Electronic supplementary materials *Mendeleev Commun.*, 2025, **35**, 269–270

An efficient solvent-free thiocyanation of indoles by grinding

Liang Wang, Dan Wang and Jie Tang

Contents

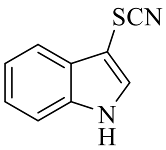
General experimental

All reagents were obtained from local commercial suppliers and used without further purification. The progress of the reaction was monitored by TLC using analytical-grade silica gel plates (GF254) under UV light. ^{1}H NMR spectra were recorded in DMSO-*d*$_6$ or $CDCl_3$ at 400 or 300 MHz instrument using TMS as internal standard. Chemical shifts are given in parts per million (δ, ppm) and the coupling constants *J* are given in Hz. Mass spectrometry was performed on an LCMS-2010 EV (Shimadzu) instrument with an ESI source. The reaction temperature of the water bath was controlled at room temperature (25 ^{o}C). All the products are known compounds and were identified by comparing their spectra data with those reported in the literature.

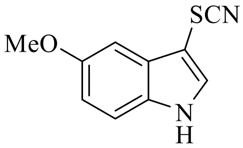
General procedure for thiocyanation of indoles

Indole **1** (1 mmol), ammonium thiocyanate (1.5 mmol, 114 mg) and $PhI(OAc)_2$ (1.5 mmol, 483 mg) were taken in a mortar, and the mixture was ground with a pestle. The reaction was kept grinding until the starting materials disappeared (monitored by TLC, *ca.* ~15 mins). After that, the residue was extracted with ethyl acetate and washed with water. The combined extracts were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel with petroleum ether/ethyl acetate (10:1, v/v) to afford the pure desired product.

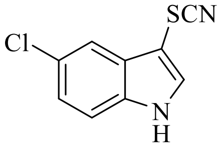
Characterization data



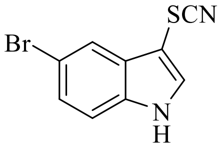
*3-Thiocyanato-1H-indole (**2a**)*.[S1] Yield: 148 mg (85%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.03 (s, 1H), 7.99 (d, *J* = 2.8 Hz, 1H), 7.68 (dd, *J* = 7.9, 6.6 Hz, 1H), 7.60 – 7.53 (m, 1H), 7.36 – 7.18 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 136.4, 133.1, 127.5, 122.9, 121.1, 117.7, 112.8, 112.3, 89.3; MS (ESI) *m/z* 175.0 [M + H]$^+$.



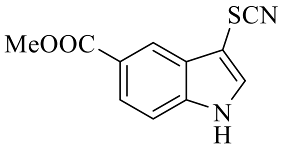
5-Methoxy-3-thiocyanato-1H-indole (***2b***).[S1] Yield: 175 mg (86%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.88 (s, 1H), 7.92 (d, *J* = 2.9 Hz, 1H), 7.43 (d, *J* = 8.8 Hz, 1H), 7.10 (d, *J* = 2.1 Hz, 1H), 6.91 (dd, *J* = 8.8, 2.3 Hz, 1H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 154.9, 133.4, 131.1, 128.2, 113.7, 113.2, 112.3, 99.1, 88.6, 55.4; MS (ESI) *m/z* 205.1 [M + H]$^+$.



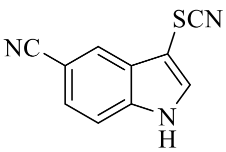
*5-Chloro-3-thiocyanato-1H-indole (**2c**).*[S2] Yield: 171 mg (82%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.19 (s, 1H), 8.06 (s, 1H), 7.66 (d, *J* = 1.8 Hz, 1H), 7.55 (d, *J* = 8.7 Hz, 1H), 7.27 (dd, *J* = 8.7, 1.9 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 134.9, 134.8, 128.7, 125.9, 123.0, 117.0, 114.5, 112.1, 89.5; MS (ESI) *m/z* 231.0 [M + Na]$^+$.



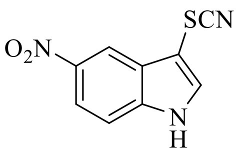
*5-Bromo-3-thiocyanato-1H-indole (**2d**).*[S1] Yield: 200 mg (80%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.21 (s, 1H), 8.06 (d, *J* = 2.6 Hz, 1H), 7.80 (s, 1H), 7.51 (d, *J* = 8.6 Hz, 1H), 7.39 (d, *J* = 8.6 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 135.1, 134.7, 129.3, 125.6, 120.0, 115.0, 113.8, 112.2, 89.4; MS (ESI) *m/z* 274.9 [M + Na]$^+$.



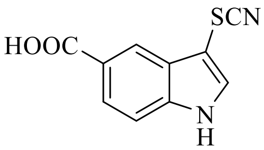
*Methyl 3-thiocyanato-1H-indole-5-carboxylate (**2e**).*[S2] Yield: 171 mg (82%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.36 (s, 1H), 8.31 (s, 1H), 8.13 (d, *J* = 2.6 Hz, 1H), 7.88 (d, *J* = 8.6 Hz, 1H), 7.62 (d, *J* = 8.6 Hz, 1H), 3.89 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.7, 139.0, 135.2, 127.1, 123.7, 122.6, 119.9, 113.1, 112.2, 91.5, 52.1; MS (ESI) *m/z* 255.0 [M + Na]$^+$.



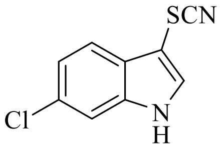
*3-Thiocyanato-1H-indole-5-carbonitrile (**2f**).*[S3] Yield: 155 mg (78%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.51 (s, 1H), 8.26 – 8.14 (m, 2H), 7.71 (d, *J* = 8.5 Hz, 1H), 7.64 (d, *J* = 8.5 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 138.2, 136.0, 127.3, 125.7, 123.4, 119.9, 114.3, 112.0, 103.4, 91.5; MS (ESI) *m/z* 200.0 [M + H]$^+$.



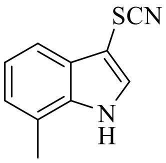
*5-Nitro-3-thiocyanato-1H-indole (**2g**).*[S3] Yield: 164 mg (75%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.63 (s, 1H), 8.53 (d, *J* = 2.0 Hz, 1H), 8.27 (d, *J* = 2.7 Hz, 1H), 8.14 (dd, *J* = 9.0, 2.2 Hz, 1H), 7.71 (d, *J* = 9.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 142.2, 139.5, 137.1, 126.9, 118.2, 114.4, 113.7, 112.0, 93.2; MS (ESI) *m/z* 242.1 [M + Na]$^+$.



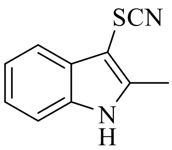
*3-Thiocyanato-1H-indole-5-carboxylic acid (**2h**).*[S2] Yield: 157 mg (72%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.11 (s, 1H), 8.08 (d, *J* = 0.7 Hz, 1H), 7.81 – 7.73 (m, 1H), 7.64 (d, *J* = 7.1 Hz, 1H), 7.42 – 7.30 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.4, 136.1, 130.1, 127.7, 125.8, 122.0, 119.5, 113.8, 111.6, 96.2; MS (ESI) *m/z* 241.1 [M + Na]$^+$.



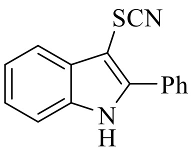
*6-Chloro-3-thiocyanato-1H-indole(**2i**).*[S1] Yield: 164 mg (79%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.11 (s, 1H), 8.03 (s, 1H), 7.66 (d, *J* = 8.5 Hz, 1H), 7.59 (s, 1H), 7.26 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 136.7, 134.3, 127.7, 126.2, 121.5, 119.2, 112.4, 112.1, 90.2; MS (ESI) *m/z* 231.0 [M + Na]$^+$.



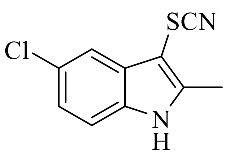
*7-Methyl-3-thiocyanato-1H-indole (**2j**).*[S4] Yield: 150 mg (80%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.02 (s, 1H), 7.99 (d, *J* = 2.9 Hz, 1H), 7.49 (d, *J* = 7.9 Hz, 1H), 7.15 (t, *J* = 7.5 Hz, 1H), 7.07 (d, *J* = 7.1 Hz, 1H), 2.50 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 135.8, 132.8, 127.2, 123.4, 122.2, 121.2, 115.2, 112.3, 89.6, 16.5; MS (ESI) *m/z* 211.0 [M + Na]$^+$.



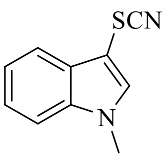
*2-Methyl-3-thiocyanato-1H-indole(**2k**).*[S5] Yield: 156 mg (83%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.95 (s, 1H), 7.59 – 7.52 (m, 1H), 7.47 – 7.39 (m, 1H), 7.24 – 7.14 (m, 2H), 2.54 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 143.0, 135.3, 128.3, 122.2, 120.8, 117.1, 112.1, 111.8, 86.6, 11.6; MS (ESI) *m/z* 211.0 [M + Na]$^+$.



*2-Phenyl-3-thiocyanato-1H-indole (**2l**).*[S2] Yield: 202 mg (81%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.41 (s, 1H), 7.86 (d, *J* = 7.5 Hz, 2H), 7.72 (d, *J* = 7.3 Hz, 1H), 7.62 (t, *J* = 7.5 Hz, 2H), 7.54 (t, *J* = 7.8 Hz, 2H), 7.37 – 7.24 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 143.2, 135.8, 130.0, 129.3, 129.2, 128.9, 128.8, 123.4, 121.4, 118.1, 112.5, 112.4, 87.1; MS (ESI) *m/z* 273.0 [M + Na]$^+$.



*5-Chloro-2-methyl-3-thiocyanato-1H-indole (**2m**).*[S2] Yield: 171 mg (77%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.15 (s, 1H), 7.53 (s, 1H), 7.43 (d, *J* = 8.6 Hz, 1H), 7.19 (dd, *J* = 8.6, 1.5 Hz, 1H), 2.52 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 144.9, 133.9, 129.6, 125.6, 122.2, 116.4, 113.5, 112.0, 86.9, 11.8; MS (ESI) *m/z* 245.1 [M + Na]$^+$.



*1-Methyl-3-thiocyanato-1H-indole (**2n**).*[S3] Yield: 158 mg (84%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78 – 7.72 (m, 1H), 7.33 – 7.23 (m, 4H), 3.67 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.1, 135.1, 128.4, 123.4, 121.6, 118.9, 112.0, 110.3, 89.6, 33.4; MS (ESI) *m/z* 189.0 [M + H]$^+$.

References

S1. W. Fan, Q. Yang, F. Xu and P. Li, *J. Org. Chem.*, 2014, **79**, 10588; https://doi.org/10.1021/jo5015799.

S2. L. Wang, C. Wang, W. Liu, Q. Chen and M. He, *Tetrahedron Lett.*, 2016, **57**, 1771; https://doi.org/10.1016/j.tetlet.2016.03.028.

