New Journal of Chemistry

p-Toluenesulfonic acid-catalyzed regioselective C4-H iodination of isoquinolin-1(2*H*)-ones with *N*-iodosuccinimide

Cai-Yun Yang[a], Lin-Ping Hu[a], De-Run Zhang[a], Xia Li[b], Ming-Yu Teng[a], Bo Liu[a] and Guo-Li Huang*[a]

[a] School of Chemistry and Chemical Engineering, [b] Department of Library, Yunnan Normal University, Kunming, P. R. China

Tel & Fax: +86-871-65941087; E-mail: hgli2005@126.com

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1. Experimental section

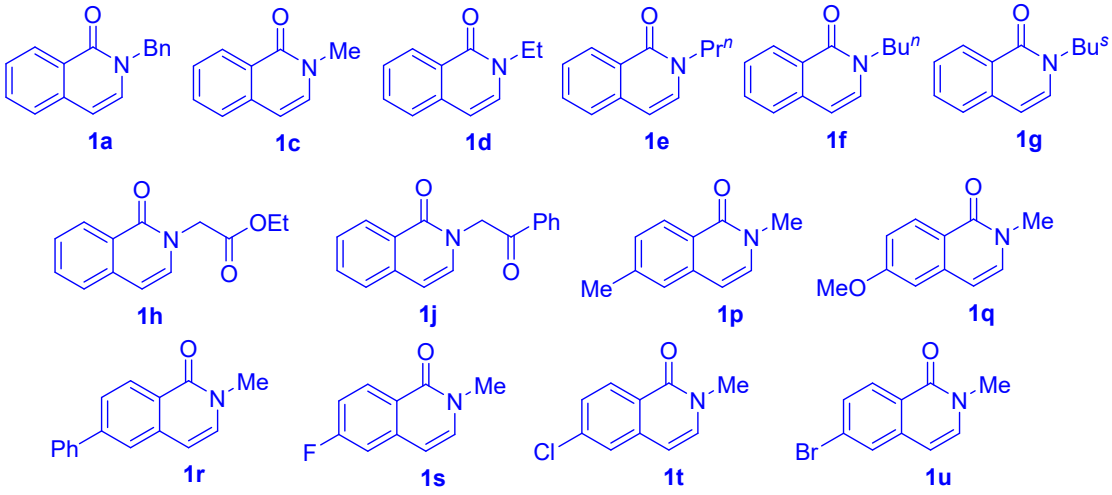
All chemicals were purchased from the Wencai New Material Technology and Merck in high purityand were used directly without any purification.Solvents were freshly distilled prior to use. All reactions were carried out under air atmosphere unless noted. ^{1}H NMR and ^{13}C NMR spectra were recorded with a Bruker Avance III 500 MHz spectrometer in $CDCl_3$ or DMSO-*d6* solution. Highresolution mass (HRMS) spectra were measured with a VG Auto Spec-3000 spectrometer. Melting points (mp) were determined with a digital electrothermal apparatus without further correction. TLC analyses were performed on commercial glass plates bearing a 0.25mm layer of Merck silica gel 60 F254. Silica gel (200-300 mesh) was used for column chromatography.

2. Experimental procedures

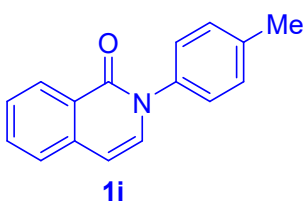
A. General procedure for preparation of N^2-alkylated isoquinolin-1(2*H*)-ones[1]

Isoquinolin-1(2*H*)-ones (1.0 mmol, 1.0 equiv.), halides (1.5 mmol, 1.5 equiv.), cesium carbonate (1.5 mmol, 1.5 equiv.) and DMF (5.0 mL) were added to a 25 mL round bottom flask, and reacted at 50 ℃ for 3 hours. After the reaction was completed, water was added and extracted by ethyl acetate (3×10 mL), then the organic phases were combined which was washed by 10 mL saturated brine and dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure and purified by silica gel column chromatography.

Isoquinolin-1(2*H*)-ones (1a, 1c-1h, 1j, 1p-1u) were synthesized using the above method:



B. Preparation of 2-(*p*-tolyl)isoquinolin-1(*2H*)-one (1i)[2]



Isoquinolin-1(2*H*)-one (0.4 mmol, 1.0 equiv.), p-iodotoluene (0.8 mmol, 2.0 equiv.), potassium carbonate (0.4 mmol, 1.0 equiv.), CuI (0.04 mmol, 0.1 equiv.), DMF (1 mL) was added to a 10 mL round-bottom flask, and reacted at 150 °C for 6 hours under N_2 protection. After the reaction was completed, 10 mL ethyl acetate was diluted and ammonia water was added. The aqueous layer was continuously extracted with ethyl acetate (10 mL). The organic phases were combined and saturated salt. It

was washed with water, dried with anhydrous magnesium sulfate, and purified by silica gel column chromatography

C. General experimental procedure for iodination of isoquinolin-1(2*H*)-ones with *N*-iodosuccinimide

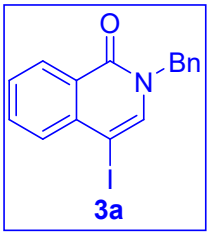
A 10 mL round-bottom flask equipped with a magnetic stir bar was charged with a mixture of isoquinolin-1(2*H*)-one (0.2 mmol, 1.0 equiv.), *N*-iodosuccinimide (0.24 mmol, 1.2 equiv.), *p*-toluenesulfonic acid monohydrate (0.02 mmol, 0.1 equiv), and DCE (1mL). The vial was capped, and the reaction mixture was stirred at room temperature for 18 h under Ar atmosphere. Upon completion, saturated $NaHSO_3$ (5 mL) and distilled deionized H_2O (10 mL) was added, and the mixture was extracted with ethyl acetate (3×10 mL). The combined organic layer was washed with saturated NaCl, dried over anhydrous $MgSO_4$, and concentrated in vacuo. The crude product was purified by SiO_2 column chromatography to afford the desired products.

Reference:

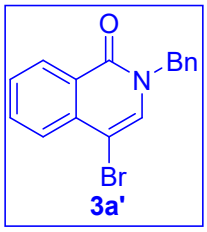
[1] A. C. Shaikh, D. R. Shinde, N. T. Patil, *Org. Lett.* **2016**, *18*, 1056-1059.

[2] J. Li, Y. Yang, Z. Wang, B. Feng, J. You, *Org. lett.* **2017**, *19*, 3083-3086.

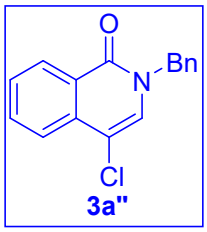
3. ^{1}H and ^{13}C NMR data of 4-iodoisoquinolin-1(2*H*)-ones (3a-3u)



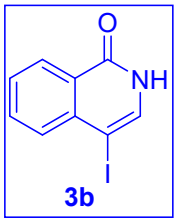
2-Benzyl-4-iodoisoquinolin-1(2*H*)-one (3a)[1]: White solid, yield: 90% (65.0 mg), Mp: 103-105 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.44 (d, *J* = 8.0 Hz, 1H), 7.76-7.70 (m, 1H), 7.67 (d, *J* = 8.0 Hz, 1H), 7.58-7.52 (m, 2H), 7.40-7.28 (m, 5H), 5.20 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.8 (*C*=O), 137.6 (Ar-C), 137.2 (Ar-C), 136.5 (Ar-C), 133.5 (Ar-C), 130.6 (Ar-C), 129.1 (Ar-C), 128.6 (Ar-C), 128.3 (Ar-C), 128.2 (Ar-C), 128.1 (Ar-C), 126.8 (Ar-C), 72.4 (*C*-I), 51.8 (-*C*H_2).



2-Benzyl-4-bromoisoquinolin-1(2*H*)-one (3a')[2]: Yellow solid, yield: 56% (35.2 mg), Mp: 68-70 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.53-8.44 (m, 1H), 7.81 (d, *J* = 7.9 Hz, 1H), 7.78-7.72 (m, 1H), 7.60-7.54 (m, 1H), 7.40-7.29 (m, 6H), 5.21 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.5 (*C*=O), 136.4 (Ar-C), 135.6 (Ar-C), 133.2 (Ar-C), 131.9 (Ar-C), 129.1 (Ar-C), 128.6 (Ar-C), 128.3 (Ar-C), 128.2 (Ar-C), 128.1 (Ar-C), 126.7(Ar-C), 126.0 (Ar-C), 100.4 (*C*-Br), 51.9 (-*C*H_2).

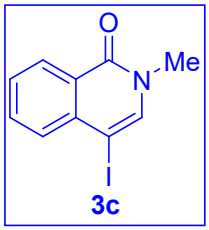


2-Benzyl-4-chloroisoquinolin-1(2*H*)-one (3a'')[3]: Yellow liquid, yield: 77% (41.5 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.50 (d, *J* = 8.0 Hz, 1H), 7.86 (d, *J* = 8.0 Hz, 1H), 7.77 (t, *J* = 7.6 Hz, 1H), 7.59 (t, *J* = 7.3 Hz, 1H), 7.34 (q, *J* = 8.9, 7.8 Hz, 5H), 7.24 (s, 1H), 5.21 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.4 (*C*=O), 136.4 (Ar-C), 134.8 (Ar-C), 133.1 (Ar-C), 129.3 (Ar-C), 129.1 (Ar-C), 128.7 (Ar-C), 128.3 (Ar-C), 128.2 (Ar-C), 128.1 (Ar-C), 126.4 (Ar-C), 123.6 (Ar-C), 111.8 (*C*-Cl), 51.9 (-*C*H_2).

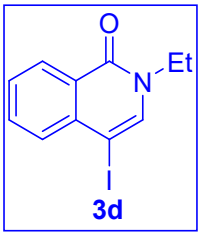


4-Iodoisoquinolin-1(2*H*)-one (3b): White solid, yield: 97% (52.6 mg), Mp: 246-248 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.50 (s, 1H), 8.18 (d, *J* = 7.9 Hz, 1H), 7.82 (t, *J* = 7.6 Hz, 1H), 7.68-7.54 (m, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 161.6 (*C*=O), 138.0 (Ar-C), 136.0 (Ar-

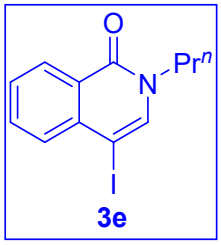
C), 134.1 (Ar-C), 130.4 (Ar-C), 128.0 (Ar-C), 127.8 (Ar-C), 127.1 (Ar-C), 70.9 (*C*-I). HRMS (ESI) [M+H$^+$] Calcd For C_9H_7INO: 271.9567, Found: 271.9570.



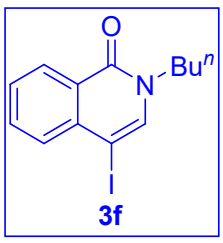
4-Iodo-2-methylisoquinolin-1(2*H*)-one (3c)[1]: Yellow solid, yield: 94% (53.6 mg), Mp: 120-122 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.41 (d, *J* = 9.0 Hz, 1H), 7.72 (td, *J* = 7.6, 7.1, 1.2 Hz, 1H), 7.67 (d, *J* = 7.3 Hz, 1H), 7.57-7.50 (m, 2H), 3.60 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.4 (*C*=O), 139.0 (Ar-C), 137.6 (Ar-C), 133.5 (Ar-C), 130.8 (Ar-C), 128.5 (Ar-C), 128.2 (Ar-C), 126.9 (Ar-C), 71.8 (*C*-I), 37.2 (-*C*H$_3$).



2-Ethyl-4-iodoisoquinolin-1(2*H*)-one (3d)[1]: Yellow solid, yield: 88% (52.6 mg). Mp: 77-79 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.45-8.37 (m, 1H), 7.71 (td, *J* = 7.6, 7.0, 1.3 Hz, 1H), 7.66 (d, *J* = 8.1 Hz, 1H), 7.55-7.49 (m, 2H), 4.04 (q, *J* = 7.2 Hz, 2H), 1.39 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.4 (*C*=O), 137.7 (Ar-C), 137.3 (Ar-C), 133.2 (Ar-C), 130.5 (Ar-C), 128.3 (Ar-C), 127.9 (Ar-C), 126.9 (Ar-C), 71.8 (*C*-I), 44.5 (-*C*H$_2$), 14.8 (-*C*H$_3$).

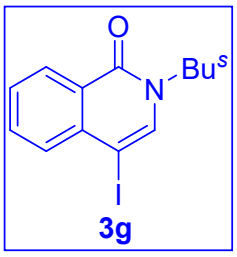


4-iodo-2-propylisoquinolin-1(2*H*)-one (3e)[1]: Yellow liquid, yield: 80% (50.1 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.40 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.73-7.69 (m, 1H), 7.66 (d, *J* = 7.4 Hz, 1H), 7.55-7.49 (m, 2H), 3.95 (t, *J* = 7.4 Hz, 2H), 1.86-1.77 (m, 2H), 0.99 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.5 (*C*=O), 138.0 (Ar-C), 137.1 (Ar-C), 133.1 (Ar-C), 130.3 (Ar-C), 128.2 (Ar-C), 127.7 (Ar-C), 126.7 (Ar-C), 71.4 (*C*-I), 50.9 (-N*C*H$_2$), 22.6 (-*C*H$_2$CH$_3$), 11.1 (-*C*H$_3$).

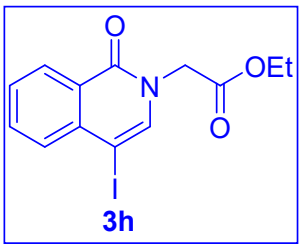


2-Butyl-4-iodoisoquinolin-1(2*H*)-one (3f)[1]: Yellow liquid, yield: 76% (49.7 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.40 (d, *J* = 7.8 Hz, 1H), 7.70 (td, *J* = 7.6, 7.1, 1.3 Hz, 1H), 7.65 (d, *J* = 7.4 Hz, 1H), 7.55-7.49 (m, 2H), 4.01-3.95 (m, 2H), 1.79-1.73 (m, 2H), 1.40 (m,

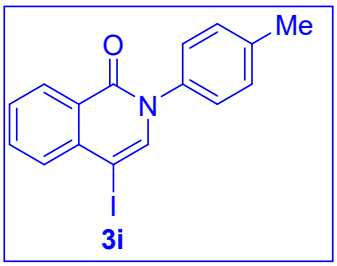
J = 7.4 Hz, 2H), 0.96 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.6 (*C*=O), 138.1 (Ar-C), 137.2 (Ar-C), 133.2 (Ar-C), 130.4 (Ar-C), 128.3 (Ar-C), 127.9 (Ar-C), 126.8 (Ar-C), 71.6 (*C*-I), 49.3 (-N*C*H_2), 31.6 (-NCH$_2$*C*H_2), 20.1 (-*C*H_2CH$_3$), 13.9 (-CH$_2$*C*H_3).



2-(sec-Butyl)-4-iodoisoquinolin-1(2*H*)-one (3g): Yellow liquid, yield: 92% (60.2 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.41 (d, J = 7.8 Hz, 1H), 7.74-7.68 (m, 1H), 7.65 (d, J = 7.8 Hz, 1H), 7.56-7.50 (m, 1H), 7.46 (s, 1H), 5.13 (h, J = 6.9 Hz, 1H), 1.76-1.72 (m, 2H), 1.37 (d, J = 6.9 Hz, 3H), 0.89 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.7 (*C*=O), 136.7 (Ar-C), 133.9 (Ar-C), 133.2 (Ar-C), 130.4 (Ar-C), 128.7 (Ar-C), 127.8 (Ar-C), 126.8 (Ar-C), 72.2 (*C*-I), 52.1 (-N*C*H), 29.2 (-*C*H_2CH$_3$), 20.3 (-NCH*C*H_3), 10.9 (-CH$_2$*C*H_3). HRMS (ESI) [M+H$^+$] Calcd For $C_{13}H_{15}INO$: 328.0193, Found: 328.0197.

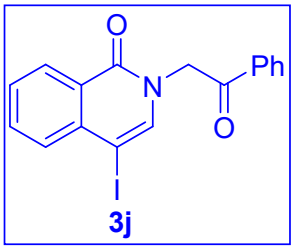


Ethyl 2-(4-iodo-1-oxoisoquinolin-2(1*H*)-yl)acetate (3h): White solid, yield: 80% (57.1 mg), Mp: 161-163 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.38 (d, J = 8.0 Hz, 1H), 7.74 (td, J = 7.6, 7.1, 1.3 Hz, 1H), 7.69 (d, J = 8.1 Hz, 1H), 7.57-7.51 (m, 1H), 7.47 (s, 1H), 4.68 (s, 2H), 4.26 (q, J = 7.1 Hz, 2H), 1.30 (t, J = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.9 (O*C*=O), 161.8 (-N*C*=O), 137.9 (Ar-C), 137.5 (Ar-C), 133.7 (Ar-C), 130.7 (Ar-C), 128.5 (Ar-C), 128.2 (Ar-C), 126.3 (Ar-C), 72.3 (*C*-I), 62.1 (-N*C*H_2), 50.1 (-*C*H_2CH$_3$), 14.3 (-CH$_2$*C*H_3). HRMS (ESI) [M+H$^+$] Calcd For $C_{13}H_{13}INO_3$: 357.9935, Found: 357.9938.

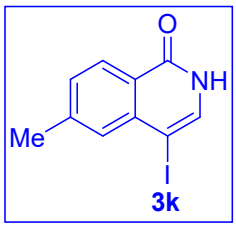


4-Iodo-2-(p-tolyl)isoquinolin-1(2*H*)-one (3i): White solid, yield: 88% (63.5 mg), Mp: 102-104 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.47-8.43 (m, 1H), 7.76 (td, J = 7.6, 7.0, 1.3 Hz, 1H), 7.74-7.71 (m, 1H), 7.64 (s, 1H), 7.59-7.54 (m, 1H), 7.30 (s, 4H), 2.42 (s, 3H). ^{13}C NMR (126

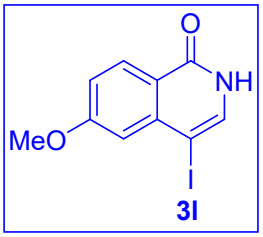
MHz, $CDCl_3$) δ 161.7 (*C*=O), 138.7 (Ar-C), 138.5 (Ar-C), 138.1 (Ar-C), 137.3 (Ar-C), 133.7 (Ar-C), 130.6 (Ar-C), 130.2 (Ar-C), 128.8 (Ar-C), 128.2 (Ar-C), 127.0 (Ar-C), 126.6 (Ar-C), 72.1 (*C*-I), 21.3 (-*C*H_3). HRMS (ESI) [M+H^+] Calcd For $C_{16}H_{13}INO$: 362.0036, Found: 362.0043.



4-Iodo-2-(2-oxo-2-phenylethyl)isoquinolin-1(2*H*)-one (3j): White solid, yield: 70% (54.5 mg), Mp: 163-165 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.43-8.36 (m, 1H), 8.08-8.00 (m, 2H), 7.73 (ddd, *J* = 14.0, 8.1, 7.0 Hz, 2H), 7.68-7.62 (m, 1H), 7.57-7.50 (m, 3H), 7.47 (s, 1H), 5.42 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.4 (*C*=O), 161.8 (-N*C*=O), 138.3 (Ar-C), 137.6(Ar-C), 134.8 (Ar-C), 134.3 (Ar-C), 133.6 (Ar-C), 130.7 (Ar-C), 129.1 (Ar-C), 128.5 (Ar-C), 128.3 (Ar-C), 128.1 (Ar-C), 126.4 (Ar-C), 72.2 (*C*-I), 54.1 (-*C*H_2). HRMS (ESI) [M+H^+] Calcd For $C_{17}H_{13}INO_2$: 389.9985, Found: 389.9989.

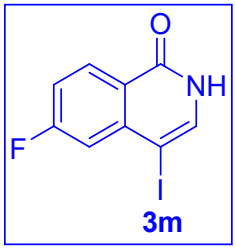


4-Iodo-6-methylisoquinolin-1(2*H*)-one (3k): Yellow solid, yield: 80% (45.6 mg), Mp: 288-290 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.42 (s, 1H), 8.10-8.06 (m, 1H), 7.58 (d, *J* = 5.0 Hz, 1H), 7.42 (s, 1H), 7.39 (d, *J* = 8.1 Hz, 1H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 161.1 (*C*=O), 143.9 (Ar-C), 137.6 (Ar-C), 135.6 (Ar-C), 129.6 (Ar-C), 128.9 (Ar-C), 127.4 (Ar-C), 124.5 (Ar-C), 70.3 (*C*-I), 21.5 (-*C*H_3). HRMS (ESI) [M+H^+] Calcd For $C_{10}H_9INO$: 285.9723, Found: 285.9728.

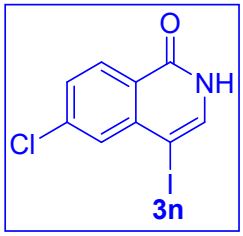


4-Iodo-6-methoxyisoquinolin-1(2*H*)-one (3l): Yellow solid, yield: 97% (58.4 mg), Mp: 263-265 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.35 (s, 1H), 8.11 (d, *J* = 8.8 Hz, 1H), 7.59 (s, 1H), 7.14 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.01 (d, *J* = 2.3 Hz, 1H), 3.92 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.3 (Ar-C), 161.0 (*C*=O), 139.9 (Ar-C), 136.5 (Ar-C), 129.9 (Ar-C), 120.4 (Ar-C), 116.1 (Ar-C),

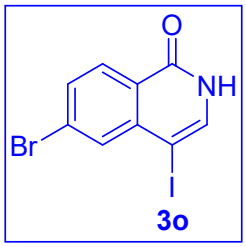
112.1 (Ar-C), 70.2 (*C*-I), 55.7 (-O*C*H$_3$). HRMS (ESI) [M+H$^+$] Calcd For $C_{10}H_9INO_2$: 301.9672, Found: 301.9677.



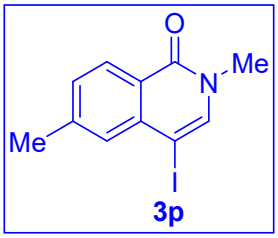
6-Fluoro-4-iodoisoquinolin-1(2*H*)-one (3m): Yellow solid, yield: 82% (47.4 mg), Mp: 289-291 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.60 (s, 1H), 8.26 (dd, J = 8.8, 6.0 Hz, 1H), 7.67 (d, J = 4.5 Hz, 1H), 7.41 (td, J = 8.6, 2.5 Hz, 1H), 7.34 (dd, J = 10.4, 2.4 Hz, 1H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 165.2 (d, J_{CF} = 250.7 Hz, Ar-C), 160.5 (*C*=O), 140.5 (d, J_{CF} = 11.3 Hz, Ar-C), 137.2 (Ar-C), 131.2 (d, J_{CF} = 10.0 Hz, Ar-C), 123.4 (d, J_{CF} = 1.3 Hz, Ar-C), 115.7 (d, J_{CF} = 26.5 Hz, Ar-C), 115.1 (d, J_{CF} = 23.9 Hz, Ar-C), 68.9 (d, J_{CF} = 2.5 Hz, *C*-I). ^{19}F NMR (471 MHz, $CDCl_3$) δ 105.2. HRMS (ESI) [M+H$^+$] Calcd For $C_9H_6FINO_2$: 289.9473, Found: 289.9479.



6-Chloro-4-iodoisoquinolin-1(2*H*)-one (3n): White solid, yield: 67% (40.9 mg), Mp: >300 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.66 (s, 1H), 8.18 (d, J = 8.4 Hz, 1H), 7.73-7.54 (m, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 160.6 (*C*=O), 139.3 (Ar-C), 138.7 (Ar-C), 137.3 (Ar-C), 129.9 (Ar-C), 129.0 (Ar-C), 127.7 (Ar-C), 125.3 (Ar-C), 68.6 (*C*-I). HRMS (ESI) [M+H$^+$] Calcd For $C_9H_6ClINO_2$: 305.9177, Found: 305.9182.

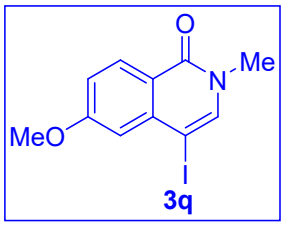


6-Bromo-4-iodoisoquinolin-1(2*H*)-one (3o): White solid, yield: 82% (57.4 mg), Mp: >300 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.65 (s, 1H), 8.09 (d, J = 8.5 Hz, 1H), 7.83-7.64 (m, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 160.7 (*C*=O), 139.4 (Ar-C), 137.2 (Ar-C), 132.1 (Ar-C), 130.5 (Ar-C), 129.8 (Ar-C), 127.8 (Ar-C), 125.6 (Ar-C), 68.5 (*C*-I). HRMS (ESI) [M+H$^+$] Calcd For $C_9H_6BrINO_2$: 349.8672, Found: 349.8675.

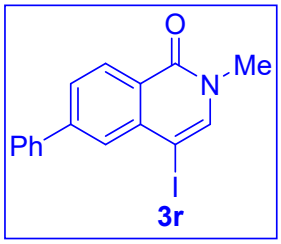


4-Iodo-2,6-dimethylisoquinolin-1(2*H*)-one (3p)[1]: Yellow liquid, yield: 85% (50.8 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ

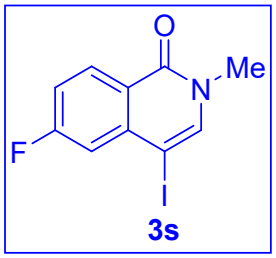
8.25 (d, J = 8.1 Hz, 1H), 7.48 (s, 1H), 7.39 (s, 1H), 7.31 (d, J = 8.2 Hz, 1H), 3.56 (s, 3H), 2.51 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.0 (*C*=O), 144.0 (Ar-C), 138.8 (Ar-C), 137.3 (Ar-C), 130.2 (Ar-C), 129.4 (Ar-C), 128.2 (Ar-C), 124.3 (Ar-C), 71.4 (*C*-I), 36.8 (-N*C*H_3), 22.0 (-*C*H_3).



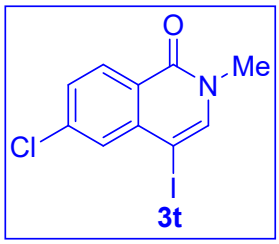
4-Iodo-6-methoxy-2-methylisoquinolin-1(2*H*)-one (3q)[1]: Yellow liquid, yield: 87% (54.8 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32 (d, J = 8.8 Hz, 1H), 7.51 (s, 1H), 7.09-7.00 (m, 2H), 3.95 (s, 3H), 3.57 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.7 (Ar-C), 161.8 (*C*=O), 139.6 (Ar-C), 139.5 (Ar-C), 130.5 (Ar-C), 120.3 (Ar-C), 116.9 (Ar-C), 112.2 (Ar-C), 71.2 (*C*-I), 55.7(-O*C*H_3), 36.8 (-N*C*H_3).



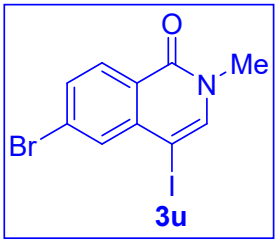
4-Iodo-2-methyl-6-phenylisoquinolin-1(2*H*)-one (3r)[1]: Yellow solid, yield: 89% (64.3 mg), Mp: 176-178 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.45 (d, J = 8.3 Hz, 1H), 7.83 (d, J = 2.2 Hz, 1H), 7.73 (dd, J = 19.0, 8.1 Hz, 3H), 7.58-7.47 (m, 3H), 7.43 (t, J = 7.3 Hz, 1H), 3.61 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.8 (*C*=O), 145.9(Ar-C), 139.7 (Ar-C), 139.0 (Ar-C), 137.5 (Ar-C), 129.0 (Ar-C), 128.8 (Ar-C), 128.6 (Ar-C), 128.4 (Ar-C), 127.6 (Ar-C), 126.9 (Ar-C), 125.2 (Ar-C), 71.6 (*C*-I), 36.8 (-N*C*H_3).



