far less attention than the OR-substituted counterparts employed in the Kabachnik-Fields or Pudovik reactions. Therefore, hydrophosphorylation using phosphine chalcogenide reagents will be the focus of this Review. While such reactions are often classified as Kabachnik-Fields or Pudovik reactions, the phosphine chalcogenides have distinct reactivity and mechanism to phosphonate/ite reagents and they should therefore be considered separately. This Review will cover seminal and selected representative contributions that address the mechanism, reactivity, and future outlook of hydrophosphorylation with (Ch)PR_2H reagents. Examples will almost exclusively focus on primary or secondary phosphine oxide or sulfide reagents since corresponding chemistry with selenide or telluride derivatives is yet to be explored. As the phosphorus reagent encompasses only half of the reaction, it is equally important to investigate the role of the C=E fragment. In the scope of this Review, we will examine carbonyl (C=O) and imine (C=N) functional groups as reaction partners. There is an intricate balance of electrophilicity/nucleophilicity and acidity that impacts the reaction, and as such, the compatibility and ideal cases between nucleophile-electrophile pairs will be highlighted. This Review is divided into the hydrophosphorylation reaction of carbonyl functional groups using phosphine oxides or phosphine sulfides (Scheme 3). The hydrophosphorylation of imine functional groups using phosphine oxides and sulfides will subsequently be outlined.



Jan-Willem Lamberink-Ilupeju completed his BSc. in Chemistry at Brock University under the supervision of Georgii Nikonov (2018). He finished his Ph.D in Chemistry at Western University under the guidance of Prof. Paul J. Ragogna, and Prof. Johanna M. Blacquiere (2023), studying the hydrophosphorylation reaction and its applications in small molecule and materials chemistry. Jan-Willem is currently a Postdoctoral Fellow in the Faculty of Chemical and Biochemical Engineering at Western University investigating depolymerization and polymer upcycling technologies.

Johanna Blacquiere is an Associate Professor in the Department of Chemistry at Western University. She obtained a B.Sc. from Mount Allison University in 2005, and a Ph.D. at the University of Ottawa under the supervison of Deryn Fogg in 2011. She was an NSERC Postdoctoral Fellow in the laboratory of Jim Mayer at the University of Washington, and in 2013 she began her independent career at Western University. Her research targets cooperative ligand design strategies for additive-free homogenous catalysis, with a focus on understanding operative mechanisms. She enjoys expanding her research into new areas through collaborations with her colleagues.

Paul Ragogna is the Associate Dean of Science (Research) and Professor in the Dept. of Chemistry at Western University. He completed his BSc. (Honours) from Brock University, a PhD from Dalhousie University (with Prof. Neil Burford) and Postdoctoral studies at the University of Toronto (with Prof. Ian Manners). Ragogna is a main group chemist, with the aim of discovering and applying novel materials and preparing thin films using atomic (molecular) layer deposition A(M)LD. He maintains numerous private/ academic partnerships that facilitate a unique research ecosystem for his trainees, where fundamental science drives their work that is informed by the needs of industry partners.



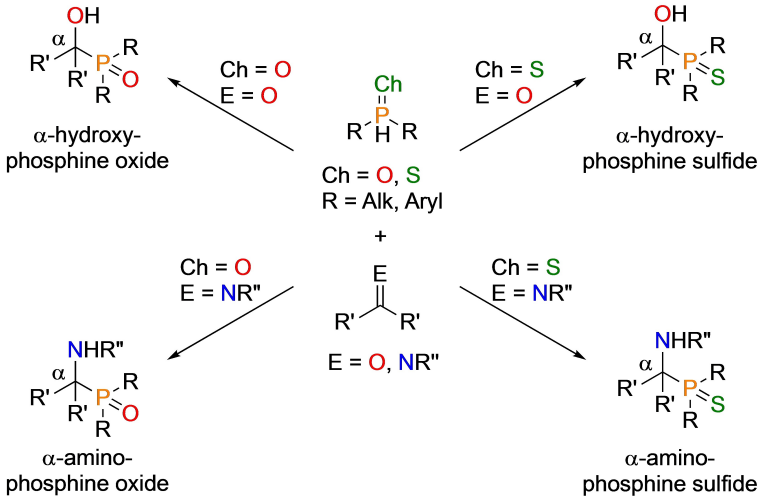
Scheme 2. a) The Kabachnik-Fields reaction between a secondary phosphonate, carbonyl, and amine to form an α-aminophosphonate, the Pudovik reaction is classified by the pre-formation and isolation of the imine moiety b) The hydrolysis of an α-aminophosphonate to generate the α-aminophosphonic acid, as an isostere of an α-amino acid. c) A general hydrophosphorylation reaction to generate an α-functionalized phosphine chalcogenide.

2. Mechanism

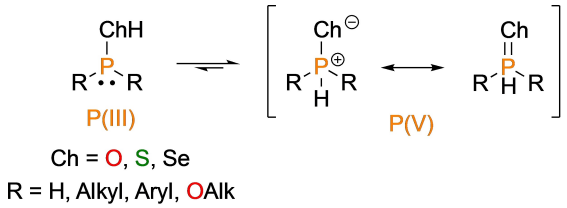
Hydrophosphorylation of C=E bonds must involve the cleavage of a P–H bond of the 1° or 2° phosphine chalcogenide, and formation of new E–H and P–C bonds. The ability for the phosphorus atom to bind to the electrophilic carbon of the C=E reagent is not immediately obvious since the P(V) precursor does not bear any non-bonding electrons, and it is therefore not inherently nucleophilic. It is well established that secondary or primary P(V) phosphine chalcogenides, phosphinates, and phosphonates that contain a P–H bond can undergo tautomerization to their corresponding P(III) form (Scheme 4).[8–14] This P(III) form has a lone pair, and the phosphorus atom can therefore act as a

© 2023 Wiley-VCH GmbH

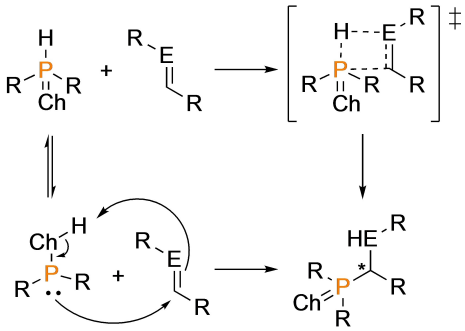
10990682c, 2024, 9, Downloaded from https://chemistry-europe.onlinelibrary.wiley.com/doi/10.1002/ejic.202300444 by Western University, Wiley Online Library on [08/05/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Scheme 3. Scope of this review: Hydrophosphorylation of carbonyl and imine functional groups with 1° or 2° phosphine chalcogenides bearing carbon-based substituents.



Scheme 4. Tautomerization of a secondary P(V) phosphine reagent (right) to the P(III) tautomer (left). Resonance structures for the former are shown within the square brackets.



Scheme 5. Two plausible pathways identified for the addition of phosphine chalcogenides to C=E bonds: a concerted [2 + 2] pathway (top), and a stepwise tautomerization and nucleophilic attack pathway (bottom).

nucleophile and attack an electrophilic partner. The tautomerization process is complex,[10–12,15] and there are several factors (such as solvent polarity) that can influence the rate,[14] but the complexity of the tautomerization process does not alter the net outcome of the reaction. In all but a few exceptional cases, the equilibrium lies drastically on the side of the P(V) form,[16] though the P(III) tautomer can be trapped using Lewis acidic reagents, or transition metals.[17,18]

The hydrophosphorylation of a C=E bond is proposed to proceed by one of two pathways. Either a concerted [2 + 2] cycloaddition (Scheme 5, top), or stepwise involving the aforementioned P(V)-P(III) tautomerization followed by nucleophilic attack and proton transfer (Scheme 5, bottom). Despite being the minor tautomer, the P(III) form can act as the nucleophile to add to the electrophilic carbon atom of the C=E reagent, and will continuously re-establish the equilibrium to reform the depleted P(III) species (Le Chatelier's Principle). The two pathways were originally identified for hydrophosphorylation with phosphonate reagents ($(OR)_2P(O)H$). While several studies have implicated these paths for organophosphine chalcogenides, the subsequent section will address evidence to support the mechanistic assignment.

