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

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Abstract

Cross-coupling catalysts are prone to unproductive side reactivity that 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, 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 substrate or free ligand to prevent irreversible dimerization and catalyst deactivation.

Graphical Abstract

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ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

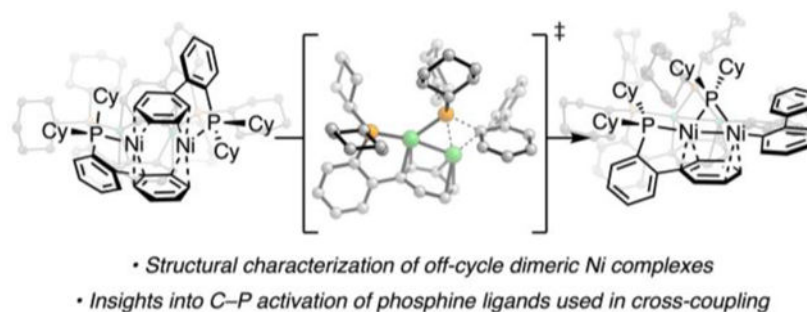
Experimental procedures, experimental data, and characterization and spectral data for new compounds (PDF).

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.

The authors declare no competing financial interest.



In transition metal catalysis, 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, cyclometallation^{8–10} and C–P bond activation^{11–13} are most commonly encountered. Herein, we report the catalyst deactivation pathway of monoligated (L_1)¹⁴ Ni^0 bound by 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 Ni^0 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 L_1Ni^{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 one minute. In stoichiometric studies of **1**, we observed that $(CyJohnPhos)_2Ni^0$ (**2**) formed following reductive elimination when one or more equivalents of free CyJohnPhos was present to trap the putative L_1Ni^0 species. However, we were interested to determine 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 $(CyJohnPhos)Ni^0$ (intermediate **i**) as the active Ni^0 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; $^{31}P\{^1H\}$ and 1H NMR analysis of the reaction mixture indicated the presence of a new diamagnetic Ni species. SCXRD analysis of the crystallized complex revealed its identity as $[(CyJohnPhos)Ni^0]_2$ (**3**, Figure 1B), the dimer of the putative monoligated $(CyJohnPhos)Ni^0$ 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 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 formally d¹⁰ 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* 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 ¹⁹F NMR. However, if 4-chlorobenzotrifluoride was combined with **1** prior to reaction with NaO*t*-Bu, oxidative addition immediately took place 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 (CyJohnPhos)Ni⁰ (**i**) forms initially following reductive elimination, which can be intercepted by the 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 Ni⁰ in the form of a mixture of Ni(COD)₂ and **2**.¹⁵ However, in the absence of added ligands and/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 ³¹P{¹H} NMR spectroscopy. One of these doublets was substantially downfield (δ = 158.2 ppm), consistent with a Ni-phosphido species formed after a C–P bond cleavage.^{12,20,21} The second doublet (δ = 35.9 ppm) was consistent with an “intact” phosphine. Over 48 hours, **3** converted completely to this putative C–P activated complex (Figure 2A).

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 bridging 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 in **3**. However, given that Ni2 is bound to the X-type biphenyl ligand and that the Ni2–P2

distance is shorter than the Ni1–P2 distance (indicative of more positive charge on Ni2), **4** is more consistent with a mixed Ni⁰/Ni^{II} species than Ni^I/Ni^I (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 hours. 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 hours) 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 itself 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 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 G^\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 off-cycle dimeric complexes that are recalcitrant towards catalytic cycle reentry. Over time, these Ni⁰ dimers decompose further via 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 is 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.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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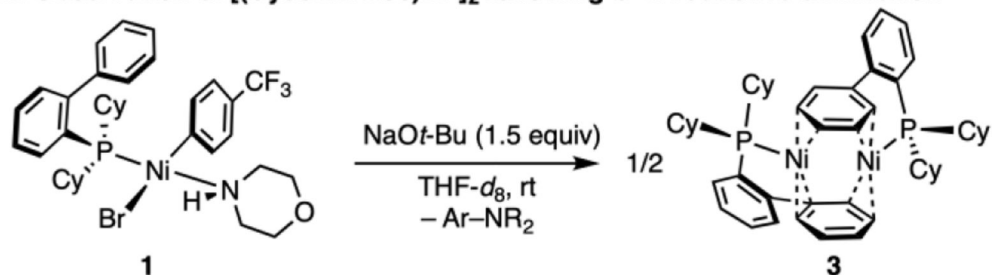
REFERENCES

