Supporting Information

Formal [4+1] heteroannulative coupling of Knoevenagel adducts derived from 2-heteroaryl acetonitriles with isocyanides: subsequent Pd-catalyzed intramolecular *N*-arylation to 6-5-5-5-6 pentacyclic core

Anamika Prajapati,[a] Manoj Kumar Saini,[b] Shashi Kant Verma,[b] Harshita Singh Korawat,[b] Ashok K. Basak*[b]

[a]*Department of Chemistry, University of Rajasthan, JLN Marg, Jaipur 302004, India*
[b]*Department of Chemistry, Institute of Science, Banaras Hindu University, Varanasi 221005, India*
*Corresponding author e-mail ID: akbasak.chem@bhu.ac.in

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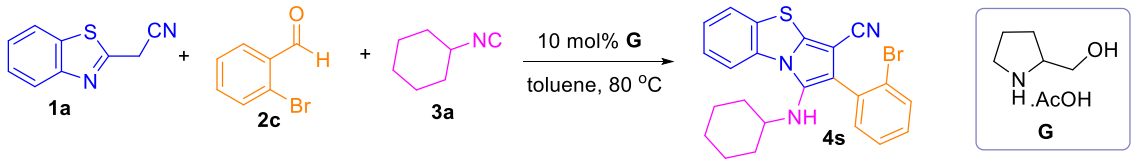
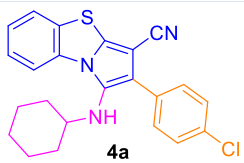
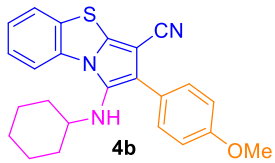
General experimental: Unless otherwise mentioned, all chemicals received from commercial sources were used without purification. All commercial grade solvents were used without any purification. HRMS spectra were recorded on SCIEX G2-SQ TOF (Waters, USA) mass spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on Jeol JNM-ECS spectrometer at operating frequencies of 400 MHz & 500 MHz (^{1}H) or 100 MHz & 125 (^{13}C) as indicated in the individual spectrum using TMS as an internal standard. Thin layer chromatography was performed on aluminum plates (silica gel 60 PF254, 0.25 mm) purchased from Merck. Melting points were recorded in open capillary method. The catalysts were purchased from commercial sources and/or prepared in the laboratory following literature procedures. The multiplicity in ^{1}H NMR spectra is presented as s for singlet, d for doublet, dd for doublet of doublet, t for triplet, apt for apparently triplet, q for quartet and m for multiplet.

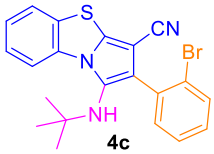
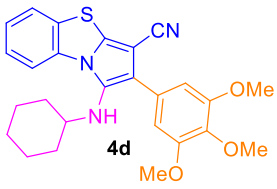
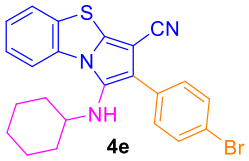
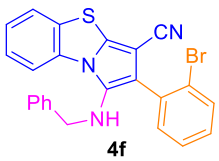
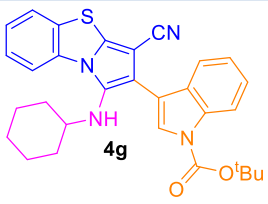
Experimental procedure for the 2-(hydroxymethyl)pyrrolidinium acetate catalyzed GBB reaction:

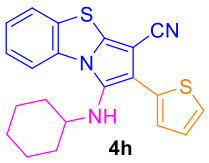
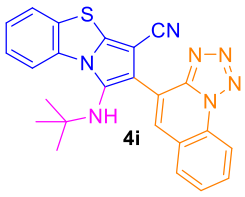
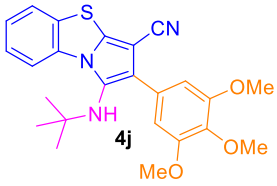
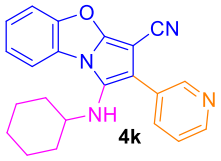
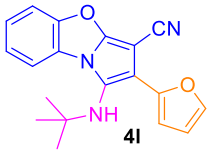


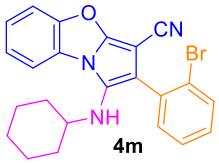
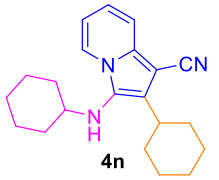
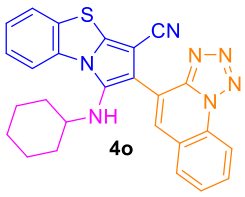
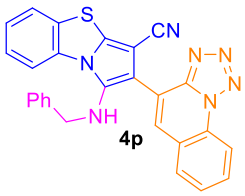
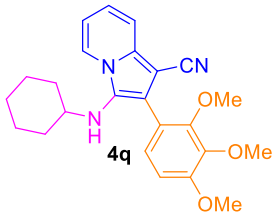
A mixture of 2-bromobenzaldehyde **2c** (46.3 mg, 0.25 mmol), 2-benzothiazole acetonitrile **1a** (43.6 mg, 0.25 mmol), cyclohexylisocyanide **3a** (27.3 mg, 0.25 mmol) and 2-(hydroxymethyl)pyrrolidinium acetate **G** (4.1 mg. 0.025 mmol) in toluene (0.75 mL) under nitrogen atmosphere was placed in a pre-heated oil bath at 80 °C and stirred for 3 hours. The reaction mixture was then cooled to rt and charged into silica gel column and eluted with 10% ethyl acetate in hexanes as eluent to obtain compound **4s** (85.4 mg, 76% yield) as a white solid.

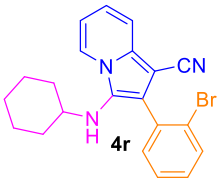
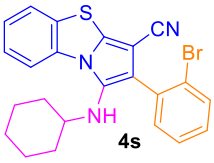
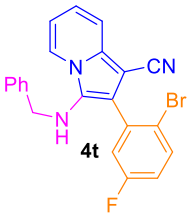
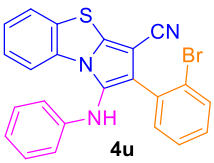
Analytical data for the synthesized compounds:

 **4a**	2-(4-chlorophenyl)-1-(cyclohexylamino)benzo[d]pyrrolo[2,1-b]thiazole-3-carbonitrile (**4a**): 79.2 mg, 78% yield; white solid, mp 240-241 °C; purified using 10% ethyl acetate in hexanes as eluent; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 8.24 (d, *J* = 8.0 Hz, 1H), 7.66 (d, *J* = 8.0 Hz, 1H), 7.47-7.39 (m, 5H), 7.34 (apt, *J* = 8.0 Hz, 1H), 3.36 (brs, 1H, NH), 2.77-2.67 (m, 1H), 1.81-1.69 (m, 2H), 1.63-1.43 (m, 3H), 1.14-0.87 (m, 5H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 134.7, 133.3, 133.2, 131.1, 130.7, 130.0, 129.9, 129.1, 126.1, 124.8, 123.6, 122.5, 116.0, 115.1, 82.1, 57.3, 33.3, 25.5, 24.7; **HRMS** (ESI-TOF) calculated for $C_{23}H_{21}ClN_3S$ $[M+H]^+$: 406.1144 found 406.1133.
 **4b**	1-(cyclohexylamino)-2-(4-methoxyphenyl)benzo[d]pyrrolo[2,1-b]thiazole-3-carbonitrile (**4b**): 82.3 mg, 82% yield; light yellow solid, mp 232-233 °C; purified using 20% ethyl acetate in hexanes as eluent; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 8.27 (d, *J* = 8.4 Hz, 1H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.48-7.31 (m, 4H), 7.01 (dd, *J* = 1.6, 8.0 Hz, 2H), 3.86 (s, 3H), 3.40 (d, *J* = 1.6 Hz, 1H), 2.73 (brs, NH, 1H), 1.83-1.72 (m, 2H), 1.65-1.53 (m, 2H), 1.52-1.42 (m, 1H), 1.15-0.86 (m, 5H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 158.9, 134.9, 132.5, 130.7, 129.9, 129.7, 126.0, 125.0, 124.5, 123.5, 123.4, 116.4, 115.0, 114.3, 82.3, 57.3, 55.3, 33.3, 25.6, 24.8; **HRMS** (ESI-TOF) calculated for $C_{24}H_{24}N_3OS$ $[M+H]^+$: 402.1639 found 402.1647.

 **4c**	2-(2-bromophenyl)-1-(tert-butylamino)benzo[d]pyrrolo[2,1-b]thiazole-3-carbonitrile (**4c**): 67.8 mg, 64% yield; white solid, mp 210-211 °C; purified using 10% ethyl acetate in hexanes as eluent; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 8.67 (d, *J* = 8.4 Hz, 1H), 7.69 (d, *J* = 8.0 Hz, 2H), 7.50 (dd, *J* = 1.6, 7.6 Hz, 2H), 7.47-7.40 (m, 2H), 7.35 (dt, *J* = 1.6, 8.0 Hz, 1H), 7.29-7.23 (m, 1H), 3.09 (brs, 1H, NH), 0.91 (s, 9H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 135.3, 134.2, 133.5, 133.1, 132.7, 130.7, 129.6, 127.7, 125.8, 125.5, 124.8, 123.5, 123.4, 116.2, 115.8, 83.4, 56.0, 29.6; **HRMS** (ESI-TOF) calculated for $C_{21}H_{19}BrN_3S$ $[M+H]^+$: 424.0482 found 424.0482.
 **4d**	1-(cyclohexylamino)-2-(3,4,5-trimethoxyphenyl)benzo[d]pyrrolo[2,1-b]thiazole-3-carbonitrile (**4d**): 87.7 mg, 76% yield; light yellow solid, mp 255-256 °C; purified using 20% ethyl acetate in hexanes as eluent; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 8.26 (d, *J* = 8.0 Hz, 1H), 7.68 (d, *J* = 7.6 Hz, 1H), 7.45 (dt, *J* = 1.2, 8.0 Hz, 1H), 7.35 (dt, *J* = 1.2, 8.0 Hz, 1H), 6.71 (s, 2H), 3.91 (s, 9H), 3.44 (brs, 1H, NH), 2.86-2.72 (m, 1H), 1.86-1.73 (m, 2H), 1.66-1.45 (m, 3H), 1.19-0.94 (m, 5H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 153.5, 137.5, 134.8, 132.9, 130.7, 129.9, 128.1, 126.1, 124.7, 123.6, 116.2, 115.0, 106.0, 82.3, 60.7, 57.3, 56.3, 33.3, 25.6, 24.7; **HRMS** (ESI-TOF) calculated for $C_{26}H_{28}N_3O_3S$ $[M+H]^+$: 462.1851 found 462.1838.
 **4e**	2-(4-bromophenyl)-1-(cyclohexylamino)benzo[d]pyrrolo[2,1-b]thiazole-3-carbonitrile (**4e**): 87.6 mg, 78% yield; light yellow solid, mp 258-260 °C; purified using 10% ethyl acetate in hexanes as eluent; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 8.25 (d, *J* = 7.6 Hz, 1H), 7.67 (dd, 0.8, 8.0 Hz, 1H), 7.59 (dd, *J* = 1.6, 8.4 Hz, 2H), 7.45 (dt, *J* = 1.2, 8.4 Hz, 1H), 7.40-7.31 (m, 3H), 3.37 (d, *J* = 8.0 Hz, 1H), 2.80-2.64 (m, 1H), 1.84-1.68 (m, 2H), 1.67-1.40 (m, 3H), 1.18-0.84 (m, 5H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 134.8, 133.2, 132.1, 131.6, 130.7, 130.2, 129.9, 126.1, 124.8, 123.6, 122.5, 121.5, 116.0, 115.1, 82.0, 57.4, 33.3, 25.5, 24.7; **HRMS** (ESI-TOF) calculated for $C_{23}H_{21}BrN_3S$ $[M+H]^+$: 450.0639 found 450.0628.
 **4f**	1-(benzylamino)-2-(2-bromophenyl)benzo[d]pyrrolo[2,1-b]thiazole-3-carbonitrile (**4f**): 91.4 mg, 80% yield; light brown solid, mp 145-146 °C; purified using 10% ethyl acetate in hexanes as eluent; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 8.35 (d, *J* = 8.4 Hz, 1H), 7.73-7.59 (m, 2H), 7.43 (dt, *J* = 1.2, 8.0 Hz, 1H), 7.39-7.25 (m, 2H), 7.25-7.13 (m, 5H), 7.08-6.98 (m, 2H), 4.05 (dd, *J* = 6.8, 13.2 Hz, 1H), 3.90 (dd, *J* = 6.8, 13.2 Hz, 1H), 3.58 (t, *J* = 6.8 Hz, 1H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 138.1, 134.7, 132.8, 132.7, 132.6, 132.4, 131.0, 130.6, 129.6, 128.5, 127.8, 127.6, 127.5, 126.3, 124.9, 123.8, 123.6, 122.3, 115.6, 115.1, 83.2, 53.5; **HRMS** (ESI-TOF) calculated for $C_{24}H_{17}BrN_3S$ $[M+H]^+$: 458.0326 found 458.0319.
 **4g**	tert-butyl 3-(3-cyano-1-(cyclohexylamino)benzo[d]pyrrolo[2,1-b]thiazol-2-yl)-1H-indole-1-carboxylate (**4g**): 94.5 mg, 74% yield; light yellow solid, mp 198-200 °C; purified using 10% ethyl acetate in hexanes as eluent; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 8.26 (d, *J* = 9.0 Hz, 1H), 8.21 (d, *J* = 6.5 Hz, 1H), 7.72 (brs, 1H), 7.68 (d, *J* = 7.0 Hz, 1H), 7.51-7.42 (m, 2H), 7.40-7.32 (m, 2H), 7.28 (apt, *J* = 8.0 Hz, 1H), 3.23 (d, *J* = 8.0 Hz, 1H), 2.81-2.69 (m, 1H), 1.83-1.74 (m, 2H), 1.71 (s, 9H), 1.58-1.49 (m, 2H), 1.48-1.40 (m, 1H), 1.10-0.82 (m, 5H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 149.6, 134.8, 132.7, 131.3, 130.7, 129.6, 126.1, 124.8, 124.7, 124.4, 123.6, 123.1, 119.5, 115.9, 115.5, 115.1, 114.3, 112.5, 84.1, 83.2, 57.3, 33.2, 28.2, 25.5, 24.7; **HRMS** (ESI-TOF) calculated for $C_{30}H_{31}N_4O_2S$ $[M+H]^+$: 511.2167 found 511.2163.

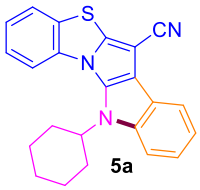
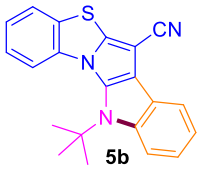
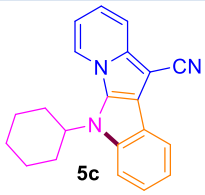
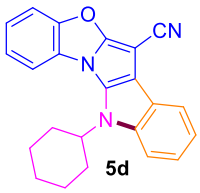
 **4h**	1-(cyclohexylamino)-2-(thiophen-2-yl)benzo[d]pyrrolo[2,1-b]thiazole-3-carbonitrile (**4h**): 73.6 mg, 78% yield; light brown viscous oil; purified using 10% ethyl acetate in hexanes as eluent; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 8.24 (d, *J* = 9.5 Hz, 1H), 7.64 (d, *J* = 8.0 Hz, 1H), 7.45 (d, *J* = 4.0 Hz, 1H), 7.42 (apt, *J* = 8.0 Hz, 1H), 7.35-7.29 (m, 2H), 7.11 (dd, *J* = 3.0, 5.0 Hz, 1H), 3.38 (d, *J* = 6.5 Hz, 1H), 2.99-2.87 (m, 1H), 1.91-1.79 (m, 2H), 1.71-1.59 (m, 2H), 1.58-1.50 (m, 1H), 1.23-1.30 (m, 5H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 134.7, 133.7, 133.4, 130.6, 129.7, 127.5, 126.0, 125.6, 124.8, 124.5, 123.5, 117.3, 116.2, 115.1, 81.7, 57.6, 33.3, 25.6, 24.9; **HRMS** (ESI-TOF) calculated for $C_{21}H_{20}N_3S_2$ $[M+H]^+$: 378.1098 found 378.1107.
 **4i**	1-(tert-butylamino)-2-(tetrazolo[1,5-a]quinolin-4-yl)benzo[d]pyrrolo[2,1-b]thiazole-3-carbonitrile (**4i**): 56.8 mg, 52% yield; white solid, mp 244-245 °C; purified using 20% ethyl acetate in hexanes as eluent; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 8.83 (d, *J* = 8.0 Hz, 1H), 8.75 (d, *J* = 8.0 Hz, 1H), 8.37 (s, 1H), 8.14 (d, *J* = 8.0 Hz, 1H), 7.91 (apt, *J* = 8.0 Hz, 1H), 7.78 (apt, *J* = 8.0 Hz, 1H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.49 (apt, *J* = 8.0 Hz, 1H), 7.40 (apt, *J* = 8.0 Hz, 1H), 4.48 (s, 1H, NH), 0.88 (s, 9H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 146.5, 135.3, 133.0, 131.9, 131.0, 130.6, 129.7, 129.4, 128.4, 125.8, 125.3, 124.3, 123.5, 119.4, 118.4, 117.0, 116.7, 115.9, 82.2, 56.6, 29.2; **HRMS** (ESI-TOF) calculated for $C_{24}H_{20}N_7S$ $[M+H]^+$: 438.1501 found 438.1512.
 **4j**	1-(tert-butylamino)-2-(3,4,5-trimethoxyphenyl)benzo[d]pyrrolo[2,1-b]thiazole-3-carbonitrile (**4j**): 67.6 mg, 62% yield; light yellow soild, mp 222-224 °C; purified using 20% ethyl acetate in hexanes as eluent; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 8.59 (d, *J* = 8.0 Hz, 1H), 7.66 (dd, *J* = 0.8, 8.0 Hz, 1H), 7.42 (dt, *J* = 0.8, 8.0 Hz, 1H), 7.33 (dt, *J* = 0.8, 7.6 Hz, 1H), 6.69 (s, 2H), 3.91 (s, 6H), 3.89 (s, 3H), 0.95 (s, 9H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 135.5, 137.7, 135.4, 133.5, 130.7, 128.8. 128.6, 127.3, 125.5, 124.3, 123.6, 116.2, 116.0, 106.4, 80.8, 61.0, 56.7, 56.4, 29.6; **HRMS** (ESI-TOF) calculated for $C_{24}H_{26}N_3O_3S$ $[M+H]^+$: 436.1695 found 436.1691.
 **4k**	1-(cyclohexylamino)-2-(pyridin-3-yl)benzo[d]pyrrolo[2,1-b]oxazole-3-carbonitrile (**4k**): 66.8 mg, 75% yield; light brown solid, mp 183-185 °C; purified using 20% ethyl acetate in hexanes as eluent; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 8.77 (s, 1H), 8.54 (d, *J* = 5.0 Hz, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.66 (d, *J* = 6.5 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 1H), 7.39-7.29 (m, 3H), 3.31 (brs, 1H, NH), 2.86-2.72 (m, 1H), 1.81-1.71 (m, 1H), 1.65-1.52 (m, 2H), 1.51-1.14 (m, 1H), 1.15-0.94 (m, 5H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 151.8, 149.1, 148.2, 148.1, 135.9, 128.8, 126.6, 124.7, 124.4, 123.6, 122.6, 116.2, 114.2, 112.3, 112.1, 64.8, 57.4, 33.5, 25.4, 24.6; **HRMS** (ESI-TOF) calculated for $C_{22}H_{21}N_4O$ $[M+H]^+$: 357.1715 found 357.1719.
 **4l**	1-(tert-butylamino)-2-(furan-2-yl)benzo[d]pyrrolo[2,1-b]oxazole-3-carbonitrile (**4l**): 43.1 mg, 54% yield; light brown viscous oil; purified using 10% ethyl acetate in hexanes as eluent; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.83 (dd, *J* = 2.5, 5.0 Hz, 1H), 7.40 (dd, *J* = 3.0, 4.0 Hz, 1H), 7.37 (s, 1H), 7.27-7.21 (m, 2H), 6.67 (d, *J* = 3.0 Hz, 1H), 6.42 (d, *J* = 5.0 Hz, 1H), 3.52 (brs, 1H, NH), 1.01 (s, 9H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 152.1, 148.5, 147.6, 140.7, 127.1, 124.5, 124.0, 121.6, 114.2, 113.4, 113.1, 112.0, 111.6, 107.0, 63.9, 56.1, 29.4; **HRMS** (ESI-TOF) calculated for $C_{19}H_{18}N_3O_2$ $[M+H]^+$: 320.1399 found 320.1403.

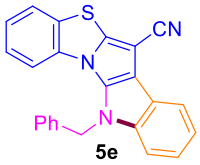
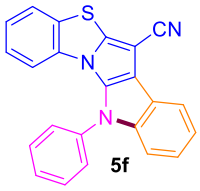
	2-(2-bromophenyl)-1-(cyclohexylamino)benzo[d]pyrrolo[2,1-b]oxazole-3-carbonitrile (**4m**): 78.1 mg, 72% yield; light yellow oil; purified using 10% ethyl acetate in hexanes as eluent; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.68-7.59 (m, 2H), 7.45 (d, *J* = 6.5 Hz, 1H), 7.38-7.32 (m, 2H), 7.31-7.24 (m, 2H), 7.18 (apt, *J* = 6.5 Hz, 1H), 3.07 (brs, 1H, NH), 2.76-2.63 (m, 1H), 1.85-1.75 (m, 1H), 1.67-1.48 (m, 2H), 1.47-1.35 (m, 2H), 1.16-0.92 (m, 4H), 0.84-0.70 (m, 1H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 152.0, 147.6, 133.3, 133.0, 132.6, 129.6, 127.6, 126.9, 124.5, 124.3, 124.2, 112.9, 118.5, 114.3, 112.5, 112.1, 66.1, 57.1, 33.5, 33.4, 25.6, 24.6, 24.3; **HRMS** (ESI-TOF) calculated for $C_{23}H_{21}BrN_3O$ $[M+H]^+$: 434.0868 found 434.0862.
	2-cyclohexyl-3-(cyclohexylamino)indolizine-1-carbonitrile (**4n**): 51.4 mg, 64% yield; light brown viscous oil; purified using 20% ethyl acetate in hexanes as eluent; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 8.07 (d, *J* = 6.5 Hz, 1H), 7.48 (d, *J* = 9.5 Hz, 1H), 6.94 (apt, *J* = 6.5 Hz, 1H), 6.93 (dd, *J* = 6.5, 9.5 Hz, 1H), 6.68 (dd, *J* = 6.5, 7.0 Hz, 1H), 2.89 (brs, 1H, NH), 2.85-2.68 (m, 2H), 2.02-1.91 (m, 2H), 1.90-1.81 (m, 4H), 1.80-1.68 (m, 5H), 1.66-1.56 (m, 1H), 1.44-1.31 (m, 4H), 1.29-1.12 (m, 5H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 135.1, 129.5, 124.7, 122.8, 121.1, 118.0, 116.8, 111.7, 77.5, 57.0, 36.0, 34.0, 32.9, 26.9, 25.7, 25.6, 24.9; **HRMS** (ESI-TOF) calculated for $C_{21}H_{28}N_3$ $[M+H]^+$: 322.4758 found 322.4766.
	1-(cyclohexylamino)-2-(tetrazolo[1,5-a]quinolin-4-yl)benzo[d]pyrrolo[2,1-b]thiazole-3-carbonitrile (**4o**): 67.3 mg, 58% yield; light brown solid, mp 248-250 °C; purified using 20% ethyl acetate in hexanes as eluent; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 8.75 (d, *J* = 8.0 Hz, 1H), 8.47 (d, *J* = 7.6 Hz, 1H), 8.33 (s, 1H), 8.13 (d, *J* = 8.0 Hz, 1H), 7.89 (dt, *J* = 0.8, 7.2 Hz, 1H), 7.77 (dt, *J* = 1.2, 7.2 Hz, 1H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.51 (dt, *J* = 1.2, 7.6 Hz, 1H), 7.40 (apt, *J* = 7.6 Hz, 1H), 2.79-2.61 (m, 1H), 1.87-1.68 (m, 2H), 1.54-1.36 (m, 3H), 1.09-0.74 (m, 5H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 146.4, 135.3, 134.8, 134.1, 130.9, 130.8, 130.6, 129.6, 129.3, 128.4, 126.4, 125.3, 124.4, 123.5, 118.6, 116.7, 116.0, 115.3, 57.7, 33.3, 29.7, 25.4, 24.9 ; **HRMS** (ESI-TOF) calculated for $C_{26}H_{22}N_7S$ $[M+H]^+$: 464.1657 found 464.1664.
	1-(benzylamino)-2-(tetrazolo[1,5-a]quinolin-4-yl)benzo[d]pyrrolo[2,1-b]thiazole-3-carbonitrile (**4p**): 66.1 mg, 56% yield; light yellow solid, mp 188-189 °C; purified using 20% hexanes as eluent; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 8.63 (d, *J* = 8.0 Hz, 1H), 8.57 (d, *J* = 8.0 Hz, 1H), 7.94 (d, *J* = 1.0 Hz, 1H), 7.84 (apt, *J* = 7.0 Hz, 1H), 7.87 (s, 1H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.71 (apt, *J* = 8.0 Hz, 1H), 7.53 (apt, *J* = 8.0 Hz, 1H), 7.43 (apt, *J* = 7.0 Hz, 1H), 6.59 (apt, *J* = 8.0 Hz, 2H), 6.50 (d, *J* = 8.0 Hz, 2H), 6.39 (apt, *J* = 8.0 Hz, 1H), 5.78 (apt, *J* = 7.0 Hz, 1H), 3.95 (d, *J* = 7.0 Hz, 2H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 146.0, 137.8, 135.4, 134.6, 133.3, 130.7, 130.5, 130.6, 129.2, 128.9, 128.2, 128.1, 127.4, 126.9, 126.7, 125.4, 124.4, 123.6, 117.6, 116.4, 116.3, 115.8, 115.7, 81.2, 53.4; **HRMS** (ESI-TOF) calculated for $C_{27}H_{18}N_7S$ $[M+H]^+$: 472.1344 found 472.1333.
	3-(cyclohexylamino)-2-(2,3,4-trimethoxyphenyl)indolizine-1-carbonitrile (**4q**): 67.1 mg, 66% yield; light brown viscous oil; purified using 20% ethyl acetate in hexanes as eluent; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 8.13 (d, *J* = 7.0 Hz, 1H), 7.58 (d, *J* = 8.0 Hz, 1H), 7.27 (d, *J* = 8.0 Hz, 1H), 7.00 (dd, *J* = 9.5, 6.5 Hz, 1H), 6.78 (d, *J* = 9.0 Hz, 1H), 6.71 (apt, *J* = 6.5 Hz, 1H), 4.01 (brs, 1H, NH), 3.94 (s, 3H), 3.91 (s, 3H), 3.60 (s, 3H), 2.63-2.49 (m, 1H), 1.68-1.38 (m, 5H), 1.10-0.88 (m, 5H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 153.5, 150.8, 142.7, 135.0, 126.1, 123.0, 121.4, 119.5, 118.9, 117.7, 117.5, 112.2, 108.6, 79.4, 61.8, 61.3, 56.1(2C), 34.1, 25.7, 24.8; **HRMS** (ESI-TOF) calculated for $C_{24}H_{28}N_3O_3$ $[M+H]^+$: 406.5058

	found 406.5053.
	2-(2-bromophenyl)-3-(cyclohexylamino)indolizine-1-carbonitrile (**4r**): 60.9 mg, 62% yield; light brown viscous oil; purified using 10% ethyl acetate in hexanes as eluent; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 8.12 (d, *J* = 6.5 Hz, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.53 (d, *J* = 9.0 Hz, 1H), 7.40-7.32 (m, 2H), 7.24-7.18 (m, 1H), 6.97 (dd, *J* = 6.5, 9.0 Hz, 1H), 6.71 (t, *J* = 6.5 Hz, 1H), 3.09 (brs, 1H, NH), 2.62-2.48 (m, 1H), 1.73-1.61 (m, 1H), 1.58-1.35 (m, 4H), 1.10-0.89 (m, 4H), 0.82-0.72 (m, 1H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 134.4, 133.6, 132.9, 132.5, 129.7, 127.6, 126.8, 123.6, 123.0, 122.8, 122.0, 117.5, 116.8, 112.4, 80.4, 56.1, 33.8, 33.7, 25.5, 24.6, 24.4; **HRMS** (ESI-TOF) calculated for $C_{21}H_{21}BrN_3$ $[M+H]^+$: 394.0919 found 394.0931.
	2-(2-bromophenyl)-1-(cyclohexylamino)benzo[d]pyrrolo[2,1-b]thiazole-3-carbonitrile (**4s**): 85.4 mg, 76% yield; white solid, mp 228-229 °C; purified using 10% ethyl aceate in hexanes as eluent; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 8.31 (d, *J* = 9.5 Hz, 2H), 7.68 (dd, *J* = 8.0, 9.5 Hz, 1H), 7.48-7.37 (m, 3H), 7.33 (apt, *J* = 8.0 Hz, 1H), 7.25 (dt, *J* = 2.5, 9.5 Hz, 1H), 3.19 (brs, 1H, NH), 2.79-2.63 (m, 1H), 1.92-1.81 (m, 1H), 1.70-1.52 (m, 2H), 1.51-1.37 (m, 2H), 1.20-0.91 (m, 4H), 0.85-0.71 (m, 1H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 134.8, 133.4, 133.0, 132.6, 132.5, 130.7, 130.6, 129.6, 127.7, 126.1, 124.8, 123.9, 123.5, 122.6, 115.7, 115.3, 83.0, 56.9, 33.3, 33.1, 25.5, 24.6, 24.3; **HRMS** (ESI-TOF) calculated for $C_{23}H_{21}N_3S$ $[M+H]^+$: 450.0639 found 450.0643.
	3-(benzylamino)-2-(2-bromo-5-fluorophenyl)indolizine-1-carbonitrile (**4t**): 60.8 mg, 58% yield; light yellow oil; purified using 10% ethyl acetate in hexanes as eluent; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 8.19 (d, *J* = 7.0 Hz, 1H), 7.61 (d, *J* = 9.5 Hz, 1H), 7.61 (d, *J* = 9.5 Hz, 1H), 7.23-7.14 (m, 3H), 7.08 (dd, *J* = 7.0, 8.0 Hz, 1H), 7.01-6.94 (m, 3H), 6.87-6.78 (m, 2H), 3.98 (dd, *J* = 2.5, 13.5 Hz, 1H), 3.87 (dd, *J* = 5.5 Hz, 13.5 Hz, 1H), 3.57 (t, *J* = 5.5 Hz, 1H, NH); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 161.5 (d, $J_{C\text{-}F}$ = 247.8 Hz), 138.5, 134.9 (d, $J_{C\text{-}F}$ = 8.3 Hz), 134.4, 133.9 (d, $J_{C\text{-}F}$ = 8.3 Hz), 128.4, 127.9, 127.6, 127.0, 122.7, 122.4, 121.7, 119.5 (d, $J_{C\text{-}F}$ = 23.2 Hz) , 117.9, 117.7, 117.1 (d, $J_{C\text{-}F}$ = 23.2 Hz), 116.2, 112.8, 80.4, 52.1; **HRMS** (ESI-TOF) calculated for $C_{22}H_{16}NBrFN_3$ $[M+H]^+$: 420.0511 found 420.0517.
	2-(2-bromophenyl)-1-(phenylamino)benzo[d]pyrrolo[2,1-b]thiazole-3-carbonitrile (**4u**): 84.2 mg, 76% yield; white solid, mp 240-241 °C; purified using 10% ethyl aceate in hexanes as eluent; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.68 (dd, *J* = 8.0, 9.0 Hz, 2H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.31-7.11 (m, 5H), 7.07-6.97 (m, 3H), 6.66 (apt, *J* = 8.0 Hz, 1H), 6.55 (d, *J* = 8.0 Hz, 2H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 145.2, 133.3, 132.1, 131.9, 131.6, 129.5, 129.1, 128.7, 126.6, 125.7, 124.4, 123.5, 123.3, 122.9, 118.6, 114.7, 114.4, 112.9, 83.0; **HRMS** (ESI-TOF) calculated for $C_{23}H_{15}BrN_3S$ $[M+H]^+$: 444.0170 found 444.0173.

