Electronic Supplementary Material (ESI) for RSC Advances
This journal is © The Royal Society of Chemistry 2013

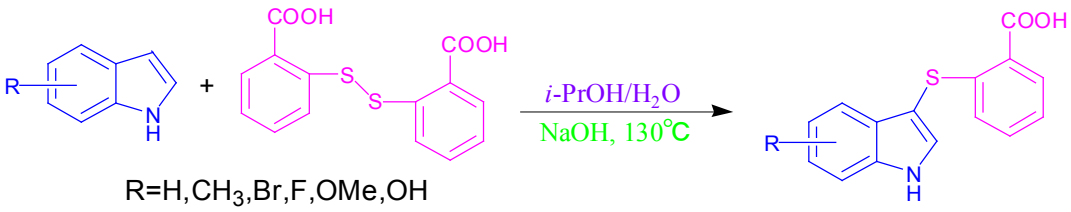
Supporting Information

Catalyst-free system for sulfenylation of free (*N*-H) indoles with 2,2'-dithiosalicylic acid under alkaline conditions

Xiaofei Zhou, Xinhua Li*

College of Chemistry and Materials Engineering, Wenzhou University, Zhejiang, Wenzhou 325035, P.R.China

Phone: (+86) 577-8659-6061, Fax: (+86) 577-8659-6063, email: lixinhua01@126.com



R=H,CH_3,Br,F,OMe,OH

This journal is © The Royal Society of Chemistry 2013

General Information

^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker advance DRX-500 MHz spectrometer in deuterated chloroform with tetramethylsilane (TMS) as an internal reference. All chemical shifts were reported relative to TMS at 0.0 ppm. Melting points were determined on a Yuhua digital melting-point apparatus and are uncorrected. Thin layer chromatography was done using commercical silica gel plates and chromatographic separations were performed using flash silica gel (200-300 mesh) columns. High resolution mass spectra were obtained using a micrOTOF-Q II. All reagents and chemicals (AR grade) were commercially obtained and used without further purification. Petroleum ether (PE) refers to the fraction boiling in the 60-90℃ range.

General Procedure for the Sulfenylation of Indoles with mercaptobenzoic acid

A mixture of an indole **1** (5mmol), a 2,2'-dithiosalicylic acid **2** (10 mmol) and sodium hydroxide (5 mmol) in 100 mL isopropanol/H_2O (v:v ratio = 9:6) was stirred at 130℃ for 48h or until complete consumption of the starting materials, as monitored by TLC. After the reaction was finished, the mixture was slowly cooled to room temperature, white solid was collected by filtration. In order to get pure product, the filtrate was poured into EtOAc (170 mL) and washed with sat. $Na_2S_2O_3$ soln (5×50 mL), followed by extraction of the aqueous layer with EtOAc (5×30 mL). The combined organic layer was dried (anhyd. Na_2SO_4) and concentrated under reduced pressure. The residue and the white solid were purified by flash chromatography (PE:EtOAc, 5:2) to afford the analytically pure sulfenylindole product **3**.

3-[(2-Carboxyphenyl)thio]-1*H*-indole (3a)

Yield, 75 %; A light brown solid; mp 254-255 °C; ^{1}H NMR (500 Hz, DMSO) δ 13.10 (s, 1H), 11.72 (s, 1H), 7.92 (dd, J = 7.7, 1.4 Hz, 1H), 7.73 (d, J = 2.6 Hz, 1H), 7.51 (d, J = 8.2 Hz, 1H), 7.31 (d, J = 7.9 Hz, 1H), 7.23-7.17 (m, 2H), 7.13-7.09 (m, 1H), 7.05 (t, J = 7.4 Hz, 1H), 6.68 (d, J = 7.6 Hz, 1H); ^{13}C NMR (126 MHz, DMSO) δ 167.4, 143.7, 136.9, 132.6, 132.0, 130.9, 128.7, 126.7, 125.6, 123.7, 122.1, 120.1,

This journal is © The Royal Society of Chemistry 2013

118.3, 112.4, 100.0. MS (ESI-Qq-TOF) m/z (amu) calcd for $C_{15}H_{12}NO_2S$ $[M + H]^+$: 270.0588. Found: 270.0583.

4-Methyl-3-[(2-Carboxyphenyl)thio]-1*H*-indole (3b)

Yield: 33%; White solid; mp 204.5-206.6℃; ^{1}H NMR(500MHz, DMSO) δ 11.72 (s,1H), 7.98 (d, J=7Hz, 1H), 7.69 (d, J=2.5Hz, 1H), 7.39 (d, J=8.5Hz, 1H), 7.33 (t, J=7.8Hz, 1H), 7.18 (t, J=7.3Hz, 1H), 7.11 (t, J=7.5Hz, 1H), 6.81 (dd, J=16.5, 7.5Hz, 2H), 2.47 (s, 3H); ^{13}C NMR (125 MHz, DMSO) δ 167.32, 145.96, 137.43, 133.16, 132.21, 130.87, 130.07, 126.59, 126.14, 125.91, 123.63, 122.20, 121.53, 110.30, 100.02, 17.91. MS (ESI-Qq-TOF) m/z (amu) calcd for $C_{16}H_{14}NO_2S$ $[M + H]^+$: 284.0740; Found: 284.0732.

7-Bromo-3-[(2-Carboxyphenyl)thio]-1*H*-indole (3c)

Yield: 44%; Light pink solid; mp 240.5℃-241.5℃; ^{1}H NMR (500MHz, DMSO) δ 12.00 (s, 1H), 7.94 (dd, J=8.0, 1.5Hz, 1H), 7.81 (d, J=3.0Hz, 1H), 7.44 (d, J=7.0Hz, 1H), 7.33 (d, J=7.5Hz, 1H), 7.26-7.23 (m, 1H), 7.15-7.12 (m, 1H), 7.03(t, J=7.5Hz, 1H), 6.66(d, J=8.0Hz, 1H); ^{13}C NMR (125 MHz, DMSO) δ 167.41, 142.99, 135.19, 133.93, 132.22, 130.99, 130.43, 126.69, 125.60, 124.88, 123.94, 121.68, 117.89, 104.97, 101.78. MS (ESI-Qq-TOF) m/z (amu) calcd for $C_{15}H_{11}BrNO_2S$ $[M + H]^+$: 347.9688; Found: 347.9676.

7-Fluoro-3-[(2-Carboxyphenyl)thio]-1*H*-indole (3d)

Yield: 60%; White solid; mp 222.7℃-224.1℃. ^{1}H NMR (500MHz,DMSO-) δ 13.13 (s, 1H), 12.25 (s, 1H), 7.93 (d, J=8.0Hz, 1H), 7.81 (d, J=2.5Hz, 1H), 7.24 (t, J=7.5, 1H), 7.14-7.11 (m, 2H), 7.05-7.02 (m, 2H), 6.66 (d, J=8.5Hz, 1H); MS (ESI-Qq-TOF) m/z (amu) calcd for $C_{15}H_{11}FNO_2S$ $[M + H]^+$: 288.0489; Found: 288.0479.

This journal is © The Royal Society of Chemistry 2013

7-Methyl-3-[(2-Carboxyphenyl)thio]-1*H*-indole (3e)

Yield: 53%; White solid; mp 234.8℃-237.5℃. ^{1}HNMR (500MHz, DMSO) δ 11.72 (s, 1H), 7.93 (dd, J=8.0, 1.5Hz, 1H), 7.72 (d, J=2.5Hz, 1H), 7.24-7.20 (m, 1H), 7.16-7.09 (m, 2H), 7.00-6.95 (m, 2H), 6.69 (d, J=8.5Hz, 1H), 2.53(s,3H). MS (ESI-Qq-TOF) m/z (amu) calcd for $C_{16}H_{14}NO_2S$ $[M + H]^+$: 284.0740; Found: 284.0734.

5-Methoxyl-3-[(2-Carboxyphenyl)thio]-1*H*-indole (3f)

Yield, 86 %; White solid; mp 202.3-203.7℃. ^{1}H NMR (500 MHz, DMSO) δ 11.58 (d, J = 1.6 Hz, 1H), 7.92 (dd, J = 7.7, 1.3 Hz, 1H), 7.65 (d, J = 2.7 Hz, 1H), 7.41 (d, J = 8.8 Hz, 1H), 7.28-7.21 (m, 1H), 7.11 (t, J = 7.5 Hz, 1H), 6.83 (dd, J = 8.8, 2.4 Hz, 1H), 6.75 (d, J = 2.3 Hz, 1H), 6.69 (d, J = 8.1 Hz, 1H), 3.66 (s, 3H); ^{13}C NMR (126 MHz, DMSO) δ 167.5, 154.4, 143.8, 133.1, 132.2, 131.8, 131.0, 129.6, 126.7, 125.5, 123.8, 113.3, 112.4, 99.7, 99.5, 55.3. MS (ESI-Qq-TOF) m/z (amu) calcd for $C_{16}H_{14}NO_3S$ $[M + H]^+$: 300.0694; Found: 300.0689.

5-Bromo-3-[(2-Carboxyphenyl)thio]-1*H*-indole (3g)

Yield, 68 %; Yellow solid; mp 231.9-232.7℃. ^{1}H NMR (500 MHz, DMSO): δ 13.18 (s, 1H), 11.94 (d, J = 1.5 Hz, 1H), 7.93 (dd, J = 7.8, 1.4 Hz, 1H), 7.81 (d, J = 2.6 Hz, 1H), 7.50 (d, J = 8.6 Hz, 1H), 7.40 (d, J = 1.8 Hz, 1H), 7.31 (dd, J = 8.6, 1.9 Hz, 1H), 7.28 -7.23 (m, 1H), 7.16-7.11 (m, 1H), 6.68-6.62 (m, 1H). ^{13}C NMR (126 MHz, DMSO): δ 167.41, 143.09, 135.71, 134.36, 132.26, 131.05, 130.66, 126.77, 125.46, 124.83, 123.98, 120.31, 114.59, 112.94, 99.83. MS (ESI-Qq-TOF) m/z (amu) calcd for $C_{15}H_{11}BrNO_2S$ $[M + H]^+$: 347.9693; Found: 347.9688.

This journal is © The Royal Society of Chemistry 2013

5-Methyl-3-[(2-Carboxyphenyl)thio]-1*H*-indole (3h)

Yield, 65 %; White solid; mp 247.3-248.6℃. ^{1}H NMR (500 MHz, DMSO): δ 11.60 (s, 1H), 7.92 (d, J = 7.7 Hz, 1H), 7.66 (d, J = 2.6 Hz, 1H), 7.40 (d, J = 8.3 Hz, 1H), 7.27-7.19 (m, 1H), 7.14-7.07 (m, 2H), 7.01 (d, J = 8.4 Hz, 1H), 6.67 (d, J = 8.2 Hz, 1H), 2.31 (s, 3H). ^{13}C NMR (126 MHz, DMSO): δ 167.51, 143.99, 135.31, 132.73, 132.17, 131.05, 129.03, 128.98, 126.62, 125.58, 123.89, 123.76, 117.80, 112.19, 99.27, 21.15. MS (ESI-Qq-TOF) m/z (amu) calcd for $C_{16}H_{14}NO_2S$ $[M + H]^+$: 284.0745; Found: 284.0740.

5-Hydroxyl-3-[(2-Carboxyphenyl)thio]-1*H*-indole (3i)

Yield, 42 %; White solid; mp 237.6-238.6℃. ^{1}H NMR (500 MHz, DMSO): δ 11.42 (d, J = 2.1 Hz, 1H), 8.82 (s, 1H), 7.90 (dd, J = 7.8, 1.5 Hz, 1H), 7.58 (d, J = 2.7 Hz, 1H), 7.30 (d, J = 8.6 Hz, 1H), 7.28-7.19 (m, 1H), 7.11 (td, J = 7.7, 1.1 Hz, 1H), 6.75-6.65 (m, 2H), 6.61 (d, J = 2.3 Hz, 1H). ^{13}C NMR (126 MHz, DMSO): δ 167.51, 151.75, 143.80, 132.76, 132.12, 131.22, 131.02, 129.71, 126.68, 125.65, 123.73, 112.98, 112.54, 102.11, 98.70. MS (ESI-Qq-TOF) m/z (amu) calcd for $C_{15}H_{12}NO_3S$ $[M + H]^+$: 286.0538; Found: 286.0532.

5-Fluoro-3-[(2-Carboxyphenyl)thio]-1*H*-indole (3j)

Yield, 68 %; Light yellow solid: mp 239.5-240.3℃. ^{1}H NMR (500 MHz, DMSO) δ 11.84 (d, J = 1.6 Hz, 1H), 7.93 (dd, J = 7.8, 1.4 Hz, 1H), 7.81 (d, J = 2.7 Hz, 1H), 7.53 (dd, J = 8.8, 4.4 Hz, 1H), 7.31-7.18 (m, 1H), 7.18- 7.09 (m, 1H), 7.04 (td, J = 9.2, 2.5 Hz, 1H), 6.99 (dd, J = 9.4, 2.5 Hz, 1H), 6.71-6.59 (m, 1H); ^{13}C NMR (126 MHz, DMSO) δ 167.5, 158.7, 156.8, 143.3, 134.8, 133.6, 132.2, 131.1, 129.5, 126.8, 125.5, 124.0, 113.8, 110.7, 110.5, 103.1, 102.9, 100.3. MS (ESI-Qq-TOF) m/z (amu) calcd for $C_{15}H_{10}FNO_2S$ $[M + H]^+$: 288.0494; Found: 288.0489.

This journal is © The Royal Society of Chemistry 2013

6-Fluoro-3-[(2-Carboxyphenyl)thio]-1*H*-indole (3k)

Yield, 51 %; White solid; mp 215.7-216.7 ℃. ^{1}H NMR (500 MHz, DMSO) δ 11.76 (s, 1H), 7.92 (dd, J = 7.7, 1.3 Hz, 1H), 7.73 (d, J = 2.5 Hz, 1H), 7.33-7.25 (m, 2H), 7.25 -7.19 (m, 1H), 7.12 (t, J = 7.2 Hz, 1H), 6.91 (td, J = 9.6, 2.3 Hz, 1H), 6.67 (d, J = 8.0 Hz, 1H). ^{13}C NMR (126 MHz, DMSO) δ 167.5, 160.3, 158.4, 143.4, 136.9, 133.4, 132.2, 131.0, 126.8, 125.6, 125.4, 123.9, 119.5, 108.9, 108.7, 100.5, 98.7, 98.4. MS (ESI-Qq-TOF) m/z (amu) calcd for $C_{15}H_{10}FNO_2S$ $[M + H]^+$: 288.0494; Found: 288.0489.

4-Fluoro-3-[(2-Carboxyphenyl)thio]-1*H*-indole (3l)

Yield, 41.72 %; White solid; mp 227.3-229.3 ℃. ^{1}H NMR (500 MHz, DMSO) δ 13.04 (s, 1H), 11.92 (s, 1H), 7.89 (dd, J=7.5, 1.5Hz, 1H), 7.70-7.63 (m, 1H), 7.32-7.23 (m, 2H), 7.14-7.08 (m, 2H), 6.76-6.72 (m, 2H). MS (ESI-Qq-TOF) m/z (amu) calcd for $C_{15}H_{11}FNO_2S$ $[M + H]^+$: 288.0489; Found: 288.0480.

