ChemPubSoc Europe

DOI: 10.1002/cctc.201700974

CHEMCATCHEM Full Papers

Hydrophosphonylation of Alkynes with Trialkyl Phosphites Catalyzed by Nickel

Rosa E. Islas and Juventino J. García*[a]

The use of simple and inexpensive $NiCl_2{\cdot}6H_2O$ as a catalyst precursor for C–P bond formation in the presence of commercially available trialkyl phosphites ($P(OR)_3$, R = Et, *i*Pr, Bu, $SiMe_3$) along with several alkynes is presented. Control experiments showed the in situ formation of $(RO)_2P(O)H$ as the species that undergo the addition into the C≡C bond at the alkynes to yield the product of P–H addition. The hydrophosphonylation of diphenylacetylene with $P(OEt)_3$, $P(OiPr)_3$, and $P(OSiMe_3)_3$ proceeds in high yields (> 92%) without the need of a specific solvent or ligand. This method is useful for the preparation of organophosphonates for both phenylacetylene as a terminal alkyne model and internal alkynes in yields that range from good to modest.

Introduction

Organophosphonates are an important family of organophosphorus compounds with multiple potential applications, which include halogen-free flame-retardant polymers and antiviral and anticancer compounds.[1] They can also be used as surface modifiers of materials, which enables the development of biological microarrays, drug delivery systems, and immobilized homogeneous and heterogeneous catalysts.[2]

Particularly, vinylphosphonates can be used in the synthesis of poly(vinylphosphonate)s[3] useful in applications as dental adhesives,[4] in studies of bone regeneration,[5] and in the development of proton-conducting membranes.[6] In addition, they can be used in a variety of organic reactions[7] and as valuable building blocks for the development of biologically active compounds.[8]

A variety of methods to obtain vinylphosphonates has already been reported.[9] Among these methods, the addition of P–H to unsaturated molecules catalyzed by costly elements, such as Pd and Rh, is an important methodology to obtain this type of compound.[10] In recent years there has been a growing interest in the development of less expensive Ni-based catalysts for C–C[11] and C–P[12] bond formation.[13]

In this regard, low-valence Ni complexes $[Ni(PPh_2Me)_4]$ or $Ni(cod)_2/PPhMe_2$ (cod = cyclooctadiene) have been reported as catalyst precursors in the addition of H-phosphonates to terminal alkynes under very mild reaction conditions to produce the corresponding vinylphosphonates.[14] In 2010, Beletskaya and co-workers showed that air-stable $[Ni(acac)_2]$ (acac = acetylacetonate) can be used instead of Ni^0 complexes as catalyst precursor along with bis(diphenylphosphino)ethane as an ancillary ligand in THF for the hydrophosphonylation of several terminal and internal alkynes.[15] Recently, a modified procedure was published by the same group, in which no specific solvents or ligands were required to achieve this kind of transformations; instead they made use of diisobutyl aluminum hydride (DIBAL-H), which is a strong reducing agent that requires special handling, in conjunction with $[Ni(acac)_2]$ to achieve the full conversion of the starting materials into the desired products.[16] Therefore, the development of new, simple, cheap, and efficient Ni-based catalytic systems able to perform the addition of P–H to unsaturated molecules is needed.

Herein, we present our findings in the study of the hydrophosphonylation of several alkynes, by a methodology that allows the in situ formation of dialkyl phosphites $(iPrO)_2P(O)H$ using commercially available trialkyl phosphites in the presence of an inexpensive and air-stable catalyst precursor ($NiCl_2{\cdot}6H_2O$). We optimized the reaction conditions made for diphenylacetylene (DPA) hydrofunctionalization with triisopropyl phosphite ($P(OiPr)_3$) to obtain the corresponding vinylphosphonate. Control experiments showed that $P(OiPr)_3$ is transformed into $(iPrO)_2P(O)H$ under the optimized reaction conditions, and we propose that this species is responsible for the alkyne hydrofunctionalization reaction. Then, $P(OR)_3$ (R = Et, Bu, $SiMe_3$) were tested under the optimized conditions, and we obtained high conversion rates and yields for the reaction with DPA, followed by the use of internal alkynes and phenylacetylene as a terminal alkyne model under the same reaction conditions to produce the corresponding vinyl- and alkylphosphonates with yields that ranged from good to modest. Finally, a plausible catalytic cycle was proposed based on our experimental findings and the results of other studies that are closely related.

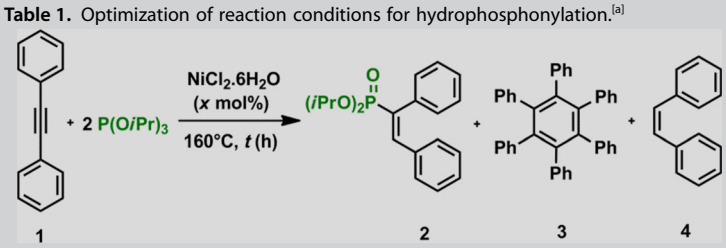
[a] R. E. Islas, Prof. J. J. García
Facultad de Química
Universidad Nacional Autónoma de México
México D. F. 04510 (México)
E-mail: juvent@unam.mx

Supporting information and the ORCID identification number(s) for the author(s) of this article can be found under https://doi.org/10.1002/cctc.201700974.