The concerted [2 + 2] hydrophosphorylation pathway (Scheme 5 top) was first proposed as a result of kinetic studies performed on the Pudovik reaction between dimethyl phosphite ($(O)P(OMe)_2H$) and *N*-benzylidene isopropylimine (Ph–CH=N-*i*-Pr).[19] The obtained negative activation energies for various imines strongly suggested that the reaction proceeds through a highly ordered 4-membered transition state. This was further corroborated by the stereochemical outcome observed in the addition of dibenzyl phosphite ($(O)P(OCH_2Ph)_2H$) to a chiral imine which ultimately followed Cram's Rules. There is no corresponding experimental or computational study to support the [2 + 2] pathway with phosphine chalcogenide reagents.

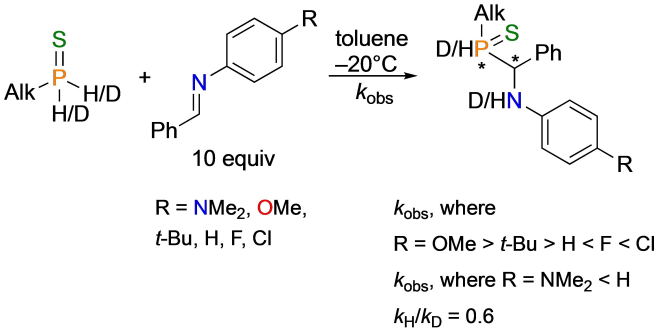
The P(III) tautomer is a key intermediate in the stepwise hydrophosphorylation mechanism since it either directly acts as a nucleophile, or it first acts as a Brønsted acid to protonate and activate the C=E functional group, so understanding factors that influence the nucleophilicity or acidity, and also formation of the P(III) species via the tautomerization equilibrium are important. Several studies have experimentally and computationally investigated the P(V)–P(III) tautomerization phenomenon to systematically quantify the rates of the reaction, as well as to determine the relative acidity of the P(III) tautomer.[8–14] However, most studies focused only on phosphorus reagents with P-OR bonds and Ch = O (*i.e.* phosphonates and phosphonites) because of the biological relevance of the hydrophosphorylation products.

© 2023 Wiley-VCH GmbH

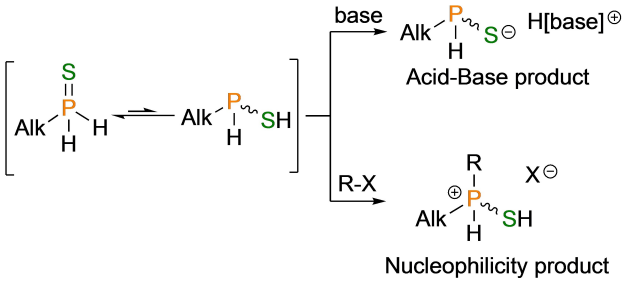
10990682c, 2024, 9, Downloaded from https://chemistry-europe.onlinelibrary.wiley.com/doi/10.1002/ejic.202300444 by Western University, Wiley Online Library on [08/05/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Some studies included reagents with P–C motifs and Ch=S, which allows for some trends in phosphine chalcogenide acidity to be extracted. It has been sporadically reported that the relative acidity of phosphine chalcogenides is greater for derivatives with heavier chalcogens. In a direct comparison between chalcogens, the secondary phosphine oxide $Me_2P(O)H$ has a $pKa_{(DMSO)}=27.1$, whereas the corresponding sulfide $Me_2P(S)H$ has a $pKa_{(DMSO)}=17.6$.[20] Showing that alkyl functionalized phosphine sulfides are 10 orders of magnitude more acidic than their oxide counterparts. The primary phosphine sulfide *i*-$BuP(S)H_2$ was indirectly shown to have a $pKa_{(MeCN)}$ less than 11.4, which is six orders of magnitude more acidic than the secondary phosphine sulfide $Me_2P(S)H$.[21] Exemplifying that a more substituted phosphine chalcogenide has attenuated acidity.[22]

Recent studies have proposed the [2+2] transition state as the key rate-determining step (RDS) in the hydrophosphorylation of C=N bonds with phosphine chalcogenides.[23–25] Yet, only one mechanistic analysis of phosphine chalcogenide reactivity has been reported, in which the experimental evidence supported the stepwise pathway involving tautomerization and nucleophilic attack. The in-depth kinetic investigation was conducted using a primary phosphine sulfide (*i*-$BuP(S)H_2$) and a family of substituted aryl imines. A KIE experiment was performed between *i*-$BuP(S)D_2$ and the imine.[21] If a P–H bond cleavage occurred in the RDS, the rate would decrease when attempted with a P–D bond and result in a primary KIE ($k_H/k_D>1$). Therefore, a KIE would be expected for both a [2+2] mechanism and a stepwise mechanism if the tautomerization or proton transfer is the RDS. A KIE is not expected for the stepwise mechanism if the RDS is the nucleophilic attack step. An inverse equilibrium isotope effect (IEIE) of *ca.* 0.6 was observed, which is inconsistent with concerted [2+2] addition via the P(V) tautomer, and is therefore consistent with the P(V)–P(III) tautomerization as a pre-equilibrium before the RDS. The incorporation of the P–D bond perturbs the equilibrium constant between the P(V) and P(III) species to slightly favour the P(III) tautomer, and the increased concentration of this reactive species overall increases the rate of the reaction. The IEIE prevented deconvolution of the KIE for the subsequent step of the reaction, though still supports the stepwise tautomerization/nucleophilic attack mechanism. To determine the electronic dependence on the rate of the reaction, a Hammett analysis displayed a "concave up" shape across a set of electron-rich and electron-poor imines (Scheme 6). This signals not only that the rates of the reaction increase despite the electronics of the electrophile, but also that there is either a change in mechanism or transition state from electron-rich to poor imines. This observation is consistent with stepwise proton transfer and nucleophilic attack, in which the order switches depending on the nature of the electrophile. An electron donating group increases the basicity of the nitrogen atom of the imine, and it is thus more amenable to protonation and activation prior to nucleophilic addition. In the case of the electron withdrawing groups, the inductive effect dominates, and the imine carbon is activated to nucleophilic addition prior to proton transfer. The acidity of *i*-$BuP(S)H_2$ was confirmed through a control reaction with dimethyl aniline, which formed the anilinium salt [*i*-BuP(H)S][$Me_2N(H)Ph$] (Scheme 7). Similar



Scheme 6. Kinetic experiments conducted on the hydrophosphorylation of C=N bonds.



Scheme 7. Trapping experiments of a primary phosphine sulfide with a base and an electrophile.

proton transfer chemistry was also operative during phosphorylation since a *p*-NMe_2 substituted imine was preferentially protonated at the tertiary amine rather than the imine nitrogen and this substantially slowed the rate of addition. This highlights that the relative acidity of the *in-situ* generated P(III) compound, as well as the basicity of the heteroatom in the unsaturated functional group, is critical to the underlying mechanism.

