Iodine-Catalyzed Oxidative System for 3-Sulfenylation of Indoles with Disulfides using DMSO as oxidant under Ambient Conditions

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R=alkyl, aryl; R^1=H, Me; R^2=H, Me; R^3=H, Br, MeO   88-97%

Experimental

All chemicals (AR grade) were obtained from commercial sources and were used without further purification. Petroleum ether (PE) refers to the fraction boiling in the 60–90 °C range. The progress of the reactions was monitored by TLC (silica gel, Polygram SILG/UV 254 plates). Column chromatography was performed on Silicycle silica gel (200–300 mesh). Melting points were obtained using aYamato melting point apparatus Model MP-21 and are uncorrected. IR spectra were recorded on a Shimadzu spectrophotometer using KBr discs. ^{1}H and ^{13}C NMR spectra were obtained using a Bruker DRX 500 (500 MHz) spectrometer in $CDCl_3$ or DMSO-d_6 with TMS as the internal standard. All the products are known compounds and they were identified by comparison of their physical and spectral data with those reported in the literature.

General procedure for iodine-catalyzed 3-sulfenylation of indoles with disulfides

A mixture of indole **1** (1 mmol), disulfide **2** (0.5 mmol) and DMSO (3 mmol) were dissolved in DMC (2ml) at 40℃ in a flask, then iodine (0.05 mmol, 5 mol%) was added. The reaction proceeded under an air atmosphere for the indicated time until complete consumption of starting material as monitored by TLC. The solution was diluted with DMC (8 ml), washed with H_2O (3× 10 mL), and then the organic layer was separated and concentrated under vacuum and the crude product was purified by column chromatography (PE:EtOAc, 15:1) or recrystallization (PE:EtOAc, 5:1) to provide the analytically pure product **3**.

3-(Phenylthio)-*1H*-indole (3a)

White solid; mp 150-151℃ (Lit.[11f] 149-151℃).

IR (KBr): 3412, 3126, 3051, 1651, 1579, 1477, 1438, 1406, 1234, 736.

^{1}H NMR (500 MHz, DMSO-d_6): δ = 11.68 (br s,1 H), 7.76 (s, 1H), 7.49 (d, 1H, J=8.0 Hz), 7.39 (d, 1H,J=7.5 Hz), 7.17-7.21 (m, 3H), 7.05-7.08 (m, 2H), 7.02 (d, 2H, J=8.0 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ=139.2, 136.5, 130.7, 129.1, 128.7, 125.9, 124.8, 123.1, 120.9, 119.7, 111.6, 102.8.

3-(p-Tolylthio)-*1H*-indole (3b)

White solid; mp 123-125℃. (Lit.[3a] 125.0-126.0℃).

1H NMR (500 MHz, CDCl3):δ= 8.37 (br s, 1 H), 7.64 (d, 1H, J=8.0 Hz), 7.50 (d, 1H, J=2.5 Hz), 7.46 (d, 1H, J=8.0 Hz), 7.27-7.30 (m, 1H), 7.17-7.20 (m, 1H), 7.06 (d, 2H, J=8.0 Hz), 7.00 (d, 2H, J=8.0 Hz), 2.28 (s, 3H).

3-[(4-Methoxyphenyl)thio]-*1H*-indole (3c)

Pale-yellow solid; mp 111-113℃.(Lit.[7] 112.2-114.1℃)

^{1}H NMR (500 MHz, DMSO-d_6): δ = 11.58 (br s, 1 H), 7.72 (d, 1H, J=2.5 Hz), 7.46 (d, 1H, J=8.0 Hz), 7.42 (d, 1H, J=8.0 Hz), 7.14-7.18 (m, 1H), 7.04-7.08 (m, 3H), 6.79-6.82 (m, 2H), 3.67 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ=157.8, 136.5, 130.0, 129.5, 129.0, 128.6, 123.0, 120.8, 119.7, 114.5, 111.5, 104.7, 55.3.

3-[(2-Aminophenyl)thio]-*1H*-indole (3d)

White solid; mp93-94.℃. (Lit.[15] 93-95℃).

^{1}H NMR (500 MHz, DMSO-d_6): δ = 11.47 (br s,1 H), 7.73-7.74 (m, 1H), 7.52 (d, 1H, J=8.0 Hz), 7.42 (d, 1H, J = 8.0 Hz), 7.12-7.15 (m, 1H), 7.00-7.06 (m, 2H), 6.87-6.91 (m, 1H), 6.65 (d, 1H, J=8.0 Hz), 6.39-6.42 (m, 1H), 5.27 (s, 2H).

3-[(4-Chlorophenyl)thio]-*1H*-indole (3e)

White solid; mp 126-128℃. (Lit.[3a] 127.5-128.3℃).

^{1}H NMR (500 MHz, DMSO-d_6): δ=11.74 (br s, 1 H), 7.79 (d, 1H, J=2.5 Hz), 7.50 (d, 1H, J=8.0 Hz), 7.38 (d, 1H, J=8.0 Hz), 7.26 (dd, 2H, J = 2.0 Hz, 7.0 Hz), 7.18-7.21 (m, 1H), 7.06-7.09 (m, 1H),7.01 (dd, 2H, J =2.0 Hz, 7.0 Hz).

3-[(4-Bromophenyl)thio]-*1H*-indole (3f)

White solid; mp 144-146℃.

IR (KBr): 3385, 2922, 1653, 1556, 1498, 1471, 1410, 1234, 1080, 1003, 808, 748.

^{1}H NMR (500 MHz, DMSO-d_6): δ= 11.74 (br s, 1 H), 7.79 (d, 1H, J=2.5 Hz), 7.50 (d, 1H, J=8.0 Hz), 7.37-7.40 (m, 3H), 7.18-7.21 (m, 1H),7.05-7.10 (m, 1H), 6.94-6.95 (d, 2H, J = 8.5 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): δ=138.5, 136.5, 131.6, 130.7, 128.8, 127.4, 123.2, 121.1, 119.5, 118.3, 111.7, 102.3.

3-[(4-Nitrophenyl)thio]-*1H*-indole (3g)

Yellow solid; mp 176-178℃. (Lit.[7] 176.1-178.0℃)

^{1}H NMR (500 MHz, $CDCl_3$): δ=8.71 (br s, 1 H), 8.00-8.03 (m, 2H), 7.52-7.57 (m, 3H), 7.32-7.35 (m, 1H), 7.20-7.24 (m, 1H), 7.14-7.17 (m, 2H).

3-(Benzylthio)-*1H*-indole (3h)

Yellow solid; mp 84-85℃. (Lit.[7] 85.2-87.0℃)

^{1}H NMR (500 MHz, DMSO-d_6): δ= 11.29 (br s, 1 H), 7.53 (d, 1H, J=8.0 Hz), 7.40 (d, 1H, J=8.0 Hz), 7.27 (d, 1H, J=2.5 Hz), 7.17-7.24 (m, 3H), 7.12-7.15 (m, 3H), 7.04-7.07 (m, 1H), 3.88 (s, 2H).

^{13}C NMR (125 MHz, $CDCl_3$): δ=139.0, 136.2, 129.8, 129.2, 129.0, 128.2, 126.7, 122.7, 120.5, 119.3, 111.4, 105.3, 41.0.