Results and Discussion

Initially, we assessed the reactivity of $P(OiPr)_3$ in the hydrophosphonylation reaction of DPA (**1**) with different amounts of $NiCl_2{\cdot}6H_2O$ at different reaction times (Table 1). Remarkably, no solvent, ligand, or any other additive was required to reach the complete conversion of DPA to diisopropyl [(*E*)-1,2-diphenylvinyl]phosphonate (**2**; >90%). The use of 1% of $NiCl_2{\cdot}6H_2O$ for 42 h produced the corresponding product **2** in a high yield (96%; entry 7). Notably, compound **2** was isolated as the only isomer as observed in the chromatograms of the crude reaction mixture (Schemes S1–S6). Moreover, this compound was isolated with a yield of 91% and its stereochemistry was assigned by using ^1H NMR spectroscopy, which showed a coupling constant of $J_{P,H\,cis}=22.3$ Hz in concordance with previous reports.[15] Thus, we decided to use these conditions for further experiments. In all cases, we detected the formation of small amounts of hexaphenylbenzene (**3**), a product of the cyclotrimerization reaction of the alkyne,[17] and *cis*-stilbene (**4**) from the semihydrogenation of the alkyne.

Table 1. Optimization of reaction conditions for hydrophosphonylation.[a]



Entry	$NiCl_2{\cdot}6H_2O$ [mol%]	*t* [h]	Conversion of **1** [%]	Selectivity [%] **2**	**3**	**4**
1	20	24	100	90	3	7
2	10	24	100	99	<1	<1
3	5	24	100	98	1	1
4	3	24	60	92	3	5
5	3	48	100	93	2	4
6	1	48	100	92	3	5
7	1	42	100	96	1	3

[a] All reactions were performed in a Schlenk flask (50 mL) equipped with a Rotaflo valve and heated at 160 °C. Reaction conditions: molar ratio of 1:2:*x* of DPA, triisopropyl phosphite, and $NiCl_2{\cdot}6H_2O$, respectively. Conversions and selectivity were determined by using GC–MS.

The performance of a variety of similar Ni catalyst precursors was evaluated in the model hydrophosphonylation reaction (Table 2). The use of $NiCl_2{\cdot}6H_2O$ showed the best results (yield 96%); however, the use of $NiBr_2{\cdot}3H_2O$ (entry 1) does not produce any addition product, instead, we observed an uncharacterized colorless polymeric byproduct. The use of NiF_2 (entry 3) allowed a poor conversion of DPA, probably because of solubility issues. If $[Ni(cod)_2]$ was used, we observed a 92% conversion of the alkyne to produce **2** in high yields. Notably, it has been reported that the use of $[Ni(cod)_2]$ only affords traces of product at 120 °C after 19 h with $(iPrO)_2P(O)H$ as the P source.[16] Thus, $NiCl_2{\cdot}6H_2O$ was selected as standard catalyst precursor for the subsequent reactions.

The effect of the variation of the concentration of the phosphites in the model reaction was examined (Table 3). The impact of the initial concentration of $P(OiPr)_3$ also influences in the performance of the reaction, that is, the use of 2 equivalents (entry 2) or more (entry 1) of the initial phosphite allowed the formation of the corresponding vinylphosphonate. However, the use of less than 2 equivalents of the phosphite decreased the conversion to 91%.

The effect of solvent was also investigated, and the results are summarized in Table 4. The use of both coordinating and non-coordinating solvents afforded the desired products. The use of non-coordinating solvents (toluene and mesitylene) led to a higher conversion of DPA (entries 1 and 2) in comparison with the use of coordinating solvents (THF and dioxane; entries 3 and 4). However, the catalytic reaction also showed a good performance under neat conditions. Consequently, these conditions were chosen to perform some control experiments, that is, without the use of the Ni catalyst precursor. These experiments showed a poor conversion of the initial alkyne (entry 6).

Additionally, to elucidate if the water molecules of the Ni precursor were responsible for the hydrolysis of the triisopropyl phosphite, the reaction was performed using 0.1 mmol of distilled water and, once again, without using the Ni catalyst (entry 7). Under these conditions, the reaction was also inhibited (entry 7); as a consequence of the hydrolysis of $P(OiPr)_3$, $(iPrO)_2P(O)H$ was also detected.[18] A homogeneity test was performed by adding a mercury

Table 2. Performance of different Ni precursors in the hydrophosphonylation reaction (Scheme 1).[a]

Entry	Catalyst precursor	Conversion of **1** [%]	Selectivity to **2** [%]
1	$NiBr_2{\cdot}3H_2O$	100	nd
2	$NiCl_2{\cdot}6H_2O$	100	96
3	NiF_2	1	100
4	$[Ni(cod)_2]$	92	92

[a] All reactions were performed in a Schlenk flask (50 mL) equipped with a Rotaflo valve and heated at 160 °C for 42 h. Reaction conditions: molar ratio of 1:2:0.01 of DPA, triisopropyl phosphite, and the nickel compound, respectively. Conversions and selectivity were determined by using GC–MS. nd = not detected.