Additional trapping experiments were performed to confirm that the nucleophilic P(III) form of the primary phosphine was present in the reaction mixture. Treatment of *i*-$BuP(S)H_2$ with MeI as a non-basic electrophile lead to the formation of the proposed phosphonium salt [*i*-$BuP(SH)Me_2$][I] (Scheme 7). The various mechanistic data all points towards the tautomerization/nucleophilic attack mechanism being operative for hydrophosphorylation with organophosphine chalcogenides, rather than the [2+2] cycloaddition pathway.

3. Addition of Phosphine Chalcogenides to C=O Bonds

The addition of a phosphine chalcogenide to a carbonyl containing compound results in the formation of an α-hydroxy phosphine chalcogenide. These are an important sub-class of phosphine chalcogenides because, in addition to the commonly known uses of phosphine chalcogenides as ligands, flame retardants, conductive materials, or organic building blocks, the presence of a hydroxyl functional group allows for subsequent

© 2023 Wiley-VCH GmbH

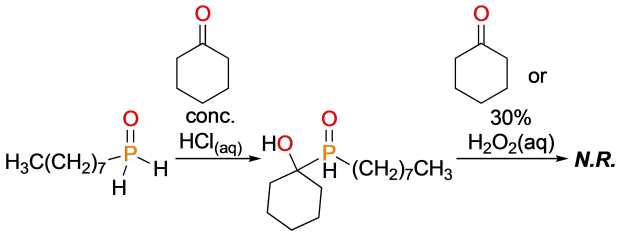
10990682c, 2024, 9, Downloaded from https://chemistry-europe.onlinelibrary.wiley.com/doi/10.1002/ejic.202300444 by Western University, Wiley Online Library on [08/05/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

transformations.[13] For instance, oxidation of the alcohol results in the formation of an acyl phosphine oxide, which is a common class of photo initiator widely used in polymer chemistry.[26,27]

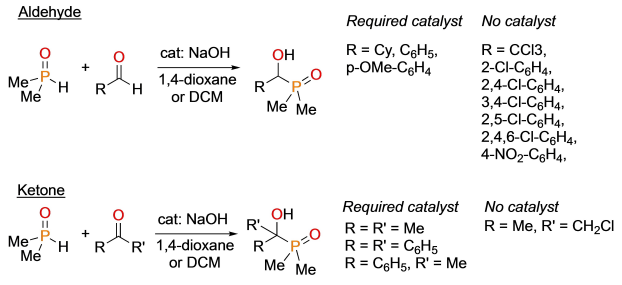
Phosphine Oxides

With the current understanding of the mechanism, we can ascertain the importance of an acid or base additive, either through the protonation of the C=E moiety or the deprotonation of the phosphorus reagent. A study performed by Epstein and Buckler, investigated a reaction in concentrated HCl between *n*-octyl phosphine oxide and an excess of cyclohexanone, which gave the corresponding mono-addition product (Scheme 8).[28] It was noted that the selectivity for the mono-addition likely occurred due to the steric profile of the cyclohexyl ring. The secondary P(O)H moiety is stable to oxidative conditions. The acid facilitates the addition of a phosphine oxide to a ketone by requisite protonation of the carbonyl to afford a sufficiently electrophilic carbon to allow for the addition of the phosphorus reagent.

The successful synthesis of the relatively unhindered compound $Me_2P(O)H$ by Kliener in 1974 allowed for the reactivity to be probed with a variety of aldehydes and ketones (Scheme 9).[29] Rather than a reaction under acidic conditions, the addition of NaOH to the mixture containing the secondary phosphine oxide and the carbonyl catalyzed the reaction. Instead of activation of the carbonyl group by a protonation step, the base likely deprotonated dimethylphosphine oxide, therefore making it a more potent nucleophile. The Brønsted base catalyst was required to achieve appreciable yields with aldehydes bearing alkyl, phenyl or electron-rich aryl substituents. The same trend



Scheme 8. Mono addition of cyclohexanone to *n*-octylphosphine oxide, and inhibition of downstream oxidation chemistry (N.R. = no reaction).

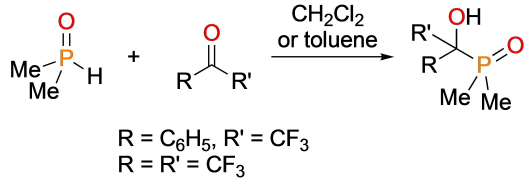


Scheme 9. Addition of dimethylphosphine oxide to various aldehydes and ketones. Electron rich carbonyls required addition of NaOH as a catalyst, and electron poor carbonyls did not require catalyst.

was also observed in the addition of $Me_2P(O)H$ to ketones, as ketones are inherently less electrophilic than aldehydes and the increased steric profile of the reaction centre. Reactions with aldehyde or ketone reagents with appended electron withdrawing group (EWG) did not require the basic reagent, rather reactions proceeded promptly under mild conditions. The increased reactivity of the electron poor C=O reagents relative to the electron rich counterparts is consistent with the expected electronic effects governing a nucleophilic addition to a carbonyl.

The above example showcases that strongly activated carbonyls undergo phosphorylation without added Brønsted acid or base reagent, and underscores that suitable substrate tuning can preclude the need for activator additives (Scheme 9). This was further corroborated by Schmutzler and Well as they investigated the addition of $Me_2P(O)H$ towards fluorinated ketones (Scheme 10).[30] Addition of $Me_2P(O)H$ to trifluoroacetophenone and hexafluoroacetone resulted in the formation of the corresponding fluorinated α-hydroxyphosphine oxides. The reactions were conducted at room temperature and required no additives to proceed. The prior two studies show that the addition of $Me_2P(O)H$ can be facilitated by the activation of either the nucleophile through deprotonation, or by activation of the carbonyl through protonation or by inductive effects.

In 2003, the Trofimov group examined the addition of secondary phosphine oxides to α,β-unsaturated aldehydes. Rather than following typical Michael-addition pathways to the β-carbon, the phosphorus reagent adds chemoselectively to the carbonyl carbon position to generate an α-hydroxyphosphine chalcogenide. Progressively longer reaction times (24, 48, and 72 hours) were required to obtain similar yields with di-*n*-butyl, di-*n*-hexyl, and bis(2-phenylethyl) (Scheme 11a).[31] The suggested mechanism invokes the P(V)-P(III) tautomerization in which the authors indicate that the more nucleophilic *n*-Bu phosphine would react quicker than the less electron rich *n*-hex or CH_2CH_2Ph derivatives (Scheme 11b). The relative nucleophilicities of the phosphorus reagents would be similar (Hammett σ_p: *n*-Bu = −0.16, *n*-pentyl = −0.15), but the steric profiles increase across the set, and this is likely a primary factor in the increased reaction times. Reactions with different aldehydes revealed that increased sterics of the phosphine oxide and electron-rich aldehydes inhibit the rate of the reaction. Substrates containing a methyl and phenyl group in the β position of the aldehyde substantially reduce the rate of the reaction (Scheme 11a). This is demonstrated by a 48% yield for the terminal alkene (R′ = H), but yields of only 2 and 12% for the methyl- and phenyl-substituted alkenes, respectively. This once again highlights that electron

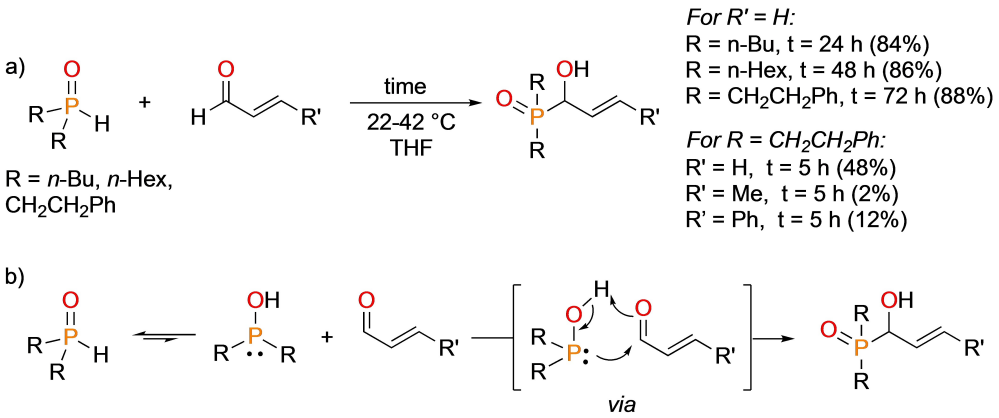


Scheme 10. Addition of $Me_2P(O)H$ to fluorinated ketones.

