Tetrahedron Letters 50 (2009) 5523–5528

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Catechol violet as new, efficient, and versatile ligand for Cu(I)-catalyzed C–S coupling reactions

Basudeb Basu *, Bablee Mandal, Sajal Das, Sekhar Kundu

Department of Chemistry, North Bengal University, Darjeeling 734 013, India

A R T I C L E I N F O

Article history:
Received 17 June 2009
Revised 15 July 2009
Accepted 16 July 2009
Available online 18 July 2009

Keywords:
C–S coupling
CuI
Catechol violet
Diaryl sulfides
Vinyl thioethers

A B S T R A C T

Combination of CuI and Catechol violet (CuI-CV) was employed as catalyst for the first time in the C–S coupling reaction of a wide variety of aromatic halides, such as aryl iodides, bromo pyridines, activated aryl chlorides, and vinyl iodide with thiols to afford the corresponding thioethers in good to excellent yields. Broad range of functional group tolerance present in both the coupling partners has been observed in this reaction protocol.

After the seminal discovery of copper-promoted Ullmann reaction[1] for the construction of carbon-hetero atom bonds, several protocols have been reported over the years to perform C–N, C–O, and C–S linkages. The carbon-sulfur bonds are prevalent in numerous pharmaceutically and biologically active compounds.[2] Traditional copper-mediated C–S couplings between thiols and aryl halides require use of copper salts in greater than stoichiometric amounts, polar solvents, and high temperatures of around 200 °C.[3] Current interests for C–S bond construction have been mostly directed toward transition metal-catalysts (mainly Fe, Cu, Ni, and Pd) complexed with suitable ligands.[4] Migita and co-workers first reported the Pd-catalyzed cross-coupling of aryl bromides with thiols using $[Pd(PPh_3)_4]$.[5] Recently, Itoh et al. screened a number of phosphine ligands for Pd-catalyzed C–S coupling of aryl bromides (or triflate) with aryl thiols using a combination of $Pd_2(dba)_3$ and xantphos.[6] Other Pd-catalyzed C–S couplings were found to be selective for alkane thiols.[7] Since copper is an inexpensive metal as compared to palladium and other late-transition metals, several studies have been directed toward copper-catalyzed C–S cross-coupling reactions. Over the last decade, Venkataraman,[8] Buchwald,[9] and Palomo[10] have investigated the combination of aryl iodides with thiols using copper catalyst. In the process of development, various Cu–ligand complexes based on Schwesinger's phosphazene P_2-Et base,[10] neo-cuproine,[8] 1,2-diol,[9] 1,2-diamines,[11] amino acids,[12] 1,1,1-tris(hydroxymethyl)ethane—a tripod,[13] as well as ligand-free CuO[4e] and Indium oxide[4g] nanoparticles have been studied with varying success. In most cases, the protocol either is substrate-specific or requires specially designed phosphine or phosphine-free ligands besides requirement of high temperature, strong base, long reaction time, etc. Therefore, the development of more efficient, inexpensive, and mild catalytic systems involving copper and more generalized mild reaction conditions for the C–S coupling reactions has been the major target of contemporary research.

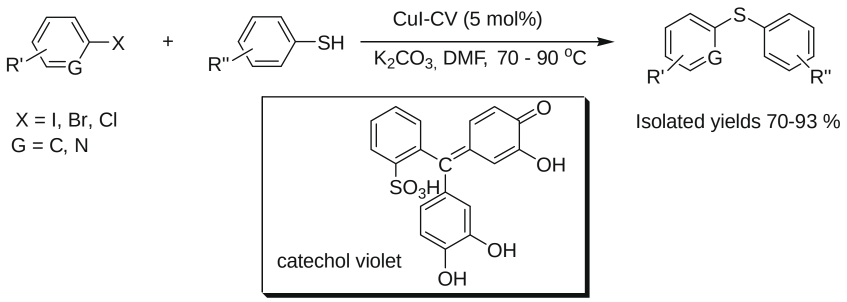
Over the last few years, we have been working on the development of several Pd- and Cu-catalyzed C–C and C–N coupling reactions.[14] In conjunction with our interest, we wish to report herein a general and efficient C–S coupling reaction between aryl halides and thiols using catalytic amounts of CuI and catechol violet (CV), as shown in Scheme 1.