1-Methyl-3-(phenylthio)-*1H*-indole (3j)

White solid; mp 86-87℃. (Lit.[7] 84.9-87.2℃)

IR (KBr): 3107, 3045, 2943, 2904, 2874, 1631, 1581, 1479, 1336, 1244, 1126, 740.

^{1}H NMR (500 MHz, $CDCl_3$): δ=7.64 (d, 1H, J=8.0 Hz), 7.42 (d, 1H, J=8.5 Hz), 7.36 (s, 1H), 7.31-7.34 (m, 1H), 7.16-7.21 (m, 3H), 7.12-7.14 (m, 2H), 7.06-7.08 (m, 1H), 3.88 (s, 3H).

2-Methyl-3-(phenylthio)-*1H*-indole (3k)

White solid; mp109-111℃. (Lit.[7] 110.9-111.2℃)

IR (KBr): 3402, 3053, 2912, 2835, 1768, 1614, 1583, 1477, 1220, 1078, 1022, 744.

^{1}H NMR (500 MHz, $CDCl_3$): δ=8.22 (br s, 1 H), 7.59 (d, 1H, J=8.0 Hz), 7.37 (d, 1H, J=8.0 Hz), 7.21-7.25 (m, 1H), 7.15-7.20 (m, 3H), 7.06-7.09 (m, 3H), 2.54 (s, 3H).

2-Methyl-3-(p-Tolylthio)-*1H*-indole (3l)

White solid; mp 97-99℃. (Lit.[7] 98.2-100.0℃)

^{1}H NMR (500 MHz, DMSO-d_6): δ= 11.60 (br s, 1 H), 7.37 (d, 1H, J=8.0 Hz), 7.31 (d, 1H, J=8.0Hz), 7.08-7.11 (m, 1H), 6.99-7.02 (m, 3H), 6.87 (d, 2H, J=8.0 Hz), 2.44 (s, 3H), 2.19 (s, 3H).

5-Bromo-3-(phenylthio)-*1H*-indole (3m)

White solid; mp 121-122℃. (Lit.[7] 120.9-123.1℃)

^{1}H NMR (500 MHz, $CDCl_3$): δ= 8.45 (br s, 1 H), 7.78 (s, 1H), 7.52 (d, 1H, J=2.5 Hz), 7.33-7.39 (m, 2H), 7.19-7.22 (m, 2H), 7.08-7.11 (m, 3H).

5-Bromo-3-(p-Tolylthio)-*1H*-indole (3n)

Oil; (Lit.[11e])

^{1}H NMR (500 MHz, DMSO-d_6): δ= 11.86 (br s, 1 H), 7.82 (d, 1H, J=3.0 Hz), 7.45-7.47 (m, 2H), 7.28-7.30 (m, 1H), 7.04 (d, 2H, J=8.0 Hz), 6.95 (d, 2H, J=8.0 Hz), 2.20 (s, 3H).

5-Methoxy-3-(phenylthio)-*1H*-indole (3o)

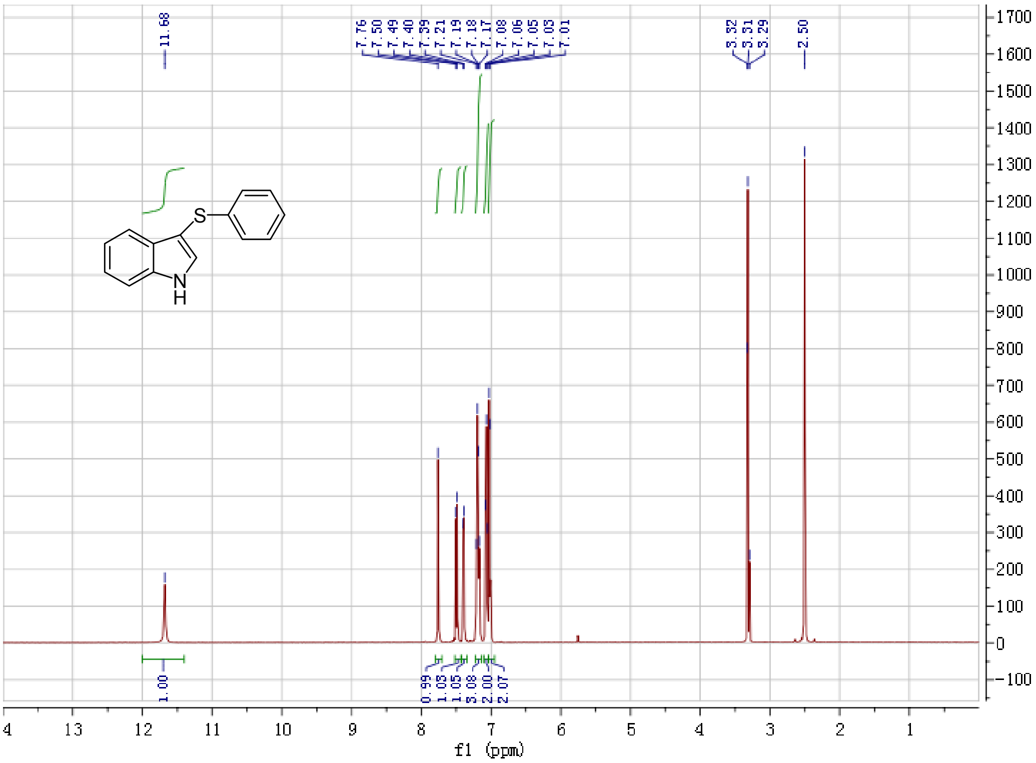
Colorless crystals; mp 78-79℃. (Lit.[11a] 78-79℃)

IR (KBr): 3412, 3066, 2958, 2937, 2835, 1680, 1627, 1577, 1475, 1282, 1201, 1095, 862, 738.

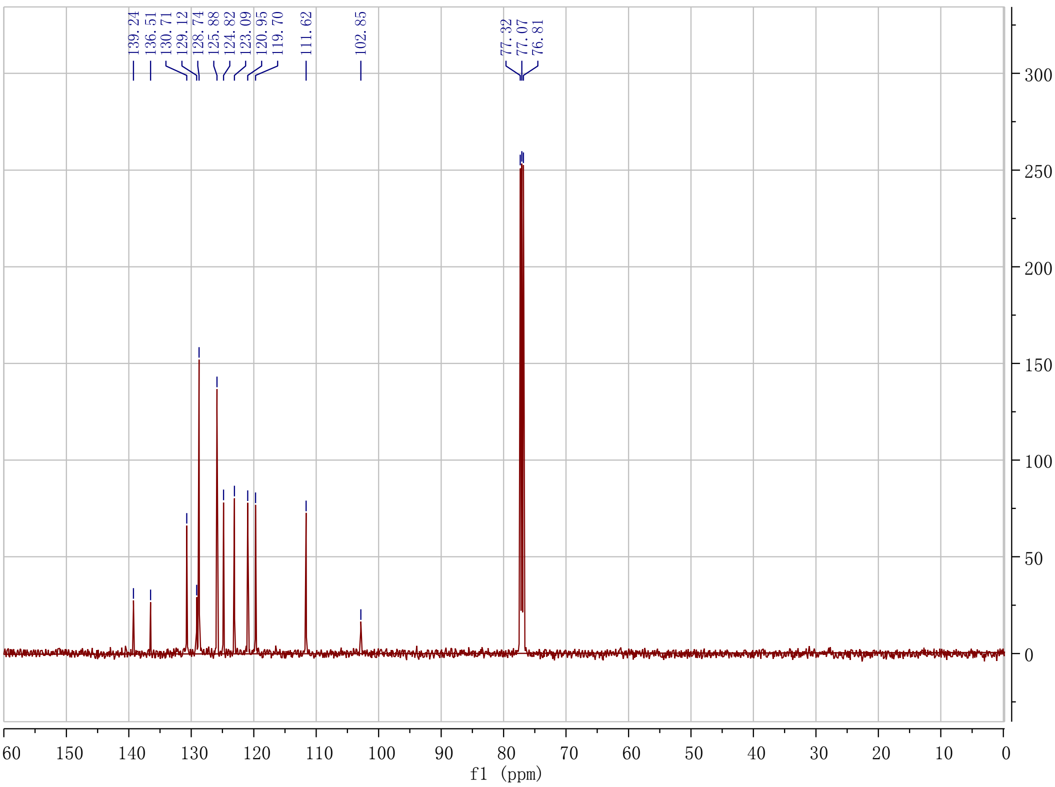
^{1}H NMR (500 MHz, $CDCl_3$): δ=8.34 (br s, 1 H), 7.47 (dd, 1H, J=2.5Hz, 10.0 Hz), 7.35 (d, 1H, J=8.5 Hz), 7.18-7.21 (m, 2H), 7.12-7.14 (m, 2H), 7.06-7.10 (m, 2H), 6.94 (dd, 1H, J= 2.5 Hz, 10.0 Hz), 3.81 (s, 3H).