6-Fluoro-4-iodo-2-methylisoquinolin-1(2*H*)-one (3s)[1]: White liquid, yield: 72% (43.6 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.43 (dd, J = 8.6, 5.9 Hz, 1H), 7.55 (s, 1H), 7.39-7.32 (m, 1H), 7.22-7.15 (m, 1H), 3.59 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.0 (d, J_{CF} = 253.3 Hz, Ar-C), 161.4 (*C*=O), 140.2 (d, J_{CF} = 11.3 Hz, Ar-C), 140.1, 131.7 (d, J_{CF} = 10.1 Hz, Ar-C), 123.1 (d, J_{CF} = 1.3 Hz, Ar-C), 116.4 (d, J_{CF} = 22.7 Hz, Ar-C), 116.1 (d, J_{CF} = 25.2 Hz, Ar-C), 69.8 (d, J_{CF} = 2.5 Hz, *C*-I), 37.0 (-N*C*H_3). ^{19}F NMR (471 MHz, $CDCl_3$) δ 104.8.

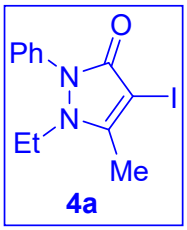


6-Chloro-4-iodo-2-methylisoquinolin-1(2*H*)-one (3t)[1]: Yellow liquid, yield: 89% (56.9 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.33 (d, *J* = 8.6 Hz, 1H), 7.66 (d, *J* = 1.9 Hz, 1H), 7.55 (s, 1H), 7.45 (dd, *J* = 8.6, 2.0 Hz, 1H), 3.59 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.5 (*C*=O), 140.1 (Ar-C), 138.9 (Ar-C), 130.2 (Ar-C), 130.0 (Ar-C), 128.5 (Ar-C), 124.9 (Ar-C), 69.5 (*C*-I), 37.0 (-N*C*H$_3$).

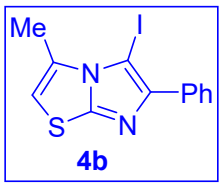


6-Bromo-4-iodo-2-methylisoquinolin-1(2*H*)-one (3u)[1]: Yellow liquid, yield: 91% (66.2 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.24 (d, *J* = 8.5 Hz, 1H), 7.83 (d, *J* = 1.7 Hz, 1H), 7.60 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.54 (s, 1H), 3.58 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.6 (*C*=O), 140.1 (Ar-C), 138.9 (Ar-C), 133.1 (Ar-C), 131.3 (Ar-C), 130.1 (Ar-C), 128.8 (Ar-C), 125.3 (Ar-C), 69.3 (*C*-I), 37.0 (-N*C*H$_3$).

4. ^{1}H and ^{13}C NMR data of iodinated products (4a-4e)

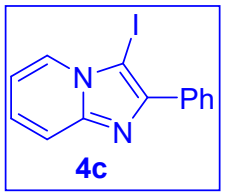


1-Ethyl-4-iodo-5-methyl-2-phenyl-1,2-dihydro-3*H*-pyrazol-3-one (4a): Yellow liquid, yield: 92% (60.4 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69-7.60 (m, 2H), 7.48-7.38 (m, 2H), 7.33-7.27 (m, 1H), 4.15 (q, *J* = 7.1 Hz, 2H), 2.27 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.6 (*C*=O), 150.5 (Ar-C), 138.7 (Ar-C), 129.1 (Ar-C), 127.0 (Ar-C), 122.4 (Ar-C), 71.1 (*C*-I), 49.6 (-N*C*H$_2$), 15.5 (-*C*H$_3$), 15.0 (-CH$_2$*C*H$_3$). HRMS (ESI) [M+H$^+$] Calcd For $C_{12}H_{14}IN_2O$: 329.0145, Found: 329.0148.

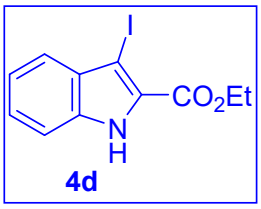


5-Iodo-3-methyl-6-phenylimidazo[2,1-*b*]thiazole (4b)[4]: White solid, yield: 64% (43.5 mg), Mp: 205-207 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (d, *J* = 7.6 Hz, 2H), 7.44 (t, *J* = 7.6 Hz, 2H), 7.35 (t, *J* = 7.3 Hz, 1H), 6.42 (s, 1H), 2.75 (s, 3H). ^{13}C NMR (126 MHz,

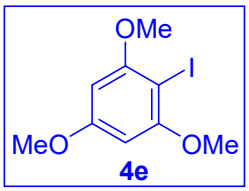
$CDCl_3$) δ 153.3 (Ar-C), 150.8 (Ar-C), 134.0 (Ar-C), 130.7 (Ar-C), 128.6 (Ar-C), 128.3 (Ar-C), 128.1 (Ar-C), 108.5 (Ar-C), 52.7 (*C*-I), 16.8 (-*C*H_3).



3-Iodo-2-phenylimidazo[1,2-a]pyridine (4c)[4]: White solid, yield: 94% (60.2 mg), Mp: 162-164 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.24 (d, *J* = 6.9 Hz, 1H), 8.07 (d, *J* = 7.3 Hz, 2H), 7.63 (d, *J* = 9.0 Hz, 1H), 7.49 (t, *J* = 7.7 Hz, 2H), 7.40 (t, *J* = 7.4 Hz, 1H), 7.30-7.26 (m, 1H), 6.94 (t, *J* = 7.2 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.3 (Ar-C), 133.7 (Ar-C), 128.7 (Ar-C), 128.5 (Ar-C), 126.7 (Ar-C), 125.7 (Ar-C), 117.8 (Ar-C), 113.3 (Ar-C), 59.6 (*C*-I).

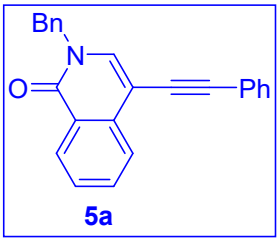


Ethyl 3-iodo-1*H*-indole-2-carboxylate (4d)[5]: White solid, yield: 73% (46.0 mg), Mp: 139-141 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.29 (bs, 1H), 7.57 (d, *J* = 8.1 Hz, 1H), 7.45-7.34 (m, 2H), 7.25-7.20 (m, 1H), 4.47 (qd, *J* = 7.1, 2.6 Hz, 2H), 1.47 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.0 (*C*=O), 136.3 (Ar-C), 131.7 (Ar-C), 127.4 (Ar-C), 126.8 (Ar-C), 123.7 (Ar-C), 121.8 (Ar-C), 112.1 (Ar-C), 66.2 (*C*-I), 61.7 (-*C*H_2), 14.5 (-*C*H_3).



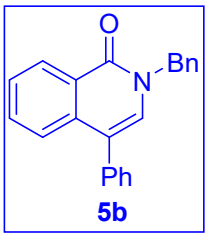
3-Iodo-1,3,5-trimethoxybenzene (4e)[5]: White solid, yield: 70% (41.2 mg), Mp: 114-116 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.14 (s, 2H), 3.86 (s, 6H), 3.82 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.3 (Ar-C), 160.0 (Ar-C), 91.4 (Ar-C), 66.9 (*C*-I), 56.6 (-O*C*H_3), 55.7 (-O*C*H_3).

5. ^{1}H and ^{13}C NMR data of coupling products (5a-5c)

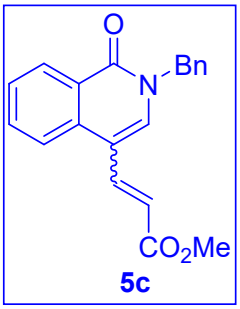


2-Benzyl-4-(phenylethynyl)isoquinolin-1(2*H*)-one (5a): Yellow solid, yield: 99% (66.4 mg), Mp: 49-51 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.49 (d, *J* = 8.0 Hz, 1H), 8.03 (d, *J* = 8.0 Hz, 1H), 7.76 (t, *J* = 7.9 Hz, 1H), 7.59-7.54 (m, 3H), 7.50 (s,

1H), 7.39-7.35 (m, 7H), 7.33-7.29 (m, 1H), 5.25 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.5 (*C*=O), 136.4 (Ar-C), 136.0 (Ar-C), 135.5 (Ar-C), 132.8 (Ar-C), 131.4 (Ar-C), 129.0 (Ar-C), 128.5 (Ar-C), 128.4 (Ar-C), 128.2 (Ar-C), 128.1 (Ar-C), 127.6 (Ar-C), 125.6 (Ar-C), 125.1 (Ar-C), 123.0 (Ar-C), 101.7 (Ar-C), 93.1 (Ph-*C*≡), 83.5 (Ph-C≡*C*), 52.0 (-*C*H_2). HRMS (ESI) [M+H^+] Calcd For $C_{24}H_{18}NO$: 336.1383, Found: 336.1388.



2-Benzyl-4-phenylisoquinolin-1(2*H*)-one (5b): Brawn solid, yield: 84% (52.3 mg), Mp: 144-146 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.57 (d, *J* = 7.4 Hz, 1H), 7.62 (td, *J* = 7.6, 7.0, 1.3 Hz, 1H), 7.58-7.52 (m, 2H), 7.48-7.43 (m, 2H), 7.43-7.40 (m, 1H), 7.39 (d, *J* = 1.5 Hz, 1H), 7.38-7.37 (m, 1H), 7.36 (d, *J* = 6.0 Hz, 2H), 7.35-7.31 (m, 2H), 7.29 (dd, *J* = 6.1, 3.6 Hz, 1H), 7.08 (s, 1H), 5.28 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.9 (*C*=O), 136.8 (Ar-C), 136.3 (Ar-C), 136.2 (Ar-C), 132.3 (Ar-C), 130.4 (Ar-C), 130.0 (Ar-C), 128.9 (Ar-C), 128.7 (Ar-C), 128.5 (Ar-C), 128.1 (Ar-C), 127.9 (Ar-C), 127.8 (Ar-C), 127.1 (Ar-C), 126.0 (Ar-C), 124.8 (Ar-C), 120.0 (Ar-C), 51.9 (-*C*H_2). HRMS (ESI) [M+H^+] Calcd For $C_{22}H_{18}NO$: 312.1383, Found: 312.1390.



Methyl (E)-3-(2-benzyl-1-oxo-1,2-dihydroisoquinolin-4-yl)acrylate (5c): White solid, yield: 96% (61.3 mg), Mp: 150-152 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.52 (d, *J* = 8.1 Hz, 1H), 7.97 (d, *J* = 15.8 Hz, 1H), 7.84 (d, *J* = 8.1 Hz, 1H), 7.74 (t, *J* = 7.6 Hz, 1H), 7.58 (d, *J* = 7.4 Hz, 1H), 7.45 (s, 1H), 7.33 (q, *J* = 8.4, 7.1 Hz, 5H), 6.24 (d, *J* = 15.8 Hz, 1H), 5.26 (s, 2H), 3.81 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.3 (O*C*=O), 162.1 (-N*C*=O), 139.1 (Ar-C), 136.4 (Ar-C), 135.0 (Ar-C), 133.0 (Ar-C), 131.6 (Ar-C), 129.2 (Ar-C), 129.0 (Ar-C), 128.4 (Ar-C), 128.3 (Ar-C), 128.2 (Ar-C), 127.7 (Ar-C), 125.9 (Ar-C), 122.8 (Ar-C), 118.0 (Ar-C), 113.0 (Ar-C), 52.2 (-*C*H_3), 51.9 (-*C*H_2). HRMS (ESI) [M+H^+] Calcd For $C_{20}H_{18}NO_3$: 320.1281, Found: 320.1285.

Reference:

[1] Z. Fang, Y. Wang, Y. Wang, *Org. Lett.* **2019**, *21*, 434-438.

[2] (a) K. A. B. Austin, E. Herdtweck, T. Bach, *Angew. Chem. Int. Ed.* **2011**, *50*, 8416-8419; (b) K.-H. Rimböck, A. Pöthig, T. Bach, *Synthesis* **2015**, *47*, 2869-2884; (c) A. Ansari, S. Satalkar, V. Patil, A. S. Shete, S. Kaur, A. Gupta, S. Singh, M. Raja, D. L. Severance, S. Bernales, S. Chakravarty, D. T. Hung, S. M. Pham, F. J. Herrera, R. Rai, *Bioorg. Med. Chem. Lett.* **2017**, *27*, 217-222.

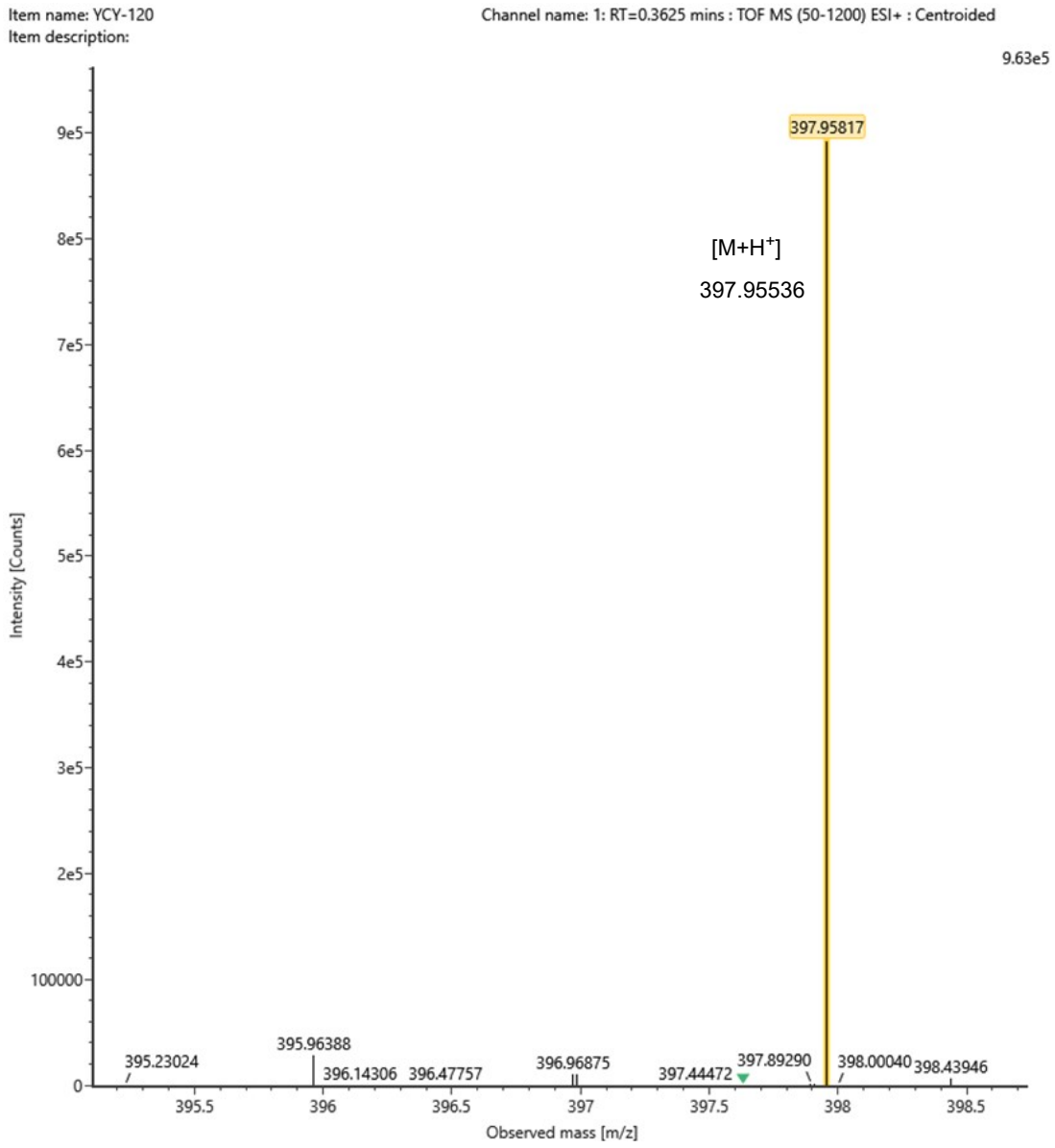
[3] P. V. Fish, C. G. Barber, D. G. Brown, R. Butt, M. G. Collis, R. P. Dickinson, B. T. Henry, V. A. Horne, J. P. Huggins, E. King, M. O'Gara, D. McCleverty, F. McIntosh, C. Phillips, R. Webster, *J. Med. Chem.* **2007**, *50*, 2341-2351.

[4] J. S. S. Neto, R. A. Balaguez, M. S. Franco, V. C. de Sá Machado, S. Saba, J. Rafique, F. Z. Galetto, A. L. Braga, *Green Chem.* **2020**, *22*, 3410-3415.

[5] L. Lu, Y. Li, X. Jiang, *Green Chem.* **2020**, *22*, 5989-5994.

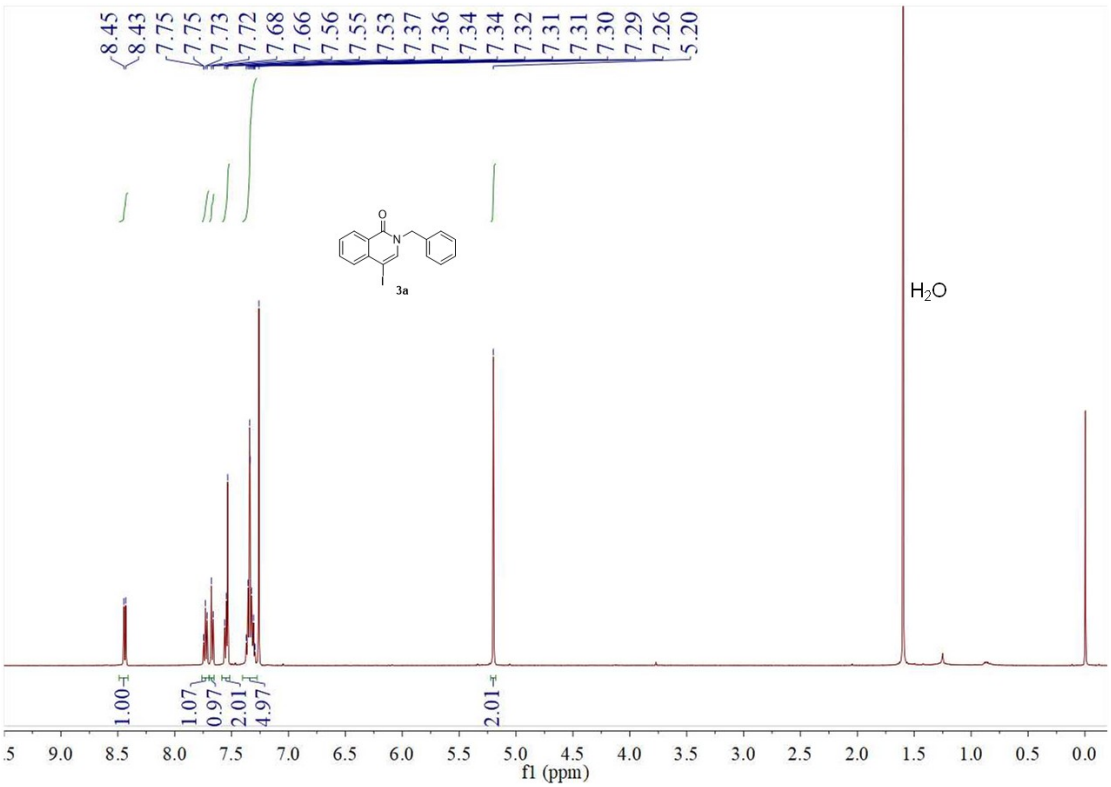
6. Mechanistic studies

HRMS spectrum of [PTSA•NIS]

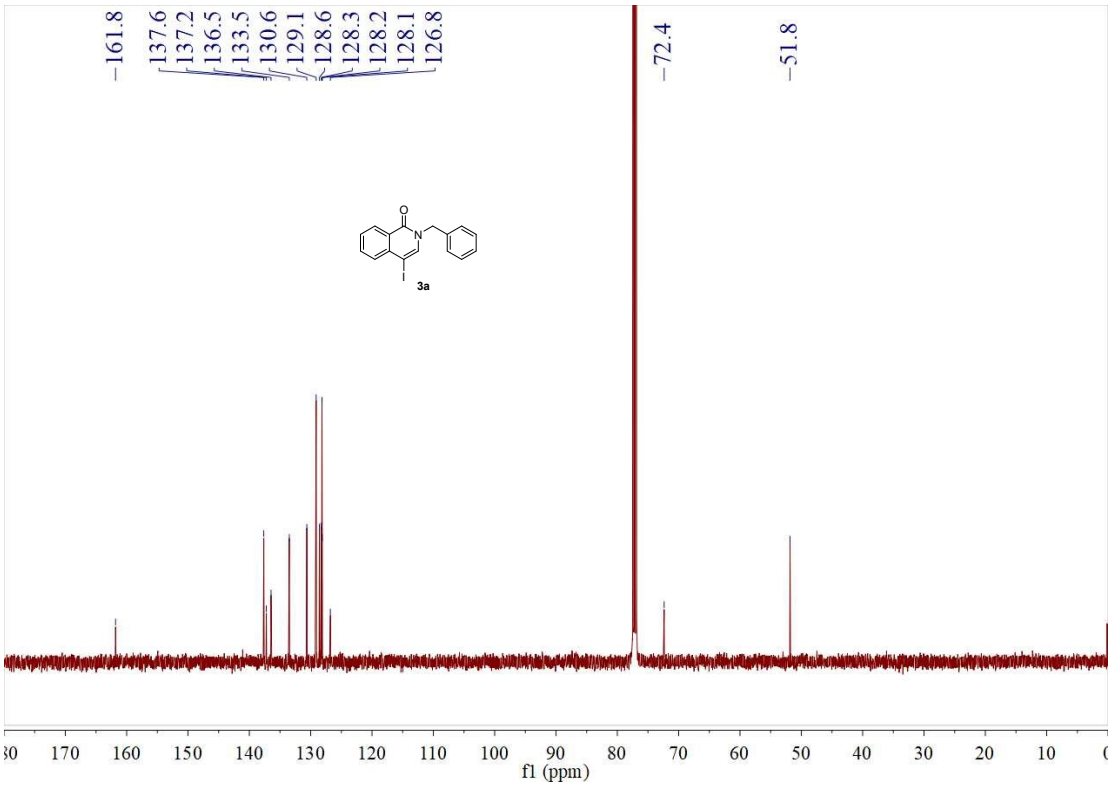


7. ^{1}H and ^{13}C NMR spectra of 4-iodoisoquinolin-1(2*H*)-ones (3a-3u)

