

Catalyst Deactivation of a Monoligated CyJohnPhos-Bound Nickel(0) Complex

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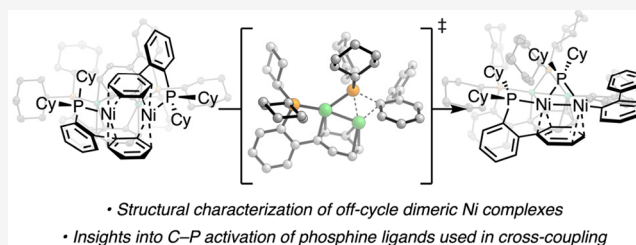


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ABSTRACT: Cross-coupling catalysts are prone to unproductive side reactivity, which can limit their practical use in synthetic chemistry. A detailed understanding of these pathways and the conditions that enable them is important for reaction optimization and rational catalyst design. In this work, we report the off-cycle reactivity of a monoligated, (2-biphenyl)dicyclohexylphosphine (CyJohnPhos)-bound Ni⁰ complex following product-forming reductive elimination. In the absence of substrate, free phosphine ligand, or π -accepting additives, dimerization of (CyJohnPhos)Ni⁰ occurs, followed by C–P bond activation of the ligand to form a phosphido-bridged Ni⁰/Ni^{II} dimer; both the Ni⁰/Ni⁰ and Ni⁰/Ni^{II} dimers were structurally characterized. Monomeric (CyJohnPhos)Ni⁰ must be intercepted by the substrate or free ligand to prevent irreversible dimerization and catalyst deactivation.



In transition-metal catalysis, a thorough mechanistic understanding of both productive and unproductive reactivity is important for the design of better catalysts and optimization of reaction conditions.^{1,2} Numerous unproductive pathways are known for cross-coupling catalysts, including aggregation,^{1,3,4} substrate/product inhibition,^{1,5} and formation of off-cycle oxidation states.^{6,7} While ancillary ligands typically serve to minimize these events, the ligand itself may deleteriously react with the metal center leading to catalyst deactivation;¹ for phosphines, cyclometalation^{8–10} and C–P bond activation^{11–13} are most commonly encountered. Herein, we report the catalyst deactivation pathway of monoligated (L₁)Ni⁰ bound by (2-biphenyl)dicyclohexylphosphine (CyJohnPhos), where interactions between low-valent Ni and the aromatic system of the phosphine enables irreversible dimerization and subsequent C–P bond cleavage. The presence of free phosphine, olefin, or substrate in solution following product-forming reductive elimination was necessary to trap monomeric Ni⁰ and prevent off-cycle speciation.

Recently, in studying Ni-catalyzed C–N cross-coupling with Buchwald-type phosphine ligands, we identified and structurally characterized amine-bound L₁Ni^{II} oxidative addition complexes.¹⁵ The CyJohnPhos/morpholine-bound complex (**1**, Figure 1A) was found to be a highly active on-cycle species, which underwent C–N reductive elimination following deprotonation in seconds with a low barrier of 13.3 kcal/mol as calculated using density functional theory (DFT). Complex **1** was also a viable precatalyst for the C–N coupling at room temperature, with 30 catalytic turnovers observed in less than 1 min. In stoichiometric studies of **1**, we observed that (CyJohnPhos)₂Ni⁰ (**2**) formed following reductive elimination when one or more equivalents of free CyJohnPhos was present

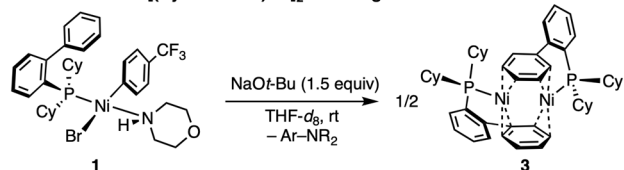
to trap the putative L₁Ni⁰ species. However, we were interested in determining the structure and reactivity of monoligated species in the absence of added ligand or substrate, given their presumed relevance in the catalytic cycle. Indeed, oxidative addition of aryl chlorides to **2** was attenuated by addition of free ligand,¹⁵ implicating (CyJohnPhos)Ni⁰ (intermediate **i**) as the active Ni⁰ species in catalysis.

