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Heterocycle Synthesis

Photocatalytic Generation of N-Centered Hydrazonyl Radicals: A Strategy for Hydroamination of β,γ-Unsaturated Hydrazones**

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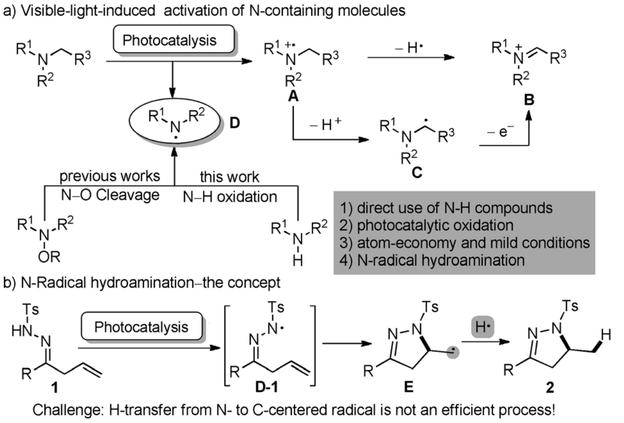
Abstract: *A visible-light photocatalytic generation of N-centered hydrazonyl radicals has been accomplished for the first time. This approach allows efficient intramolecular addition of hydrazonyl radical to terminal alkenes, thus providing hydroamination and oxyamination products in good yields. Importantly, the protocol involves deprotonation of an N−H bond and photocatalytic oxidation to an N-centered radical, thus obviating the need to prepare photolabile amine precursors or the stoichiometric use of oxidizing reagents.*

Nitrogen-containing heterocycles are ubiquitous in biologically active natural isolates and pharmaceuticals,[1] and have also found broad application in chemical, medical, and life sciences.[2] The development of atom-economic and direct synthetic approaches to these heterocycles has received considerable attention. In this context, intramolecular alkene hydroamination has been emerging as a versatile method for the synthesis of structurally diverse N-heterocycles.[3] Despite impressive achievements in the field of transition-metal-catalyzed hydroamination, the catalytic modes, substrate scope, and functional-group tolerance of this protocol are still limited.[4] Therefore, the exploration of new strategies and reagents to develop more efficient and greener methodologies for the rapid assembly of N-heterocycles is highly desirable. Given the functional-group compatibility and versatile reactivity of radicals, radical hydroamination involving neutral N-centered radicals should be a powerful and important platform for identifying new inter- and intramolecular hydroamination by using suitable N-radical precursors and radical initiators.[5,6] In this regard, both 1,3-diazaallyl radicals, derived from amidine by copper-catalyzed oxidation,[7] and hydrazonyl radicals, generated from hydrazones by stoichiometric use of TEMPO or azodicarboxylates, have proven to be valuable N-radicals for intramolecular cyclization.[8] To our knowledge, however, direct catalytic transformation of the N−H bond of hydrazone into an N-centered radical, and exploitation of such radical species in hydroamination of alkenes remains largely unexplored.

Recently, visible-light photocatalysis has spurred extensive research efforts because of its ability to generate various reactive radical or ionic species, thus allowing the design of new reactions proceeding under mild reaction conditions.[9] In this regard, three main activation modes for N-containing molecules have been developed using such a catalytic strategy (Scheme 1 a), including: 1) direct oxidation of amines to the nitrogen radical cation **A** by the excited state of a photocatalyst;[10] 2) further transformation of **A** into the iminium ion **B** upon release of a hydrogen atom, and its trapping by a wide range of nucleophiles;[11] and, 3) further conversion of **A** into the radical **C** after deprotonation.[12] Despite these advances, little attention has been devoted to the application of visible-light photocatalysis to the generation of neutral N-centered radicals of the type **D**. Reaction design with such radical species remain largely unexploited because of the



Scheme 1. Visible-light-induced photocatalytic activation of N-containing compounds and reaction design on N-centered radical. Ts = 4-toluenesulfonyl.

