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$Pd_2(dba)_3$/Xantphos-catalyzed cross-coupling of thiols and aryl bromides/triflates

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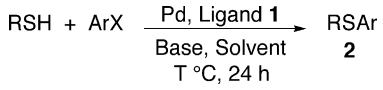
Abstract—The cross-coupling of aliphatic and aromatic thiols and aryl bromides/triflates mediated by a $Pd_2(dba)_3$/Xantphos catalytic system in refluxing xylene (140 °C) affords the corresponding aryl thioethers in good to excellent yields.

1. Introduction

Aryl sulfides are useful intermediates in organic synthesis. In addition, this sulfur fragment is incorporated in a number of natural products or compounds exhibiting important biological activities.[1] The more conventional route to these compounds involves the displacement reaction of an arenethiolate with the appropriate alkyl halide.[2] Other reported procedures are based on the creation of the aryl–sulfur bond, thus including nucleophilic aromatic substitution[3] or treatment[4] of aryllithium or Grignard reagents with sulfurated electrophiles. In 1980, Migita introduced the Pd-catalyzed cross-coupling reaction of aryl bromides with thiols.[5] Since then, various efficient catalytic systems using bidentate phosphines or dialkylphosphine oxides **1** have been described (Scheme 1).[6–9] Furthermore, reactions mediated with other transition metals (Ni, Cu) have been investigated very recently.[10–11]



Scheme 1. Pd-catalyzed Ar–S bond formation.

The Pd-catalyzed strategy previously mentioned is particularly attractive for industry, as revealed by the recent contributions in this area.[12] One major reason of this interest is the use of readily available phenol derivatives (i.e., triflates) or aryl bromides as starting materials. As part of our program concerning the creation of a carbon–sulfur bond on an aromatic ring, our motivation turned towards this chemistry.[13] Among the few examples already described when we initiated the project, we paid particularly attention to a work from Merck dedicated to the palladium cross-coupling of thiols with aryl triflates.[6] The protocol involves an initial deprotonation of the mercaptan with sodium *t*-butoxide followed by heating the resulting sodium thiolate with the aromatic triflate in the presence of $Pd(OAc)_2$ and (*R*)-(+)-Tol-BINAP **1a** (see Table 1 for the ligand structure). However the methodology suffers from a few limitations, such as the incompatibility with aromatic thiols. As a consequence, the search of novel conditions leading to various thioethers, especially both alkyl aryl and diaryl compounds remained of interest. Additional attractive features would be to proceed under mild and friendly conditions (base, solvent) compatible with industrial constraints and allow bromo arenes[14] as substrates. We wish to present herein the results from our investigation that led to the development of a new catalytic system.

2. Results and discussion

In our initial screening experiments, *n*-butanethiol and phenyltriflate were selected as substrates for discovery of optimal conditions. Reaction times were arbitrary set at 24 h. Selected conditions we tested are listed in Table 1. We began with the conditions developed by the Merck group for, which *n*-butyl phenyl sulfide was isolated in 71.5% yield (entry 1). Various bidentate phosphine ligands,

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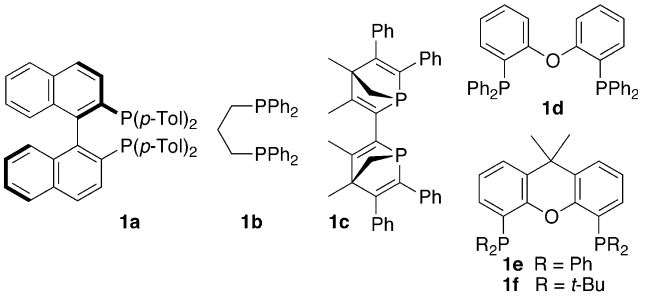
Table 1. Evaluation of various catalytic systems for cross-coupling of *n*-BuSH and PhOTf to give sulfide **2a** (R=*n*-Bu, Ar=Ph) according to Scheme 1[a]



Entry	Base	Pd source	Ligand	Solvent, *T* (°C)	Yield (%)
1	*t*-BuONa	$Pd(OAc)_2$	**1a**	Toluene, 80	71.5
2	*t*-BuONa	$Pd(OAc)_2$	**1b**	Toluene, 80	7.5
3	*t*-BuONa	$Pd(OAc)_2$	**1c**	Toluene, 80	33
4	*t*-BuONa	$Pd(OAc)_2$	**1d**	Toluene, 80	0
5	*t*-BuONa	$Pd(OAc)_2$	**1e**	Toluene, 80	20
6	*t*-BuONa	$Pd_2(dba)_3$	**1a**	Toluene, 80	88
7	*t*-BuONa	$Pd_2(dba)_3$	**1e**	Toluene, 80	0
8	*t*-BuONa	$Pd_2(dba)_3$	**1e**	Toluene, 110	74
9	*t*-BuONa	$Pd_2(dba)_3$	**1e**	Xylene, 140	82
10	K_2CO_3	$Pd_2(dba)_3$	**1e**	Xylene, 140	80
11	K_2CO_3	$Pd_2(dba)_3$	**1f**	Xylene, 140	Traces
12	K_2CO_3	$Pd_2(dba)_3$	**1f**	Toluene, 110	0

