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# Merging Photoredox Catalysis with Lewis Acid Catalysis: Activation of Carbon-Carbon Triple Bond

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Photoredox catalysis can be merged with Lewis acid catalysis, providing fundamentally new activation mode of C-C triple bond.

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Here we demonstrate that merging photoredox catalysis with Lewis acid catalysis provides fundamentally new activation mode of C-C triple bond to achieve the bond-forming reaction of alkynes with weak nucleophiles. Using this synergistic merger of Eosin Y and Cu(OTf)<sub>2</sub>, a highly efficient cyclization reaction of arene-ynes was developed.

Sunlight, an almost inexhaustible energy source, is the basis of all lives on the earth. Huge amounts of biochemical reactions are powered by solar energy every day in Nature. In such transformations, the bond cleavage and/or construction are very effective at ambient temperature. Utilization of solar energy to realize efficient organic chemistry transformations has recently regained much research interest to replace traditional processes that employs stoichiometric oxidants. As a result, much attention have been paid to visible light-mediated photoredox catalysis over the past decades.<sup>1</sup> Indeed, numerous novel synthetic methods have been developed in this field. Several reports<sup>2</sup> demonstrated that photoredox catalysis could be merged with transition-metal catalysis, among which some examples uncovered fundamentally novel reactivities.<sup>2b-2f</sup> Compared with transition-metal catalyst, Lewis acid catalyst shows much fewer organometallic reactivities. Therefore, novel reactions achieved by merging photoredox catalysis with Lewis acid catalysis via currently unknown or inaccessible mechanistic pathways remained undeveloped.

Alkyne, a very important class of organic compounds, has been extensively applied in organic synthesis as building blocks and versatile synthons.<sup>3</sup> Studies on its reactivity have received extensive attention, resulting in many important protocols for C-C bond formation.<sup>4</sup> The direct cleavage of C-C triple bond is non-trivial due to its high bond energy.  $\pi$ -Philic Lewis acid activation of alkynes represents an important method for functionalization of alkynes, which enables  $\pi$ -bond cleavage and simultaneous formation of two  $\sigma\text{-bonds.}^{\scriptscriptstyle 5}$  Copper, an inexpensive metal, is well known as an efficient Lewis acid catalyst to activate the C-C triple bond for nucleophilic attack from a strong nucleophile.<sup>6</sup> However, for typical weak nucleophiles, copper does not show enough Lewis acidity, which is determined by its natural attribute. We questioned whether photoredox catalysis could be merged with Lewis acid copper salt to create a dual-catalytic system for the activation of alkyne to enable the nucleophilic attack from a weak nucleophile.



Department of Chemistry, Fudan University, 220 Handan Road, Shanghai, 200433, P. R. China. Tel: +86-21-55664361, Fax: +86-21-55664361, E-mail: Hao\_Guo@fudan.edu.cn In the model of a Cu(II)-alkyne complex, the bond between the copper center and alkyne unit can be described by the standard Dewar-Chatt-Duncanson model.<sup>7</sup> The filled  $\pi$  orbital from one of the triple bonds can form a  $\sigma$ -bonding interaction with an empty orbital of the copper(II) atom, together with synergistic  $\pi$ -back-donation from one of the filled *d* orbitals of

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copper(II) to  $\pi^*$  empty orbital of the alkyne. In such a complex, the  $\pi$  electrons of the alkyne are redistributed between alkyne and copper(II) atom, resulting in a three-center two-electron (3c-2e) delocalized system. As a result, the electron density of the  $\pi$  bond decreases, which weakens the bond order, rendering it easier to be oxidized via single electron transfer (SET) process. On the other hand, the electron density of the copper(II) atom is increased, i.e., it becomes easier to be oxidized. In view of the overall model, SET from the Cu(II)-alkyne complex to an external oxidant should be easier (Scheme 1).

Based on the above consideration, the following question was raised: is it possible to break the  $\pi$  bond of alkyne via single electron oxidation catalyzed by Lewis acid and photoredox catalysts? We believe such a desired reaction must run via two key and independent SET steps: firstly, oxidation of Cu(II)-alkyne complex into (Cu(II)-alkyne)<sup>+</sup> complex, which results in the cleavage of the  $\pi$  bond; secondly, reduction of Cu(III) into Cu(II), which regenerates the Lewis acid and photoredox catalysts. If this idea works, a novel activation mode of C-C triple bond will be developed.