3-Methyl -2-[(2-Carboxyphenyl)thio]-1*H*-indole (3m)

Yield, 20.34 %; White solid; mp 210.4-211.7 ℃. ^{1}H NMR (500 MHz, DMSO) δ 13.18 (s, 1H), 11.23 (s, 1H), 7.88 (dd, J=8.0, 1.5Hz, 1H), 7.49 (d, J=8.0Hz, 1H), 7.27-7.23 (m, 2H), 7.12-7.08 (m, 2H), 6.97 (t, J=7Hz, 1H), 6.41 (d, J=8.0Hz, 1H), 2.19 (s, 3H). MS (ESI-Qq-TOF) m/z (amu) calcd for $C_{16}H_{14}NO_2S$ $[M + H]^+$: 284.0740; Found: 284.0736.

This journal is © The Royal Society of Chemistry 2013

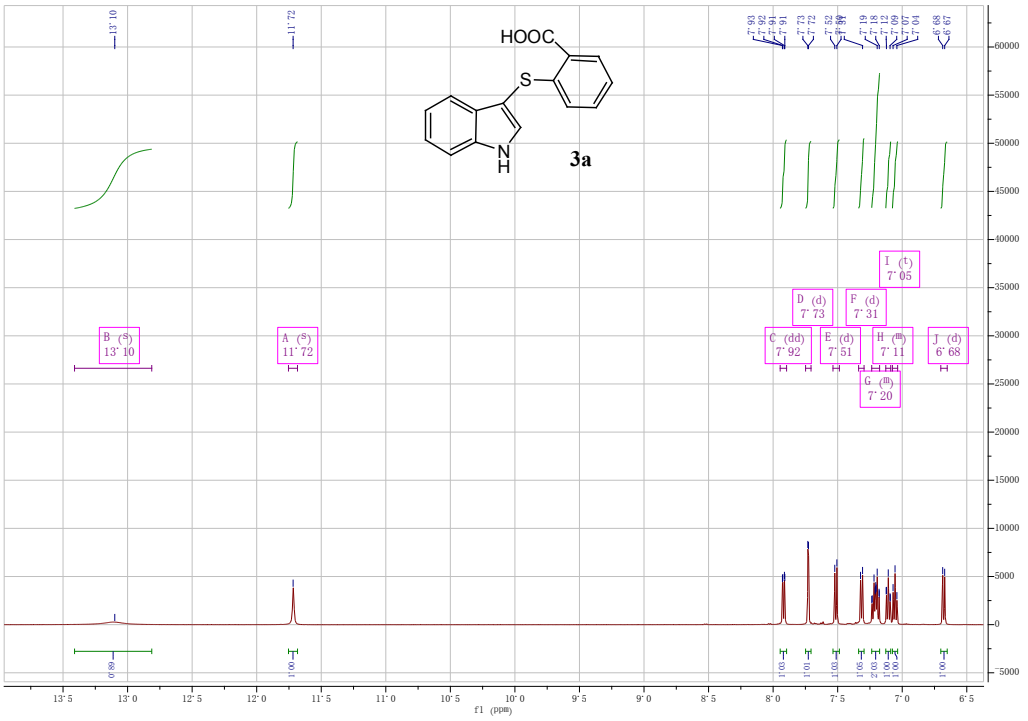


Figure S1. ^{1}H spectrum for 3-[(2-Carboxyphenyl)thio]-1*H*-indole (**3a**).

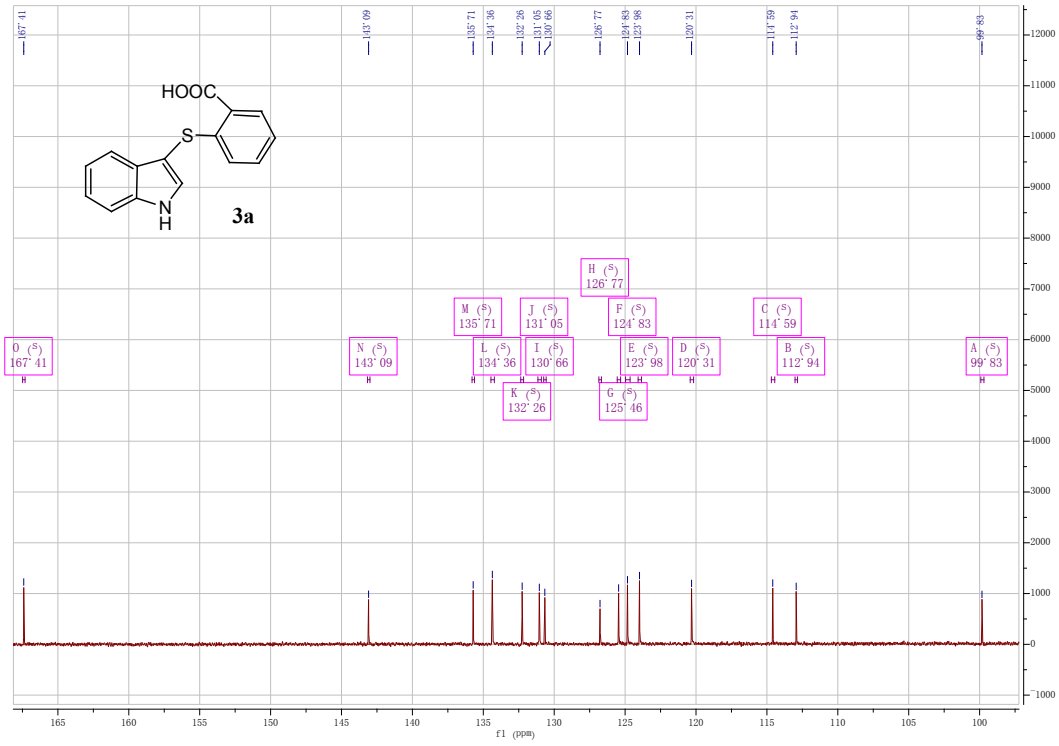


Figure S2. ^{13}C NMR spectrum for 3-[(2-Carboxyphenyl)thio]-1*H*-indole (**3a**).

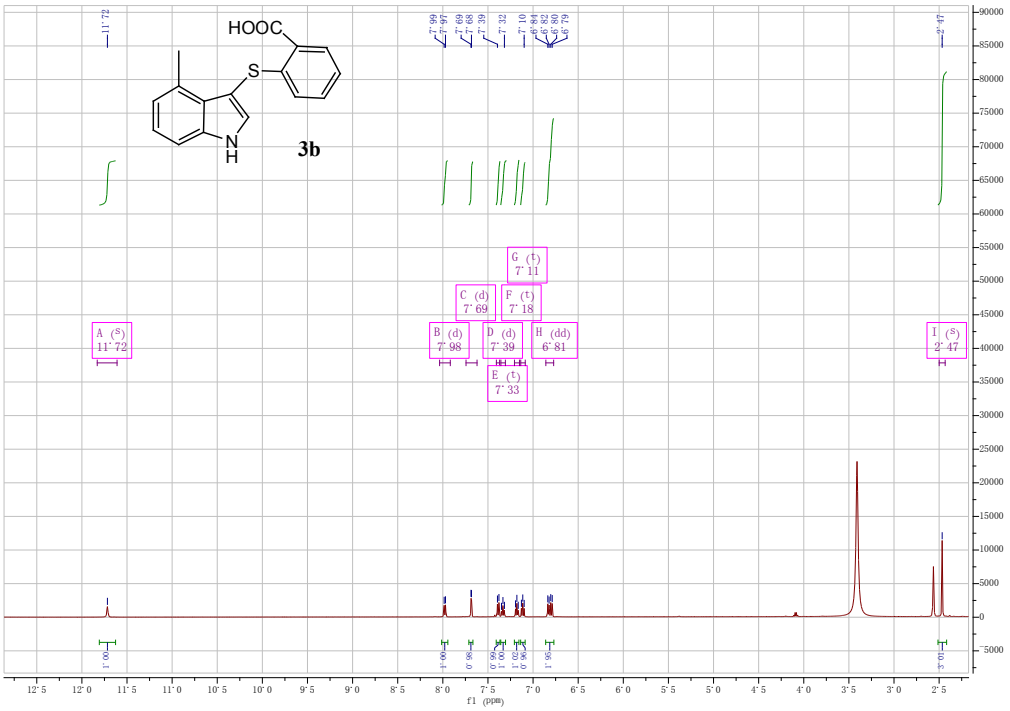


Figure S3. [1]H spectrum for 4-Methyl-3-[(2-Carboxyphenyl)thio]-1*H*-indole (**3b**)

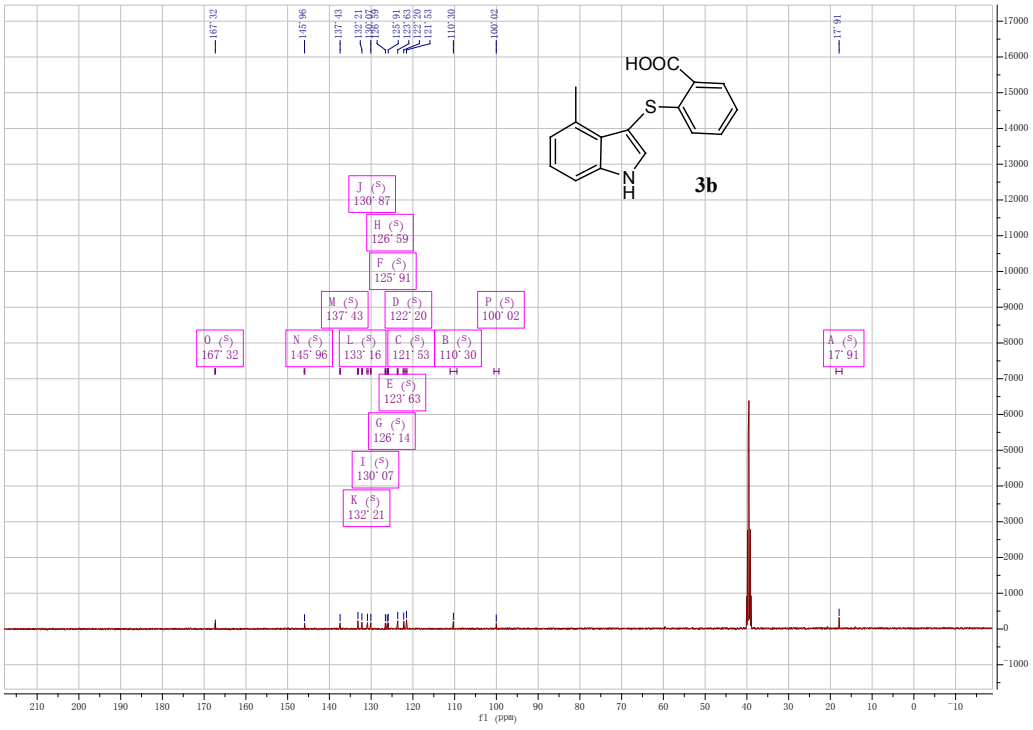


Figure S4. [13]C NMR spectrum for 4-Methyl-3-[(2-Carboxyphenyl)thio]-1*H*-indole (**3b**)

This journal is © The Royal Society of Chemistry 2013

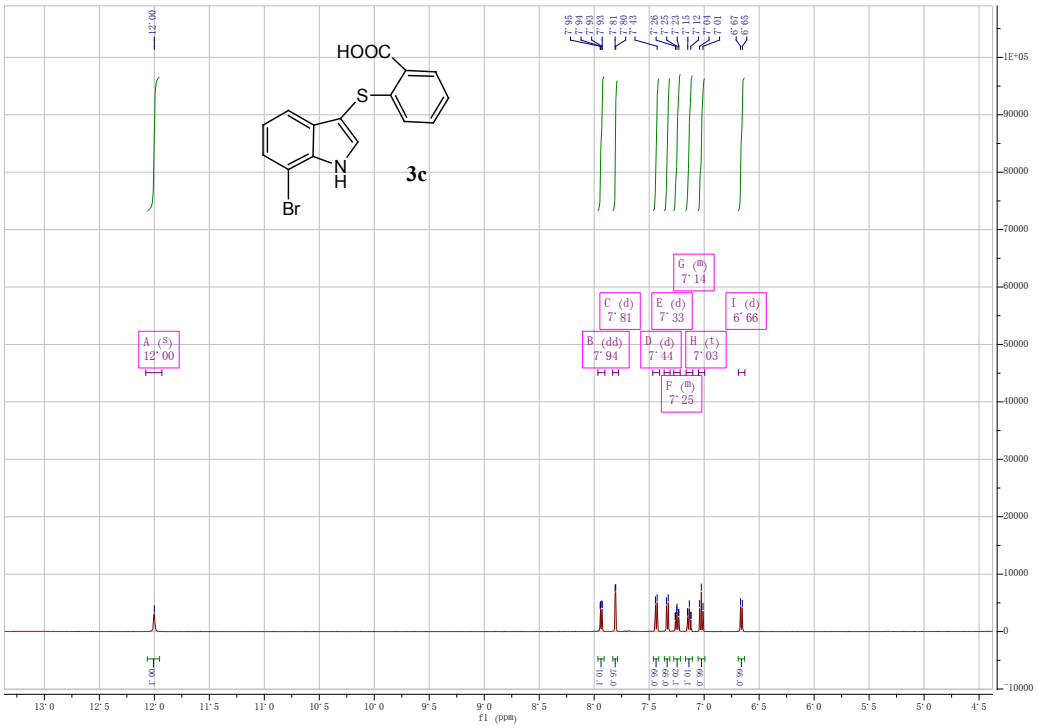


Figure S5. ^{1}H spectrum for 7-Bromo-3-[(2-Carboxyphenyl)thio]-1*H*-indole (**3c**)

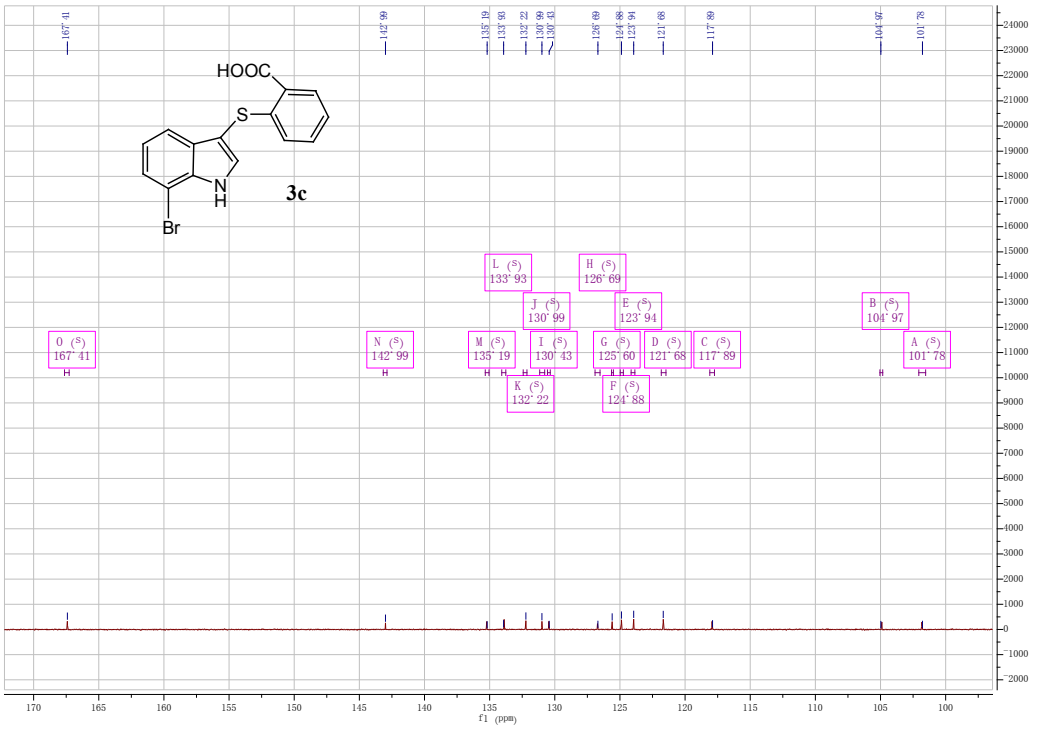


Figure S6. ^{13}C NMR spectrum for 7-Bromo-3-[(2-Carboxyphenyl)thio]-1*H*-indole (**3c**)