- (1). Crabtree RH Deactivation in Homogeneous Transition Metal Catalysis: Causes, Avoidance, and Cure. *Chem. Rev* 2015, 115, 127–150. [PubMed: 25493420]
- (2). Hartwig JF *Organotransition Metal Chemistry: From Bonding to Catalysis*; University Science Books, 2010.

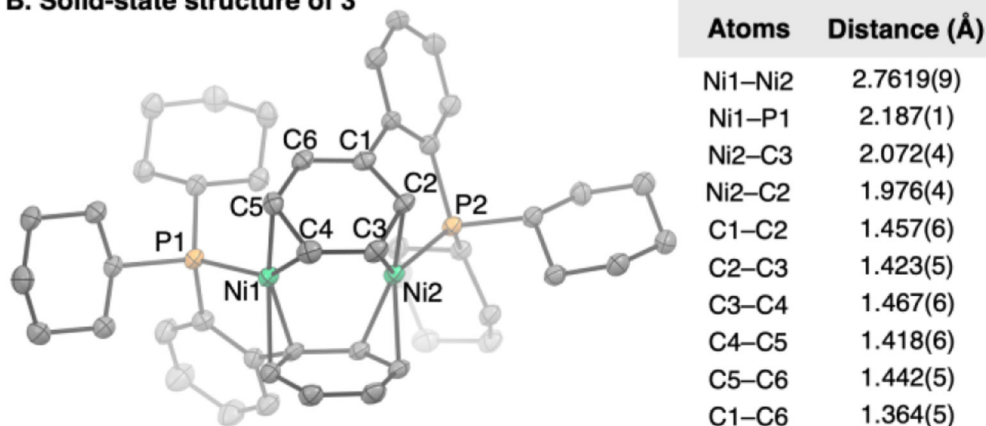
- (3). Payard P-A; Perego LA; Ciofini I; Grimaud L. Taming Nickel-Catalyzed Suzuki-Miyaura Coupling: A Mechanistic Focus on Boron-to-Nickel Transmetalation. *ACS Catal.* 2018, 8, 4812–4823.
- (4). Beromi MM; Brudvig GW; Hazari N; Lant HMC; Mercado BQ Synthesis and Reactivity of Paramagnetic Nickel Polypyridyl Complexes Relevant to C(Sp²)–C(Sp³) Coupling Reactions. *Angew. Chem. Int. Ed* 2019, 58, 6094–6098.
- (5). Ruiz-Castillo P; Buchwald SL Applications of Palladium-Catalyzed C–N Cross-Coupling Reactions. *Chem. Rev* 2016, 116, 12564–12649.
- (6). Guard LM; Beromi MM; Brudvig GW; Hazari N; Vinyard DJ Comparison of Dppf-Supported Nickel Precatalysts for the Suzuki–Miyaura Reaction: The Observation and Activity of Nickel(I). *Angew. Chem. Int. Ed* 2015, 54, 13352–13356.
- (7). Dicciani JB; Diao T. Mechanisms of Nickel-Catalyzed Cross-Coupling Reactions. *Trends. Chem* 2019, 1, 830–844.
- (8). Albrecht M. Cyclometalation Using D-Block Transition Metals: Fundamental Aspects and Recent Trends. *Chem. Rev* 2010, 110, 576–623. [PubMed: 20017477]
- (9). Strieter ER; Buchwald SL Evidence for the Formation and Structure of Palladacycles during Pd-Catalyzed C–N Bond Formation with Catalysts Derived from Bulky Monophosphinoboryl Ligands. *Angew. Chem. Int. Ed* 2006, 45, 925–928.
- (10). Reid SM; Boyle RC; Mague JT; Fink MJ A Dicoordinate Palladium(0) Complex with an Unusual Intramolecular η -Arene Coordination. *J. Am. Chem. Soc* 2003, 125, 7816–7817. [PubMed: 12822996]
- (11). Parkins AW The Migration and Cleavage of Substituents from Donor Atoms in Coordination Compounds of the Transition Metals. *Coord. Chem. Rev* 2006, 250, 449–467.
- (12). Touchton AJ; Wu G; Hayton TW Generation of a Ni³ Phosphinidene Cluster from the Ni(0) Synthon, Ni(η^3 -CPh₃)₂. *Organometallics* 2020, 39, 1360–1365.
- (13). Fahey DR; Mahan JE Reversible Oxidative Addition of Triphenylphosphine to Zero-Valent Nickel and Palladium Complexes. *J. Am. Chem. Soc* 1976, 98, 4499–4503.