[a] Reaction conditions: *n*-BuSH (1 mmol), base (0.5 mmol), PhOTf (0.8 mmol), Pd source (0.08 mmol), ligand **1** (0.09 mmol), solvent (12 mL) for 24 h.

including dppp **1b**, *meso*-BIPNOR **1c**, DPEphos **1d** and Xantphos **1e** were tested but all afforded disappointing results, with chemical yields below 33% (entries 2–5). Use of $Pd_2(dba)_3$ as a direct palladium(0) source in the presence of (*R*)-(+)-Tol-BINAP **1a** led to an excellent 88% yield (entry 6). In contrast, no cross-coupling was observed when combined with Xantphos **1e** (entry 7). However, an elevation of the temperature to 110 °C (refluxing toluene) and even to 140 °C (reflux of xylene) in the presence of this ligand **1e** led to a dramatic improvement. In the last case, the product was obtained in 82% yield (entry 9). Using potassium carbonate as base instead of sodium *t*-butoxide gave an analogous excellent yield (entry 10). As the use of a bulkier and more electron-rich ligand could in principle allow a reduced reaction temperature, we designed the unprecedented Xantphos analogue **1f** with bis-(*t*-butylphosphino) substituents (see Fig. 1 for the X-ray structure). Unfortunately, all attempts with this ligand failed and a total inhibition of the coupling was observed (entries 11 and 12).

In summary, these preliminary studies revealed that the best reaction conditions involve potassium thiolates obtained by mixing the thiol precursor with a stoichiometric amount of potassium carbonate and a Xantphos **1e**/$Pd_2(dba)_3$ as the catalytic system in refluxing xylene (entry 10).[15] The main features of these cross-coupling conditions are the combined use of a cheap, stable, mild and easy handling mineral base and the readily available ligand **1e**. Even if the boiling point of xylene is relatively high (140 °C), this is not a crucial drawback for further industrial applications, the products being in general non-volatile solids. The catalyst loading was deliberately not optimized at our laboratory scale (1 mmol) and more significant results involving until 500 ppm of Pd can in principle be obtained during a scale-up investigation on a specific substrate. In addition the effect of the Pd/ligand ratio was not examined at this point. Important to note is that during the preparation of this manuscript, a Japanese group reported the same catalytic system for this reaction.[16] The difference consists in the use of *i*-Pr_2NEt or Cs_2CO_3 (2 equiv) and 1,4-dioxane, respectively, as base and solvent.

To investigate the scope of the reaction, a broad range of aliphatic thiols including primary, secondary and tertiary structures were then used. The thiolate was generated by deprotonation of the thiol at 0 °C and was then added to a mixture of all other reagents. When all reaction components were simply mixed together, lower conversions to the desired product were observed. For example, sulfide **2a** was

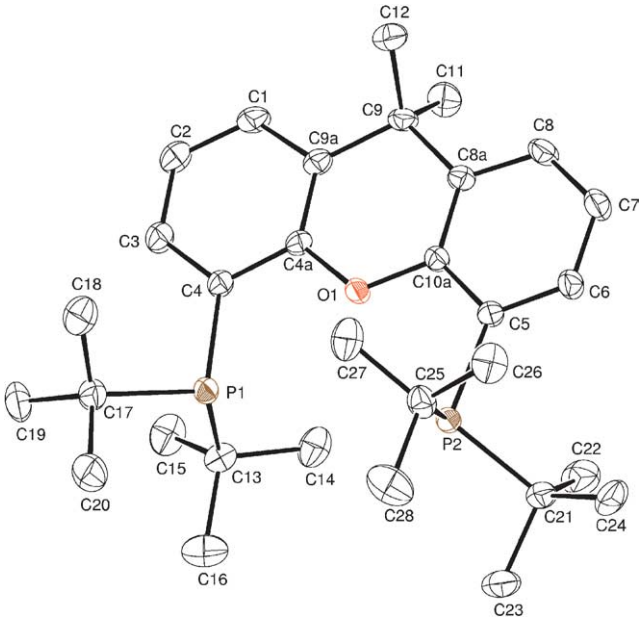


Figure 1. ORTEP diagram of ligand **1f**.

