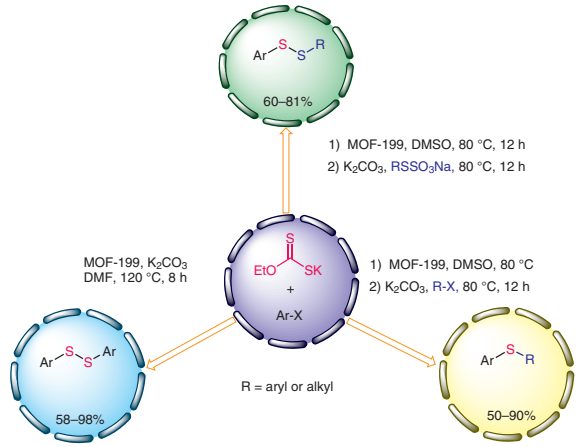
Synlett M. Soleiman-Beigi, Z. Arzehgar Letter

A Novel Method for the Direct Synthesis of Symmetrical and Unsymmetrical Sulfides and Disulfides from Aryl Halides and Ethyl Potassium Xanthogenate

M. Soleiman-Beigi*
Z. Arzehgar

Department of Chemistry, Basic of Sciences Faculty, Ilam University, PO Box 69315-516, Ilam, Iran
SoleimanBeigi@yahoo.com



Received: 06.11.2017
Accepted after revision: 24.12.2017
Published online: 31.01.2018
DOI: 10.1055/s-0037-1609081; Art ID: St-2017-d0819-l

Abstract An efficient and new method for the synthesis of disulfides and sulfides via the reaction of aryl halides with ethyl potassium xanthogenate in the presence of MOF-199 is described. *O*-Ethyl-*S*-aryl carbonodithioate has a key role as an intermediate in this procedure; it was converted into symmetrical diaryl disulfides in DMF. Additionally, this could be applied to the synthesis of unsymmetrical aryl alkyl(aryl′) disulfides by the reaction with *S*-alkyl(aryl) sulfurothioates (Bunte salts) as well as unsymmetrical aryl alkyl(aryl′) sulfides in DMSO.

Key words MOF-199, unsymmetrical disulfides, ethyl potassium xanthogenate, sulfides

Organosulfur derivatives represent an important class of compounds with applications in the pharmaceutical industry, materials science, food chemistry, and synthetic chemistry.[1,2] The most common methods used to synthesize these compounds include the use of thiols.[3] Consequently, the thioalkylation of thiols–thiolysis is appropriate for the synthesis of unsymmetrical disulfides and sulfides.[4] Although thiols are readily available they have significant drawbacks such as being toxic and having unpleasant odors with associated environmental issues. Furthermore, the ready overoxidation of thiols to their corresponding symmetrical disulfides during the synthesis of unsymmetrical disulfides or sulfides is another drawback of using these compounds. In order to overcome these difficulties significant attention has been directed towards the search for alternative pathways. Nowadays, C–S cross-coupling reactions of aryl halides with *S*-transfer reagents have attracted a lot of attention for the direct syntheses of organosulfur derivatives.[5] As such, interest continues in finding new reagents and procedures that can afford, in particular, unsymmetrical disulfides. Hence, sodium *S*-alkyl (*S*-aryl) sulfurothioates[6] (Bunte salts reported in 1897 by Hans Bunte) and ethyl potassium xanthogenate[5f–h] have been successfully used as the sulfur source for the synthesis of aryl alky(aryl′) disulfides in the presence of metal–organic frameworks (MOF-199). Bunte salts were previously used as a thiolate source in the synthesis of disulfides and trisulfides by the reactions with thiols, Na_2S, and sulfinates.[7]

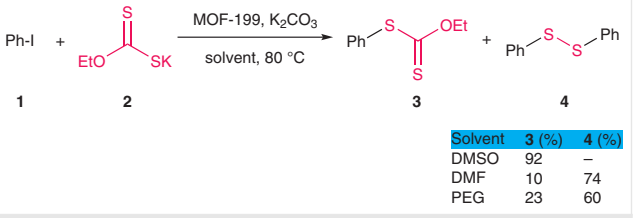
Metal–organic frameworks (MOFs) are important crystalline materials in heterogeneous catalysis that are used for a variety of transformations including cross-coupling reactions.[8,9] Important features of MOFs when used as heterogeneous catalysts are their high internal surface area, high activity, microporosity, ease of product separation, stability, diffusion, and high metal content.[10]

Herein, in an extension of our previous studies on the synthesis of disulfides,[11] we report a novel method for the synthesis of unsymmetrical aryl alkyl(aryl′) disulfides by reaction of aryl halides, ethyl potassium xanthogenate, and Bunte salts in the presence of MOF-199. The procedure was also extended to the synthesis of unsymmetrical organic sulfides and symmetrical disulfides.