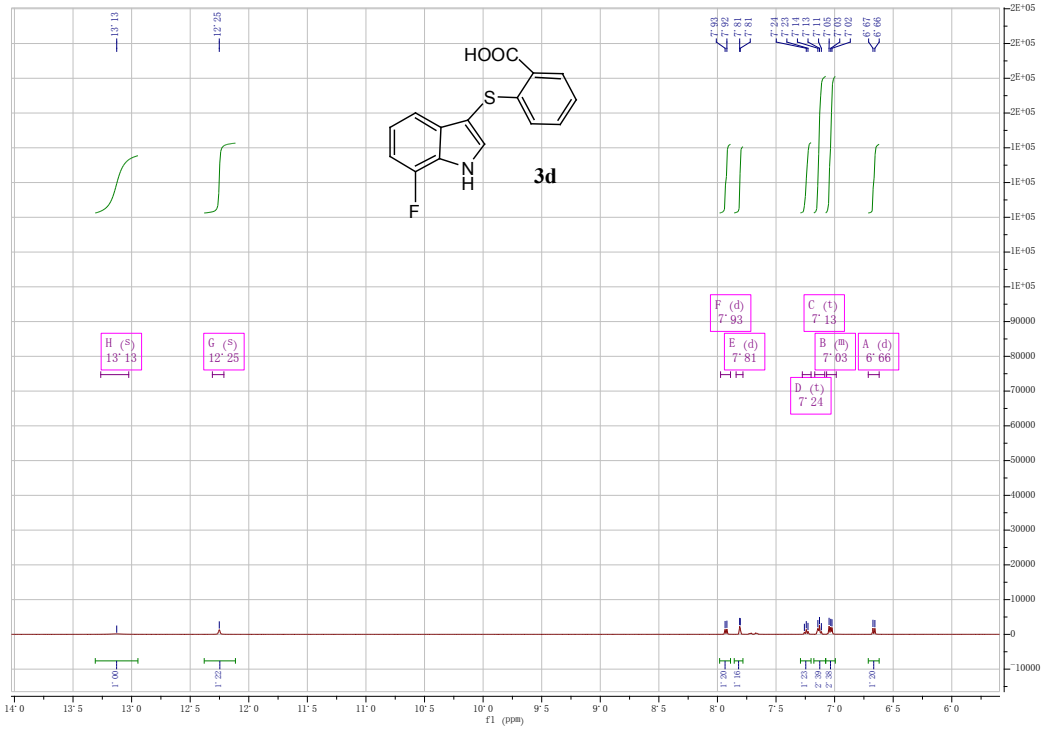


Figure S7. [1]H spectrum for 7-Fluoro-3-[(2-Carboxyphenyl)thio]-1*H*-indole (**3d**)

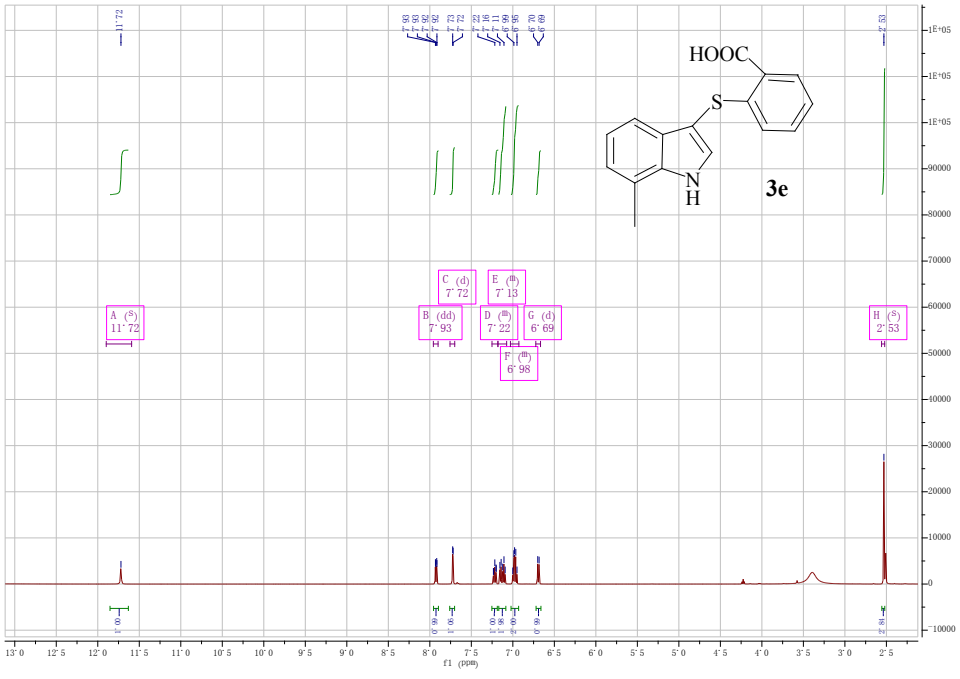


Figure S8. [1]H spectrum for 7-Methyl-3-[(2-Carboxyphenyl)thio]-1*H*-indole (**3e**)

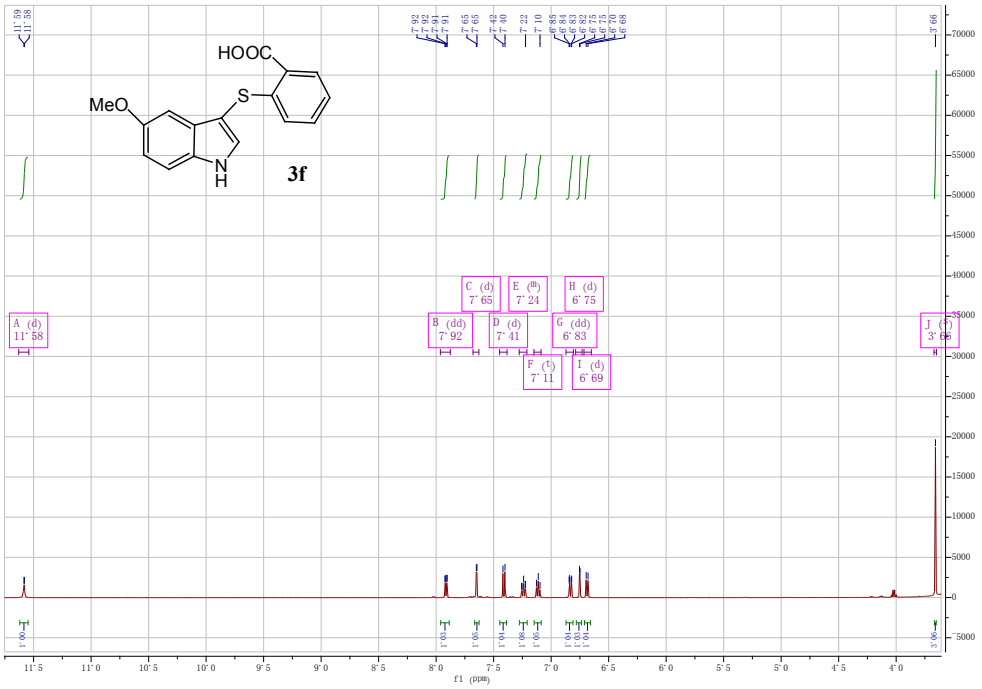


Figure S9. ^{1}H NMR spectrum for 5-Methoxyl-3-[(2-Carboxyphenyl)thio]-1*H*-indole (**3f**)

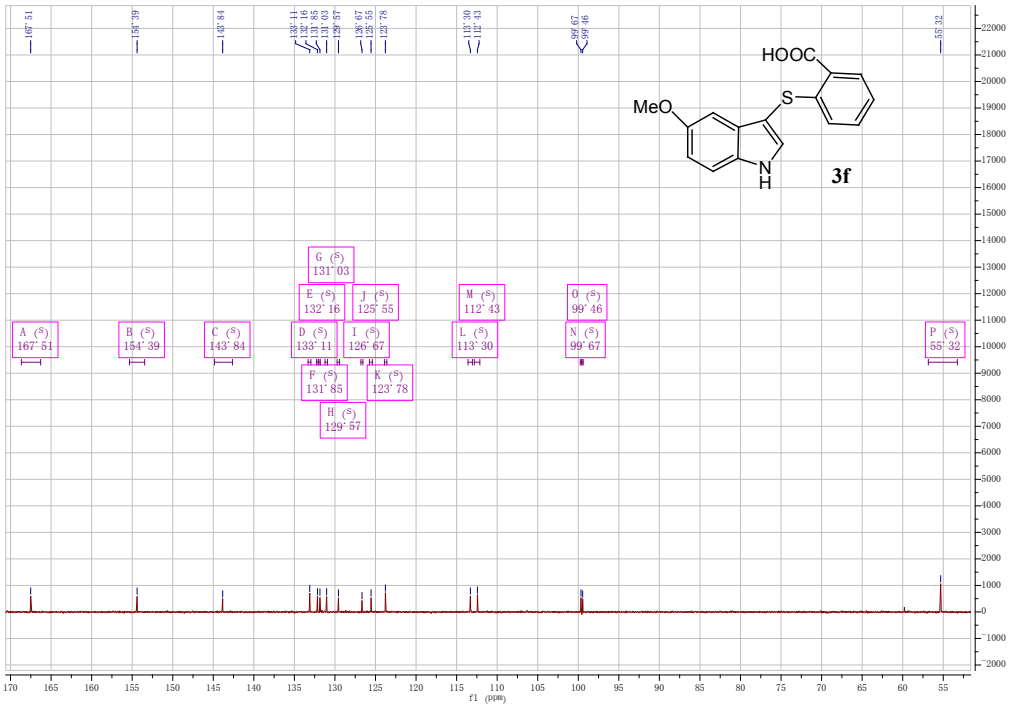


Figure S10. ^{13}C NMR spectrum for 5-Methoxyl-3-[(2-Carboxyphenyl)thio]-1*H*-indole (**3f**)

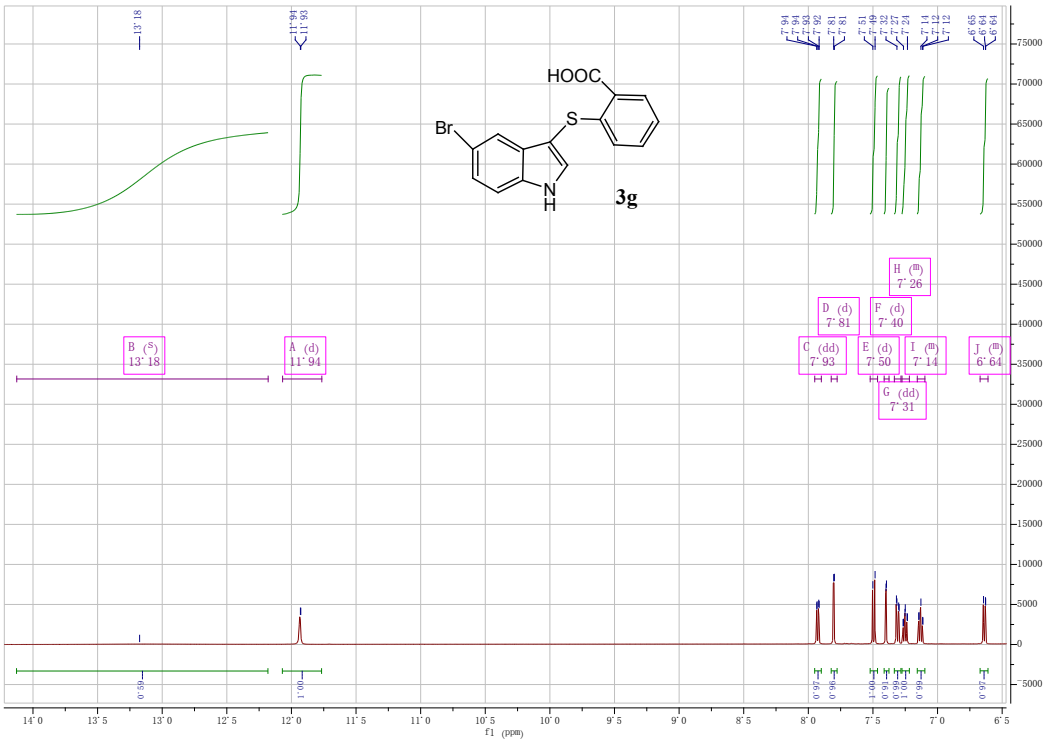


Figure S11. ^{1}H NMR spectrum for 5-Bromo-3-[(2-Carboxyphenyl)thio]-1*H*-indole (**3g**).

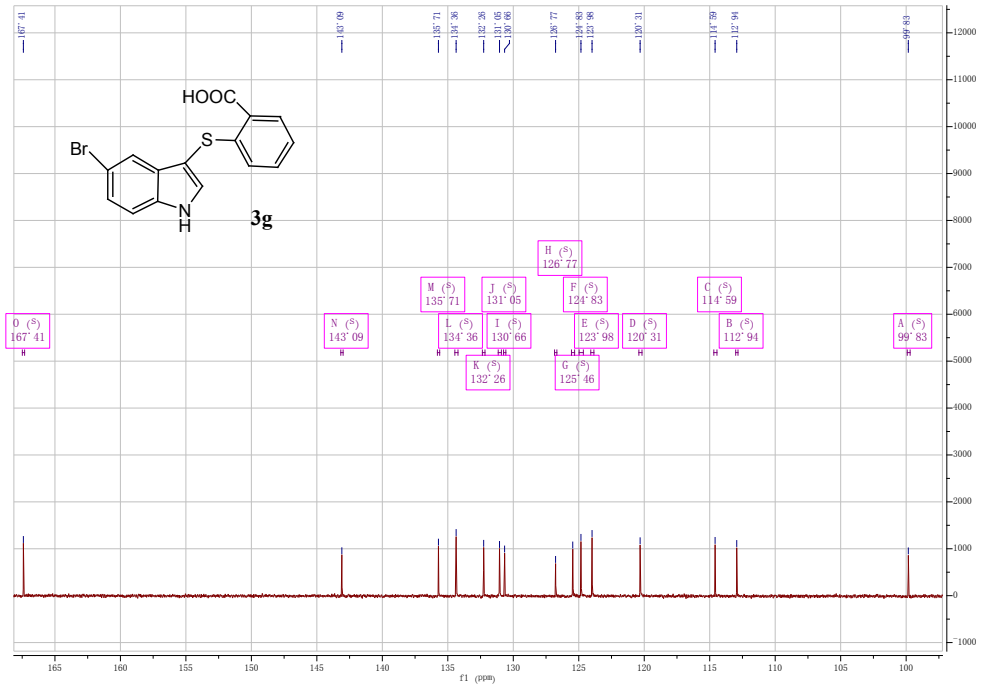


Figure S12. ^{13}C NMR spectrum for 5-Bromo-3-[(2-Carboxyphenyl)thio]-1*H*-indole (**3g**).

