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# **Isocyanide-Induced Activation of Copper Sulfate: Direct Access to Functionalized Heteroarene Sulfonic Esters**

Xiaohu Hong<sup>+</sup>, Qitao Tan<sup>+</sup>, Bingxin Liu, and Bin Xu<sup>\*</sup>

Dedicated to Professor Shizheng Zhu on the occasion of his 70th birthday

**Abstract:** A novel and direct approach to alkyl/aryl heteroarene sulfonic esters using copper sulfate as the environmentally benign inorganic sulfonation reagent was first realized with the aid of isocyanide. A variety of heterocycles reacted to afford the corresponding sulfonic esters through C– H functionalization. In this transformation, the otherwise inert copper sulfate was unusually activated by an isocyanide and employed as the source of the sulfonic substituents in an unprecedented fashion. The findings suggest that an appropriate activator may liberate the chemical activities of some relatively inert inorganic salts for organic synthesis.

**C**opper salts, which are inexpensive and of low toxicity, have been widely used in organic reactions as catalysts or mediators.<sup>[1]</sup> Recently, many copper salts have been frequently involved in C–H bond functionalization for the formation of C–X, C–O, and C–N bonds by assembling their anions to the substrates (Scheme 1).<sup>[2]</sup> Copper sulfate, known as bluestone in its pentahydrate form, is abundant in nature and has found vast practical uses including herbicide, wood impregnation, and algae control in swimming pools. However,



Scheme 1. The utilities of copper salt anions in C–H bond functionalization.

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in a stark contrast to other frequently used copper salts, copper sulfate is employed at a limited level in organic synthesis.<sup>[3]</sup> The principal uses of copper sulfate in organic synthesis stem from the chemical properties of copper(II) cation, and it is utilized as a dehydrating agent,<sup>[4]</sup> Lewis acid,<sup>[5]</sup> oxidant,<sup>[6]</sup> or catalyst.<sup>[7]</sup> To our knowledge, the utilization of the sulfate anion of copper sulfate has remained unexplored, which is probably due to the robustness of the O–S bond in many sulfate moieties.<sup>[8]</sup> For example, copper(II) sulfate was reported to decompose into copper(II) oxide and sulfur trioxide at elevated temperature (>600 °C).<sup>[9]</sup> Therefore, to utilize the sulfate anion in organic transformation, such as sulfonation reaction, the cleavage of the inert O–S bond is necessary and challenging.

Sulfonates are one of the most important classes in surfactant industry as detergents and surface active agents.<sup>[10]</sup> However, the traditional sulfonates are conventionally prepared under harsh conditions by heating at elevated temperatures with corrosive or environmentally unfriendly oleum, sulfur trioxide, or chlorosulfonic acid. Improved results could be achieved using easily handling sulfur trioxide amine complexes in sulfonation reactions.<sup>[11]</sup> Generally, the sulfonic esters are accessible by several steps through tedious procedures.<sup>[12]</sup> Thus, direct sulfonation using the sulfate anion of copper sulfate will be remarkably different from traditional or recently developed methods, which do not involve the cleavage of O-S bonds.<sup>[13]</sup> Herein, we report an unprecedented sulfonation process employing copper sulfate as the novel environmentally benign inorganic sulfonation reagent to afford various heteroarene sulfonic esters in good yields (Scheme 1). The significance of the given chemistry is threefold: 1) It is the first direct transformation of safe and low-cost copper sulfate to sulfonic esters, avoiding the traditional use of corrosive hazards such as concentrated sulfuric acid or chlorosulfonic acid; 2) the chemically inert copper sulfate is activated unusually for the first time in the presence of an isocyanide;<sup>[14]</sup> 3) the valuable mechanistic insights could be expanded for promoting the discovery of other new types of sulfonation reactions.

