

Rongalite-promoted transition metal-free synthesis of *S*-aryl phosphorothioates

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General experimental

Unless otherwise noted, all chemicals were purchased from commercial suppliers (Aladdin) and used without further purification. ¹H and ¹³C NMR spectra were performed on a Bruker Advance III 300 analyzer in Chloroform-*d* (CDCl₃) using TMS as an internal standard. Chemical shifts are reported in δ units, parts per million (ppm), and were referenced to CDCl₃ as the internal standard. The coupling constants *J* are given in Hz. Mass spectrometry was performed on an LCMS-2010 EV (Shimadzu) instrument with an ESI source. Column chromatography was performed using EM Silica gel 60 (300-400 mesh). All the products are known compounds and were identified by comparing their physical and spectra data with those reported in the literature.

Experimental procedures, spectral and analytical data

General procedure for the synthesis of **3a-o**

A sealed tube equipped with a magnetic stirrer bar was charged with S₈ (0.4 mmol, 13 mg), *H*-phosphonate **2** (0.4 mmol), Et₃N (0.4 mmol, 40 mg), DMSO (1 ml), and this was stirred for 30 min. Then iodoarene **1** (0.2 mmol), rongalite (0.4 mmol, 47 mg) and KOH (0.6 mmol, 34 mg) were added. The reaction mixture was then heated to 80 °C and stirred overnight. Upon reaction completion, the resulting solution was quenched with water and extracted by ethyl acetate. The combined organic extracts were dried over Na₂SO₄. The solvent was then removed under reduced pressure and the residue was purified by silica gel column chromatography using petroleum ether/ethyl acetate (4:1, *v/v*) as eluent to afford product **3a-o**.

Characterization data of products **3**

O,O-Diethyl *S*-phenyl phosphorothioate (**3a**).^[S1] Yellow oil (85%). ¹H NMR (300 MHz, CDCl₃) δ 7.54 – 7.44 (m, 2H), 7.35 – 7.21 (m, 3H), 4.21 – 4.01 (m, 4H), 1.23 (td, *J* = 7.1, 0.6 Hz, 6H). ¹³C NMR (75 MHz, CDCl₃) δ 134.5 (d, *J* = 5.2 Hz), 129.3 (d, *J* = 2.3 Hz), 129.0 (d, *J* = 2.8 Hz), 126.6 (d, *J* = 7.2 Hz), 64.1 (d, *J* = 6.2 Hz), 16.1 (d, *J* = 7.2 Hz). MS-ESI: *m/z* = 268.9 [M + Na]⁺.

O,O-Diethyl *S*-(*o*-tolyl) phosphorothioate (**3b**).^[S1] Yellow oil (80%). ¹H NMR (300 MHz, CDCl₃) δ 7.58 – 7.49 (m, 1H), 7.20 (dd, *J* = 4.1, 2.7 Hz, 2H), 7.14 – 7.07 (m, 1H), 4.15 – 4.01 (m, 4H), 2.45 (d, *J* = 1.4 Hz, 3H), 1.22 (td, *J* = 7.1, 0.8 Hz, 6H). ¹³C NMR (75 MHz, CDCl₃) δ 142.4 (d, *J* = 5.6 Hz), 136.3 (d, *J* = 4.2 Hz), 131.0 (d, *J* = 2.6 Hz), 129.5 (d, *J* = 3.1 Hz), 126.8 (d, *J* = 2.7 Hz), 64.3 (d, *J* = 6.7 Hz), 21.5, 16.1 (d, *J* = 7.1 Hz). MS-ESI: *m/z* = 283.0 [M + Na]⁺.

