

# Cu-Catalyzed Arylcarbocyclization of Alkynes with Diaryliodonium Salts through C–C Bond Formation on Inert C<sub>(sp3)</sub>–H Bond

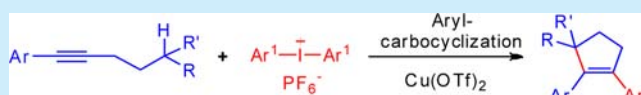
Jing Peng,<sup>†</sup> Chao Chen,<sup>\*,†</sup> Junjie Chen,<sup>†</sup> Xiang Su,<sup>†</sup> Chanjuan Xi,<sup>†</sup> and Hui Chen<sup>\*,‡</sup>

<sup>†</sup>Key Laboratory of Bioorganic Phosphorus Chemistry & Chemical Biology (Ministry of Education), Department of Chemistry, Tsinghua University, Beijing 100084, China

<sup>‡</sup>Beijing National Laboratory for Molecular Sciences, CAS Key Laboratory of Photochemistry, Institute of Chemistry, Chinese Academy of Sciences, Beijing 100190, China

**S** Supporting Information

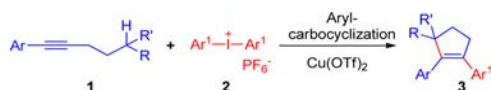
**ABSTRACT:** Copper-catalyzed arylcarbocyclization reaction of alkynes was realized with diaryliodonium salts through C–C bond formation on an inert C<sub>(sp3)</sub>–H bond. This method provides an efficient cyclization of alkyl alkynes to generate carbocycles with good step-economy. Theoretical study revealed an interesting Cu-catalyzed concerted pathway of the C–C bond formation.



Theoretical study revealed an interesting Cu-catalyzed concerted pathway of the C–C bond formation.

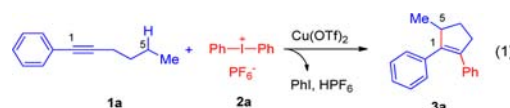
C–C bond formation on an inert C–H bond features good atom- and step-economy and hence has attracted much interest. This strategy provides an alternative to traditional functional group synthesis, which is hardly in line with the concept of green chemistry. According to the recent literature, major achievements in this field focused on the activation of the C<sub>(sp2)</sub>–H bond,<sup>1</sup> while the report of inert C<sub>(sp3)</sub>–H bond activation is relatively rare.<sup>2</sup> A part of the reported work concerning C<sub>(sp3)</sub>–H bond activation mainly dealt with relatively active allylic and benzylic C–H bonds.<sup>3</sup> While the tougher goal on the unreactive C<sub>(sp3)</sub>–H bonds has been successively accomplished by many groups lately, it is a bit flawed in that most of the approaches require a suitably situated heteroatom (e.g., adjacent N or O atom),<sup>4</sup> directing groups,<sup>5</sup> and/or the aid of precious metal catalysts (often in carbenoid chemistry).<sup>6</sup> Hence, the C–C bond formation on an inert C<sub>(sp3)</sub>–H bond (e.g., a C<sub>(sp3)</sub>–H bond in a alkyl chain) is still particularly challenging, especially for regioselective cases. Herein, we report an arylcarbocyclization reaction of acetylenes with diaryliodonium salts through C–C bond formation on an inert C<sub>(sp3)</sub>–H bond. Such a reaction enabled an efficient cyclization of simple alkylacetylenes to give carbocycles with good step-economy (Scheme 1).