Experimental procedure for intramolecular *N*-arylation:

Compound **4s** (90 mg, 0.20 mmol), LiO^{t}Bu (40 mg, 0.50 mmol), SPhos (16.4 mg, 0.040 mmol) and toluene (2.0 mL) were charged into a 35 mL pressure tube. After purging the mixture with nitrogen, $Pd(OAc)_2$ (4.4 mg, 0.020 mmol) was added. The pressure tube was then sealed with Teflon® screw cap, placed in a pre-heated oil bath at 150 °C and stirred for 18 h. After cooling to rt, the reaction mixture was diluted with ethyl acetate (25 mL) and filtered through short celite pad, washed the celite pad with ethyl acetate (2 x 10 mL). The combined filtrate was evaporated and the crude product was purified by silica gel column chromatography using 15% ethyl acetate in hexanes as eluent to obtain compound **5a** (53.2 mg, 72%) as a brown solid.

 **5a**	5-cyclohexyl-5H-benzo[4',5']thiazolo[3',2':1,5]pyrrolo[2,3-b]indole-12-carbonitrile (**5a**): 53.2 mg, 72% yield; Brown solid, mp 168-169 °C; purified using 15% ethyl acetate in hexanes as eluent; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.81 (d, *J* = 7.5 Hz, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.64 (d, *J* = 8.0 Hz, 1H), 7.55 (d, *J* = 8.0 Hz, 1H), 7.42 (apt, *J* = 8.0 Hz, 1H), 7.30 (apt, *J* = 8.0 Hz, 1H), 7.22-7.12 (m, 2H), 4.69-4.57 (m, 1H), 2.38-2.21 (m, 2H), 2.03-1.88 (m, 4H), 1.82-1.17 (m, 1H), 1.46-1.25 (m, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 139.7, 136.6, 134.0, 133.4, 130.5, 126.3, 124.6, 124.5, 122.0, 121.8, 120.7, 119.4, 115.9, 114.7, 113.4, 113.3, 76.5, 59.4, 31.9, 26.5, 25.3; **HRMS** (ESI-TOF) calculated for $C_{23}H_{20}N_3S$ $[M+H]^+$: 370.1378 found 370.1368.
 **5b**	5-(tert-butyl)-5H-benzo[4',5']thiazolo[3',2':1,5]pyrrolo[2,3-b]indole-12-carbonitrile (**5b**): 43.9 mg, 64% yield; light yellow solid, mp 156-157 °C; purified using 15% ethyl acetate in hexanes as eluent; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.90 (d, *J* = 8.0 Hz, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.57-7.51 (m, 2H), 7.31 (apt, *J* = 8.0 Hz, 1H), 7.21 (apt, *J* = 8.0 Hz, 1H), 7.18-7.07 (m, 2H), 1.56 (s, 9H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 146.9, 138.1, 136.0, 134.6, 130.5, 125.0, 124.6, 124.2, 122.2, 122.1, 118.8, 117.6, 115.6, 114.7, 77.9, 60.9, 31.1; **HRMS** (ESI-TOF) calculated for $C_{21}H_{18}N_3S$ $[M+H]^+$: 344.1221 found 344.1212.
 **5c**	5-cyclohexyl-5H-indolizino[3,2-b]indole-11-carbonitrile (**5c**): 42.7 mg, 68% yield; white solid, mp 188-189 °C; purified using 20% ethyl aceate in hexanes as eluent; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 8.27 (d, *J* = 6.5 Hz, 1H), 7.98 (d, *J* = 8.0 Hz, 1H), 7.64 (d, *J* = 9.5 Hz, 1H), 7.51 (d, *J* = 9.5 Hz, 1H), 7.17 (apt, *J* = 8.0 Hz, 1H), 6.86 (dd, *J* = 6.5 Hz, 7.0 Hz, 1H), 6.71 (dd, *J* = 6.5, 7.0 Hz, 1H), 4.61(tt, *J* = 4.0, 8.0, 12.0 Hz, 1H), 2.83 (apt, *J* = 6.5 Hz, 1H), 2.25-1.91 (m, 6H), 1.88-1.75 (m, 1H), 1.58-1.42 (m, 2H), 1.40-1.27 (m, 1H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 140.9, 138.8, 131.4, 123.5, 122.5, 120.7, 119.9, 119.2, 118.9, 117.3, 113.3, 112.0, 72.3, 57.0, 32.8, 26.3, 25.3; **HRMS** (ESI-TOF) calculated for $C_{21}H_{20}N_3$ $[M+H]^+$: 314.1657 found 314.1652.
 **5d**	5-cyclohexyl-5H-benzo[4',5']oxazolo[3',2':1,5]pyrrolo[2,3-b]indole-12-carbonitrile (**5d**): 41.1 mg, 58% yield; brown oil; purified using 15% ethyl aceate in hexanes as eluent; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.84 (d, *J* = 8.0 Hz, 1H), 7.69 (d, *J* = 7.0 Hz, 1H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.51 (d, *J* = 8.0 Hz, 1H), 7.39-7.28 (m, 2H), 7.23-7.11 (m, 2H), 4.65-4.57 (m, 1H), 2.42-2.29 (m, 2H), 2.14-2.00 (m, 3H), 1.19-1.79 (m, 2H), 1.64-1.45 (m, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 151.7, 136.7, 126.5, 125.5, 124.9, 124.7, 124.3, 124.0, 121.6, 120.0, 119.3, 114.7, 112.8, 112.7, 111.7, 77.5, 59.1, 32.0, 26.5, 25.2; **HRMS** (ESI-TOF) calculated for $C_{23}H_{20}N_3O$ $[M+H]^+$: 354.1606 found 354.1613.

 **5e**	5-benzyl-5H-benzo[4',5']thiazolo[3',2':1,5]pyrrolo[2,3-b]indole-12-carbonitrile (**5e**): 55.8 mg, 74% yield; white solid, mp 162-163 °C; purified using 15% ethyl aceate in hexanes as eluent; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.92 (d, *J* = 6.0 Hz, 1H), 7.60 (apt, *J* = 8.0 Hz, 2H), 7.32 (dd, *J* = 6.5, 8.0 Hz, 2H), 7.30-7.16 (m, 8H), 5.76 (s, 2H), 3.67 (s, 1H, NH); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 140.6, 136.7, 132.8, 132.3, 129.8, 129.3, 128.0, 126.3, 125.6, 124.6, 124.2, 123.1, 120.9, 119.5, 119.1, 115.9, 113.6, 113.1, 110.2, 76.3, 49.7; **HRMS** (ESI-TOF) calculated for $C_{24}H_{16}N_3S$ $[M+H]^+$: 378.1065 found 378.1058.
 **5f**	5-phenyl-5H-benzo[4',5']thiazolo[3',2':1,5]pyrrolo[2,3-b]indole-12-carbonitrile (**5f**): 49.4 mg, 68% yield; light brown solid, mp 198-199 °C; purified using 10% ethyl aceate in hexanes as eluent; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.95 (d, *J* = 6.0 Hz, 1H), 7.64-7.60 (m, 4H), 7.55-7.49 (m, 2H), 7.32-7.15 (m, 4H), 6.96 (t, *J* = 8.0 Hz, 1H), 6.13 (d, *J* = 8.0 Hz, 1H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 141.9, 138.3, 136.4, 132.9, 132.5, 130.1, 129.8, 129.3, 128.8, 128.4, 125.9, 124.4, 123.7, 123.1, 121.4, 119.7, 114.3, 114.1, 111.2, 76.2; **HRMS** (ESI-TOF) calculated for $C_{23}H_{14}N_3S[M+H]^+$: 364.0908 found 364.0903.

