Electronic Supplementary Information

Calix[8]arene Nanoreactor for Cu(I)-Catalysed C–S Coupling

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1. General Experimental Procedures. All manipulations were carried out under an inert atmosphere using a nitrogen-filled glovebox or standard Schlenk techniques. Reagents were purchased from commercial suppliers and used as received. Toluene, THF, DMSO, MeOH, and DMF solvents were distilled and degassed prior to use. Deuterated solvents were distilled and degassed prior to use. 1, 5-phenanthroline-bridged *p*-tert-butylcalix[8]arene (**L**) was prepared following our previously reported method. All spectral data of coupled thioether products correspond to those reported in the literature. Infrared spectra were obtained with a Bruker Tensor 27 spectrometer in the 4000–400 cm^{-1} spectral region as KBr disks. Combustion analyses were performed at the microanalytical laboratory of Instituto de Química. NMR spectra were recorded with a Bruker 300 with tetramethylsilane (TMS) as an internal standard. Molecular modeling on catalysts was performed with Merck Molecular Force Field (MMFF) methods on Spartan '08 software (Wavefunction, Irvine, CA). Electron Ionization mass spectrometry (ESI MS) experiments were performed with a Bruker Daltonics Esquire 6000 spectrometer with ion trap. Positive ion FAB+ MS were acquired with a JEOL JMS-SX-102A mass spectrometer operated at an accelerating voltage of 10 kV from a nitrobenzyl alcohol matrix by using xenon atoms at 6 keV. EI MS were acquired with a JEOL JMS-SX 102A mass spectrometer.

2. Synthesis of Supramolecular complexes [LCuCl-THF] (1) and LCuSPh (2)

Preparation of [LCuCl-THF] (1). A solution of 1, 5-phenanthroline-bridged *p*-tert-butylcalix[8]arene (**L**) (500 mg, 0.33 mmol) in anhydrous THF (10 mL) was added CuCl (32.9 mg, 0.33 mmol), and the red suspension was stirred at room temperature for 8h. The resultant red solution was evaporated to dryness and the solid was washed with 1 mL of cold THF and cold diethyl ether to give complex **1** as dark red solid. Yield: 506 mg, 95%. IR (KBr): ν = [2956m, 2902w, 2866w] (C─H), 1480m (br) (C═C), 1361w, 1199m, 799m (br). ^{1}H NMR (300 MHz, $CDCl_3$, 25°C): δ = 8.37 (d, $^3J_{H–H}$ = 16.2 Hz, 2H, Phen), 8.08–7.76 (m, 4H, Phen), 7.34–6.74 (m, 18H, ArH), 6.10 (d, $^2J_{H–H}$ = 15.5 Hz, 2H, –OCH_2–Phen), 5.61 (d, $^2J_{H–H}$ = 15.6 Hz, 2H, –OCH_2–Phen), 4.73 (d, $^2J_{H–H}$ = 16.2 Hz, 2H, Ar–CH_2–Ar), 4.35 (br, 2H, Ar–CH_2–Ar), 4.18 (d, $^2J_{H–H}$ = 16.2 Hz, 2H, Ar–CH_2–Ar), 4.00 (br, 2H, Ar–CH_2–Ar), 3.76 (m, 6H, THF/Ar–CH_2–Ar), 3.49 (br, 2H, Ar–CH_2–Ar), 3.24 (m, 3H, Ar–CH_2–Ar), 2.88 (br, 1H, Ar–CH_2–Ar), 1.86 (br, 4H, THF), 1.38–1.07 (m, 72H, t-Bu). MS (+ESI, MeOH/CH_2Cl_2): *m/z* = 1770.1 [**LCuCl**–H^++CuCl+THF]$^+$, 1563.3 [**LCuCl**–Cl^-]$^+$. Elemental analysis calcd (%) for $C_{102}H_{124}N_2O_{10}CuCl$•2THF C 73.43, H

7.95, N 1.56; found C 73.52, H 7.54, N 1.96. Note: *THF molecule could be involved in fast exchange according to* ^{1}*H-DOSY, VT-NMR, MS, and elemental analysis (Figures S1-S4).*

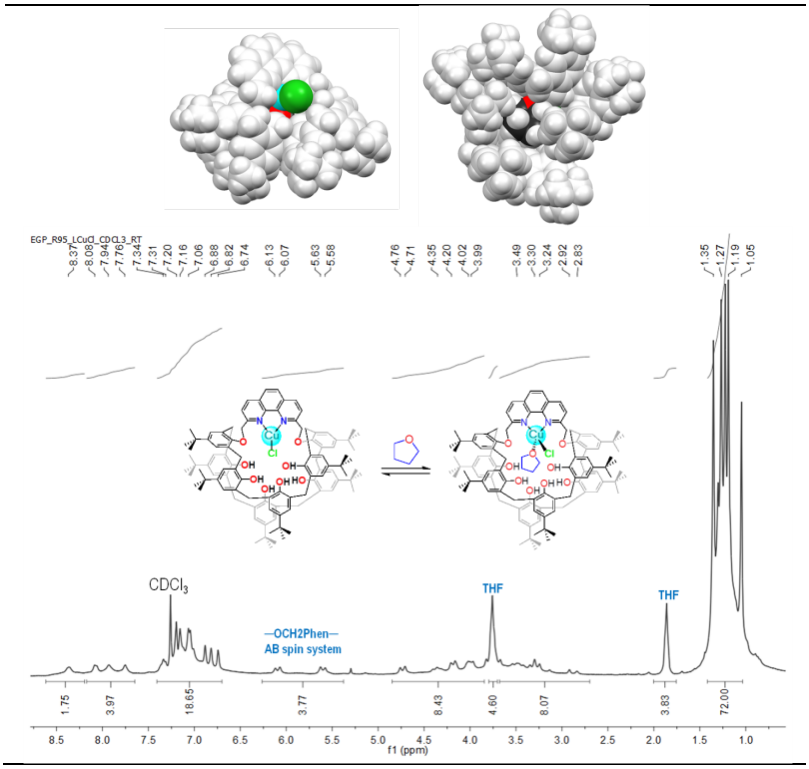


Figure S1. Two perspectives of complex **1** containing THF; MMFF simulations (*top*), and ^{1}H NMR spectrum of complex **1** as $CDCl_3$ solution at 298 K (*bottom*).

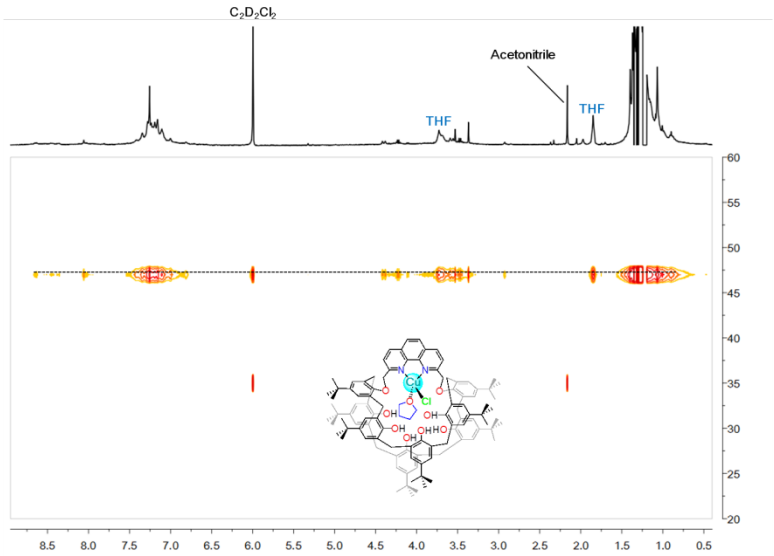


Figure S2. ^{1}H DOSY NMR of complex **1** as $C_2D_2Cl_4$ at 298 K showing that THF is part of the complex on the NMR time scale.

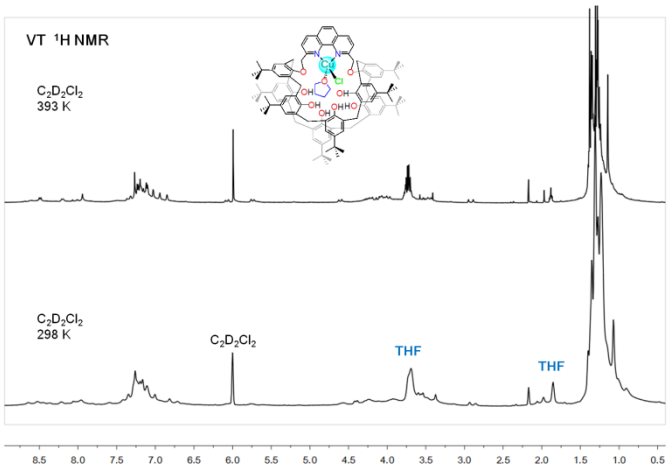


Figure S3. VT ^{1}H NMR spectra of complex **1** in $C_2D_2Cl_4$.

