Supporting information

Novel C–H Functionalization of Arenes: Palladium-catalyzed Synthesis of Diaryl Sulfides

Pazhamalai Anbarasan, Helfried Neumann, and Matthias Beller*

Leibniz-Institut für Katalyse e.V. an der Universität Rostock, Albert-Einstein-Straße 29a, 18059 Rostock, Germany.

Table of contents

1. General Comments S2
2. Analytical Methods S2
3. Optimization for the synthesis of diaryl thioethers S3
4. General procedure for the synthesis of diaryl thioethers S3
5. Properties of isolated diaryl thioethers S4
6. NMR spectra of isolated diaryl thioethers S12
1. General Comments:

All reactions were carried out under air using Wheaton vial. Trifluoroacetic acid, acetic acid, trifluoromethanesulfonic acid and formic acid were purchased from Aldrich, stored in Schlenk tube and used as received. Pd(OAc)$_2$, AuCl$_3$, HAuCl$_4$ were purchased from Aldrich, FeCl$_3$ was purchased from Merck and used as received. $p$-Toluenesulfonyl cyanide and benzenesulfonyl cyanides were purchased from Aldrich and used as received. The handling of these cyanides is not problematic, but they shouldn’t come in contact with acids and moisture. Arenes were purchased either from Aldrich or from Alfa Aesar. Column chromatography was performed using Merck Silicagel 60 (0.043-0.06 mm). In general, the purity of the resulting products is $>$95%. However, in case of Table 2, entries 4, 5 and 11 the separation of the major product from the minor regioisomer or the di-addition product is difficult. Hence, the purity in these three examples is lower (80-90%), which is seen in $^{13}$C NMR.

2. Analytical Methods:

NMR data were recorded on Bruker ARX 300 and 400 spectrometers. $^{13}$C and $^1$H NMR spectra were referenced to signals of deuterio solvents and residual protiated solvents, respectively. Gas chromatography analysis was performed on a Agilent HP-5890 instrument with a FID detector and HP-5 capillary column (polydimethylsiloxane with 5% phenyl groups, 30 m, 0.32 mm i.d., 0.25 μm film thickness) using argon as carrier gas. Gas chromatography-mass analysis was carried out on a Agilent HP-5890 instrument with an Agilent HP-5973 Mass Selective Detector (EI) and HP-5 capillary column (polydimethylsiloxane with 5% phenyl groups, 30 m, 0.25 mm i.d., 0.25 μm film thickness) using helium as carrier gas. ESI HR-MS measurements were performed on an Agilent 1969A TOF mass-spectrometer.
3. Optimization for the synthesis of diaryl thioethers:

A 12 mL Wheaton vial was charged with metal source, \( p \)-toluenesulfonyl cyanide, mesitylene and magnetic stir bar (as described in Table 1). To the vial solvent (acid) was added, caped and stirred at room temperature for 1 h (after the addition of acid generation of heat is observed). After 1 h, hexadecane was added as internal GC standard; the reaction mixture was diluted with ethyl acetate and analyzed by GC. Results of the GC analysis are depicted in the Table 1.

4. General procedure for the synthesis of diaryl thioethers:

A 12 mL Wheaton vial was charged with \( \text{Pd(OAc)}_2 \) (10 mol\%), arenesulfonyl cyanide (2 mmol) and magnetic stir bar. To the vial 1 mL of trifluoroacetic acid was added, caped and stirred at room temperature for 10 min. After 10 min, arene (1 mmol) was added at room temperature and stirred for further 1 h (after the addition of arene reaction mixture turned to dark color). Next, the reaction mixture was diluted with ethyl acetate and neutralized by slow addition to saturated aq. \( \text{NaHCO}_3 \) and extracted with ethyl acetate. To the extract silica gel was added and the solvent was removed under reduced pressure. The slurry was subjected to column chromatography to yield the diaryl thioethers.
5. Properties of isolated diaryl thioethers:

2,4,4’,6-Tetramethyldiphenyl thioether:

According to the general procedure product was isolated in 72% yield using the mixture of diethyl ether/pentane (4:96) as an eluent for column chromatography.

