Title

Oxidative Cascade Cyclization of 1,2-Dicyanoarenes by a Dicopper(I,I) Nitrite Complex to Phthalimide Ligands

Journal

Organometallics, 45(5)

ISSN

0276-7333

Authors

Fernandez, Jose Martinez

Nguyen, Ai Vy

Tilley, T Don

Publication Date

2026-03-09

DOI

10.1021/acs.organomet.6c00031

Oxidative Cascade Cyclization of 1,2-Dicyanoarenes by a Dicopper(I,I) Nitrite Complex to Phthalimide Ligands

Jose Martinez Fernandez,[†] Ai Vy Nguyen,[†] and T. Don Tilley[†*]

[†]Department of Chemistry, University of California, Berkeley, Berkeley, California 94720, United States; Chemical Sciences Division, Lawrence Berkeley National Laboratory, Berkeley, California 94720, United States

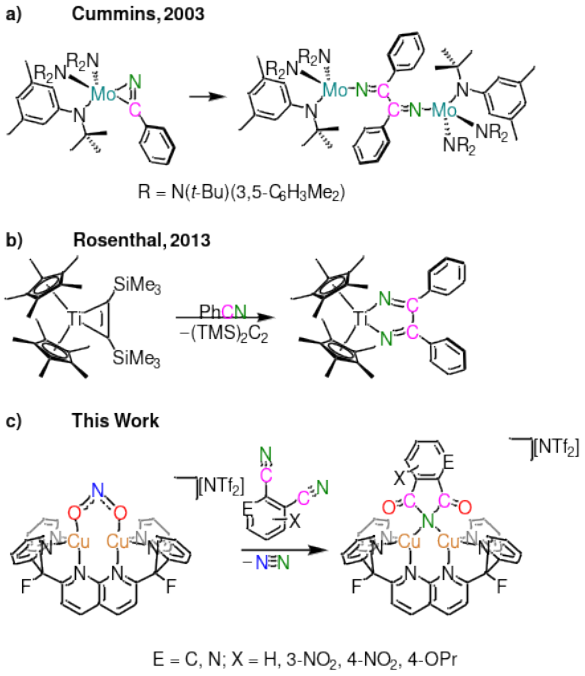
Supporting Information Placeholder

ABSTRACT: The reactions of $[Cu_2(\mu\text{-}\kappa^1\text{:}\kappa^1\text{-}O_2N)DPFN][NTf_2]$ (**1**; DPFN = 2,7-bis(fluoro-di(2-pyridyl)methyl)-1,8-naphthyridine, NTf_2^- = $N(SO_2CF_3)_2^-$) with 1,4-dicyanobenzene and 1,2-dicyanoarenes are discussed. Treatment of **1** with 1,4-dicyanobenzene produces a tetra-Cu(I) terephthalate complex (**2**) and dinitrogen via a discrete C≡N triple bond cleavage at each cyano group. However, reactions of **1** with 1,2-dicyanoarenes appear to proceed *via* a cascade reaction involving two intertwined C≡N triple bond activations to yield a series of di-Cu(I) phthalimides, $[Cu_2(\mu\text{-}N(CO)_2(Ar)DPFN][NTf_2]$ (**3-(Ar)**; **Ar** = 1,2-arylenes C_6H_4, 3-$NO_2C_6H_3$, 4-$NO_2C_6H_3$, 4-$PrOC_6H_3$, 3-NC_5H_3) and dinitrogen. The dicopper phthalimide bonding interaction in these compounds is robust enough to resist protonation by pentafluorophenol and alkylation by methyl triflate or benzyl chloride at the imide nitrogen. This characteristic presents an opportunity for post-synthetic modifications of the phthalimide ligand. Nevertheless, treatment of **3-(C_6H_4)** with bistriflimidic acid ($HNTf_2$) results in release of the neutral phthalimide, making the dicopper core available to coordinate other ligands such as nitrite and thus, completing a stoichiometric cycle.

INTRODUCTION

Nitriles are essential and versatile building blocks in organic synthesis.[1,2] Their chemistry with transition metals beyond their use as ligands has been extensively studied, with reported transformations ranging from simple metal-mediated hydrolysis to more complex cross metathesis reactions.[3,4] However, reactions in which two organonitriles are coupled by a transition metal are not commonly observed.[5] The products of such reactions are usually bimetallic complexes with a bridging diiminato ($[N=C(R)\text{-}C(R')=N]^{2-}$) ligand resulting from C-C bond formation between two nitriles.[6–9] Such dimerizations are most often mediated by highly reducing, low-valent early transition metals complexes. In these cases, the nitrile binding mode, sterics, and metal-ligand cooperation have all been reported to play key functions. Clear depictions of this are seen in the reactions of Cummins' molybdenum trisanilide complex $Mo(N[t\text{-}Bu]Ar)_3$ (Ar = 3,5-$C_6H_3Me_2$; Scheme 1a) and Hey-Hawkins' zirconocene phosphanido complex $[Cp°_2Zr(PHCy)]$ (Cp° = η^5-C_5EtMe).[10,11] While such chemistry is unusual with late transition metals, cases such as that of the electron-rich iridium pincer complex, $(PC_{sp2}P)Ir\text{-}N(H)Ar$ ($PC_{sp2}P$ = $(iPr_2PC_6H_4)_2C$, Ar = C_6H_5, 2,6-$iPr_2C_6H_3$) reported by Piers and coworkers, have been shown to engage in nitrile–nitrile coupling.[12]