O,O-Diethyl *S*-(*m*-tolyl) phosphorothioate (**3c**).^[S1] Yellow oil (82%). ¹H NMR (300 MHz, CDCl₃) δ 7.38 – 7.31 (m, 2H), 7.21 (t, *J* = 7.5 Hz, 1H), 7.14 (dd, *J* = 7.6, 0.7 Hz, 1H), 4.25 – 4.10 (m, 4H), 2.33 (s, 3H), 1.29 (td, *J* = 7.1, 0.9 Hz, 6H). ¹³C NMR (75 MHz, CDCl₃) δ 139.3 (d, *J* = 2.3 Hz), 135.2 (d, *J* = 5.2 Hz), 131.6 (d, *J* = 5.2 Hz), 129.9 (d, *J* = 2.9 Hz), 129.2 (d, *J* = 2.3 Hz), 126.2 (d, *J* = 7.2 Hz), 64.1 (d, *J* = 6.2 Hz), 21.3, 16.07 (d, *J* = 7.3 Hz). MS-ESI: *m/z* = 283.0 [M + Na]⁺.

O,O-Diethyl *S*-(*p*-tolyl) phosphorothioate (**3d**).^[S2] Yellow oil (84%). ¹H NMR (300 MHz, CDCl₃) δ 7.46 – 7.39 (m, 2H), 7.16 – 7.11 (m, 2H), 4.25 – 4.09 (m, 4H), 2.33 (d, *J* = 2.0 Hz, 3H), 1.30 (td, *J* = 7.1, 0.9 Hz, 6H). ¹³C NMR (75 MHz, CDCl₃) δ 139.4 (d, *J* = 3.2 Hz), 134.7 (d, *J* = 5.1 Hz), 130.2 (d, *J* = 2.4 Hz), 122.9 (d, *J* = 7.3 Hz), 64.1 (d, *J* = 6.1 Hz), 21.3 (d, *J* = 0.9 Hz), 16.1 (d, *J* = 7.2 Hz). MS-ESI: *m/z* = 283.0 [M + Na]⁺.

S-(4-Chlorophenyl) *O,O*-diethyl phosphorothioate (**3e**).^[S2] Yellow oil (66%). ¹H NMR (300 MHz, CDCl₃) δ 7.54 – 7.45 (m, 2H), 7.35 – 7.28 (m, 2H), 4.29 – 4.07 (m, 4H), 1.31 (td, *J* = 7.1, 0.8 Hz, 6H). ¹³C NMR (75 MHz, CDCl₃) δ 135.2 (d, *J* = 5.2 Hz), 131.6 (d, *J* = 5.2 Hz), 129.9 (d, *J* = 2.9 Hz), 126.2 (d, *J* = 7.2 Hz), 64.1 (d, *J* = 6.2 Hz), 16.1 (d, *J* = 7.3 Hz). MS-ESI: *m/z* = 302.9 [M + Na]⁺.

S-(4-Fluorophenyl) *O,O*-diethyl phosphorothioate (**3f**).^[S2] Yellow oil (72%). ¹H NMR (300 MHz, CDCl₃) δ 7.53 (ddd, *J* = 8.8, 5.1, 2.1 Hz, 2H), 7.03 (t, *J* = 8.6 Hz, 2H), 4.24 – 4.08 (m, 4H), 1.29 (t, *J* = 7.1 Hz, 6H). ¹³C NMR (75 MHz, CDCl₃) δ 163.4 (dd, *J* = 250, 3.2 Hz), 136.8 (dd, *J* = 6.3, 3.7 Hz), 121.6 (dd, *J* = 6.8, 2.6 Hz), 116.5 (dd, *J* = 37.3, 22.3 Hz), 64.2 (d, *J* = 6.4 Hz), 16.1 (d, *J* = 7.2 Hz). MS-ESI: *m/z* = 286.8 [M + Na]⁺.

O,O-Diethyl *S*-(4-(trifluoromethyl)phenyl) phosphorothioate (**3g**).^[S1] Yellow oil (70%). ¹H NMR (300 MHz, CDCl₃) δ 7.74 – 7.68 (m, 2H), 7.60 (d, *J* = 8.6 Hz, 2H), 4.30 – 4.14 (m, 4H), 1.33 (td, *J* = 7.1, 0.8 Hz, 6H). ¹³C NMR (75 MHz, CDCl₃) δ 134.2 (d, *J* = 5.2 Hz), 132.0 (dd, *J* = 32.8 Hz, *J* = 1.8 Hz), 131.2 (d, *J* = 2.5 Hz), 130.8 (d, *J* = 2.6 Hz), 125.8 (q, *J* = 3.2 Hz), 123.6 (d, *J* = 272.5 Hz), 64.5 (d, *J* = 6.4 Hz), 16.0 (d, *J* = 7.2 Hz). MS-ESI: *m/z* = 337.0 [M + Na]⁺.

