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Cu(II)-Mediated Methylthiolation of Aryl C−H Bonds with DMSO

Lingling Chu,[†] Xuyi Yue,[†] and Feng-Ling Qing*[,†,‡]

Key Laboratory of Organofluorine Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Lingling Lu, Shanghai 200032, China and College of Chemistry, Chemical Engineering and Biotechnology, Donghua University, 2999 North Renmin Lu, Shanghai 201620, China

flq@mail.sioc.ac.cn

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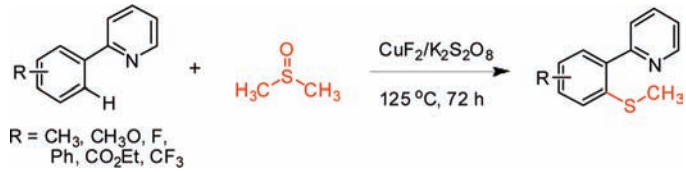
ABSTRACT



An unprecedented Cu(II)-mediated methylthiolation of aryl C−H bonds under oxidative conditions that employs the widely available DMSO as the methylthiolation reagent is described. Various functional groups in the substrates were tolerated, and ethylthiolation was also successfully achieved directly from diethyl sulfoxide under the same reaction conditions.

Aryl sulfides are indispensable in many fields of biology and material sciences, especially in the pharmaceutical area.[1] Among them, aryl methyl thioethers are important compounds with biological activities or skeletons that lead to biologically active compounds.[2] The classic method for preparing aryl methyl thioethers directly from aromatics usually consists of directed or heteroatom-facilitated lithiation and subsequent electrophilic substitution with dimethyl disulfide (Scheme 1).[3] A multistep transformation has also been reported, that is, chlorosulfonylation of electron-rich aromatics using chlorosulfonic acid followed by reduction with zinc powder and 30% HCl and then S-methylation with MeI (Scheme 1).[2c] These methods have become common and reliable methods in application, although the limitation of their harsh or multistep reaction conditions could be inevitable.[2c,3] Although carbon−sulfur bond formation via the cross-coupling reaction of thiols and aryl halides or vinyl halides catalyzed by the transition metals has recently gained significant developments,[4] no example for preparation of aryl methyl thioethers in this fashion has appeared so far.

Recently, the development of selective functionalization of C−H bonds catalyzed by transition metals combining with directing groups has witnessed tremendous progress.[5] Among the transition metals, copper is particularly attractive for C−H bond activation because of its low cost and low toxicity.[6]

Scheme 1. Traditional Methods versus Our Method

However, the formation of a C−S bond through transition-metal-mediated C−H functionalization has been less fruitful.[7] To our knowledge, only Yu reported $Cu(OAc)_2$-catalyzed thioetherification of the C−H bond of 2-phenylpyridine with PhSH and MeSSMe using O_2 as the oxidant.[7a] Doi and Batey independently described the palladium-catalyzed synthesis of 2-substituted benzothiazoles from thiobenzanilides via C−H functionalization/intramolecular C−S bond formation,[7b−d] and Dong disclosed a Pd-catalyzed C−H bond activation/

[†] Shanghai Institute of Organic Chemistry.
[‡] Donghua University.

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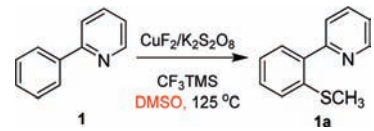
coupling with $ArSO_2Cl$ to produce sulfones.[7e] Described herein is the unprecedented Cu(II)-mediated methylthiolation of aryl C−H bonds under oxidative condition that employs the widely available DMSO as the methylthiolation reagent.

