Synthesis of spiro[4.4]thiadiazole derivatives via double 1,3-dipolar cycloaddition of hydrazonyl chlorides with carbon disulfide

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Supporting Information

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1. General methods

NMR data were obtained for $^1$H at 400 MHz, and for $^{13}$C at 100 MHz. Chemical shifts were given in parts per million (δ) from tetramethylsilane with the solvent resonance as the internal standard in CDCl$_3$ solution. Data were reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz), integration. ESI HRMS was recorded on a Waters SYNAPT G2. Column chromatography was performed on silica gel (200-300 mesh) eluting with ethyl acetate and petroleum ether. TLC was performed on glass-backed silica plates. UV light, I$_2$, and solution of potassium permanganate were used to visualize products. All chemicals were used without purification as commercially available unless otherwise noted. Petroleum ether (PE) and ethyl acetate (EtOAc) were distilled. THF was freshly distilled from sodium/benzophenone. Unless otherwise noted, experiments involving moisture and/or air sensitive components were performed under a positive pressure of argon in oven-dried glassware equipped with a rubber septum inlet. Dried solvents and liquid reagents were transferred by oven-dried syringes. The hydrazonyl chlorides 1 were prepared according to the literature procedures [1].


\[ \begin{array}{c}
\text{Cl} \\
\text{R} \\
\text{N} \\
\text{H} \\
\text{N} \\
\text{R}^1 \\
\end{array} + \begin{array}{c}
\text{CS}_2 \\
\end{array} \rightarrow \begin{array}{c}
\text{S} \\
\text{N} \\
\text{S} \\
\text{N} \\
\text{R}^1 \\
\end{array}
\]

The nitrile imine precursor of the hydrazonyl chlorides 1 (0.2 mmol), carbon disulfide 2 (0.3 mmol), and the cesium carbonate (0.2 mmol) were dissolved in CH$_2$Cl$_2$ (1.0 mL). Then the solution was stirred at rt for 12 h. After completion, the mixture was directly purified by column chromatography on silica gel eluting with petroleum ether/ethyl acetate (50:1 to 25:1) to afford the product 3.

\[ \begin{array}{c}
\text{Ph} \\
\text{N} \\
\text{S} \\
\text{N} \\
\text{Ph} \\
\end{array} \text{3a, 42.7 mg, 92% yield, pale white solid.} \\
\text{H NMR (400 MHz, CDCl$_3$) δ 7.64 (dd, } J = 7.6, 3.6 \\
\text{Hz, 4H), 7.49 (d, } J = 8.4 \text{ Hz, 4H), 7.40 – 7.38 (m, 6H), 7.27 – 7.22 (m, 4H), 7.03 (t, } J = 7.2 \\
\text{Hz, 2H).} \] \[ \begin{array}{c}
\text{Ph} \\
\text{N} \\
\text{S} \\
\text{N} \\
\text{Ph} \\
\end{array} \text{\textsuperscript{13}C NMR (100 MHz, CDCl$_3$) δ 144.3, 141.4, 130.8, 130.0, 128.9, 128.7, 126.2, 123.6, 121.6, 118.8. ESI-HRMS: C$_{27}$H$_{30}$N$_4$S$_2$+H$^+$ 465.1202, found 465.1198.} \]
3b, 44.3 mg, 90% yield, pale white solid. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.53 (d, $J = 8.0$ Hz, 4H), 7.47 (d, $J = 8.4$ Hz, 4H), 7.25 – 7.18 (m, 8H), 7.00 (t, $J = 7.6$ Hz, 2H), 2.36 (s, 6H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 144.4, 141.5, 140.3, 129.4, 128.8, 128.0, 126.1, 123.3, 121.3, 118.6, 21.4. ESI-HRMS: C$_{29}$H$_{34}$N$_4$S$_2$+H$^+$ 493.1515, found 493.1510.

3c, 47.5 mg, 95% yield, pale white solid. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.62 (dd, $J = 8.8$, 5.2 Hz, 4H), 7.47 (d, $J = 7.6$ Hz, 4H), 7.28 – 7.24 (m, 4H), 7.11 – 7.03 (m, 6H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 163.7 (d, $J = 249.6$ Hz), 143.4, 141.3, 128.9, 128.0 (d, $J = 8.3$ Hz), 127.0 (d, $J = 3.3$ Hz), 123.8, 122.4, 118.9, 115.9 (d, $J = 22.2$ Hz). ESI-HRMS: C$_{27}$H$_{18}$F$_2$N$_4$S$_2$+H$^+$ 501.1014, found 501.1009.