3-(Phenylthio)-*1H*-indole (3a)

^{1}H NMR (500 MHz, DMSO-d_6)

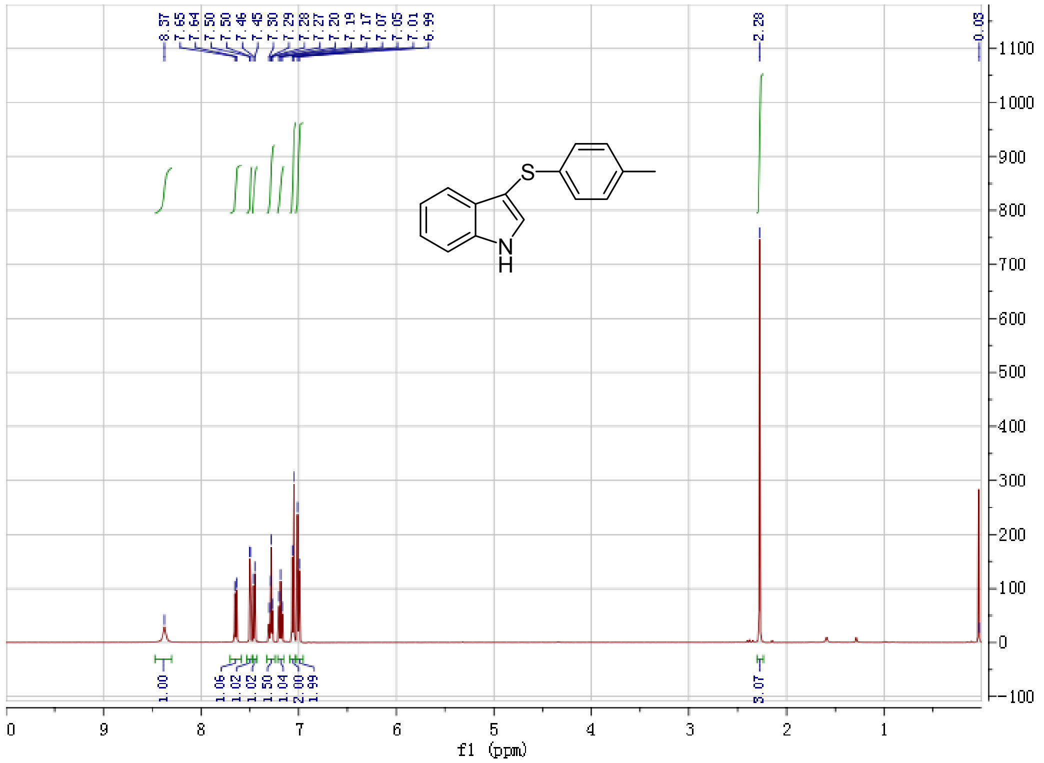


^{13}C NMR (125 MHz, $CDCl_3$)



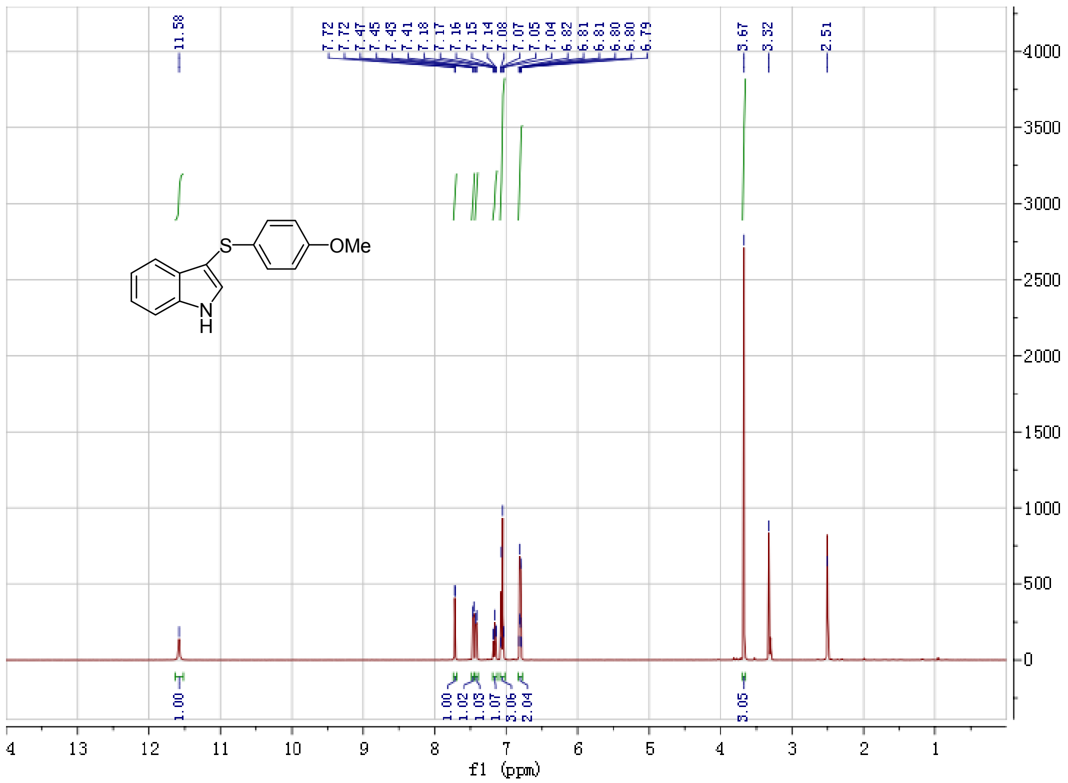
3-(*p*-Tolylthio)-*1H*-indole (3b)

^{1}H NMR (500 MHz, $CDCl_3$)



