# Oxidative Addition of a Phosphinite P–O Bond at Nickel

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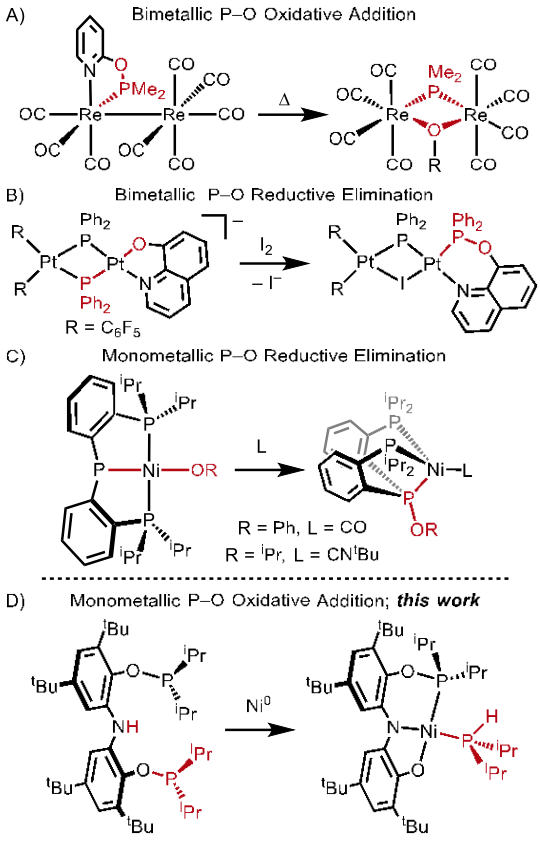
**ABSTRACT:** Oxidative addition is an essential elementary reaction in organometallic chemistry and catalysis. While a diverse array of oxidative addition reactions have been reported to date, examples of P–O bond activation are surprisingly rare. Herein we report the ligand-templated oxidative addition of a phosphinite P–O bond in the diphosphinito aniline compound HN(2-OP$^i$Pr$_2$-3,5-$^t$Bu-C$_6$H$_2$)$_2$ (H(P$_2$ONO)) at Ni$^0$ to form (PONO)Ni(HP$^i$Pr$_2$) after proton rearrangement. Notably, the P–O cleavage occurs selectively over an intramolecular amine N–H bond activation. Additionally, the ligand cannibalization is reversible, as addition of XPR$_2$ (X = Cl, Br; R = $^i$Pr, Cy) to (PONO)Ni(HP$^i$Pr$_2$) readily produces either symmetric or unsymmetric (P$_2$ONO)NiX species and free HP$^i$Pr$_2$. Finally, the mechanism of both the initial P–O bond cleavage and its subsequent reconstruction are investigated to provide further insight into how to target P–O bond activation.

## INTRODUCTION

Oxidative addition is a fundamental elementary reaction in organometallic chemistry and serves as a key entry point into metal-mediated functionalizations.[1] While bonds between elements spanning the periodic table have been cleaved via oxidative addition, the insertion of transition metals into phosphorus–element bonds is relatively undeveloped. Oxidative addition in catalytic processes is largely limited to P–H bonds and phosphonium P–C bonds.[2–5] Even stoichiometric activation of P–O bonds, such as in phosphinites (PR$_2$(OR')), remains rare.[6–10] In fact, the activation of C–H,[11–14] B–H,[15] C–Br,[16] C–C,[17,18] S–S,[19] S–C,[20] and N–C[20] bonds have all occurred preferentially over phosphinite P–O bonds during either (i) initial coordination of multidentate ligands or (ii) during metal-mediated transformations using phosphinites as ancillary ligands.