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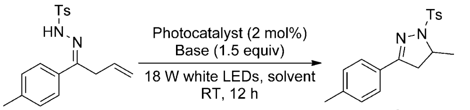
requisite use of unstable precursors (e.g., N-halogen, N-nitrosoamides) or tedious preparation procedure.[5] Moreover, traditional methods involving high-energy UV irradiation or high reaction temperature has also caused limitations in functional-group tolerance and substrate scope.

Recently, the group of MacMillan reported an imidazolidinone-catalyzed enantioselective α-amination of aldehydes by using electrophilic N-centered radicals generated from carbamate reagents by photocatalysis (Scheme 1 a).[13] Sanford and co-workers developed a photocatalytic C–H amination of arenes using *N*-acyloxyphthalimides as N-centered radical precursors.[14] In these processes, the incorporation of a photolabile group as a handle for the amine substrates was essential to the formation of the N-radical. Based on our recent success in photocatalytic synthesis of heterocycles,[15] we hypothesized that the direct transformation of the N–H bond into an N-centered radical by photocatalysis would provide a new strategy for the hydroamination of alkenes. However, realization of this concept would encounter a major challenge in that H-atom transfer from an N- to C-centered radical usually is not an efficient process.[16] Herein, we report a photocatalytic entry to N-centered hydrazonyl radicals from β,γ-unsaturated hydrazones,[17] and show that this activation mode leads to efficient intramolecular hydroamination reactivity (Scheme 1 b).

Initially, we selected the β,γ-unsaturated hydrazone **1a** as a model substrate to test the feasibility of its intramolecular hydroamination using $[Ir(ppy)_2(dtbbpy)]PF_6$ as a photocatalyst under irradiation by an 18W white LED light (Table 1). Gratifyingly, the reaction does indeed occur with Cs_2CO_3 as the base in CH_2Cl_2 at room temperature, thus giving the desired 4,5-dihydropyrazole **2a** in 17 % yield (entry 1). The structure of **2a** was unambiguously confirmed by NMR spectroscopy and X-ray diffraction analysis.[18] Encouraged by this result, other reaction parameters were then extensively investigated to improve the efficiency. A brief survey of reaction media showed that the reaction in $CHCl_3$ gave rise to a 40 % yield of **2a** (entry 5), while DMF and DMSO only led to low yields (entries 3 and 4). In addition, the effect of photocatalysts on the reaction was also examined, and the yield of **2a** was dramatically improved to 57 % with $[Ru(bpy)_3]Cl_2{\cdot}6H_2O$ as the catalyst (entry 9). Interestingly, a screen of common inorganic bases identified NaOH as the best of choice, thus affording **2a** in 71 % yield, when using 3 W blue LEDs as light source (entry 13). To confirm that the observed reactivity was due to the visible-light photocatalytic activation, some control experiments were performed. It was found that the photocatalyst, base, and light source are all critical to this transformation (entries 14–16).

Table 1: Optimization for the photocatalytic N-radical hydroamination[a]



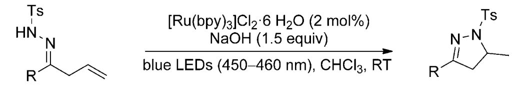
1a

2a
(characterized by
X-ray crystallography)