S3. S. Saha, A. B. Pinheiro, A. Chatterjee, Z. T. Bhutiab and M. Banerjee, *Green Chem.*, 2024, **26**, 5879; https://doi.org/10.1039/D4GC00486H.

S4. X.-Q. Pan, M.-Y. Lei, J.-P. Zou and W. Zhang, *Tetrahedron Lett.*, 2009, **50**, 347; https://doi.org/10.1016/j.tetlet.2008.11.007.

S5. D. Khalili, *Chin. Chem. Lett.*, 2015, **26**, 547; https://doi.org/10.1016/j.cclet.2015.01.007.

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

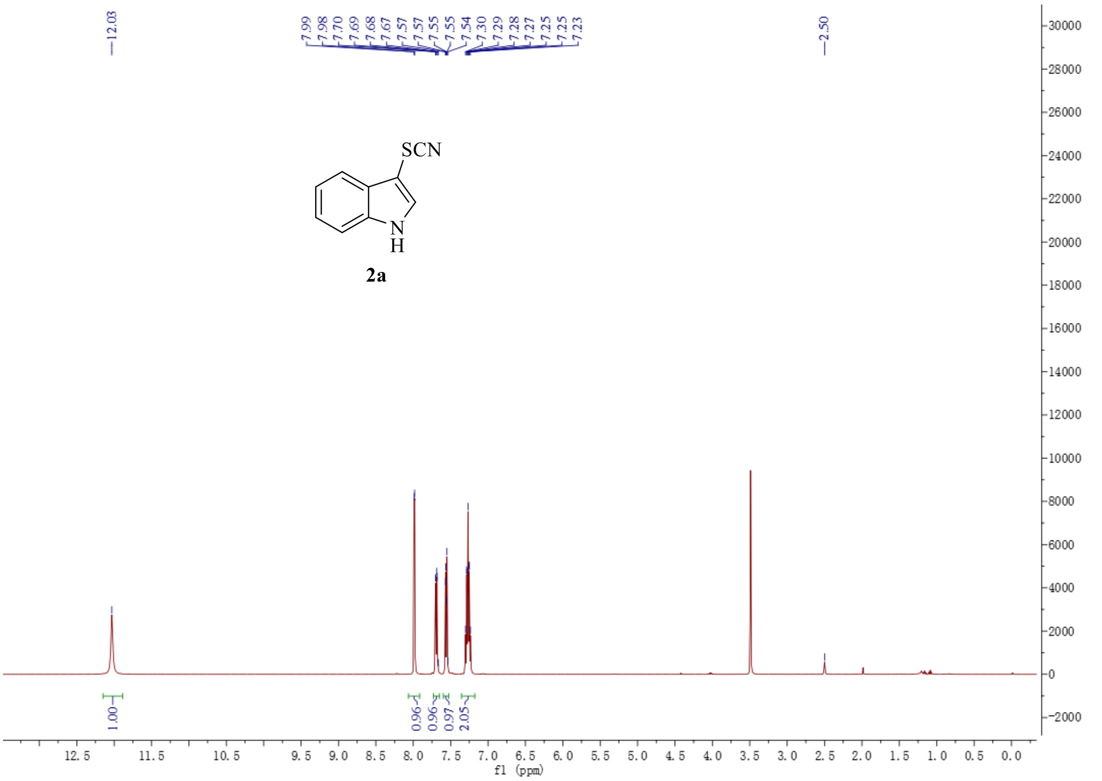


Figure S1. ^{1}H NMR of **2a**

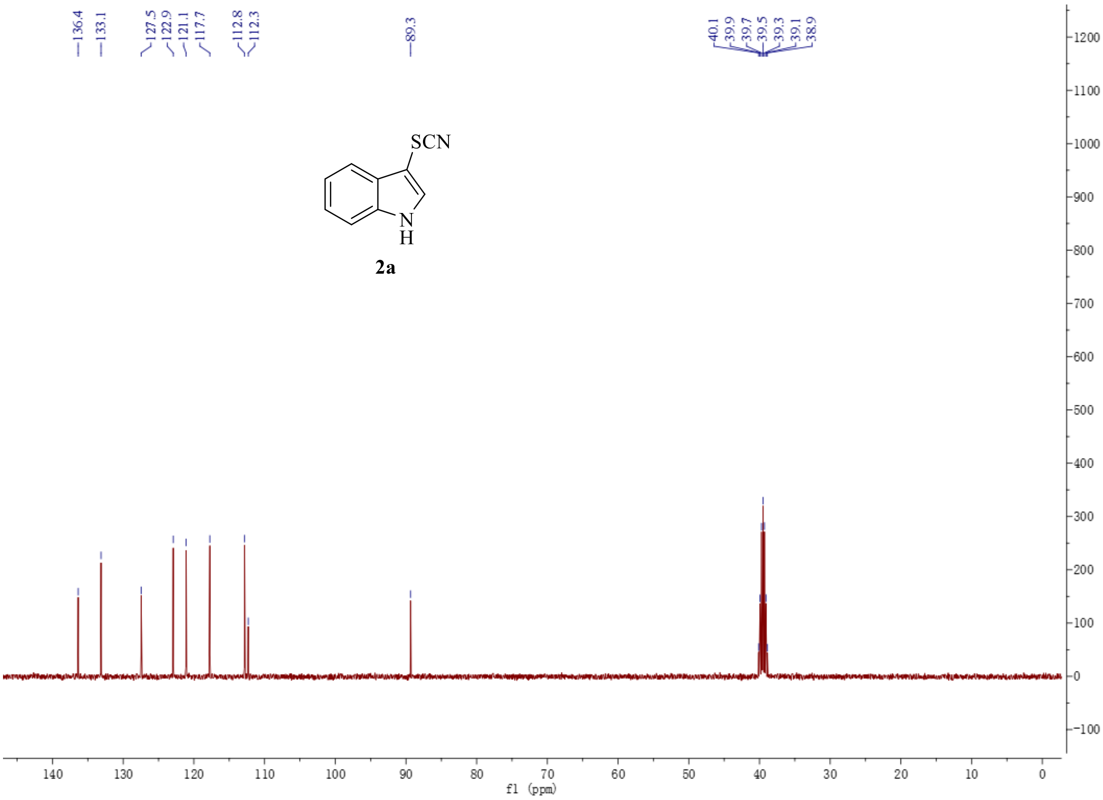


Figure S2. ^{13}C NMR of **2a**

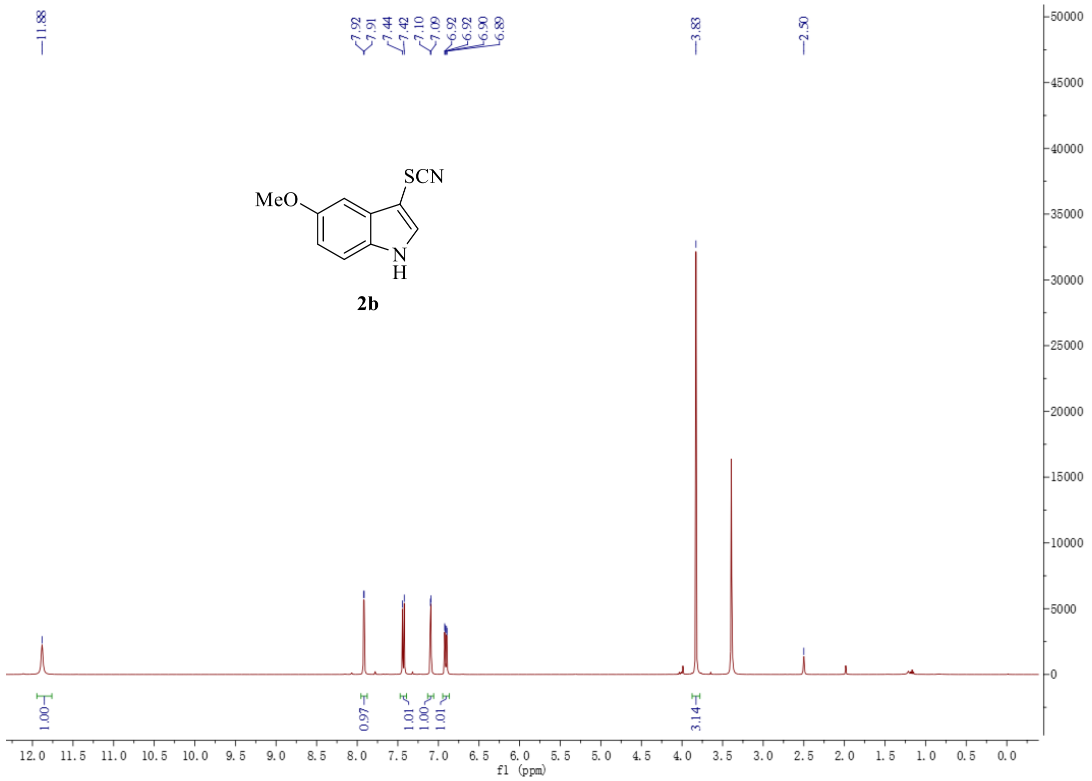


Figure S3. ^{1}H NMR of **2b**

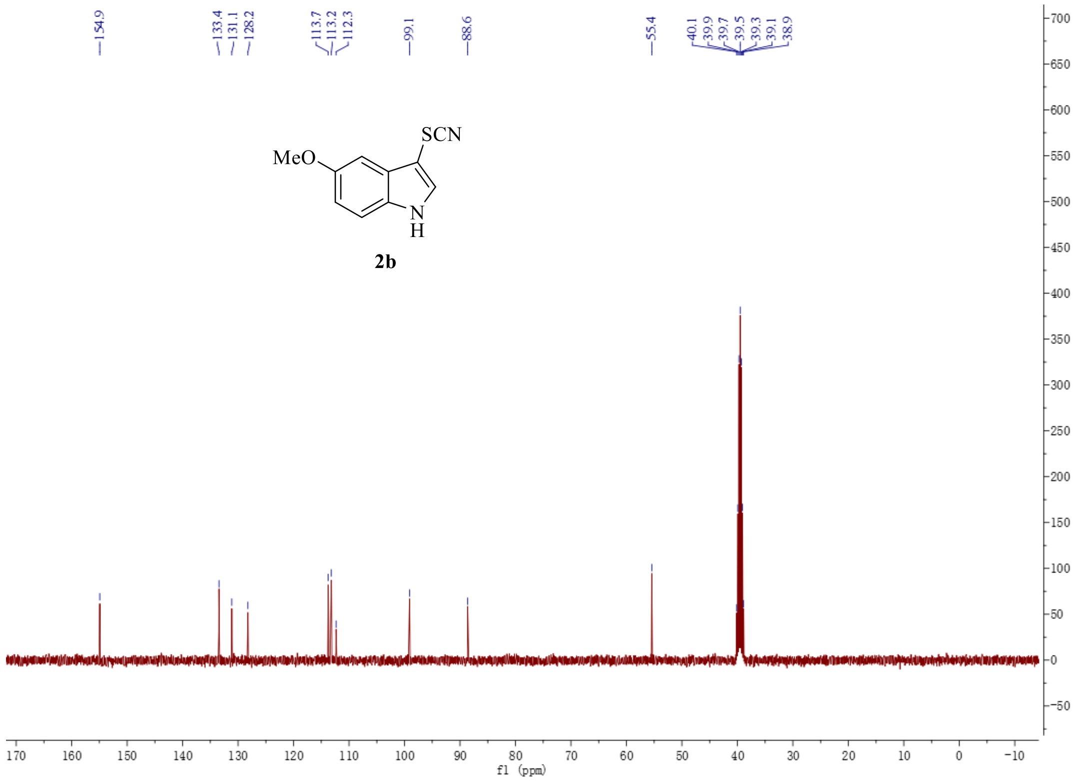


Figure S4. ^{13}C NMR of **2b**