The dearth of examples of P–O oxidative addition could be due to several factors, but one possibility is that the formation of high-energy phosphido moieties renders the reactions thermodynamically unfavorable. This is supported by the fact that in the rare cases in which P–O bond oxidative addition *has* been observed, the resultant phosphido ligand bridges two metal centers, providing additional stabilization (e.g. in Scheme 1A).[6–10] Notably, the reverse transformation of reductive elimination to generate a P–O bond has been demonstrated in structurally analogous systems: addition of I$_2$ as an oxidant to a Pt$_2$($\mu_2$-PR$_2$) species induced formation of a phosphinite ligand (Scheme 1B).[21] Similarly, while we are not aware of oxidative addition reactions to yield terminal M–PR$_2$ fragments, the microscopic reverse reaction of P–O reductive elimination of a chelating terminal phosphide complex was recently reported upon addition of CO or CN$^t$Bu to (PPP)Ni(OR) (PPP = [P(2-P$^i$Pr$_2$-C$_6$H$_4$)$_2$]$^-$ , R = Ph, $^i$Pr; Scheme 1C).[22,23]




**Scheme 1.** Examples of bimetallic[6,21] and monometallic[22,23] phosphinite P–O reductive elimination and oxidative addition.

Herein we report the oxidative addition of a phosphinite P–O bond at Ni$^0$ to generate a monometallic nickel secondary phosphine complex (Scheme 1D). This is achieved by combining the H(P$_2$ONO) ligand (H(P$_2$ONO) = HN(2-OP$^i$Pr$_2$-3,5-$^t$Bu-C$_6$H$_2$)$_2$, **1**) and Ni(COD)$_2$ at room temperature, suggesting that P–O bond activation is kinetically and thermodynamically facile. Of note, the observed P–O oxidative addition occurs preferentially over an intramolecular N–H bond activation, with the amine functional group instead serving as a proton donor to trap the reactive phosphido intermediate as a nickel-bound secondary

