New β-carboline fluorophores with superior sensitivity and endoplasmic reticulum specificity for tracking ER changes

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Supporting Information

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General Information

All solvents were purified according to standard methods prior to use. Melting points were recorded on a BÜCHI B-540 melting point apparatus. NMR spectra were recorded for ^{1}H NMR at 500 MHz and for ^{13}C NMR at 125 MHz. For ^{1}H NMR, tetramethylsilane (TMS) (δ=0) or DMSO (δ=2.50) served as internal standard and data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), and coupling constant(s) in Hz. For ^{13}C NMR, TMS (δ=0) or DMSO (δ=39.52) was used as internal standard and spectra were obtained with complete proton decoupling. HPLC analysis and the HRMS of all final products were confirmed on a Agilent 1290 HPLC-6224 Time of Fight Mass Spectrometer using PhenomenexLuna 5μ C18, 100 Å, 150 X 4.60 mm 5 micron column at a flow rate of 0.5 mL/min using liner gradients buffer B in A (B: CH_3OH containing 0.1 % formic acid, A: H_2O containing 0.1% formic acid). Mobile phase B was increased linearly from 5% to 95% over 7 min and 95% over the next 2 min, after which the column was equilibrated to 5% for 1 min. The glyoxal monohydrates 2 were synthesized according to the method of acetophenone oxidation by DMSO-HBr system or using selenium dioxide in 1, 4-dioxane-water mixture [1-2].

1. Karpova, S. V.; Kayukova, Y. S.; Grigor'eva, A. A.; Tafeenko, V. A. *Tetrahedron Lett.* 2015, **56**, 1732-1734.
2. Antoinea M.; Gerlachb M.; Güntherb, E.; Schusterb, T.; Czechb, M.; Seipeltb, I.; Marchand, P. *Synthesis* 2012, **1**, 69-82.

General Procedure for the Synthesis of 3:

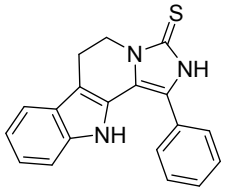
1 2 3

TFA (2.0mmol) was added to a mixture of tryptamine derivatives**1** (2.0 mmol), glyoxal hydrates **2** (2.0mmol) and KSCN (4.0 mmol) in CH_3CN (10 mL) and stirred at 40°C. After the reaction was completed (monitored by TLC), the reaction mixture was filtered, and the precipitation was washed with cold CH_3CN and crystallized with

EtOHto afford **3**.

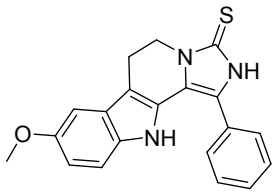
Characterization data of compound 3

1-phenyl-2,5,6,11-tetrahydro-3*H*-imidazo[1',5':1,2]pyrido[3,4-b]indole-3-thione (3a)



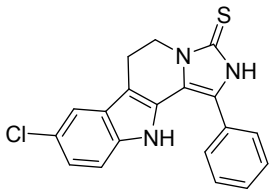
Yellow solid, m.p. >250°C.^{1}H NMR (500 MHz, DMSO) δ 12.70 (s, 1H), 10.66 (s, 1H), 7.69-7.67 (m, 2H), 7.54-7.51 (m, 3H), 7.46-7.43 (m, 1H), 7.39 (d, *J* = 8.0 Hz, 1H), 7.12-7.09 (m, 1H), 7.06-7.02 (m, 1H), 4.14 (t, *J* = 6.5 Hz, 2H), 3.13 (t, *J* = 6.5 Hz, 2H).^{13}C NMR (125 MHz, DMSO) δ 161.3, 137.5, 129.2, 128.4, 128.1, 127.0, 125.6, 124.1, 122.3, 121.9, 119.6, 118.1, 117.6, 112.3, 109.8, 41.7, 19.6.HRMS (ESI): m/z calcd for $(C_{19}H_{15}N_3S+H)^+$: 318.1059; found: 348.1060

8-methoxy-1-phenyl-2,5,6,11-tetrahydro-3*H*-imidazo[1',5':1,2]pyrido[3,4-b]indole-3-thione (3b)



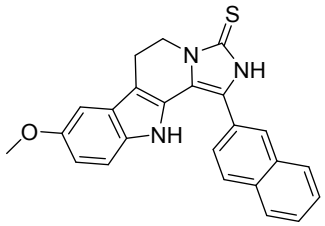
Yellow solid, m.p. >250°C.^{1}H NMR (500 MHz, DMSO) δ 12.66 (s, 1H), 10.48 (s, 1H), 7.67 (d, *J* = 7.5 Hz, 2H), 7.52 (t, *J* = 7.5 Hz, 2H), 7.43 (t, *J* = 7.3 Hz, 1H), 7.27 (d, *J* = 8.8 Hz, 1H), 7.03 (s, 1H), 6.74 (dd, *J* = 8.8, 2.3 Hz, 1H), 4.13 (t, *J* = 6.5 Hz, 2H), 3.77 (s, 3H), 3.10 (t, *J* = 6.5 Hz, 2H).^{13}C NMR (125 MHz, DMSO) δ 161.8, 154.4, 138.1, 133.0, 129.7, 128.8, 127.4, 126.5, 125.2, 122.2, 118.2, 113.5, 113.1, 110.1, 100.2, 55.9, 42.2, 20.1.HRMS (ESI): m/z calcd for $(C_{20}H_{17}N_3OS+H)^+$: 348.1165; found: 348.1167.

8-chloro-1-phenyl-2,5,6,11-tetrahydro-3H-imidazo[1',5':1,2]pyrido[3,4-b]indole-3-thione (3c)



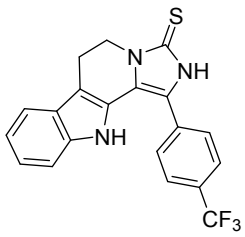
White solid, m.p.>250°C.^{1}H NMR (500 MHz, DMSO) δ 12.73 (s, 1H), 10.83 (s, 1H), 7.66 (d, *J* = 7.4 Hz, 2H), 7.60 (d, *J* = 1.6 Hz, 1H), 7.53 (t, *J* = 7.6 Hz, 2H), 7.45 (t, *J* = 7.4 Hz, 1H), 7.38 (d, *J* = 8.6 Hz, 1H), 7.09 (dd, *J* = 8.6, 1.9 Hz, 1H), 4.13 (t, *J* = 6.6 Hz, 2H), 3.12 (t, *J* = 6.6 Hz, 2H).^{13}C NMR (125 MHz, DMSO) δ 162.0, 136.4, 129.7, 129.0, 128.4, 127.6, 127.3, 126.3, 124.7, 123.1, 122.6, 117.9, 117.6, 114.2, 109.8, 42.0, 19.9.HRMS (ESI): m/z calcd for $(C_{19}H_{14}ClN_3S+H)^+$: 352.0670; found: 352.0670

8-methoxy-1-(naphthalen-2-yl)-2,5,6,11-tetrahydro-3H-imidazo[1',5':1,2]pyrido[3,4-b]indole-3-thione (3d)



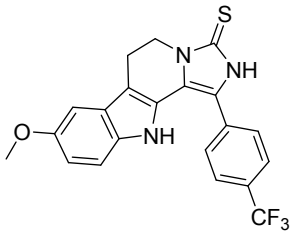
Yellow solid, m.p. >250°C.^{1}H NMR (500 MHz, DMSO) δ 12.61 (s, 1H), 9.85 (s, 1H), 8.15 -8.09 (m, 1H), 8.06 (d, *J* = 8.2 Hz, 1H), 7.79 (d, *J* = 8.4 Hz, 1H), 7.66 (q, *J* = 6.7 Hz, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.5 Hz, 1H), 7.05 (d, *J* = 8.8 Hz, 1H), 7.01 (d, *J* = 2.1 Hz, 1H), 6.65 (dd, *J* = 8.8, 2.4 Hz, 1H), 4.23 (t, *J* = 6.7 Hz, 2H), 3.75 (s, 3H), 3.17 (t, *J* = 6.5 Hz, 2H). ^{13}C NMR (125MHz, DMSO) δ 161.7, 154.2, 134.2, 133.0, 132.1, 130.2, 129.3, 128.9, 127.2, 126.8, 126.4, 126.4, 126.1, 125.6, 124.9, 120.0, 119.8, 113.2, 112.7, 108.9, 100.3, 55.8, 42.2, 20.2.HRMS (ESI): m/z calcd for $(C_{24}H_{19}N_3OS+H)^+$: 398.1322; found: 398.1322.

1-(4-(trifluoromethyl)phenyl)-2,5,6,11-tetrahydro-3H-imidazo[1',5':1,2]pyrido[3,4-b]indole-3-thione (3e)



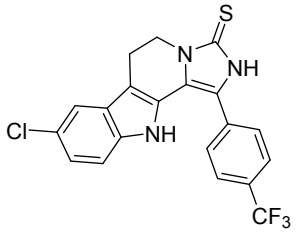
Yellow solid, m.p. >250°C.^{1}H NMR (500 MHz, DMSO) δ 12.86 (s, 1H), 10.80 (s, 1H), 7.86 (d, *J* = 8.0 Hz, 4H), 7.55 (d, *J* = 7.9 Hz, 1H), 7.39 (d, *J* = 8.1 Hz, 1H), 7.14 (dd, *J* = 11.1, 3.9 Hz, 1H), 7.06 (t, *J* = 7.4 Hz, 1H), 4.15 (t, *J* = 6.7 Hz, 2H), 3.15 (t, *J* = 6.7 Hz, 2H).^{13}C NMR (125 MHz, DMSO) δ 162.4, 138.0, 132.6, 128.6 (q, *J* = 31.25 Hz), 128.0, 126.5(q, *J* = 3.75 Hz), 126.0, 124.7 (q, *J* = 270 Hz), 124.2,123.1, 120.7, 120.1, 119.4, 118.7, 112.7, 111.1, 42.1, 20.0. HRMS (ESI): m/z calcd for ($C_{20}H_{14}F_3N_3S$+H) $^{+}$: 386.0933; found: 386.0934.

8-methoxy-1-(4-(trifluoromethyl) phenyl)-2,5,6,11-tetrahydro-3H-imidazo [1',5':1,2] pyrido[3,4-b] indole-3-thione (3f)



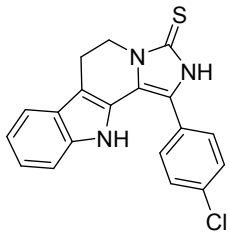
Yellow solid, m.p. >250 °C. ^{1}H NMR (500 MHz, DMSO) δ 12.84 (s, 1H), 10.64 (s, 1H), 8.02-7.72 (m, 4H), 7.27 (d, *J* = 8.8 Hz, 1H), 7.06 (d, *J* = 2.2 Hz, 1H), 6.77 (dd, *J* = 8.8, 2.4 Hz, 1H), 4.14 (t, *J* = 6.7 Hz, 2H), 3.78 (s, 3H), 3.12 (t, *J* = 6.7 Hz, 2H). ^{13}C NMR (125 MHz, DMSO) δ 162.3, 154.4, 133.2, 132.6, 128.6 (q, *J* = 31.25 Hz), 127.9, 126.5(q, *J* = 3.75 Hz), 126.4, 124.7 (q, *J* = 270 Hz), 124.7, 120.5, 119.6, 113.5, 113.5, 111.0, 100.3, 55.8, 42.2, 20.1. HRMS (ESI): m/z calcd for ($C_{21}H_{16}F_3N_3OS$+H) $^{+}$: 416.1039; found: 416.1041.

8-chloro-1-(4-(trifluoromethyl) phenyl)-2,5,6,11-tetrahydro-3H-imidazo [1',5':1,2] pyrido[3,4-b] indole-3-thione (3g)



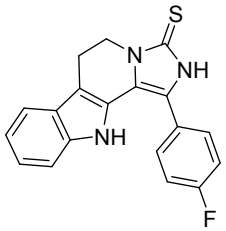
Yellow solid, m.p. >250°C, ^{1}H NMR (500 MHz, DMSO) δ 12.91 (s, 1H), 10.98 (s, 1H), 8.02-7.72 (m, 4H), 7.63 (d, *J* = 2.0 Hz, 1H), 7.37 (d, *J* = 8.5 Hz, 1H), 7.12 (dd, *J* = 9.0, 2.5 Hz, 1H), 4.13 (t, *J* = 6.5 Hz, 2H), 3.14 (t, *J* = 6.5 Hz, 2H). ^{13}C NMR (125 MHz, DMSO) δ 162.6, 136.5, 132.4, 128.8 (q, *J* = 32.5 Hz), 128.2, 127.2, 126.6 (q, *J* = 3.75 Hz), 125.8, 124.7 (q, *J* = 270 Hz), 124.8, 122.9, 121.5, 118.9, 118.1, 114.2, 110.6, 42.1, 19.9. HRMS (ESI): m/z calcd for $(C_{20}H_{13}ClF_3N_3S+H)^+$: 420.0544; found: 420.0545

1-(4-chlorophenyl)-2,5,6,11-tetrahydro-3H-imidazo [1',5':1,2] pyrido[3,4-b] indole-3-thione (3h)



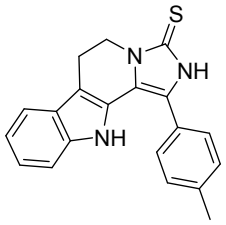
Yellow solid, m.p. >250°C, ^{1}H NMR (500 MHz, DMSO) δ 12.74 (s, 1H), 10.69 (s, 1H), 7.66 (d, *J* = 8.6 Hz, 2H), 7.58 (d, *J* = 8.5 Hz, 2H), 7.53 (d, *J* = 7.8 Hz, 1H), 7.38 (d, *J* = 8.1 Hz, 1H), 7.17-7.09 (m, 1H), 7.04 (t, *J* = 7.4 Hz, 1H), 4.13 (t, *J* = 6.7 Hz, 2H), 3.12 (t, *J* = 6.7 Hz, 2H). ^{13}C NMR (125 MHz, DMSO) δ 162.0, 138.0, 133.3, 129.6, 129.3, 127.4, 126.1, 124.3, 122.8, 121.1, 120.0, 118.6, 118.5, 112.6, 110.4, 42.1, 20.0. HRMS (ESI): m/z calcd for $(C_{19}H_{14}ClN_3S+H)^+$: 352.0670; found: 352.0672

1-(4-fluorophenyl)-2,5,6,11-tetrahydro-3H-imidazo [1',5':1,2] pyrido[3,4-b] indole-3-thione (3i)



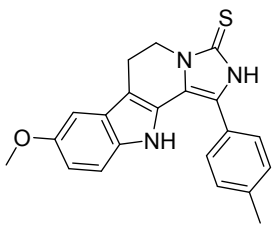
Brown solid, m.p. >250°C, ^{1}H NMR (500 MHz, DMSO) δ 12.70 (s, 1H), 10.64 (s, 1H), 7.70-7.66 (m, 2H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.39-7.35 (m, 3H), 7.13-7.09 (m, 1H), 7.04 (t, *J* = 7.5 Hz, 1H), 4.13 (t, *J* = 6.5 Hz, 2H), 3.12 (t, *J* = 6.5 Hz, 2H). ^{13}C NMR (125 MHz, DMSO) δ 162.6 (d, *J* = 245 Hz), 161.7, 137.9, 130.0 (d, *J* = 7.5 Hz), 126.1, 125.1 (d, *J* = 2.5 Hz), 124.5, 122.8, 121.4, 120.0, 118.6, 118.2, 116.7 (d, *J* = 21.25 Hz), 112.7, 110.1, 42.1, 20.1.HRMS (ESI): m/z calcd for $(C_{19}H_{14}FN_3S+H)^+$: 336.0965; found: 336.0963.

1-(p-tolyl)-2, 5, 6, 11-tetrahydro-3H-imidazo [1', 5':1, 2] pyrido[3,4-b] indole-3-thione (3j)



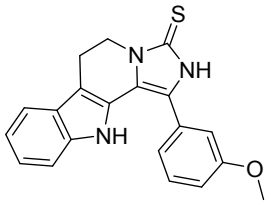
Yellow solid, m.p. >250°C, ^{1}H NMR (500 MHz, DMSO) δ 12.63 (s, 1H), 10.59 (s, 1H), 7.56 (d, *J* = 8.0 Hz, 2H), 7.52 (d, *J* = 7.8 Hz, 1H), 7.39 (d, *J* = 8.1 Hz, 1H), 7.34 (d, *J* = 7.9 Hz, 2H), 7.10 (t, *J* = 7.5 Hz, 1H), 7.03 (t, *J* = 7.4 Hz, 1H), 4.13 (t, *J* = 6.6 Hz, 2H), 3.11 (t, *J* = 6.6 Hz, 2H), 2.39 (s, 3H). ^{13}C NMR (125 MHz, DMSO) δ 161.7, 138.4, 137.9, 130.2, 127.4, 126.1, 125.8, 124.7, 122.7, 122.5, 120.0, 118.5, 117.8, 112.8, 110.0, 42.1, 21.4, 20.1. HRMS (ESI): m/z calcd for $(C_{20}H_{17}N_3S+H)^+$: 332.1216; found: 332.1216.

8-methoxy-1-(p-tolyl)-2,5,6,11-tetrahydro-3H-imidazo [1',5':1,2] pyrido[3,4-b] indole-3-thione (3k)



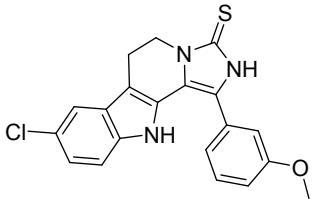
Orange solid, m.p. >250°C, ^{1}H NMR (500 MHz, DMSO) δ 12.61 (s, 1H), 10.43 (s, 1H), 7.55 (d, *J* = 8.1 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.27 (d, *J* = 8.8 Hz, 1H), 7.03 (d, *J* = 2.4 Hz, 1H), 6.74 (dd, *J* = 8.8, 2.4 Hz, 1H), 4.12 (t, *J* = 6.7 Hz, 2H), 3.77 (s, 3H), 3.09 (t, *J* = 6.7 Hz, 2H), 2.38 (s, 3H). ^{13}C NMR (125 MHz, DMSO) δ 161.6, 154.3, 138.3, 133.0, 130.2, 127.4, 126.5, 125.8, 125.2, 122.3, 117.9, 113.5, 113.0, 109.8, 100.2, 55.8, 42.2, 21.4, 20.1. HRMS (ESI): m/z calcd for $(C_{21}H_{19}N_3OS+H)^+$: 362.1322; found: 362.1322.

1-(3-methoxyphenyl)-2,5,6,11-tetrahydro-3H-imidazo [1',5':1,2] pyrido[3,4-b] indole-3-thione (3l)



Red solid, m.p. >250°C, ^{1}H NMR (500 MHz, DMSO) δ 12.69 (s, 1H), 10.75 (s, 1H), 7.53 (d, *J* = 7.8 Hz, 1H), 7.42 (dd, *J* = 15.9, 8.1 Hz, 2H), 7.29- 7.24 (m, 2H), 7.15-7.09 (m, 1H), 7.04 (dd, *J* = 10.9, 3.9 Hz, 1H), 7.01- 6.97 (m, 1H), 4.14 (t, *J* = 6.7 Hz, 2H), 3.81 (s, 3H), 3.13 (t, *J* = 6.7 Hz, 2H).^{13}C NMR (125 MHz, DMSO) δ 161.8, 160.1, 138.0, 130.8, 129.7, 126.1, 124.6, 122.8, 122.3, 120.0, 119.4, 118.6, 118.3, 115.5, 112.7, 111.8, 110.4, 55.5, 42.1, 20.1. HRMS (ESI): m/z calcd for $(C_{20}H_{17}N_3OS+H)^+$: 348.1165; found: 348.1163.

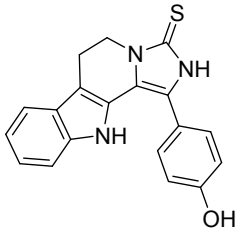
8-chloro-1-(3-methoxyphenyl)-2,5,6,11-tetrahydro-3H-imidazo [1',5':1,2] pyrido[3,4-b] indole-3-thione (3m)



White solid, m.p. >250°C, ^{1}H NMR (500 MHz, DMSO) δ 12.73 (s, 1H), 10.92 (s, 1H), 7.60 (s, 1H), 7.47-7.32 (m, 2H), 7.25 (d, *J* = 7.7 Hz, 2H), 7.10 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.05-6.95 (m, 1H), 4.12 (t, *J* = 6.6 Hz, 2H), 3.81 (s, 3H), 3.12 (t, *J* = 6.6 Hz, 2H). ^{13}C NMR (125 MHz, DMSO) δ 162.0, 160.1, 136.4, 130.8, 129.6, 127.3, 126.2, 124.7, 123.0, 122.6, 119.6, 117.9, 117.8, 115.7, 114.2, 112.0, 109.9, 55.5, 42.1, 19.9. HRMS

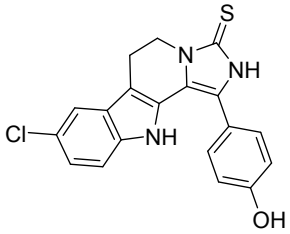
(ESI): m/z calcd for $(C_{20}H_{16}ClN_3OS+H)^+$: 382.0775; found: 382.0774.

1-(4-hydroxyphenyl)-2,5,6,11-tetrahydro-3H-imidazo [1',5':1,2] pyrido[3,4-b] indole-3-thione (3n)



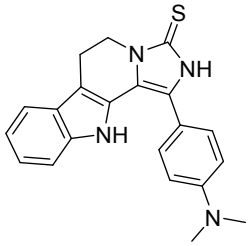
Pale solid, m.p. >250°C, ^{1}H NMR (500 MHz, DMSO) δ 12.53 (s, 1H), 10.54 (s, 1H), 9.83 (s, 1H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.46 (d, *J* = 8.5 Hz, 2H), 7.38 (d, *J* = 8.0 Hz, 1H), 7.11-7.06 (m, 1H), 7.04-7.00 (m, 1H), 6.90 (d, *J* = 8.5 Hz, 2H), 4.11 (t, *J* = 6.5 Hz, 2H), 3.10 (t, *J* = 6.5 Hz, 2H). ^{13}C NMR (125 MHz, DMSO) δ 160.7, 157.8, 137.4, 128.6, 125.7, 124.4, 122.4, 122.0, 119.5, 118.8, 117.9, 116.5, 116.0, 112.3, 108.9, 41.6, 19.6. HRMS (ESI): m/z calcd for $(C_{19}H_{15}N_3OS+H)^+$: 334.1009; found: 334.1008.

8-chloro-1-(4-hydroxyphenyl)-2,5,6,11-tetrahydro-3H-imidazo [1',5':1,2] pyrido[3,4-b] indole-3-thione (3o)



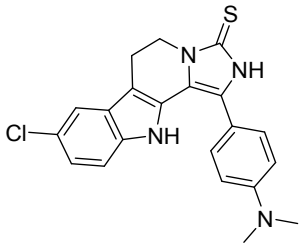
White solid, m.p. >250°C, ^{1}H NMR (500 MHz, DMSO) δ 12.58 (s, 1H), 10.74 (s, 1H), 9.97 (s, 1H), 7.57 (d, *J* = 1.5 Hz, 1H), 7.44 (d, *J* = 8.5 Hz, 2H), 7.38 (d, *J* = 8.5 Hz, 1H), 7.07 (dd, *J* = 8.5, 2.0 Hz, 1H), 6.92 (d, *J* = 8.5 Hz, 2H), 4.09 (t, *J* = 6.5 Hz, 2H), 3.09 (t, *J* = 6.5 Hz, 2H). ^{13}C NMR (125 MHz, DMSO) δ 160.9, 158.1, 135.8, 128.7, 126.9, 126.1, 124.1, 123.2,121.8, 118.5, 117.2, 116.1, 116.0, 113.7, 108.5, 41.6, 19.5. HRMS (ESI): m/z calcd for $(C_{19}H_{14}ClN_3OS+H)^+$: 368.0619; found: 368.0619.

1-(4-(dimethylamino) phenyl)-2,5,6,11-tetrahydro-3H-imidazo [1',5':1,2] pyrido[3,4-b] indole-3-thione (3p)



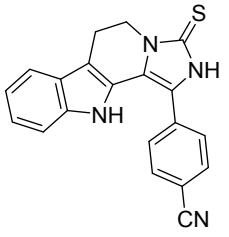
Light green solid, m.p. >250°C, ^{1}H NMR (500 MHz, DMSO) δ 12.49 (s, 1H), 10.57 (s, 1H), 7.51-7.48 (m, 3H), 7.39 (d, *J* = 8.0 Hz, 1H), 7.08 (t, *J* = 7.5 Hz, 1H), 7.02 (t, *J* = 7.5 Hz, 1H), 6.85 (d, *J* = 8.5 Hz, 2H), 4.10 (t, *J* = 6.5 Hz, 2H), 3.10 (t, *J* = 6.5 Hz, 2H), 2.99 (s, 6H). ^{13}C NMR (125 MHz, DMSO) δ 160.6, 150.3, 137.3, 127.8, 125.7, 124.7, 122.9, 121.9, 119.4, 117.8, 116.0, 115.4, 112.5, 112.3, 108.6, 41.7, 39.9, 19.6. HRMS (ESI): m/z calcd for $(C_{21}H_{20}N_4S+H)^+$: 361.1481; found: 361.1482.

8-chloro-1-(4-(dimethylamino) phenyl)-2,5,6,11-tetrahydro-3H-imidazo [1',5':1,2] pyrido[3,4-b] indole-3-thione (3q)



Green solid, m.p. >250°C, ^{1}H NMR (500 MHz, DMSO) δ 12.55 (s, 1H), 10.77 (s, 1H), 7.57 (d, *J* = 2.0 Hz, 1H), 7.46 (d, *J* = 8.5 Hz, 2H), 7.38 (d, *J* = 8.5 Hz, 1H), 7.06 (dd, *J* = 8.5, 2.0 Hz, 1H), 6.85 (d, *J* = 8.5 Hz, 2H), 4.09 (t, *J* = 6.5 Hz, 2H), 3.09 (t, *J* = 6.5 Hz, 2H), 2.99 (s, 6H). ^{13}C NMR (125 MHz, DMSO) δ 160.8, 150.3, 135.8, 127.9, 126.9, 126.4, 124.1, 123.6, 121.7, 117.1, 115.5, 115.2, 113.7, 112.5, 108.2, 41.6, 39.9, 19.5. HRMS (ESI): m/z calcd for $(C_{21}H_{19}ClN_4S+H)^+$: 395.1092; found: 395.1090.

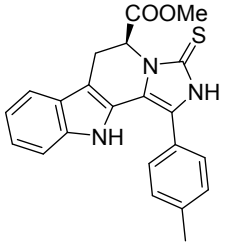
4-(3-thioxo-2,5,6,11-tetrahydro-3H-imidazo [1',5':1,2] pyrido[3,4-b] indol-1-yl) benzonitrile (3r)



Yellow solid, m.p. >250°C, ^{1}H NMR (500 MHz, DMSO)δ 12.85 (s, 1H), 10.80 (s, 1H), 7.96 (d, *J* = 8.0 Hz, 2H), 7.84 (d, *J* = 8.0 Hz, 2H), 7.56 (d, *J* = 7.5 Hz, 1H),

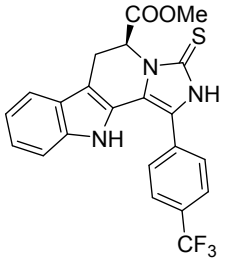
7.38(d, *J* = 8.0 Hz, 1H), 7.14 (t, *J* = 7.5 Hz, 1H), 7.06 (t, *J* = 7.5 Hz, 1H), 4.14 (t, *J* = 6.5 Hz, 1H), 3.15 (t, *J* = 6.5 Hz, 1H).^{13}C NMR (125 MHz, DMSO)δ 162.1, 137.6, 133.0, 132.5, 127.5, 125.5, 123.6, 122.7, 120.1, 119.7, 119.4, 118.7, 118.3, 112.2, 110.9, 110.2, 41.6, 19.5. HRMS (ESI): m/z calcd for $(C_{20}H_{14}N_4S+H)^+$: 343.1012; found: 343.1010.