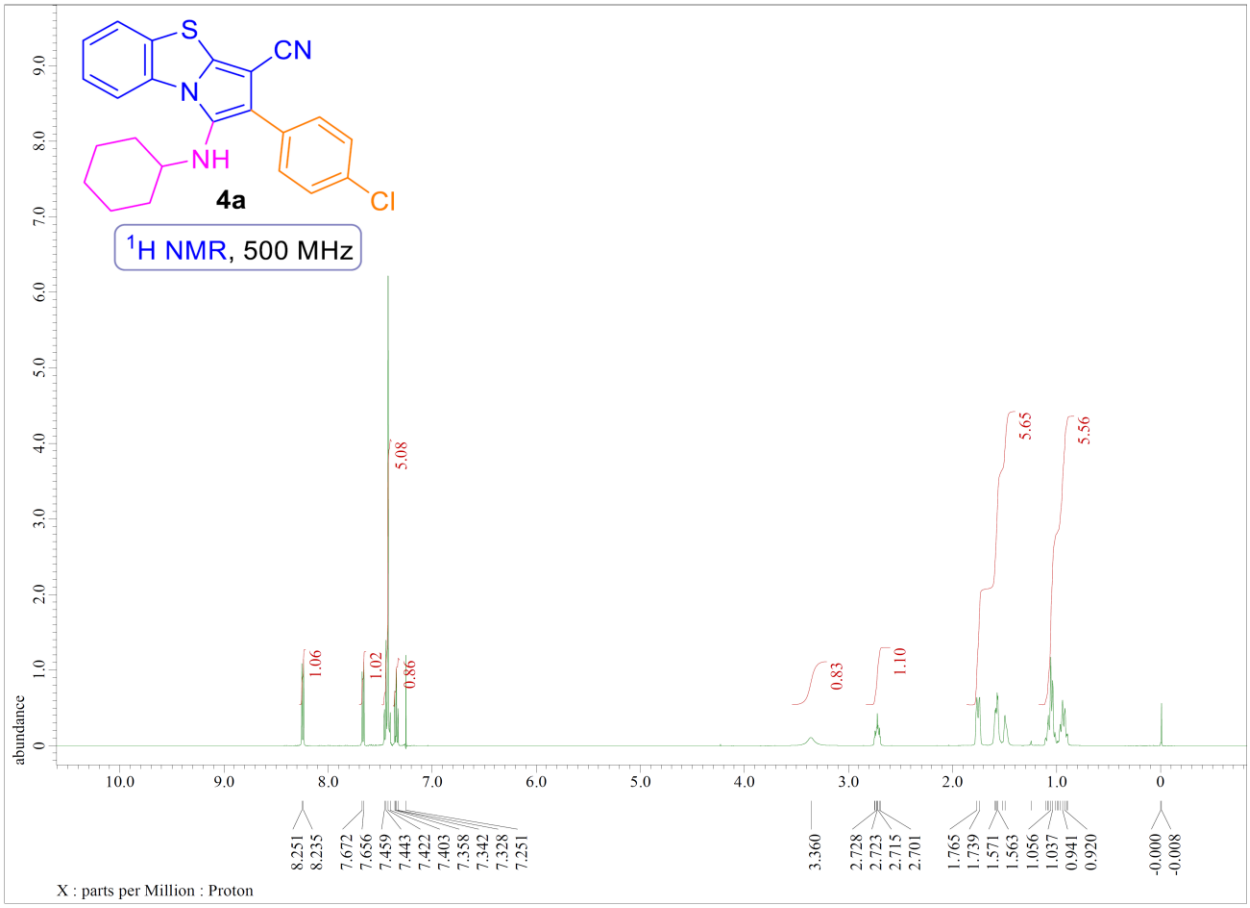


Figure S1: ^{1}H NMR of compound **4a** in $CDCl_3$

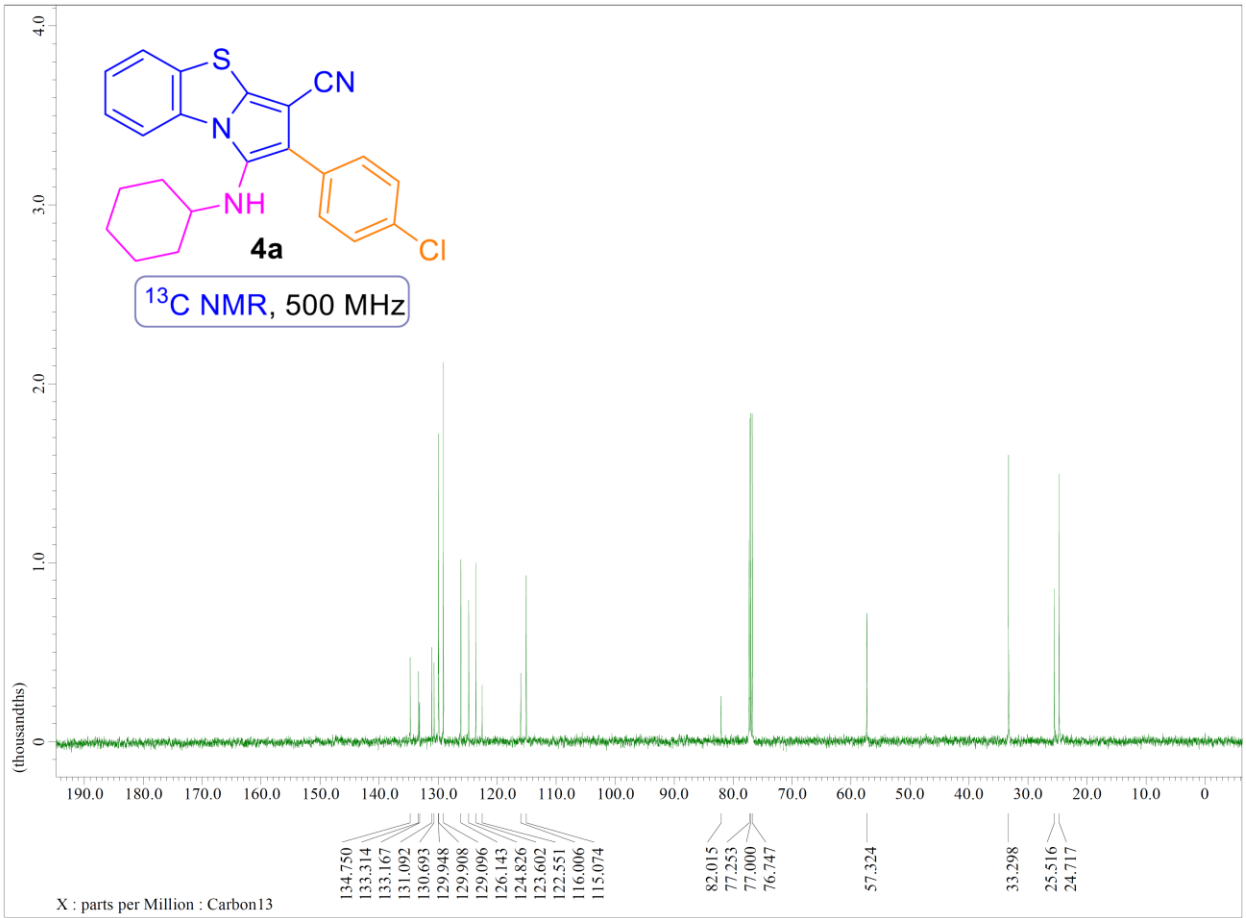


Figure S2: ^{13}C NMR of compound **4a** in $CDCl_3$

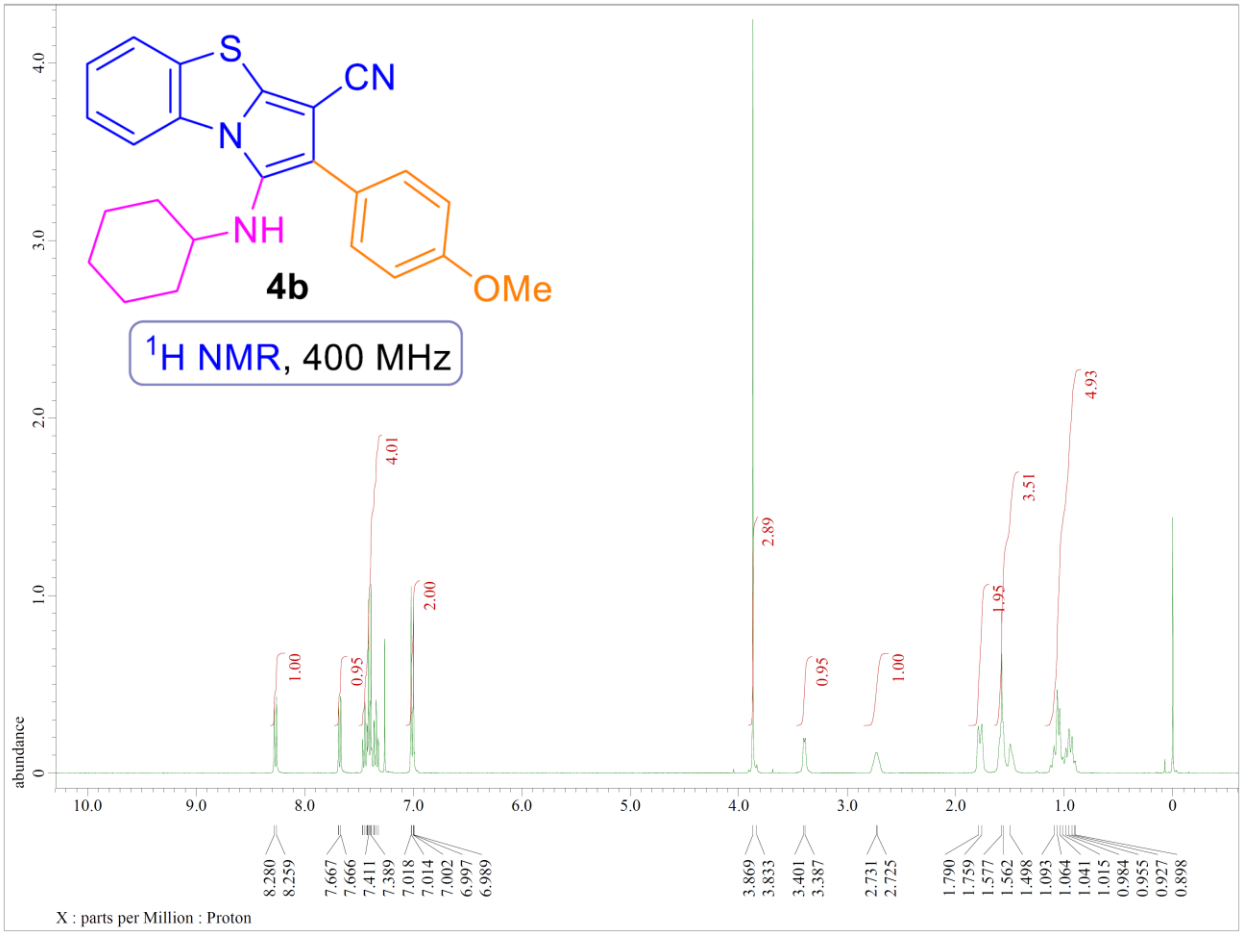


Figure S3: ^{1}H NMR of compound **4b** in $CDCl_3$

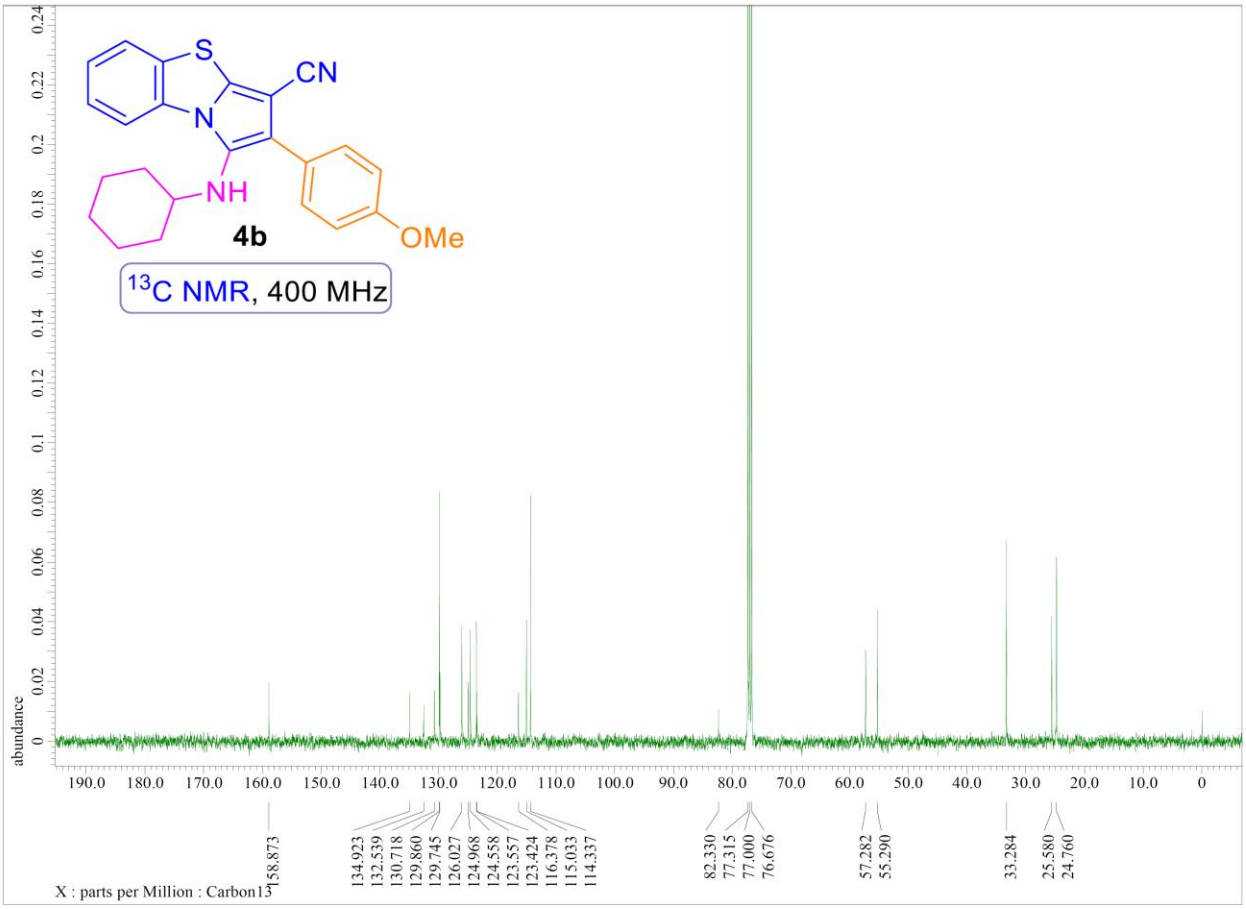


Figure S4: ^{13}C NMR of compound **4b** in $CDCl_3$

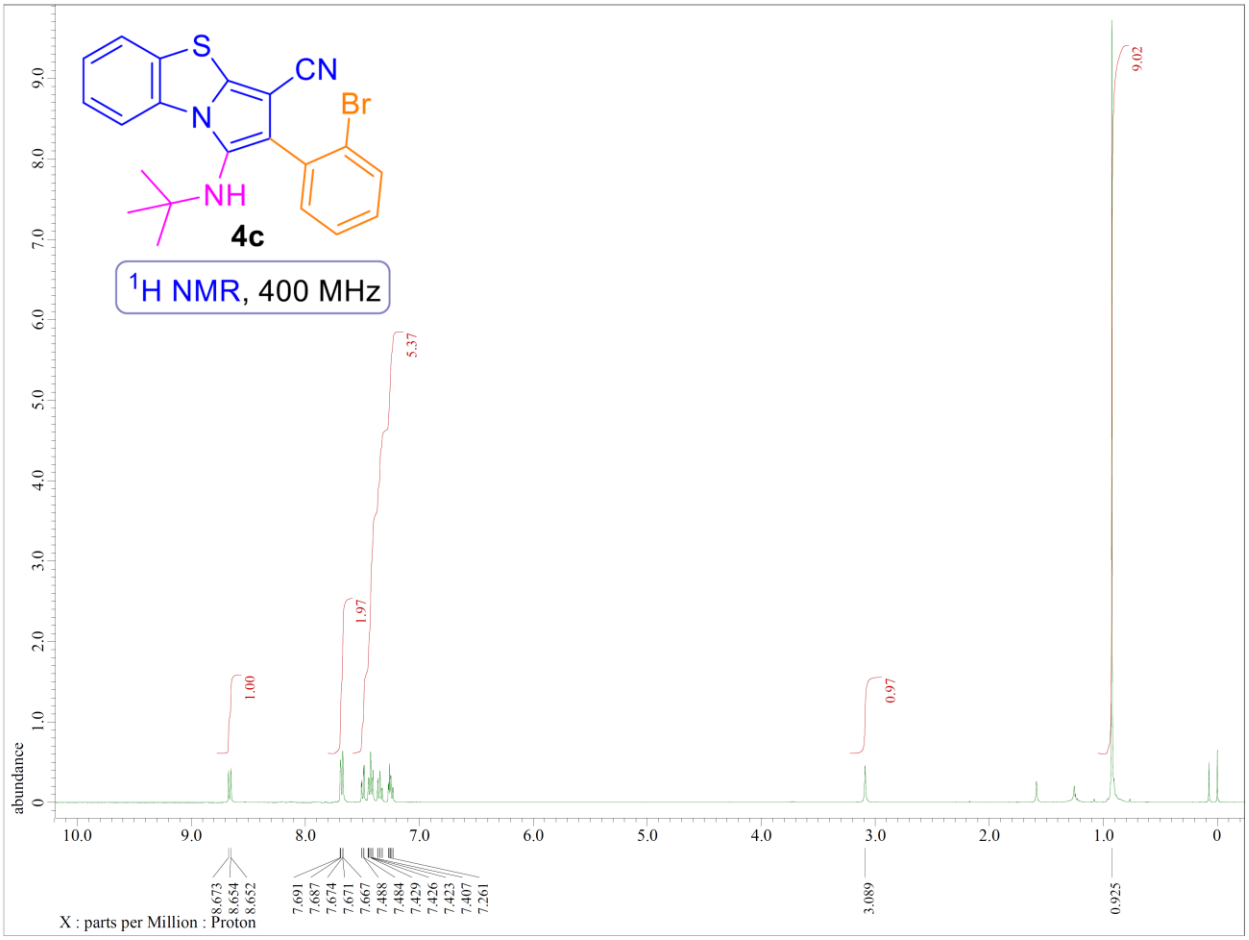


Figure S5: ^{1}H NMR of compound **4c** in $CDCl_3$

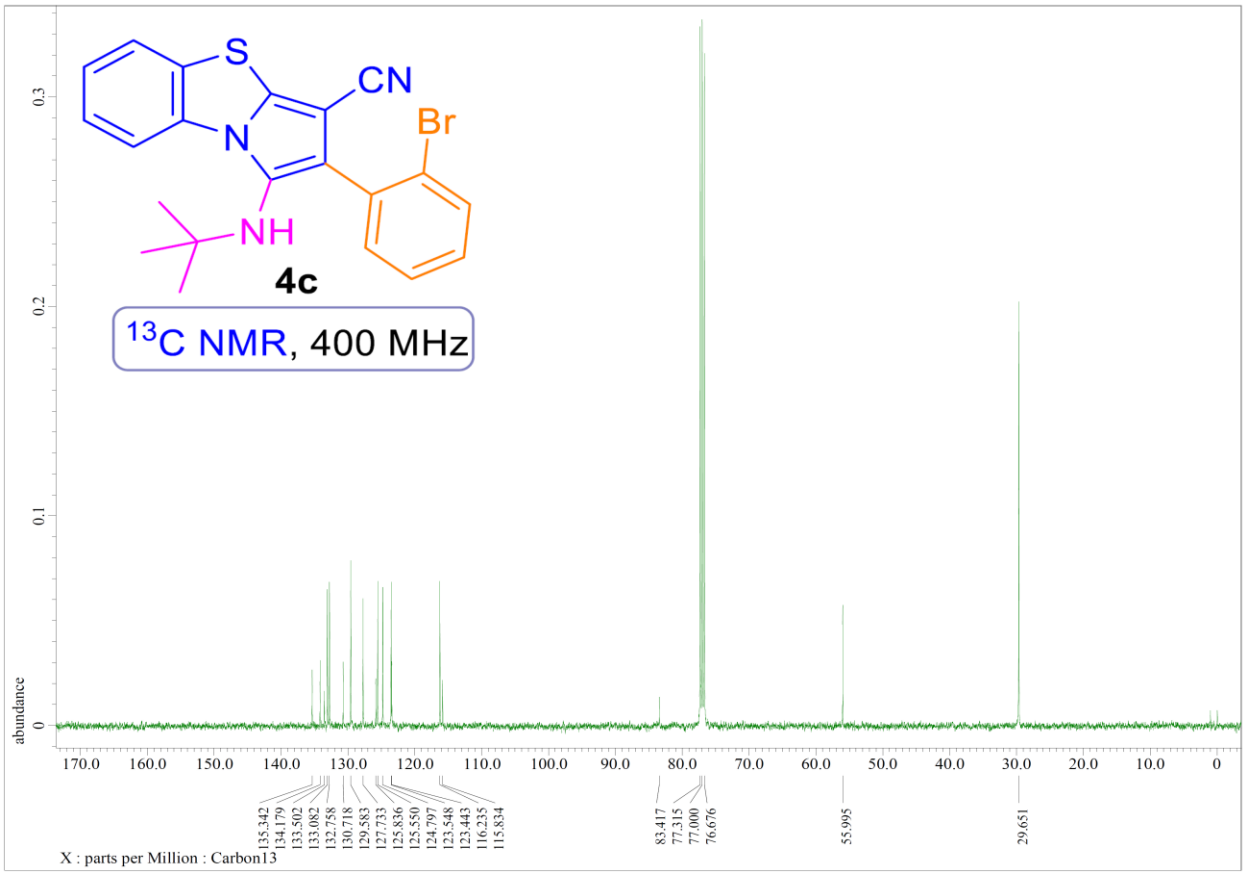


Figure S6: ^{13}C NMR of compound **4c** in $CDCl_3$

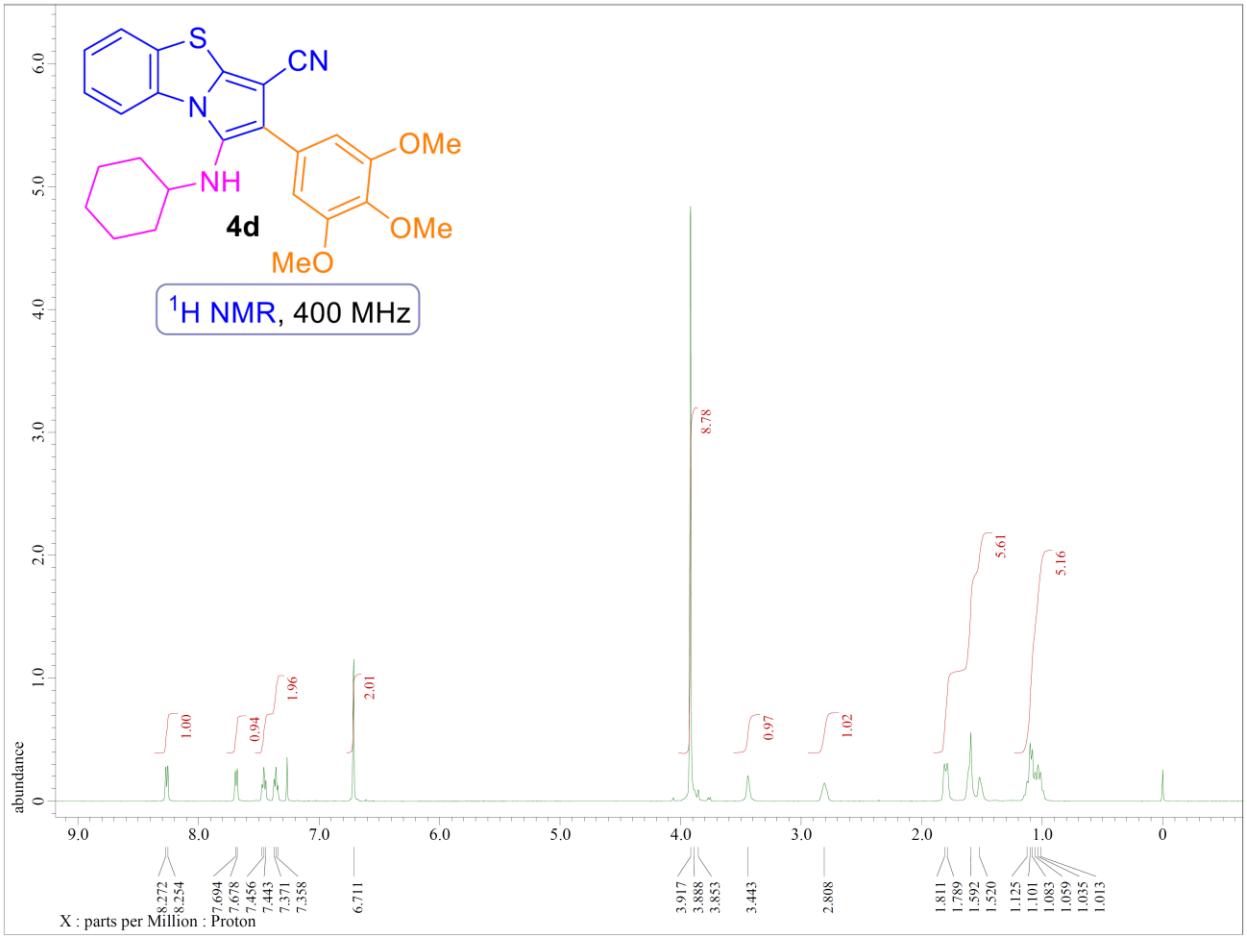


Figure S7: ^{1}H NMR of compound **4d** in $CDCl_3$

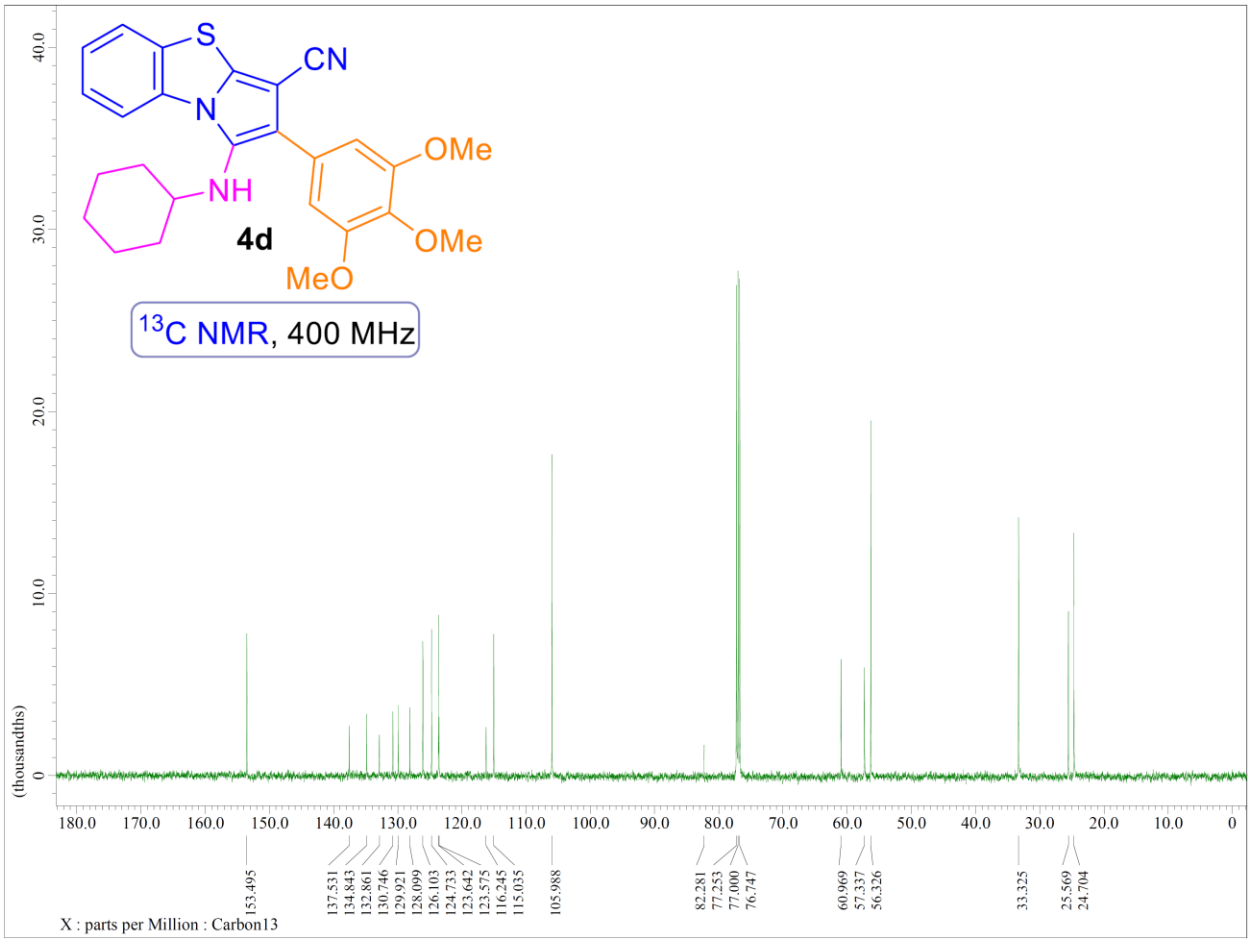


Figure S8: ^{13}C NMR of compound **4d** in $CDCl_3$

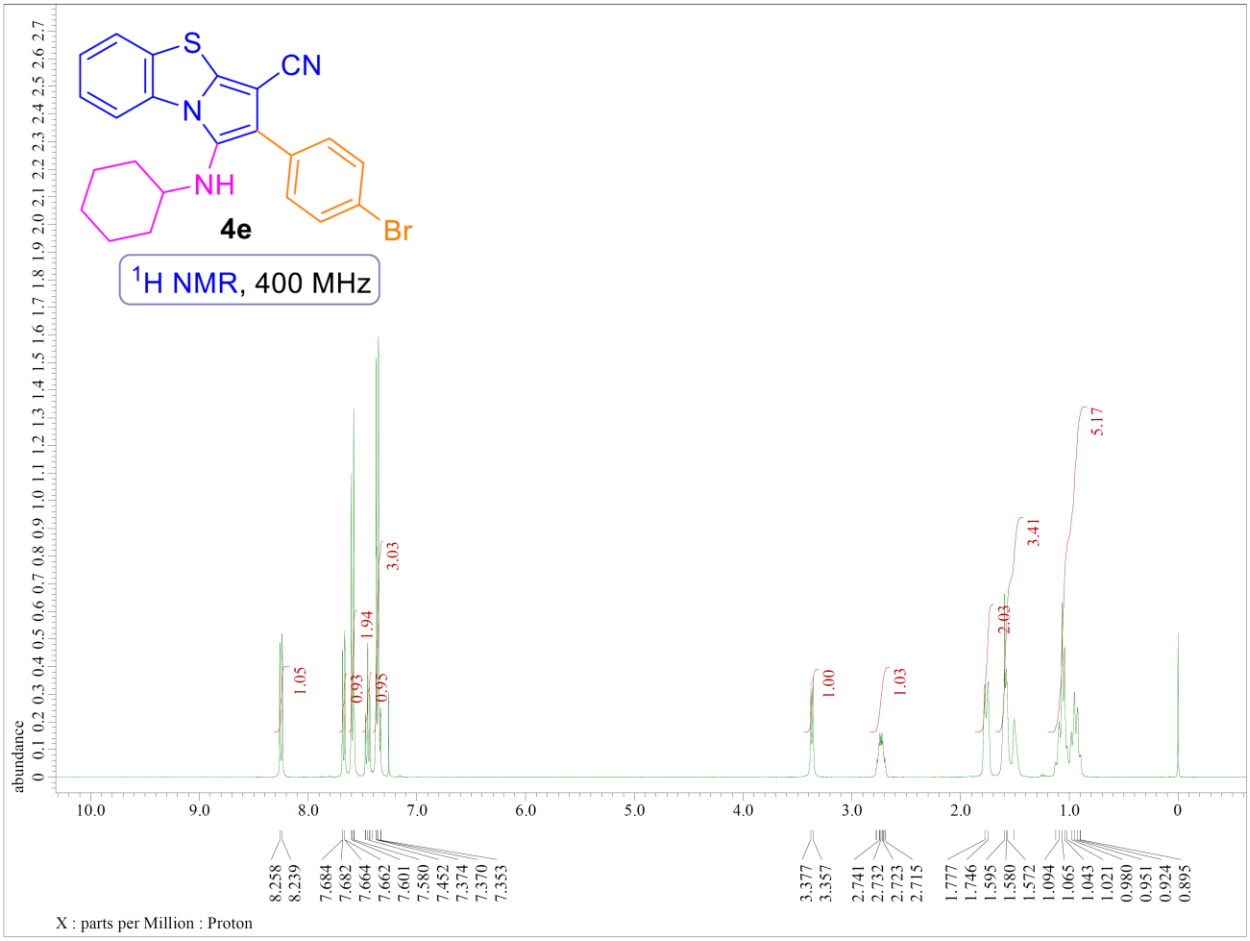