Table 3. Effect of $P(OiPr)_3$ concentration in the model hydrophosphonylation of DPA (Scheme 1).[a]

Entry	$P(OiPr)_3$ [mmol/equiv.]	Conversion of **1** [%]	Selectivity to **2** [%]
1	5.04/3	100	97
2	3.36/2	100	96
3	2.52/1	91	89

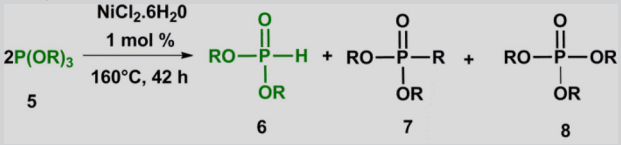
[a] All reactions were performed in a Schlenk flask (50 mL) equipped with a Rotaflo valve and heated at 160 °C for 42 h. Reaction conditions: molar ratio of 1:*x*:0.01 of DPA, triisopropyl phosphite, and $NiCl_2{\cdot}6H_2O$, respectively. Conversions and selectivity were determined by using GC–MS.

Table 4. Solvent variations and control experiments (Scheme 1).[a]

Entry	Solvent	Conversion of **1** [%]	Selectivity to **2** [%]
1	Toluene	100	97
2	Mesitylene	100	98
3	Dioxane	32	100
4	THF	28	98
5	Neat	100	96
6[b]	Neat	24	73
7[c]	Neat	16	90
8[d]	Neat	99	97

[a] All reactions were performed in a Schlenk flask (50 mL) equipped with a Rotaflo valve and 1.5 mL of solvent at 160 °C for 42 h. Reaction conditions: molar ratio of 1:2:0.01 of DPA, triisopropyl phosphite, and $NiCl_2{\cdot}6H_2O$, respectively. [b] Control experiment: molar ratio of 1:2 of DPA, and triisopropyl phosphite. [c] Molar ratio of 1:2:0.1 of DPA, triisopropyl phosphite, and distilled water, respectively. [d] Molar ratio of 1:2:0.01:0.05 of DPA, triisopropyl phosphite, $NiCl_2{\cdot}6H_2O$, and metallic Hg, respectively. Conversions and selectivity were determined by using GC–MS.

Table 5. Formation of $(i\text{PrO})_2\text{P(O)H}$ (P^V species) from trialkyl phosphites $P(OR)_3$.[a]



Entry	R	Conversion of **5** [%]	Selectivity [%] **6**	**7**	**8**
1	*i*Pr	42	90	1	9
2	Et	29	55	21	24
3	Bu	12	58	17	25
4	$Si(Me)_3$	45	91	nd	9
5[b]	*i*Pr	4	12	13	75

[a] All reactions were performed in a Schlenk flask (50 mL) equipped with a Rotaflo valve. Reaction conditions: molar ratio of 2:0.01 of trialkyl phosphite and $NiCl_2{\cdot}6H_2O$, respectively. [b] Control experiment under Ni-free conditions. nd = not detected. Conversions and selectivity were determined by using GC–MS.

drop into the $NiCl_2{\cdot}6H_2O$ reaction system (entry 8), and no decrease in the DPA conversion or yield was observed. Therefore, we conclude that the reaction was homogeneous.

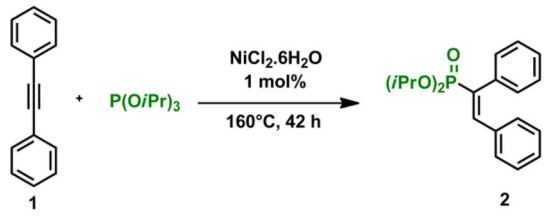
The P^{III} atom in the starting phosphite was oxidized to the corresponding P^V phosphonate (Scheme 1). A similar transformation was reported by Lu and Zhu who used $NiCl_2$ to promote the oxidation of P^{III} to P^V (Scheme 2).[19]

If we consider the above, we propose that under the optimized conditions $NiCl_2{\cdot}6H_2O$ promotes the in situ formation of $(i\text{PrO})_2\text{P(O)H}$ (a P^V species) from $P(Oi\text{Pr})_3$, which is involved in the formation of the alkyne hydrophosphonylation product. To corroborate this, we performed a series of hydrophosphonylation experiments to confirm the formation of P^V (Table 5). $(Oi\text{Pr})_2\text{P(O)H}$ was obtained as the major product from $P(Oi\text{Pr})_3$ in the presence of the Ni catalyst (entry 1). The formation of the phosphonates $(O)P(i\text{Pr})(Oi\text{Pr})_2$ and the phosphates $(O)P(Oi\text{Pr})_3$ was also detected under the optimized hydrophosphonylation conditions. If a control experiment was performed without $NiCl_2{\cdot}6H_2O$, only a trace amount of $(Oi\text{Pr})_2\text{P(O)H}$ was observed (entry 5). $P(OEt)_3$, $P(OBu)_3$, and $P(OSiMe_3)$ were also used as starting materials for the synthesis of $(RO)_2\text{P(O)H}$ (entries 2–4). Notably, $P(Oi\text{Pr})_3$ and $P(OSiMe_3)$ gave a better yield of $(RO)_2\text{P(O)H}$ than the other two P^{III} sources (entries 1 and 4).