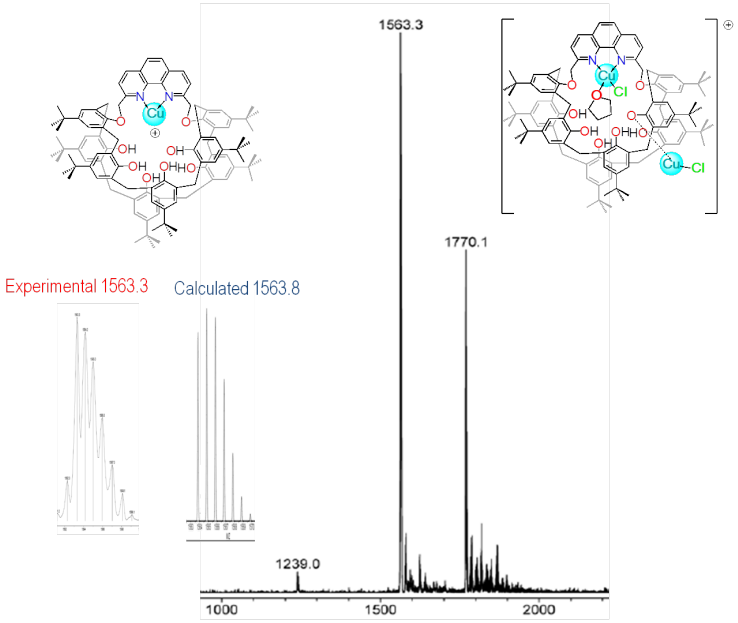


Figure S4. ESI–MS spectrum of **[LCuCl-THF]** (**1**).

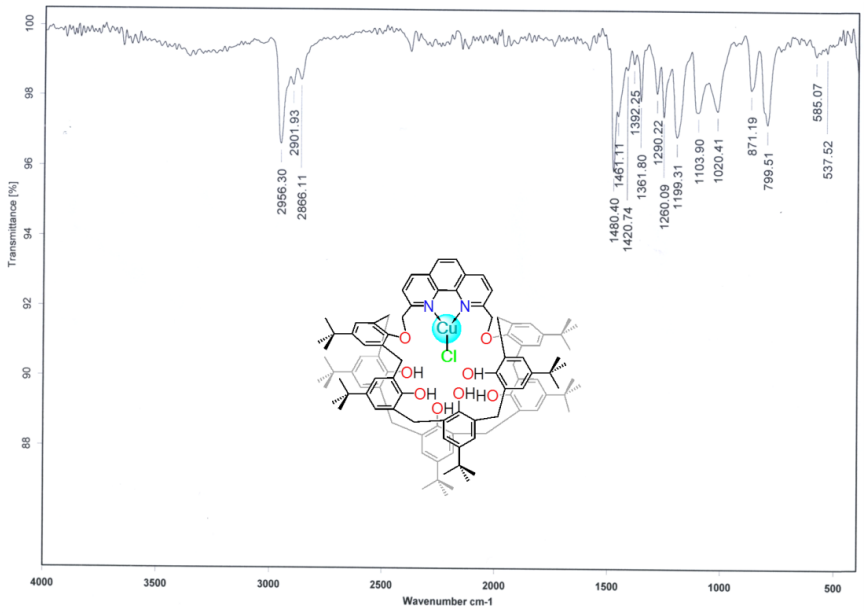


Figure S5. IR spectrum of **1** in KBr.

Preparation of [LCuSPh] (2). To a solution of **[LCuCl-THF]** (**1**) (400 mg, 0.25 mmol) in anhydrous THF was added sodium thiophenolate (33 mg, 0.25 mmol), after 3h of stirring at room temperature the reaction mixture was filtered and the obtained red solution was evaporated, the solid was washed with 2 mL of cold THF and cold hexanes to give **2a** as an burnt orange solid. The corresponding species should content one molecule of THF and one Na^+ ion according to MS, NMR, and Elemental analyses. Yield: 389 mg, 93%. IR (KBr): ν = 3239w, 3191w (br) (O─H), [2954s, 2902w, 2865w] (C─H), 1593w (C═N), 1479s (br) (C═C), 1361s, 1199s, 731m. ^{1}H NMR (300 MHz, $CDCl_3$, 25°C): δ = 8.26–8.18 (br, 2H, Phen), 7.78–7.73 (m, 4H, Phen), 7.19–6.92 (m, 21H, ArH/–SPh), 5.23 (br, 4H, –OCH_2–Phen), 4.31 (br, 4H, Ar–CH_2–Ar), 4.06 (br, 4H, Ar–CH_2–Ar), 3.40–3.31 (m, 8H, Ar–CH_2–Ar), 1.24–1.11 (m, 72H, t-Bu). MS (+FAB, MeOH/CH_2Cl_2): *m/z* = 1768.3 [**LCuSPh**+THF+Na]$^+$, 1564.4 [**LCu**]$^+$. Elemental analysis calcd (%) for $C_{108}H_{125}N_2O_8SCu$•THF•Na C 76.01, H 7.57, N 1.58; found C 76.01, H 7.70, N 1.73.

As an effort to characterise the sodium-free thiophenolate complex, a methanolic solution of **2** was passed through a short column of celite and silica gel (230:400); solvent evaporation resulted in a pale orange solid. ^{1}H NMR (300 MHz, $CDCl_3$, 25°C): δ = 8.31 (d, $^3J_{H–H}$ = 7.4 Hz, 1H, Phen), 8.23 (d, $^3J_{H–H}$ = 6.2 Hz, 1H, Phen), 8.04–7.70 (m, 4H, Phen), 7.53–6.71 (m, 21H, ArH/–SPh), 5.80 (br, 2H, –OCH_2–Phen), 5.48 (d, $^2J_{H–H}$ = 13.4 Hz, 2H, –OCH_2–Phen), 4.70–2.92 (m, 16H,

Ar–CH_2–Ar), 1.31–1.12 (m, 72H, t-Bu). The NMR spectra of both sodium-containing (**2a**) and sodium-free (**2**) complexes are shown below.

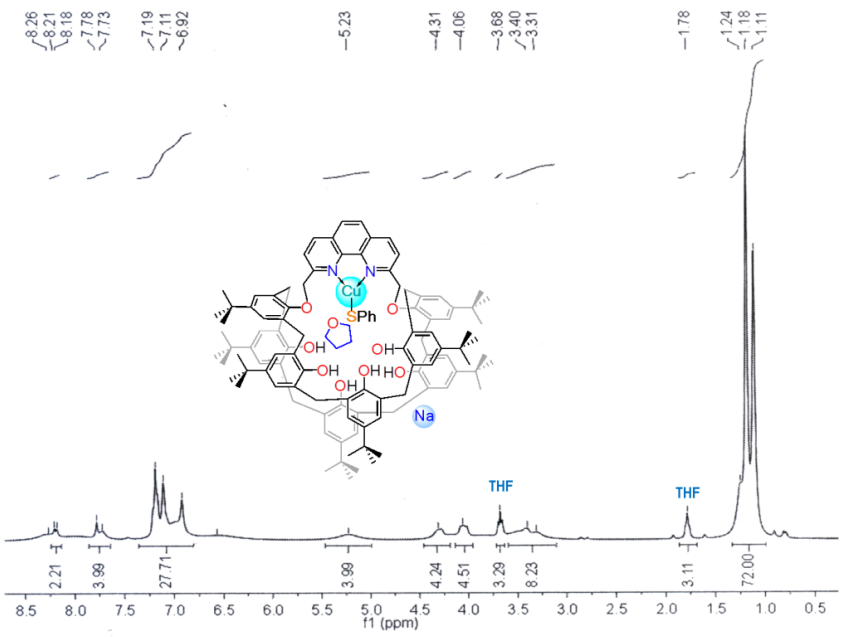


Figure S6. ^{1}H NMR spectrum of **[(L-H)CuSPh⊂THF·Na]** (**2a**) in $CDCl_3$ at 298 K.

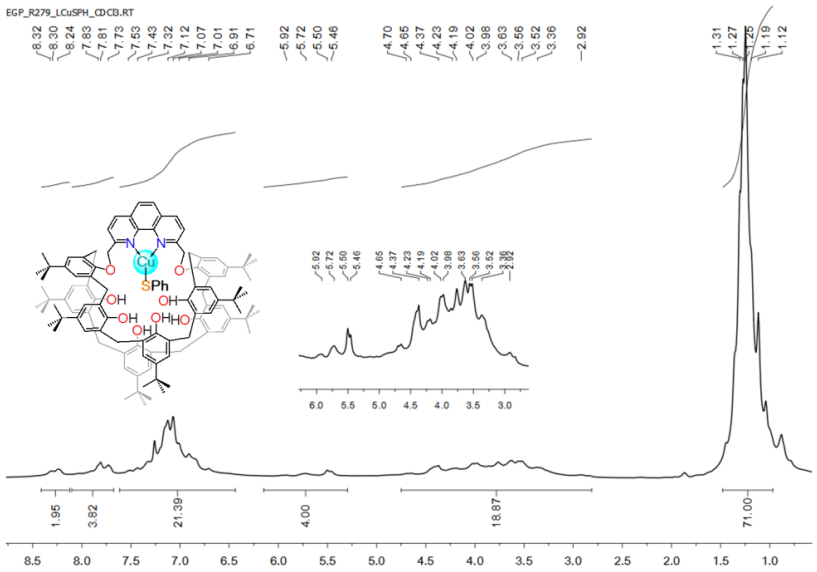


Figure S7. ^{1}H NMR spectrum of **LCuSPh** (**2**) in $CDCl_3$ at 298 K.