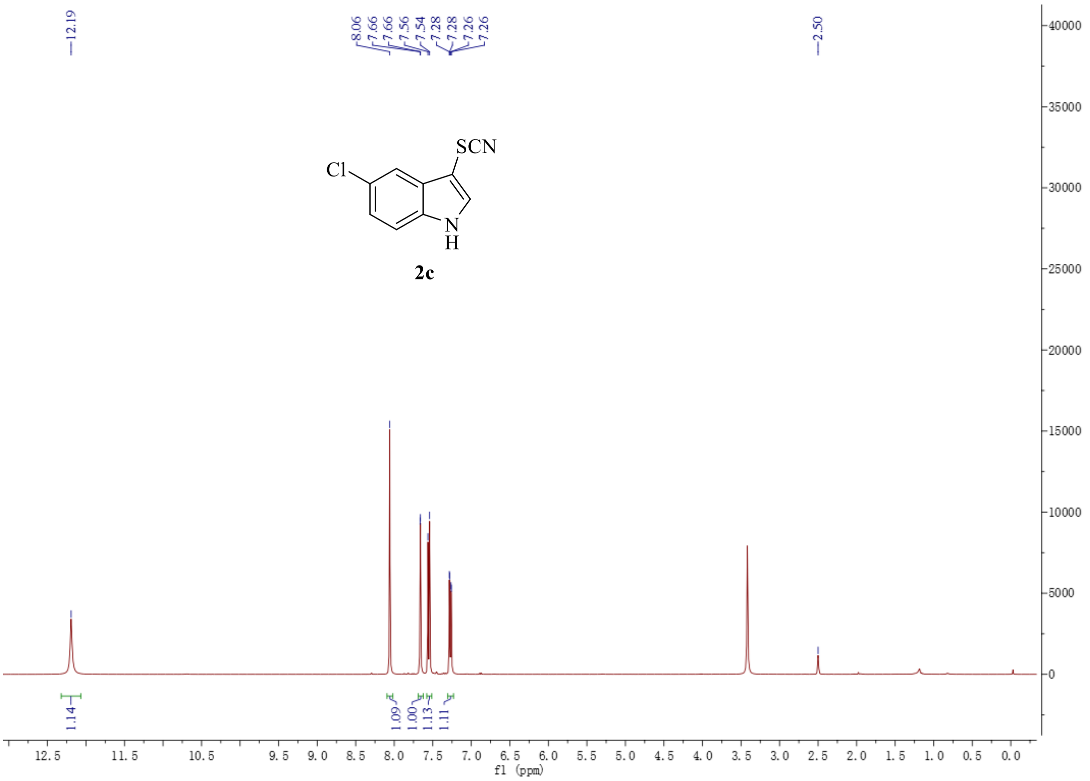


Figure S5. ^{1}H NMR of **2c**

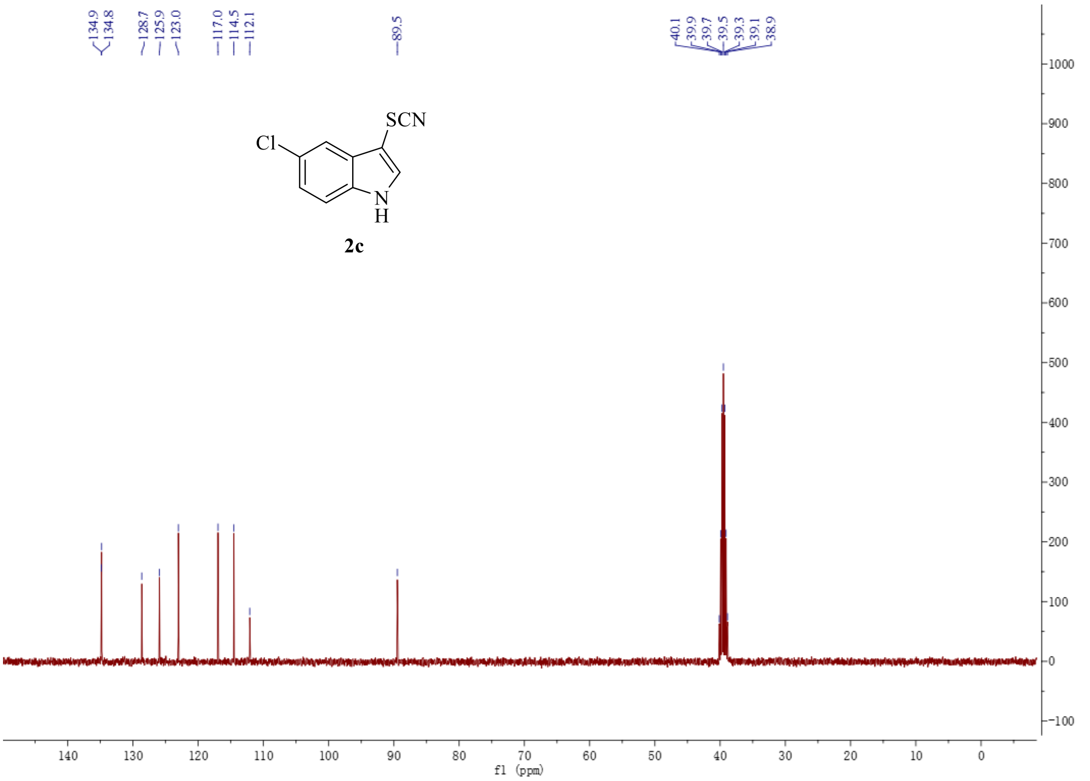


Figure S6. ^{13}C NMR of **2c**

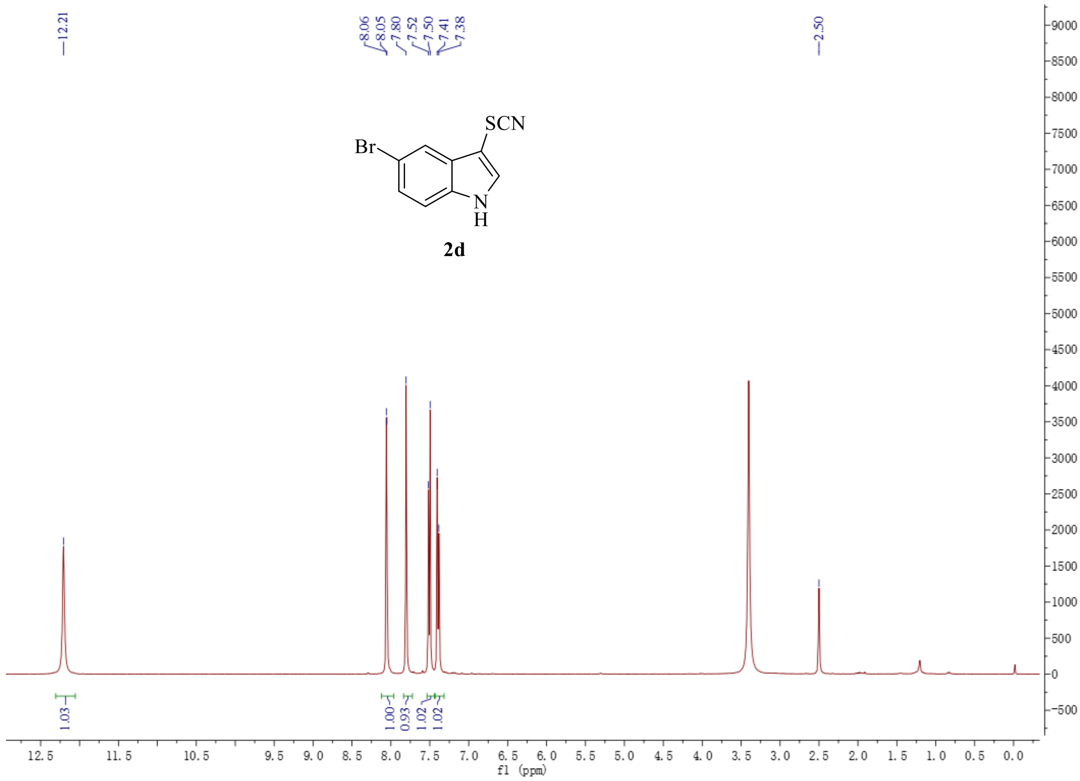


Figure S7. ^{1}H NMR of **2d**

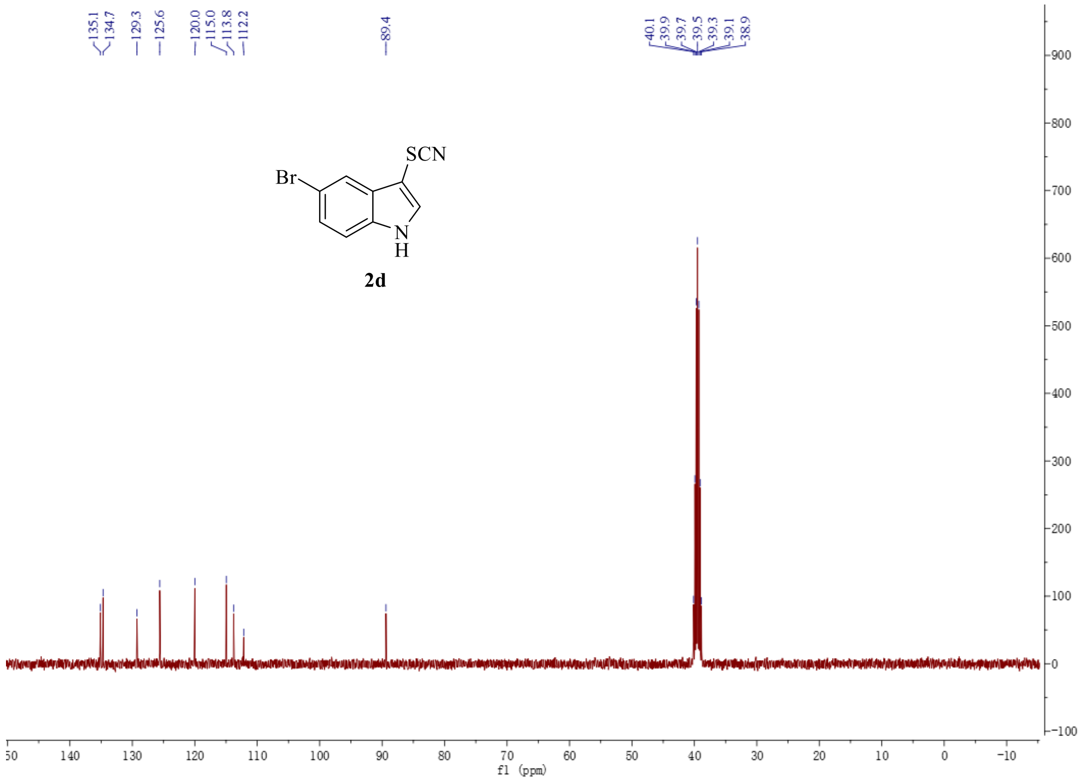


Figure S8. ^{13}C NMR of **2d**

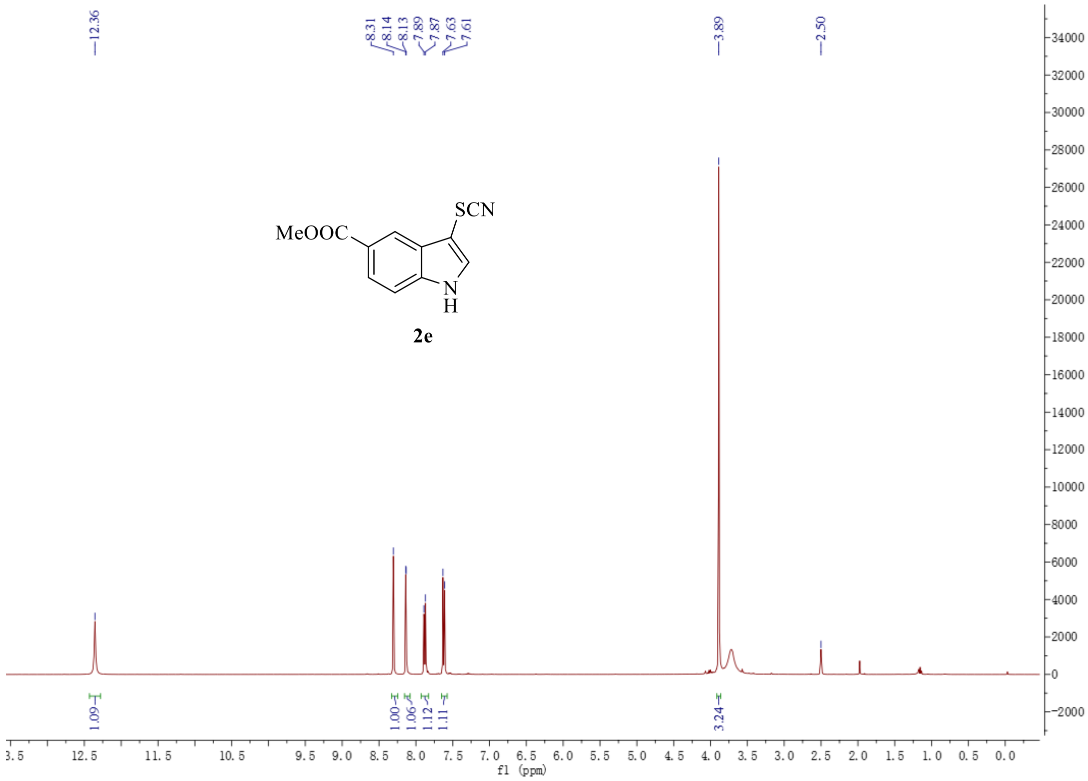