$^1$H NMR (400 MHz, CDCl$_3$, 24 °C): $\delta$ 6.94-6.86 (m, 4H, H$_{Ar}$), 6.74 (d, $J = 8.2$ Hz, 2H, H$_{Ar}$), 2.30 (s, 6H, CH$_3$), 2.23 (s, 3H, CH$_3$), 2.18 (s, 3H, CH$_3$).

$^{13}$C{$^1$H} NMR (100 MHz, CDCl$_3$, 24 °C): $\delta$ 143.6 (C), 139.1 (C), 134.8 (C), 134.2 (C), 129.6 (CH), 129.3 (CH), 127.5 (C), 125.7 (CH), 21.7 (CH$_3$), 21.1 (CH$_3$), 20.8 (CH$_3$).

MS (EI): 242 (100) [M]$^+$, 150 (24).

HRMS: calcd. for C$_{16}$H$_{18}$S: 242.11237; found: 242.11208.

2,3,4,4’,5,6-Hexamethyldiphenyl thioether:

According to the general procedure product was isolated in 76% yield using the mixture of diethyl ether/pentane (4:96) as an eluent for column chromatography.

$^1$H NMR (400 MHz, CDCl$_3$, 24 °C): $\delta$ 6.89 (d, $J = 8.2$ Hz, 2H, H$_{Ar}$), 6.73 (d, $J = 8.2$ Hz, 2H, H$_{Ar}$), 2.38 (s, 6H, CH$_3$), 2.20 (s, 3H, CH$_3$), 2.18 (s, 6H, CH$_3$), 2.17 (s, 3H, CH$_3$).

$^{13}$C{$^1$H} NMR (100 MHz, CDCl$_3$, 24 °C): $\delta$ 139.0 (C), 136.6 (C), 135.6 (C), 133.9 (C), 133.5 (C), 129.6 (CH), 128.4 (C), 125.6 (CH), 20.9 (CH$_3$), 19.3 (CH$_3$), 17.5 (CH$_3$), 17.2 (CH$_3$).
2,4,4’-Trimethyldiphenyl thioether:

According to the general procedure product was isolated in 57% yield using the mixture of diethyl ether/pentane (4:96) as an eluent for column chromatography.

$^1$H NMR (400 MHz, CDCl$_3$, 24 °C): δ 7.10 (d, $J = 7.8$ Hz, 1H, H$_{Ar}$), 7.03-6.95 (m, 5H, H$_{Ar}$), 6.89-6.83 (m, 1H, H$_{Ar}$), 2.25 (s, 3H, CH$_3$), 2.23 (s, 3H, CH$_3$), 2.22 (s, 3H, CH$_3$).

$^{13}$C{$_1$H} NMR (100 MHz, CDCl$_3$, 24 °C): δ 139.8 (C), 137.8 (C), 136.1 (C), 133.1 (CH), 133.0 (C), 131.4 (CH), 130.6 (C), 129.8 (CH), 129.6 (CH), 127.4 (CH), 21.07 (CH$_3$), 21.05 (CH$_3$), 20.5 (CH$_3$).

MS (EI): 228 (100) [M]$^+$, 213 (11), 198 (11), 136 (11).
HRMS: calcd. for C$_{15}$H$_{16}$S: 228.09672; found: 228.09693.

4-Methoxy-2,4’,6-trimethyldiphenyl thioether:

According to the general procedure, product was isolated in 43% yield with 1:3 ratio of ortho:para using the mixture of diethyl ether/pentane (5:95) as an eluent for column chromatography.

Experimental data of major compound (para):
1H NMR (400 MHz, CDCl3, 24 °C): δ 6.91 (d, J = 8.2 Hz, 2H, H\textsubscript{Ar}), 6.73 (d, J = 8.2 Hz, 2H, H\textsubscript{Ar}), 6.65 (s, 2H, H\textsubscript{Ar}), 3.73 (s, 3H, OCH\textsubscript{3}), 2.32 (s, 6H, CH\textsubscript{3}), 2.18 (s, 3H, CH\textsubscript{3}).

13C\textsubscript{1}H NMR (100 MHz, CDCl3, 24 °C): δ 160.0 (C), 145.5 (C), 135.1 (C), 134.1 (C), 129.6 (CH), 125.4 (CH), 113.8 (CH), 55.2 (OCH\textsubscript{3}), 22.1 (CH\textsubscript{3}), 20.8 (CH\textsubscript{3}).