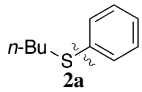
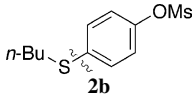
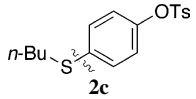
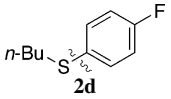
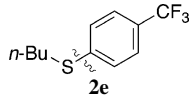
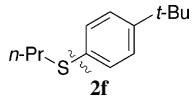
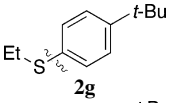
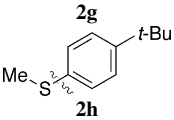
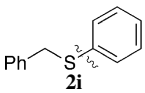
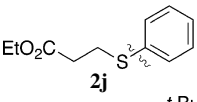
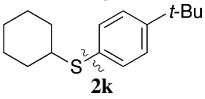
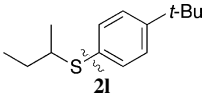
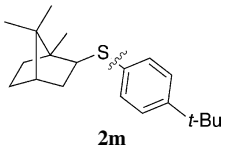
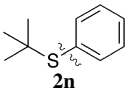
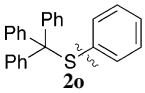
obtained only in 43% yield (compare with the 80% yield obtained above).

All alkyl aryl sulfides were produced in good to excellent yields as outlined in Table 2, except for the trityl derivative (entry 17). Bromobenzene was shown to be an efficient electrophile (entry 2) and the use of the chloride analogue led to a lower 19% yield (entry 3). However, chlorinated arenes can be suitable substrates when activated with an electron withdrawing group. For example, the cross-coupling of compound possessing a trifluoromethyl substituent gave rise to a 75% yield (entry 7). Total chemoselectivities were observed with substrates possessing two potential leaving groups. Substitution took place only at the more reactive C–Br or C–OTf bonds and the mesyl, tosyl and fluoro groups remained unchanged (entries 4–6). Interestingly, sterically hindered thiols were also suitable substrates, thioethers derived from bornane-2-thiol and *t*-butanethiol being isolated in 59 and quantitative yields, respectively. With ethanethiol, a disappointing 35% yield was obtained and this was interpreted by the volatility of the precursor (entry 9). A significant improvement leading to a 94% yield was observed employing an isolated and accurately weighted thiolate (deprotonation with NaOH followed by concentration and drying under vacuum until constant weight). As a consequence, we were also able to couple efficiently commercially available sodium methanethiolate (entry 10). A base sensitive functional groups, namely a methyl ester, in the starting thiol was also tolerated (entry 12). Interestingly, β-sulfanylesters that can thus be produced have very recently been identified as convenient and efficient thiol surrogates.[17]

Arenethiols were also found to be effective nucleophiles under the reactions conditions as can be seen from Table 3. Important to remember is that such substrates were problematic with the Merck procedure. Reaction of simple thiophenol with bromobenzene and phenyltriflate afforded diphenyl sulfide **2p** in quantitative yields (entries 1 and 2). Extension to the access of a naphthyl derivative was also achieved in an excellent 93% yield (entry 3). Introduction of an *ortho*-methoxy group on the aromatic thiol led to the sulfide product in a moderate 41% yield. As can be seen from the results in entries 4 and 6, the protocol can be even applied to electron-deficient thiols. A lower conversion was however observed with the thiol possessing an *N*,*N*-dimethylaminoethyl group (entry 7), probably due to a competing complexation of the nitrogen atom on palladium. Furthermore, pyridine-2-thiol did not react under these reaction conditions (entry 8).

While the precise mechanistic details of the C–S coupling reaction remain to be established, it is assumed that the overall catalytic cycle of the synthesis is similar to that postulated for palladium catalyzed aminations and etherations.[18] The reasons for the beneficial influence of the Xantphos **1e** ligand are not straightforward to elucidate. It is likely that the close proximity of the oxygen atom to the palladium center (with the possibility of assisting the displacement of the leaving group from palladium)[19] and the known ability of chelating diphosphines with large bite angles[20] to accelerate reductive elimination rates[21] play a crucial role.

Table 2. Coupling of aliphatic thiols with $Pd_2(dba)_3$/Xantphos **1e** according to Scheme 1[a]

Entry	X of ArX	Sulfide	Yield (%)[b]
1	OTf		80
2	Br	 **2a**	80
3	Cl		19[c]
4	Br	 **2b**	80
5	Br	 **2c**	87
6	Br	 **2d**	93[c]
7	Cl	 **2e**	75[d]
8	Br	 **2f**	75
9	Br	 **2g**	35 (94)
10	Br	 **2h**	−(86)
11	Br	 **2i**	97
12	Br	 **2j**	84
13	Br	 **2k**	94
14	Br	 **2l**	89
15	Br	 **2m**	59
16	Br	 **2n**	100
17	Br	 **2o**	0

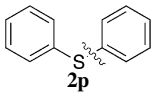
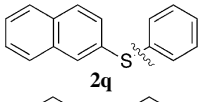
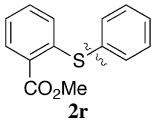
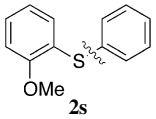
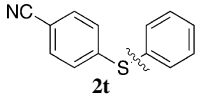
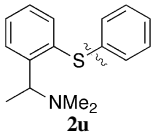
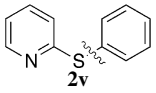
[a] Reaction conditions: RSH (1 mmol), K_2CO_3 (0.5 mmol), ArX (0.8 mmol), $Pd_2(dba)_3$ (0.08 mmol), Xantphos **1e** (0.09 mmol) in xylene (12 mL) at 140 °C for 24 h.