Methyl (R)-3-thioxo-1-(p-tolyl)-2, 5, 6, 11-tetrahydro-3H-imidazo [1', 5':1, 2] pyrido[3,4-b] indole-5-carboxylate (3s)



Yellow solid, m.p. >250^{o}C, ^{1}H NMR (500 MHz, DMSO) δ 12.81 (s, 1H), 10.69 (s, 1H), 7.58 (d, *J* = 8.1 Hz, 2H), 7.53 (d, *J* = 7.8 Hz, 1H), 7.37 (t, *J* = 7.8 Hz, 3H), 7.10 (t, *J* = 7.5 Hz, 1H), 7.03 (t, *J* = 7.4 Hz, 1H), 5.64 (d, *J* = 6.9 Hz, 1H), 3.62 (d, *J* = 16.2 Hz, 1H), 3.56 (s, 3H), 3.44 (dd, *J* = 16.4, 7.4 Hz, 1H), 2.40 (s, 3H). ^{13}C NMR (125 MHz, DMSO) δ 170.3, 163.0, 138.6, 137.9, 130.3, 127.4, 122.9, 122.8, 120.2, 118.5, 117.2, 112.8, 106.8, 53.8, 53.1, 23.8, 21.4. HRMS (ESI): m/z calcd for $(C_{22}H_{19}N_3O_2S+H)^+$: 390.1271; found: 390.1275.

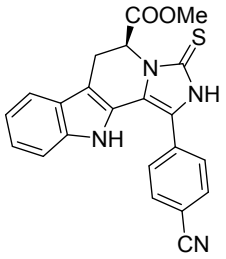
Methyl (R)-3-thioxo-1-(4-(trifluoromethyl) phenyl)-2, 5, 6, 11-tetrahydro-3H-imidazo [1', 5':1, 2] pyrido[3,4-b] indole-5-carboxylate (3t)



Yellow solid, m.p. >250^{o}C, ^{1}H NMR (500 MHz, DMSO) δ 13.08 (s, 1H), 10.91 (s, 1H), 7.90 (s, 4H), 7.57 (d, *J* = 8.5 Hz, 1H), 7.36 (d, *J* = 8.0 Hz, 1H), 7.16-7.11 (m, 1H), 7.07-7.03 (m, 1H), 5.66 (d, *J* = 6.5 Hz, 1H), 3.66-3.62 (m, 1H), 3.56 (s, 3H), 3.47 (dd, *J* = 16.5, 7.5 Hz, 1H).^{13}C NMR (125 MHz, DMSO) δ 169.7, 163.2, 137.6, 131.9, 128.4 (q, *J* =31.25 Hz), 127.6, 126.2 (q, *J* = 2.5 Hz), 125.6, 124.2 (d, *J* =

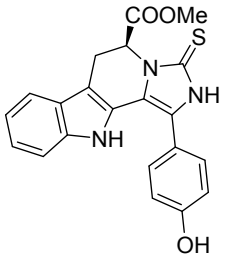
271.25 Hz), 123.6, 122.8, 120.6, 119.9, 118.4, 118.3, 112.3, 107.4, 53.3, 52.7, 20.8. HRMS (ESI): m/z calcd for $(C_{22}H_{16}F_3N_3O_2S+H)^+$: 444.0988; found: 444.0991.

Methyl (R)-1-(4-cyanophenyl)-3-thioxo-2, 5, 6, 11-tetrahydro-3H-imidazo [1', 5':1, 2] pyrido[3,4-b] indole-5-carboxylate (3u)



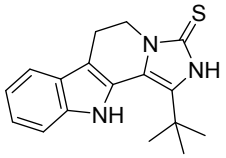
Yellow solid, m.p. >250°C, ^{1}H NMR (500 MHz, DMSO) δ 13.02 (s, 1H), 10.86 (s, 1H), 8.00-7.98 (m, 2H), 7.87-7.85 (m, 2H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.36 (d, *J* = 8.0Hz, 1H), 7.16-7.13 (m, 1H), 7.07-7.04 (m, 1H), 5.65 (d, *J* = 6.5 Hz, 1H), 3.66-3.63 (m, 1H), 3.56 (s, 3H), 3.47 (dd, *J* = 16.5, 7.5 Hz, 1H).^{13}C NMR (125 MHz, DMSO) δ 169.6, 163.4, 137.6, 133.0, 132.3, 127.5, 125.5, 123.5, 122.9, 120.4, 119.9, 118.8, 118.7, 118.3, 112.2, 110.4, 107.7, 53.3, 52.6, 23.2. HRMS (ESI): m/z calcd for $(C_{22}H_{16}N_4O_2S+H)^+$: 401.1067; found: 401.1064.

Methyl (R)-1-(4-hydroxyphenyl)-3-thioxo-2, 5, 6, 11-tetrahydro-3H-imidazo [1', 5':1, 2] pyrido[3,4-b] indole-5-carboxylate (3v)



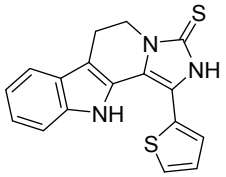
Yellow solid, m.p. >250°C, ^{1}H NMR (500 MHz, DMSO) δ 12.63 (s, 1H), 10.57 (s, 1H), 9.80 (s, 1H), 7.51-7.47 (m, 3H), 7.37 (d,*J* = 8.5 Hz,1H), 7.10-1.07 (m, 1H), 7.03-7.00 (m, 1H), 6.93-6.91 (m, 2H), 5.62 (d, *J* = 6.5 Hz, 1H), 3.61-3.58 (m, 1H), 3.56 (s, 3H), 3.41 (dd, *J* = 16.5, 7.5 Hz, 1H).^{13}C NMR (125 MHz, DMSO) δ 169.8, 162.2, 157.9, 137.3, 128.6, 124.3, 122.6, 122.1, 119.6, 118.5, 117.8, 116.0, 115.9, 112.2, 105.7, 54.8, 53.3, 52.5, 23.2. HRMS (ESI): m/z calcd for $(C_{21}H_{17}N_3O_3S+H)^+$: 392.1063; found: 392.1067.

1-(Tert-butyl)-2, 5, 6, 11-tetrahydro-3H-imidazo [1', 5':1, 2] pyrido[3,4-b] indole-3-thione (3w)



Yellow solid, m.p. >250°C, ^{1}H NMR (500 MHz, DMSO) δ 11.94 (s, 1H), 10.47 (s, 1H), 7.52 (t, *J* = 6.9 Hz, 2H), 7.12 (t, *J* = 7.6 Hz, 1H), 7.04 (t, *J* = 7.5 Hz, 1H), 4.04 (t, *J* = 6.5 Hz, 2H), 2.99 (t, *J* = 6.5 Hz, 2H), 1.46 (s, 9H). ^{13}C NMR (125 MHz, DMSO) δ 159.9, 137.9, 132.4, 126.1, 125.3, 122.4, 120.0, 118.4, 116.8, 112.7, 110.1, 42.3, 31.8, 30.6, 20.2. HRMS (ESI): m/z calcd for $(C_{17}H_{19}N_3S+H)^+$: 298.1372; found: 298.1376.

1-(thiophen-2-yl)-2, 5,6,11-tetrahydro-3H-imidazo [1', 5':1, 2] pyrido[3,4-b] indole-3-thione (3x)



Grey solid, m.p. >250°C, ^{1}H NMR (500 MHz, DMSO) δ 12.74 (s, 1H), 10.71 (s, 1H), 7.74-7.67 (m, 1H), 7.58-7.49 (m, 2H), 7.43 (d, *J* = 8.1 Hz, 1H), 7.23 (dd, *J* = 5.0, 3.7 Hz, 1H), 7.12 (dd, *J* = 11.6, 4.3 Hz, 1H), 7.05 (t, *J* = 7.4 Hz, 1H), 4.13 (t, *J* = 6.7 Hz, 2H), 3.11 (t, *J* = 6.7 Hz, 2H). ^{13}C NMR (125 MHz, DMSO) δ 162.0, 138.1, 129.5, 128.5, 127.8, 127.3, 126.1, 124.2, 123.0, 120.1, 118.6, 116.2, 112.8, 110.6, 42.1, 20.1. HRMS (ESI): m/z calcd for $(C_{17}H_{13}N_3S_2+H)^+$: 324.0624; found: 324.0624.

General Procedure for the biological evaluation of compound 3

Cell culture

The human umbilical vein/vascular cell line (HUVEC), the HeLa cell line and the HCT116 cell line were purchased from ATCC. Briefly, the cells were cultured in Dulbecco's modified Eagle medium (DMEM, Thermo Fisher Scientific) for HUVEC, or Eagle's Minimal Essential Medium (EMEM, Thermo Fisher Scientific) for HeLa cells, or McCoy's 5A Medium (Thermo Fisher Scientific), for HCT116 cells supplemented with 10% heat-inactivated fatal bovine serun (Thermo Fisher Scientific), penicillin (100 U/mL, Thermo Fisher Scientific), and streptomycin (100 U/mL, Thermo Fisher Scientific). The cultures were maintained at 37 ^{o}C in a 95% humidified atmosphere with 5% CO_2.

Cytotoxicity assay for Probe

HeLa cells were seeded in 96-well plates at a density of 5×10^3 cells/well at 37 ^{o}C in a 95% humidified atmosphere with 5% CO_2 for 24 h. After washing with PBS twice, **3t**/**3q** with concentration of 1 μM, 5 μM, 60 μM, 80 μM, and 100 μM were added to the cells, which were allowed an incubation period of 24 h. After introducing 10 μL of CCK8 solution for 1 h, the absorption at 450 nm was measured by Microplate Spectrophotometer (MD I3X). Each experiment was repeated three times, and the average values were taken in analyses.

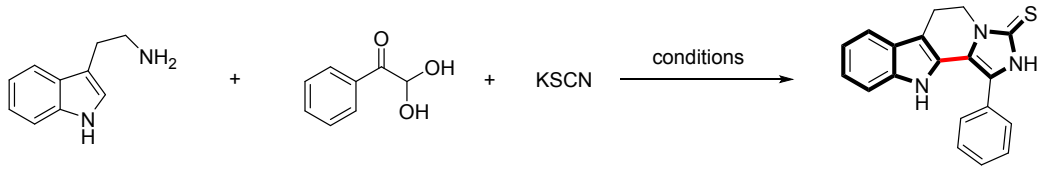
Confocal fluorescence imaging

For confocal microscopy imaging of subcellular distribution of **3t**, **3q** or **3u** in living cells, HeLa or HUVEC cells were incubated with 1μM probe for 30 min at 37 ^{o}C and followed by staining with of ER-Tracker(1 μM)/Mito-Tracker(0.5 μM)/Lyso-Tracker (1 μM) for 30min, then washed with PBS (pH 7.4) and replaced with flesh medium. For evaluate the photo-stability of **3t**, **3q** or **3u** in the live cells, the HeLa cells were incubated with **3t** (1 μM) or **3q** (1 μM) or **3u** (1 μM) with increasing number of scans (irradiation time: 5.36 s/scan). The laser power used for **3t**, **3q** and **3u**was 0.1%. For visualization of **3t** in HeLa cells native or upon ER stress, HeLa cells were incubated with **3t** for 30 min at 37 ^{o}C, and then washed with PBS (pH 7.4) followed by tunicamycin (TM, 10 μM) treatment. For visualization of **3t** in HeLa

cellsduring apoptosis, HeLa cells were pre-treated with 100 ng/ml TNFα for 72 h, and then incubated with 1μM **3t**or ER-Tracker Red (1 μM)for 30 min. After that, cells were washed with PBS (pH 7.4) and replaced with fresh medium. For analyze the sensitivity of **3t** in HeLa cells, cells were incubated with **3t** (1 μM) and ER-Tracker (1 μM) for 30 min at 37 ^{o}C, then the images were obtained by confocal microscopy with 0.1%, 1%, 10%, 25%, 50% and 75% laser power. For analyze the efficiency of **3t** in staining ER at different concentrations. HeLa cells were incubated with **3t**, ER-Tracker RedorER-Tracker Blue at the concentration of 250 nM, 500 nM and 1μM, respectively, then washed with PBS (pH 7.4) and replaced with fresh medium. The images were obtained by confocal microscopy with 20% laser power. The fluorescence of **3t**, **3q** or **3u** was monitored at λ_{em}=440-480nm (λ_{ex}=405nm). Fluorescent signal from ER-Tracker red/Mito-Tracker/Lyso-Tracker was obtained at λ_{em}=600-650nm (λ_{ex}=543nm), fluorescent signal from ER-Tracker Blue was obtained at λ_{em}=430-530 nm (λ_{ex}=405nm).The fluorescence was obtained by fluoview FV1000 laser scanning confocal microscope (Olympus). Digital images were captured using the FV10-ASW 3.0 viewer software (Olympus), and performed using a 60× objective in at least four fields of view randomly selected from each culture dish. At least 3 independent experiments were counted. The fluorescence density was analyzed using Image J software (NIH, Bethesda, MD, USA).

Supplementary Tables and Figures

Table S1. Optimization of reaction conditions [a]



1a 2a 3a

Entry	Additive(equiv.)	Solvent	T/ °C	Yield/% [b]
1	/	CH_3CN	25	trace
2	Conc. HCl (1.0)	CH_3CN	25	22
3	HOAc (1.0)	CH_3CN	25	46
4	Conc. H_2SO_4 (1.0)	CH_3CN	25	67
5	$MeSO_3H$ (1.0)	CH_3CN	25	52
6	TFA (1.0)	CH_3CN	25	69
7	TFA (1.0)	EtOH	25	43
8	TFA (1.0)	THF	25	62
9	TFA (1.0)	DCE	25	51
10	TFA (1.0)	DMSO	25	13
11	TFA (1.0)	DMF	25	25
12	TFA (1.0)	CH_3CN	40	80
13	TFA (1.0)	CH_3CN	80	70
14	TFA (0.5)	CH_3CN	25	64
15	TFA (1.5)	CH_3CN	25	71

[a.]Reaction conditions: 0.3 mmol**1a**, 1.0 equiv **2a**, 2.0 equiv KSCN, solvent (2 mL) at 40 °C.[b.] Yield of isolated products.

Table S2. Photo-physical properties of Carboline-Fluor[a]

Compd.	λ_{abs}/nm	λ_{ex}/nm	λ_{em}/nm	Stokes shift/cm^{-1}	Φ_F
3a	350	350	412	4300	0.09
3b	353	360	418	3854	0.12
3c	350	350	414	4417	0.26
3d	327	328	480	9654	0.05
3e	368	368	442	4549	0.14
3f	371	370	448	4706	0.23
3g	365	364	438	4641	0.52
3h	356	358	428	4568	0.08
3i	340	346	410	4511	0.08
3j	347	346	410	4511	0.19
3k	352	352	412	4137	0.20
3l	352	354	418	4325	0.15
3m	352	356	422	4393	0.33
3n	336	338	410	5196	0.61
3o	353	356	418	4166	0.12
3p	354	360	426	4304	0.32
3q	359	366	434	4281	0.66
3r	396	389	504	5866	0.11
3s	350	354	412	3977	0.06
3t	368	370	444	4505	0.29
3u	380	397	503	5308	0.16
3v	351	351	409	4040	0.07
3w	324	320	372	4368	0.11
3x	352	356	428	4725	0.09

[a.] Photo-physical properties in EtOH at 10.0 μM

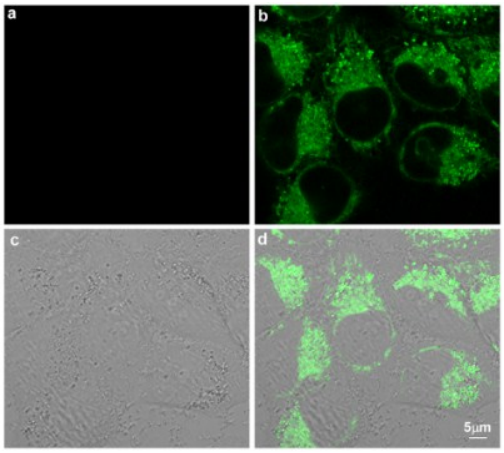


Fig S1. Confocal fluorescence images of HeLa cells cultured with **3t** in EMEM medium (λ_{ex}= 405 nm, λ_{em}= 440-480 nm). (**a**) **3t** without HeLa cells; (**b**) **3t** with HeLa cells, the fluorescence of **3t** was indicated as green color; (**c**) bright field image; (**d**) merged image of **b** and **c**. Scale bar=5 μm.

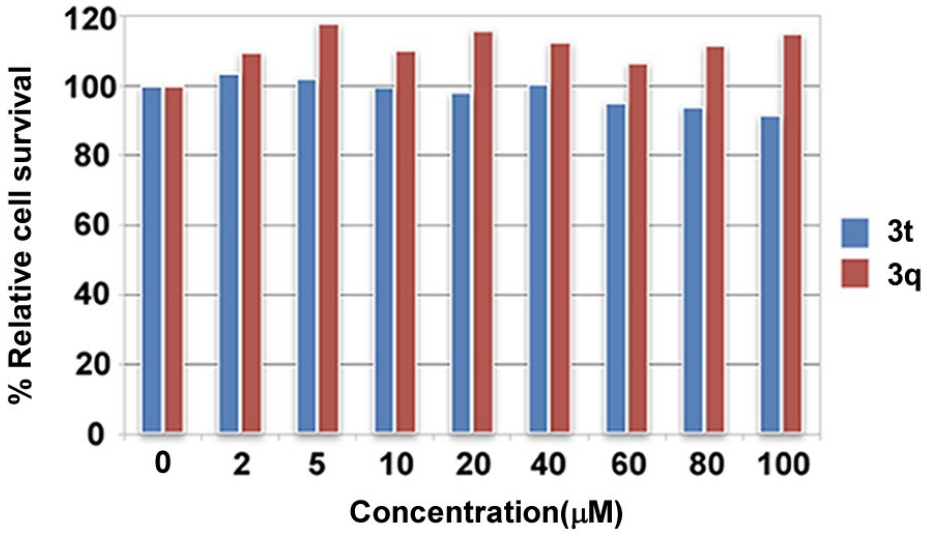


Figure S2 Cytotoxicity of **3t** and **3q** was assessed in HeLa by CCK8 assays. **3t** with concentration of 2 μM, 5 μM, 10 μM, 20 μM, 40 μM, 60 μM, 80 μM and 100 μM were added to cells, and incubated for of 24 h. After introducing CCK8 (10 μL) solution at 37℃ in a 95% humidified atmosphere with 5% CO_2 for 1 h, the absorption at 450 nm was measured by Microplate Spectrophotometer (MD I3X).

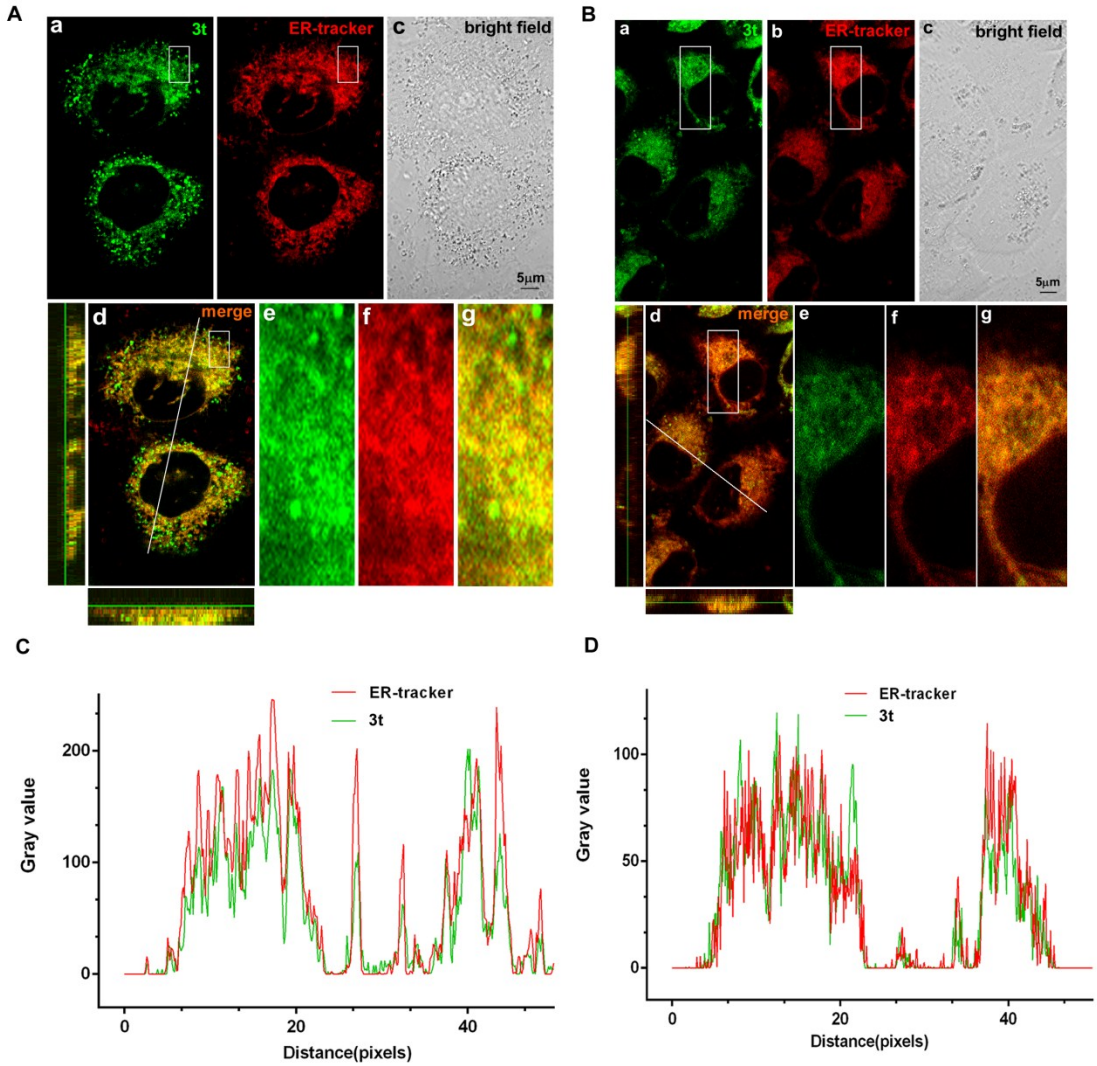


Figure S3 Confocal microscopic images of subcellular localization of **3t** in HUVEC cells. (A, B) Cells were incubated with **3t** (A: 1μM, B: 10μM)for 30 min at 37 ^{o}C and subsequently stained with 1 μM of ER-tracker, then washed with PBS (pH 7.4). a) Green fluorescent of **3t**; b) Red fluorescent of ER-tracker; c) Bright field; d) Merge of a and b, orthogonal projection onto the x-z and y-z planes as shown to confirm the co-localization of **3t** and ER-tracker Red; e, f, g) themagnification of the pane in the a, b, d, respectively. (C, D) Intensity profile of regions of interest across HUVECcells.The **3t** fluorescence was monitored at λ_{em}=440-480 nm (λ_{ex}=405 nm). Fluorescent signal from ER-trackers were obtained at λ_{em}= 600-650 nm (λ_{ex}=543 nm). Scale bar=5 μm.

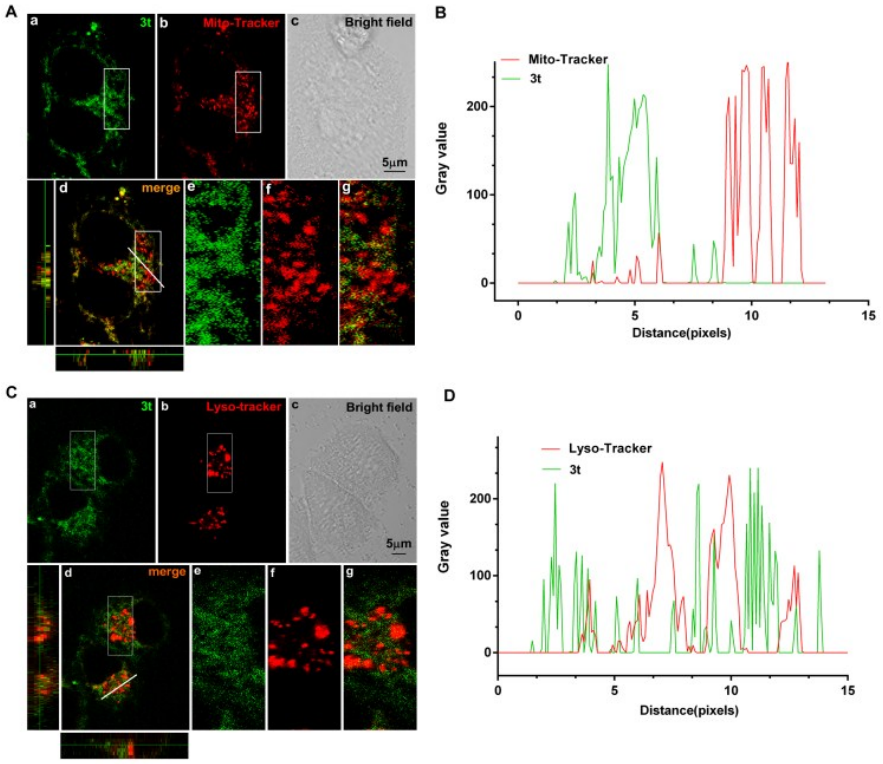


Fig S4. Confocal microscopic images of subcellular localization of **3t** in HeLa cells. **A, C)** Cells were incubated with 1 μM **3t** for 30 min at 37 °C and subsequently stained with 0.5 μM **MTR** (A) or 1 μM of **LTR** (C). a) Green fluorescent of **3t**; b) Red fluorescent of Mito-Tracker or Lyso-Tracker; c) Bright field; d) Merge of a and b, orthogonal projection onto the x-z and y-z planes as shown to confirm the co-localization of **3t** and **MTR** (A) or **LTR** (C); e, f, g) the magnification of the pane in the a, b, d, respectively. **B, D)** Intensity profile of regions of interest across HeLa cells. The **3t** fluorescence was monitored at λ_{em}=440-480 nm (λ_{ex}=405 nm). Fluorescent signal from Mito-Tracker or Lyso-Tracker were obtained at λ_{em}= 600-650 nm (λ_{ex}=543 nm). Scale bar=5 μm.