Entry	Solvent	Photocatalyst	Base	Yield [%][b]
1	CH_2Cl_2	$[Ir(ppy)_2(dtbbpy)]PF_6$	Cs_2CO_3	17
2	MeOH	$[Ir(ppy)_2(dtbbpy)]PF_6$	Cs_2CO_3	26
3	DMF	$[Ir(ppy)_2(dtbbpy)]PF_6$	Cs_2CO_3	15
4	DMSO	$[Ir(ppy)_2(dtbbpy)]PF_6$	Cs_2CO_3	<5
5	$CHCl_3$	$[Ir(ppy)_2(dtbbpy)]PF_6$	Cs_2CO_3	40
6	CH_3CN	$[Ir(ppy)_2(dtbbpy)]PF_6$	Cs_2CO_3	11
7	$CHCl_3$	EosinY	Cs_2CO_3	43
8	$CHCl_3$	$[Ir(ppy)_2(dtbbpy)]PF_6$	Cs_2CO_3	54
9	$CHCl_3$	$[Ru(bpy)_3]Cl_2{\cdot}6H_2O$	Cs_2CO_3	57
10	$CHCl_3$	$[Ru(bpy)_3]Cl_2{\cdot}6H_2O$	K_2CO_3	68
11	$CHCl_3$	$[Ru(bpy)_3]Cl_2{\cdot}6H_2O$	$NaHCO_3$	67
12	$CHCl_3$	$[Ru(bpy)_3]Cl_2{\cdot}6H_2O$	NaOH	71
13[c]	$CHCl_3$	$[Ru(bpy)_3]Cl_2{\cdot}6H_2O$	NaOH	74 (71)
14[d]	$CHCl_3$	–	NaOH	trace
15[e]	$CHCl_3$	$[Ru(bpy)_3]Cl_2{\cdot}6H_2O$	–	trace
16[f]	$CHCl_3$	$[Ru(bpy)_3]Cl_2{\cdot}6H_2O$	NaOH	trace

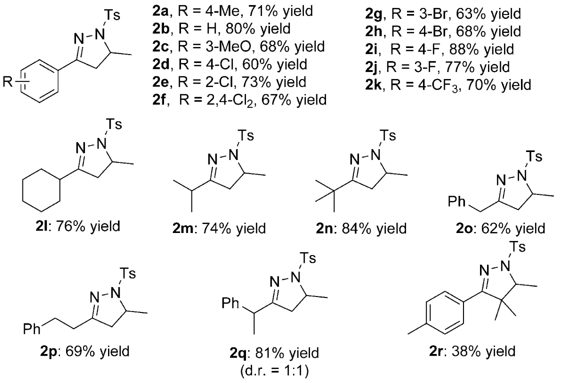
[a] Reaction conditions: **1a** (0.2 mmol), photocatalysts (2 mol %), base (0.3 mmol), solvents (3.0 mL), 18 W white LEDs, at room temperature. [b] Determined by GC using biphenyl as an internal standard. [c] Using 3 W blue LEDs as the light source. Yield of isolated product given within parentheses. [d] Without photocatalyst. [e] Without base. [f] Without visible light irradiation. bpy = 2,2′-bipyridine, dtbbpy = 4,4′-di-*tert*-butyl-2,2′-bipyridine, ppy = 2-phenylpyridine, DMF = *N*,*N*-dimethylformamide, DMSO = dimethylsulfoxide.

Table 2: Scope of photocatalytic N-radical hydroamination of β,γ-unsaturated hydrazones.[a,b]



1

2

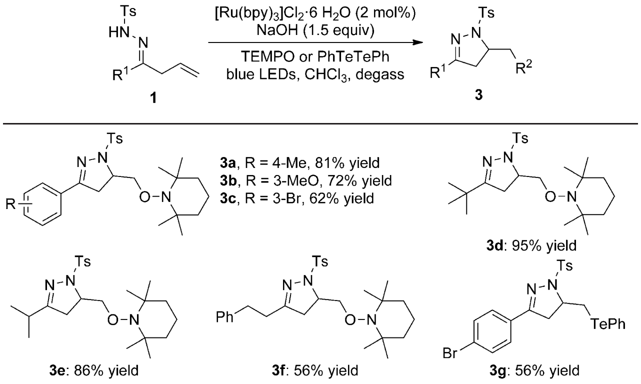


[a] Reaction conditions: **1** (0.3 mmol), $[Ru(bpy)_3]Cl_2{\cdot}6H_2O$ (2 mol %), NaOH (0.45 mmol), $CHCl_3$ (4.5 mL), 3 W blue LEDs (450–460 nm), at room temperature for 12–16 h. [b] Yield is that of the isolated product.