Figure S9: ^{1}H NMR of compound **4e** in $CDCl_3$

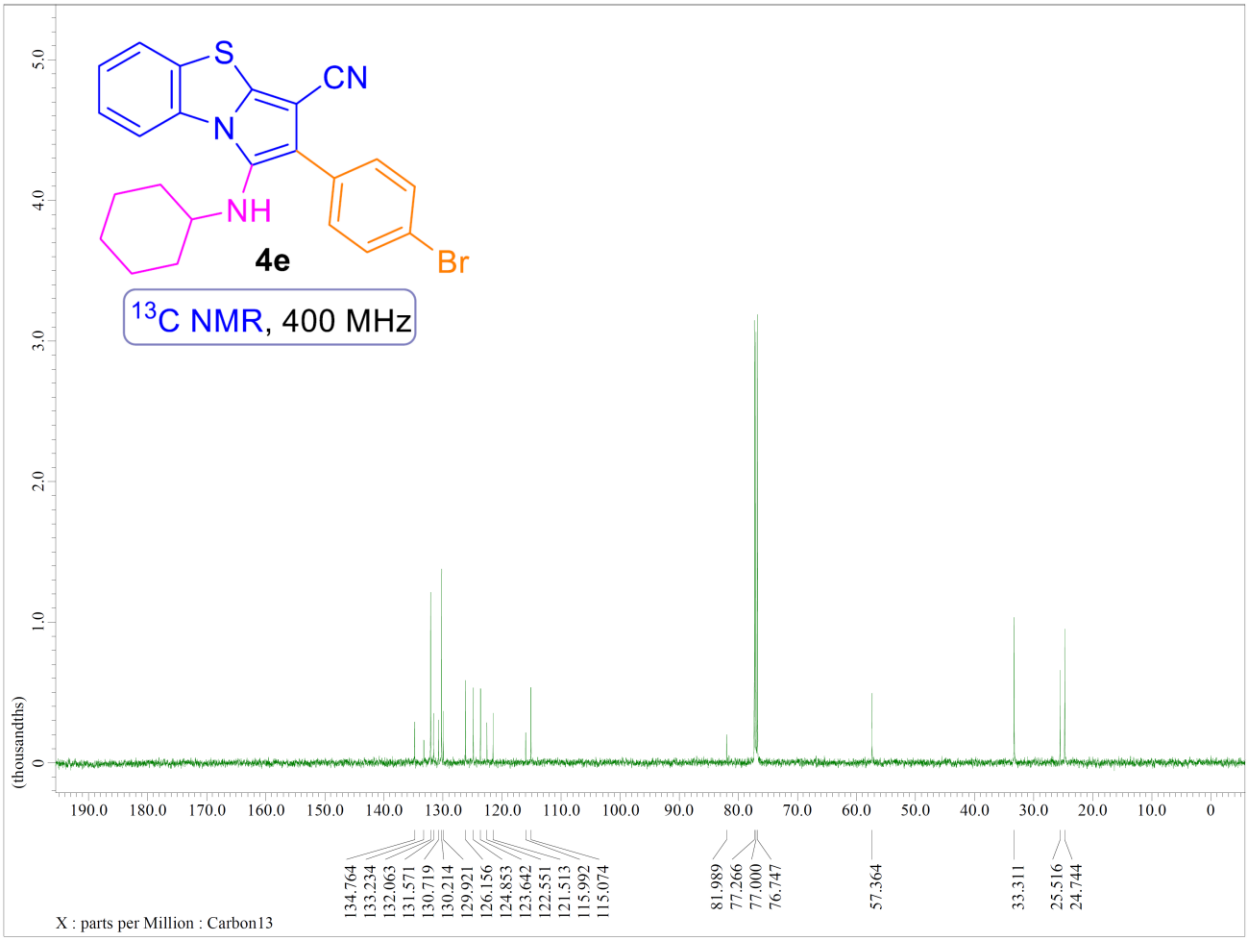


Figure S10: ^{13}C NMR of compound **4e** in $CDCl_3$

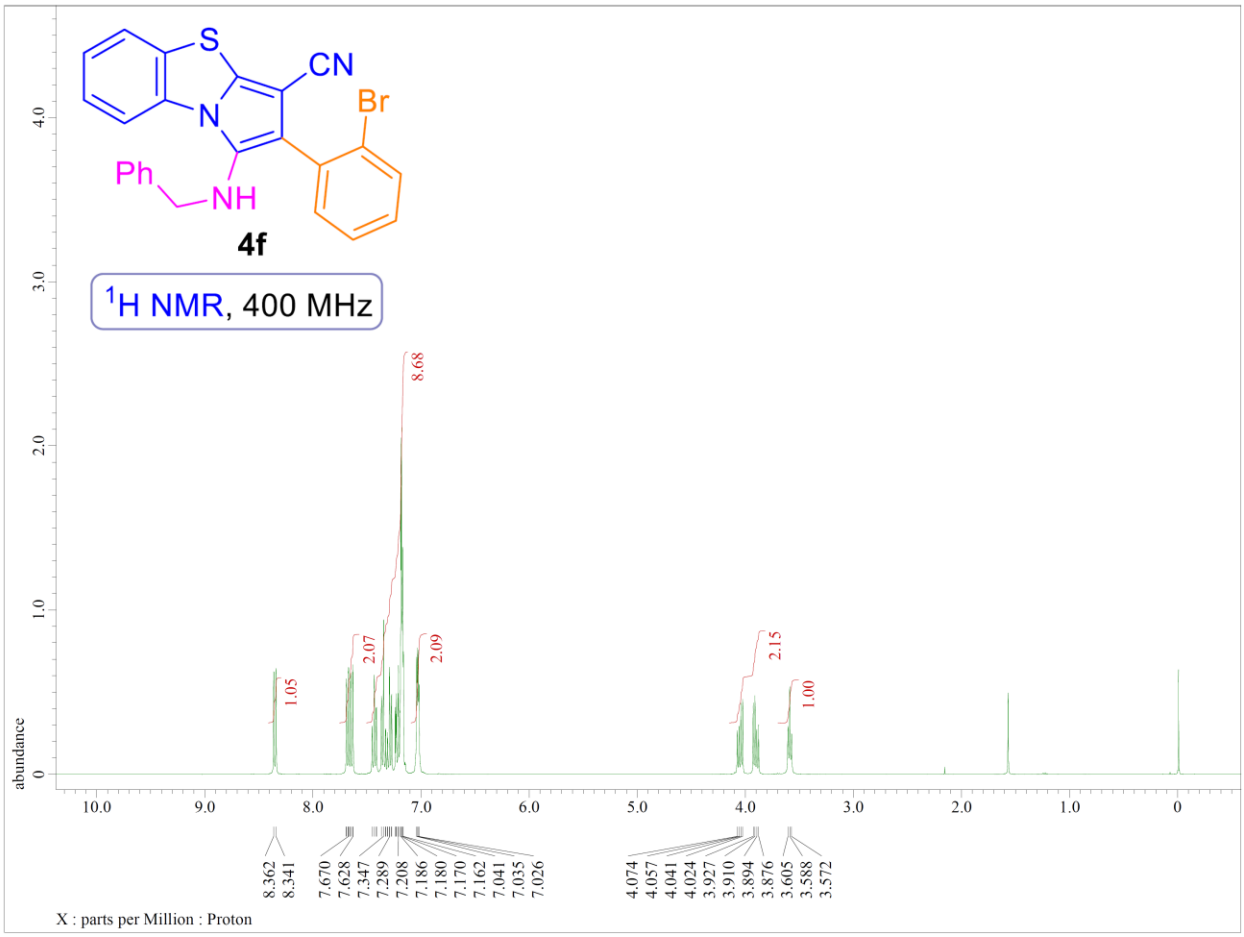


Figure S11: ^{1}H NMR of compound **4f** in $CDCl_3$

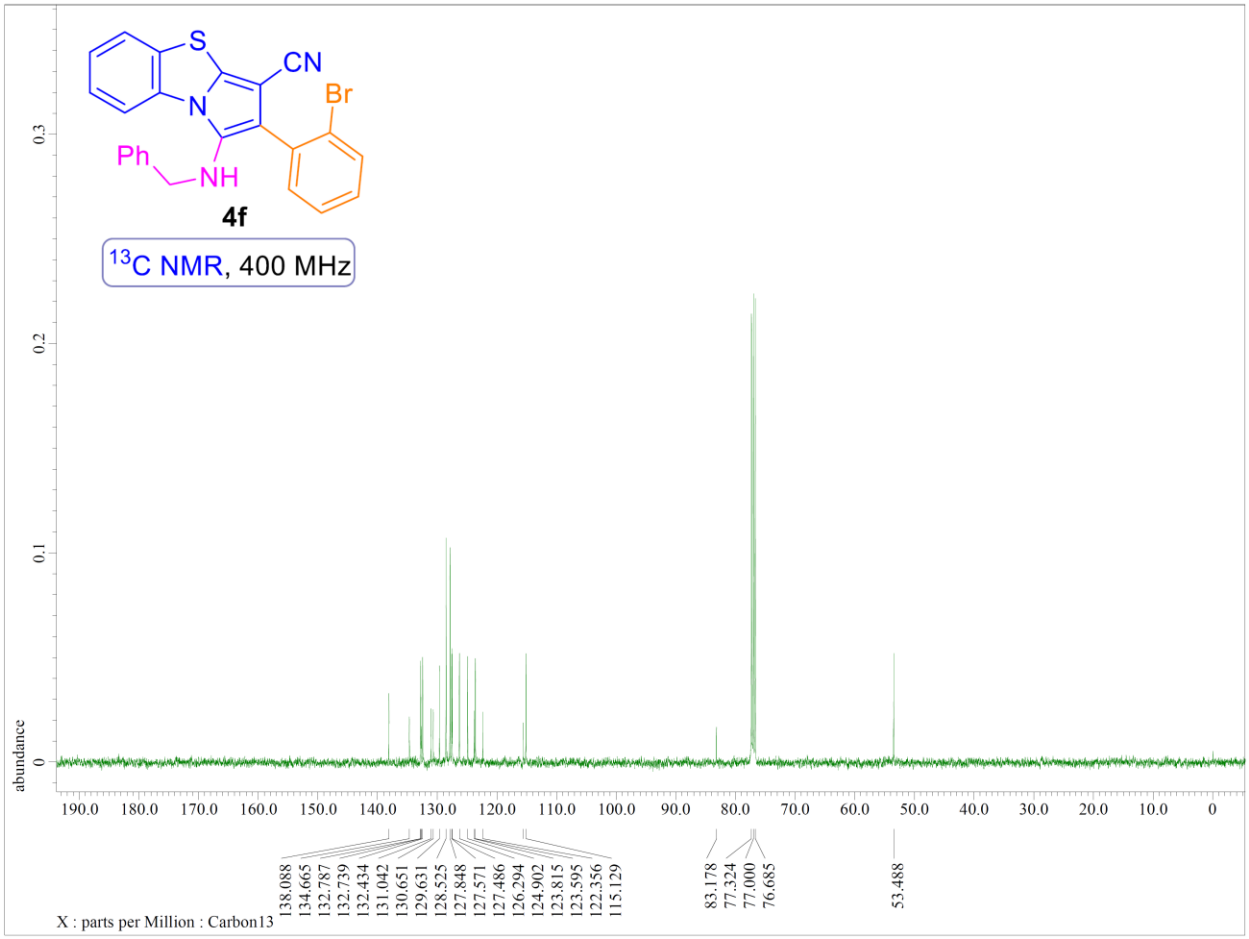


Figure S12: ^{13}C NMR of compound **4f** in $CDCl_3$

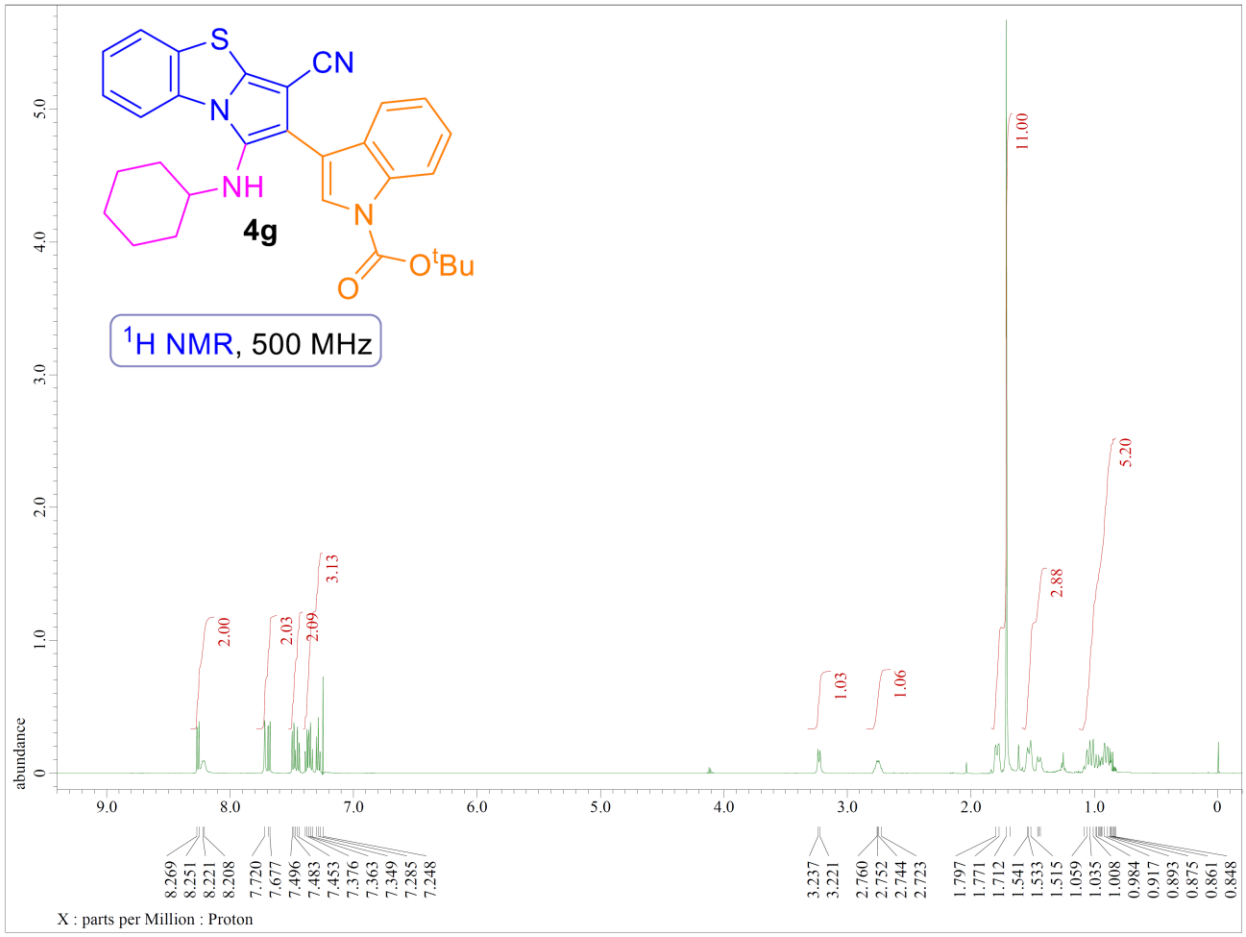


Figure S13: ^{1}H NMR of compound **4g** in $CDCl_3$

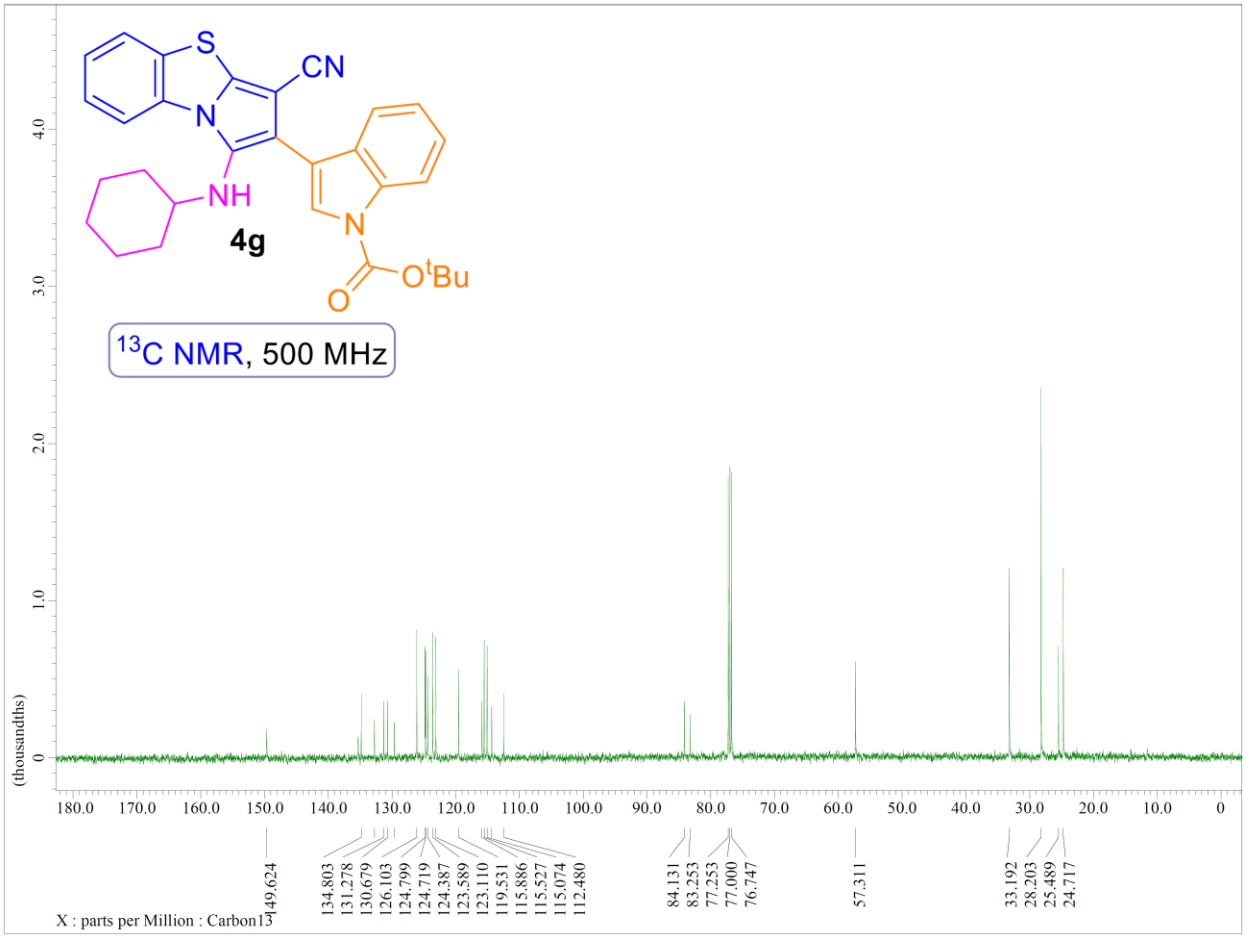


Figure S14: ^{13}C NMR of compound **4g** in $CDCl_3$

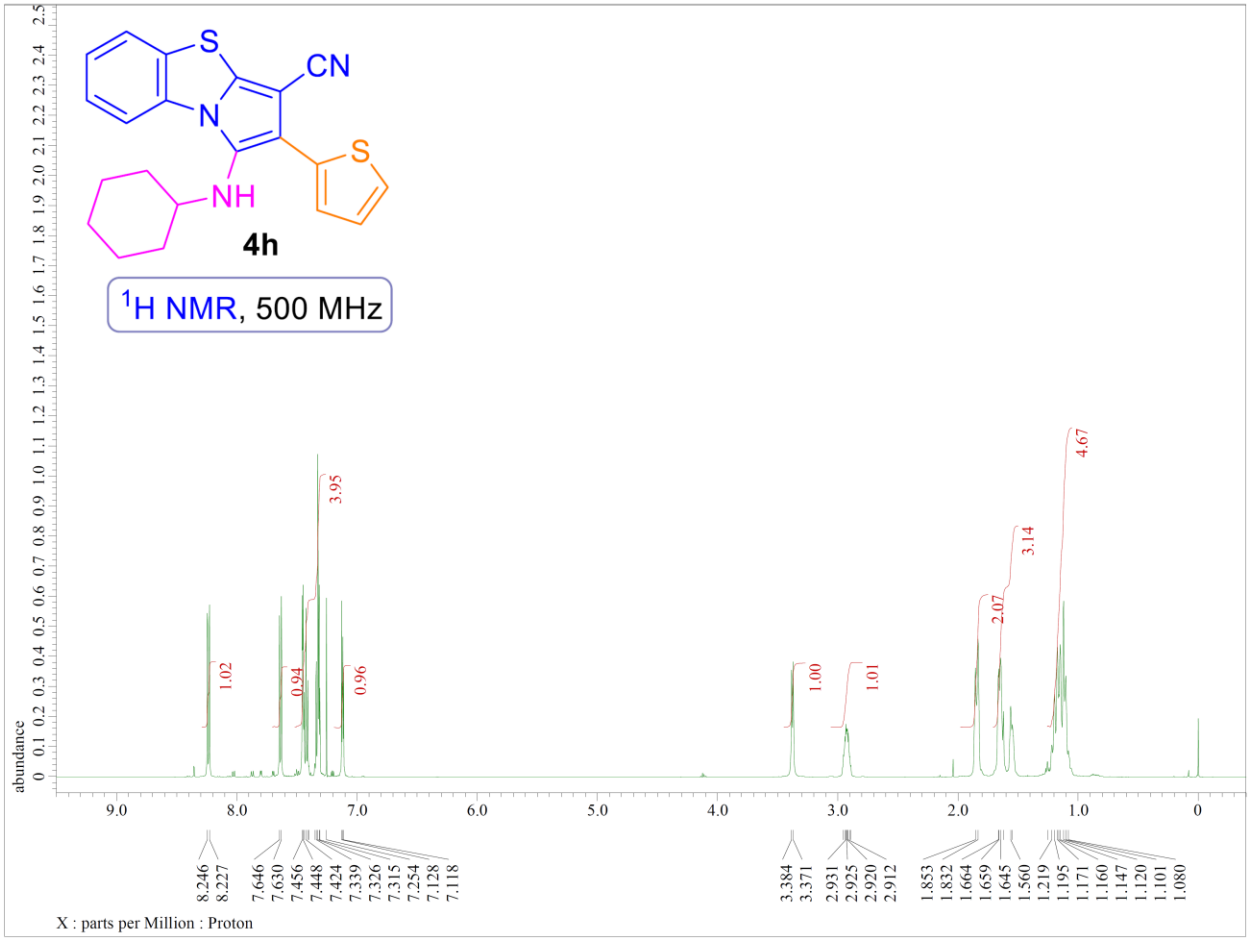


Figure S15: ^{1}H NMR of compound **4h** in $CDCl_3$

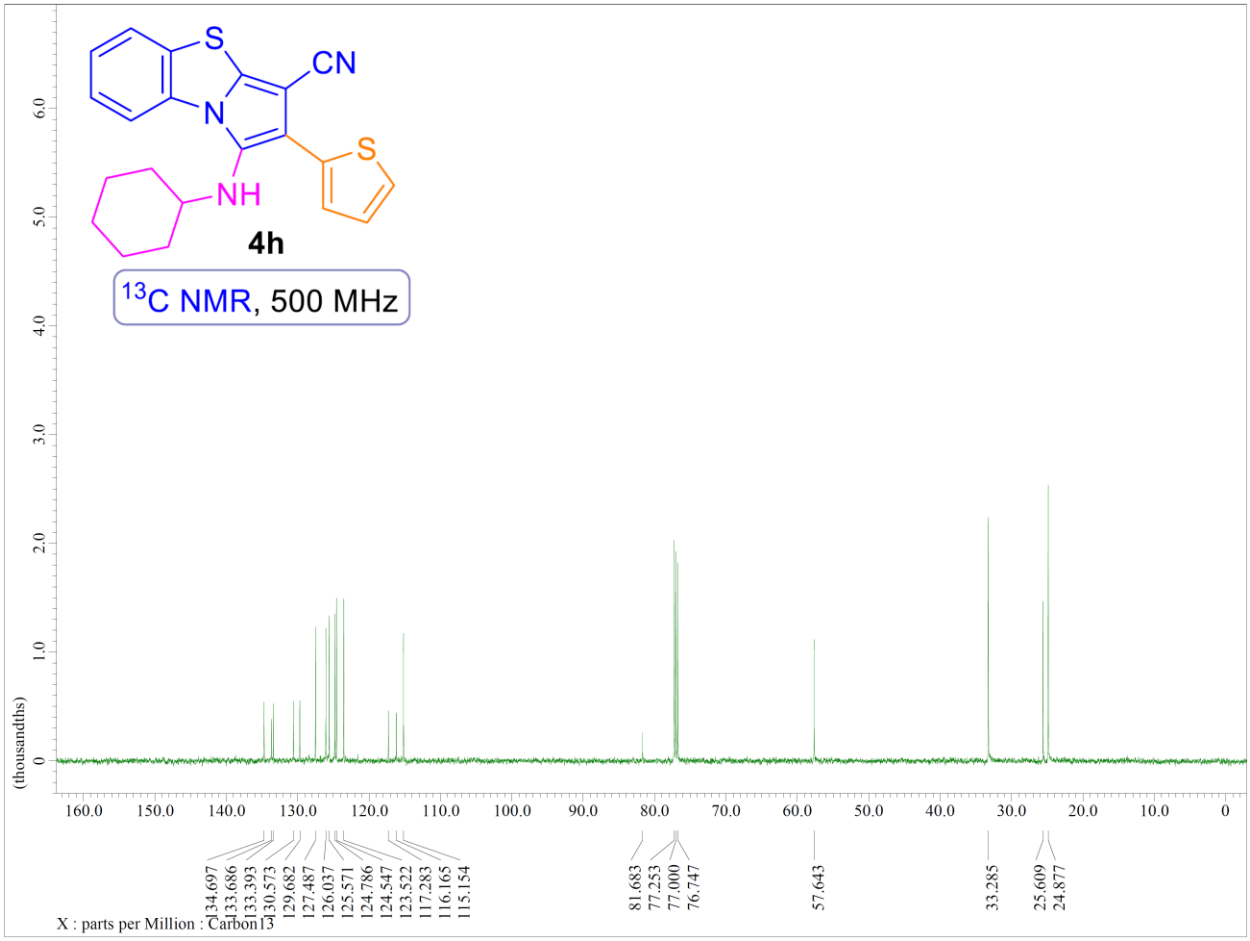


Figure S16: ^{13}C NMR of compound **4h** in $CDCl_3$

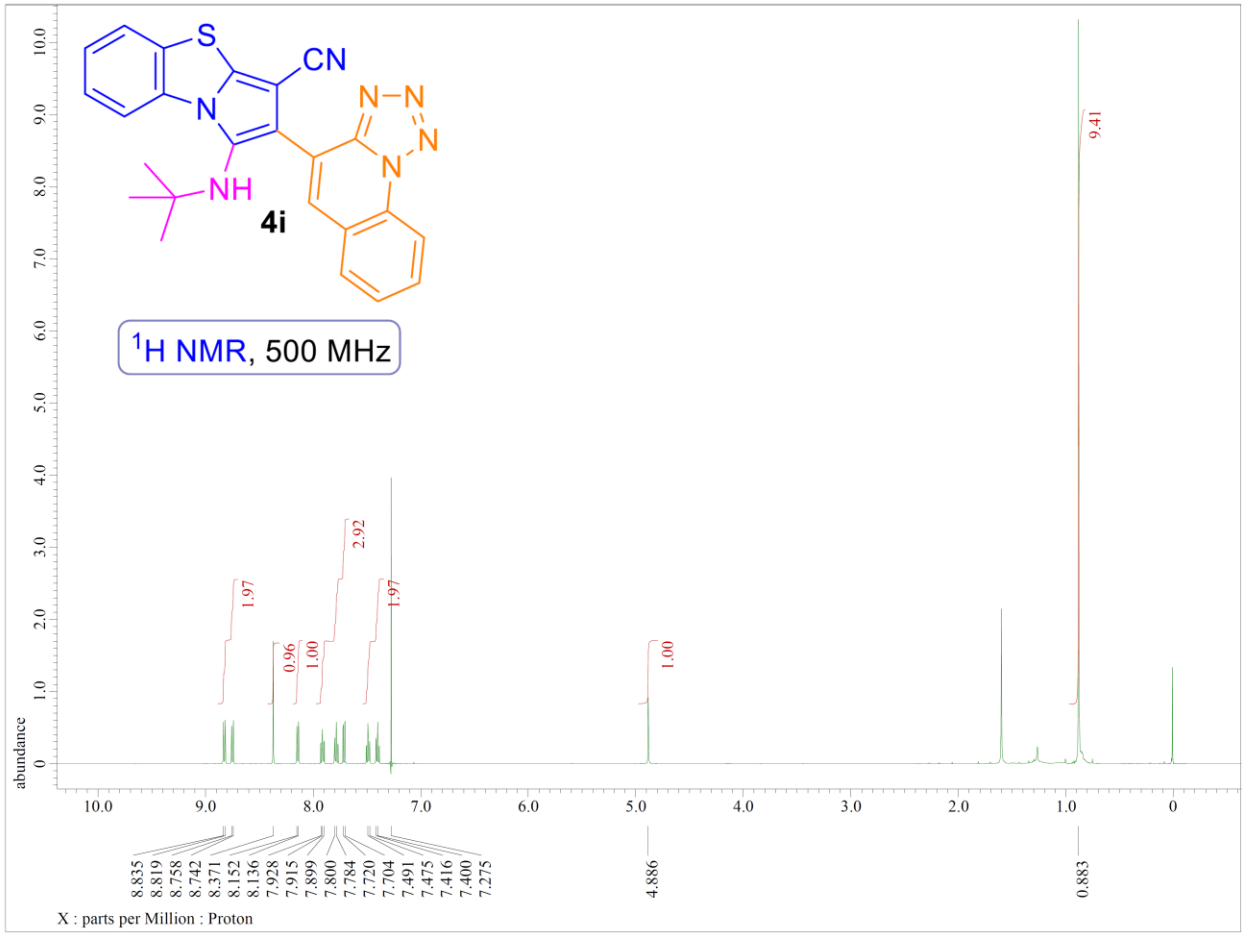


Figure S17: ^{1}H NMR of compound **4i** in $CDCl_3$