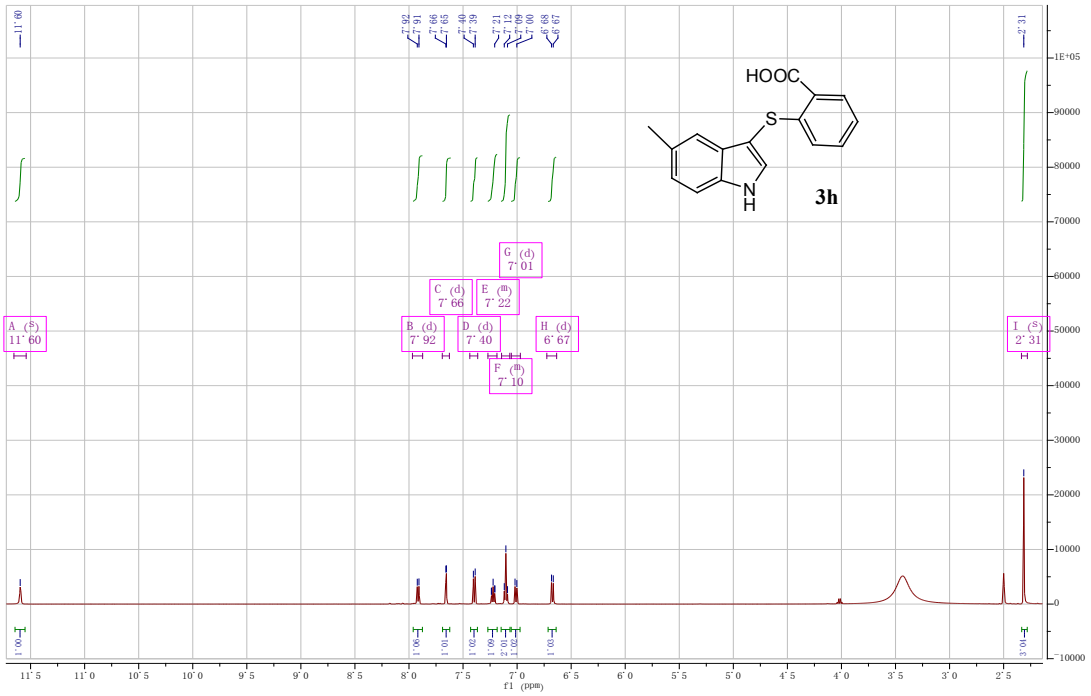


Figure S13. [1]H NMR spectrum for 5- Methyl-3-[(2-Carboxyphenyl)thio]-1*H*-indole (**3h**).

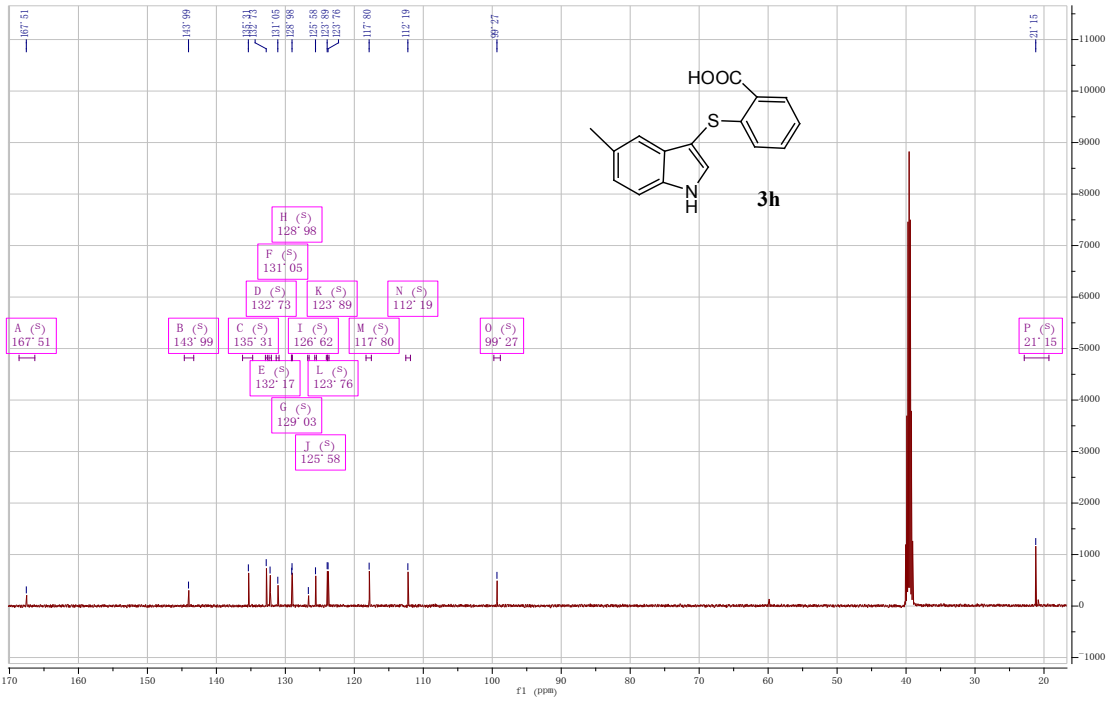


Figure S14. [13]C NMR spectrum for 5- Methyl-3-[(2-Carboxyphenyl)thio]-1*H*-indole (**3h**).

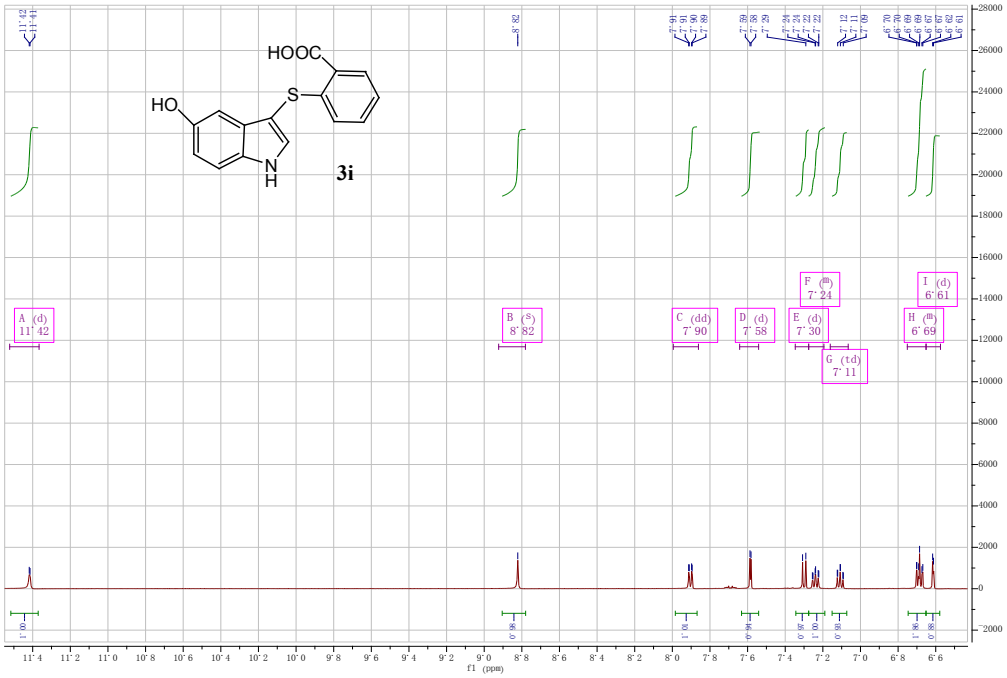


Figure S15. ^{1}H NMR spectrum for 5-Hydroxyl-3-[(2-Carboxyphenyl)thio]-1*H*-indole (**3i**)

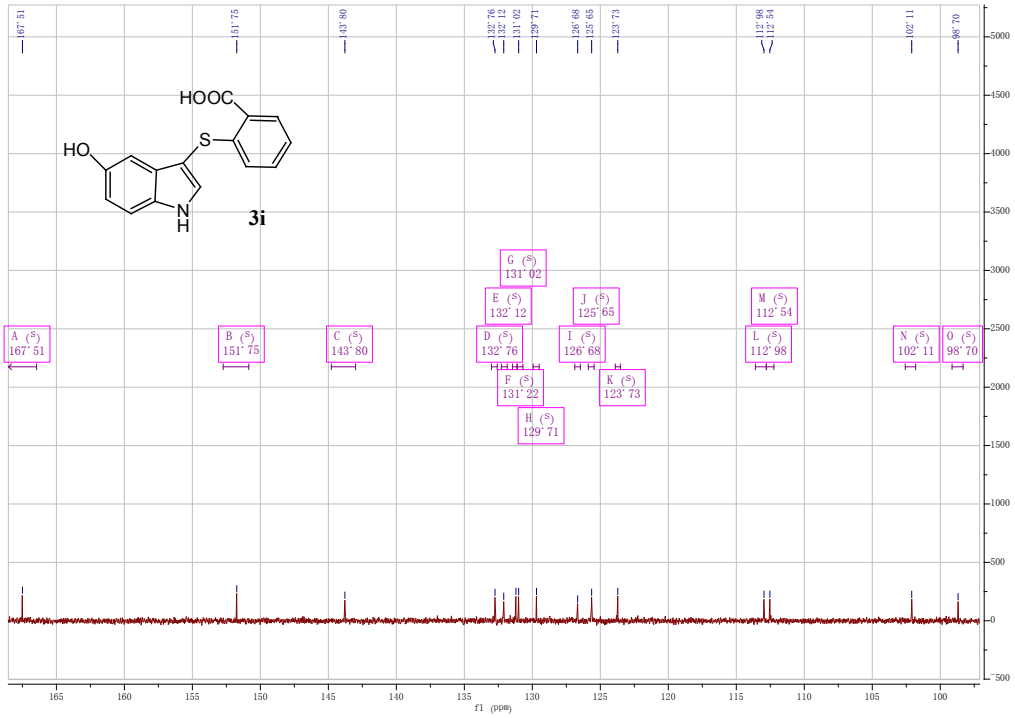


Figure S16. ^{13}C NMR spectrum for 5-Hydroxyl-3-[(2-Carboxyphenyl)thio]-1*H*-indole (**3i**)

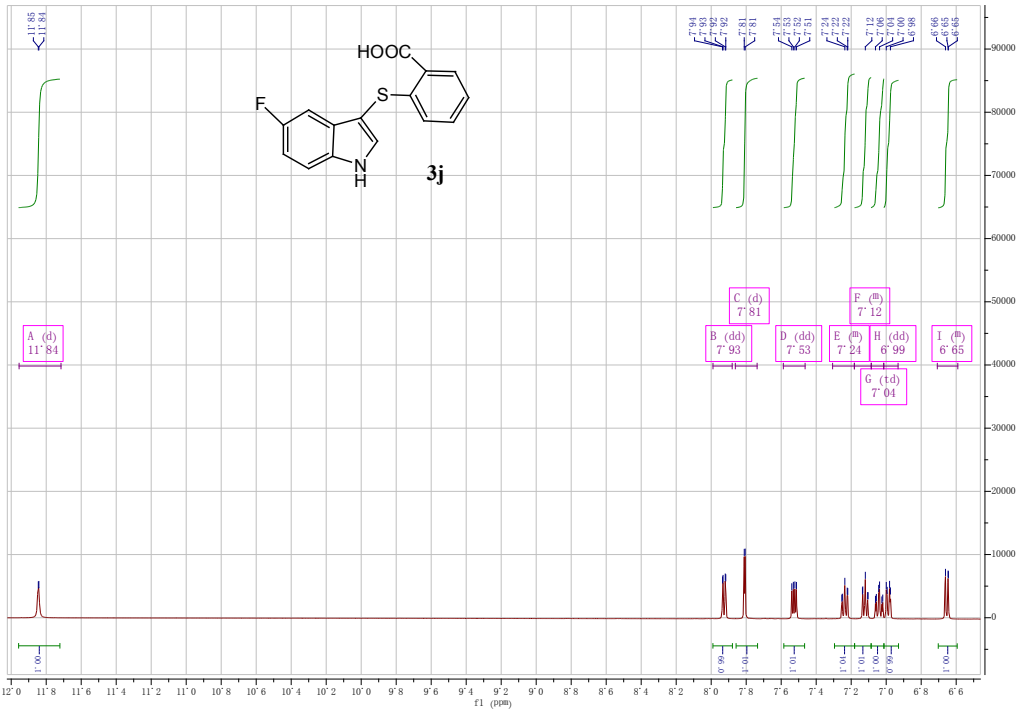


Figure S17. ^{1}H NMR spectrum for 5-Fluoro-3-[(2-Carboxyphenyl)thio]-1*H*-indole (**3j**)

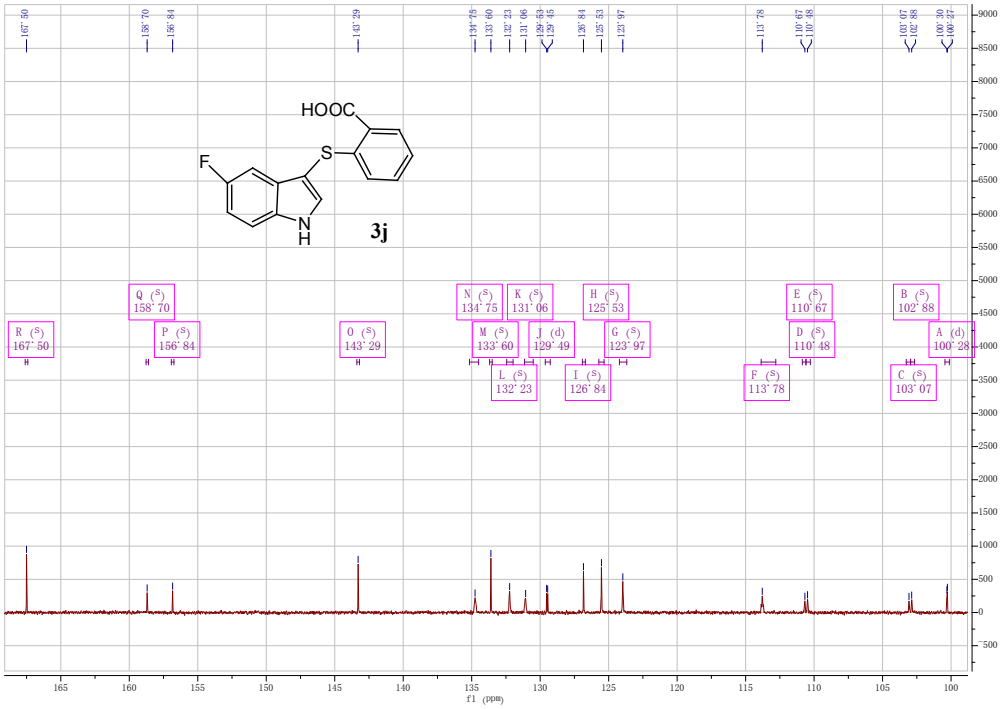


Figure S18. ^{13}C NMR spectrum for 5-Fluoro-3-[(2-Carboxyphenyl)thio]-1*H*-indole (**3j**)