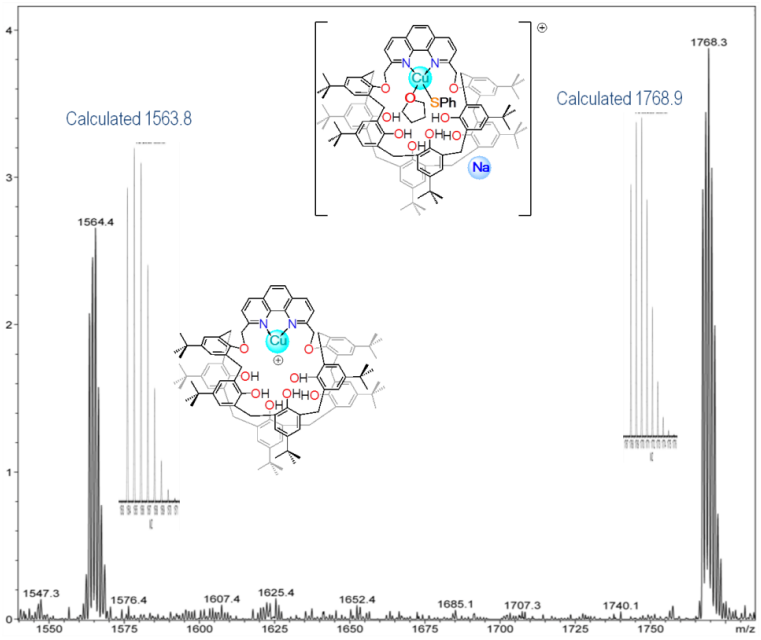


Figure S8. FAB–MS spectrum of **2a**.

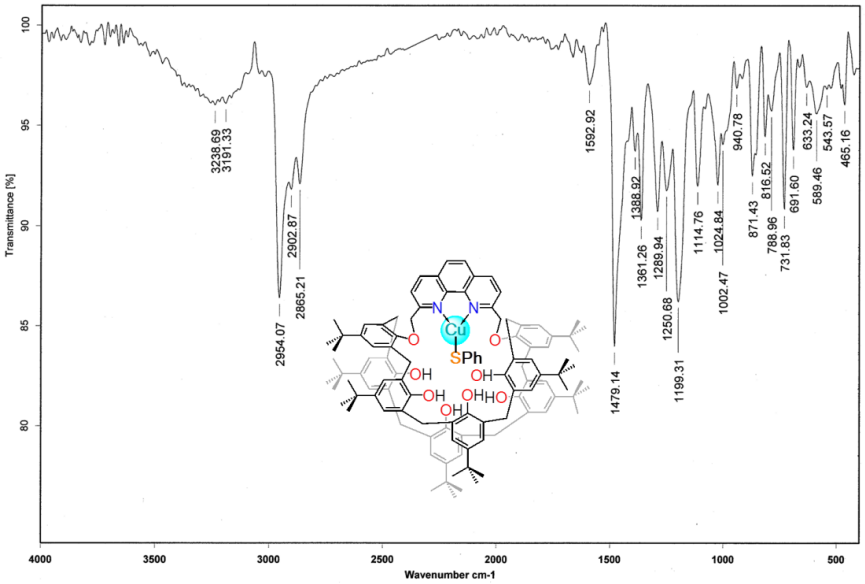
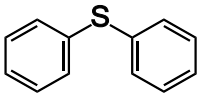


Figure S9. IR spectrum of **2a** in KBr.

3. General procedure for C–S Cross-Coupling Reactions using *in situ* formed LCuCl (1) catalyst. The same procedure was implemented for all reactions presented in (Table 1) as well as the analogous reactions tested in the diverse polar solvents we screened (DMSO, DMF, THF, MeOH, MeOH/H_2O). Calixarene (**L**) (2.5% mol), CuCl (2.5% mol), sodium thiophenolate (100 mg, 0.76 mmol), the corresponding haloarene (0.76 mmol), and dried and degassed solvent (2 mL) were placed in an oven-dried Schlenk tube in the glovebox. The Schlenk tube was stirred and heated at 110°C, and the progress of the reaction was monitored by TLC chromatography. The reaction was stopped until the starting materials disappeared, or when a significant amount of the likely coupling products was evident on the TLC plate. The products were purified by column chromatography using silica gel 70:230 and hexane as eluant (unless noted); the yields are reported based on isolated pure products. All spectral data correspond to those given in the literature.



Entries 1 and 2; Biphenyl sulfide: Colourless oil; Yield: Entry 1: 124 mg, 88%; Entry 2: 134 mg, 95%. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.32–7.19 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 135.8, 131.1, 129.3, 127.4. MS (EI): *m/z* = 186 (M^+).

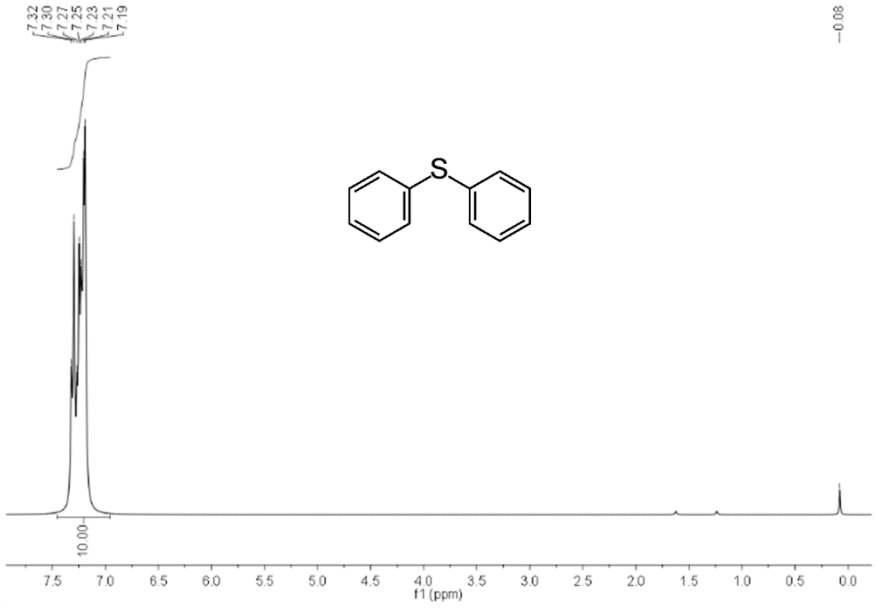


Figure S10. ^{1}H NMR spectrum of **Biphenyl disulfide** in $CDCl_3$ at 298K.

Figure S11. ^{13}C NMR spectrum of **Biphenyl disulfide** in $CDCl_3$ at 298K.

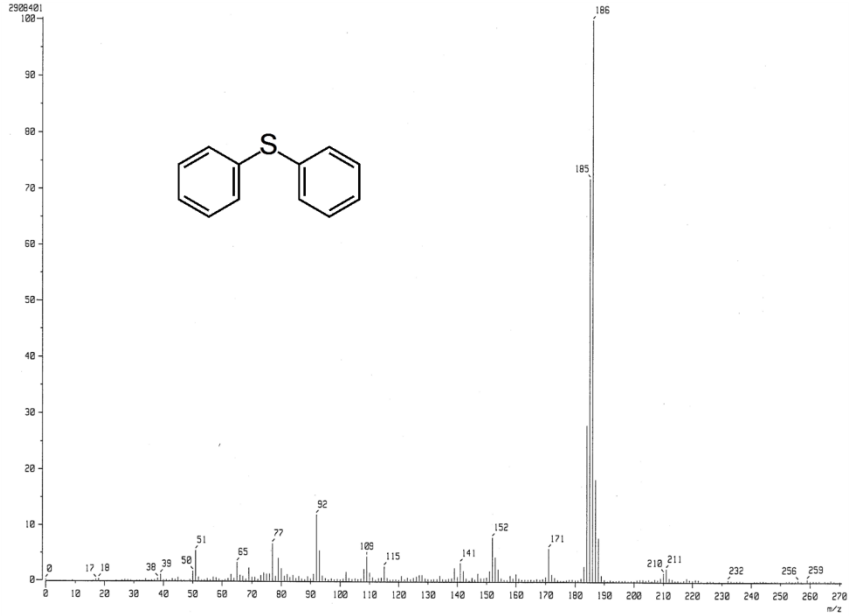
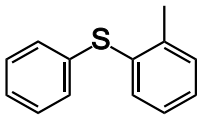


Figure S12. EI-MS spectrum of **Biphenyl disulfide**.