A detailed description of our dual-catalytic arene-yne cyclization is shown in Scheme 2. The coordination of Cu(II) with the alkyne 1 generated complex 2. In a thermal reaction, intramolecular attack of the weakly nucleophilic aryl moiety to the alkyne does not occur (vide infra). However, as discussed above, this complex should be easier to be oxidized. On the other hand, in the photoredox catalytic circle, the photoexcited Eosin Y<sup>\*</sup> is highly oxidizing.<sup>8</sup> We assumed that the copper and photoredox catalysis cycles would merge via SET for the first time. The photoexcited Eosin Y\* would abstract one electron from the copper-alkyne complex to yield cationic intermediate 3 and the corresponding Eosin Y<sup>-</sup>, after which the three-center two-electron (3c-2e) delocalized system was transferred into a new three-center one-electron (3c-1e) delocalizeared system. At this moment, the original  $\pi$  bond of the alkyne had already been broken. The alkyne moiety, (in fact, it should be the threecenter one-electron (3c-1e) delocalized system), became electropositive. Its chemical behavior would be no longer to accept nucleophilic attack to break the  $\pi$  bond and build two  $\sigma$ bonds, just as what a normal Lewis acid shows. Alternatively, as a positive intermediate, it tends to electrophilicly add to the former "nucleophile" (the aryl ring) to build a new C-C  $\sigma$  bond, after which the rest single electron of the highly unstable threecenter one-electron (3c-1e) delocalized system would certainly fill into the empty orbital of the copper(II) atom to form a new C-Cu bond and the valence of copper rose up to three. After this step, the three-membered ring system disintegrated. In the whole process the cleavage of the  $\pi$  bond and the formation of two  $\sigma$  bonds occurred at three different steps. Next, protonation of the C-Cu bond (in species 5) by the in situ generated proton (from intermediate 4) resulted in the final product phenanthrene derivative 6 and delivered the free Cu(III) species.9 Given that the Cu(III) species is highly oxidizing,10 meanwhile, the resulting Eosin Y- is quite reducing,8 we envisioned these two catalytic cycles merging for the second time, enabling the single electron oxidization of Eosin Y- into



Scheme 2 Proposed mechanism of the dual-catalysis.

Eosin Y and reduction of Cu(III) into Cu(II). Thus, both the copper and photoredox catalytic cycles closes simultaneously.

Based on the above design, our attempts were carried out using 2-((4-methoxyphenyl)ethynyl)-1,1'-biphenyl 1a as the model substrate, along with a catalyst combination of Cu(OTf)<sub>2</sub> and Eosin Y under the photo irradiation of a 23 W household lamp. To our great delight, careful optimizations (see Table S1 in Supporting Information) proved that our dual-cycle design worked quite well to yield the desired cyclized product 9-(4methoxyphenyl)phenanthrene 6a in quantitive yield (entry 10, Table S1). After establishing the optimal conditions, we turned to the examination of the scope of the arene-ynes.<sup>11</sup> As listed in Table 1, a wide range of mono-, di-, or tri-substituted areneynes with various functional groups were amenable to this dualcatalysis strategy. Electron-rich substrates showed very nice reactivities, affording the desired products in excellent yields (6a-e, 6h, 6k, 6m-n, 6p-s, and 6x-y). In case of reactants with a weak electron withdrawing group, temperature as high as 60 °C was required, which should be due to its lower reactivity (6g, 6i, and 6t). Further studies indicated that no reaction occurred under the standard condition when a strong electron withdrawing group was introduced to the arene-ynes. After extensive optimizations, it was found that the photo reactions of such substrates could proceed in MeCN at 90 °C, affording the desired products in excellent yields (6j, 6l, 6o, 6u-w, and 6zaa). The above results clearly indicated that the substrate scope was broad. Numerous functional groups, such as alkoxy, acetoxyl, alkyl, halogen atom, methoxycarbonyl, acetyl, nitro, nitrile, and trifluoromethyl, were all well tolerated in this reaction. There might be two possible reasons for the observed electronic effect. For electron-deficient arene-ynes, the lower