**Scheme 1. Arylcarbocyclization Reaction of Alkynes with Diaryliodonium Salts through C–C Bond Formation on the C<sub>(sp3)</sub>–H Bond**



Lately, diaryliodonium salts, Ar<sub>2</sub>I<sup>+</sup>X<sup>−</sup>, have received considerable attention due to their powerful arylation for numerous nucleophiles to produce valuable aromatic compounds in a new reaction mode.<sup>7</sup> During our synthetic study with diaryliodonium salts,<sup>8</sup> we were tempted to explore their capability to induce arylcyclization reaction of alkynes.<sup>9</sup> The initial investigation

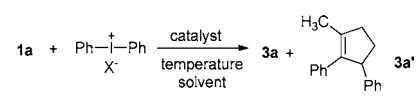
stemmed from the reaction of 1-phenyl-1-hexyne **1a** with diphenyliodonium hexafluorophosphate **2a**. It is delightful to observe that in the presence of Cu(OTf)<sub>2</sub> (10 mol %) **1a** could be conjugated with a phenyl group of **2a**. More importantly, a dramatic cyclization occurred between the C1 and C5 positions to give product **3a**, in which a new C–C bond was formed on the traditionally inert C<sub>(sp3)</sub>–H bond of the alkyl chain (eq 1).



The primary result showed us an efficient way to generate 1,2-diphenyl cyclopentene much easier compared with some known methods,<sup>10</sup> which encouraged us to seek the best reacting conditions (Table 1). Different metal salts were examined as catalysts, and Cu(OTf)<sub>2</sub> proved to be the best one. CuBr and Fe(OTf)<sub>2</sub> showed lower catalytic activity, and no reaction was observed in the presence of Ni(OTf)<sub>2</sub> as well as in the absence of any metal catalyst (entries 1–5). Surprisingly, when the amount of the Cu(OTf)<sub>2</sub> was decreased to 5 mol %, a better yield of desired product was detected (entry 10). Moreover, it was crucial to observe that a dramatic anion effect, indicating that diaryliodonium salt with PF<sub>6</sub><sup>−</sup>, showed much better activity than other anions including OTf<sup>−</sup>, Cl<sup>−</sup>, and BF<sub>4</sub><sup>−</sup> (entries 11–13). While optimizing the reaction conditions (for more details, see the Supporting Information), we noticed that the reaction was quite sensitive to moisture so that the system had to be completely free from moisture. After various attempts, optimal conditions were found (Table 1, entry 10). It should be noted that **3a** was isolated in 75% yield by slow column chromatography with hexane with small amount of **3a'**, a double-bond migrating isomer (ca. 10%).

Received: June 8, 2014

Published: July 10, 2014

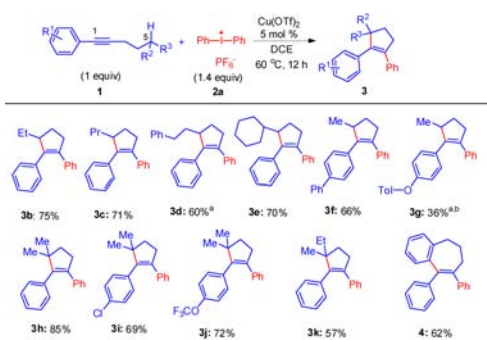
**Table 1. Condition Optimization of Arylcarbo-cyclization of Alkyne 1a**


entry	catalyst (mol %)	X <sup>-</sup>	solvent	temp (°C)	yield <sup>a</sup> (%)
1	Cu(OTf) <sub>2</sub> (10)	PF <sub>6</sub> <sup>-</sup>	DCE	60	78
2	CuBr (10)	PF <sub>6</sub> <sup>-</sup>	DCE	60	63
3	Ni(OTf) <sub>2</sub> (10)	PF <sub>6</sub> <sup>-</sup>	DCE	60	0
4	Fe(OTf) <sub>2</sub> (10)	PF <sub>6</sub> <sup>-</sup>	DCE	60	21
5	none	PF <sub>6</sub> <sup>-</sup>	DCE	60	0
6	Cu(OTf) <sub>2</sub> (10)	PF <sub>6</sub> <sup>-</sup>	DCM	60	70
7	Cu(OTf) <sub>2</sub> (10)	PF <sub>6</sub> <sup>-</sup>	EtOAc	60	0
8	Cu(OTf) <sub>2</sub> (10)	PF <sub>6</sub> <sup>-</sup>	DCE	40	57
9	Cu(OTf) <sub>2</sub> (10)	PF <sub>6</sub> <sup>-</sup>	DCE	80	32
10	Cu(OTf) <sub>2</sub> (5)	PF <sub>6</sub> <sup>-</sup>	DCE	60	83 <sup>b</sup>
11	Cu(OTf) <sub>2</sub> (5)	OTf <sup>-</sup>	DCE	60	53
12	Cu(OTf) <sub>2</sub> (5)	Cl <sup>-</sup>	DCE	60	0
13	Cu(OTf) <sub>2</sub> (5)	BF <sub>4</sub> <sup>-</sup>	DCE	60	0

<sup>a</sup>Determined by GC analysis using dodecane as an internal standard.

