

Communication

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Observation of a Photogenerated Rh₂ Nitrenoid Intermediate in C–H Amination

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Supporting Information Placeholder

ABSTRACT: Rh₂-catalyzed C–H amination is a powerful method for nitrogenating organic molecules. While Rh₂ nitrenoids are often invoked as reactive intermediates in these reactions, the exquisite reactivity and fleeting lifetime of these species has precluded their observation. Here, we report the photogeneration of a transient Rh₂ nitrenoid that participates in C–H amination. The developed approach to Rh₂ nitrenoids, based on photochemical cleavage of N–Cl bonds in *N*-chloroamido ligands, has enabled characterization of a reactive Rh₂ nitrenoid by mass spectrometry and transient absorption spectroscopy. We anticipate that photogeneration of metal nitrenoids will contribute to the development of C–H amination catalysis by providing tools to directly study the structures of these critical intermediates.

Since Kwart and Khan demonstrated that metal nitrenoids participate in C–H amination chemistry in 1967,¹ metal-catalyzed nitrogen-group-transfer catalysis has become an important technology for the construction of C–N bonds.² In particular, Rh₂ nitrenoids — typically generated by the combination of Rh₂ catalysts with iminoiodinane reagents (*e.g.* PhI=NR) — have emerged as powerful intermediates for C–H amination.^{1,3} The exceptional reactivity of Rh₂ nitrenoids has precluded the spectroscopic or structural characterization of these critical species.⁴ Thus ongoing efforts to develop new amination reactions must rely on computational descriptions of the reactive nitrenoid intermediates.⁵

Characterization of reactive intermediates is inherently challenging due to the fleeting nature of these species. Stable model complexes are often pursued in order to gain insight into the structure and reactivity of reactive intermediates.⁶ We have been attracted to synthetic photochemistry as a tool to access authentic reactive intermediates under conditions that allow their characterization without attenuating their reactivity.⁷ In contrast to metal oxo and nitrido complexes, which can be generated by photolysis of metal-bound oxyanions⁸ and azido ligands,⁹ respectively, there are no readily available photoprecursors to metal nitrenoid complexes. Here, we report the development of a new photochemical synthesis of metal nitrenoids, which has enabled the first spectroscopic observation of a Rh₂ nitrenoid intermediate in C– H amination.

We envisioned that a Rh₂ nitrenoid could be generated by photochemical homolysis of an N–X bond in an axially bound *N*-haloamide ligand (Scheme 1). Such a transformation would reduce the Rh₂ fragment by one electron, and thus a Rh₂[II,III] precursor is required to access the Rh₂[II,II] nitrenoids that mediate Rh₂-catalyzed C–H amination with iminoiodinanes.¹⁰ In contrast to the well-recognized facility of photochemical N–Cl homolysis in *N*-chloroamines to generate nitrogen-centered radicals (*i.e.* the Hofmann-Löffler-Freytag reaction),^{11,12} the photochemistry of transition-metal-bound *N*-chloroamido ligands is less well explored.¹³ Here we report the synthesis of a Rh₂ *N*-chloroamide complex and demonstrate



Scheme 1. Rh₂-catalyzed amination chemistry proceeds through a reactive nitrenoid intermediate generated by nitrene transfer from an iminoiodinane reagent. Here, we demonstrate that photogeneration of a Rh₂ nitrenoid enables direct spectroscopic observation of this critical reactive intermediate.



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Scheme 2. Synthesis of Rh₂ *N*-chloroamide 3. Complex 3 crystallizes from CH₃CN as a salt of Rh₂[II,III] ions: [Rh₂(espn)₂(MeCN)₂][Rh₂(espn)₂(NTsCI)₂].

that photolysis of this compound unveils a reactive Rh₂ nitrenoid that participates in C–H amination.

