Supporting Information

Silver-Catalyzed Generation of Acyl Radicals from α-Imino-Oxy Acids: Access to Acylated 3-CF_3-2-Oxindoles

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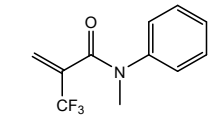
Contents

1. General information

^{1}H and ^{13}C NMR spectra were recorded on a Bruker AVANCE NEO 400 spectrometer (400 MHz for ^{1}H, 101 MHz for ^{13}C) in $CDCl_3$. Chemical shifts (ä) were measured in ppm relative to TMS ä = 0 for ^{1}H, or to chloroform ä = 77.0 for ^{13}C as internal standard. Data are reported as follows: Chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), and Coupling constants, *J*, are reported in hertz. High resolution mass spectroscopy (HRMS) data were measured with Waters Xevo TQ-XS mass spectrometer. The starting materials were purchased from Aldrich, Acros Organics, J&K Chemicals, or TCI and used without further purification. Solvents were dried and purified according to the "Purification of Laboratory Chemicals book" procedure. Column chromatography was performed on silica gel (particle size 200-400 mesh ASTM).

2. Numberings and structures of *N*-aryl Acrylamides



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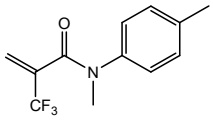

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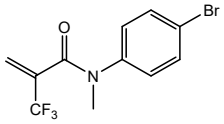

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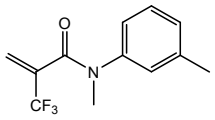

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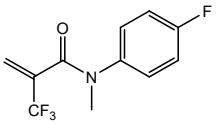

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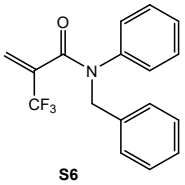

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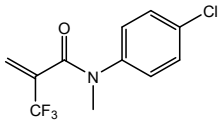

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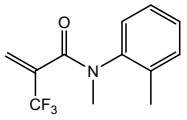

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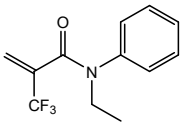

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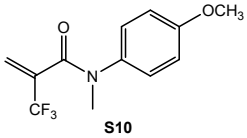

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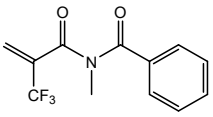

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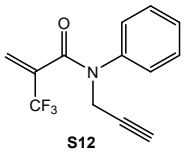

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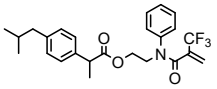

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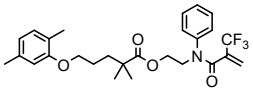

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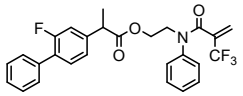

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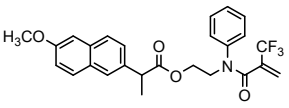

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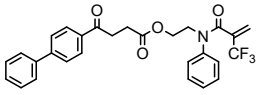

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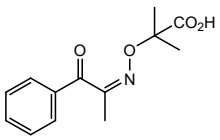

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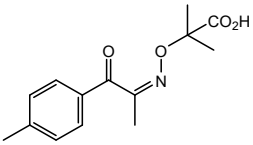

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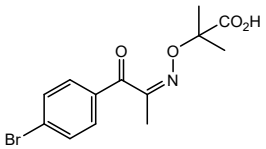


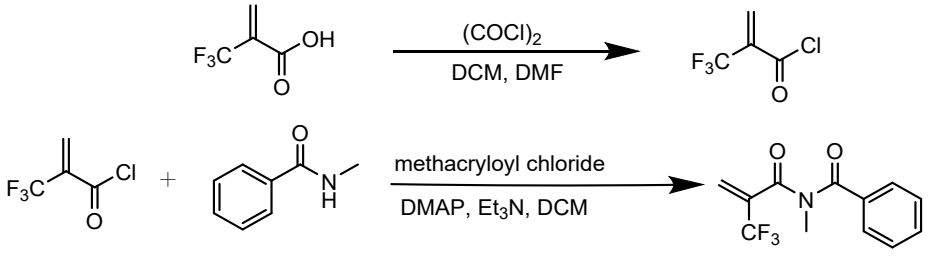
S20

3. General procedures for *N*-aryl Acrylamides

3.1 General procedure I (S1-S10)

A two-neck round-bottom flask (100 mL) equipped with a magnetic stir-bar was charged with 2-(trifluoromethyl)acrylic acid (1.0 equiv) and purged with nitrogen gas using a standard schlenk line technique. Next, amine (1.5 equiv) and dry DCM (5 mL $mmol^{-1}$) were sequentially added to the above flask. The corresponding reaction mixture was cooled to -30 ℃ using Eyela low-temperature bath. Afterward, a pre-prepared solution of 1-Ethyl-3-(3-dimethyl aminopropyl) carbodiimide hydrochloride (EDC·HCl, 1.5 equiv) and 4-dimethylamino pyridine (DMAP, 20 mol%) in dry DCM (5 ml $mmol^{-1}$) under nitrogen was added to the above-mentioned cooled reaction mixture dropwise for about 10-15 min. The resulting mixture was brought to room temperature and stirred overnight. After completion of the reaction (as monitored by TLC), the reaction mixture was washed with water (water solution extracted 2-3 times with DCM and combined all the organic layers). The combined organic layer was washed with 1N HCl solution, 1N NaOH solution, and brine, respectively. The final organic solution was dried over Na_2SO_4 and then concentrated in a rotary evaporator. The crude product was purified by silica-column chromatography (100-200 mesh) using a mixture of hexane and ethyl acetate as the eluent.[1]

3.2 The synthesis of S11.

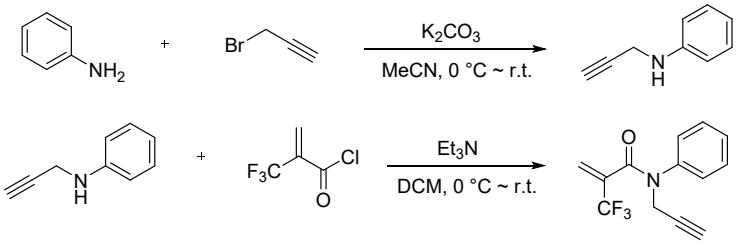


A two neck round bottom flask (100 mL) equipped with a magnetic stir-bar was charged with 2-(trifluoromethyl)acrylic acid (1.0 equiv) and dry DCM (10 mL) under a nitrogen atmosphere, and the ensuing reaction solution was cooled to 0 ℃ using an

ice bath. Afterward, a dropwise addition of freshly distilled oxalyl chloride (2.0 equiv) and 2-4 drops of dry DMF under a nitrogen atmosphere was done. The resulting mixture was stirred at room temperature for 6-8 hours and used directly for the next step.[1]

A 100 mL round bottom flask was charged with *N*-methyl benzamide (10 mmol), DMAP (1 mmol), triethylamine (20 mmol) in dichloromethane (20 mL) and 2-(trifluoromethyl)acryloyl chloride (15 mmol) was added slowly to the reaction mixture at 0 ℃. After that, the residue was stirred at room temperature for 4-6 h. The reaction was completed by TLC monitoring, the organic phase was separated, dried over $MgSO_4$, and concentrated under vacuum. The resulting residue was purified by flash silica gel column chromatography (eluent: hexane/EtOAc, v/v = 10/1) to afford the desired products with 75% yield.[2]

3.3 The synthesis of S12.

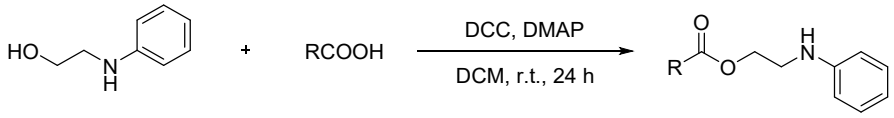


To a round bottom flask were added with aniline (1.2 equiv), K_2CO_3 (2.0 equiv), and MeCN (10.0 mL), then cooled to 0 ℃ in the ice water bath. 3-Bromo-1-propyne was slowly added to the solution at 0 ℃ and then the mixture was stirred at room temperature for 7 h. The solution was concentrated under reduced pressure, and the mixture was purified by flash column chromatography over silica gel to afford *N*-(prop-2-yn-1-yl) aniline (eluent: petroleum ether/ethyl acetate, v/v = 5:1).