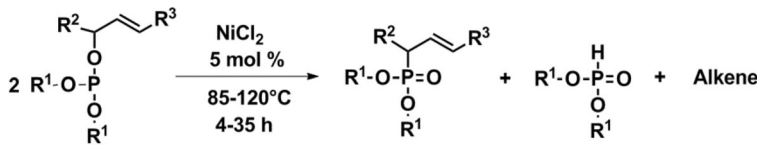
We extended the scope of the hydrophosphonylation reaction using $P(OEt)_3$, $P(OBu)_3$, and $P(OSiMe_3)$, and the results were compared with those obtained with $P(Oi\text{Pr})_3$ (Table 6). If $P(OSiMe_3)$ was used as the P^{III} source, it was possible to detect the hydrophosphonylation product in high conversion and yields (Table 6, entry 4), which can be related to the higher concentration of the P^V species $(Me_3SiO)_2\text{P(O)H}$ (Table 5, entry 4). The use of $P(OEt)_3$ and $P(OBu)_3$ led to low yields of the hydrophosphonylation product (Table 6, entries 1 and 3) in concordance with the low yields of the P^V species $(OR)_2\text{P(O)H}$ (Table 5, entries 2 and 3). However, the low yields obtained with the use of $P(OEt)_3$ and $P(OBu)_3$ can be overcome by using a higher catalyst loading (10%; Table 6, entries 5 and 6).

Several aromatic alkynes were used under the catalytic reaction conditions, and the results are summarized in Table 7. In general, high conversions of functionalized DPAs (**1a**, **1c**–**1e**) were observed, with the exception of 1-methyl-4-(2-phenylethynyl)benzene (Me-DPA; **1b**), which produced 76% conversion. 1-(4-phenylethynyl-phenyl)-ethanone (MeOC-DPA; **1a**; entry 1) and the symmetric alkyne **1e** (entry 5) both gave the corresponding vinylphosphonates in high yields. If 1-methoxy-4-(2-phenylethynyl)benzene (MeO-DPA; **1c**) was used, the side reaction product that corresponds to the semihydrogenation of the alkynes was preferred to produce the corresponding stilbenes (**17d**) in high yields (82%; entry 4) with a low preference to the hydrophosphonylation products (11%; entry 4).

To extend the scope of this reaction, a series of nonaromatic alkynes was assessed (Table 8). Notably, a higher load of catalytic precursor was required to perform the alkyne hydrophosphonylation with $P(OEt)_3$ in comparison to $P(Oi\text{Pr})_3$. Again, this can be related to the lower concentration of $(EtO)_2\text{P(O)H}$ formed with $P(OEt)_3$ (vide supra). The hydrophosphonylation of disubstituted alkynes required more

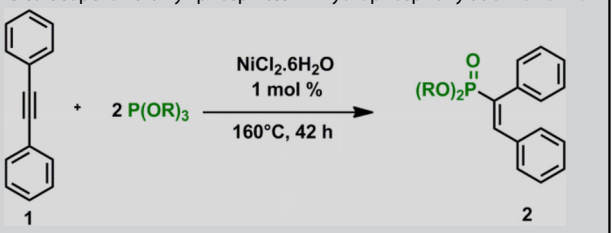


Scheme 1. Hydrophosphonylation of DPA using $NiCl_2{\cdot}6H_2O$.



Scheme 2. Reported formation of P^V by trialkyl phosphites using $NiCl_2$.[19]

Table 6. Scope of trialkyl phosphites in hydrophosphonylation of DPA.[a]



Entry	$NiCl_2{\cdot}6H_2O$ [equiv.]	$P(OR)_3$	Conversion of **1** [%]	Selectivity to **2** [%]
1	0.01	$P(OEt)_3$	32	10
2		$P(OiPr)_3$	100	96
3		$P(OBu)_3$	18	22
4		$P(OSiMe_3)_3$	100	98
5[b]	0.1	$P(OEt)_3$	100	92
6[b]		$P(OBu)_3$	56	100

[a] All reactions were performed in a Schlenk flask (50 mL) equipped with a Rotaflo valve and 1.5 mL of solvent. Reaction conditions: molar ratio of 1:2:0.01 of DPA, trialkyl phosphite, and $NiCl_2{\cdot}6H_2O$, respectively. [b] Molar ratio of 1:2:0.1 of DPA, trialkyl phosphite, and $NiCl_2{\cdot}6H_2O$, respectively. Conversions and selectivity were determined by using GC–MS.