This new reaction was accidentally found during the course of our recent investigation on Cu(II)-mediated trifluoromethylation of an aryl C−H bond in the presence of an oxidant. Upon treatment of 2-phenylpyridine **1** with CuF_2 (1 equiv), $K_2S_2O_8$ (2 equiv), and CF_3SiMe_3 (2 equiv) in DMSO at 125 °C for 72 h, it was surprisingly found that only the methylthiolation of aryl C−H bond product **1a** was formed in 14% yield determined by GC (Scheme 2). This result showed that DMSO was used as methylthiolation agent in the C−S bond formation which is rare and attractive.[8] Intrigued by this experimental observation, we decided to optimize the conditions of methylthiolation. A screening of the catalysts showed copper salts profoundly affected the reaction outcomes. CuF_2 was infinitely superior to other copper salts ($Cu(OTf)_2$, $Cu(OAc)_2$, $CuCl_2$, and $CuBr_2$) as no product was observed with the latter four catalysts (Table 1, entries 1−5). Considering the organic sulfur compound may bind to Cu(II) salt which leads to catalyst deactivation,[9] an excess amount of Cu(II) is most likely required. Thus, we increased the amount of CuF_2 from 1 equiv to 4 equiv and were delighted to find that **1** was almost totally consumed (entries 5−8). Under the reaction conditions of entry 8, the GC−MS analysis of the reaction mixture showed that the

Scheme 2. Methylthiolation of Aryl C−H Bond Found Accidentally



(1) (a) Alcaraz, M.-L.; Atkinson, S.; Cornwall, P.; Foster, A. C.; Gill, D. M.; Humphries, L. A.; Keegan, P. S.; Kemp, R.; Merifield, E.; Nixon, R. A.; Noble, A. J.; O'Beirne, D.; Patel, Z. M.; Perkins, J.; Rowan, P.; Sadler, P.; Singleton, J. T. *Org. Proc. Res. Dev.* **2005**, *9*, 555. (b) Kaldor, S. W.; Kalish, V. J.; Davies, J. F.; Shetty, B. V.; Fritz, J. E.; Appelt, K.; Burgess, J. A.; Campanale, K. M.; Chirgadze, N. Y.; Clawson, D. K.; Dressman, B. A.; Hatch, S. D.; Khalil, D. A.; Kosa, M. B.; Lubbehusen, P. P.; Muesing, M. A.; Patick, A. K.; Reich, S. H.; Su, K. S.; Tatlock, J. H; Tornos, J.; Watts, A. J.; Woodland, I. A. *J. Med. Chem.* **1997**, *40*, 3979. (c) Liu, G.; Huth, J. R.; Olejniczak, E. T.; Mendoza, R.; DeVries, P.; Leitza, S.; Reilly, E. B.; Okasinski, G. F.; Fesik, S. W.; von Geldern, T. W. *J. Med. Chem.* **2001**, *44*, 1202. (d) De Martino, G.; Edler, M. C.; La Regina, G.; Coluccia, A.; Barbera, M. C.; Barrow, D.; Nicholson, R. I.; Chiosis, G.; Brancale, A.; Hamel, E.; Artico, M.; Silvestri, R. *J. Med. Chem.* **2006**, *49*, 947. (e) Gangjee, A.; Zeng, Y.; Talreja, T.; McGuire, J. J.; Kisliuk, R. L.; Queener, S. F. *J. Med. Chem.* **2007**, *50*, 3046. (f) De Martino, G.; La Regina, G.; Coluccia, A.; Edler, M. C.; Barbera, M. C.; Brancale, A.; Wilcox, E.; Hamel, E.; Artico, M.; Silvestri, R. *J. Med. Chem.* **2004**, *47*, 6120. (g) Nielsen, S. F.; Nielsen, E. Ø; Olsen, G. M.; Liljefors, T.; Peters, D. *J. Med. Chem.* **2000**, *43*, 2217. (h) Wang, Y.; Chackalamannil, S.; Chang, W.; Greenlee, W.; Ruperto, V.; Duffy, R. A.; McQuade, R.; Lachowicz, J. E. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 891. (i) Bonnet, B.; Soullez, D.; Girault, S.; Maes, L.; Landry, V.; Davioud-Charvet, E.; Sergheraert, C. *Bioorg. Med. Chem.* **2000**, *8*, 95. (j) Sawyer, J. S.; Schmittling, E. A.; Palkowitz, J. A.; Smith, W. J. *J. Org. Chem.* **1998**, *63*, 6338. (k) Baird, C. P.; Rayner, C. M. *J. Chem. Soc., Perkin Trans. 1* **1998**, 1973. (l) Procter, D. J. *J. Chem. Soc., Perkin Trans. 1* **2001**, 335. (m) Herradura, P. S.; Pendola, K. A.; Guy, R. K. *Org. Lett.* **2000**, *2*, 2019.