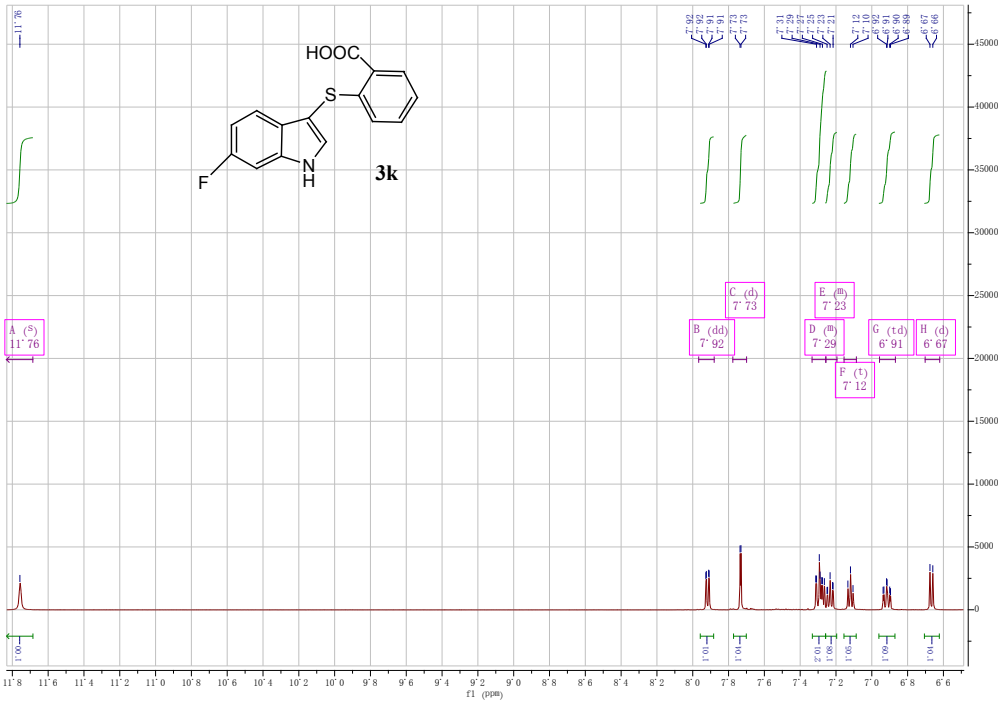


Figure S19. [1]H NMR spectrum for 6-Fluoro-3-[(2-Carboxyphenyl)thio]-1*H*-indole (**3k**)

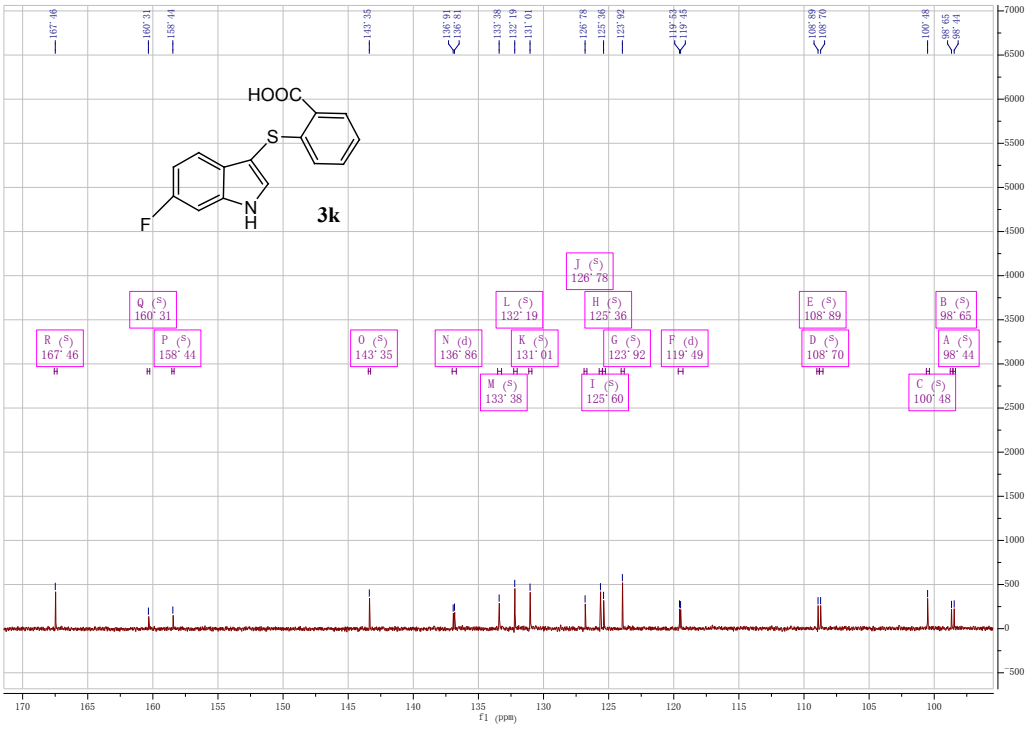


Figure S20. [13]C NMR spectrum for 6-Fluoro-3-[(2-Carboxyphenyl)thio]-1*H*-indole (**3k**)

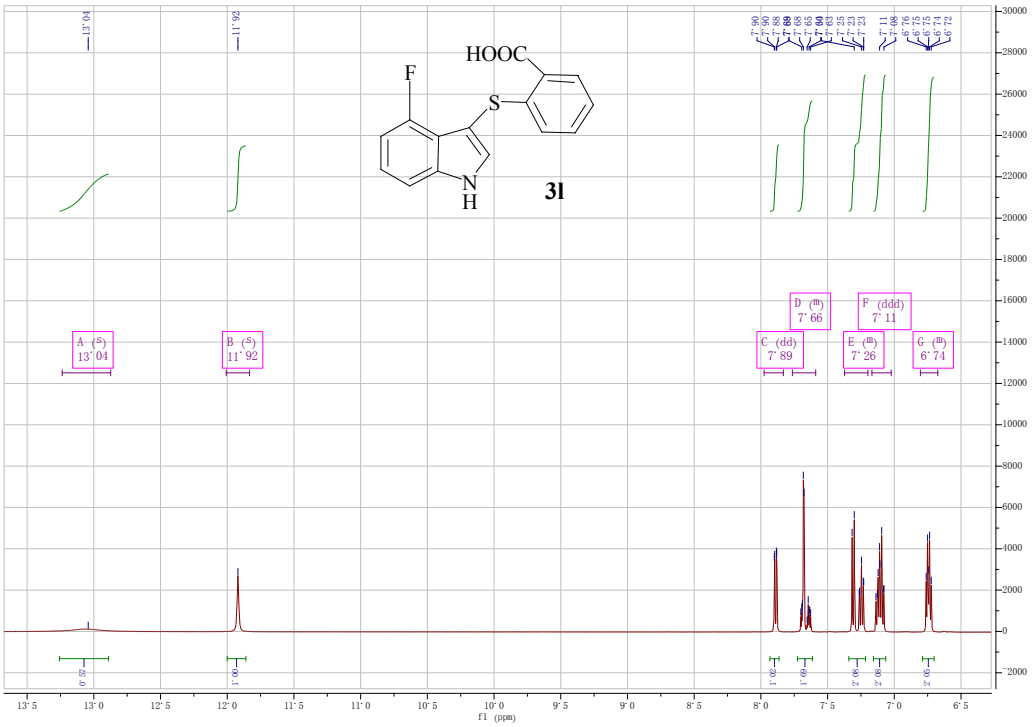


Figure S21. [1]H NMR spectrum for 4-Fluoro-3-[(2-Carboxyphenyl)thio]-1*H*-indole (**3l**)

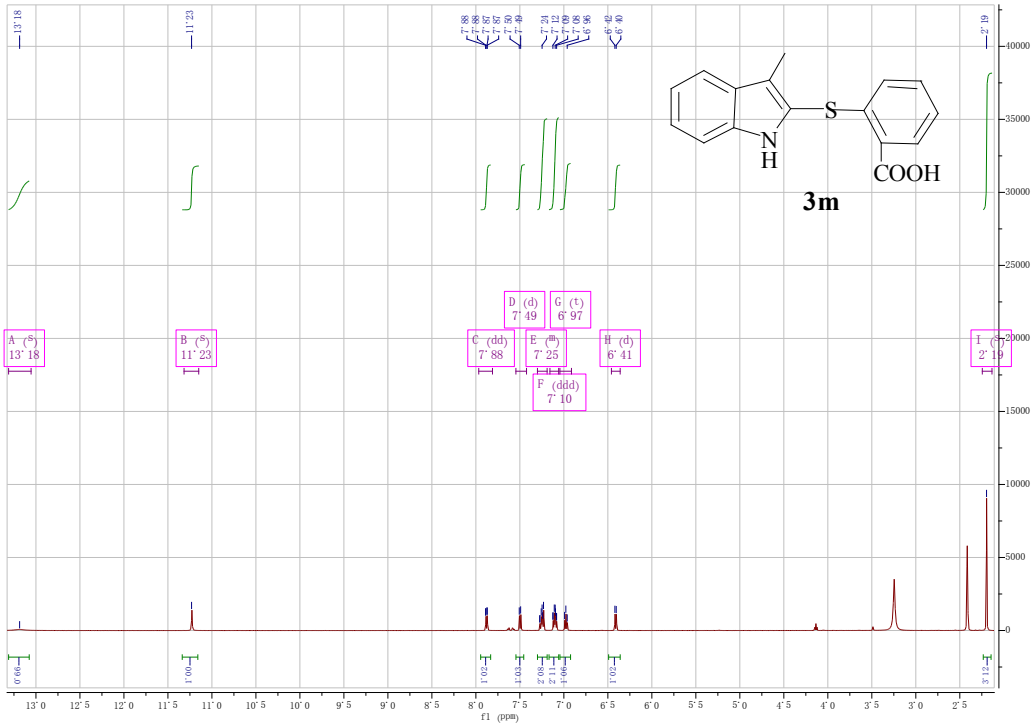


Figure S22. [1]H NMR spectrum for 3-Methyl -2-[(2-Carboxyphenyl)thio]-1*H*-indole (**3m**)

This journal is © The Royal Society of Chemistry 2013

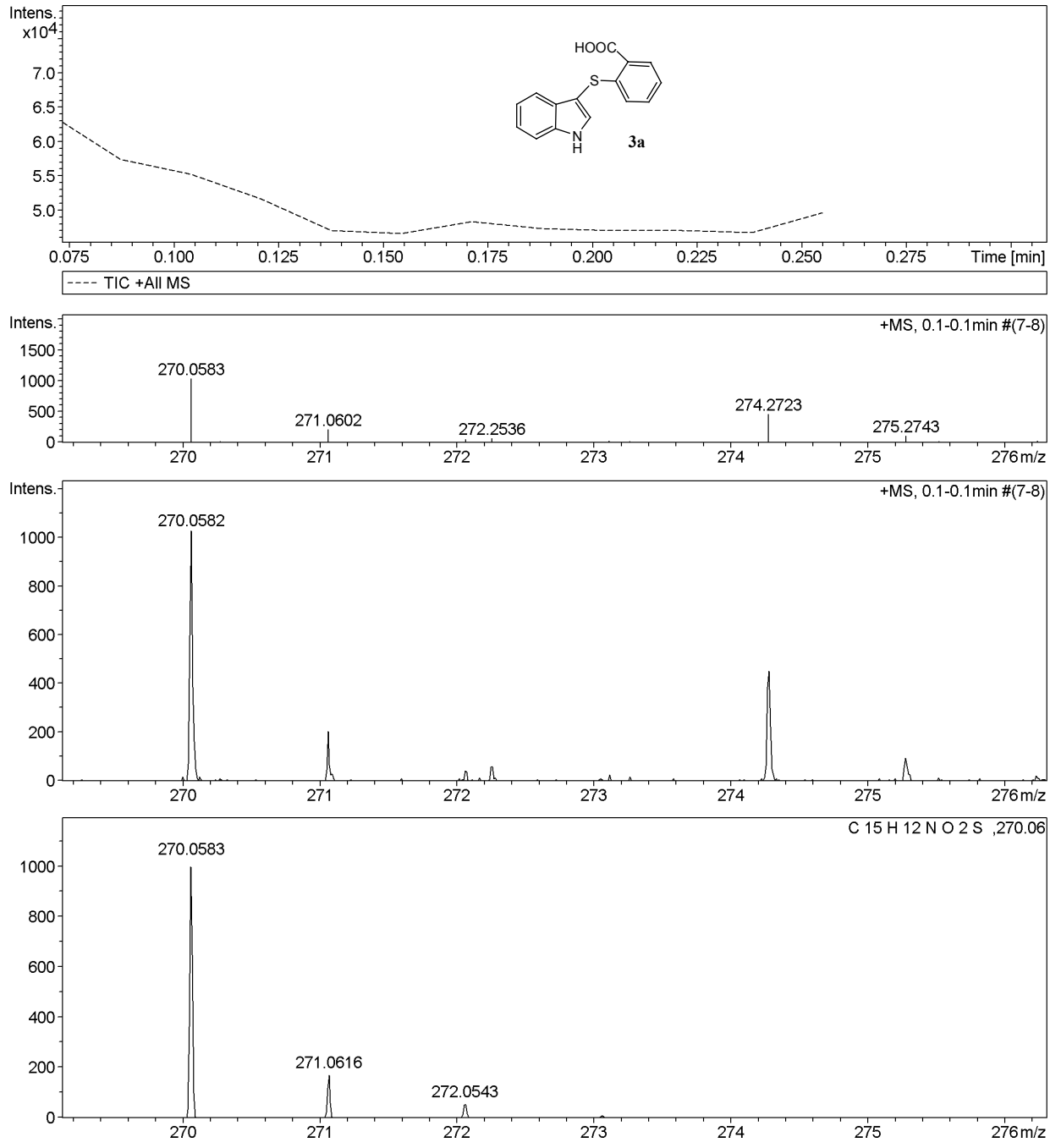


Figure S23. ESI-Qq-TOF mass spectrum for 3-[(2-Carboxyphenyl)thio]-1*H*-indole (**3a**)