Treatment of Rh₂[II,III] chloride^{10b,14} **1** with AgBF₄ affords [Rh₂(espn)₂]BF₄ (**2**). Subsequent exposure of **2** to Na[NTsCI] affords Rh₂[II,III] *N*-chloroamido complex **3** (Scheme 2, espn = α , α , α' , α' -tetramethyl-1,3-benzenedipropanamidate, Ts = *p*-toluenesulfonate). Complex **3** crystallizes as a red-colored [Rh₂L₂S₂][Rh₂L₂X₂] salt from CH₃CN (L =espn, S = CH₃CN, X = NTsCI); the crystal structure of **3** features a cationic Rh₂[II,III] unit with two bound acetonitrile ligands and an anionic Rh₂[II,III] unit with two *N*-chloroamide ligands. For comparison, Rh₂ chloride **1** crystallizes from CH₂Cl₂ as extended (Rh–Rh–Cl–)_n chains^{10b} but crystallizes from CH₃CN as a [Rh₂(espn)₂(MeCN)₂][Rh₂(espn)₂Cl₂] salt.

34 Based on EPR, IR, and electronic absorption spectros-35 copies, as well as Evans method and DC susceptibility 36 measurements, Rh₂[II,III] complexes 1, 2, and 3 share a 37 common S = 1/2 ground state in which the unpaired elec-38 tron resides in a Rh–Rh δ^* orbital (Figures S1–S4).^{5,15} ESI-39 MS analysis of a MeCN solution of 3 displays a signal at 40 959.168, which is consistent with [Rh₂(espn)₂(NTsCl)]⁺. 41 The ¹H NMR spectrum of **3** measured in MeCN displays 42 more features than expected for 43 [Rh₂(espn)₂(NTsCl)(MeCN)] (Figure S5). Comparison of 44 the ¹H NMR spectrum of **3** with those of [Rh₂(espn)₂]BF₄ 45 46 (2) and Na[Rh₂(espn)₂(NTsCl)₂] (4), obtained by treat-47 ment of complex 1 with excess Na[NTsCl], indicates that 48 the solution structure of 3 is comprised of a ligand ex-49 change equilibrium mixture of the neutral complex 50 Rh₂(espn)₂(NTsCl)(MeCN) and salt 51 [Rh₂(espn)₂][Rh₂(espn)₂(NTsCl)₂] (see Supporting Infor-52 mation for additional discussion of the solution-phase 53 structure of 3). 54

Photolysis of a THF solution of Rh₂ complex **3** (λ > 400 nm) results in a red-to-green color change (Scheme 3).



Scheme 3. Photolysis of red-colored complex 3 ($\lambda > 400$ nm) results in consumption of 3 with concurrent evolution of green-colored Rh₂[II,II] complex 5 and amine 6. The observed reaction products – Rh₂[II,II] complex 5 and amine 6 – are consistent with amination by a photogenerated Rh₂ nitrenoid.

UV-vis analysis of the reaction mixture following photolysis indicates evolution of green-colored Rh₂[II,II] complex 5 (~100%, Figure S6) and ¹H NMR analysis of the reaction mixture indicates evolution of 6 (47 \pm 2%), the product of THF amination (Figure S7). The balance of nitrogen content is accounted for by $T_{S}NH_2$ (45 \pm 3%). Rh₂[II,II] complex 5 and tosylamide 6 are the products expected from initial N–Cl cleavage to generate a Rh₂ nitrenoid and Cl•. Nitrene-transfer from the Rh₂ nitreneoid to THF would generate Rh₂[II,II] complex 5 and amine 6 and H-atom abstraction (HAA) between THF and Cl• would generate HCl and THF radicals. We have not detected products derived from THF radicals but the evolution of HCl was confirmed by the formation of Et₃N·HCl upon addition of Et₃N to the photolysis reaction mixture (Figures S8 and S9). See Supporting Information for discussion of the amination of 2-methyl-THF and toluene.

In concept, the observed amination of THF could arise from a variety of reactive nitrogen species. For example, initial Rh–N cleavage could generate Rh₂[II,II] complex **5** and an aminyl radical that could engage in C–H amination. Alternately, photolysis could generate free tosylnitrene which could also engage in C–H amination. We have carried out a series of kinetic isotope effect (KIE) experiments to interrogate the nature of the reactive nitrogen species generated during photolysis of **3** (Table 1). Photolysis of **3** in a 1:1 THF : THF-*d*₈ mixture affords a KIE of 2.72(8). This value is well-matched to KIEs that have been previously measured for Rh₂-catalyzed C–H amination using iminoiodinanes as nitrene sources.¹⁶ In comparison, photolysis of Na[NTSCI] affords tosylamide **6** with a KIE of 4.4(3), which is consistent with amination via initial 