3d, 50.0 mg, 94% yield, pale white solid. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.55 (d, $J = 8.4$ Hz, 4H), 7.45 (d, $J = 8.0$ Hz, 4H), 7.36 (d, $J = 8.4$ Hz, 4H), 7.28 – 7.24 (m, 4H), 7.06 (t, $J = 7.2$ Hz, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 143.2, 141.2, 135.9, 129.2, 123.9, 122.2, 119.0. ESI-HRMS: C$_{27}$H$_{18}$Cl$_2$N$_4$S$_2$+H$^+$ 533.0423, found 533.0416.

3e, 56.0 mg, 93% yield, pale white solid. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.49 (s, 4H), 7.43 (d, $J = 8.8$ Hz, 4H), 7.37 (s, 2H), 7.30 (t, $J = 7.6$ Hz, 4H), 7.11 (t, $J = 7.2$ Hz, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 141.6, 140.8, 135.5, 133.4, 129.7, 129.1, 124.6, 124.3, 122.9, 119.4. ESI-HRMS: C$_{27}$H$_{18}$Cl$_2$N$_4$S$_2$+H$^+$ 600.9643, found 600.9639.

3f, 58.8 mg, 95% yield, pale white solid. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.68 – 7.64 (m, 4H), 7.49 (d, $J = 8.4$ Hz, 4H), 7.35 (t, $J = 7.6$ Hz, 2H), 7.30 – 7.22 (m, 6H), 7.06 (t, $J = 7.6$ Hz, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 142.3, 141.1, 134.2, 131.4, 130.85, 130.83, 128.9, 127.5, 123.7, 121.5, 121.3, 119.0. ESI-HRMS: C$_{27}$H$_{18}$Br$_2$N$_4$S$_2$+H$^+$ 622.9392, found 622.9383.
3g 59.4 mg, 96% yield, pale white solid. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.83 (s, 2H), 7.50 – 7.44 (m, 8H), 7.29 – 7.25 (m, 4H), 7.23 – 7.21 (m, 2H), 7.06 (t, $J$ = 7.2 Hz, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 142.8, 141.1, 132.9, 132.7, 130.3, 129.1, 128.8, 124.9, 124.2, 123.0, 122.3, 119.2. ESI-HRMS: C$_{27}$H$_{18}$Br$_2$N$_4$S$_2$+H$^+$ 622.9392, found 620.9384.

3h, 58.8 mg, 95% yield, pale white solid. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.54 – 7.44 (m, 12H), 7.28 – 7.24 (m, 4H), 7.06 (t, $J$ = 7.6 Hz, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 143.3, 141.1, 131.9, 129.6, 129.0, 127.5, 124.1, 124.0, 122.2, 119.0. ESI-HRMS: C$_{27}$H$_{18}$Br$_2$N$_4$S$_2$+H$^+$ 622.9392, found 622.9384.

3i, 56.4 mg, 94% yield, pale white solid. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.73 (d, $J$ = 8.0 Hz, 4H), 7.65 (d, $J$ = 8.4 Hz, 4H), 7.47 (d, $J$ = 8.0 Hz, 4H), 7.28 (t, $J$ = 7.2 Hz, 4H), 7.09 (t, $J$ = 7.2 Hz, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 142.8, 141.0, 134.0, 131.6 (q, $J$ = 32.5 Hz), 129.1, 126.3, 125.8 (q, $J$ = 3.7 Hz), 125.1, 124.4, 122.5, 121.3 (q, $J$ = 220.3 Hz), 119.3. ESI-HRMS: C$_{29}$H$_{18}$F$_6$N$_4$S$_2$+H$^+$ 601.0950, found 601.0942.