<sup>b</sup>Isolated yield: 75%.

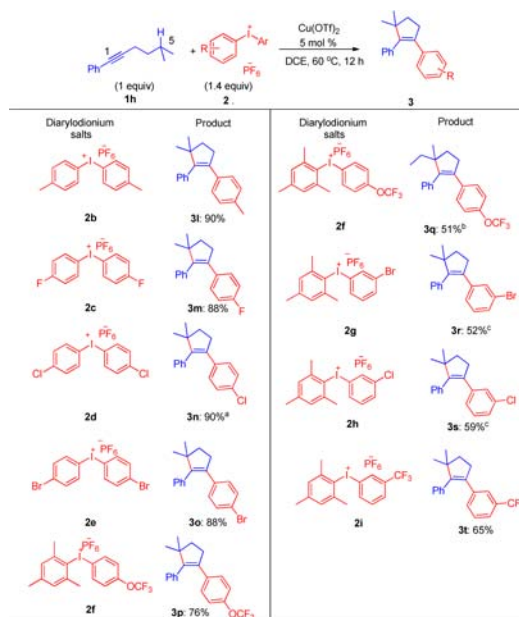
With the optimized conditions established, the scope of this novel cyclization process was first explored by varying the substituents on alkynes **1** (Scheme 2). When alkynes with extended

**Scheme 2. Reaction Scope of Alkynes with 2a**


<sup>a</sup>Around 15% of double-bond migrating isomers were observed. <sup>b</sup>The reaction was carried out at 30 °C.

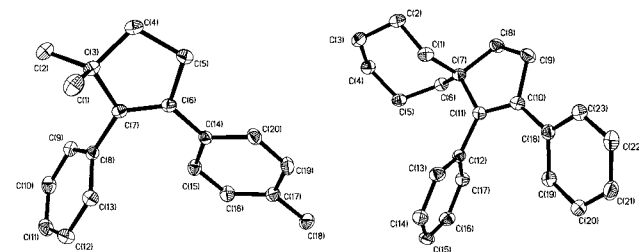
alkyl groups (**1b–e**) were employed, the corresponding 1,2-diphenyl-substituted cyclopentene derivatives were isolated in fairly good yields with a regioselectivity forming the product of five-membered ring instead of any larger one. In addition, alkynes bearing a shorter alkyl chain such as 1-phenyl-1-pentyne gave fewer desired products. Alkynes with different functional groups (**1f, 1g**) on the phenyl ring at C1 position also worked well to give desired products. Next, we challenged alkynes with branched-chain alkyl groups (**1h–k**) possessing tertiary C–H bonds. To our delight, 1,2-diphenyl-3,3-dimethylcyclopentene **3h** and more complicated product **3k** were also obtained with good selectivity in synthetically useful yield. However, when alkyne **1z** (1,5-diphenylpentyne) was used, a Friedel–Crafts-type reaction took place instead of C–H activation to give product **4**, whose structure was clearly shown by X-ray diffraction (see the SI). This type of reaction with alkyne was reported by Gaunt et al. very recently, where diphenyliodonium triflate was used instead.<sup>9</sup>

Inspired by the successful arylcarbo-cyclization of various alkyl acetylenes, a variety of symmetric and unsymmetric diaryliodonium hexafluorophosphates **2** were investigated with

**Scheme 3. Various Diaryliodonium Salts with 1h**


<sup>a</sup>The reaction was preformed at 100 °C for 8 h. <sup>b</sup>The reactant was 5-methyl-1-phenyl-1-heptyne **1k**. <sup>c</sup>2 equiv of diaryliodonium salts was added.

alkyl acetylene **1h** (listed in Scheme 3). Symmetric diaryliodonium hexafluorophosphates with halogen and methyl substituents (**2b–2e**) reacted smoothly with **1a** producing the corresponding products in excellent yields. The structure of **3l** was unequivocally confirmed with X-ray diffraction (Figure 1, left).