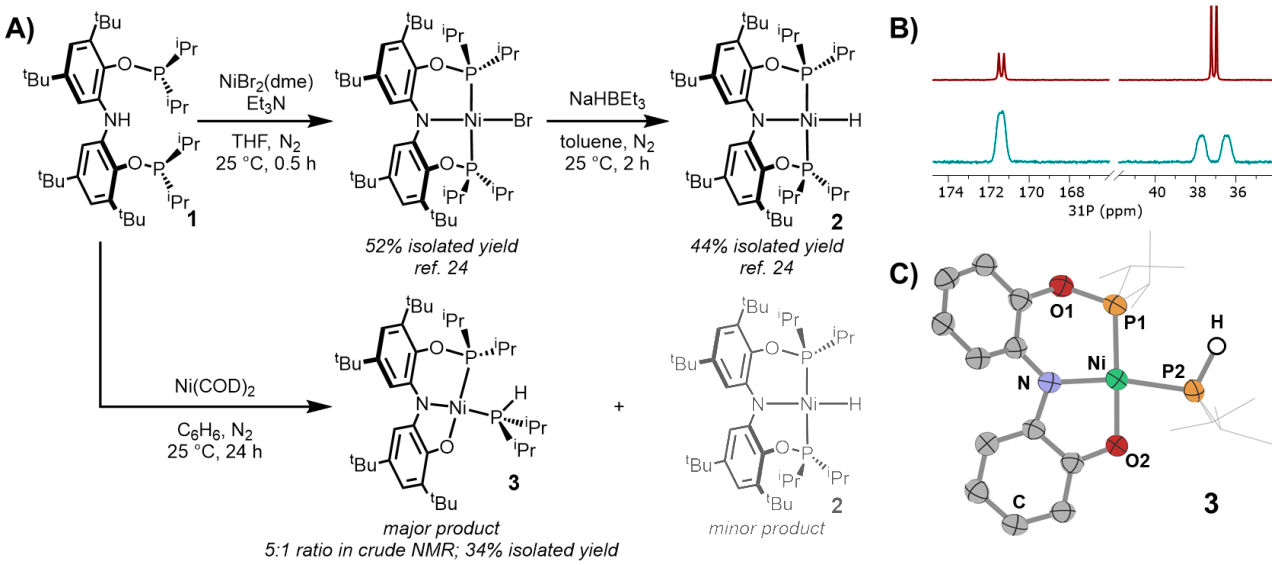



**Figure 1.** (A) Reactivity of H(P$_2$ONO) (**1**) with Ni(COD)$_2$ to generate (PONO)Ni(HP$^i$Pr$_2$) (**3**).[24] (B) $^{31}$P{$^1$H} (top) and $^{31}$P (bottom) NMR spectrum of **3** displaying the large $J_{HP}$ coupling of 306 Hz. (C) Structural representation of (PONO)Ni(HP$^i$Pr$_2$) (**3**) determined using single-crystal X-ray diffraction. Ellipsoids are set at 50% and all *tert*-butyl groups and hydrogens *except* for the P–H are omitted for clarity. See SI Section VII for additional details.

phosphine. The mechanism of the P–O oxidative addition was interrogated experimentally and subsequent reactivity studies revealed that the pincer ligand platform was capable of reconstructing P–O bonds upon addition of phosphorus electrophiles.

## RESULTS AND DISCUSSION

The P–O bond activation of **1** was initially encountered during attempts to abbreviate the synthesis of the nickel hydride complex (P$_2$ONO)NiH (**2**). We previously reported the synthesis of **2** in two steps by (i) initial metalation of the pincer ligand **1** with NiBr$_2$(dme) to generate (P$_2$ONO)NiBr followed by (ii) treatment with NaHBEt$_3$ (Figure 1A, top).[24] Alternatively, we sought to access **2** in a single step via oxidative addition of the central amine N–H bond at low-valent Ni.[25] To our surprise, upon mixing **1** and Ni(COD)$_2$ in C$_6$H$_6$, the solution immediately turned dark blue-green as opposed to the pale yellow color of the anticipated hydride **2**. Analysis of the crude reaction mixture by $^1$H and $^{31}$P{$^1$H} NMR spectroscopy in C$_6$D$_6$ revealed an unknown major product (**3**) and hydride **2** formed in a 5:1 ratio. Extraction of **2** into pentane enabled isolation of **3** as a dark blue-green powder.

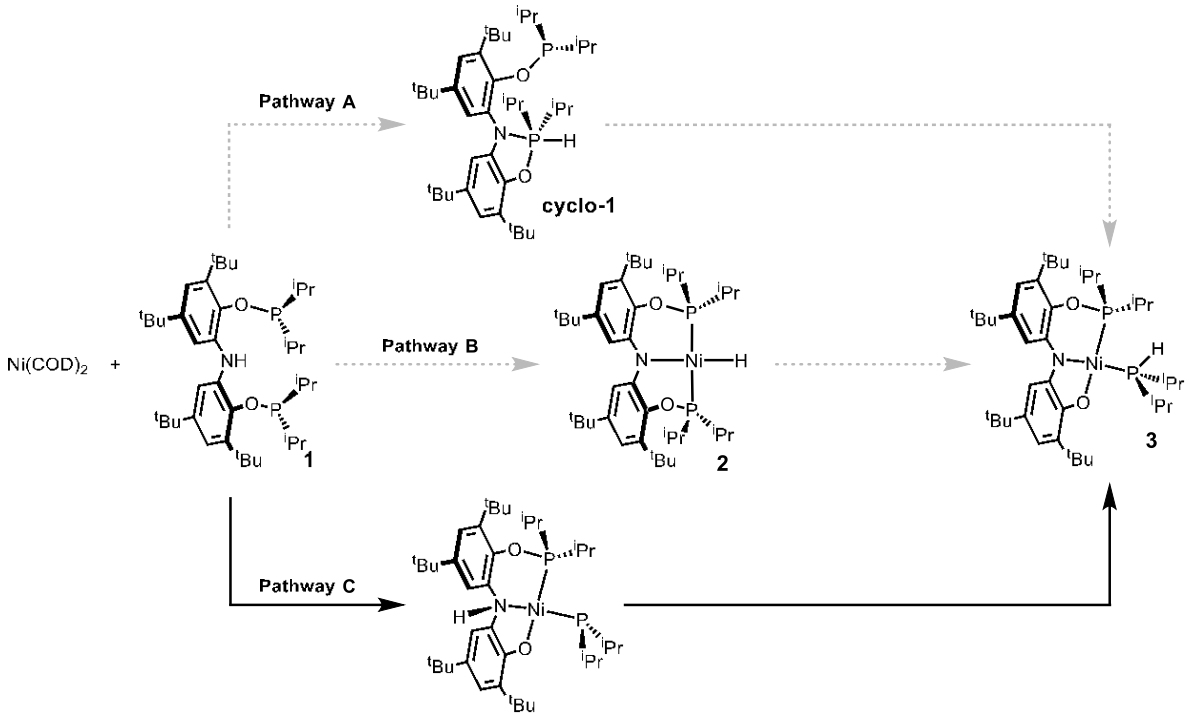
$^1$H NMR spectroscopy of isolated **3** in C$_6$D$_6$ indicated a $C_s$ symmetric species, matching the observation of two weakly coupled phosphorus nuclei in vastly different regions of the $^{31}$P{$^1$H} spectrum (δ 171.4, 37.1; $J_{PP}$ = 62 Hz). Without the decoupler, the upfield $^{31}$P NMR signal featured strong proton coupling (d, $J_{HP}$ = 306 Hz; Figure 1B) which correlated to a $^1$H resonance (δ 2.98, $J_{HP}$ = 304 Hz). The P–H bond was also apparent in the IR spectrum ($\nu_{P-H}$ = 2333 cm$^{-1}$).[26] In sum, these spectroscopic data are consistent with assignment of **3** as the secondary phosphine complex, (PONO)Ni(HP$^i$Pr$_2$), a constitutional isomer of the originally targeted nickel hydride species **2**.