Figure S9. ^{1}H NMR of **2e**

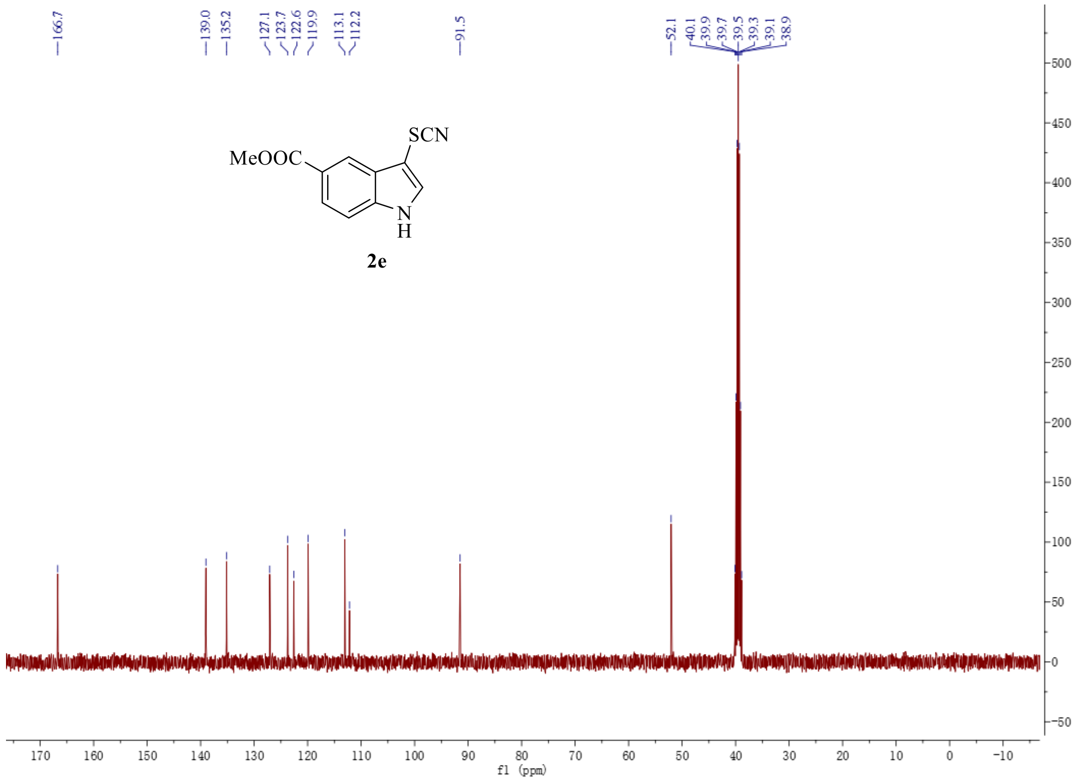


Figure S10. ^{13}C NMR of **2e**

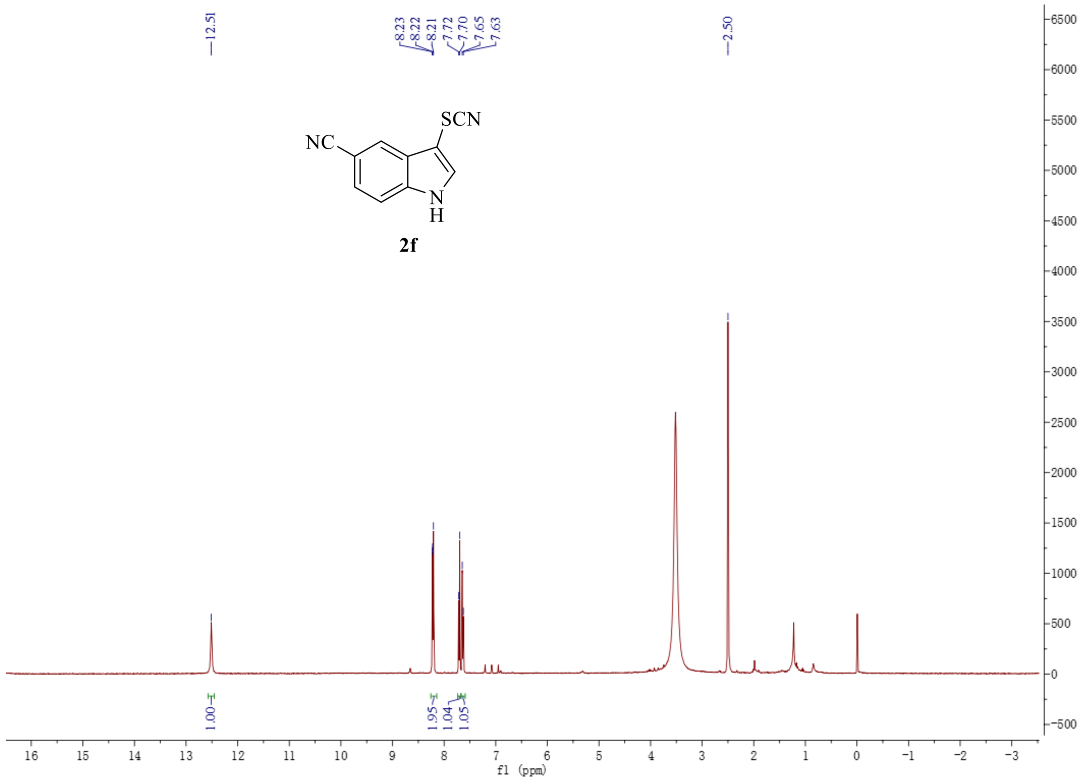


Figure S11. ^{1}H NMR of **2f**

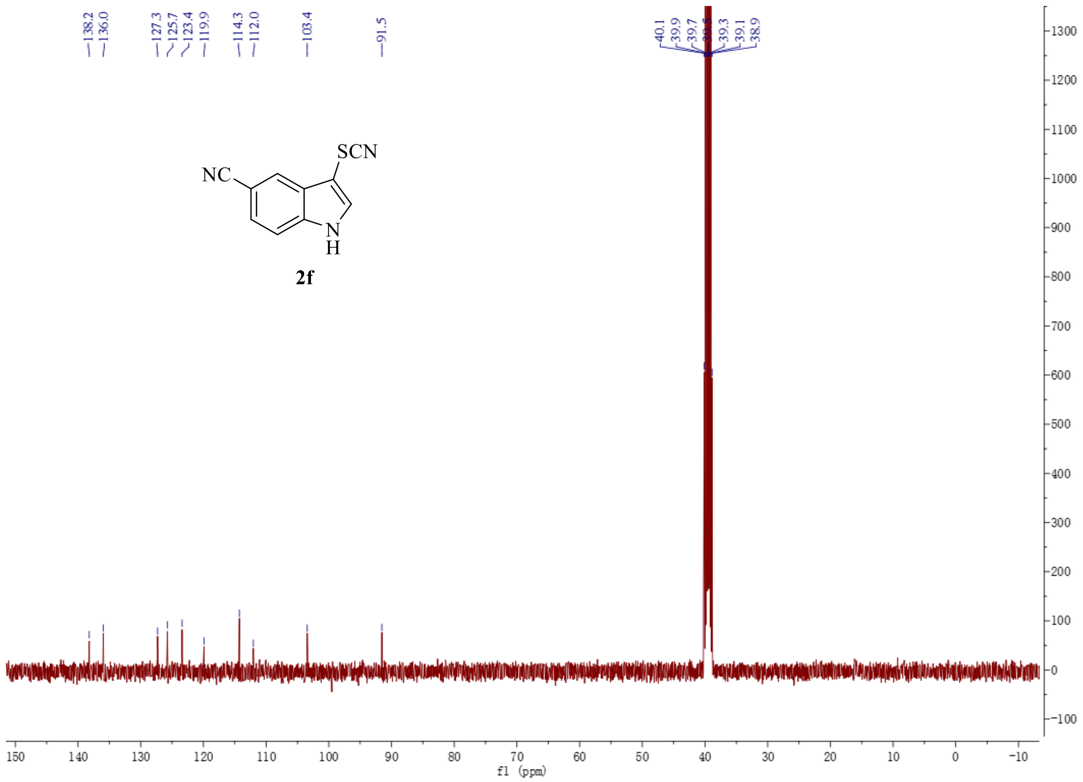


Figure S12. ^{13}C NMR of **2f**

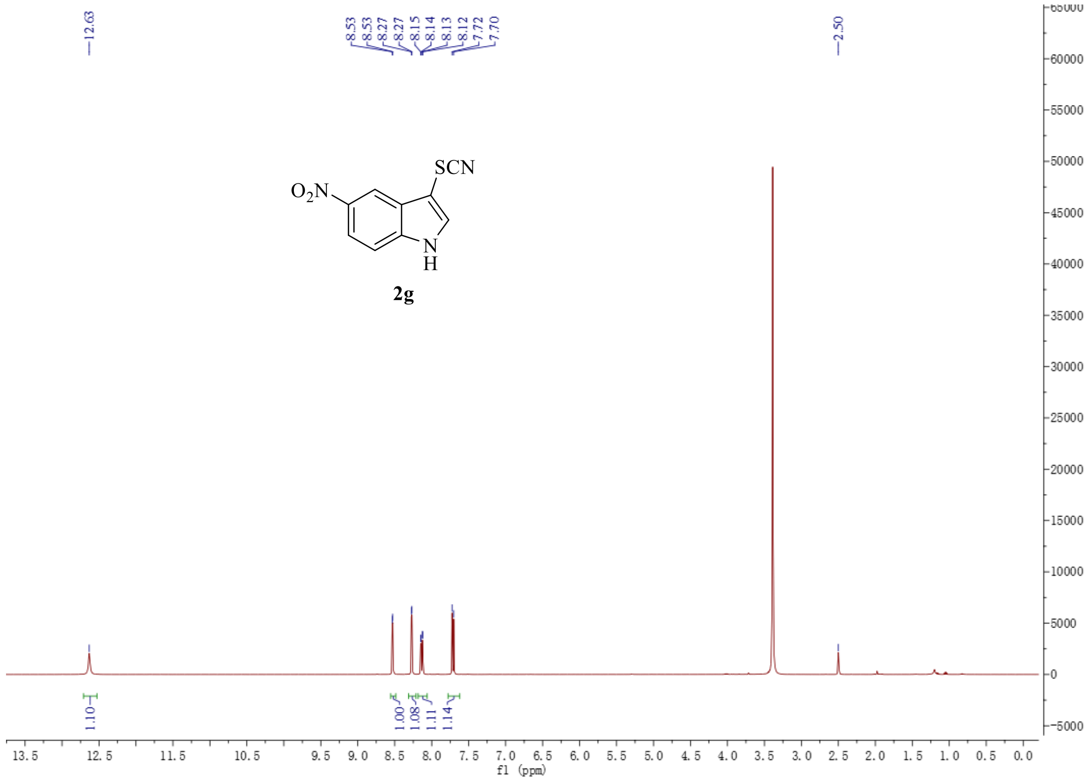


Figure S13. ^{1}H NMR of **2g**

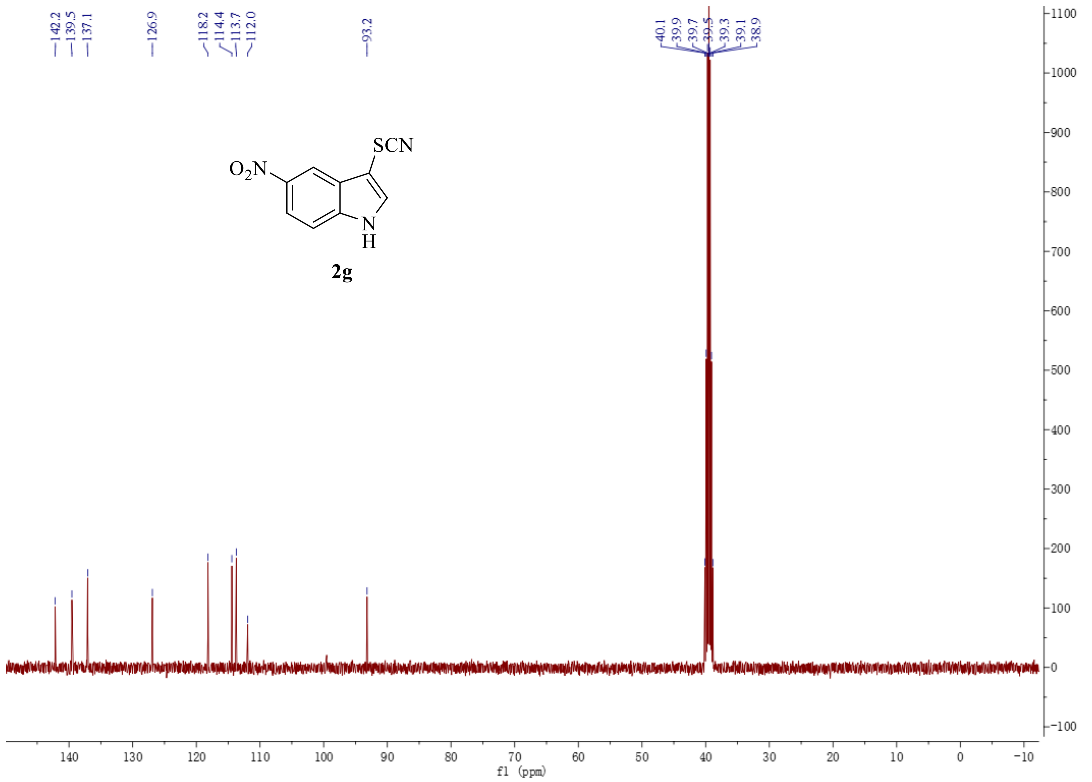