MS (EI): 258 (100) [M]\textsuperscript{+}, 210 (10), 166 (10), 91 (11).

HRMS: calcd. for C\textsubscript{16}H\textsubscript{18}OS: 258.10729; found: 258.10703.

2,4-Dimethoxy-6,4’-dimethyldiphenyl thioether:

According to the general procedure product was isolated in 58% yield using the mixture of diethyl ether/pentane (5:95) as an eluent for column chromatography.

1H NMR (400 MHz, CDCl3, 24 °C): δ 6.88 (d, J = 8.3 Hz, 2H, H\textsubscript{Ar}), 6.80 (d, J = 8.3 Hz, 2H, H\textsubscript{Ar}), 6.41 (d, J = 2.5 Hz, 1H, H\textsubscript{Ar}), 6.31 (d, J = 2.5 Hz, 1H, H\textsubscript{Ar}), 3.74 (s, 3H, OCH\textsubscript{3}), 3.69 (s, 3H, OCH\textsubscript{3}), 2.32 (s, 3H, CH\textsubscript{3}), 2.16 (s, 3H, CH\textsubscript{3}).

13C\textsubscript{1}H NMR (100 MHz, CDCl3, 24 °C): δ 161.9 (C), 161.5 (C), 146.2 (C), 135.1 (C), 134.2 (C), 129.5 (CH), 125.8 (CH), 110.8 (C), 107.3 (CH), 96.8 (CH), 56.2 (OCH\textsubscript{3}), 55.3 (OCH\textsubscript{3}), 21.8 (CH\textsubscript{3}), 20.9 (CH\textsubscript{3}).

MS (EI): 274 (100) [M]\textsuperscript{+}, 226 (14).

HRMS: calcd. for C\textsubscript{16}H\textsubscript{18}O\textsubscript{2}S: 274.10220; found: 274.10169.
2,4,6-Trimethoxy-4’-methyldiphenyl thioether:

According to the general procedure product was isolated in 44% yield using the mixture of diethyl ether/pentane (8:92) as an eluent for column chromatography.

$^1$H NMR (300 MHz, CDCl₃, 24 °C): $\delta$ 6.90 (d, $J = 8.6$ Hz, 2H, H$_{Ar}$), 6.86 (d, $J = 8.6$ Hz, 2H, H$_{Ar}$), 6.13 (s, 2H, H$_{Ar}$), 3.79 (s, 3H, OCH₃), 3.73 (s, 6H, OCH$_3$), 2.17 (s, 3H, CH$_3$).

$^{13}$C$^{[1H]}$ NMR (75 MHz, CDCl₃, 24 °C): $\delta$ 162.8 (C), 162.5 (C), 135.0 (C), 134.1 (C), 129.3 (CH), 126.0 (CH), 99.2 (C), 91.1 (CH), 56.3 (OCH₃), 55.4 (OCH$_3$), 20.9 (CH$_3$).

MS (EI): 290 (100) [M]$^+$, 242 (11).

HRMS: calcd. for C$_{16}$H$_{18}$O$_3$S: 290.09712; found: 290.09678.

2,4-Dimethoxy-4’-methyldiphenyl thioether:

According to the general procedure product was isolated in 39% yield using the mixture of diethyl ether/pentane (6:94) as an eluent for column chromatography.

$^1$H NMR (400 MHz, CDCl₃, 24 °C): $\delta$ 7.15 (d, $J = 8.4$ Hz, 1H, H$_{Ar}$), 7.02 (d, $J = 8.3$ Hz, 2H, H$_{Ar}$), 6.96 (d, $J = 8.3$ Hz, 2H, H$_{Ar}$), 6.42 (d, $J = 2.5$ Hz, 1H, H$_{Ar}$), 6.37 (dd, $J = 8.4, 2.5$ Hz, 1H, H$_{Ar}$), 3.73 (s, 3H, OCH$_3$), 3.72 (s, 3H, OCH$_3$), 2.20 (s, 3H, CH$_3$).