[b] The yields obtained using isolated sodium thiolates are shown in parentheses.

[c] Deprotonation with *t*-BuONa.

[d] Yield of the corresponding sulfone **3** obtained after oxidation of sulfide **2e** with *m*-CPBA.

Table 3. Coupling of aromatic thiols with $Pd_2(dba)_3$/Xantphos **1e** according to Scheme 1[a]

Entry	X of ArX	Sulfide	Yield (%)
1	Br	 **2p**	100
2	OTf		100
3	Br	 **2q**	93
4	Br	 **2r**	83
5	Br	 **2s**	41
6	Br	 **2t**	57
7	Br	 **2u**	25[19]
8	Br	 **2v**	0

[a] Reaction conditions: RSH (1 mmol), K_2CO_3 (0.5 mmol), ArX (0.8 mmol), $Pd_2(dba)_3$ (0.08 mmol), Xantphos **1e** (0.09 mmol) in xylene (12 mL) at 140 °C for 24 h.

In conclusion, we have developed an efficient and fairly general Pd(0)-catalyzed aryl–sulfur bond formation from aromatic and aliphatic thiols. The successful reaction partners are aryl bromides, triflates and even activated chlorobenzenes. An important value of the protocol we described lies in the use of a classical mild mineral base (K_2CO_3) and a readily available and cheap catalytic system based on $Pd_2(dba)_3$ and Xantphos.

3. Experimental

3.1. General

All reactions were performed in oven-dried Schlenk tubes, under an atmosphere of dry nitrogen. Due to the stench of thiols, all glassware and syringes were washed with bleach after use. Reactions were purified by chromatography column with Merck silica gel Geduran Si 60 (0.040–0.063 nm). Thin layer chromatography was carried out on silica gel 60 F_{254} (1.1 mm, Merck) with spot detection under UV light or through I_2 or $KMnO_4$ oxidation. Melting points were obtained on a Reichert 7905 hot-stage microscope or an Electrothermal IA9000 capillary apparatus and are uncorrected. NMR spectra were recorded at room temperature on Bruker DPX 250 or DRX 400 spectrometers. All chemical shifts (δ) and coupling constants are quoted in parts per million (ppm) and Hertz (Hz), respectively. The following abbreviations are used to designate the multiplicity of the signals: s = singlet; d = doublet; t = triplet; q = quartet; m = multiplet, and combinations thereof. The chemical shifts are calibrated to TMS (δ H 0.00) or residual proton and carbon resonance of the solvent $CDCl_3$ (δ H 7.26 and δ C 77.16). ^{31}P and ^{19}F chemical shifts are referred to external 85% phosphoric acid and $CFCl_3$, respectively. IR spectra were recorded on a Perkin–Elmer 16 PC FT-IR instrument. Mass spectra were recorded on a Varian GC/MS/MS instrument. Only peaks of an intensity $>10\%$ (except decisive ones) are listed. Elemental analyses were performed with a C, H, N, S, O Thermoquest apparatus.

3.2. Ligand 1f

3.2.1. Synthesis of 1f. *n*-BuLi (1.7 mL of a 1.6 M solution in hexanes, 2.9 mmol) was added dropwise at room temperature to a stirred solution of 9,9-dimethylxantene (200 mg, 0.9 mmol) and TMEDA (360 µL, 2.3 mmol) in heptane (6 mL). After stirring for 15 h, neat chlorodi-*t*-butylphosphine (3 mmol) was added dropwise and the reaction mixture was stirred at 60 °C for 24 h. The solvent was removed in vacuo and the resulting beige residue was dissolved in CH_2Cl_2 (10 mL). The resulting solution was washed with water, dried over $MgSO_4$ and concentrated to dryness. The resulting oil was then washed with petroleum ether and crystallized from *n*-propyl alcohol to afford the desired diphosphine **1f** as air-stable crystals (170 mg, 0.34 mmol, 38%). White crystals, mp 155–156 °C (*n*-propyl alcohol). ^1H NMR (250 MHz): δ 1.21–1.26 (m, 36H), 1.57 (s, 6H), 7.02 (t, $J=7.6$ Hz, 2H), 7.38 (dd, $J=7.6$, 1.5 Hz, 2H), 7.60 (d, $J=7.6$ Hz, 2H). ^{13}C NMR (100.63 MHz): δ 30.8 (m), 31.1, 32.7 (m), 35.0, 121.5, 125.5 (m), 126.6 (m), 130.7 (m), 133.7, 155.8 (m). ^{31}P NMR (101.3 MHz): δ 12.4. Anal Calcd for $C_{31}H_{48}OP_2$, C: 74.65, H: 9.71. Found: C: 74.71, H: 9.63.