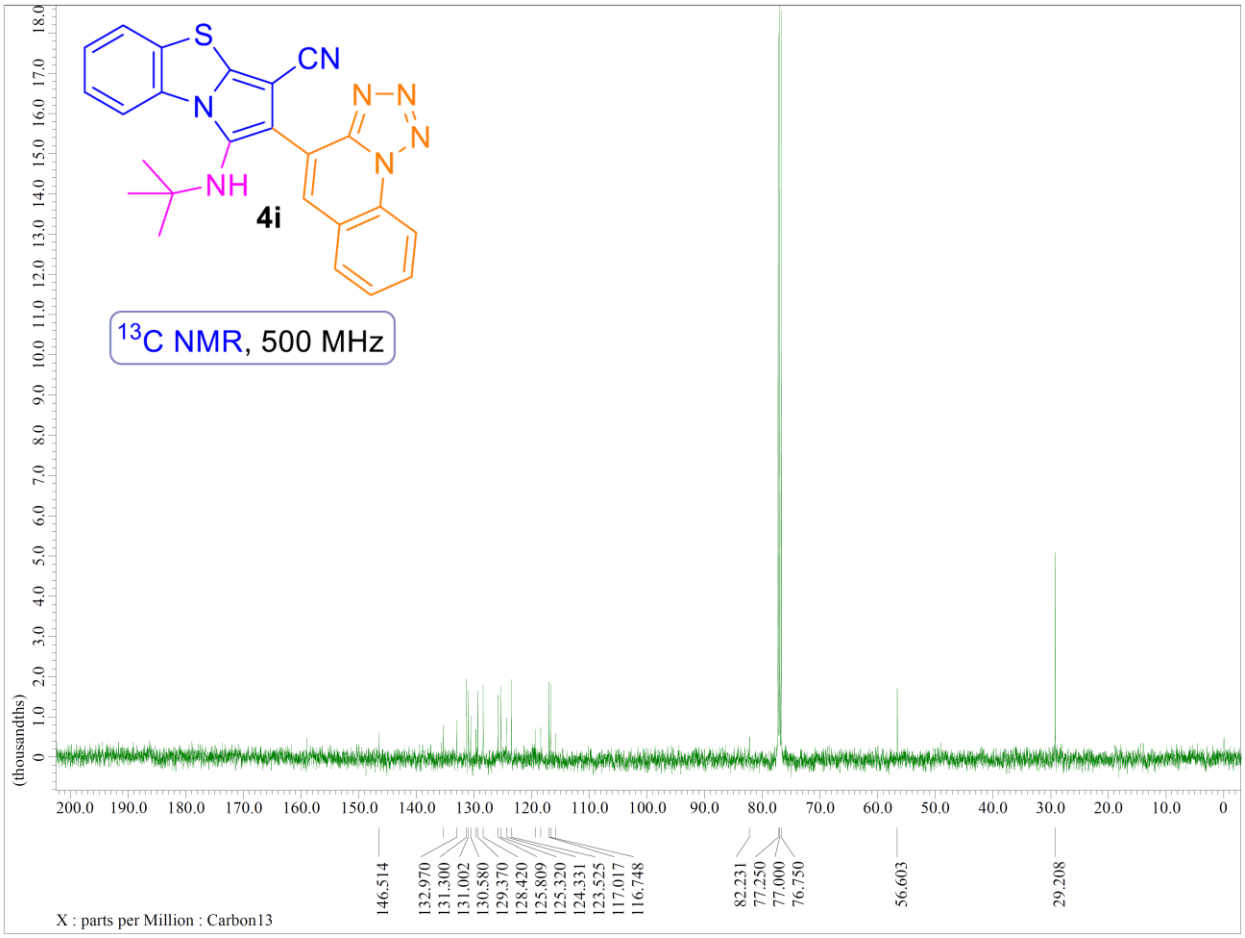


Figure S18: ^{13}C NMR of compound **4i** in $CDCl_3$

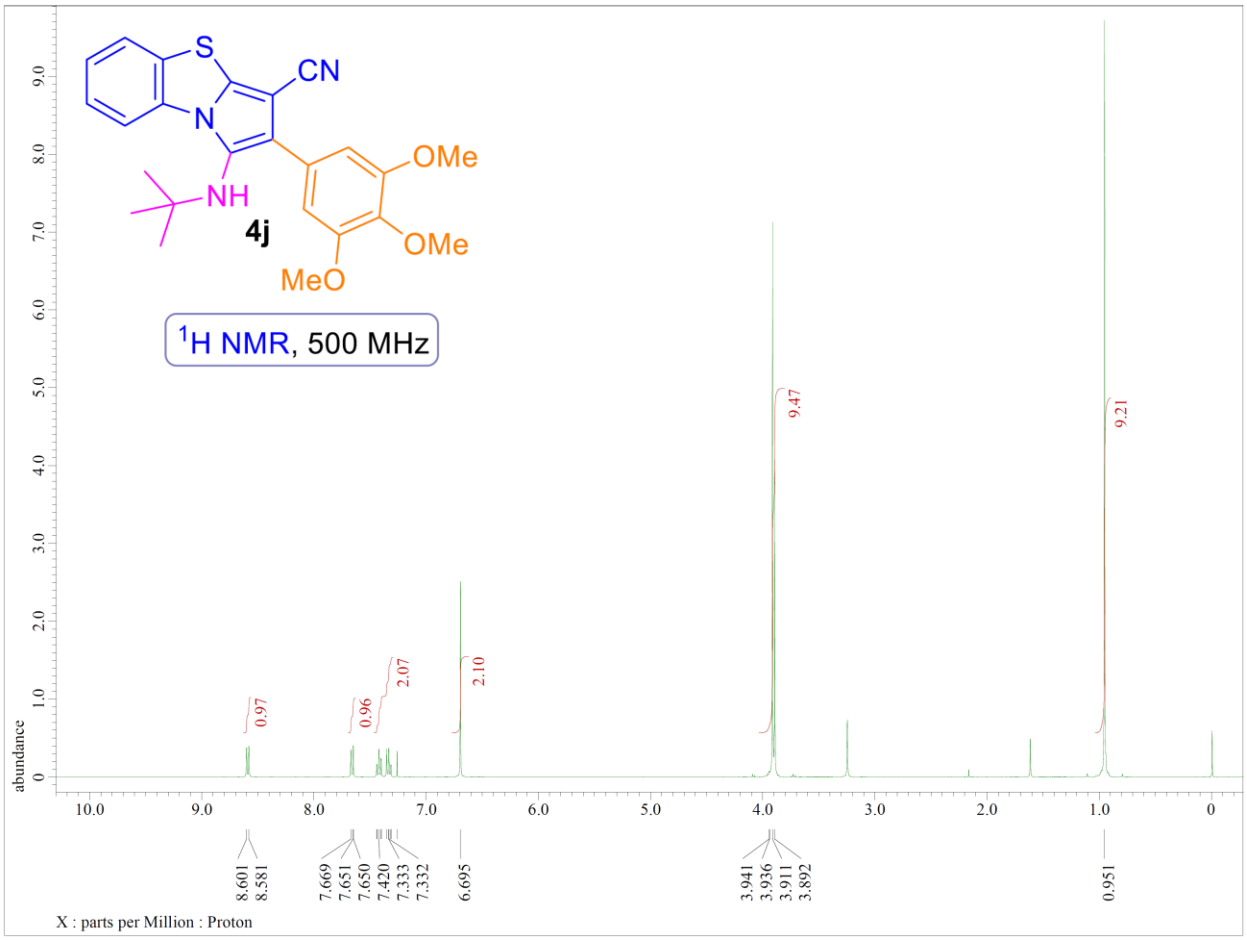


Figure S19: ^{1}H NMR of compound **4j** in $CDCl_3$

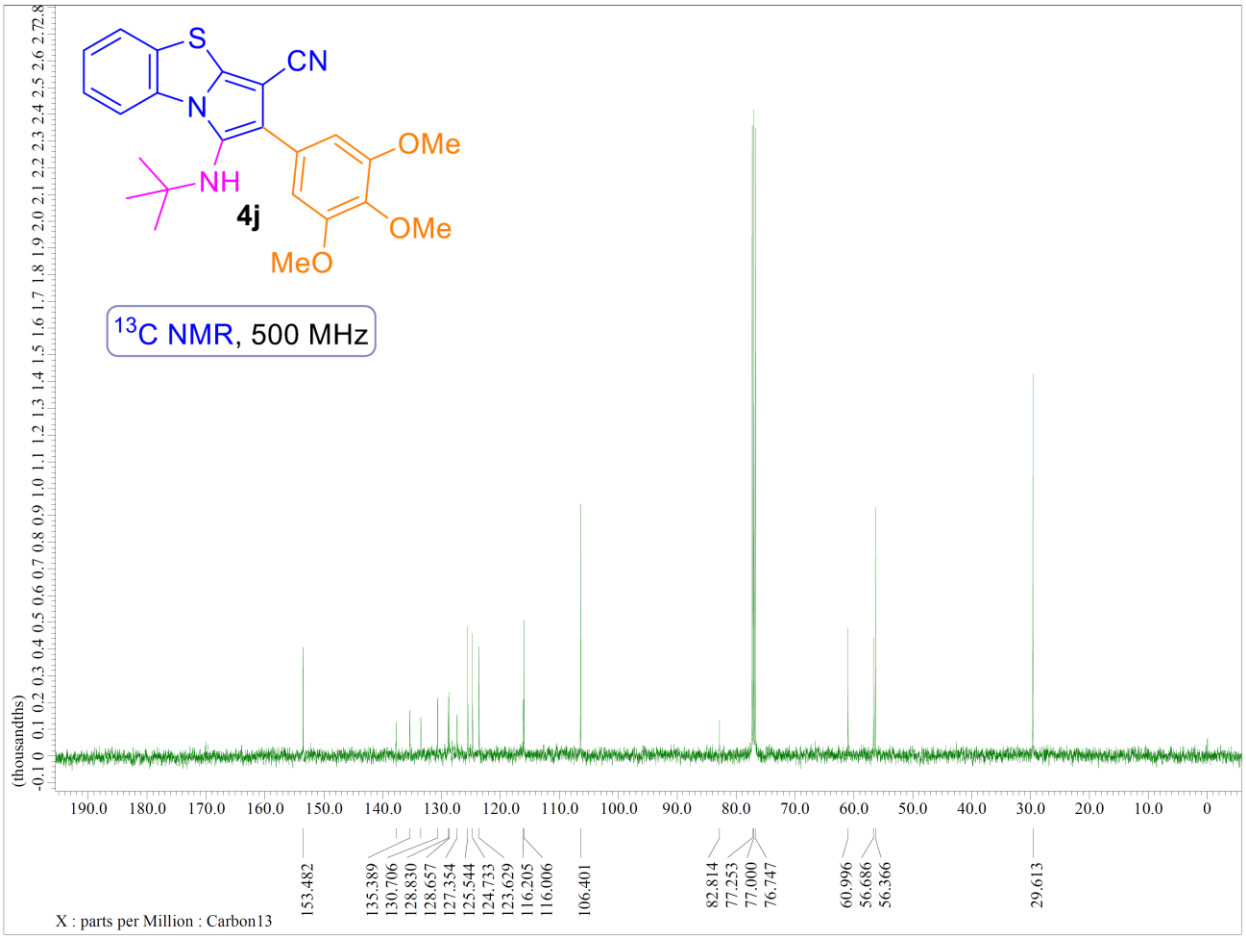


Figure S20: ^{13}C NMR of compound **4j** in $CDCl_3$

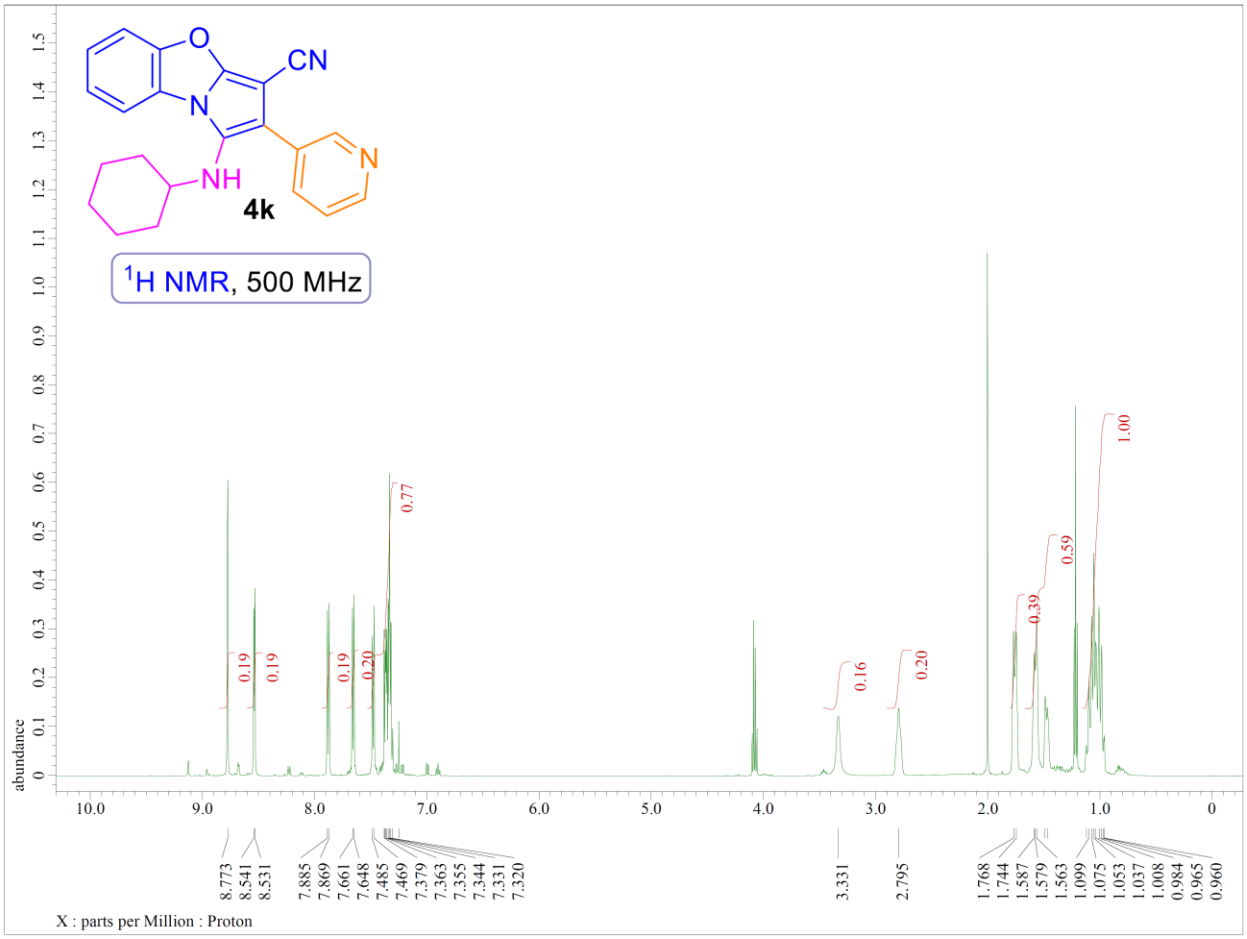


Figure S21: ^{1}H NMR of compound **4k** in $CDCl_3$

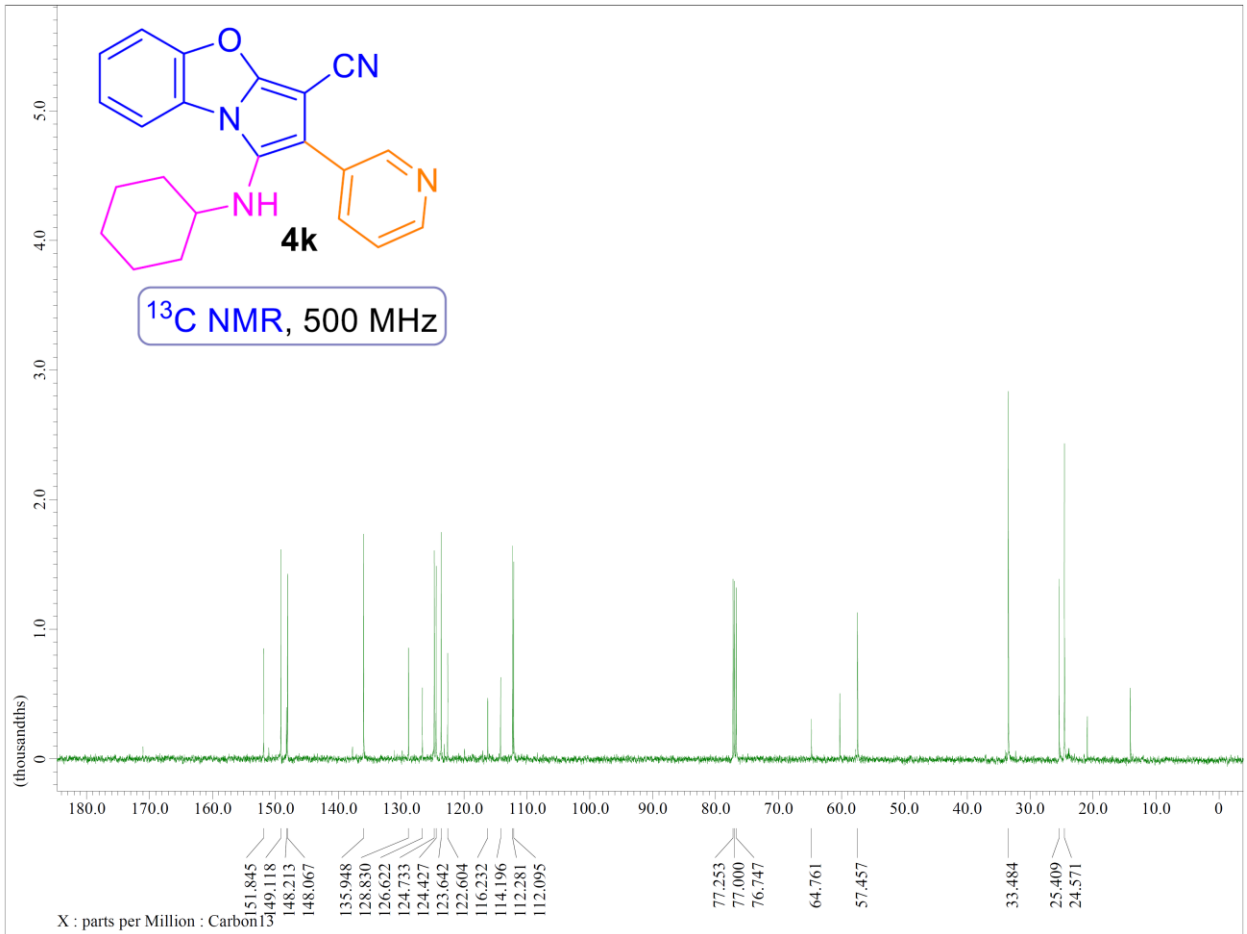


Figure S22: ^{13}C NMR of compound **4k** in $CDCl_3$

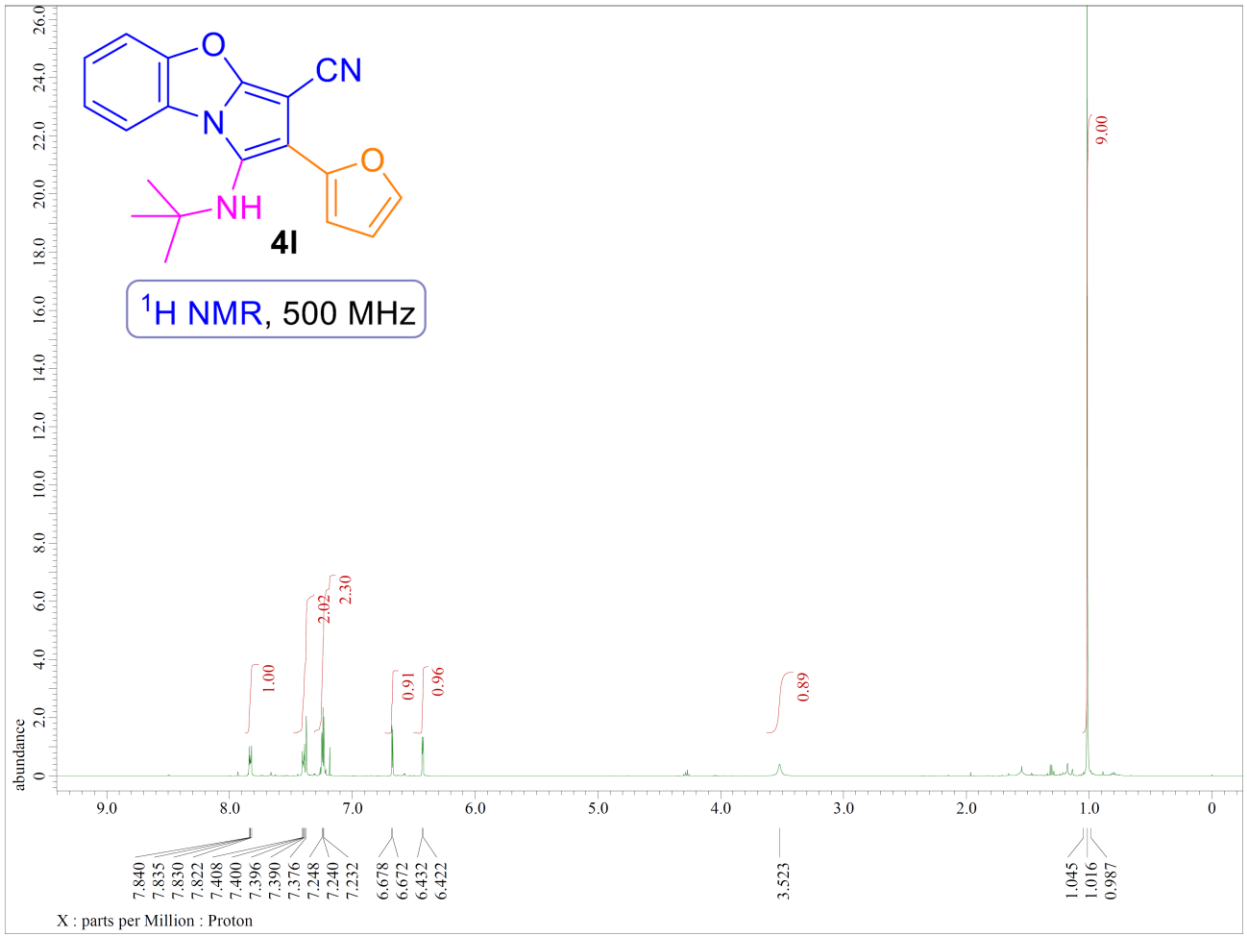


Figure S23: ^{1}H NMR of compound **4l** in $CDCl_3$

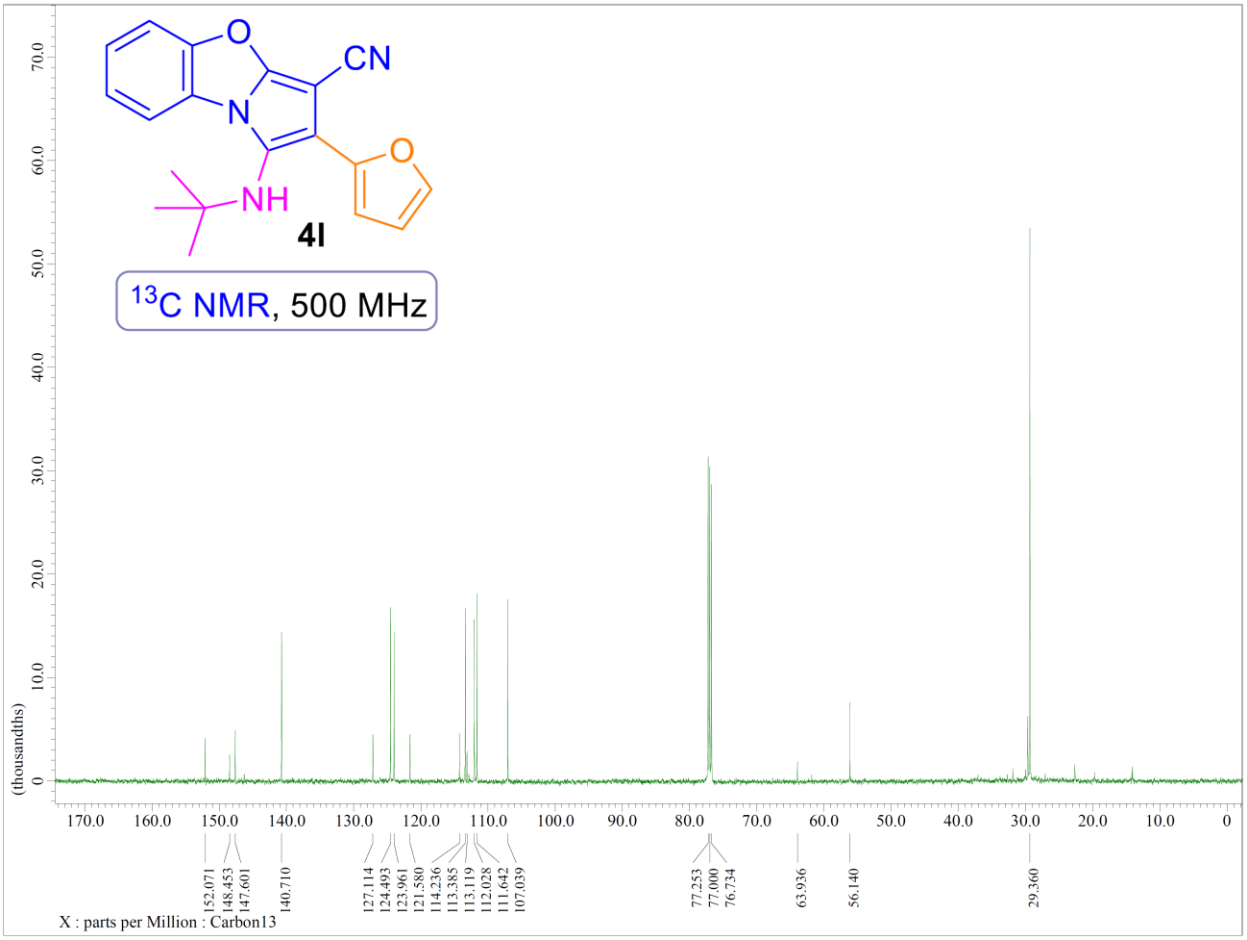


Figure S24: ^{13}C NMR of compound **4l** in $CDCl_3$

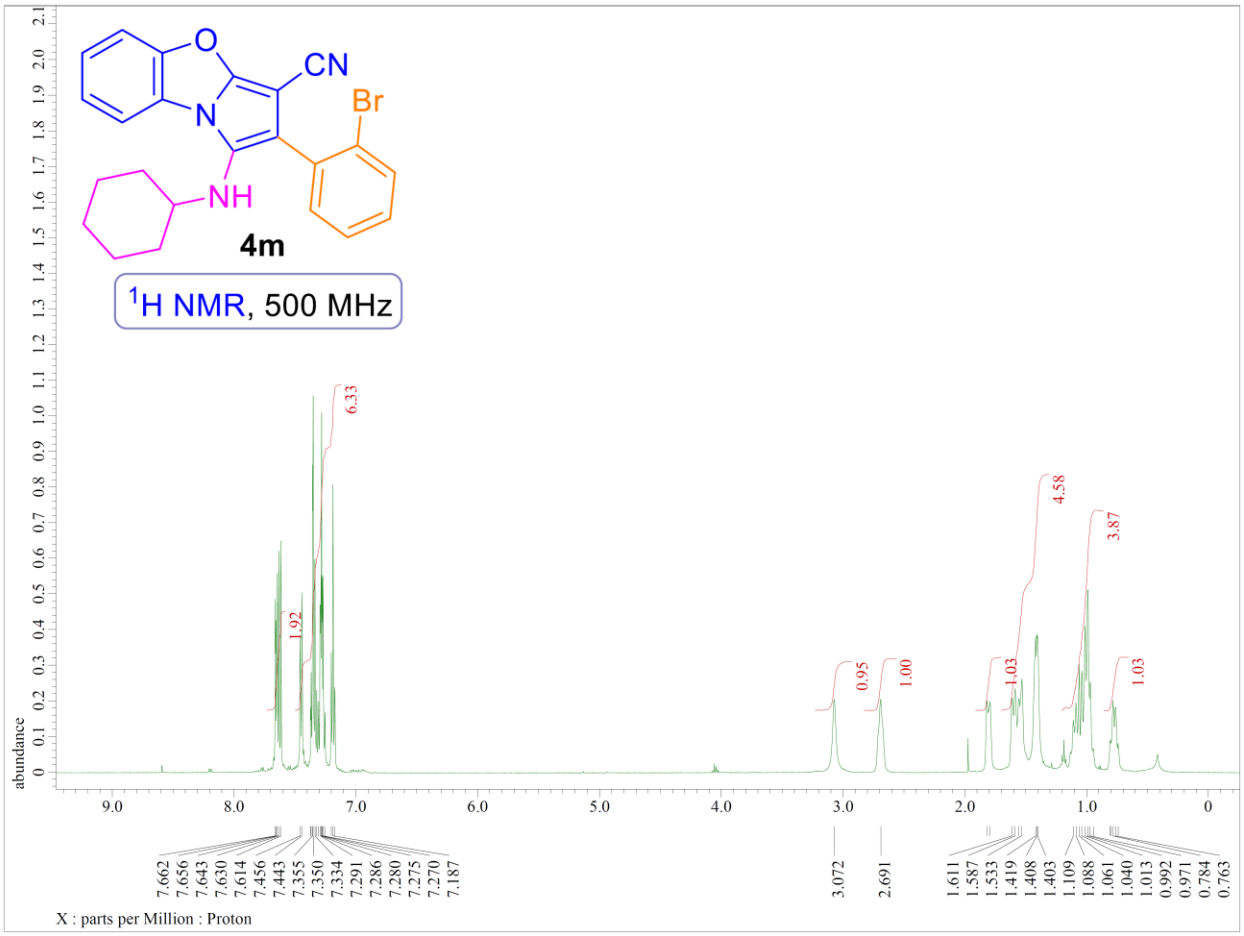


Figure S25: ^{1}H NMR of compound **4m** in $CDCl_3$

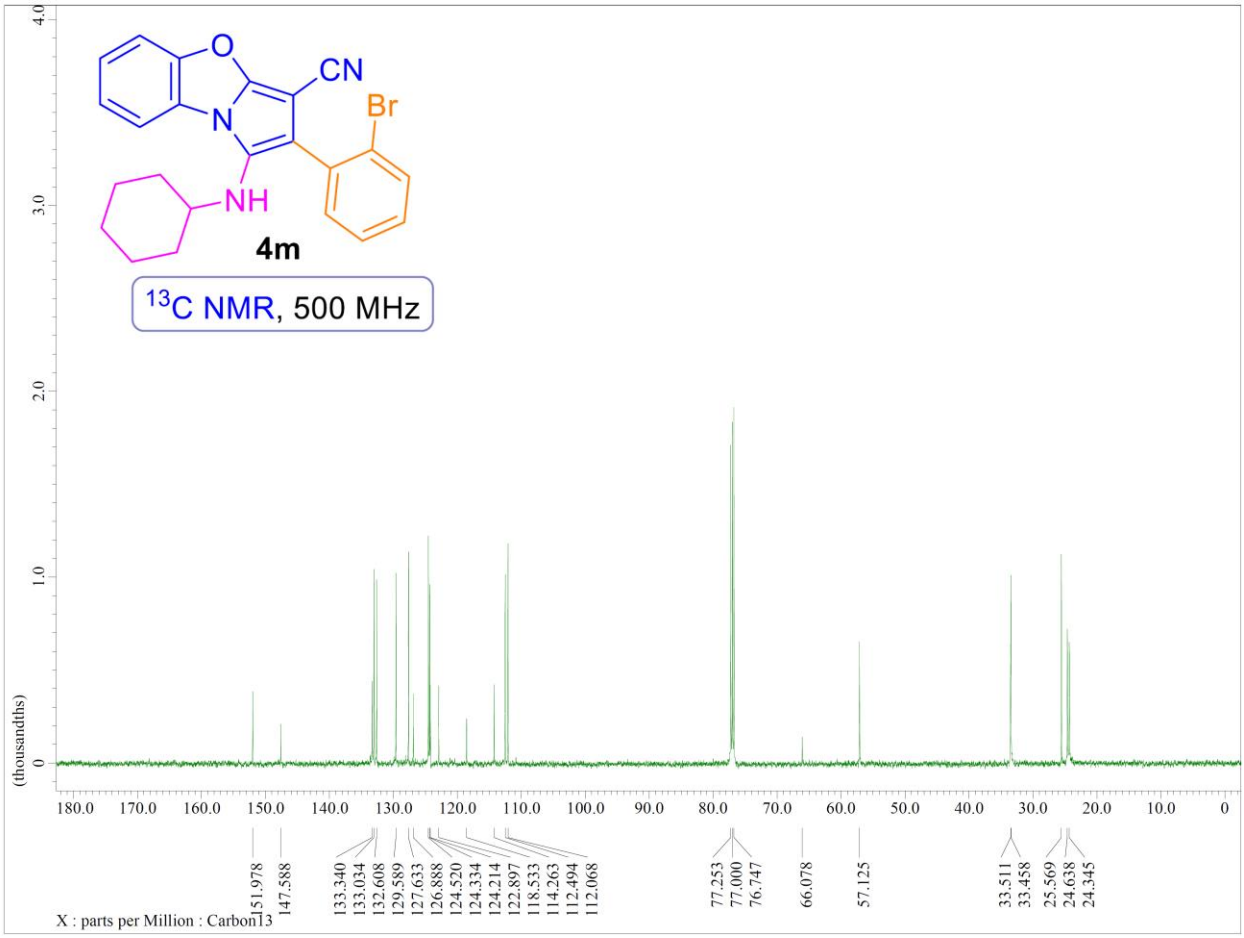