Conditions	Yield (6 + 6-d ₇)	к н / к р
Rh2(espn)2Cl, PhINTs	(ref. 5) ¹⁵	2.6
Rh ₂ complex 3, hv	48%	2.72(8)
Chloramine-T, hv	63%	4.4(3)
TsN ₃ , <i>hv</i>	7%	1.48(2)

HAA from THF.¹⁷ The potential intermediacy of free nitrenes was investigated by photolysis of TsN₃.¹⁸ Analysis of the amination of THF under these conditions affords a KIE of 1.48(2). The similarity of the KIE measured for photochemical amination of THF with that of Rh₂-catalyzed amination, and the dissimilarity with the KIEs measured for amination via aminyl radical and free nitrene intermediates, suggests photolysis of Rh₂ complex **3** generates a Rh₂ nitrenoid.

With a photosynthetic approach to a chemically and kinetically competent Rh_2 nitrenoid in hand, we turned our attention to observation of the reactive intermediate involved in amination chemistry. At low laser intensity, MALDI mass spectrometric analysis of **3** displayed an m/z = 754.153, which corresponds to $[Rh_2(espn)_2]^+$. As the laser intensity was increased, we observed the emergence of an m/z signal at 923.458, which corresponds to nitrenoid **7** (Scheme 4a). Mass spectrometry analysis of ¹⁵N-labeled **3** displays a shift to 924.555, which is expected for replacement of the ¹⁴N with ¹⁵N. In addition to the parent ions, m/z signals at 962.464 and 963.547 are also observed, which correspond to the mass of ¹⁴N- and ¹⁵N labeled nitrenoid **7** with a bound MeCN ligand (Figure S10).

We have carried out transient absorption (TA) experiments to obtain spectroscopic information regarding the reactive intermediate in amination. Laser-flash photolysis (λ = 280 nm or 355 nm¹⁹) of Rh₂ complex **3** in CH₂Cl₂ reveals a transient growth centered at ~580 nm in the prompt spectrum (red, Scheme 4b). The decay of this lower-energy feature is accompanied by the development of a spectral bleach centered at ~450 nm. The spectrum acquired after a delay of 200 µs corresponds to the difference spectrum expected for consumption of 3 and formation of Rh₂[II,II] complex 5 (blue, Scheme 4b). The time constants for the decay of the feature at 580 nm and for the bleach at 450 nm are 11.6 \pm 2.7 μs and 10.1 \pm 3.8 us, respectively. This similarity of temporal evolution of the two observed transient features suggests that they arise from the same chemical process. Time-dependent density functional theory (TD-DFT) calculations of Rh₂[II,III] complexes 1, 2, 3, and nitrenoid 7 have been



Scheme 4. (a) Rh₂ nitrenoid has been observed by MALDI-MS. ¹⁵N-labeled 3 provides the expected M+1 *m/z* shift. (b) TA spectra obtained by laser flash photolysis of a THF solution of 3 (λ_{pump} = 280 nm). The prompt spectrum (red) displays a transient growth centered at 580 nm that we attribute to Rh₂ nitreneoid **7**. The prompt spectrum evolves over the course of 200 µs to a spectrum (blue) that displays a spectral bleach that corresponds to consumption of **3**. Single wavelength kinetics indicate that the disappearance of the growth at 580 nm and the appearance of the bleach at 450 nm are temporally coupled, suggesting evolution of these two signals is related to the same chemical process. (c) The low-energy feature (580 nm) observed in the spectrum of nitrenoid **7** arises from predominantly Rh–Rh π (left) to Rh–N π^* (right) excitation.

carried out to gain insight into the TA spectra observed (see Supporting Information for computational details). Each of the Rh₂[II,III] complexes **1**, **2**, and **3** share a common absorbance that is primarily derived from a Rh–Rh π to Rh–O π^* transition. The computed spectrum of nitrenoid **7** shares the absorbance of the Rh₂[II,III] structures as well as a lower-energy absorbance that predominantly arises from Rh–Rh π to Rh–N π^* excitation. The computed spectra of **3** and **7** are consistent with the TA spectra that display a prompt low-energy growth and the subsequent evolution of a higher energy bleach. In conclusion, we have described photogeneration of a Rh₂ nitrenoid intermediate in C–H amination. Based on the observed photochemical C–H amination, the similarity of the KIE for C–H amination to that of Rh₂-catalyzed amination reactions, the observation of *m/z* for a molecular Rh₂ nitrenoid, and TA spectroscopy correlated with TD-DFT calculations, the developed photochemistry enables the first spectroscopic observation of critical Rh₂ nitrenoid (*i.e.* **7**) implicated in amination chemistry. We anticipate that photochemical access to reactive metal nitrenoids will facilitate direct characterization of these critical amination intermediates, and thus contribute to the rational development of C–H amination chemistry.