3.2.2. Crystal structure determination of 1f. Single crystals of ligand **1f** suitable for X-ray crystallographic analysis were obtained by slow evaporation of *n*-propyl alcohol solution. X-ray diffraction experiments for monocrystal of **1f** were performed at 293.2 K with graphite-monochromatized Mo K_α radiation on an Enraf-Nonius CAD-4 diffractometer. Formula $C_{31}H_{48}OP_2$, formula weight 498, crystal system triclinic, space group P^{-1} (no 2), $a=12.477(4)$ Å, $b=12.550(4)$ Å, $c=12.934(3)$ Å, $\alpha=117.00(2)°$, $\beta=92.82(4)°$, $\gamma=116.98(3)°$, $V=1523.(1)$ Å^3, $Z=2$, $\rho_{calcd}=1.087$ g/cm^3, $\mu=1.430$ mm^{-1}, $R=0.046$, $wR=0.056$. Selected bond lengths (Å) and angles (deg): P1–C4 1.847(2), P1–C13 1.882(3), P1–C17 1.901(2), P2–C5 1.850(2), P2–C21 1.892(2), P2–C25 1.881(2), O1–C4a 1.378(2), O1–C10a 1.378(2), C4–P1–C13 100.6(1), C4–P1–C17 105.7(1), C13–P1–C17 111.4(1), C5–P2–C21 105.3(1), C5–P2–C25 100.2(1), C21–P2–C25 111.1(1), C4a–O1–C10a 120.6(2). Data reduction: TEXSAN (Molecular Structure Corporation). Program(s) used to solve structure: SIR92. Program(s) used to refine structure: TEXSAN. Software used to prepare material for publication: TEXSAN. Crystallographic data for compound **1f** have been deposited at the Cambridge Crystallographic Data Centre, CCDC No 255820. Copies of this information may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (+44 1223

336408; e-mail: deposit@ccdc.cam.ac.uk or http://www.ccdc.cam.ac.uk).

3.3. Typical experimental procedure for cross-coupling

In a Schlenk tube were charged successively K_2CO_3 (74 mg, 0.5 mmol) and degassed xylene (2 mL). After purging with N_2 using 3 evacuate-fill cycles, the slurry was cooled to 0 °C and the thiol (1 mmol) was added dropwise. The resulting mixture was then allowed to warm to room temperature and stirred for 1 h. To a Schlenk tube were placed successively the aryl substrate (0.8 mmol), $Pd_2(dba)_3$ (0.08 mmol), Xantphos **1e** (0.09 mmol) and degassed xylene (10 mL). After purging with N_2 using 3 evacuate-fill cycles, the mixture was stirred at room temperature for 20 min and transferred via a cannula to the previously formed potassium thiolate. The dark solution was then purged with N_2 and heated to reflux for 24 h. After cooling to room temperature, the mixture was diluted with EtOAc (20 mL), washed with water (3×20 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was then purified by silica gel chromatography to afford the anticipated thioether **2**.

3.4. Spectral data of sulfides 2

3.4.1. Butylsulfanylbenzene 2a (entries 1–3, Table 1).[11e] Colorless oil. ^{1}H NMR (250 MHz): δ0.90 (t, J=7.4 Hz, 3H), 1.43 (sextet, J=7.4 Hz, 2H), 1.62 (quint, J=7.4 Hz, 2H), 2.90 (t, J=7.4, 2H), 7.12–7.33 (m, 5H, m). ^{13}C NMR (62.9 MHz): δ 13.7, 22.0, 31.3, 33.3, 125.6, 128.7, 128.8, 137.1. MS (EI) *m/z* (relative intensity) 166 (M+, 46), 123 (28), 110 (100), 45 (38), 41 (53), 39 (478).

3.4.2. 4-Butylsulfanylphenyl methanesulfonate 2b (entry 4, Table 1). White solid, mp 54 °C. ^{1}H NMR (250 MHz): δ 0.93 (t, J=7.2 Hz, 3H), 1.44 (sextet, J=7.2 Hz, 2H), 1.61 (quint, J=7.2 Hz, 2H), 2.92 (t, J=7.2 Hz, 2H), 3.13 (s, 3H), 7.17–7.35 (m, 4H). ^{13}C NMR (62.9 MHz): δ 13.7, 22.1, 31.2, 33.6, 37.5, 122.6, 130.1, 137.0, 147.2. MS (EI) *m/z* (relative intensity) 260 (M+, 44), 181 (100), 125 (97), 57 (72). HRMS (EI) *m/z* 260.0499 (Calcd for $C_{11}H_{16}O_3S_2$ 260.0541).