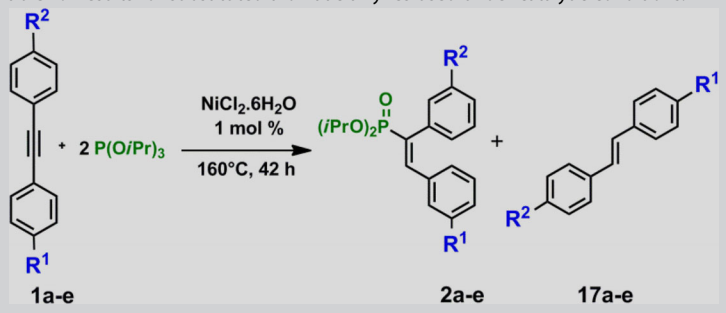
forceful reaction conditions than those used for terminal alkynes.[20] Steric effects have an important effect on the selectivity, as evidenced by the higher number of byproducts observed by using $P(OEt)_3$ than $P(OiPr)_3$.[21]

However, if we used phenylacetylene as the substrate, the formation of bisphosphonated species **10 f** is favored if $P(OEt)_3$ is used as a P^{III} source (Table 8, entry 1), whereas the monophosphonated species **9 g** is preferred if the more sterically hindered $P(OiPr)_3$ is used as the P^{III} source (Table 8, entry 2). In both cases, 1,3,5-triphenylbenzene was also obtained as a result of the cyclotrimerization of phenylacetylene. Moreover, the use of low loadings of the Ni precatalyst (1% mol) (entry 3) favored the cyclotrimerization (89% yield) over the alkyne hydrophosphonylation. This kind of cyclotrimerization product is formed frequently in the presence of Ni^{II} precursors.[22]

If we performed the reaction with $P(OEt)_3$ and 1-phenyl-1-propyne, the corresponding monophosphonate **9 i** was obtained in good yield (entry 4) along with the formation of the mono- and divinylphosphonates **13 i** and **14 i** in poor yields. If $P(OiPr)_3$ was used, compound **9 j** was the only phosphonate produced, along with the corresponding cyclotrimer **16 j** (entry 5). Notably, the cyclotrimerization products can be reduced or halted by adding an excess of the P^{III} source (entries 6 and 7).

The selectivity was affected by using 4-phenyl-3-butyn-2-one (entries 8–9) in which the formation of alkylphosphonates is preferred over that of the vinylphosphonates. The introduction of an electron-withdrawing substituent conjugated to the triple bond modified the electron density around this triple bond to undergo a Ni-catalyzed hydrogenation. The hydrogenation of α,β-unsaturated carbonyl compounds has already been performed with the use of Ni^{I} and Ni^{II} catalytic precursors.[23] The formation of alkylphosphonates **11 n** and **15 n** was preferred in the presence of $P(OiPr)_3$ over the corresponding vinylphosphonates **9 n** and **13 n**. We also found the opposite if we used $P(OSiMe_3)$: vinylbisphosphonate **10 o** species were preferred over the less sterically hindered monophosphonated species (entry 10).

Table 7. Results for substituted aromatic alkynes used under catalytic conditions.[a]



Entry	**1**	R^1	R^2	Conversion of **1** [%]	Selectivity [%] **2**	**17**
1	**1 a**	COMe	H	100	98[c]	nd
2	**1 b**	Me	H	76	100[c]	nd
3	**1 c**	Cl	H	97	nd	>99
4	**1 d**	OMe	H	80	11[c]	82[b]
5	**1 e**	OMe	OMe	96	98	nd

[a] All reactions were performed in a Schlenk flask (50 mL) equipped with a Rotaflo valve and 1.5 mL of toluene. Reaction conditions: molar ratio of 1:2:0.01 of functionalized DPA, triisopropyl phosphite, and $NiCl_2{\cdot}6H_2O$, respectively. [b] (*E*/*Z*)-Stilbenes were detected. [c] Regioisomeric mixture of the corresponding hydrophosphonylation products were detected. nd = not detected. Conversions and selectivity were determined by using GC–MS.