Preliminary optimization of the C–S coupling reactions between aryl halide and aryl thiol with the aid of catalytic CuI and catechol violet was tested with *p*-iodoanisole and thiophenol (Table 1). As expected, in the absence of copper no aryl sulfide was detected (entry 1). Using only CuI (5 mol %) and carrying out the reaction at 90 °C for 21 h in DMF yielded the desired diaryl sulfide in 78% (Table 1, entry 2). On the other hand, similar reaction in presence of CuI and catechol violet (5 mol % each) afforded the desired diaryl sulfide in 93% yield in only 2 h (entry 3). Since formation of disulfide as a by-product is dependent on the reaction medium (i.e., the solvent), screening of a number of solvents and base was done at various temperatures. It was revealed that use of polar aprotic solvents resulted in the formation of the desired diaryl sulfide in substantial amount, whereas a polar protic or a non-polar solvent gave the disulfide as the main product (Table 1, entries 3, 7–13).

---

* Corresponding author. Tel.: +91 353 2776381; fax: +91 353 2699001.
E-mail addresses: basu_nbu@hotmail.com, basudeb.basu@yahoo.co.in (B. Basu).

0040-4039/$ - see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2009.07.076



Scheme 1. The CuI-CV-catalyzed synthesis of diarylsulfides is represented.

Table 1
Optimization of conditions for the CuI-CV-catalyzed coupling of *p*-iodoanisole and thiophenol

Entry[a]	Solvent	Base	Temperature (°C)	Time (h)	Yield[b] (%)
1[c]	DMF	K_2CO_3	90	24	00
2[d]	DMF	K_2CO_3	90	21	78
3	DMF	K_2CO_3	90	2	93
4	DMF	K_2CO_3	70	4	80
5	DMF	K_2CO_3	50	17	20
6	DMF	K_2CO_3	rt	9 days	15
7	Dioxane	K_2CO_3	80	8	72
8	THF	K_2CO_3	65	8	76
9	CH3CN	K_2CO_3	80	6	70
10	Toluene	K_2CO_3	70	10	00
11	Cyclohexane	K_2CO_3	80	8	08
12	Water	K_2CO_3	70	10	00
13	Methanol	K_2CO_3	65	10	10
14	DMF	KO^tBu	70	9	61
15	DMF	KF	70	9	49
16	DMF	Et_3N	70	9	55

[a] Reactions carried out with 5 mol % each of CuI and CV.
[b] Yield based on HPLC analysis.
[c] Reactions carried out in absence of CuI and CV.
[d] Reactions carried out using 5 mol % CuI only.

Performing the reaction at room temperature for a long time (9 days) afforded the desired diaryl sulfide in only 15% yield (entry 6). Use of K_2CO_3 as the base was found to be superior to KO*t*-Bu, KF, or trialkyl amine (entries 14–16). Thus, the optimized reaction conditions utilized 5 mol % of Cu(I), 5 mol % of catechol violet, and K_2CO_3 (1 equiv) in DMF as a solvent at 70–90 °C under nitrogen.

In the first part of this study, these reaction conditions[15] were applied to the coupling of various functionalized aryl iodides and aryl thiols (Table 2). No significant electronic effects were observed. Sterically hindered (*ortho*-substituted) aryl iodides underwent C–S coupling smoothly to furnish corresponding diaryl sulfide in good to excellent yield (Table 2, entries 2–4, 6). However, selectivity has been noted when the aryl iodides bearing chloro- or bromo- substituent afforded C–S coupling substituting only the iodo group (Table 2, entries 5 and 6). Furthermore, polythioethers, which are commercially important and widely used as thermosensitive recording materials,[16] were also prepared employing the same protocol and thus *bis*(phenylthio)benzene derivatives were obtained in fairly good yields (Table 2, entries 8 and 9).