© 2023 Wiley-VCH GmbH

10990682c, 2024, 9, Downloaded from https://chemistry-europe.onlinelibrary.wiley.com/doi/10.1002/ejic.202300444 by Western University, Wiley Online Library on [08/05/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Review
doi.org/10.1002/ejic.202300444

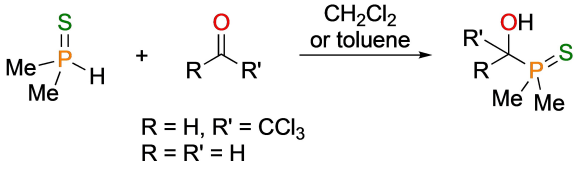


Scheme 11. a) Addition of secondary phosphine oxides to α,β-unsaturated aldehydes. b) Proposed mechanism, invoking a P(V)-P(III) tautomerization followed by a nucleophilic attack at the carbonyl carbon.

donating groups and steric bulk deactivate the carbonyl carbon toward electrophilic attack.

Phosphine Sulfides

Several of the prior studies with phosphine oxide reagents concurrently investigated the addition of phosphine sulfide reagents. The investigations performed by Schmutzler and Well also examined the addition of $Me_2P(S)H$ towards fluorinated ketones, formaldehyde, 1,1,1-trichloroethanal (chloral), dialdehydes, diketones, acetone, and cyclohexanone.[30] Analogous reaction products to those with the phosphine oxide reagent were observed. Unfortunately, several of the reactions performed with $Me_2P(S)H$ were not conducted in parallel with $Me_2P(O)H$. This leads to difficulties in direct comparison of the reactivity of the oxide vs the sulfide, but still allows for some conclusions to be drawn. Reactions with formaldehyde and 1,1,1-trichloroethanal both resulted in an exotherm (Scheme 12), demonstrating that both the strong withdrawing effect of the trichloro group, and the minimal steric profile of formaldehyde, can lead to

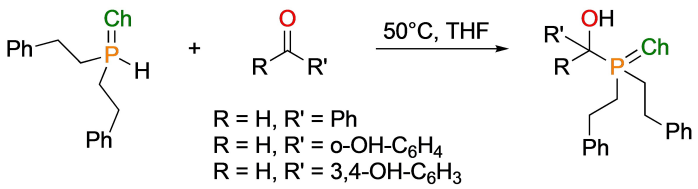


Scheme 12. Addition of $Me_2P(S)H$ to 1,1,1-trichloroethanal and formaldehyde resulting in noticable exotherms.

vigorous reactions and in both these cases no additive was required.

The 2006 studies by Trofimov utilized both bis-(2-phenylethyl)phosphine oxide and sulfide, and showed that the reaction with the phosphine oxide proceeded quicker, and in greater yields than that of the phosphine sulfide. With the same aldehyde, the phosphine oxide required 6 hours to react completely, and the sulfide required 10 hours, almost twice as long (Scheme 13).[32] The reduced reaction time for the phosphine oxide is suggestive that either the concentration of the P(III) tautomer is greater for the phosphine oxide than that of the phosphine sulfide, or that the nucleophilic addition of the P(III) tautomer to the aldehyde is faster for the oxide vs the sulfide. As noted above, the sulfide reagent is inherently more acidic than the oxide, which shows that proton transfer does not significantly influence reaction rates in this case.

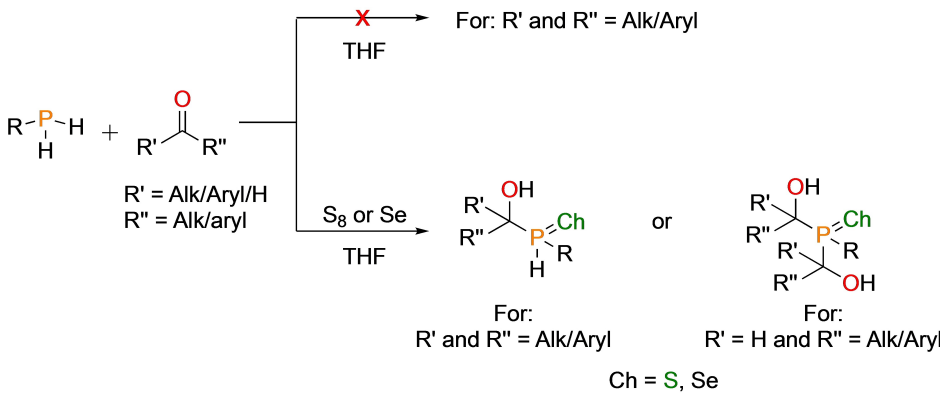
One of the first examples of P–H bond addition using primary phosphines was performed by Uhlig and co-workers who investigated the reactivity of primary phosphine sulfides and selenides towards aldehydes and ketones to generate bis(α-hydroxy)phosphine sulfides/selenides.[33] These reactions were performed as a three-component mixture between carbonyl, phosphine and chalcogen. Since the reaction was performed by the portion-wise addition of solid sulfur or selenium to the mixture, the overall rate of the reaction was limited by mass transfer of the oxidant into the solution. The transient primary phosphine chalcogenide was not isolated, although it was prepared and characterized *in-situ* using ^{31}P NMR spectroscopy. In the absence of chalcogen or acid to activate the P(III) or ketone reagents, respectively, P–H bond addition did not occur



Scheme 13. Addition of bis-(2-phenylethyl) phosphine chalcogenides (Ch = O, S) to hydroxyaldehydes.

© 2023 Wiley-VCH GmbH

10990682c, 2024, 9, Downloaded from https://chemistry-europe.onlinelibrary.wiley.com/doi/10.1002/ejic.202300444 by Western University, Wiley Online Library on [08/05/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Scheme 14. Top) No reaction between 1° phosphine and ketone in absence of chalcogen. Bottom: Addition of ketones and aldehydes to primary phosphine sulfides/selenides. Addition in presence of chalcogen to ketones provides the mono addition products, and addition to aldehyde afford the double addition products.