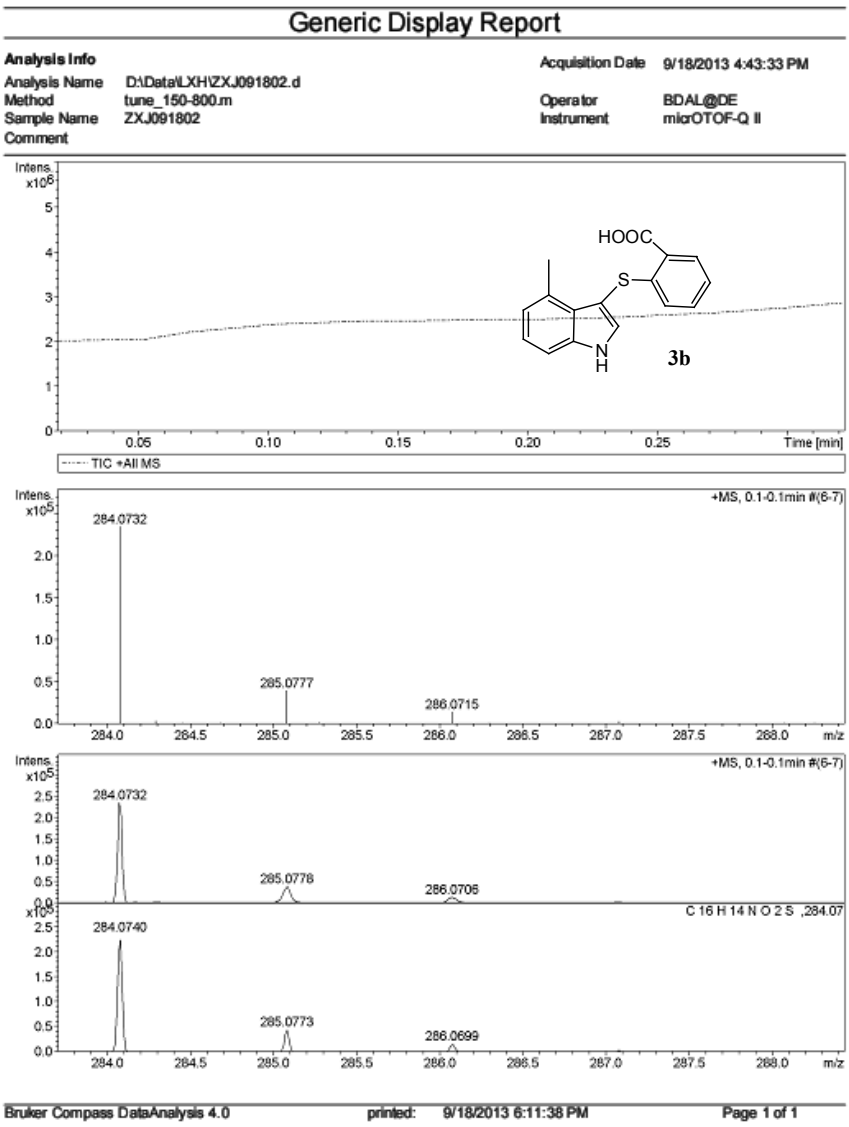


Figure S24. ESI-Qq-TOF mass spectrum for 4-Methyl-3-[(2-Carboxyphenyl)thio]-1*H*-indole (**3b**)

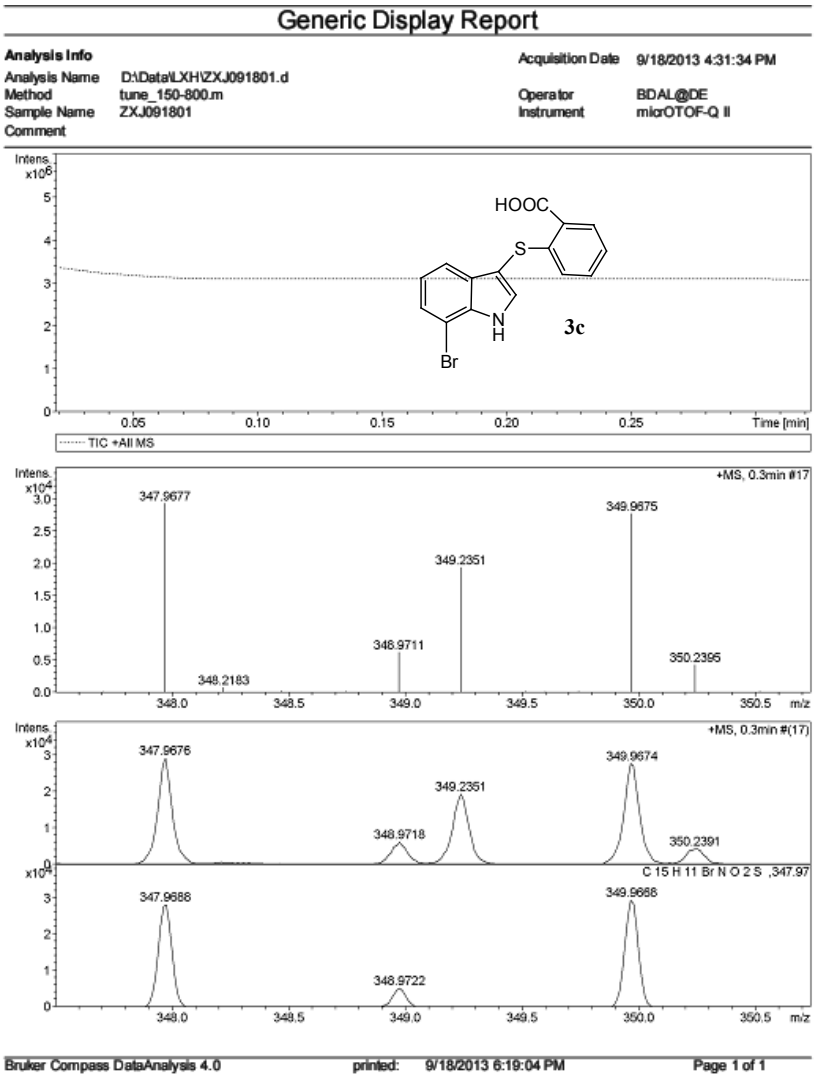


Figure S25. ESI-Qq-TOF mass spectrum for 7-Bromo-3-[(2-Carboxyphenyl)thio]-1*H*-indole (**3c**)

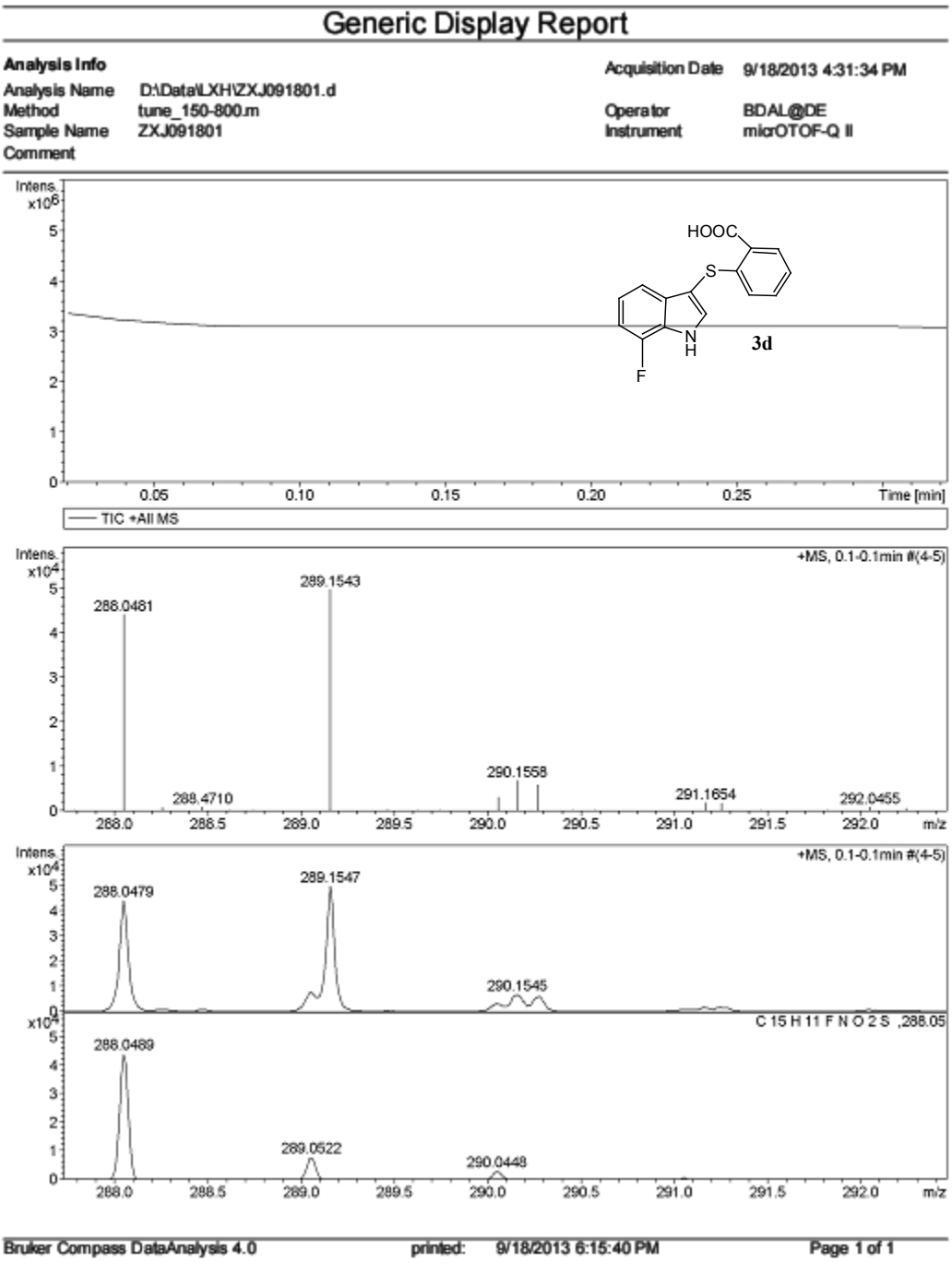


Figure S26. ESI-Qq-TOF mass spectrum for 7-Fluoro-3-[(2-Carboxyphenyl)thio]-1*H*-indole (**3d**)

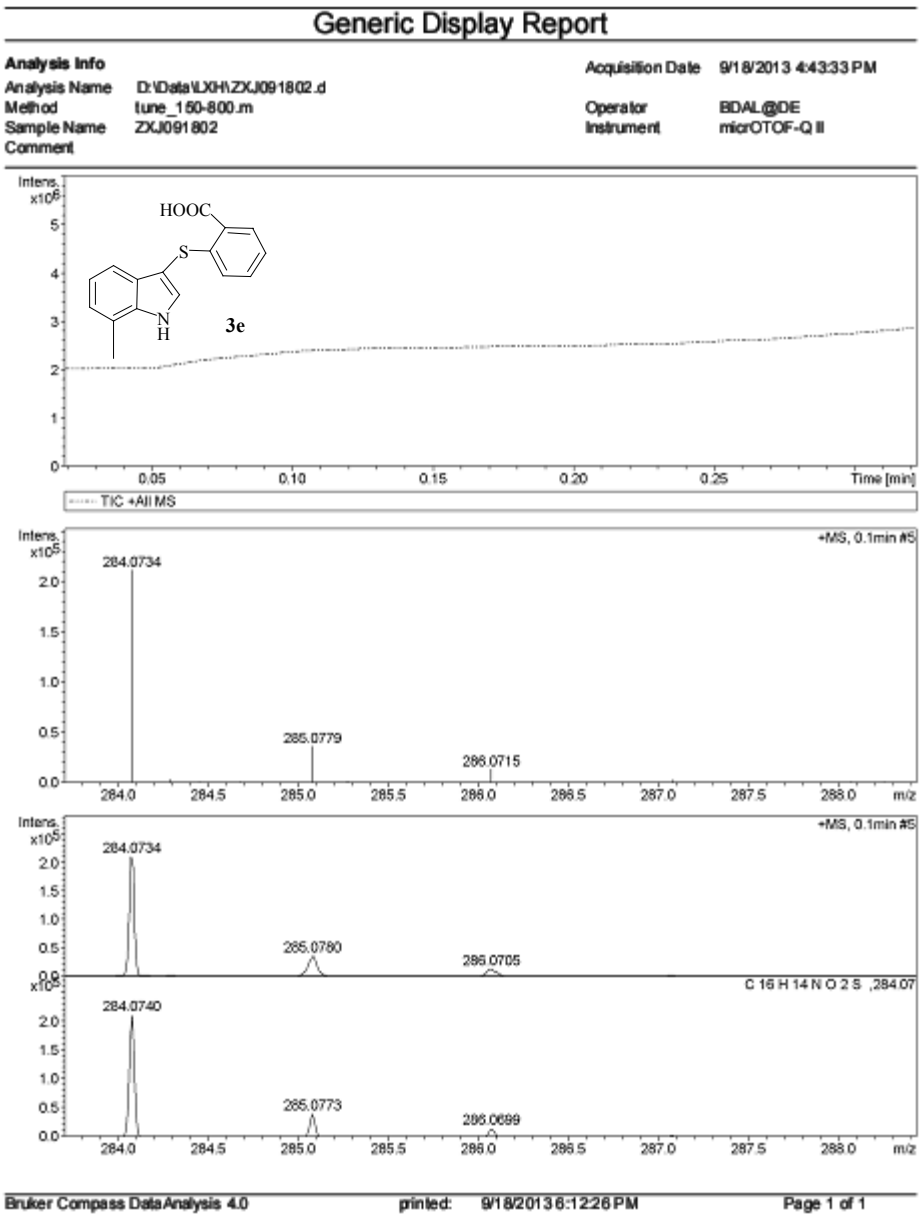


Figure S27. ESI-Qq-TOF mass spectrum for 7-Methyl-3-[(2-Carboxyphenyl)thio]-1*H*-indole (**3e**)