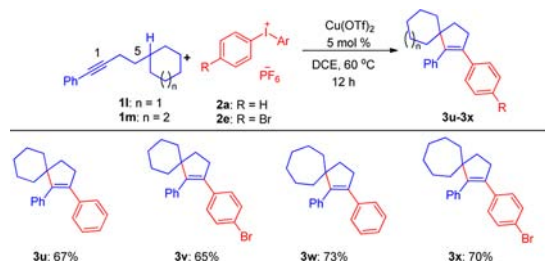
**Figure 1.** Crystal structure of **3l** (left) and **3w** (right). Hydrogen atoms are omitted for clarity.

Unsymmetric **2f** enabled the reaction with **1h** and **1k** to transfer aryl groups generating corresponding *para*-substituted arylated products. It is also pleasant to find that aryl(mesityl)-iodonium salts (**2g–2i**) could also accommodate substituents at the *meta* positions on arene groups to conduct the transformation. Few product was observed when the reaction was carried out with *ortho*-substituted iodonium salt or diaryliodonium salt with strongly electron-withdrawing group.

Inspired by the facile and efficient cyclization reactions of the alkylacetylenes, we made further attempts to use more complicated molecules, for instance, some spirocyclic compounds utilizing this new strategy. Direct construction of spirocyclic molecules through a forming C–C bond at the spiro-center has always been a challenging subject because of the steric hindrance and indeterminate reactivity of the functionalized tertiary carbon atom.<sup>11</sup> Our findings might disclose a potential way to spiro-cyclic molecules through forming C–C bonds at a tertiary carbon atom without prefunctionality. For this goal, acetylenes **1l** and **1m** were

easily prepared through Cu-catalyzed Kumada-coupling reactions.<sup>12</sup> To our delight, the newly developed method could be applied to substrates like **11** and **1m** giving 1,2-diaryl-substituted spiro compounds in high isolated yields with elegant selectivity (**3u–x**, Scheme 4), and the structure of **3w** was clearly confirmed

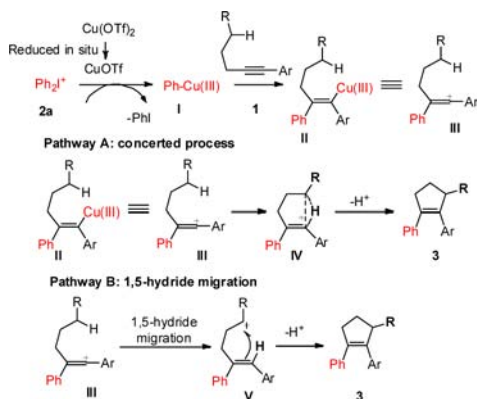
#### Scheme 4. Synthesis of Spiro Compounds



by X-ray diffraction (Figure 1, right). Such a straightforward process might vitally reduce the synthetic steps of carbocycles with complicated structures.

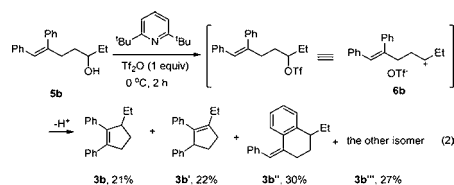
Recent reports have shown that the diaryliodonium salts could generate Ar–Cu(III) species in situ in the presence of Cu(OTf)<sub>2</sub>.<sup>13</sup> These Ar–Cu(III) **I** species are generally highly electrophilic and could be easily attacked by acetylene to produce vinylcopper(III) species **II**, resembling a vinylic cation **III** (Scheme 5).<sup>9,14</sup> Various vinylic cation species were previously