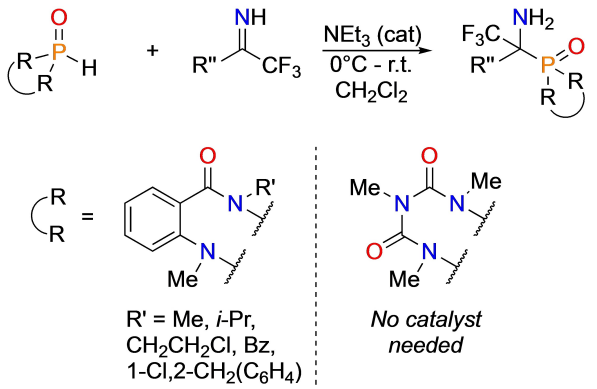
(Scheme 14; top). When a ketone was employed in the three component reaction, only the mono-addition product was formed, once again likely due to the increased steric profile as compared to the aldehydes which give bis-α-hydroxyphosphine chalcogenide products (Scheme 14; bottom). The assignment of the rate determining step should be taken with care, as the solubility and multicomponent nature of the reaction complicates the determination of the reaction rate. This unfortunately results in the inability to compare the overall reaction rates of the primary phosphine sulfide to the primary phosphine selenide, but still shows the ephemeral nature of the P(V) reagent in the presence of an electrophile.

4. Addition of Phosphine Chalcogenides to C=N Bonds

Addition of phosphine chalcogenides to C=N bonds generate the corresponding α-aminophosphine chalcogenides. When Ch = O, the α-aminophosphine oxide bears similarity to the α-aminophosphonate moiety formed by the Kabachnik-Fields reaction. Therefore, the α-aminophosphine oxide fragment is considered a valuable target for biological studies. In comparison to the Kabachnik-Fields reaction, a limited number of studies have been performed on the synthesis of α-aminophosphine oxides. In relation to the hydrophosphorylation of C=O bonds, the C=N moiety is less polarized, because of the decreased electronegativity of the nitrogen atom relative to oxygen. It is expected that an inherently less electrophilic reagent would impede phosphorylation and this is indirectly observed through longer reaction times and harsher reaction conditions for additions to imines as compared to ketones and aldehydes. The nitrogen offers an additional site for functionalization, which can be exploited to tune the electrophilicity of the C=N fragment, without the need for additives. Although the electrophilicity of the C=N fragment is decreased relative to C=O, the basicity of the imine is greater than that of C=O. With the acidic nature of the P(III) tautomer, protonation of the imine to the iminium allows for facile addition of nucleophiles to the C=N moiety.

Phosphine Oxides

The first reported addition of a phosphine oxide to a C=N bond was performed in 1995 by Schmutzler.[34] The reaction was performed between a variety of phosphine oxides and aryltrifluoromethylketimines (Scheme 15). It was found that in most cases a catalytic amount of NEt_3 was required for the reaction to proceed, with a notable exception being the addition of 1,3,5-triaza-4,6-dione phosphine oxide. The 1,3,5-triaza-4,6-dione phosphine oxide reactant was proposed to be sufficiently acidic to protonate the ketimine substrate, which eliminated the need for an external base. However, when the reaction was attempted with the less basic bis(trifluoromethyl)ketimine, the addition of NEt_3 was required. These observations suggest that all reactions proceed by initial deprotonation of the P–H moiety, followed by nucleophilic attack on the ketimine. Since NEt_3 was an effective external base, the phosphine chalcogenides must have lower p*K*a values than the conjugate acid $H[NEt_3]^+$ ($pKa_{(H2O)}$ = 10.75). Consequently, decreasing the basicity of the imine



Scheme 15. Phosphine oxide addition to trifluoromethylketimines.

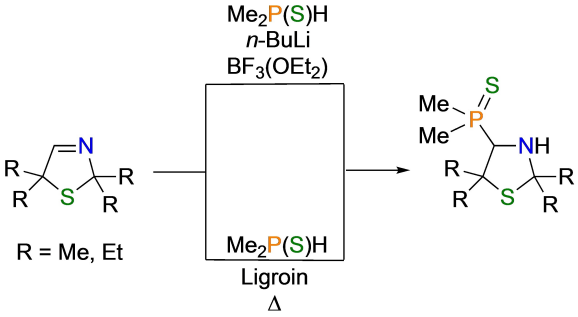
© 2023 Wiley-VCH GmbH

10990682c, 2024, 9, Downloaded from https://chemistry-europe.onlinelibrary.wiley.com/doi/10.1002/ejic.202300444 by Western University, Wiley Online Library on [08/05/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

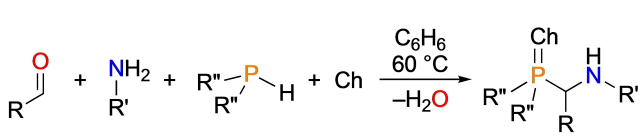
moiety impedes deprotonation of the phosphine oxide, and the reaction does not occur. Even with the incorporation of strong electron withdrawing groups (CF_3) to activate the electrophile, the addition of a nucleophile still depends heavily on the acidity and basicity of the substrates. This is a common trend amongst hydrophosphorylation reactions towards imines. As previously noted, the phosphorylation reactions are sensitive to sterically bulky substituents, and, consistent with that, the bis(1-adamantyl) phosphine oxide showed no reactivity.

Phosphine Sulfides

The first reported addition of a phosphine sulfide to an imine was performed in 1993 by Schmutzler.[35] This study utilized a triazine as an imine synthon. However, the first reported addition of a phosphine sulfide was performed on a formal C=N bond in 1997.[36] Using a variety of very electron rich substituted 3-thiazolines, the addition of $Me_2P(S)H$ proceeded under two drastically different conditions (Scheme 16). First, by refluxing the phosphine sulfide and thiazoline in ligroin for 48 hours afforded the products in poor to moderate yield (Scheme 16, bottom; 23–63%). Alternatively, higher yields under milder conditions were achieved on addition of BF_3 as a Lewis acid additive, in conjunction with a *n*-BuLi as a strong base additive to deprotonate $Me_2P(S)H$ (Scheme 16, top). In other addition reactions to C=E moieties, adduct formation between a Lewis acid and the heteroatom (E) increases the electrophilicity of the carbon atom. Thus, effective activation of C=E with BF_3 for hydrophosphorylation further supports a tautomerization and nucleophilic attack mechanism. As the 3-thiazolines are considered electron-rich heterocycles, they are not as amenable to nucleophilic attack, thus the activation of both the nucleophile and electrophile was required to promote the reactions in reasonable yields (Scheme 16, top, 26–78%).



Scheme 16. Addition of $Me_2P(S)H$ to 3-thiazolines.



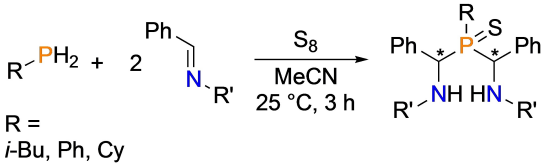
Scheme 17. The four-component reaction between aldehyde, amine, chalcogen, and secondary phosphine to generate an α-aminophosphine chalcogenide.

The next reported addition to imines was not until 2017 by Trofimov and co-workers in which a four-component mixture of aldehyde, amine, chalcogenide, and secondary phosphine was reacted to afford the α-aminophosphine chalcogenide in a one-pot procedure (Scheme 17).[23] While monitoring the reaction, the authors noted the formation of secondary phosphine chalcogenides as well as imines. This indicates that the overall transformation can be viewed as a hydrophosphorylation of a C=N bond. An aliphatic aldehyde was ineffective in the reaction, once again showing the importance of an electrophilic C=E bond when there is no additive acid or base present in the mixture. However, in examining the scope of the amine reagent, the authors describe little to no effect on the yield of the reaction. An α,β-unsaturated aldehyde was also used, and chemoselective nucleophilic attack at the *in situ*-generated imine carbon occured, rather than the Michael-addition product.