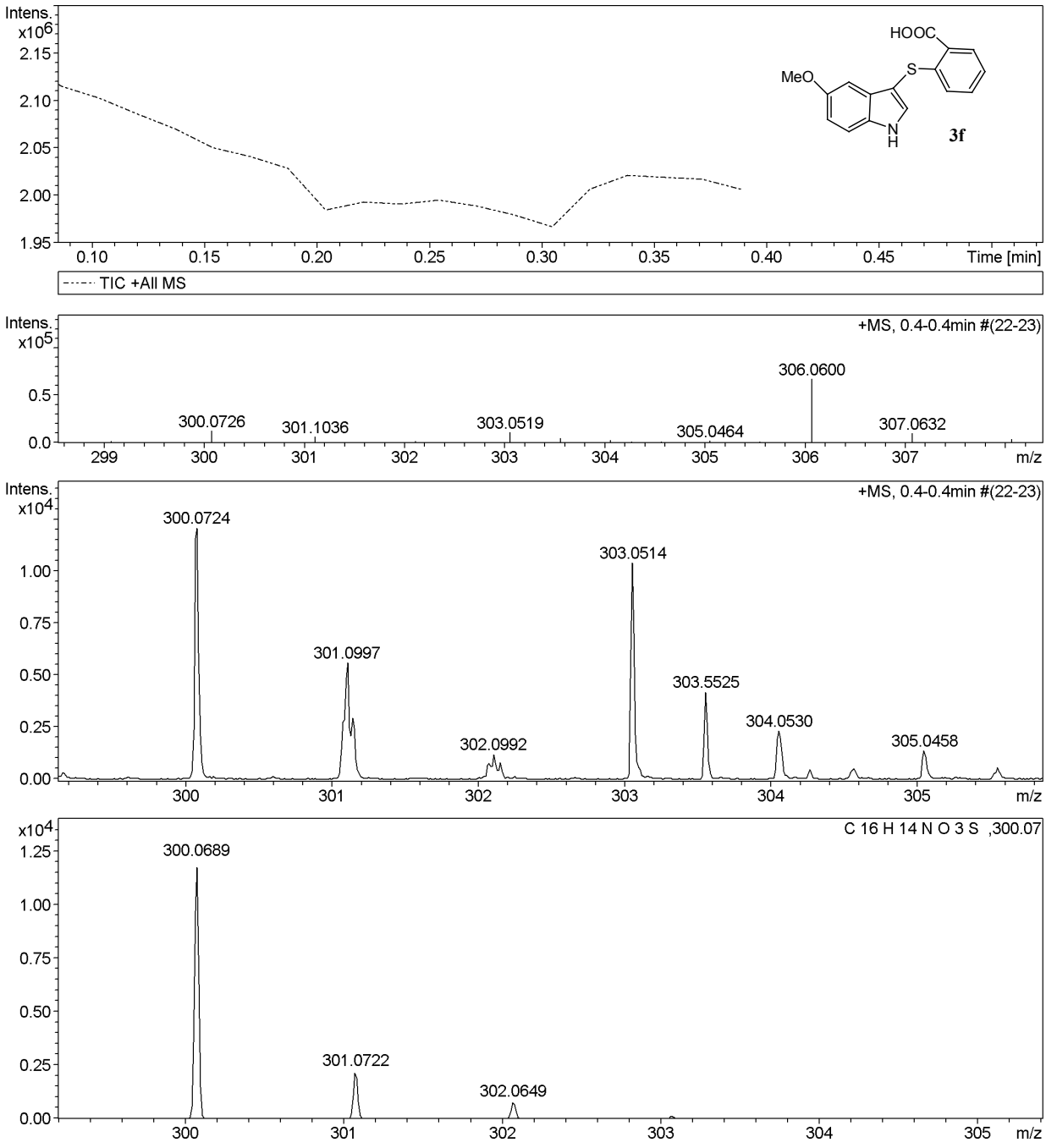


Figure S28. ESI-Qq-TOF mass spectrum for 5-Methoxyl-3-[(2-Carboxyphenyl)thio]-1*H*-indole (**3f**).

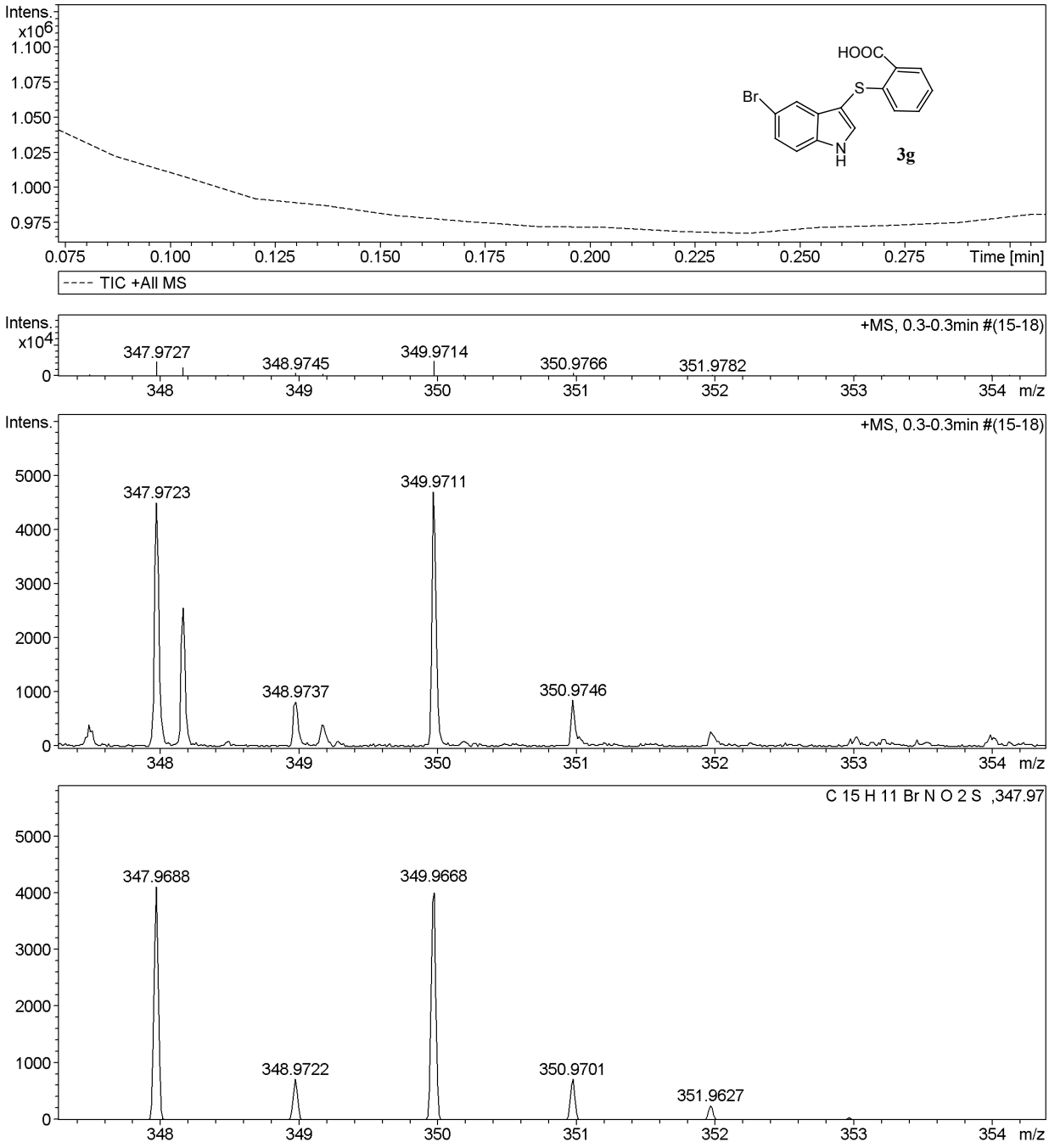


Figure S29. ESI-Qq-TOF mass spectrum for 5-Bromo-3-[(2-Carboxyphenyl)thio]-1*H*-indole (**3g**).

This journal is © The Royal Society of Chemistry 2013

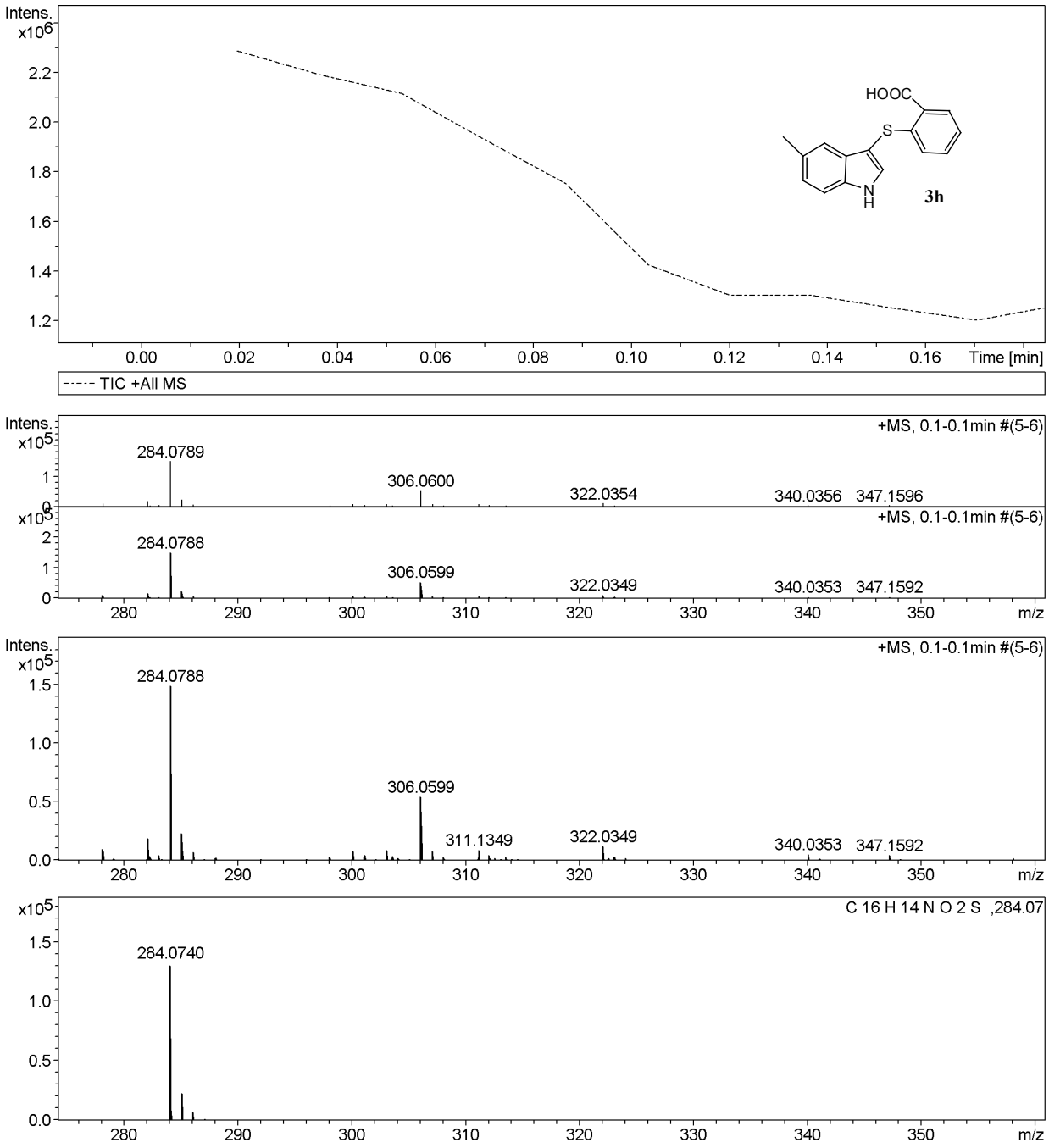


Figure S30. ESI-Qq-TOF mass spectrum for 5- Methyl-3-[(2-Carboxyphenyl)thio]-1*H*-indole (**3h**).

This journal is © The Royal Society of Chemistry 2013

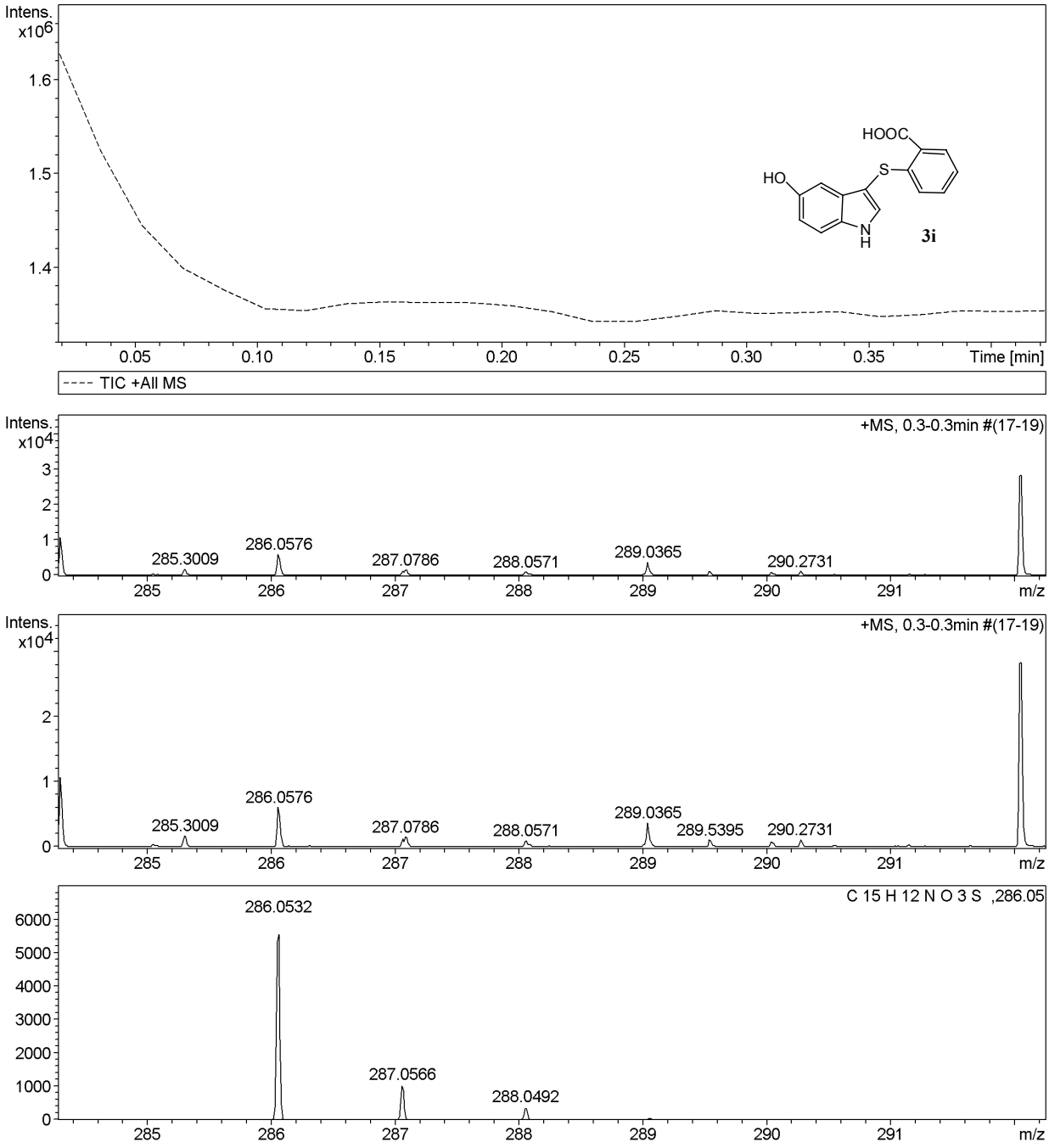


Figure S31. ESI-Qq-TOF mass spectrum for 5-Hydroxyl-3-[(2-Carboxyphenyl)thio]-1*H*-indole (**3i**)