To a round bottom flask were added with *N*-(prop-2-yn-1-yl) aniline (1.0 equiv), Et_3N (2.0 equiv), and CH_2Cl_2 (10.0 mL). Then the solution was cooled to 0 ℃ in the ice water bath. 2-(Trifluoromethyl)acryloyl chloride (3.0 mmol) was slowly added to the solution at 0 ℃ and then the mixture was stirred at room temperature for 7 h. The solution was concentrated under reduced pressure and purified by flash column

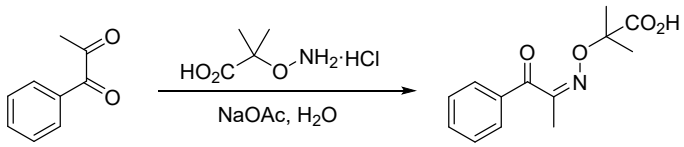
chromatography over silica gel to *N*-phenyl-*N*-(prop-2-yn-1-yl) methacrylamide.[3]

3.4 General procedure II (S13-S17).



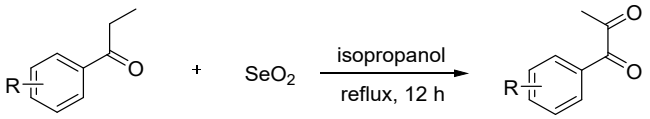
To a solution of 2-anilinoethanol (5.0 mmol) in DCM (25 mL) was added acid (1.0 equiv), DCC (2.0 equiv) and DMAP (0.5 equiv), this mixture was stirred at r.t. for 24 h. Then the obtained solution was poured into water and the aqueous layer was extracted with DCM (25 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was used without further purification for the next step.[4] Post-drug synthesis, Watch next General procedure I.

3.5 The synthesis of S18.



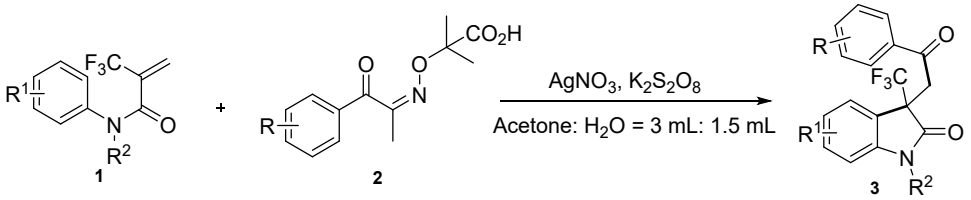
A mixture of indoline-2,3-dione (10 mmol) and hydroxylamine hydrochloride (10.6 mmol) in water (25 mL) was heated to reflux for 30 min. Then sodium acetate (10 mmol) was added in one portion, and the solution continued to stir for 30 min. The mixture was cooled down to room temperature. The solid was filtered out and dried to afford a yellow solid.[5] These solid bypass purification and proceed straight to the next step reaction.

3.6 General procedure Ⅲ (S19, S20).



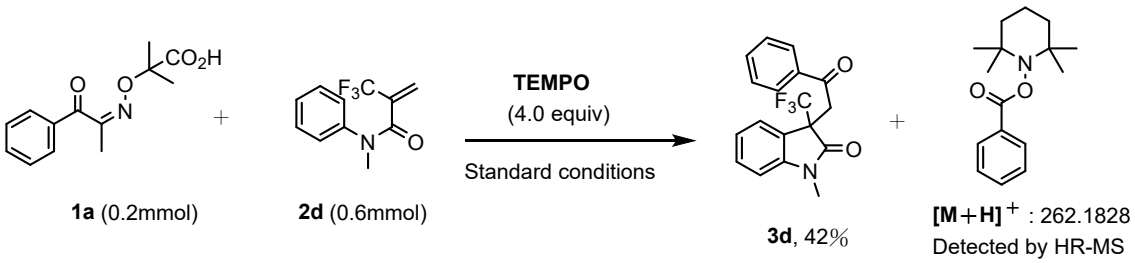
1.11 g (0.01 mol) of SeO_2 and 1.2 g (0.01 mol) of acetophenone were dissolved in a mixture of 10 mL of isopropyl alcohol and 5 mL of water. The solution was refluxed until the precipitation of metallic selenium was complete. The precipitate was separated by decantation. To the resulting solution, after cooling, the product is obtained. Next look at the S18 synthesis steps.

4. General procedure for the synthesis of 3-CF_3-2-Oxindoles



An oven-dried 10 mL Schlenk bottle fitted with a magnetic stir-bar was charged with **1** (0.2 mmol), **2** (0.6 mmol), $AgNO_3$ (0.04 mmol), $K_2S_2O_8$ (1.0 mmol), acetone (3 mL), and water (1.5 mL). Seal the mouth and line the surface with a layer of tinfoil, and then charged with nitrogen. The reaction mixture was stirred at 60 ℃ for 48 h. After the reaction was completed, the residue was diluted with EtOAc, washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated under vacuum. The residue was purified by flash chromatography on silica gel to afford the desired compound.

5. Control experiments



With TEMPO: An oven-dried 10 mL shrek bottle fitted with a magnetic stir-bar was charged with **1a** (50 mg, 0.2 mmol), **2d** (137 mg, 0.6 mmol), $AgNO_3$ (6.8 mg, 0.04 mmol), $K_2S_2O_8$ (270 mg, 1 mmol), TEMPO (125 mg, 0.8 mmol), acetone (3 mL), and water (1.5 mL). Seal the mouth and line the surface with a layer of tinfoil, and then charged with nitrogen. The reaction mixture was stirred at 60 ℃ for 48 h. Finally, the target products 3d and radical-trapped product were obtained, and the yield of 3d was reduced to 42%.

Qualitative Analysis Report

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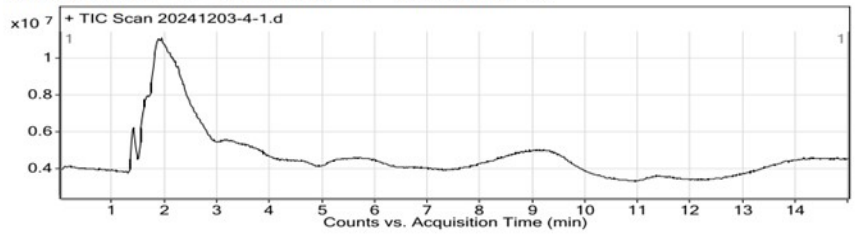
Comment			
Sample Group		**Info.**	
Acquisition SW Version	6200 series TOF/6500 series Q-TOF B.05.01 (B5125.2)		

User Chromatograms

Fragmentor Voltage 160 **Collision Energy** 0 **Ionization Mode** ESI



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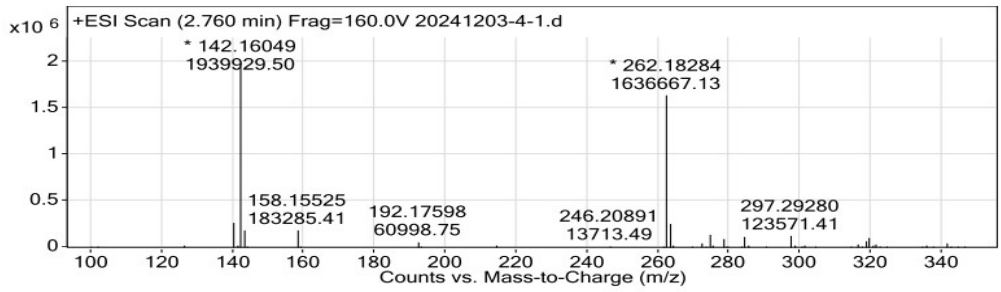
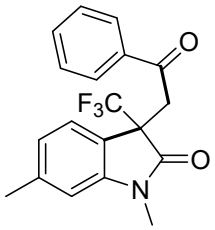


Peak List

m/z	z	Abund
140.14468	1	267337.5
142.16049	1	1939929.5
143.16351	1	181759.59
158.15525	1	183285.41
262.18284	1	1636667.13
263.18586	1	259934.25
274.27672	1	136983.63
284.16473	1	111680.52

6. Characterization Date of New Product



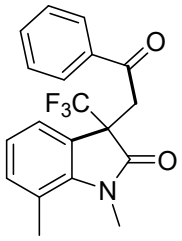
1,6-dimethyl-3-(2-oxo-2-phenylethyl)-3-(trifluoromethyl)indolin-2-one (3a)

^{1}H NMR (400 MHz, Chloroform-d) δ 7.88 – 7.85 (m, 2H), 7.58 – 7.53 (m, 1H), 7.45 – 7.39 (m, 2H), 7.28 – 7.10 (m, 1H), 6.84 – 6.78 (m, 2H), 4.38 – 3.98 (q, *J* = 119.5,

18.1 Hz, 2H), 3.33 (d, *J* = 4.9 Hz, 3H), 2.33 (d, *J* = 39.3 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-d) δ 194.2, 167.8, 164.0, 135.5, 134.3, 133.8, 133.0, 129.9, 129.4, 129.0, 128.2, 127.2, 125.8, 53.8, 53.6 (q, *J* = 24.1 Hz), 41.7, 28.1.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{16}F_3NO_2Na$: 370.1025, found 370.1026.