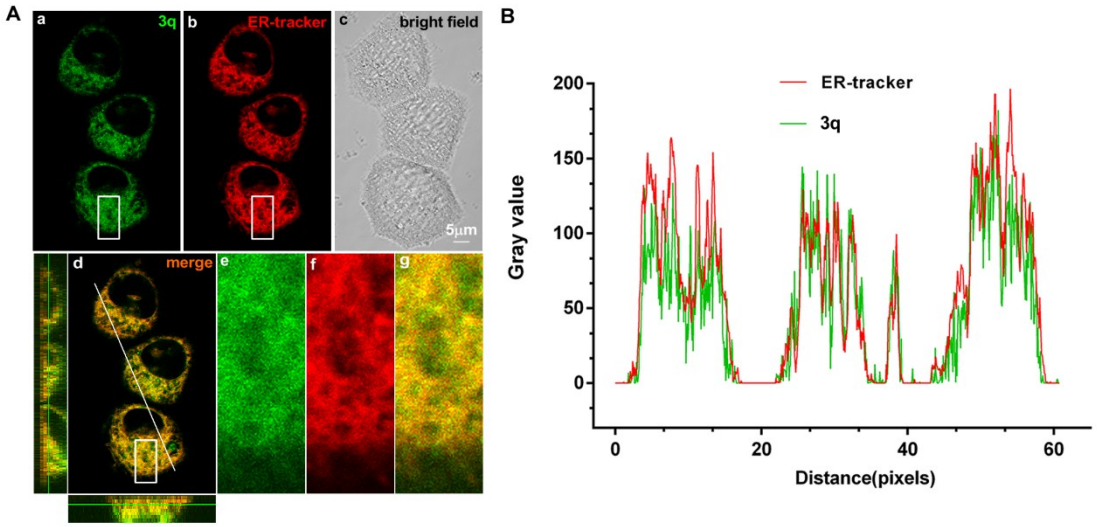


Figure S5 Confocal microscopic images of subcellular localization of **3q** in HeLa cells. (A) Cells were incubated with 1μM**3q**for 30 min at 37 ^{o}C and subsequently stained with 1 μM of ER-tracker. a) Green fluorescent of **3q**; b) Red fluorescent of ER-tracker; c) Bright field; d) Merge of a and b, orthogonal projection onto the x-z and y-z planes as shown to confirm the co-localization of **3q** and ER-tracker Red; e, f, g) themagnification of the pane in the a, b, d, respectively. (B) Intensity profile of regions of interest across HeLacells.The **3q** fluorescence was monitored at λ_{em}=440-480 nm (λ_{ex}=405 nm). Fluorescent signal from ER-trackers were obtained at λ_{em}= 600-650 nm (λ_{ex}=543 nm). Scale bar=5 μm.

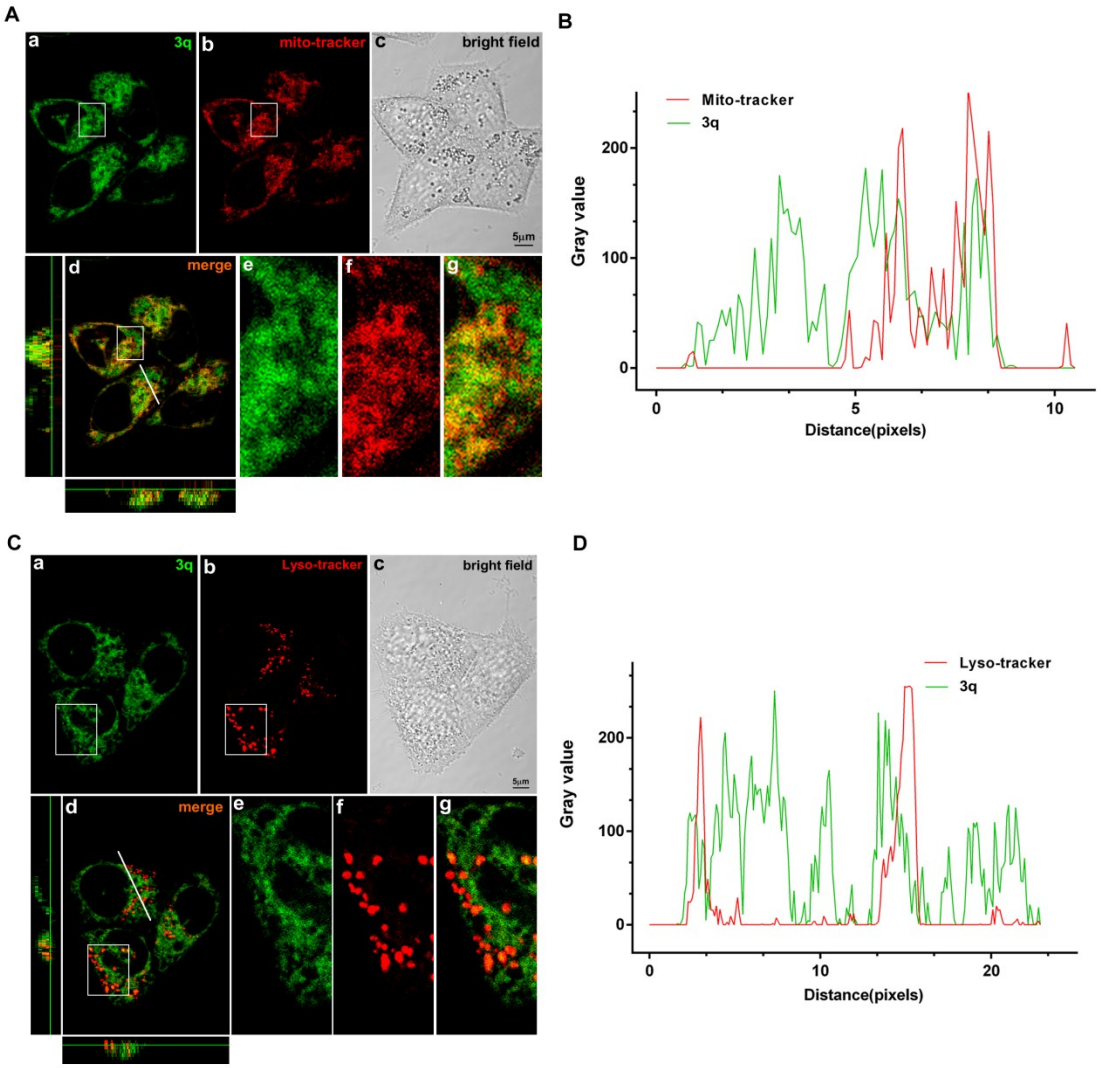


Figure S6 Confocal microscopic images of subcellular localization of **3q** in HeLa cells. (A, C) Cells were incubated with 1 μM**3q**for 30 min at 37 °C and subsequently stained with 0.5 μM Mito-tracker (A) or1 μM of Lyso-tracker (C). a) Green fluorescent of **3q**; b) Red fluorescent of Mito-tracker or Lyso-tracker; c) Bright field; d) Merge of a and b, orthogonal projection onto the x-z and y-z planes as shown to confirm the co-localization of **3t** and Mito-tracker (A) or Lyso-tracker (C); e, f, g) themagnification of the pane in the a, b, d, respectively. (B, D) Intensity profile of regions of interest across HeLacells.The **3q** fluorescence was monitored at λ_{em}=440-480 nm (λ_{ex}=405 nm). Fluorescent signal from Mito-tracker or Lyso-tracker were obtained at λ_{em}= 600-650 nm (λ_{ex}=543 nm). Scale bar=5 μm.

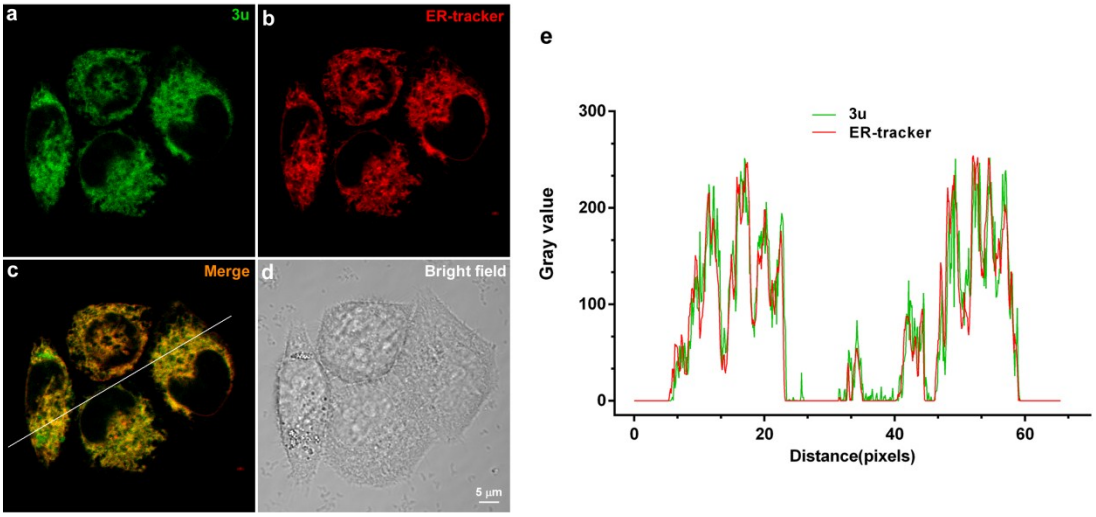


Figure S7 Confocal microscopic images of subcellular localization of **3u** in HeLa cells. (A) Cells were incubated with 1μM**3u**for 30 min at 37 °C and subsequently stained with 1 μM of ER-tracker, then washed with PBS (pH 7.4). a) green fluorescent of; b) red fluorescent of ER-tracker; c) bright field; d) merge of a and b, (B) Intensity profile of regions of interest across HeLa cells.The **3u** fluorescence was monitored at λ_{em}=440-480 nm (λ_{ex}=405 nm). Fluorescent signal from ER-tracker was obtained at λ_{em}= 600-650 nm (λ_{ex}=543 nm). Scale bar=5 μm.

a

Probe name	Pearson's correlation factors
3t	0.8333 ± 0.0252
3q	0.8433 ± 0.0058
3u	0.8125 ± 0.0486

b

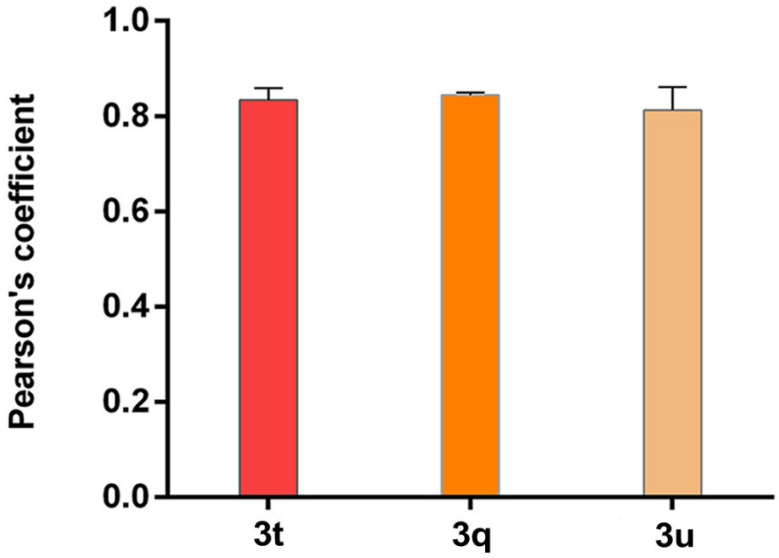


Figure S8 Quantification of colocalization analysis. (A) The colocalization of **3t**, **3q**, **3u** with ER was quantified with Pearson's coefficient calculated using the Image J software and averaged across 4 separate fields of cells. (B) Data were expressed as mean ± S. E. M, *n*=4.

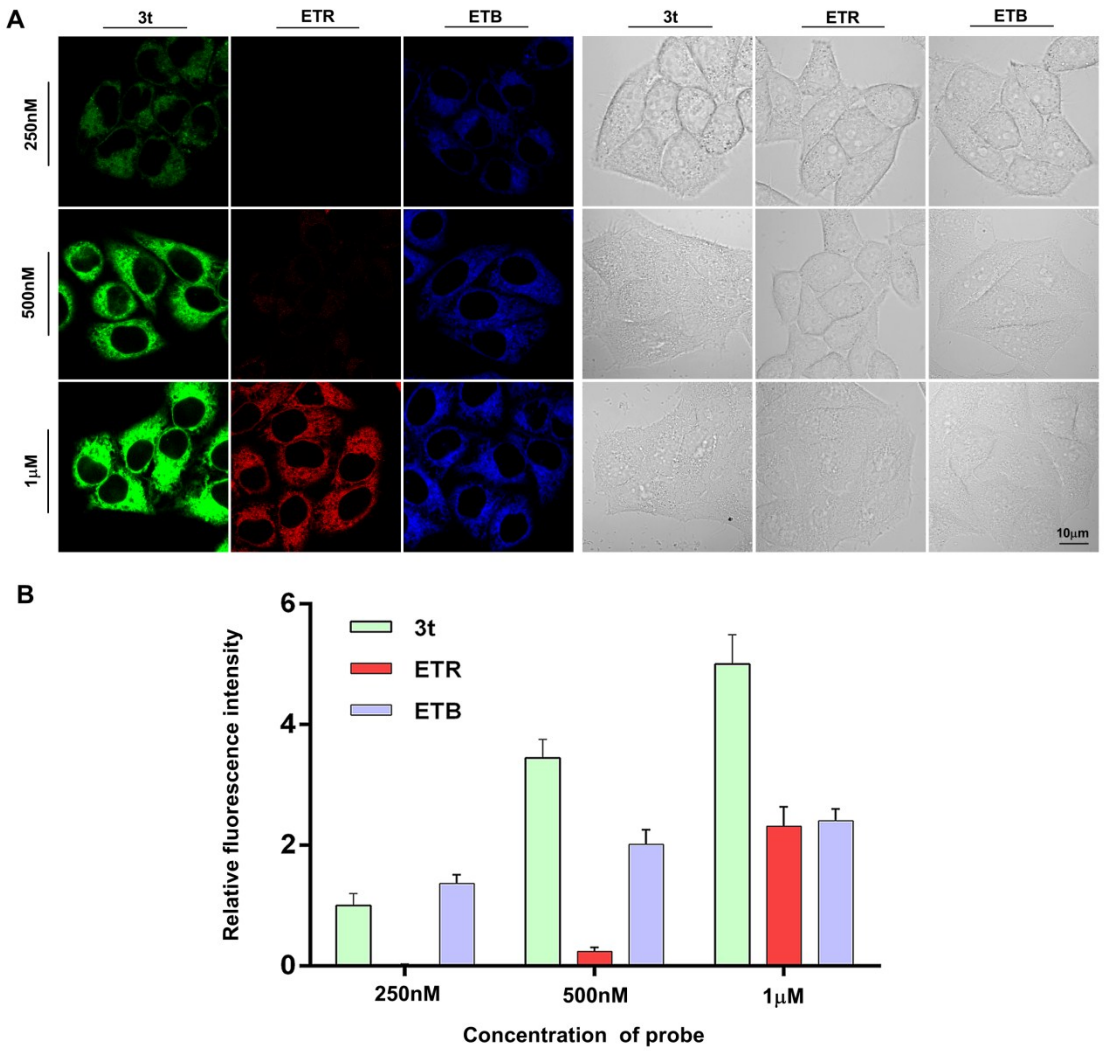


Figure S9. The efficiency of **3t** in staining ER at different concentrations. (A) HeLa cells were incubated with **3t**, **ETR** or **ETB** at the concentration of 250 nM, 500 nM and 1μM, respectively. The images were obtained by confocal microscopy with 20% laser power. The fluorescence of **3t**and **ETB**was monitored at 440-480 nm (λ_{ex}=405 nm), and **ETR**was monitored at 600-650 nm (λ_{ex}= 543 nm). Scale bar=10 μm. (B) Quantification of image data. The fluorescence was normalized to the group of **3t** at 250 nM. Data were expressed as mean ± S.E.M., a minimum of 3 images were quantified and averaged.

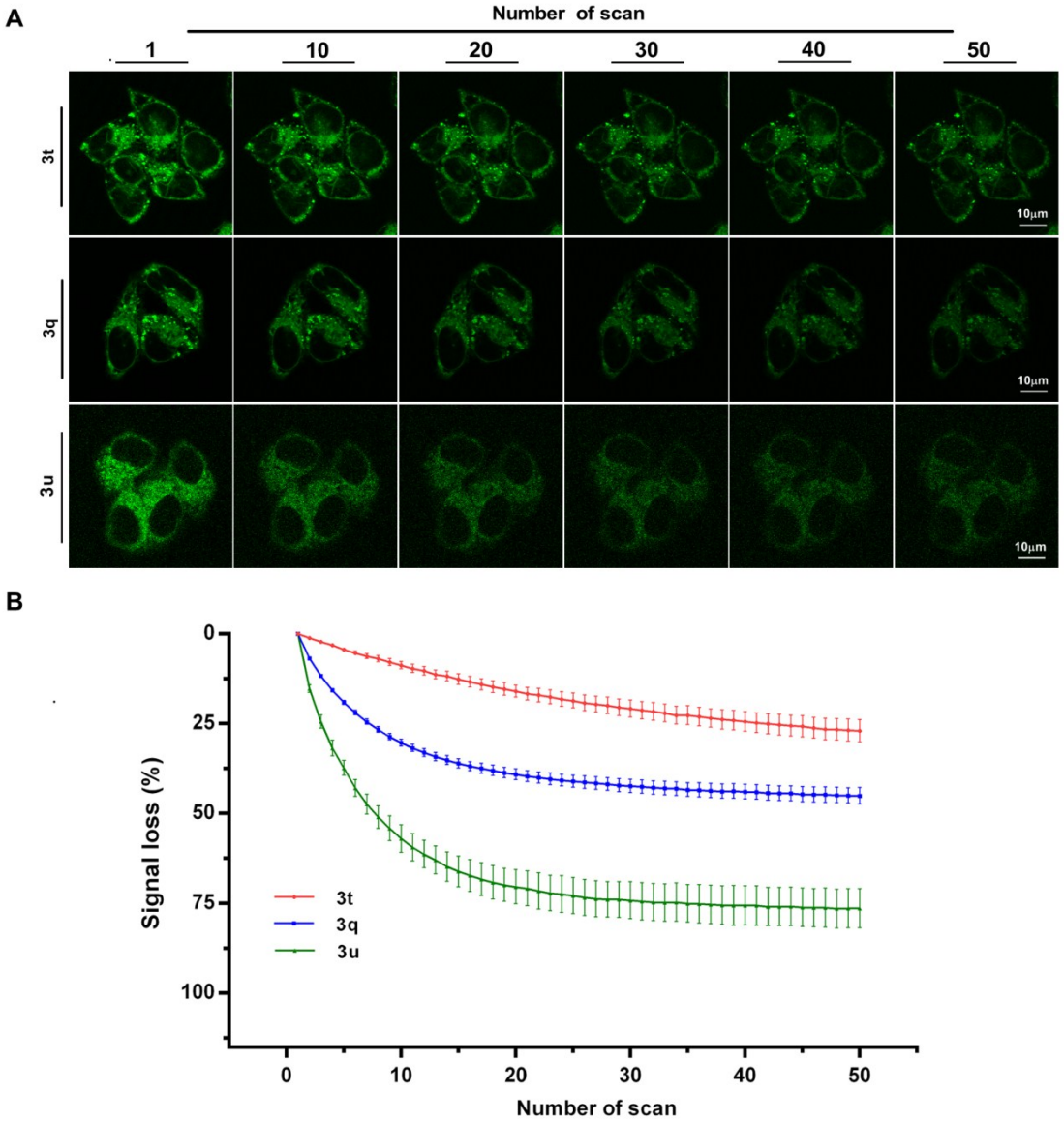
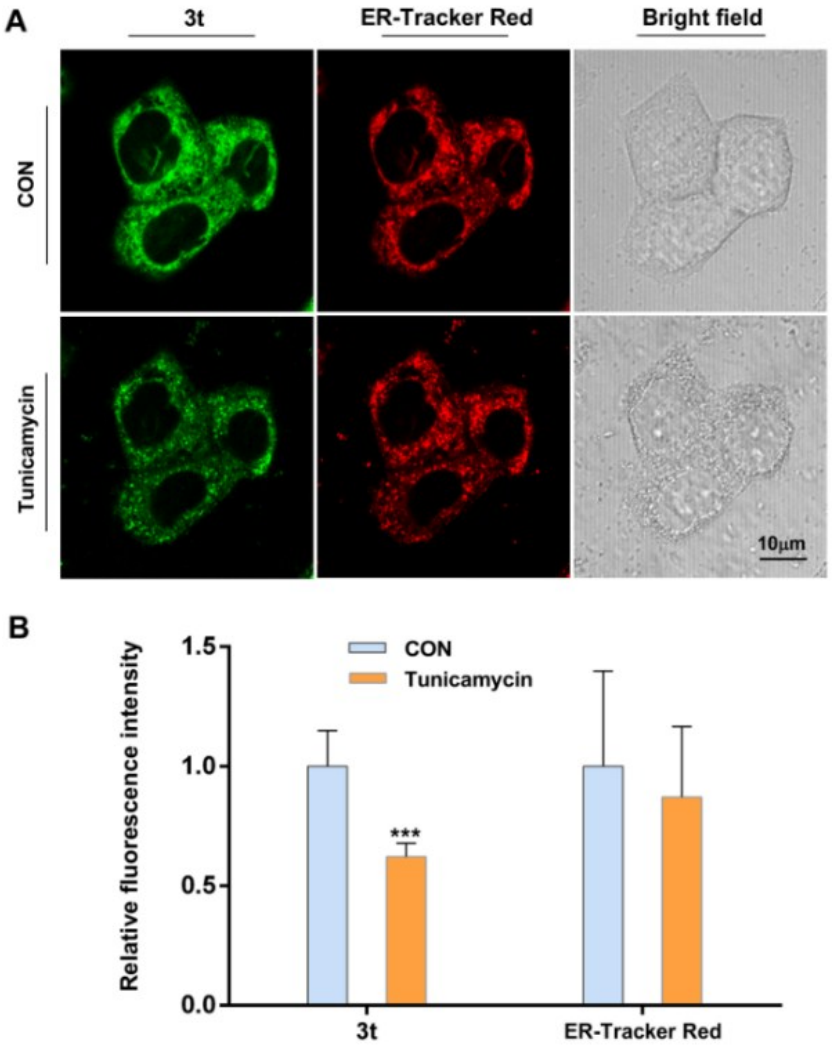
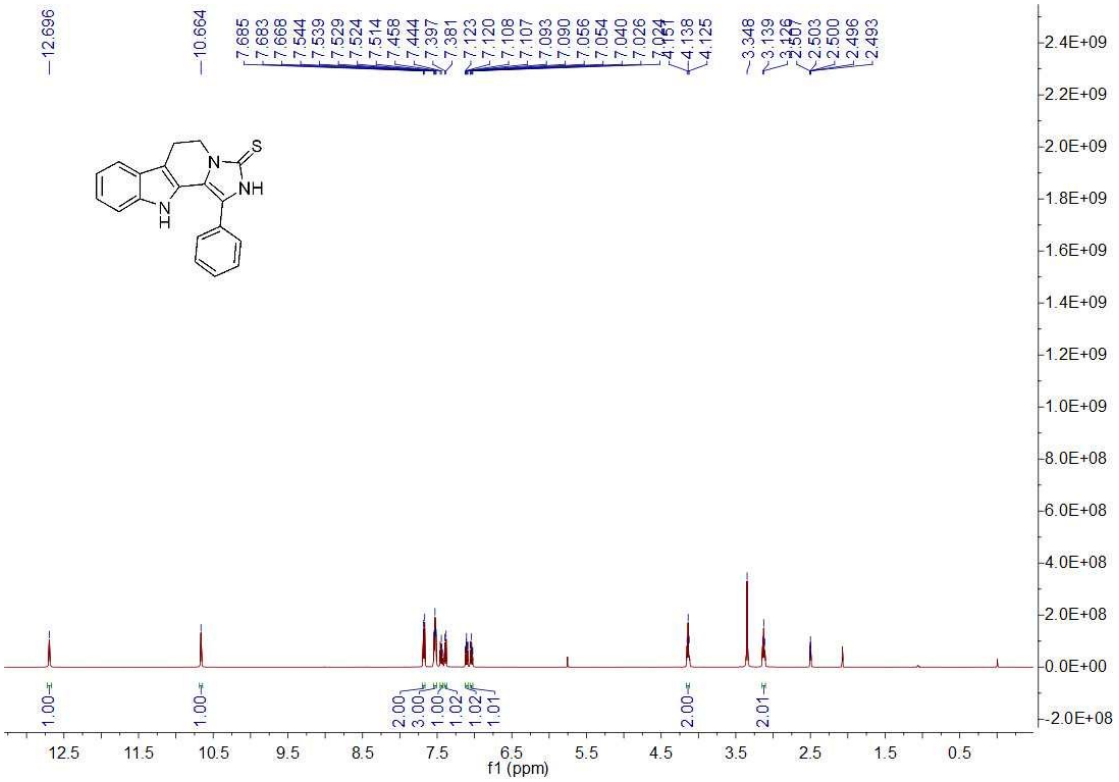


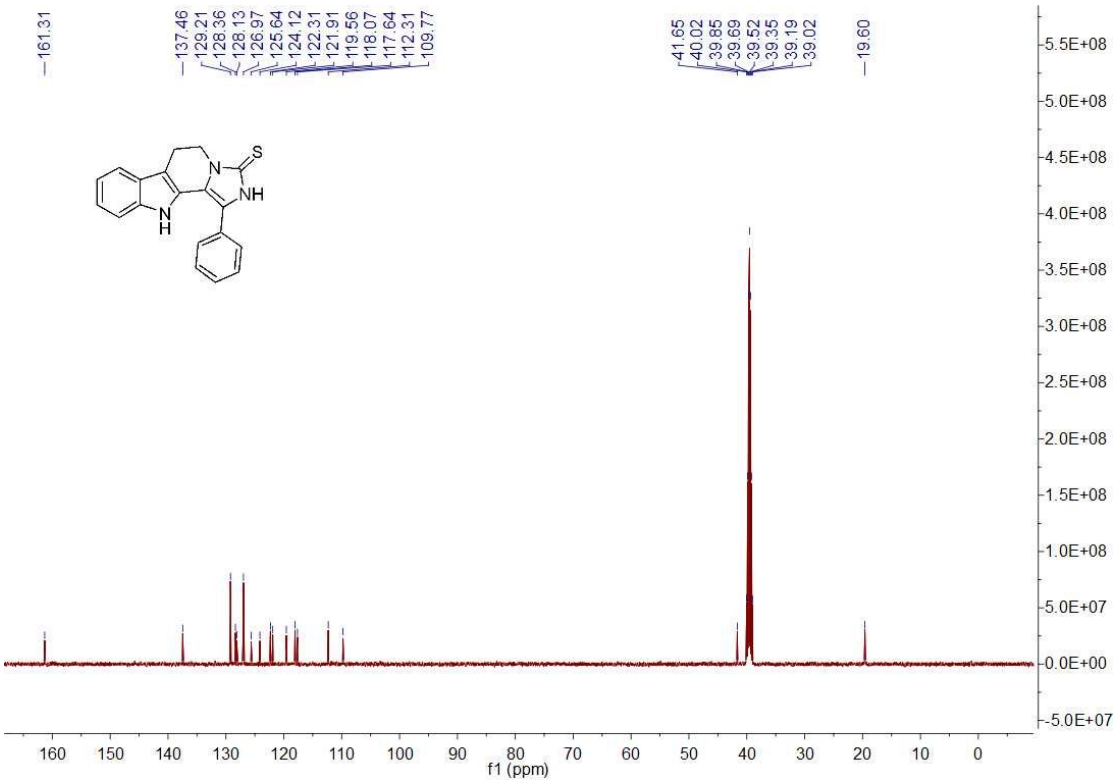
Figure S10. Photo-stability analysis of probes in Hela cells. (A) Confocal fluorescence images of the HeLa cells incubated with **3t** (1 μM), **3q** (1 μM) and **3u** (1 μM) with increasing number of scans (irradiation time: 5.36 s/scan).λ_{ex}= 405 nm, λ_{em}= 440-480 nm, 0.1%laser power, scale bar=10 μm; (B) Signal loss (%) of fluorescent emission of probes in the HeLa cells with increasing number of scans using confocal microscope. The scan number was shown in the X-axis.