We recently demonstrated the addition of a primary phosphine sulfide to *N*-aryl imines, which generated a family of *bis*-α-aminophosphine sulfides (Scheme 18).[21] The reaction showed good functional group tolerance, as a variety of aryl halides, electron-donating and electron withdrawing groups, and phenols were unaffected by the reaction conditions. As noted above in the mechanistic section, the NMe_2 moiety was sufficiently basic to competitively deprotonate the phosphine chalcogenide reagent, which had a detrimental effect on the isolated yield of the target hydrophosphorylation product. Throughout the course of the reaction, the secondary phosphine sulfide (*i.e.*, the mono-addition product) was identified as an intermediate and was ultimately consumed by imine in the mixture. Reactions were also carried out in the absence of oxidant, and the addition occurred to varying degrees depending on the imine. Under all reaction conditions an equilibrium was operative between the P(III) reagent and the imine. When the reaction was performed using $CyPH_2$, only the mono addition product was detected in 65% conversion. However, when an oxidant was added, the double addition product was observed and isolated in good yield (75%).

5. Critical Comparison of Phosphine Chalcogenide to H-Phosphonate Reactivity.

The accepted mechanisms for phosphonate ($(RO)_2P(O)H$) addition consist of the [2+2] cycloaddition, as well as the P(V)–P(III) tautomerization with subsequent nucleophilic attack. In contrast, the current mechanistic understanding for phosphine chalcoge-



Scheme 18. Double hydrophosphorylation of imines to generate bis-α-aminophosphine sulfide.

© 2023 Wiley-VCH GmbH

10990682c, 2024, 9, Downloaded from https://chemistry-europe.onlinelibrary.wiley.com/doi/10.1002/ejic.202300444 by Western University, Wiley Online Library on [08/05/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

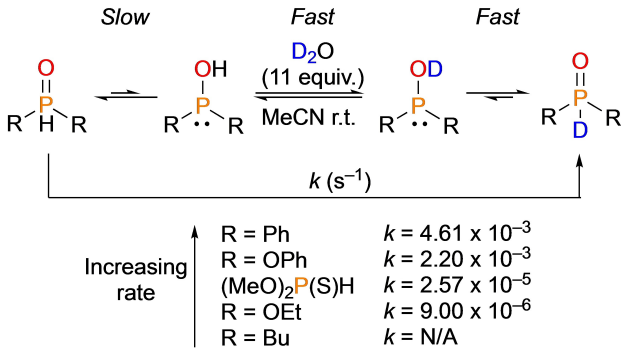
nide (i.e. $R_2P(Ch)H$ or $RP(Ch)H_2$) addition only support the tautomerization and nucleophilic attack pathway. There is an important distinction between phosphonates and phosphine chalcogenides that must be considered when conducting a nucleophilicity driven hydrophosphorylation reaction. The first of which is the inherent nucleophilicity of the phosphorus reagent. The quantification of nucleophilicity has been the subject of several pioneering studies by Mayr.[37] The nucleophilicity of P–H containing P(III) and P(V) molecules has yet to be probed, but tertiary P(III) reagents have been explored. This can provide an excellent reference point, since the P(V) reagent must tautomerize to a P(III) species to undergo nucleophilic attack. The nucleophilicity of tertiary phosphines are consistently greater than that of the phosphonate analogues.[38] This shows simply that R-substituted phosphines are more nucleophilic than their RO-substituted counterparts. However, as these studies have not investigated P–H containing phosphines or any P(V) reagent, the tautomerization process has not been considered in this quantification.

A second governing factor of the hydrophosphorylation reaction is rate of tautomerization of the P(V) species to the nucleophilic P(III) species. As determined experimentally by Montchamp, the kinetics of the tautomerization were faster for phosphonates than phosphine chalcogenides.[12] By treating a sample of P(V) reagent with an excess of D_2O, deuterium was incorporated into the P(V) form and was easily observed and monitored by ^{31}P NMR spectroscopy (Scheme 19). The rate of the D incorporation was quantified and comparisons between substitution patterns and chalcogens were tabulated. The only di-alkyl substituted phosphine oxide ($(n\text{-Bu})_2P(O)H$) examined in this study resulted in such a slow rate of reaction, that the rate constant could not be obtained. The corresponding diethyl H-phosphonate ($(EtO)_2P(O)H$) had a rate constant of 9.00×10^{-6} s^{-1}. An inverse relationship was observed with aryl substituted phosphine oxides $Ph_2P(O)H$ and phosphonates $(PhO)_2P(O)H$, in which the phosphine oxide was about two-fold faster than the phosphonate analogue (4.61×10^{-3} s^{-1} and 2.20×10^{-3} s^{-1}, respectively). The thiophosphonate, $(MeO)_2P(S)H$ resulted in a rate constant of 2.57×10^{-5} s^{-1}, almost three times the rate of the corresponding phosphonate, showing that the tautomerization rate increases for the derivative with the heavier chalcogen. Consolidating this and other data shows that H-phosphonates typically exhibit the more rapid tautomerization as compared to their phosphine chalcogenide counterparts. Except, a unique effect was observed with aryl-substituted phosphine chalcogenides, which demonstrated faster rates than analogous phosphonates. Diphenylphosphine oxide displayed one of the most rapid tautomerization processes amongst the phosphorus reagents that were studied.

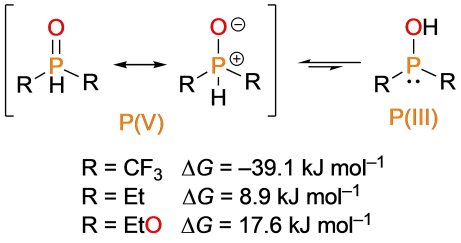
To thermodynamically assess the tautomerization process, Keglevich and co-workers computationally examined the Gibbs free energy (ΔG) values for the tautomeric equilibrium of a large variety of H-phosphonates and phosphine chalcogenides (Scheme 20).[10] The incorporation of strong electron withdrawing groups (CF_3, F, CH_2NO_2) to the phosphine oxide resulted in a large negative ΔG, indicating a more thermodynamically favourable P(III) form. This can be corroborated experimentally in the isolation of the formal P(III) phosphinous acid $(CF_3)_2P(OH)$.[16] The ΔG for the tautomerization of phosphine chalcogenide $Et_2P(O)H$ and the phosphonate analogue $(EtO)_2P(O)H$ were determined to be 8.9 kJ mol^{-1} and 17.6 kJ mol^{-1}, respectively.[39] This result clearly shows that the P(III) form of the alkyl phosphine oxide is more thermodynamically stable than that of the phosphonate. This should help facilitate the hydrophosphorylation reaction using phosphine chalcogenides relative to their phosphonate analogues.

The final aspect to consider is in the pK_a of the corresponding H-phosphonates or phosphine chalcogenides. Since the dominant form of the H-phosphonates and phosphine chalcogenides in solution are in the P(V) form, the computationally determined pK_a values are understood to be of the P(V)–H bond, rather than the P(III)–OH bond. Gratifyingly, comprehensive investigations have established the pK_as of organophosphines.[22] The pK_a of $Me_2P(O)H$, Me(MeO)P(O)H, and $(MeO)_2P(O)H$ were computationally determined. The trend of pK_a values follows the order: phosphine oxide > phosphinates > phosphonates. As H-phosphonates have the lowest pK_a it is unsurprising that the addition of a proton mediator in the Kabachnik-Fields reaction is seldom used. The reactivity is likely facilitated by the H-phosphonate acting as the required proton mediator. Whereas in the cases of phosphine oxides, the addition of an acid, base, or Lewis acid is required to facilitate the desired nucleophilic reactivity unless the pK_a is inherently lowered through the use of strong electron withdrawing substituents on the phosphorus reagent.