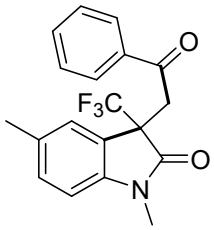


1,7-dimethyl-3-(2-oxo-2-phenylethyl)-3-(trifluoromethyl)indolin-2-one (3b)

^{1}H NMR (400 MHz, Chloroform-d) δ 7.77 – 7.75 (m, 2H), 7.48 – 7.45 (m, 1H), 7.36 – 7.31 (m, 2H), 7.02 – 6.97 (m, 2H), 6.82 (t, *J* = 7.6 Hz, 1H), 3.96 (q, *J* = 35.5, 17.7 Hz, 2H), 3.53 (s, 3H), 2.54 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-d) δ 194.0, 172.7, 143.6, 135.9, 134.1, 133.9, 128.9, 128.2, 124.7, 122.7, 121.7, 120.4, 53.1 (q, *J* = 25.5 Hz), 40.2, 30.5, 19.3.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{16}F_3NO_2Na$: 370.1025, found 370.1024.

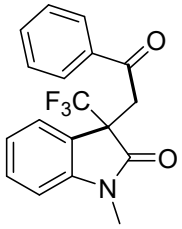


1,5-dimethyl-3-(2-oxo-2-phenylethyl)-3-(trifluoromethyl)indolin-2-one (3c)

^{1}H NMR (400 MHz, Chloroform-d) δ 7.77 – 7.74 (m, 2H), 7.45 (t, *J* = 7.7 Hz, 1H), 7.32 (t, J = 7.8 Hz, 2H), 7.07 (dd, *J* = 8.0, 1.6 Hz, 1H), 6.95 (s, 1H), 6.75 (d, *J* = 7.9 Hz, 1H), 3.96 (q, *J* = 37.9, 17.9 Hz, 2H), 3.23 (s, 3H), 2.18 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-d) δ 193.9, 171.8, 143.4, 135.8, 133.9, 132.4, 130.5, 128.9, 128.2, 124.6, 124.2, 108.6, 53.6 (q, *J* = 25.6 Hz), 40.0, 27.1, 21.3.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{16}F_3NO_2Na$: 370.1025, found 370.1034.

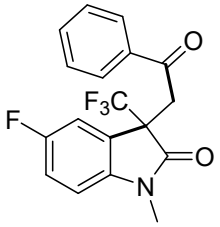


1-methyl-3-(2-oxo-2-phenylethyl)-3-(trifluoromethyl)indolin-2-one (3d)

^{1}H NMR (400 MHz, Chloroform-d) δ 7.71 – 7.68 (m, 2H), 7.41 – 7.37 (m, 1H), 7.28 – 7.21 (m, 3H), 7.10 (d, *J* = 8.0 Hz, 1H), 6.88 (m, 1H), 6.80 (d, *J* = 8.0 Hz, 1H), 3.94 (q, *J* = 27.0, 18.4 Hz, 2H), 3.20 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-d) δ 193.8, 171.8, 145.6, 135.6, 133.8, 130.1, 128.7, 128.0, 124.1, 123.7, 122.7, 108.8, 53.5 (q, *J* = 26.3 Hz), 39.8, 27.0.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{15}F_3NO_2$: 334.1049, found 334.1053.

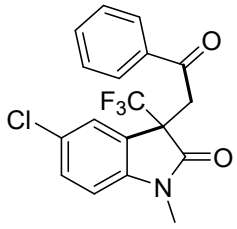


5-fluoro-1-methyl-3-(2-oxo-2-phenylethyl)-3-(trifluoromethyl)indolin-2-one (3e)

^{1}H NMR (400 MHz, Chloroform-d) δ 7.85 – 7.83 (m, 2H), 7.58 – 7.54 (m, 1H), 7.44 – 7.40 (m, 2H), 7.08 (td, *J* = 8.9, 2.6 Hz, 1H), 7.01 – 6.98 (m, 1H), 6.88 (dd, *J* = 8.5, 4.1 Hz, 1H), 4.06 (q, *J* = 51.4, 18.3 Hz, 2H), 3.33 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-d) δ 199.8, 171.7, 142.1, 136.9, 133.2, 133.1, 130.4, 128.7, 128.1, 125.6, 124.3, 108.5, 56.9 (q, *J* = 26.5 Hz), 38.2, 30.9, 26.7, 24.0, 23.2, 21.3.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{18}H_{13}F_4NO_2Na$: 374.0775, found 374.0783.

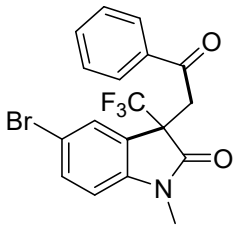


5-chloro-1-methyl-3-(2-oxo-2-phenylethyl)-3-(trifluoromethyl)indolin-2-one (3f)

^{1}H NMR (400 MHz, Chloroform-d) δ 7.78 – 7.75 (m, 2H), 7.51 – 7.47 (m, 1H), 7.37 – 7.35 (m, 2H), 7.29 – 7.26 (m, 1H), 7.13 (s, 1H), 6.80 (dd, *J* = 8.3, 1.6 Hz, 1H), 3.98 (q, *J* = 53.7, 18.3 Hz, 2H), 3.26 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-d) δ 194.0, 171.9, 146.2, 145.7, 140.6, 135.6, 135.2, 134.0, 133.9, 129.8, 128.9, 128.8, 128.2, 126.1, 123.5, 123.4, 121.6, 121.2, 54.8 (q, *J* = 26.2 Hz), 39.9, 38.2, 27.2, 27.1, 22.1, 19.3.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{18}H_{13}ClF_3NO_2Na$: 390.0479, found 390.0489.

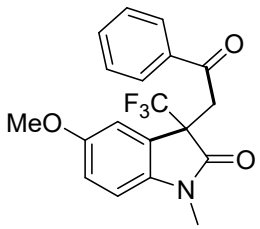


5-bromo-1-methyl-3-(2-oxo-2-phenylethyl)-3-(trifluoromethyl)indolin-2-one (3g)

^{1}H NMR (400 MHz, Chloroform-d) δ 7.86 – 7.83 (m, 2H), 7.58 – 7.54 (m, 1H), 7.50 (dd, *J* = 8.3, 2.0 Hz, 1H), 7.45 – 7.41 (m, 2H), 7.35 (s, 1H), 6.84 (d, J = 8.3 Hz, 1H), 4.07 (q, *J* = 52.9, 18.1 Hz, 2H), 3.33 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-d) δ 193.7, 171.3, 144.9, 135.5, 134.2, 133.1, 128.9, 128.2, 127.0, 126.2, 115.3, 110.3, 53.8 (q, *J* = 26.8 Hz), 53.6, 40.1, 27.2.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{14}BrF_3NO_2$: 412.0155, found 412.0147.



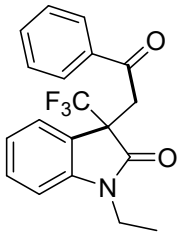
5-methoxy-1-methyl-3-(2-oxo-2-phenylethyl)-3-(trifluoromethyl)indolin-2-one (3h)

^{1}H NMR (400 MHz, Chloroform-d) δ 7.77 – 7.75 (m, 2H), 7.49 – 7.45 (m, 1H), 7.36 – 7.32 (m, 2H), 6.82 – 6.76 (m, 3H), 3.97 (q, *J* = 45.3, 17.8 Hz, 2H), 3.65 (s, 3H),

3.24 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-d) δ 193.8, 171.5, 156.0, 139.3, 135.8, 134.0, 128.9, 128.2, 113.8, 112.0, 109.1, 55.9, 53.9 (q, *J* = 26.6 Hz), 54.1, 40.0, 27.2.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{16}F_3NO_3Na$: 386.0974, found 386.0982.

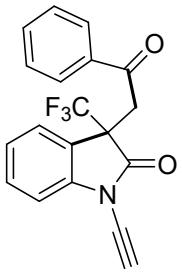


1-ethyl-3-(2-oxo-2-phenylethyl)-3-(trifluoromethyl)indolin-2-one (3i)

^{1}H NMR (400 MHz, Chloroform-d) δ 7.76 – 7.74 (m, 2H), 7.47 – 7.43 (m, 1H), 7.34 – 7.25 (m, 3H), 7.15 (d, *J* = 7.6 Hz 1H), 6.94 – 6.86 (m, 2H), 3.97 (q, J = 32.6, 17.8 Hz, 2H), 3.83 – 3.76 (m, 2H), 1.28 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-d) δ 193.7, 171.4, 144.9, 135.9, 133.9, 130.1, 128.9, 128.2, 124.5, 124.0, 122.6, 109.0, 53.6 (q, 26.4 Hz), 39.8, 35.5, 12.2.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{16}F_3NO_2Na$: 370.1025, found 370.1018.