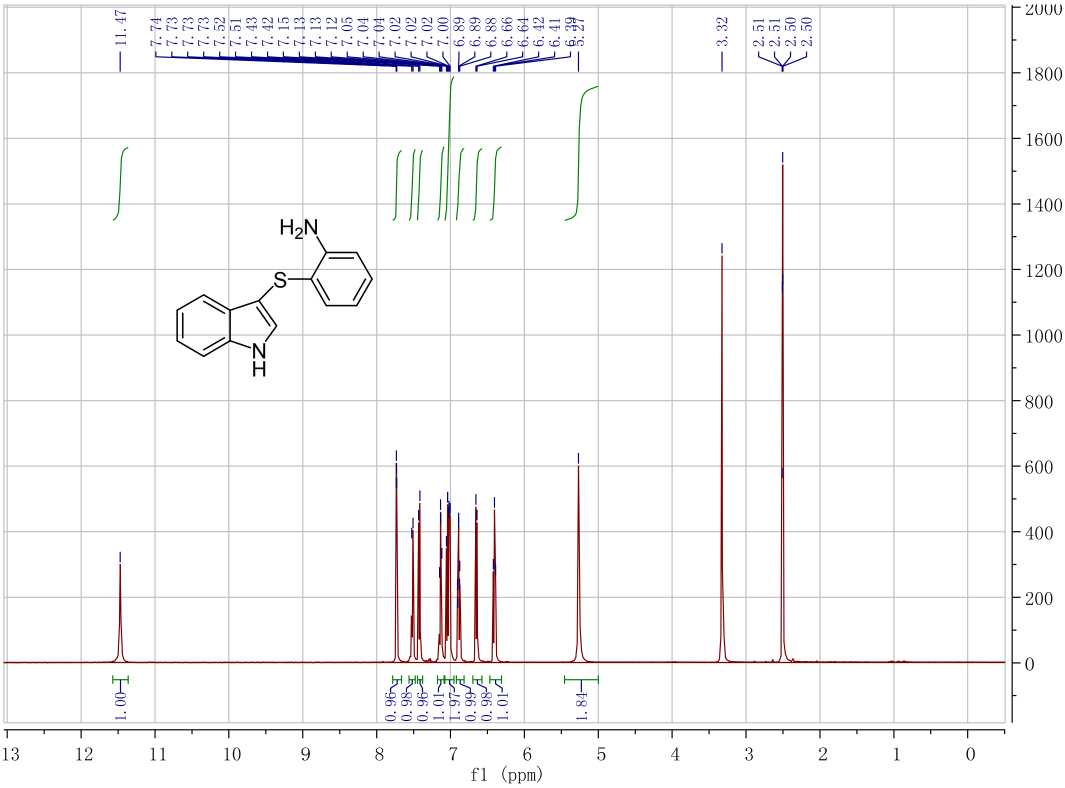
3-[(4-Methoxyphenyl)thio]-*1H*-indole (3c)

^{1}H NMR (500 MHz, DMSO-d_6)



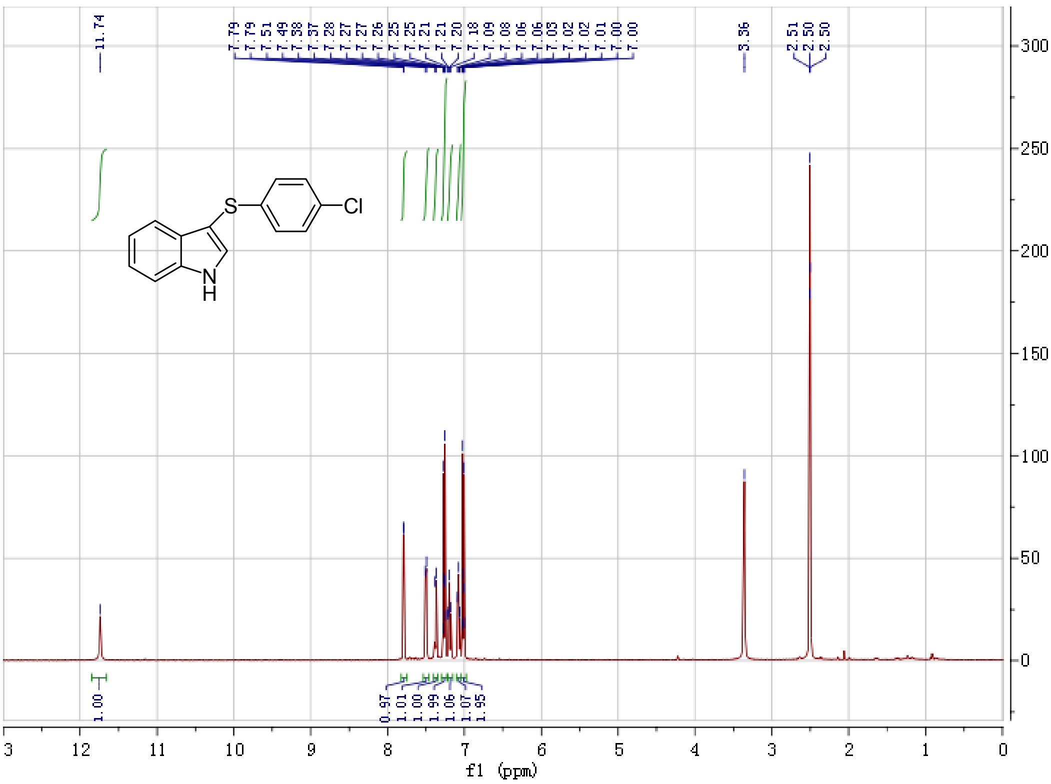
3-[(2-Aminophenyl)thio]-*1H*-indole (3d)

^{1}H NMR (500 MHz, DMSO-d_6)



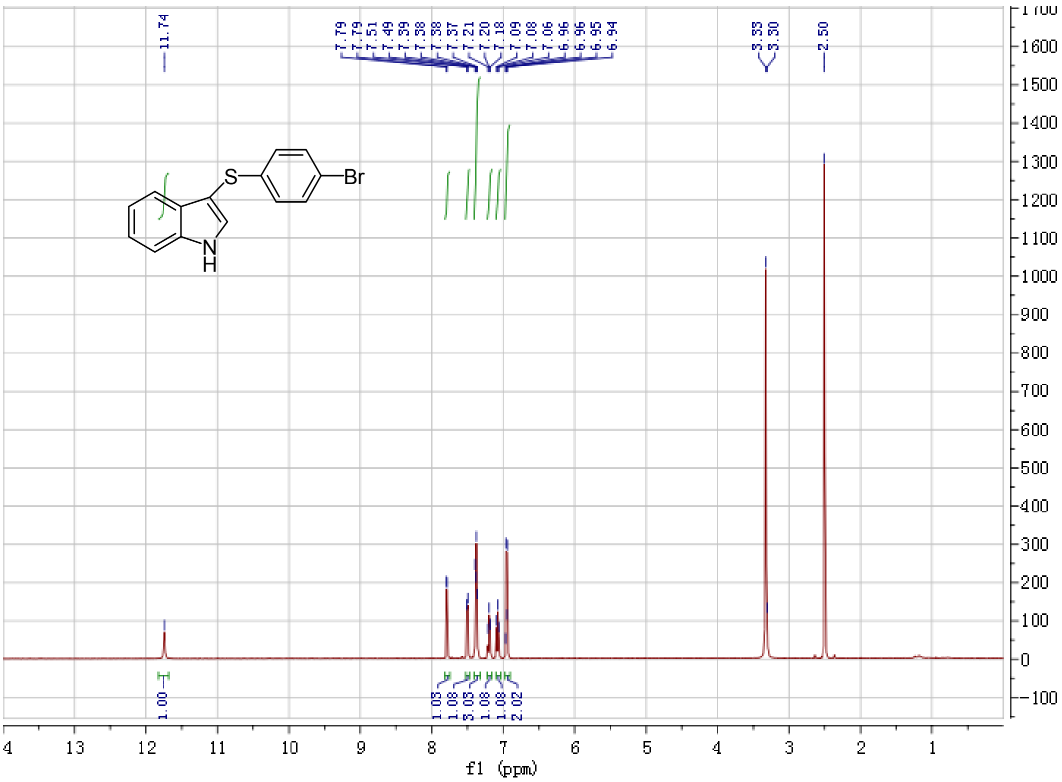
3-[(4-Chlorophenyl)thio]-*1H*-indole (3e)