Figure S26: ^{13}C NMR of compound **4m** in $CDCl_3$

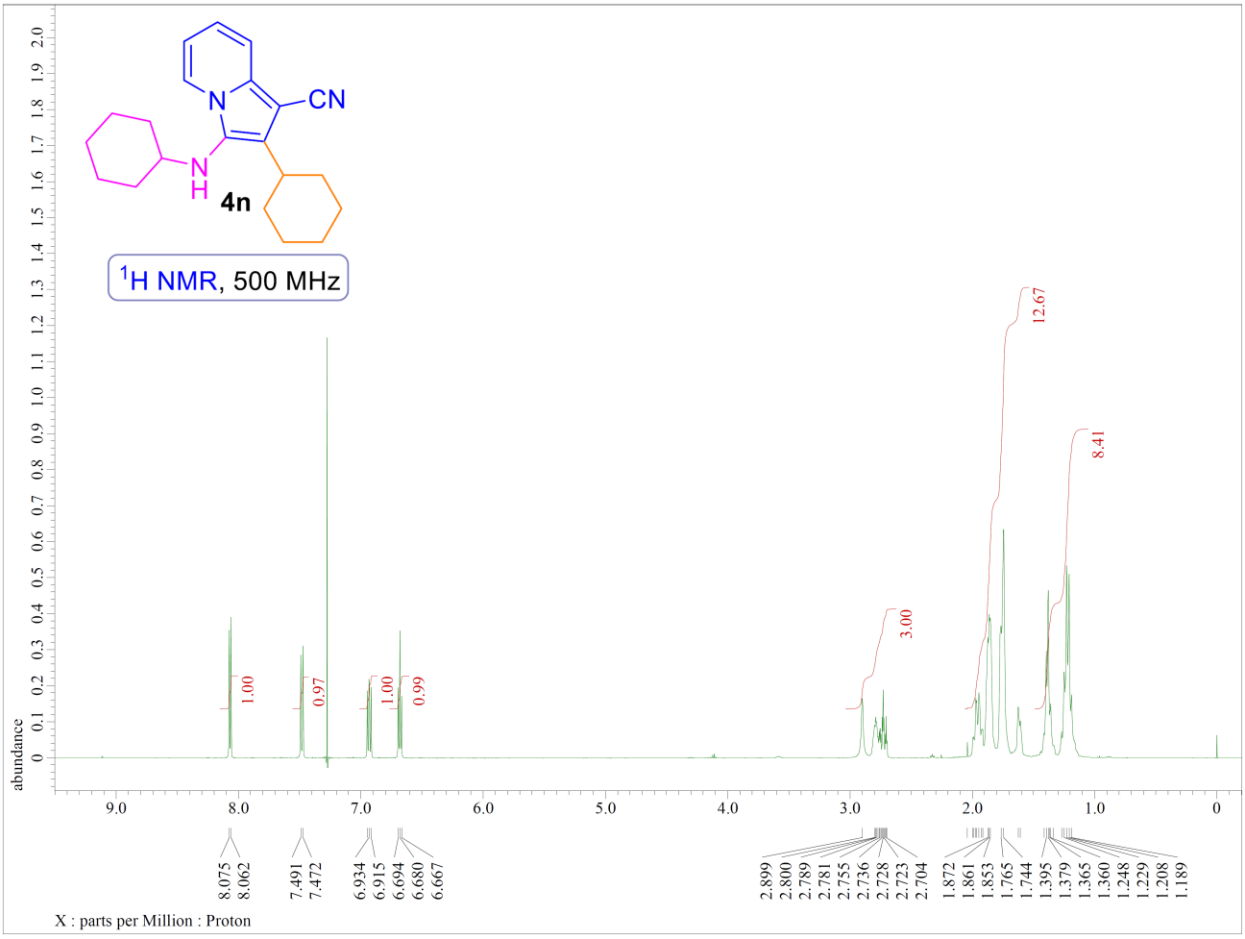


Figure S27: ^{1}H NMR of compound **4n** in $CDCl_3$

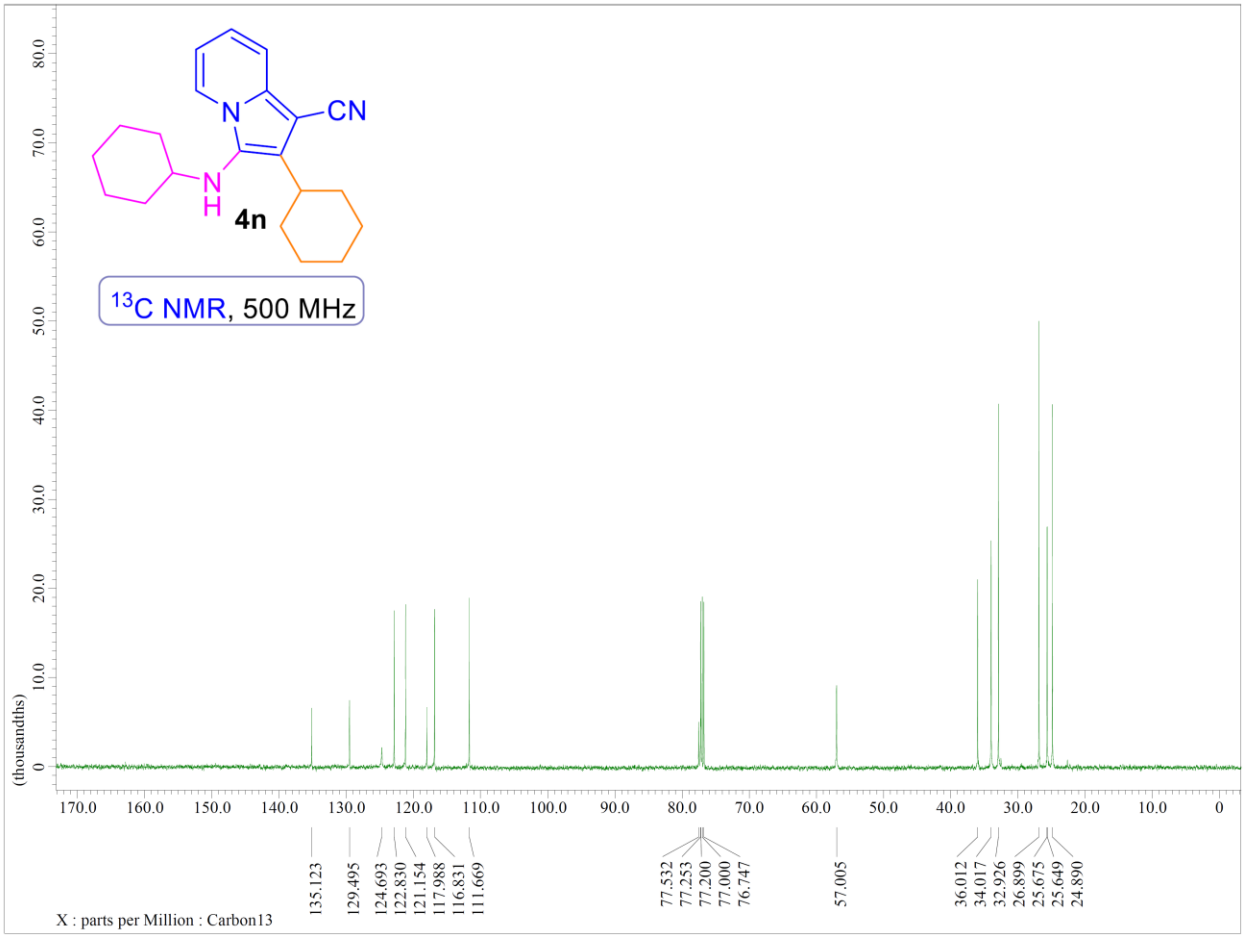


Figure S28: ^{13}C NMR of compound **4n** in $CDCl_3$

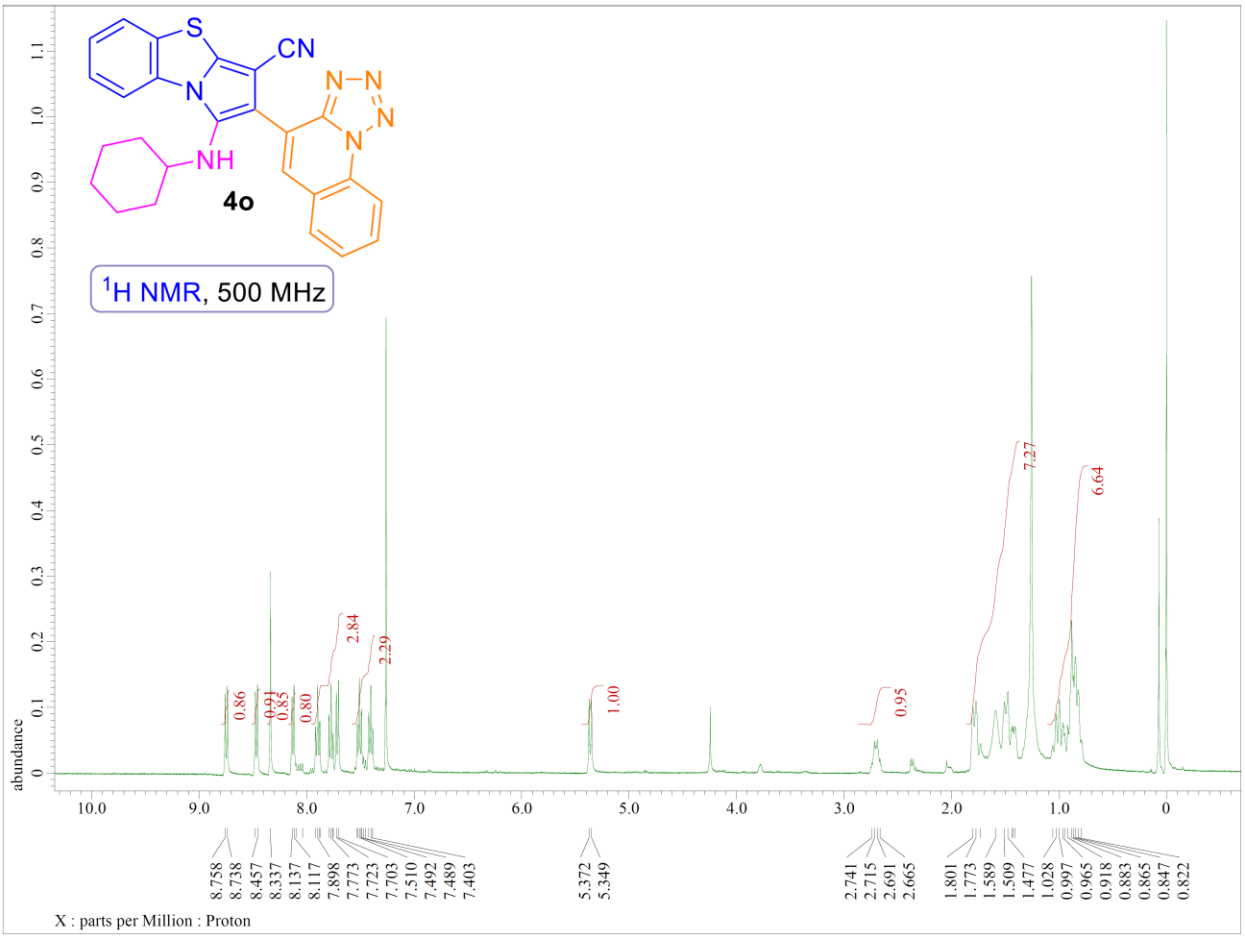


Figure S29: ^{1}H NMR of compound **4o** in $CDCl_3$

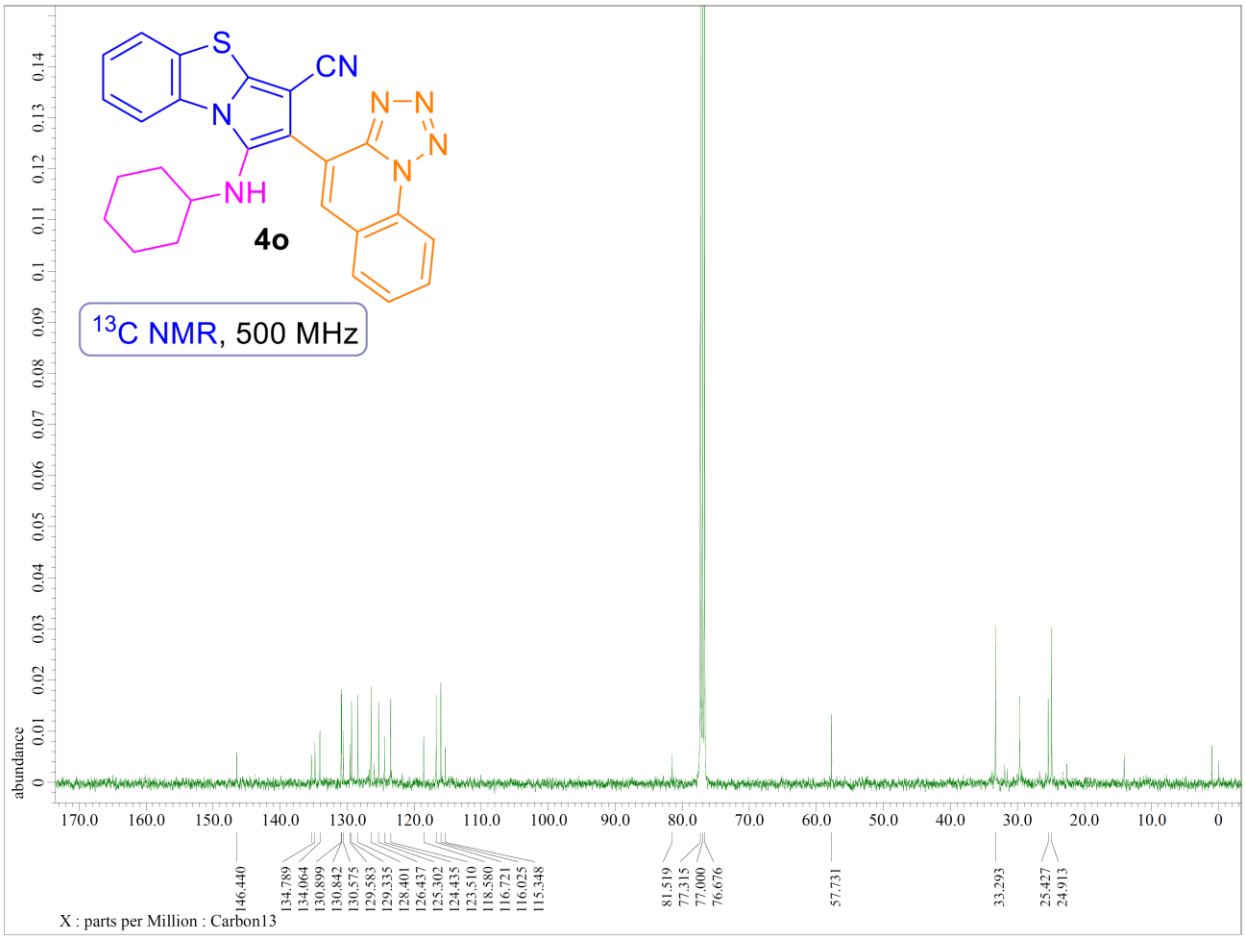


Figure S30: ^{13}C NMR of compound **4o** in $CDCl_3$

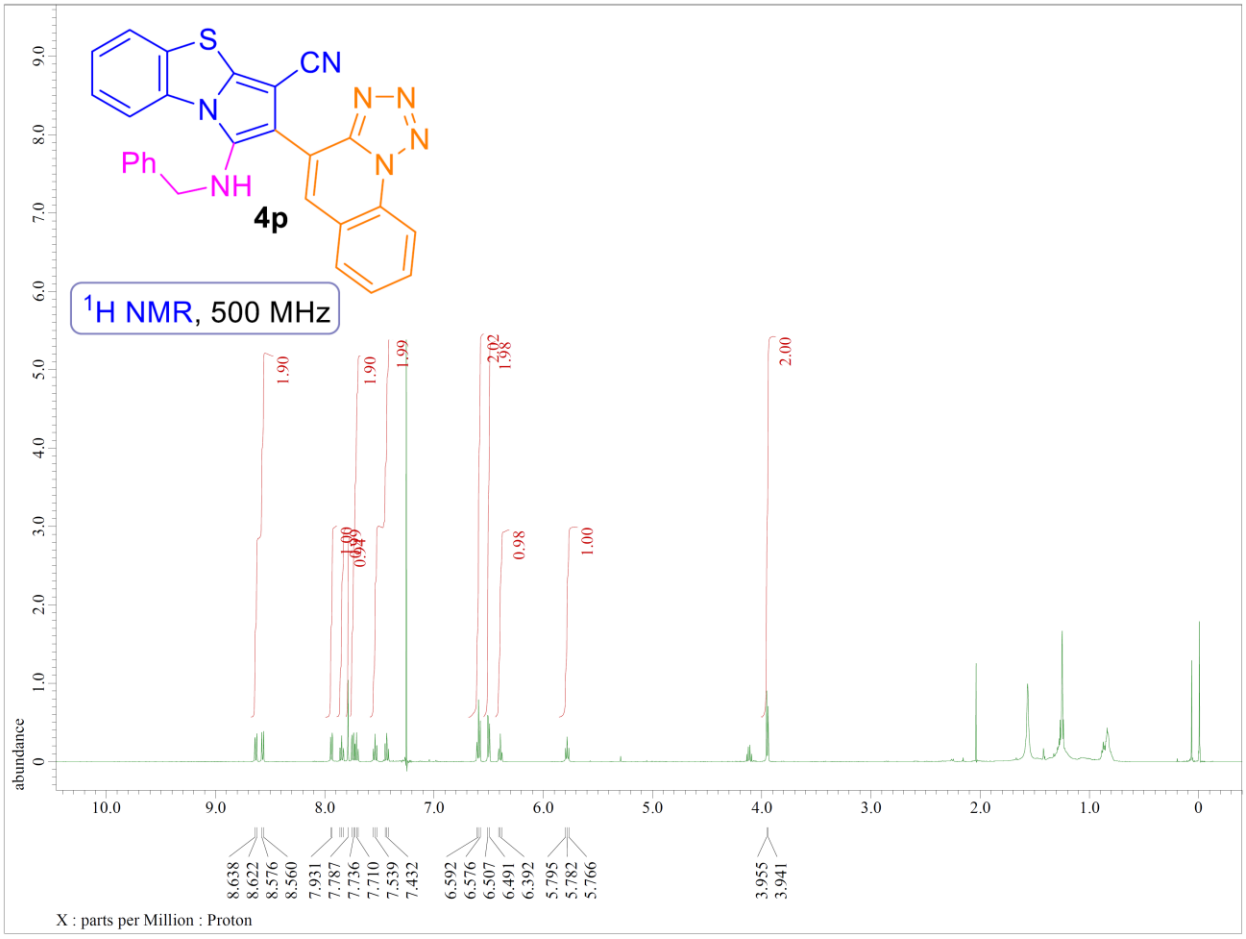


Figure S31: ^{1}H NMR of compound **4p** in $CDCl_3$

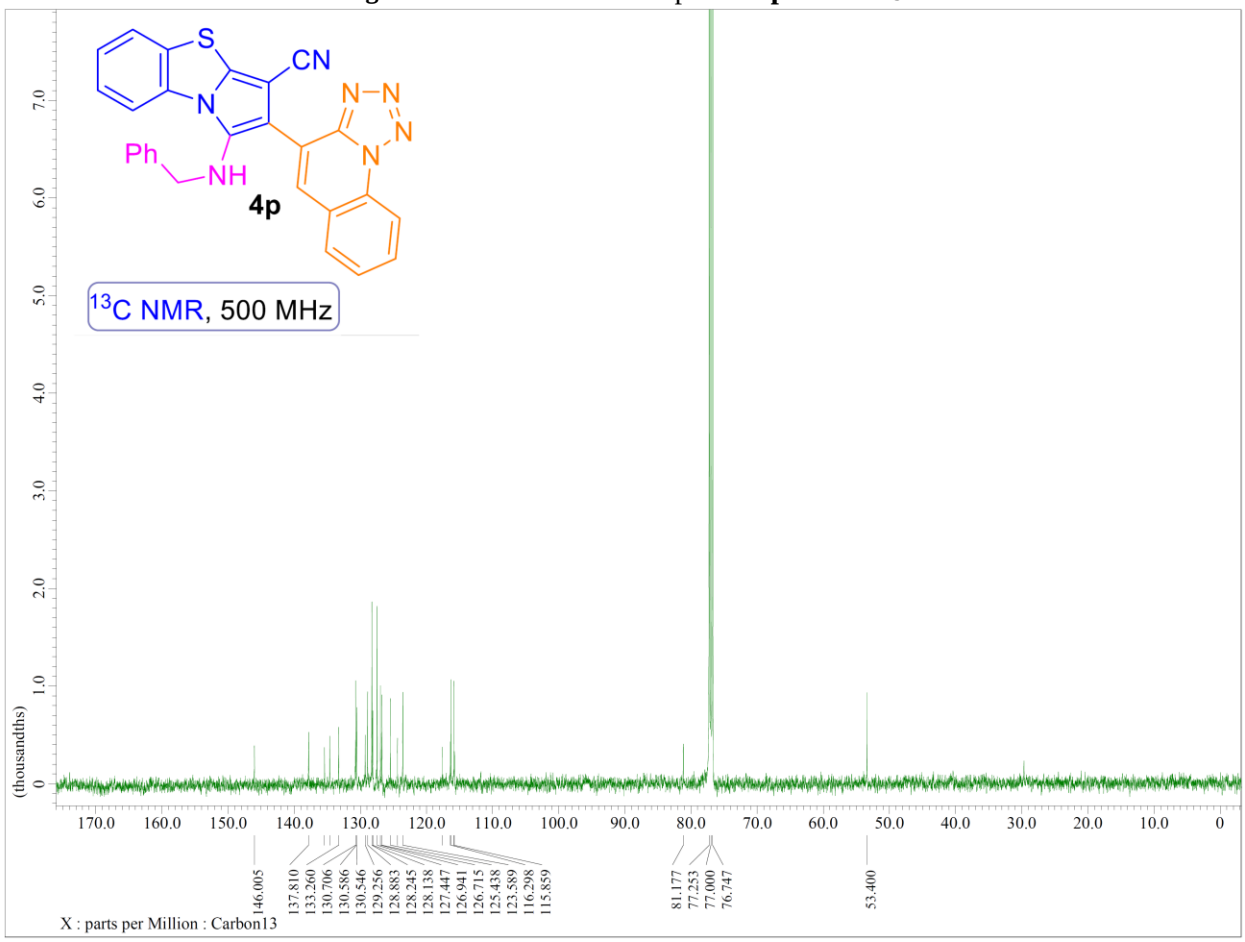


Figure S32: ^{13}C NMR of compound **4p** in $CDCl_3$

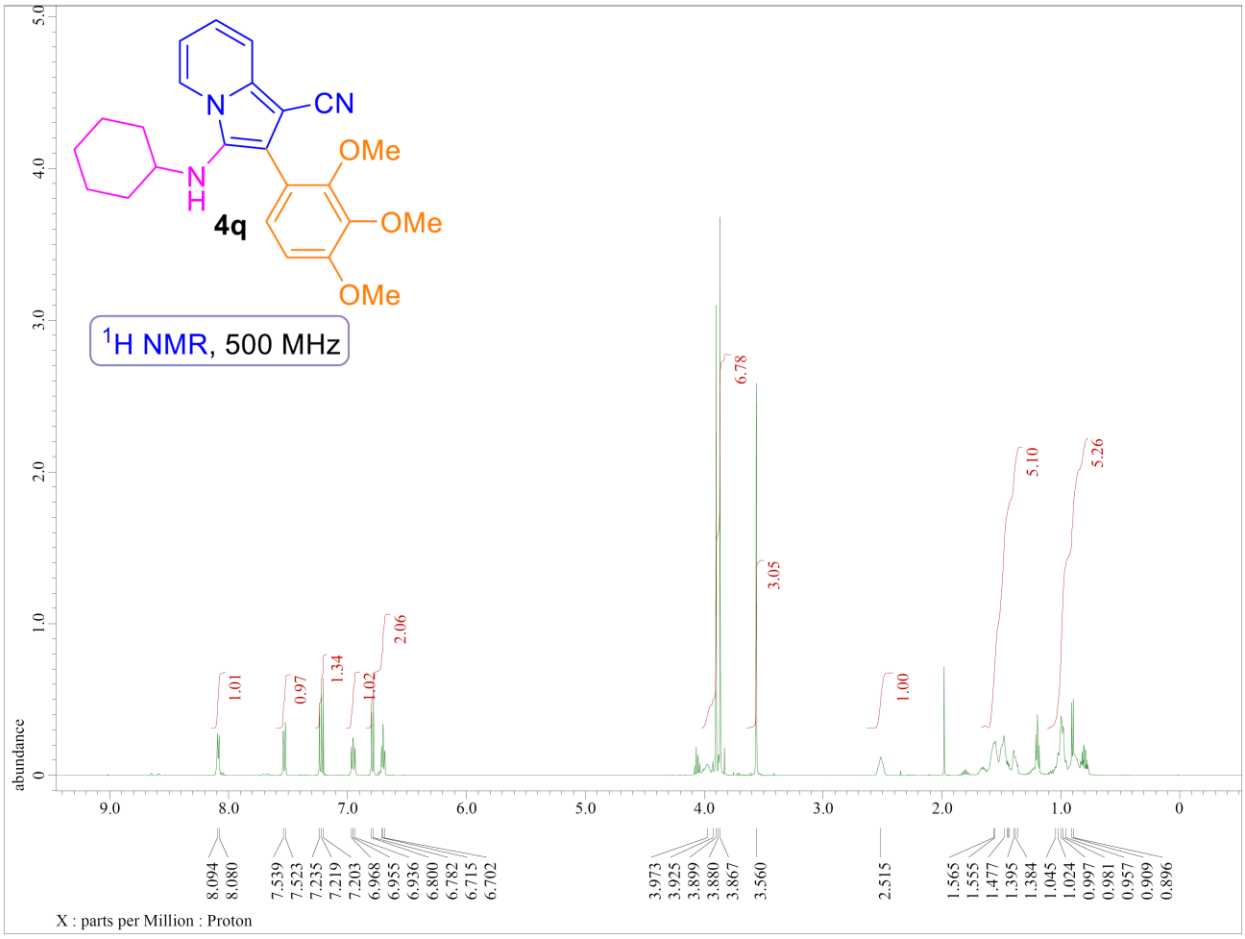


Figure S33: ^{1}H NMR of compound **4q** in $CDCl_3$

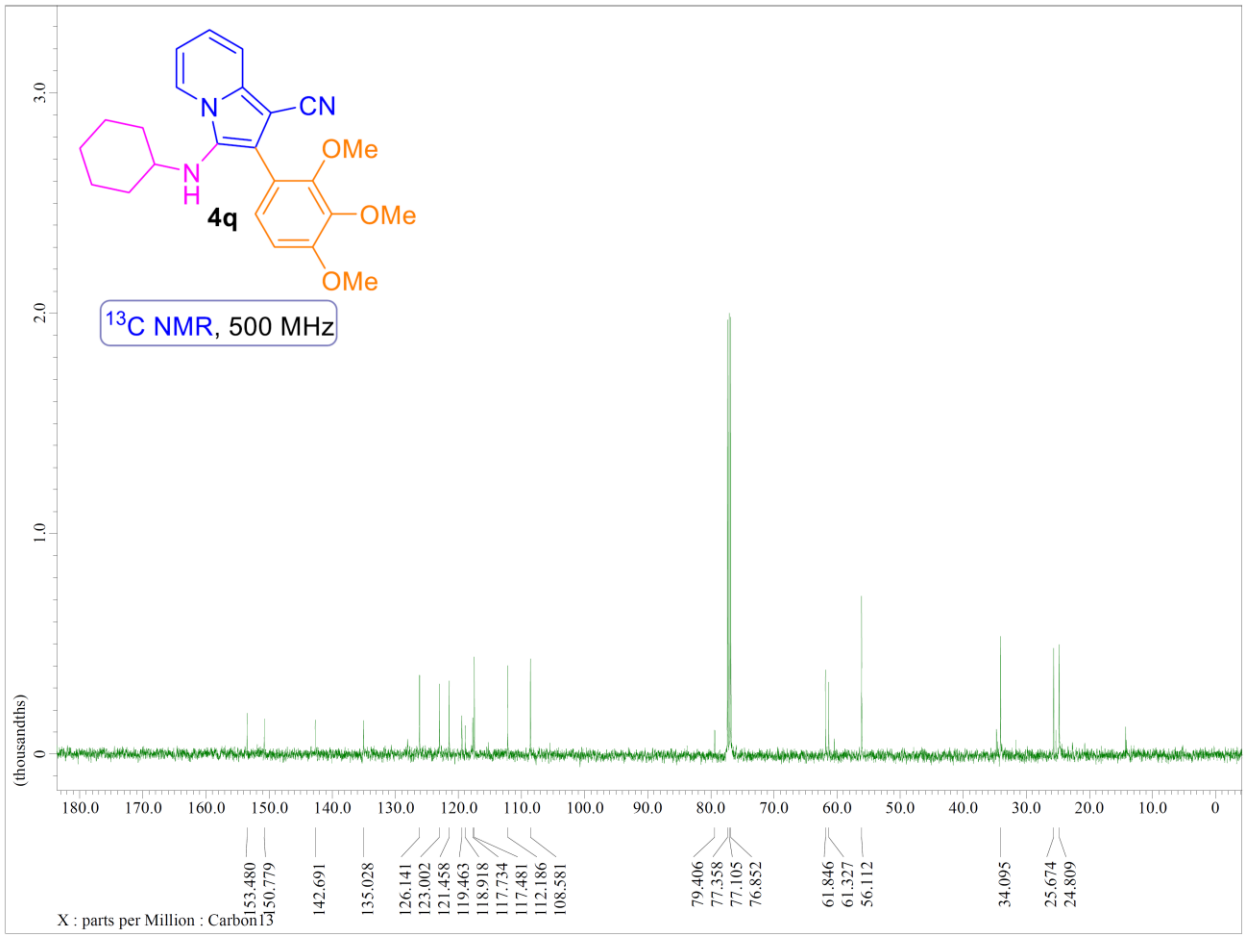


Figure S34: ^{13}C NMR of compound **4q** in $CDCl_3$