Entry 3; 2-Tolyl phenyl sulfide: Pale yellow liquid; Yield: 144 mg, 95%. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.36–7.16 (m, 9H), 2.38 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 135.8, 131.1, 129.3, 127.4.

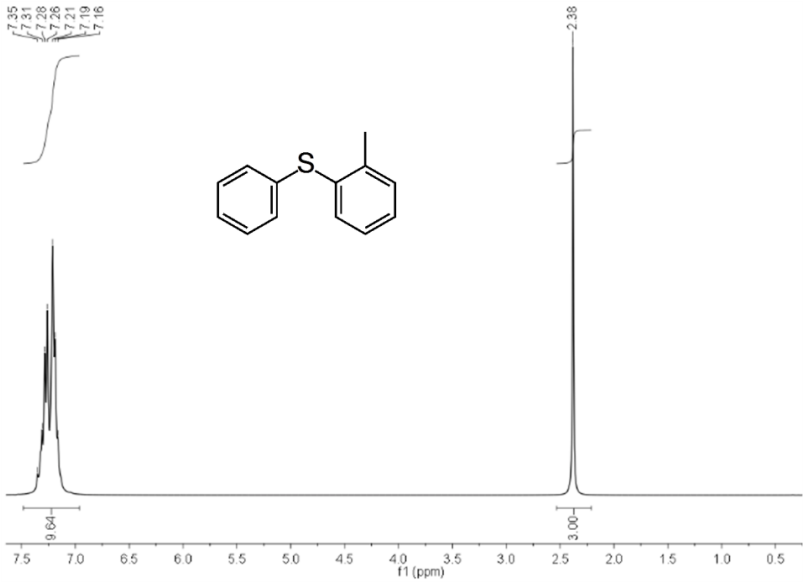


Figure S13. ^{1}H NMR spectrum of **2-Tolyl phenyl sulfide** in $CDCl_3$ at 298K.

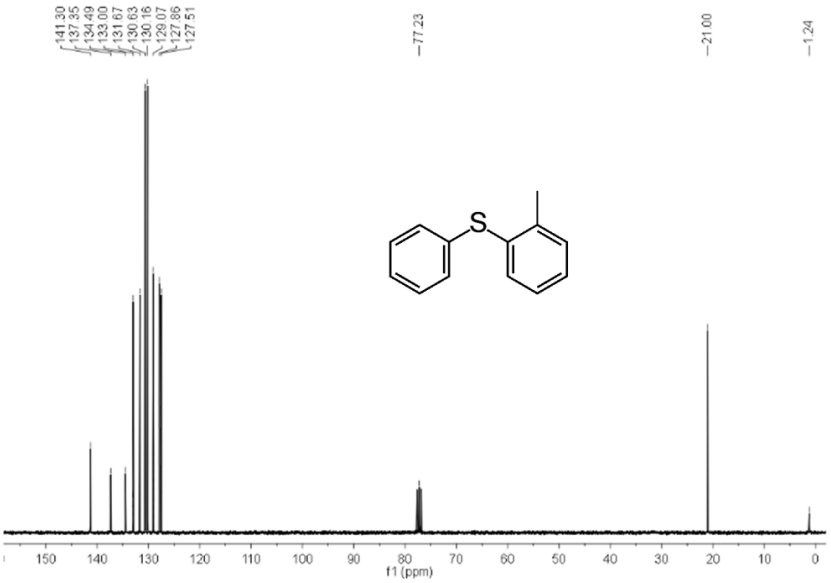
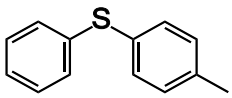


Figure S14. ^{13}C NMR spectrum of **2-Tolyl phenyl sulfide** in $CDCl_3$ at 298K.



Entries 4 and 5; 4-Tolyl phenyl sulfide: Pale yellow liquid; Yield: Entry 4: 141 mg, 93%; Entry 5: 144 mg, 95%. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.37–7.19 (m, 9H), 2.40 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 137.5, 137.1, 133.3, 131.3, 130.1, 129.3, 129.0, 126.4, 21.3. MS (EI): *m/z* = 200 (M^+).

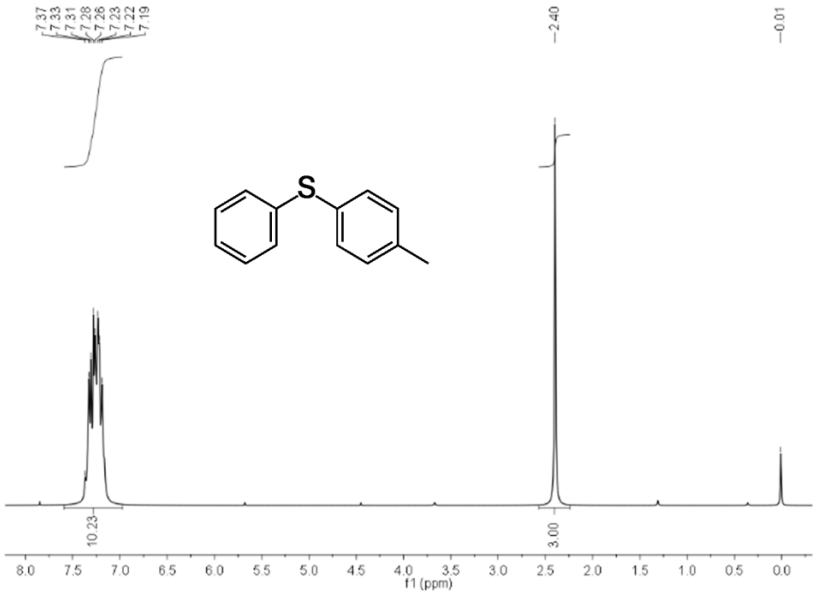


Figure S15. ^{1}H NMR spectrum of **4-Tolyl phenyl sulfide** in $CDCl_3$ at 298K.

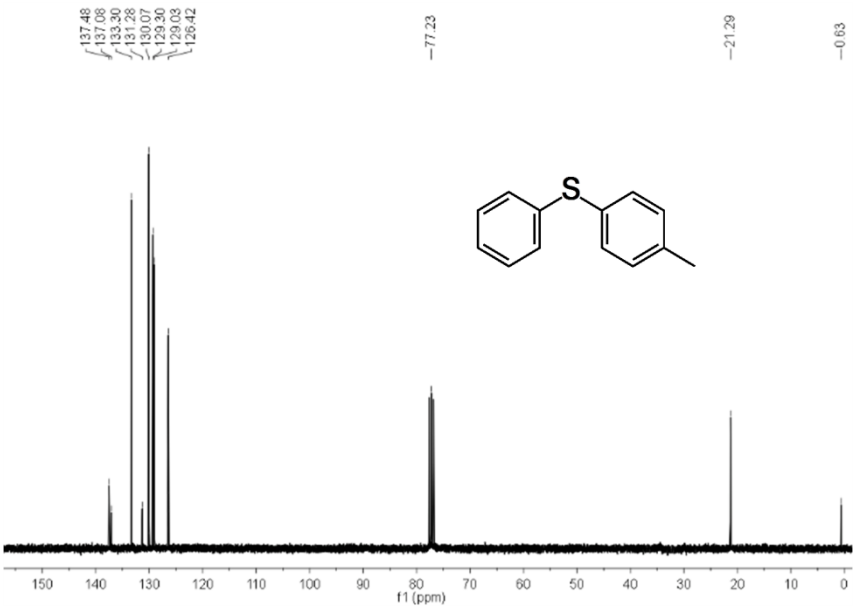


Figure S16. ^{13}C NMR spectrum of **4-Tolyl phenyl sulfide** in $CDCl_3$ at 298K.

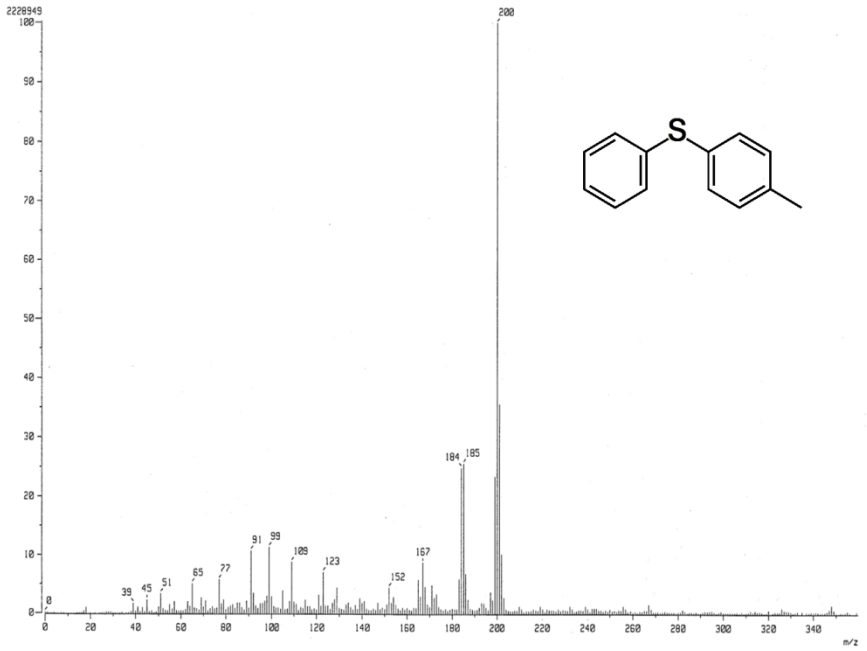
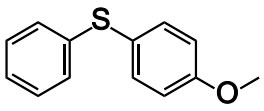


Figure S17. EI-MS spectrum of **4-Tolyl phenyl sulfide**.