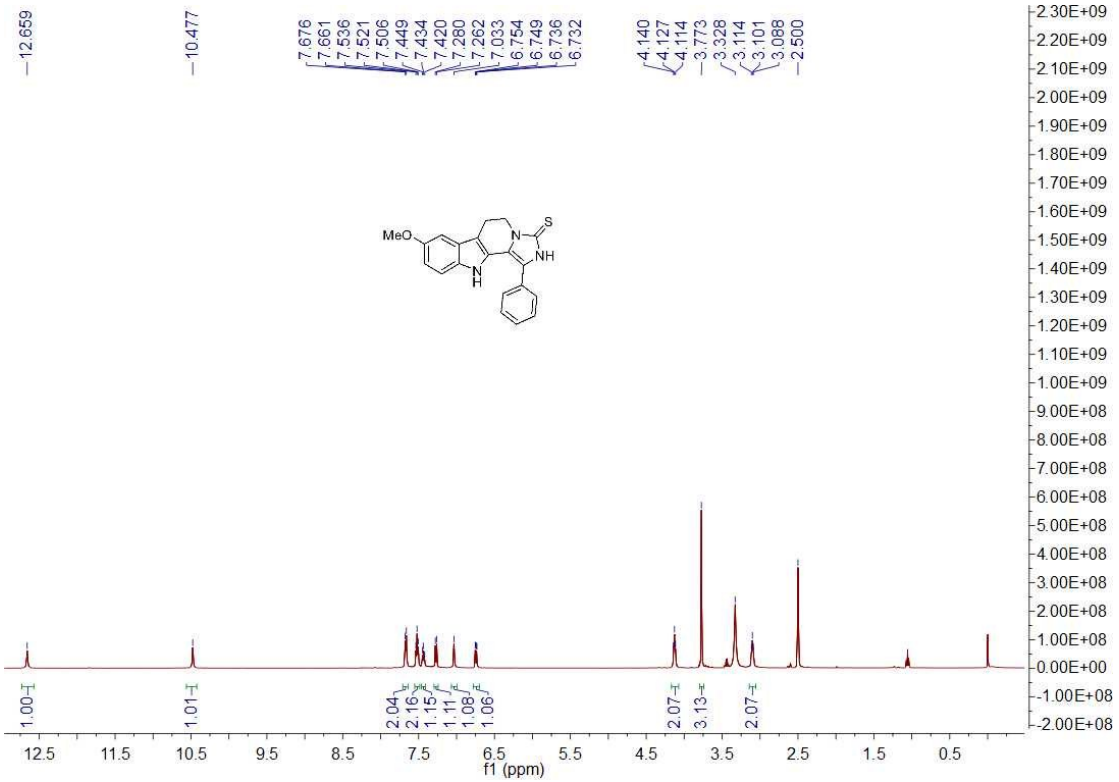


FigureS11. Imaging **3t** in living HeLa cells upon ER stress. (A) HeLa cells were incubated with **3t** and **ETR** for 30 min at 37 °C, and then washed with PBS (pH 7.4) followed by tunicamycin (TM, 10 μM) treatment. Fluorescence was obtained at 10 min after TM incubation. Scale bar=10 μm. The fluorescence of **3t** fluorescence was monitored at 440-480 nm (λ_{ex}=405 nm), the fluorescence of **ETR**was monitored at 600-650 nm (λ_{ex}= 543 nm). Scale bar=10 μm. (B) Quantification of image data. Data were expressed as mean ± S.E.M., a minimum of 4 images were quantified and averaged, ****P*<0.001 versus control.