#### Scheme 5. Discussion of Two Pathways

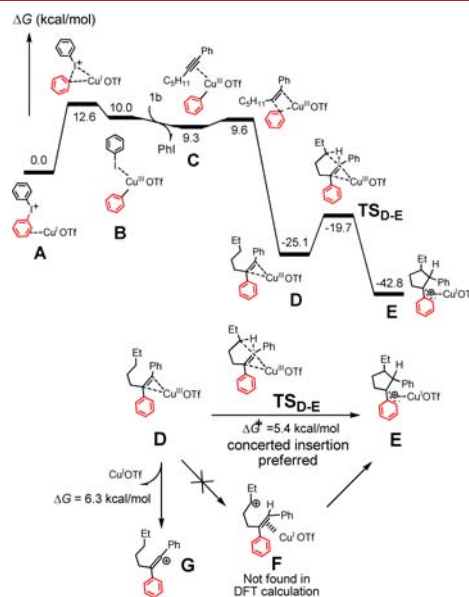


generated via alkylation or acylation of acetylenes and found to form a C–C bond on the C<sub>(sp<sup>3</sup>)</sub>–H bond via a concerted or stepwise pathway, depending on the substituents.<sup>14a,b</sup> Hence, in the case of acetylene with an appropriate alkyl chain, vinylcopper(III) species **II** would initiate the activation of C–H bond and form C–C bond via a concerted process (pathway A). This hypothesis is preferred by theoretical calculations (vide infra). On the other hand, the reactivity of vinylcopper(III) species **II** resembled that of the vinylic cation, which would initiate a 1,5-hydride migration to give alkyl cation **V** (pathway B). The cation **V** would undergo cyclization on the double bond to produce **3**. To seek the possibility of this pathway, alcohol **5b** was prepared according to a known procedure (see SI) and treated with Tf<sub>2</sub>O to generate the proposed cationic intermediate **6b**. However, the cyclization of **6b** produced a mixture of four isomers, and **3b** was only the minor product among them (eq 2).<sup>15</sup>

To shed more light on the reaction mechanism at the molecular level, density functional theory (DFT) calculations were then conducted. The mechanism obtained from DFT calculations



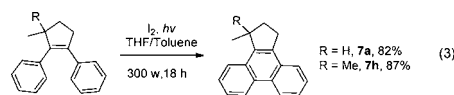
inspired by the experimental results and the known research work<sup>10</sup> is described in Figure 2 (upper), taking the reaction of **1b**



**Figure 2.** DFT-calculated pathway of reaction of **1b** with **2a** catalyzed by CuOTf (top); comparison of different C<sub>(sp<sup>3</sup>)</sub>–H activation steps in DFT calculations (bottom).

and **2a** as an example. The diaryliodonium salt combined with copper catalyst to generate the species of **C** which is highly electrophilic.<sup>9,13</sup> It would attack C–C triple bond and form a three-membered ring intermediate **D** through of aryl transfer. It is remarkable that TS<sub>D–E</sub> proves to be the transition state for the further cyclization process since concerted insertion of vinylcopper(III) into the C<sub>(sp<sup>3</sup>)</sub>–H bond is preferred instead of forming a carbocation intermediate. From Figure 2 (bottom), it is likely that the formation of Ar–Cu(III) species **B**, rather than a C–H activation process from **D**, is the rate-determining step. Copper catalyst is also likely to be involved in the C–H activation process, since its dissociation from **D** need to consume a certain free energy that is larger than the free energy barrier of the subsequent C–H activation with copper catalyst in the system, as shown in Figure 2 (bottom).<sup>16</sup>

Cyclic alkenes are important synthetic intermediates, organic optic materials, and motifs in natural products. The newly formed alkenes **3a** and **3h** were simply applied to a photocyclization reaction to produce phenanthrene derivatives **7a** and **7h** in high yields, respectively (eq 3).<sup>17</sup>



In summary, we reported a novel arylcarbocyclization reaction of alkynes induced by diaryliodonium salts. This new finding of iodonium chemistry disclosed an efficient way to generate

carbocycles and even spirocycles with alkylalkynes via C–C bond formation on an inert C<sub>(sp<sup>3</sup>)</sub>–H bond. Theoretical study revealed an interesting Cu-catalyzed concerted pathway of the C–C bond formation.