Entries 6 and 7; 4-Methoxyphenyl phenyl sulfide: Colourless oil; Yield: Entry 6: 139 mg, 85%; Entry 7: 155 mg, 95%. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.41 (d, ^{3}J = 8.8 Hz, 2H), 7.13–7.23 (m, 5H), 6.89 (d, ^{3}J = 8.6 Hz, 2H), 3.82 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 159.9, 138.6, 135.5, 129.0, 128.2, 125.8, 124.3, 115.1, 55.4. MS (DART+): *m/z* = 217 ($M+H^+$).

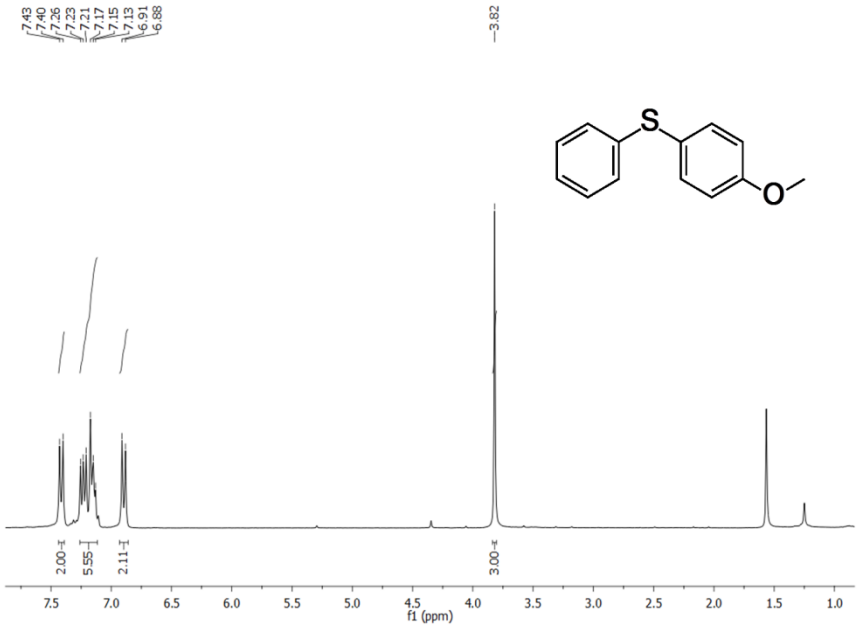


Figure S18. ^{1}H NMR spectrum of **4-Methoxyphenyl phenyl sulfide** in $CDCl_3$ at 298K.

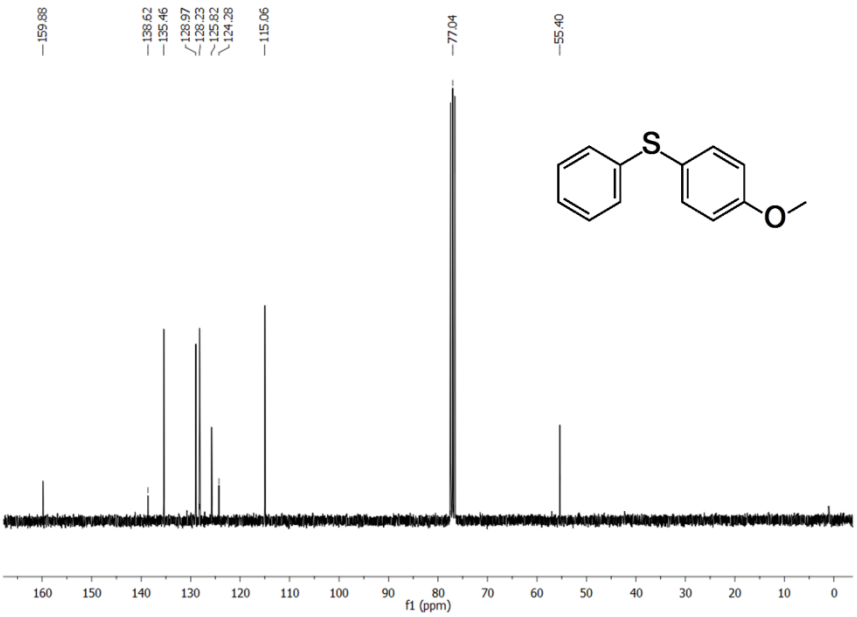


Figure S19. ^{13}C NMR spectrum of **4-Methoxyphenyl phenyl sulfide** in $CDCl_3$ at 298K.

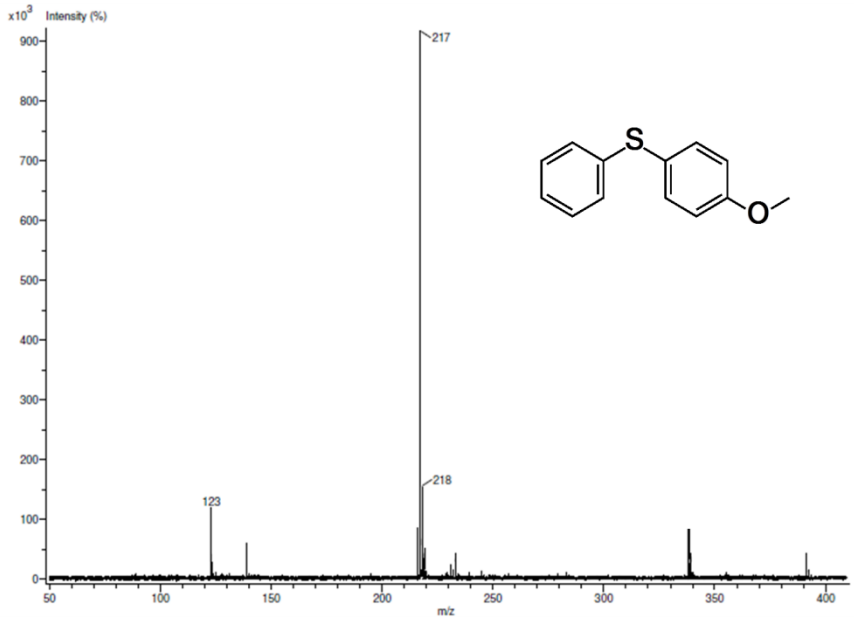
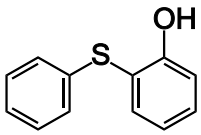


Figure S20. EI-MS spectrum of **4-Methoxyphenyl phenyl sulfide**.



Entry 8; 2-Hydroxyphenyl phenyl sulfide: Pale yellow liquid; Yield: 108 mg, 70%. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.47 (t, ^{3}J = 7.6 Hz, 1H), 7.37 (t, ^{3}J = 7.6 Hz, 1H), 7.24–7.20 (m, 2H), 7.11 (t, ^{3}J = 7.6 Hz, 1H), 7.03 (d, ^{3}J = 7.6 Hz, 2H), 6.95 (t, ^{3}J = 7.6 Hz, 1H), 6.51 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 157.3, 137.0, 135.9, 132.4, 129.2, 126.9, 126.2, 121.3, 116.3, 115.6. MS (EI): *m/z* = 218 (M^+). Eluant: Hex:AcOEt 20:1.

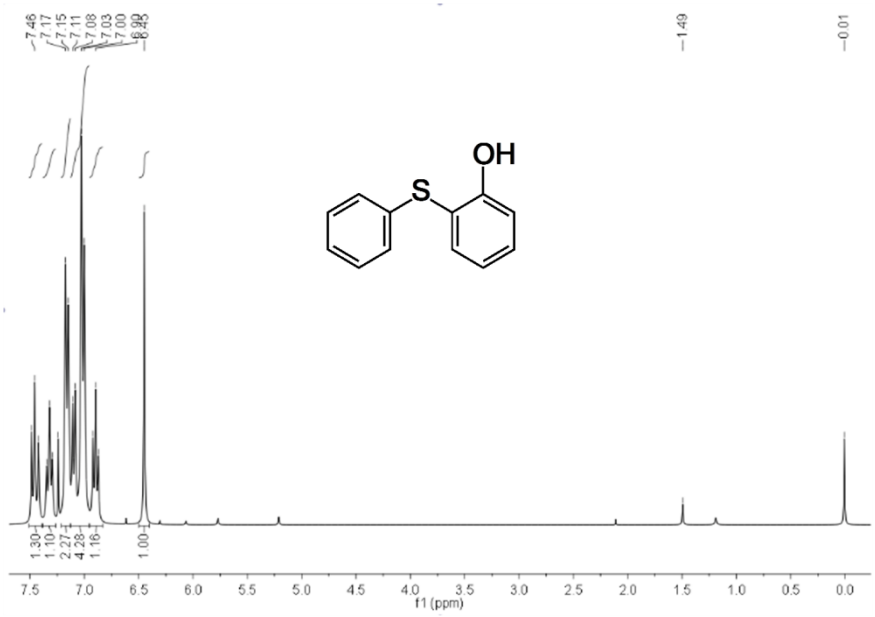


Figure S21. ^{1}H NMR spectrum of **2-Hydroxyphenyl phenyl sulfide** in $CDCl_3$ at 298K.