^{1}H and ^{13}C NMR spectra



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NH
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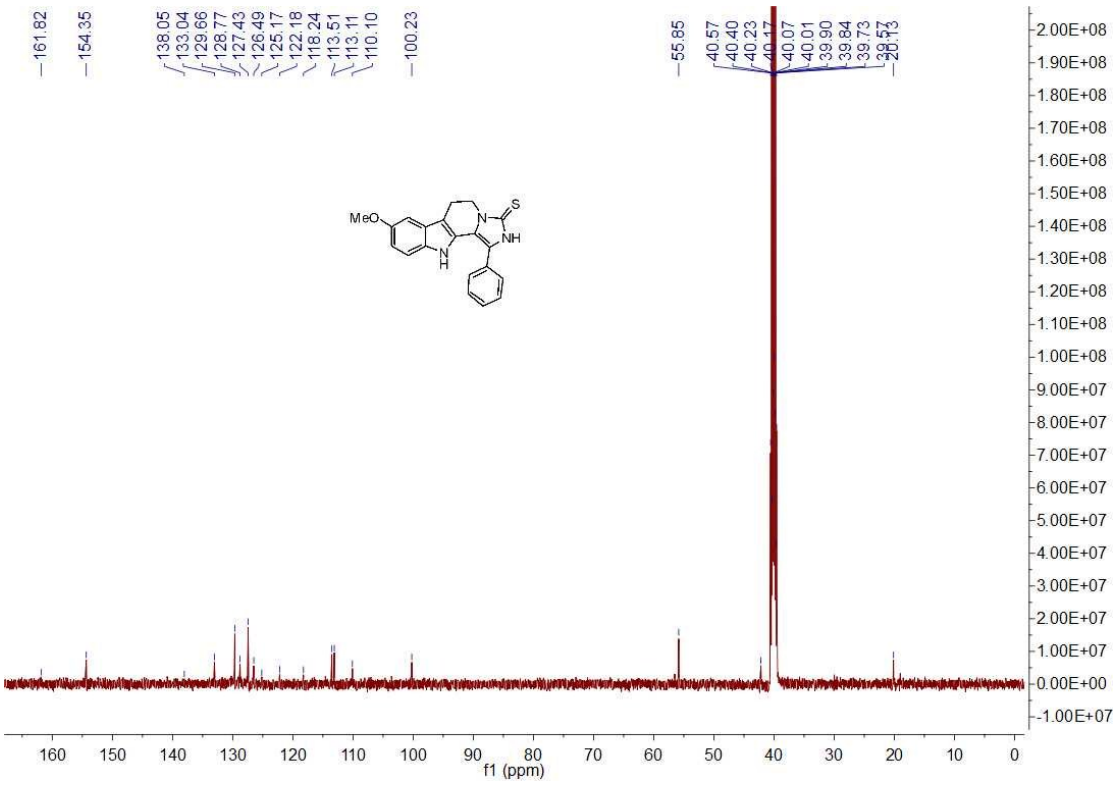
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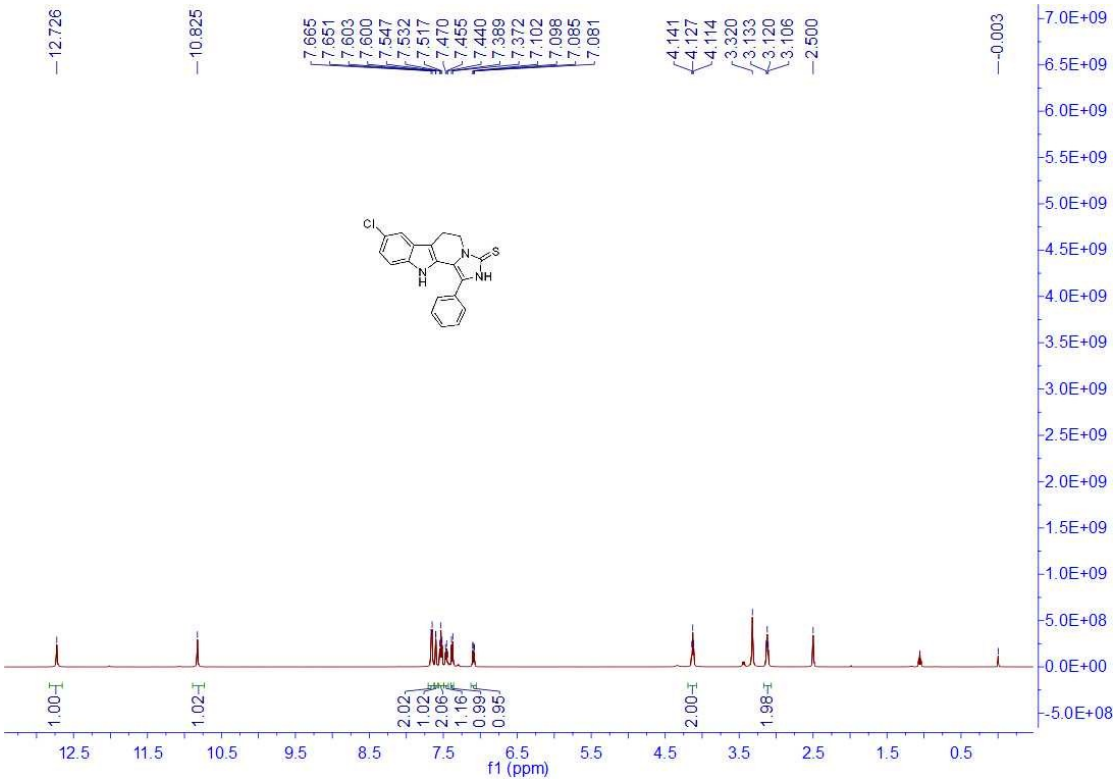
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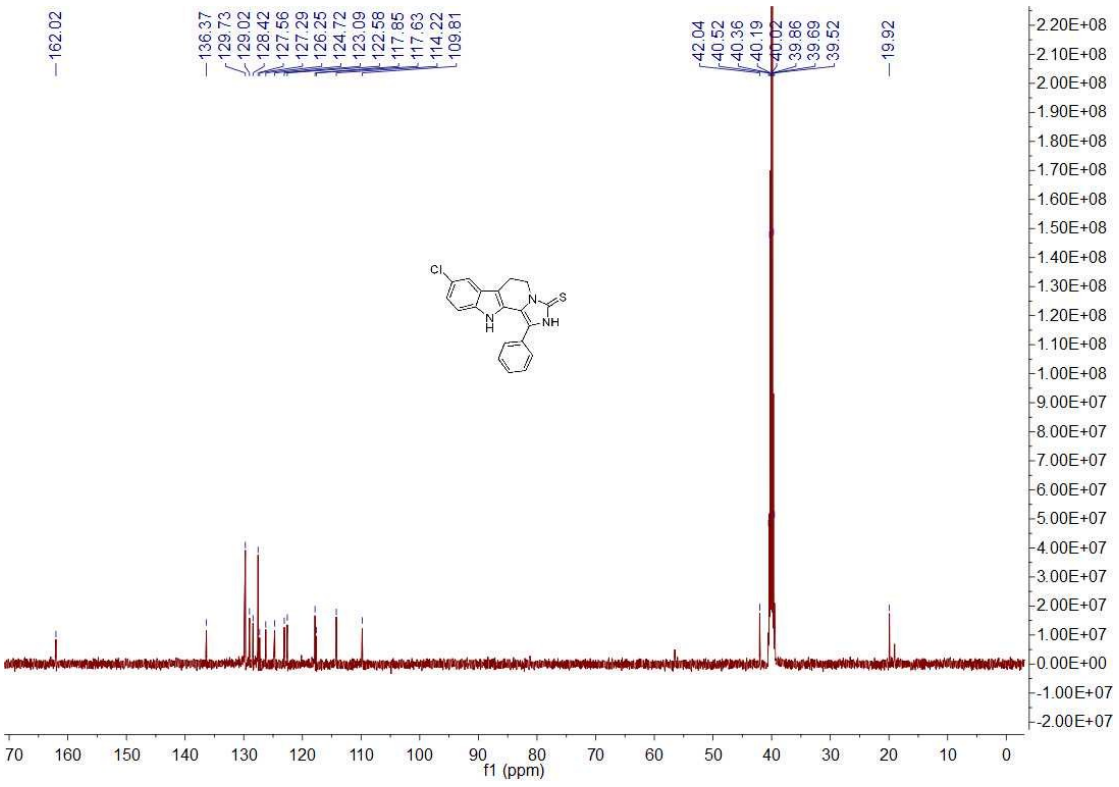
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Cl
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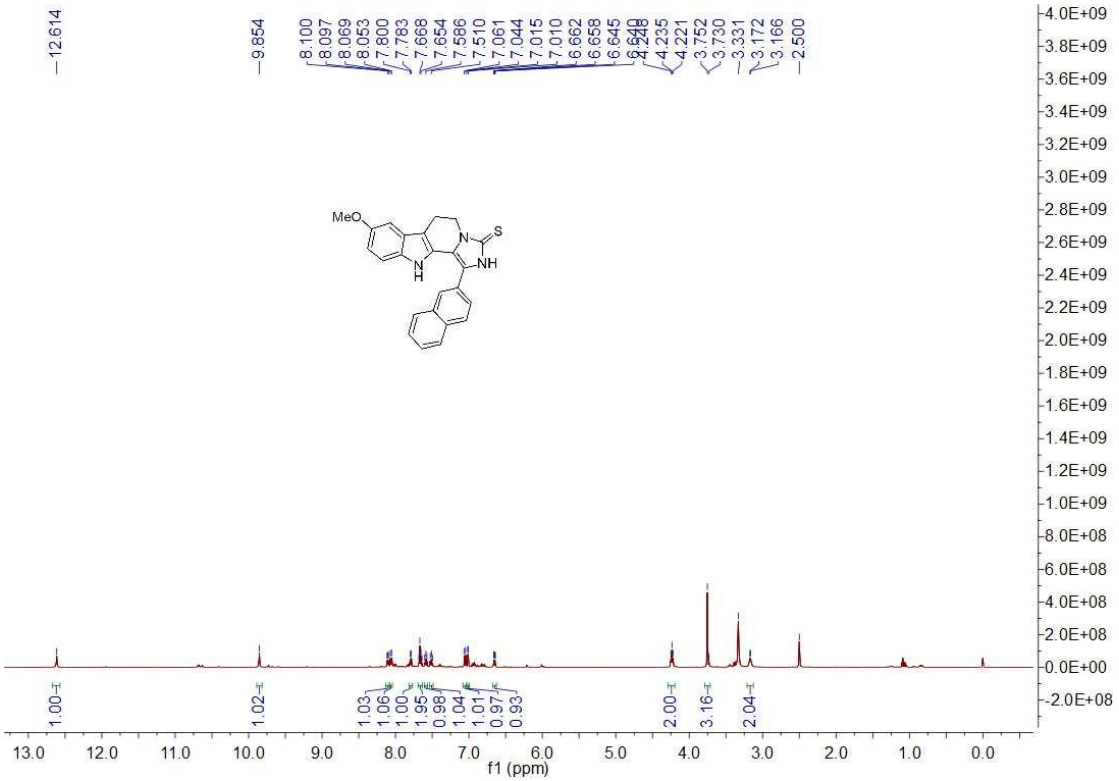
S
NH
f1 (ppm)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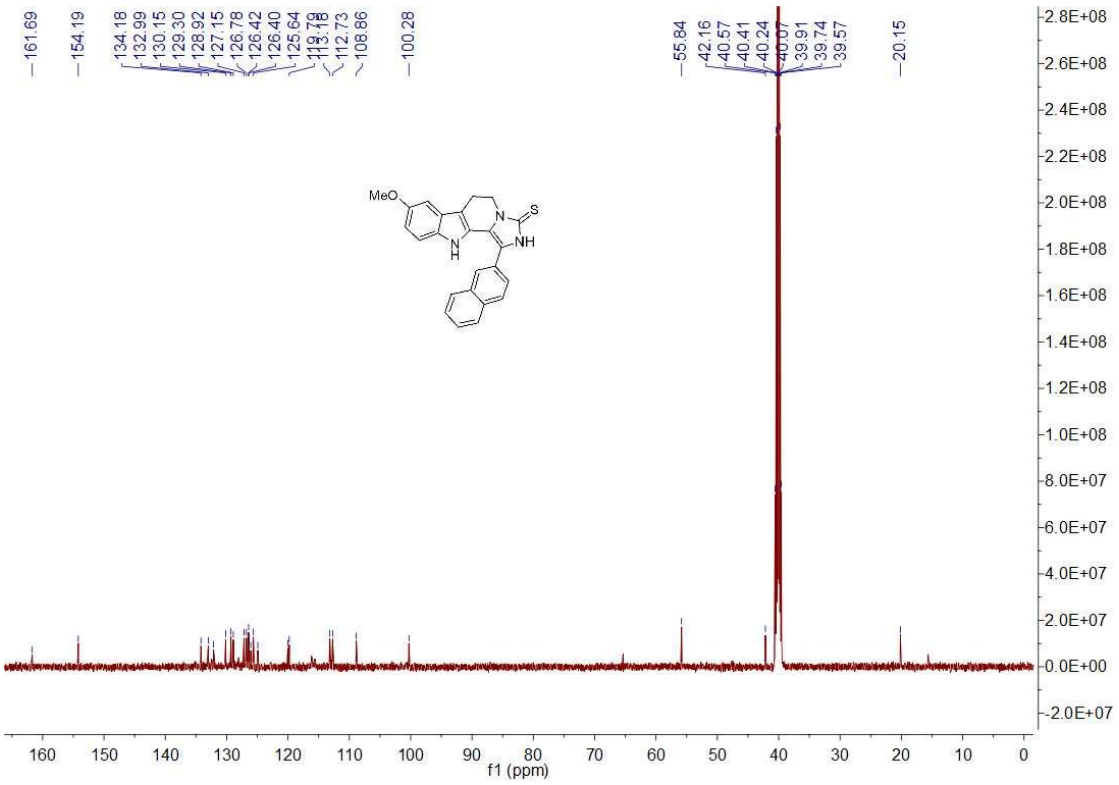
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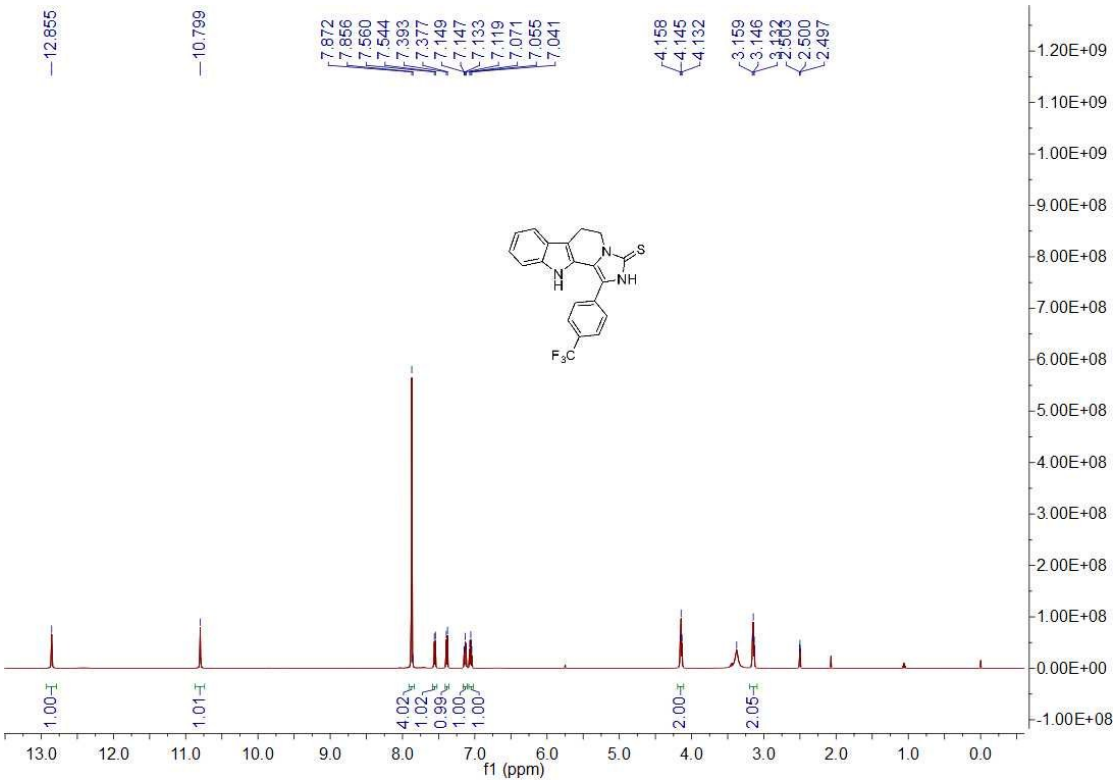
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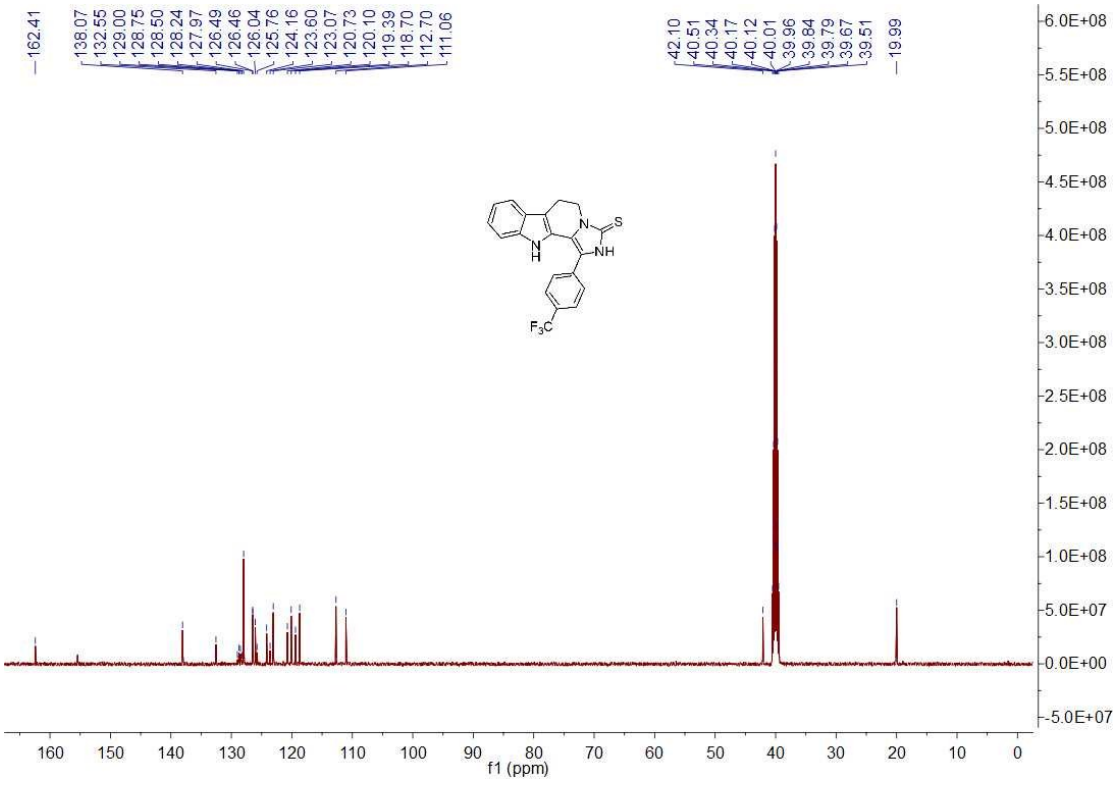
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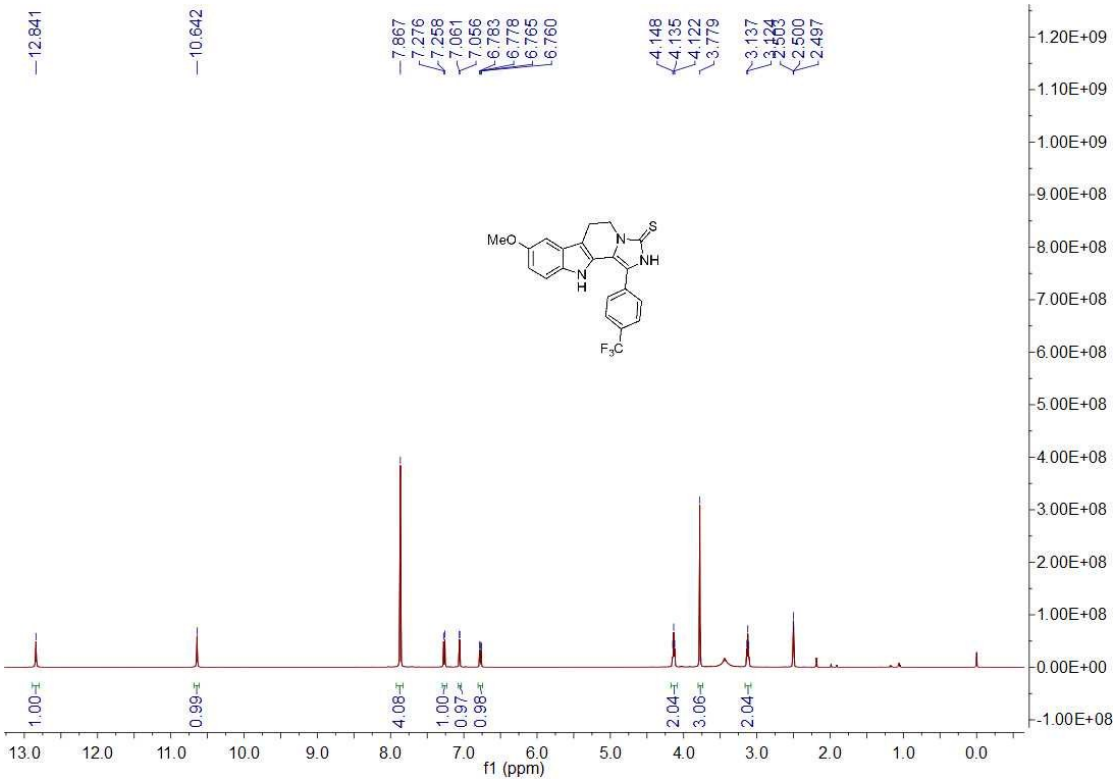
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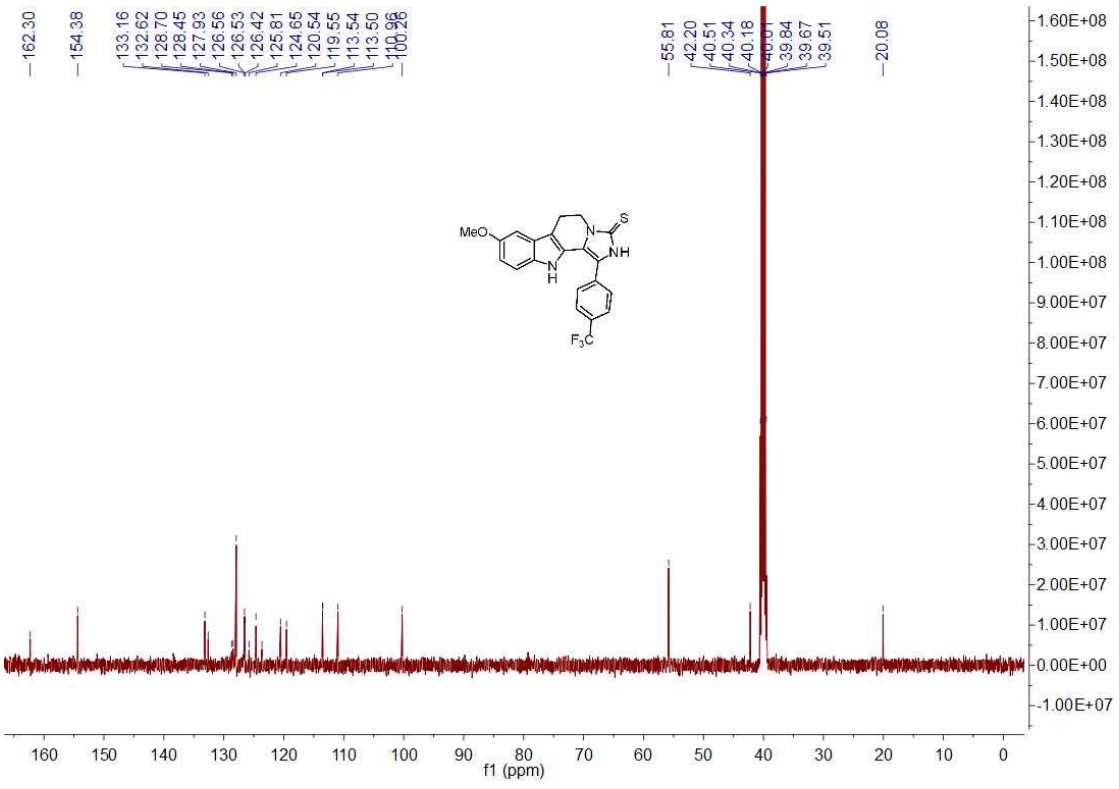
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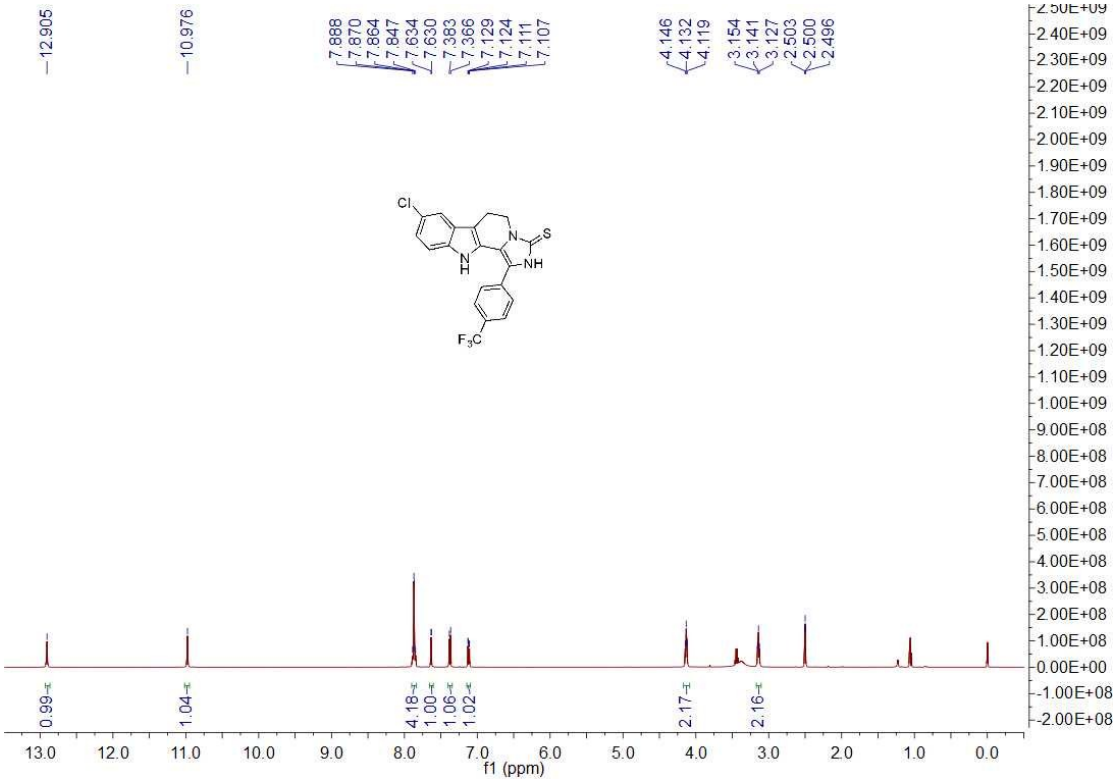
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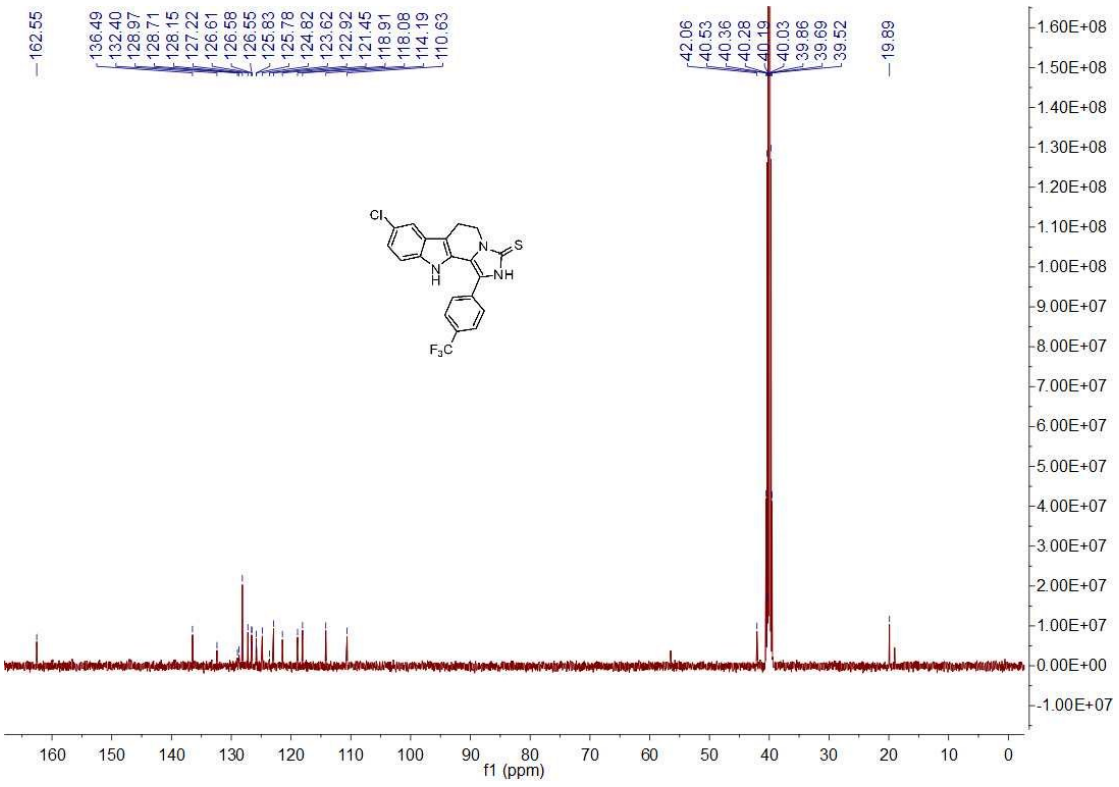
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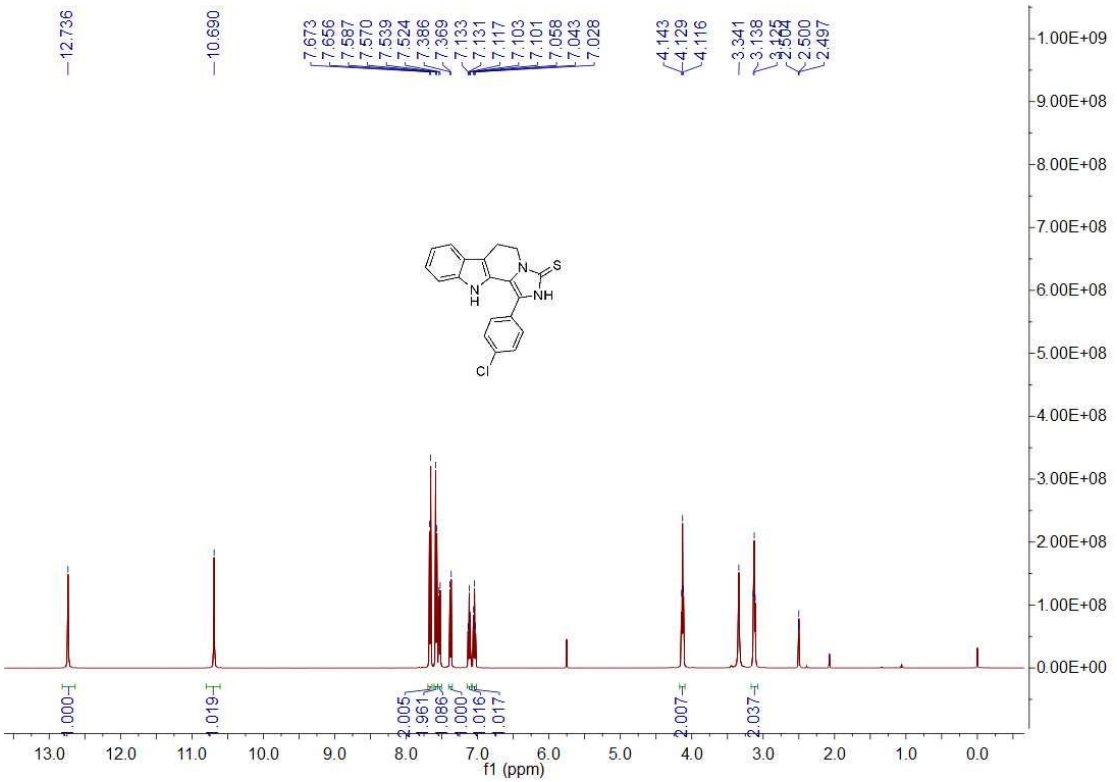
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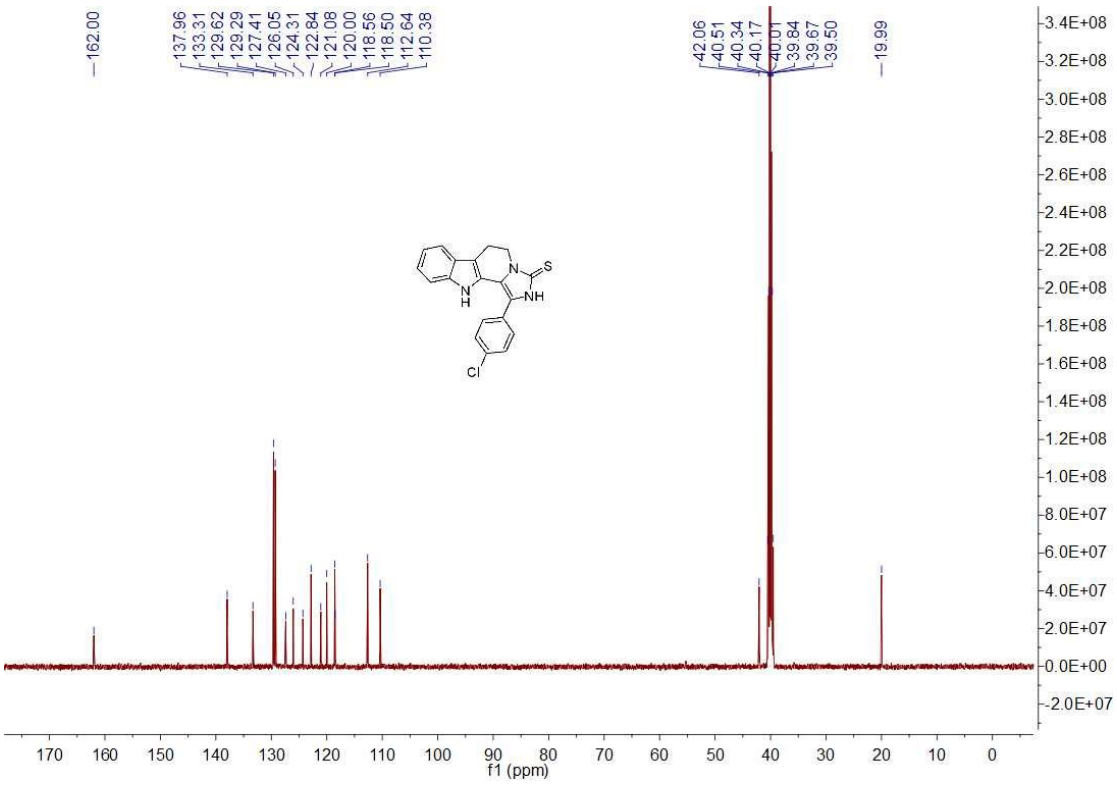
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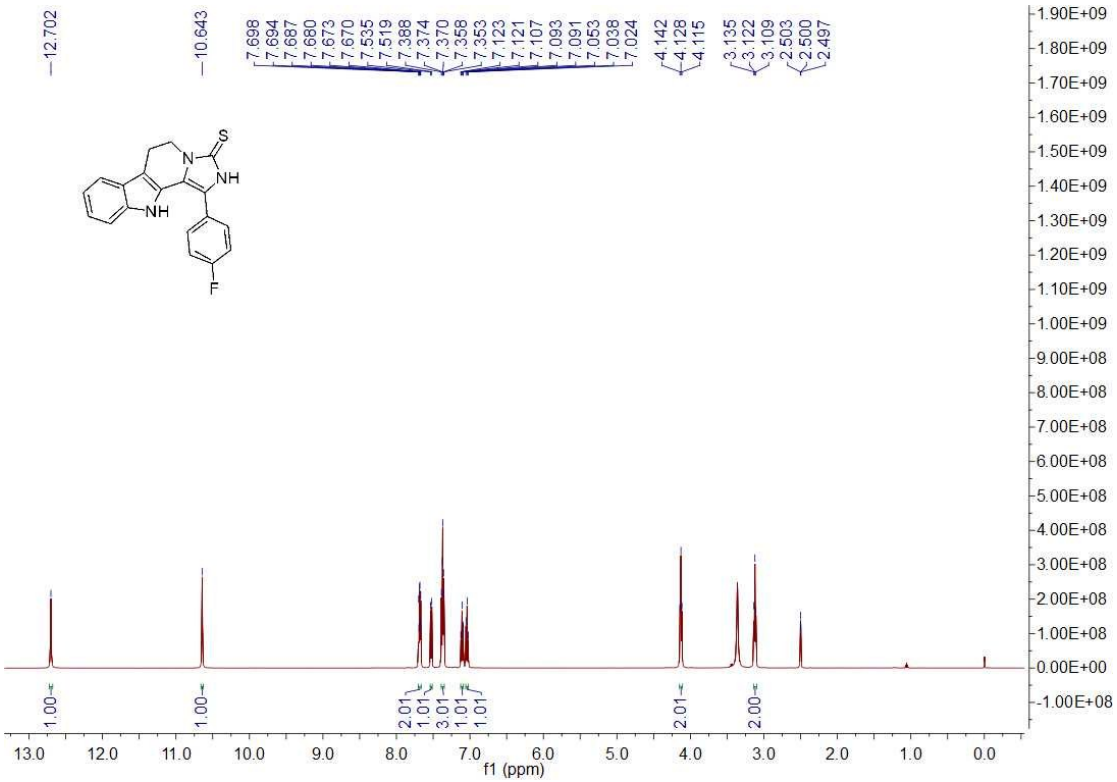
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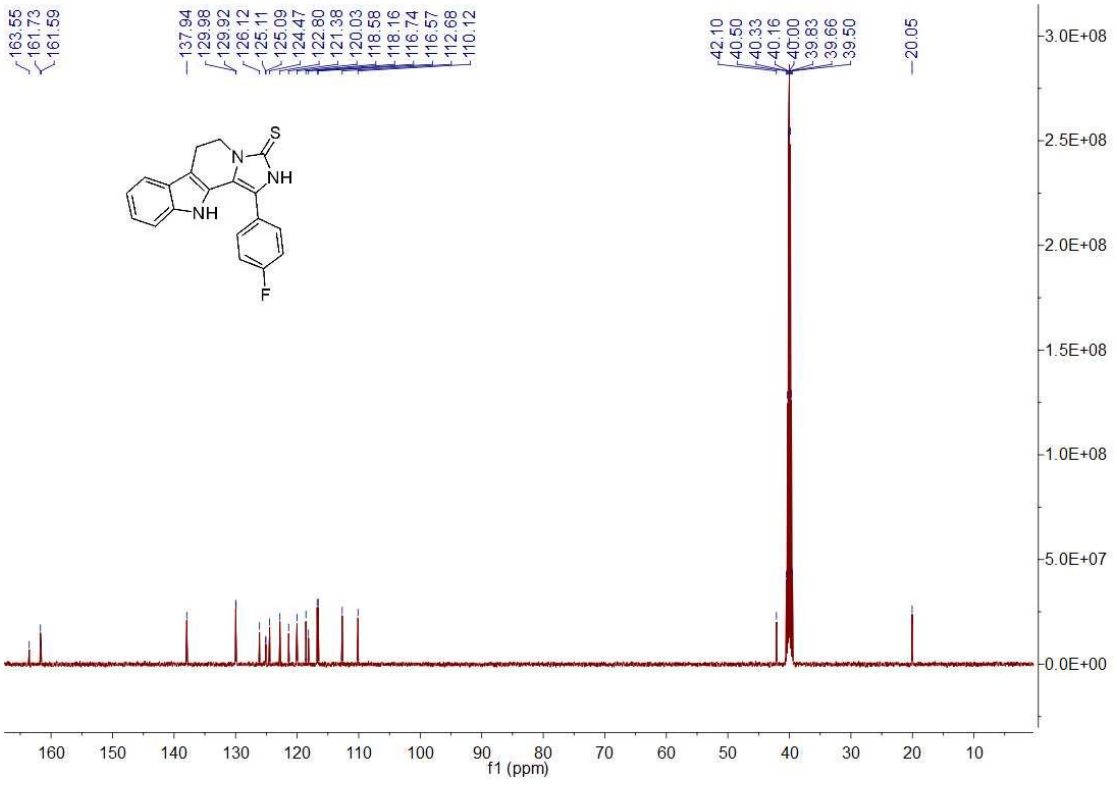
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112.68
110.12
42.10
40.50
40.33
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40.00
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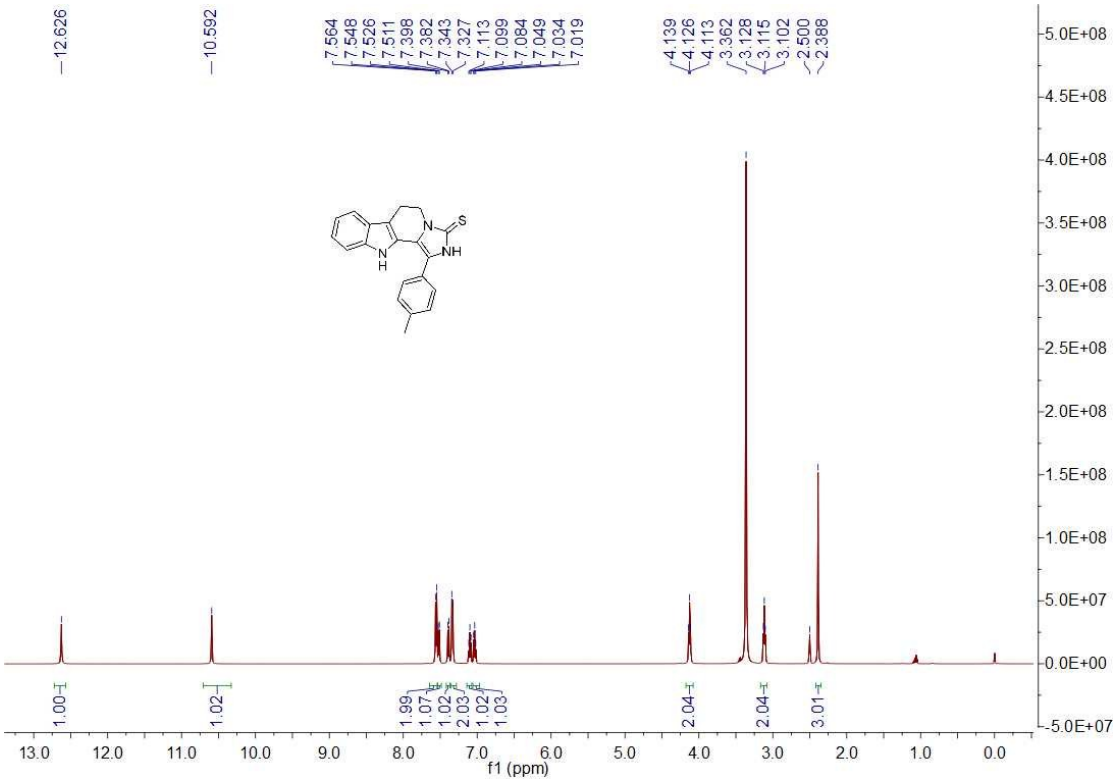
39.66
39.50
20.05
S
N
NH
NH
F
f1 (ppm)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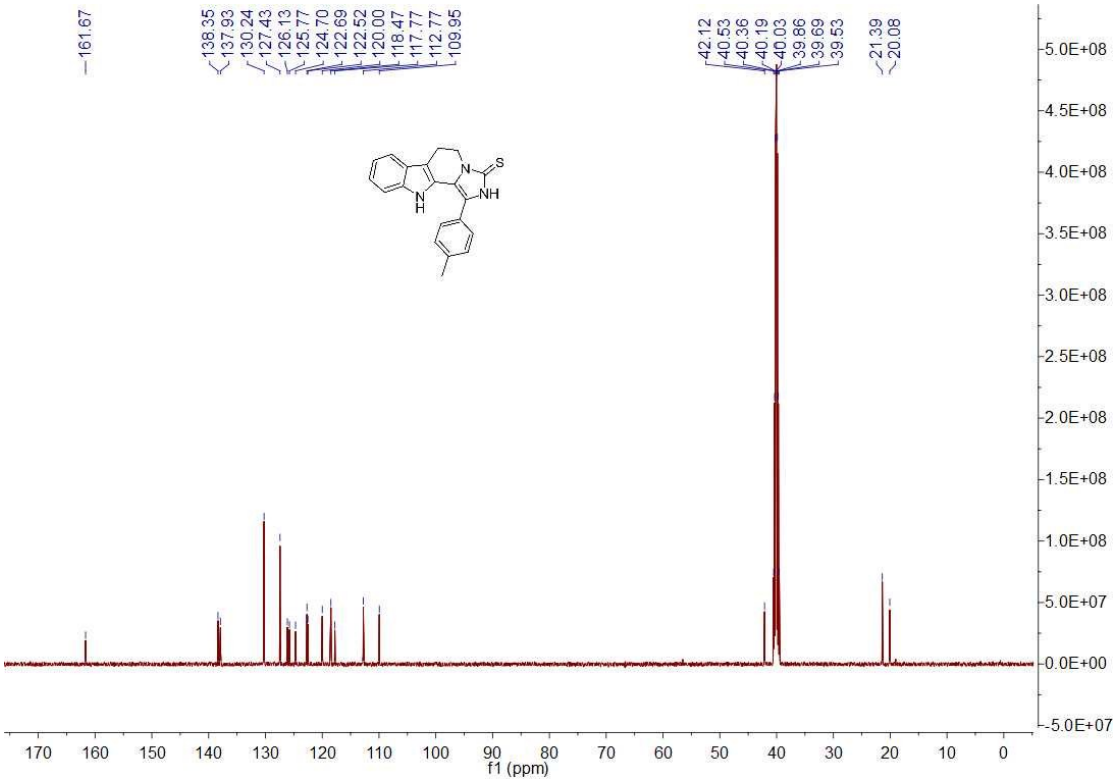
7.113
7.099
7.084
7.049
7.034
7.019
4.139
4.126
4.113
3.362
3.128
3.115
3.102
2.500
2.388
1.00
1.02
1.99
1.07
1.02
2.03
1.02
1.03
2.04
2.04
3.01
f1 (ppm)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124.70
122.69
122.52
120.00
118.47
117.77
112.77
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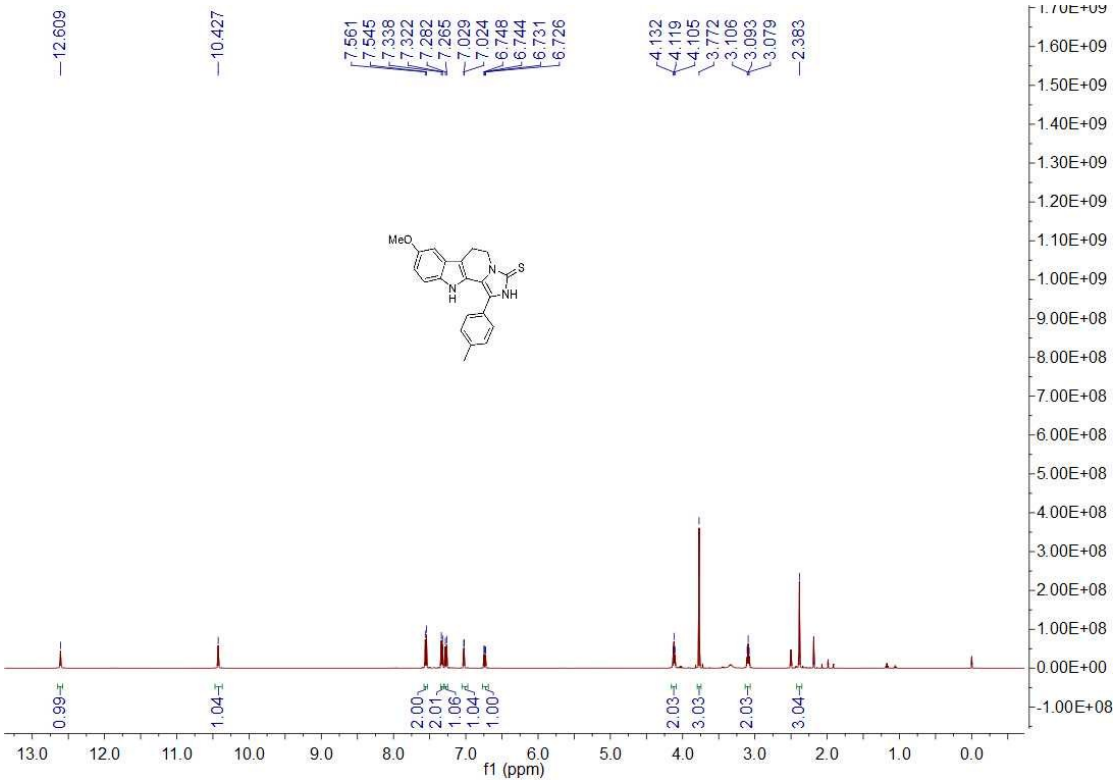
40.36
40.19
40.03
39.86
39.69
39.53
21.39
20.08
f1 (ppm)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7.282
7.265
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7.024
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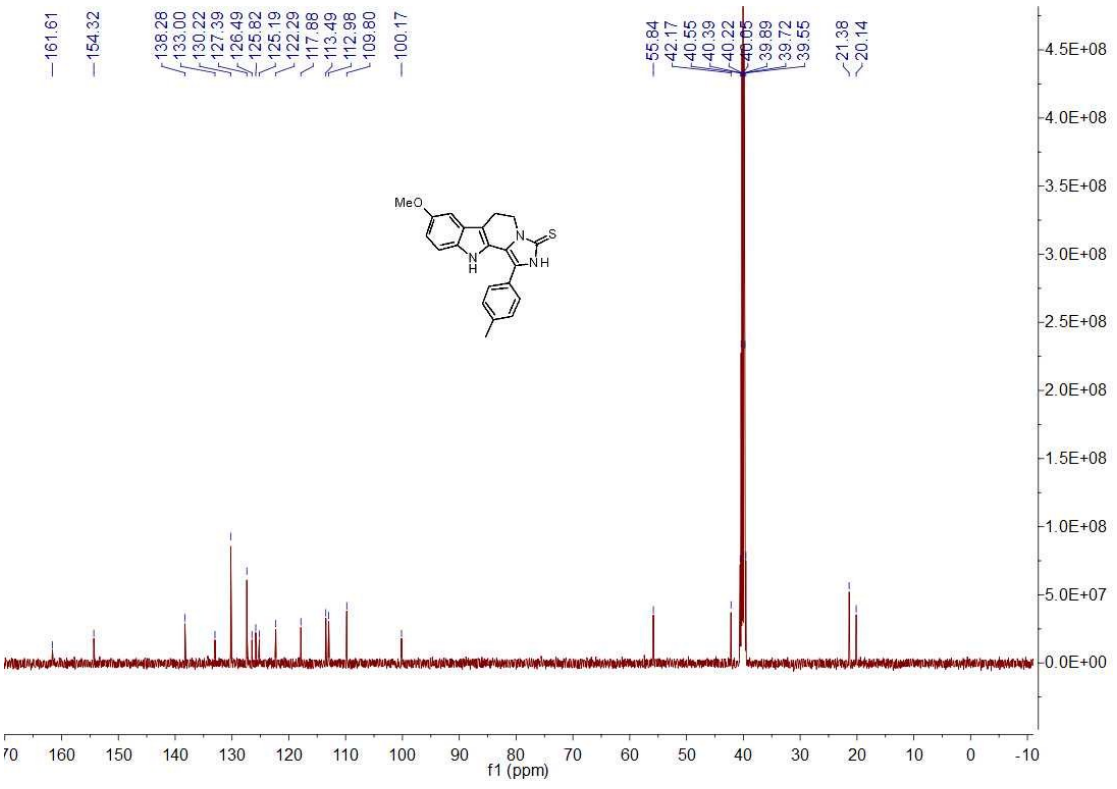
6.731
6.726
4.132
4.119
4.105
3.772
3.106
3.093
3.079
2.383
MeO
N
S
NH
H
0.99
1.04
2.00
2.01
1.06
1.04
1.00
2.03
3.03
2.03
3.04
f1 (ppm)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127.39
126.49
125.82
125.19
122.29
117.88
113.49
112.98
109.80
100.17
55.84
42.17
40.55
40.39
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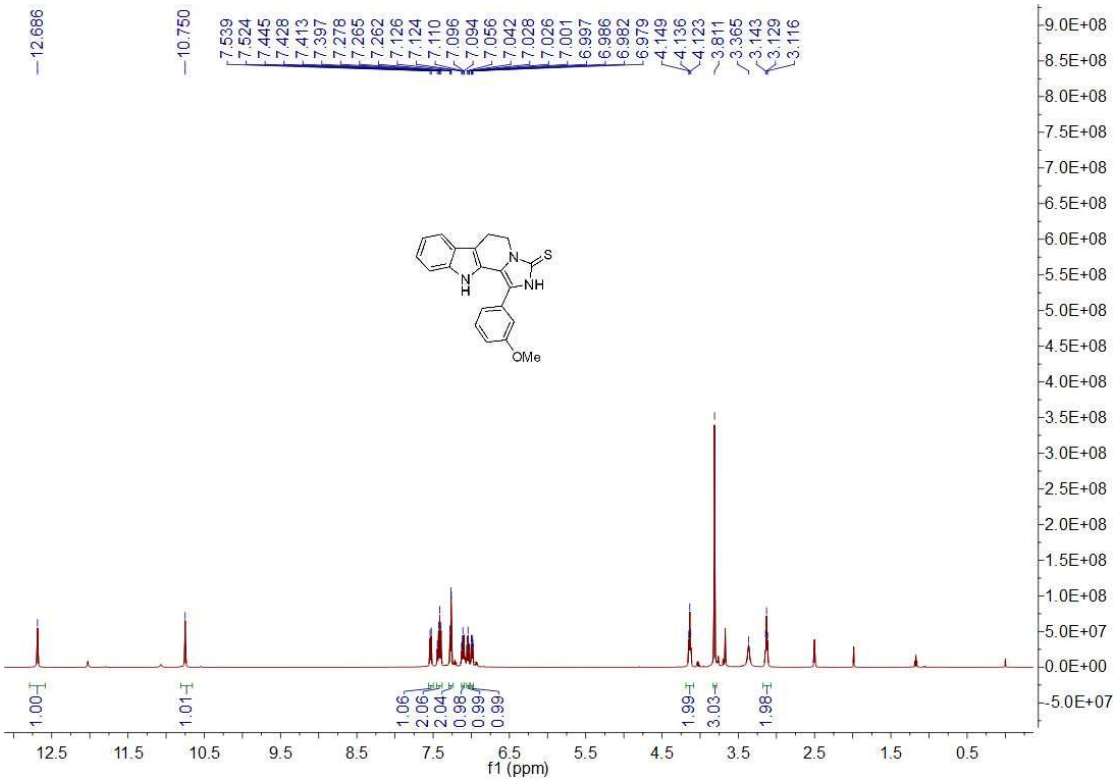
39.89
39.72
39.55
21.38
20.14
MeO
N
S
NH
H
f1 (ppm)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7.265
7.262
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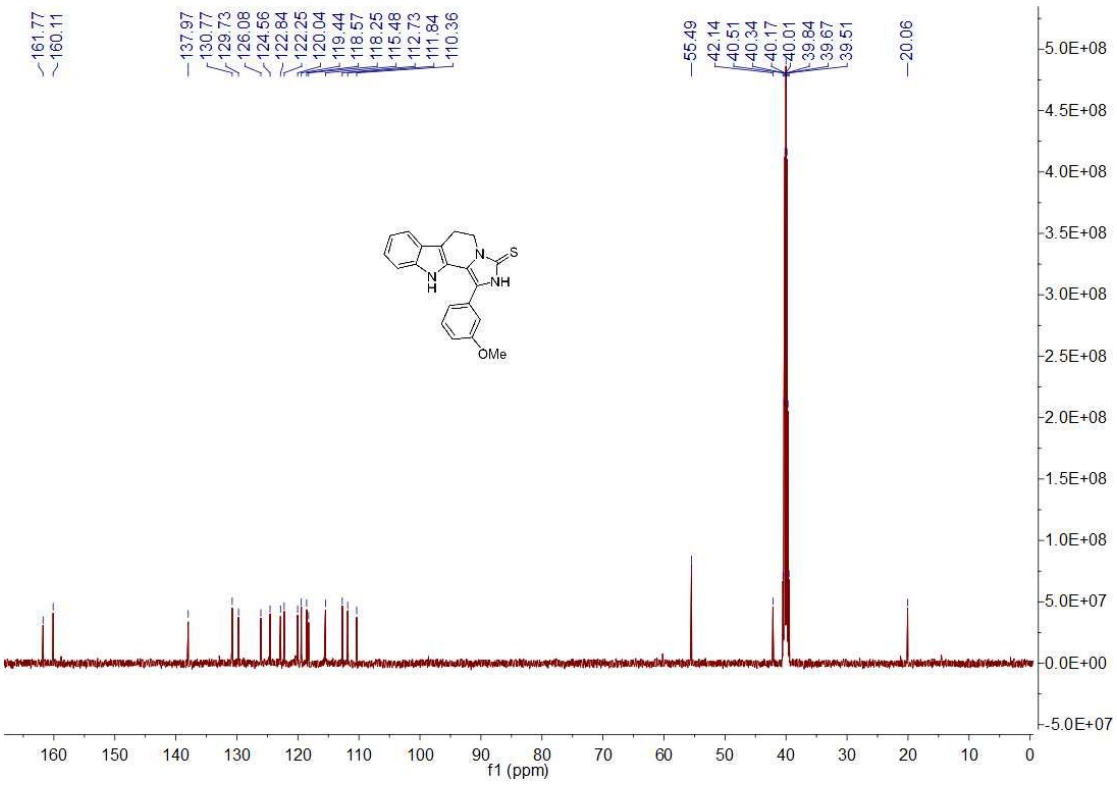
7.124
7.110
7.096
7.094
7.056
7.042
7.028
7.026
7.001
6.997
6.986
6.982
6.979
4.149
4.136
4.123
3.811
3.365
3.143
3.129
3.116
N
S
NH
OMe
1.00
1.01
1.06
2.05
2.04
0.98
0.99
0.99
1.99
3.03
1.98
f1 (ppm)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122.84