The MOF-199 was prepared in 87% yield using the reaction of benzenetricarboxylic acid and $Cu(OAc)_2{\cdot}H_2O$ in a 1:1:1 mixture of DMF/EtOH/H_2O following the literature.[12] The structures of MOF-199 were deduced from their FT-IR, EDX, X-ray, and SEM analytical data.[13]

Initially, we commenced our study with a model reaction of iodobenzene **1**, ethyl potassium xanthogenate **2**, and a catalytic amount of MOF-199 at 80 °C, in order to optimize conditions for forming the key intermediate *O*-ethyl-*S*-phenyl carbonodithioate (**3**), because this project was

aimed towards applying *O*-ethyl-*S*-phenyl carbonodithioate as an aryl thiolate (ArS^-) source. The desired product **3** was obtained using DMSO as the reaction solvent in 92% yield and was the only product. When using PEG and DMF as the reaction solvent, diphenyl disulfide was formed as the major product in 60% and 74% yields, respectively (Scheme 1).



Solvent	3 (%)	4 (%)
DMSO	92	–
DMF	10	74
PEG	23	60

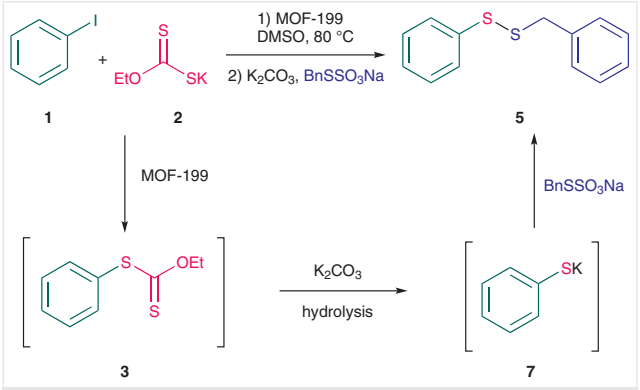
Scheme 1 Synthesis of *O*-ethyl-*S*-phenyl carbonodithioate as an aryl thiolate (ArS^-) source. *Reagents and conditions*: PhI (2.0 mmol), ethyl potassium xanthogenate (**2**, 3.0 mmol), MOF-199 (8.0 mg), DMF (3.0 mL), K_2CO_3 (1.0 mmol) 80 °C, and 8 h.

We were able to extend these reaction conditions as a novel and efficient method for the synthesis of symmetrical disulfides using potassium ethyl xanthogenate **2** (*S* source) by increasing the temperature to 120 °C in DMF in the presence of K_2CO_3 (Scheme 2).

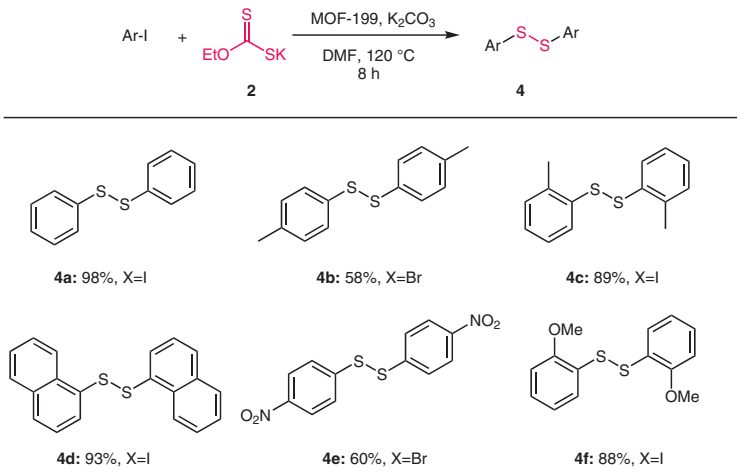
Next, we focused on the major aim of this project; namely the one-pot synthesis of unsymmetrical disulfides **5** from aryl halides and potassium ethyl xanthogenate **2** in the presence of MOF-199. After, conversion of potassium ethyl xanthogenate (**2**) into *O*-ethyl-*S*-aryl carbonodithioate (**3**) and K_2CO_3, a range of sodium *S*-alkyl(benzyl,aryl)sulfurothioates was added to the reaction mixture and heating was continued for 12 h to give the corresponding unsymmetrical disulfides in moderate to good yields (Table 1).