Upon deprotonation of **1** with a slight excess of NaOt-Bu and no added ligand or electrophile, an immediate color change from orange to dark brown was observed; ³¹P{¹H} and ¹H NMR analyses of the reaction mixture indicated the presence of a new diamagnetic Ni species. Single-crystal X-ray diffraction (SCXRD) analysis of the crystallized complex revealed its identity as [(CyJohnPhos)Ni⁰]₂ (**3**, Figure 1B), the dimer of the putative monoligated (CyJohnPhos)Ni⁰ complex (**i**, Figure 1C) formed after reductive elimination. In the crystal structure of **3**, each Ni is coordinated by a single phosphorus, and the two Ni centers are “sandwiched” between the B rings of the two CyJohnPhos ligands.^{16,17} Each Ni is engaged in two η^2 -C_{arene} interactions—one on each B ring of the sandwich—for a total of four η^2 interactions in the complex (two total per B ring).^{17,18} The arenes are considerably dearomatized due to substantial backdonation from the two Ni⁰ centers; both C–C bond lengthening (up to 1.467(6) Å for C3–C4) and

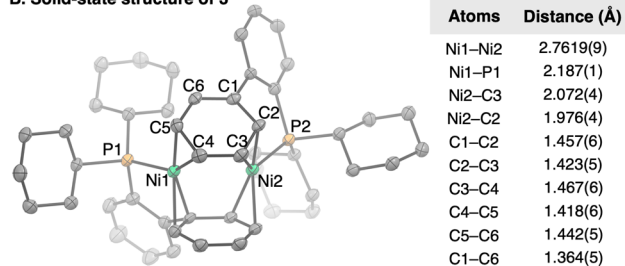
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A. Observation of $[(\text{CyJohnPhos})\text{Ni}^0]_2$ following C–N reductive elimination

B. Solid-state structure of 3



C. Stoichiometric Reactivity

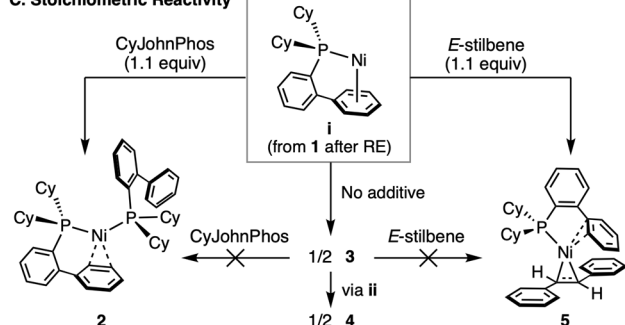


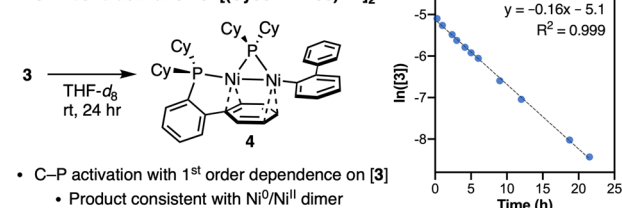
Figure 1. (A) Formation of $[(\text{CyJohnPhos})\text{Ni}^0]_2$ (**3**). (B) Structural characterization of **3**. Solid-state structure with thermal ellipsoids at 50% probability shown. Hydrogen atoms omitted for clarity. (C) Stoichiometric reactivity studies following C–N reductive elimination at room temperature in deuterated tetrahydrofuran.

contraction (down to 1.364(5) Å for C1–C6) compared with unbound CyJohnPhos is observed (Figure 1B). By ^1H NMR spectroscopy, several of the B ring aromatic protons of **3** are shifted significantly upfield; the most shifted aromatic resonance is found at 3.9 ppm—corroborating the solid-state observation. The Ni–Ni distance is relatively long at 2.7618(9) Å (formal shortness ratio of 1.20), longer than a typical Ni–Ni single bond.¹⁹ Given the formal d^{10} electronic configuration of both Ni centers, their proximity in the complex is likely due more to the sandwiched nature of the metals between the B ring arenes than to Ni–Ni bonding.

