Microwave-assisted Ullmann–Buchwald C–S bond formation using a copper(I) catalyst and *trans*-cyclohexane-1,2-diol as ligand

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Dedicated to Professor Keith Smith on the occasion of his 65th anniversary

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Abstract

Microwave irradiation of a thiophenol or alkyl thiol (1 equiv.) and an aryl halide (1 equiv.) in 2-propanol at 120 °C for three hours in the presence of K_2CO_3 (2 equiv.) as base using copper(I) iodide as catalyst (5 mol%) and *trans*-cyclohexane-1,2-diol (2 equiv.) as ligand provides a rapid and convenient method for C–S bond formation. The process is most efficient using thiophenol and aryl iodide precursors, both of which may contain electron-donating and electron-withdrawing groups, to give the corresponding diaryl sulfide in good to excellent yield.

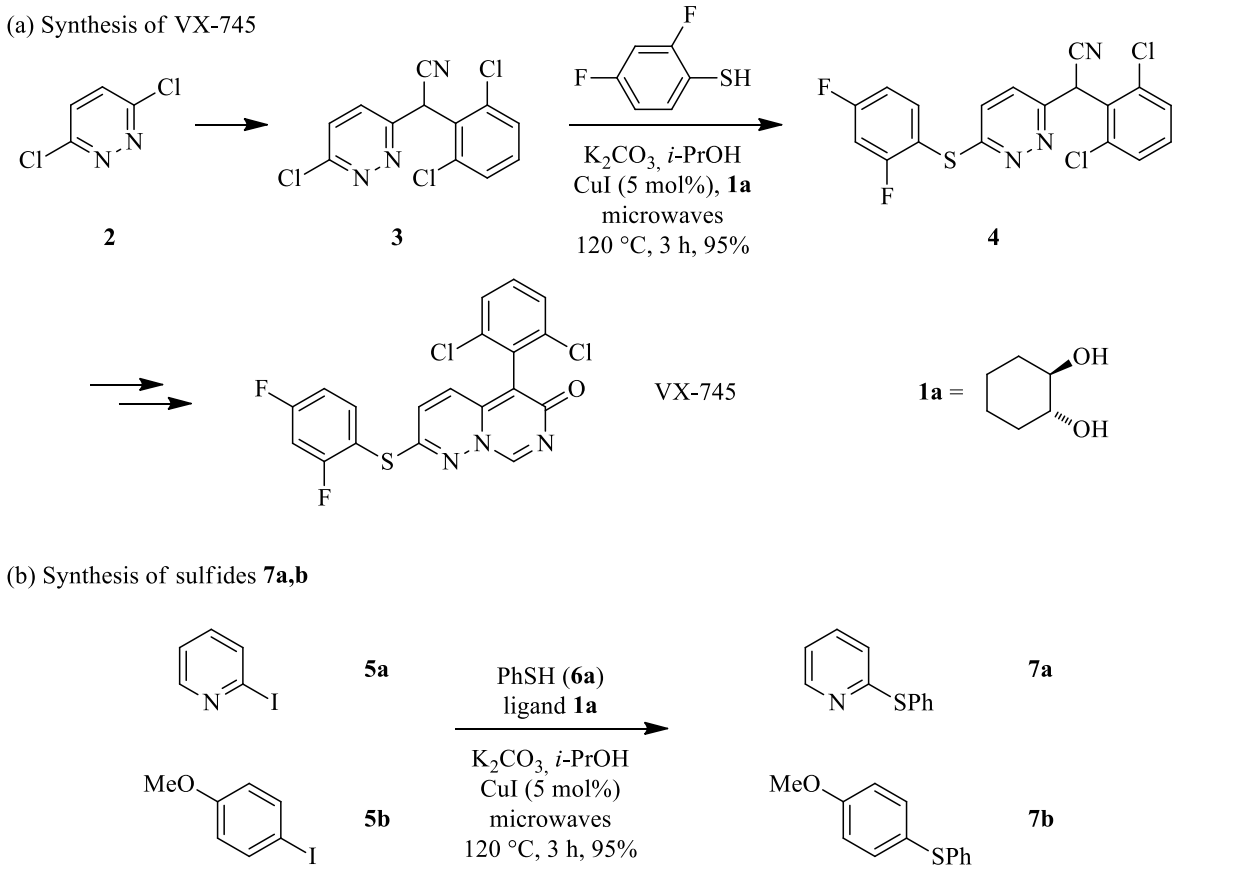
Keywords: Ullmann condensation, sulfides, copper, microwaves

Introduction

Aryl sulfides are valuable intermediates in organic synthesis. Many of them display useful pharmacological and biological properties and there have been many synthetic routes developed for their synthesis.[1] Since the discovery of the copper-catalyzed Ullmann homocoupling reaction over 100 years ago, the related Ullmann heterocoupling, first described in 1903,[2] has been a valuable method for the formation of C–O, C–S and C–N bonds and has received much recent attention in the literature.[3] The copper-mediated synthesis of aryl sulfides by the reaction of a thiol and an aryl iodide under classical Ullmann conditions is a challenging transformation that often exhibits poor functional group tolerance, can give varied outcomes depending upon the copper source and requires harsh conditions. The process often requires high temperatures and

prolonged reaction time, can give low yields of product and can require strong bases, stoichiometric copper and toxic solvents; and yet the so-called Ullmann condensation reaction still stands as an important route to these valuable targets. There have been many recent efforts to overcome the problems associated with this transformation, in certain cases using metal-free strategies,[4] by variation in metal[5] or ligand,[6] with or without the use of additives,[7] but the challenge remains to find a simple but effective method for this process that is compatible with a broad range of substrates. One strategy adopted by Wu and He employed the use of microwave heating in order to access the high temperature conditions necessary for C–S bond formation,[8] and in a landmark study, Kwong and Buchwald adopted the use of an ethylene glycol ligand and copper catalyst under conventional heating for efficient conversion to the sulfide products.[9]

Microwave dielectric heating has received considerable attention in recent years as a valuable alternative to the use of conductive heating for accelerating synthetic transformations[10] and in the biosciences.[11] Furthermore, transition-metal mediated processes seem to benefit greatly from this technology,[12] which has found widespread use in medicinal chemistry,[13] and so this heating method seemed appropriate for use in promoting the Ullmann condensation reaction.



Scheme 1. (a) Microwave-assisted synthesis of sulfide **4** from chloropyridazine **3** using CuI (5 mol%) and a 1,2-diol ligand **1a**. (b) Microwave-assisted synthesis of sulfides **7a,b** from aryl iodides **5a,b** and thiophenol (**6a**) using CuI (5 mol%) and a 1,2-diol ligand **1a**.

Recently we described a new method of C–S bond formation for the synthesis of the clinical candidate VX-745[14] to examine inhibition of p38α mitogen-activated protein kinase (MAPK) in Werner syndrome cells.[15] This method[16] combined microwave heating in a sealed reaction vessel with the use of a copper(I) catalyst and *trans*-cyclohexane-1,2-diol (**1a**) ligand and was found to promote transformation of chloropyridazine **3**, derived from 3,6-dichloropyridazine (**2**), to give sulfide **4** as an intermediate in the synthesis of VX-745 (Scheme 1a).[14] This catalyst/ligand system also mediated the reaction of 2-iodopyridine (**5a**) and thiophenol (**6a**) to give sulfide **7a** and the transition metal catalyzed transformation of 4-iodoanisole (**5b**) into sulfide **7b** in excellent yield (Scheme 1b). Furthermore, the process was found to be amenable to scale up using a stop-flow microwave reactor to deliver gram quantities of VX-745 for biological evaluation.[17]

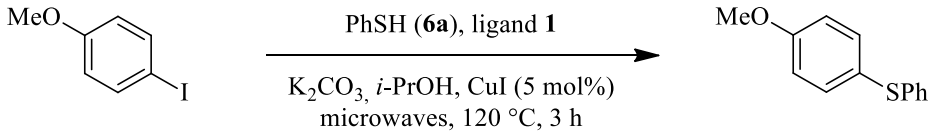
Given the apparent broad scope of this process, from the observation that the transformation was efficient for both electron-poor and electron-rich substrates, **5a** and **5b** respectively, this manuscript now describes the use of microwave dielectric heating to promote Ullmann C–S bond formation for a range of substrates to establish the scope of this rapid and efficient method for the synthesis of aryl sulfides so that it may find widespread use in synthetic chemistry.