The procedure was successful with *sec*-butyl, benzyl, and *n*-butyl sulfurothioates with various aryl iodides (and bromides) and benzyl bromide. However, in the case of aryl *sec*-butyl disulfide products the reaction yield was lower when compared to the others (Table 1, 5l–n). The procedure could also be applied to the synthesis of unsymmetrical diaryl disulfides from sodium aryl sulfurothioates. In this regard, sodium phenyl sulfurothioate was examined under the optimal reaction conditions; 1-(4-methoxyphenyl) 2-phenyl disulfide and 1-phenyl 2-(*p*-tolyl) disulfide were obtained in 71% and 63% 1-phenyl 2-(*p*-tolyl) disulfide and 1-(4-methoxyphenyl) 2-phenyl disulfide were obtained in 63% and 71% yields, respectively (Table 1, **5o** and **5p**)

The procedure was also extended to the synthesis of unsymmetrical sulfides by the addition of aryl (alkyl) halides to the reaction mixture after the first step was complete (Table 2). In this way, a range of diaryl and aryl alkyl sulfides was synthesized in good to excellent yield (Table 2).



Scheme 3 Purposed mechanism for the unsymmetrical disulfide formation

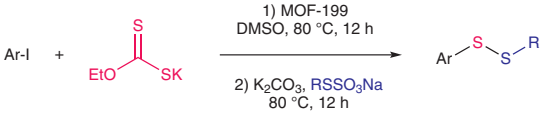


Scheme 2 Scope for the synthesis of symmetrical disulfides.[a] [a] *Reagents and conditions*: ArI (2.0 mmol), ethyl potassium xanthogenate **2** (3.0 mmol), MOF-199 (8.0 mg), DMF (3.0 mL), K_2CO_3 (1.0 mmol) 120 °C, 8 h. [b] Isolated yield.

Mechanistically, the coupling reaction for the formation of the C–S bond between iodobenzene (**1**) and potassium ethyl xanthogenate (**2**, xanthate coupling) gives the key intermediate *O*-ethyl-*S*-phenyl carbonodithioate (**3**). Hydrolysis using K_2CO_3 gives the corresponding thiolate **7**, which reacts with sodium *S*-benzyl sulfurothioate to give unsymmetrical disulfide **5** (Scheme 3).

In the case of diaryl and aryl alkyl sulfides, according to a possible mechanistic pathway based on the one suggested by Akkilagunta et al., thiolate **7** undergoes a second cross-coupling reaction with alkyl or aryl halides to form the unsymmetrical sulfides **6** (Scheme 4).[5f]

Table 1 Scope for the Synthesis of Unsymmetrical Disulfides[a]