Then, we investigated the scope of this N-radical hydroamination reaction by using a series of β,γ-unsaturated hydrazones. As shown in Table 2, substitution patterns and electronic properties of the phenyl ring of the β,γ-unsaturated hydrazones had no obvious influence on the reaction efficiency. A range of β,γ-unsaturated hydrazones bearing electron-donating and electron-withdrawing groups at either the 2-, 3-, or 4-position of the aromatic ring underwent the desired reaction smoothly to give the corresponding products **2b–k** in 60–88 % yield. Notably, the hydrazones **1g** and **1h**, having sensitive groups such as 3-Br and 4-Br substituents, were also well tolerated and produced **2g** (63 %) and **2h** (68 %), respectively. Strong electron-withdrawing group such as CF_3 group can be present on the aromatic ring, thus furnishing a 70% yield of **2k**. Moreover, the reaction also proceeds efficiently with aliphatic hydrazones. The cyclohexyl-substituted hydrazone **1l** proved to be suitable for this reaction to provide **2l** in 76% yield. An array of other representative alkyl groups, such as isopropyl, *tert*-butyl, benzyl, and phenylethyl groups, were tolerated under the standard reaction conditions, thus giving **2m–q** in 62–84% yield. The reaction with **1r**, bearing geminal methyl groups at the α-position also worked well to give **2r** in 38% yield.

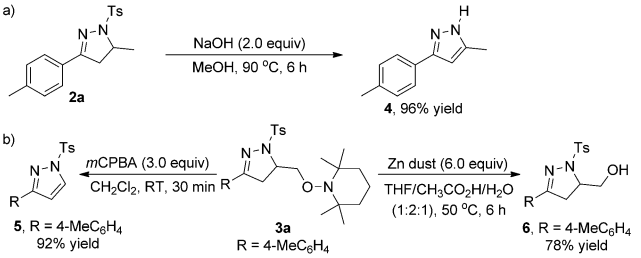
According to the reaction design, a C-centered radical is likely a key intermediate during the process, and might be intercepted by radical quenchers. As expected, addition of TEMPO (2.0 equiv) to the model reaction resulted in the formation of **3a** in 81% yield (Table 3). This finding suggests that the process does indeed involve radical intermediates. It should also be noted that this reactivity provides an opportunity to develop photocatalytic oxyamination of olefins. Thus, we quickly surveyed the scope of the reaction. The hydrazones bearing electron-donating (4-MeO) or electron-withdrawing (3-Br) groups participated in the reaction smoothly to give the products **3b** (72%) and **3c** (62%), respectively. Importantly, *tert*-butyl, isopropyl-, and phenylethyl-substituted β,γ-unsaturated hydrazones can also undergo the desired reaction efficiently, thus affording the oxyamination products **3d** and **3f**, respectively, in 56–95% yield. When using PhTeTePh, the radical cyclization/intermolecular addition cascade proceeded well to produce **3g** in 56% yield.

Table 3: Trapping of C-centered radical intermediates with TEMPO or PhTePh: Preliminary scope study.[a,b]



[a] Reaction conditions: **1** (0.3 mmol), TEMPO (0.6 mmol) or PhTeTePh (1.2 mmol), $[Ru(bpy)_3]Cl_2{\cdot}6\,H_2O$ (2 mol%), NaOH (0.45 mmol), $CHCl_3$ (4.5 mL), 3 W blue LEDs (450–460 nm), at room temperature for 12–16 h. [b] Yield is that of the isolated product. TEMPO = 2,2,6,6-tetramethylpiperidine-*N*-oxyl.

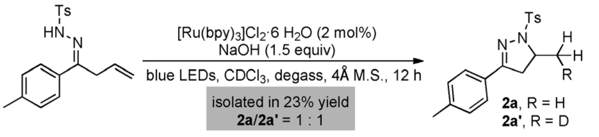
To demonstrate the synthetic potential of this methodology, several transformations of 4,5-dihydropyrazole products were carried out. The Ts group of **2a** can be easily removed under basic conditions to give the pyrazole **4** in 96% yield (Scheme 2a). Moreover, the oxyamination product **3a** can be oxidized directly to the biologically important pyrazole **5** by *m*CPBA through a Baeyer–Villiger oxidation/elimination sequence. The N−O bond of **3a** can easily be cleaved to afford the alcohol **6** in 78% yield (Scheme 2b).