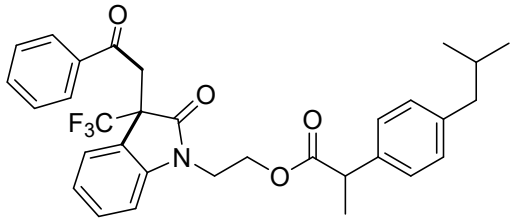


1-ethynyl-3-(2-oxo-2-phenylethyl)-3-(trifluoromethyl)indolin-2-one (3j)

^{1}H NMR (400 MHz, Chloroform-d) δ 7.92 – 7.90 (m, 2H), 7.64 – 7.60 (m, 1H), 7.50 – 7.45 (m, 3H), 7.32 – 7.30 (m, 1H), 7.25 (d, *J* = 7.8 Hz, 1H), 7.13 (td, *J* = 7.5, 1.0 Hz, 1H), 4.83 (dd, *J* = 17.7, 2.6 Hz, 1H), 4.58 (dd, *J* = 17.7, 2.5 Hz, 1H), 4.14 (q, *J* = 27.2, 17.8 Hz, 2H), 2.39 (t, *J* = 2.5 Hz, 1H).

^{13}C NMR (101 MHz, Chloroform-d) δ 193.7, 171.0, 144.0, 135.7, 134.0, 130.3, 128.9, 128.2, 124.1, 123.9, 123.2, 109.9, 76.5, 72.9, 53.8 (q, 26.7 Hz), 40.0, 30.2.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{14}F_3NO_2Na$: 380.0869, found 380.0867.

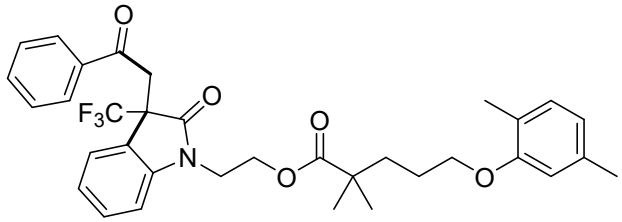


2-(2-oxo-3-(2-oxo-2-phenylethyl)-3-(trifluoromethyl)indolin-1-yl)ethyl 2-(4-isobutylphenyl)propanoate (3k)

^{1}H NMR (400 MHz, Chloroform-d) δ 7.83 – 7.80 (m, 2H), 7.55 (t, J = 7.5 Hz, 1H), 7.43 – 7.39 (m, 2H), 7.34 – 7.29 (m, 1H), 7.22 (d, *J* = 7.4 Hz, 1H), 7.16 – 7.13 (m, 2H), 7.06 – 6.94 (m, 4H), 4.48 – 4.29 (m, 2H), 4.18 – 3.91 (m, 4H), 3.67 – 3.61 (m, 1H), 2.42 (dd, *J* = 7.1, 1.8 Hz, 2H), 1.86 – 1.81 (m, 1H), 1.43 (dd, *J* = 7.2, 1.5 Hz, 3H), 0.89 (dd, *J* = 6.6, 1.8 Hz, 6H).

^{13}C NMR (101 MHz, Chloroform-d) δ 193.6, 174.8, 145.1, 145.0, 140.7, 137.6 , 135.8, 135.7, 134.0, 130.2, 129.5, 128.9, 128.2, 127.4, 124.1, 123.9, 122.8, 109.4, 109.3, 61.6, 53.5 (q, *J* = 27.2 Hz), 45.2, 40.1, 39.5, 30.3, 22.6, 18.5.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{32}H_{32}F_3NO_4Na$: 574.2176, found 574.2167.



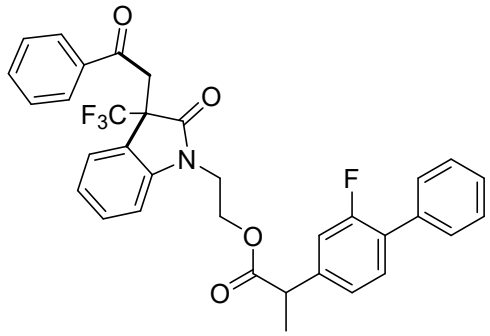
2-(2-oxo-3-(2-oxo-2-phenylethyl)-3-(trifluoromethyl)indolin-1-yl)ethyl 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoate (3l)

^{1}H NMR (400 MHz, Chloroform-d) δ 7.84 – 7.82 (m, 2H), 7.58 – 7.53 (m, 1H), 7.44 – 7.34 (m, 3H), 7.23 (d, *J* = 7.4 Hz, 1H), 7.07 (d, *J* = 7.9 Hz, 1H), 7.03 – 6.98 (m, 2H), 6.65 (d, *J* = 7.5 Hz 1H), 6.55 (s, 1H), 4.45 – 4.35 (m, 2H), 4.19 – 4.00 (m, 4H), 3.82 – 3.79 (m, 2H), 2.30 (s, 3H), 2.16 (s, 3H), 1.72 – 1.63 (m, 4H), 1.15 (d, *J* = 2.4 Hz, 6H).

^{13}C NMR (101 MHz, Chloroform-d) δ 193.6, 178.0, 157.1, 145.1, 136.6, 135.8,

134.0, 130.5, 130.2, 128.9, 128.2, 124.2, 124.0, 123.7, 122.9, 120.8, 112.1, 109.4, 68.0, 61.6, 53.6 (q, J = 26.3 Hz), 42.3, 40.0, 39.6, 37.1, 25.2, 21.6, 16.0.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{34}H_{36}F_3NO_5Na$: 618.2438, found 618.2440.

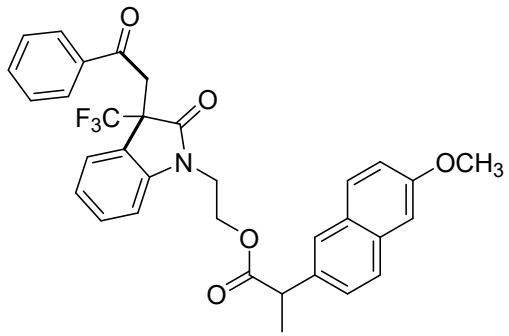


2-(2-oxo-3-(2-oxo-2-phenylethyl)-3-(trifluoromethyl)indolin-1-yl)ethyl 2-(2-fluoro-[1,1'-biphenyl]-4-yl)propanoate (3m)

^{1}H NMR (400 MHz, Chloroform-d) δ 7.84 – 7.80 (m, 2H), 7.57 – 7.47 (m, 3H), 7.45 – 7.39 (m, 4H), 7.38 – 7.29 (m, 3H), 7.23 (d, J = 7.4 Hz, 1H), 7.09 – 6.96 (m, 4H), 4.53 – 4.37 (m, 2H), 4.21 – 4.00 (m, 4H), 3.73 – 3.66 (m, 1H), 1.50 – 1.46 (m, 3H).

^{13}C NMR (101 MHz, Chloroform-d) δ 193.5, 173.9, 160.8, 158.4, 144.9, 135.5, 133.8, 130.7, 130.0, 129.0, 128.9, 128.7, 128.4, 128.0, 127.6, 123.8 (t, J = 30.4 Hz), 123.6, 122.7, 115.5, 115.2, 109.1, 61.9, 53.4 (q, J = 27.6 Hz), 45.0, 39.9, 39.3, 26.9, 18.2.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{34}H_{37}F_3NO_5$: 590.1949, found 590.1953.

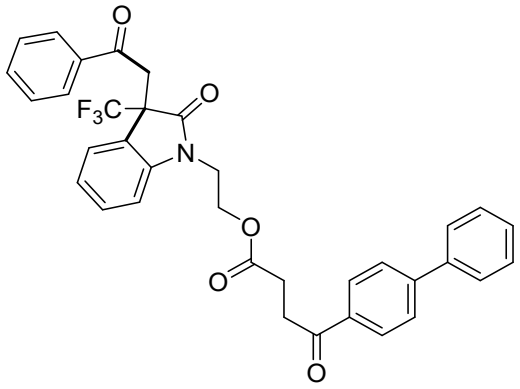


2-(2-oxo-3-(2-oxo-2-phenylethyl)-3-(trifluoromethyl)indolin-1-yl)ethyl 2-(6-methoxynaphthalen-2-yl)propanoate (3n)

^{1}H NMR (400 MHz, Chloroform-d) δ 7.82 – 7.77 (m, 2H), 7.66 – 7.62 (m, 2H), 7.60 – 7.58 (m, 1H), 7.57 - 7.52 (m, 2H), 7.43 – 7.37 (m, 2H), 7.35 – 7.32 (m, 1H), 7.21 – 7.07 (m, 4H), 6.96 (tt, *J* = 7.7, 1.3 Hz, 1H), 6.87 (dd, *J* = 9.3, 7.9 Hz, 1H), 4.51 – 4.32 (m, 2H), 4.16 – 3.97 (m, 4H), 3.91 (d, *J* = 2.8 Hz, 3H), 3.80 (tt, *J* = 7.2, 3.6 Hz, 1H), 1.52 (dd, *J* = 7.2, 3.6 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-d) δ 193.6, 174.7, 157.8, 145.0, 135.7, 135.6, 133.9, 130.1, 129.5, 129.1, 128.9, 128.2, 127.4, 126.4, 126.3, 124.1, 123.9, 122.8, 119.1, 109.3, 105.8, 61.8, 55.5, 53.6 (q, *J* = 26.5 Hz), 45.5, 40.1, 39.6, 29.9, 18.5.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{33}H_{28}F_3NO_5Na$: 598.1812, found 598.1803.