3.4.3. 4-Butylsulfanylphenyl 4-methylbenzenesulfonate 2c (entry 5, Table 1). Yellowish oil. ^{1}H NMR (250 MHz): δ 0.90 (t, J=7.2 Hz, 3H), 1.49 (sextet, J=7.2 Hz, 2H), 1.59 (quint, J=7.2 Hz, 2H), 2.42 (s, 3H), 2.87 (t, J=7.2 Hz, 2H), 6.84–6.91 (m, 2H), 7.15–7.20 (m, 2H), 7.27–7.31 (m, 2H), 7.66–7.70 (m, 2H). ^{13}C NMR (62.9 MHz): δ 13.6, 21.7, 21.9, 31.0, 33.3, 122.8, 128.5, 129.4, 129.5, 132.3, 136.4, 145.5, 147.5. MS (EI) *m/z* (relative intensity) 336 (M+, 55), 181 (100), 125 (33), 91 (15). HRMS (EI) *m/z* 336.0820 (Calcd for $C_{17}H_{20}O_3S_2$ 336.0854).

3.4.4. 1-(Butylsulfanyl)-4-fluorobenzene 2d (entry 6, Table 1).[22a] Colorless oil. ^{1}H NMR (250 MHz): δ0.90 (t, J=7.2 Hz, 3H), 1.37–1.62 (m, 4H), 2.85 (t, J=7.2 Hz, 2H), 6.93–7.00 (m, 2H), 7.24–7.35 (m, 2H). ^{13}C NMR (62.9 MHz): δ13.5, 21.7, 31.2, 34.6, 115.8 (d, J_{CF}= 21.4 Hz), 131.9 (d, J_{CF}=3.1 Hz), 132.0 (d, J_{CF}=7.5 Hz), 161.6 (d, J_{CF}=245.3 Hz). ^{19}F NMR (235.3 MHz): δ−116.6. MS (EI) *m/z* (relative intensity) 184 (M+, 41), 128 (100), 83 (29), 45 (44).

3.4.5. 1-(Butylsulfanyl)-4-trifluoromethylbenzene 2e (entry 7, Table 1).[22b] Due to contamination with di-*n*-butyl disulfide and difficult separation of both products, the mixture was subjected to oxidation with *m*-CPBA. Spectral data of the sulfone **3** derived from sulfide **2e** thus obtained.

1-(Butylsulfonyl)-4-trifluoromethylbenzene **3**. White solid, mp 40 °C. ^{1}H NMR (250 MHz): δ0.91 (t, J=7.3 Hz, 3H), 1.42 (sextet, J=7.3 Hz, 2H), 1.64–1.77 (m, 2H), 3.09–3.16 (m, 2H), 7.75–7.79 (m, 2H), 7.97–8.00 (m, 2H). ^{13}C NMR (62.9 MHz): δ13.5, 21.6, 24.6, 56.1, 123.2 (q, J_{CF}= 270.4 Hz), 126.5 (q, J_{CF}=3.8 Hz), 128.9, 135.4 (q, J_{CF}= 33.3 Hz), 142.9. ^{19}F NMR (235.3 MHz): δ−63.6. MS (EI) *m/z* (relative intensity) 267 (MH+, 1), 145 (26), 57 (100), 56 (37). HRMS (EI) *m/z* 266.0629 (Calcd for $C_{11}H_{13}F_3O_2S$ 266.0588).

3.4.6. 1-(1,1-Dimethylethyl)-4-propylsulfanylbenzene 2f (entry 8, Table 1).[22c] Yellowish oil. ^{1}H NMR (250 MHz): δ1.01 (t, J=7.3 Hz, 3H), 1.29 (s, 9H), 1.65 (sextet, J= 7.3 Hz, 2H), 2.86 (t, J=7.3 Hz, 2H), 7.25–7.31 (m, 4H). ^{13}C NMR (62.9 MHz): δ 13.5, 22.8, 31.4, 34.5, 36.2, 126.0, 129.4, 133.4, 149.0. MS (EI) *m/z* (relative intensity) 209 (MH+, 49), 208 (89), 195 (40), 194 (80), 193 (100), 149 (34), 45 (54), 43 (95).

3.4.7. 1-Ethylsulfanyl-4-(1,1-dimethylethyl)benzene 2g (entry 9, Table 1).[22d] Colorless oil. ^{1}H NMR (250 MHz): δ1.30 two signals overlapping (t, J=7.3 Hz, 3H) and (s, 9H), 2.92 (q, J=7.3 Hz, 2H), 7.25–7.35 (m, 4H). ^{13}C NMR (62.9 MHz): δ14.7, 28.2, 31.4, 34.6, 126.0, 129.5, 133.1, 149.3. MS (EI) *m/z* (relative intensity) 194 (M+, 27), 179 (100), 151 (38), 116 (31), 77 (35).