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118.25
115.48
112.73
111.84
110.36
55.49
42.14
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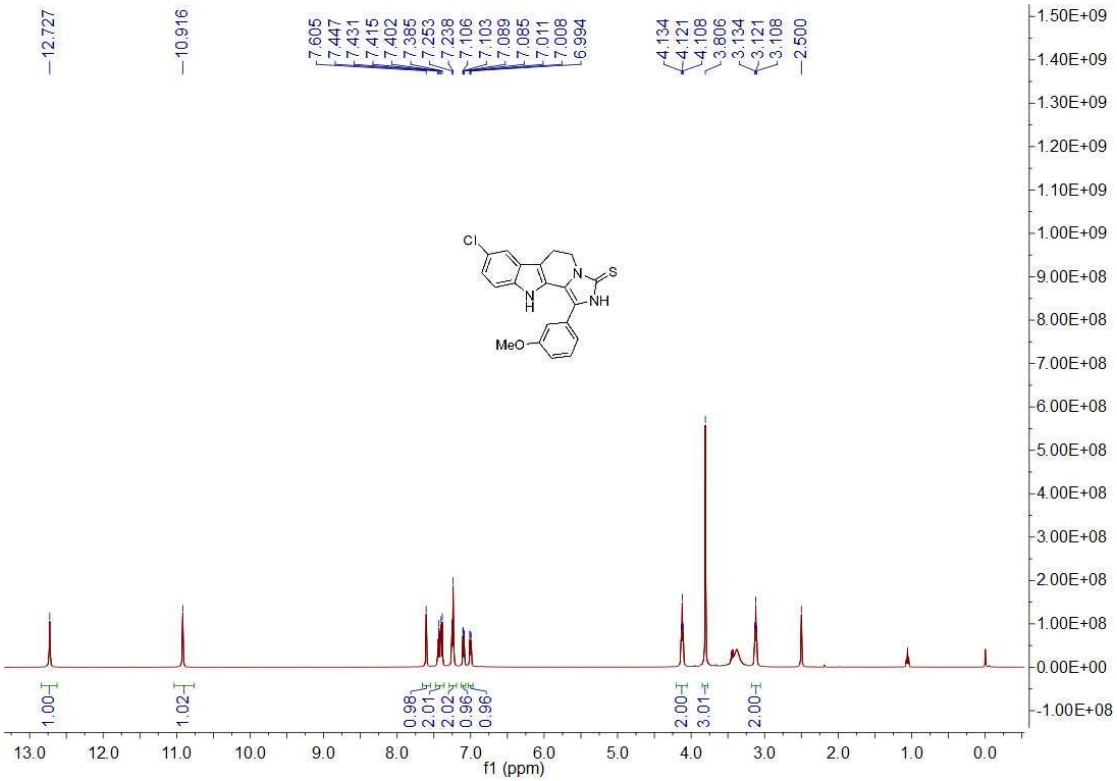
40.34
40.17
40.01
39.84
39.67
39.51
20.06
N
S
NH
OMe
f1 (ppm)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7.385
7.253
7.238
7.106
7.103
7.089
7.085
7.011
7.008
6.994
4.134
4.121
4.108
3.806
3.134
3.121
3.108
2.500
Cl
N
S
NH
H
MeO
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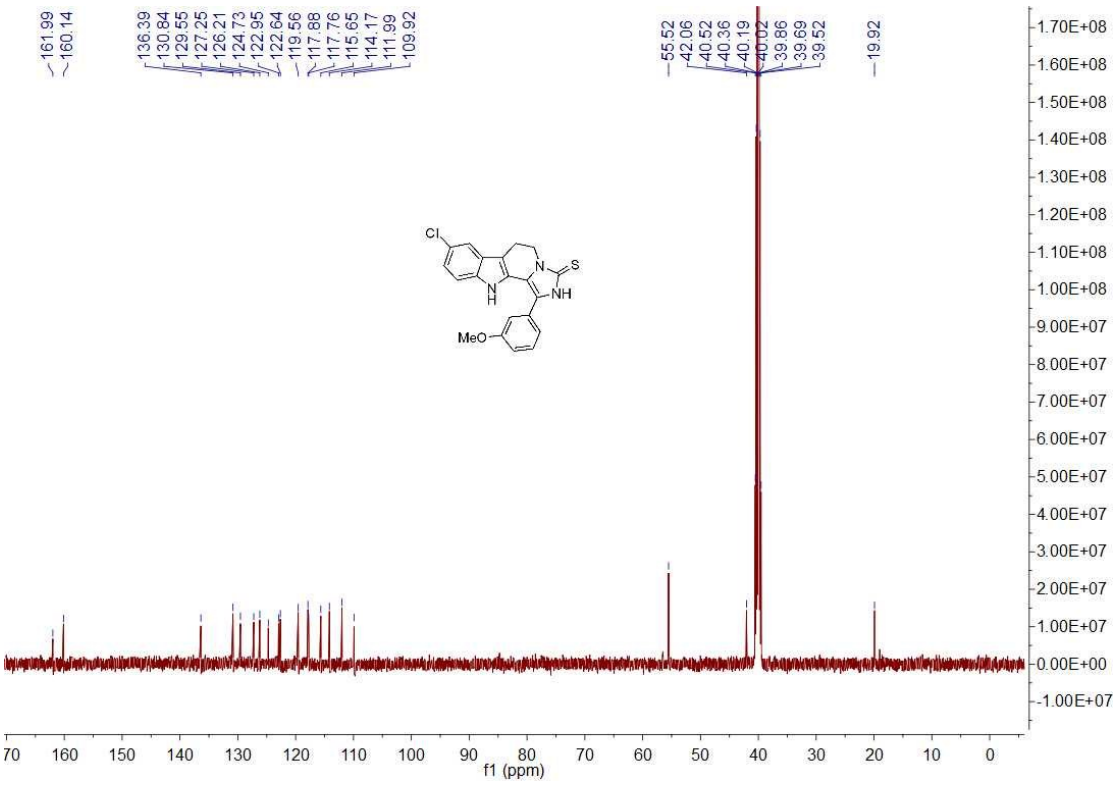
0.98
2.01
2.02
0.96
0.96
2.00
3.01
2.00
f1 (ppm)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117.88
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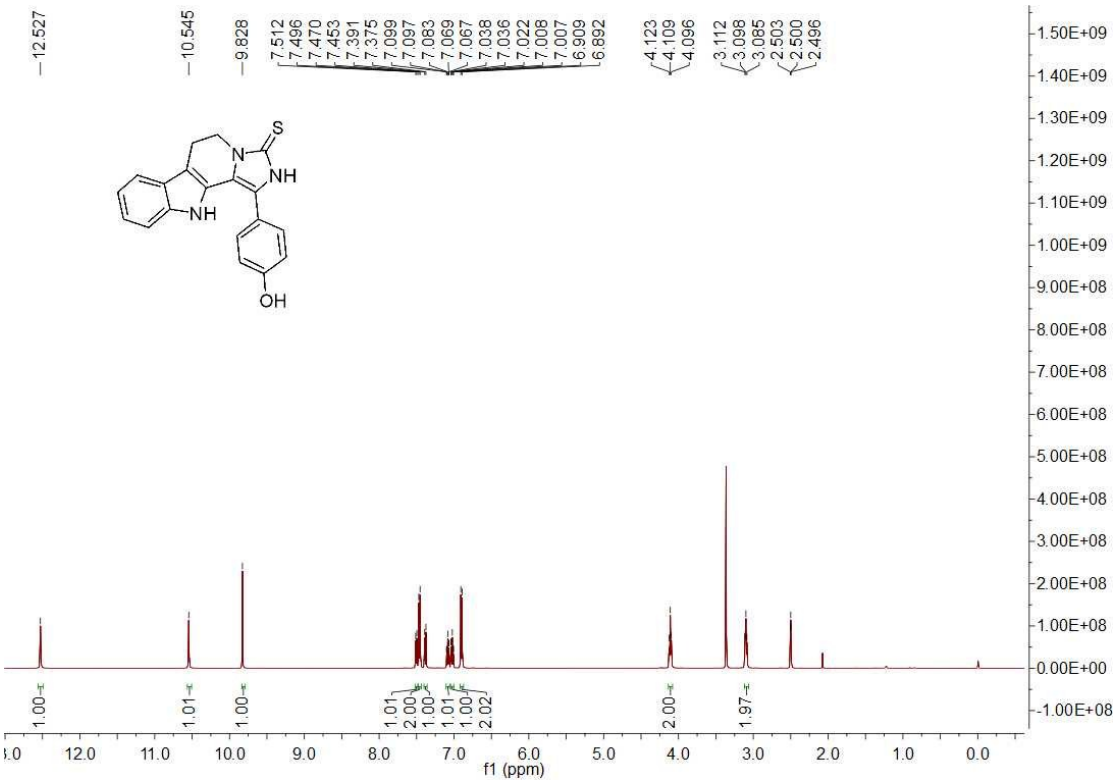
114.17
111.99
109.92
55.52
42.06
40.52
40.36
40.19
40.02
39.86
39.69
39.52
19.92
Cl
N
S
NH
H
MeO
f1 (ppm)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7.391
7.375
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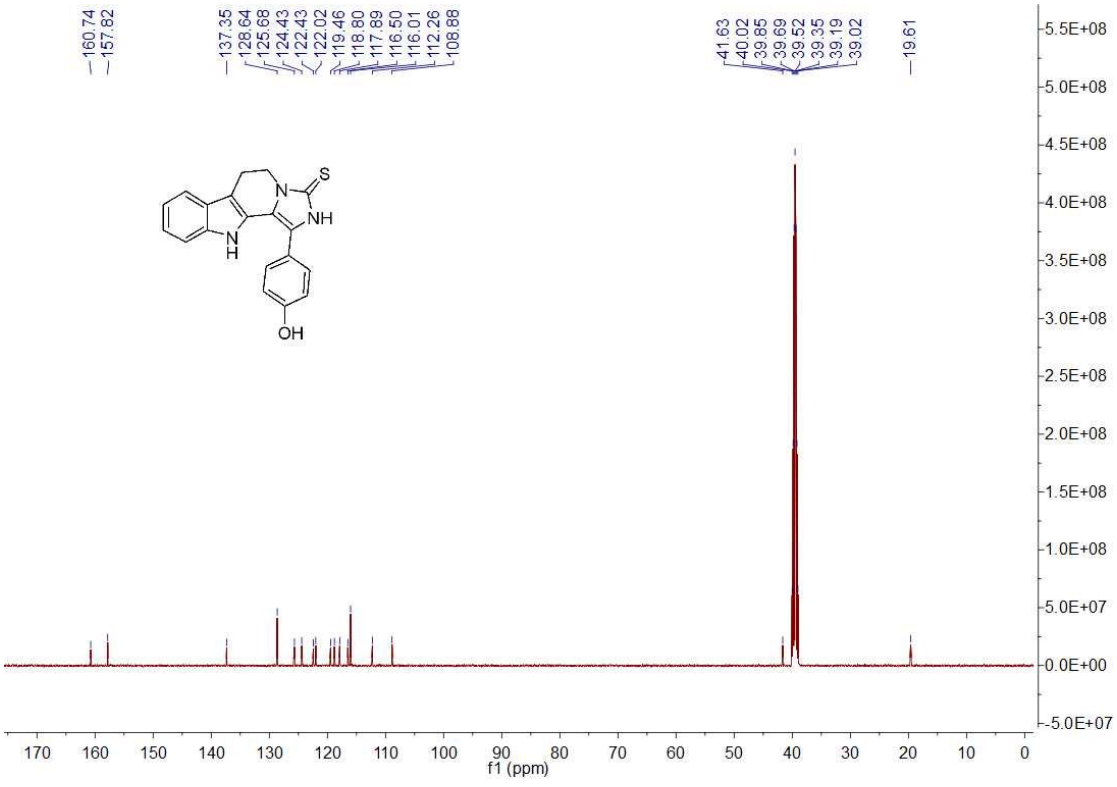
7.097
7.083
7.069
7.067
7.038
7.036
7.022
7.008
7.007
6.909
6.892
4.123
4.109
4.096
3.112
3.098
3.085
2.503
2.500
2.496
S
N
NH
NH
OH
1.50E+09
1.40E+09
1.30E+09
1.20E+09
1.10E+09
1.00E+09
9.00E+08
8.00E+08
7.00E+08
6.00E+08
5.00E+08
4.00E+08
3.00E+08
2.00E+08
1.00E+08
0.00E+00
-1.00E+08
1.00
1.01
1.00
1.01
2.00
1.00
1.01
1.00
2.02
2.00
1.97
f1 (ppm)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124.43
122.43
122.02
119.46
118.80
117.89
116.50
116.01
112.26
108.88
41.63
40.02
39.85
39.69
39.52
39.35
39.19
39.02
19.61
S
N
NH
N
H
OH
5.5E+08
5.0E+08
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
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1.5E+08
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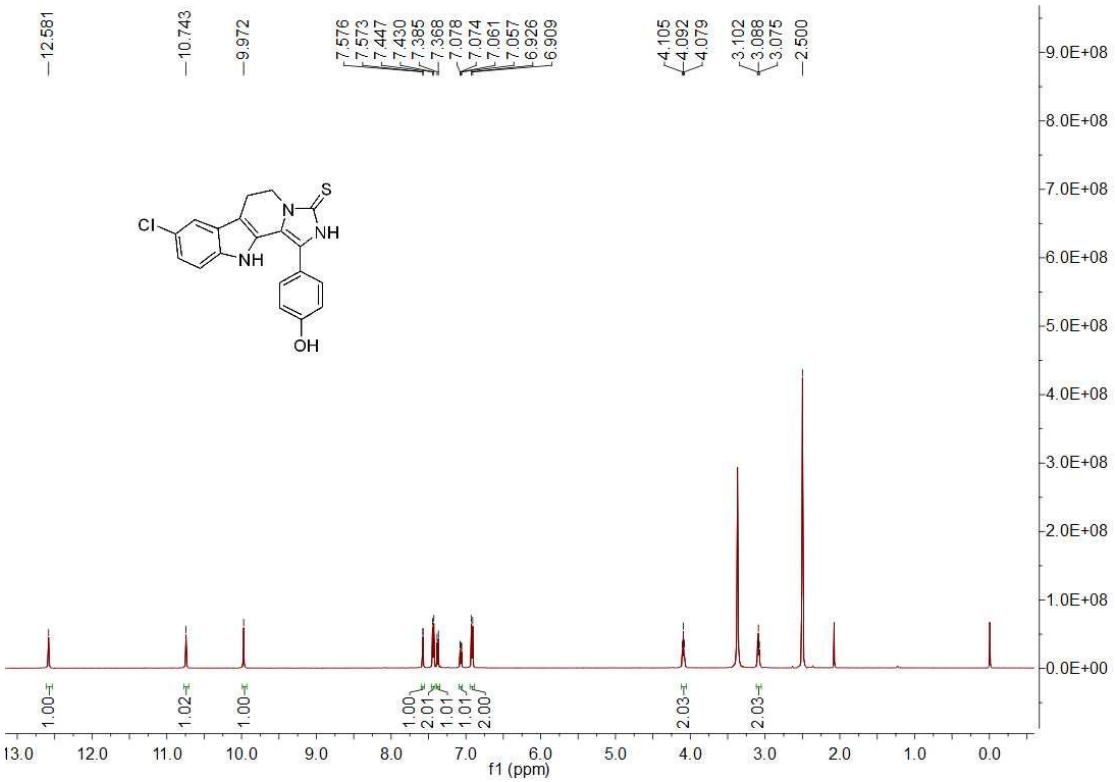
5.0E+07
0.0E+00
-5.0E+07
f1 (ppm)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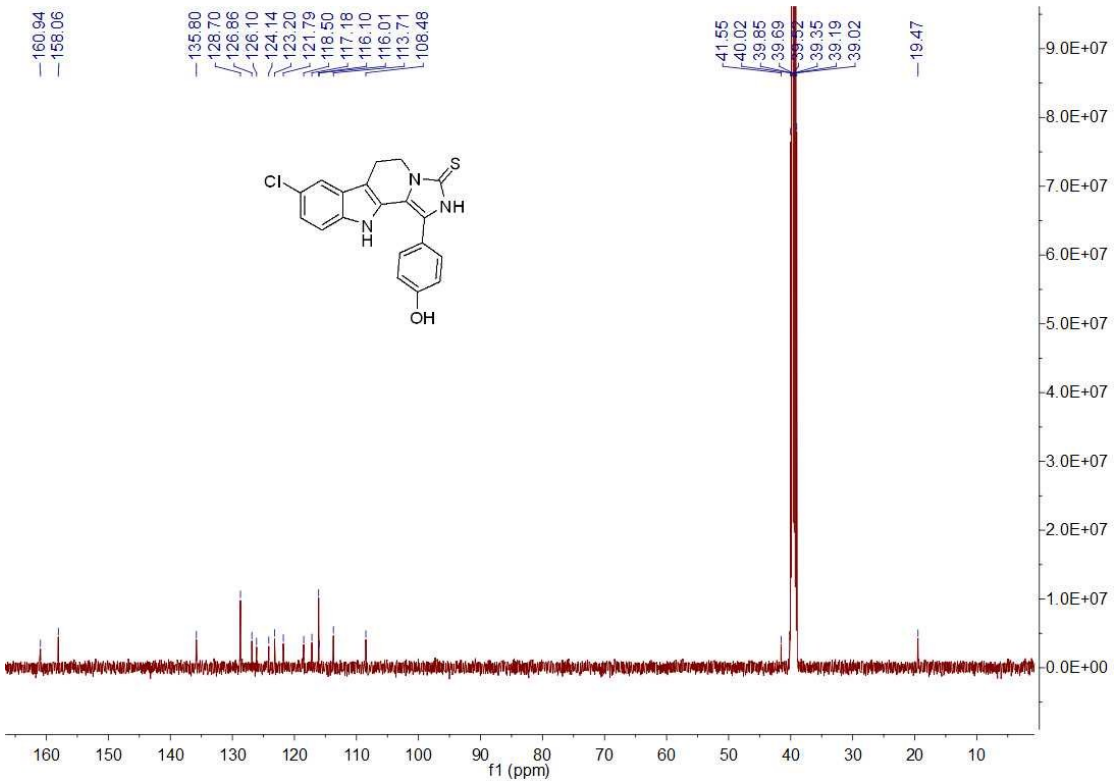
7.385
7.368
7.078
7.074
7.061
7.057
6.926
6.909
4.105
4.092
4.079
3.102
3.088
3.075
2.500
Cl
NH
NH
S
OH
1.00
1.02
1.00
1.00
2.01
1.01
1.01
2.00
2.03
2.03
f1 (ppm)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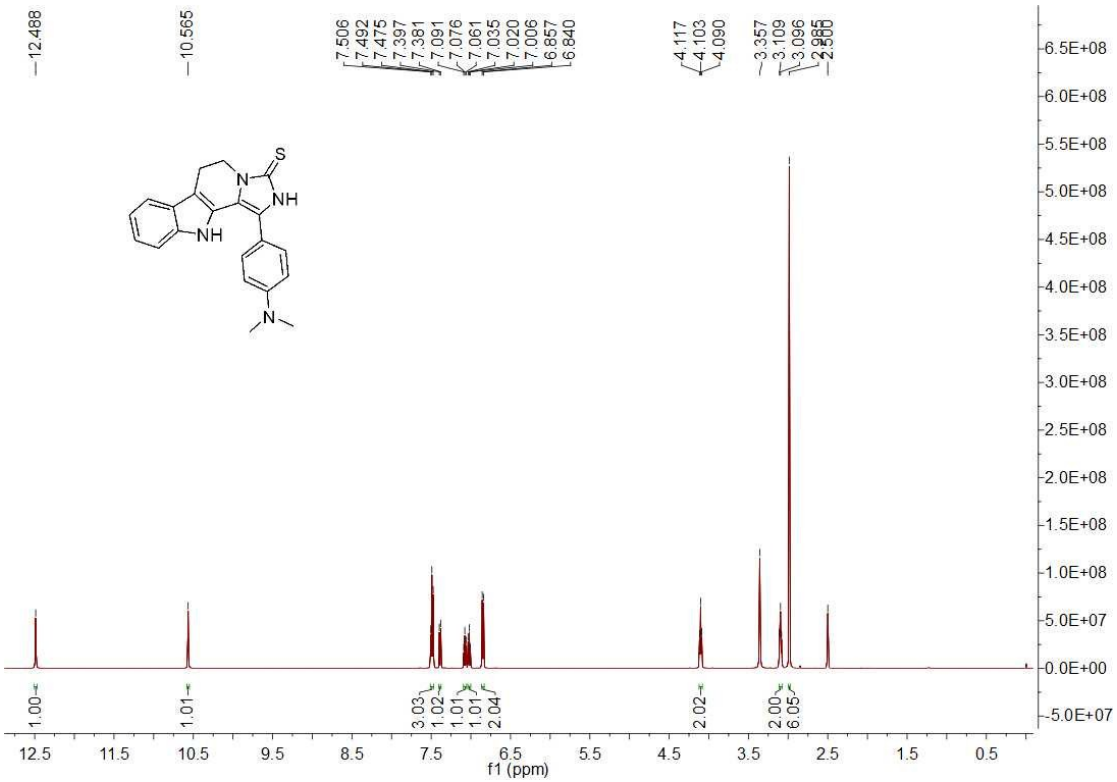
158.06
135.80
128.70
126.86
126.10
124.14
123.20
121.79
118.50
117.18
116.10
116.01
113.71
108.48
41.55
40.02
39.85
39.69
39.52
39.35
39.19
39.02
19.47
Cl
N
H
NH
S
OH
f1 (ppm)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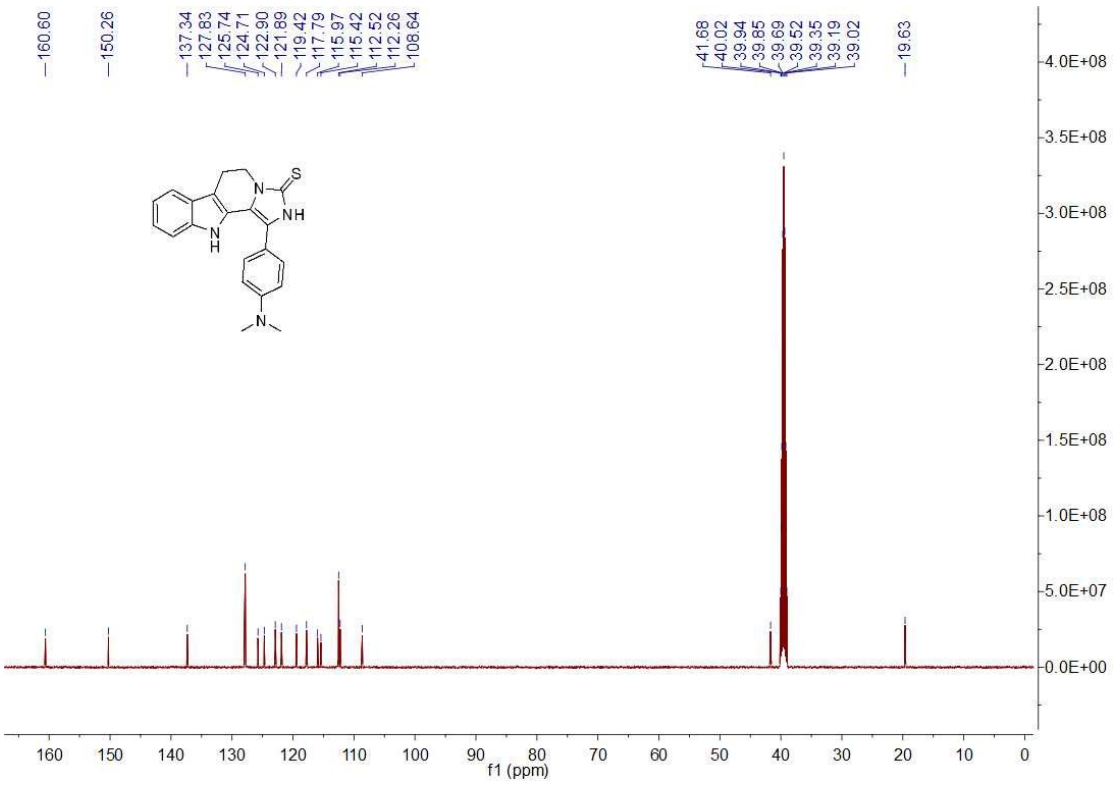
7.091
7.076
7.061
7.035
7.020
7.006
6.857
6.840
4.117
4.103
4.090
3.357
3.109
3.096
1.00
1.01
3.03
1.02
1.01
1.01
2.04
2.02
2.00
6.05
f1 (ppm)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121.89
119.42
117.79
115.97
115.42
112.52
112.26
108.64
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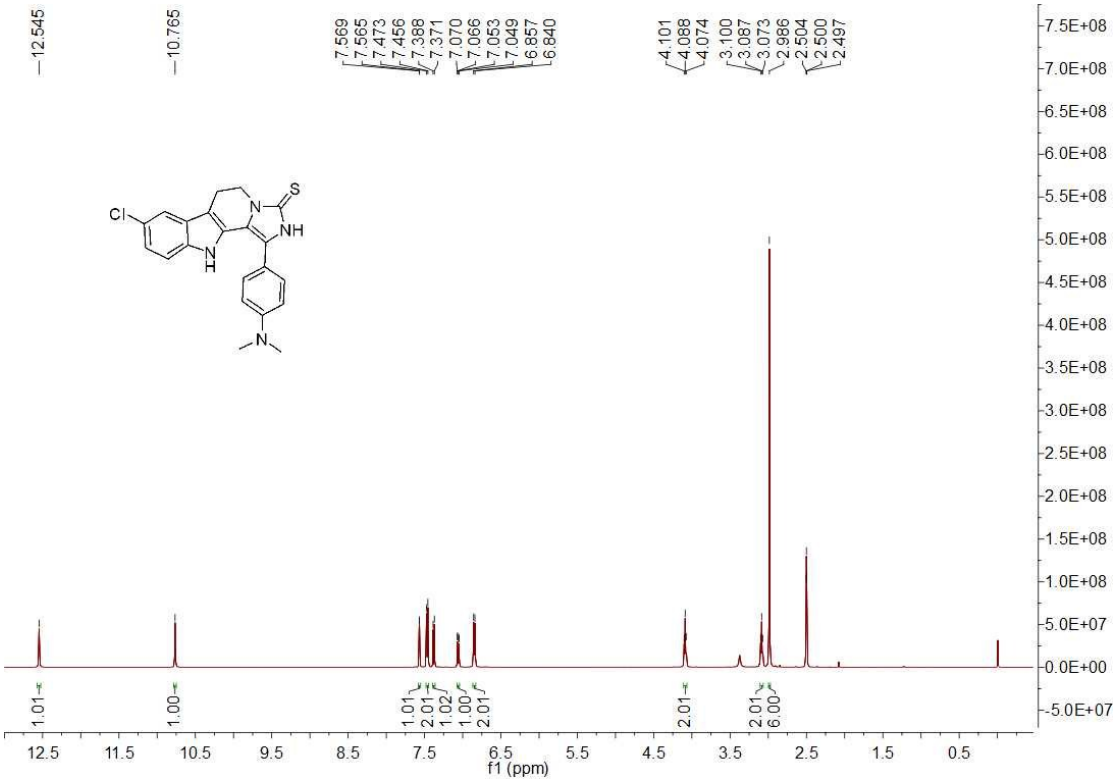
39.94
39.85
39.69
39.52
39.35
39.19
39.02
19.63
f1 (ppm)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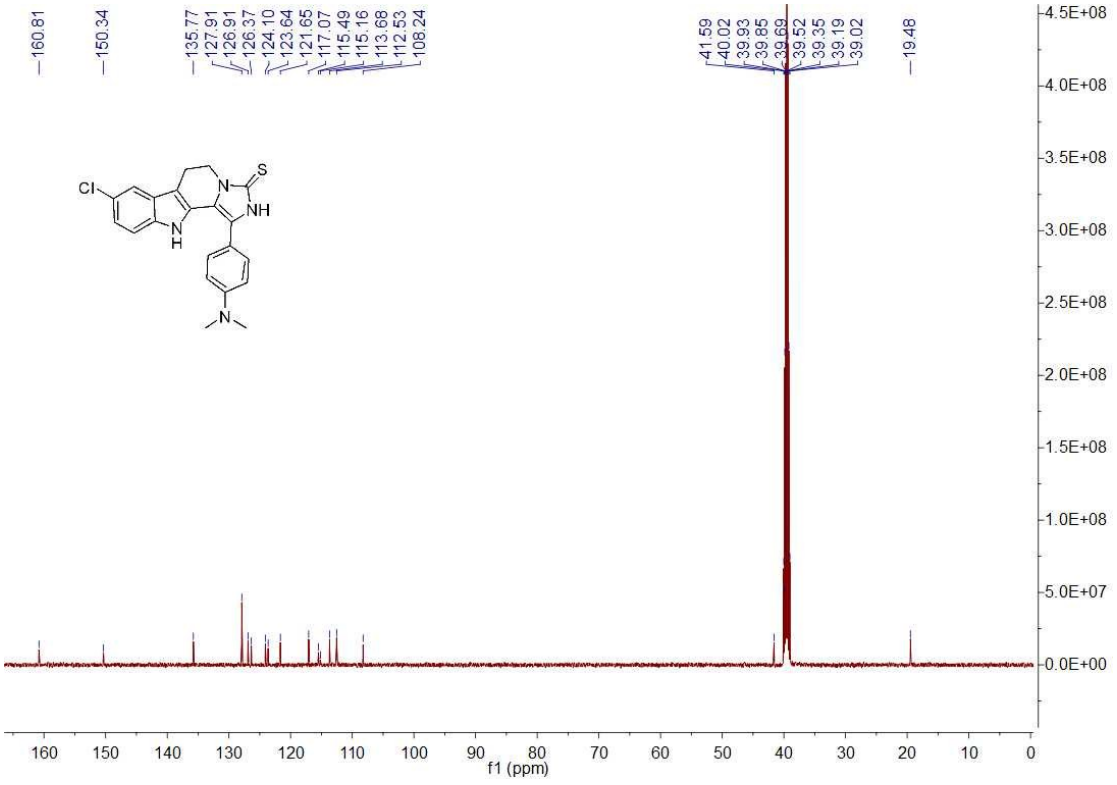
7.456
7.388
7.371
7.070
7.066
7.053
7.049
6.857
6.840
4.101
4.088
4.074
3.100
3.087
3.073
2.986
2.504
2.500
2.497
Cl
S
N
NH
H
N
1.01
1.00
1.01
2.01
1.02
1.00
2.01
2.01
2.01
6.00
f1 (ppm)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117.07
115.49
115.16
113.68
112.53
108.24
41.59
40.02
39.93
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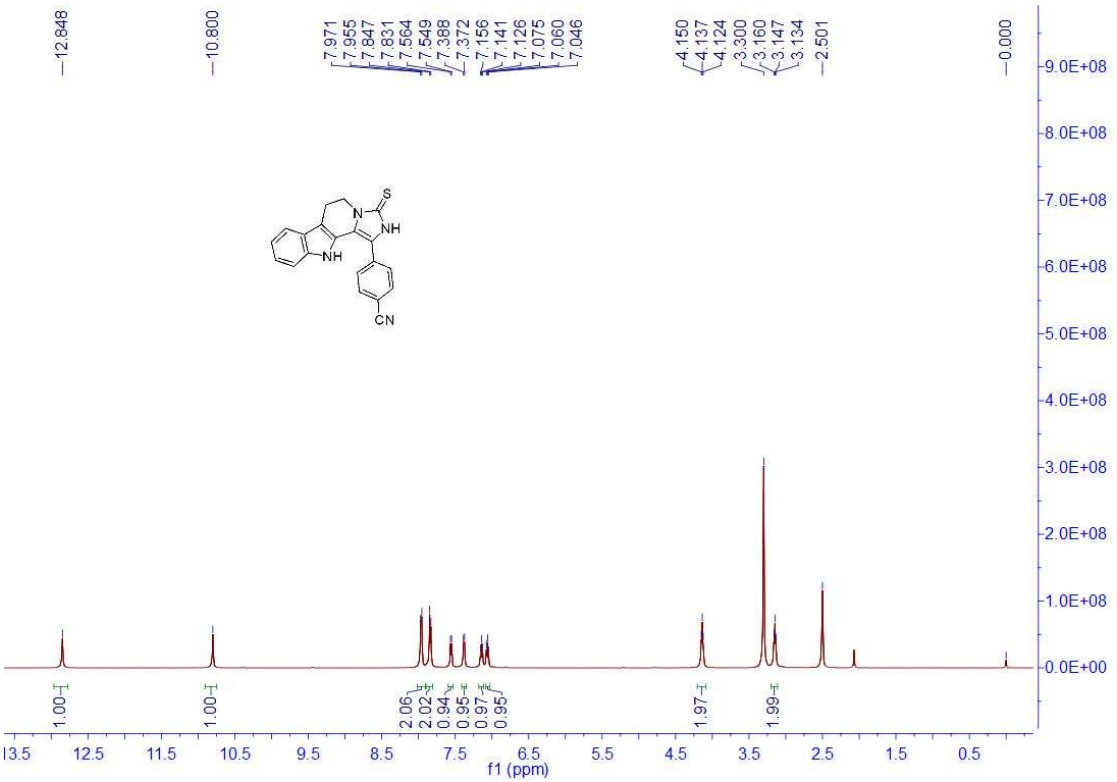
39.52
39.35
39.19
39.02
19.48
Cl
S
N
NH
H
N