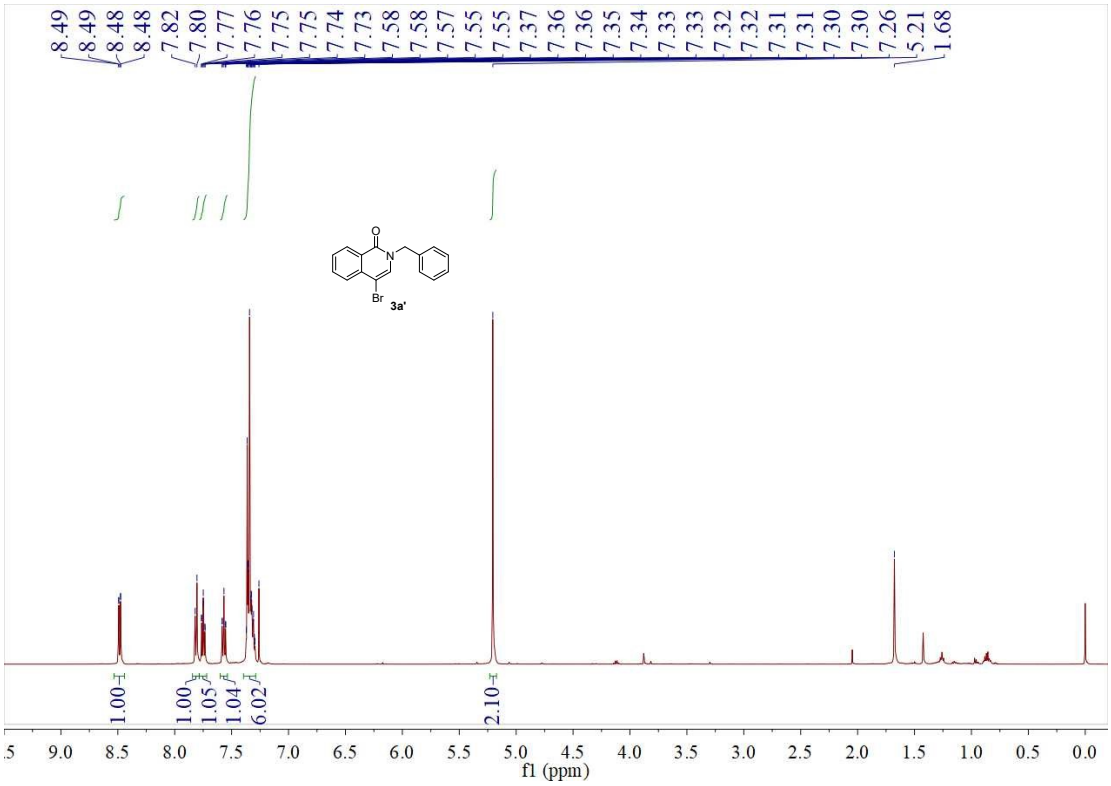
^{1}H NMR of **3a** in $CDCl_3$



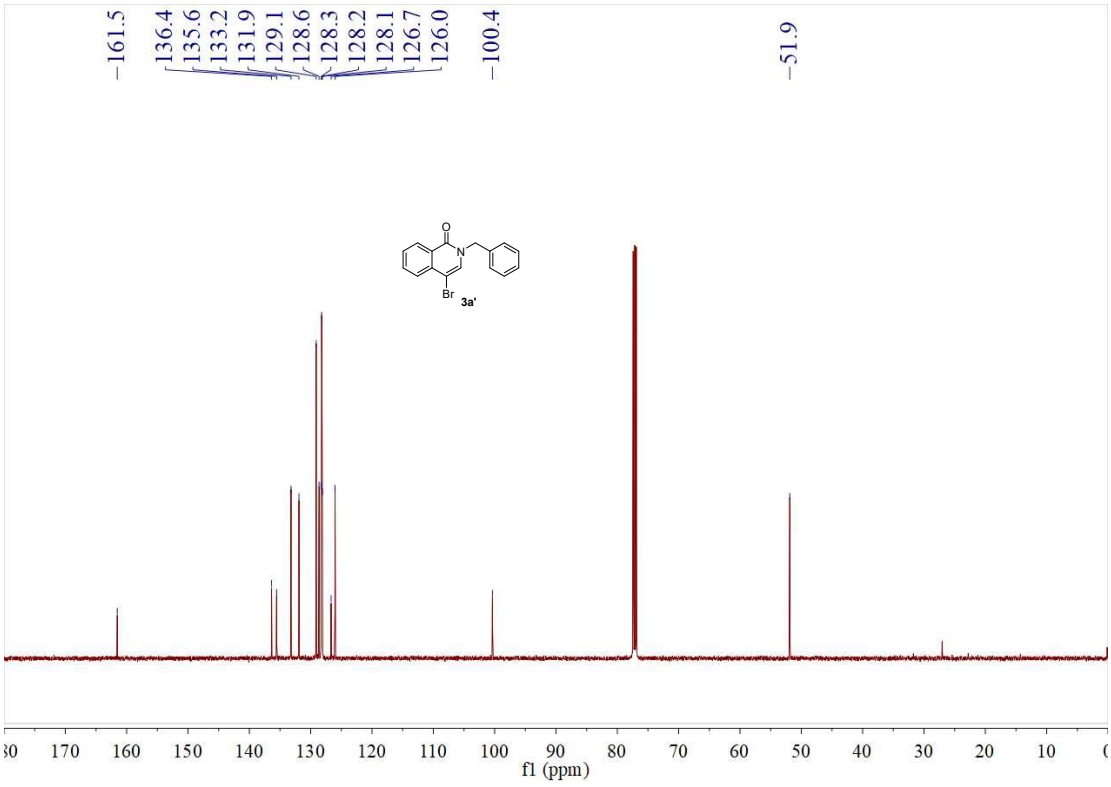
^{13}C NMR of **3a** in $CDCl_3$



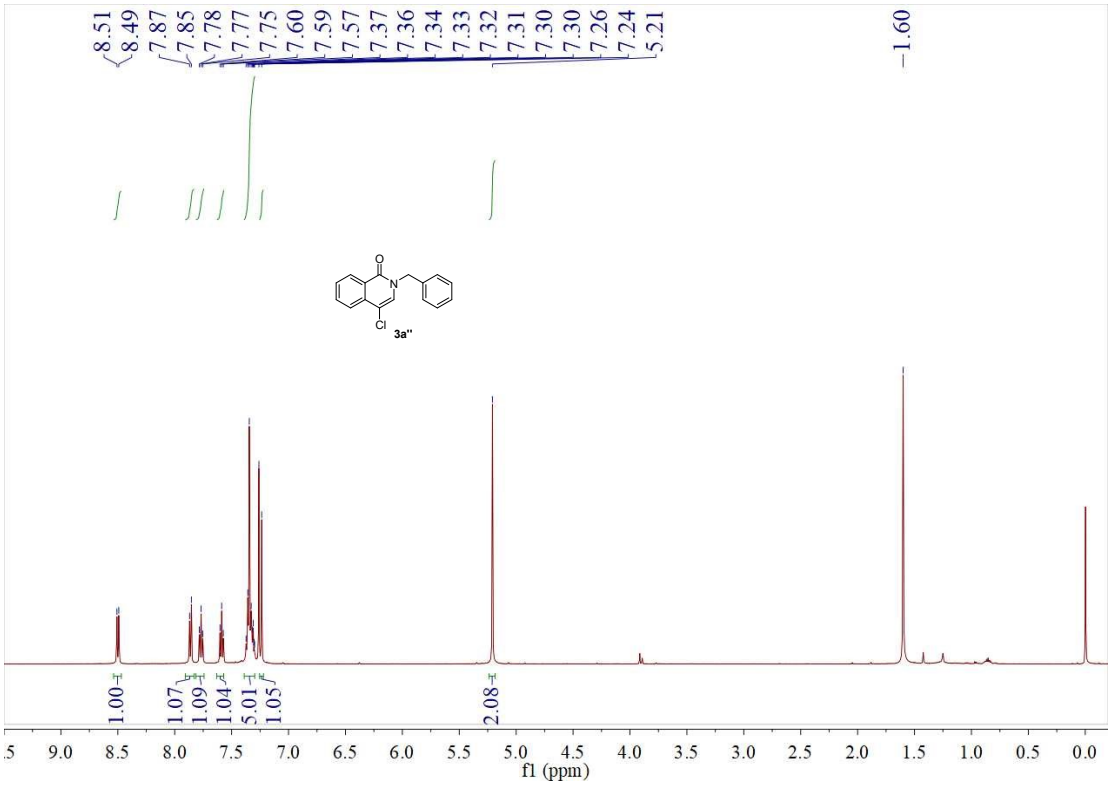
^{1}H NMR of **3a'** in $CDCl_3$



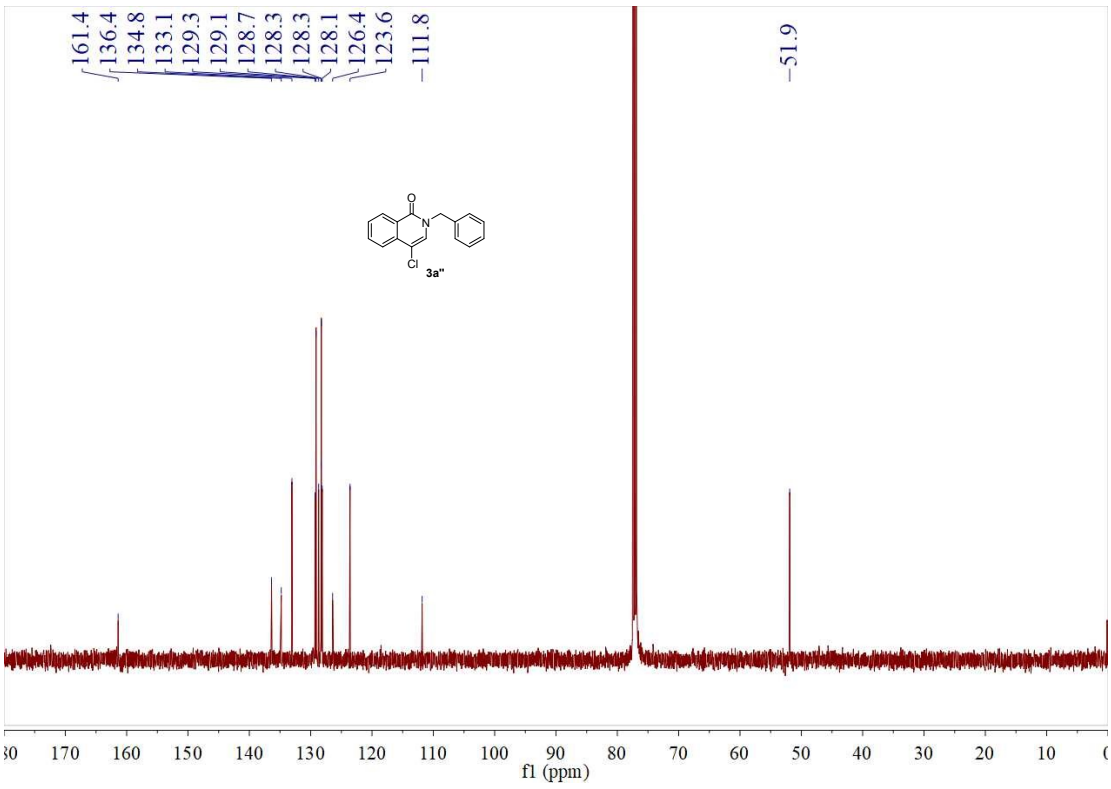
^{13}C NMR of **3a'** in $CDCl_3$



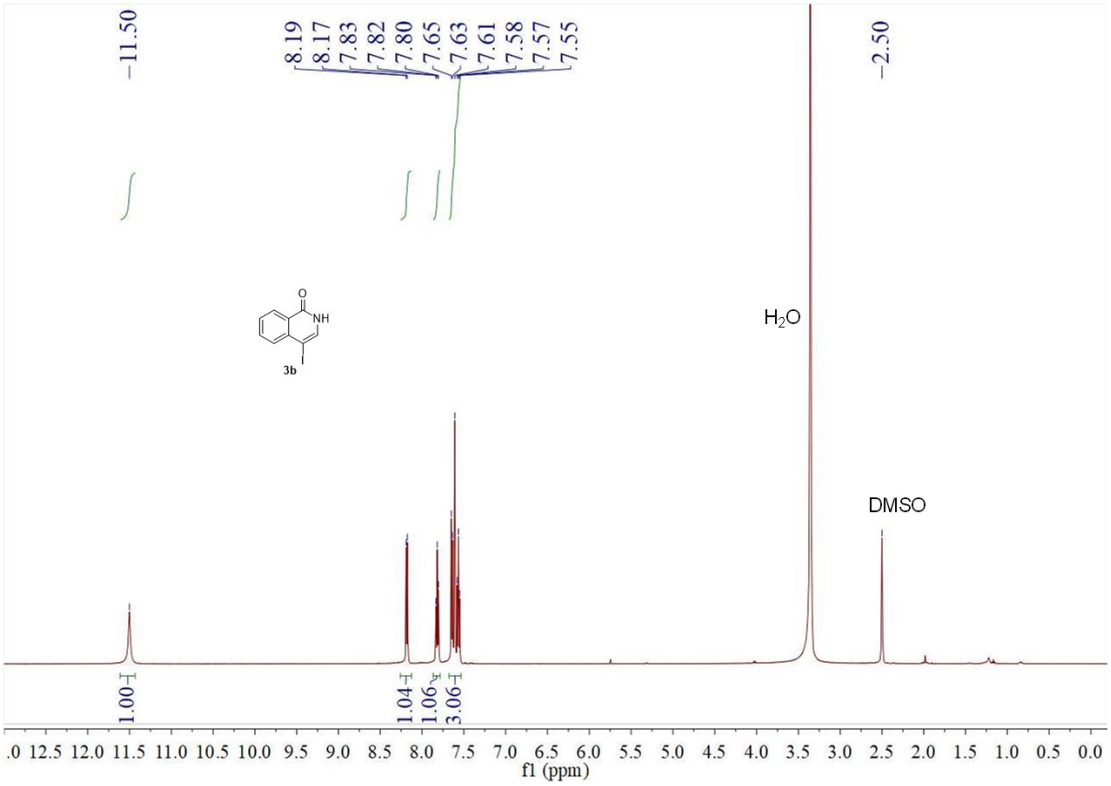
^{1}H NMR of **3a''** in $CDCl_3$



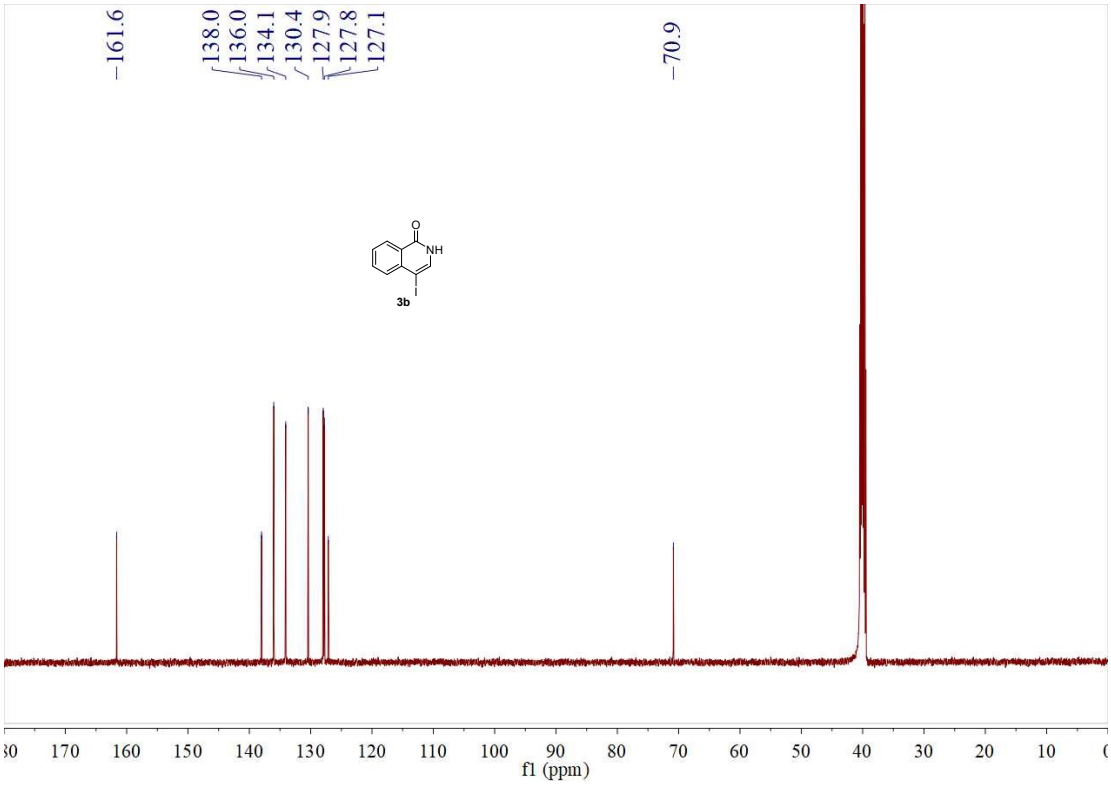
^{13}C NMR of **3a''** in $CDCl_3$



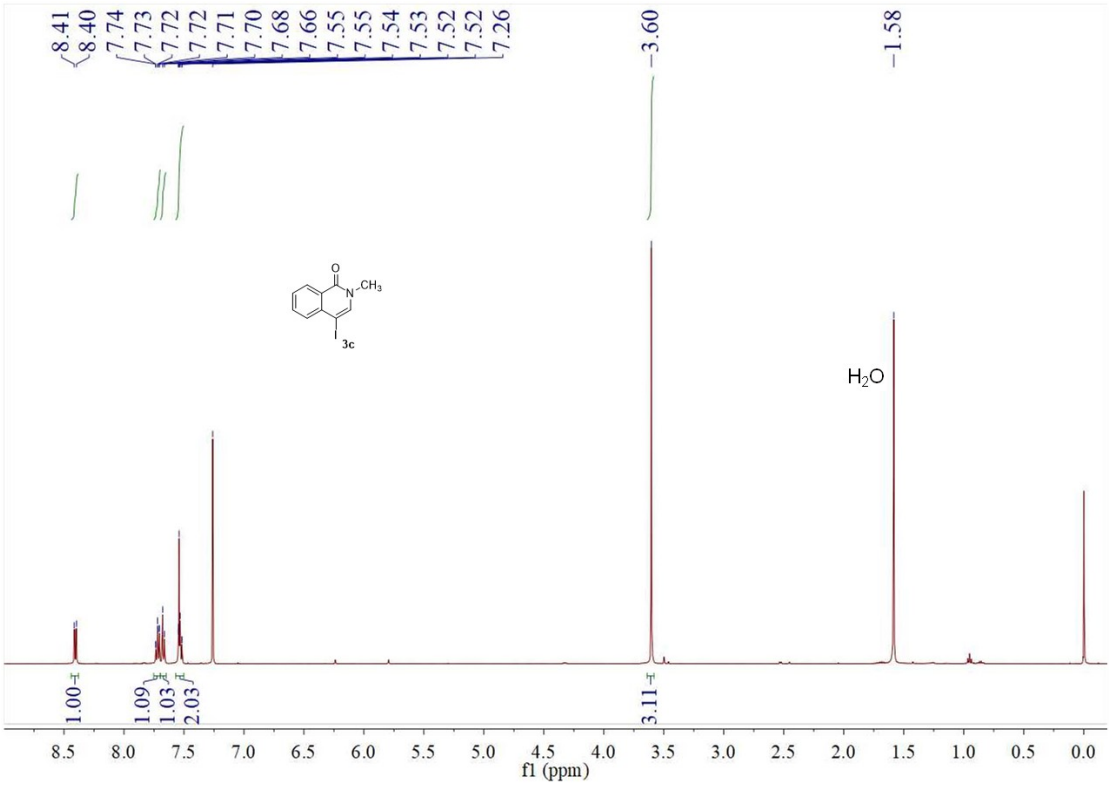
^{1}H NMR of **3b** in DMSO-d_6



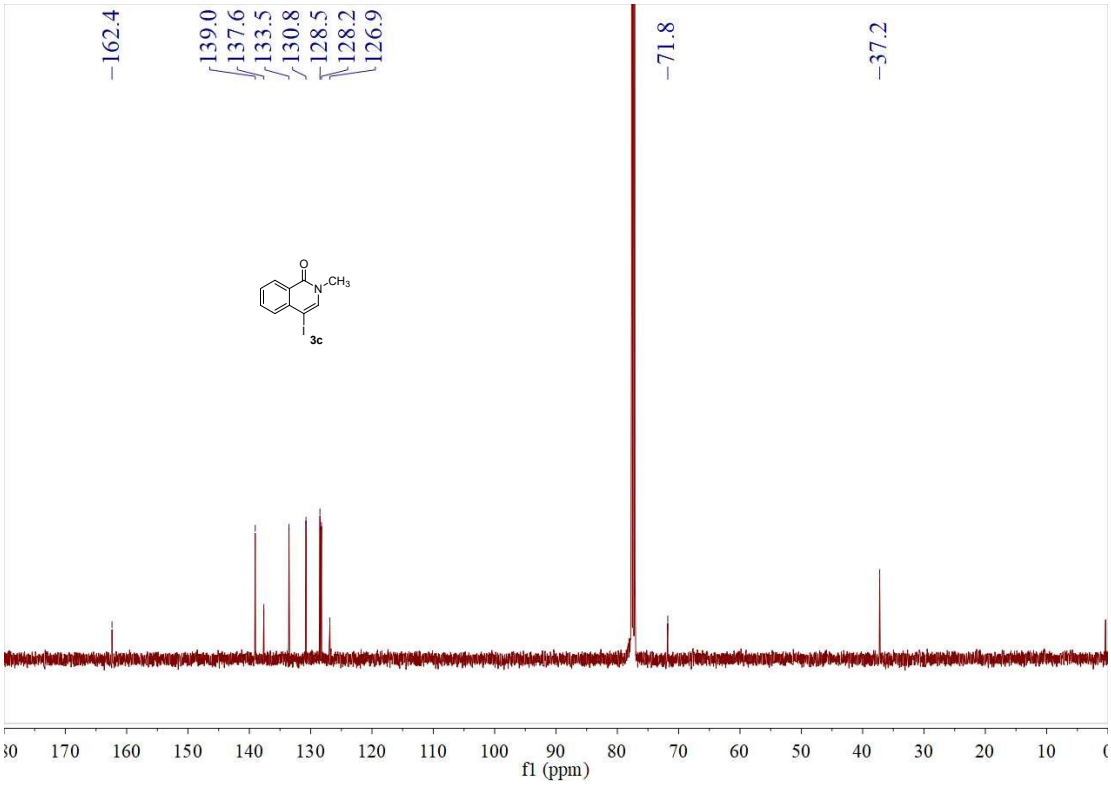
^{13}C NMR of **3b** in DMSO-d_6



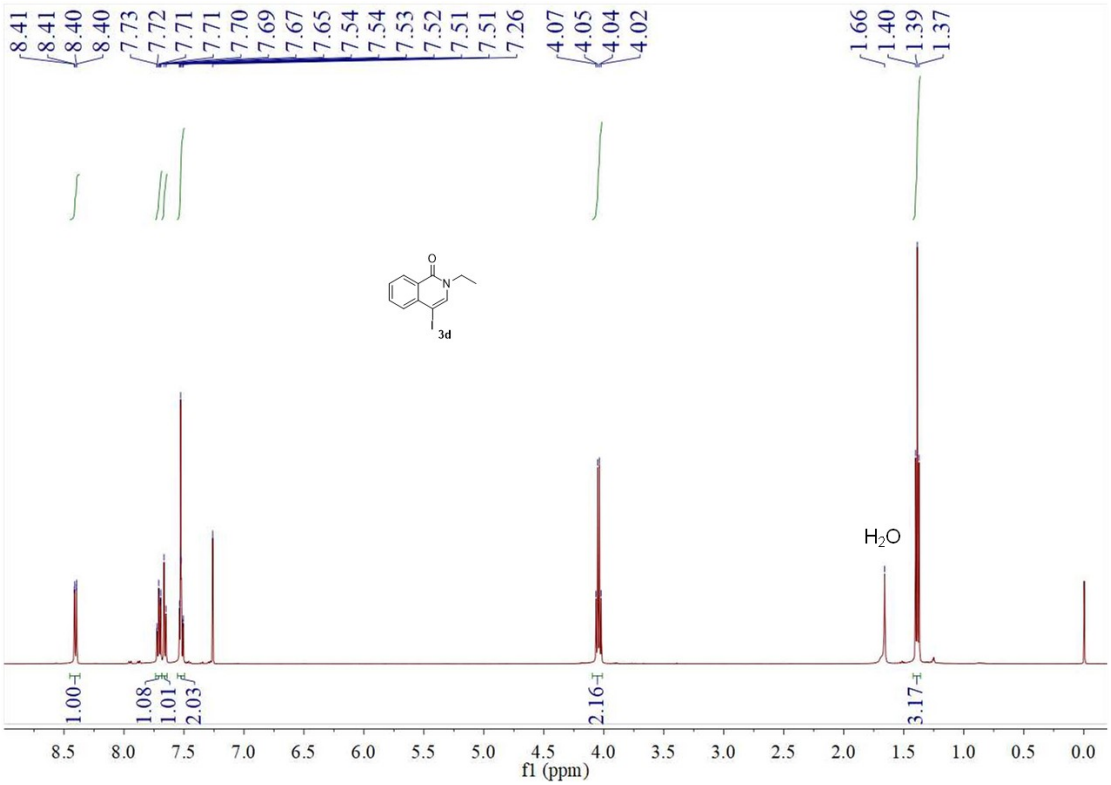
^{1}H NMR of **3c** in $CDCl_3$



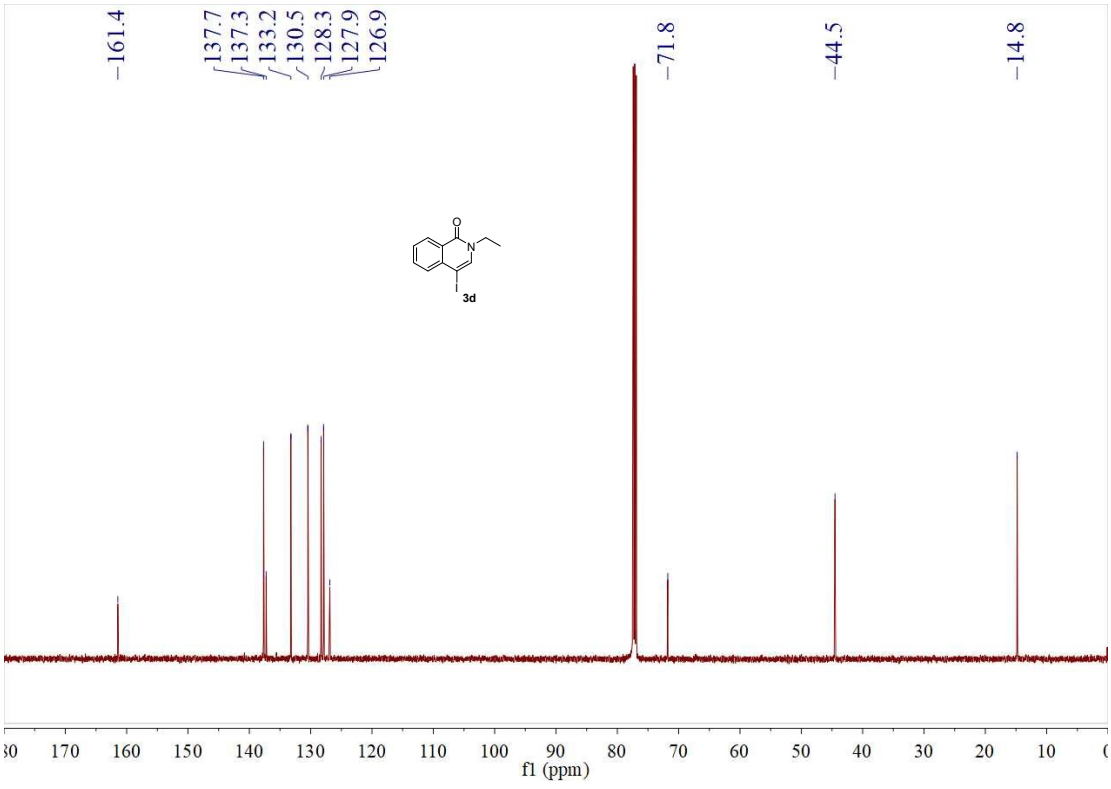