Scheme 1. Examples of nitrile–nitrile coupling and this work



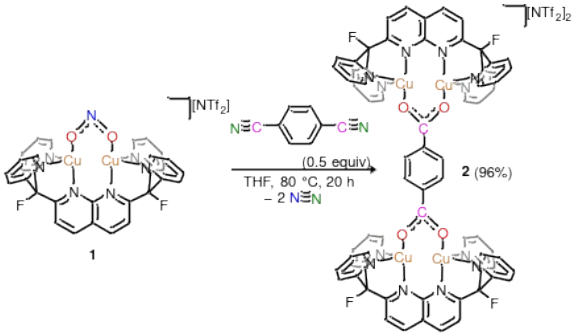
Nitrogen-containing metallocycles can result from the coupling of two or more organonitriles at a transition metal center.[13] In 1988, Walton and coworkers reported a triply bonded dirhenium(II) complex, $Re_2X_4(\mu\text{-dppm})_2$ (X =Cl, Br, dppm = $Ph_2PCH_2PPh_2$) that couples two acetonitrile molecules to form a 5-membered ring, while retaining the dirhenium core.[14] There are several reports, including a study on titanocene-mediated coupling of oligo-dinitriles from this laboratory, showcasing the ability of group IV metallocenes to form 1-metalla-2,5-diaza-cyclopenta-2,4-dienes in reactions with nitriles (Scheme 1b).[15−18] Rosenthal and coworkers reported that these transformations are in fact reversible as shown by nitrile exchange after the initial coupling has taken place.[19]

Recently, the Tilley laboratory reported reactions of $[Cu_2(\mu\text{-}\kappa^1\text{:}\kappa^1\text{-}O_2N)DPFN][NTf_2]$ (**1**) with organonitriles to yield $[Cu_2(\mu\text{-}\kappa^1\text{:}\kappa^1\text{-}O_2CR)DPFN][NTf_2]$ (R = Me, Ph, 4-Ac C_6H_4, *t*-Bu) and dinitrogen *via* C≡N triple bond cleavage.[20] This contribution builds on that work by showcasing the divergent reactivity of the nitrite complex with 1,2-dicyanoarenes, resulting in di-Cu(I) phthalimides complexes $[Cu_2(\mu\text{-}N(CO)_2(Ar)DPFN][NTf_2]$ (**3-(Ar)**; **Ar** = 1,2-arylenes C_6H_4, 3-$NO_2C_6H_3$, 4-$NO_2C_6H_3$, 4-$PrOC_6H_3$, 3-NC_5H_3), and dinitrogen (Scheme 1c). The nitrile–nitrile coupling in this contribution is not only unique because it occurs through a cascade reaction mediated by late transition metals, but also because it proceeds *via* formation of a new C–N bond rather than the more common C–C bond formation.

RESULTS AND DISCUSSION

To investigate the ability of $[Cu_2(\mu\text{-}\kappa^1\text{:}\kappa^1\text{-}O_2N)DPFN][NTf_2]$ (**1**) to activate more than one C≡N triple bond on a single substrate, the complex was allowed to react with dicyanoarenes. Treatment of **1** with 0.5 equiv of 1,4-dicyanobenzene in THF at 80 °C for 20 h resulted in the slow formation of $[Cu_4(\mu_4\text{-}\kappa^1\text{:}\kappa^1\text{:}\kappa^1\text{:}\kappa^1\text{-}(O_2C)_2C_6H_4)(DPFN)_2][NTf_2]_2$ (**2**; Scheme 2). Precipitation of the compound with diethyl ether resulted in isolation of an analytically pure light brown powder (96% yield). The ^1H and ^{19}F NMR spectra of **2** corroborate the symmetrical binding of both cationic dicopper(DPFN) fragments to the terephthalate ligand. Similar dinuclear Cu(I)/Cu(II) complexes have been synthesized in the study of self-assembled metallomacrocycles, mixed valency, and DNA cleavage activity.[21−23]

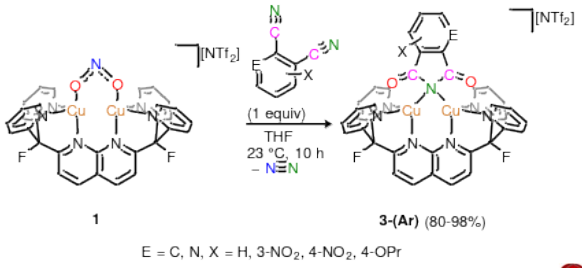
Scheme 2. Synthesis of the tetra-Cu(I) terephthalate complex (2)