S-(4-Cyanophenyl) *O,O*-diethyl phosphorothioate (**3h**).^[S3] Yellow oil (73%). ¹H NMR (300 MHz, CDCl₃) δ 7.70 – 7.65 (m, 2H), 7.62 – 7.58 (m, 2H), 4.27 – 4.11 (m, 4H), 1.30 (td, *J* = 7.1, 0.8 Hz, 6H). ¹³C NMR (75 MHz, CDCl₃) δ 134.2 (d, *J* = 5.9 Hz), 134.0 (d, *J* = 6.7 Hz), 132.7 (d, *J* = 1.6 Hz), 118.1 (d, *J* = 1.4 Hz), 112.5 (d, *J* = 2.4 Hz), 64.7 (d, *J* = 6.4 Hz), 16.1 (d, *J* = 7.1 Hz). MS-ESI: *m/z* = 294.0 [M + Na]⁺.

O,O-Diethyl *S*-(3-nitrophenyl) phosphorothioate (**3i**).^[S3] Yellow oil (65%). ¹H NMR (300 MHz, CDCl₃) δ 8.41 (dd, *J* = 3.9, 1.9 Hz, 1H), 8.20 (ddd, *J* = 8.3, 2.8, 2.1 Hz, 1H), 7.90 (ddd, *J* = 7.8, 2.8, 1.8 Hz, 1H), 7.54 (t, *J* = 8.0 Hz, 1H), 4.29 – 4.14 (m, 4H), 1.32 (td, *J* = 7.1, 0.9 Hz, 6H). ¹³C NMR (75 MHz, CDCl₃) δ 148.4, 140.5 (d, *J* = 5.4 Hz), 140.0, 130.5, 129.7 (dd, *J* = 13.5, 9.8 Hz), 129.1 (dd, *J* = 15.2, 5.3 Hz), 124.1, 123.7, 64.7 (d, *J* = 6.5 Hz), 16.1 (d, *J* = 7.1 Hz). MS-ESI: *m/z* = 314.0 [M + Na]⁺.

S-(4-Acetylphenyl) *O,O*-diethyl phosphorothioate (**3j**).^[S3] Yellow oil (74%). ¹H NMR (300 MHz, CDCl₃) δ 7.92 – 7.87 (m, 2H), 7.69 – 7.61 (m, 2H), 4.27 – 4.11 (m, 4H), 2.58 (s, 3H), 1.30 (td, *J* = 7.1, 0.9 Hz, 6H). ¹³C NMR (75 MHz, CDCl₃) δ 197.3, 137.0 (d, *J* = 2.4 Hz), 134.0 (d, *J* = 5.7 Hz), 133.3 (d, *J* = 6.9 Hz), 129.1 (d, *J* = 1.8 Hz), 64.5 (d, *J* = 6.3 Hz), 26.7, 16.1 (d, *J* = 7.1 Hz). MS-ESI: *m/z* = 310.9 [M + Na]⁺.

Ethyl 4-((diethoxyphosphoryl)thio)benzoate (**3k**).^[S2] Yellow oil. ¹H NMR (300 MHz, CDCl₃) δ 7.98 (d, *J* = 8.2

Hz, 2H), 7.62 (dd, $J = 8.5, 1.8$ Hz, 2H), 4.35 (q, $J = 7.1$ Hz, 2H), 4.25 – 4.10 (m, 4H), 1.36 (t, $J = 7.1$ Hz, 3H), 1.29 (td, $J = 7.1, 0.8$ Hz, 6H). ^{13}C NMR (75 MHz, CDCl_3) δ 165.9, 133.8 (d, $J = 5.7$ Hz), 132.8 (d, $J = 6.9$ Hz), 130.8 (d, $J = 2.5$ Hz), 130.3 (d, $J = 1.8$ Hz), 64.4 (d, $J = 6.3$ Hz), 61.3, 16.1 (d, $J = 7.2$ Hz), 14.4. MS-ESI: $m/z = 341.0$ [M + Na] $^+$.