Results and Discussion

Our previous work established the role of the copper catalyst in this transformation and compared a variety of additives, bases and other catalyst systems to validate the choice of ligand.[14a] Thus, we started these studies by examining the stoichiometry of reagents, varying the amount of ligand and catalyst to verify the process was optimum. 4-Iodoanisole (**5b**) was reacted with thiophenol (**6a**) in the presence of CuI (5 mol%) using K_2CO_3 (2 equiv.) as base in *i*-PrOH under microwave irradiation at 120 °C, varying the amount of ligand **1a** (Table 1). When the amount of ligand was decreased from 2 equiv. (entry 1) to 1.1 (entry 2) or 1.0 equiv. (entry 3), with respect to the two substrates, a slight decrease in the isolated yield was observed (88 or 85%, respectively). Further decrease in stoichiometry, using 5 mol% of ligand, gave a further reduction in the isolated yield (70%, entry 4). Changing the stereochemistry of the ligand and replacing (±)-*trans*-**1a** with *cis*-1,2-cyclohexanediol (**1b**) gave the desired sulfide but caused a dramatic reduction in the efficiency of reaction (68%, entry 5). Removing the ligand altogether did provide the product, but again the yield was reduced (64%; entry 6). Furthermore, carrying out the reaction in the absence of the CuI catalyst (entry 7), gave no reaction and returned only unreacted starting materials indicating that a copper-mediated process was operating for this substrate. Gratifyingly, these conditions using microwave heating at a higher reaction temperature were also effective using the Buchwald-Kwong ligand system[9] although gave sulfide **7b** in slightly reduced yield (entry 8). Finally, the reaction was carried out using a silicon carbide (SiC) passive heating element (entry 9). We,[18] and others,[19] have shown that for some microwave-assisted processes this can improve the thermal profile and outcome of reaction.

However, for this transformation, the passive heating element gave a less reliable heating profile, causing dramatic changes in temperature between 115 and 125 °C which accompanied bursts of power, and this gave a slightly lower yield of sulfide product **7b** (85%).

Table 1. Effect of ligand on the microwave-assisted synthesis of sulfide **7b**



5b **7b**

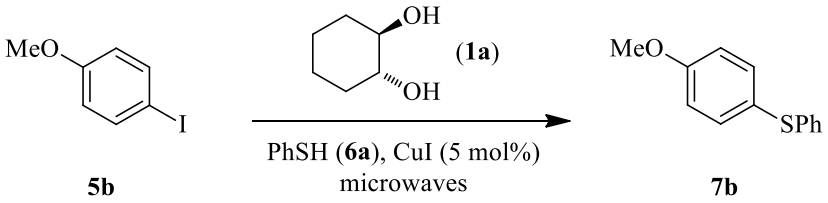
Entry	Ligand **1**	**1** equiv.	Conditions[a]	Yield%[b]
1	**1a**	2	[a]	95
2	**1a**	1.05	[a]	88
3	**1a**	1	[a]	85
4	**1a**	5 mol%	[a]	70
5	**1b**[c]	2	[a]	68
6	No ligand	–	[a]	64
7	**1a**	2	No CuI[d]	–
8	**1c**[e]	2	[a]	89
9	**1a**	2	SiC[f]	85

[a] Reactions were carried out under microwave dielectric heating in a CEM Discover single-mode cavity at 120 °C for 3 h, measured by the in-built IR sensor, using 4-iodoanisole (**5b**) (1 equiv.) and thiophenol (**6a**) (1 equiv.) in the presence of copper(I) iodide (5 mol%), (±)-*trans*-1,2-cyclohexanediol (**1a**) (at the stated stoichiometry), K_2CO_3 (2 equiv.), and *i*-PrOH as solvent under anhydrous conditions, unless stated otherwise. [b] Isolated yield of sulfide **7b** after purification by column chromatography. [c] Reaction was carried out using *cis*-1,2-cyclohexanediol (**1b**) in place of (±)-*trans*-**1a**. [d] Reaction was carried out in the absence of copper(I) iodide. [e] Reaction was carried out using ethylene glycol in place of (±)-*trans*-**1a**. [f] Reaction was carried out in the presence of a silicon carbide passive heating element.[18,19]

It was concluded that the use of 2 equiv. of (±)-*trans*-1,2-cyclohexanediol (**1a**) as ligand was optimal under these conditions. However, a second series of optimization studies was undertaken to examine the role of the chosen base and solvent (Table 2). Carrying out the reaction in water (entry 1) gave a very low yield (31%) but predictably suffered from issues of solubility. Changing the base from potassium carbonate to triethylamine and carrying out the reaction in 2-propanol did provide sulfide **7b** but in only 60% yield (entry 2). Shortening the reaction time (entries 3 and 4) did little to improve the yield of the triethylamine-mediated reaction which was much less efficient than the use of potassium carbonate (95%; entry 5). For the most part, the outcome from the microwave-assisted reaction could be reproduced under conventional heating

(entries 6 and 7) using Schlenk apparatus, but the microwave-assisted procedure is favored for its convenience and speed.

Table 2. Effect of base and solvent on the microwave-assisted synthesis of sulfide **7b**



5b **7b**

Entry	Base–solvent	Conditions[a]	Yield%[b]
1	K_2CO_3–H_2O	3 h, 120 °C	31
2	NEt_3–*i*-PrOH	3 h, 120 °C	60
3	NEt_3–*i*-PrOH	1.5 h, 120 °C	45
4	NEt_3–*i*-PrOH	45 min, 120 °C	58
5	K_2CO_3– *i*-PrOH	3 h, 120 °C	95
6	K_2CO_3– *i*-PrOH	4 d, 120 °C[c]	81
7	K_2CO_3– *i*-PrOH	24 h, 110 °C[c]	84

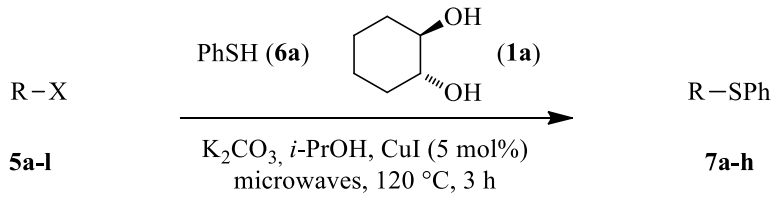
[a] Reactions were carried out under microwave dielectric heating in a CEM Discover single-mode cavity at 120 °C for 3 h, measured by the in-built IR sensor, using 4-iodoanisole (**5b**) (1 equiv.) and thiophenol (**6a**) (1 equiv.) in the presence of copper(I) iodide (5 mol%) and (±)-*trans*-1,2-cyclohexanediol (**1a**) (2 equiv.) using the specified base (2 equiv.) and solvent, unless stated otherwise.

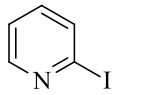
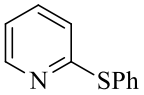
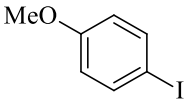
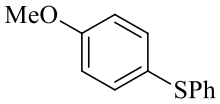
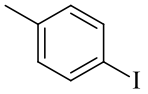
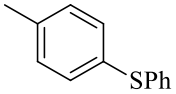
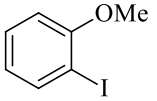
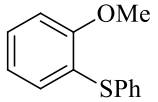
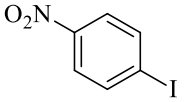
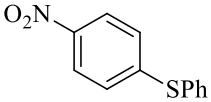
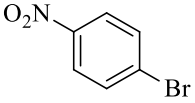
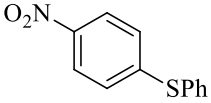
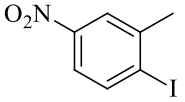
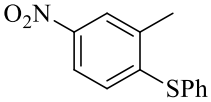
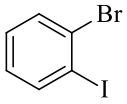
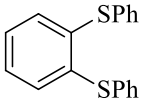
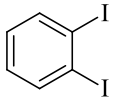
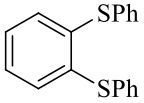
[b] Isolated yield of sulfide **7b** after purification by column chromatography.

[c] Reaction was carried out using conventional heating methods under an anhydrous atmosphere.

Using the optimum conditions, a series of both electron-rich and electron-poor aryl halides **5** was submitted to microwave-assisted Ullmann condensation with thiophenol (**6a**) (Table 3) in the presence of diol ligand **1a** (2 equiv.) and K_2CO_3 as base. The reaction of iodobenzene (**5c**) under these conditions (entry 3) was comparable to previously studied substrates (entries 1 and 2), giving diphenyl sulfide (**7c**) in 86% yield without any competing formation of the corresponding disulfide, shown to be problematic in the presence of oxygen,[14a] as confirmed by spectroscopic and mass spectrometric analysis. Replacing iodobenzene (**5c**) with the corresponding bromide **5d** (entry 4) still gave sulfide **7c** as the product but in much reduced yield. Use of the chloride **5e** (entry 5) failed to give any of the desired product at all. Thus it was concluded that the copper-catalyzed reaction was highly efficient for aryl iodides, but less so for aryl bromides. As expected, the process was tolerant of a tolyl-derived aryl iodide (**5f**; entry 6). The presence of an *ortho*-methoxy group (entry 7) had no detrimental effect on the efficiency of reaction producing the corresponding sulfide **7e** in 95% yield.