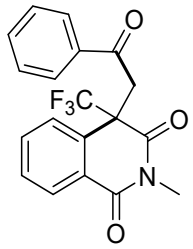


2-(2-oxo-3-(2-oxo-2-phenylethyl)-3-(trifluoromethyl)indolin-1-yl)ethyl 4-([1,1'-biphenyl]-4-yl)-4-oxobutanoate (3o)

^{1}H NMR (400 MHz, Chloroform-d) δ 8.00 – 7.98 (m, 2H), 7.84 – 7.82 (m, 2H), 7.66 – 7.61 (m, 4H), 7.57 – 7.53 (m, 1H), 7.50 – 7.46 (m, 2H), 7.43 – 7.35 (m, 4H), 7.23 (d, *J* = 7.4 Hz, 1H), 7.09 (d, *J* = 7.9 Hz, 1H), 7.01 (td, *J* = 7.6, 1.0 Hz, 1H), 4.54 – 4.41 (m, 2H), 4.21 – 4.05 (m, 4H), 3.28 (t, *J* = 6.8 Hz, 2H), 2.75 (t, *J* = 6.8 Hz, 2H).

^{13}C NMR (101 MHz, Chloroform-d) δ 197.8, 193.7, 173.0, 146.0, 145.1, 140.1, 135.8, 135.3, 134.0, 130.3, 129.2, 128.9, 128.8, 128.4, 128.2, 127.5, 127.4, 124.2, 124.0, 122.9, 109.3, 61.4, 53.7 (q, *J* = 26.7 Hz), 53.5, 40.0, 39.6, 33.6, 28.5.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{35}H_{28}F_3NO_5Na$: 622.1812, found 622.1821.

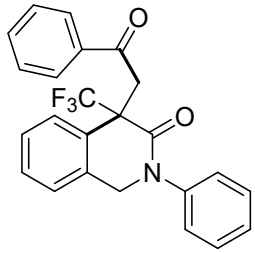


2-methyl-4-(2-oxo-2-phenylethyl)-4-(trifluoromethyl)isoquinoline-1,3(2*H*,4*H*)-dione (3p)

^{1}H NMR (400 MHz, Chloroform-d) δ 8.37 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.90 – 7.88 (m, 2H), 7.60 – 7.50 (m, 3H), 7.47 – 7.38 (m, 3H), 4.59 (d, *J* = 18.1 Hz, 1H), 4.32 (d, *J* = 18.1 Hz, 1H), 3.47 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-d) δ 193.7, 171.5, 160.3, 157.9, 141.8, 135.6, 134.1, 128.9, 128.2, 116.5 (d, *J* = 23.5 Hz), 112.3 (d, *J* = 25.6 Hz), 109.4, 109.36 , 53.9 (q, *J* = 25.3 Hz), 40.0, 27.2.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{14}F_3NO_3Na$: 384.0818, found 384.0822.

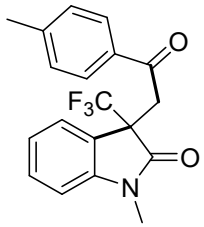


4-(2-oxo-2-phenylethyl)-2-phenyl-4-(trifluoromethyl)-1,4-dihydroisoquinolin-3(2*H*)-one (3q)

^{1}H NMR (400 MHz, Chloroform-d) δ 7.88 – 7.86 (m, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.45 – 7.41 (m, 4H), 7.37 – 7.33 (m, 2H), 7.30 – 7.26 (m, 1H), 7.24 – 7.20 (m, 2H), 6.98 (td, *J* = 7.6, 1.0 Hz, 1H), 6.75 (d, *J* = 7.6 Hz, 1H), 5.24 (d, *J* = 16.0 Hz, 1H), 4.90 (d, *J* = 15.9 Hz, 1H), 4.19 – 4.05 (m, 2H).

^{13}C NMR (101 MHz, Chloroform-d) δ 193.8, 172.0, 144.9, 135.8, 135.6, 134.0, 130.1, 129.0, 128.9, 128.3, 127.8, 127.3, 124.2, 123.8, 122.9, 110.0, 53.8 (q, *J* = 26.3 Hz), 44.7, 39.9.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{24}H_{18}F_3NO_2Na$: 432.1182, found 432.1172.

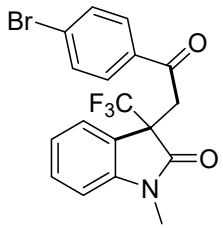


1-methyl-3-(2-oxo-2-(p-tolyl)ethyl)-3-(trifluoromethyl)indolin-2-one (3r)

^{1}H NMR (400 MHz, Chloroform-d) δ 7.76 – 7.73 (m, 2H), 7.37 (td, *J* = 7.8, 1.2 Hz, 1H), 7.23 – 7.21 (m, 3H), 7.02 (td, *J* = 7.6, 1.0 Hz, 1H), 6.95 (d, *J* = 7.8 Hz, 1H), 4.10 – 3.98 (m, 2H), 3.36 (s, 3H), 2.39 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-d) δ 193.3, 171.8, 145.6, 144.8, 133.2, 130.0, 129.4, 128.1, 124.2, 123.6, 122.6, 108.7, 53.5 (q, *J* = 27.4 Hz), 39.7, 27.0, 21.7.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{16}F_3NO_2Na$: 370.1025, found 370.1028.

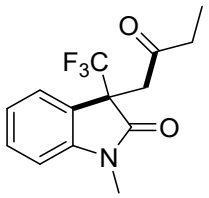


3-(2-(4-bromophenyl)-2-oxoethyl)-1-methyl-3-(trifluoromethyl)indolin-2-one (3s)

^{1}H NMR (400 MHz, Chloroform-d) δ 7.72 – 7.68 (m, 2H), 7.58 – 7.55 (m, 2H), 7.39 (td, *J* = 7.7, 1.2 Hz, 1H), 7.23 (d, *J* = 7.4 Hz, 1H), 7.04 (td, *J* = 7.6, 1.0 Hz, 1H), 6.95 (d, *J* = 7.8 Hz, 1H), 4.09 – 3.94 (m, 2H), 3.35 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-d) δ 192.9, 171.7, 145.8, 134.5, 132.2, 130.4, 129.7, 129.3, 124.1, 123.8, 122.9, 108.9, 53.6 (q, *J* = 26.2 Hz), 39.9, 27.2.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{18}H_{13}BrF_3NO_2Na$: 433.9974, found 433.9969.



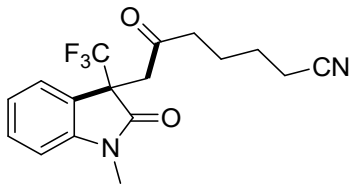
1-methyl-3-(2-oxobutyl)-3-(trifluoromethyl)indolin-2-one (3t)

^{1}H NMR (400 MHz, Chloroform-d) δ 7.37 (t, *J* = 7.2 Hz, 1H), 7.21 (d, *J* = 7.2 Hz,

1H), 7.05 (t, *J* = 7.2 Hz, 1H), 6.90 (d, *J* = 7.6 Hz, 1H), 3.54 (d, *J* = 17.6 Hz, 1H), 3.37 (d, *J* = 18.0 Hz, 1H), 3.30 (s, 3H), 2.37–2.47 (m, 1H), 2.23–2.33 (m, 1H), 0.90 (t, *J* = 7.6 Hz, 1H).

^{13}C NMR (101 MHz, Chloroform-d) δ 204.8, 171.4, 145.4, 130.0, 128.5, 125.7, 123.8, 123.4, 122.9, 122.6, 120.1, 53.1 (q, *J* = 26.3 Hz), 42.7, 35.8, 26.8, 7.2.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{14}H_{14}F_3NO_2Na$: 308.0869, found 308.0866.



7-(1-methyl-2-oxo-3-(trifluoromethyl)indolin-3-yl)-6-oxoheptanenitrile (3u)

^{1}H NMR (400 MHz, Chloroform-d) δ 7.37 (t, J = 7.6 Hz, 1H), 7.21 (d, J = 7.6 Hz, 1H), 7.05 (t, J = 7.6 Hz, 1H), 6.90 (d, J = 8.0 Hz, 1H), 3.52 (d, J = 17.6 Hz, 1H), 3.36 (d, J = 18.0 Hz, 1H), 3.28 (s, 3H), 2.41–2.49 (m, 1H), 2.29–2.37 (m, 1H), 2.17–2.26 (m, 2H), 1.42–1.58 (m, 4H).