The molecular structure of **3** was unambiguously confirmed by single-crystal X-ray diffraction (Figure 1C). Complex **3** features a distorted square planar geometry with an unsymmetrical pincer ligand forming both 5- and 6-membered metallacycles. The monodentate secondary phosphine ligand (HP$^i$Pr$_2$) lies *cis* to the phosphine of the PONO pincer fragment (consistent with the small $J_{PP}$) and the P–H bond is oriented towards the bulky phosphinite arm, avoiding steric interactions between the isopropyl groups. The exocyclic Ni–P2 bond distance of 2.182(7) Å is similar to complexes of the formula NiX$_2$(HPR$_2$)$_2$ (X = Cl, Br; R = $^i$Pr, Cy)[27] while the endocyclic Ni–P1 bond in **3** is very similar to that of **2** (2.098(5) Å and 2.1092(4), respectively).

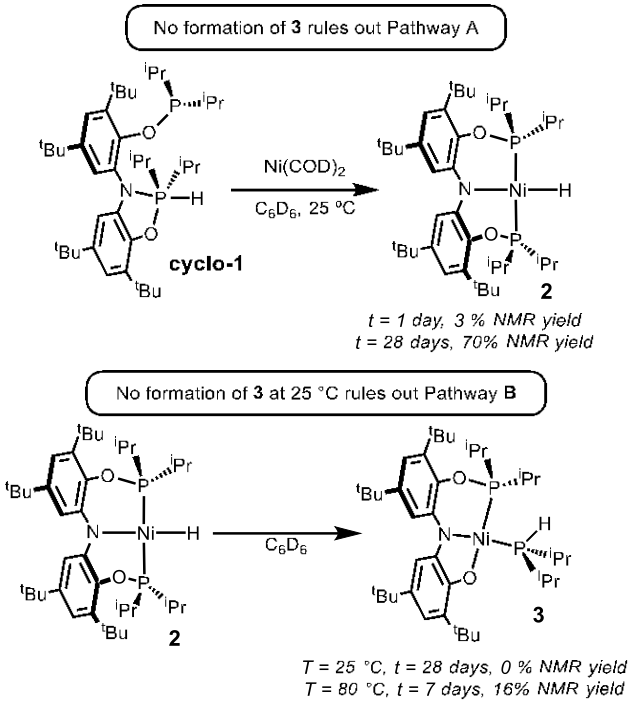
Surprised by the formation and structure of **3**, we sought to better understand how the unanticipated net P–O bond activation occurred. We initially considered three possibilities as shown in Scheme 2: (A) *in situ* cyclization of **1** to known isomer ***cyclo*-1**[24] affording access to facile P–O bond activation from a P$^V$ intermediate; (B) *in situ* isomerization of **2** to **3**; or (C) direct oxidative addition of the P–O bond.