Table 3. Microwave-assisted synthesis of sulfides **7a-h** using a range of aryl halides **5a-l**[a]



Entry	Halide	5	ArSH	6	Product	7	Yield%[b]
1[c]		**a**	PhSH	**a**		**a**	91[c]
2		**b**	PhSH	**a**		**b**	95
3	PhI	**c**	PhSH	**a**	Ph_2S	**c**	86
4	PhBr	**d**	PhSH	**a**	Ph_2S	**c**	32
5	PhCl	**e**	PhSH	**a**		**c**	–
6		**f**	PhSH	**a**		**d**	76
7		**g**	PhSH	**a**		**e**	95
8		**h**	PhSH	**a**		**f**	81
9		**i**	PhSH	**a**		**f**	74
10		**j**	PhSH	**a**		**g**	66
11		**k**	PhSH (2 equiv.)	**a**		**h**	94
12		**l**	PhSH (2 equiv.)	**a**		**h**	81

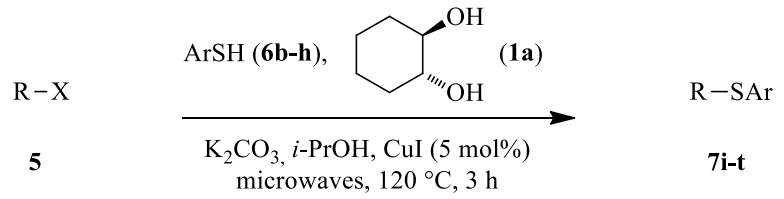
[a] Reactions were carried out under microwave dielectric heating in a CEM Discover single-mode cavity at 120 °C for 3 h, measured by the in-built IR sensor, using an aryl halide **5** (1 equiv.) and thiophenol (**6a**) (1 equiv.) in the presence of copper(I) iodide (5 mol%), (±)-*trans*-1,2-cyclohexanediol (**1a**) (2 equiv.), K_2CO_3 (2 equiv.), and *i*-PrOH as solvent under anhydrous conditions, unless stated otherwise. [b] Isolated yield of the corresponding sulfide **7** after purification by column chromatography. [c] As described previously.[14a]

Interestingly, for electron-poor aryl halides there was much less variability in yield using different halides: 4-iodonitrobenzene (**5h**; entry 8) and 4-bromonitrobenzene (**5i**; entry 9) gave very similar yields of sulfide **7f** using this procedure. Although the presence of an *ortho*-methyl group in an electron-poor halide **5i** (entry 10) did reduce the efficiency of reaction, giving the sulfide product **7g** in 66% yield. With this process, it was possible to use dihalides **5k** and **5l** in Ullmann condensation with 2 equiv. of thiophenol (**6a**) (entries 11 and 12), both of which gave sulfide **7h** in very good yield. Thus, in conclusion, the reaction of thiophenol (**6a**) with a range of electron-poor and electron-rich alkyl bromides and iodides was found, for the most part, to be a rapid and reliable route to phenyl sulfides **7a-h** in good yields.

Next our attention turned to screening a range of thiophenols **6b-h** in the same process using a selection of aryl halides (Table 4). Reaction of an electron-rich halide **5b** with 2-thionaphthol (**6b**) gave a much higher yield of the corresponding sulfide product **7i** (91%; entry 1) than the electron-poor analogue (**7j** was isolated in 78% yield; entry 2), although both reactions were considered a success. Electron-rich and electron-poor aryl halides were also screened in the reactions of 4-mercaptothiophenol (**6c**) (entries 3 and 4). For this substrate it was anticipated that Ullmann C–S bond formation would be favored over C–O bond formation and this was indeed observed to be the case, with sulfides **7k** and **7l** generated in similar yields (74 and 68%, respectively). Curiously, the corresponding *O*-methyl analogue **6d** showed a dramatic difference in the efficiency of reaction: with 4-iodoanisole **5b** it gave sulfide **7m** in 99% yield (entry 5) whereas with 4-nitroiodobenzene (**5h**) it gave barely any yield of the sulfide product **7n** (13%; entry 6) and instead returned significant quantities of unreacted thiol (**6d**; 34% recovery). A similar trend was observed in the reactions of 2,4-dichlorothiophenol **6e** which gave efficient conversion with the electron-rich halide **5b** (83%; entry 7) but a much lower isolated yield following the reaction with the electron-poor halide **5h** (37%; entry 8). The reaction of 4-aminothiophenol (**6f**) with 4-iodoanisole (**5b**) was poorly efficient (38%; entry 9), whereas 3,5-bistrifluoromethylbenzenethiol (**6g**) and 4-(trifluoromethyl)benzenethiol (**6h**) gave very good and comparable yields of sulfides **7r-t** (entries 10-12; 82, 87 and 75%, respectively). In conclusion, by varying the thiophenol substrate some variation in the isolated yield of the corresponding sulfide was observed – the process being most efficient and reliable for reactions with the electron-rich aryl iodide **5b** for which a copper-mediated mechanism could be expected to dominate.

Given the success with thiophenol substrates, the reaction of the more-challenging alkyl thiols **8a,b** was briefly examined (**Table 5**). Benzylthiol (**8a**) was reacted with 4-iodoanisole (**5b**) (entry 1) and an electron-poor halide, 2-chloropyridine (**5m**) (entry 2), under the established conditions. Although the yield of the corresponding alkyl sulfide **9a,b** was on average lower, both processes were successful. Similarly, the use of cyclohexanethiol (**8b**) with either an electron-rich **5b** or electron-poor halide **5i** both gave respectable yields of the corresponding alkyl sulfide products **9c,d** (entries 3 and 4). Thus although slightly less efficient, this process can be used for the synthesis of alkyl sulfides.

Table 4. Microwave-assisted synthesis of aryl sulfides **7i-t** using a range of thiophenols **6b-h**[a]



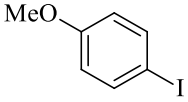
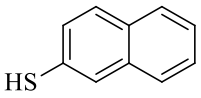
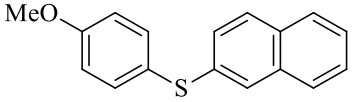
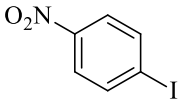
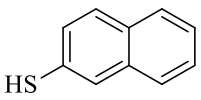
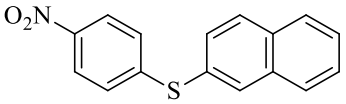
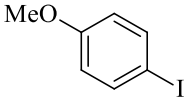
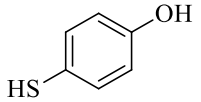
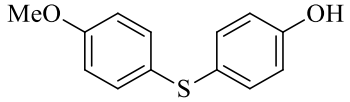
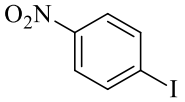
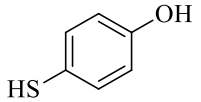
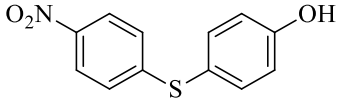
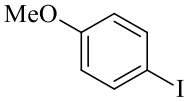
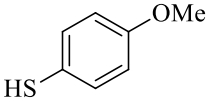
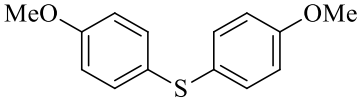
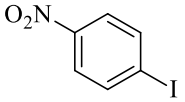
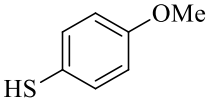
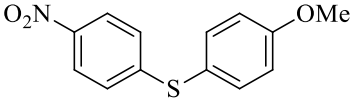
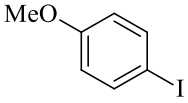
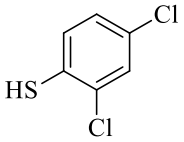
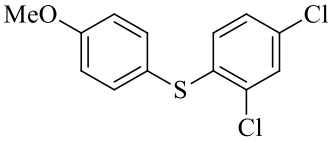
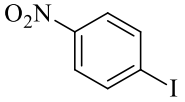
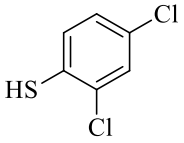
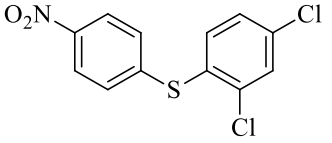
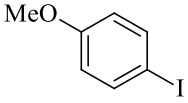
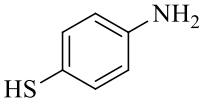
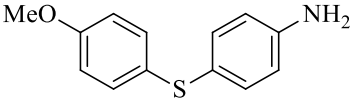
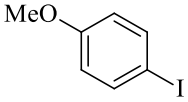
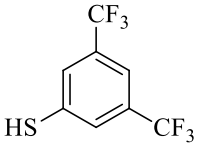
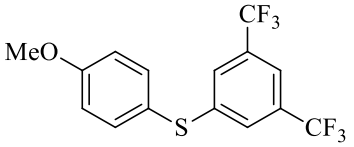
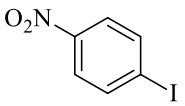
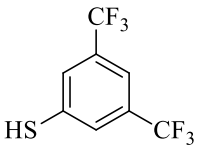
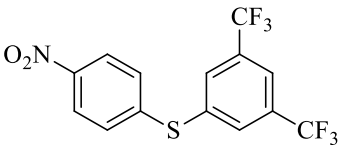
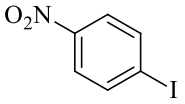
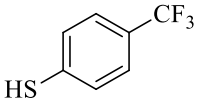
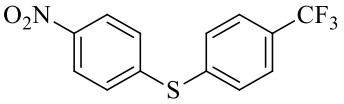
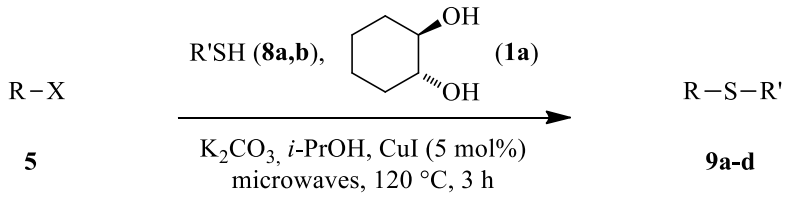
Entry	Halide	5	Thiol	6	Product	7	Yield%[b]
1		**b**		**b**		**i**	91
2		**h**		**b**		**j**	78
3		**b**		**c**		**k**	74
4		**h**		**c**		**l**	68
5		**b**		**d**		**m**	99
6		**h**		**d**		**n**	13
7		**b**		**e**		**o**	83
8		**h**		**e**		**p**	37
9		**b**		**f**		**q**	38
10		**b**		**g**		**r**	82
11		**h**		**g**		**s**	87