The next part of this study involved the application of our protocol to the CuI-CV-catalyzed S-arylation of thiols with aryl bromides and aryl chlorides. It was noted that in case of bromoiodoarene, S-arylation selectively occurred with iodide keeping the bromide unchanged. While attempting with only aryl bromides, similar observations were obtained. The results are presented in Table 3 (entries 1 and 2). However, electron-deficient pyridine ring bearing bromo substituents (Table 3, entries 3–5) or bromoarenes bearing electron-withdrawing groups such as nitro, acyl, or aldehyde function (Table 3, entries 6–8) underwent C–S coupling smoothly yielding unsymmetrical diaryl sulfides in excellent yield using CuI-CV (10 mol % each) and K_2CO_3 as the base. Although Zhang et al.[4d] reported C–S coupling of aryl bromides bearing electron-donating groups in presence of NHC-based Ni catalyst, our conditions were effective only for activated aryl bromides.

Itoh et al. reported palladium-catalyzed C–S coupling reactions of activated aryl chlorides.[6] Here, we employed our optimized reaction conditions with minor modifications (Table 4). Changing the catalytic amount of CuI-CV from 5 to 10 mol % resulted in the formation of desired diaryl sulfides from activated aryl chlorides in high yields (86–92%) (Table 4, entries 2–4), though unactivated aryl chloride did not give the corresponding sulfide even after prolonging the reaction time (20 h) (Table 4, entry 1). C–S coupling reactions of activated aryl chloride have been considered to follow the nucleophilic substitution mechanism and thus do not ordinarily need a catalyst. However, the competition between nucleophilic substitution and metal-catalyzed oxidative addition followed by reductive elimination pathways still remains unclear. We did observe a clear advantage between the presence and absence of metal-ligand catalyst, the former combination being much more efficient even for activated aryl chloride.

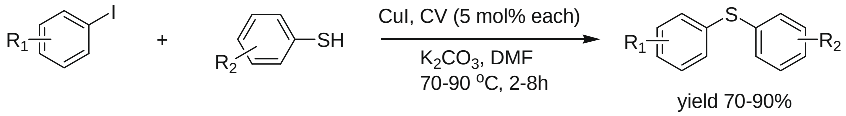
Vinyl sulfides are very important intermediates in organic chemistry. They are used as enolate ion equivalents,[17] Michael acceptors,[18] as intermediates in the synthesis of oxetanes,[19] cyclopentanones,[20] and cyclopentanes.[21] Due to the importance of these compounds a number of methods have been reported. Most noteworthy among them involves the addition of thiol to an alkyne.[22] More recently, Venkataraman et al.[23] reported the synthesis of vinyl sulfides by the thiolation of vinyl iodides using $[Cu(phen)(PPh_3)_2]NO_3$ as catalyst. To broaden the scope of our reaction protocol, we performed C–S coupling of vinyl iodides with aryl thiols using 5 mol % of CuI-CV. Gratifyingly, coupling occurred selectively and smoothly yielding the corresponding aryl vinyl sulfides in 83–93% isolated yields. Both aromatic and aliphatic thiols worked efficiently and the results are shown in Table 5.

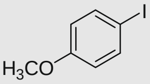
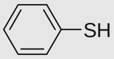
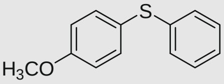
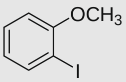
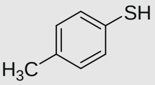
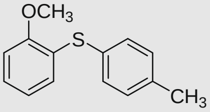
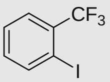
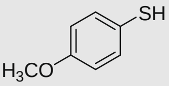
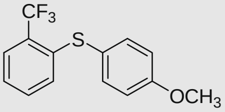
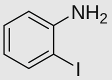
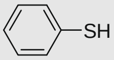
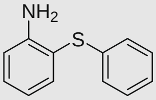
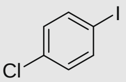
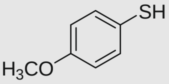
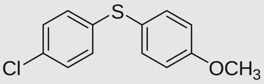
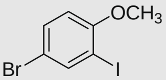
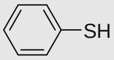
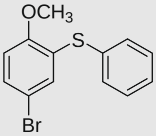
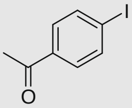
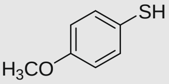
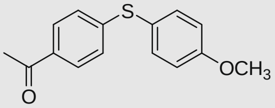
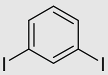
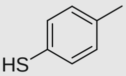
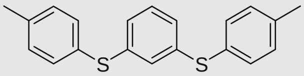
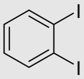
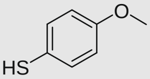
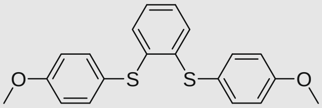
Finally, we extended our protocol to aliphatic thiols bearing free hydroxyl group. Thus, 2-mercaptoethanol was used as the aliphatic thiol for coupling with various aryl iodides. The cross-coupling reactions were carried out under optimal catalytic conditions: aryl iodide (1 mmol), CuI (5 mol %), CV (5 mol %), 2-mercaptoethanol (1.1 mmol), and K_2CO_3 (1 mmol) in DMF at 90 °C for 8 h. The results are presented in Table 6, which showed excellent conversion to the aryl alkyl sulfides with free terminal hydroxyl group. No by-product was isolated or observed while monitoring by TLC.