Since the reaction of **1** with 1,2-dicyanobenzene seemed unlikely to result in a similar tetra-Cu(I) product, differently substituted 1,2-dicyanoarenes were investigated to probe the selectivity of oxidative couplings by the di-Cu(I) nitrite complex. Surprisingly, treatment of **1** with each 1,2-dicyanoarene (1,2-$(NC)_2Ar$; Ar = 1,2-arylenes C_6H_4, 3-$NO_2C_6H_3$, 4-$NO_2C_6H_3$, 4-$PrOC_6H_3$, 3-NC_5H_3) in THF at 23 °C for 10 h resulted in formation of nitrile–nitrile

coupling products $[Cu_2(\mu\text{-}N(CO)_2(Ar)DPFN][NTf_2]$ (**3-(Ar)**; Scheme 3). For each complex, precipitation from solution with diethyl ether resulted in isolation of an analytically pure red-brown powder in high yield (80-98%). As with the previously reported alkyl and aryl nitrile C≡N triple bond cleavages, the presence of the ^{15}N-labeled dinitrogen byproduct was confirmed by ^{15}N NMR (*vide infra*; Figure S22) in reactions involving the isotopologue of **1**.[20] Control experiments performed with $[n\text{-}Bu_4N][NO_2]$ and 1,2-$(NC)_2Ar$ (Ar = 1,2-arylenes 3-$NO_2C_6H_3$, 4-$NO_2C_6H_3$, 4-$PrOC_6H_3$, 3-NC_5H_3) in THF at 60 °C for 14 d did not produce the corresponding phthalimide (Figure S23-S26).

Scheme 3. Synthesis of the di-Cu(I) phthalimide complexes 3-(C_6H_4), 3-(3-$NO_2C_6H_3$), 3-(4-$NO_2C_6H_3$), 3-(4-$PrOC_6H_3$), and 3-(3-NC_5H_3)



The solid-state structures of **3-(3-$NO_2C_6H_3$)**, **3-(4- $NO_2C_6H_3$)**, and **3-(3-NC_5H_3)** were determined by single crystal X-ray diffraction (Figure 1). Compared to the structural metrics of another di-Cu(I) amido complex, $[Cu_2(\mu\text{-}NHTosyl)DPFN][NTf_2]$ (Cu-Cu = 2.6652(5) Å, Cu-N_{am} = 1.980(3) Å), previously reported by this laboratory, compounds **3-(Ar)** have shorter Cu-Cu interatomic distances (2.5154(4)-2.5309(7) Å) and longer average Cu-N_{im} bond distances ranging from 2.030(3) to 2.041(2) Å.[24] All phthalimide ligands bridge symmetrically and are positioned perpendicular to the plane defined by the naphthyridine scaffold. However, they should be able to freely rotate as indicated by the faux C_{2v} symmetry observed in the ^1H NMR spectra of each compound. While some monometallic Cu(I) phthalimide complexes have previously been reported, to our knowledge, complexes **3-(Ar)** are the first

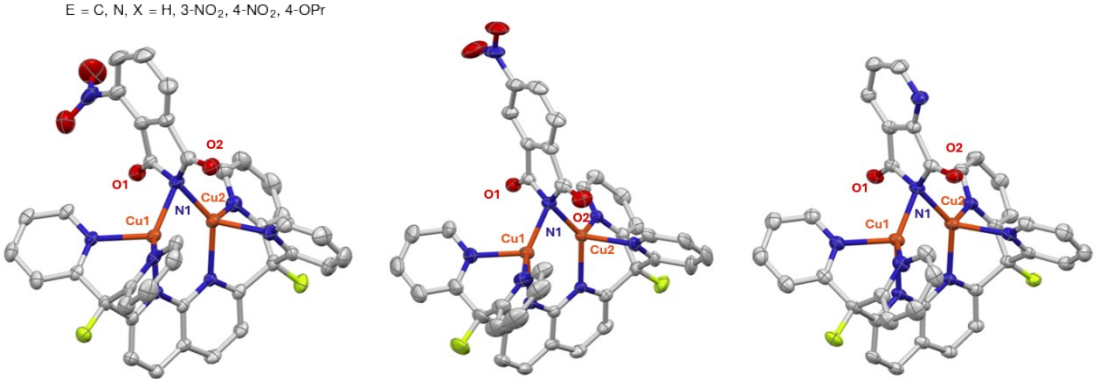


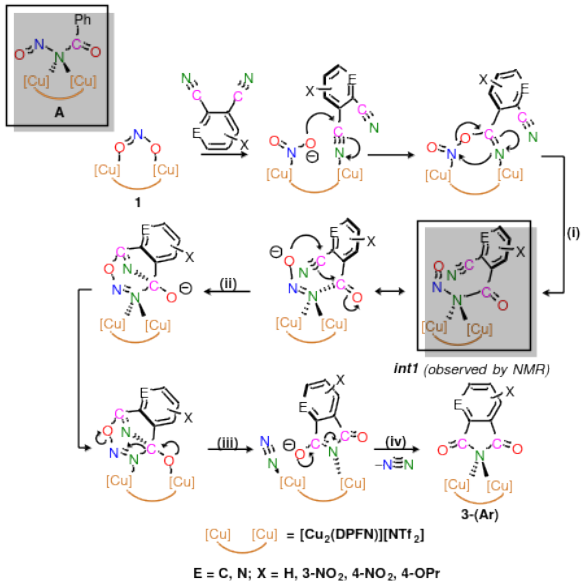
Figure 1. Solid-state molecular structures of compounds **3-(3-$NO_2C_6H_3$)**, **3-(4-$NO_2C_6H_3$)**, and **3-(3-NC_5H_3)** with thermal ellipsoids drawn at 50% probability. Hydrogen atoms, solvent molecules, and bistriflimide (NTf_2^-) anions are omitted for clarity.

phthalimide-bridged bimetallic complexes to be reported and crystallographically characterized.[25–28]

The release of isotopically labeled dinitrogen as a byproduct of these reactions suggests that the imide nitrogen in complexes **3-(Ar)** originates from one of the cyano groups of the 1,2-dicyanoarene.[29] In no case was a $^{15}N\{^1H\}$ NMR signal for an imide nitrogen belonging to any of the **3-(Ar)** complexes detected. After addition of excess 4-propoxy-1,2-dicyanobenzene to the ^{15}N isotopologue of **1**, a fleeting intermediate (**int1**) closely resembling the previously reported

[Cu_2(μ-N(NO)C(O)Ph)DPFN][NTf_2] (**A**) was observed by ^{1}H NMR and mass spectrometry (Figure S27 and S58). This suggests that just like the reactions of **1** with alkyl/aryl nitriles, reactions with 1,2-dicyanoarenes proceed through a di-Cu(I) N-nitrosamide intermediate (Scheme 4).