## ■ ASSOCIATED CONTENT

### Supporting Information

Experimental procedures, spectral data, computational details, and results. This material is available free of charge via the Internet at <http://pubs.acs.org>.

## ■ AUTHOR INFORMATION

### Corresponding Authors

\*E-mail: [chenchao01@mails.tsinghua.edu.cn](mailto:chenchao01@mails.tsinghua.edu.cn).

\*E-mail: [chenh@iccas.ac.cn](mailto:chenh@iccas.ac.cn).

### Notes

The authors declare no competing financial interest.

## ■ ACKNOWLEDGMENTS

This work was supported by the National Natural Science Foundation of China (21102080, 21372138, 21290194, 21221002, and 21032004) and Tsinghua University Initiative Scientific Research Program (2011Z02150).

## ■ REFERENCES

- (1) (a) Alberico, D.; Campeau, L. C.; Fagnou, K. *Chem. Commun.* **2006**, 1253. (b) Chen, X.; Engle, K. M.; Wang, D.-H.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2009**, *48*, 5094. (c) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147. (d) Colby, D. A.; Bergman, R. G.; Ellman, J. A. *Chem. Rev.* **2010**, *110*, 624. (e) Yeung, C. S.; Dong, V. M. *Chem. Rev.* **2011**, *111*, 1215. (f) Wencle-Dlord, J.; Droge, T.; Liu, F.; Glorius, F. *Chem. Soc. Rev.* **2011**, *40*, 4740.
- (2) (a) Culkun, D. A.; Hartwig, J. F. *Acc. Chem. Res.* **2003**, *36*, 234. (b) Davies, H. M. L. *Angew. Chem., Int. Ed.* **2006**, *45*, 6422. (c) Godula, K.; Sames, D. *Science* **2009**, *312*, 67. (d) Doyle, M. P.; Duffy, R.; Ratnikov, M.; Zhou, L. *Chem. Rev.* **2010**, *110*, 704. (e) Baudoin, O. *Chem. Soc. Rev.* **2011**, *40*, 4902. (f) Sun, C.-L.; Li, B.-J.; Shi, Z.-J. *Chem. Rev.* **2011**, *111*, 1293. (g) Li, H.; Li, B.-J.; Shi, Z.-J. *Catal. Sci. Technol.* **2011**, *1*, 191.
- (3) (a) Kalyani, D.; Deprez, N. R.; Desai, L. V.; Sanford, M. S. *J. Am. Chem. Soc.* **2005**, *127*, 7330. (b) Li, Z.-P.; Li, C.-J. *J. Am. Chem. Soc.* **2005**, *128*, 56. (c) Yin, G.; Wu, Y.; Liu, G. *J. Am. Chem. Soc.* **2010**, *132*, 11978. (d) Paradine, S. M.; White, M. C. *J. Am. Chem. Soc.* **2012**, *134*, 2036. (e) Xie, P.; Xie, Y.; Qian, B.; Zhou, H.; Xia, C.; Huang, H. *J. Am. Chem. Soc.* **2012**, *134*, 9902.
- (4) (a) Desai, L. V.; Hull, K. L.; Sanford, M. S. *J. Am. Chem. Soc.* **2004**, *126*, 9542. (b) Chen, X.; Goodhue, C. E.; Yu, J.-Q. *J. Am. Chem. Soc.* **2006**, *128*, 12634. (c) Shabashov, D.; Daugulis, O. *J. Am. Chem. Soc.* **2010**, *132*, 3965. (d) Stowers, K. J.; Fortner, K. C.; Sanford, M. S. *J. Am. Chem. Soc.* **2011**, *133*, 6541. (e) Qian, B.; Xie, P.; Xie, Y.-J.; Huang, H.-M. *Org. Lett.* **2011**, *13*, 2580. (f) Nadres, E. T.; Daugulis, O. *J. Am. Chem. Soc.* **2012**, *134*, 7. (g) Pan, F.; Shen, P.-X.; Zhang, L.-S.; Wang, X.; Shi, Z.-J. *Org. Lett.* **2013**, *15*, 4758.
- (5) (a) Chatani, N.; Asaumi, T.; Yorimitsu, S.; Ikeda, T.; Kakiuchi, F.; Murai, S. *J. Am. Chem. Soc.* **2001**, *123*, 10935. (b) Li, Z.-P.; Li, C.-J. *J. Am. Chem. Soc.* **2004**, *126*, 11810. (c) Li, Z.-P.; Li, C.-J. *J. Am. Chem. Soc.* **2005**, *127*, 3672. (d) Campos, K. R. *Chem. Soc. Rev.* **2007**, *36*, 1069. (e) Pastine, S. J.; Gribkov, D. V.; Sames, D. *J. Am. Chem. Soc.* **2006**, *128*, 14220. (f) Baslé, O.; Li, C.-J. *Org. Lett.* **2008**, *10*, 3661. (g) Kumaraswamy, G.; Murthy, A. N.; Pitchaiah, A. *J. Org. Chem.* **2010**, *75*, 3916. (h) Gogoi, A.; Guin, S.; Rout, S. K.; Patel, B. K. *Org. Lett.* **2013**, *15*, 1802.
- (6) (a) Davies, H. M. L.; Beckwith, R. E. *J. Chem. Rev.* **2003**, *103*, 2861. (b) Bhunia, S.; Liu, R.-S. *J. Am. Chem. Soc.* **2008**, *130*, 16488. (c) Horino,