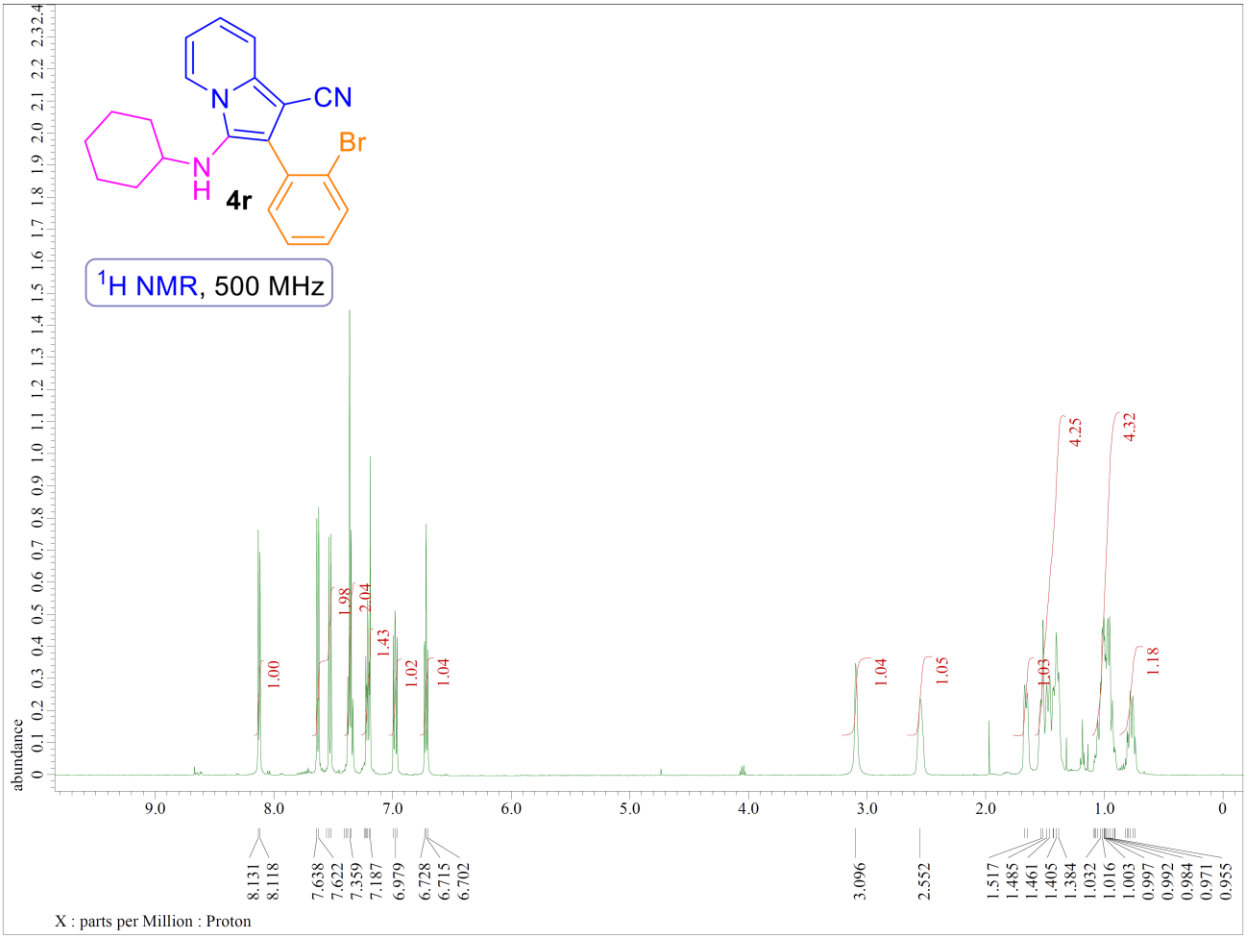


Figure S35: ^{1}H NMR of compound **4r** in $CDCl_3$

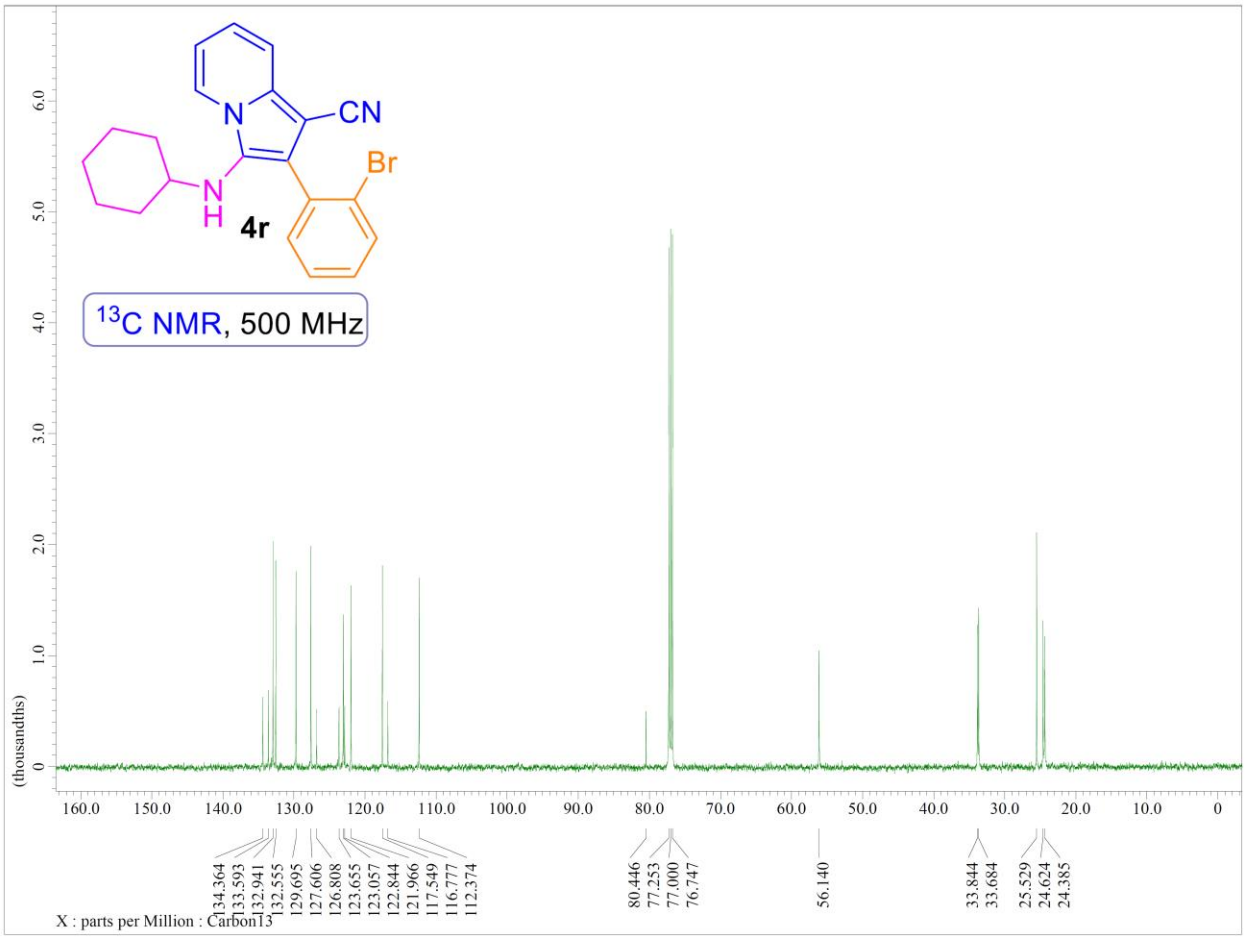


Figure S36: ^{13}C NMR of compound **4r** in $CDCl_3$

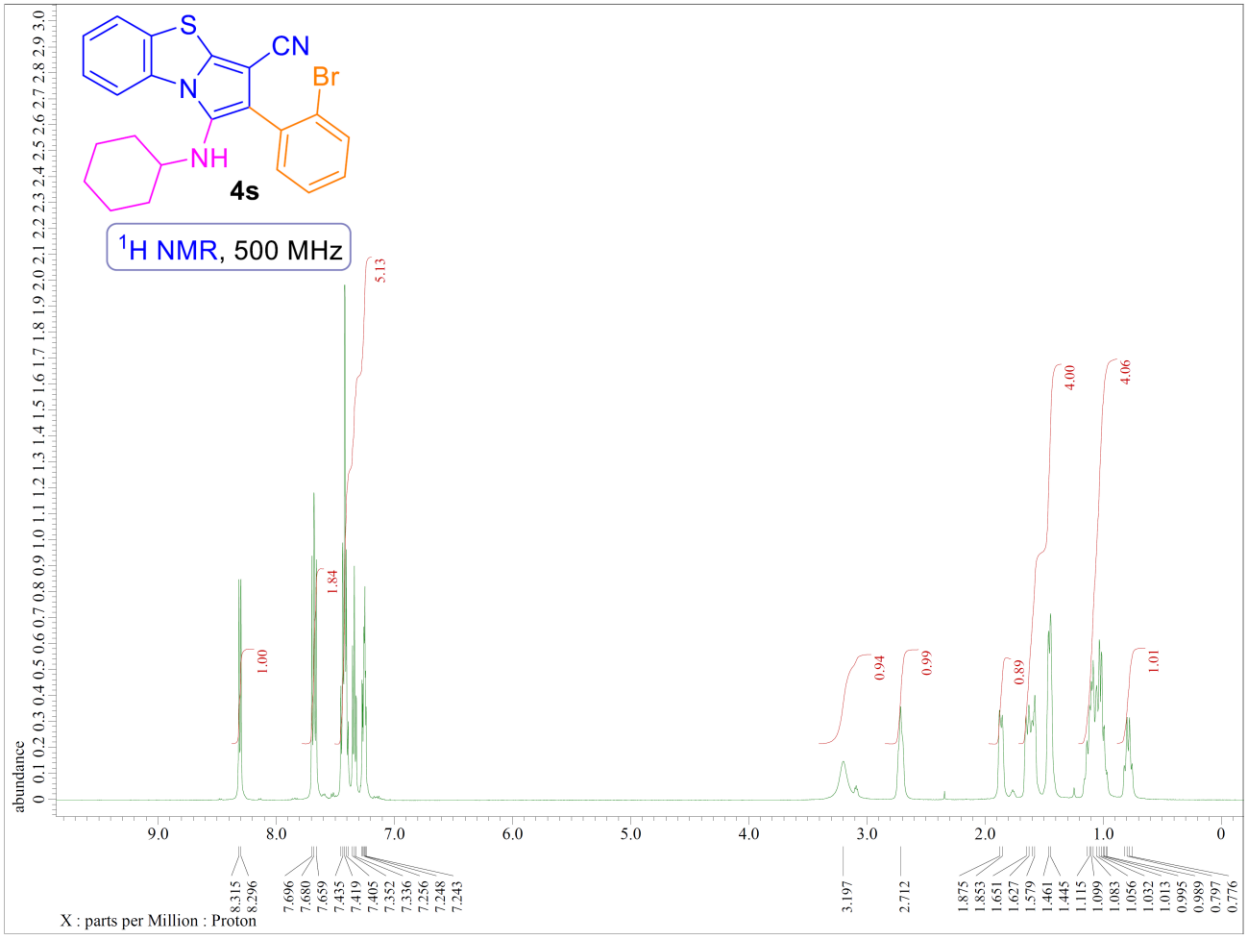


Figure S37: ^{1}H NMR of compound **4s** in $CDCl_3$

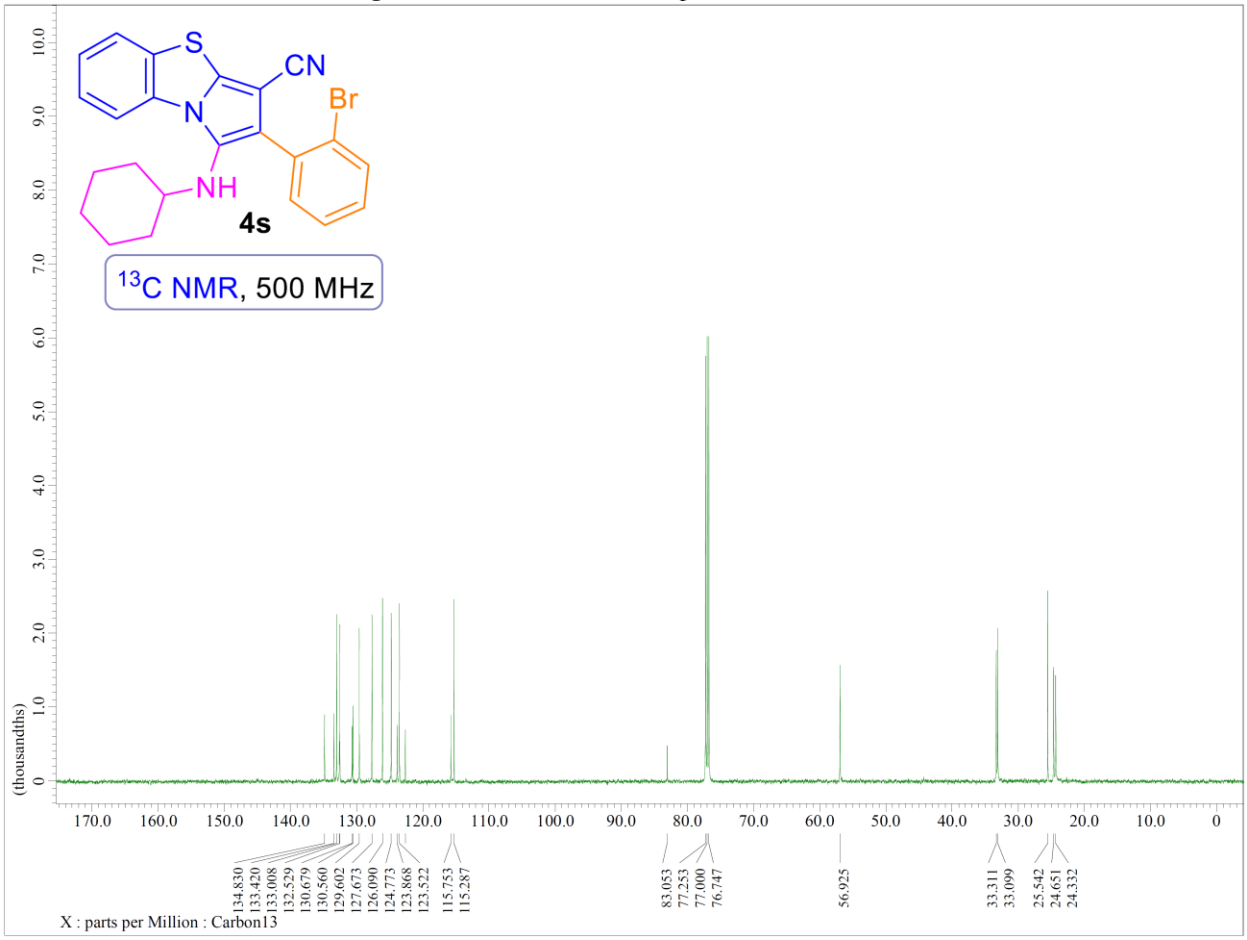


Figure S38: ^{13}C NMR of compound **4s** in $CDCl_3$

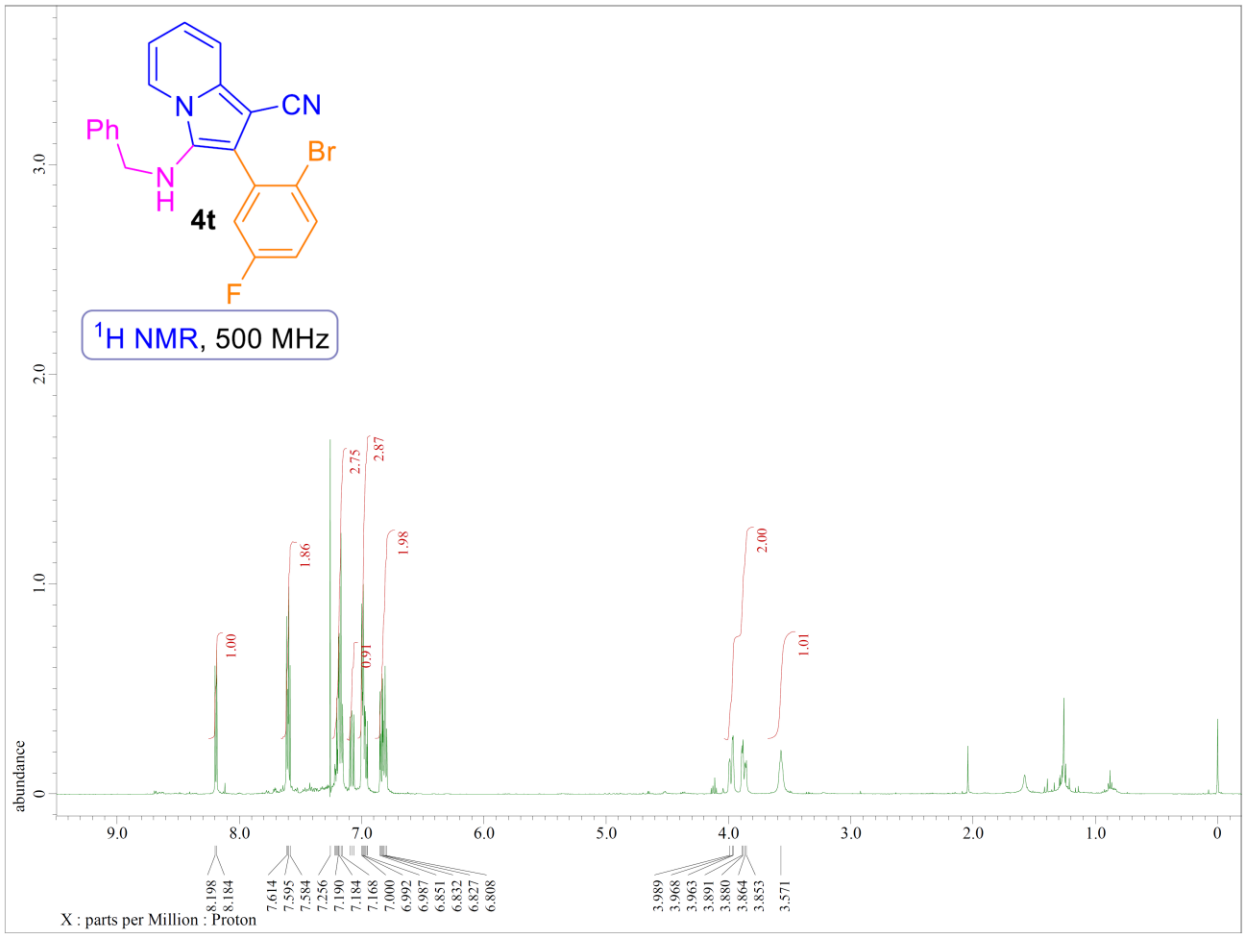


Figure S39: ^{1}H NMR of compound **4t** in $CDCl_3$

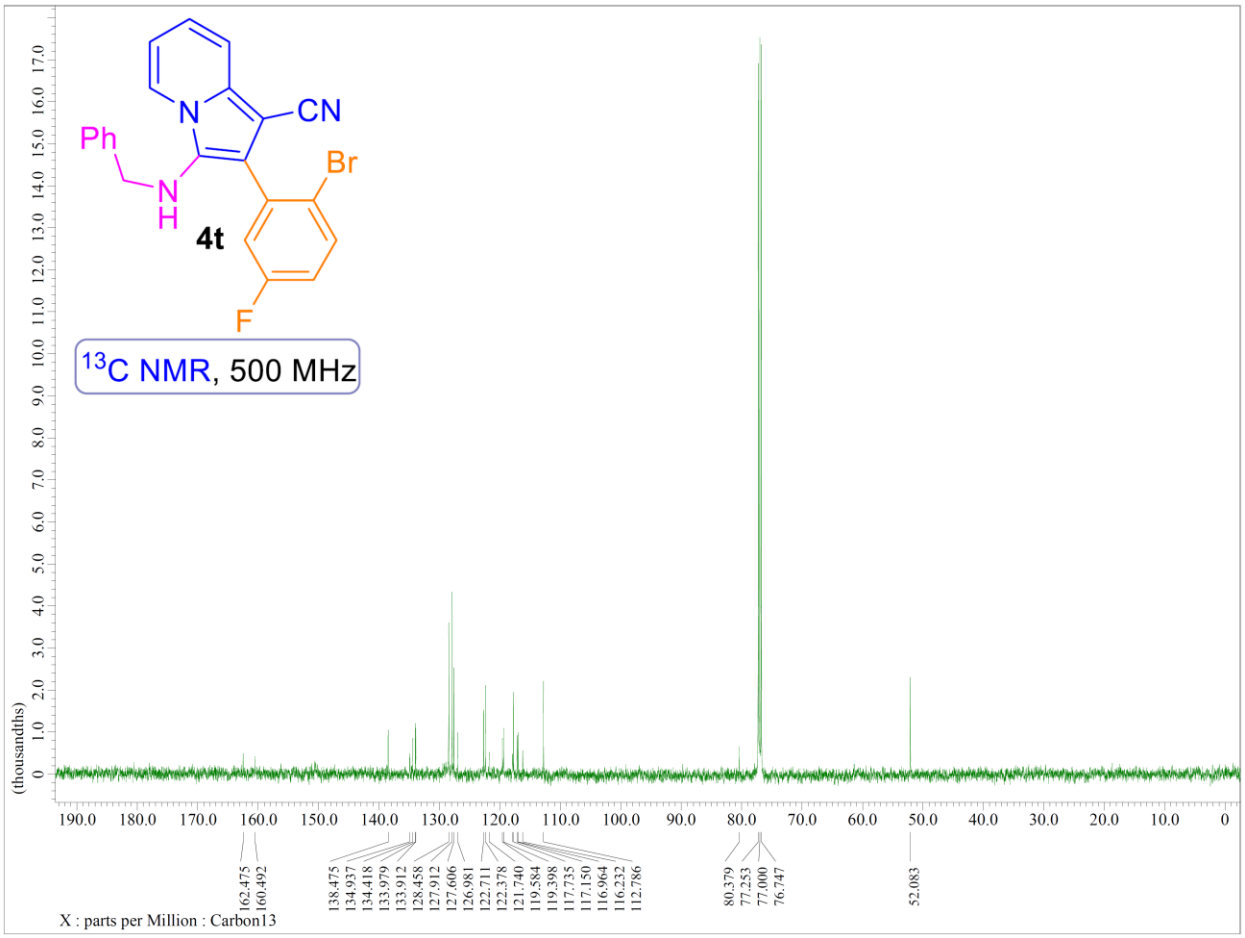


Figure S40: ^{13}C NMR of compound **4t** in $CDCl_3$

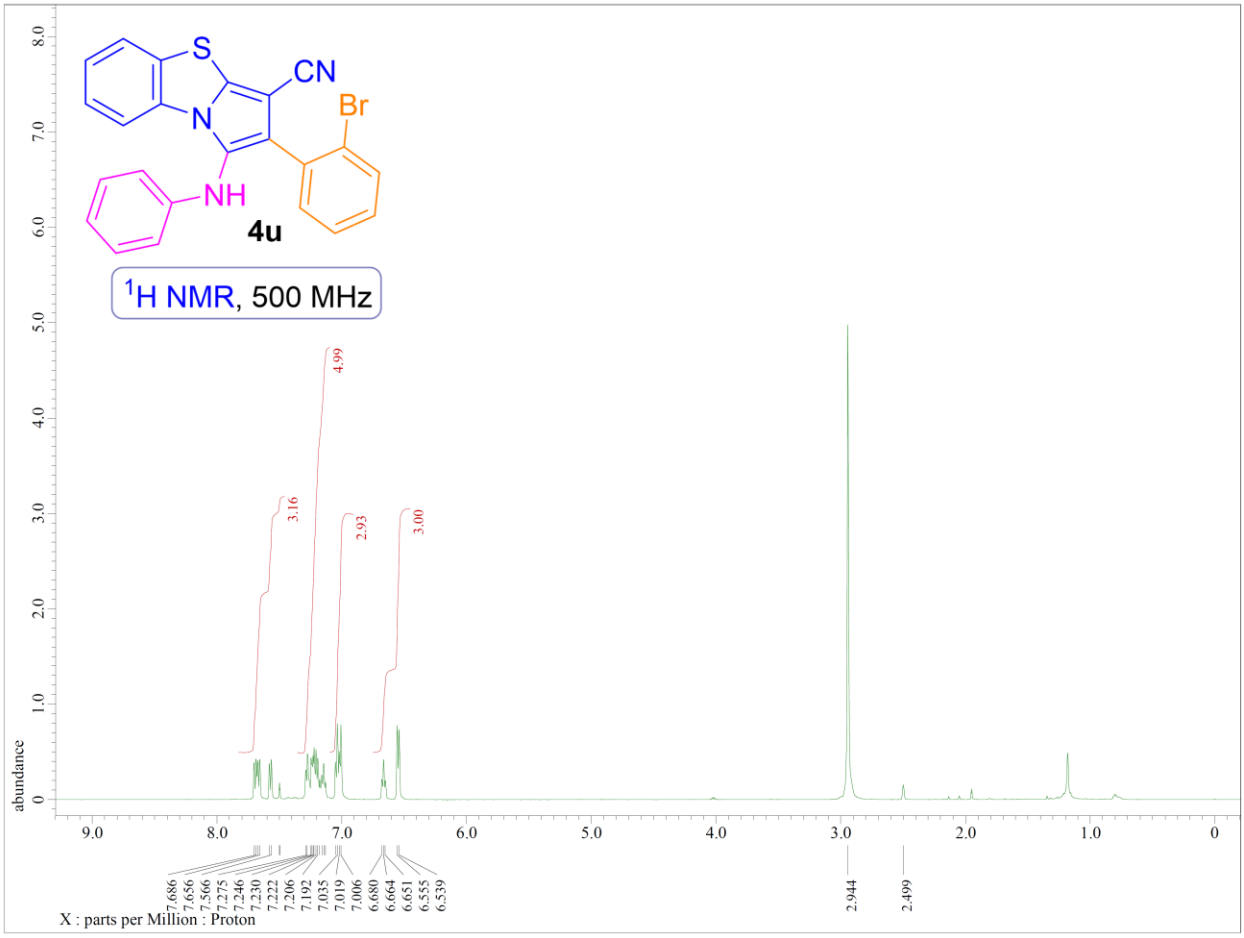


Figure S41: ^{1}H NMR of compound **4t** in ($CDCl_3$ + DMSO-d6)

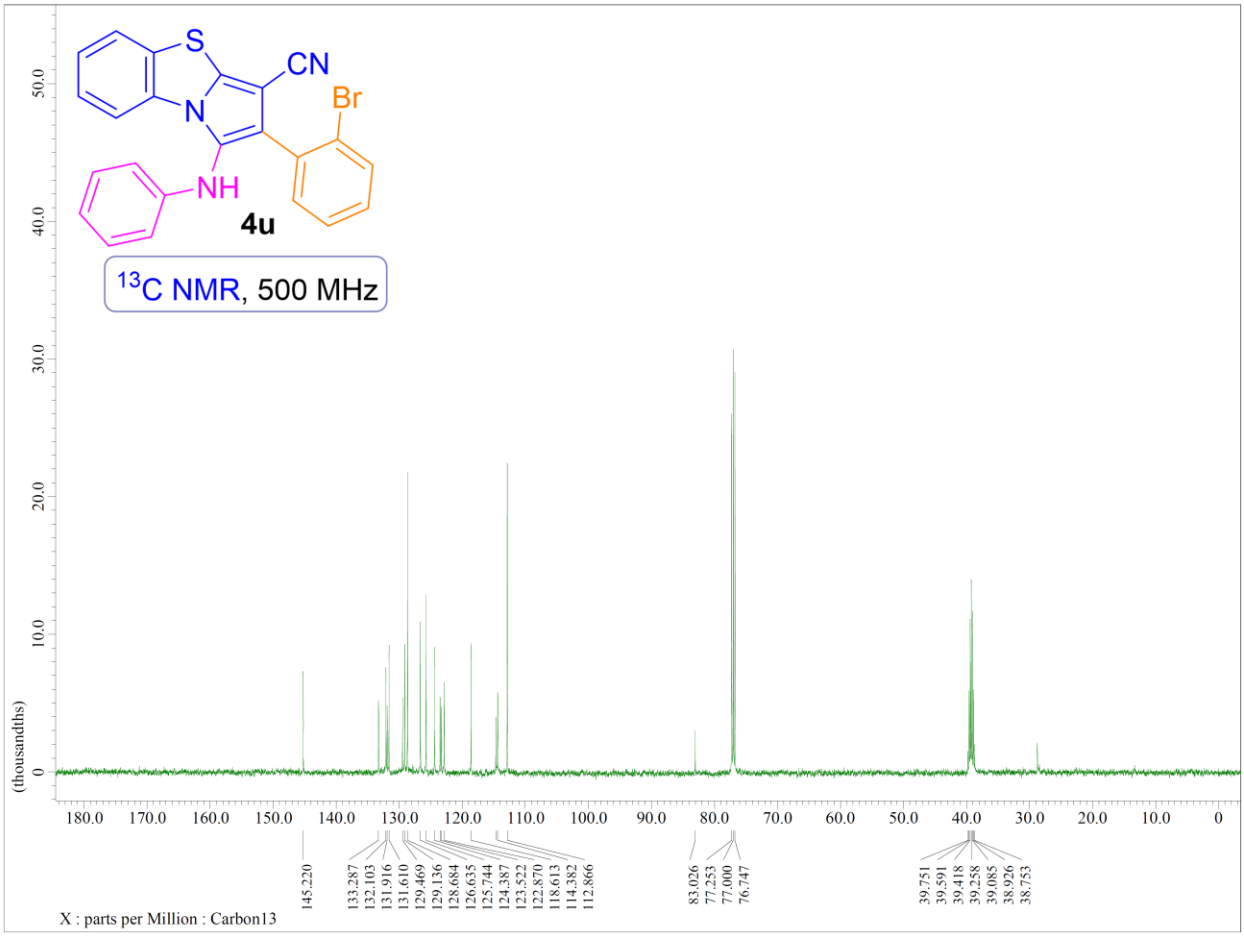


Figure S42: ^{13}C NMR of compound **4u** in ($CDCl_3$ + DMSO-d6)