- (14). Monoligated (L₁) is defined as a single monophosphine ligand bound to the metal center (L:M of 1:1).₁
- (15). Newman-Stonebraker SH; Wang JY; Jeffrey PD; Doyle AG Structure–Reactivity Relationships of Buchwald-Type Phosphines in Nickel-Catalyzed Cross-Couplings. *J. Am. Chem. Soc* 2022, 144, 19635–19648. [PubMed: 36250758]
- (16). Barder TE Synthesis, Structural, and Electron Topographical Analyses of a Dialkylbiaryl Phosphine/Arene-Ligated Palladium(I) Dimer: Enhanced Reactivity in Suzuki–Miyaura Coupling Reactions. *J. Am. Chem. Soc* 2006, 128, 898–904. [PubMed: 16417380]
- (17). Jones C; Schulten C; Fohlmeister L; Stasch A; Murray KS; Moubaraki B; Kohl S; Ertem MZ; Gagliardi L; Cramer CJ Bulky Guanidinato Nickel(I) Complexes: Synthesis, Characterization, Isomerization, and Reactivity Studies. *Chem. Eur. J* 2011, 17, 1294–1303. [PubMed: 21243697]
- (18). For selected examples of arene-bridged Ni dimers see: (a) Koch F; Berkefeld A; Schubert H; Grauer C. Redox and Acid–Base Properties of Binuclear 4-Terphenyldithiophenolate Complexes of Nickel. *Chem. Eur. J* 2016, 22, 14640–14647. [PubMed: 27554625] (b) Ito M; Matsumoto T; Tatsumi K. Synthesis and Reactions of Mono- and Dinuclear Ni(I) Thiolate Complexes. *Inorg. Chem.* 2009, 48, 2215–2223. [PubMed: 19235981] (c) Velian A; Lin S; Miller AJM; Day MW; Agapie T. Synthesis and C–C Coupling Reactivity of a Dinuclear Ni^I–Ni^I Complex Supported by a Terphenyl Diphosphine. *J. Am. Chem. Soc* 2010, 132, 6296–6297. [PubMed: 20397653] (d) Tsui E; Agapie T. Carbon dioxide cleavage by a Ni₂ complex supported by a binucleating bis(N-heterocyclic carbene) framework. *Polyhedron* 2014, 84, 103–110. [PubMed: 30393421] (e) Zhou Y-Y; Hartline DR; Steiman TJ; Fanwick PE; Uyeda C. Dinuclear Nickel Complexes in Five States of Oxidation Using a Redox-Active Ligand. *Inorg. Chem* 2014, 53, 11770–11777. [PubMed: 25337719]
- (19). Pauling L. Atomic Radii and Interatomic Distances in Metals. *J. Am. Chem. Soc* 1947, 69, 542–553.
- (20). Chen Y; Sui-Seng C; Zargarian D. Tetraphenylborate as a Novel Bridging Ligand in a Zwitterionic Nickel(I) Dimer. *Angew. Chem. Int. Ed* 2005, 44, 7721–7725.