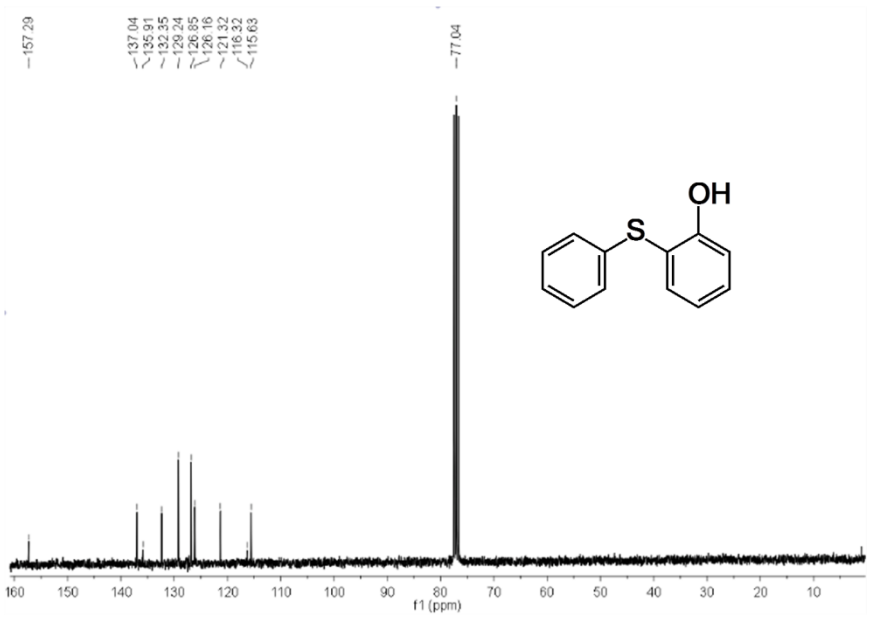


Figure S22. ^{13}C NMR spectrum of **2-Hydroxyphenyl phenyl sulfide** in $CDCl_3$ at 298K.

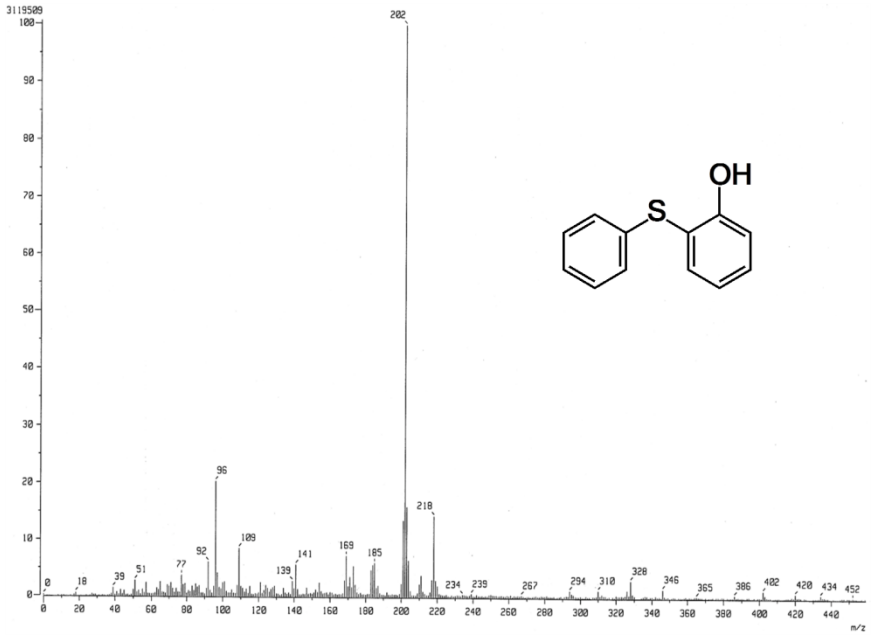
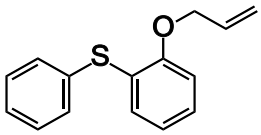


Figure S23. EI-MS spectrum of **2-Hydroxyphenyl phenyl sulfide**.



Entry 9; 2-(Allyloxy)phenyl phenyl sulfide: Light yellow solid; Yield: 147 mg, 80%. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.31–7.00 (m, 9H), 6.81 (d, 2H), 6.00–5.82 (m, 1H), 5.30 (d, ^{3}J = 17.0 Hz, 1H), 5.15 (d, ^{3}J = 5.2 Hz, 1H), 4.52 (d, ^{3}J = 5.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 156.4, 134.7, 133.0, 131.9, 131.6, 129.3, 128.3, 127.3, 125.2, 121.6, 177.7, 112.7, 69.5. MS (EI): *m/z* = 242 (M^+). Eluant: Hex:AcOEt 20:1.

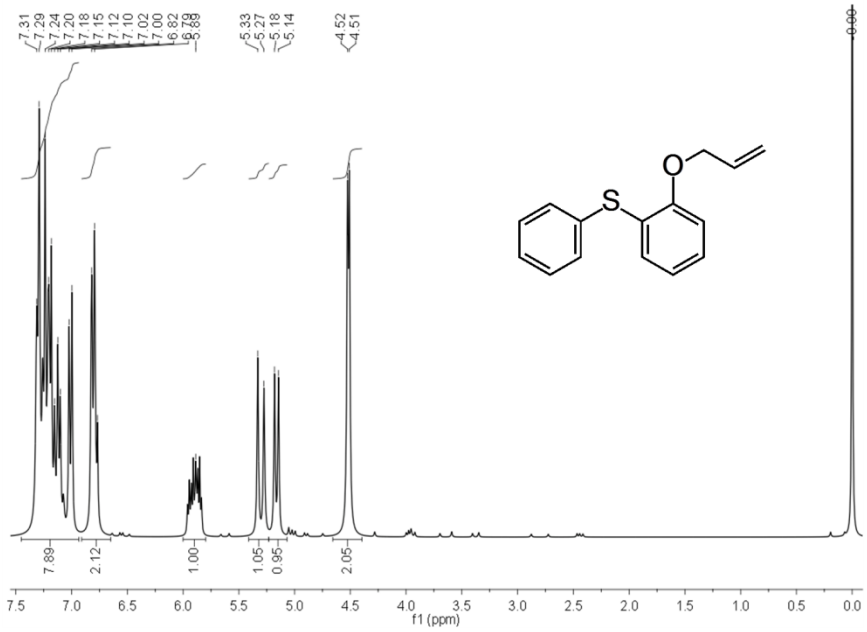


Figure S24. ^{1}H NMR spectrum of **2-(Allyloxy)phenyl phenyl sulfide** in $CDCl_3$ at 298K.

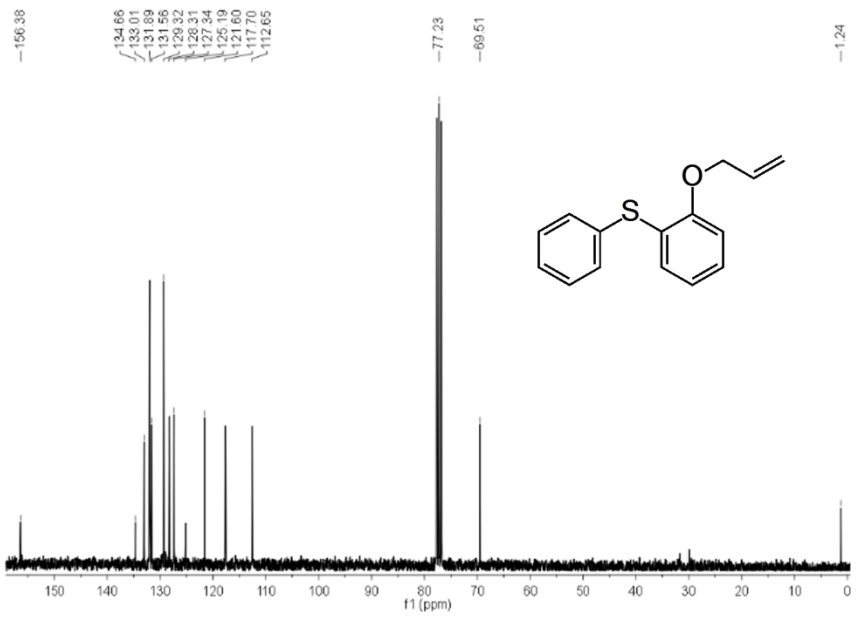
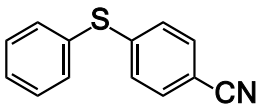


Figure S25. ^{13}C NMR spectrum of **2-(Allyloxy)phenyl phenyl sulfide** in $CDCl_3$ at 298K.