R = Aryl or Alkyl

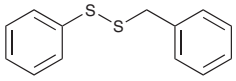
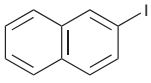
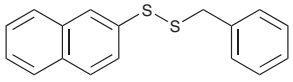
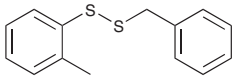
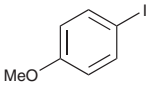
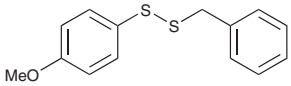
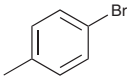
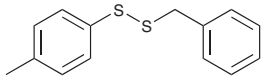
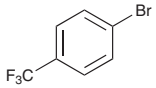
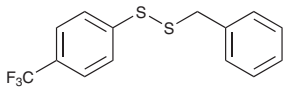
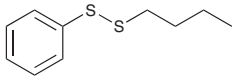
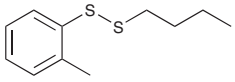
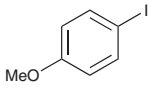
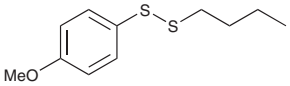
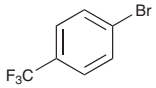
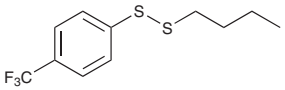
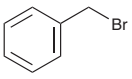
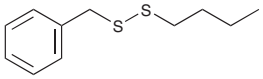
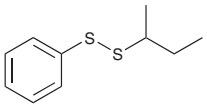
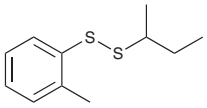
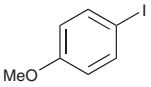
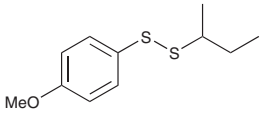
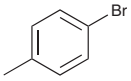
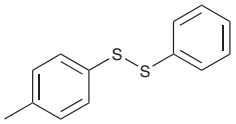
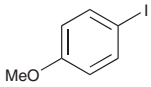
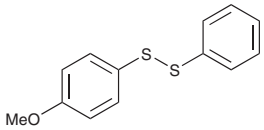
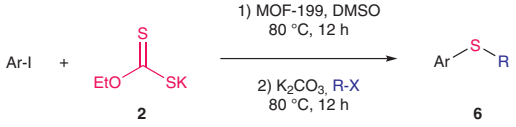
Entry	ArI	$RSSO_3Na$	Product		Yield of **5** (%)[b]
1		$BnSSO_3Na$		**5a**	81
2		$BnSSO_3Na$		**5b**	80
3		$BnSSO_3Na$		**5c**	74
4		$BnSSO_3Na$		**5d**	75
5		$BnSSO_3Na$		**5e**	70
6		$BnSSO_3Na$		**5f**	79
7		*n*-$BuSSO_3Na$		**5g**	71
8		*n*-$BuSSO_3Na$		**5h**	68
9		*n*-$BuSSO_3Na$		**5i**	67
10		*n*-$BuSSO_3Na$		**5j**	67
11		*n*-$BuSSO_3Na$		**5k**	80

Table 2 (continued)

Entry	ArI	$RSSO_3Na$	Product		Yield of **5** (%)[b]
12		*s*-BuSSO_3Na		**5l**	65
13		*s*-BuSSO_3Na		**5m**	63
14		*s*-BuSSO_3Na		**5n**	60
15		PhSSO_3Na		**5o**	63
16		PhSSO_3Na		**5p**	71

[a] Reagents and conditions: (1) aryl halide (1.0 mmol), ethyl potassium xanthogenate (**2**, 1.5 mmol), MOF-199 (4.0 mg), DMSO (2.0 mL), 80 °C, 12 h. (2) RS_2O_3Na (1.0 mmol), K_2CO_3 (1.0 mmol), reflux, 12 h.
[b] Isolated yields.

Table 2 Scope for the Synthesis of Unsymmetrical Sulfides[a]



R = Aryl or Alkyl

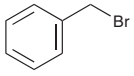
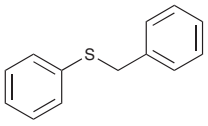
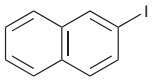
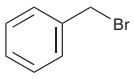
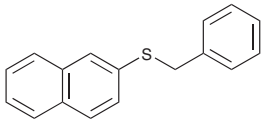
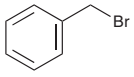
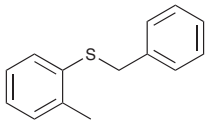
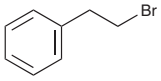
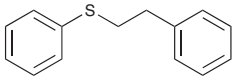
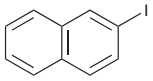
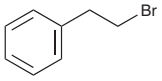
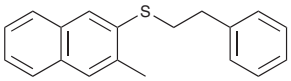
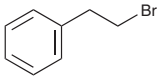
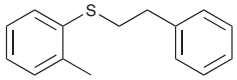
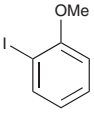
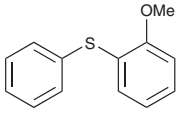
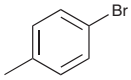
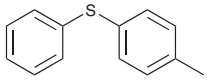
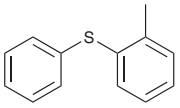
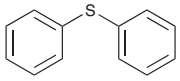
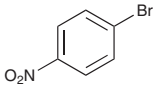
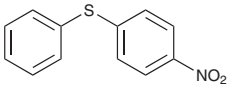
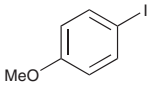
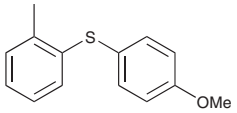
Entry	ArI	RX	Product		Yield of **6** (%)[b]
1				**6a**	90
2				**6b**	81
3				**6c**	85
4				**6d**	84