^{1}H NMR (500 MHz, DMSO-d_6)

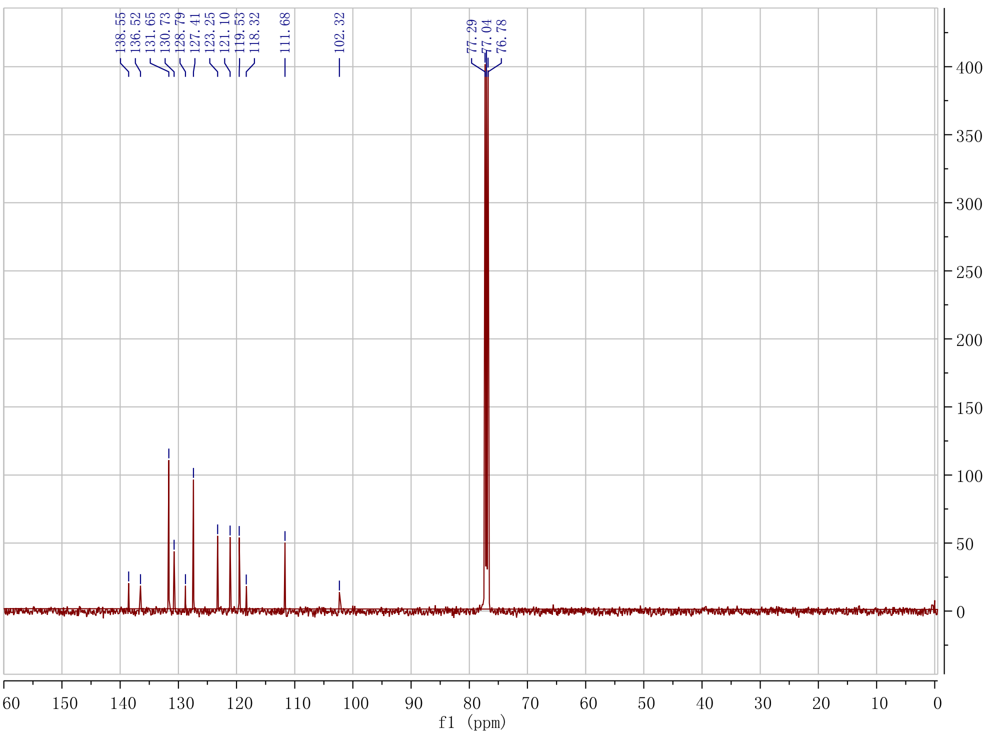


3-[(4-Bromophenyl)thio]-*1H*-indole (3f)

^{1}H NMR (500 MHz, DMSO-d_6)



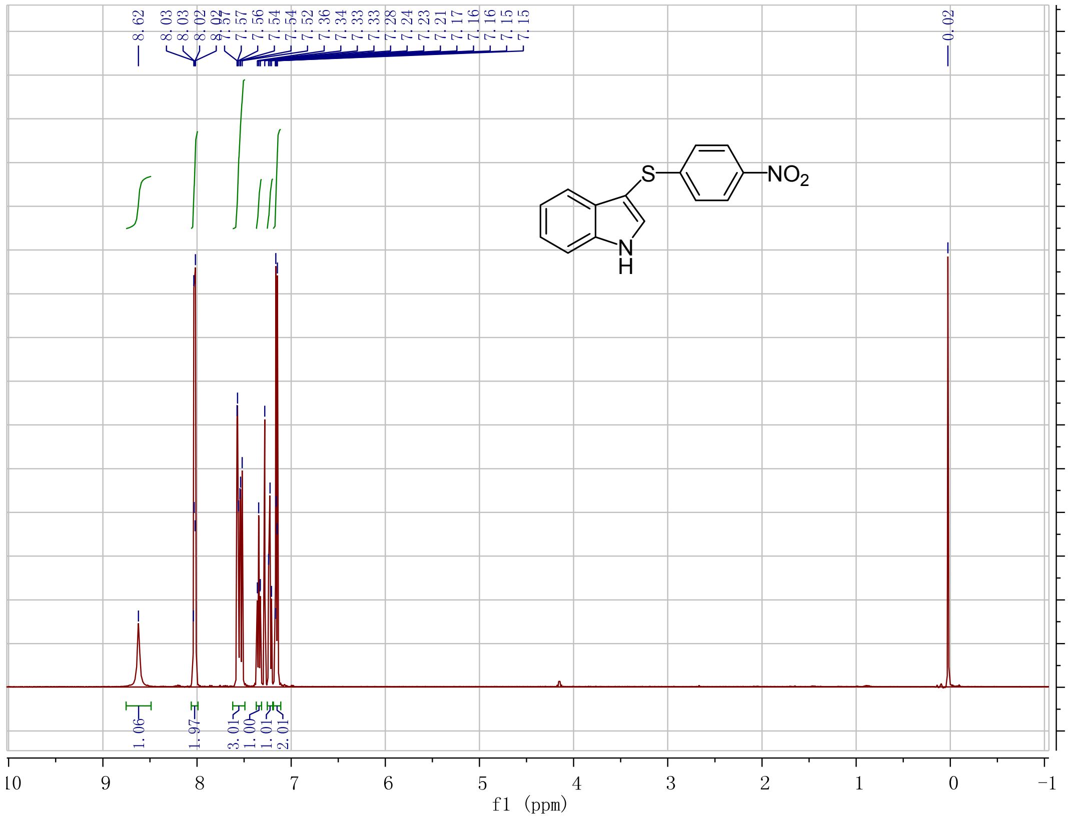
^{13}C NMR (125 MHz, $CDCl_3$)