Scheme 4. Structure of A and a proposed mechanism for the formation of complexes 3-(Ar)

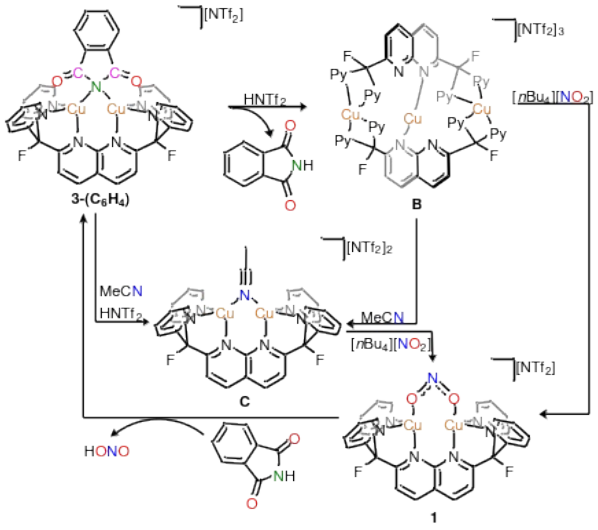


A plausible mechanism for the formation of **3-(Ar)** is shown in Scheme 4. Upon formation of the *N*-nitrosamide complex, **int1**, by an initial nucleophilic attack of the nitrite on a cyano *sp*-hybridized carbon **(i)**, a second nucleophilic attack by the nitroso group on the other cyano group leads to an N-C bond between the cyano nitrogen atom and the acyl carbon **(ii)**. Reconstitution of the acyl C=O double bond results in dinitrogen formation and full oxo transfer to the cyano carbon **(iii)**. Finally, dinitrogen extrusion forms the coupling product **3-(Ar) (iv)**. Thus, this transformation can be best understood as an unusual cascade reaction facilitated by bimetallic copper(I) complex.

The unique nature of these reactions motivated attempts to complete a stoichiometric synthetic cycle that allows production of a phthalimide derivative from a 1,2-dicyanoarene. This would involve release of the phthalimide group (e.g., by protonation or alkylation) followed by regeneration of the nitrite complex **1**. In the Gabriel synthesis, phthalimide salts are known to react with alkyl halides in an S_N2 reaction to form an *N*-alkyl phthalimide, which can then be treated with hydrazine to produce the corresponding primary amine.[30] Given this, **3-(4-PrOC$_6$H$_3$)** was treated with benzyl chloride (1 equiv) in THF at 80 °C for 1 d. Surprisingly, **3-(4-PrOC$_6$H$_3$)** remained completely unconsumed (Figure S28). The same results were observed when treating the complex with stoichiometric amounts of methyl triflate in *o*-DFB (Figure S29). These results suggest that the bonding interaction between the phthalimide ligand and the dicopper core is very strong, contributing to its low nucleophilicity. The more electrophilic character of the phthalimide ligands is highlighted by the rapid reaction of **3-(4-PrOC$_6$H$_4$)** and LiCl to yield [Cu_2(μ-Cl)DPFN][NTf_2][31] and the lithium phthalimide salt *in situ*, in 68 and 99% yield, respectively (vs. an internal standard; Figure S30).

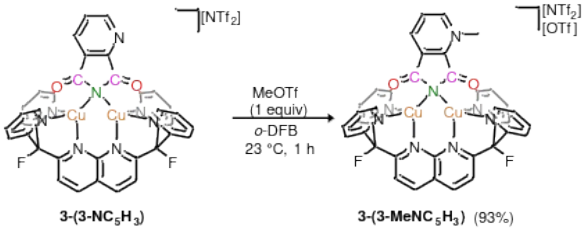
Free phthalimide is fairly acidic (pK_a = 8.3) due to conjugate base stabilization provided by the resonance of its two carbonyl groups.[32,33] However, treatment of **3-(C$_6$H$_4$)** with 1 equiv of pentafluorophenol (pK_a = 5.5) in THF at 60 °C for 4 days did not produce the neutral phthalimide, again demonstrating the stability of the fragment (Figure S32).[34] Complex **3-(C$_6$H$_4$)** was successfully protonated with bistriflimidic acid ($HNTf_2$; pK_a = -12.3), causing release of the phthalimide from the dicopper core.[35] As previously reported, ligand loss at the dicopper core promotes formation of the tricationic complex [Cu_3(DPFN)$_2$][NTf_2]$_3$ (**B**), which was observed (97% vs. an internal standard) in the reaction solution by ^{1}H NMR spectroscopy (Scheme 5, Figure S34).[31] Addition of a stoichiometric amount of [*n*-Bu_4N][NO_2] to the THF solution at 23 °C led to an instantaneous color change from orange to red and formation of **3-(C$_6$H$_4$)** in 70% yield (assuming that only 0.75 equiv of **3-(C$_6$H$_4$)** can form from 1 equiv of **B**).