Isocyanides are not only important C1 synthons in organic synthesis but also strong ligands towards transition metals.<sup>[14b,15]</sup> They could be generally activated as versatile reactants for a variety of transformations when coordinated to metals. Recently, we have successfully explored isocyanides as crucial ligands to promote various copper-mediated transformations.<sup>[2h,16]</sup> Inspired by these results, we started our investigation by exploring the reaction of 1-phenyl-1*H*-indole (**1a**) with copper sulfate in the presence of *t*-BuNC in 1,2dichloroethane at 130 °C under a nitrogen atmosphere. After an extensive screening of the ratios of the starting materials (Supporting Information, Table S1),  $1a/CuSO_4/t$ -BuNC = 1:4:5 was found to be the best choice, affording the indolyl sulfonic ester 2a in 86% yield (Table 1, entry 1).<sup>[17]</sup> Under

*Table 1:* Optimization of reaction conditions.<sup>[a]</sup>



Entry	Change from standard conditions	Yield [%] <sup>[b]</sup>
1	none	86
2	no <i>t</i> -BuNC	-
3	50 mol % <i>t</i> -BuNC	trace
4	CuSO <sub>4</sub> ·5 H <sub>2</sub> O instead of CuSO <sub>4</sub>	36
5	Na <sub>2</sub> SO <sub>4</sub> instead of CuSO <sub>4</sub>	-
6	8 mol% CuSO <sub>4</sub> , 10 mol% <i>t</i> -BuNC and 4.0 equiv of	-
	Na <sub>2</sub> SO <sub>4</sub> were used	
7	MgSO₄ instead of CuSO₄	-
8	MnSO <sub>4</sub> instead of CuSO <sub>4</sub>	-
9	ZnSO <sub>4</sub> instead of CuSO <sub>4</sub>	-
10	FeSO <sub>4</sub> ·7H <sub>2</sub> O instead of CuSO <sub>4</sub>	-
11	XyNC instead of <i>t</i> -BuNC	65
12	PPh₃ instead of <i>t</i> -BuNC	32 (83)
13	Xantphos instead of <i>t</i> -BuNC	52
14	bipyridine instead of t-BuNC	-
15	1,10-phen instead of <i>t</i> -BuNC	-
16	3.0 equiv of CuSO <sub>4</sub>	72 (95)
17	110°C instead of 130°C	55 (62)
18	under air instead of N2 atmosphere	79

[a] Reaction conditions: 1a (0.2 mmol), CuSO<sub>4</sub> (0.8 mmol), *t*-BuNC (1.0 mmol) in DCE (3.0 mL), 130 °C, under nitrogen atmosphere, sealed tube, 20 h. DCE = 1,2-dichloroethane, XyNC = 2,6-dimethylphenylisoni-trile. Xantphos = 4,5-bis-di-phenylphosphanyl-9,9-dimethylxanthene. [b] Isolated yield with the conversion of 1a shown in parentheses.

otherwise identical conditions in the absence or using catalytic amount of *t*-BuNC, none or just trace amount of sulfonic ester **2a** was observed (entries 2 and 3). If copper sulfate pentahydrate was employed instead of the anhydrous form, significant lower yield was obtained (entry 4). Interestingly, among the sulfate salts screened (entries 5–10), only copper sulfate could give the desired product in an appreciable yield indicating its unique role in this transformation. XyNC and phosphine ligands<sup>[18]</sup> could also afford the desired product, albeit in decreased yields (entries 11–13). Nitrogencontaining ligands such as bipyridine or 1,10-phenanthroline, however, could not afford the desired product (entries 14 and 15). Reducing the amount of copper sulfate, lowering the reaction temperature, or performing the reaction under air atmosphere caused somewhat lower yields (entries 16–18).

The scope of this reaction was next investigated, as shown in Scheme 2. Substrates bearing electron-donating or electron-withdrawing groups at the *N*-phenyl rings underwent sulfonation reaction smoothly (**2a–2h**), and functional groups such as methyl, methoxyl, halide, and ester groups were all tolerated. This sulfonation reaction also worked well with substrates bearing methyl or phenyl group at the indole C2 position (**2i** and **2j**). Furthermore, *N*-phenyl indoles having



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**Scheme 2.** Sulfonation scope of indoles. Reaction conditions: 1 (0.4 mmol), CuSO<sub>4</sub> (1.6 mmol), *t*-BuNC (2.0 mmol) in DCE (6.0 mL), under nitrogen atmosphere, sealed tube, 20–36 h. Yields shown are of the isolated products.

halides, -OMe or  $-CO_2Me$  at the C5 or C6 position could also undertake this reaction smoothly with moderate to good yields (**2k-2n**). Primary and secondary alkyl, benzyl, allyl, and pyridyl indoles could efficiently convert into the desired sulfonation products in good yields (**2o-2w**). However, less electron-rich *N*-acyl indoles (Ac, Ts, and Boc) did not give the corresponding products. This newly established protocol was not limited to indoles; azaindoles were also found to be suitable substrates, affording products **2x** and **2y** in good yields. The identity of **2m** was determined by spectral analysis and further confirmed by X-ray crystallographic analysis.<sup>[19]</sup>