(2) (a) Kalgutkar, A. S.; Kozak, K. R.; Crews, B. C.; Marnett, L. J. *J. Med. Chem.* **1998**, *41*, 4800. (b) Laufer, S. A.; Striegel, H.-G.; Wagner, G. K. *J. Med. Chem.* **2002**, *45*, 4695. (c) Gallardo-Godoy, A.; Fierro, A.; McLean, T. H.; Castillo, M.; Cassels, B. K.; Reyes-Parada, M.; Nichols, D. E. *J. Med. Chem.* **2005**, *48*, 2407. (d) Pradhan, T. K.; De, A.; Mortier, J. *Tetrahedron* **2005**, *61*, 9007.

(3) (a) Stanetty, P.; Koller, H.; Mihovilovic, M. *J. Org. Chem.* **1992**, *57*, 6833. (b) Ranken, P. F.; McKinnie, B. G. *J. Org. Chem.* **1989**, *54*, 2985. (c) Fort, Y.; Rodriguez, A. L. *J. Org. Chem.* **2003**, *68*, 4918. (d) Pratt, S. A.; Goble, M. P.; Mulvaney, M. J.; Wuts, P. G. M. *Tetrahedron Lett.* **2000**, *41*, 3559.

(4) (a) Fernández-Rodríguez, M. A.; Shen,; Hartwig, J. F. *J. Am. Chem. Soc.* **2006**, *128*, 2180. (b) Rout, L.; Sen, T.; Punniyamurthy, T. *Angew. Chem., Int. Ed.* **2007**, *46*, 5583. (c) Wu, J.-R.; Lin, C.-H.; Lee, C.-F. *Chem. Commun.* **2009**, 4450. (d) Bryan, C. S.; Braunger, J. A.; Lautens, M. *Angew. Chem., Int. Ed.* **2009**, *48*, 7064. (e) Beletskaya, I. P.; Ananikov, V. P. *Eur. J. Org. Chem.* **2007**, 3431. (f) Kondo, T.; Mitsudo, T.-A. *Chem. Rev.* **2000**, *100*, 3205. (g) Wong, Y.-C.; Jayanth, T. T.; Cheng, C.-H. *Org. Lett.* **2006**, *8*, 5613. (h) Correa, A.; Carril, M.; Bolm, C. *Angew. Chem., Int. Ed.* **2008**, *47*, 2880. (i) Reddy, V. P.; Kumar, A. V.; Swapna, K.; Rao, K. R. *Org. Lett.* **2009**, *11*, 1697. (j) Mispelaere-Canivet, C.; Spindler, J.-F.; Perrio, S.; Beslin, P. *Tetrahedron* **2005**, *61*, 5253. (k) Itoh, T.; Mase, T. *Org. Lett.* **2004**, *6*, 4587. (l) Murata, M.; Buchwald, S. L. *Tetrahedron* **2004**, *60*, 7397. (m) Schopfer, U.; Schlapbach, A. *Tetrahedron* **2001**, *57*, 3069. (n) Li, G. Y. *Angew. Chem., Int. Ed.* **2001**, *40*, 1513. (o) Mann, G.; Baranano, D.; Hartwig, J. F.; Rheingold, A. L.; Guzei, I. A. *J. Am. Chem. Soc.* **1998**, *120*, 9205. (p) Millois, C.; Diaz, P. *Org. Lett.* **2000**, *2*, 1705. (q) Bates, C. G.; Gujadhur, R. K.; Venkataraman, D. *Org. Lett.* **2002**, *4*, 2803. (r) Wu, Y.-J.; He, H. *Synlett* **2003**, 1789. (s) Bates, C. G.; Saejueng, P.; Doherty, M. Q.; Venkataraman, D. *Org. Lett.* **2004**, *6*, 5005. (t) Chen, Y.-J.; Chen, H.-H. *Org. Lett.* **2006**, *8*, 5609. (u) Ranu, B. C.; Saha, A.; Jana, R. *Adv. Synth. Catal.* **2007**, *349*, 2690. (v) Ley, S. V.; Thomas, A. W. *Angew. Chem., Int. Ed.* **2003**, *42*, 5400.