- (21). Vivic DA; Anderson TJ; Cowan JA; Schultz AJ Synthesis, Structure, and Reactivity of a Dinuclear Metal Complex with Linear M–H–M Bonding. *J. Am. Chem. Soc* 2004, 126, 8132–8133. [PubMed: 15225051]
- (22). Beck R; Johnson SA Mechanistic Implications of an Asymmetric Intermediate in Catalytic C–C Coupling by a Dinuclear Nickel Complex. *Chem. Commun* 2011, 47, 9233–9235.
- (23). Beck R; Johnson SA Structural Similarities in Dinuclear, Tetranuclear, and Pentanuclear Nickel Silyl and Silylene Complexes Obtained via Si–H and Si–C Activation. *Organometallics* 2012, 31, 3599–3609.
- (24). The rate limiting step of the C–P activation pathway likely occurs during the reorganization of 3 to intermediate ii. We were unable to locate a transition state for this process, but an intermediate in the reorganization was calculated with a ΔG^\ddagger of 23.6 kcal/mol above 3 (see SI for more information).
- (25). Appleby KM; Dzotsi E; Scott NWJ; Dexin G; Jeddi N; Whitwood AC; Pridmore NE; Hart S; Duckett SB; Fairlamb IJS Bridging the Gap from Mononuclear PdII Precatalysts to Pd Nanoparticles: Identification of Intermediate Linear [Pd3(XPh3)4]2+ Clusters as Catalytic Species for Suzuki–Miyaura Couplings (X = P, As). *Organometallics* 2021, 40, 3560–3570.
- (26). Martin R; Buchwald SL Palladium-Catalyzed Suzuki–Miyaura Cross-Coupling Reactions Employing Dialkylbiaryl Phosphine Ligands. *Acc. Chem. Res* 2008, 41, 1461–1473. [PubMed: 18620434]
- (27). Hartwig JF Evolution of a Fourth Generation Catalyst for the Amination and Thioetherification of Aryl Halides. *Acc. Chem. Res* 2008, 41, 1534–1544. [PubMed: 18681463]
- (28). Fu GC The Development of Versatile Methods for Palladium-Catalyzed Coupling Reactions of Aryl Electrophiles through the Use of P(t-Bu)3 and PCy3 as Ligands. *Acc. Chem. Res* 2008, 41, 1555–1564. [PubMed: 18947239]
- (29). Marion N; Nolan SP Well-Defined N-Heterocyclic Carbenes–Palladium(II) Precatalysts for Cross-Coupling Reactions. *Acc. Chem. Res* 2008, 41, 1440–1449. [PubMed: 18774825]
- (30). Johansson Seechurn CCC; Kitching MO; Colacot TJ; Snieckus V. Palladium-Catalyzed Cross-Coupling: A Historical Contextual Perspective to the 2010 Nobel Prize. *Angew. Chem. Int. Ed* 2012, 51, 5062–5085.

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



B. Solid-state structure of **3**



C. Stoichiometric Reactivity

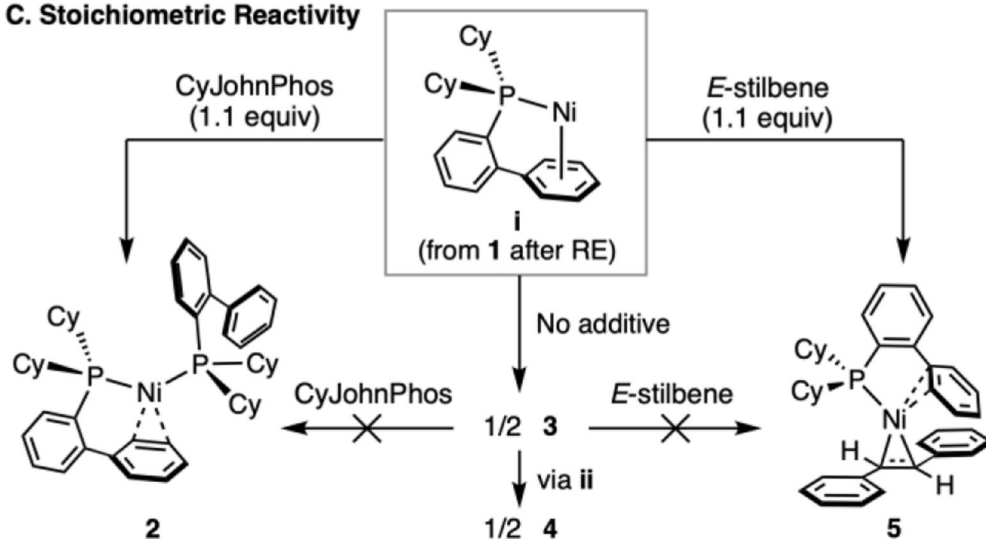
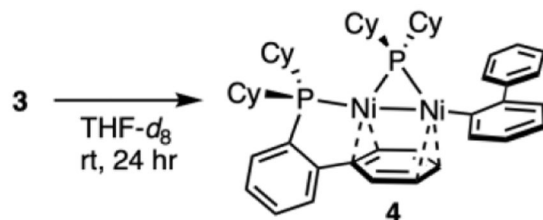