Figure S14. ^{13}C NMR of **2g**

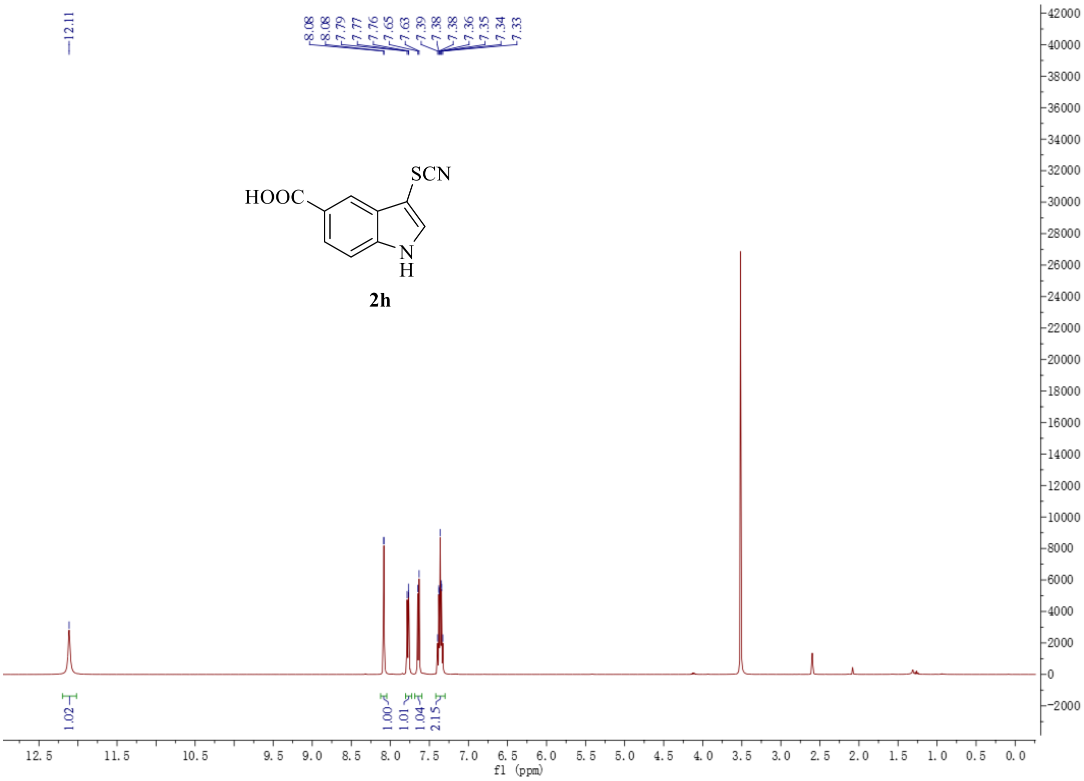


Figure S15. ^{1}H NMR of **2h**

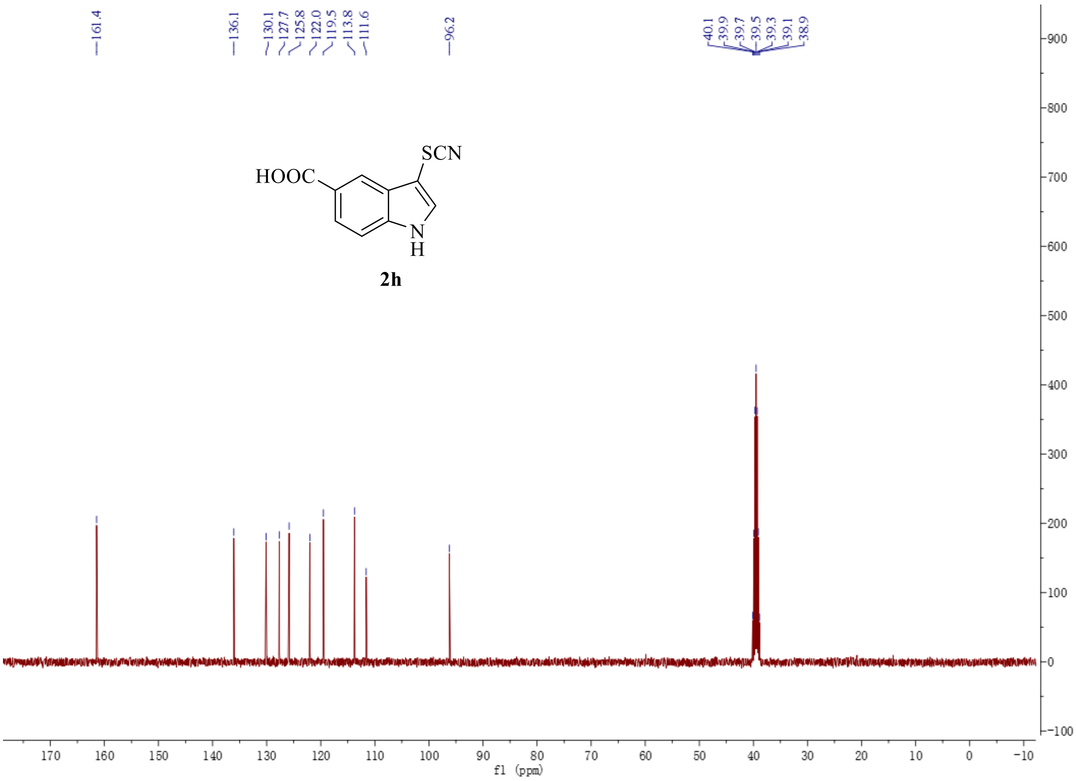


Figure S16. ^{13}C NMR of **2h**

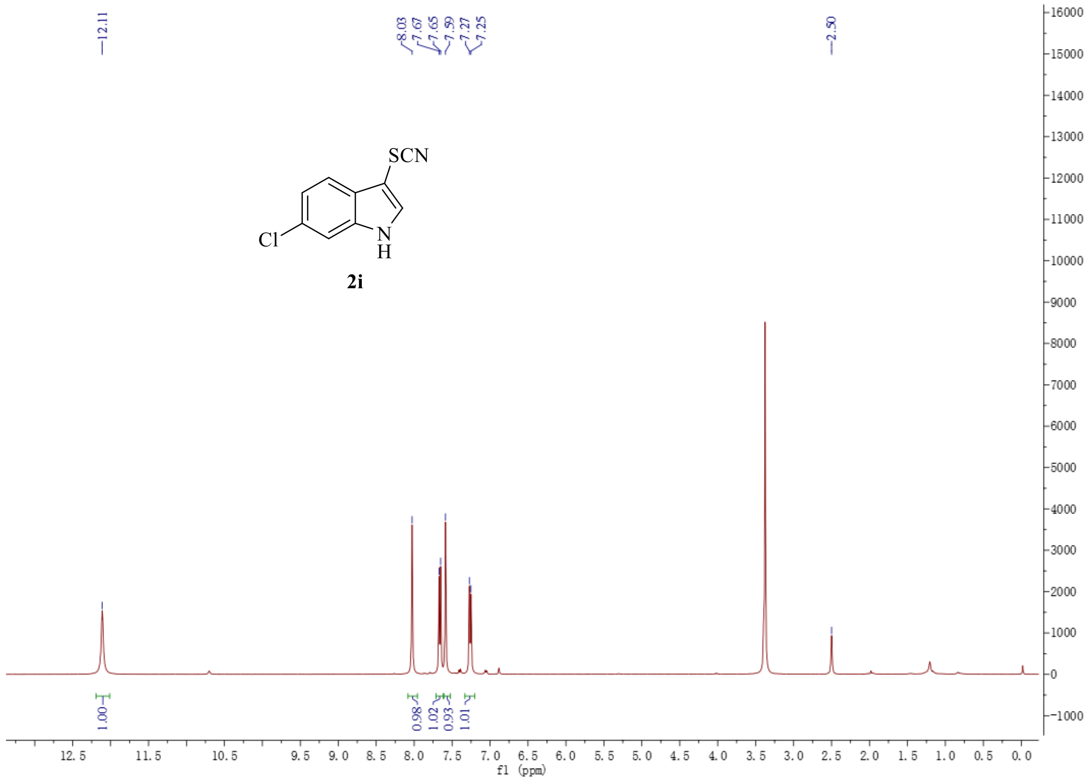


Figure S17. [1]H NMR of **2i**

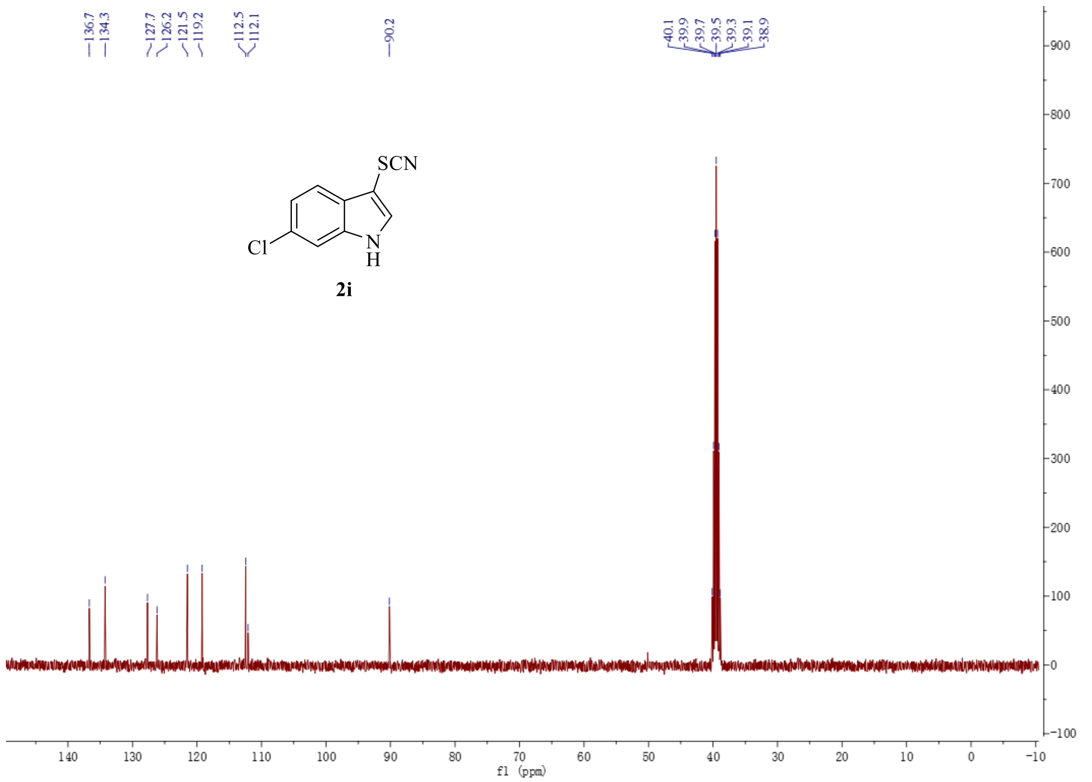


Figure S18. [13]C NMR of **2i**

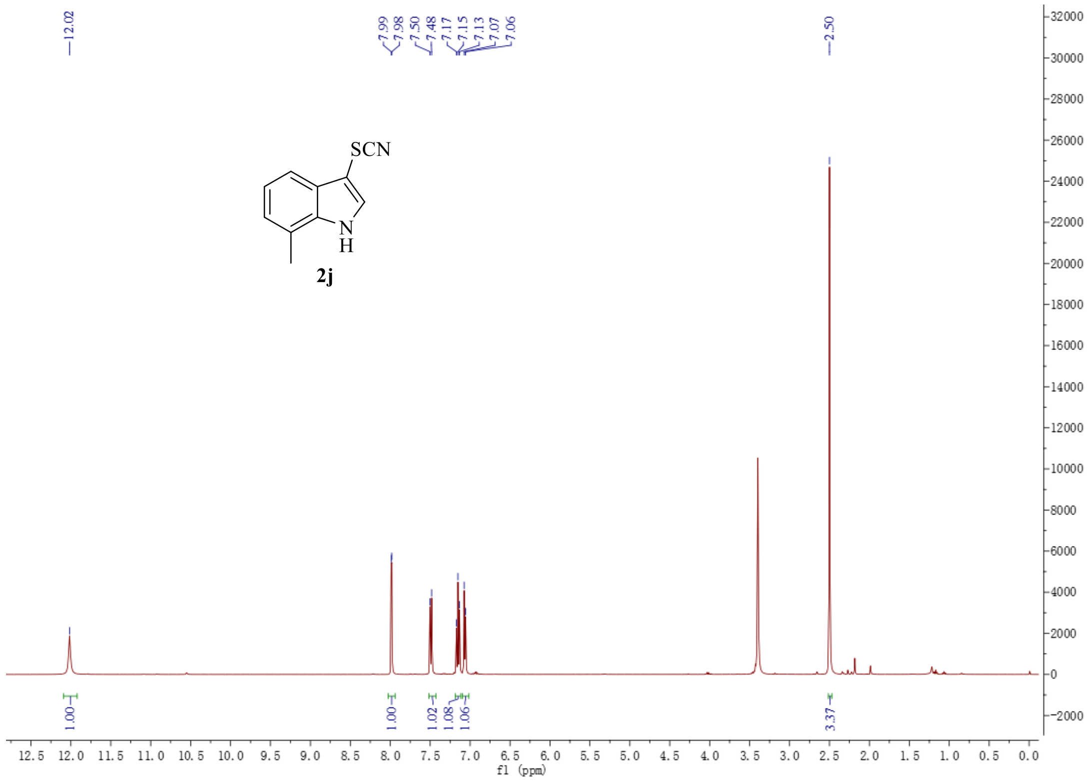