(5) For recent reviews on directed C−H activation reactions, see: (a) Yu, J.-Q.; Giri, R.; Chen, X. *Org. Biomol. Chem.* **2006**, *4*, 4041. (b) Godula, K.; Sames, D. *Science* **2006**, *312*, 67. (c) Alberico, D.; Scott, M. E.; Lautens, M. *Chem. Rev.* **2007**, *107*, 174. (d) Li, B.-J.; Yang, S.-D.; Shi, Z.-J. *Synlett* **2008**, 949. (e) Herreras, C. I.; Yao, X.; Li, Z.; Li, C.-J. *Chem. Rev.* **2007**, *107*, 2546. (f) Campos, K. R. *Chem. Soc. Rev.* **2007**, *36*, 1069. (g) Seregin, I. V.; Gevorgyan, V. *Chem. Soc. Rev.* **2007**, *36*, 1173. (h) Davies, H. M. L.; Manning, J. R. *Nature* **2008**, *451*, 417. (i) Chen, X.; Engle, K. M.; Wang, D.-H.; Yu, J. Q. *Angew. Chem., Int. Ed.* **2009**, *48*, 5094. (j) Giri, R.; Shi, B.-F.; Engle, K. M.; Maugelc, N.; Yu, J.-Q. *Chem. Soc. Rev.* **2009**, *38*, 3242. (k) McGlacken, G. P.; Bateman, L. M. *Chem. Soc. Rev.* **2009**, *38*, 2447. (l) Daugulis, O.; Do, H.-Q.; Shabashov, D. *Acc. Chem. Res.* **2009**, *42*, 1074. (m) Muniz, K. *Angew. Chem., Int. Ed.* **2009**, *48*, 9412. (n) Ackermann, L.; Vicente, R.; Kapdi, A. R. *Angew. Chem., Int. Ed.* **2009**, *48*, 9792. (o) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147.

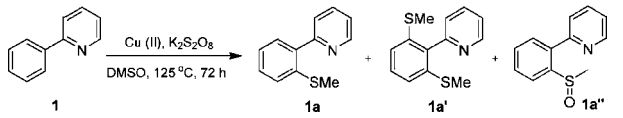
(6) (a) Brasche, G.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2008**, *47*, 1932. (b) Do, H.-Q.; Daugulis, O. *J. Am. Chem. Soc.* **2007**, *129*, 12404. (c) Li, Z.; Li, C.-J. *Proc. Natl. Acad. Sci. U.S.A.* **2006**, *103*, 8928. (d) Baslé, O.; Li, C.-J. *Green Chem.* **2007**, *9*, 1047. (e) Perry, A.; Taylor, R. J. K. *Chem. Commun.* **2009**, 3249. (f) Phipps, R. J.; Grimster, N. P.; Gaunt, M. J. *J. Am. Chem. Soc.* **2008**, *130*, 8172. (g) Phipps, R. J.; Gaunt, M. J. *Science* **2009**, *323*, 1593. (h) Uemura, T.; Imoto, S.; Chatani, N. *Chem. Lett.* **2006**, *35*, 842. (i) Yoo, W. J.; Correia, C. A.; Zhang, Y. H.; Li, C. J. *Synlett* **2009**, 138. (j) Baslé, O.; Li, C.-J. *Chem. Commun.* **2009**, 4124. (k) Monguchi, D.; Fujiwara, T.; Furukawa, H.; Mori, A. *Org. Lett.* **2009**, *11*, 1607. (l) Hamada, T.; Ye, X.; Stahl, S. S. *J. Am. Chem. Soc.* **2008**, *130*, 833. (m) Ban, I.; Sudo, T.; Taniguchi, T.; Itami, K. *Org. Lett.* **2008**, *10*, 3607. (n) Brasche, G.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2008**, *47*, 1932. (o) Ueda, S.; Nagasawa, H. *Angew. Chem., Int. Ed.* **2008**, *47*, 6411. (p) Hewgley, J. B.; Stahl, S. S.; Kozlowski, M. C. *J. Am. Chem. Soc.* **2008**, *130*, 12232. (q) Li, X. L.; Hewgley, J. B.; Mulrooney, C. A.; Yang, J. M.; Kozlowski, M. C. *J. Org. Chem.* **2003**, *68*, 5500. (r) Huffman, L. M.; Stahl, S. S. *J. Am. Chem. Soc.* **2008**, *130*, 9196. (s) Yao, B.; Wang, D.-X.; Huang, Z.- T.; Wang, M.- X. *Chem. Commun.* **2009**, 2899.