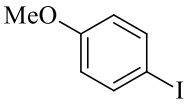
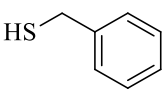
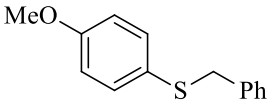
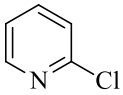
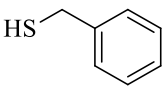
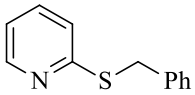
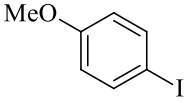
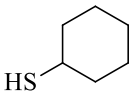
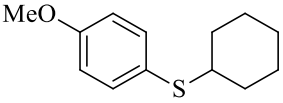
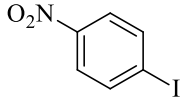
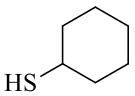
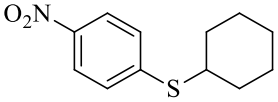
Table 4 (continued)

12		**h**		**h**		**t**	75

[a] Reactions were carried out under microwave dielectric heating in a CEM Discover single-mode cavity at 120 °C for 3 h, measured by the in-built IR sensor, using an aryl halide **5** (1 equiv.) and thiophenol **6b-h** (1 equiv.) in the presence of copper(I) iodide (5 mol%), (±)-*trans*-1,2-cyclohexanediol (**1a**) (2 equiv.), K_2CO_3 (2 equiv.), and *i*-PrOH as solvent under anhydrous conditions. [b] Isolated yield of the corresponding sulfide **7** after purification by column chromatography.

Table 5. Microwave-assisted synthesis of sulfides **9a-d** using alkyl thiols **8a,b**[a]



Entry	Halide	**5**	Thiol	**8**	Product	**9**	Yield%[b]
1		**b**		**a**		**a**	66
2		**m**		**a**		**b**	50
3		**b**		**b**		**c**	48
4		**h**		**b**		**d**	64

[a] Reactions were carried out under microwave dielectric heating in a CEM Discover single-mode cavity at 120 °C for 3 h, measured by the in-built IR sensor, using an aryl halide **5** (1 equiv.) and alkyl thiol **8** (1 equiv.) in the presence of copper(I) iodide (5 mol%), (±)-*trans*-1,2-cyclohexanediol (**1a**) (2 equiv.), K_2CO_3 (2 equiv.), and *i*-PrOH as solvent under anhydrous conditions, unless stated otherwise. [b] Isolated yield of the corresponding sulfide **9** after purification by column chromatography.

Conclusions

The use of microwave irradiation when combined with a copper(I) catalyst and two equivalents of the (±)-*trans*-1,2-cyclohexanediol ligand (**1a**) using K_2CO_3 as base promotes the Ullmann condensation of a thiophenol and an aryl iodide or bromide. On the whole, yields are very good to excellent and reaction times comparatively short (3 hours). Furthermore, the process is compatible with both electron-rich and electron-poor aryl halide precursors: in general the former tend to provide the corresponding sulfide product in higher yield as one might expect for a copper-catalyzed process. The same process can be used to generate alkyl sulfide products, although in general the yields for this transformation were more moderate. This procedure is fast and convenient and gives rise to a wide variety of sulfide products and so should find widespread use in the future.

Experimental Section

General. Commercially available reagents were used without further purification; solvents were dried by standard procedures. Light petroleum refers to the fraction with bp 40–60 °C. Flash chromatography was carried out using Merck Kieselgel 60 H silica or Matrex silica 60. Analytical thin layer chromatography was carried out using aluminium-backed plates coated with Merck Kieselgel 60 GF_{254} that were visualized under UV light (at 254 and/or 360 nm). Microwave irradiation experiments were performed in a sealed tube using a self-tunable CEM Discover focused monomodal microwave synthesizer at the given temperature using the instrument's in-built temperature measuring device, by varying the irradiation power (initial power given in parentheses). For experiments with a passive heating element, an Anton Paar cylindrical insert of sintered silicon carbide was added to the reaction vessel. Fully characterized compounds were chromatographically homogeneous. Melting points were determined on a Kofler hot stage apparatus and are uncorrected. Infra-red spectra were recorded in the range 4000–600 cm^{-1} on a Perkin–Elmer 1600 series FTIR spectrometer using KBr disks or as a nujol mull for solid samples and thin films between NaCl plates for liquid samples and are reported in cm^{-1}. NMR spectra were recorded using a Bruker DPX 400 instrument, 500 Avance instrument or Varian VNMRS instrument operating at 400 or 500 MHz for ^1H spectra and 100 or 126 MHz for ^{13}C spectra; *J* values were recorded in Hz and multiplicities were expressed by the usual conventions. Low resolution mass spectra were determined using a Fisons VG Platform II Quadrupole instrument using atmospheric pressure chemical ionization (APcI) unless otherwise stated. High resolution mass spectra were obtained courtesy of the EPSRC Mass Spectrometry Service at University College of Wales, Swansea, UK using the ionization methods specified.

General experimental procedure for microwave-assisted C–S bond formation. A solution of aryl halide **5** (0.5 mmol), thiol **6** (0.5 mmol), CuI (5 mg, 25 μmol), (±)-*trans*-cyclohexane-1,2-

diol (**1**) (116 mg, 1.0 mmol), K_2CO_3 (138 mg, 1.0 mmol) in 2-propanol (2 mL) was irradiated at 120 °C for 3 × 1 h in a pressure-rated glass tube (10 mL) using a CEM Discover® microwave synthesizer by moderating the initial power (150 W unless otherwise stated). After cooling in a flow of compressed air, the reaction mixture was filtered and evaporated *in vacuo*.

4-(Phenylthio)anisole (**7b**). According to the general experimental procedure, a solution of 4-iodoanisole (**5b**) (117 mg, 0.5 mmol), thiophenol (**6a**) (55 mg, 0.05 mL, 0.5 mmol), CuI (5 mg, 0.025 mmol), (±)-*trans*-1,2-cyclohexanediol (**1a**) (116 mg, 1 mmol), and K_2CO_3 (138 mg, 1 mmol) in 2-propanol (2 mL) was irradiated at 120 °C in a pressure-rated glass tube (10 mL) for 3 × 1 h. After cooling in a flow of compressed air, the reaction mixture was filtered and evaporated *in vacuo*. Purification by column chromatography on SiO_2, eluting with hexane–CH_2Cl_2 (3:1), gave the *title compound* (103 mg, 95%) as a yellow oil (found: M^+, 216.0607. $C_{13}H_{12}OS$ requires M, 216.0609); IR (nujol)/cm^{-1} ν_{max} 3058, 3002, 2938, 2835, 2537, 2044, 1594, 1573, 1505, 1491, 1474, 1439, 1286, 1180, 1094, 1081, 1023; ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.35 (2H, m), 7.15 (2H, m), 7.11 – 7.05 (3H, m), 6.83 (2H, m), 3.75 (3H, s); ^{13}C NMR (125 MHz; $CDCl_3$) δ 158.8 (C), 137.6 (C), 134.3 (CH), 127.9 (CH), 127.2 (CH), 124.7 (C), 123.4 (CH), 113.9 (CH), 54.4 (Me); MS (EI) *m/z* (rel. intensity) 216 ($M^{\bullet+}$, 100), 201 (55).

Diphenyl sulfide (**7c**). A solution of iodobenzene (**5c**) (102 mg, 0.5 mmol), thiophenol (**6a**) (55 mg, 0.05 mL, 0.5 mmol), CuI (5 mg, 0.025 mmol), (±)-*trans*-1,2-cyclohexanediol (116 mg, 1 mmol), K_2CO_3 (138 mg, 1 mmol) in 2-propanol (2 mL) was irradiated at 120 °C in a pressure-rated glass tube (10 mL) for 3 × 1 h. After cooling in a flow of compressed air, the reaction mixture was filtered and evaporated *in vacuo*. Purification by column chromatography on SiO_2, eluting with hexane–CH_2Cl_2 (3:1), gave the title compound (80 mg, 86%) as a yellow oil (found: M^+, 186.0502. $C_{12}H_{10}S$ requires M, 186.0503); ^{1}H NMR (400 MHz; d_6-DMSO*)* δ 7.41 – 7.37 (4H, m), 7.34 – 7.31 (4H, m), 7.29 (2H, m); ^{13}C NMR (100 MHz; d_6-DMSO) δ 136.2 (C), 130 (CH), 128.1 (CH), 127.6 (CH); MS (EI) *m/z* (rel. intensity) 186 ($M^{\bullet+}$, 100%), 171 (10).