^{13}C NMR (101 MHz, Chloroform-d) δ 203.3, 171.3, 145.2, 130.1, 128.4, 125.6, 123.6, 123.4, 122.8, 122.6, 120.0, 119.2, 108.7, 53.0 (q, J = 26.6 Hz), 43.0, 41.4, 26.8, 24.3, 22.0, 16.8.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{17}H_{17}F_3N_2O_2Na$: 361.1134, found 361.1138.

7. Reference

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2. (a) Y. -Q. Yuan, P. S. Kumar, C. -N. Zhang, M. -H. Yang, S. -R. Guo, *Org. Biomol. Chem.,* **2017**, *15*, 7330. (b) C. -B. Liu, W. -W. Zhao, Y. Huang, H. -M. Wang, B. Zhang, *Tetrahedron.,* **2015**, *71*, 4344.
3. X. -X. Meng, Q. -Q. Kang, J. -Y. Zhang, Q. Li, W. -T. Wei, W. -M. He, *Green Chem.,* **2020**, *22*, 1388-1392.
4. A. Hossian, M. K. Manna, K. Manna, R. Jana, *Org. Biomol. Chem.* **2017**, *15*, 6592.
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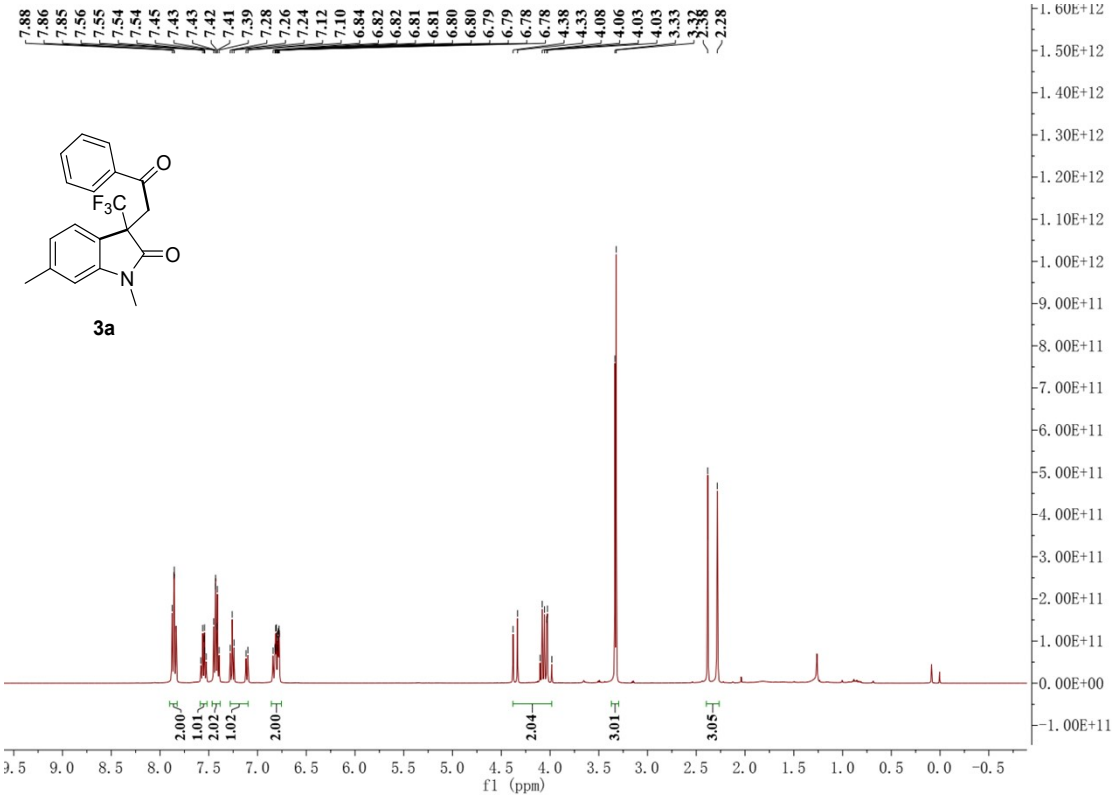
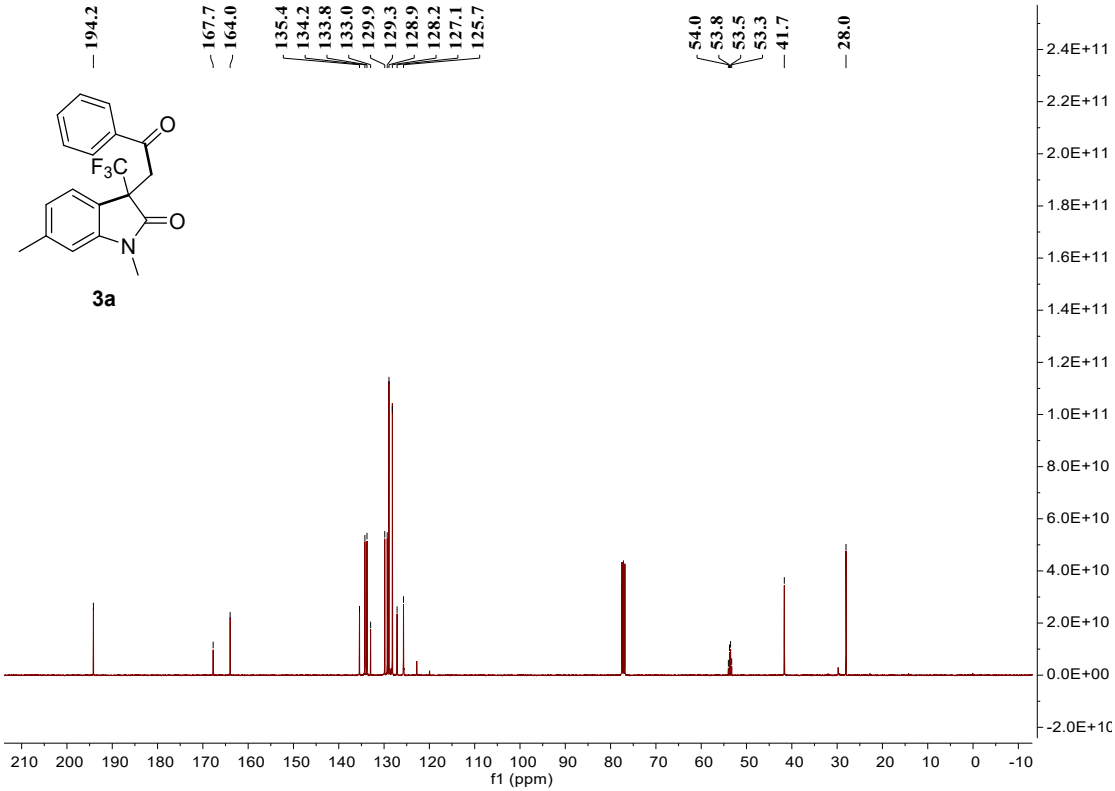
8. NMR Spectra of Products

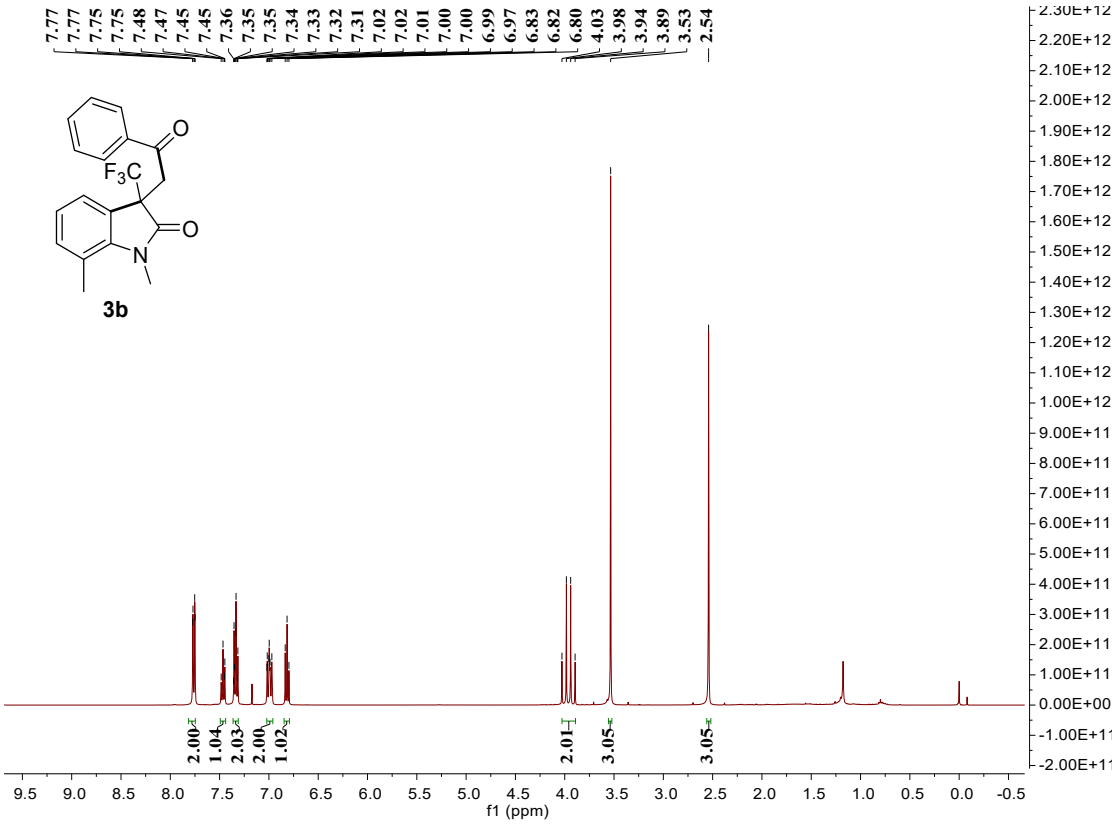
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3a**