Figure S26. EI-MS spectrum of **2-(Allyloxy)phenyl phenyl sulfide**.



Entries 10 and 11; 4-Cyanophenyl phenyl sulfide: Light yellow oil; Yield: Entry 10: 149 mg, 94%; Entry 11: 146 mg, 92%. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.44–7.34 (m, 7H), 7.08 (d, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 145.9, 134.7, 132.5, 131.0, 130.1, 129.6, 127.4, 119.0, 108.8. MS (EI): *m/z* = 211 (M^+). Eluant: Hex:AcOEt 20:1.

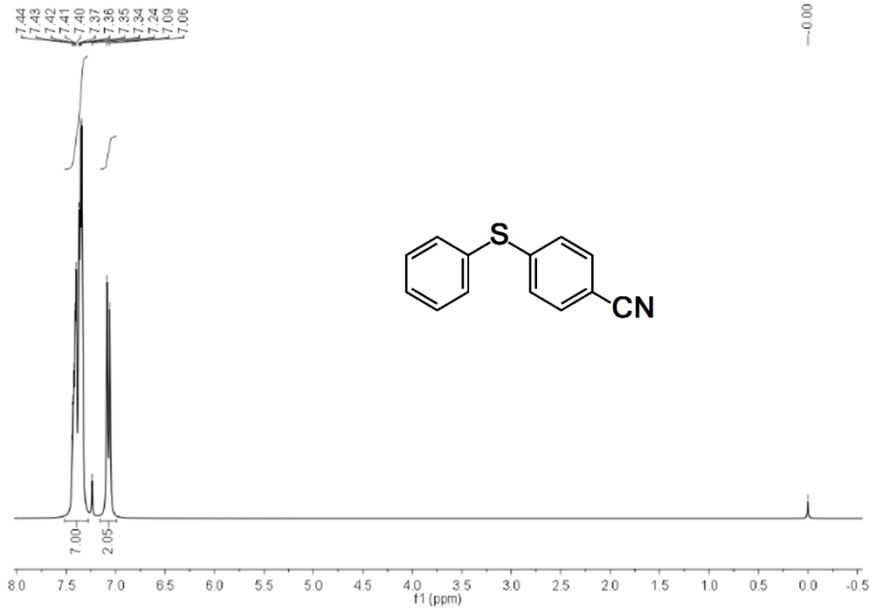


Figure S27. ^{1}H NMR spectrum of **4-Cyanophenyl phenyl sulfide** in $CDCl_3$ at 298K.

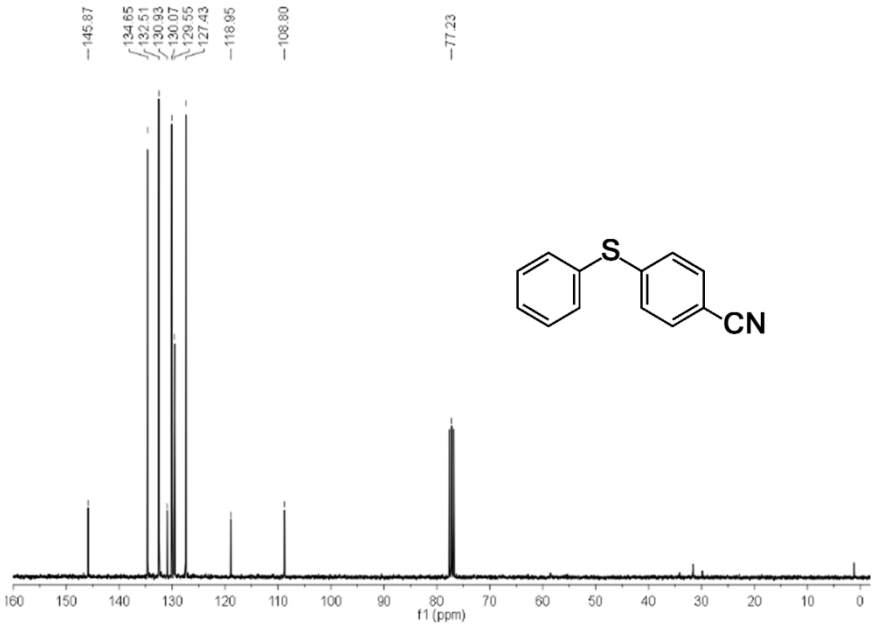


Figure S28. ^{13}C NMR spectrum of **4-Cyanophenyl phenyl sulfide** in $CDCl_3$ at 298K.

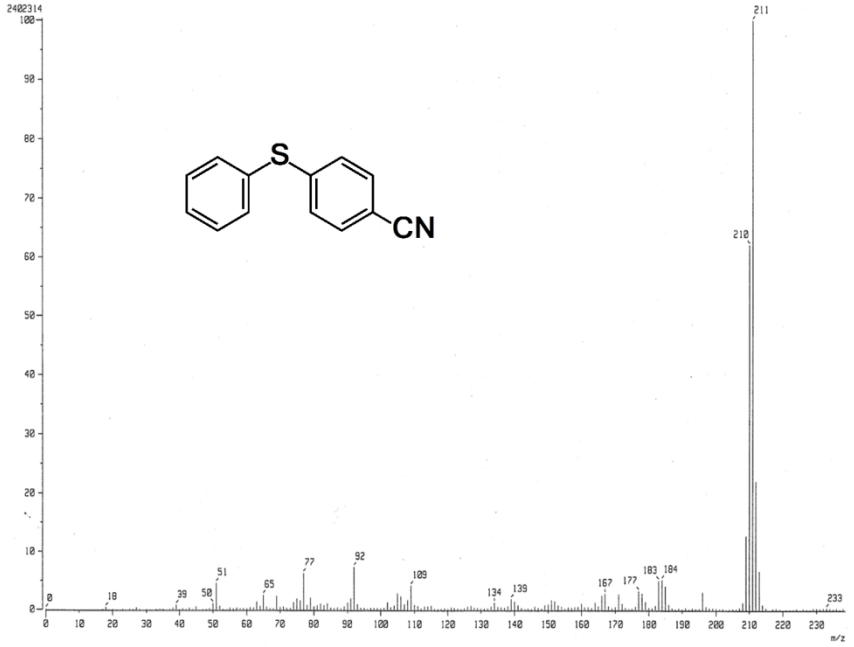
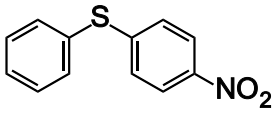


Figure S29. EI-MS spectrum of **4-Cyanophenyl phenyl sulfide**.



Entries 12 and 13; 4-Nitrophenyl phenyl sulfide: Yellow oil; Yield: Entry 12: 166 mg, 95%; Entry 13: 165 mg, 94%. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.03 (d, ^{3}J = 8.7 Hz, 2H), 7.51–7.49 (m, 2H), 7.43–7.40 (m, 3H), 7.14 (d, ^{3}J = 8.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 148.9, 145.9, 134.6, 130.9, 130.1, 129.5, 127.0, 124.3. MS (EI): *m/z* = 231 (M^+).

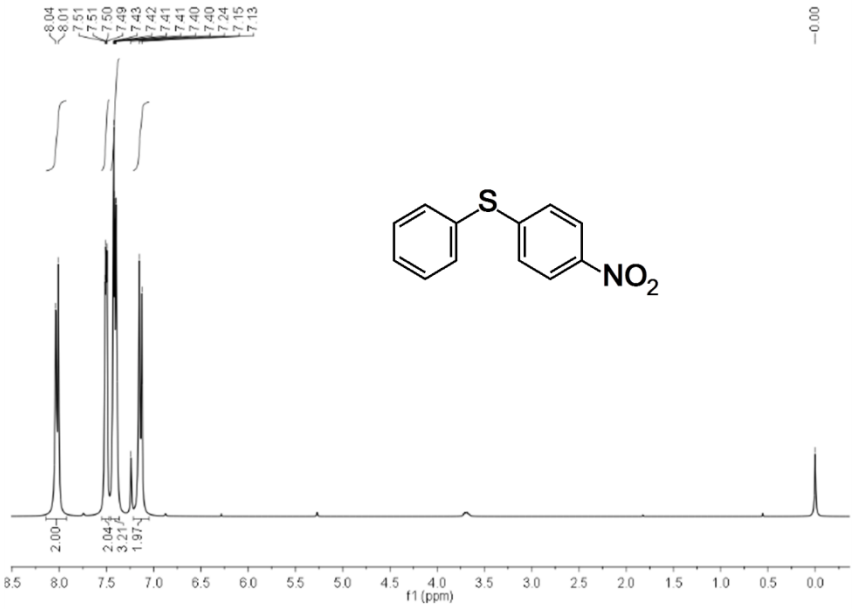


Figure S30. ^{1}H NMR spectrum of **4-Nitrophenyl phenyl sulfide** in $CDCl_3$ at 298K.