In summary, we found that inexpensive and commercially available catechol violet is a new, efficient, and versatile ligand, which could promote CuI-catalyzed C–S cross-coupling reactions between aryl or vinyl halides and various thiophenols. Generally,

Table 2

CuI-CV-catalyzed C–S coupling of aryl iodides with aryl thiols



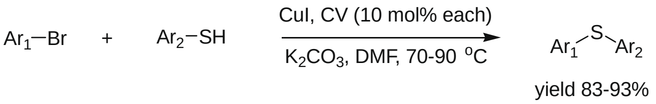
Entry	Aryl iodide	Thiol	Conditions[a] temp/time	Product	Yield[c] (%)
1			90 °C/2 h		90
2			70 °C/8 h		75
3			85 °C/6 h		89
4			90 °C/4 h		90
5			80 °C/6 h		87
6			90 °C/8 h		70
7			70 °C/5 h		86
8[b]			80 °C/4 h		71
9[b]			80 °C/4 h		69

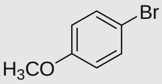
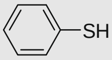
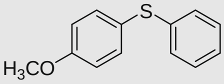
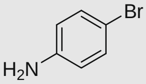
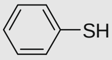
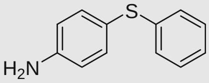
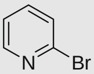
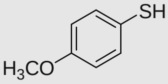
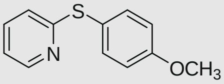
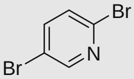
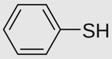
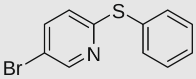
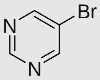
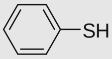
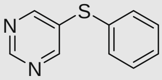
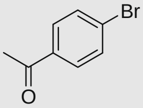
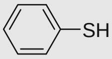
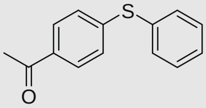
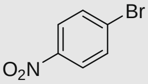
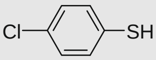
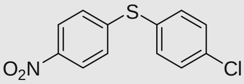
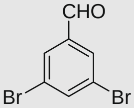
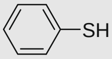
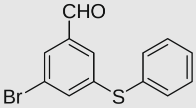
[a] Aryl iodide: thiol: CuI-CV (1 mmol: 1.1 mmol: 5 mol %) and K_2CO_3 (1 mmol) was taken in DMF (2 mL).

[b] Aryl iodide: thiol: CuI-CV (0.5 mmol: 1.1 mmol: 10 mol %) and K_2CO_3 (1 mmol) was taken in DMF (2 mL).

[c] Yield refers to pure isolated products characterized by spectroscopic (^{1}H, ^{13}C NMR, and IR) data.