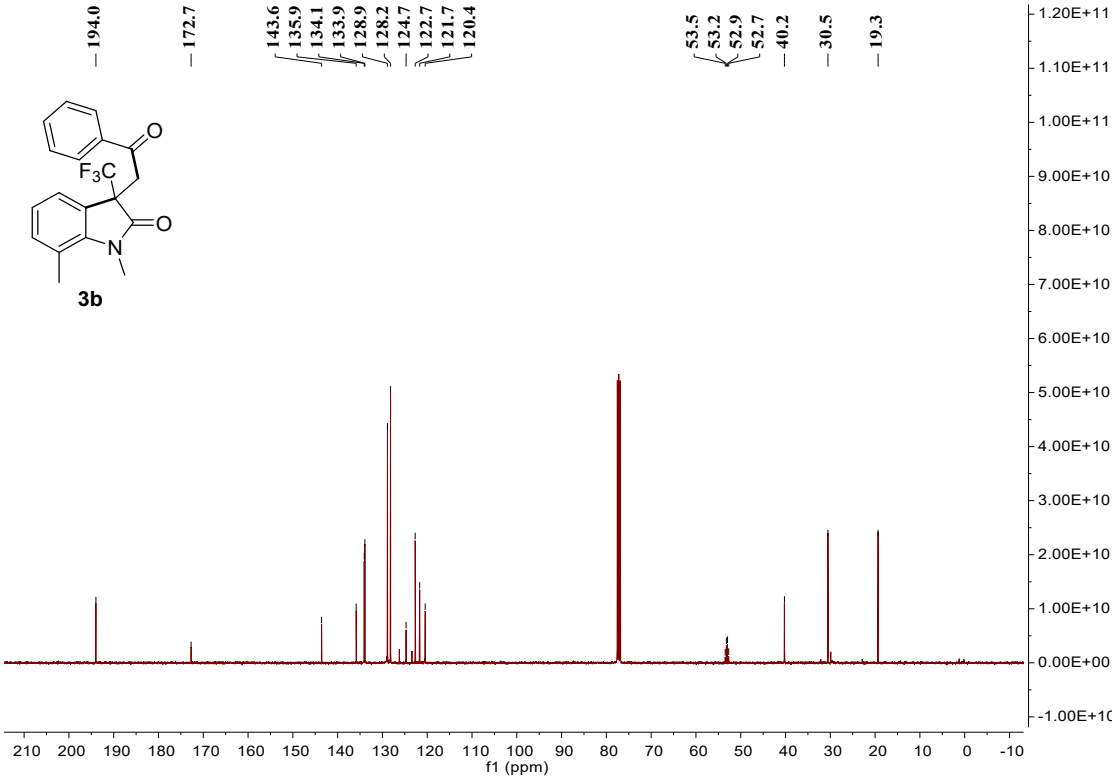
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3a**



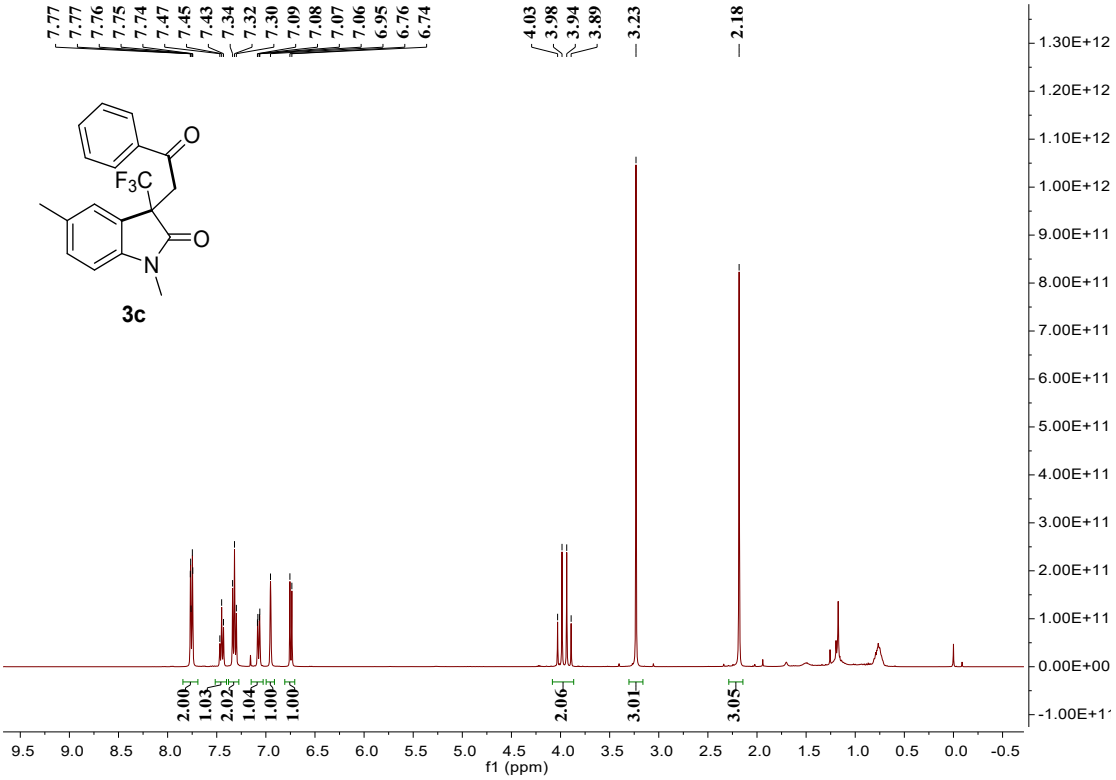
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3b**



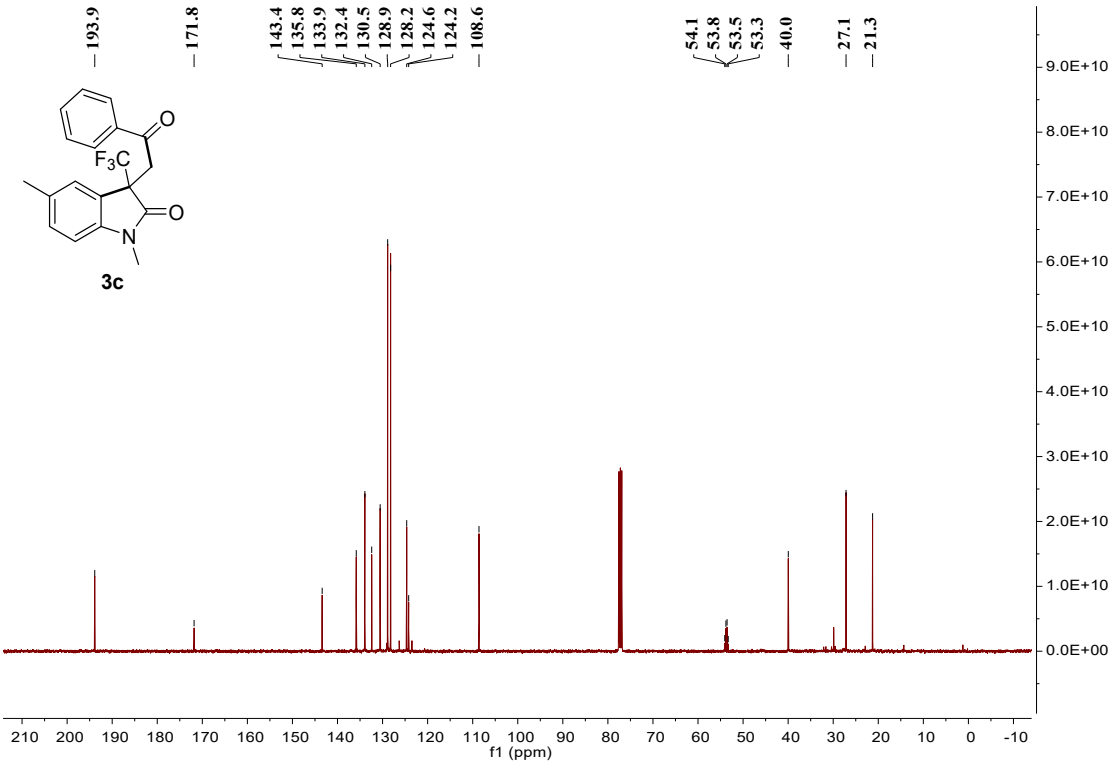
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3b**