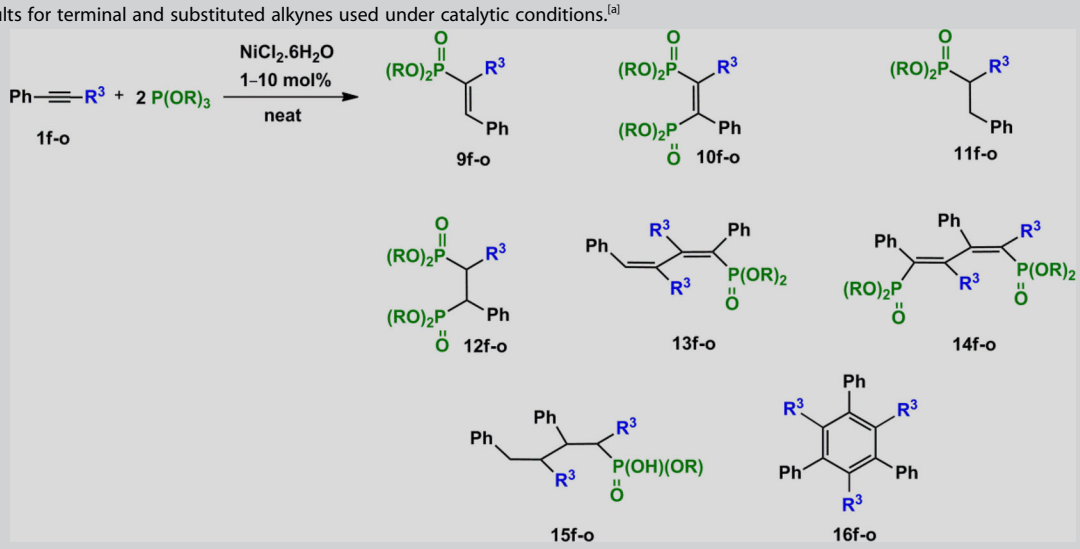
Proposed mechanism

If we consider both the findings of the current work and the results of studies that are related closely,[16,24] a mechanism is proposed for the hydrophosphonylation of alkynes (Scheme 3). The first step involves the formation of a Ni^0 complex from $NiCl_2{\cdot}6H_2O$ and $P(OR)_3$. It is known that Ni^{II} halides are reduced to Ni^0 by trialkyl phosphites, which are strong reducing agents, to obtain trialkyl phosphates as the main oxidation product.[24a–c] The formation of the trialkyl phosphates was detected experimentally under the optimized hydrophosphonylation conditions (Figure S1) also in the experiments in which the formation of P^V species takes place from P^{III} sources (Table 5, entries 1–4, Figures S9–S12). Once the Ni^0 species is formed, the next step is the oxidative addition of $(RO)_2P(O)H$, to produce **A**. This is followed by the coordination of the alkyne to the metal–hydride complex to yield **B**, which evolves into the alkenyl complex **C** by an insertion of the alkyne into the Ni–H bond.[24d] The vinylphosphonate was obtained by the reductive elimination of the product and catalyst regeneration.

Conclusions

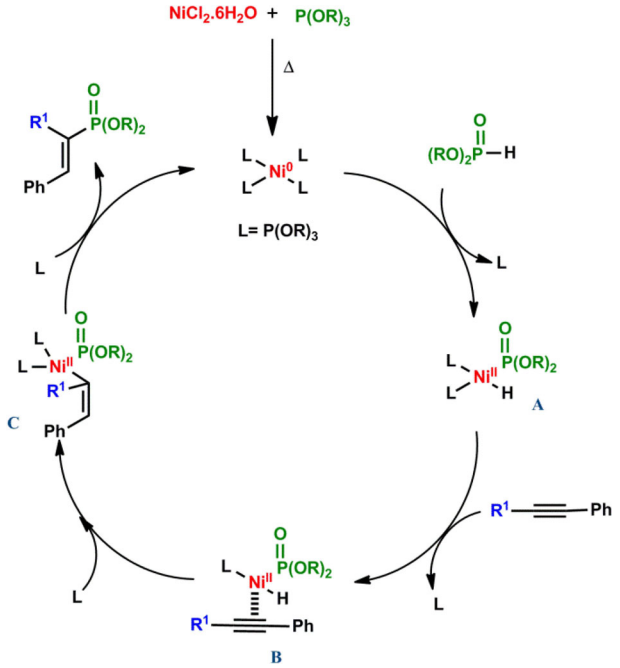
We have demonstrated that inexpensive and easy to handle $NiCl_2{\cdot}6H_2O$ is an effective catalyst precursor for P–C bond formation reactions using alkynes and

Table 8. Results for terminal and substituted alkynes used under catalytic conditions.[a]



Entry	Alkyne, phosphite	*t* [h]	*T* [°C]	Selectivity [%] 9	10	11	12	13	14	15	16
1[b,d,e]	**1 f** = R^3 = H, R = Et	24	130	4	38	nd	nd	9	7	nd	24
2[b,d]	**1 g** = R^3 = H, R = *i*Pr	24	130	46	9	nd	10	nd	nd	nd	35
3[a,d]	**1 h** = R^3 = H, R = *i*Pr	24	130	7	4	nd	nd	nd	nd	nd	89
4[b,d]	**1 i** = R^3 = Me, R = Et	24	160	66	nd	nd	nd	7	17	nd	10
5[a,d]	**1 j** = R^3 = Me, R = *i*Pr	42	160	43	nd	nd	nd	nd	nd	nd	57
6[c,d]	**1 k** = R^3 = Me, R = *i*Pr	42	160	92	nd	nd	nd	nd	nd	nd	8
7[c,d]	**1 l** = R^3 = Me, R = $SiMe_3$	42	160	99	nd	nd	nd	nd	nd	nd	nd
8[b]	**1 m** = R^3 = COMe, R = Et	24	160	nd	nd	12	84	nd	nd	nd	4
9[a]	**1 n** = R^3 = COMe, R = *i*Pr	42	160	nd	nd	37	nd	nd	nd	55	nd
10[a]	**1 o** = R^3 = COMe, R = $SiMe_3$	42	160	3	94	3	nd	nd	nd	nd	nd

[a] All reactions were performed in a Schlenk flask (50 mL) equipped with a Rotaflo valve. Reaction conditions: molar ratio of 1:2:0.01 of alkyne, trialkyl phosphite, and $NiCl_2{\cdot}6H_2O$, respectively. [b] Molar ratio of 1:2:0.1 of alkyne, trialkyl phosphite, and $NiCl_2{\cdot}6H_2O$, respectively. [c] Molar ratio of 1:4:0.01 of alkyne, trialkyl phosphite, and $NiCl_2{\cdot}6H_2O$, respectively. [d] Regioisomeric mixtures of the corresponding hydrophosphonylation products were detected. [e] Additionally, 18% *E*/*Z* isomers of [4-phenylbut-1-en-3-ynyl]benzene was observed. nd = not detected. Conversions and selectivity were determined by using GC–MS.