Electronic Supplementary Material (ESI) for Green Chemistry

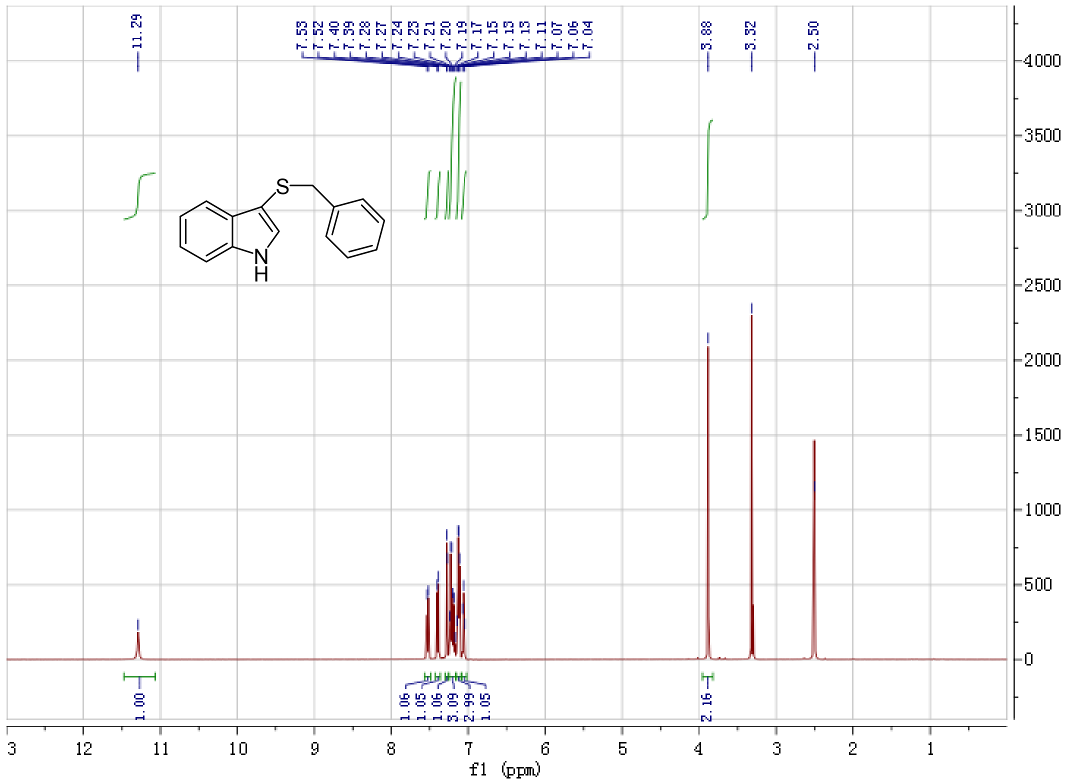
3-[(4-Nitrophenyl)thio]-*1H*-indole (3g)

^{1}H NMR (500 MHz, $CDCl_3$)

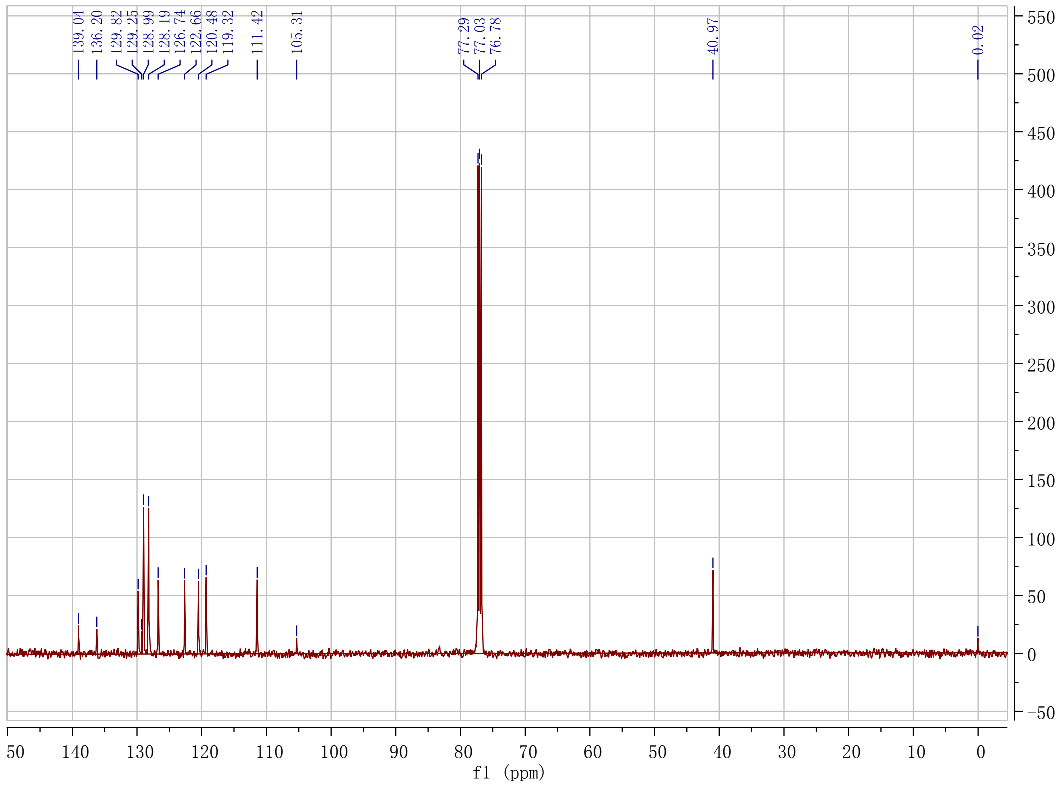


3-(Benzylthio)-*1H*-indole (3i)

^{1}H NMR (500 MHz, DMSO-d_6)

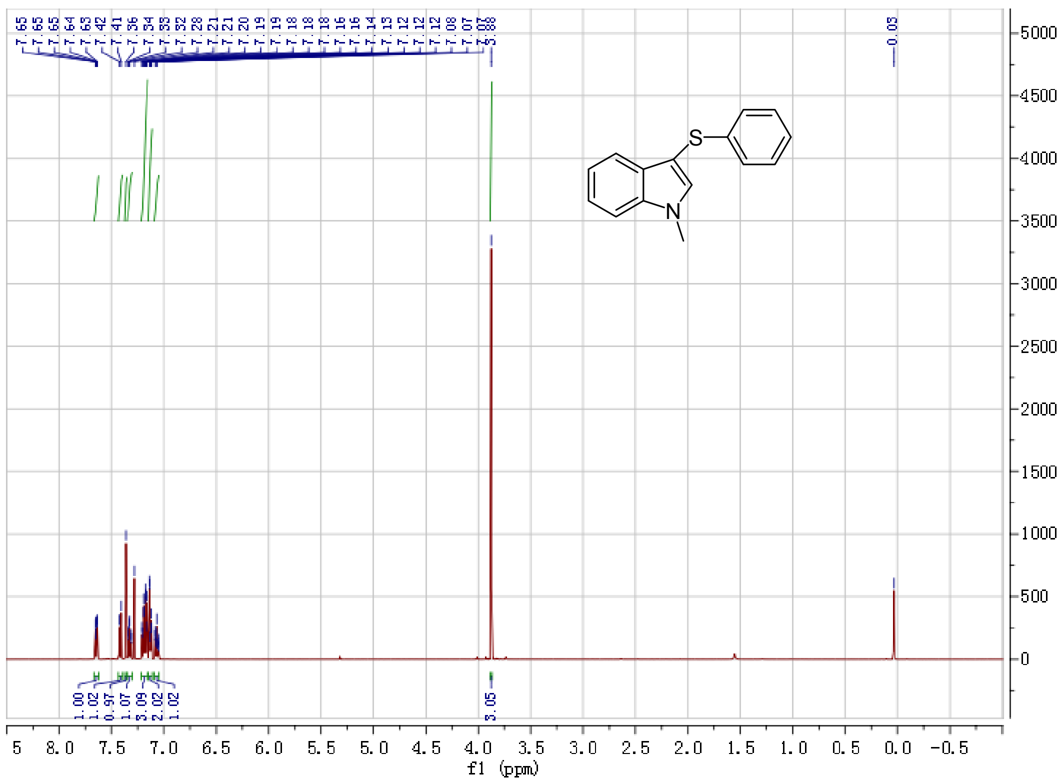


^{13}C NMR (125 MHz, $CDCl_3$)