^{13}C NMR of **3c** in $CDCl_3$



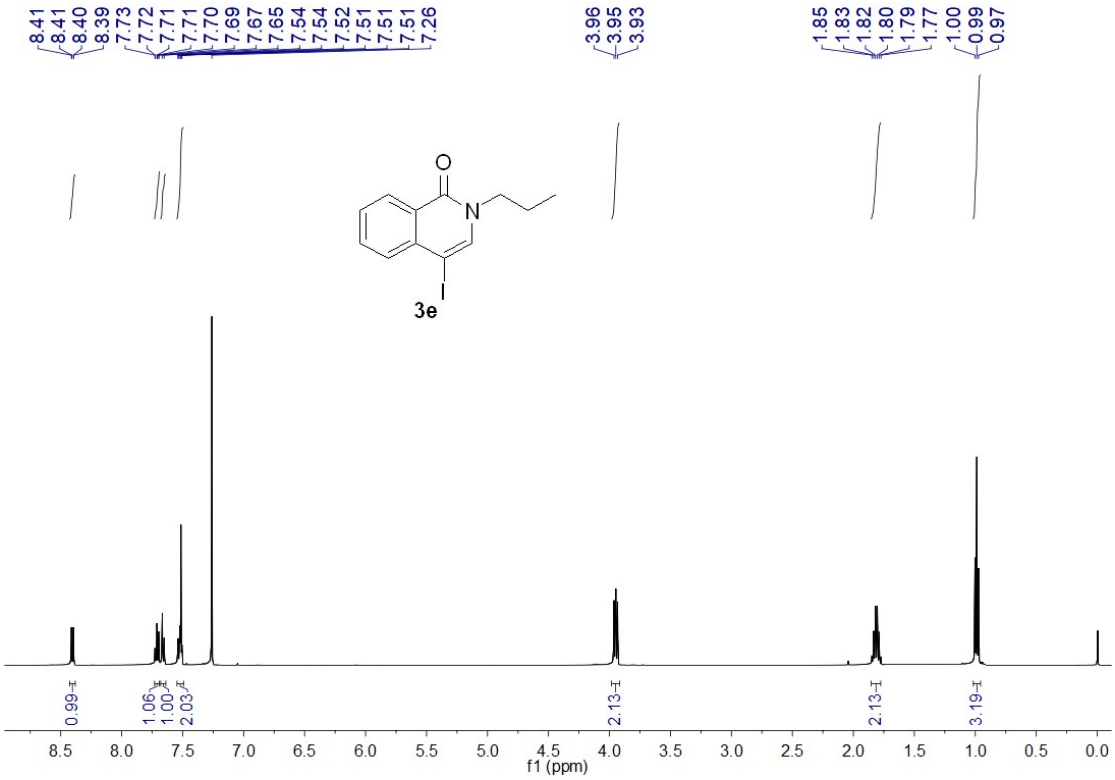
^{1}H NMR of **3d** in $CDCl_3$



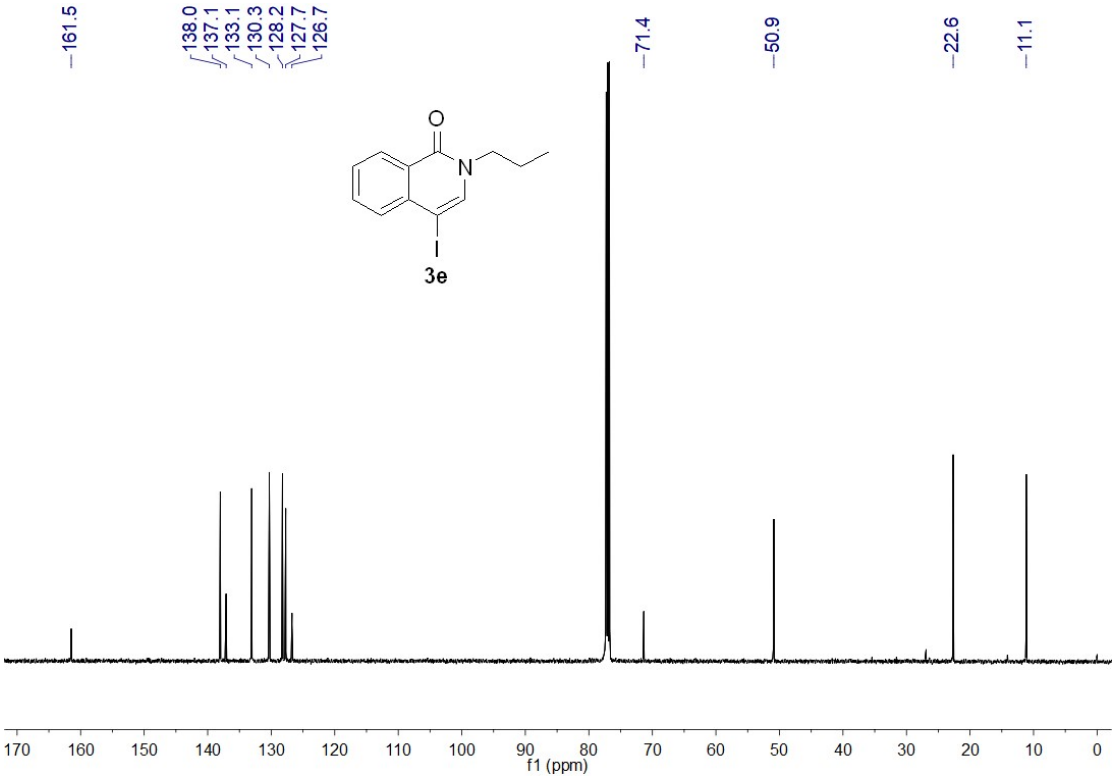
^{13}C NMR of **3d** in $CDCl_3$



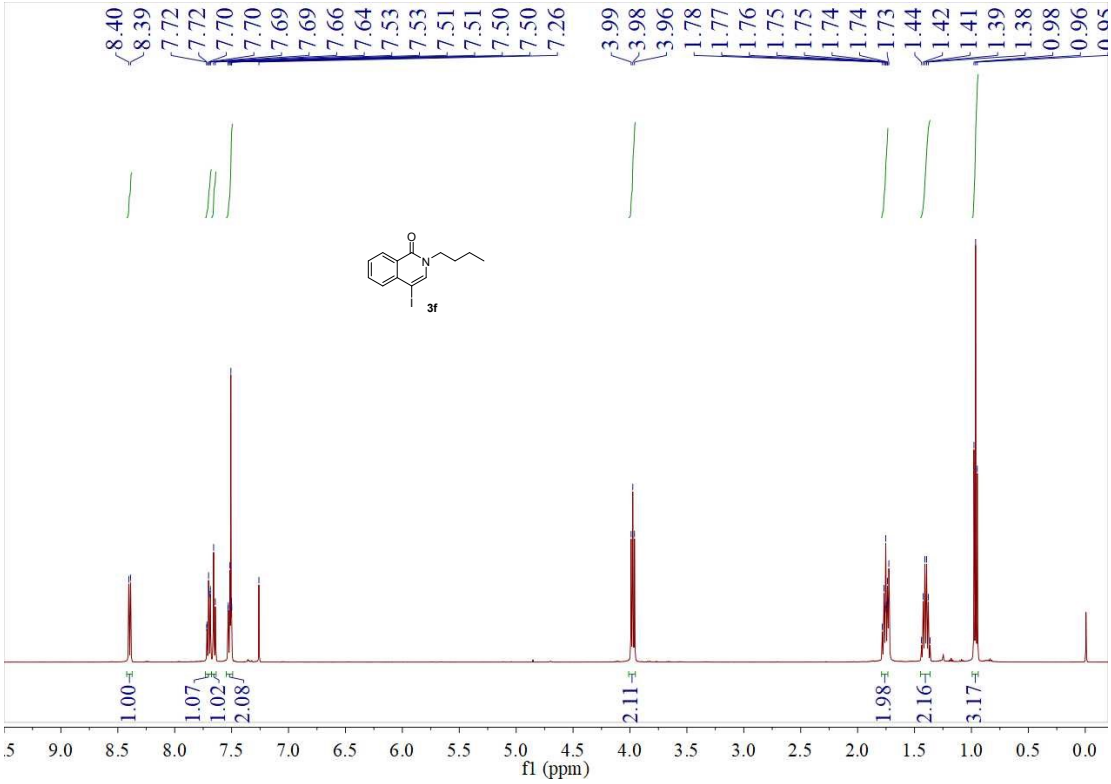
^{1}H NMR of **3e** in $CDCl_3$



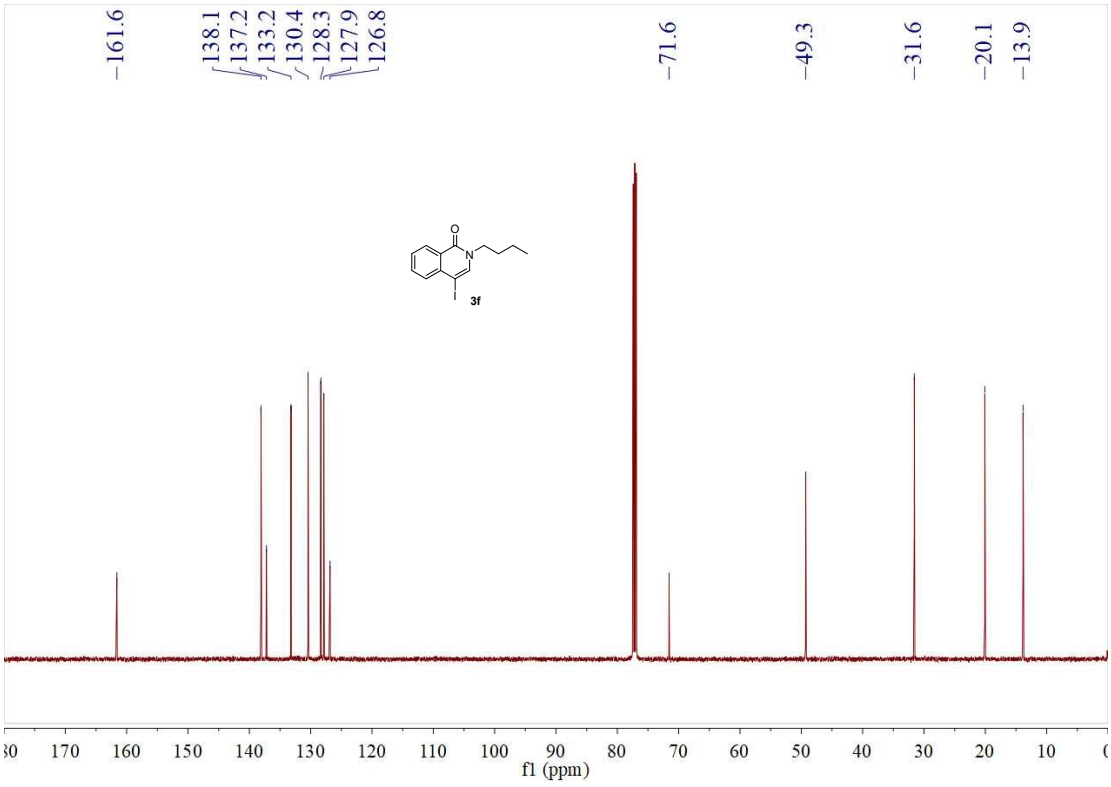
^{13}C NMR of **3e** in $CDCl_3$



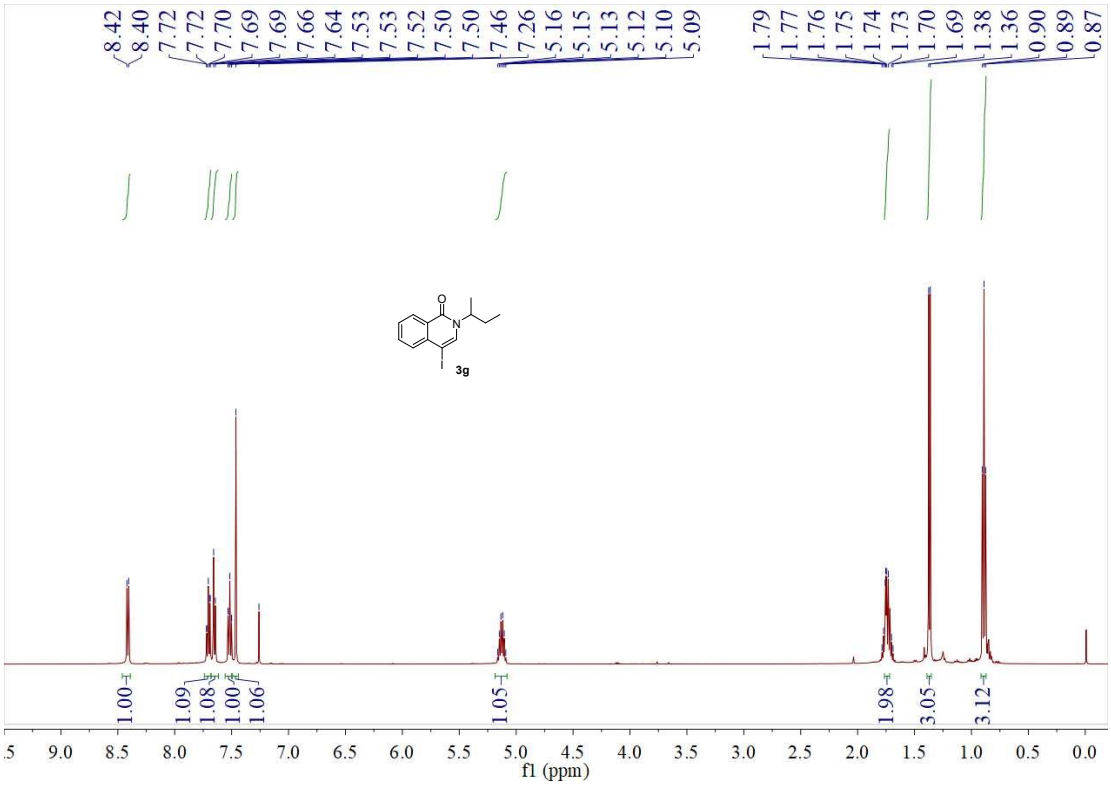
^{1}H NMR of **3f** in $CDCl_3$



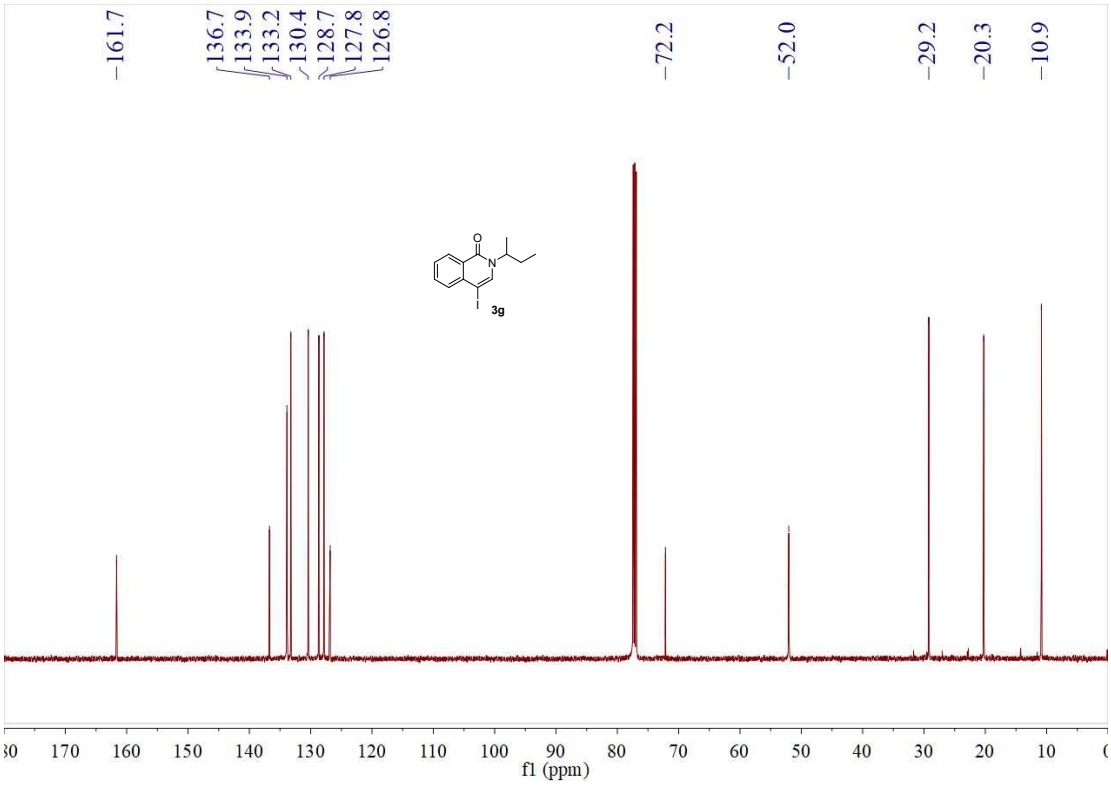
^{13}C NMR of **3f** in $CDCl_3$



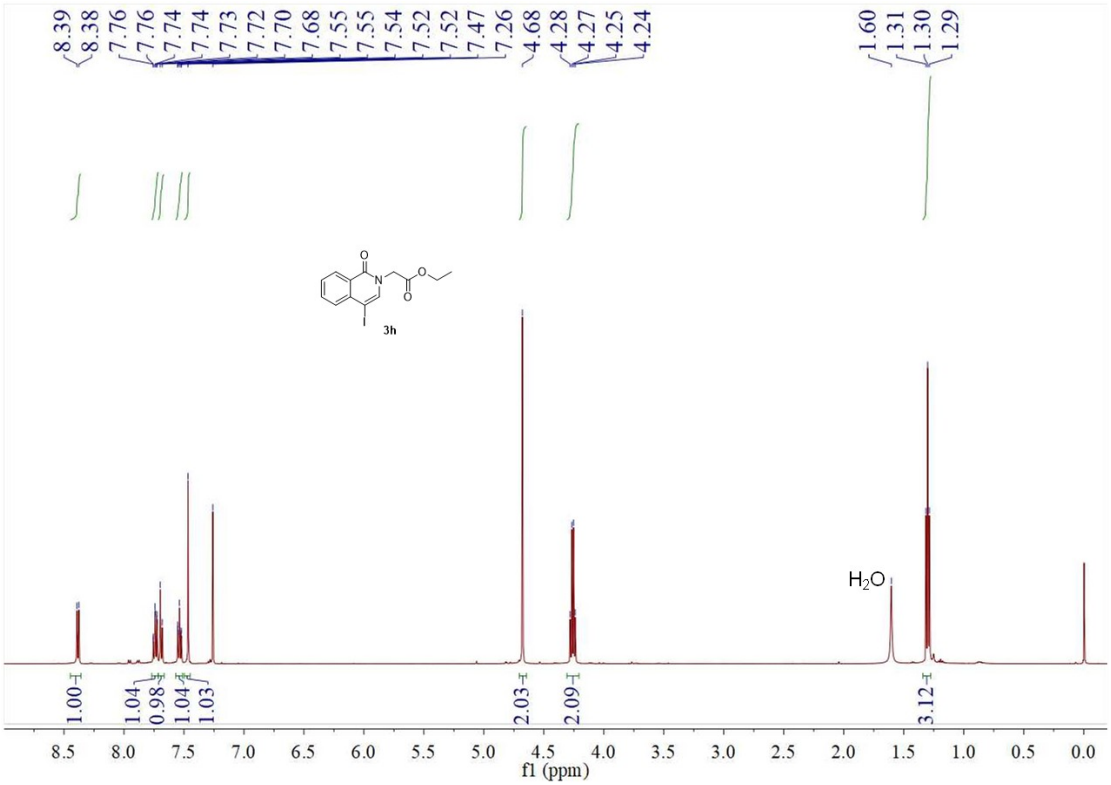
^{1}H NMR of **3g** in $CDCl_3$



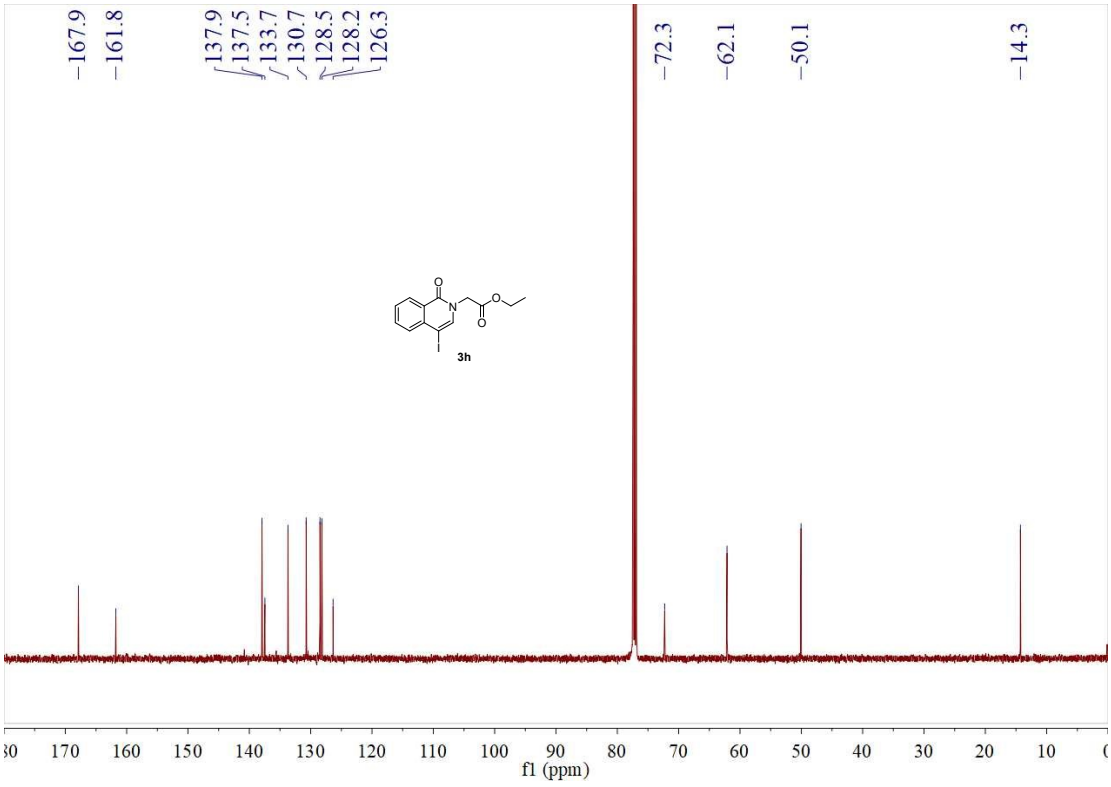
^{13}C NMR of **3g** in $CDCl_3$



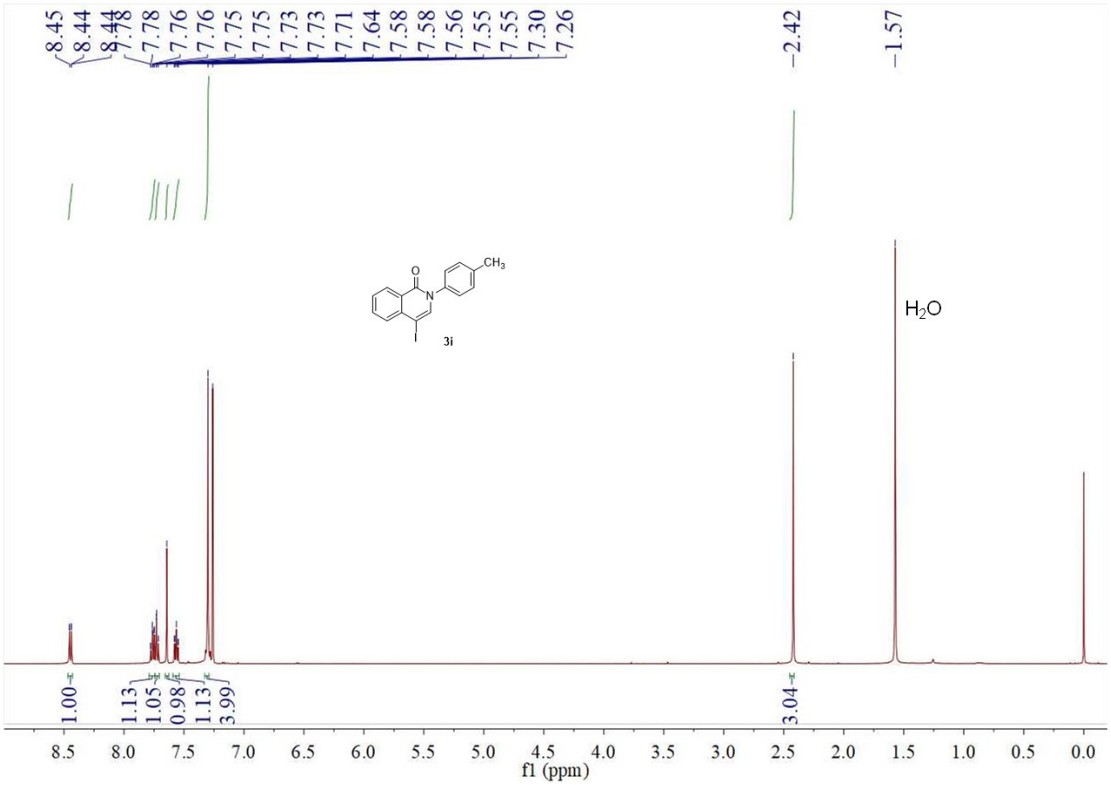
^{1}H NMR of **3h** in $CDCl_3$



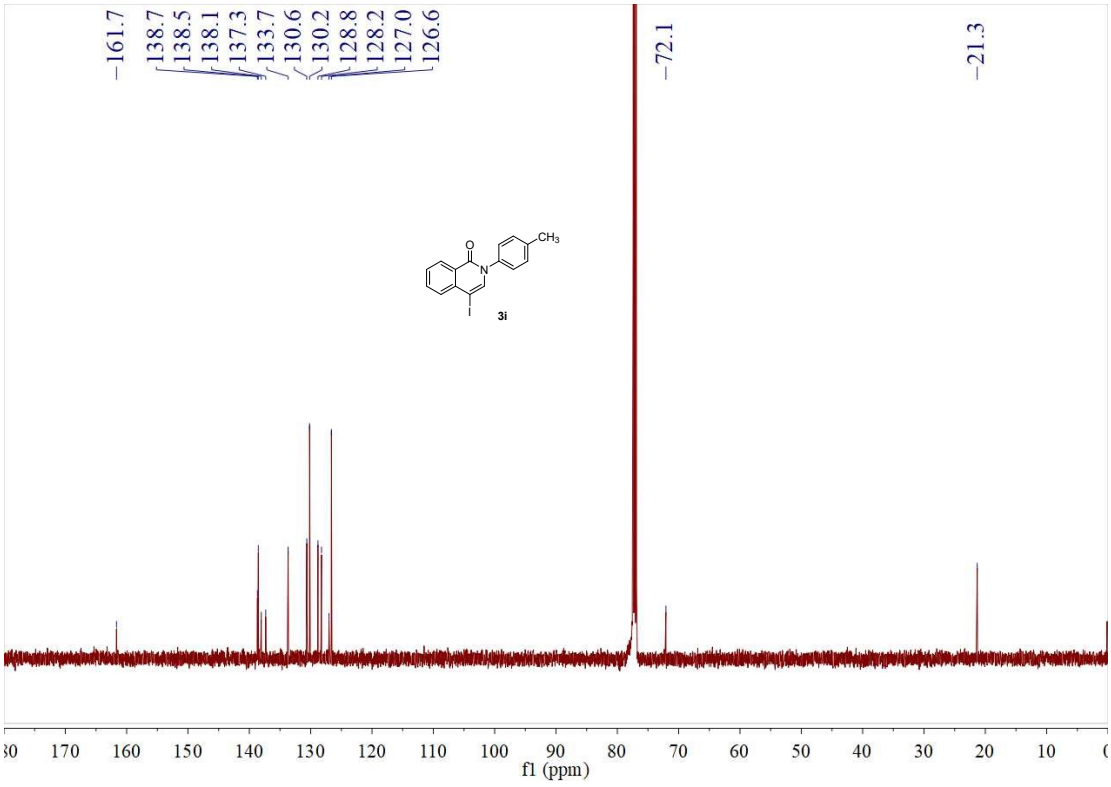