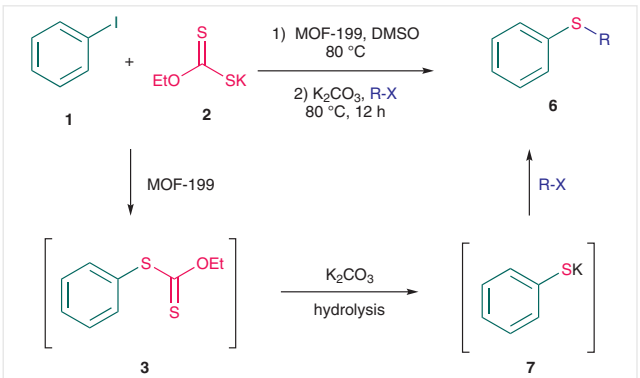
Table 2 (continued)

Entry	ArI	RX	Product		Yield of **6** (%)[b]
5				**6e**	80
6				**6f**	85
7				**6g**	73
8				**6h**	72
9				**6i**	75
10				**6j**	84
11				**6k**	50
12				**6l**	66

[a] Reagents and conditions: (1) aryl halide (1.0 mmol), ethyl potassium xanthogenate (**2**, 1.5 mmol), MOF-199 (4.0 mg), DMSO (2.0 mL), 80 °C, 12 h. (2) RX (1.0 mmol), K_2CO_3 (1.0 mmol), reflux, 12 h.
[b] Isolated yields.

To confirm the recyclability of the MOF-199, the fresh and reused catalyst was characterized by FT-IR, XRD, EDX, and SEM spectroscopy. All of the data are similar to that of other MOF-199 samples previously described in the literature.[13] It was found that MOF-199 could be reused for further runs (demonstrated for up to five cycles) without decrease in activity.

In conclusion, an efficient and novel method is described for the synthesis of various organosulfur compounds from aryl halides and ethyl potassium xanthogenate in the presence of MOF-199.[14–18] This procedure is not only applicable to the synthesis of *O*-ethyl-*S*-aryl xanthogenate as the reaction intermediate, but can also be used for synthesis of unsymmetrical disulfides and sulfides on adding K_2CO_3, Bunte salts, and organic halides to the previously generated intermediate. The procedure was also extended to synthesize symmetrical diaryl disulfides in good to excellent yields by changing the reaction solvent to DMF. In this work, MOF-199 as an affective heterogeneous, porous, and recyclable catalyst, and *O*-ethyl-*S*-aryl xanthogenate as a new, stable, solid, and odorless sulfurating reagent were successfully investigated.



Scheme 4 Proposed pathway for unsymmetrical sulfide formation

Funding Information

Financial support from the Ilam University Research Council is gratefully acknowledged.

Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0037-1609081.

References and Notes

(1) (a) Cremlyn, R. J. W. *An Introduction to Organosulfur Chemistry*; John Wiley and Sons: Chichester, **1996**. (b) Oae, S. *Organic Chemistry of Sulfur*; Springer: Berlin, **2012**. (c) Schaumann, E. *Sulfur-Mediated Rearrangements I*; Springer: Berlin: Heidelberg, **2007**. (d) Dubbaka, S. R.; Vogel, P. *Angew. Chem. Int. Ed.* **2005**, *44*, 7674. (e) Sahu, S. C. *J. Environ. Sci. Health, Part C: Environ. Carcinog. Ecotoxicol. Rev.* **2002**, *20*, 61.

(2) (a) Zhang, L.; Chou, C. P.; Moo-Young, M. *Biotechnol. Adv.* **2011**, *29*, 923. (b) Saito, G.; Swanson, J. A.; Lee, K.-D. *Adv. Drug Delivery Rev.* **2003**, *55*, 199. (c) Dar, A. A.; Enjamuri, N.; Shadab, M.; Ali, N.; Khan, A. T. *ACS Comb. Sci.* **2015**, *17*, 671. (d) Bodanszky, M. *Principles of Peptide Synthesis*; Springer: Berlin, **1984**.