Scheme 3. Proposed mechanism for the hydrophosphonylation of alkynes.

readily available trialkyl phosphites, which make this method suitable for practical application in the preparation of organophosphorated compounds of relevance in organic synthesis. Remarkably, this reaction did not require any additives to reach the complete conversion of the reactants into the desired organophosphorus products. Experimental evidence led us to propose that $(i\text{PrO})_2\text{P(O)H}$ is an active species.

It was also demonstrated that this method is applicable to a variety of alkynes. Symmetrical aromatic alkynes (diphenylacetylene and 1,2-bis(4-methoxyphenyl)ethyne) produced the corresponding vinylphosphonates in high yields in the presence of $P(OR)_3$ (R = Et, $SiMe_3$, or *i*Pr). Phenylacetylene produced mono- or diphosphonated species under milder reaction conditions than those used with other disubstituted alkynes, and the regioselectivity was determined by the steric hindrance of the trialkyl phosphite used. With the use of substrates such as 1-phenylpropyne in the presence of $P(OEt)_3$, several products were observed because of a low reaction selectivity; this can be improved by using more sterically hindered phosphites ($P(Oi\text{Pr})_3$ or $P(OSiMe_3)_3$) to yield the monophosphonated species.

The use of 4-phenyl-3-butyn-2-one allowed the production of alkylphosphonates instead of vinylphosphonates in the presence of $P(OiPr)_3$ and $P(OEt)_3$, whereas the use of $P(OSiMe_3)$ produced the corresponding diphosphonate as the main product. The regioselectivity with unsymmetrical alkynes needs further investigation.

Experimental Section

All experiments were performed in oven-dried Schlenk tubes in a glovebox (MBraun Unilab) under high-purity Ar (Praxair 99.998%) and controlled concentrations of water and oxygen (<1 ppm). All liquid reagents were purchased from Aldrich and Merck and they were degassed and stored in a glovebox for further use. All solvents were dried using standard techniques and stored in the glovebox before use. Alkynes **1a**–**1d** were prepared following a method reported previously.[25] Alkynes (diphenylacetylene, phenylacetylene, 1-phenyl-1-propyne, and 4-phenyl-3-butyn-2-one) and phosphites $P(OEt)_3$, $P(OiPr)_3$, $P(OBu)_3$, and $P(OSiMe_3)_3$ were purchased from Aldrich and stored in the glovebox before use. Column chromatography was performed using Silica Gel 60 (particle size 63–200 μm). Deuterated solvents were purchased from Cambridge Isotope Laboratories. NMR spectra of organic products were acquired at RT by using a 300 MHz Varian Unity spectrometer. Chemical shifts in the ^{1}H NMR spectra (δ, ppm) are reported according to the residual solvent peaks. $^{31}P\{^1H\}$ NMR spectra are referenced to the $\delta = 0$ ppm signal of external 85% H_3PO_4. GC–MS was performed by using an Agilent Technologies G3171A equipped with a 5% phenylmethylsilicone (30 m × 0.25 mm × 0.25 μm) column.

Catalytic hydrophosphonylation of DPA

Typically, $NiCl_2{\cdot}6H_2O$ (4 mg, 0.0168 mmol), DPA (300 mg, 1.68 mmol), and $P(OiPr)_3$ (701 mg, 3.36 mmol) were placed in a Schlenk flask (50 mL) fitted with Rotaflo valve. The color of the solution turned immediately to dark blue. Then, the flask was taken out from the glovebox and heated at 160 °C for 42 h (except in the experiments indicated in Table 1). After this time, the reaction mixture was cooled to RT, exposed to air, filtered through Celite, and then analyzed by using GC–MS. Usually, orange-colored solutions were observed.

After the completion of the reaction, product **2** was purified by column chromatography with silica gel (particle size 63–200 μm, hexane/ethyl acetate as eluent), and the product was isolated in 91% yield as a yellow oil.

Mercury drop test

Following the procedure described above, the same reaction was performed with the addition of one drop of elemental Hg to the reaction mixture. At the end of each run, the reaction mixture was cooled to RT, exposed to air, filtered through Celite, and analyzed by using GC–MS. Usually, orange-colored solutions were observed.

Use of different Ni compounds as catalytic precursors

Typically, a given Ni compound (0.0168 mmol), DPA (300 mg, 1.68 mmol), and $P(OiPr)_3$ (701 mg, 3.36 mmol) were placed in a Schlenk flask (50 mL) fitted with a Rotaflo valve. The flask was taken out from the glovebox and heated at 160 °C for 42 h. After this time, the reaction mixture was cooled to RT, exposed to air, filtered through Celite, and then analyzed by using GC–MS.