^{13}C NMR of **3h** in $CDCl_3$



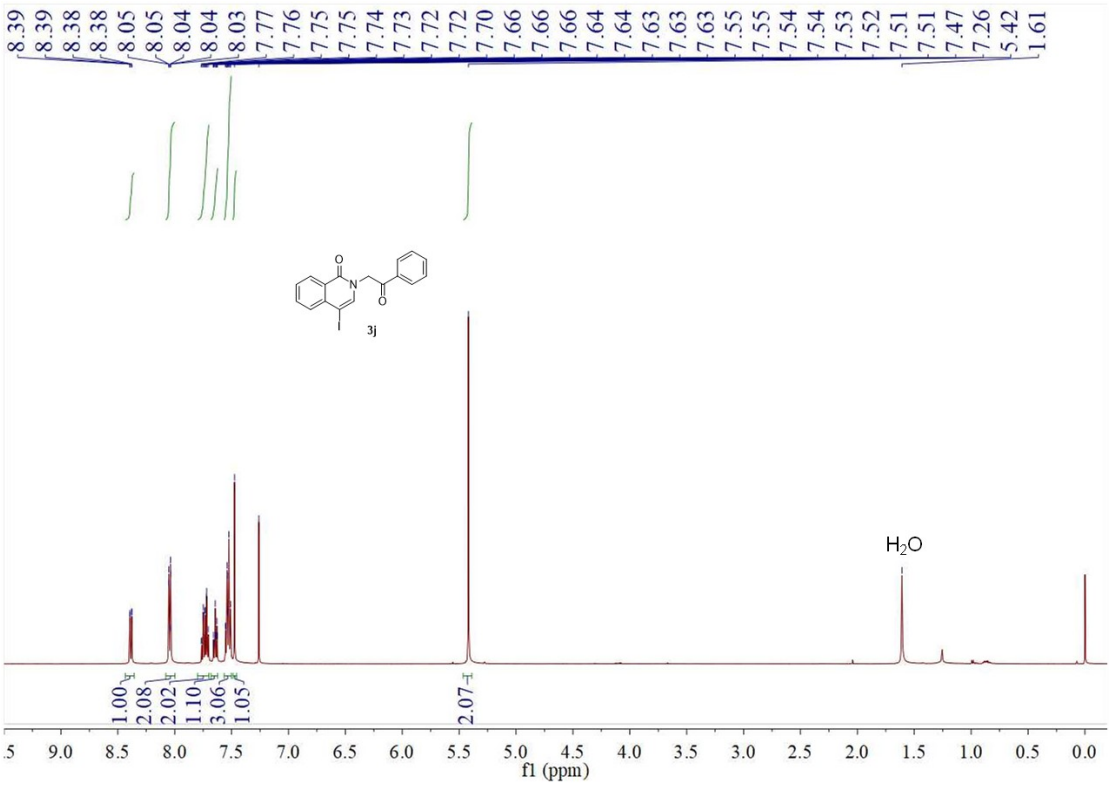
^{1}H NMR of **3i** in $CDCl_3$



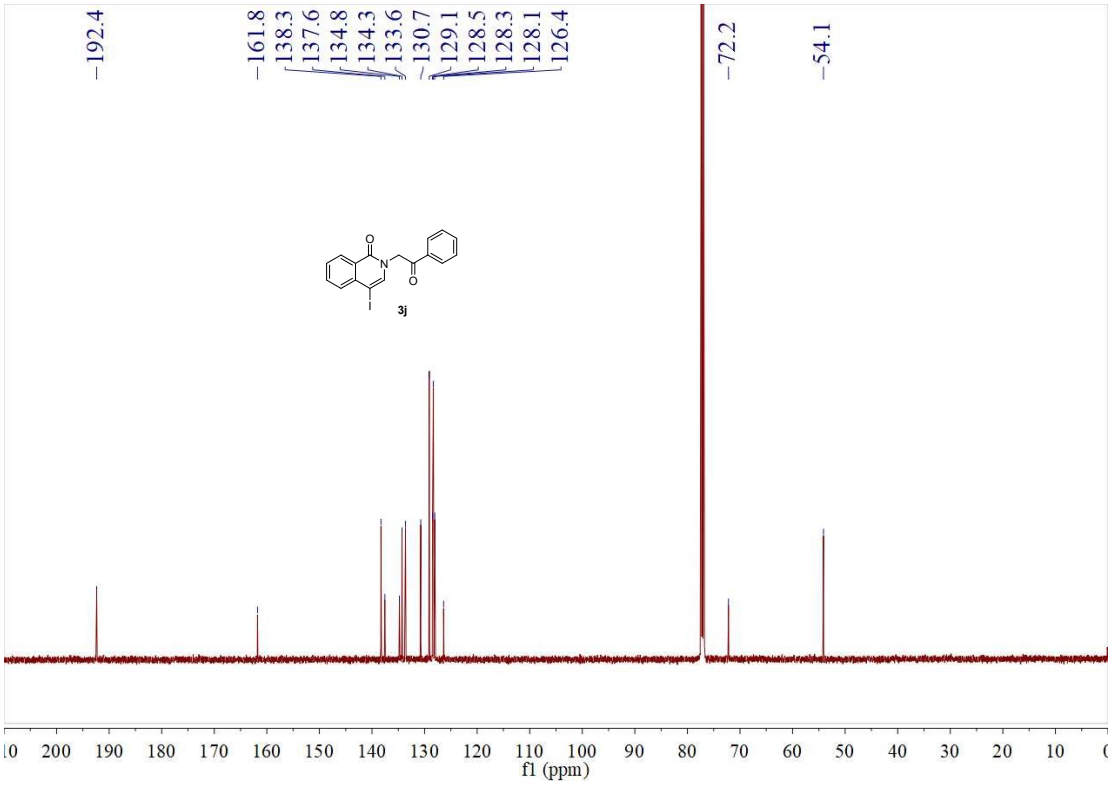
^{13}C NMR of **3i** in $CDCl_3$



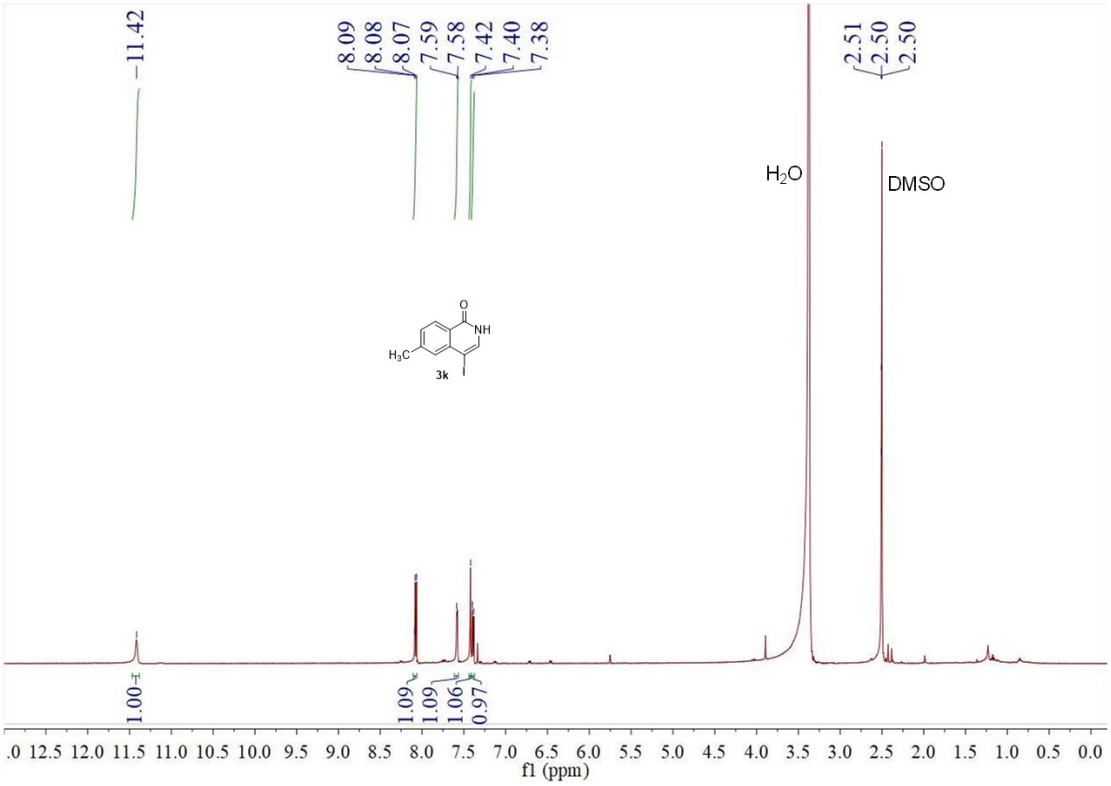
^{1}H NMR of **3j** in $CDCl_3$



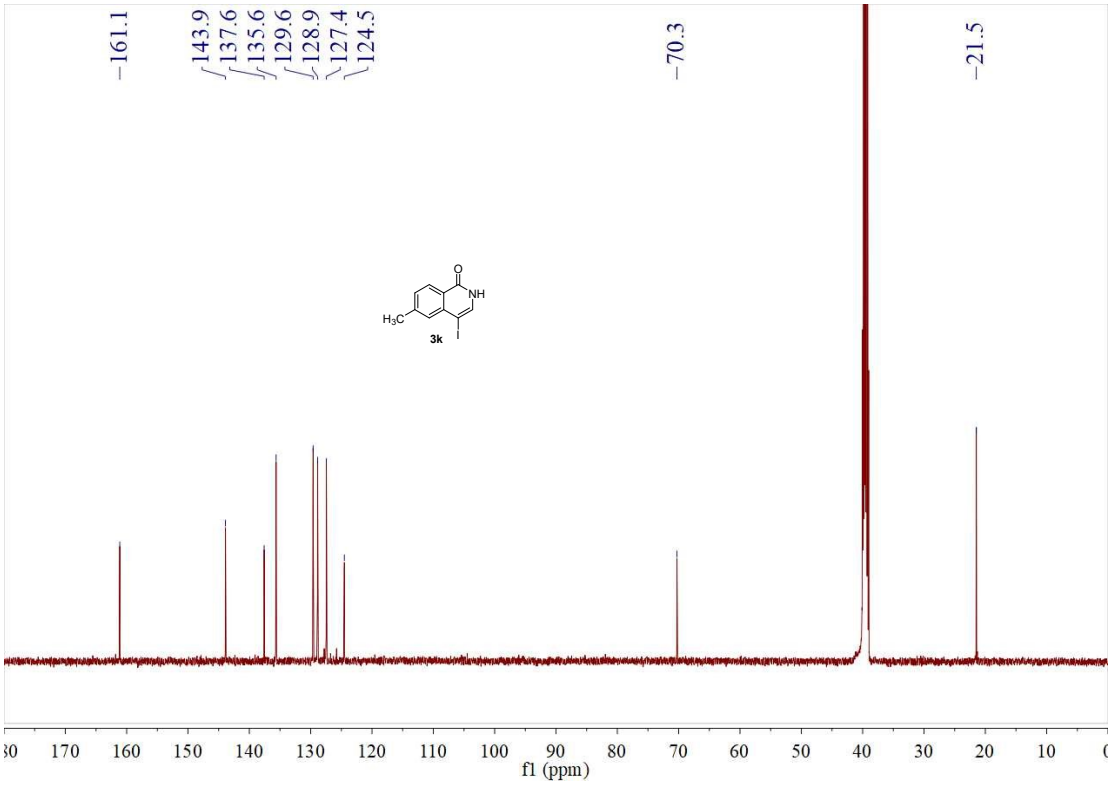
^{13}C NMR of **3j** in $CDCl_3$



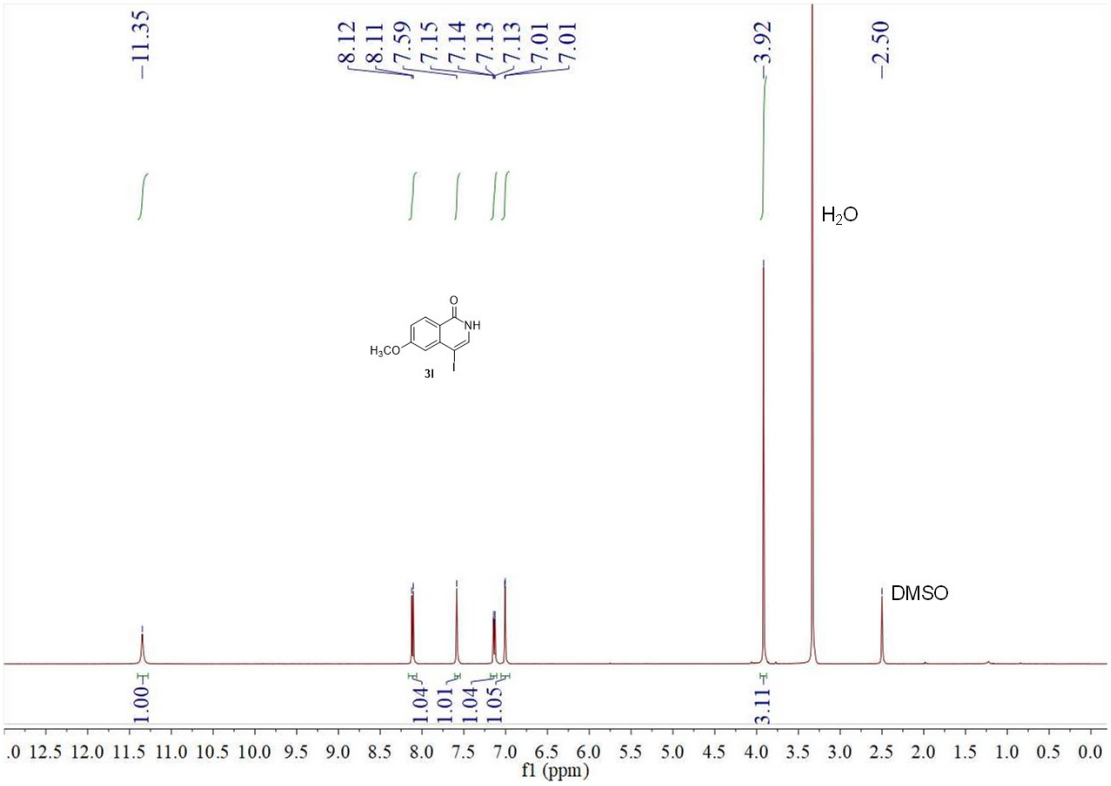
^{1}H NMR of **3k** in DMSO-d_6



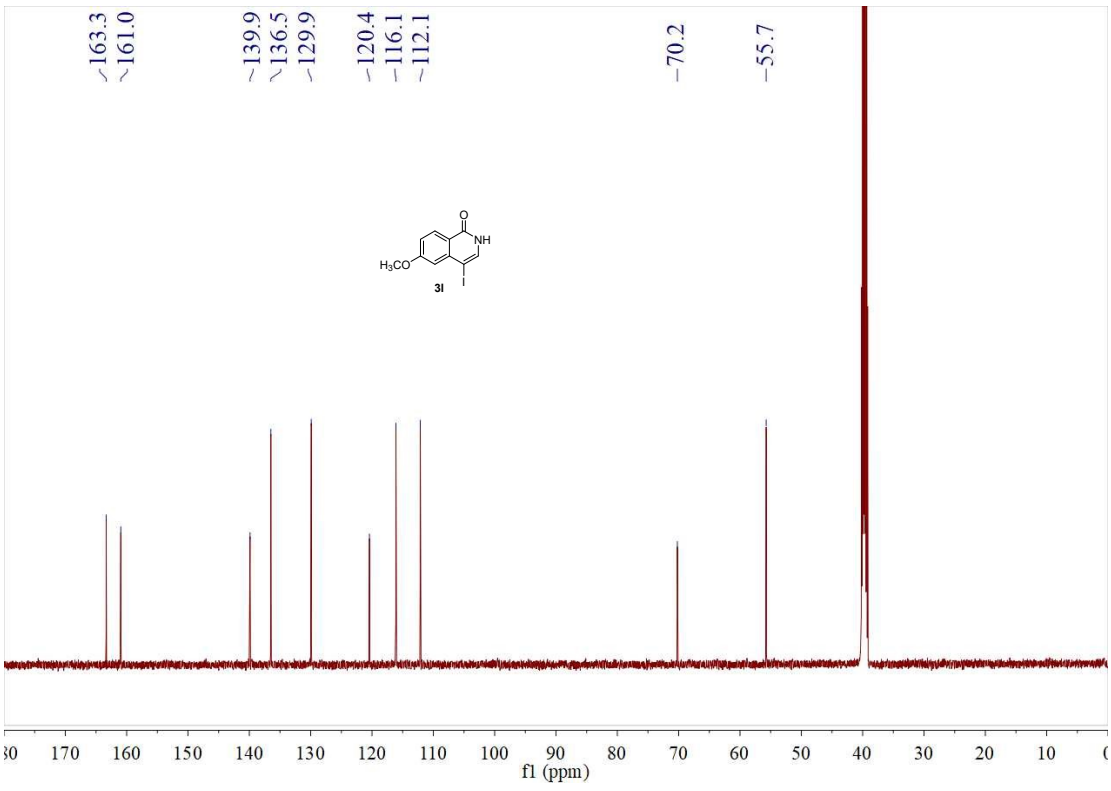
^{13}C NMR of **3k** in DMSO-d_6



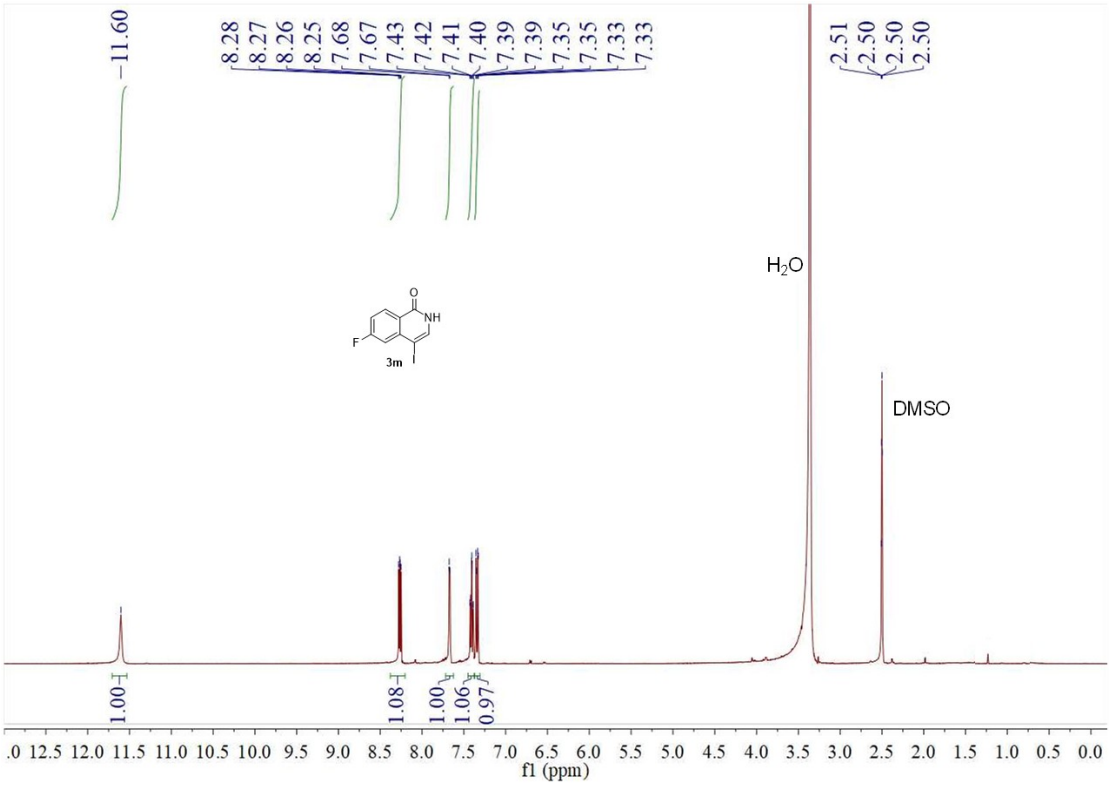
^{1}H NMR of **3l** in DMSO-d_6



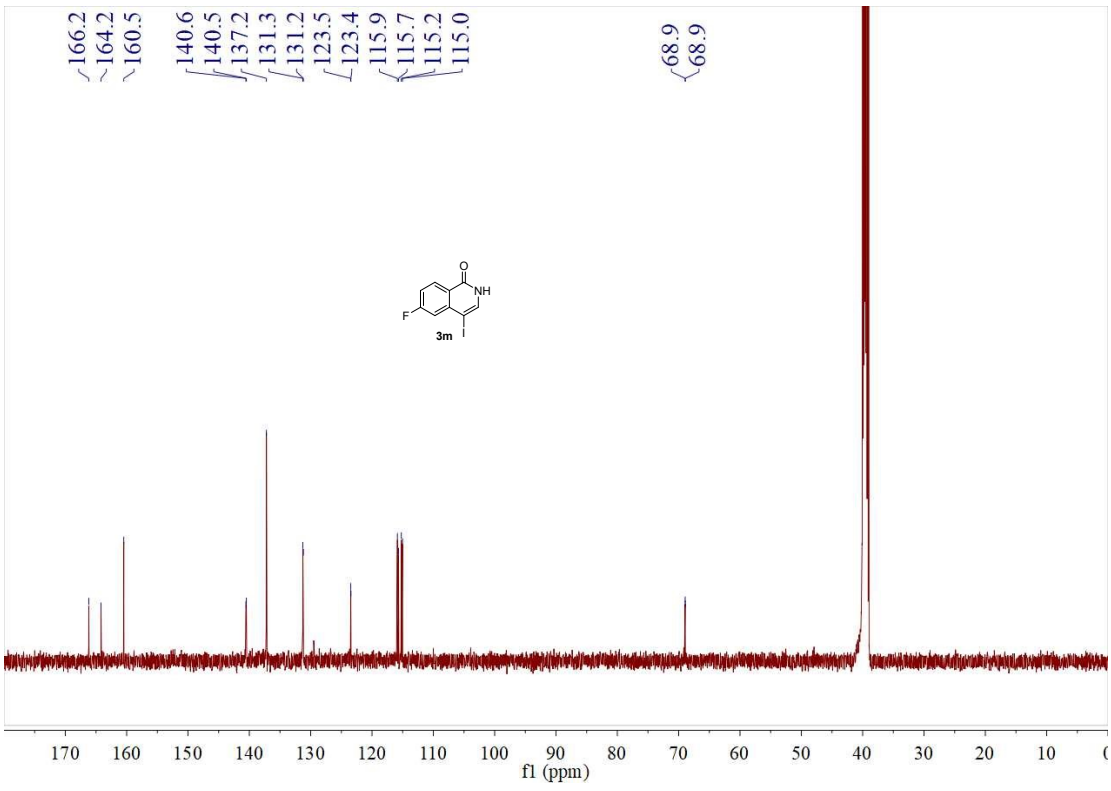
^{13}C NMR of **3l** in DMSO-d_6



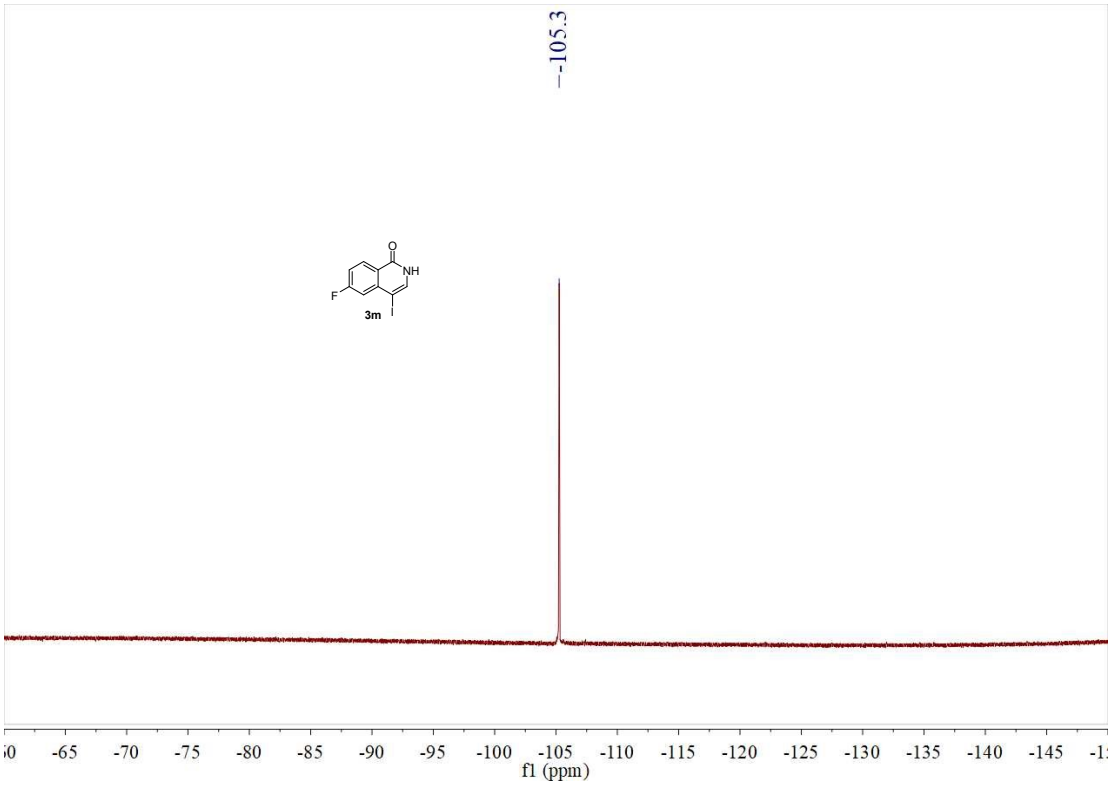
^{1}H NMR of **3m** in DMSO-d_6



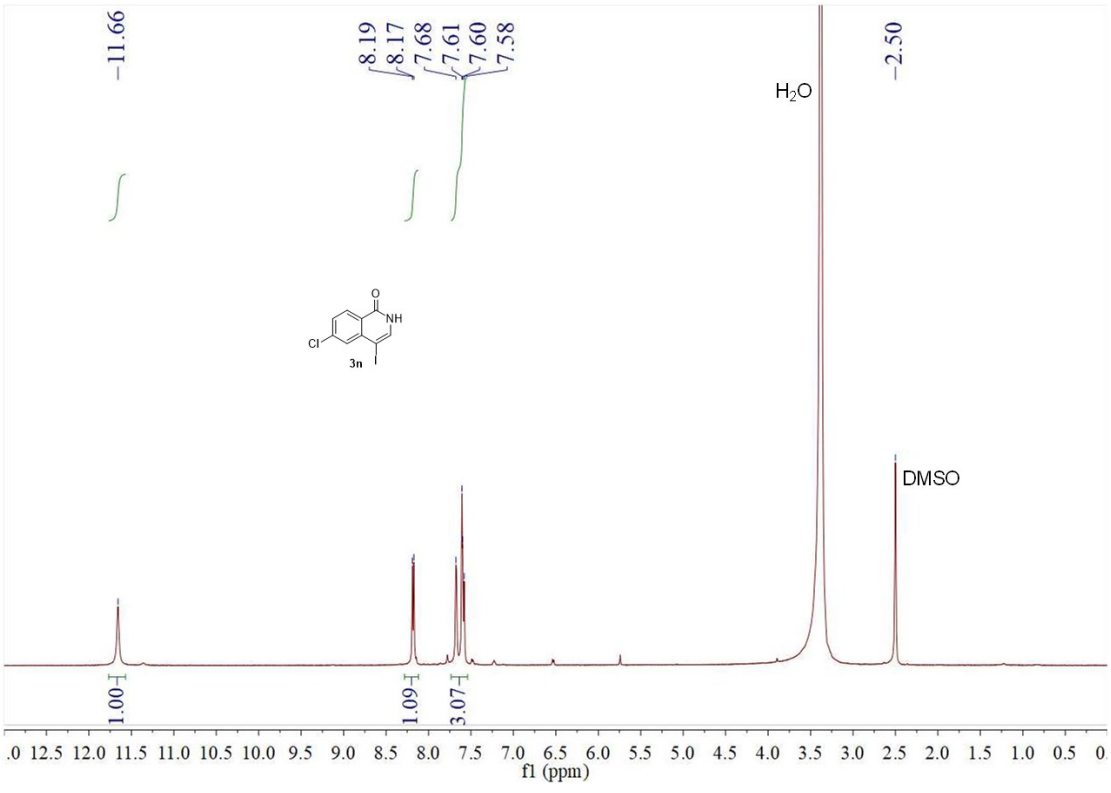