(3) (a) Jones, R. C.; Katritzky, A. R. *Comprehensive Organic Functional Group Transformations II: Carbon with Two Attached Heteroatoms with at Least One Carbon-to-heteroatom Multiple Link*; Elsevier: Amsterdam, **2005**. (b) Mandal, B.; Basu, B. *RSC Adv.* **2014**, *4*, 13854. (c) Witt, D. *Synthesis* **2008**, 2491. (d) Rayner, C. M. *Contemp. Org. Synth.* **1995**, *2*, 409.

(4) (a) Fernández-Rodríguez, M. A.; Shen, Q.; Hartwig, J. F. *J. Am. Chem. Soc.* **2006**, *128*, 2180. (b) Bastug, G.; Nolan, S. P. *J. Org. Chem.* **2013**, *78*, 9303. (c) Murata, M.; Buchwald, S. L. *Tetrahedron* **2004**, *60*, 7397. (d) Oderinde, M. S.; Frenette, M.; Robbins, D. W.; Aquila, B.; Johannes, J. W. *J. Am. Chem. Soc.* **2016**, *138*, 1760. (e) Xu, H.-J.; Zhao, Y.-Q.; Feng, T.; Feng, Y.-S. *J. Org. Chem.* **2012**, *77*, 2649. (f) Uyeda, C.; Tan, Y.; Fu, G. C.; Peters, J. C. *J. Am. Chem. Soc.* **2013**, *135*, 9548. (g) Hunter, R.; Caira, M.; Stellenboom, N. *J. Org. Chem.* **2006**, *71*, 8268. (h) Antoniow, S.; Witt, D. *Synthesis* **2007**, 363. (i) Bao, M.; Shimizu, M. *Tetrahedron* **2003**, *59*, 9655. (j) Wu, X.-m.; Yan, G.-b. *Synlett* **2015**, *26*, 537. (k) Mukherjee, N.; Chatterjee, T.; Ranu, B. C. *J. Org. Chem.* **2013**, *78*, 11110.

(5) (a) Kondo, T.; Mitsudo, T. *Chem. Rev.* **2000**, *100*, 3205. (b) Beletskaya, I. P.; Ananikov, V. P. *Chem. Rev.* **2011**, *111*, 1596. (c) Li, Y.; Pu, J.; Jiang, X. *Org. Lett.* **2014**, *16*, 2692. (d) Singh, N.; Singh, R.; Raghuvanshi, D. S.; Singh, K. N. *Org. Lett.* **2013**, *15*, 5874. (e) Qiao, Z.; Wei, J.; Jiang, X. *Org. Lett.* **2014**, *16*, 1212. (f) Akkilagunta, V. K.; Kakulapati, R. R. *J. Org. Chem.* **2011**, *76*, 6819. (g) Prasad, D. J. C.; Sekar, G. *Org. Lett.* **2011**, *13*, 1008. (h) Wang, L.; Zhou, W.-Y.; Chen, S.-C.; He, M.-Y.; Chen, Q. *Synlett* **2011**, 3041. (i) Lee, J.-Y.; Lee, P. H. *J. Org. Chem.* **2008**, *73*, 7413.

(6) Bunte, H. *Ber. Dtsch. Chem. Ges.* **1874**, *7*, 646.

(7) (a) Milligan, B.; Swan, J. M. *J. Chem. Soc.* **1963**, 6008. (b) Milligan, B.; Saville, B.; Swan, J. M. *J. Chem. Soc.* **1961**, 4850. (c) Xiao, X.; Feng, M.; Jiang, X. *Chem. Commun.* **2015**, *51*, 4208.

(8) (a) Chughtai, A. H.; Ahmad, N.; Younus, H. A.; Laypkov, A.; Verpoort, F. *Chem. Soc. Rev.* **2015**, *44*, 6804. (b) Gascon, J.; Corma, A.; Kapteijn, F.; Llabrés, F. X. *ACS Catal.* **2014**, *4*, 361. (c) Dhakshinamoorthy, A.; Alvaro, M.; Corma, A.; Garcia, H. *Dalton Trans.* **2011**, *40*, 6344. (d) Deria, P.; Mondloch, J. E.; Karagiaridi, O.; Bury, W.; Hupp, J. T.; Farha, O. K. *Chem. Soc. Rev.* **2014**, *43*, 5896.