Figure S19. ^{1}H NMR of **2j**

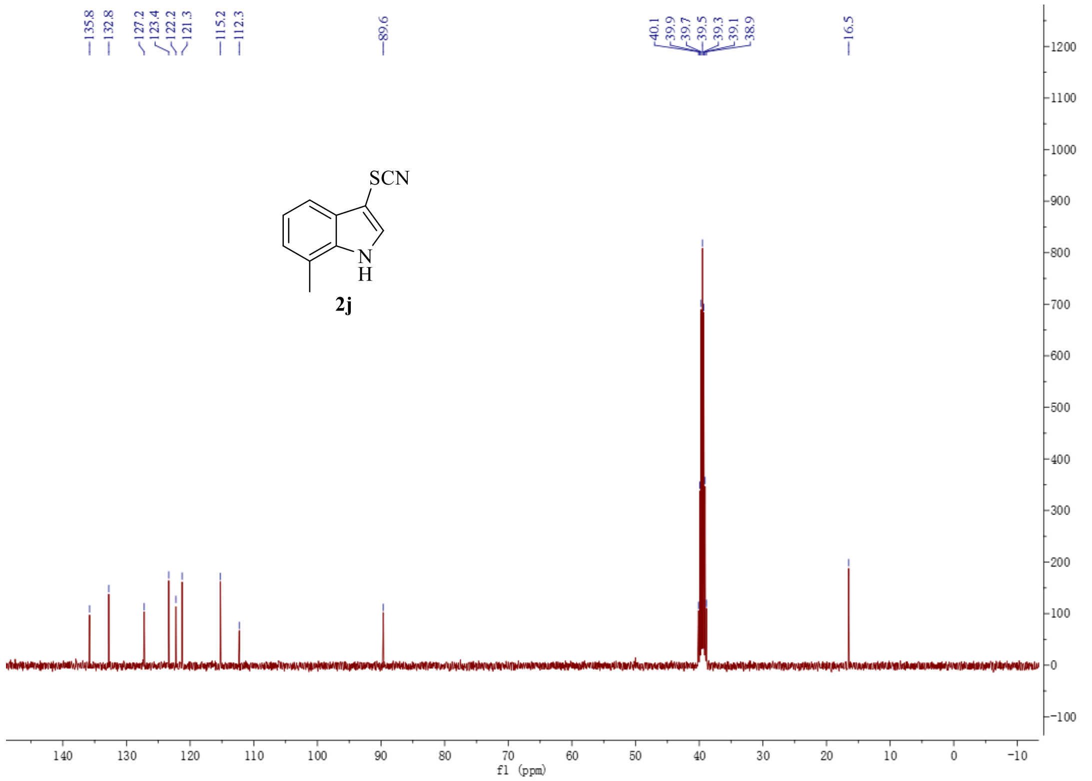


Figure S20. ^{13}C NMR of **2j**

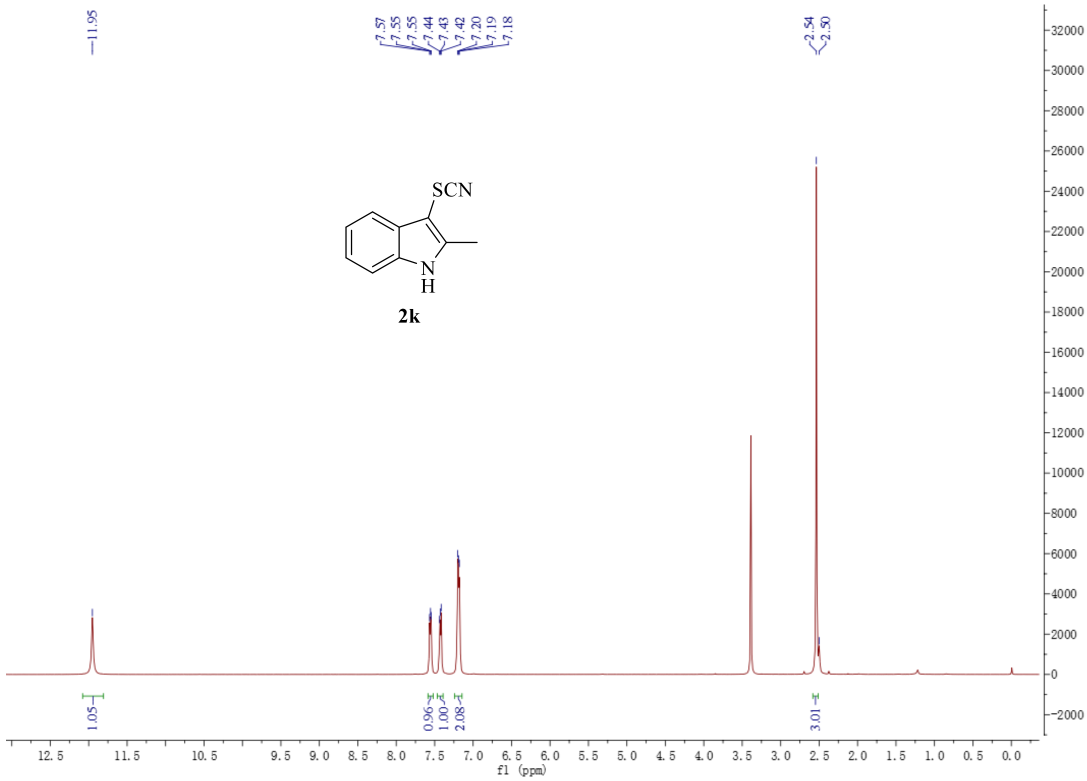


Figure S21. [1]H NMR of **2k**

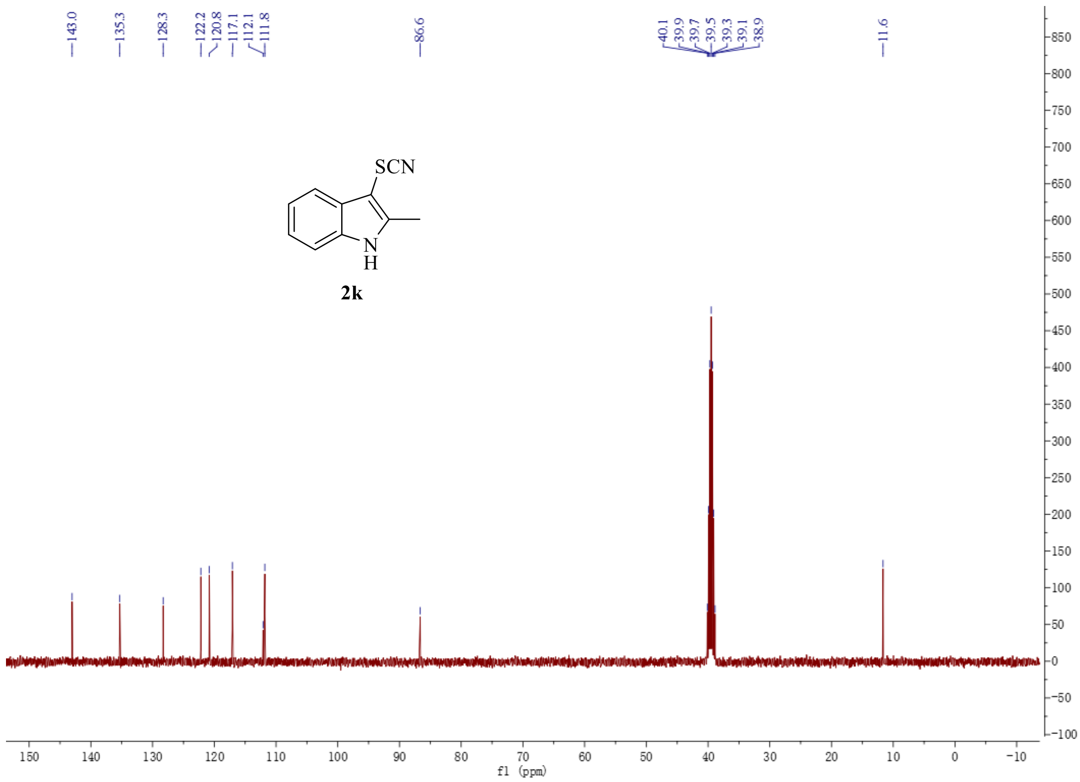


Figure S22. [13]C NMR of **2k**

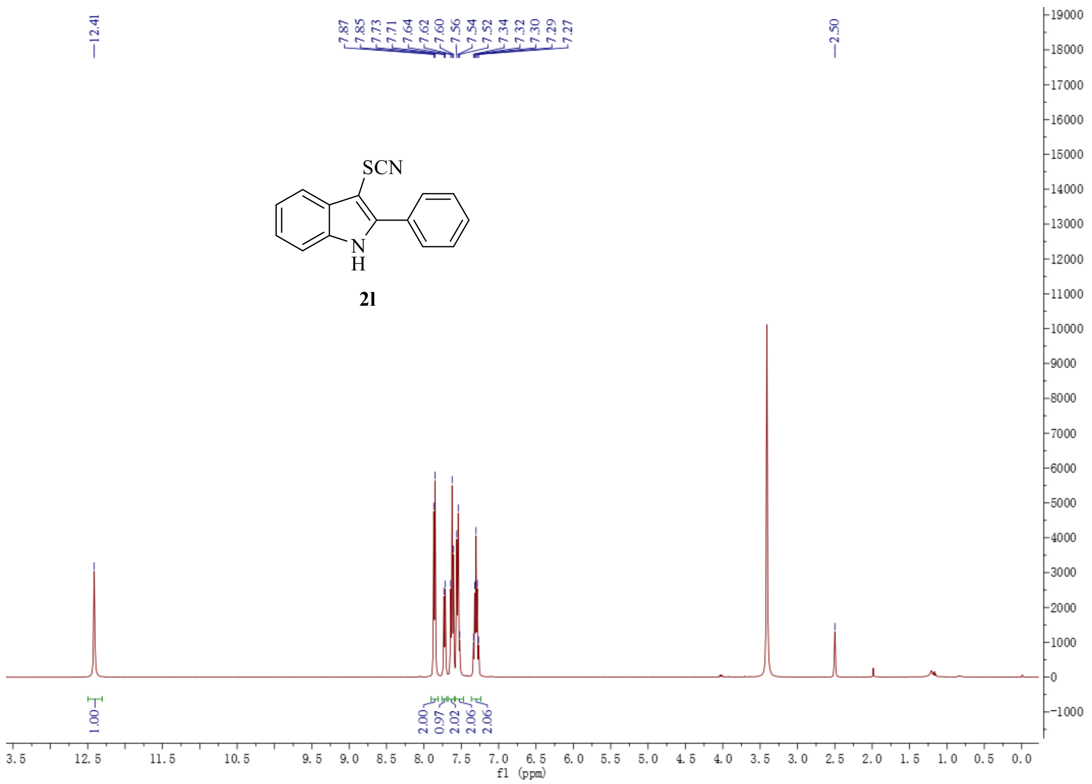


Figure S23. ^{1}H NMR of **2l**