To probe pathway A, we first interrogated whether the formation of ***cyclo*-1** *in situ* could influence reactivity, as the insertion of low-valent metals into the P–X bonds of P$^V$ species has been previously reported.[28] To test this, isolated ***cyclo*-1** and Ni(COD)$_2$ were combined in C$_6$D$_6$ and the reaction was monitored by NMR spectroscopy (Scheme 3, top). NMR spectral monitoring showed just a 3% yield of hydride **2** after 24 h, while **3** was not detected. During continued monitoring over the course of 28 days, the reaction proceeded to 70% NMR yield of **2** with still no evidence for the formation of **3**. This clearly rules out the activation of the P$^V$ center in ***cyclo*-1** in pathway A as a viable mechanism for the formation of **3**. Additionally, this suggests that the P–O bond activation occurs at a P$^{III}$ phosphinite center. Finally, in a spot of irony, the reaction of Ni(COD)$_2$ and ***cyclo*-1** also demonstrates the initially desired goal of developing a one-step synthesis of **2**, albeit from a counter-intuitive hydridophosphorane precursor.

**Scheme 3.** Probing the mechanism of P–O oxidative addition via a ***cyclo*-1** intermediate (top) and isomerization of **2** (bottom).



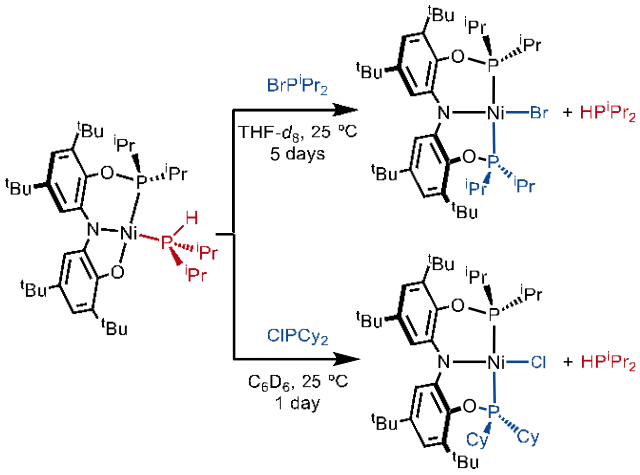

**Scheme 2.** Mechanistic possibilities for the formation of **3** via (A) *in situ* isomerization of **1** to ***cyclo*-1**, (B) isomerization of **2** to **3**, (C) direct oxidative addition of the P–O bond.




Next, we considered whether N–H bond activation followed by isomerization of **2** to its constitutional isomer **3** could be possible (pathway B, Scheme 2B). While no evidence for isomerization of isolated samples of **2** was observed at room temperature (*vide supra*), we did find that heating solutions of **2** in $C_6D_6$ at 80 ˚C resulted in partial conversion of **2** to **3** after 7 days (16% NMR yield) along with a decomposition product (Scheme 3, bottom; see SI Section V for more details). This temperature and timeframe, however, mean that the thermal isomerization is simply kinetically incompatible with the observed formation of **3** from **1** and $Ni(COD)_2$, which occurs overnight at room temperature. After ruling out pathways A and B, this left the direct oxidative addition of the P–O bond in **1** at $Ni^0$ in pathway C to initially generate a nickel phosphido species that was subsequently stabilized via proton transfer from the amine pincer backbone (Scheme 2C).