$^{13}$C$^{[1H]}$ NMR (100 MHz, CDCl₃, 24 °C): $\delta$ 161.4 (C), 159.8 (C), 135.8 (C), 135.5 (CH), 133.4 (C), 129.7 (CH), 129.0 (CH), 113.6 (C), 105.3 (CH), 99.2 (CH), 55.9 (OCH$_3$), 55.5 (OCH$_3$), 21.0 (CH$_3$).
MS (EI): 260 (100) [M]+, 245 (12), 212 (12).

HRMS: calcd. for C_{15}H_{16}O_{2}S: 260.08655; found: 260.08573.

4-Methoxy-2,4’-dimethyldiphenyl thioether:

According to the general procedure product was isolated in 66% yield using the mixture of diethyl ether/pentane (5:95) as an eluent for column chromatography.

$^1$H NMR (300 MHz, CDCl$_3$, 24 °C): δ 7.29 (d, $J = 8.4$ Hz, 1H, H$_{Ar}$), 6.95 (d, $J = 8.2$ Hz, 2H, H$_{Ar}$), 6.90 (d, $J = 8.2$ Hz, 2H, H$_{Ar}$), 6.75 (d, $J = 2.8$ Hz, 1H, H$_{Ar}$), 6.64 (dd, $J = 8.4$, 2.8 Hz, 1H, H$_{Ar}$), 3.72 (s, 3H, OCH$_3$), 2.27 (s, 3H, OCH$_3$), 2.20 (s, 3H, CH$_3$).

$^{13}$C{$_1$H} NMR (75 MHz, CDCl$_3$, 24 °C): δ 160.0 (C), 143.1 (C), 136.5 (CH), 135.3 (C), 134.4 (C), 129.7 (CH), 127.8 (CH), 123.7 (C), 116.4 (CH), 112.1 (CH), 55.3 (OCH$_3$), 21.1 (CH$_3$), 20.9 (CH$_3$).

MS (EI): 244 (100) [M]+, 229 (30).

HRMS: calcd. for C$_{15}$H$_{16}$OS: 244.09164; found: 244.09174.

4-Methoxy-4’-methyldiphenyl thioether:

According to the general procedure product was isolated in 61% yield using the mixture of diethyl ether/pentane (5:95) as an eluent for column chromatography.

$^1$H NMR (300 MHz, CDCl$_3$, 24 °C): δ 7.28 (d, $J = 8.9$ Hz, 2H, H$_{Ar}$), 7.05 (d, $J = 8.3$ Hz, 2H, H$_{Ar}$), 6.98 (d, $J = 8.3$ Hz, 2H, H$_{Ar}$), 6.78 (d, $J = 8.9$ Hz, 2H, H$_{Ar}$), 3.72 (s, 3H, OCH$_3$), 2.22 (s, 3H, CH$_3$).
13C{1H} NMR (75 MHz, CDCl3, 24 °C): δ 159.4 (C), 136.1 (C), 134.4 (CH), 129.8 (CH), 129.4 (CH), 125.6 (C), 114.9 (CH), 55.3 (OCH3), 21.0 (CH3).

MS (EI): 230 (100) [M]+, 215 (43), 171 (13).


6-Bromo-2,4-dimethoxy-4'-methyldiphenyl thioether:

According to the general procedure product was isolated in 37% yield using the mixture of diethyl ether/pentane (8:92) as an eluent for column chromatography.

1H NMR (300 MHz, CDCl3, 24 °C): δ 6.94 (d, J = 8.6 Hz, 2H, HAr), 6.90 (d, J = 8.6 Hz, 2H, HAr), 6.82 (d, J = 2.5 Hz, 1H, HAr), 6.39 (d, J = 2.5 Hz, 1H, HAr), 3.75 (s, 3H, OCH3), 3.70 (s, 3H, OCH3), 2.19 (s, 3H, CH3).

13C{1H} NMR (75 MHz, CDCl3, 24 °C): δ 162.3 (C), 161.8 (C), 135.0 (C), 133.8 (C), 133.7 (C), 129.5 (CH), 126.8 (CH), 113.7 (C), 110.1 (CH), 98.8 (CH), 56.5 (OCH3), 55.7 (OCH3), 20.9 (CH3).

MS (EI): 340 & 338 (100) [M]+, 244 (36), 229 (17), 201 (19).

HRMS: calcd. for C15H15O279BrS: 337.99706; found: 337.99606.