Table 3
CuI-CV-catalyzed C–S coupling of aryl bromides with aryl thiols

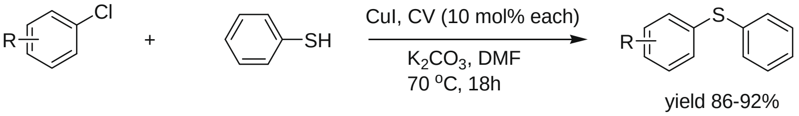


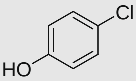
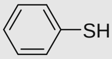
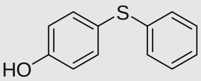
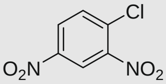
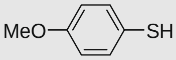
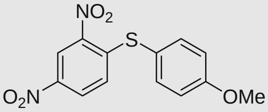
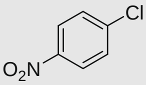
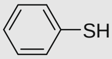
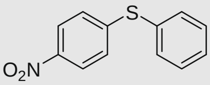
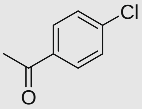
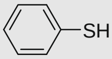
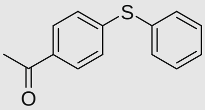
Entry	Bromoarene	Thiol	Conditions[a] temp/time	Product	Yield[b] (%)
1			90 °C/12 h		00
2			90 °C/14 h		00
3			70 °C/6 h		88
4			70 °C/2 h		93
5			70 °C/7 h		84
6			70 °C/18 h		87
7			70 °C/20 h		90
8			70 °C/8 h		83

[a] Bromoarene: thiol: CuI-CV (1 mmol: 1.1 mmol: 10 mol %) and K_2CO_3 (1 mmol) was taken in DMF (2 mL).

[b] Yield refers to the pure isolated products characterized by spectroscopic (^{1}H, ^{13}C NMR, and IR) data.

Table 4
CuI-CV-catalyzed C–S coupling of aryl chlorides with aryl thiols

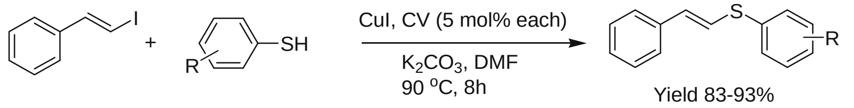


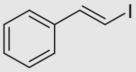
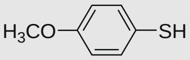
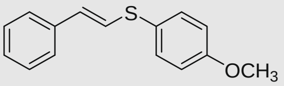
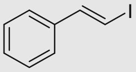
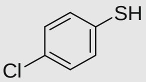
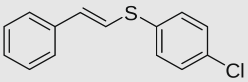
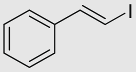
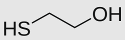
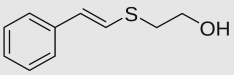
Entry	Aryl chloride	Thiol	Conditions[a] temp/time	Product	Yield[b] (%)
1			70 °C/20 h		00
2			70 °C/18 h		86
3			70 °C/20 h		88
4			70 °C/12 h		92

[a] Aryl chloride: thiol: CuI-CV (1 mmol: 1.1 mmol: 10 mol %) and K_2CO_3 (1 mmol) was taken in DMF (2 mL).

[b] Yield refers to the pure isolated products characterized by spectroscopic (^{1}H, ^{13}C NMR, and IR) data.

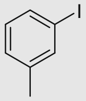
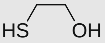
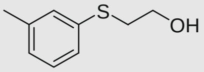
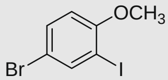
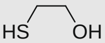
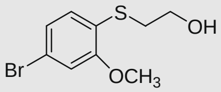
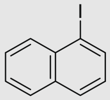
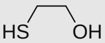
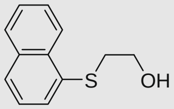
Table 5
CuI-CV-catalyzed C–S coupling of styryl iodides with thiols



Entry	Styryl iodide	Thiol	Conditions[a] temp/time	Product	Yield[b] (%)
1			90 °C/8 h		83
2			90 °C/8 h		83
3			90 °C/8 h		93

[a] Styryl iodide: thiol: CuI-CV (1 mmol: 1.1 mmol: 5 mol %) and K_2CO_3 (1 mmol) was taken in DMF (2 mL).
[b] Yield refers to the pure isolated products characterized by spectroscopic (^{1}H, ^{13}C NMR, and IR) data.