Scheme 2. Synthetic applications. *m*CPBA = *m*-chloroperbenzoic acid, THF = tetrahydrofuran.

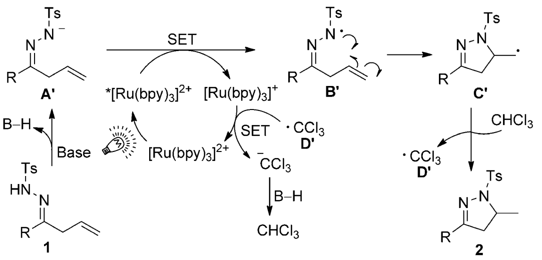
To gain some insight into the mechanism, we first carried out a series of luminescence-quenching experiments to support the hypothesis that the β,γ-unsaturated hydrazone **1a** might be initially oxidized by the excited state of the photocatalyst $*[Ru(bpy)_3]^{2+}$.[19] Surprisingly, no decrease of $[Ru(bpy)_3]^{2+}$ luminescence was observed by only adding **1a**. Based on studies from the group of Nicewicz on photocatalytic alkene hydrofunctionalization,[20] the low oxidizing power of the excited state of the photocatalyst $*[Ru(bpy)_3]^{2+}$ rendered it unable to oxidize the terminal double bond of **1a** to the corresponding radical cation. Given the important role of the base on the reaction, we conducted the luminescence quenching experiments under basic conditions. A significant decrease of $[Ru(bpy)_3]^{2+}$ luminescence was observed, and suggested that the nitrogen anion of **1a** quenched the excited photocatalyst $*[Ru(bpy)_3]^{2+}$.

The photocatalytic oxyamination of β,γ-unsaturated hydrazones with TEMPO further indicated that the reaction is a radical process and the C-centered radical was involved as a key intermediate (Table 3). To identify the hydrogen source of the desired product **2a**, the model reaction of **1a** was performed in $CDCl_3$. It was found that the reaction afforded a mixture of **2a** and **2a′** (1:1 ratio) in 23% combined yield (Scheme 3). These results confirmed that $CHCl_3$ worked as hydrogen source to facilitate the hydroamination process, while the direct H-transfer from N−H to the C-based radical is unfavorable.[16] The on-off light experiments also support that a radical chain process is not the predominant pathway under the reaction conditions.[19]



Scheme 3. Deuterium-labeling experiment.

Finally, a possible reaction mechanism was proposed (Scheme 4). Deprotonation of the hydrazone **1** occurs under basic conditions to affords the anionic intermediate **A′**. A single-electron oxidation of **A′** by the excited state of the photocatalyst ($*[Ru(bpy)_3]^{2+}$) gives the N-centered radical **B′** through a reductive quenching process. A 5-*exo*-trig cycliza-



Scheme 4. Plausible reaction mechanism.

tion of **B′** affords the C-centered radical **C′**. Subsequent H-transfer from CHCl$_3$ to **C′** gives the product **2**, together with generation of trichloromethyl radical **D′**. The formed radical intermediate **D′** can regenerate the photocatalyst ([Ru(bpy)$_3$]$^{2+}$) through a single electron-transfer process.