4-(Methylphenyl)phenyl sulfide (**7d**). According to the general experimental procedure, a solution of 4-iodotoluene (**5f**) (109 mg, 0.5 mmol), thiophenol (**6a**) (55 mg, 0.05 mL, 0.5 mmol), CuI (5 mg, 0.025 mmol), (±)-*trans*-1,2-cyclohexanediol (**1a**) (116 mg, 1 mmol), and K_2CO_3 (138 mg, 1 mmol) in 2-propanol (2 mL) was irradiated at 120 °C in a pressure-rated glass tube (10 mL) for 3 × 1 h. After cooling in a flow of compressed air, the reaction mixture was filtered and evaporated *in vacuo*. Purification by column chromatography on SiO_2, eluting with hexane–CH_2Cl_2 (3:1), gave the title compound (76 mg, 76%) as a yellow oil (found: M^+, 200.0657. $C_{13}H_{12}S$ requires M, 200.0660); ^{1}H NMR (400 MHz; d_6-DMSO*)* δ 7.18 (2H, d, *J* 8), 7.16 – 7.13 (4H, m), 7.09 – 7.05 (1H, m), 7.02 – 6.99 (2H, d, *J* 8), 2.30 (3H, s); ^{13}C NMR (100 MHz; d_6-DMSO) δ 139.2 (CH), 137 (C), 132.6 (C), 131.1 (CH), 130.6 (CH), 129.7 (CH), 128.5 (CH), 127.2 (CH), 22.5 (CH); MS (EI) *m/z* (rel. intensity) 200 ($M^{\bullet+}$, 100), 185 (50).

2-(Phenylthio)anisole (**7e**). According to the general experimental procedure, a solution of 2-iodoanisole (**5g**) (117 mg, 0.5 mmol), thiophenol (**6a**) (55 mg, 0.05 mL, 0.5 mmol), CuI (5 mg, 0.025 mmol), (±)-*trans*-1,2-cyclohexanediol (**1a**) (116 mg, 1 mmol), and K_2CO_3 (138 mg, 1 mmol) in 2-propanol (2 mL) was irradiated at 120 °C in a pressure-rated glass tube (10 mL) for 3

× 1 h. After cooling in a flow of compressed air, the reaction mixture was filtered and evaporated *in vacuo*. Purification by column chromatography on SiO_2, eluting with hexane–CH_2Cl_2 (3:1), gave the *title compound* (103 mg, 95%) as a pale yellow oil (found: M^+, 216.0612. $C_{13}H_{12}OS$ requires M, 216.0609); ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.35 (2H, d, *J* 8.8), 7.16 – 7.15 (2H, m), 7.11 – 7.05 (3H), 6.83 (2H, d, *J* 8.8), 3.75 (3H, s); ^{13}C NMR (125 MHz; $CDCl_3$) δ 158.8 (C), 137.6 (C), 134.3 (CH), 127.9 (CH), 127.2 (CH), 124.7 (C), 123.4 (CH), 113.9 (CH), 54.4 (Me); MS (EI) *m/z* (rel. intensity) 216 ($M^{\bullet+}$, 100), 168 (15).

4-Nitrophenyl phenyl sulfide (**7f**). According to the general experimental procedure, a solution of 4-nitroiodobenzene (**5h**) (124 mg, 0.5 mmol), thiophenol (**6a**) (55 mg, 0.05 mL, 0.5 mmol), CuI (5 mg, 0.025 mmol), (±)-*trans*-1,2-cyclohexanediol (**1a**) (116 mg, 1 mmol), and K_2CO_3 (138 mg, 1 mmol) in 2-propanol (2 mL) was irradiated at 120 °C in a pressure-rated glass tube (10 mL) for 3 × 1 h. After cooling in a flow of compressed air, the reaction mixture was filtered and evaporated *in vacuo*. Purification by column chromatography on SiO_2, eluting with hexane–CH_2Cl_2 (3:1), gave the *title compound* (94 mg, 81%) as a yellow solid, mp 50 °C (lit.[20] 50–55 °C) (found: M^+, 231.0360. $C_{12}H_9NO_2S$ requires M, 231.0354); IR (nujol)/cm^{-1} ν_{max} 3060, 2915, 2599, 2444, 2223, 1915, 1573, 1505, 1474, 1439, 1396, 1331, 1179, 1080, 1023, 1009; ^{1}H NMR (400 MHz; d_6-DMSO) δ 8.19 (2H, m), 7.66 – 7.63 (2H, m), 7.59 (3H, m), 7.33 (2H, m); ^{13}C NMR (400 MHz; d_6-DMSO) δ 148.5 (C), 145.4 (C), 134.7 (C), 130.5 (CH), 130 (CH), 129.7 (CH), 126.7 (CH), 124 (CH); MS (EI) *m/z* (rel. intensity) 231 ($M^{\bullet+}$, 100), 201 (16), 184 (70), 152 (10).

2-Methyl-4-nitro-1-(phenylthio)benzene (**7g**). According to the general experimental procedure, a solution of 2-iodo-5-nitrotoluene (**5j**) (132 mg, 0.5 mmol), thiophenol (**6a**) (55 mg, 0.05 mL, 0.5 mmol), CuI (5 mg, 0.025 mmol), (±)-*trans*-1,2-cyclohexanediol (**1a**) (116 mg, 1 mmol), and K_2CO_3 (138 mg, 1 mmol) in 2-propanol (2 mL) was irradiated at 120 °C in a pressure-rated glass tube (10 mL) for 3 × 1 h. After cooling in a flow of compressed air, the reaction mixture was filtered and evaporated *in vacuo*. Purification by column chromatography on SiO_2, eluting with hexane–CH_2Cl_2 (3:1), gave the title compound (81 mg, 66%) as a colorless oil (found: M^+, 245.0503. $C_{13}H_{11}NO_2S$ requires M, 245.0511); ^{1}H NMR (400 MHz; d_6-DMSO) δ 8.16 (1H, d, *J* 2.5), 7.96 (1H, dd, *J* 8.7, 2.5), 6.88 (1H, d, *J* 8.7), 7.57 – 7.53 (5H, m), 2.44 (3H, s); ^{13}C NMR (100 MHz; d_6-DMSO) δ 148.7 (C), 145.1 (C), 141.2 (C), 135.8 (C), 132.8 (CH), 132.6 (CH), 131.5 (CH), 129.7 (CH), 129.4 (CH), 127.7 (CH), 121.4 (CH), 119.1 (CH), 18.3 (CH); MS (EI) *m/z* (rel. intensity) 245 ($M^{\bullet+}$, 23%), 215 (100), 199 (14).

1,2-Bis(phenylthio)benzene (**7h**). According to the general experimental procedure, a solution of 2-bromoiodobenzene (**5k**) (132 mg, 0.06 mL, 0.5 mmol), thiophenol (**6a**) (118 mg, 0.11 mL, 1 mmol), CuI (5 mg, 0.025 mmol), (±)-*trans*-1,2-cyclohexanediol (**1a**) (116 mg, 1 mmol), and K_2CO_3 (207 mg, 1.5 mmol) in 2-propanol (2 mL) was irradiated at 120 °C in a pressure-rated glass tube (10 mL) for 3 × 1 h. After cooling in a flow of compressed air, the reaction mixture was filtered and evaporated *in vacuo*. Purification by column chromatography on SiO_2, eluting with hexane–CH_2Cl_2 (3:1), gave the *title compound* (138 mg, 94%) as a colorless oil (found: M^+, 294.0539. $C_{18}H_{14}S_2$ requires M, 294.0537); IR (nujol)/cm^{-1} ν_{max} 3056, 1575, 1558, 1475, 1446,

1426, 1327, 1305, 1250, 1104, 1018, 999; ^{1}H NMR (500 MHz; $CDCl_3$) δ 7.57 (1H, dd, *J* 8, 1.5), 7.54 – 7.21 (10H), 7.15 (1H, td, *J* 8, 1.5), 7.03 (1H, m), 6.94 (1H, dd, *J* 8, 1.5); ^{13}C NMR (126 MHz; $CDCl_3$) δ 138.8 (C), 137.1 (C), 133.4 (CH), 133.0 (CH), 133.0 (C), 129.9 (CH), 129.6 (CH), 129.0 (CH), 128.4 (CH), 127.8 (CH), 127.6 (CH), 127.2 (CH), 127.1 (C), 123.1 (C); MS (EI) *m/z* (rel. intensity) 294 ($M^{\bullet+}$, 100%), 184 (55).