Various alkyl halides were subsequently examined in the sulfonation of N-(p-methoxyphenyl)indole (1c) using toluene as solvent (Scheme 3). A wide range of primary alkyl bromides could be employed in this reaction (3a-3f). Reaction using n-butyl chloride or n-butyl tosylate as alkylating reagent afforded the corresponding 3c in diminished yield, while n-butyl iodide gave comparable yield to n-butyl bromide. Secondary alkyl bromides, such as 2-bromopropane and 2-bromobutane, reacted with 1c to afford the sulfonation products (3g and 3h) in 52% and 21% yield, respectively, while tertiary alkyl bromides were not applicable to the reaction. Notably, N-alkyl indoles and azaindole were also found to be suitable substrates in the reaction (3i-3k).

For the efficient preparation of corresponding aryl sulfonic esters, diaryliodonium salts were then selected as

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**Scheme 3.** Sulfonation scope of alkyl halides. Reaction conditions: 1 (0.4 mmol), CuSO<sub>4</sub> (1.6 mmol), *t*-BuNC (2.0 mmol) in toluene/Alkyl-Br (6.0 mL/1.0 mL), under nitrogen atmosphere, sealed tube, 20 h. PMP = p-methoxyphenyl. Yields shown are of the isolated products.

the arylation reagent.<sup>[20]</sup> With the optimized reaction conditions in hand (Supporting Information, Table S2, entry 15), several substrates were investigated with diphenyliodonium triflate or tetrafluoroborate as the arylation reagent at 120 °C (Scheme 4). This sulfonation reaction proceeded well with functionalized indoles bearing various substitutions at the N1,



**Scheme 4.** Sulfonation scope of diaryliodonium salts. Reaction conditions: 1 (0.4 mmol),  $CuSO_4$  (1.2 mmol), *t*-BuNC (1.44 mmol) and  $Ar_2IX$  (1.2 mmol) in  $CH_3CN$  (6.0 mL), under nitrogen atmosphere, sealed tube, 20 h. Yields shown are of the isolated products.

C2, or C5 position with different electronic properties, affording the corresponding phenyl sulfonates in moderate to good yields (4a-4h). *N*-Phenyl azaindole was also functionalized in a similar manner (4i) and various symmetrical diaryliodonium salts could be successfully employed to react with *N*-phenyl indole (1a), affording indolyl C3 aryl sulfonates in good yields (4j-4p). The identity of 4g was further confirmed by X-ray crystallographic analysis.<sup>[19]</sup>

To further explore the generality and scope of this approach, various heterocycles were investigated with slight modifications to the standard reaction conditions (Scheme 5),



**Scheme 5.** Sulfonation scope of heterocycles. Reaction Conditions: Reactions were conducted on 0.4 mmol scale,  $CuSO_4$  (1.6 mmol), *t*-BuNC (2.0 mmol), 130 °C, under nitrogen atmosphere, sealed tube, 20–48 h. Yields shown are of the isolated products. [a] DCE (6.0 mL). [b] Yield based on 80% conversion. [c] *n*-Propyl bromide (1.0 mL) in toluene (6.0 mL). [d] CuSO<sub>4</sub> (1.2 mmol), *t*-BuNC (1.44 mmol), Ar<sub>2</sub>IX (1.2 mmol) in CH<sub>3</sub>CN (6.0 mL), 120 °C. [e] *n*-Propyl bromide (1.0 mL) in CH<sub>3</sub>CN (6.0 mL).

due to the different electronic properties of each class of heterocycles. To our delight, benzo[g]indole gave sulfonation products **5a–5c** in good yields, and 3,5-dimethyl-1-phenyl-pyrazole could also be functionalized in a similar manner to furnish **6a–6c** in moderate yields. However, non-substituted 1-phenylpyrazole failed to react under the reaction conditions which may be due to the electronic effects. Sulfonation of *N*-phenyl pyrrole afforded **7a** in 64 % yield, while the reaction of *N*-methyl carbazole with copper sulfate and *n*-propyl bromide was sluggish under the standard condition. Intriguingly, when changing the solvent from toluene to acetonitrile, the reaction was improved and gave the *n*-propyl sulfonated product **8a** in 72 % yield. Furthermore, the phenyl sulfonic ester **8b** could be generated successfully in high yield from *N*-methyl carbazole.