ASSOCIATED CONTENT

Supporting Information. Experimental procedures, spectroscopic data, optimized structure coordinates (PDF, cif). Crystallographic data deposited in Cambridge Crystal Structure Database (1845233–1845238, 1855308). The Supporting Information is available free of charge on the ACS Publications website.

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31 Notes

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The authors declare no competing financial interest.

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REFERENCES

46 (1) Kwart, H.; Khan, A. A. J. Am. Chem. Soc. **1967**, 87, 1951–1953.

47 (2) (a) Park, Y.; Kim, Y.; Chang, S. Chem. Rev. 2017, 117, 9247-9301. 48 (b) Brandenberg, O. F.; Fasan, R.; Arnold, F. H. Curr. Opin. Biotech. 49 2017, 47, 102-111. (c) Dequirez, G.; Pons, V.; Dauban, P. Angew. Chem. Int. Ed. 2012, 51, 7384–7395. (d) Roizen, J. L.; Harvey, M. E.; Du 50 Bois, J. Acc. Chem. Res. 2012, 45, 911-922. (e) Du Bois, J. Org. Proc. 51 Res. Dev. 2011, 15, 758-762. (f) Zalatan, D. N.; Du Bois, J. Top. Curr. 52 Chem. 2010, 292, 347-378. (g) Davies, H. M. L.; Manning, J. R. Davies, 53 H. M. L.; Manning, J. R. Nature 2008, 451, 417-424. (h) Godula, K.; 54 Sames, D. Science 2006, 312, 67-72. 55

(3) (a) Paudyal, M. P.; Adebesin, A. M.; Burt, S. R.; Ess, D. H.; Ma, Z.;
Kürti, L.; Falck, J. R. *Science* 2016, *353*, 1144–1147. (b) Jat, J. L.;
Paudyal, M. P.; Gao, H; Xu, Q.-L.; Yousufeddin, M.; Devarajan, D.; Ess,

D. H.; Kürti, L.; Falck, J. R. *Science* **2014**, *343*, 61–65. (c) Kornecki, K. P.; Berry, J. F. *Chem. Commun.* **2012**, *48*, 12097–12099. (d) Fiori, K. W.; Du Bois, J. *J. Am. Chem. Soc.* **2007**, *129*, 562–568. (e) Espino, C. G.; Fiori, K. W.; Kim, M.; Du Bois, J. *J. Am. Chem. Soc.* **2004**, *126*, 15378– 15379. (f) Espino, C. G.; Du Bois, J. *Angew. Chem. Int. Ed.* **2001**, *40*, 598–600. (g) Müller, P.; Baud, C.; Jacquier, Y. *Tetrahedron* **1996**, *52*, 1543–1548. (h) Breslow, R. Gellman, S. H. J. Am. Chem. Soc. **1983**, *105*, 6728–6729.

(4) Perry, R. H.; Cahill, T. J., III; Roizen, J. L.; Du Bois, J.; Zare, R. N. *Proc. Nat. Acad. Sci.* **2012**, *109*, 18295–18299.

(5) Varela-Álvarez, A.; Yang, T.; Jennings, H.; Kornecki, K. P.; Macmillan, S. N.; Lancaster, K. M.; Mack, J. B. C.; Du Bois, J.; Berry, J. F.; Musaev, D. G. *J. Am. Chem. Soc.* **2016**, *138*, 2327–2341.

(6) (a) Iovan, D. A.; Betley, T. A. *J. Am. Chem. Soc.* **2016**, *138*, 1983– 1993. (b) Kornecki, K. P.; Briones, J. F.; Boyarskikh, V.; Fullilove, F.; Autschbach, J.; Schrote, K. E.; Lancaster, K. M.; Davies, H. M. L.; Berry, J. F. *Science* **2013**, *342*, 351–354. (c) Rohde, J.-U.; In, J. H.; Lim, M. H.; Brennessel, W. W.; Bukowski, M. R.; Stubna, A.; Munck, E.; Nam, W. Que, L., Jr. *Science* **2003**, *299*, 1037–1039.