Having identified a plausible mechanism of P–O bond activation, we next sought to determine whether the initial "cannibalization" of ligand **1** could be reversed. To drive the reconstruction of the P–O bond and regenerate the $P_2ONO$ ligand, **3** was treated with 1 equiv of $BrP^iPr_2$ as a phosphorus electrophile. Upon mixing $BrP^iPr_2$ and **3**, the blue-green solution slowly converted to a dark green color over the course of 5 days while $^{31}P$ and $^1H$ NMR spectroscopy showed formation of ($P_2ONO$)NiBr and free $HP^iPr_2$ (Scheme 4, top). This reaction restores the pincer ligand to its original composition as $P_2ONO$.

**Scheme 4.** Reconstruction of the P–O bond to regenerate symmetric (top) and unsymmetric (bottom) $P_2ONO$ ligands.




An analogous reaction of **3** with $ClPCy_2$ led to a dark green solution. Monitoring the reaction by $^{31}P$ NMR spectroscopy showed consumption of **3**, the appearance of free $HP^iPr_2$, and a major product featuring two closely spaced doublets as part of an AB spin system (δ 141.6, 138.7; $J_{PP}$ = 425 Hz) (Figure S16-17). These resonances appear in a similar region to ($P_2$ONO)NiBr (δ 146) while the large $J_{PP}$ is consistent with the *trans* phosphine configuration expected in an unsymmetrical PP'ONO ligated-species (Scheme 4, bottom). Although P-containing side products are present (Figure S16), the formulation of the sole nickel-containing product as an unsymmetrical PP'ONO ligand is further supported by the presence of four different aromatic and $^t$Bu resonances in the $^1$H NMR spectrum (Figure S18-19). This experiment confirms that the halophosphine is the source of the restored phosphinite arm rather than the $HP^iPr_2$ ligand. The combination of these reactivity and mechanistic studies demonstrates that the $P_2$ONO platform supports the activation and reformation of P–O bonds. This is notable, as it offers insight into ligand-templating as a potential strategy for driving P–O bond functionalization.

## CONCLUSION

In summary, oxidative addition of a phosphinite P–O bond at $Ni^0$ generates a monometallic secondary phosphine complex, (PONO)Ni($HPiPr_2$). Mechanistic studies revealed that the observed reactivity is due to a kinetic preference for $P^{III}$–O bond activation over the N–H bond present in the ligand **1**, and is also faster than any $P^V$–O bond activation of the cyclic isomer ***cyclo*-1**. In fact, the cyclic ligand state preferentially reacted with $Ni^0$ to solely generate the nickel hydride, ($P_2$ONO)NiH. Addition-ally, the initial cannibalization of the pincer ligand framework was found to be reversible, as addition of phosphorus electro-philes readily afforded reconstruction of the P–O bond. This demonstrates the potential feasibility of a ligand-templated approach to target P–O bond functionalization.

## ASSOCIATED CONTENT

**Supporting Information**.
Experimental details, characterization data (PDF)
Crystallographic data (CIF)

**Accession codes**

CCDC 2216707 contains the supplementary crystallographic datum for this paper. This datum can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44-1223-336033.
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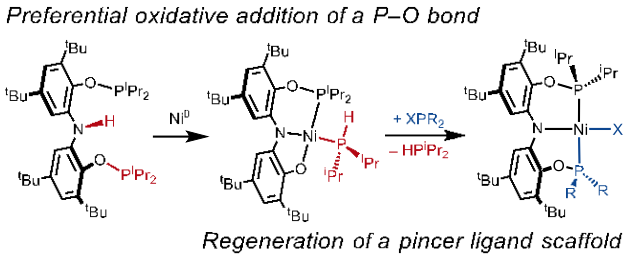
**TOC GRAPHIC**




**SYNOPSIS**

Oxidative addition reactions play a key role in generating reactive transition metal complexes to drive the functionalization of organic substrates. However, the activation of phosphorus-oxygen bonds remains essentially untapped. Herein we report the preferential oxidative addition of a phosphinite P–O bond at Ni over an N–H bond and interrogate both the mechanism of this bond activation and the microscopic reverse reaction by reconstructing the P–O bond using phosphorus electrophiles.