To gain insight into the possible pathway of this novel sulfonation reaction, several control experiments were carried out as shown in Scheme 6. Comparable yields could be

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Scheme 6. Preliminary mechanistic studies.

achieved when 2,2,6,6-tetramethyl-piperidine-1-oxy (TEMPO) or *p-tert*-butylphenol (PTBP) was used as radical scavengers [Eq. (1)].<sup>[21]</sup> Moreover, when **1c** was reacted with a radical clock substrate 6-bromohex-1-ene, sulfonic ester 9 was obtained in 66% yield without observation of the corresponding cyclization product [Eq. (2)]. These results may rule out the possibility of radical pathways for this transformation.<sup>[22]</sup> As isocyanides were well documented to promote the transformation of Cu<sup>II</sup> to Cu<sup>I</sup>, [16b,23] we speculated that the use of Cu<sub>2</sub>SO<sub>4</sub> may also lead to the desired product. To address this, N-phenyl indole 1a was treated with relatively unstable Cu<sub>2</sub>SO<sub>4</sub>, which was freshly prepared from  $Cu_2O$  and  $(CH_3)_2SO_4$ <sup>[24]</sup> in the absence of *t*-BuNC in DCE [Eq. (3)]. This reaction did afford the sulfonated product 2a, albeit in only 9% yield [Eq. (3)]. The low yield may attribute to the instability of Cu<sub>2</sub>SO<sub>4</sub> at elevated temperature. Interestingly, when the reaction was carried out in the presence of t-BuNC, significantly improved yield was obtained, which indicated that the isocyanide may play the second role, that is, as a ligand.

Although the detailed reaction mechanism remains to be clarified, a plausible mechanism for this reaction was proposed in Scheme 7. Copper sulfate was initially reduced by *t*-BuNC to form the complex **A**, where the isocyanide also acted as a ligand. The coordination of the isocyanide to copper center may stabilize the Cu<sup>1</sup> species and weaken the O–S bond thus activating the sulfate anion. The given complex **A** reacted with electron-rich heteroarene substrate to afford Cu<sup>1</sup> heteroaryl sulfonic intermediate **B** via a Friedel–Crafts-type S<sub>E</sub>Ar reaction, which finally reacted with different



Scheme 7. Plausible mechanism (Ligands are omitted for clarity).

electrophiles, such as alkyl halides or aryl iodonium salts, to give the corresponding alkyl or aryl sulfonates, respectively.

In summary, we have developed a direct synthesis of functionalized alkyl/aryl sulfonic esters using copper sulfate as the novel sulfonating source through the activation effect of *tert*-butyl isocyanide. Various heterocycles such as indoles, azaindoles, pyrroles, pyrazoles, and carbazoles worked well to afford the corresponding sulfonic esters smoothly. The given approach represents the first example to use copper sulfate as an environmentally benign inorganic sulfonation reagent and provides a novel protocol for the activation of chemically inert inorganic salts for application in organic synthesis. The isocyanide is conceived to play a threefold role in the activation of conventionally inert copper sulfate: 1) reducing copper(II) to copper (I); 2) acting as a ligand; 3) facilitating the dissociation of the robust O–S bond. Further research are currently being investigated in our lab.

#### **Experimental Section**

1a (77.6 mg, 0.4 mmol), copper sulfate anhydrous (255.2 mg, 1.6 mmol), and *t*-BuNC (166.0 mg, 2.0 mmol) in DCE (6.0 mL) were added to a 35 mL sealed tube. The tube was sealed and the reaction mixture was stirred at 130 °C under nitrogen atmosphere. After 20 h, the reaction mixture was diluted with water (10 mL) and extracted with EtOAc ( $3 \times 10$  mL) and the combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated in vacuo. The given residue was purified by column chromatography (petroleum ether/EtOAc 5:1) to give the sulfonation product **2a** (109.0 mg, 81%) as a yellow solid.

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### **Conflict of interest**

The authors declare no conflict of interest.