Y.; Yamamoto, T.; Ueda, K.; Kuroda, S.; Toste, F. D. *J. Am. Chem. Soc.* **2009**, *131*, 2809.

(7) For reviews, see: (a) Yusubov, M. S.; Maskae, A. V.; Zhdankin, V. V. *ARKIVOC* **2011**, No. i, 370. (b) Merritt, E. A.; Olofsson, B. *Angew. Chem., Int. Ed.* **2009**, *48*, 9052. (c) Zhdankin, V. V.; Stang, P. J. *Chem. Rev.* **2008**, *108*, 5299. (d) Zhdankin, V. V.; Stang, P. J. *Chem. Rev.* **2002**, *102*, 2523. (e) Grushin, V. V. *Chem. Soc. Rev.* **2000**, *29*, 315. (f) Stang, P. J.; Zhdankin, V. V. *Chem. Rev.* **1996**, *96*, 1123.

(8) (a) Wang, Y.; Chen, C.; Peng, J.; Li, M. *Angew. Chem., Int. Ed.* **2013**, *52*, 5323. (b) Peng, J.; Chen, C.; Wang, Y.; Lou, Z.-B.; Li, M.; Xi, C.; Chen, H. *Angew. Chem., Int. Ed.* **2013**, *52*, 7574. (c) Su, X.; Chen, C.; Wang, Y.; Peng, J.; Lou, Z.-B.; Li, M. *Chem. Commun.* **2013**, *49*, 6752. (d) Wang, Y.; Su, X.; Chen, C. *Synlett* **2013**, *24*, 2619.

(9) (a) Suero, M. G.; Bayle, E. D.; Collins, B. S. L.; Gaunt, M. J. *J. Am. Chem. Soc.* **2013**, *135*, 5332. (b) Walkinshaw, A. J.; Xu, W.-S.; Suero, M. G.; Gaunt, M. J. *J. Am. Chem. Soc.* **2013**, *135*, 12532. (c) Copper-catalyzed reactions between alkynes and diaryliodonium salts form carbocyclic products was reported during the time this paper was revised: Zhang, F.; Das, S.; Walkinshaw, A. J.; Casitas, A.; Taylor, M.; Suero, M. G.; Gaunt, M. J. *J. Am. Chem. Soc.* **2014**, *136*, 8851.