4-Bromo-2-methoxy-4'-methyldiphenyl thioether:

According to the general procedure product was isolated in 55% yield using the mixture of diethyl ether/pentane (6:94) as an eluent for column chromatography.
$^1$H NMR (300 MHz, CDCl$_3$, 24 °C): $\delta$ 7.17-6.99 (m, 6H, H$_{Ar}$), 6.69 (dd, $J$ = 8.7, 2.7 Hz, 1H, H$_{Ar}$), 3.75 (s, 3H, OCH$_3$), 3.70 (s, 3H, OCH$_3$), 2.25 (s, 3H, CH$_3$).

$^{13}$C$^{[1]$H} NMR (75 MHz, CDCl$_3$, 24 °C): $\delta$ 159.4 (C), 137.2 (C), 133.7 (CH), 131.7 (C), 131.0 (CH), 130.1 (CH), 128.0 (C), 126.7 (C), 118.6 (CH), 114.5 (CH), 55.6 (OCH$_3$), 21.1 (CH$_3$).

MS (EI): 310 & 308 (100) [M]$^+$, 293 (10), 214 (49), 199 (11), 185 (22), 171 (18).

HRMS: calcd. for C$_{14}$H$_{13}$O$_7$BrS: 307.98650; found: 307.98588.

2-(4-Methylphenylthio)-9,9-dimethylxanthene:

According to the general procedure product was isolated in 57% yield using the mixture of diethyl ether/pentane (6:94) as an eluent for column chromatography.

$^1$H NMR (300 MHz, CDCl$_3$, 24 °C): $\delta$ 7.41 (d, $J$ = 2.2 Hz, 1H, H$_{Ar}$), 7.31 (dd, $J$ = 7.7, 1.6 Hz, 1H, H$_{Ar}$), 7.16-7.05 (m, 4H, H$_{Ar}$), 7.04-6.93 (m, 4H, H$_{Ar}$), 6.91 (d, $J$ = 8.4 Hz, 1H, H$_{Ar}$), 2.23 (s, 3H, CH$_3$), 1.51 (s, 6H, CH$_3$).

$^{13}$C$^{[1]$H} NMR (75 MHz, CDCl$_3$, 24 °C): $\delta$ 150.2 (C), 150.17 (C), 136.4 (C), 133.7 (C), 131.6 (CH), 131.1 (C), 130.5 (CH), 129.9 (CH), 129.7 (CH), 128.5 (C), 127.5 (CH), 126.1 (CH), 123.3 (CH), 117.5 (CH), 116.4 (CH), 34.1 (CH$_3$), 32.4 (CH$_3$), 21.1 (CH$_3$).

MS (EI): 332 (23) [M]$^+$, 317 (100).

HRMS: calcd. for C$_{22}$H$_{20}$OS: 332.12294; found: 332.12319.
2,4,6-Trimethyldiphenyl thioether:

According to the general procedure product was isolated in 33% yield using the mixture of diethyl ether/pentane (4:96) as an eluent for column chromatography.

$^1$H NMR (300 MHz, CDCl$_3$, 24 °C): $\delta$ 7.12-7.03 (m, 2H, H$_{Ar}$), 6.99-6.94 (m, 1H, H$_{Ar}$), 6.94-6.90 (m, 2H, H$_{Ar}$), 6.86-6.80 (m, 2H, H$_{Ar}$), 2.30 (s, 6H, CH$_3$), 2.23 (s, 3H, CH$_3$).

$^{13}$C$^1$H NMR (75 MHz, CDCl$_3$, 24 °C): $\delta$ 143.7 (C), 139.3 (C), 138.4 (C), 129.3 (CH), 128.9 (CH), 127.0 (C), 125.5 (CH), 124.5 (CH), 21.7 (CH$_3$), 21.2 (CH$_3$).

MS (EI): 228 (100) [M$^+$], 150 (22), 91 (13).

HRMS: calcd. for C$_{15}$H$_{16}$S: 228.09672; found: 228.09635.

4-Methoxydiphenyl thioether:

According to the general procedure product was isolated in 41% yield using the mixture of diethyl ether/pentane (6:94) as an eluent for column chromatography.