Table 6
CuI-CV-catalyzed C–S coupling of aryl iodides with aliphatic thiol

Entry	Aryl iodide	Thiol	Conditions[a] temp/time	Product	Yield[b] (%)
1			90 °C/4 h		83
2			90 °C/4 h		87
3			90 °C/ 4 h		78

[a] Aryl iodide: thiol: CuI-CV (1 mmol: 1.1 mmol: 5 mol %) and K_2CO_3 (1 mmol) was taken in DMF (2 mL).
[b] Yield refers to the pure isolated products characterized by spectroscopic (^{1}H, ^{13}C NMR, IR, and HRMS) data.

very good to excellent yields of the desired diaryl or aryl alkyl sulfides could be obtained successfully under mild reaction conditions. The catalytic combination CuI-CV offers general applicability and avoids use of expensive phosphines or other specially designed ligands. Further applications of this catalytic combination are currently under investigation.

Acknowledgments

We are grateful to the Department of Science & Technology, New Delhi for financial support (Grant No. SR/S1/OC–49/2006). We also thank CSIR, New Delhi for awarding senior research fellowships to BM and SD.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2009.07.076.

References and notes

1. (a) Ullmann, F. *Ber. Dtsch. Chem. Ges.* **1903**, *36*, 2382; For review, see: (b) Lindley, J. *Tetrahedron* **1984**, *40*, 1433; (c) Hassan, J.; Sévignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359.
2. (a) Jones, D. N.. In *Comprehensive Organic Chemistry*; Barton, D. H., Ollis, D. W., Eds.; Pergamon: New York, 1979; Vol. 3, (b) Tiecco, M. *Synthesis* **1988**, 749; (c) Rayner, C. M. *Contemp. Org. Synth.* **1996**, *3*, 499; (d) Baird, C. P.; Rayner, C. M. *J. Chem. Soc., Perkin Trans. 1* **1998**, 1973; (e) Procter, D. J. *J. Chem. Soc., Perkin Trans. 1* **1999**, 641; (f) Procter, D. J. *J. Chem. Soc., Perkin Trans. 1* **2000**, 835; (g) Procter, D. J. *J. Chem. Soc., Perkin Trans. 1* **2001**, 335; (h) Herradura, P. S.; Pendola, K. A.; Guy, R. K. *Org. Lett.* **2000**, *2*, 2019 and references cited therein.
3. (a) Yamamoto, T.; Sekine, Y. *Can. J. Chem.* **1984**, *62*, 1544; (b) Hickman, R. J. S.; Christie, B. J.; Guy, R. W.; White, T. J. *Aust. J. Chem.* **1985**, *38*, 899.
4. (a) Correa, A.; Carril, M.; Bolm, C. *Angew. Chem., Int. Ed.* **2008**, *47*, 2880; (b) Fernández-Rodríguez, M. A.; Shen, Q.; Hartwig, J. F. *Chem. Eur. J.* **2006**, *12*, 7782; (c) Baldovino-Pantaleón, O.; Hernández-Ortega, S.; Morales-Morales, D. *Inorg. Chem. Commun.* **2005**, *8*, 955; (d) Zhang, Y.; Ngeow, K. C.; Ying, J. Y. *Org. Lett.* **2007**, *9*, 3495; (e) Rout, L.; Sen, T. K.; Punniyamurthy, T. *Angew. Chem., Int. Ed.* **2007**, *46*, 5583; (f) Rout, L.; Saha, P.; Jammi, S.; Punniyamurthy, T. *Eur. J. Org. Chem.* **2008**, 640; (g) Reddy, V. P.; Kumar, A. V.; Swapna, K.; Rao, K. R. *Org. Lett.* **2009**, *11*, 1697.
5. Migita, T.; Shimizu, T.; Asami, Y.; Shiobara, J.; Kato, Y.; Kosugi, M. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 1385.
6. Itoh, T.; Mase, T. *Org. Lett.* **2004**, *6*, 4587.
7. Ham, J.; Yang, I.; Kang, H. *J. Org. Chem.* **2004**, *69*, 3236.
8. (a) Gujadhur, R. K.; Bates, C. G.; Venkataraman, D. *Org. Lett.* **2001**, *3*, 4315; (b) Bates, C. G.; Gujadhur, R. K.; Venkataraman, D. *Org. Lett.* **2002**, *4*, 2803.
9. Kwong, F. Y.; Buchwald, S. L. *Org. Lett.* **2002**, *4*, 3517.
10. Palomo, C.; Oiarbide, M.; López, R.; Gómez-Bengoa, E. *Tetrahedron Lett.* **2000**, *41*, 1283.
11. Carril, M.; SanMartin, R.; Domínguez, E.; Tellitu, I. *Chem. Eur. J.* **2007**, *13*, 5100.
12. Deng, W.; Zou, Y.; Wang, Y.-F.; Liu, L.; Guo, Q.-X. *Synlett* **2004**, 1254.
13. Chen, Y.-J.; Chen, H.-H. *Org. Lett.* **2006**, *8*, 5609.
14. (a) Basu, B.; Das, P.; Nanda, A. K.; Das, S.; Sarkar, S. *Synlett* **2005**, 1275; (b) Das, P.; Basu, B. *Synth. Commun.* **2004**, *34*, 2177; (c) Basu, B.; Das, P.; Bhuiyan, M. M.