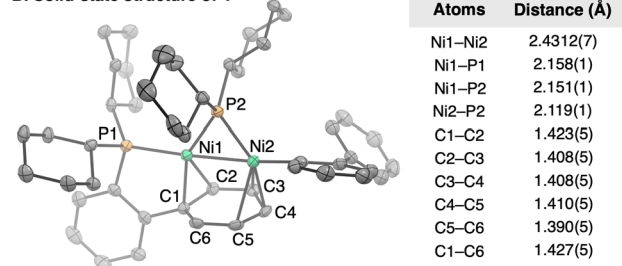
We then investigated the room-temperature reactivity of **3** with added free CyJohnPhos and π -accepting *E*-stilbene. We observed that if either CyJohnPhos or stilbene was added following the formation of dimeric **3**, no reaction occurred. However, if either CyJohnPhos or stilbene was added to **1** before deprotonation/reductive elimination, **2** or **5** were observed to form, respectively.¹⁵ Similarly, if 4-chlorobenzotrifluoride was added after reductive elimination and formation of **3**, no consumption of the electrophile was observed by ^{19}F NMR. However, if 4-chlorobenzotrifluoride was combined with **1** prior to reaction with NaOt-Bu, oxidative addition immediately occurred following reductive elimination. This suggests that **3** is an off-cycle species and that its formation is deleterious to efficient catalysis. We hypothesize that monomeric $(\text{CyJohnPhos})\text{Ni}^0$ (**i**) forms initially following reductive elimination, which can be intercepted by free phosphine, olefin, or aryl halide. The presence of one or

more equivalent (relative to Ni) of 1,5-cyclooctadiene (COD) in solution also serves to trap monomeric Ni^0 in the form of a mixture of $\text{Ni}(\text{COD})_2$ and **2**.¹⁵ However, in the absence of added ligands or substrates, irreversible dimerization of **i** occurs to form **3** (Figure 1C).

Furthermore, we observed that **3** itself was not indefinitely stable in solution at room temperature. Over time, two sets of doublets with 1:1 integration and J_{PP} values of 34.3 Hz were observed downfield of **3** by $^{31}\text{P}\{^1\text{H}\}$ NMR spectroscopy. One of these doublets was substantially downfield ($\delta = 158.2$ ppm), consistent with a Ni-phosphido species formed after a C–P bond cleavage.^{12,20,21} The second doublet ($\delta = 35.9$ ppm) was consistent with an “intact” phosphine. Over 48 h, **3** converted completely to this putative C–P activated complex (Figure 2A).

A. C–P bond activation of $[(\text{CyJohnPhos})\text{Ni}^0]_2$ 

B. Solid-state structure of 4



C. DFT-computed structures for the C–P bond cleavage pathway

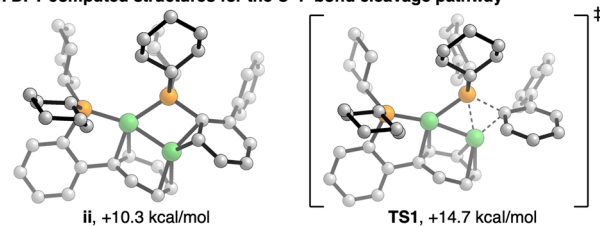


Figure 2. (A) C–P bond activation of **3** observed and monitored in situ at room temperature by $^{31}\text{P}\{^1\text{H}\}$ NMR spectroscopy at 298 K. (B) Structural characterization of **4**. Solid-state structure with thermal ellipsoids at 50% probability; hydrogen atoms omitted for clarity. (C) DFT-computed structures for C–P bond cleavage at the M06/def2-TZVP//B3LYP-D3/def2-SVP (SMD solvation model for tetrahydrofuran) level of theory. Energies were relative to **3** (0.0 kcal/mol).