(7) (a) Chen, X.; Hao, X.-S.; Goodhue, C. E.; Yu, J. Q. *J. Am. Chem. Soc.* **2006**, *128*, 6790. (b) Inamoto, K.; Arai, Y.; Hiroya, K.; Doi, T. *Chem. Commun.* **2008**, 5529. (c) Inamoto, K.; Hasegawa, C.; Hiroya, K.; Doi, T. *Org. Lett.* **2008**, *10*, 5147. (d) Joyce, L. L.; Batey, R. A. *Org. Lett.* **2009**, *11*, 2792. (e) Zhao, X.; Dimitrijevic, E.; Dong, V. M. *J. Am. Chem. Soc.* **2009**, *131*, 3466.

(8) Only one patent described the thioetherification of aromatics with electron-donating-groups using sulfoxides in HF; see: Adolf, W. Arylsulfonium salts. Ger. Offen. DE 2644591A1, Apr 8, 1978.

(9) (a) Kondo, T.; Mitsudo, T. *Chem. Rev.* **2000**, *100*, 3205. (b) Alvaro, E.; Hartwig, J. F. *J. Am. Chem. Soc.* **2009**, *131*, 7858. (c) Mann, G.; Baranano, D.; Hartwig, J. F.; Rheingold, A. L.; Guzei, I. A. *J. Am. Chem. Soc.* **1998**, *120*, 9205. (d) Louie, J.; Hartwig, J. F. *J. Am. Chem. Soc.* **1995**, *117*, 11598.

Table 1. Optimization Studies for Cu-Mediated C−H Methylthiolation[a]



entry	Cu(II) (equiv)	oxidant (2 equiv)	convn[b] (%)	yield of **1a**[b] (%)
1	$Cu(OTf)_2$ (1)	$K_2S_2O_8$	13	none
2	$Cu(OAc)_2$ (1)	$K_2S_2O_8$	18	trace
3	$CuCl_2$ (1)	$K_2S_2O_8$	25	none
4	$CuBr_2$ (1)	$K_2S_2O_8$	17	none
5	CuF_2 (1)	$K_2S_2O_8$	48	14
6	CuF_2 (2)	$K_2S_2O_8$	59	27
7	CuF_2 (3)	$K_2S_2O_8$	82	59
8	CuF_2 (4)	$K_2S_2O_8$	95	83
9	CuF_2 (4)	no	29	26
10	CuF_2 (4)	O_2	22	12[c]
11	CuF_2 (4)	CAN	29	21
12	CuF_2 (4)	BPO	38	17
13	CuF_2 (4)	OXONE	31	25
14	CuF_2 (4)	BQ	21	trace
15	No	$K_2S_2O_8$	11	none

[a] All of the reactions were carried out with 0.4 mmol of **1** in 0.8 mL of DMSO. [b] Determined by GC analysis. [c] The reaction was carried out under oxygen atmosphere.

desired product **1a** was formed in 83% yield along with the dimethylthiolated product **1a′** (7%), sulfoxide product **1a″** (3%), dimethyl sulfone ($(CH_3)_2SO_2$ 5%), and dimethyl sulfate ($(CH_3O)_2SO_2$ 10%). Compound **1a″** and dimethyl sulfone were produced from the oxidation of **1a** and DMSO with $K_2S_2O_8$, respectively. Oxidants also highly affected this reaction. Switching the oxidant from $K_2S_2O_8$ to no oxidant or other oxidants, such as oxygen, ammonium cerium(IV) nitrate (CAN), benzoyl peroxide (BPO), *p*-benzoquinone (BQ), and potassium monopersulfate compound (OXONE), resulted in the incomplete conversion of **1** and a decreased amount of **1a** (entries 9−14). These results further indicated that the S atom in **1a** was transferred from DMSO[10] instead of $K_2S_2O_8$. No reaction was observed in the absence of