^{13}C NMR of **3m** in DMSO-d_6



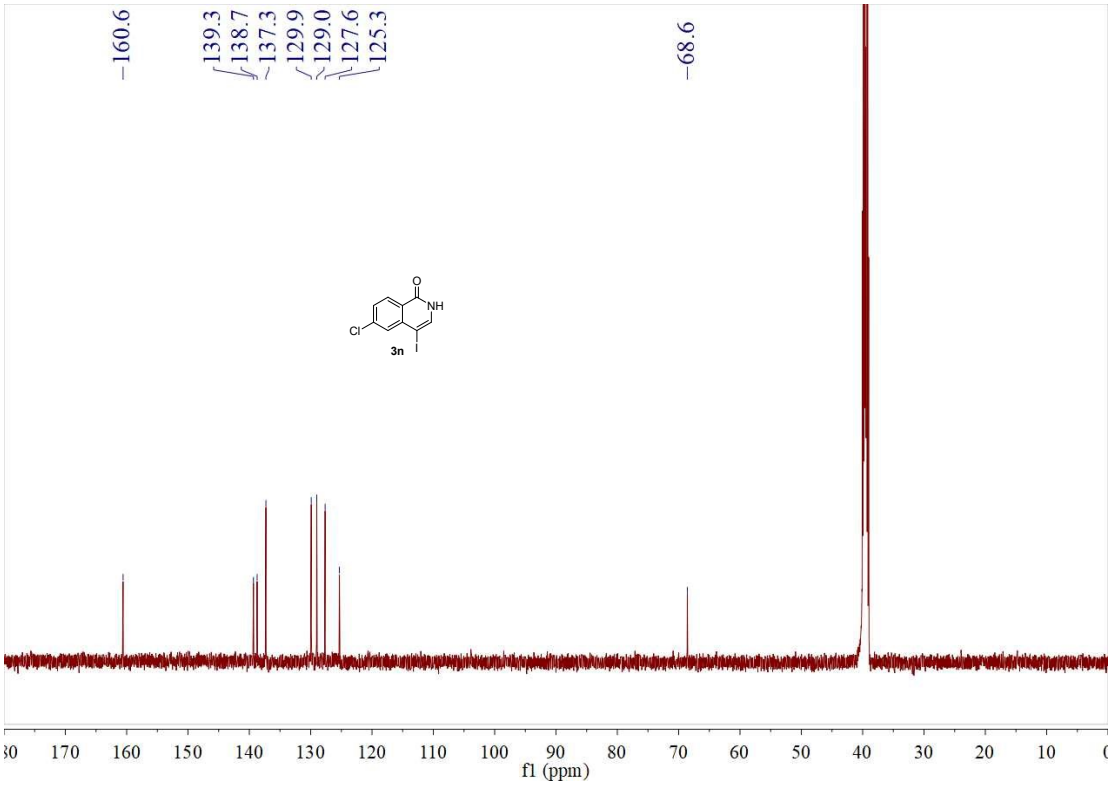
^{19}F NMR of **3m** in DMSO-d_6



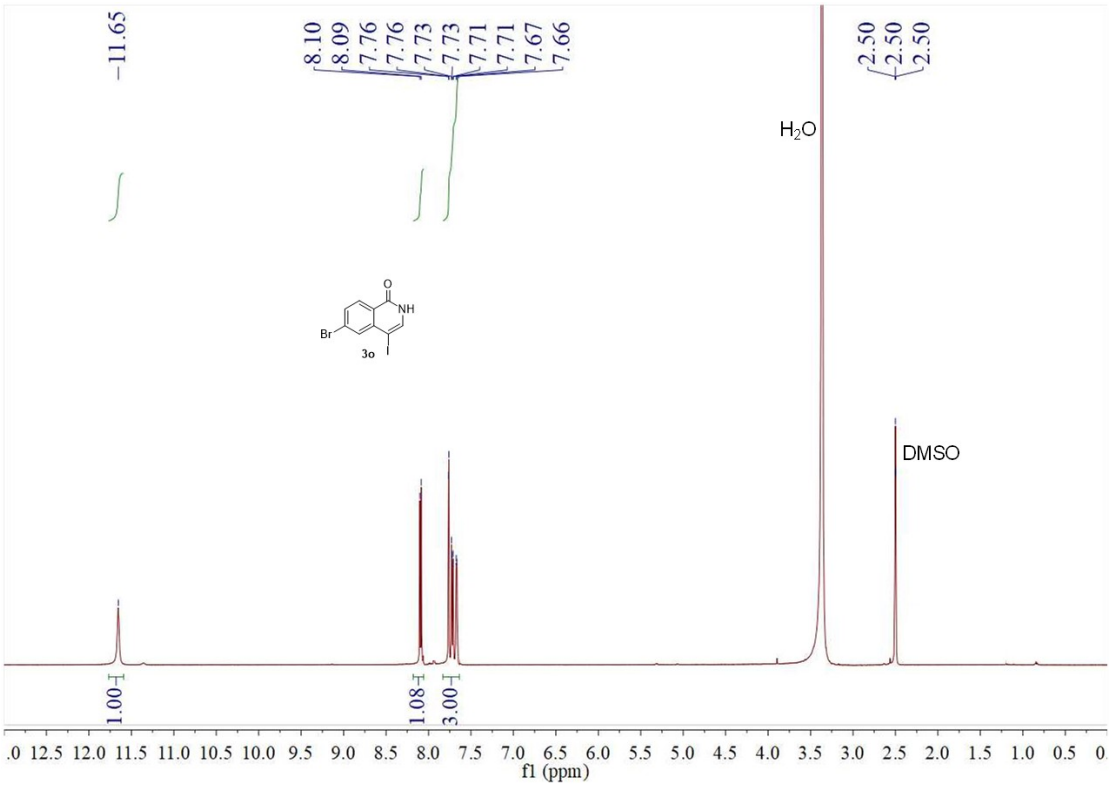
^{1}H NMR of **3n** in DMSO-d_6



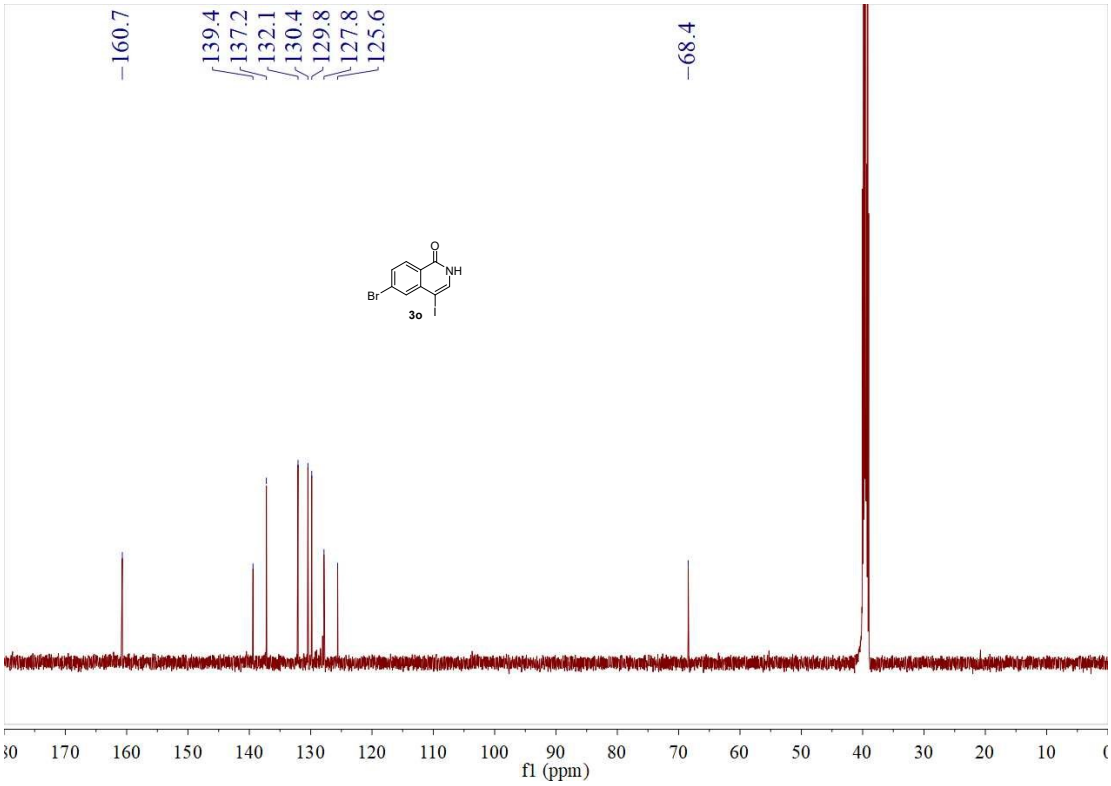
^{13}C NMR of **3n** in DMSO-d_6



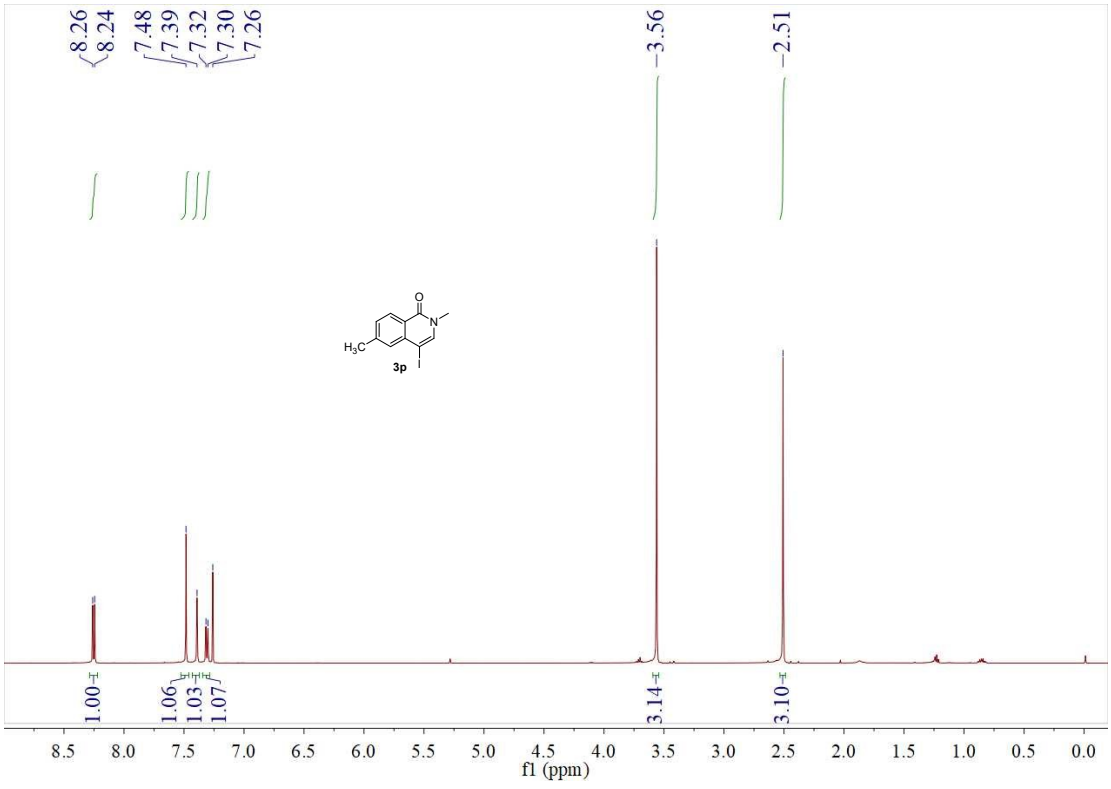
^{1}H NMR of **3o** in DMSO-d_6



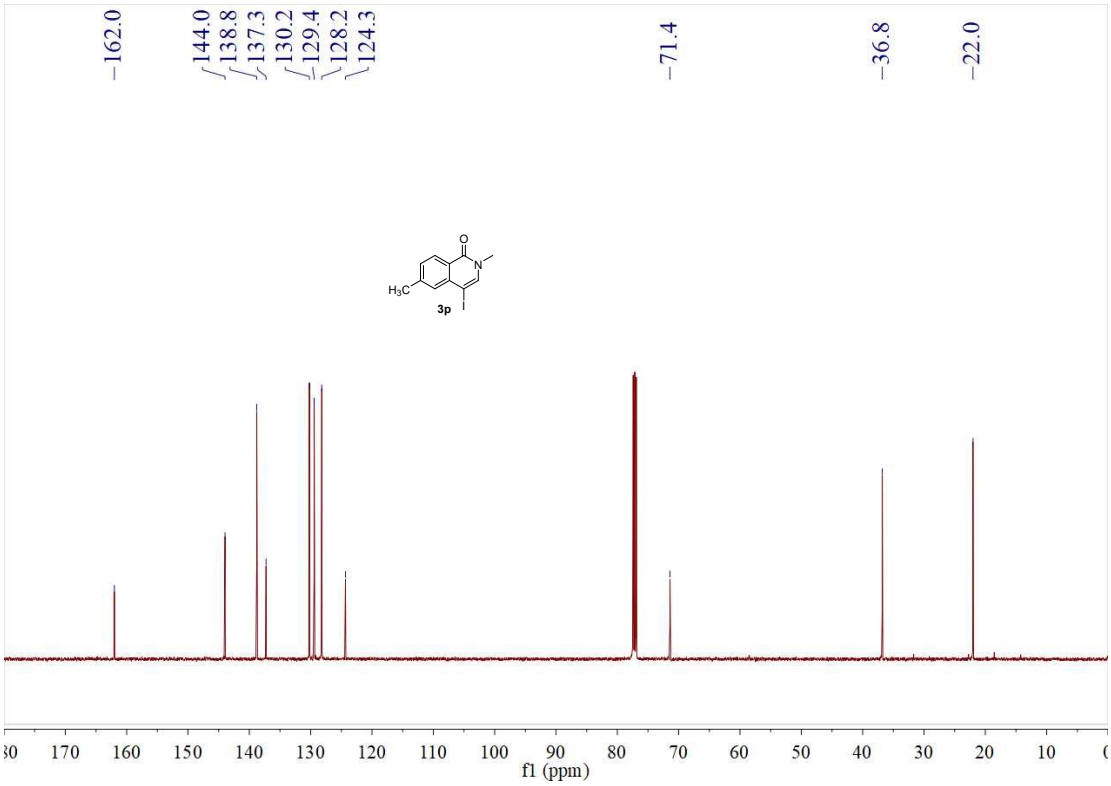
^{13}C NMR of **3o** in DMSO-d_6



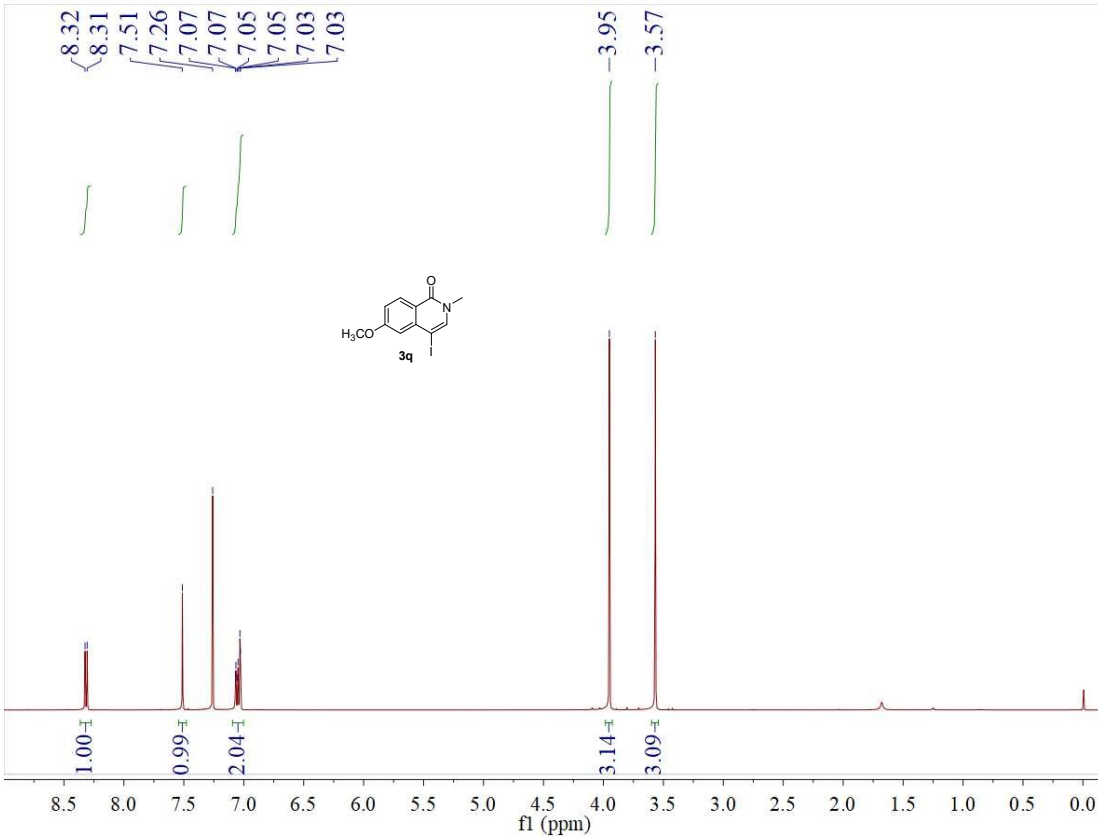
^{1}H NMR of **3p** in $CDCl_3$



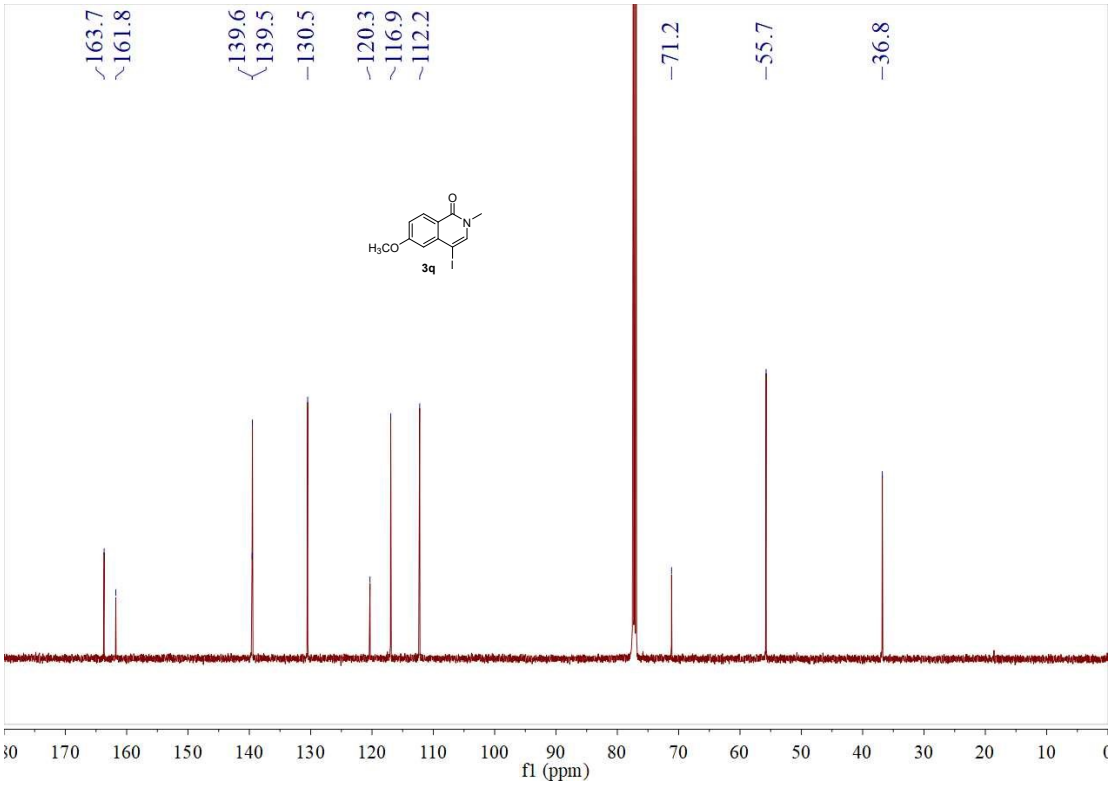
^{13}C NMR of **3p** in $CDCl_3$



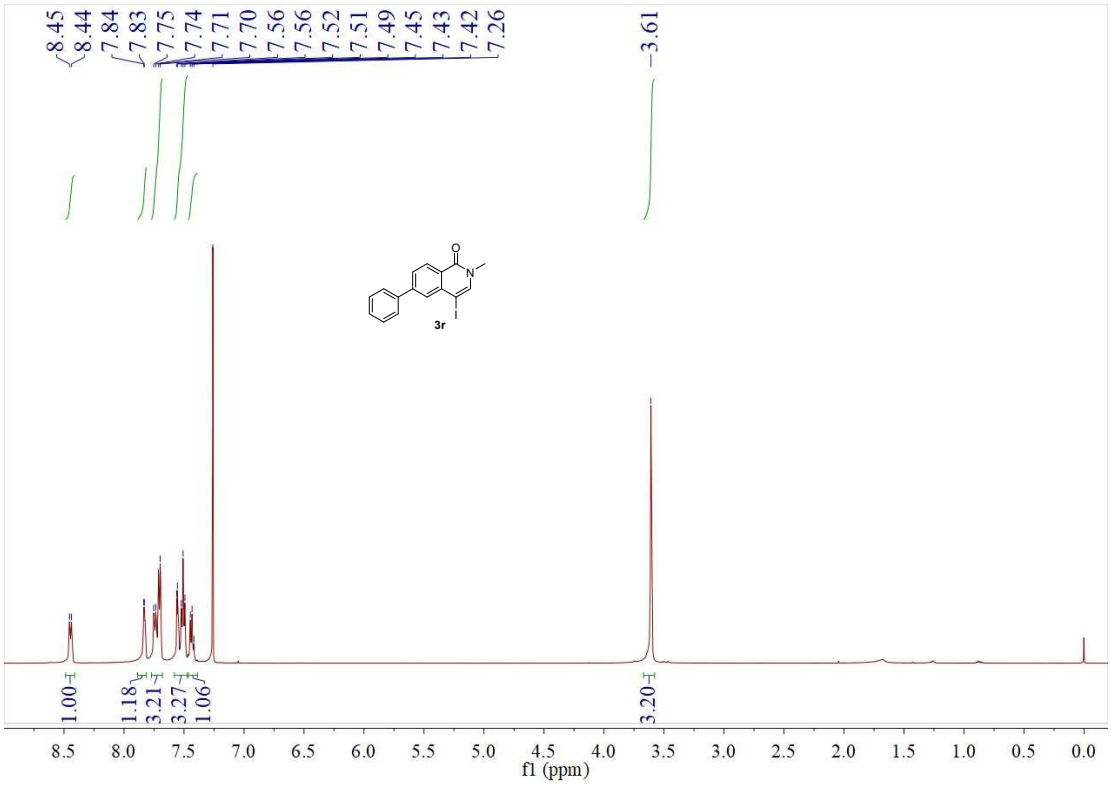
^{1}H NMR of **3q** in $CDCl_3$



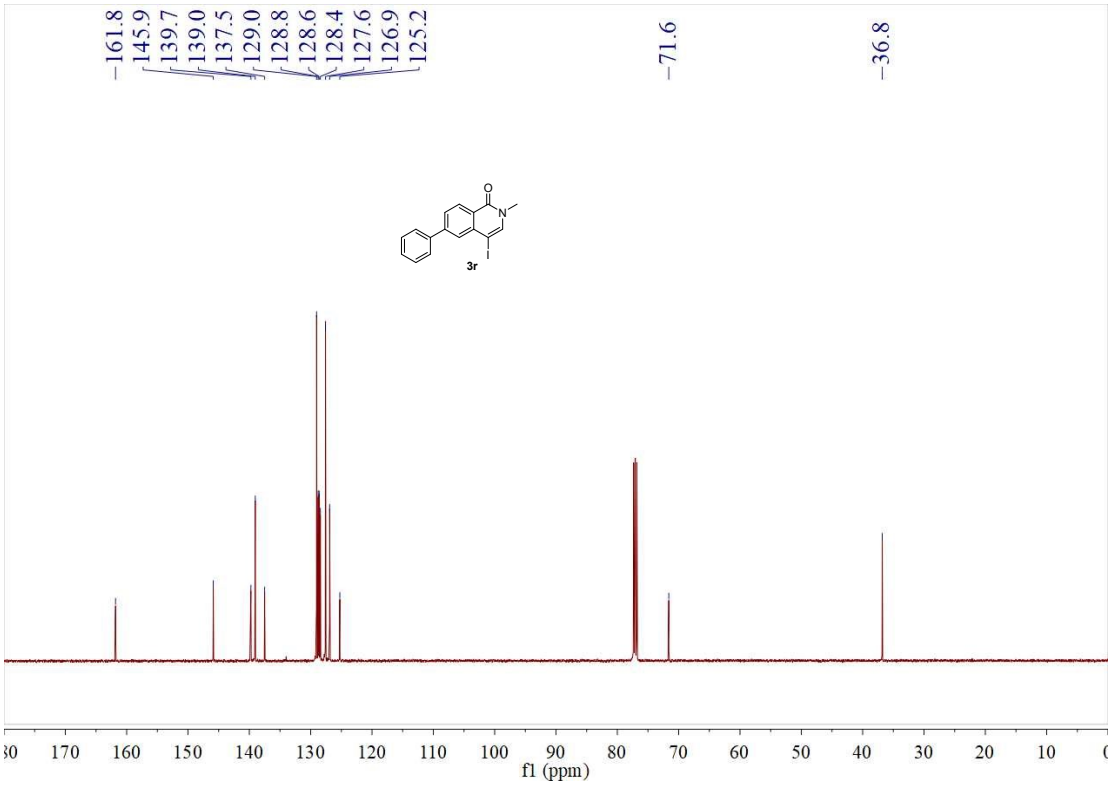
^{13}C NMR of **3q** in $CDCl_3$