Scheme 5. Production of 1 from 3-(C$_6$H$_4$) *via* protonation



These results establish the stoichiometric, synthetic cycle of Scheme 5, and provide two valuable insights: (i) The reaction of compound **C** and a suitable bridging ligand can reconstitute the dicopper(DPFN) motif. (ii) Complex **1** can indeed be produced from **3-(Ar)** given subsequent addition of a strong acid and a nitrite source to achieve a synthetic cycle, but **1** quickly reacts with the neutral phthalimide in solution in an acid-base exchange to yield **3-(Ar)** and presumably nitrous acid (HONO) in a fashion akin to its reactions with thiols (Scheme 5).[36] Independently treating compound **1** with phthalimide yields the same result (Figure S36). This is also supported by the formation of $[Cu_2(\mu\text{-MeCN})DPFN][NTf_2]_2$ (**C**) in 97% yield (vs. an internal standard) when the protonation with $HNTf_2$ is conducted in the presence of MeCN-d_3 (Scheme 5, Figure S35).[37] If $[n\text{-Bu}_4N][NO_2]$ is added after the phthalimide is removed, then the stoichiometric cycle can be closed from **B** or **C** to form the di-Cu(I) nitrite complex. However, the similar solubility profiles of the air-sensitive dicopper complexes discussed so far and phthalimides make their separation non-trivial.

Scheme 6. Methylation of 3-(3-NC_5H_3) with MeOTf to yield 3-(3-$MeNC_5H_3$)



The stability of the dicopper-phthalimide bonding interaction presents an opportunity for post-synthetic modification of the phthalimide ligand. To explore this possibility, **3-(3-NC_5H_3)** was treated with methyl triflate (1 equiv) in *o*-DFB at 23 °C.[38] Over the course of 1 h, the solution changed from red to purple and ^{1}H NMR analysis indicated successful methylation of the pyridine nitrogen to form $[Cu_2(\mu\text{-N(CO)}_2(3\text{-MeNC}_5H_3)DPFN][NTf_2]$ (**3-(3-$MeNC_5H_3$)**; Scheme 6) in high yield (93%). Purple crystalline blocks grew in the reaction vessel as the reaction transpired. These were subjected to single crystal X-ray diffraction, and the solid-state structure of compound **3-(3-$MeNC_5H_3$)** was determined (Figure 2). The average Cu-Cu distance and Cu-N bond length of 2.5374(8) Å and 2.047(4) Å, respectively, in this compound are slightly longer than those of the parent compound **3-(3-NC_5H_3)** (Cu-Cu = 2.5284(6) Å and Cu-N = 2.0295(3) Å). While pyridine methylation by MeOTf is known, these results suggest that the dicopper phthalimide bonding interaction could withstand more elaborate post-synthetic modifications to the phthalimide ligand.[39] Such alterations may provide more accessible ways to close the stoichiometric cycle.

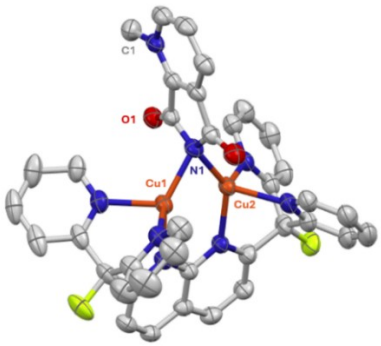


Figure 3. Solid-state molecular structure of compound **3-(3-$MeNC_5H_3$)** with thermal ellipsoids drawn at 50% probability. Hydrogen

atoms, bistriflimide (NTf_2^-), and triflate (OTf^-) anions are omitted for clarity.

CONCLUSION

This study demonstrates the divergent reactivity of the di-Cu(I) nitrite complex with 1,2-dicyanoarenes. The phthalimide complexes **3-(Ar)** likely result from an intramolecular nucleophilic attack by the nitroso fragment of a di-Cu(I) *N*-nitrosamide intermediate on its remaining cyano group. The phthalimide ligands on compounds **3-(Ar)** appear to have a strong bonding interaction with the dicopper core, allowing for further functionalization after their synthesis. The preference of the *N*-nitrosamide intermediate for an intramolecular nucleophilic attack rather than a 1,3-acyl shift suggests that other types of intramolecular cascade reactions, involving electrophilic carbon centers *ortho* to the nitrile (in e.g., alkynyl, acyl, formyl, etc.), could provide new routes to heterocycles.

ASSOCIATED CONTENT

Supporting Information

The supporting information is available free of charge at http://journal.org.
Detailed experimental methods, including characterization data, spectra, and details of X-ray crystallography (PDF)

Accession Codes

CCDC 2499266-2499269 contain the supplementary crystallographic data for this paper. This data can be obtained free of charge via www.ccdc.cam.ac.uk, or by contacting the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

AUTHOR INFORMATION

Corresponding Authors

T. Don Tilley - Department of Chemistry, University of California, Berkeley, Berkeley, California 94720-1460, United States; Chemical Sciences Division, Lawrence Berkeley National Laboratory, Berkeley, California 94720, United States; orcid.org/0000-0002-6671-9099

Email: tdtilley@berkeley.edu

Authors

Jose Martinez Fernandez - Department of Chemistry, University of California, Berkeley, Berkeley, California 94720-1460, United States; Chemical Sciences Division, Lawrence Berkeley National Laboratory, Berkeley, California 94720, United States; orcid.org/0000-0001-5618-9322

Email: jose_m.f@berkeley.edu

Ai Vy Nguyen - Department of Chemistry, University of California, Berkeley, Berkeley, California 94720-1460, United States; Chemical Sciences Division, Lawrence Berkeley National Laboratory, Berkeley, California 94720, United States; orcid.org/0009-0001-5349-8880

Email: aivy.nguyen@berkeley.edu

Notes

The authors declare no competing financial interests.