$^1$H NMR (300 MHz, CDCl$_3$, 24 °C): $\delta$ 7.34 (d, $J = 8.9$ Hz, 2H, H$_{Ar}$), 7.25-6.96 (m, 5H, H$_{Ar}$), 6.82 (d, $J = 8.9$ Hz, 2H, H$_{Ar}$), 3.74 (s, 3H, OCH$_3$).

$^{13}$C$^1$H NMR (75 MHz, CDCl$_3$, 24 °C): $\delta$ 159.8 (C), 138.6 (C), 135.4 (CH), 130.7 (C), 128.9 (CH), 128.2 (CH), 125.7 (CH), 115.0 (CH), 55.4 (OCH$_3$).

MS (EI): 216 (100) [M$^+$], 201 (49).

HRMS: calcd. for C$_{13}$H$_{12}$OS: 216.06034; found: 216.06043.
6. NMR spectra of isolated diaryl thioether:

2,4,4',6-Tetramethyldiphenyl thioether

$^1$H NMR (400 MHz, CDCl$_3$, 24 °C)

$^{13}$C{$^1$H} NMR (100 MHz, CDCl$_3$, 24 °C)
2,3,4,4',5,6-Hexamethyldiphenyl thioether

$^1$H NMR (400 MHz, CDCl$_3$, 24 °C)

$^{13}$C{$^1$H} NMR (100 MHz, CDCl$_3$, 24 °C)
2,4,4’-Trimethyldiphenyl thioether

$^1$H NMR (400 MHz, CDCl$_3$, 24 °C)

$^{13}$C$^1$H NMR (100 MHz, CDCl$_3$, 24 °C)
4-Methoxy-2,4',6-trimethyldiphenyl thioether

$^1$H NMR (400 MHz, CDCl$_3$, 24 °C)

$^{13}$C{$_1^H$} NMR (100 MHz, CDCl$_3$, 24 °C)
2,4-Dimethoxy-6,4’-dimethyldiphenyl thioether

$^1$H NMR (400 MHz, CDCl$_3$, 24 °C)

$^{13}$C{$^1$H} NMR (100 MHz, CDCl$_3$, 24 °C)
2,4,6-Trimethoxy-4’-methyldiphenyl thioether

$^1$H NMR (300 MHz, CDCl$_3$, 24 °C)

$^{13}$C{$^1$H} NMR (75 MHz, CDCl$_3$, 24 °C)
2,4-Dimethoxy-4’-methyldiphenyl thioether

$^1$H NMR (400 MHz, CDCl$_3$, 24 °C)

$^{13}$C{$^1$H} NMR (100 MHz, CDCl$_3$, 24 °C)
4-Methoxy-2,4’-dimethyldiphenyl thioether

$^1$H NMR (300 MHz, CDCl$_3$, 24 °C)

$^{13}$C{$_1$H} NMR (75 MHz, CDCl$_3$, 24 °C)
4-Methoxy-4'-methyldiphenyl thioether

$^1$H NMR (300 MHz, CDCl$_3$, 24 °C)

$^{13}$C{$^1$H} NMR (75 MHz, CDCl$_3$, 24 °C)
6-Bromo-2,4-dimethoxy-4'-methyldiphenyl thioether

$^1$H NMR (300 MHz, CDCl$_3$, 24 °C)

$^{13}$C{$^1$H} NMR (75 MHz, CDCl$_3$, 24 °C)
4-Bromo-2-methoxy-4’-methylphenyl thioether

$^1$H NMR (300 MHz, CDCl$_3$, 24 °C)

$^{13}$C{$_^1$H} NMR (75 MHz, CDCl$_3$, 24 °C)
2-(4-Methylphenylthio)-9,9-dimethylxanthene

$^1$H NMR (300 MHz, CDCl$_3$, 24 °C)

$^{13}$C{$^1$H} NMR (75 MHz, CDCl$_3$, 24 °C)
2,4,6-Trimethyldiphenyl thioether

$^1$H NMR (300 MHz, CDCl$_3$, 24 °C)

$^{13}$C{$_1$H} NMR (75 MHz, CDCl$_3$, 24 °C)
4-Methoxydiphenyl thioether

\(^1\)H NMR (300 MHz, CDCl\(_3\), 24 °C)

MeO

\[^{13}\text{C}\] NMR (75 MHz, CDCl\(_3\), 24 °C)