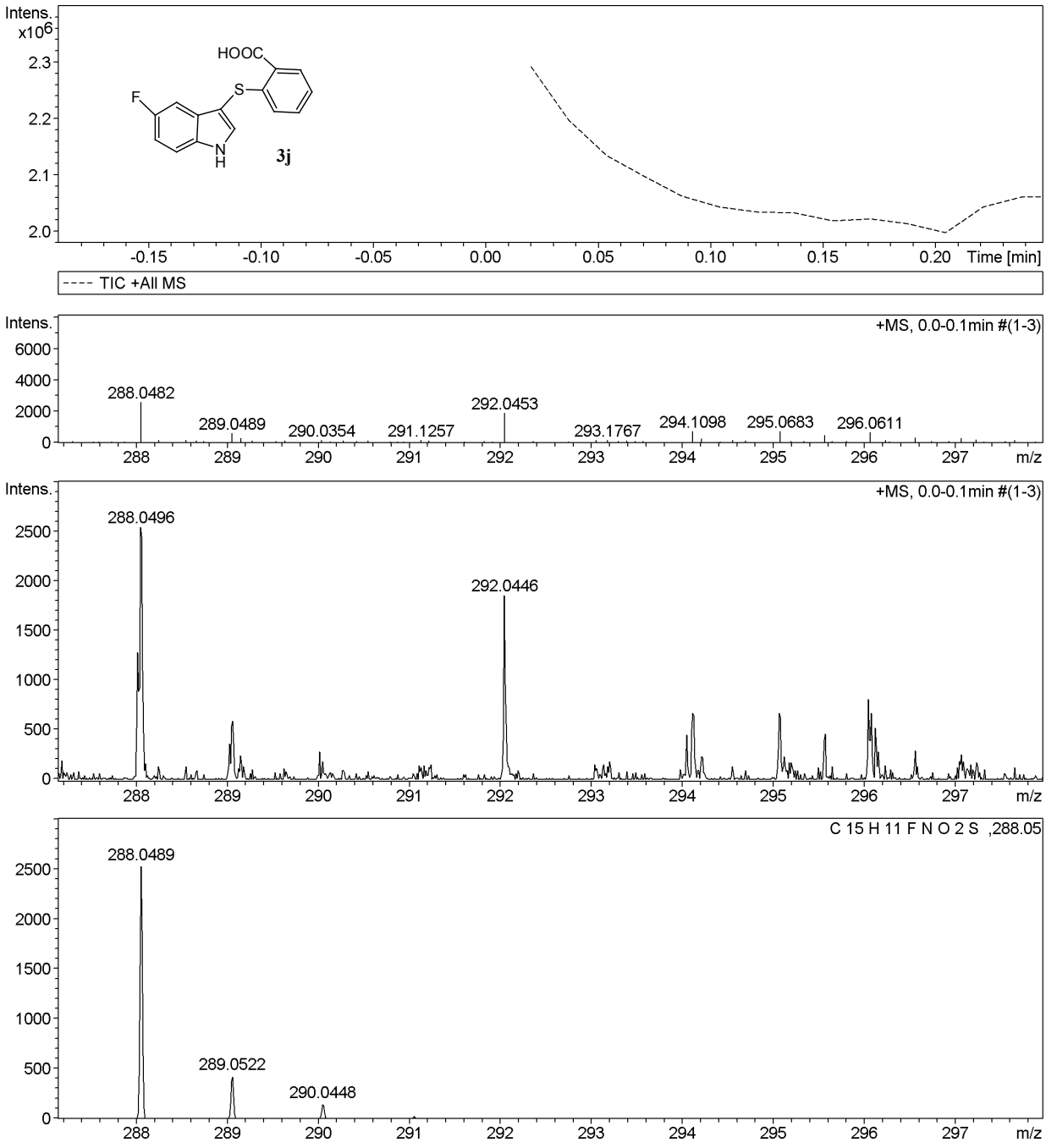


Figure S32. ESI-Qq-TOF mass spectrum for 5-Fluoro-3-[(2-Carboxyphenyl)thio]-1*H*-indole (**3j**)

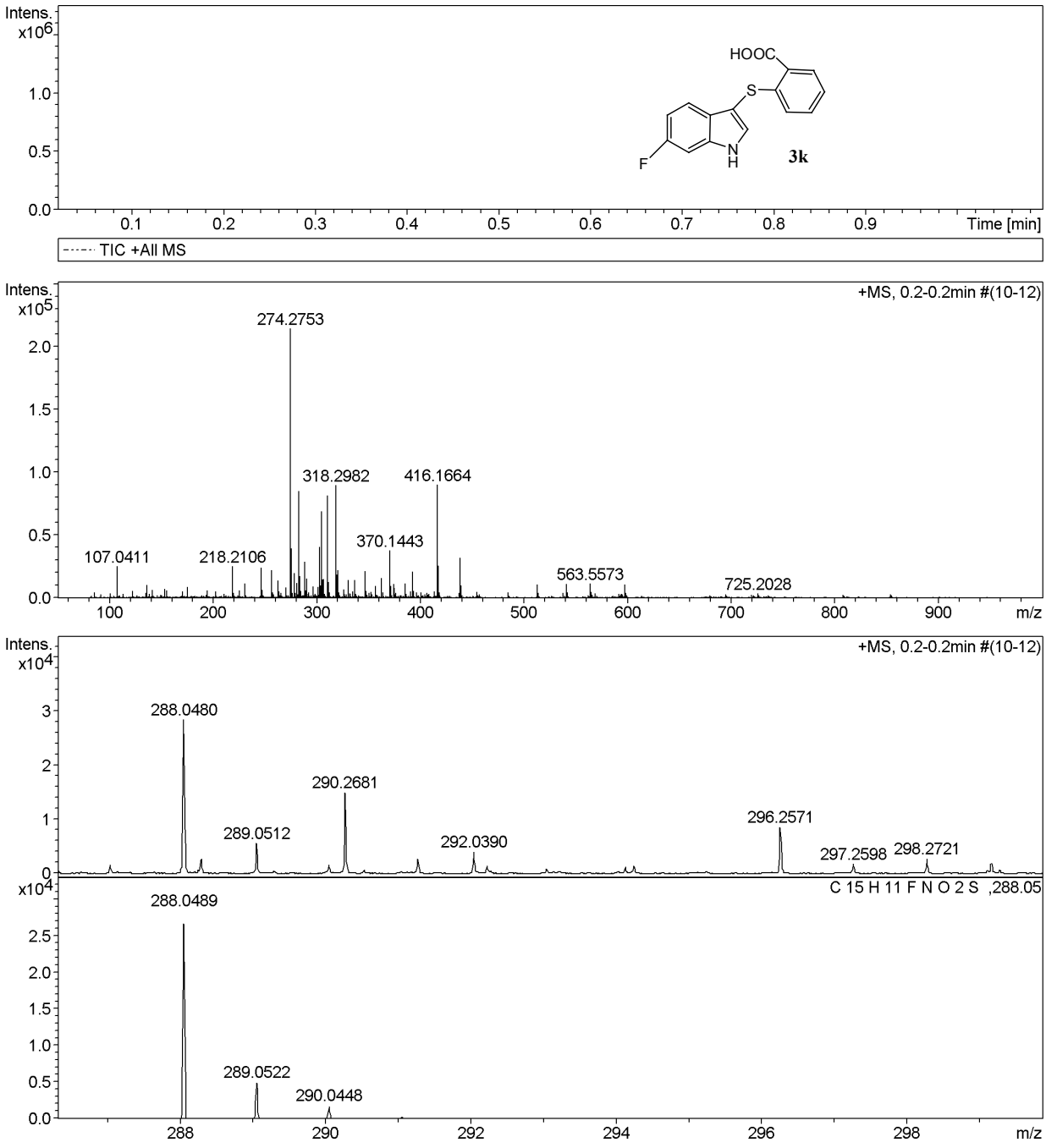


Figure S33. ESI-Qq-TOF mass spectrum for 6-Fluoro-3-[(2-Carboxyphenyl)thio]-1*H*-indole (**3k**)

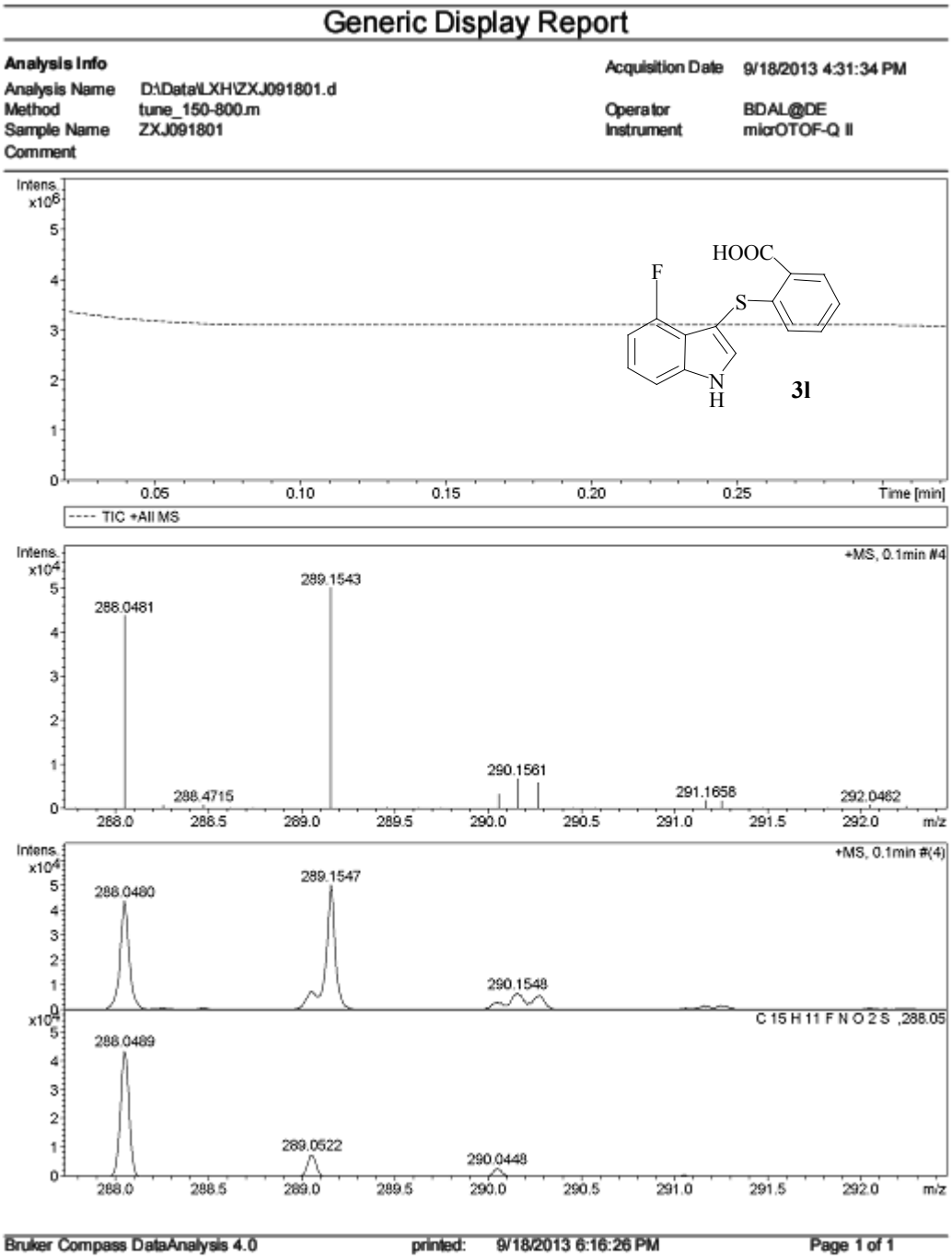


Figure S34. ESI-Qq-TOF mass spectrum for 4-Fluoro-3-[(2-Carboxyphenyl)thio]-1*H*-indole (**3l**)

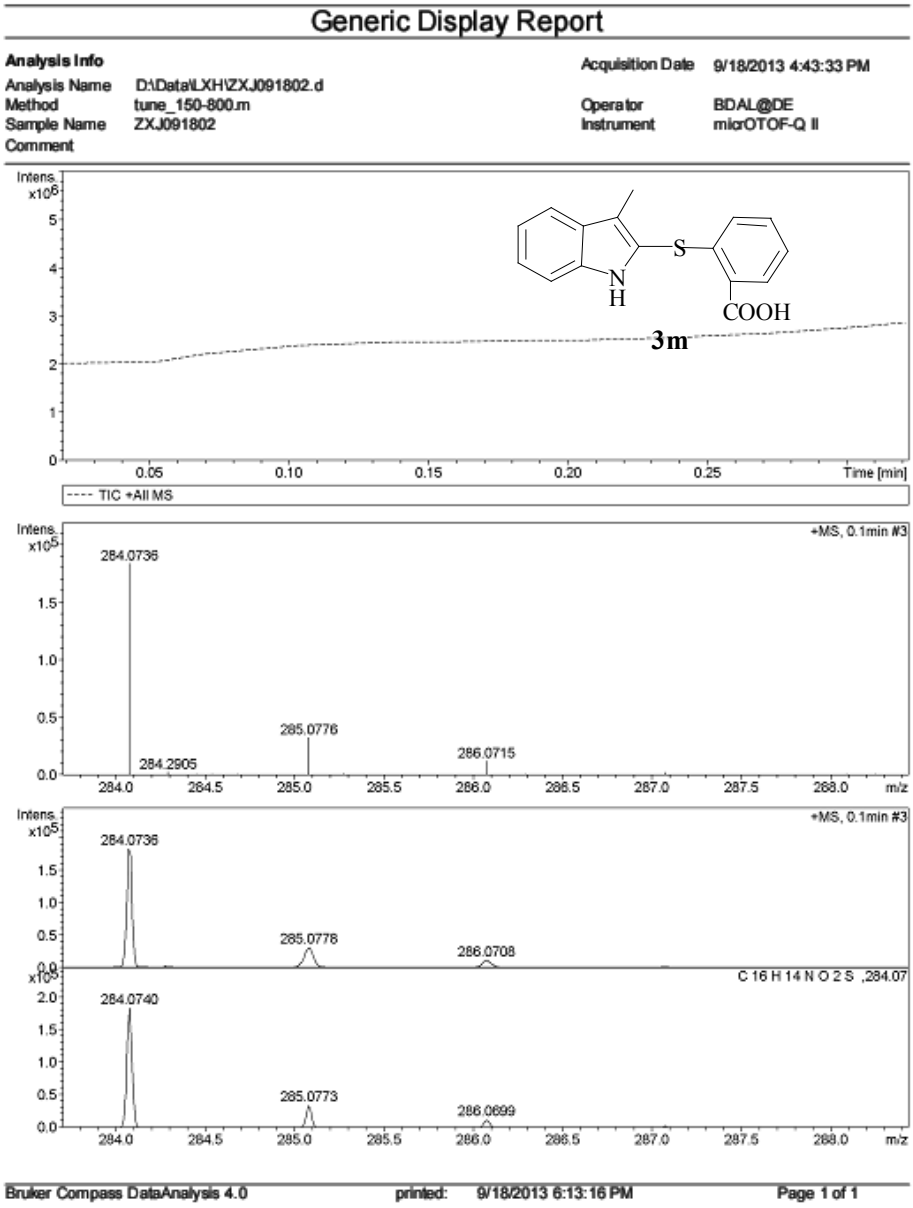


Figure S35. ESI-Qq-TOF mass spectrum for 3-Methyl -2-[(2-Carboxyphenyl)thio]-1*H*-indole (**3m**)