3.4.8. 1-(1,1-Dimethylethyl)-4-methylsulfanylbenzene 2h (entry 10, Table 1).[22e] White solid, mp 30–31 °C. ^{1}H NMR (250 MHz): δ1.29 (s, 9H), 2.45 (s, 3H), 7.18–7.33 (m, 4H). ^{13}C NMR (62.9 MHz): δ16.2, 31.2, 34.3, 125.8, 126.8, 134.8, 148.3. MS (EI) *m/z* (relative intensity) 180 (M+, ·99), 165 (100), 150 (22), 137 (46), 117 (24), 45 (22).

3.4.9. (Phenylmethylsulfanyl)benzene 2i (entry 11, Table 1).[16] White solid, mp 41–41.5 °C. ^{1}H NMR (250 MHz): δ3.98 (s, 2H), 7.00–7.22 (m, 10H). ^{13}C NMR (100 MHz): δ39.48, 126.76, 127.59, 128.90, 129.25, 130.26, 136.80, 137.89. MS (EI) *m/z* (relative intensity) 200 (M+, 100), 51 (50).

3.4.10. 3-Phenylsulfanylpropanoic acid ethyl ester 2j (entry 12, Table 2).[22f] Colorless oil. ^{1}H NMR (250 MHz): δ1.24 (t, J=7.1 Hz, 3H), 2.61 (t, J=7.4 Hz, 2H), 3.16 (t, J=7.4 Hz, 2H), 4.13 (q, J=7.1 Hz, 2H), 7.16–7.38 (m, 5H). ^{13}C NMR (62.9 MHz): δ14.2, 29.1, 34.5, 60.7, 126.5, 129.0, 130.1, 135.4, 171.7. IR (NaCl, cm^{-1}) 1732 (C=O). MS (EI) *m/z* (relative intensity) 210 (M+, 77), 196 (35), 137 (100), 135 (30), 123 (32), 109 (25).

3.4.11. 1-Cyclohexylsulfanyl-4-(1,1-dimethylethyl)-benzene 2k (entry 13, Table 1).[11b] Colorless oil. ^{1}H NMR (250 MHz): δ1.22–1.34 (m, 5H), 1.29 signal

overlapping with the previous multiplet (s, 9H), 1.54–1.62 (m, 1H), 1.74–1.78 (m, 2H), 1.90–1.99 (m, 2H), 2.99–3.09 (m, 1H), 7.26–7.35 (m, 4H). ^{13}C NMR (62.9 MHz): δ25.9, 26.1, 31.4, 33.5, 34.5, 46.9, 125.8, 131.9, 132.2, 149.9. MS (EI) *m/z* (relative intensity) 248 (M+, 25), 166 (42), 151 (100), 122 (40), 90 (33), 55 (96).

3.4.12. 1-(1,1-Dimethylethyl)-4-(1-methylpropylsulfanyl)benzene 2l (entry 14, Table 1). Colorless oil. ^{1}H NMR (250 MHz): δ 1.01 (t, *J*=7.4 Hz, 3H), 1.25 (d, *J*=6.7 Hz, 3H), 1.31 (s, 9H), 1.42–1.72 (m, 2H), 3.10 (sextet, *J*=6.7 Hz, 1H), 7.27–7.32 (m, 4H). ^{13}C NMR (62.9 MHz): δ 11.6, 20.7, 29.6, 31.4, 34.6, 45.2, 125.8, 131.9, 132.2, 150.0. MS (EI) *m/z* (relative intensity) 222 (M+, 100), 207 (49), 166 (70), 151 (28). HRMS (EI) *m/z* 222.1368 (Calcd for $C_{14}H_{22}S$ 222.1442). Anal Calcd for $C_{14}H_{22}S$, C: 75.61, H: 9.97, S: 14.42. Found: C: 75.57, H: 9.86, S: 14.77.

3.4.13. (*exo*)-2-Phenylsulfanylbornane 2m (entry 15, Table 1). Orange oil. ^{1}H NMR (250 MHz): δ 0.77 (s, 3H), 0.94 and 0.95 (2 s, 3H each), 1.12–1.16 (m, 2H), 1.30 (s, 9H), 1.60–1.80 (m, 3H), 1.95–2.05 (m, 2H), 3.15–3.30 (m, 1H), 7.26–7.30 (m, 4H). ^{13}C NMR (62.9 MHz): δ 14.0, 20.2, 20.5, 27.8, 31.4, 34.4, 38.5, 41.2, 45.9, 47.5, 49.8, 56.7, 125.8, 129.4, 135.8, 148.8. MS (EI) *m/z* (relative intensity) 302 (M+, 14), 137 (66), 95 (26), 81 (100). HRMS (EI) *m/z* 302.2082 (Calcd for $C_{20}H_{30}S$ 302.2068).