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<sup>a</sup> All reactions were carried out using **1** (0.2 mmol), Cu(OTf)<sub>2</sub> (5 mol%), and Eosin Y (3 mol%) in anhydrous DCM (5 mL) in a thick sealed tube irradiated by a 23 W household lamp at rt under argon atmosphere. Isolated yields were reported. <sup>b</sup> Reactions were carried out at 60 °C.<sup>c</sup> Reactions were carried out in anhydrous MeCN (5 mL) at 90 °C.

electron density of the  $\pi$  bond in the alkyne renders oxidation of the copper-alkyne complex more difficult. Meanwhile, the

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low electron density of the aryl ring also makes electrophilic addition to the aryl ring more challenging. It was also worthy to note that this reaction could easily proceed in a high yield on a gram scale (**6q**).

After the above explorations, a series of control experiments were carried out in order to gain more informations of this designed dual-cycle reaction mechanism. First of all, Cu(OTf) and some other Lewis acids were surveyed as the catalyst in this reaction (entries 11-16, Table S1). The fact that no reaction occurred in the presence of such catalysts clearly demonstrated that only Cu(OTf)<sub>2</sub> could catalyze this reaction. To examine whether this reaction was catalyzed by the in situ generated proton, reaction of 1a in the presence of 5 mol% of HOAc was carried out. The results indicated that no reaction took place under the catalysis of HOAc, which ruled out the above possibility (see Scheme S1 in Electronic Supplymentary Information). Omission of either Cu(OTf)<sub>2</sub> (entry 17, Table S1) or Eosin Y (entry 18, Table S1) from the standard reaction conditions led to no conversion, indicating that both catalysts were key factors in this transformation. The fact that no reaction took place under dark conditions (entry 19, Table S1) clearly illustrated that light was necessary. Notably, under the irradiation of 254 nm UV light, dramatically increased reaction rate and higher yield were obtained in the absence of Eosin Y (entry 20, Table S1), but no reaction occurred in the absence of Cu(OTf)<sub>2</sub> under UV irradiation (entry 21, Table S1). In such a UV reaction, we assumed that the reaction proceeded via Cucatalyzed photolytic  $\pi$  bond cleavage process which is distinct from catalytic SET procedure. Considering that the household lamp operates with a wide spectral window (around 400 to 760 nm) and the Eosin Y absorbs green light (characteristic peak at 539 nm,8 the green LED lamp (520 to 530 nm, 2 W) was used instead of the household lamp. As a result, the reaction was greatly accelerated (entry 22, Table S1). Moreover, the reaction under the same irradiation conditions in the absence of Eosin Y showed no conversion (entry 23, Table S1). These results strongly suggested that the excited state of Eosin Y was a key intermediate in this dual-catalysis mechanism.

In conclusion, the strategy reported herein represents a novel activation mode of carbon-carbon triple bond. In contrast to the traditional reaction pathway, wherein the metal-coordinated alkyne "passively" accepts the nucleophilic attack resulting in concomitant cleavage of the  $\pi$  bond and construction of two new  $\sigma$  bonds at the same step, this new strategy proceeds via electrophilic addition with the former "nucleophile" to an initially formed positive species by SET-induced cleavage of the  $\pi$  bond. In such a new reaction procedure, the cleavage of the  $\pi$  bond and the constructions of two new  $\sigma$  bonds proceed step by step. This new activation mode will probably find wide applications in the design of organic reactions.