Detection of $(OR)_2P(O)H$ from $P(OR)_3$ using $NiCl_2{\cdot}6H_2O$

Typically, a Schlenk flask (50 mL) fitted with a Rotaflo valve was charged with $NiCl_2{\cdot}6H_2O$ (4 mg, 0.0168 mmol) and a given trialkyl phosphite (3.36 mmol). The flask was heated at 160 °C for 42 h. After this time, the reaction mixture was cooled to RT, exposed to air, filtered through Celite, and analyzed by using GC–MS. White precipitates were observed.

Reaction scope with trialkyl phosphites

Typically, a 50 mL Schlenk flask fitted with a Rotaflo valve was charged with $NiCl_2{\cdot}6H_2O$ (4 mg, 0.0168 mmol), DPA (300 mg, 1.68 mmol), and a given trialkyl phosphite (3.36 mmol). The flask was heated at 160 °C for 42 h. After this time, the reaction mixture was cooled to RT, exposed to air, filtered through Celite, and analyzed by using GC–MS. Orange-colored solutions were observed.

Reaction scope with alkynes

Typically, a 50 mL Schlenk flask fitted with a Rotaflo valve was charged with $NiCl_2{\cdot}6H_2O$ (4 mg, 0.0168 mmol), $P(OR)_3$ (3.36 mmol), a given alkyne (1.68 mmol), and toluene (1.5 mL; the experiments indicated in Table 8 were performed under neat conditions). The flask was heated at 160 °C for 42 h. After this time, the reaction mixture was cooled to RT, exposed to air, filtered through Celite, and analyzed by using GC–MS.

Diisopropyl[(*E*)-1,2-diphenylvinyl]phosphonate]: ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.18$ (d, $J_{H,H} = 6.0$ Hz, 6H), 1.25 (d, $J_{H,H} = 6.0$ Hz, 6H), 4.60 (m, 2H), 6.99–7.02 (m, 2H), 7.08–7.11(m, 3H), 7.24–7.26 (m, 5H), 7.57 ppm (d, $J_{H,H} = 24.0$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 23.89$, 23.96, 24.13, 24.18, 71.01,127.62, 128.22, 128.69, 128.82, 129.53, 129.6, 130.39, 132.74 ($J_{P,C} = 179.25$ Hz), 134.93, 135.23, 135.91,136.01,142.78 ppm ($J_{P,C} = 10.5$ Hz); ^{31}P NMR (121.44 MHz, $CDCl_3$): $\delta = 15.83$ ppm.

Acknowledgements

We thank CONACYT 178265 and PAPIIT-DGAPA-UNAM 202516 for their financial support of this work. R.E.I. thanks CONACYT (245557) for a graduate studies grant. We also thank Dr. Alma Arévalo for her technical assistance.

Keywords: alkynes · homogeneous catalysis · nickel · phosphorus · reaction mechanisms

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Manuscript received: June 14, 2017
Revised manuscript received: July 7, 2017
Accepted manuscript online: July 21, 2017
Version of record online: ■■ ▮▮, 0000

These are not the final page numbers! ↗↗

*R. E. Islas, J. J. García**

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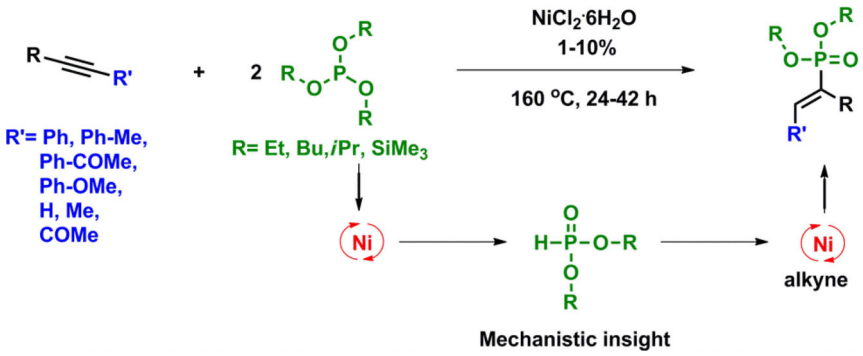
Hydrophosphonylation of Alkynes with Trialkyl Phosphites Catalyzed by Nickel



Back to the hydrophosphonylation: The use of inexpensive $NiCl_2{\cdot}6H_2O$ as a catalyst precursor for C–P bond formation in the presence of commercially available trialkyl phosphites ($P(OR)_3$, R = Et, *i*Pr, Bu, $SiMe_3$) along with several alkynes is presented. $(RO)_2P(O)H$ formed in situ undergoes addition to the alkyne C≡C bond. The hydrophosphonylation of diphenylacetylene with $P(OEt)_3$, $P(OiPr)_3$, and $P(OSiMe_3)_3$ proceeds in high yields (> 92%) without the need of a specific solvent or ligand.