ACKNOWLEDGMENTS

This work was primarily funded by the US Department of Energy, Office of Science, Office of Basic Energy Sciences, Chemical Sciences, Geosciences, and Biosciences Division, under Contract no. DE-AC02-05CH11231 (to T.D.T.). The LBNL Catalysis Laboratory provided HR-ESI-MS instrumentation. The work carried out at the Molecular Foundry was supported by the Office of Science, Office of Basic Energy Sciences, of the U.S. Department of Energy under Contract no. DE-AC02-05CH11231. T.D.T. is grateful to Mr. and Ms. Chen for their funding of the PMP Tech Chancellor's Chair in Chemistry. This material is based upon work supported by the National Science Foundation Graduate Research Fellowship Program under Grant No. DGE 1752814 (to JMF). Any opinions, findings, and conclusions or recommendations expressed in this material are those of the authors and do not necessarily reflect the views of the National Science Foundation. We thank Dr. Nick Settineri and the UC Berkeley CheXray crystallographic facility under grant no. S10RR027172 for crystallographic assistance. We

thank Drs. Hasan Celik, Raynald Giovine, and the Pines Magnetic Resonance Center's Core NMR Facility (PMRC Core) for spectroscopic assistance. We also thank Drs. Tianchang Liu and Marcel Bamberg for useful conversations and advice.

REFERENCES

(1) Huang, W.; He, D.; Jiang, H.; Wu, W. Recent Advances in the Transformation of Nitriles into Diverse *N*-Heterocycles. *Chem. Soc. Rev.* **2025**, 10.1039.D5CS00024F. https://doi.org/10.1039/D5CS00024F.

(2) Wu, P.; Zhang, X.; Pang, J.; Wei, G.; Zheng, M.; Zhang, T. State-of-the-Art Advancements in Synthesis of Nitriles from Primary Alcohols. *ACS Catal.* **2024**, *14* (19), 14436–14474. https://doi.org/10.1021/acscatal.4c04460.

(3) Kukushkin, V. Yu.; Pombeiro, A. J. L. Additions to Metal-Activated Organonitriles. *Chem. Rev.* **2002**, *102* (5), 1771–1802. https://doi.org/10.1021/cr0103266.

(4) Geyer, A. M.; Wiedner, E. S.; Gary, J. B.; Gdula, R. L.; Kuhlmann, N. C.; Johnson, M. J. A.; Dunietz, B. D.; Kampf, J. W. Synthetic, Mechanistic, and Computational Investigations of Nitrile-Alkyne Cross-Metathesis. *J. Am. Chem. Soc.* **2008**, *130* (28), 8984–8999. https://doi.org/10.1021/ja800020w.

(5) Beaumier, E. P.; Pearce, A. J.; See, X. Y.; Tonks, I. A. Modern Applications of Low-Valent Early Transition Metals in Synthesis and Catalysis. *Nat Rev Chem* **2018**, *3* (1), 15–34. https://doi.org/10.1038/s41570-018-0059-x.

(6) Finn, P. A.; King, M. S.; Kilty, P. A.; McCarley, R. E. Synthesis and Structure of Dinuclear Niobium and Tantalum Complexes Containing an Unusual Bridging Ligand Derived from Acetonitrile. *J. Am. Chem. Soc.* **1975**, *97* (1), 220–221. https://doi.org/10.1021/ja00834a056.

(7) Cotton, F. A.; Hall, W. T. A Binuclear Tantalum Compound Containing Bridging 1,2-Dimethyl-1,2-Diimidoethene Formed by Dimerization of Acetonitrile. *Inorg. Chem.* **1978**, *17* (12), 3525–3528. https://doi.org/10.1021/ic50190a039.

(8) Tsai, Y.-C.; Johnson, M. J. A.; Mindiola, D. J.; Cummins, C. C.; Klooster, W. T.; Koetzle, T. F. A Cyclometalated Resting State for a Reactive Molybdenum Amide: Favorable Consequences of β-Hydrogen Elimination Including Reductive Cleavage, Coupling, and Complexation. *J. Am. Chem. Soc.* **1999**, *121* (44), 10426–10427. https://doi.org/10.1021/ja9917464.

(9) Young, C. G.; Philipp, C. C.; White, P. S.; Templeton, J. L. Two-Electron Reductive Coupling of Acetonitrile to Form a (μ-Butane-2,3-Diimino(2-)-N:N')Ditungsten Complex. *Inorg. Chem.* **1995**, *34* (25), 6412–6414. https://doi.org/10.1021/ic00129a029.