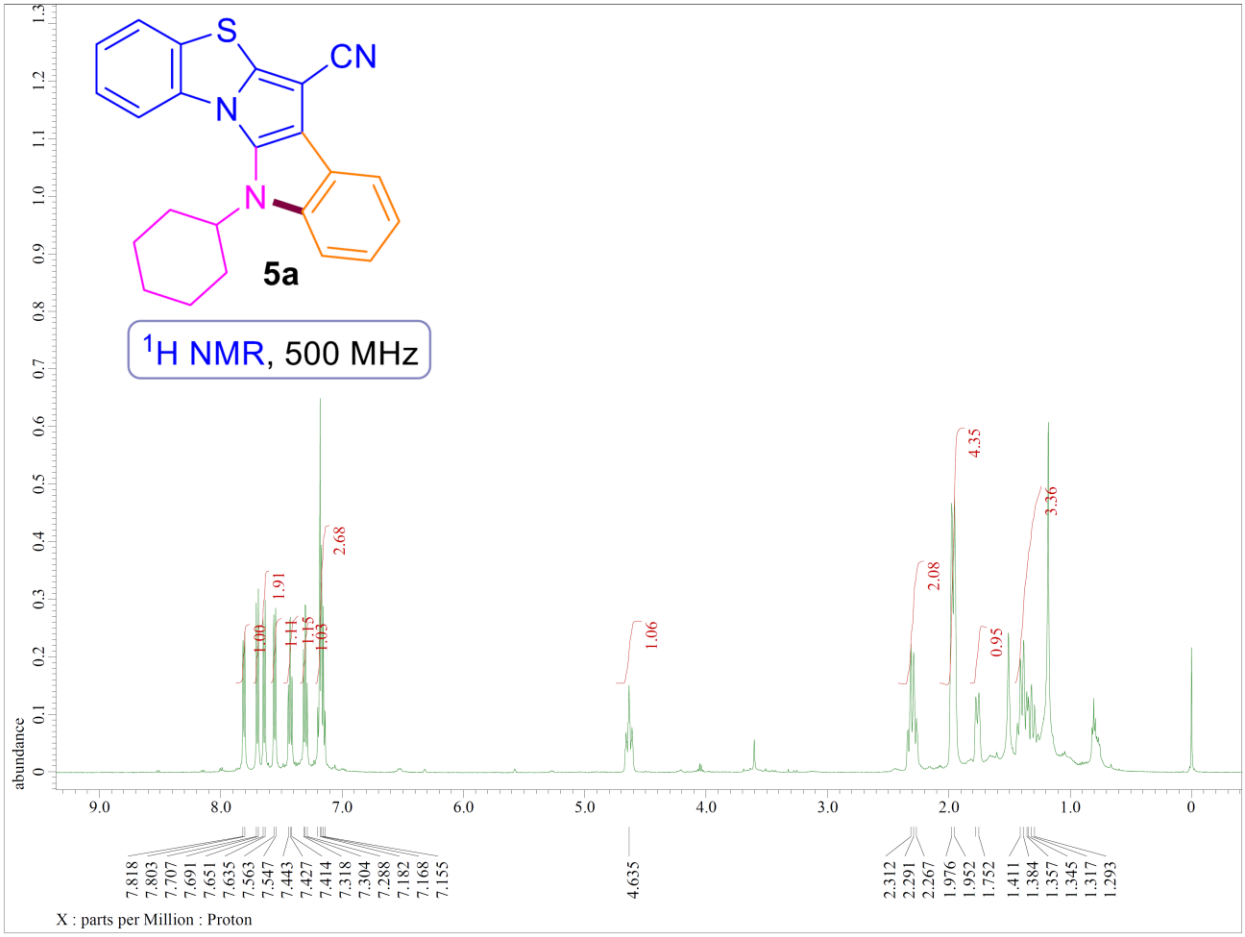


Figure S43: ^{1}H NMR of compound **5a** in $CDCl_3$

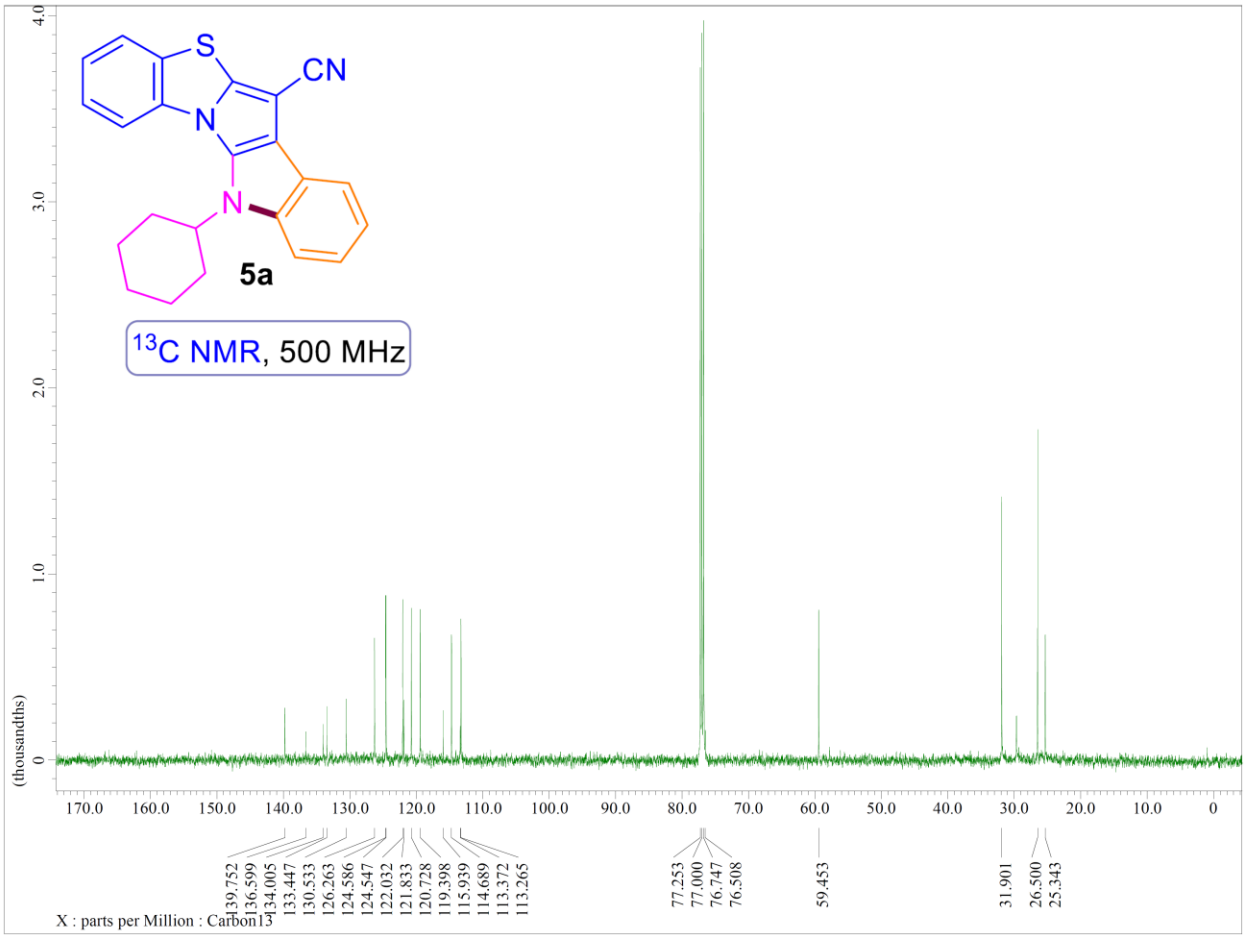


Figure S44: ^{13}C NMR of compound **5a** in $CDCl_3$

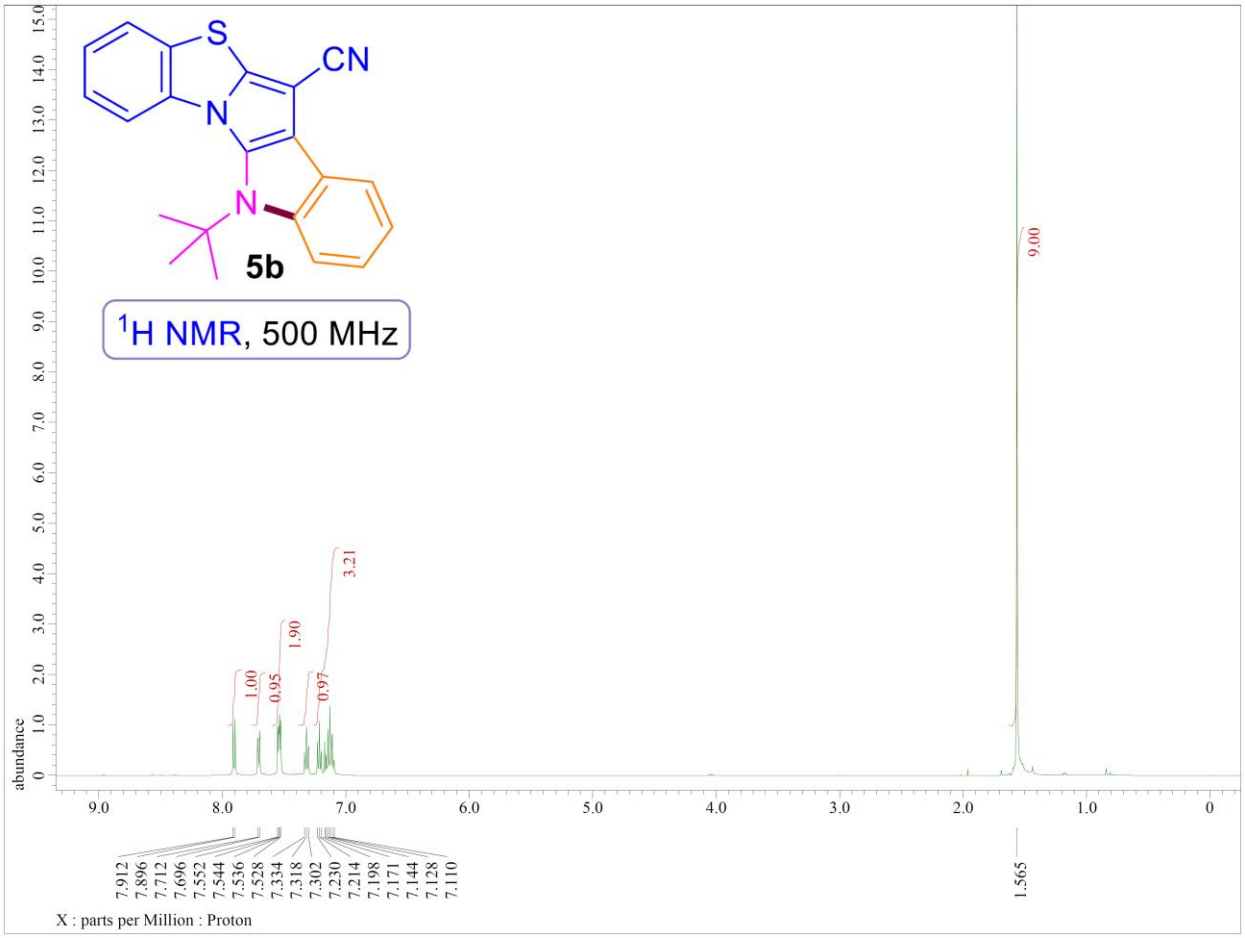


Figure S45: ^{1}H NMR of compound **5b** in $CDCl_3$

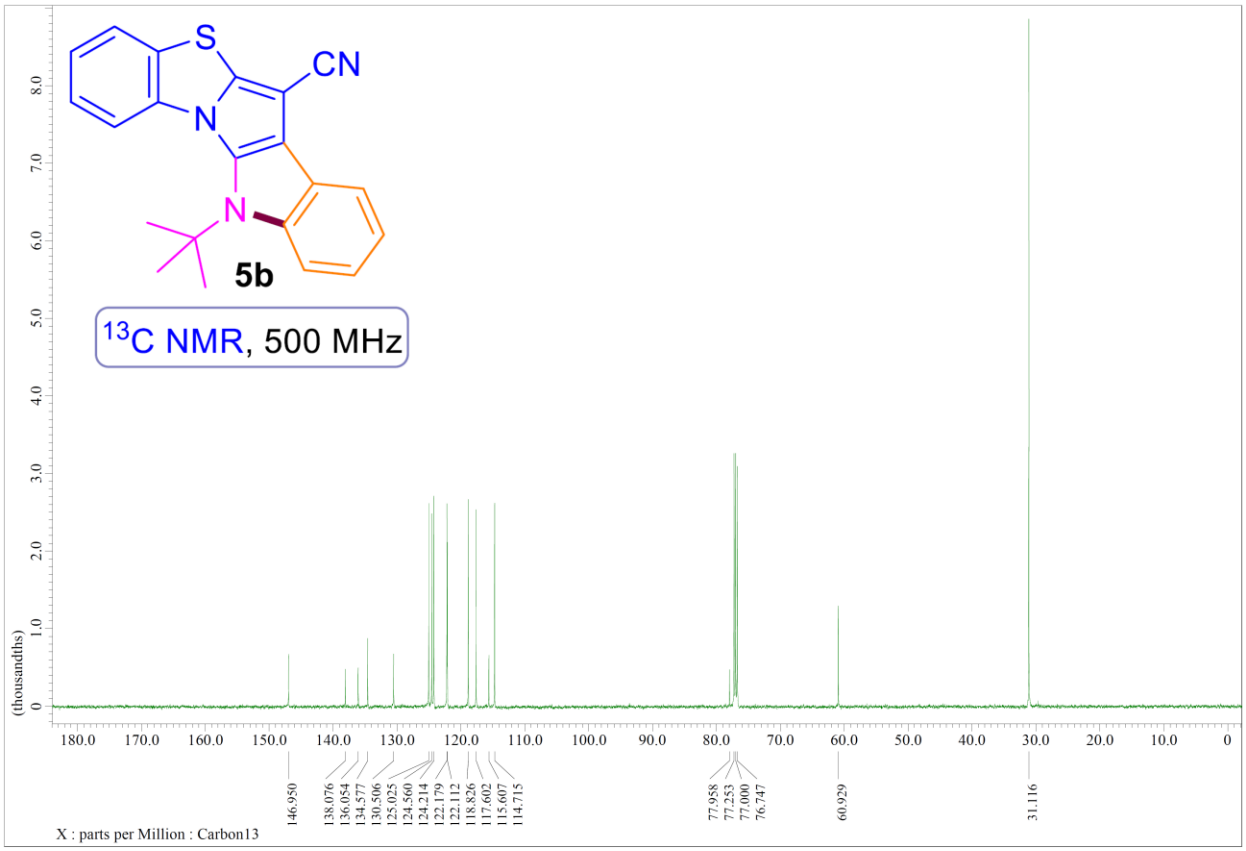


Figure S46: ^{13}C NMR of compound **5b** in $CDCl_3$

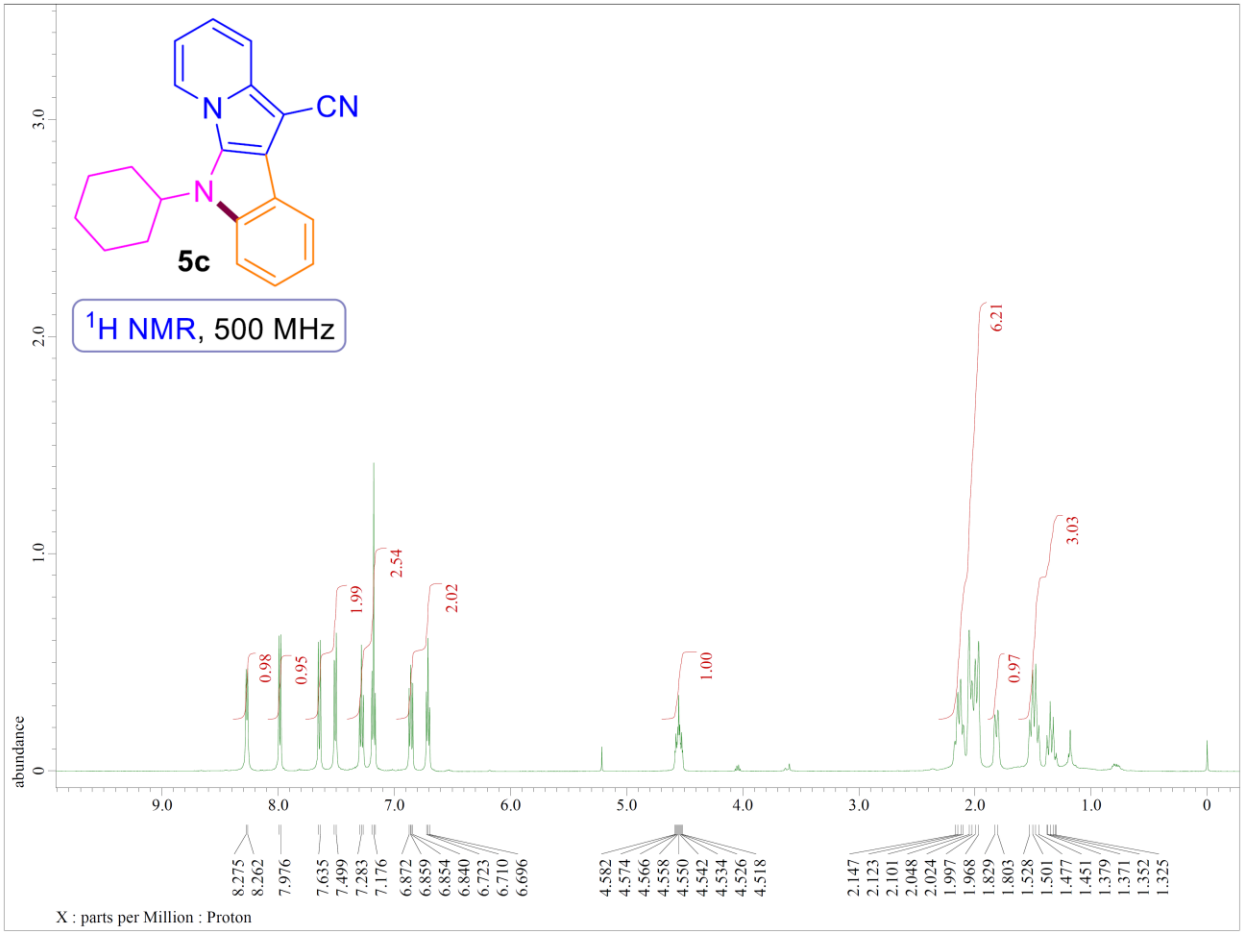


Figure S47: ^{1}H NMR of compound **5c** in $CDCl_3$

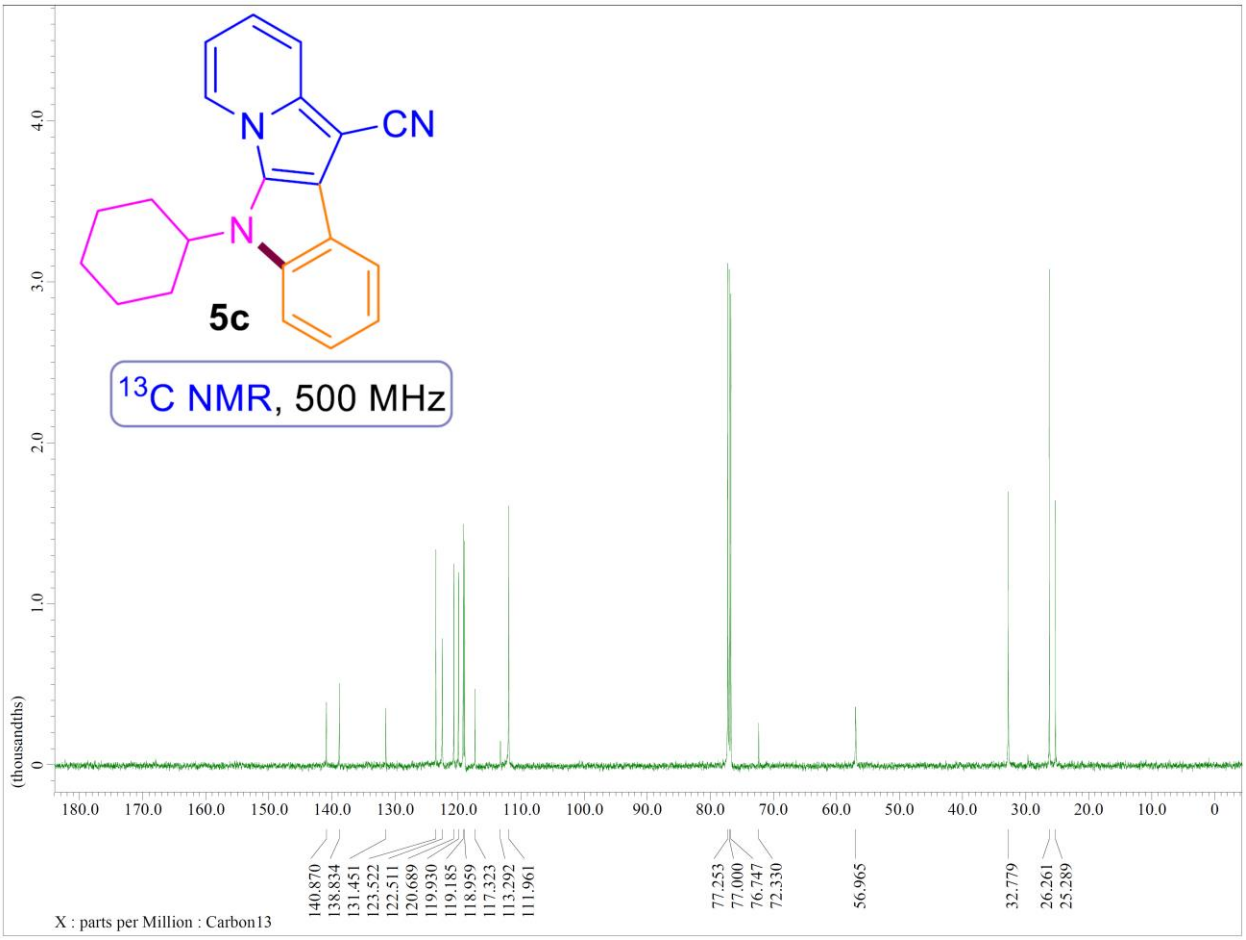


Figure S48: ^{13}C NMR of compound **5c** in $CDCl_3$

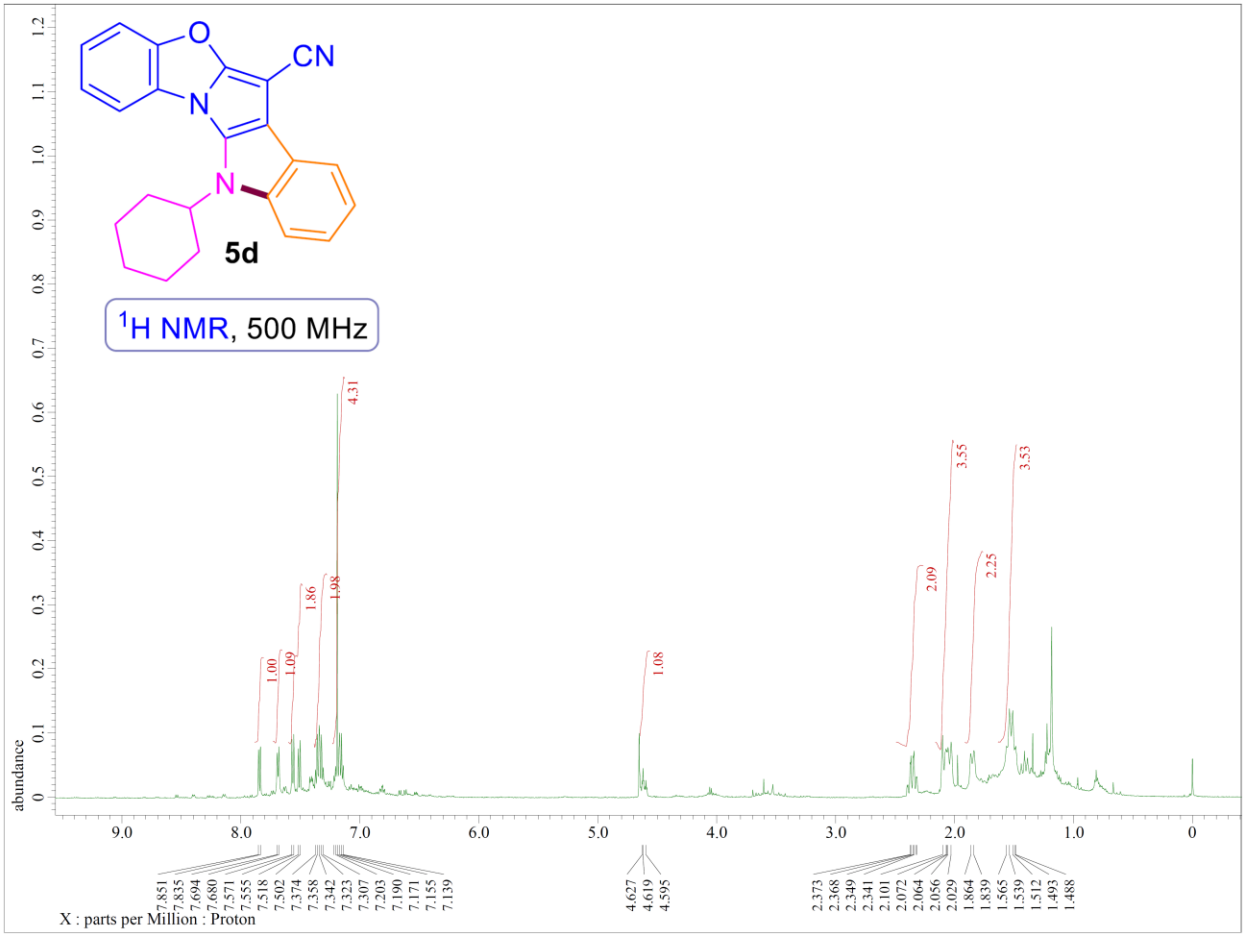


Figure S49: ^{1}H NMR of compound **5d** in $CDCl_3$

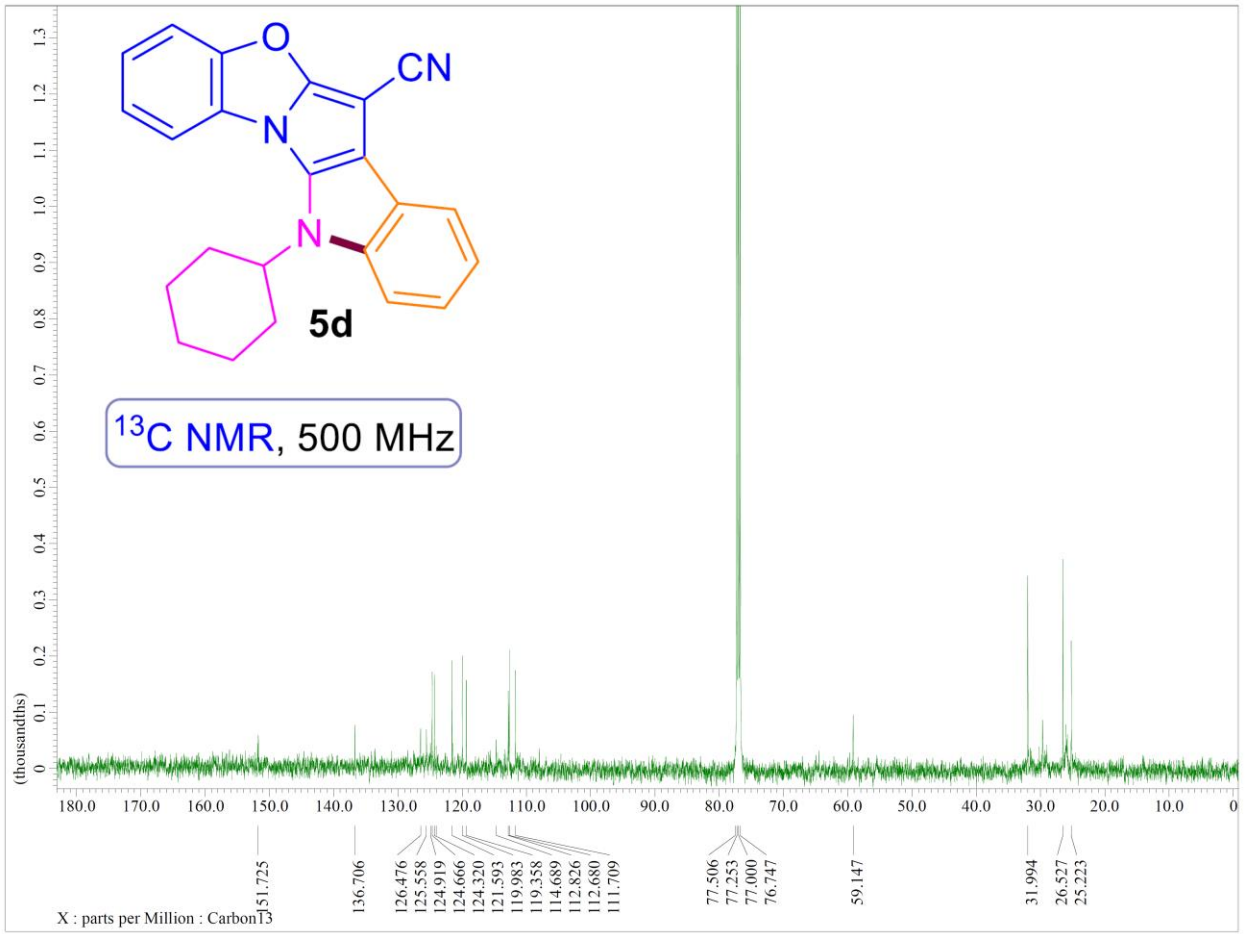


Figure S50: ^{13}C NMR of compound **5d** in $CDCl_3$

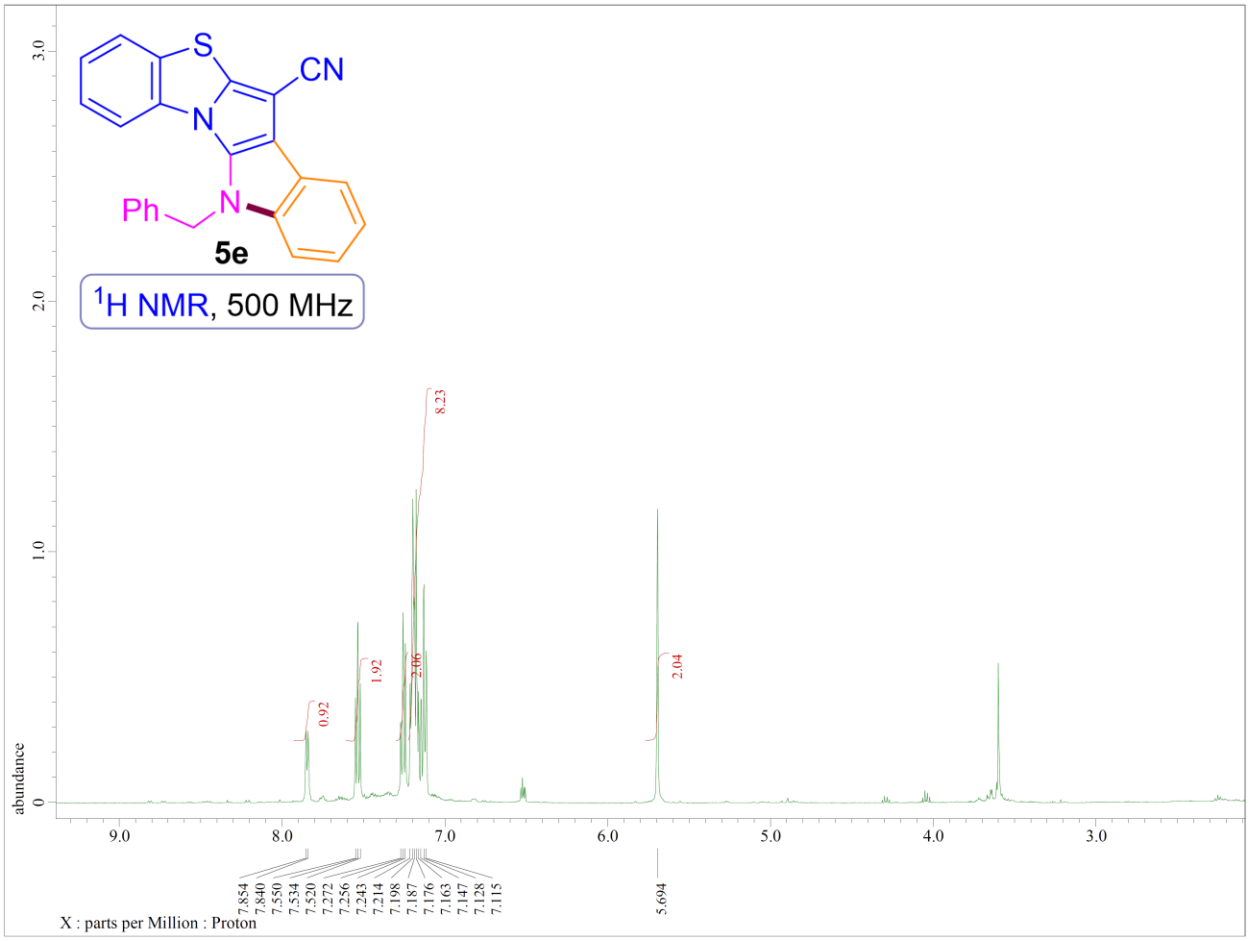


Figure S51: ^{1}H NMR of compound **5e** in $CDCl_3$

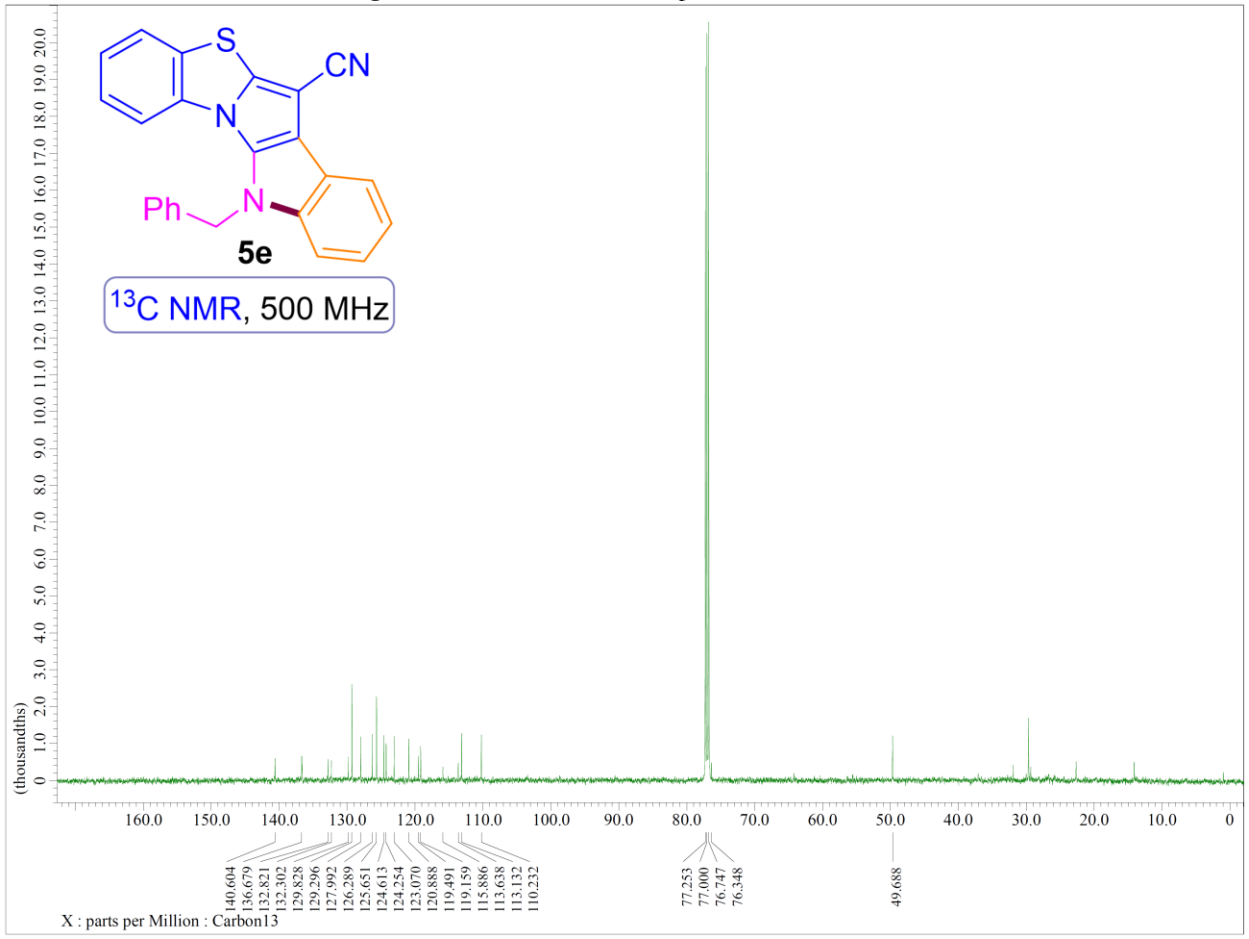


Figure S52: ^{13}C NMR of compound **5e** in $CDCl_3$

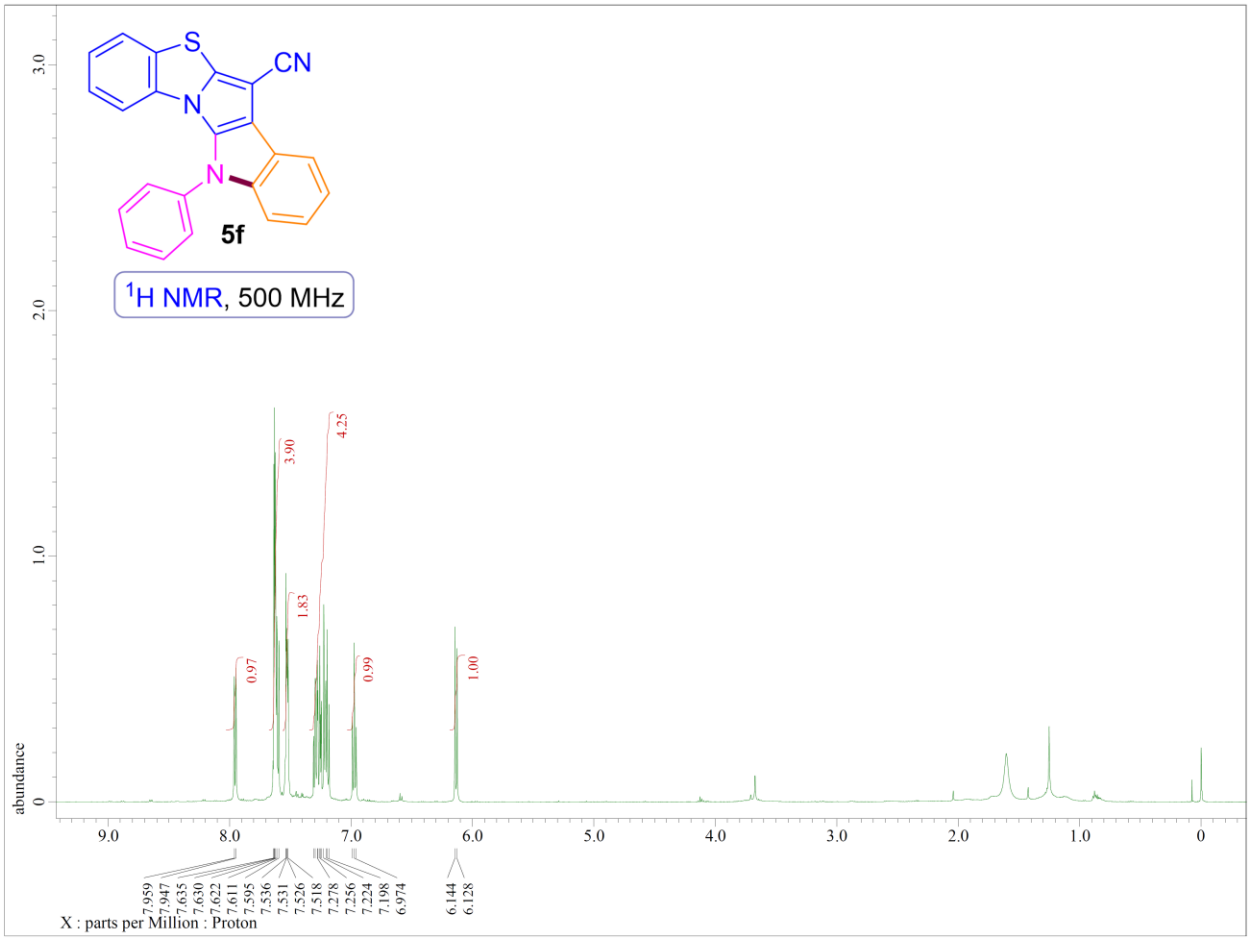


Figure S53: ^{1}H NMR of compound **5e** in $CDCl_3$

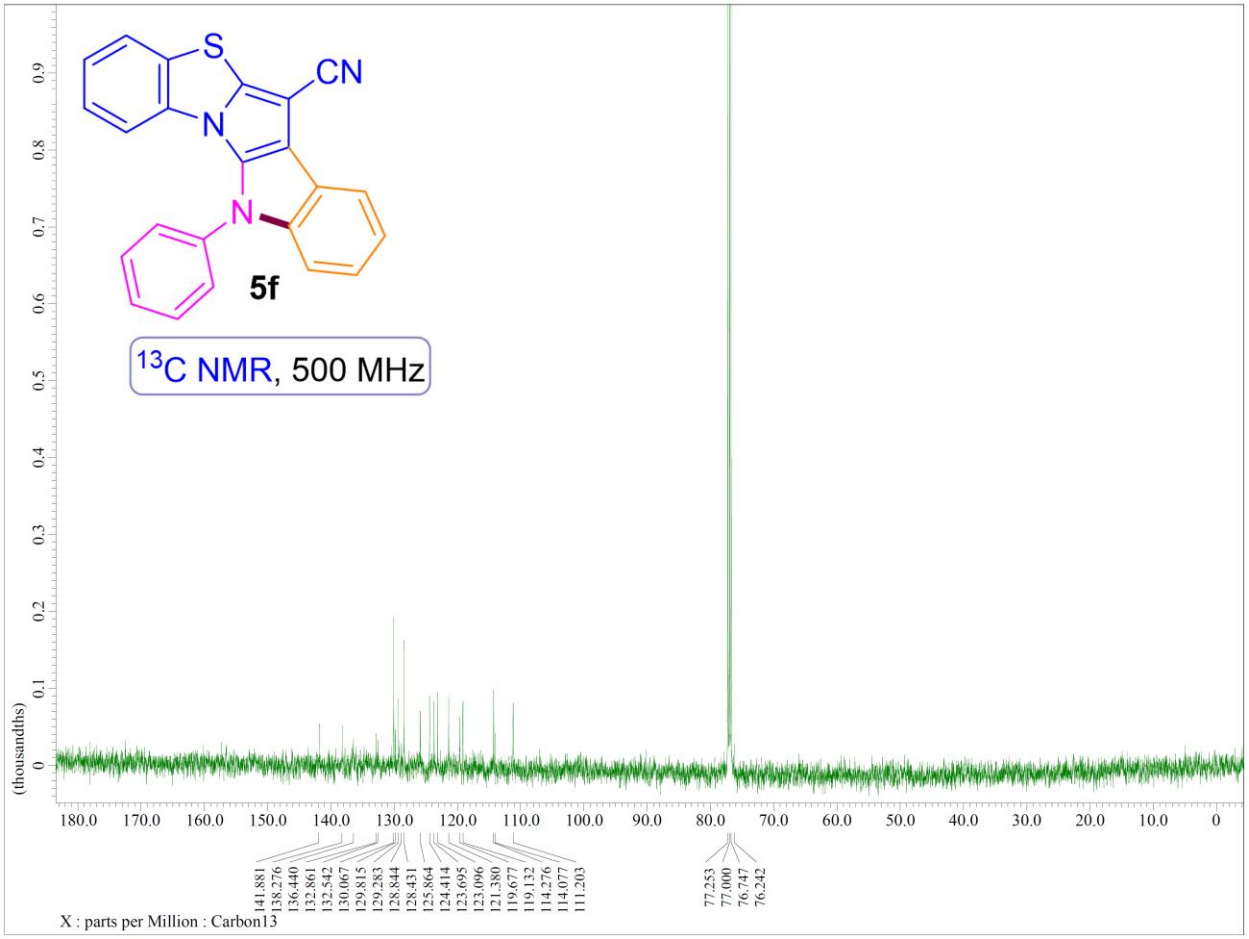


Figure S54: ^{1}H NMR of compound **5e** in $CDCl_3$