2-(4-Methoxyphenylthio)naphthalene (**7i**). According to the general experimental procedure, a solution of 4-iodoanisole (**5b**) (117 mg, 0.5 mmol), 2-thionaphthol (**6b**) (80 mg, 0.5 mmol), CuI (5 mg, 25 µmol), (±)-*trans*-cyclohexane-1,2-diol (**1a**) (116 mg, 1.0 mmol), and K_2CO_3 (138 mg, 1.0 mmol) in 2-propanol (2 mL) was irradiated at 120 °C in a pressure-rated glass tube (10 mL) for 3 × 1 h. After cooling in a flow of compressed air, the reaction mixture was filtered and evaporated *in vacuo*. Purification by column chromatography on silica gel, eluting with hexane–CH_2Cl_2 (3:1), gave the *title compound* (121 mg, 91%) as a colorless solid, mp 66–67 °C (hexane) (lit.[21] 63–64 °C) (found: MH^+, 267.0848. $C_{17}H_{15}OS$ requires MH, 267.0844); IR (KBr)/cm^{-1} ν_{max} 2024, 2853, 1183, 1106; ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.63 (3H, m), 7.52 (1H, d, *J* 1.3), 7.38 (2H, d, *J* 8.8), 7.36 – 7.30 (2H, m), 7.21 (1H, dd, *J* 8.8, 1.8), 6.84 (2H, AA′XX′, J_{AX} 8.8), 3.75 (3 H, s); ^{13}C NMR (62.5 MHz; $CDCl_3$) 159.7 (C), 135.1 (C), 128.8 (C), 127.6 (C), 127.0 (CH), 126.8 (CH), 126.3 (CH), 125.9 (CH), 121.0 (CH), 115.4 (CH), 55.3 (Me); MS (AP^+) *m/z* (rel. intensity) 267 (MH^+, 84%), 266 (13), 115 (100).

2-(4-Nitrophenylthio)naphthalene (**7j**). According to the general experimental procedure, a solution of 1-iodo-4-nitrobenzene (**5h**) (124 mg, 0.5 mmol), 2-thionaphthol (**6b**) (80 mg, 0.5 mmol), CuI (5 mg, 25 µmol), (±)-*trans*-cyclohexane-1,2-diol (**1a**) (116 mg, 1.0 mmol), and K_2CO_3 (138 mg, 1.0 mmol) in 2-propanol (2 mL) was irradiated at 120 °C for 3 × 1 h in a pressure-rated glass tube (10 mL). After cooling in a flow of compressed air, the reaction mixture was filtered and evaporated *in vacuo*. Purification by column chromatography on silica gel, eluting with hexane–CH_2Cl_2 (3:1), gave the *title compound* (109 mg, 78%) as a pale yellow solid, mp 94 °C (lit.[7d] 92–93 °C) (found: M^+, 281.0509. $C_{16}H_{11}NO_2S$ requires M, 281.0511); IR (KBr)/cm^{-1} ν_{max} 3089, 1574, 1509, 1341; ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.04 (1H, d, *J* 1.4), 8.00 (2H, AA′XX′, J_{AX} 9.0), 7.81 (3H, ddd, *J* 9, 7, 4), 7.55 – 7.47 (2H, m), 7.45 (1H, dd, *J* 9, 1.8), 7.15 (2H, AA′XX′, J_{AX} 9); ^{13}C NMR (62.5 MHz; $CDCl_3$) δ 148.4 (C) 145.5 (C), 134.6 (C), 133.9 (CH), 133.4 (C), 130.8 (CH), 129.9 (C), 127.9 (CH), 127.9 (CH), 127.7 (CH), 127.6 (CH), 127.1 (CH), 126.9 (CH), 124.1 (CH); MS (EI^+) *m/z* (rel. intensity) 281 ($M^{\bullet+}$, 50%), 251 (100), 234 (37), 127 (5).

4-Hydroxy-4′-methoxydiphenyl sulfide (7k). According to the general experimental procedure, a solution of 4-iodoanisole (**5b**) (117 mg, 0.5 mmol), 4-mercaptophenol (**6c**) (63 mg, 0.5 mmol), CuI (5 mg, 25 µmol), (±)-*trans*-cyclohexane-1,2-diol (**1a**) (116 mg, 1.0 mmol), and K_2CO_3 (138 mg, 1.0 mmol) in 2-propanol (2 mL) was irradiated at 120 °C for 3 x 1 h in a pressure-rated glass tube (10 mL). After cooling in a flow of compressed air, the reaction mixture was filtered and evaporated *in vacuo*. Purification by column chromatography on silica gel, eluting with hexane–CH_2Cl_2 (1;10), gave the *title compound*[5i] (86 mg, 74%) as a light yellow solid, mp 60 °C (found: M^+, 232.0555. $C_{13}H_{12}O_2S$ requires *M*, 232.0558); IR (KBr)/cm^{-1} ν_{max} 3390, 1584, 1490,

1237, 1100, 818; ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.17 (2H, app dd, *J* 6.7, 2.1), 7.11 (2H, app dd, *J* 6.6, 2.0), 6.74 (2H, app dd, *J* 6.7, 2.1), 6.65 (2H, app dd, *J* 6.6, 2.0), 5.09 (1H, s), 4.00 – 3.49 (3H, m); ^{13}C NMR (62.5 MHz; $CDCl_3$) δ 158.9 (C), 155.0 (C), 133.0 (C), 132.8 (C), 132.6 (CH), 127.5 (CH), 127.5 (CH), 116.4 (CH), 116.3 (CH), 114.9 (CH), 55.5 (Me); MS (EI^+) *m/z* (rel. intensity) 232 ($M^{\bullet+}$, 100), 217 (97), 189 (21), 86 (50), 84 (82).

4-Hydroxy-4′-nitrodiphenyl sulfide (**7l**). According to the general experimental procedure, a solution of 1-iodo-4-nitrobenzene (**5h**) (124 mg, 0.5 mmol), 4-mercaptophenol (**6c**) (63 mg, 0.5 mmol), CuI (5 mg, 25 μmol), (±)-*trans*-cyclohexane-1,2-diol (**1a**) (116 mg, 1.0 mmol), and K_2CO_3 (138 mg, 1.0 mmol) in 2-propanol (2 mL) was irradiated at 120 °C for 3 × 1 h in a pressure-rated glass tube (10 mL). After cooling in a flow of compressed air, the reaction mixture was filtered and evaporated *in vacuo*. Purification by column chromatography on silica gel, eluting with hexane–CH_2Cl_2 (1:3), gave the *title compound* (84.5 mg, 68%) as a yellow solid, mp 143.5–146.5 (dec.) °C (lit.[22] 143–145 °C) (found: M^+, 247.0306. $C_{12}H_9NO_3S$ requires *M*, 247.0303); IR (KBr)/cm^{-1} ν_{max} 3434, 2130, 1652, 1506, 1335, 1025; ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.96, 7.01 (4H, AA′XX′, J_{AX} 9.0), 7.32, 6.88 (4H, AA′XX′, J_{AX} 8.7),5.69 (1H, s); ^{13}C NMR (62.5 MHz; $CDCl_3$) δ 159.4 (C), 149.9 (C), 144.4 (C), 137.2 (C), 125.2 (CH), 124.0 (CH), 117.3 (CH), 116.8 (CH); MS (EI^+) *m/z* (rel. intensity) 247 ($M^{\bullet+}$, 87), 200 (19), 183 (17), 84 (100).

Bis(4-methoxyphenyl) sulfide (**7m**). According to the general experimental procedure, a solution of 4-iodoanisole (**5b**) (117 mg, 0.5 mmol), 4-methoxythiophenol (**6d**) (70 mg, 0.06 ml, 0.5 mmol), CuI (5 mg, 25 μmol), (±)-*trans*-cyclohexane-1,2-diol (**1a**) (116 mg, 1.0 mmol), and K_2CO_3 (138 mg, 1.0 mmol) in 2-propanol (2 mL) was irradiated at 120 °C for 3 × 1 h in a pressure-rated glass tube (10 mL). After cooling in a flow of compressed air, the reaction mixture was filtered and evaporated *in vacuo*. Purification by column chromatography on silica gel, eluting with hexane–CH_2Cl_2 (3:1), gave the *title compound*[5j] (122 mg, 99%) as a colorless solid, mp 38 °C (lit.[23] 37.6–37.9 °C) (found: M^+, 246.0717. $C_{14}H_{14}O_2S$ requires M, 246.0715); IR (KBr)/cm^{-1} ν_{max} 3450, 2938, 2838, 1590; ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.20, 6.76 (8H, AA′XX′, J_{AX} 8.6), 3.72 (6H, s); ^{13}C NMR (62.5 MHz; $CDCl_3$) δ 159.0 (C), 132.8 (CH), 127.5 (C), 114.8 (CH), 55.4 (Me); MS (EI^+) *m/z* (rel. intensity) 246 ($M^{\bullet+}$, 100), 231 (95), 203 (24), 188 (20).