**Keywords:** C–H activation  $\cdot$  copper sulfate  $\cdot$  heterocycles  $\cdot$  isocyanide  $\cdot$  sulfonation

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For selected reviews, see: a) X. Guo, D. Gu, Z. Wu, W. Zhang, *Chem. Rev.* 2015, 115, 1622; b) S. E. Allen, R. R. Walvoord, R. Padilla-Salinas, M. C. Kozlowski, *Chem. Rev.* 2013, 113, 6234; c) C. Zhang, C. Tang, N. Jiao, *Chem. Soc. Rev.* 2012, 41, 3464; d) K. Hirano, M. Miura, *Chem. Commun.* 2012, 48, 10704; e) A. E. Wendlandt, A. M. Suess, S. S. Stahl, *Angew. Chem. Int. Ed.* 2011, 50, 11062; *Angew. Chem.* 2011, 123, 11256; f) D. Ma, Q. Cai, Acc. Chem. Res. 2008, 41, 1450; g) Modern Organocopper *Chemistry* (Ed.: N. Krause), Wiley-VCH, Weinheim, 2002.

<sup>[2]</sup> For selected C-X bond formation using CuX or CuX<sub>2</sub>, see: a) L. Yang, Z. Lu, S. S. Stahl, *Chem. Commun.* **2009**, 6460; b) X. Wan,

Z. Ma, B. Li, K. Zhang, S. Cao, S. Zhang, Z. Shi, J. Am. Chem. Soc. 2006, 128, 7416; c) D. Kalyani, A. R. Dick, W. Q. Anani, M. S. Sanford, Org. Lett. 2006, 8, 2523; For selected acetoxylation using Cu(OAc)<sub>2</sub>, see: d) Z. Wang, Y. Kuninobu, M. Kanai, Org. Lett. 2014, 16, 4790; e) X. Chen, X. S. Hao, C. E. Goodhue, J.-Q. Yu, J. Am. Chem. Soc. 2006, 128, 6790; For selected nitration using Cu(NO<sub>3</sub>)<sub>2</sub>, see: f) Y. Li, M. Gao, B. Liu, B. Xu, Org. Chem. Front. 2017, 4, 445; g) M. Gao, B. Xu, Org. Lett. 2016, 18, 4746; h) M. Gao, Y. Li, Y. Gan, B. Xu, Angew. Chem. Int. Ed. 2015, 54, 8795; Angew. Chem. 2015, 127, 8919; i) L. Zhang, Z. Liu, H. Li, G. Fang, B. Barry, T. A. Belay, Q. Liu, Org. Lett. 2011, 13, 6536.

- [3] Copper(II) sulfate: R. V. Hoffman, Encyclopedia of Reagents for Organic Synthesis, Wiley, New York, 2001.
- [4] R. P. Hanzlik, M. Leinwetter, J. Org. Chem. 1978, 43, 438.
- [5] R. V. Hoffman, R. D. Bishop, P. M. Fitch, R. Hardenstein, J. Org. Chem. 1980, 45, 917.
- [6] C. W. Jefford, Y. Li, Y. Wang, Org. Synth. 1993, 71, 207.
- [7] a) C. Zhang, Y. Ou, W. Lei, L. Wan, J. Ji, Z. Xu, Angew. Chem. Int. Ed. 2016, 55, 3054; Angew. Chem. 2016, 128, 3106; b) Y. Li, J. Pu, X. Jiang, Org. Lett. 2014, 16, 2692.
- [8] The dissociation energy of the single O–S bond in sulfuric acid was reported to be as high as 92.0 kcalmol<sup>-1</sup>; see: Y.-R. Luo, *Comprehensive Handbook of Chemical Bond Energies*, CRC, Boca Raton, FL, **2007**, pp. 363.
- [9] R. V. Siriwardane, J. A. Poston, E. P. Fisher, M. S. Shen, A. L. Miltz, *Appl. Surf. Sci.* **1999**, *152*, 219.
- [10] a) L. Suárez, M. A. Díez, R. García, F. A. Riera, J. Ind. Eng. Chem. 2012, 18, 1859; b) J. R. Lu, R. K. Thomas, J. Penfold, Adv. Colloid Interface Sci. 2000, 84, 143.
- [11] For selected reviews, see: a) R. A. Al-Horani, U. R. Desai, *Tetrahedron* 2010, 66, 2907; b) D. Kelly, *Synlett* 2003, 2263.
- [12] J. Hoyle in *The Chemistry of Sulphonic Acids, Esters and Their Derivatives* (Eds.: S. Patai, Z. Rappoport), Wiley, Chichester, 1991, pp. 351–399.
- [13] a) A. S. Deeming, C. J. Russell, M. C. Willis, Angew. Chem. Int. Ed. 2016, 55, 747; Angew. Chem. 2016, 128, 757; b) D. Zheng, Y. An, Z. Li, J. Wu, Angew. Chem. Int. Ed. 2014, 53, 2451; Angew. Chem. 2014, 126, 2483.
- [14] For recent reviews on isocyanides, see: a) B. Song, B. Xu, Chem. Soc. Rev. 2017, 46, 1103; b) V. P. Boyarskiy, N. A. Bokach, K. V.