The crystal structure of the complex confirmed its identity as a C–P-activated dimer (**4**, Figure 2B). Complex **4** consists of one intact CyJohnPhos ligand bound to one of the two Ni centers and a μ_2 -PCy₂ bridge spanning the second Ni center, which is also bound to the biphenyl moiety. The B ring of the intact CyJohnPhos supports both Ni centers via an η^2 interaction to Ni1 and an η^3 interaction to Ni2. The Ni–Ni distance is 2.4312(7) Å (formal shortness ratio of 1.06), far shorter than that observed in **3**, and consistent with a Ni–Ni bonding interaction.¹⁹ The formal oxidation states of the Ni centers in **4** are more ambiguous than those in **3**. However,

given that Ni^{II} is bound to the X-type biphenyl ligand and that the Ni^{II}–P₂ distance is shorter than the Ni^I–P₂ distance (indicative of more positive charge on Ni^{II}), **4** is more consistent with a mixed Ni⁰/Ni^{II} species than a Ni^I/Ni^I species (Figure 2B).^{22,23}

To investigate the mechanism of C–P bond cleavage, conversion of **3** and formation of **4** were monitored by ³¹P{¹H} NMR spectroscopy over 24 h. The results were consistent with a first-order dependence on [**3**], with a rate constant of $4.4 \times 10^{-5} \text{ s}^{-1}$ (half-life of 4.3 h) at 298 K (Figure 2A). Addition of free CyJohnPhos to trap any monomeric species that would form due to dissociation did not affect the reaction. Overall, these results suggest that the C–P bond activation likely takes place from **3** and not from **i** or a higher nuclearity aggregate. DFT calculations were performed to further interrogate this process (Figures 2C and S27). In the computed pathway, **3** reorganizes to form intermediate **ii** (10.3 kcal/mol above **3**),²⁴ wherein one Ni center is coordinated by both phosphines and the lower (B ring) of one CyJohnPhos ligand. The second Ni atom in **ii** is sandwiched between this B ring and the upper (A ring) of the second CyJohnPhos; the η^2 interaction with the A ring includes the C–P ipso carbon. The transition state of the subsequent C–P bond cleavage was located with a ΔG^\ddagger of 4.4 kcal/mol above **ii** (14.7 kcal/mol above **3**).²⁴ See Figure S27 for the full free energy profile. A similar multinuclear C–P activation mechanism likely occurs with other coordinatively unsaturated Ni⁰ complexes bound by aryl phosphines (e.g., PPh₃).^{12,25}

In conclusion, we found that in the absence of additional ligand equivalents, π -acceptors, and/or electrophile substrate, monoligated (CyJohnPhos)Ni⁰ forms a Ni⁰/Ni⁰ dimer that is recalcitrant toward catalytic cycle reentry. Over time, this Ni⁰/Ni⁰ dimer decomposes further via a C–P bond cleavage to generate a Ni⁰/Ni^{II} dimer. Knowledge of these off-cycle complexes and an understanding of the conditions that lead to their formation are helpful in the design of new ligands and Ni precursors as well as in the fine-tuning of reaction conditions to maximize productive Ni-catalyzed cross-coupling. Continued effort by the field to fully elucidate these pathways, as has been done for precious metal complexes,^{26–30} will undoubtedly lead to more practical and efficient use of Ni in valuable bond-forming methodologies.

■ ASSOCIATED CONTENT

SI Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acs.organomet.3c00450>.

Experimental procedures, experimental data, and characterization and spectral data for new compounds (PDF)

XYZ coordinates for DFT-computed structures (ZIP)

Accession Codes

CCDC 2204444 (**3**) and 2204458 (**4**) contain the supplementary crystallographic data for this paper (CIF). These data 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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Author Contributions

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Notes

The authors declare no competing financial interest.

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