In conclusion, we have developed a photocatalytic generation of N-centered hydrazonyl radicals from β,γ-unsaturated hydrazones. This strategy provides efficient access to intramolecular alkene hydroamination and oxyamination, thus furnishing the corresponding 4,5-dihydropyrazoles in good yields. We believe that this photocatalytic strategy will find broad applications in nitrogen-containing molecule synthesis. Further study on the reaction mechanism as well as intermolecular variants is underway.[21]

Experimental Section

Representative procedure: **1a** (0.3 mmol), [Ru(bpy)$_3$]Cl$_2$·6 H$_2$O (0.006 mmol), NaOH (0.45 mmol), and dry CHCl$_3$ (4.5 mL) were added to a 10 mL Schlenk flask equipped with a stirring bar. The resulting mixture was degassed by using a freeze-pump-thaw procedure (3 times). Then, the solution was stirred at a distance of about 5 cm from a 3 W blue LEDs (450–460 nm) at room temperature for 12 h. Upon the completion of reaction, as monitored by TLC, the solvent was removed in vacuum. The crude reaction mixture was purified by flash chromatography on silica gel (silica: 200–300; eluent: petroleum ether/ethyl acetate (20:1–10:1) to provide product **2a** as a white solid in 71 % yield.

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[1] a) B. A. Trofimov, L. N. Sobenina, A. P. Demenev, A. b. I. Mikhaleva, *Chem. Rev.* **2004**, *104*, 2481–2506; b) F. Bellina, R. Rossi, *Tetrahedron* **2006**, *62*, 7213–7256; c) M. A. P. Martins, C. P. Frizzo, D. N. Moreira, N. Zanatta, H. G. Bonacorso, *Chem. Rev.* **2008**, *108*, 2015–2050; d) G. S. Singh, Z. Y. Desta, *Chem. Rev.* **2012**, *112*, 6104–6155; e) A. V. Gulevich, A. S. Dudnik, N. Chernyak, V. Gevorgyan, *Chem. Rev.* **2013**, *113*, 3084–3213.

[2] *Privileged Chiral Ligands and Catalysts* (Ed.: Q.-L. Zhou), Wiley-VCH, Weinheim, **2011**.

[3] For selected reviews, see: a) T. E. Müller, K. C. Hultzsch, M. Yus, F. Foubelo, M. Tada, *Chem. Rev.* **2008**, *108*, 3795–3892; b) S. R. Chemler, *Org. Biomol. Chem.* **2009**, *7*, 3009–3019; c) R. I. McDonald, G. Liu, S. S. Stahl, *Chem. Rev.* **2011**, *111*, 2981–3019; d) T. J. Donohoe, C. K. Callens, A. Flores, A. R. Lacy, A. H. Rathi, *Chem. Eur. J.* **2011**, *17*, 58–76.

[4] For recent transition-metal-free intramolecular hydroaminations, see: a) J.-G. G. Roveda, C. Clavette, A. D. Hunt, S. I. Gorelsky, C. J. Whipp, A. M. Beauchemin, *J. Am. Chem. Soc.* **2009**, *131*, 8740–8741; b) N. Guimond, M. J. MacDonald, V. Lemieux, A. M. Beauchemin, *J. Am. Chem. Soc.* **2012**, *134*, 16571–16577; c) A. R. Brown, C. Uyeda, C. A. Brotherton, E. N. Jacobsen, *J. Am. Chem. Soc.* **2013**, *135*, 6747–6749.

[5] For reviews, see: a) S. Z. Zard, *Chem. Soc. Rev.* **2008**, *37*, 1603–1618; b) G. J. Rowlands, *Tetrahedron* **2010**, *66*, 1593–1636.

[6] For applications of carbamoyl radicals in transfer hydroamination, see: a) J. Kemper, A. Studer, *Angew. Chem. Int. Ed.* **2005**, *44*, 4914–4917; *Angew. Chem.* **2005**, *117*, 4993–4995; b) J. Guin, C. Mück-Lichtenfeld, S. Grimme, A. Studer, *J. Am. Chem. Soc.* **2007**, *129*, 4498–4503; c) J. Guin, R. Frohlich, A. Studer, *Angew. Chem. Int. Ed.* **2008**, *47*, 779–782; *Angew. Chem.* **2008**, *120*, 791–794; for IBX-mediated formation of *N*-aryl amide radical, see: d) K. C. Nicolaou, P. S. Baran, Y.-L. Zhong, S. Barluenga, K. W. Hunt, R. Kranich, J. A. Vega, *J. Am. Chem. Soc.* **2002**, *124*, 2233–2244.