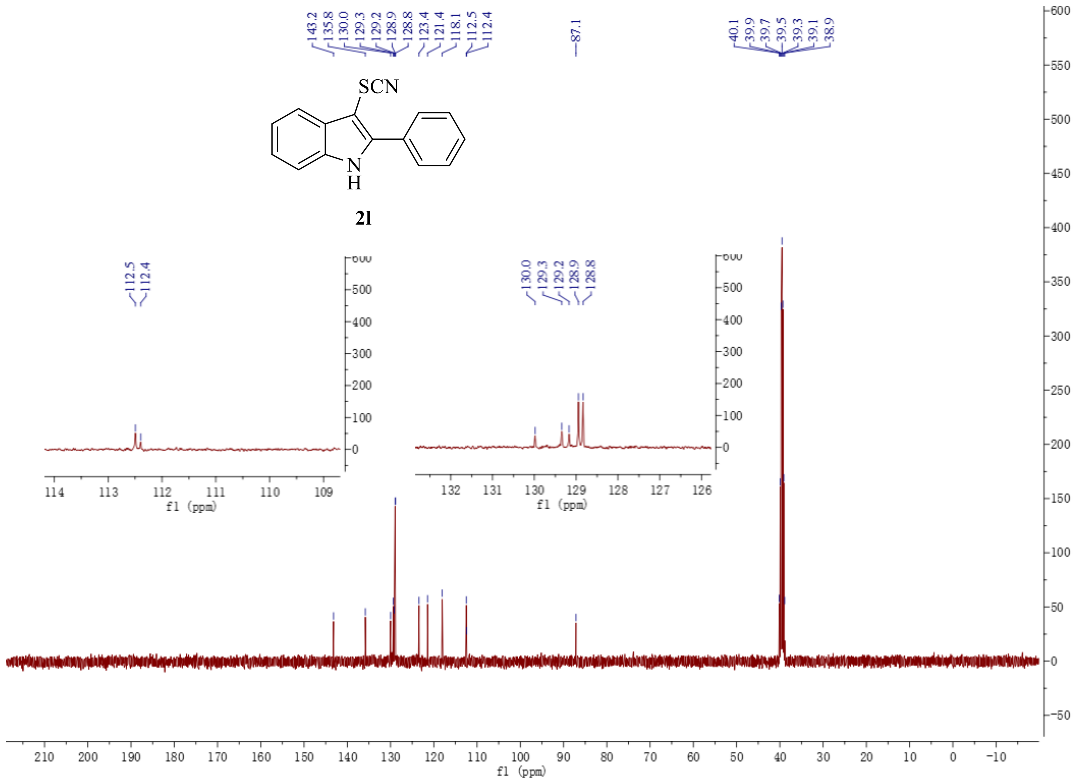


Figure S24. ^{13}C NMR of **2l**

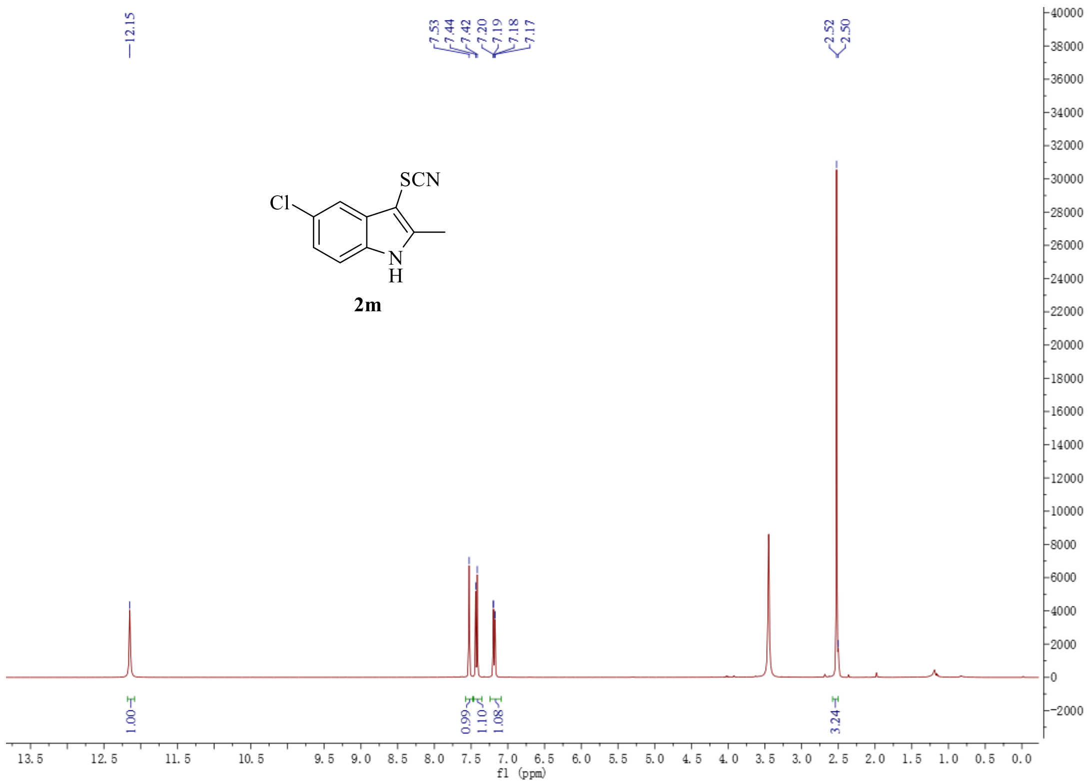


Figure S25. ^{1}H NMR of **2m**

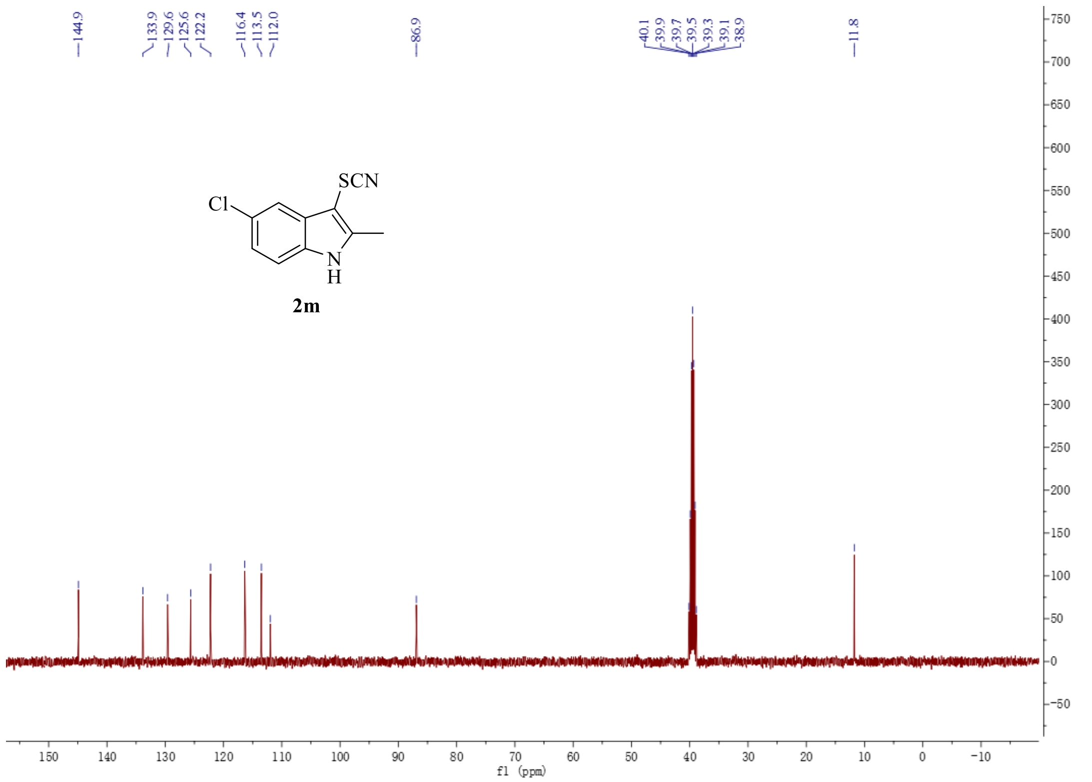


Figure S26. ^{13}C NMR of **2m**

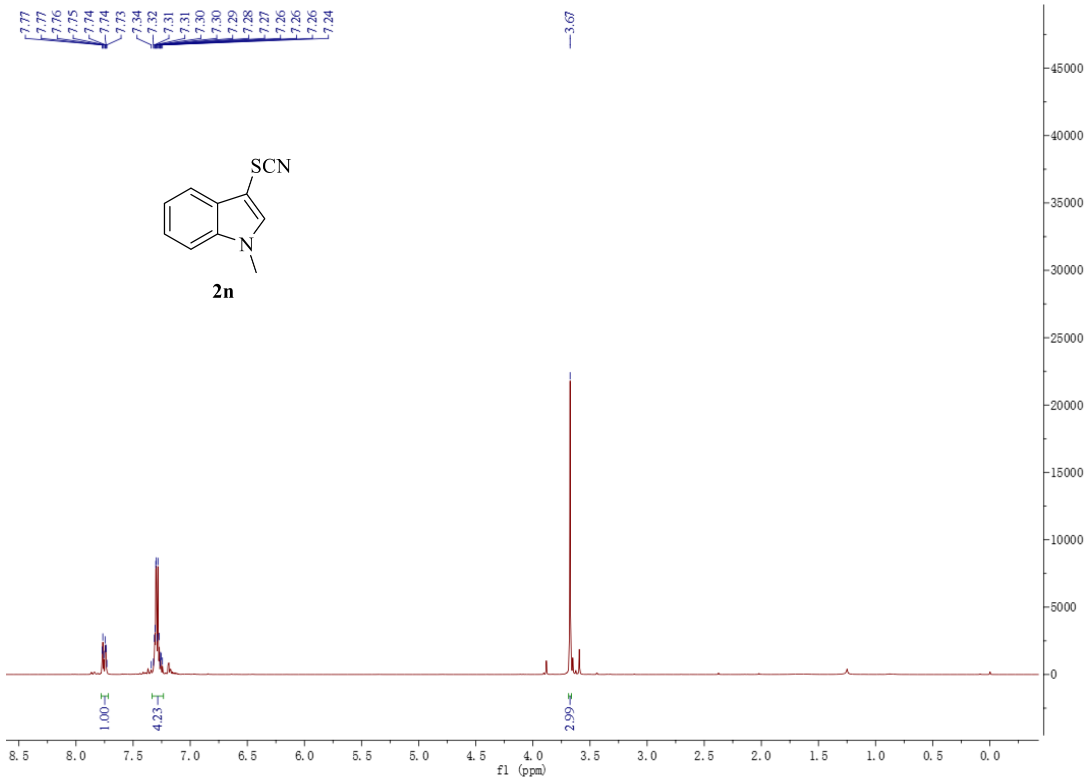


Figure S27. ^{1}H NMR of **2n**

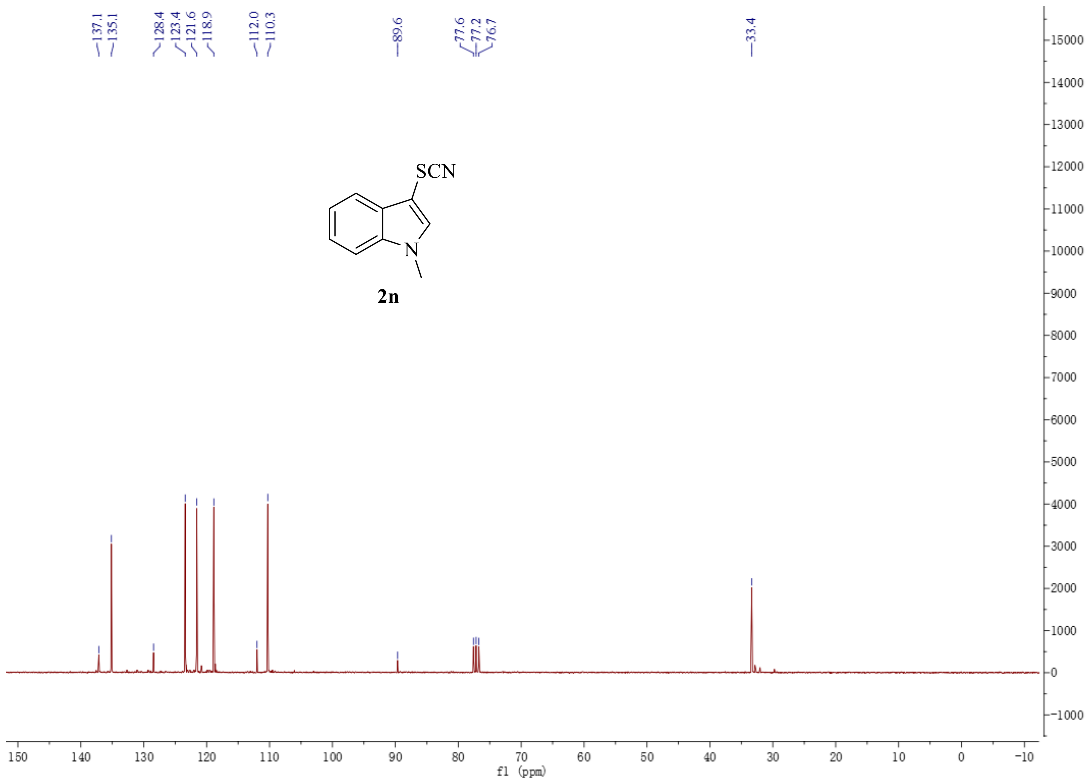


Figure S28. ^{13}C NMR of **2n**