4-(4-Methoxyphenylthio)nitrobenzene (**7n**). According to the general experimental procedure, a solution of 1-iodo-4-nitrobenzene (**5h**) (124 mg, 0.5 mmol), 4-methoxythiophenol (**6d**) (70 mg, 0.06 ml, 0.5 mmol), CuI (5 mg, 25 μmol), (±)-*trans*-cyclohexane-1,2-diol (**1a**) (116 mg, 1.0 mmol), and K_2CO_3 (138 mg, 1.0 mmol) in 2-propanol (2 mL) was irradiated at 120 °C for 3 × 1 h in a pressure-rated glass tube (10 mL). After cooling in a flow of compressed air, the reaction mixture was filtered and evaporated *in vacuo*. Purification by column chromatography on silica gel, eluting with hexane–CH_2Cl_2 (1;3), gave the *title compound* (16 mg, 13%) as a yellow solid, mp 56 °C (lit.[4c] 58–60 °C) (found: M^+, 261.0453. $C_{13}H_{11}NO_3S$ requires M, 261.0460); IR (KBr)/cm^{-1} ν_{max} 2925, 1593, 1494, 1336, 1172, 1080; ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.97, 7.02 (4H, AA′XX′, J_{AX} 8.8), 7.42, 6.92 (4H, AA′XX′, J_{AX} 8.6), 3.80 (3H, s); ^{13}C NMR (62.5 MHz;

$CDCl_3$) δ 161.3 (C), 150.1 (C), 145.0 (C), 137.2 (C), 125.6 (CH), 124.0 (CH), 120.2 (CH), 115.7 (CH), 55.5 (Me); MS (EI^+) *m/z* (rel. intensity) 261 ($M^{\bullet+}$, 100), 231 (90), 215 (52), 200 (59), 184 (44), 139 (61).

4-(2,4-Dichlorophenylthio)anisole (**7o**). According to the general experimental procedure, a solution of 4-iodoanisole (**5b**) (117mg, 0.5 mmol), 2,4-dichlorobenzenethiol (**6e**) (90 mg, 0.13 ml, 0.5 mmol), CuI (5 mg, 25 μmol), (±)-*trans*-cyclohexane-1,2-diol (**1a**) (116 mg, 1.0 mmol), and K_2CO_3 (138 mg, 1.0 mmol) in 2-propanol (2 mL) was irradiated at 120 °C for 3 × 1 h in a pressure-rated glass tube (10 mL). After cooling in a flow of compressed air, the reaction mixture was filtered and evaporated *in vacuo*. Purification by column chromatography on silica gel, eluting with hexane–CH_2Cl_2 (10:1), gave the *title compound* (118 mg, 83%) as a pale yellow oil (found: M^+,283.9831. $C_{13}H_{10}Cl_2OS$ requires M, 283.9829); IR (KBr)/cm^{-1} ν_{max} 3082, 3004, 1570 1494, 564; ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.37, 6.88 (4H, AA′XX′, J_{AX} 8.6), 7.27 (1H, d, *J* 2.2), 6.95 (1H, dd, *J* 8.6, 2.2), 6.56 (1H, d, *J* 8.6), 3.78 (3H, s); ^{13}C NMR (62.5 MHz; $CDCl_3$) δ 160.8 (C), 137.8 (C), 136.9 (C), 131.5 (CH), 131.1 (C), 129.2 (C), 128.3 (CH), 127.3 (CH), 121.2 (CH), 115.4 (CH), 55.4 (Me); MS (EI^+) *m/z* (rel. intensity) 284 ($M^{\bullet+}$, 100), 269 (62), 206 (30), 171 (39).

4-(2,4-Dichlorophenylthio)nitrobenzene (**7p**). According to the general experimental procedure, a solution of 1-iodo-4-nitrobenzene (**5h**) (124 mg, 0.5 mmol), 2,4-dichlorobenzene-thiol (**6e**) (90 mg, 0.13 ml, 0.5 mmol), CuI (5 mg, 25 μmol), (±)-*trans*-cyclohexane-1,2-diol (**1a**) (116 mg, 1.0 mmol), and K_2CO_3 (138 mg, 1.0 mmol) in 2-propanol (2 mL) was irradiated at 120 °C for 3 × 1 h in a pressure-rated glass tube (10 mL). After cooling in a flow of compressed air, the reaction mixture was filtered and evaporated *in vacuo*. Purification by column chromatography on silica gel, eluting with hexane–CH_2Cl_2 (1:3), gave the *title compound* (54.9 mg, 37%) as a brown oil (found: MH^+, 299.97. $C_{12}H_7Cl_2NO_2S$ requires MH, 299.9653); IR (KBr)/cm^{-1} ν_{max} 1620, 1596, 1568, 1486, 1372, 564; ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.25 (1H, d, *J* 2), 7.24, 6.65 (4H, AA′XX′, J_{AX} 8.5), 6.93 (1H, dd, *J* 8.6, 2), 6.53 (1H, d, *J* 8.6); ^{13}C NMR (62.5 MHz; $CDCl_3$) δ 148.0 (C), 138.6 (C), 137.3 (C), 130.6 (CH), 129.0 (C), 127.7 (CH), 127.2 (CH), 117.3 (CH), 116.2 (CH); MS (AP^+) *m/z* (rel. intensity) 300 (MH^+, 100), 177 (32).

4-(4-Aminophenylthio)anisole (**7q**). According to the general experimental procedure, a solution of 4-iodoanisole (**5b**) (117 mg, 0.5 mmol), 4-aminothiophenol (**6f**) (63 mg, 0.5 mmol), CuI (5 mg, 25 μmol), (±)-*trans*-cyclohexane-1,2-diol (**1a**) (116 mg, 1.0 mmol), and K_2CO_3 (138 mg, 1.0 mmol) in 2-propanol (2 mL) was irradiated at 120 °C for 3 × 1 h in a pressure-rated glass tube (10 mL). After cooling in a flow of compressed air, the reaction mixture was filtered and evaporated *in vacuo*. Purification by column chromatography on silica gel, eluting with hexane–CH_2Cl_2 (1:3), gave the *title compound* (7.7 mg, 7%) as a brown solid, mp 85–86 °C (lit.[24] 96 °C) (found: MH^+, 232.0791. $C_{13}H_{14}NOS$ requires MH, 232.0791); ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.19 – 7.11 (4H), 6.74 (2H, AA′XX′, J_{AX} 6.7, 2), 6.59 (2H, AA′XX′, J_{AX} 6.7, 2), 3.70 (3H); ^{13}C NMR (62.5 MHz; $CDCl_3$) δ 158.8 (C), 133.4 (C), 132.0 (CH), 128.1 (C), 116.66 (CH), 116.62 (CH), 114.7 (CH), 55.4 (Me); MS (AP^+) *m/z* (rel. intensity) 232 (MH^+, 5%), 184 (3).

4-[3,5-Bis(trifluoromethyl)phenylthio]anisole (**7r**). According to the general experimental procedure, a solution of 4-iodoanisole (**5b**) (117 mg, 0.5 mmol), 3,5-bis(trifluoromethyl)benzenethiol (**6g**) (123 mg, 0.09 mL, 0.5 mmol), CuI (5 mg, 25 μmol), (±)-*trans*-cyclohexane-1,2-diol (**1a**) (116 mg, 1.0 mmol), and K_2CO_3 (138 mg, 1.0 mmol) in 2-propanol (2 mL) was irradiated at 120 °C for 3 × 1 h in a pressure-rated glass tube (10 mL). After cooling in a flow of compressed air, the reaction mixture was filtered and evaporated *in vacuo*. Purification by column chromatography on silica gel, eluting with hexane–CH_2Cl_2 (6:1), gave the *title compound* (144 mg, 82%) as a pale yellow solid, mp 52 °C (found: M^+, 352.0351. $C_{15}H_{10}F_6OS$ requires *M*, 352.0357); IR (KBr)/cm^{-1} ν_{max} 2962, 2836, 1592, 1572, 1352, 1171, 1141; ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.49 (1H, bs), 7.41, 6.91 (4H, AA′XX′, J_{AX} 8.9), 7.37 (2H, bs), 3.80 (3H, s); ^{13}C NMR (62.5 MHz; $CDCl_3$) δ 161.1 (C), 143.6 (C), 136.8 (CH), 132.0 (C, q, $^2J_{CF}$ 33), 126.1 (CH, m), 123.1 (C, q, $^1J_{CF}$ 273), 120.4 (C), 118.8 (CH, hept, $^3J_{CF}$ 4), 115.7 (CH), 55.4 (Me); MS (EI^+) *m/z* (rel. intensity) 352 ($M^{\bullet+}$, 50%), 337 (23), 240 (8), 84 (100).