[7] For examples, see: a) Y.-F. Wang, X. Zhu, S. Chiba, *J. Am. Chem. Soc.* **2012**, *134*, 3679–3682; b) Y.-F. Wang, H. Chen, X. Zhu, S. Chiba, *J. Am. Chem. Soc.* **2012**, *134*, 11980–11983; c) H. Chen, S. Sanjaya, Y.-F. Wang, S. Chiba, *Org. Lett.* **2013**, *15*, 212–215.

[8] a) X. Zhu, Y.-F. Wang, W. Ren, F.-L. Zhang, S. Chiba, *Org. Lett.* **2013**, *15*, 3214–3217; b) M.-K. Zhu, Y.-C. Chen, T. P. Loh, *Chem. Eur. J.* **2013**, *19*, 5250–5254; c) X.-Y. Duan, X.-L. Yang, R. Fang, X.-X. Peng, W. Yu, B. Han, *J. Org. Chem.* **2013**, *78*, 10692–10704; d) X.-Y. Duan, N.-N. Zhou, R. Fang, X.-L. Yang, W. Yu, B. Han, *Angew. Chem. Int. Ed.* **2014**, *53*, 3158–3162; *Angew. Chem.* **2014**, *126*, 3222–3226; e) L.-L. Zhou, S. Tang, X.-T. Qi, C.-T. Lin, K. Liu, C. Liu, Y. Lan, A.-W. Lei, *Org. Lett.* **2014**, *16*, 3404–3407.

[9] For reviews, see: a) T. P. Yoon, M. A. Ischay, J. Du, *Nat. Chem.* **2010**, *2*, 527–532; b) F. Teplý, *Collect. Czech. Chem. Commun.* **2011**, *76*, 859–917; c) J. M. R. Narayanam, C. R. J. Stephenson, *Chem. Soc. Rev.* **2011**, *40*, 102–113; d) J. Xuan, W.-J. Xiao, *Angew. Chem. Int. Ed.* **2012**, *51*, 6828–6838; *Angew. Chem.* **2012**, *124*, 6934–6944; e) L. Shi, W.-J. Xia, *Chem. Soc. Rev.* **2012**, *41*, 7687–7697; f) Y.-M. Xi, H. Yi, A.-W. Lei, *Org. Biomol. Chem.* **2013**, *11*, 2387–2403; g) C. K. Prier, D. A. Rankic, D. W. C. MacMillan, *Chem. Rev.* **2013**, *113*, 5322–5363; h) D. M. Schultz, T. P. Yoon, *Science* **2014**, *343*, 985–994; i) M. N. Hopkinson, B. Sahoo, J.-L. Li, F. Glorius, *Chem. Eur. J.* **2014**, *20*, 3874–3886.

[10] For pioneering examples, see: a) S. Maity, M. Zhu, R. S. Shinabery, N. Zheng, *Angew. Chem. Int. Ed.* **2012**, *51*, 222–226; *Angew. Chem.* **2012**, *124*, 226–230; b) S. Maity, N. Zheng, *Angew. Chem. Int. Ed.* **2012**, *51*, 9562–9566; *Angew. Chem.* **2012**, *124*, 9700–9704.