3j, 40.4 mg, 91% yield, pale white solid. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.48 – 7.45 (m, 6H), 7.28 – 7.24 (m, 4H), 7.05 (t, $J$ = 7.2 Hz, 2H), 6.70 (d, $J$ = 3.2 Hz, 2H), 6.49 – 6.48 (m, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 145.2, 143.9, 141.3, 135.8, 129.0, 124.0, 119.5, 111.9, 110.3. ESI-HRMS: C$_{23}$H$_{16}$N$_4$O$_2$S$_2$+H$^+$ 445.0787, found 445.0783.

3k, 44.3 mg, 93% yield, pale white solid. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.50 – 7.45 (m, 6H), 7.38 – 7.34 (m, 4H), 7.28 – 7.24 (m, 4H), 7.04 (t, $J$ = 7.2 Hz, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 141.4, 140.2, 132.6, 128.9, 126.7, 125.2, 124.5, 123.6, 121.8, 118.9. ESI-HRMS: C$_{23}$H$_{16}$N$_4$S$_4$+H$^+$ 477.0331, found 477.0326.

3l, 53.6 mg, 95% yield, pale white solid. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.12 – 7.99 (m, 2H), 7.88 (s, 1H), 7.85 – 7.80 (m, 7H), 7.56 (d, $J$ = 8.0 Hz, 4H), 7.49 (dd, $J$ = 7.6, 3.6 Hz, 4H), 7.28 (d, $J$ = 7.6 Hz, 3H), 7.23 (s, 1H), 7.04 (t, $J$ = 7.2
3 m, 44.3 mg, 90% yield, pale white solid. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.64 – 7.62 (m, 4H), 7.40 – 7.38 (m, 10H), 7.06 (d, $J = 8.4$ Hz, 4H), 2.26 (s, 6H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 143.9, 139.1, 133.3, 131.0, 129.8, 129.5, 128.7, 126.1, 119.1, 20.7. ESI-HRMS: C$_{29}$H$_{24}$N$_4$S$_2$+H$^+$ 493.1515, found 493.1512.

3 n, 49.5 mg, 93% yield, pale white solid. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.64 – 7.62 (m, 4H), 7.42 – 7.41 (m, 6H), 7.38 – 7.36 (m, 4H), 7.24 – 7.20 (m, 4H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 145.0, 139.7, 130.4, 130.3, 129.0, 128.8, 126.2, 120.9, 119.7. ESI-HRMS: C$_{27}$H$_{18}$Cl$_2$N$_4$S$_2$+H$^+$ 533.0423, found 533.0421.

3 o, 41.5 mg, 91% yield, pale white solid. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.37 (d, $J = 8.0$ Hz, 4H), 7.31 (t, $J = 7.8$ Hz, 4H), 7.18 (t, $J = 7.2$ Hz, 2H), 4.35 (q, $J = 6.4$ Hz, 4H), 1.36 (t, $J = 7.2$ Hz, 6H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 159.6, 140.1, 135.9, 129.3, 125.9, 123.2, 120.9, 62.7, 14.2. ESI-HRMS: C$_{21}$H$_{20}$N$_4$O$_4$S$_2$+H$^+$ 457.0999, found 457.0990.

3. Crystal data and structural refinement for 3h

Identification code 3h
Empirical formula C$_{27}$H$_{18}$Br$_2$N$_4$S$_2$
Formula weight 622.39
Temperature/K 273
Crystal system triclinic
Space group P -1 (2)
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<tr>
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<td>Final R indexes [I&gt;=2σ (I)]</td>
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<tr>
<td>Final R indexes [all data]</td>
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<tr>
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</tr>
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4. Copies of NMR spectra
\[
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  \node at (-1.5,0) {F};
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  \node at (-2.5,0) {Ph-N-S-N-Ph};
  \node at (2.5,0) {Ph-N-S-N-Ph};
  \node at (-3.5,0) {S};
  \node at (3.5,0) {S};
  \node at (-4.5,0) {N};
  \node at (4.5,0) {N};
\end{tikzpicture}
\end{center}}
\]
$^{19}$F-NMR

![Chemical Structure]

$\text{Ph-N}_2\text{S-S-Ph}$

$3c$
$^{19}$F-NMR

![Chemical structure](image)

$\text{F}_3\text{C} - \text{N} = \text{S} - \text{N} = \text{S} - \text{N} - \text{Ph}$

$3i$