Figure S31. ^{13}C NMR spectrum of **4-Nitrophenyl phenyl sulfide** in $CDCl_3$ at 298K.

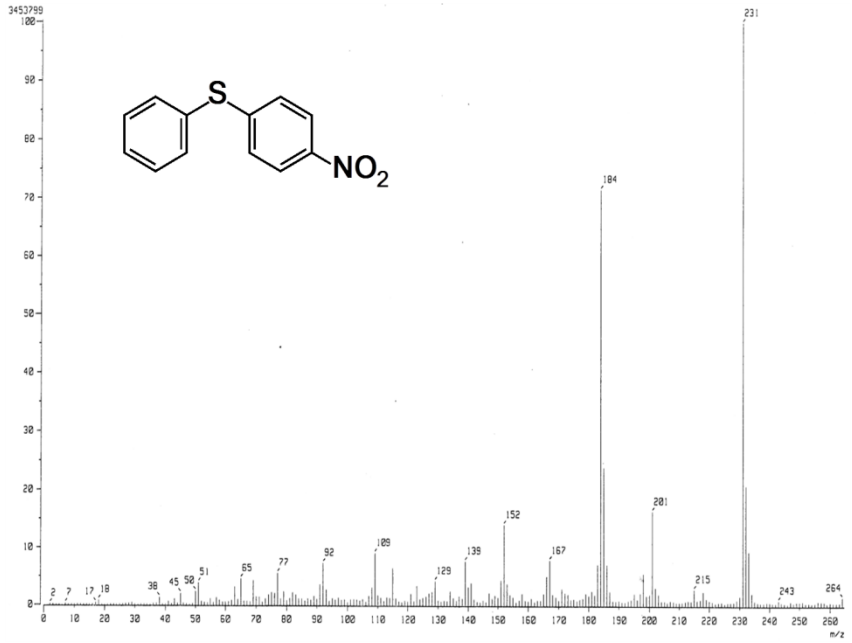


Figure S32. EI-MS spectrum of **4-Nitrophenyl phenyl sulfide**.

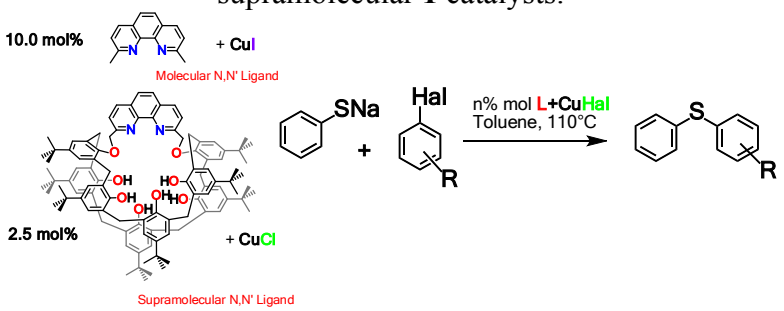
4. C–S Cross-Coupling Reactions using [LCuSPh⊂THF·Na] (2a). The same procedure was used for all selected reactions presented in Scheme 1. **2a** (150 mg, 0.09 mmol), the corresponding haloarene (0.09 mmol), and degassed toluene (2 mL) were placed in an oven-dried Schlenk tube in the glovebox. The Schlenk tube was stirred and heated at 110°C, the progress of the reaction was monitored by TLC chromatography and the reaction was stopped until the starting materials disappeared. The products were purified by column chromatography using silica gel 70:230 and hexane as eluant; the yields are reported based on isolated pure products.

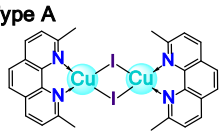
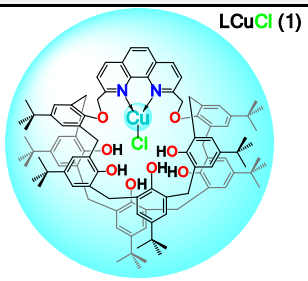
5. Selected Selectivity C–S Cross-Coupling Experiments. The same procedure was used for reactions presented in Scheme 1. **2a** (150 mg, 0.09 mmol), one equivalent of each haloarene (0.09 mmol), and degassed toluene (2 mL) were placed in an oven-dried Schlenk tube in the glovebox. The Schlenk tube was stirred and heated at 110°C for 20 h. The products were purified by column chromatography using silica gel 70:230 and hexane as eluant; the yields are reported based on isolated pure products.

6. Comparative of supramolecular complexes 1 and 2 versus their molecular A and B counterparts.

Cu(I)–catalyzed C–S couplings reported by the groups of Venkataraman and Hartwig were used for comparative purposes. In the former report, the conditions are virtually identical (toluene, 110°C) [Venkataraman et al., *Org. Lett.* **2002**, *4*, 2803]; 2,9-dimethyl-1,10-phenanthroline was used for the *in situ* formation of the catalysts with CuI and CuCl. The following table summarizes the experimental conditions in our supramolecular system and Venkataraman's.

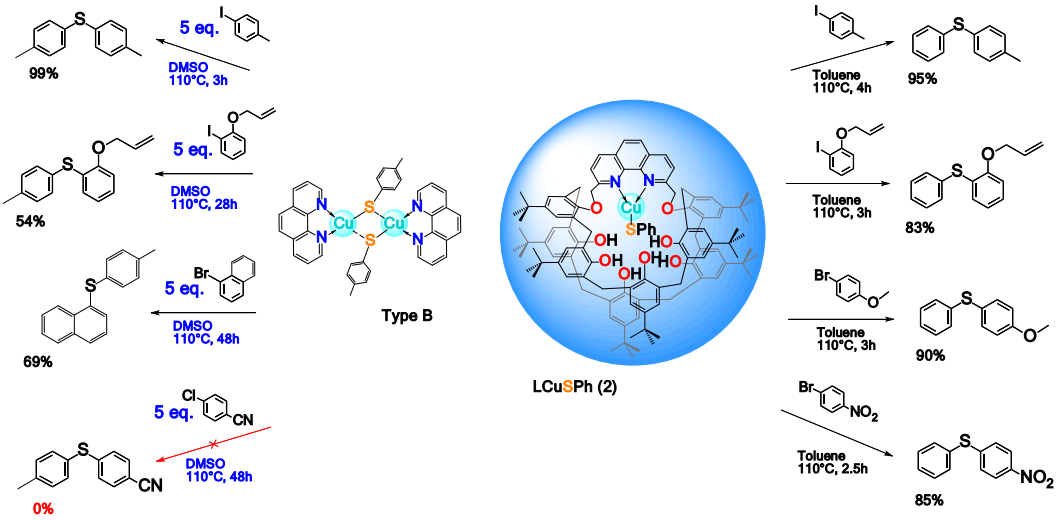
Table S1. Comparison between C–S coupling protocols using molecular type-**A** and supramolecular **1** catalysts.



	Molecular Catalyst	Supramolecular Catalyst
	Type A  Venkataraman, *Org. Lett.*, **2002**	LCuCl (1) 
Molecular Structure	Dimeric complex[a]	Monomeric complex
Catalyst Loading	Necuproine and CuI **10 mol%**	Calixarene and CuCl **2.5 mol%**
Solvent and Temperature	Toluene, 110°C	Toluene, 110°C
Yields	77–98%	80–95%
Reaction Time	Roughly 24 h	14 h average
Reactivity using CuCl	Incomplete conversion	Complete conversion
Versatility and reactivity towards aryl halides	Only effective to couple aryl iodides	Effective with aryl iodides, bromides, and some chlorides
Other Effects	N/A	Size selectivity and solvent dependence due to calixarene cavity

[a]Although Venkataraman and coworkers did not isolate the putative Necuproine-CuI catalyst, it is well known that phenanthroline derivatives form dimeric complexes with Cu(I) salts; the X-ray structure of the dimeric [Necuproine-Cu(μ-I)]$_2$ complex has been reported elsewhere.

The catalytic performance of supramolecular complex **2** can be compared to the molecular analogue reported by Hartwig and coworkers [Hartwig et al., *Organometallics* **2012**, *31*, 8031]. They described the thioetherification reactions of aryl halides using isolated Cu(I)-thiophenolate complexes coordinated by 1,10-phenanthroline and 2,9-dimethyl-1,10-phenanthroline as precursors. Scheme S1 shows the reactions carried out by Hartwig's group and the reactions we performed.



Scheme S1. Thioetherifications reactions of molecular type-**B N,N'-CuSPh** (*left*) and supramolecular **L(N,N')-CuSPh** (**2**) complexes (*right*).