(10) Segerer, U.; Blaurock, S.; Sieler, J.; Hey-Hawkins, E. Insertion of Acetonitrile into the Zr-P Bond of [Cp°$_2$ZrCl(PHCy)] (Cy = Cyclohexyl, Cp° = η^5-C_5EtMe_4) Followed by PHCy Elimination to Give [Cp°$_2$(Cl)Zr(μ-NCMe-CMeN)Zr(Cl)Cp°$_2$]. *Organometallics* **1999**, *18* (15), 2838–2842. https://doi.org/10.1021/om9901271.

(11) Tsai, Y.-C.; Stephens, F. H.; Meyer, K.; Mendiratta, A.; Gheorghiu, M. D.; Cummins, C. C. Reactions of Organic Nitriles with a Three-Coordinate Molybdenum(III) Complex and with a Related Molybdaziridine-Hydride. *Organometallics* **2003**, *22* (14), 2902–2913. https://doi.org/10.1021/om030124v.

(12) Burford, R. J.; Piers, W. E.; Parvez, M. Acetonitrile Coupling at an Electron-Rich Iridium Center Supported by a PCP Pincer Ligand. *Eur J Inorg Chem* **2013**, *2013* (22–23), 3826–3830. https://doi.org/10.1002/ejic.201300152.

(13) Hsieh, J. Transition-Metal-Catalyzed Addition/Cyclization Reactions of the C-N Multiple Bonds Containing Species. *The Chemical Record* **2021**, *21* (12), 3370–3381. https://doi.org/10.1002/tcr.202100008.

(14) Esjornson, D.; Fanwick, P. E.; Walton, R. A. Carbon-Carbon Bond Formation in the Reductive Coupling of Nitriles at a Multiply Bonded Dirhenium Center. *Inorg. Chem.* **1988**, *27* (18), 3066–3067. https://doi.org/10.1021/ic00291a004.

(15) Rosenthal, U. Reactions of Group 4 Metallocene Bis(Trimethylsilyl)Acetylene Complexes with Nitriles and Isonitriles. *Angew Chem Int Ed* **2018**, *57* (45), 14718–14735. https://doi.org/10.1002/anie.201805157.

(16) Becker, L.; Haehnel, M.; Spannenberg, A.; Arndt, P.; Rosenthal, U. Reactions of Group 4 Metallocenes with Monosubstituted Acetonitriles: Keteniminate Formation versus C-C Coupling. *Chemistry A European J* **2015**, *21* (8), 3242–3248. https://doi.org/10.1002/chem.201406219.

(17) Rehbaum, F.; Thiele, K.-H.; Trojanov, S. I. Darstellung und Molekülstruktur des (μ-Alkylidenamido)titanocenkomplexes [(C_5H_5)$_2$TiCl]$_2$[μ-{N=C($CH_2C_6H_5$)C($CH_2C_6H_5$)=N}]. *Journal of Organometallic Chemistry* **1991**, *410* (3), 327–333. https://doi.org/10.1016/0022-328X(91)83006-P.

(18) Kiel, G. R.; Samkian, A. E.; Nicolay, A.; Witzke, R. J.; Tilley, T. D. Titanocene-Mediated Dinitrile Coupling: A Divergent Route to Nitrogen-Containing Polycyclic Aromatic Hydrocarbons. *J. Am. Chem. Soc.* **2018**, *140* (7), 2450–2454. https://doi.org/10.1021/jacs.7b13823.

(19) Becker, L.; Arndt, P.; Jiao, H.; Spannenberg, A.; Rosenthal, U. Nitrile–Nitrile C-C Coupling at Group 4 Metallocenes to Form 1-Metalla-2,5-diaza-cyclopenta-2,4-dienes: Synthesis and Reactivity.

Angew Chem Int Ed **2013**, *52* (43), 11396–11400. https://doi.org/10.1002/anie.201303748.

(20) Martinez Fernandez, J.; Nguyen, A. V.; Gharaee, M.; Haji Seyed Javadi, A.; Cundari, T.; Tilley, T. D. Nitrile RC≡N Triple Bond Cleavage by a Dicopper Nitrite Complex with N_2 Elimination and Formation of RCO_2^- Carboxylate Ligands. *J. Am. Chem. Soc.* **2025**, *Accepted Pending Revisions*.

(21) Dry, E. F. V.; Clegg, J. K.; Breiner, B.; Whitaker, D. E.; Stefak, R.; Nitschke, J. R. Reversible Anion-Templated Self-Assembly of [2+2] and [3+3] Metallomacrocycles Containing a New Dicopper(I) Motif. *Chem. Commun.* **2011**, *47* (21), 6021. https://doi.org/10.1039/c1cc11206f.

(22) Zhang, X.-M.; Tong, M.-L.; Chen, X.-M. Hydroxylation of *N*-Heterocycle Ligands Observed in Two Unusual Mixed-Valence Cu^{I}/Cu^{II} Complexes. *Angew. Chem. Int. Ed.* **2002**, *41* (6), 1029–1031. https://doi.org/10.1002/1521-3773(20020315)41:6%253C1029::AID-ANIE1029%253E3.0.CO;2-B.

(23) Dhara, K.; Roy, P.; Ratha, J.; Manassero, M.; Banerjee, P. Synthesis, Crystal Structure, Magnetic Property and DNA Cleavage Activity of a New Terephthalate-Bridged Tetranuclear Copper(II) Complex. *Polyhedron* **2007**, *26* (15), 4509–4517. https://doi.org/10.1016/j.poly.2007.06.009.