Each pair of H–P nucleophile (Figure 1) and C=E electrophile are unique since there are several factors that influence the reactivity. Based on mechanistic analysis for the addition of



Scheme 19. Determination of the rate of P(V)–P(III) tautomerization through deuterium incorporation.



Scheme 20. Gibbs free energy of the P(III)–P(V) equilibrium for phosphonates, alkyl phosphine chalcogenides and phosphine chalcogenides bearing electron withdrawing substituents.

© 2023 Wiley-VCH GmbH

10990682c, 2024, 9, Downloaded from https://chemistry-europe.onlinelibrary.wiley.com/doi/10.1002/ejic.202300444 by Western University, Wiley Online Library on [08/05/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

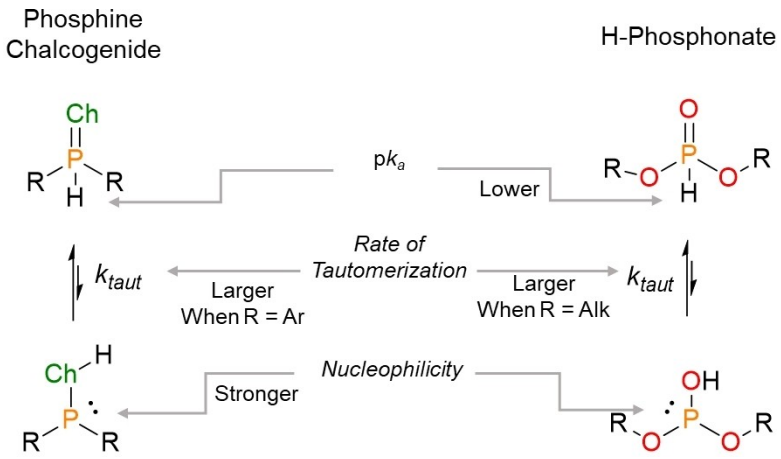


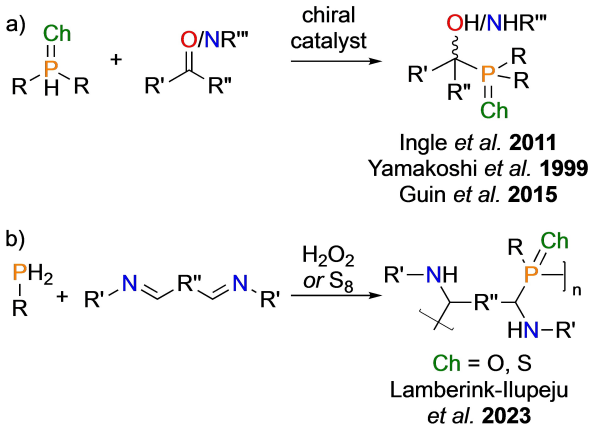
Figure 1. Comparison of properties between phosphine chalcogenides and H-phosphonates.

phosphine chalcogenides to C=N bonds, only the stepwise tautomerization and nucleophilic attack pathway is supported. Yet, hydrophosphorylation with 1° and 2° phosphine chalcogenides remains underexplored, and the alternative [2+2] concerted pathway cannot be ruled out for every example. As such, the mechanistic investigations of hydrophosphorylation reactions should be considered on a case-by-case basis, rather than assume phosphine chalcogenides act similarly to the corresponding H-phosphonates.

6. Summary and Outlook

The simple difference between an H-phosphonate and a secondary phosphine chalcogenide is the presence of an oxygen atom between the substituent and the phosphorus atom. The implications of this substitution can be significant, including differences in nucleophilicity, acidity, and rates of tautomerization. The current understanding of the mechanism of phosphine chalcogenide addition to C=E bonds favours a stepwise tautomerization and nucleophilic attack pathway. The presence of an acid, either generated *in-situ* or as an additive, assists the reaction for less activated electrophiles such as ketones or electron rich C=E groups. The phosphine chalcogenide structure also greatly impacts the reaction, as less nucleophilic or sterically hindered phosphines limit product formation. The hydrophosphorylation of C=E bonds with phosphine oxides or sulfides provides a subtly complex, yet functionally convenient method of accessing heteroatom- and functional group-rich materials.

With the seemingly limitless combinations of P nucleophiles and C=E electrophiles, the development of novel hydrophosphorylation methodologies allows for even larger libraries of potentially interesting α-functionalized phosphine chalcogenide compounds to be formed. The variety of formed products can be applied to biological applications, given their structural similarity to α-amino acids, or to coordination chemistry, as fundamentally unique ligands. It is our hope with this review to expand the accessibility of this hydrophosphorylation reaction to more subdisciplines of chemistry. Understanding the power and limitations of the hydrophosphorylation reaction can lead to easier synthetic targets to allow for more rapid development of products with diverse applications. For example, only a few chiral catalysts exist to mediate this transformation enantioselectively (Scheme 21a).[40–42] Development of new catalysts can further increase the interdisciplinary impact of the hydrophosphorylation reaction. The implementation of hydrophosphorylation chemistry in polymer/materials chemistry offers interesting avenues into the synthesis of heteroatom-rich materials, with drastically different properties than carbon-rich materials.[43–48] Recently, we have published the synthesis of poly-(α-aminophosphine chalcogenide)s from primary phosphines, diimines, and a chalcogen (Scheme 21b). These, and other α-aminophosphine chalcogenide containing materials have an incredible potential for downstream reactivity, as there are many tolerated functional groups that can be leveraged to manipulate structure-property relationships to tune the desired properties. Overall, the hydrophosphorylation of C=O and C=N bonds is a powerful reaction that can afford intriguing biologically active molecules, as well as unique and applicable main group-rich small molecules and materials. Further investigations into the scope and utility of this



Scheme 21. Future avenues for hydrophosphorylation methodology, a) Chiral catalyst development, and b) Linear polymer synthesis.

© 2023 Wiley-VCH GmbH

10990682c, 2024, 9, Downloaded from https://chemistry-europe.onlinelibrary.wiley.com/doi/10.1002/ejic.202300444 by Western University, Wiley Online Library on [08/05/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

reaction will only serve to improve the efficacy of the products in their given application.

Acknowledgements

We are very grateful for the Nuclear Waste Management Organization (NWMO, Toronto, Canada), the Natural Sciences and Engineering Research Council of Canada (NSERC), Canada Foundation for Innovation (CFI), Ontario Research Fund – Research Excellence (ORF-RF), Western University and Solvay for support.

Conflict of Interests

The authors declare no competing financial interest.