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- Journal Name
- (a) D. A. Nicewicz and D. W. C. MacMillan, *Science*, 2008, 322, 77. (b) C. K. Prier, D. A. <u>Rankig and Contract</u> MacMillan, *Chem. Rev.*, 2013, 113, 5322. (c) D. M. Schultz and T. P. Yoon, *Science*, 2014, 343, 985. (d) P. Wang, M. Cheng and Z. Zhang, *J. Saudi Chem. Soc.*, 2014, 18, 308-316. (e) M. O. Ansari, M. M. Khan, S. A. Ansari and M. H. Cho, *J. Saudi Chem. Soc.*, 2015, 19, 494-504.
- 2 (a) T. Bach, Angew. Chem. Int. Ed., 2015, 54, 11294. (b) J. C. Tellis, D. N. Primer and G. A. Molander, Science 2014. 345, 433. (c) Z. Zuo, D. T. Ahneman, L. Chu, J. A. Terrett, A. G. Doyle and D. W. C.MacMillan, Science, 2014, 345, 437. (d) J. A. Terrett, J. D. Cuthbertson, V. W. Shurtleff and D. W. C. MacMillan, Nature, 2015, 524, 330. (e) Q. M. Kainz, C. D. Matier, A. Bartoszewicz, S. L. Zultanski, J. C. Peters and G. C. Fu, Science, 2016, 351, 681. (f) A. Sagadevan, A. Ragupathi, C. Lin, J. R. Hwu and K. C. Hwang, Green. Chem., 2015, 17, 1113. (g) Y. Ye and M. S. Sanford, J. Am. Chem. Soc., 2012, 134, 9034. (h) B. Sahoo, M. N. Hopkinson and F. Glorius, J. Am. Chem. Soc., 2013, **135**, 5505. (i) X. Shu, M. Zhang, Y. He, H. Frei and F. D. Toste, J. Am. Chem. Soc., 2014, 136, 5844. (j) M. N. Hopkinson, B. Sahoo, J. Li and F. Glorius, Chem.- Eur. J., 2014, 20, 3874. (k) J. M. Narayanam and C. R. J. Stephenson, Chem. Soc. Rev., 2011, 40, 102.
- 3 (a) B. M. Trost and A. H. Weiss, *Adv. Synth. Catal.*, 2009,
  351, 963. (b) R. Chinchilla and C. Nájera, *Chem. Rev.*,
  2014, 114, 1783. (c) Y. Luo, X. Pan, X. Yu and J. Wu, *Chem. Soc. Rev.*, 2014, 43, 834.
- 4 (a) G. Fang and X. Bi, Chem. Soc. Rev., 2015, 44, 8124. (b)
  R. Chinchilla and C. Nájera, Chem. Soc. Rev., 2011, 40, 5084. (c)
  K. Sonogashira, Y. Tohda and N. Hagihara, Tetrahedron Lett, 1975, 16, 4467. (d)
  S. M. R. Mohammad, J. Saudi Chem. Soc., 2014, 18, 115.
- 5 (a) W. Debrouwer, T. S. A. Heugebaert, B. I. Roman and C. V. Stevens, *Adv. Synth. Catal.*, 2015, **357**, 2975. (b) R. Dorel and A. M. Echavarren, *Chem. Rev.*, 2015, **115**, 9028. (c) S. M. A. Sohel and R. Liu, *Chem. Soc. Rev.*, 2009, **38**, 2269.
- 6 (a) A. Peng and Y. Ding, J. Am. Chem. Soc., 2003, 125, 15006. (b) Y. Fukudome, H. Naito, T. Hata and H. Urabe, J. Am. Chem. Soc., 2008, 130, 1820. (c) V. Rauniyar, Z. J. Wang, H. E. Burks and F. D. Toste, J. Am. Chem. Soc., 2011, 133, 8486. (d) M. Jithunsa, M. Ueda and O. Miyata, Org. Lett., 2011, 13, 518. (e) N. Fei, H. Yin, S. Wang, H. Wang and Z. Yao, Org. Lett., 2011, 13, 4208.
- 7 (a) M. J. S. Dewar, *Bull. Soc. Chim. Fr.*, 1951, **18**, 71. (b) J.
   Chatt, and L. A. Duncanson, *J. Chem. Soc.*, 1953, 2939.
- 8 M. Neumann, S. Füldner, B. König and K. Zeitler, Angew. Chem., Int. Ed., 2011, **50**, 951.
- 9 W. Liu, J. Chen, R. Jin, D. Xu, Y. Li, F. Ba, G. Gu, Y. Kuang and H. Guo, *Org. Chem. Front.*, 2016, **3**, 852-855.
- 10 M. Orbán, React. Kinet. Catal. Lett., 1990, 42, 343.
- 11 Note please: All the optimization reactions were carried out in a thin glass tube (Table S1). All the scope exploration reactions were carried out in a thick sealed tube (Table 1). The transmittance of the thin glass tube is more excellent than the thick sealed tube. Thus, the corresponding reaction time of the same substrate under the same reaction condition was not the same. Reactions in a thick sealed tube took longer time.

## Notes and references