3.4.14. 1,1-Dimethylethylsulfanylbenzene 2n (entry 16, Table 1).[6a] Colorless oil. ^{1}H NMR (250 MHz): δ1.29 (s, 9H), 7.31–7.55 (m, 5H). ^{13}C NMR (62.9 MHz): δ31.1, 45.9, 128.6, 128.8, 132.9, 137.6. MS (EI) *m/z* (relative intensity) 166 (M+, 34), 110 (100), 109 (36), 65 (28), 57 (75).

3.4.15. Phenylsulfanylbenzene 2p (entries 1 and 2, Table 2).[11e] Colorless oil. ^{1}H NMR (250 MHz): δ7.31–7.48 (m, 10H). ^{13}C NMR (62.9 MHz): δ126.9, 129.1, 130.9, 135.7. MS (EI) *m/z* (relative intensity) 186 (M+, 100), 77 (24), 65 (25), 51 (57).

3.4.16. 2-Phenylsulfanylnaphthalene 2q (entry 3, Table 2).[22g] White solid, mp 50 °C. ^{1}H NMR (250 MHz): δ7.22–7.46 (m, 8H), 7.71–7.82 (m, 4H). ^{13}C NMR (62.9 MHz): δ 126.7, 127.0, 127.5, 127.9, 128.2, 129.2, 129.3, 129.7, 130.4, 131.4, 132.8, 133.5, 134.3, 136.3. MS (EI) *m/z* (relative intensity) 236 (M+, 100), 235 (67), 234 (48), 118 (27).

3.4.17. 2-Phenylsulfanylbenzoic acid methyl ester 2r (entry 4, Table 2).[11e] White solid, mp 46–47.5 °C. ^{1}H NMR (250 MHz): δ3.93 (s, 3H), 6.81 (d, *J*=8.0 Hz, 1H), 7.13 (t, *J*=7.2 Hz, 1H), 7.21 (dt, *J*=8.0, 1.6 Hz, 1H), 7.39–7.42 (m, 3H), 7.53–7.57 (m, 2H), 7.97 (dd, *J*=8.0, 1.6 Hz, 1H). ^{13}C NMR (62.9 MHz): δ52.1, 124.3, 126.8, 127.4, 129.0, 129.7, 131.0, 132.3, 132.6, 135.5, 143.1, 166.8. IR (KBr, cm^{-1}) 1716 (C=O). MS (EI) *m/z* (relative intensity) 244 (M+, 73), 200 (100), 50 (93).

3.4.18. 1-Methoxy-2-phenylsulfanylbenzene 2s (entry 5, Table 2).[11e] Colorless oil. ^{1}H NMR (250 MHz): δ3.85 (s, 3H), 6.82–6.90 (m, 2H), 7.06–7.10 (m, 1H), 7.19–7.37 (m, 6H, m). ^{13}C NMR (62.9 MHz): δ56.0, 111.0, 121.3, 124.2, 127.1, 128.4, 129.2, 131.5, 131.7, 134.6, 157.4. MS (EI) *m/z* (relative intensity) 216 (M+, 100), 201 (11).

3.4.19. 2-Phenylsulfanylbenzonitrile 2t (entry 6, Table 2).[11c] White solid, mp 39–40 °C. ^{1}H NMR (250 MHz): δ7.14–7.21 (m, 2H), 7.33–7.52 (m, 7H). ^{13}C NMR (62.9 MHz): δ108.8, 118.8, 127.4, 129.8, 130.0, 130.9, 132.4, 134.6, 145.8. IR (KBr, cm^{-1}) 2224 (C≡N). MS (EI) *m/z* (relative intensity) 211 (M+, 100), 210 (70), 51 (25).

3.4.20. 1-[1-(*N*,*N*-Dimethylaminoethyl)]-2-phenylsulfanylbenzene 2u (entry 7, Table 2). Brown oil. ^{1}H NMR (250 MHz): δ 1.28 (d, *J*=6.6 Hz, 3H), 2.20 (s, 6H), 3.93 (q, *J*=6.6 Hz, 1H), 7.14–7.29 (m, 9H), 7.54–7.58 (m, 1H). ^{13}C NMR (62.9 MHz): δ 19.7, 43.4, 62.0, 126.6, 127.4, 127.6, 128.1, 129.2, 130.4, 133.4, 134.0, 137.4, 146.9. MS (EI) *m/z* (relative intensity) 257 (M+, 28), 242 (100), 72 (68). HRMS (EI) *m/z* 257.1288 (Calcd for $C_{16}H_{19}NS$ 257.1238).

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