Scheme 3. Proposed Mechanism for the Methylthiolation

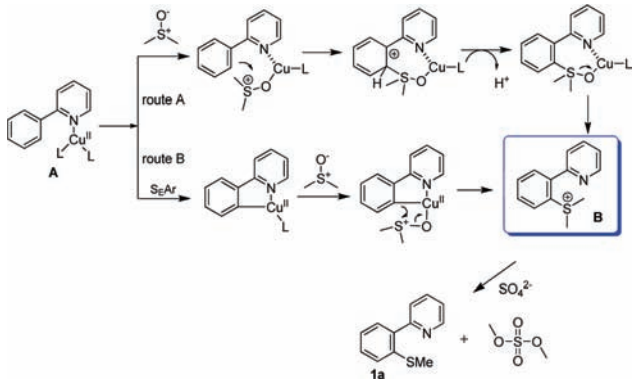
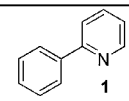
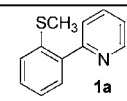
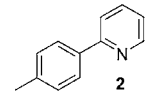
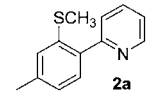
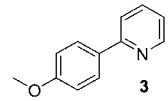
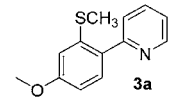
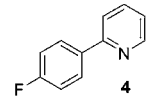
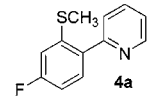
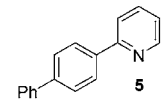
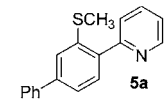
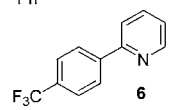
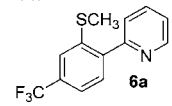
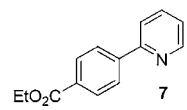
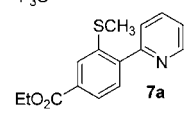
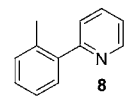
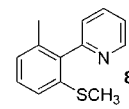
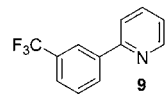
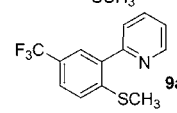
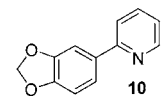
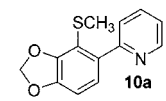
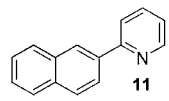
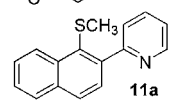
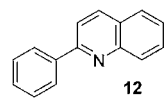
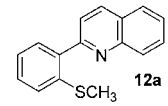
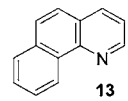
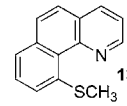
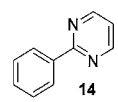
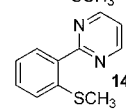
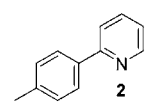
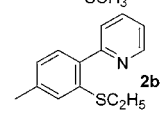


Table 2. Cu(II)-Mediated C−H Methylthiolation of Aryl C−H Bonds

entry	substrate	product	convn [%][b]	yield [%][c]
1			95	67 (7)
2			100	68 (6)
3			100	65 (15)
4			100	55 (15)
5			100	71 (8)
6			81	69 (10)
7			89	66 (9)
8			48	23
9			79	54
10			100	62 (14)
11			100	72 (6)
12			56	64 (9)
13			57	69
14			44	47
15[d]			89	63

a Reaction conditions: substrate (0.4 mmol), $K_2S_2O_8$ (0.8 mmol), CuF_2 (1.6 mmol), DMSO (11.2 mmol), 125 °C for 72 h. [b] Determined by GC. [c] Isolated yield based on conversion. The yield of corresponding dimethylthiolated product is shown in parentheses and determined by GC−MS of the reaction mixture. [d] 4-*p*-Tolylpyridine (0.4 mmol), $K_2S_2O_8$ (0.8 mmol), CuF_2 (1.6 mmol), diethyl sulfoxide (11.2 mmol), 125 °C for 72 h.

copper salt, indicating that the mediation of Cu(II) is necessary (entry 15).