H.; Jha, S. *Tetrahedron Lett.* **2003**, *44*, 3817; (d) Basu, B.; Jha, S.; Mridha, N. K.; Bhuiyan, M. M. H. *Tetrahedron Lett.* **2002**, *43*, 7967; (e) Basu, B.; Das, S.; Das, P.; Mandal, B.; Banerjee, D.; Almqvist, F. *Synthesis* **2009**, 1137; (f) Basu, B.; Das, S.; Kundu, S.; Mandal, B. *Synlett* **2008**, 255; (g) Basu, B.; Das, S.; Mandal, B. *Indian J. Chem., Sect B* **2008**, *47*, 1701.

15. *Typical experimental procedure for the thiolation reaction of aryl iodides* (Table 2, entry 1): A mixture of 4-iodoanisole (234 mg, 1 mmol), CuI (9.5 mg, 5 mol %), catechol violet (19 mg, 5 mol %), K_2CO_3 (138 mg, 1 mmol), and thiophenol (121 mg, 1.1 mmol) was taken in a screw-capped vial. DMF (2 mL) was added to it and it was placed on a preheated oil-bath at 90 °C for 2 h. The mixture was then cooled to room temperature followed by dilution with water (6 mL). It was then extracted with ether (3 × 10 mL) and the combined organic layer was washed with brine and dried over anhydrous sodium sulfate. Removal of the solvent left an oily residue which was passed through a short column of silica gel (60–120 mesh). Elution with light petroleum afforded the desired product as a colorless liquid (194 mg, yield 90%). IR (neat): $v_{\max}$ 2959, 2835, 1529, 1478, 1172 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 7.41 (2H, d, J = 8.2 Hz); 7.23 (2H, m); 7.15 (3H, m); 6.90 (2H, d, J = 8.2 Hz), 3.82 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 159.8, 138.6, 135.3, 128.9, 128.2, 125.7, 124.3, 115.0, 55.3.
16. Vicente, J.; Abad, J. A.; López-Nicolás, R. M. *Tetrahedron* **2008**, *64*, 6281.
17. Trost, B. M.; Lavoie, A. C. *J. Am. Chem. Soc.* **1983**, *105*, 5075.
18. Miller, R. D.; Hässig, R. *Tetrahedron Lett.* **1985**, *26*, 2395.
19. Morris, T. H.; Smith, E. H.; Walsh, R. *J. Chem. Soc., Chem. Commun.* **1987**, 964.
20. Magnus, P.; Quagliato, D. *J. Org. Chem.* **1985**, *50*, 1621.
21. (a) Mizuno, H.; Domon, K.; Masuya, K.; Tanino, K.; Kuwajima, I. *J. Org. Chem.* **1999**, *64*, 2648; (b) Domon, K. M. K.; Tanino, K.; Kuwajima, I. *Synlett* **1996**, 157.
22. (a) Beauchemin, A.; Gareau, Y. *Phosphorus Sulfur Silicon Relat. Elem.* **1998**, *139*, 187; (b) Benati, L.; Capella, L.; Montevecchi, P. C.; Spagnolo, P. *J. Chem. Soc., Perkin Trans. 1* **1995**, 1035.
23. Bates, C. G.; Saejueng, P.; Doherty, M. Q.; Venkataraman, D. *Org. Lett.* **2004**, *6*, 5005.