f1 (ppm)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7.141
7.126
7.075
7.060
7.046
4.150
4.137
4.124
3.300
3.160
3.147
3.134
2.501
0.000
S
N
NH
NH
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1.00
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2.02
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0.95
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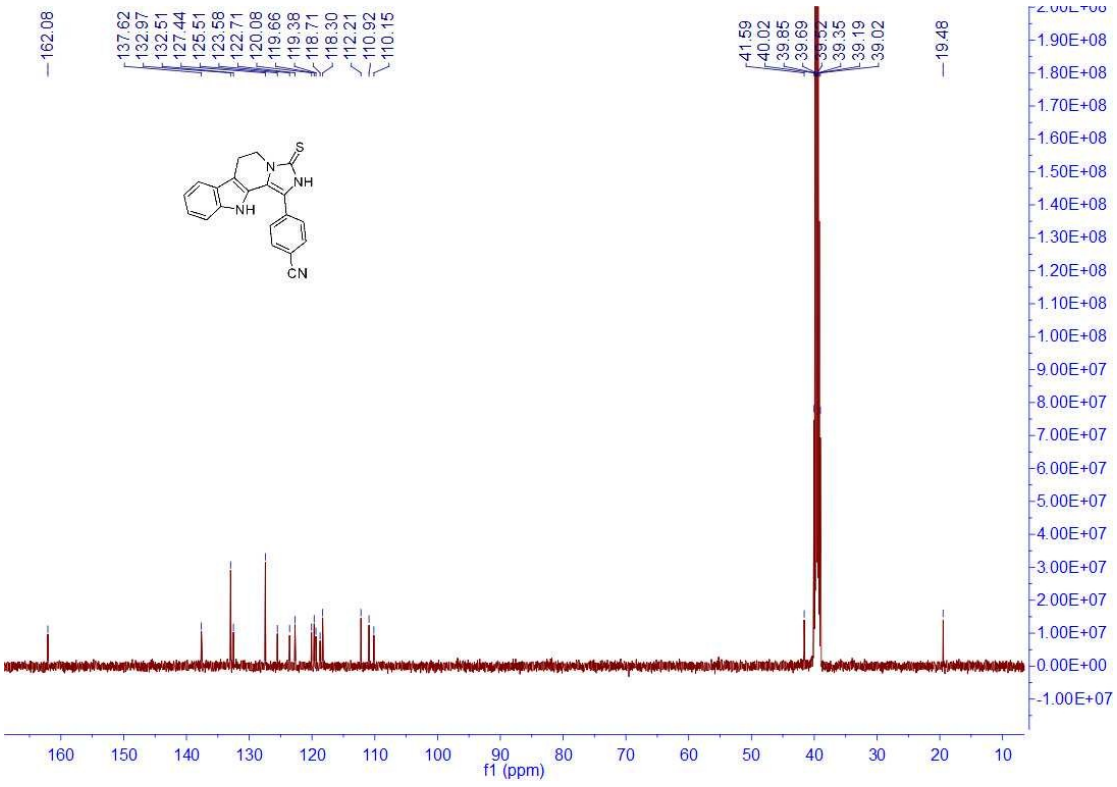
0.95
1.97
1.99
f1 (ppm)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125.51
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122.71
120.08
119.66
119.38
118.71
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112.21
110.92
110.15
41.59
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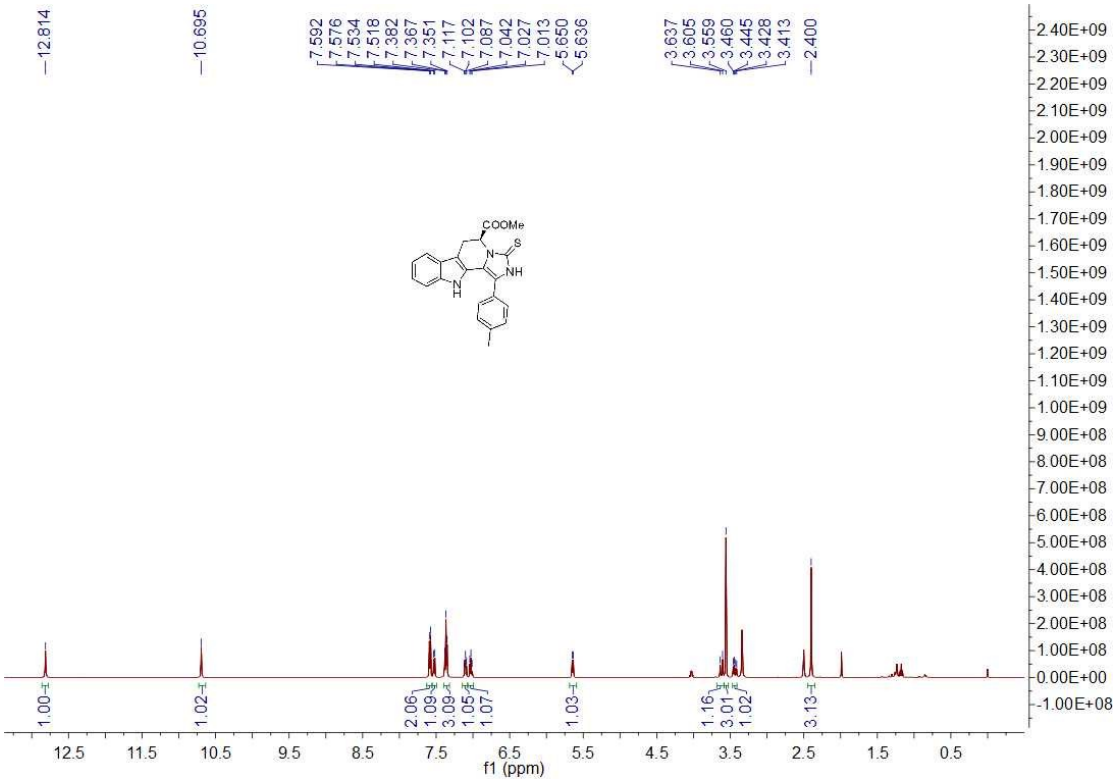
39.69
39.52
39.35
39.19
39.02
19.48
S
NH
NH
CN
f1 (ppm)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7.087
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7.027
7.013
5.650
5.636
3.637
3.605
3.559
3.460
3.445
3.428
3.413
2.400
COOMe
S
NH
N
H
1.00
1.02
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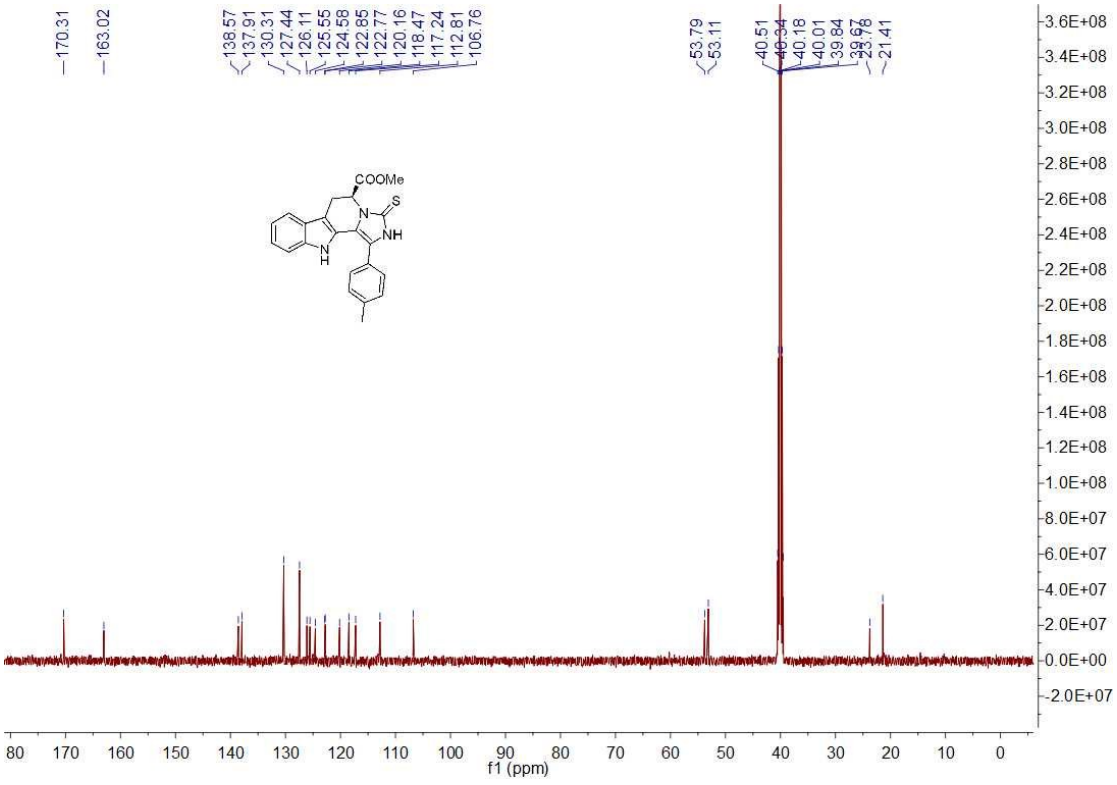
3.09
1.05
1.07
1.03
1.16
3.01
1.02
3.13
f1 (ppm)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125.55
124.58
122.85
122.77
120.16
118.47
117.24
112.81
106.76
53.79
53.11
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40.18
40.01
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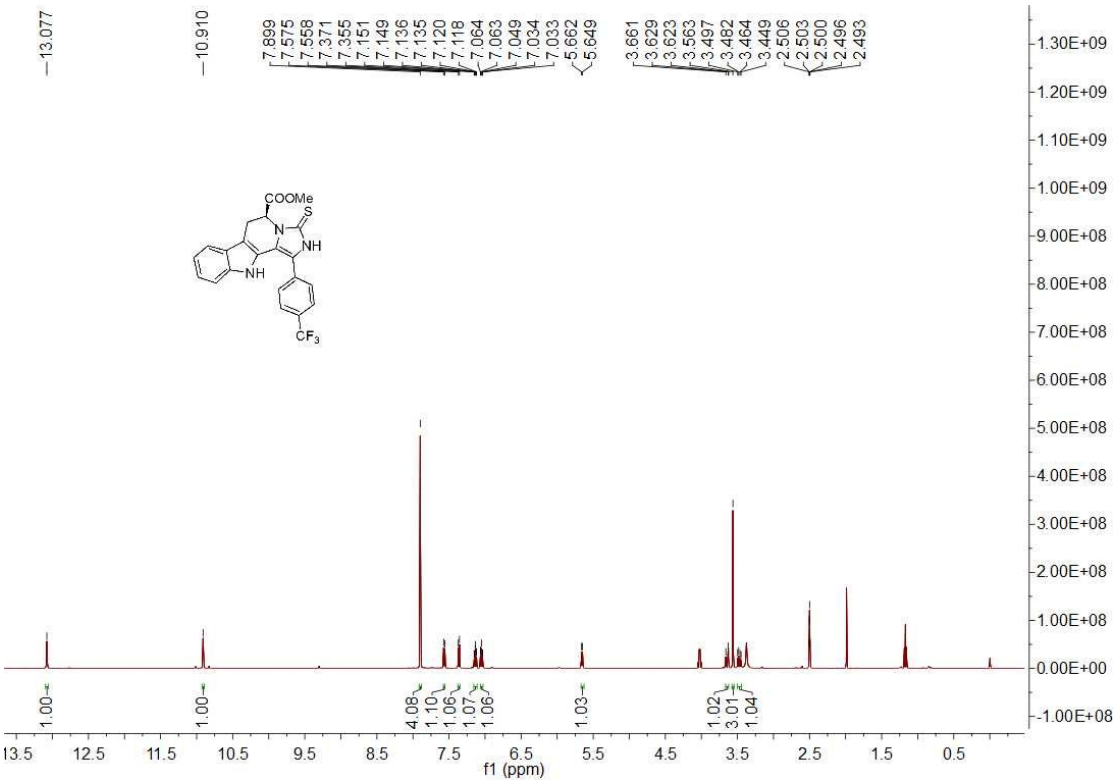
21.41
COOMe
S
NH
N
H
f1 (ppm)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7.135
7.120
7.118
7.064
7.063
7.049
7.034
7.033
5.662
5.649
3.661
3.629
3.623
3.563
3.497
3.482
3.464
3.449
2.506
2.503
2.500
2.496
2.493
COOMe
S
N
NH
NH
CF3
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1.07
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1.03
1.02
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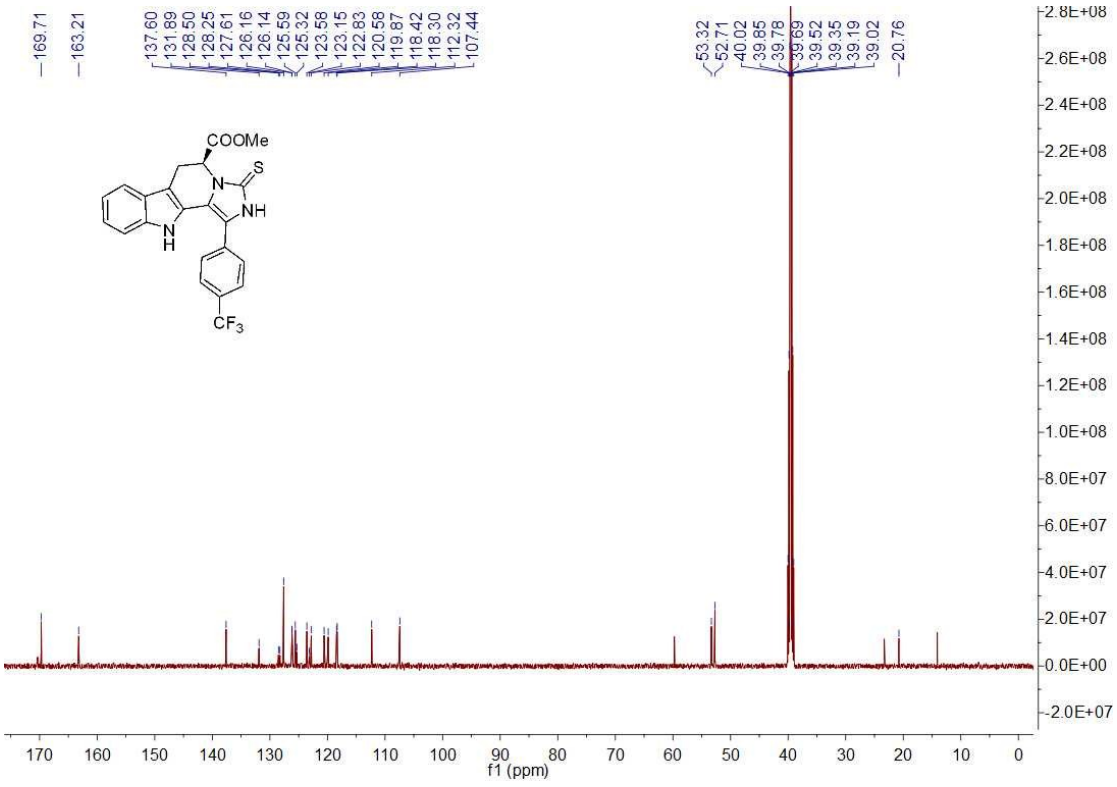
1.04
f1 (ppm)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128.25
127.61
126.16
126.14
125.59
125.32
123.58
123.15
122.83
120.58
119.87
118.42
118.30
112.32
107.44
53.32
52.71
40.02
39.85
39.78
39.69
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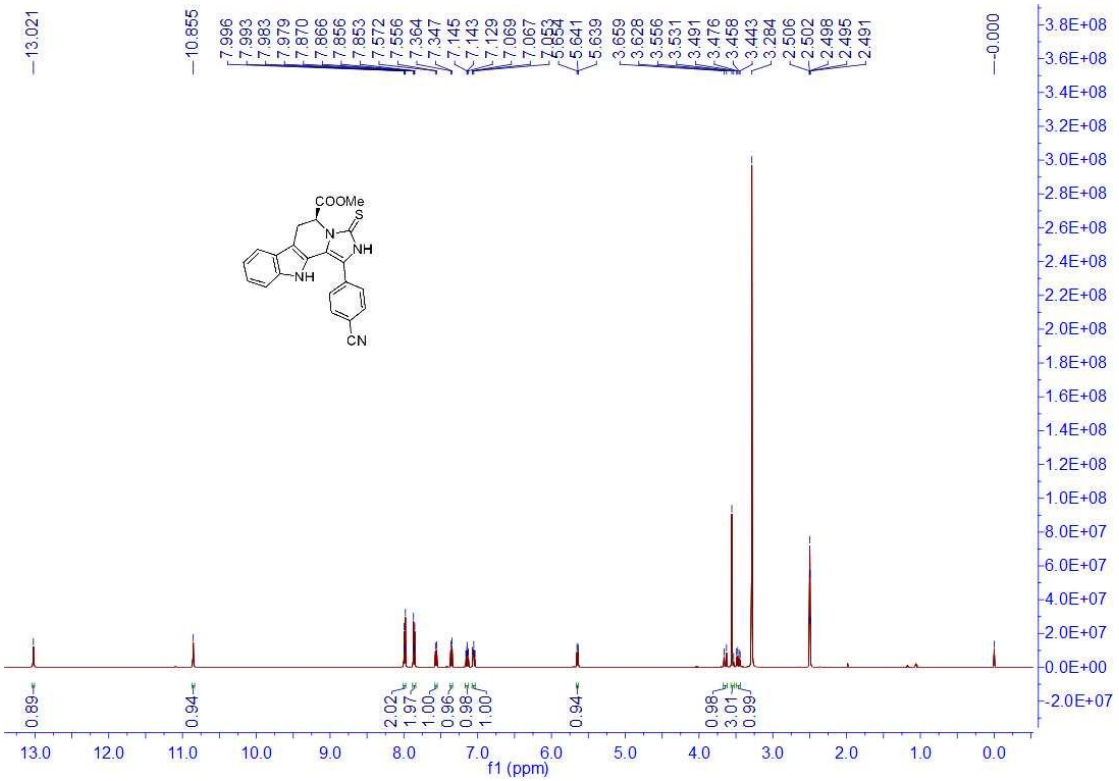
COOMe
S
N
NH
N
H
CF3
f1 (ppm)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7.556
7.364
7.347
7.145
7.143
7.129
7.069
7.067
7.053
5.641
5.639
3.659
3.628
3.556
3.531
3.491
3.476
3.458
3.443
3.284
2.506
2.502
2.498
2.495
2.491
0.000
COOMe
S
N
NH
NH
CN
0.89
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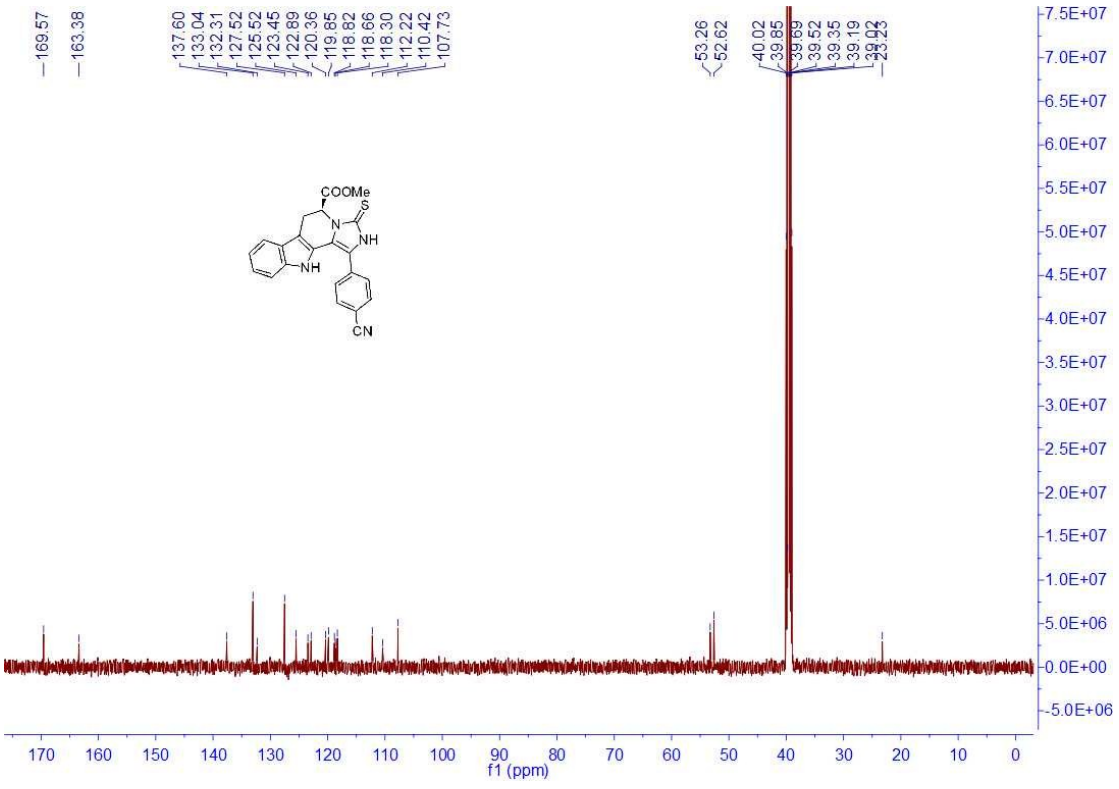
2.02
1.97
1.00
0.96
0.98
1.00
0.94
0.98
3.01
0.99
f1 (ppm)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125.52
123.45
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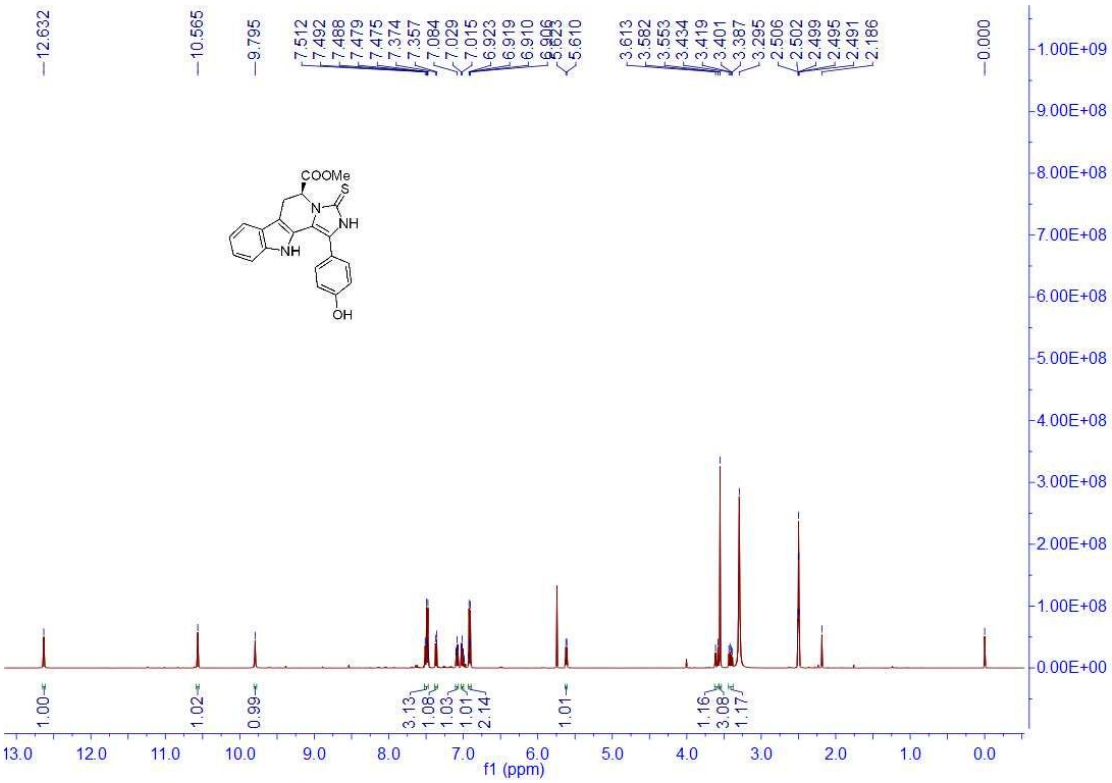
120.36
119.85
118.82
118.66
118.30
112.22
110.42
107.73
53.26
52.62
40.02
39.85
39.69
39.52
39.35
39.19
39.02
23.23
COOMe
S
N
NH
NH
CN
f1 (ppm)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7.512
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7.488
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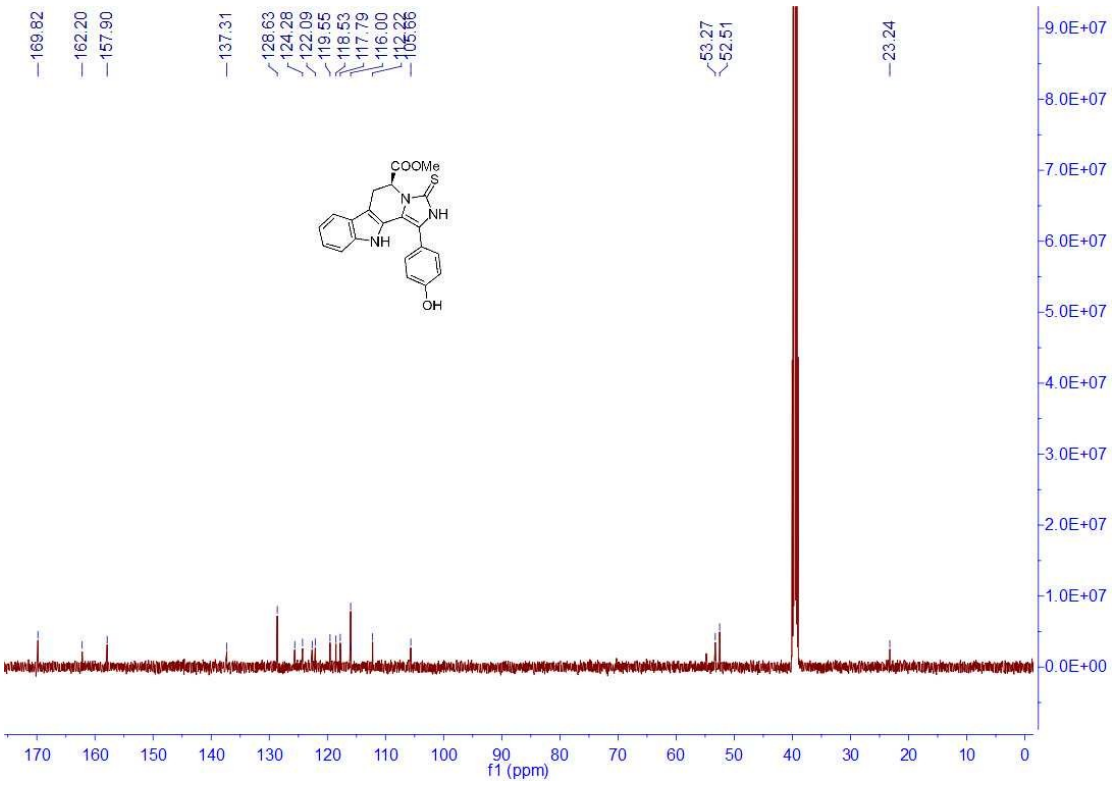
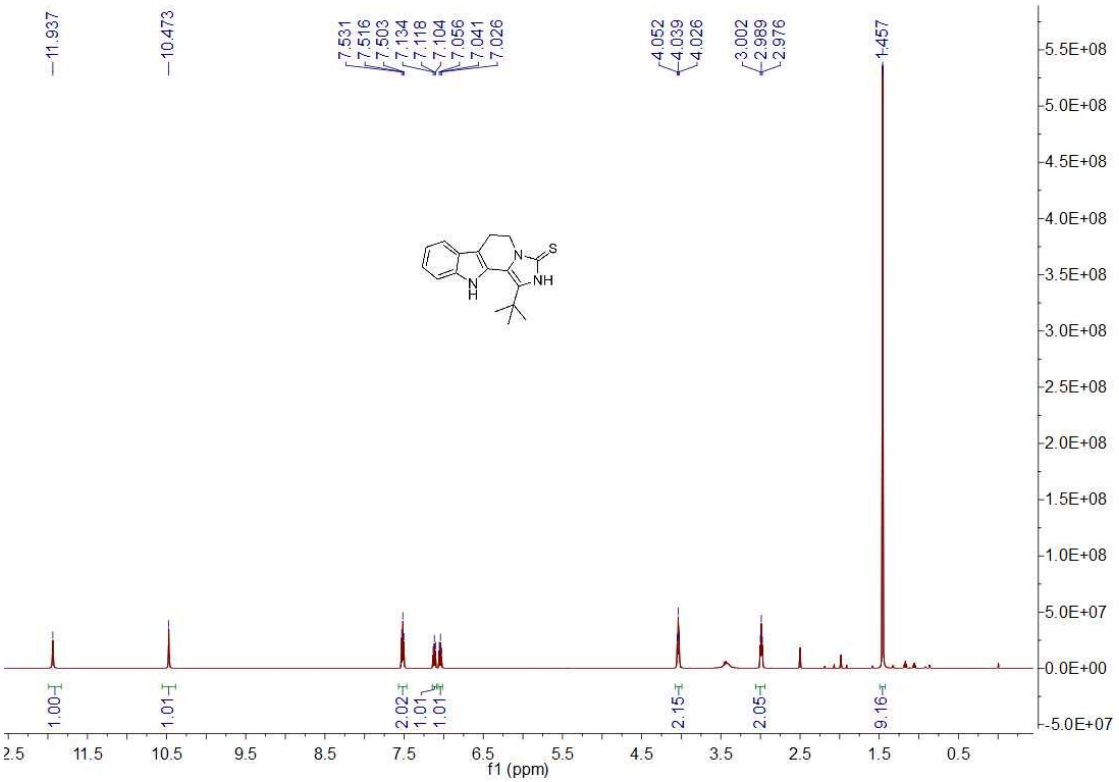
7.357
7.084
7.029
7.015
6.923
6.919
6.910
5.610
3.613
3.582
3.553
3.434
3.419
3.401
3.387
3.295
2.506
2.502
2.499
2.495
2.491
2.186
0.000
COOMe
S
N
NH
NH
OH
1.00
1.02
0.99
3.13
1.08
1.03
1.01
2.14
1.01
1.16
3.08
1.17
f1 (ppm)