4-[3,5-Bis(trifluoromethyl)phenylthio]nitrobenzene (**7s**). According to the general experimental procedure, a solution of 1-iodo-4-nitrobenzene (**5h**) (124 mg, 0.5 mmol), 3,5-bis(trifluoromethyl)benzenethiol (**6g**) (123 mg, 0.09 mL, 0.5 mmol), CuI (5 mg, 25 μmol), (±)-*trans*-cyclohexane-1,2-diol (**1a**) (116 mg, 1.0 mmol), and K_2CO_3 (138 mg, 1.0 mmol) in 2-propanol (2 mL) was irradiated at 120 °C for 3 × 1 h in a pressure-rated glass tube (10 mL). After cooling in a flow of compressed air, the reaction mixture was filtered and evaporated *in vacuo*. Purification by column chromatography on silica gel, eluting with hexane–CH_2Cl_2 (3:1), gave the *title compound* (143 mg, 87%) as an orange solid, mp 51 °C (found: M^+, 367.0088. $C_{14}H_7F_6NO_2S$ requires M, 367.0102); IR (KBr)/cm^{-1} ν_{max} 2921, 2853, 1672, 1598, 1574, 1524, 1351, 1167, 1131; ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.12, 7.31 (4H, AA′XX′, J_{AX} 8.7), 7.82–7.79 (3H); ^{13}C NMR (62.5 MHz; $CDCl_3$) δ 147.3 (C), 143.5 (C), 136.1 (C), 133.5 (C, q, $^2J_{CF}$ 34), 132.6 (CH, m), 129.6 (CH), 124.8 (CH), 122.5 (CH, hept, $^3J_{CF}$ 4), 122.8 (C, q, $^1J_{CF}$ 275); MS (EI^+) *m/z* (rel. intensity) 367 ($M^{\bullet+}$, 30%), 337 (68), 252 (15), 86 (100).

4-[4-(Trifluoromethyl)phenylthio]nitrobenzene (**7t**). According to the general experimental procedure, a solution of 1-iodo-4-nitrobenzene (**5h**) (124 mg, 0.5 mmol), 4-(trifluoromethyl)-benzenethiol (**6h**) (89 mg, 0.07 mL, 0.5 mmol), CuI (5 mg, 25 μmol), (±)-*trans*-cyclohexane-1,2-diol (**1a**) (116 mg, 1.0 mmol), and K_2CO_3 (138 mg, 1.0 mmol) in 2-propanol (2 mL) was irradiated at 120 °C for 3 × 1 h in a pressure-rated glass tube (10 mL). After cooling in a flow of compressed air, the reaction mixture was filtered and evaporated *in vacuo*. Purification by column chromatography on silica gel, eluting with hexane–CH_2Cl_2 (3:1), gave the *title compound* (112 mg, 75%) as a dark orange solid, mp ~200 °C (found: M^+, 299.0220. $C_{13}H_8F_3NO_2S$ requires M, 299.0228); IR (KBr)/cm^{-1} ν_{max} 1583, 1503, 1477, 1402, 1325, 1169, 1125; ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.04, 7.24 (4H, AA′XX′, J_{AX} 8.7), 7.58 (2H, d, *J* 8.4), 7.50 (2H, d, *J* 8.4); ^{13}C NMR (62.5 MHz; $CDCl_3$) δ 146.3 (C), 145.4 (C), 136.9 (C), 133.1 (CH), 131.0 (C, q, $^2J_{CF}$ 33), 128.9 (CH), 126.8 (CH, q, $^3J_{CF}$ 4), 123.7 (C, q, $^1J_{CF}$ 272), 124.3 (CH); MS (EI^+) *m/z* (rel. intensity) 299 ($M^{\bullet+}$, 100%), 269 (91), 233 (29), 184 (67).

4-(Benzylthio)anisole (**9a**). According to the general experimental procedure, a solution of 4-iodoanisole (**5b**) (117 mg, 0.5 mmol), benzyl mercaptan (**8a**) (68 mg, 0.5 mmol), CuI (5 mg, 0.025 mmol), (±)-*trans*-1,2-cyclohexanediol (**1a**) (116 mg, 1 mmol), and K_2CO_3 (138 mg, 1 mmol) in 2-propanol (2 mL) was irradiated at 120 °C in a pressure-rated glass tube (10 mL) for 3 × 1 h. The reaction mixture was filtered and evaporated *in vacuo*. Purification by column chromatography on SiO_2, eluting with hexane–CH_2Cl_2 (3:1), gave the *title compound* (66 mg, 66%) as a pale yellow solid[9]; ^{1}H NMR (400 MHz; d_6-DMSO) δ 7.29 – 7.19 (7H, m), 6.85 (2H, app dt, *J* 8.8), 4.1 (2H, s), 3.72 (3H, s).

2-(Benzylthio)pyridine (**9b**). According to the general experimental procedure, a solution of 2-chloropyridine (**5m**) (57 mg, 0.5 mmol), benzyl mercaptan (**8a**) (68 mg, 0.5 mmol), CuI (5 mg, 0.025 mmol), (±)-*trans*-1,2-cyclohexanediol (**1a**) (116 mg, 1 mmol), and K_2CO_3 (138 mg, 1 mmol) in 2-propanol (2 mL) was irradiated at 120 °C in a pressure-rated glass tube (10 mL) for 3 × 1 h. The reaction mixture was filtered and evaporated *in vacuo*. Purification by column chromatography on SiO_2, eluting with hexane–CH_2Cl_2 (3:1), gave the *title compound*[25] (100 mg, 50%) as a yellow solid, mp 30 °C (found: M^+, 201.0605. $C_{12}H_{11}NS$ requires M, 201.0612); ^{1}H NMR (400 MHz; d_6-DMSO) δ 8.45 (1H, m), 7.47 (1H, m), 7.42 – 7.28 (5H, m), 7.15 (1H, m), 6.95 (1H, m), 4.34 (2H, s); ^{13}C NMR (400 MHz; d_6-DMSO) δ 159 (C), 150.5 (CH), 138.9 (C), 136.8 (CH), 130.4 (CH), 129.1 (CH), 127.3 (CH), 123.1 (CH), 118.5 (CH), 35.2 (CH_2); MS (EI) *m/z* (rel. intensity) 201 ($M^{\bullet+}$, 68), 168 (100).

4-(Cyclohexylthio)anisole (**9c**). According to the general experimental procedure, a solution of 4-iodoanisole (**5b**) (117 mg, 0.5 mmol), cyclohexyl mercaptan (**8b**) (58 mg, 0.06 mL, 0.5 mmol), CuI (5 mg, 0.025 mmol), (±)-*trans*-1,2-cyclohexanediol (**1a**) (116 mg, 1 mmol), and K_2CO_3 (138 mg, 1 mmol) in 2-propanol (2 mL) was irradiated at 120 °C in a pressure-rated glass tube (10 mL) for 3 × 1 h. After cooling in a flow of compressed air, the reaction mixture was filtered and evaporated *in vacuo*. Purification by column chromatography on SiO_2, eluting with hexane–CH_2Cl_2 (3:1), gave the *title compound* (53 mg, 48%) as a light brown oil (found: M^+, 222.1078. $C_{13}H_{18}OS$ requires M, 222.1078); IR (nujol)/cm^{-1} ν_{max} 2926, 2851, 1591, 1570, 1492, 1462, 1447, 1283, 1241, 1171, 1101, 1031, 997; ^{1}H NMR (250 MHz; $CDCl_3$) δ 7.42 (2H, m), 6.87 (2H, m), 3.83 (3H, s), 2.97 – 2.87 (1H, m), 1.99 – 1.23 (10H); ^{13}C NMR (100 MHz; d_6-DMSO) δ 159.7 (C), 129.8 (C), 128.2 (CH), 116.5 (CH), 57.2 (Me), 54.2 (CH), 37.3 (CH_2), 29.5 (CH_2), 26.0 (CH_2); MS (EI) *m/z* (rel. intensity) 222 ($M^{\bullet+}$, 46%), 140 (100).

4-(Cyclohexylthio)nitrobenzene (**9d**). According to the general experimental procedure, a solution of 1-iodo-4-nitrobenzene (**5h**) (124 mg, 0.5 mmol), cyclohexyl mercaptan (**8b**) (58 mg, 0.06 mL, 0.5 mmol), CuI (5 mg, 25 µmol), (±)-*trans*-cyclohexane-1,2-diol (**1a**) (116 mg, 1.0 mmol), and K_2CO_3 (138 mg, 1.0 mmol) in 2-propanol (2 mL) was irradiated at 120 °C for 3 × 1 h in a pressure-rated glass tube (10 mL). After cooling in a flow of compressed air, the reaction mixture was filtered and evaporated *in vacuo*. Purification by column chromatography on silica gel, eluting with hexane–CH_2Cl_2 (1:1), gave the *title compound* (75 mg, 64%) as a yellow solid, mp 49–51 °C (found: M^+, 237.0826. $C_{12}H_{15}NO_2S$ requires M, 237.0824); IR (KBr)/cm^{-1} ν_{max} 2923, 1577, 1331, 1097, 851; ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.14, 7.37 (4H, AA′XX′ J_{AX} 9.0),

3.50 – 3.31 (1H, m), 2.08 (2H, d, *J* 10), 1.88 – 1.79 (2H, m), 1.74 – 1.63 (1H, m), 1.57 – 1.31 (5H, m); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 147.0 (C), 145.1 (C), 127.7 (CH), 123.9 (CH), 44.9 (CH), 32.9 (CH_2), 25.8 (CH_2), 25.6 (CH_2); MS (EI^+) *m/z* (rel. intensity) 237 ($M^{\bullet+}$, 70), 207 (33), 155 (54), 125 (98).

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