(10) (a) Couture, A.; Ho, K.; Hoshino, M.; Mayo, P.; Suau, R.; Ware, W. R. *J. Am. Chem. Soc.* **1976**, *98*, 6218. (b) Somers, J. B. M.; Couture, A.; Lablache-Combiere, A.; Laarhoven, W. H. *J. Am. Chem. Soc.* **1985**, *107*, 1387. (c) Schwiebert, K. E.; Stryker, J. M. *J. Am. Chem. Soc.* **1994**, *116*, 11570. (d) Xia, Y.; Liu, Z.-X.; Xia, Q.; Qu, P.-Y.; Ge, Y.; Zhang, Y.; Wang, J.-B. *Angew. Chem., Int. Ed.* **2012**, *51*, 5714.

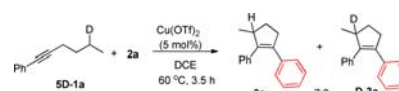
(11) (a) Yang, Y.-H.; Petersen, J. L.; Wang, K.-K. *J. Org. Chem.* **2003**, *68*, 5832. (b) Camps, P.; Domingo, L. R.; Formosa, X.; Galdeano, C.; González, D.; Muñoz-Torrero, D.; Segalés, S.; Font-Bardia, M.; Solans, X. *J. Org. Chem.* **2006**, *71*, 3464. (c) Wu, Y. G.; Zhang, J. Y.; Bo, Z. S. *Org. Lett.* **2007**, *9*, 4435. (d) Sánchez-Larios, E.; Holmes, J. M.; Daschner, C. L.; Gravel, M. *Org. Lett.* **2010**, *12*, 5772. (e) Singh, C.; Hassam, M.; Naikade, N. K.; Verma, V. P.; Singh, A. S.; Puri, S. K. *J. Med. Chem.* **2010**, *53*, 7587.

(12) (a) Ren, P.; Stern, L.-A.; Hu, X.-L. *Angew. Chem., Int. Ed.* **2012**, *51*, 9110. (b) Yang, C.-T.; Zhang, Z.-Q.; Liang, J.; Liu, J.-H.; Lu, X.-Y.; Chen, H.-H.; Liu, L. *J. Am. Chem. Soc.* **2012**, *134*, 11124.

(13) (a) Phipps, R. J.; McMurray, L.; Ritter, S.; Duong, H. A.; Gaunt, M. J. *J. Am. Chem. Soc.* **2012**, *134*, 10773. (b) Chen, B.; Hou, X.-L.; Li, Y.-X.; Wu, Y.-D. *J. Am. Chem. Soc.* **2011**, *133*, 7668. (c) Xiao, B.; Fu, Y.; Xu, J.; Gong, T.-J.; Dai, J.-J.; Yi, J.; Liu, L. *J. Am. Chem. Soc.* **2010**, *132*, 468. (d) Phipps, R. J.; Gaunt, M. J. *Science* **2009**, *323*, 1593. (e) Phipps, R. J.; Grimster, N. P.; Gaunt, M. J. *J. Am. Chem. Soc.* **2008**, *130*, 8172.

(14) (a) Biermann, U.; Koch, R.; Metzger, J. O. *Angew. Chem., Int. Ed.* **2006**, *45*, 3076. (b) Kanishchev, M. I.; Shegolev, A. A.; Smit, W. A.; Caple, R.; Kelner, M. J. *J. Am. Chem. Soc.* **1979**, *101*, 5660. (c) Schegolev, A. A.; Smit, W. A.; Kucherov, V. F.; Caple, R. *J. Am. Chem. Soc.* **1975**, *97*, 6604.

(15) The KIE experiment was carried out with **5D-1a** and **2a**. After the majority of **5D-1a** was converted, the mixture of **3a** and **D-3a** was isolated at a ratio around 7:3. The deuterium of **D-3a** is located at the allylic position and may be exchanged by protons in the reaction system. Therefore, this KIE result is not sufficient to reveal the process of cyclization.



(16) This mechanism of pathway A is similar to that proposed in ref **14a**, but the role of Cu catalyst cannot be neglected as calculated.

(17) Talele, H. R.; Gohil, M. J.; Bedekar, A. V. *Bull. Chem. Soc. Jpn.* **2009**, *82*, 1182. (b) Rahmahan, A. U.; Vuano, B. *J. Org. Chem.* **1969**, *34*, 763.