(7) Das, A.; Reibenspies, J. H.; Chen, Y.-S.; Powers, D. C. J. Am. Chem. Soc. **2017**, 139, 2912–2915.

(8) (a) Corcos, A. R.; Pap, J. S.; Yang, T.; Berry, J. F. *J. Am. Chem. Soc.* **2016**, *138*, 10032–10040. (b) Zhang, R.; Newcomb, M. *Acc. Chem. Res.* **2008**, *41*, 468–477. (c) Cheng, M.; Bakac, A. J. Am. Chem. Soc. 2008, 130, 5600. (d) Kunkely, H.; Vogler, A. *J. Am. Chem. Soc.* **1995**, *117*, 540–541.

(9) (a) Smith, J. M. Prog. Inorg. Chem. **2014**, 58, 417–470. (b) Berry, J. F. Comm. Inorg. Chem. **2009**, 30, 28–66.

(10) Mixed-valent Rh₂[II,III] complexes have also been observed in amination reactions, although the role of Rh₂[II,III]-derived nitrenoid intermediates continues to be discussed. For discussion, see (a) ref. 5,
(b) Kornecki, K. P.; Berry, J. F. *Chem. Eur. J.* **2011**, *17*, 5827–5832. (c) Zalatan, D. N.; Du Bois, J. J. Am. Chem. Soc. **2009**, *131*, 7558–7559.

(11) (a) Stateman, L. M.; Nakafuku, K. M. Nagib, D. A. Synthesis 2018, 50, 1569–1586. (b) Zard, S. Z. Chem. Soc. Rev. 2008, 37, 1603–1618.
(c) Neale, R. S. Synthesis 1971, 1–15. (d) Wolff, M. E. Chem. Rev. 1961, 63, 55–64.

(12) For discussion of the photochemical N–Cl homolysis in Chloramine-T, see: Evans, J. C.; Jackson, S. K.; Rowlands, C. C.; Barratt, M. D. *Tetrahedron* **1985**, *41*, 5191–5194.

(13) The only crystallographically characterized example of a metal complex with an *N*-chlorosulfonamide ligand is a Sn complex reported in: Shcherbakov, V. I.; Kuznetsova, V. P.; Chuprunov, E. V.; Ovsetsina, T. I.; Stolyarova, N. E.; Zakharov, L. N.; Novgorod, N. *Organomet. Chem. (USSR)* **1991**, *4*, 1350–1354.

(14) A number of isomers of Rh₂[II,III] complex **3** are known. All experiments reported here utilize the *cis*-(2,2) isomer in which each Rh center features RhN₂O₂ ligation.

(15) (a) Lutterman, D. A.; Degtyareva, N. N.; Johnston, D. H.; Gallucci, J. C.; Eglin, J. L.; Turro, C. *Inorg. Chem.* **2005**, *44*, 5388–5396.
(b) Kawamura, T.; Maeda, M.; Miyamoto, M.; Usami, H.; Imaeda, K.; Ebihara, M. *J. Am. Chem. Soc.* **1998**, *120*, 8136–8142.

(16) The $k_h/k_D = 2.9$ was measured for the intramolecular amination of 3-phenylpropyl-3-*d* sulfamate (ref. 5). The KIE for Rh₂-catalyzed amination of THF cannot be directly measured due to fast background reactions of PhINTs with THF to generate **6**.

(17) For examples of kinetic isotope effects of HAA by aminyl radicals, see: (a) Martínez, C.; Muñiz, K. *Angew. Chem. Int. Ed.* **2015**, *54*, 8287–8291. (b) Corey, E. J.; Hertler, W. R. *J. Am. Chem. Soc.* **1960**, *82*, 1657–1668.

(18) Shainyan, B. A.; Kuzmin, A. V. J. Phys. Org. Chem. 2014, 27, 156–162.

(19) Flash photolysis at these wavelengths afforded qualitatively identical spectra. Steady-state photolysis of **3** with a 325–385 nm bandpass filter also afforded **5** and **6**.