Luzyanin, V. Y. Kukushkin, *Chem. Rev.* **2015**, *115*, 2698; c) H. Wang, B. Xu, *Chin. J. Org. Chem.* **2015**, *35*, 588; d) G. Qiu, Q. Ding, J. Wu, *Chem. Soc. Rev.* **2013**, *42*, 5257; e) S. Lang, *Chem. Soc. Rev.* **2013**, *42*, 4867; f) T. Vlaar, E. Ruijter, B. U. W. Maes, R. V. A. Orru, *Angew. Chem. Int. Ed.* **2013**, *52*, 7084; *Angew. Chem.* **2013**, *125*, 7222.

- [15] R. A. Michelin, A. J. L. Pombeiro, M. F. C. Guedes da Silva, *Coord. Chem. Rev.* 2001, 218, 75.
- [16] a) G. Qian, X. Hong, B. Liu, H. Mao, B. Xu, Org. Lett. 2014, 16, 5294; b) X. Huang, S. Xu, Q. Tan, M. Gao, M. Li, B. Xu, Chem. Commun. 2014, 50, 1465; c) S. Xu, X. Huang, X. Hong, B. Xu, Org. Lett. 2012, 14, 4614.
- [17] For selected examples on direct sulfonation of indoles, see: a) C. Schneider, E. Broda, V. Snieckus, Org. Lett. 2011, 13, 3588;
  b) G. F. Smith, D. A. Taylor, Tetrahedron 1973, 29, 669.
- [18] Phosphine ligands were reported to reduce CuSO<sub>4</sub> to Cu<sup>1</sup> complexes; see: a) W. Yuan, Y. Chen, J. Chen, *Inorg. Chem. Commun.* 2009, *12*, 1197; b) H. Shi, C. Xu, A. Jia, X. Huang, Q. Zhang, *Inorg. Chim. Acta* 2014, *419*, 55.
- [19] For crystallographic data of compounds **2m** and **4g**, see the Supporting Information.
- [20] a) V. V. Zhdankin, P. J. Stang, Chem. Rev. 2002, 102, 2523; b) P. J. Stang, V. V. Zhdankin, Chem. Rev. 1996, 96, 1123.
- [21] a) J. Liu, C. Fan, H. Yin, C. Qin, G. Zhang, X. Zhang, H. Yi, A. Lei, *Chem. Commun.* 2014, 50, 2145; b) U. M. V. Basavanag, A. D. Santos, L. E. Kaim, R. Gámez-Montaño, L. Grimaud, *Angew. Chem. Int. Ed.* 2013, 52, 7194; *Angew. Chem.* 2013, 125, 7335.
- [22] C. W. Cheung, F. E. Zhurkin, X. Hu, J. Am. Chem. Soc. 2015, 137, 4932.
- [23] a) T. Tsuda, H. Habu, S. Horiguchi, T. Saegusa, J. Am. Chem. Soc. 1974, 96, 5930; b) T. Saegusa, Y. Ito, S. Kobayashi, K. Hirota, H. Yoshioka, Bull. Chem. Soc. Jpn. 1969, 42, 3310.
- [24] H. J. Berthold, J. Born, Z. Anorg. Allg. Chem. 1987, 550, 7.

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## **Communications**



## **Communications**

C—H Activation	
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+ R=LG

of isocyanide. The otherwise chemically inert copper sulfate was unusually activated by an isocyanide and employed as the source of the sulfonic substituents in an unprecedented fashion.

OR

uSC

tBuNC as additive

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