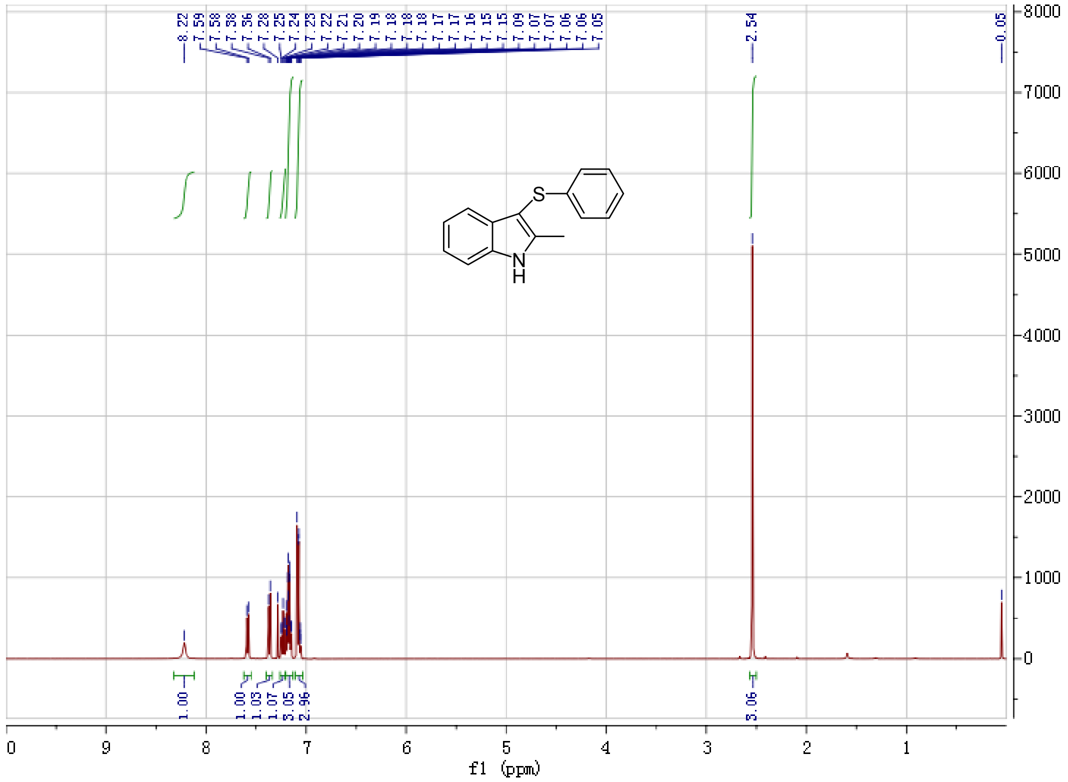
1-Methyl-3-(phenylthio)-1H-indole (3j)

^{1}H NMR (500 MHz, $CDCl_3$)



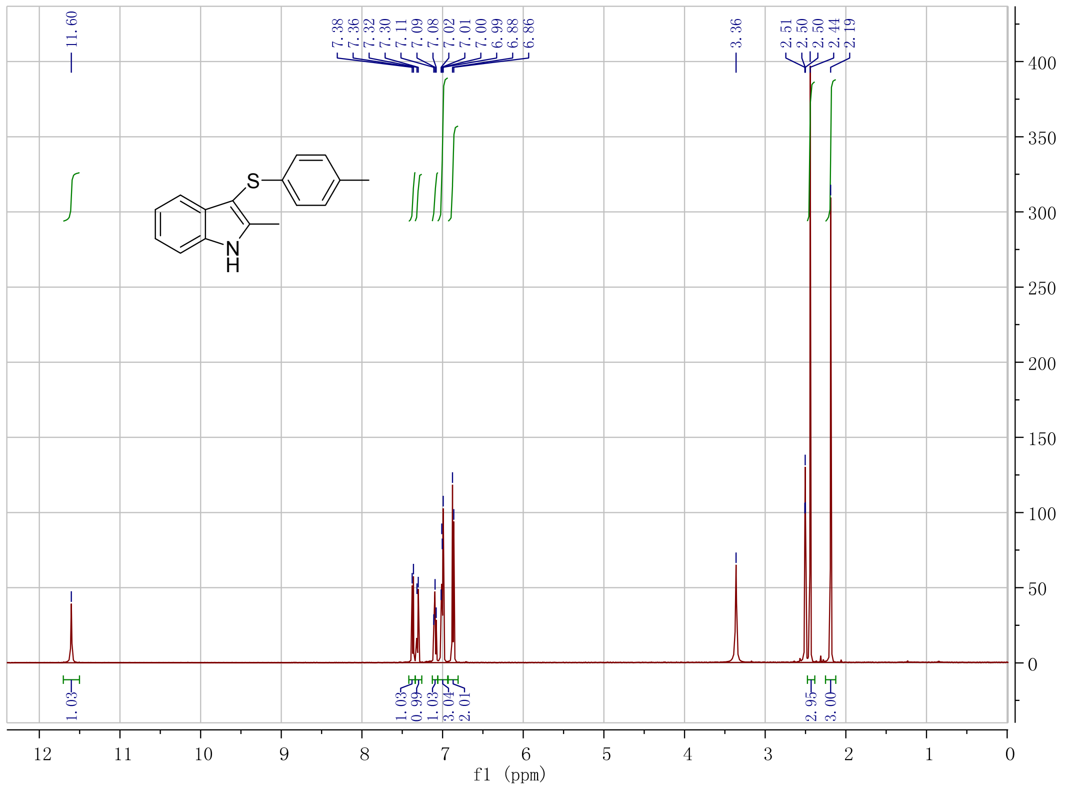
2-Methyl-3-(phenylthio)-1H-indole (3k)

^{1}H NMR (500 MHz, $CDCl_3$)