(9) Furukawa, H.; Cordova, K. E.; O'Keeffe, M.; Yaghi, O. M. *Science* **2013**, *341*, 974.

(10) Dhakshinamoorthy, A.; Asiric, A. M.; Garcia, H. *Chem. Soc. Rev.* **2015**, *44*, 1922.

(11) (a) Soleiman-Beigi, M.; Arzehgar, Z. *Heteroat. Chem.* **2015**, *26*, 355. (b) Soleiman-Beigi, M.; Yavari, I.; Sadeghizadeh, F. *RSC Adv.* **2015**, *5*, 87564. (c) Soleiman-Beigi, M.; Sadeghizadeh, F.; Basereh, A. *J. Sulfur Chem.* **2017**, *38*, 572. (d) Soleiman-Beigi, M.; Yavari, I.; Sadeghizadeh, F. *Phosphorus, Sulfur Silicon Relat. Elem.* **2018**, *193*, 41. (e) Soleiman-Beigi, M.; Mohammadi, F. *J. Sulfur Chem.* **2016**, *38*, 134.

(12) Savegnago, L. *Environ. Toxicol. Pharmacol.* **2006**, *21*, 86.

(13) Britt, D.; Tranchemontagne, D.; Yaghi, O. M. *Proc. Natl. Acad. Sci. U.S.A.* **2008**, *105*, 11623.

(14) **General Procedure for the Synthesis of *S*-Alkyl Sulfurothioates**

The requisite alkyl halide (10.0 mmol) and sodium thiosulfate pentahydrate (2.98 g, 12.0 mmol) dissolved in methanol–water (3:1, 20 mL). The reaction mixture was stirred and heated to 65 °C. Upon completion of the reaction, the mixture was cooled to room temperature, and then concentrated at 40–45 °C. The resultant solid was treated with methanol (50 mL), heated to 50 °C (most solid dissolved), and filtered. This removed the excess sodium thiosulfate and sodium chloride. The filtrate was concentrated to a white solid. The mixture was washed with *n*-hexane, filtered, and dried under vacuum at 50 °C.

(15) **General Procedure for the Synthesis of *S*-Aryl Sulfurothioates**

To a stirred mixture of iodobenzene (1.02 g, 5.0 mmol), sodium thiosulfate pentahydrate (1.88 g, 7.5 mmol) and CuI (0.09 g, 0.5 mmol, 10 mol%) in DMSO (5 mL) was added 1,10-phenanthroline (0.18 g, 1.0 mmol, 20 mol%), and the mixture was stirred for 5 min at room temperature and then heated to 80 °C for 4 h under a nitrogen atmosphere until completion of reaction. The reaction mixture was cooled to room temperature, brine (15 mL) was added, and the mixture was stirred vigorously at room temperature for 1 h. The mixture was filtered, and the solid was washed successively with brine and *n*-hexanes. The solid was dried under vacuum at 50 °C for 3 h.

(16) **General Procedure for the Synthesis of Unsymmetrical Disulfides**

The requisite alkyl (aryl) halide (1.0 mmol), potassium *O*-ethylcarbonodithioate (0.24 g, 1.5 mmol) and MOF-199 (4.0 mg) were added to DMSO (2.0 mL) and the mixture heated to 80 °C for 12 h. After complete conversion of the alkyl (aryl) halide into *O*-ethyl-*S*-phenyl carbonodithioate, RS_2O_3Na (1.0 mmol) and K_2CO_3 (0.14 g, 1.0 mmol) were added and the mixture heated to 80 °C for a further 12 h. The progress of reaction was monitored by TLC. Upon completion of the reaction, the mixture was cooled to room temperature and then filtered. The filtrate was evaporated under vacuum, CH_2Cl_2 (20 mL) was added, and the mixture was washed with H_2O (2 × 15 mL). The combined organic layers were dried over Na_2SO_4, filtered, and evaporated to afford the crude unsymmettrical alkyl (aryl) disulfide, which was purified by thick-layer chromatography (silica gel, eluting wth *n*-hexane–ethyl acetate, 20:1; in the case of **5d**,**f**,**i**,**j**,**n**,**p**, 4:1).