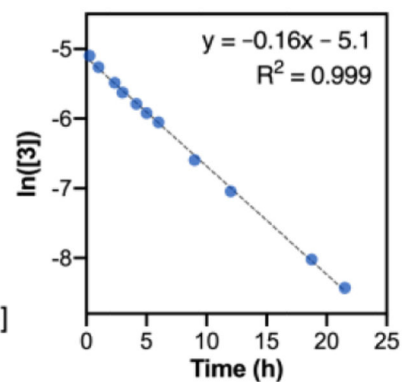
Figure 1.

(A) Stoichiometric 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 THF-d_8 .

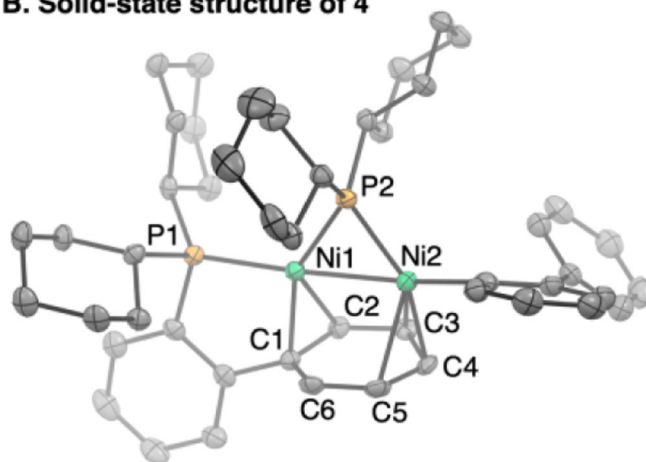
A. C–P bond activation of $[(\text{CyJohnPhos})\text{Ni}^0]_2$



- C–P activation with 1st order dependence on [3]
- Product consistent with Ni⁰/Ni^{II} dimer



B. Solid-state structure of 4



Atoms	Distance (Å)
Ni1–Ni2	2.4312(7)
Ni1–P1	2.158(1)
Ni1–P2	2.151(1)
Ni2–P2	2.119(1)
C1–C2	1.423(5)
C2–C3	1.408(5)
C3–C4	1.408(5)
C4–C5	1.410(5)
C5–C6	1.390(5)
C1–C6	1.427(5)

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

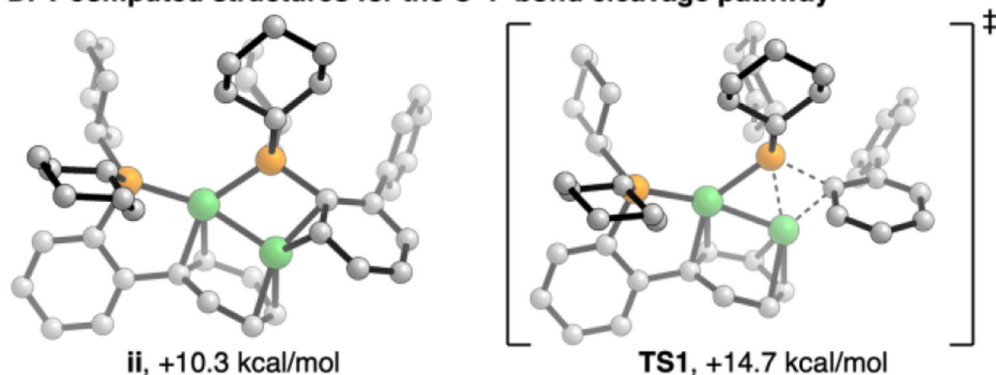


Figure 2.

(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 THF) level of theory. Energies relative to **3** (0.0 kcal/mol).