169.82
162.20
157.90
137.31
128.63
124.28
122.09
119.55
118.53
117.79
116.00
53.27
52.51
23.24
COOMe
S
N
NH
NH
OH
f1 (ppm)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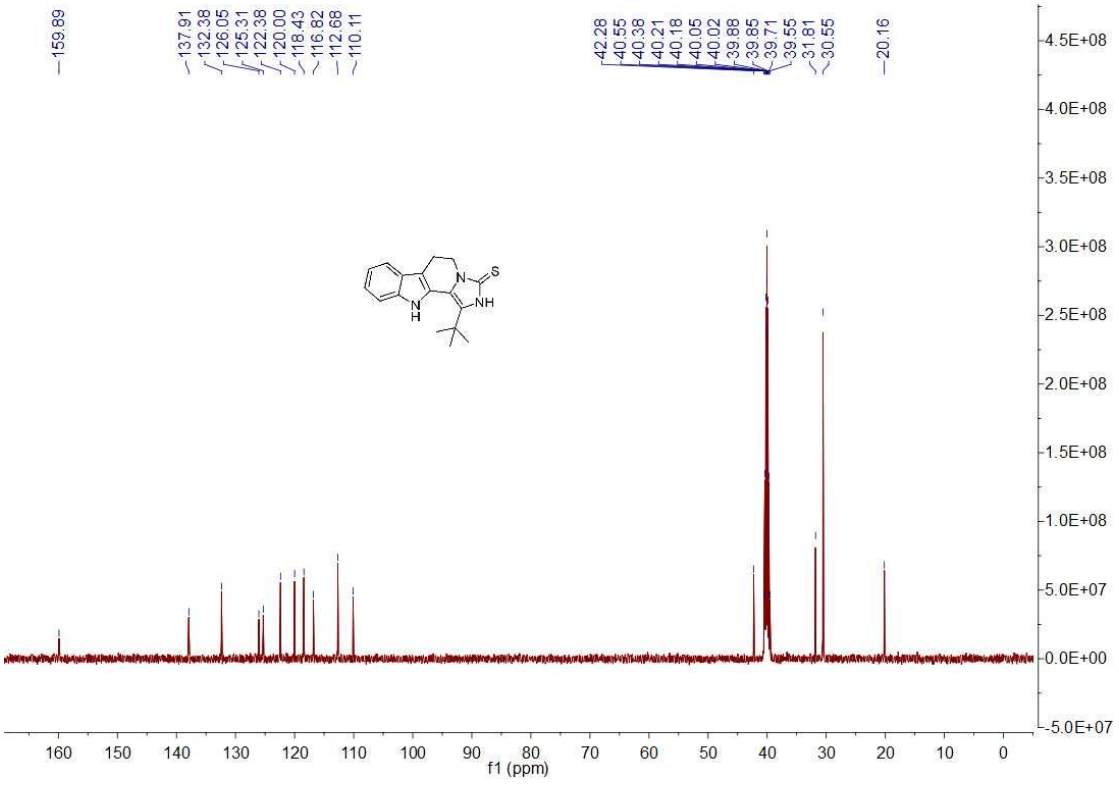
10.473
7.531
7.516
7.503
7.134
7.118
7.104
7.056
7.041
7.026
4.052
4.039
4.026
3.002
2.989
2.976
1.457
1.00
1.01
2.02
1.01
1.01
2.15
2.05
9.16
f1 (ppm)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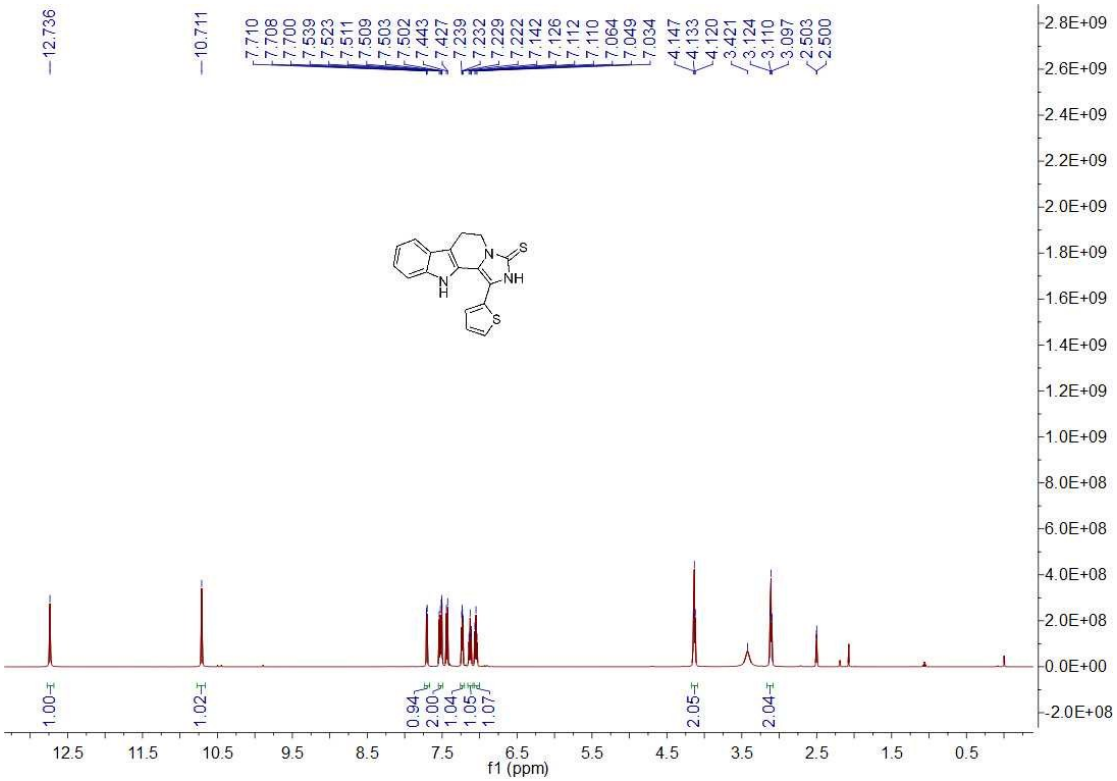
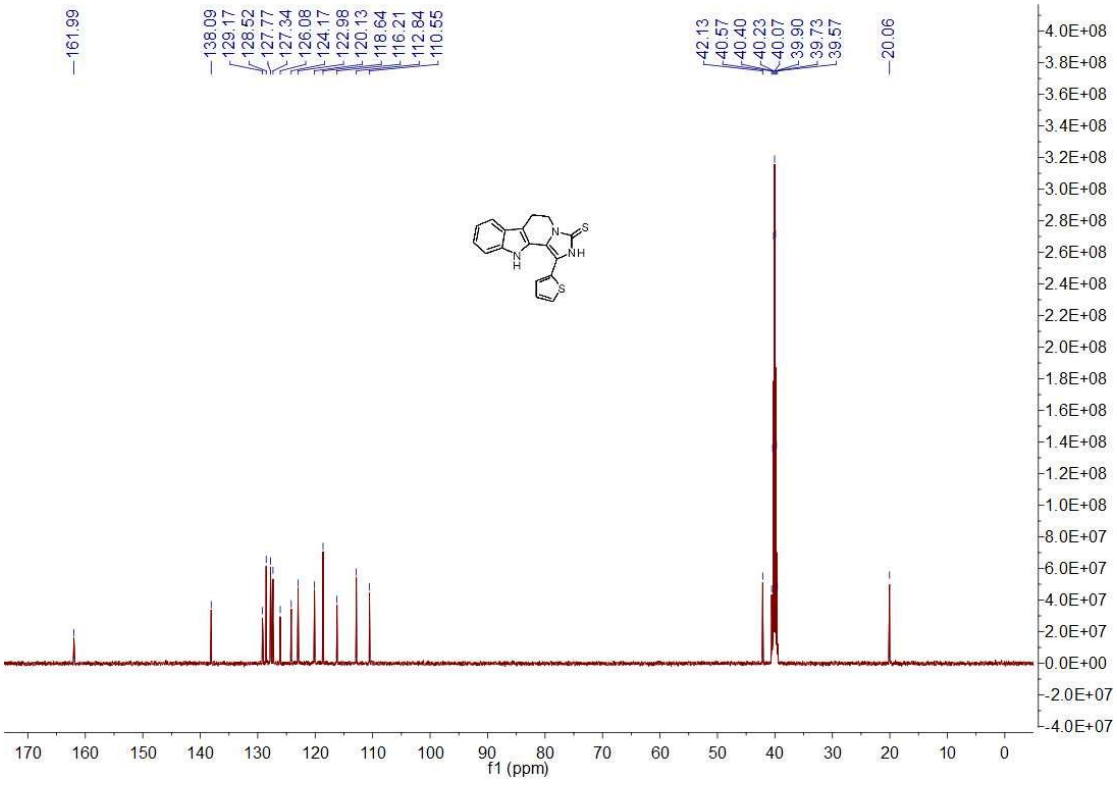
137.91
132.38
126.05
125.31
122.38
120.00
118.43
116.82
112.68
110.11
42.28
40.55
40.38
40.21
40.18
40.05
40.02
39.88
39.85
39.71
39.55
31.81
30.55
20.16
f1 (ppm)


12.736
10.711
7.710
7.708
7.700
7.539
7.523
7.511
7.509
7.503
7.502
7.443
7.427
7.239
7.232
7.229
7.222
7.142
7.126
7.112
7.110
7.064
7.049
7.034
4.147
4.133
4.120
3.421
3.124
3.110
3.097
2.503
2.500
1.00
1.02
0.94
2.00
1.04
1.05
1.07
2.05
2.04
f1 (ppm)


161.99
138.09
129.17
128.52
127.77
127.34
126.08
124.17
122.98
120.13
118.64
116.21
112.84
110.55
42.13
40.57
40.40
40.23
40.07
39.90
39.73
39.57
20.06
f1 (ppm)