O-Ethyl-*S*-phenyl Carbonodithioate (3)

Oil.^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.76 (d, 2 HAr), 7.37–7.12 (m, 3 HAr), 3.26 (q, 2 HOEt), 1.14 (t, 3 HOEt) ppm.^{13}C NMR (100

MHz, $CDCl_3$): δ = 210.2 (C=S), 138.7, 136.4, 131.4, 126.4 (CAr), 66.0 (CH_2), 13.7 (CH_3) ppm. GC–MS (EI): *m/z* = 198.3 [M^+].

1-Benzyl -2-(naphthalen-2-yl)disulfide (**5b**)

Oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.82–7.55 (m, 12 HAr), 2.32 (s, 2 HCH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.3, 158.4, 147.1, 136.1, 130.4, 129.5, 129.0, 128.8, 127.9, 127.3, 125.2, 124.9, 122. 6, 115.8, 31.4 ppm.

1-(4-Methoxyphenyl)-2-phenyldisulfide (**5p**)

White solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.73–7.09 (m, 9 HAr), 3.80 (s, 3 HOMe) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.1, 132.5, 129.8, 127.9, 125.2, 123.2, 115.9, 127.2, 31.9 ppm. For other compounds, see the Supporting Information.

(17) **General Procedure for the Synthesis of Symmetrical Disulfides**

A mixture of the requisite alkyl (aryl) halide (2.0 mmol), potassium *O*-ethylcarbonodithioate (0.48 g, 3.0 mmol) and MOF-199 (8 mg) in DMF (15.0 mL) in a 25 mL round-bottom flask was stirred at 120 °C for 8 h. The reaction was monitored by TLC analysis. Upon completion of the reaction, the mixture was cooled to room temperature and then filtered. The filtrate was evaporated under vacuum, CH_2Cl_2 (20 mL) was added, and the mixture was washed with H_2O (2 × 15 mL). The combined organic layers were dried over Na_2SO_4, filtered, and solvent was removed in vacuo. The residue was purified by thick-layer chromatography on silica gel (eluting with *n*-hexane–ethyl acetate, 20:1; in the case of **4e** and **4f**, 4:1 and 2:1, respectively) to give the corresponding products.

Diphenyl Disulfide (4a)

White solid.^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.24–7.36 (m, 6 H), 7.54 (m, 4 H) ppm.^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.0, 129.1, 127.5, 127.2 ppm. GC–MS (EI): *m/z* = 218.0 [M^+].

(18) **General Procedure for the Synthesis of Unsymmetrical Sulfides**

The aryl halide (1.0 mmol), potassium *O*-ethylcarbonodithioate (0.24 g, 1.5 mmol) and MOF-199 (4.0 mg) were added to DMSO (2 mL) and the mixture heated to 80 °C for 12 h. After complete conversion of the alkyl (aryl) halide into *O*-ethyl-*S*-phenyl carbonodithioate, the requisite alkyl (aryl) halide (1.0 mmol) and K_2CO_3(0.058 g, 1.0 mmol) were added and the mixture heated at 80 °C for a further 12 h. The progress of reaction was monitored by TLC. Upon completion of the reaction, the mixture was cooled to room temperature and filtered. The filtrate was evaporated under vacuum, CH_2Cl_2 (20 mL) was added, and the mixture was washed with H_2O (2 × 15 mL). The combined organic layers were dried over Na_2SO_4, filtered, and evaporated to afford the crude unsymmetrical alkyl (aryl) sulfide, which was purified by thick-layer chromatography (silica gel, *n*-hexane–ethyl acetate, 20:1; in the case of **6g**,**k**,**l**, 4:1).

Phenyl(*o*-tolyl)sulfide (6i)

The product was obtained as a oil.^{1}H NMR (300 MHz, CDCl3): δ = 7.85–7.00 (m, 9 HAr), 2.34 (s, 3 HMe) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.4, 137.8, 136.4, 131.4, 131.3, 130.8, 129.1, 128.4, 127.2, 127.1, 29.1 ppm. GC–MS (EI): *m/z* = 200.0 [M^+].

Benzyl(*o*-tolyl)sulfide (6c)

The product was obtained as a oil.^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39–7.28 (m, 9 H), 4.23 (s, 2 H), 2.31 (s, 3 HMe) ppm.^{13}C NMR (100 MHz, $CDCl_3$): δ = 130.0, 129.5, 129.2, 128.8, 128.0, 127.9, 127.6, 127.5, 126.1, 39.6, 21.6 ppm. GC–MS (EI): *m/z* = 214.0 [M^+].