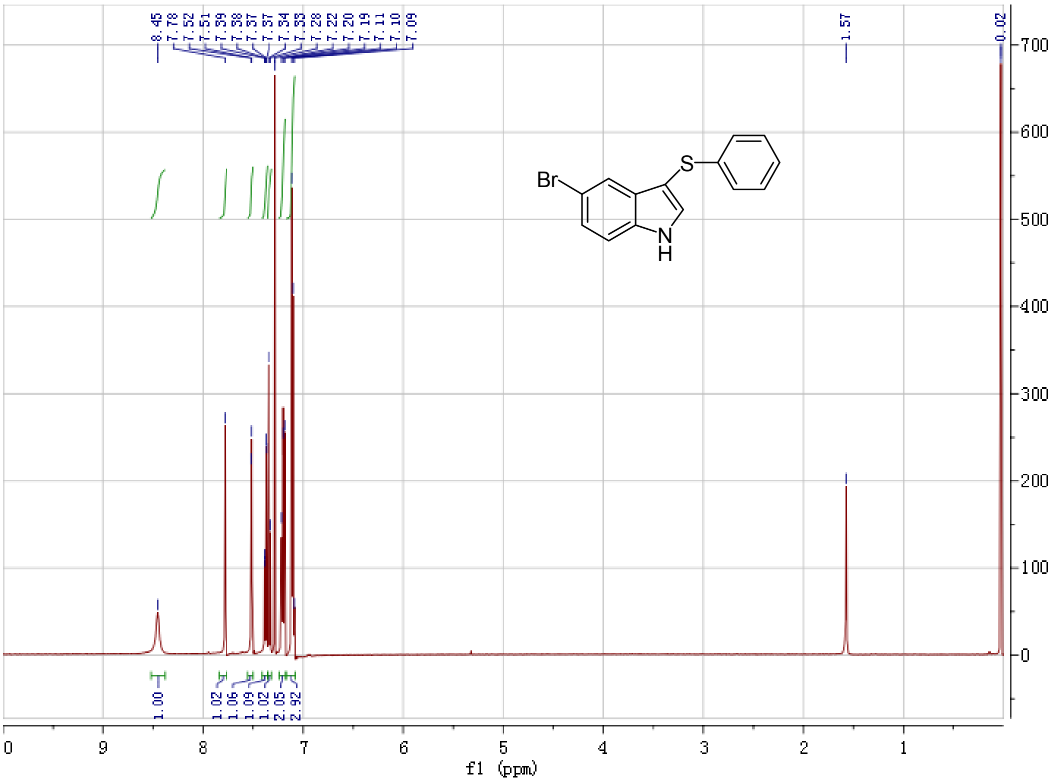
2-Methyl-3-(p-Tolylthio)-1H-indole (3l)

^{1}H NMR (500 MHz, DMSO-d_6)



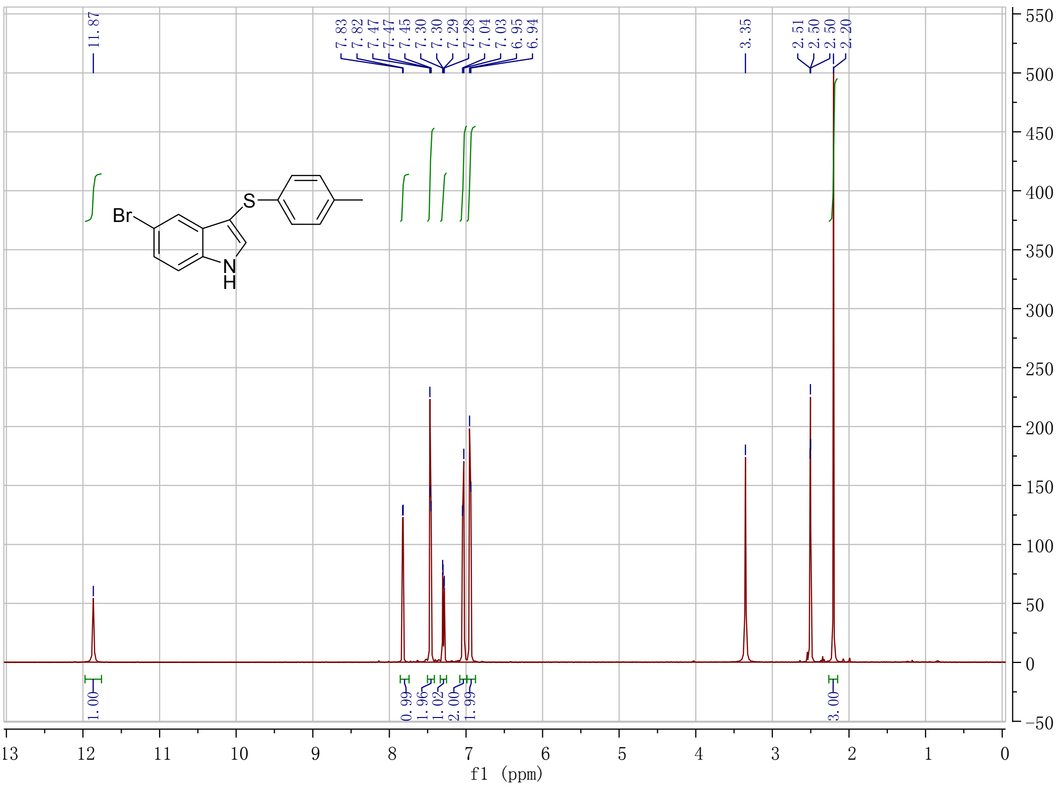
5-Bromo-3-(phenylthio)-1H-indole (3m)

[1]H NMR (500 MHz, $CDCl_3$)



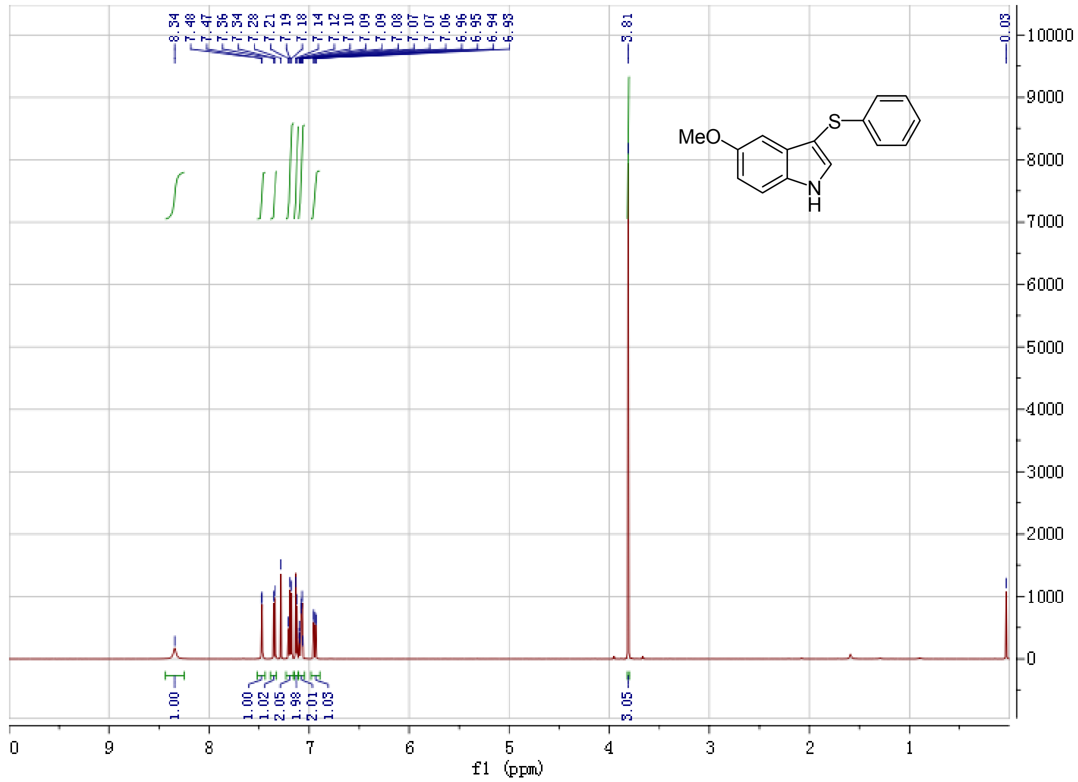
5-Bromo-3-(p-Tolylthio)-1H-indole (3n)

[1]H NMR (500 MHz, DMSO-d_6)



5-Methoxy-3-(phenylthio)-1H-indole (3o)

^{1}H NMR (500 MHz, $CDCl_3$)



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