We also conducted a preliminary mechanistic investigation to gain insight into this novel reaction. It is reasonable to assume that sulfonium intermediate **B** would be formed in this reaction and then one methyl transferred in the presence of a nucleophile (Scheme 3).[8,11] No reaction was observed in the absence of copper salt, and biphenyl was an ineffective substrate, suggesting that copper is involved in the reaction and the coordination of Cu(II) to the N atom of the pyridine in the substrate promoted the formation of the sulfonium **B** with high *ortho*-selectivity. Two potential pathways led to intermediate **B** from the copper complex **A**. Route A involved an intramolecular eletrophilic aromatic substitution and then cleavage of the S−O bond in the assistance of Cu(II). In route B, a metalacycle could be formed from **A** via S_EAr and then rearranged to give the intermediated **B**.[12] A subsequent methyl-transfer process promoted by a nucleophile would deliver the methylthiolated product **1a**.[11] Since a small amount (10% by GC−MS) of dimethyl sulfate ($(CH_3O)_2SO_2$) was detected (Table 1, entry 8), it is very likely that one methyl group of sulfonium **B** was captured by the sulfate ion generated by the decomposition of $K_2S_2O_8$. However, the reaction did not give an appreciable amount of dimethyl sulfate (it should be 41.5% by GC−MS), and we surmised that sulfuric acid monomethyl ester and its corresponding potassium methyl sulfate were also generated and could not be detected by GC−MS.

With a set of optimized conditions in hand, we promptly examined the scope of the arylpyridine motif in the C−H methylthiolation process. We found that the 2-phenylpyridine derivatives bearing either electron-donating or electron-withdrawing functional groups on the phenyl ring reacted smoothly to afford the desired monomethylthiolated products in 54−72% yield, while the reaction afforded higher conversion when the phenyl group bore electron-donating groups (Table 2, entries 1−11). It should be noted that the chemoselectivity of 2-(3-(trifluoromethyl)phenyl)pyridine was different from that of 2-(benzo[*d*][1,3]dioxol-5-yl)pyridine, and we ascribed the chemoselectivity of the former mainly to steric factors and the latter to electronic effects (entries 9 and 10). Functional groups such as MeO, F, and CO_2Et were tolerated (entries 3, 4, and 7). The reactions of 2-*o*-tolylpyridine, 2-phenylquinoline, and benzo[*h*]quinoline were very sluggish, and only moderate portion of starting materials were consumed (entries 8, 12, and 13). We surmise that the low reactivity is due to the restricted conformation of these compounds.[13] Other directing groups such as pyrimidine were also effective for aryl C−H methylthiolation under the optimized conditions, while the yields were lower than the pyridine counterpart **1** (entry 14). Furthermore, the ethylthiolation is also successfully achieved directly from diethyl sulfoxide under the same reaction conditions (entry 15). It was noteworthy that the corresponding dimethylthiolated products were also detected by GC−MS of the reaction mixtures, but the yields were very low for most of the substrates.

In conclusion, this communication highlights the direct use of DMSO as the reagent for Cu(II)-mediated C−H bond methylthiolation and the tolerance of various functional groups in substrates. Compared to the traditional methods for preparing aryl methyl thioethers, our method is more direct and convenient.

Acknowledgment. The National Natural Science Foundation of China is greatly acknowledged for funding this work.

Supporting Information Available: Detailed experimental procedures and characterization for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(10) No any MeSSMe or MeSH was detected by LC−MS in our used DMSO.

(11) Coward, J. K.; Sweet, W. D. *J. Org. Chem.* **1971**, *36*, 2337.

(12) Brasche, G.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2008**, *47*, 1932.

(13) Norinder, J.; Matsumoto, A.; Yoshikai, N.; Nakamura, E. *J. Am. Chem. Soc.* **2008**, *130*, 5858.