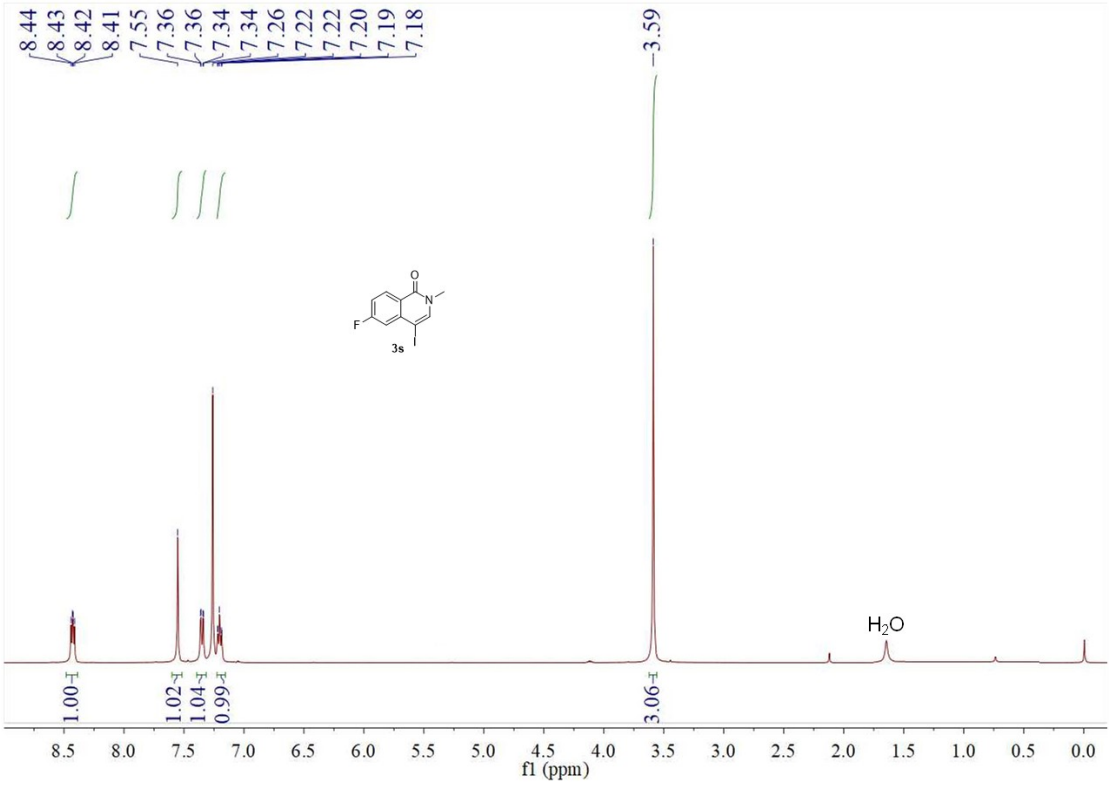
^{1}H NMR of **3r** in $CDCl_3$



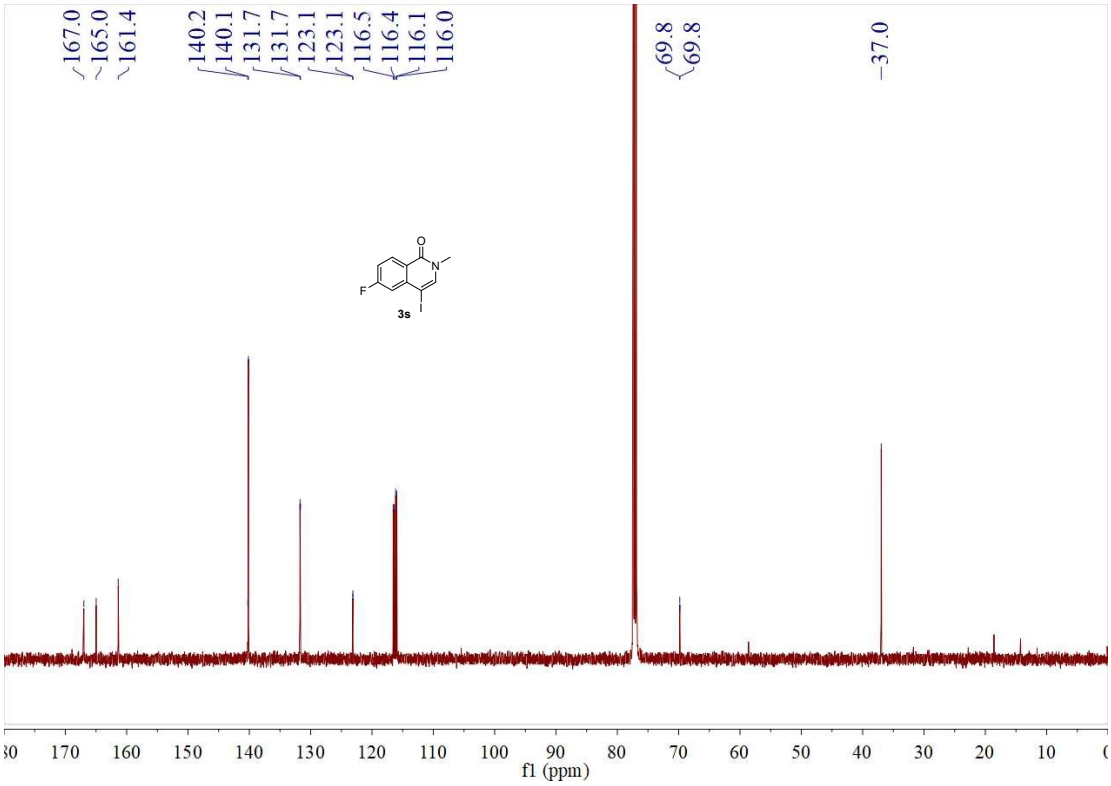
^{13}C NMR of **3r** in $CDCl_3$



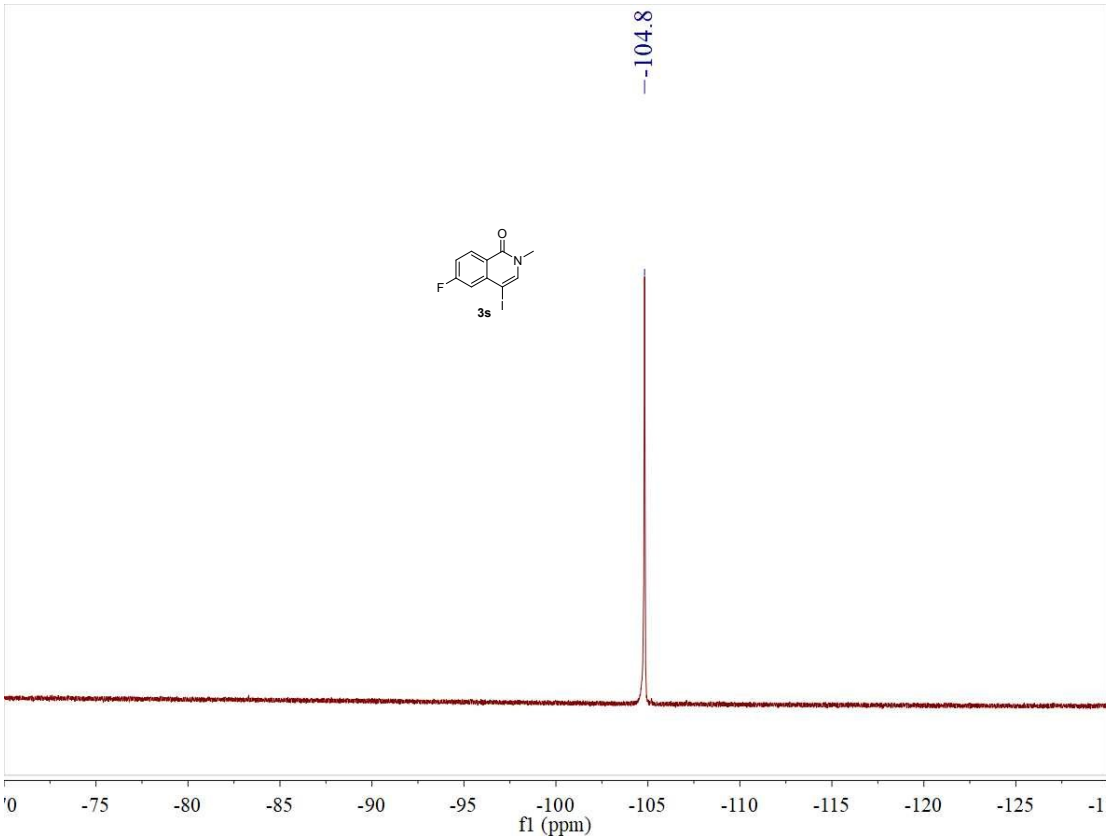
^{1}H NMR of **3s** in $CDCl_3$



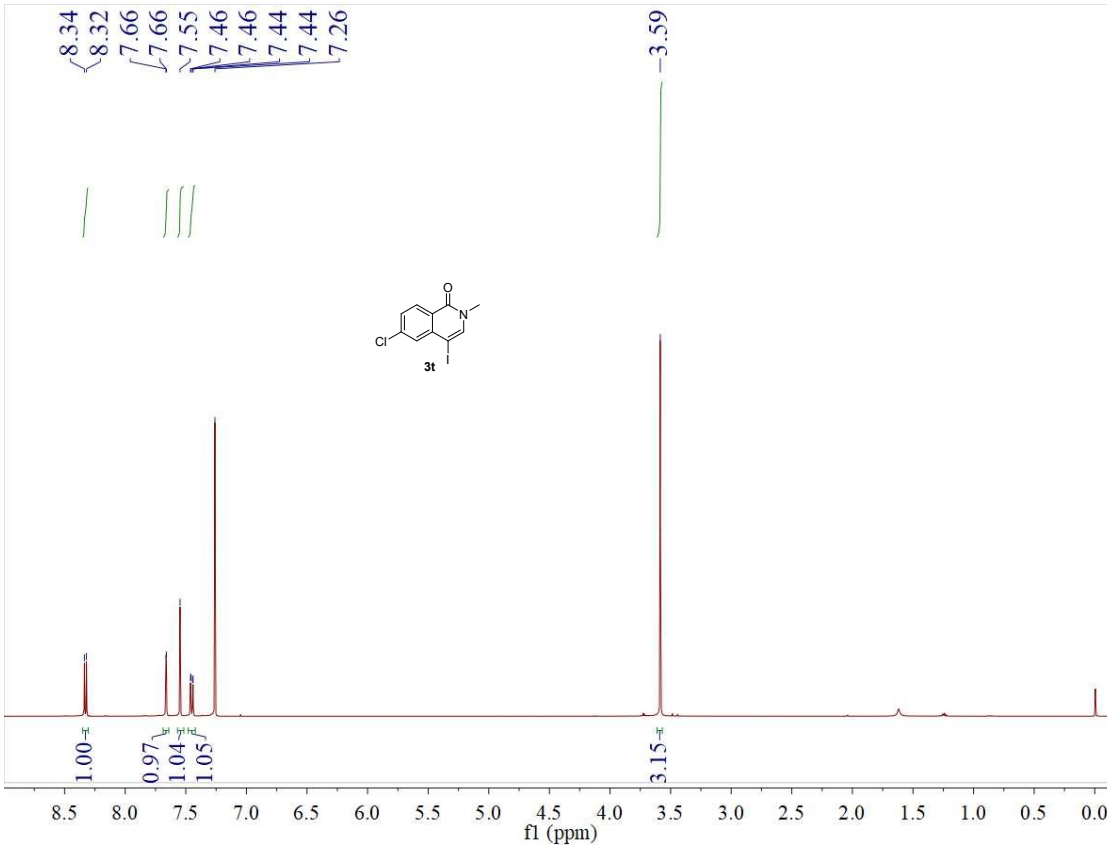
^{13}C NMR of **3s** in $CDCl_3$



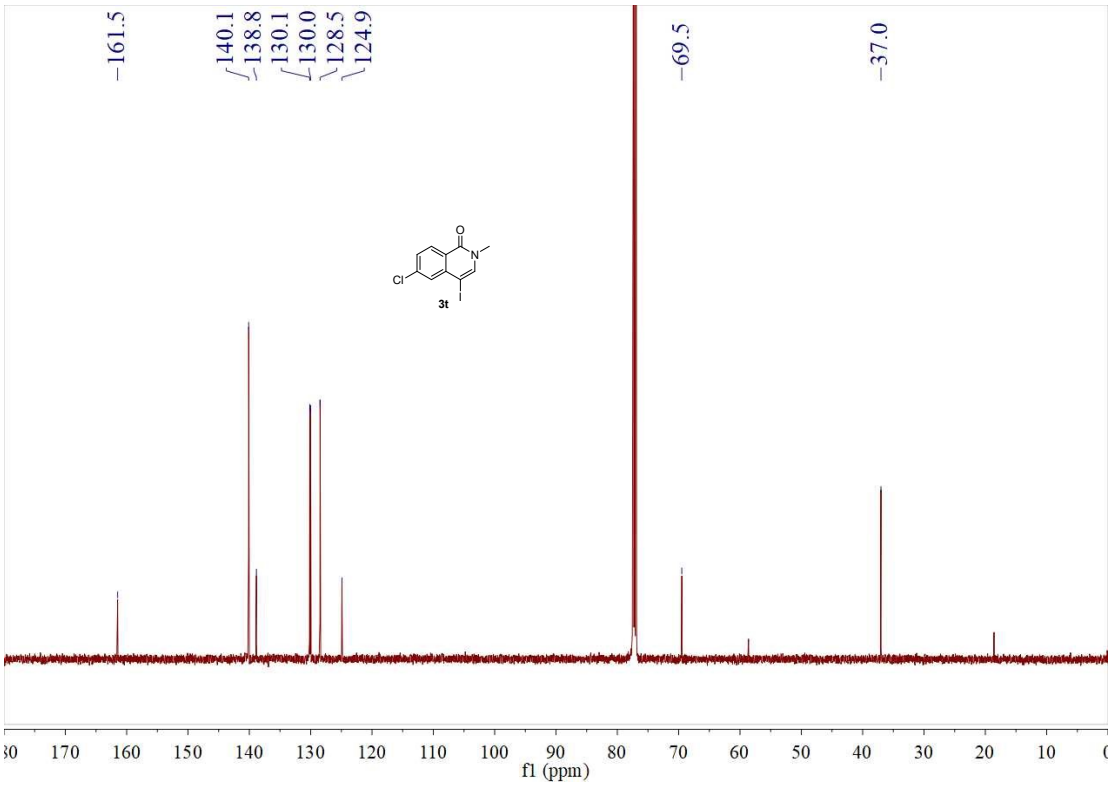
^{19}F NMR of **3s** in $CDCl_3$



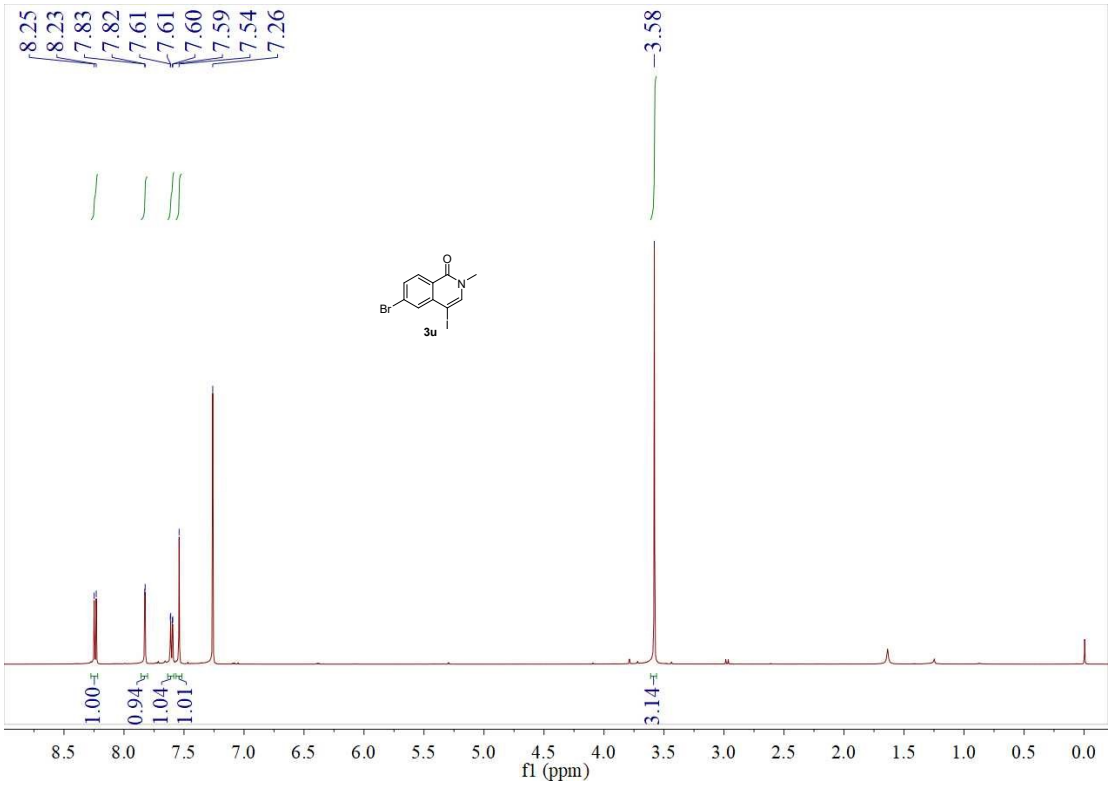
^{1}H NMR of **3t** in $CDCl_3$



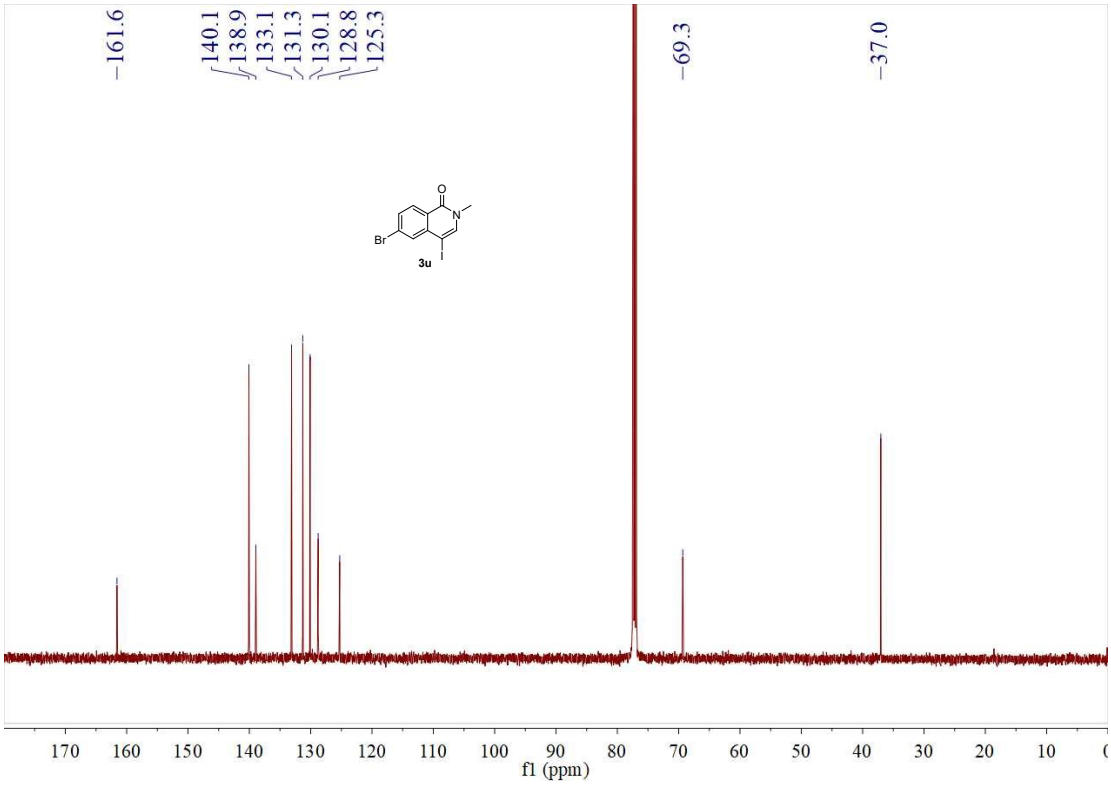
^{13}C NMR of **3t** in $CDCl_3$



^{1}H NMR of **3u** in $CDCl_3$

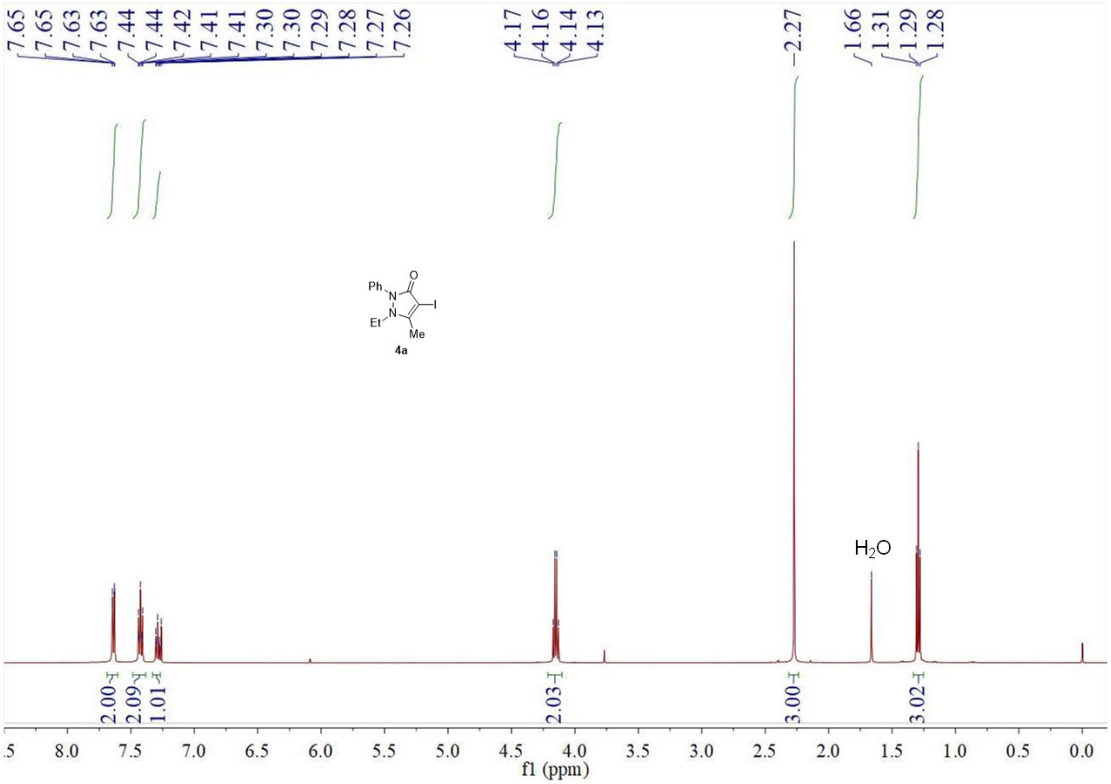


^{13}C NMR of **3u** in $CDCl_3$

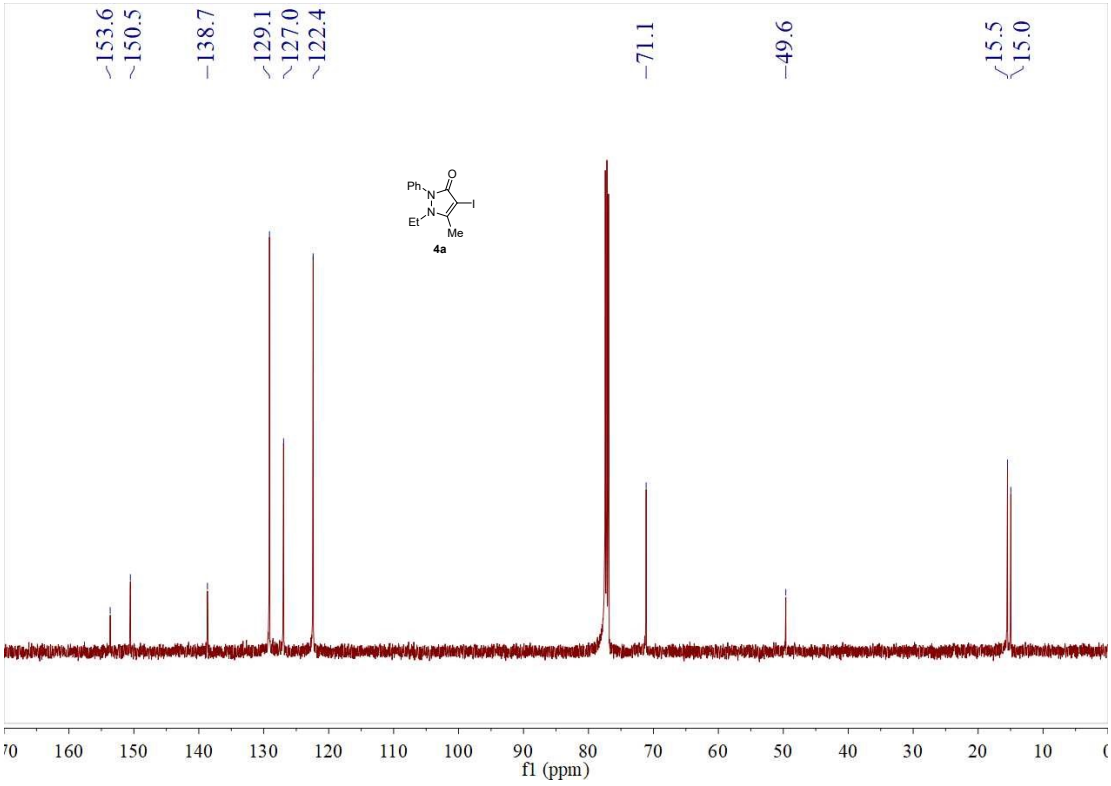


8. ^{1}H and ^{13}C NMR spectra of iodinated products (4a-4e)