O,O-Diethyl *S*-(*naphthalen-1-yl*) phosphorothioate (**3l**).^[S3] Yellow oil (80%). ^1H NMR (300 MHz, CDCl_3) δ 8.53 (d, $J = 8.4$ Hz, 1H), 7.92 – 7.84 (m, 3H), 7.63 – 7.43 (m, 3H), 4.22 – 4.02 (m, 4H), 1.18 (td, $J = 7.1, 0.6$ Hz, 6H). ^{13}C NMR (75 MHz, CDCl_3) δ 135.3 (d, $J = 5.6$ Hz), 134.8 (d, $J = 4.1$ Hz), 134.3 (d, $J = 2.3$ Hz), 130.4 (d, $J = 3.5$ Hz), 128.6, 127.1, 126.6, 125.9 (dd, $J = 17.5, 2.1$ Hz), 123.8 (d, $J = 8.1$ Hz), 64.3 (d, $J = 6.5$ Hz), 16.0 (d, $J = 7.2$ Hz). MS-ESI: $m/z = 319.0$ [M + Na] $^+$.

O,O-Dimethyl *S*-phenyl phosphorothioate (**3m**).^[S4] Yellow oil (87%). ^1H NMR (300 MHz, CDCl_3) δ 7.57 – 7.51 (m, 2H), 7.37 – 7.30 (m, 3H), 3.82 (s, 3H), 3.77 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 134.7 (d, $J = 5.2$ Hz), 129.4 (dd, $J = 21.7, 2.6$ Hz), 126.0 (d, $J = 7.3$ Hz), 54.3 (d, $J = 6.1$ Hz). MS-ESI: $m/z = 240.8$ [M + Na] $^+$.

O,O-Diisopropyl *S*-phenyl phosphorothioate (**3n**).^[S1] Yellow oil (84%). ^1H NMR (300 MHz, CDCl_3) δ 7.61 – 7.55 (m, 2H), 7.34 – 7.29 (m, 3H), 4.75 (ddt, $J = 12.4, 8.7, 6.2$ Hz, 2H), 1.31 (d, $J = 6.2$ Hz, 6H), 1.24 (d, $J = 6.2$ Hz, 6H). ^{13}C NMR (75 MHz, CDCl_3) δ 134.6 (d, $J = 5.5$ Hz), 129.6 (d, $J = 5.2$ Hz), 128.7 (d, $J = 1.8$ Hz), 127.4 (d, $J = 5.2$ Hz), 73.4 (d, $J = 5.5$ Hz), 23.9 (d, $J = 4.1$ Hz), 23.6 (d, $J = 6.0$ Hz). MS-ESI: $m/z = 297.0$ [M + Na] $^+$.

O,O-Dibenzyl *S*-phenyl phosphorothioate (**3o**).^[S4] Yellow oil (81%). ^1H NMR (300 MHz, CDCl_3) δ 7.42 – 7.37 (m, 2H), 7.26 – 7.15 (m, 13H), 5.08 – 4.98 (m, 4H). ^{13}C NMR (75 MHz, CDCl_3) δ 135.4 (d, $J = 7.6$ Hz), 134.9 (d, $J = 5.3$ Hz), 129.3 (dd, $J = 18.0, 2.7$ Hz), 128.6 (d, $J = 2.0$ Hz), 128.1, 126.0 (d, $J = 7.3$ Hz), 69.5 (d, $J = 6.3$ Hz). MS-ESI: $m/z = 370.9$ [M + Na] $^+$.

References

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Copies of ^1H and ^{13}C NMR Spectra





