(24) Desnoyer, A. N.; Nicolay, A.; Ziegler, M. S.; Lakshmi, K. V.; Cundari, T. R.; Tilley, T. D. A Dicopper Nitrenoid by Oxidation of a $Cu^{I}Cu^{I}$ Core: Synthesis, Electronic Structure, and Reactivity. *J. Am. Chem. Soc.* **2021**, *143* (18), 7135–7143. https://doi.org/10.1021/jacs.1c02235.

(25) Tran, B. L.; Li, B.; Driess, M.; Hartwig, J. F. Copper-Catalyzed Intermolecular Amidation and Imidation of Unactivated Alkanes. *J. Am. Chem. Soc.* **2014**, *136* (6), 2555–2563. https://doi.org/10.1021/ja411912p.

(26) Tye, J. W.; Weng, Z.; Johns, A. M.; Incarvito, C. D.; Hartwig, J. F. Copper Complexes of Anionic Nitrogen Ligands in the Amidation and Imidation of Aryl Halides. *J. Am. Chem. Soc.* **2008**, *130* (30), 9971–9983. https://doi.org/10.1021/ja076668w.

(27) Ponikiewski, L.; Shi, W.; Rothenberger, A. Synthesis and Structures of Metallated *N*-Heterocyclic Derivatives. *Zeitschrift anorg allge chemie* **2008**, *634* (10), 1770–1774. https://doi.org/10.1002/zaac.200800044.

(28) Sonawane, S. C.; Sabharwal, G.; Balakrishna, M. S. Cu^{I}–Amidobis(Phosphine)-Catalyzed Direct Amidation of Unactivated Alkanes via C(sp^3)–H Activation. *Org. Lett.* **2024**, *26* (22), 4589–4593. https://doi.org/10.1021/acs.orglett.4c01063.

(29) Liu, T.; Gau, M. R.; Tomson, N. C. Mimicking the Constrained Geometry of a Nitrogen-Fixation Intermediate. *J. Am. Chem. Soc.* **2020**, *142* (18), 8142–8146. https://doi.org/10.1021/jacs.0c01861.

(30) Gibson, M. S.; Bradshaw, R. W. The Gabriel Synthesis of Primary Amines. *Angew. Chem. Int. Ed. Engl.* **1968**, *7* (12), 919–930. https://doi.org/10.1002/anie.196809191.

(31) Ziegler, M. S.; Torquato, N. A.; Levine, D. S.; Nicolay, A.; Celik, H.; Tilley, T. D. Dicopper Alkyl Complexes: Synthesis, Structure, and Unexpected Persistence. *Organometallics* **2018**, *37* (16), 2807–2823. https://doi.org/10.1021/acs.organomet.8b00443.

(32) Kushwaha, N.; Kaushik, D. Recent Advances and Future Prospects of Phthalimide Derivatives. *J App Pharm Sci* **2016**, 159–171. https://doi.org/10.7324/JAPS.2016.60330.

(33) Bordwell, F. G. Equilibrium Acidities in Dimethyl Sulfoxide Solution. *Acc. Chem. Res.* **1988**, *21* (12), 456–463. https://doi.org/10.1021/ar00156a004.

(34) Bansal, D.; Sivaganesan, P.; Elanchezhian, C.; Nataraj, G.; Das, M. K.; Chaudhuri, S. Pentafluorophenol-Catalyzed Metal-Free Fischer Indole Synthesis: A Novel Approach to Carbazole Derivatives and Desbromoarborescidine A*. *Chemistry An Asian Journal* **2025**, *20* (10), e202500246. https://doi.org/10.1002/asia.202500246.

(35) Paenurk, E.; Kaupmees, K.; Himmel, D.; Kütt, A.; Kaljurand, I.; Koppel, I. A.; Krossing, I.; Leito, I. A Unified View to Brønsted Acidity Scales: Do We Need Solvated Protons? *Chem. Sci.* **2017**, *8* (10), 6964–6973. https://doi.org/10.1039/C7SC01424D.

(36) Martinez Fernandez, J.; Haji Seyed Javadi, A.; Teat, S. J.; Cundari, T. R.; Tilley, T. D. Synthetically Reversible, Proton-Mediated Nitrite N–O Bond Cleavage at a Dicopper Site. *J. Am. Chem. Soc.* **2024**, *146* (50), 34962–34969. https://doi.org/10.1021/jacs.4c14642.

(37) Ziegler, M. S.; Levine, D. S.; Lakshmi, K. V.; Tilley, T. D. Aryl Group Transfer from Tetraarylborato Anions to an Electrophilic Dicopper(I) Center and Mixed-Valence μ-Aryl Dicopper(I,II) Complexes. *J. Am. Chem. Soc.* **2016**, *138* (20), 6484–6491. https://doi.org/10.1021/jacs.6b00802.

(38) Zhao, W.; Sun, J. Triflimide ($HNTf_2$) in Organic Synthesis. *Chem. Rev.* **2018**, *118* (20), 10349–10392. https://doi.org/10.1021/acs.chemrev.8b00279.

(39) Rubinsztajn, S.; Fife, W. K.; Zeldin, M. Synthesis and Reactivity of 1-Methyl-4-Ethynylpyridinium Triflate. *Tetrahedron Letters* **1992**, *33* (14), 1821–1824. https://doi.org/10.1016/S0040-4039(00)74151-7.

For Table of Contents Only