Data Availability Statement

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

Keywords: Phosphorus · Chalcogen · Multiple bonds · Hydrophosphorylation · Reaction mechanisms

[1] M. I. Kabachnik, T. Y. Medved, *Dokl. Akad. Nauk SSSR* **1952**, *83*, 689–692.
[2] E. K. Fields, *J. Am. Chem. Soc.* **1952**, *74*, 1528–1531.
[3] A. N. Pudovik, I. V. Konovalova, *Synthesis* **1979**, *1979*, 81–96.
[4] V. P. Kukhar, H. R. Hudson, *Aminophosphonic and Aminophosphinic Acids: Chemistry and Biological Activity* **2000**, p. 1–33.
[5] R. A. Cherkasov, V. I. Galkin, *Russ. Chem. Rev.* **1998**, *67*, 857.
[6] G. Keglevich, E. Bálint, *Molecules* **2012**, *17*, 12821–12835.
[7] P. R. Varga, G. Keglevich, *Molecules* **2021**, *26*, 2511.
[8] J. P. Guthrie, *Can. J. Chem.* **1979**, *57*, 236–239.
[9] P. R. Hammond, *J. Chem. Soc. Resumed* **1962**, 1365–1369.
[10] D. Vincze, P. Ábrányi-Balogh, P. Bagi, G. Keglevich, *Molecules* **2019**, *24*, 3859.
[11] D. Vincze, P. Bagi, P. Ábrányi-Balogh, *Phosphorus Sulfur Silicon Relat. Elem.* **2019**, *194*, 359–360.
[12] B. G. Janesko, H. C. Fisher, M. J. Bridle, J.-L. Montchamp, *J. Org. Chem.* **2015**, *80*, 10025–10032.
[13] L. Ackermann, *Synthesis* **2006**, *2006*, 1557–1571.
[14] B. Kurscheid, W. Wiebe, B. Neumann, H.-G. Stammler, B. Hoge, *Eur. J. Inorg. Chem.* **2011**, *2011*, 5523–5529.
[15] N. S. Golubev, R. E. Asfin, S. N. Smirnov, P. M. Tolstoi, *Russ. J. Gen. Chem.* **2006**, *76*, 915–924.
[16] J. E. Griffiths, A. B. Burg, *J. Am. Chem. Soc.* **1960**, *82*, 1507–1508.
[17] F. Horký, I. Císařová, P. Štěpnička, *Chem. Eur. J.* **2021**, *27*, 1282–1285.
[18] F. Horký, I. Císařová, P. Štěpnička, *Organometallics* **2021**, *40*, 427–441.
[19] A. A. Sobanov, A. V. Zolotukhin, V. I. Galkin, R. A. Cherkasov, A. N. Pudovik, *Russ. J. Gen. Chem.* **2002**, *72*, 1067–1070.
[20] E. N. Tsvetkov, M. I. Terekhova, É. S. Petrov, R. A. Malevannaya, S. P. Mesyats, A. I. Shatenshtein, M. I. Kabachnik, *Bull. Acad. Sci. USSR Div. Chem. Sci. (Engl. Transl.)* **1978**, *27*, 1743–1746.
[21] J.-W. Lamberink, P. D. Boyle, J. B. Gilroy, J. J. Noël, J. M. Blacquiere, P. J. Ragogna, *Chem. Eur. J.* **2022**, *28*, e202201565.
[22] J.-N. Li, L. Liu, Y. Fu, Q.-X. Guo, *Tetrahedron* **2006**, *62*, 4453–4462.
[23] A. V. Artem'ev, N. A. Kolyvanov, L. A. Oparina, N. K. Gusarova, A. O. Sutyrina, I. Y. Bagryanskaya, B. A. Trofimov, *Synthesis* **2017**, *49*, 677–684.
[24] S. N. Arbuzova, S. I. Verkhoturova, S. V. Zinchenko, N. A. Kolyvanov, N. A. Chernysheva, G. K. Bishimbaeva, B. A. Trofimov, *ChemistrySelect* **2022**, *7*, e202202757.
[25] L. Cottier, G. Descotes, J. Lewkowski, R. Skowroński, *Phosphorus Sulfur Silicon Relat. Elem.* **1996**, *116*, 93–100.
[26] S. Jockusch, I. V. Koptyug, P. F. McGarry, G. W. Sluggett, N. J. Turro, D. M. Watkins, *J. Am. Chem. Soc.* **1997**, *119*, 11495–11501.
[27] C. Chatgilialoglu, D. Crich, M. Komatsu, I. Ryu, *Chem. Rev.* **1999**, *99*, 1991–2070.
[28] S. A. Buckler, M. Epstein, *Tetrahedron* **1962**, *18*, 1221–1230.
[29] H.-J. Kleiner, *Justus Liebigs Ann. Chem.* **1974**, *1974*, 751–764.
[30] M. Well, R. Schmutzler, *Phosphorus Sulfur Silicon Relat. Elem.* **1992**, *72*, 171–187.
[31] N. I. Ivanova, N. K. Gusarova, E. A. Nikitina, A. I. Albanov, L. M. Sinegovskaya, M. V. Nikitin, N. A. Konovalova, B. A. Trofimov, *Phosphorus Sulfur Silicon Relat. Elem.* **2004**, *179*, 7–18.
[32] N. I. Ivanova, N. K. Gusarova, N. A. Konovalova, L. M. Sinegovskaya, V. G. Samoilov, S. M. Markosyan, N. D. Avseenko, B. G. Sukhov, B. A. Trofimov, *Russ. J. Gen. Chem.* **2006**, *76*, 98–102.
[33] F. Uhlig, E. Herrmann, D. Schädler, G. Ohms, G. Großmann, S. Besser, R. Herbst-Irmer, *Z. Anorg. Allg. Chem.* **1993**, *619*, 1962–1970.
[34] I. Neda, V. A. Pinchuk, A. Fischer, P. G. Jones, R. Schmutzler, Y. G. Shermolovich, *J. Fluorine Chem.* **1995**, *70*, 127–133.
[35] J. R. Goerlich, I. Neda, M. Well, A. Fischer, P. G. Jones, R. Schmutzler, *Z. Naturforschung B* **1993**, *48*, 1161–1168.
[36] H. Gröger, J. Martens, J. R. Goerlich, R. Schmutzler, *Phosphorus Sulfur Silicon Relat. Elem.* **1997**, *128*, 153–163.
[37] T. B. Phan, M. Breugst, H. Mayr, *Angew. Chem. Int. Ed.* **2006**, *45*, 3869–3874.
[38] B. Kempf, H. Mayr, *Chem. Eur. J.* **2005**, *11*, 917–927.
[39] The ΔG values have had their signs reversed for clarity, as the original publication investigated the tautomerization in the P(III)-P(V) direction.
[40] G. K. Ingle, Y. Liang, M. G. Mormino, G. Li, F. R. Fronczek, J. C. Antilla, *Org. Lett.* **2011**, *13*, 2054–2057.
[41] K. Yamakoshi, S. J. Harwood, M. Kanai, M. Shibasaki, *Tetrahedron Lett.* **1999**, *40*, 2565–2568.
[42] J. Guin, Q. Wang, M. van Gemmeren, B. List, *Angew. Chem. Int. Ed.* **2015**, *54*, 355–358.
[43] P. Theato, *Multi-Component and Sequential Reactions in Polymer Synthesis*, Springer International Publishing, **2015**, p. 5–6.
[44] R. Kakuchi, P. Theato, *ACS Macro Lett.* **2014**, *3*, 329–332.
[45] F. Moldenhauer, R. Kakuchi, P. Theato, *ACS Macro Lett.* **2016**, *5*, 10–13.
[46] P. R. Bachler, M. D. Schulz, C. A. Sparks, K. B. Wagener, B. S. Sumerlin, *Macromol. Rapid Commun.* **2015**, *36*, 828–833.
[47] X. He, L. Yang, G. Liu, Y. Wei, Y. Zeng, L. Tao, *Chem. Mater.* **2022**, *34*, 9558–9568.
[48] J.-W. Lamberink-Ilupeju, M. J. Willans, J. B. Gilroy, J. J. Noël, J. M. Blacquiere, P. J. Ragogna, *Inorg. Chem.* **2023**, *62*, 15104–15109.

Manuscript received: July 17, 2023
Revised manuscript received: November 6, 2023
Accepted manuscript online: November 8, 2023
Version of record online: November 30, 2023

© 2023 Wiley-VCH GmbH

10990682c, 2024, 9, Downloaded from https://chemistry-europe.onlinelibrary.wiley.com/doi/10.1002/ejic.202300444 by Western University, Wiley Online Library on [08/05/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License