[11] For recent examples, see: a) A. G. Condie, J. C. Gonzalez-Gomez, C. R. Stephenson, *J. Am. Chem. Soc.* **2010**, *132*, 1464–1465; b) J. W. Tucker, Y. Zhang, T. F. Jamison, C. R. Stephenson, *Angew. Chem. Int. Ed.* **2012**, *51*, 4144–4147; *Angew. Chem.* **2012**, *124*, 4220–4223; c) J. Xie, Q.-C. Xue, H.-M. Jin, H.-M. Li, Y.-X. Cheng, C.-J. Zhu, *Chem. Sci.* **2013**, *4*, 1281–1286; d) D. A. DiRocco, T. Rovis, *J. Am. Chem. Soc.* **2012**, *134*, 8094–8097; e) J.-J. Zhong, Q.-Y. Meng, G.-X. Wang, Q. Liu, B. Chen, K. Feng, C.-H. Tung, L.-Z. Wu, *Chem. Eur. J.* **2013**, *19*, 6443–6450; f) Z.-Q. Wang, M. Hu, X.-C. Huang, L.-B. Gong, Y.-X. Xie, J.-H. Li, *J. Org. Chem.* **2012**, *77*, 8705–8711; g) S.-Q. Zhu, M. Rueping, *Chem. Commun.* **2012**, *48*, 11960–11962; h) M. Rueping, C. Vila, *Org. Lett.* **2013**, *15*, 2092–2095.

[12] a) A. McNally, C. K. Prier, D. W. MacMillan, *Science* **2011**, *334*, 1114–1117; b) P. Kohls, D. Jadhav, G. Pandey, O. Reiser, *Org. Lett.* **2012**, *14*, 672–675; c) Y. Miyake, K. Nakajima, Y.

Nishibayashi, *J. Am. Chem. Soc.* **2012**, *134*, 3338 – 3341; d) Y. Miyake, K. Nakajima, Y. Nishibayashi, *Chem. Eur. J.* **2012**, *18*, 16473 – 16477; e) S.-Q. Zhu, A. Das, L. Bui, H.-J. Zhou, D. P. Curran, M. Rueping, *J. Am. Chem. Soc.* **2013**, *135*, 1823 – 1829; f) L. Ruiz Espelt, E. M. Wiensch, T. P. Yoon, *J. Org. Chem.* **2013**, *78*, 4107 – 4114.

[13] G. Cecere, C. M. Konig, J. L. Alleva, D. W. MacMillan, *J. Am. Chem. Soc.* **2013**, *135*, 11521 – 11524.

[14] L. J. Allen, P. J. Cabrera, M. Lee, M. S. Sanford, *J. Am. Chem. Soc.* **2014**, *136*, 5607 – 5610.

[15] a) Y.-Q. Zou, L.-Q. Lu, L. Fu, N.-J. Chang, J. Rong, J.-R. Chen, W.-J. Xiao, *Angew. Chem. Int. Ed.* **2011**, *50*, 7171 – 7175; *Angew. Chem.* **2011**, *123*, 7309 – 7313; b) J. Xuan, X.-D. Xia, T.-T. Zeng, Z.-J. Feng, J.-R. Chen, L.-Q. Lu, W.-J. Xiao, *Angew. Chem. Int. Ed.* **2014**, *53*, 5653 – 5656; *Angew. Chem.* **2014**, *126*, 5759 – 5762.

[16] It has been documented that the H transfer from C- to N-radical is unfavored in the Hoffmann – Löffler – Freytag reaction, see: P. Mackiewicz, R. Furstoss, *Tetrahedron* **1978**, *34*, 3241 – 3260.

[17] For a recent review, see: a) O. A. Attanasi, L. De Crescentini, G. Favi, P. Filippone, F. Mantellini, F. R. Perrulli, S. Santeusanio, *Eur. J. Org. Chem.* **2009**, 3109 – 3127.

[18] CCDC 1004591 (**2a**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[19] We also tried the hydroamination of **1a** using AIBN and DTBP as classical radical initiators and thiol (PhSH) as a catalyst. However, all the reactions resulted in no formation of the desired product.

[20] a) D. Nicewicz, D. Hamilton, *Synlett* **2014**, 1191 – 1196; b) J. M. Grandjean, D. A. Nicewicz, *Angew. Chem. Int. Ed.* **2013**, *52*, 3967 – 3971; *Angew. Chem.* **2013**, *125*, 4059 – 4063; c) M. Riener, D. A. Nicewicz, *Chem. Sci.* **2013**, *4*, 2625 – 2629.

[21] All the attempts for the intermolecular variants met failure.