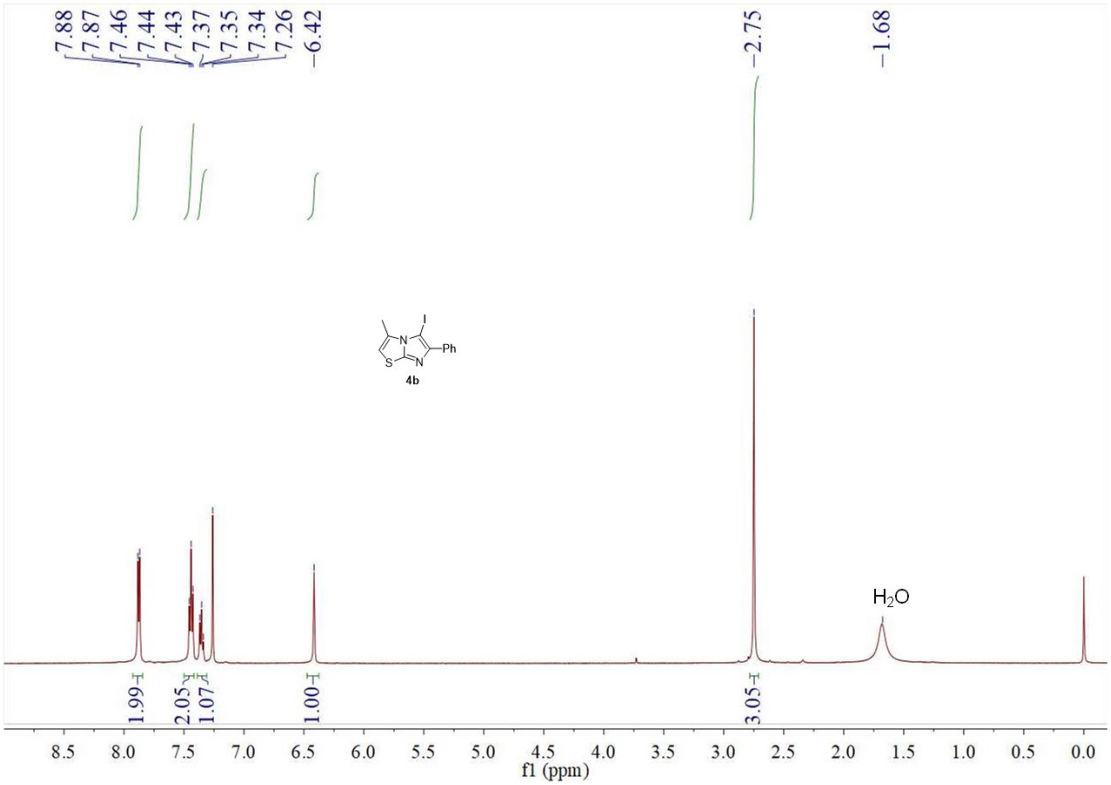
^{1}H NMR of **4a** in $CDCl_3$



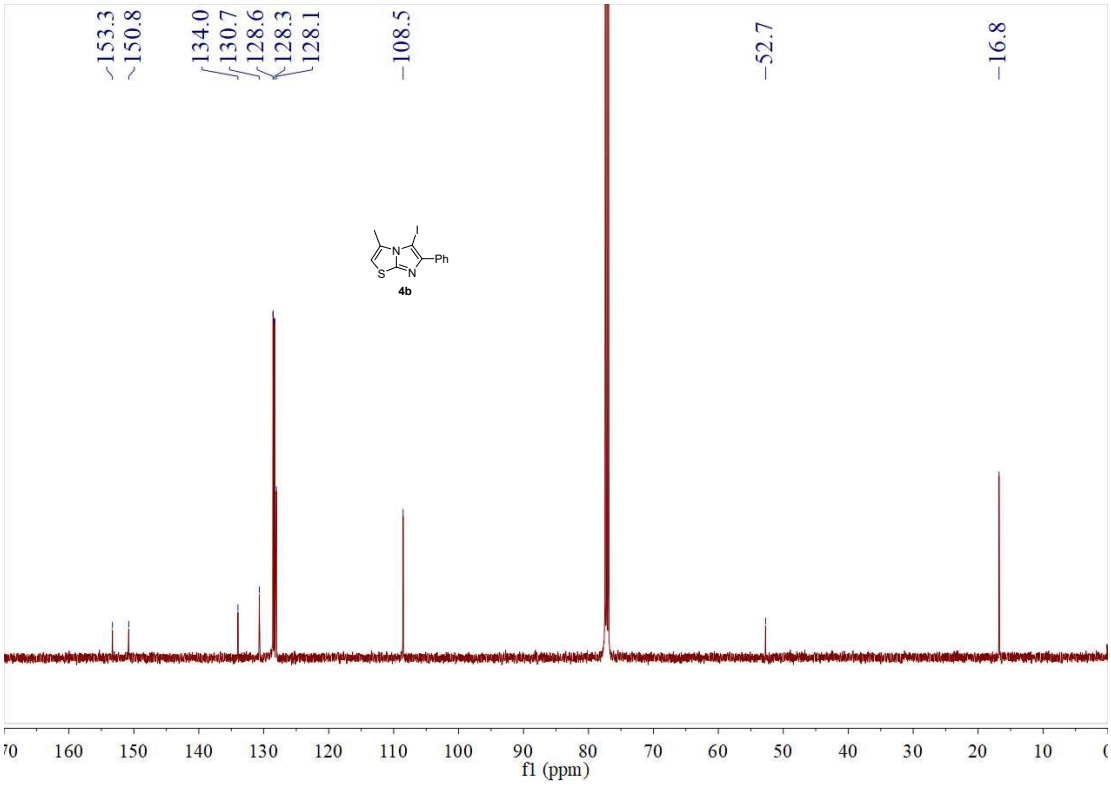
^{13}C NMR of **4a** in $CDCl_3$



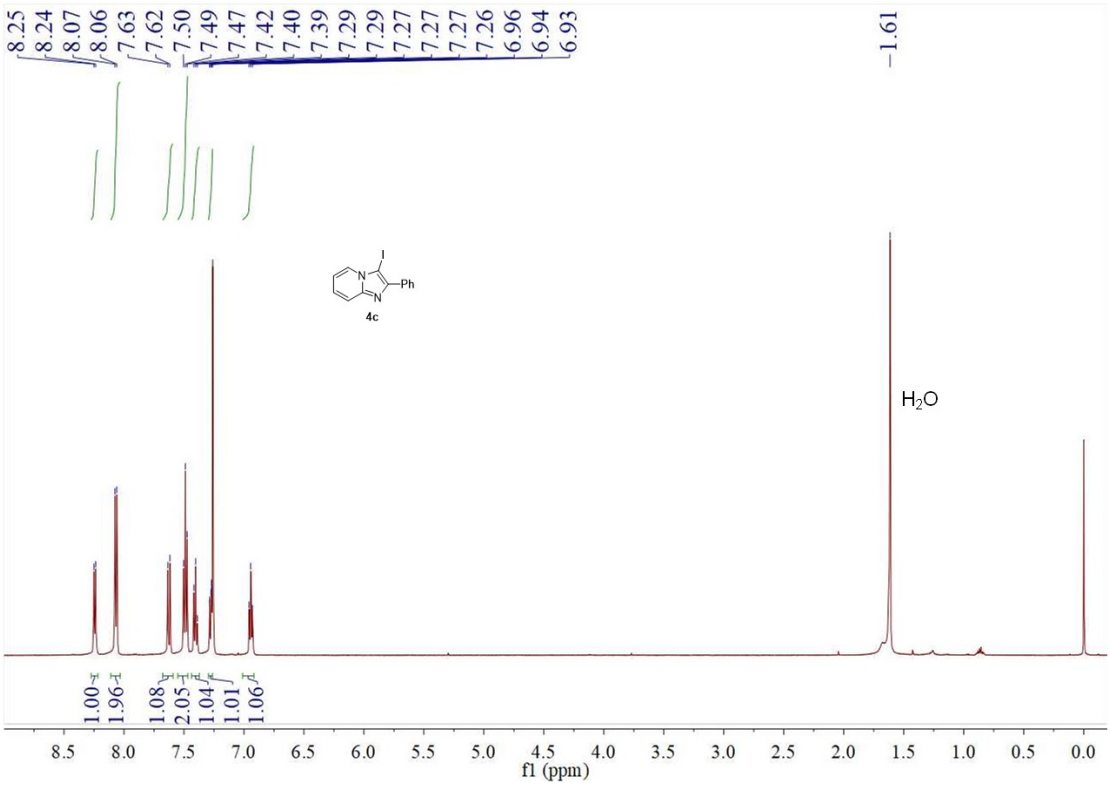
^{1}H NMR of **4b** in $CDCl_3$



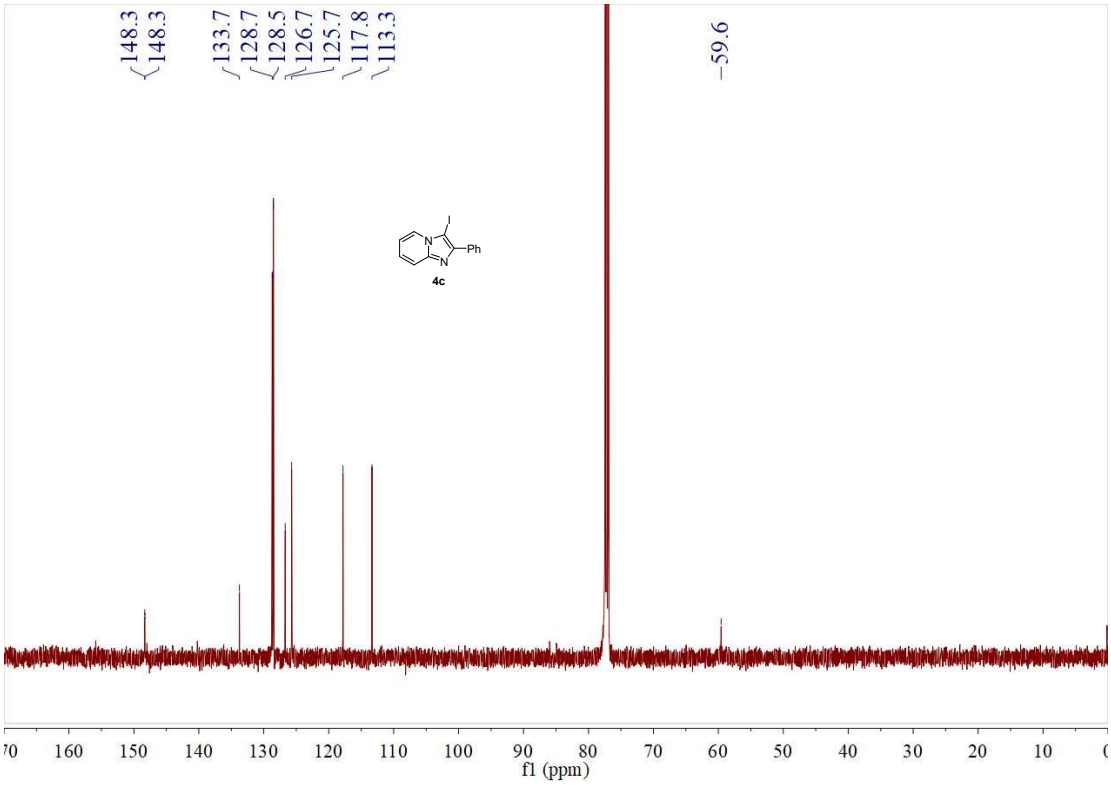
^{13}C NMR of **4b** in $CDCl_3$



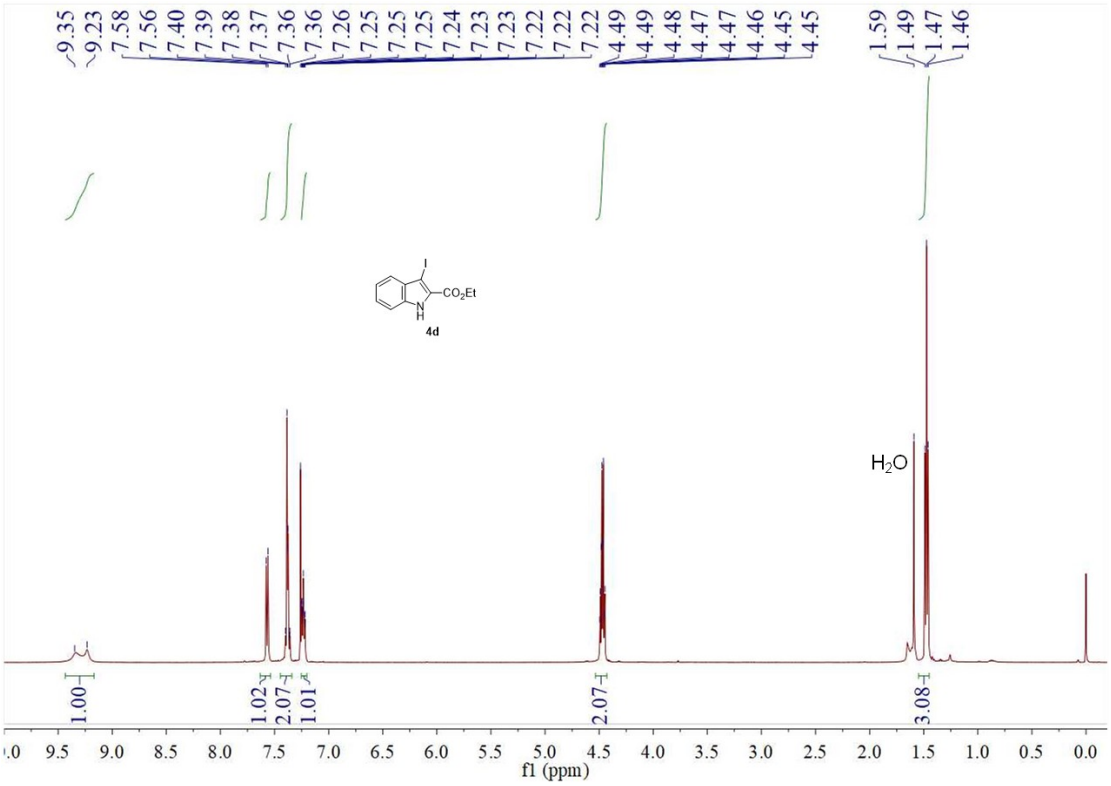
^{1}H NMR of **4c** in $CDCl_3$



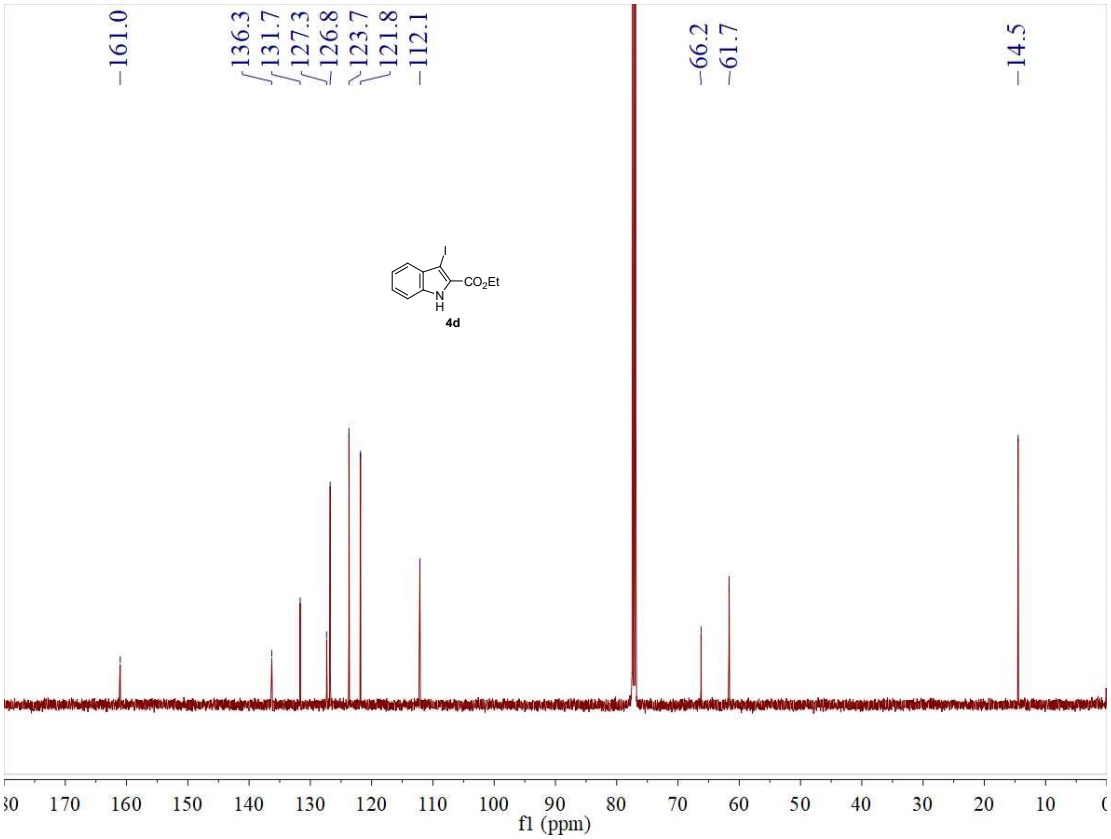
^{13}C NMR of **4c** in $CDCl_3$



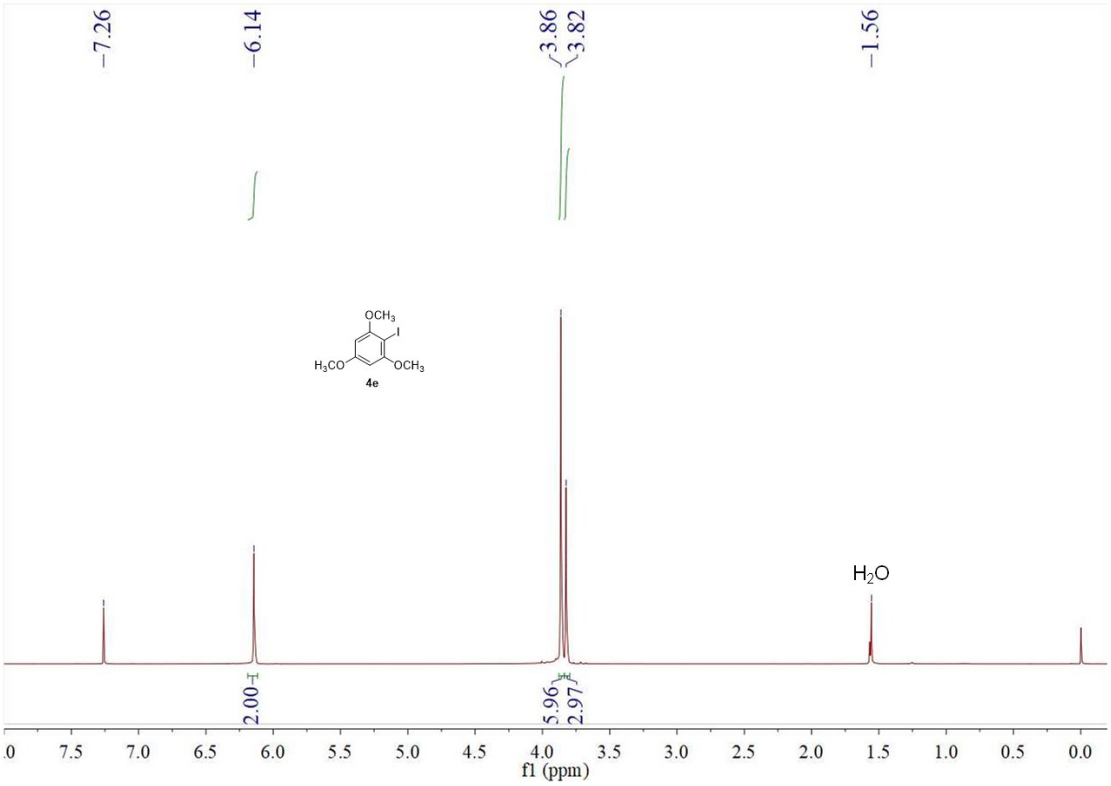
^{1}H NMR of **4d** in $CDCl_3$



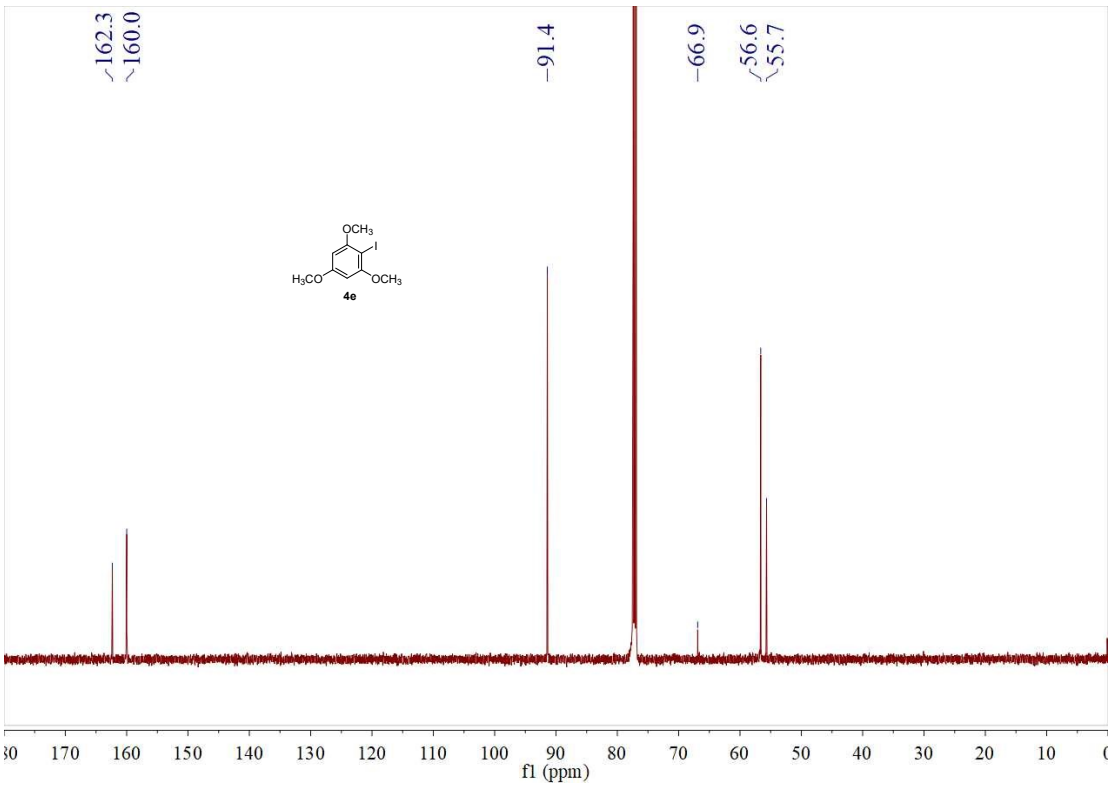
^{13}C NMR of **4d** in $CDCl_3$



^{1}H NMR of **4e** in $CDCl_3$

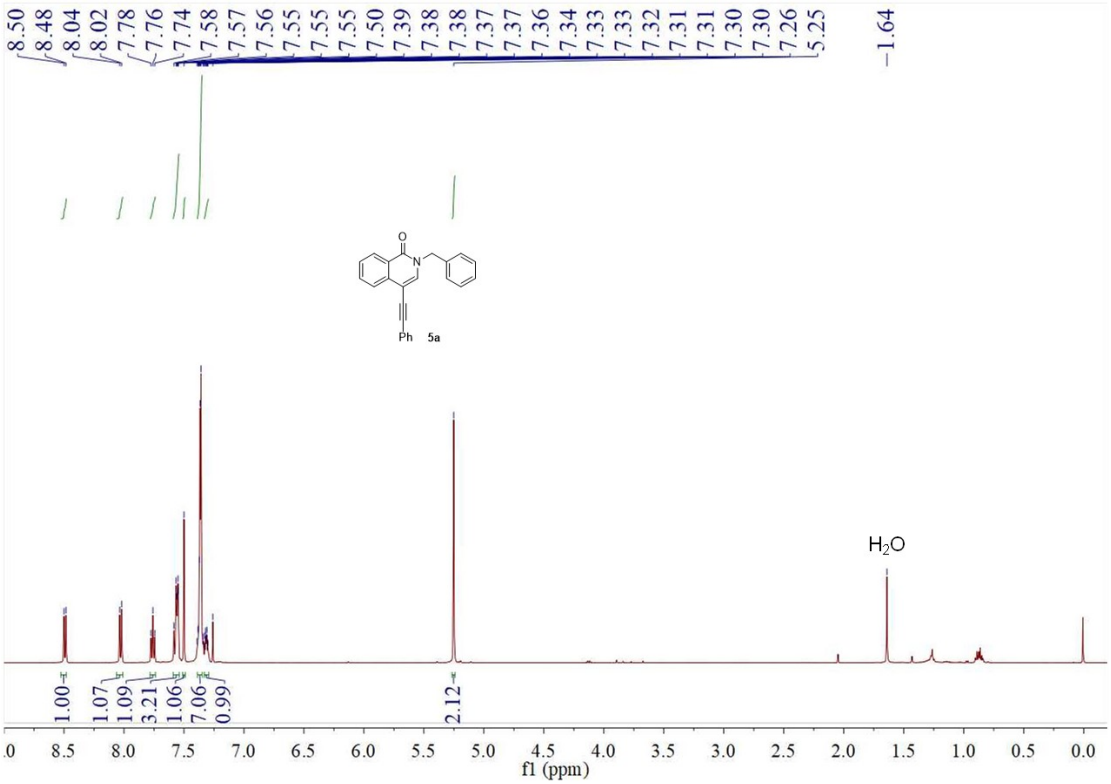


^{13}C NMR of **4e** in $CDCl_3$

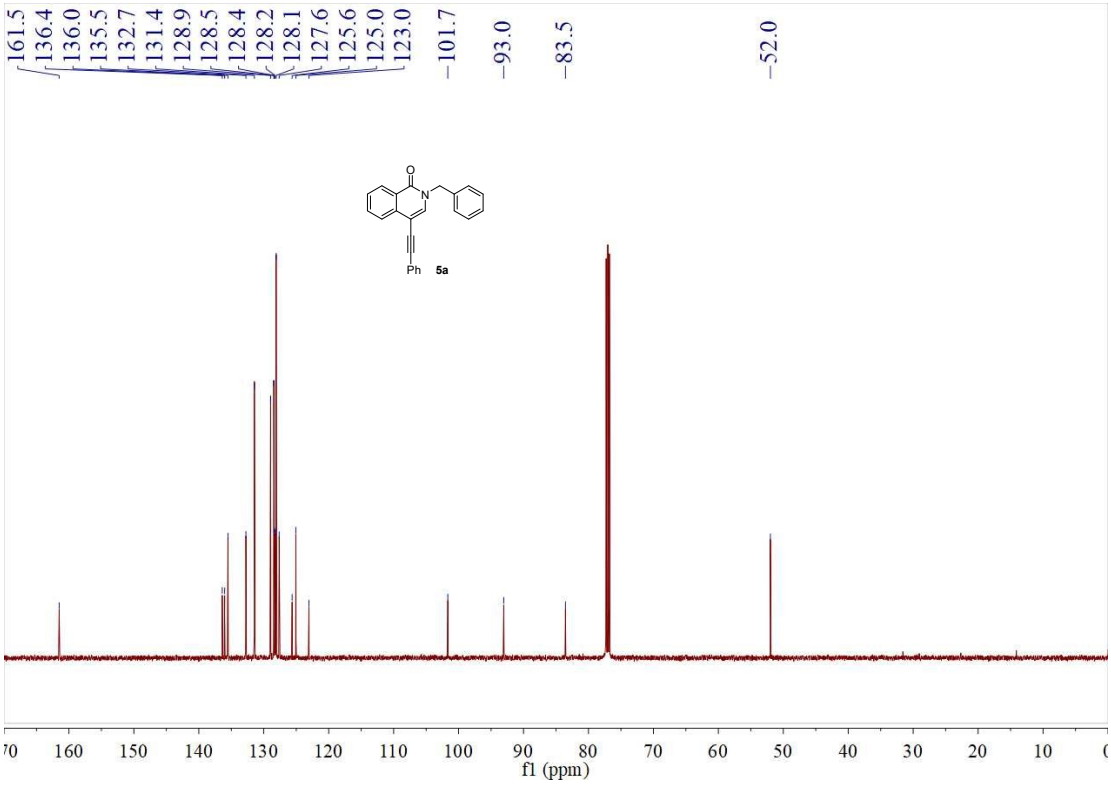


9. ^{1}H and ^{13}C NMR spectra of coupling products (5a-5c)

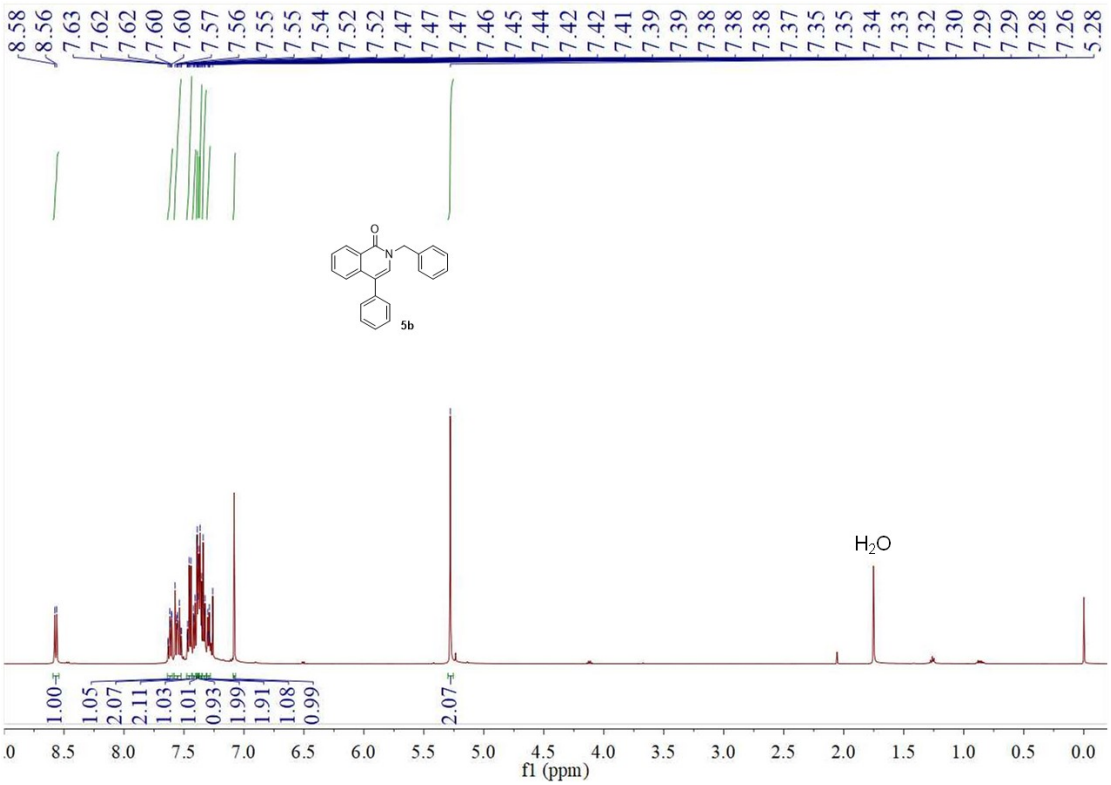
^{1}H NMR of **5a** in $CDCl_3$



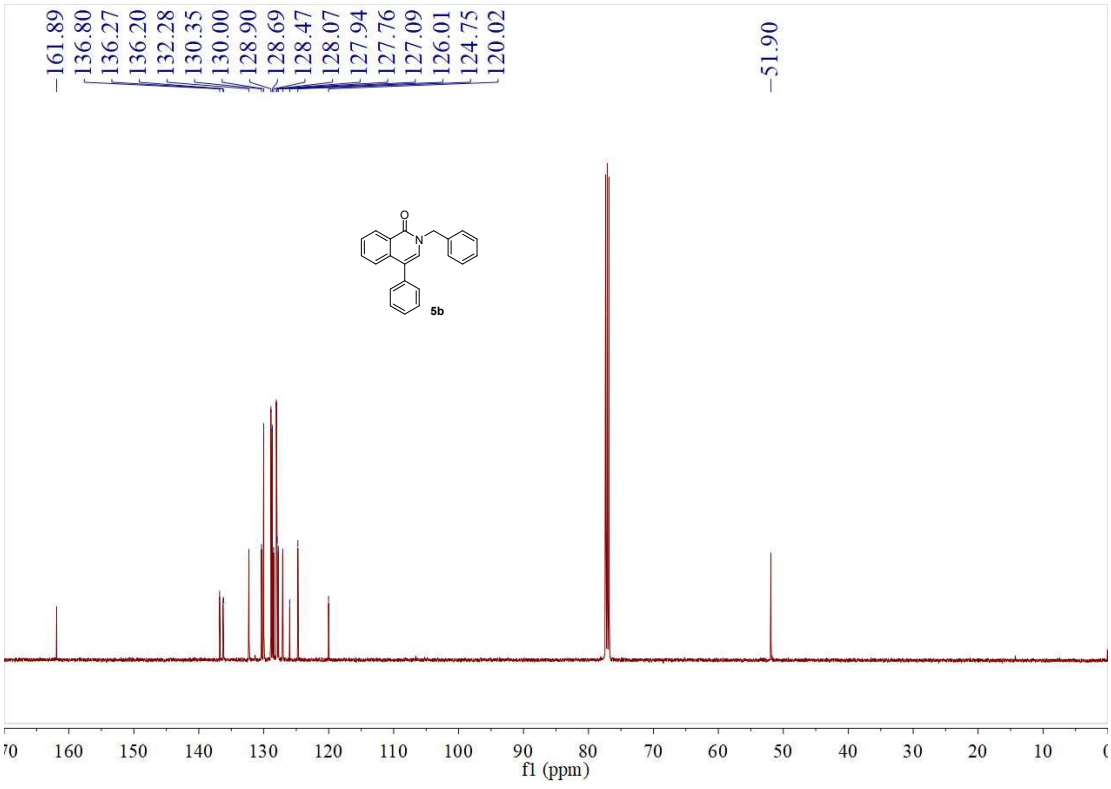
^{13}C NMR of **5a** in $CDCl_3$



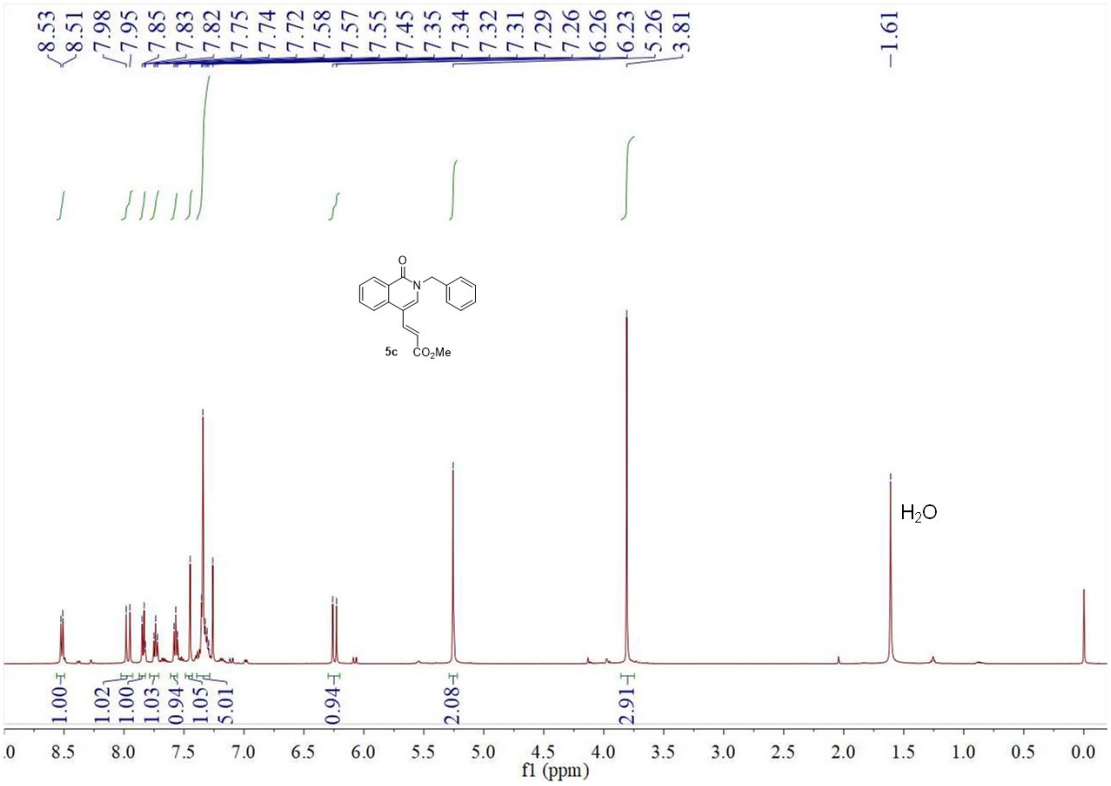
^{1}H NMR of **5b** in $CDCl_3$



^{13}C NMR of **5b** in $CDCl_3$



^{1}H NMR of **5c** in $CDCl_3$



^{13}C NMR of **5c** in $CDCl_3$