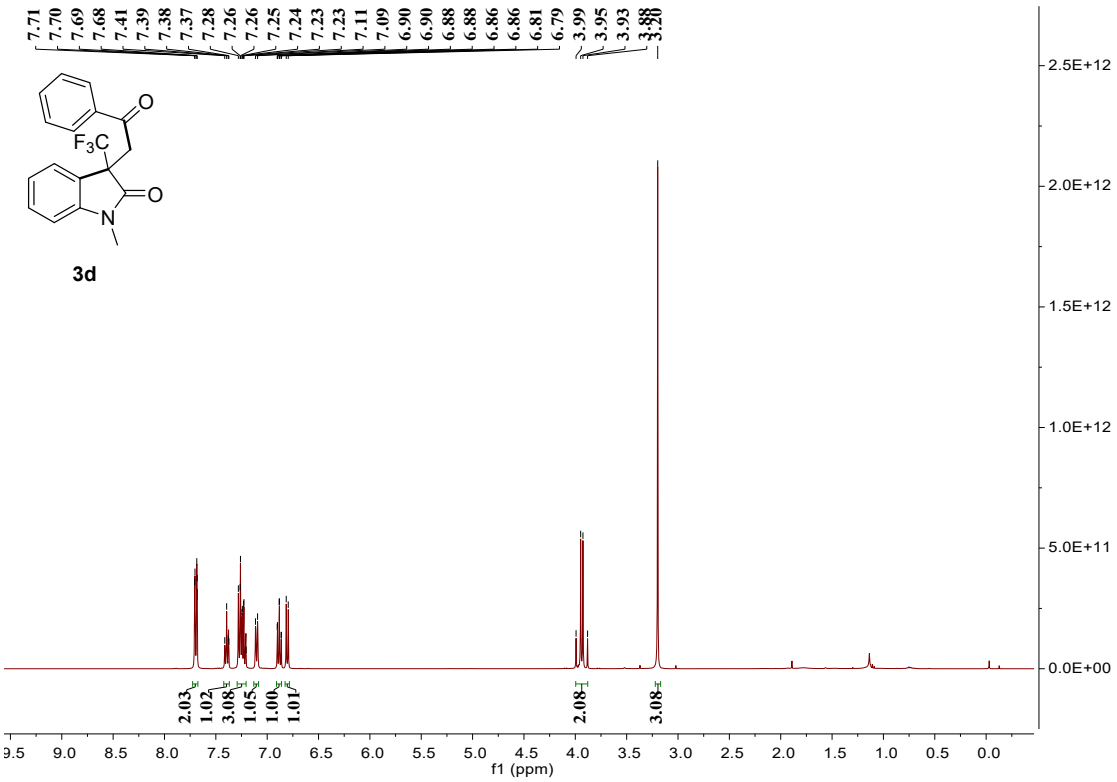
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3c**



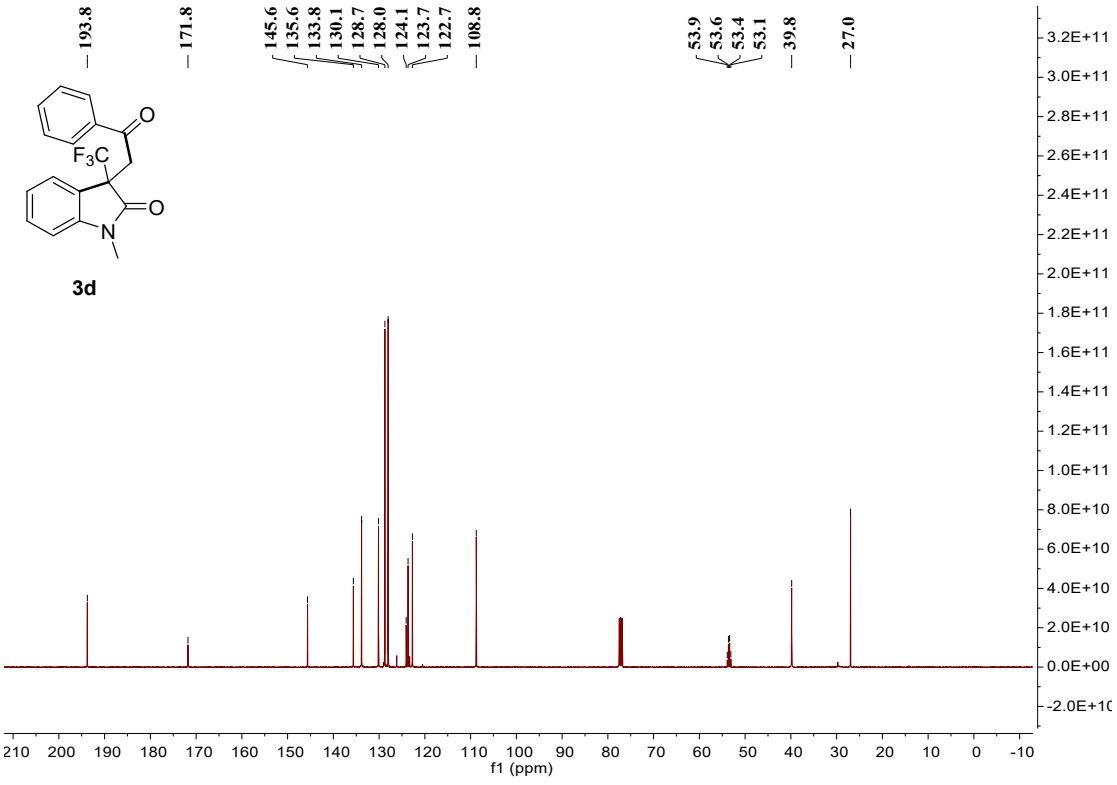
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3c**



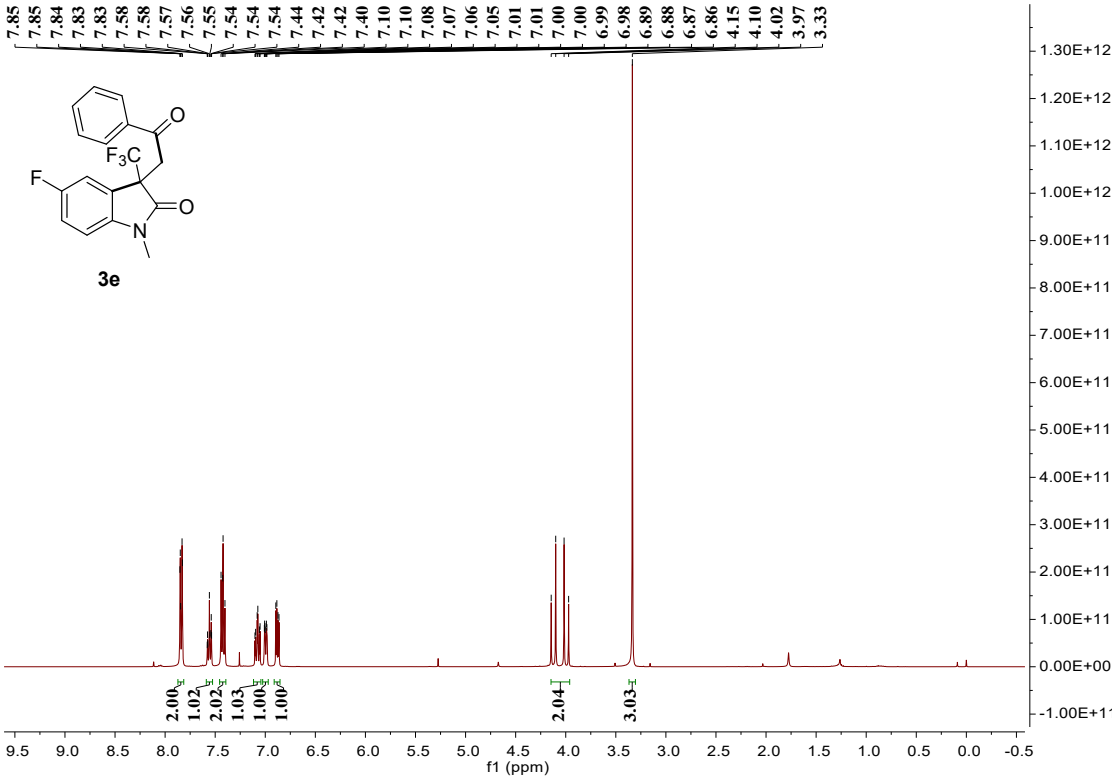
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3d**



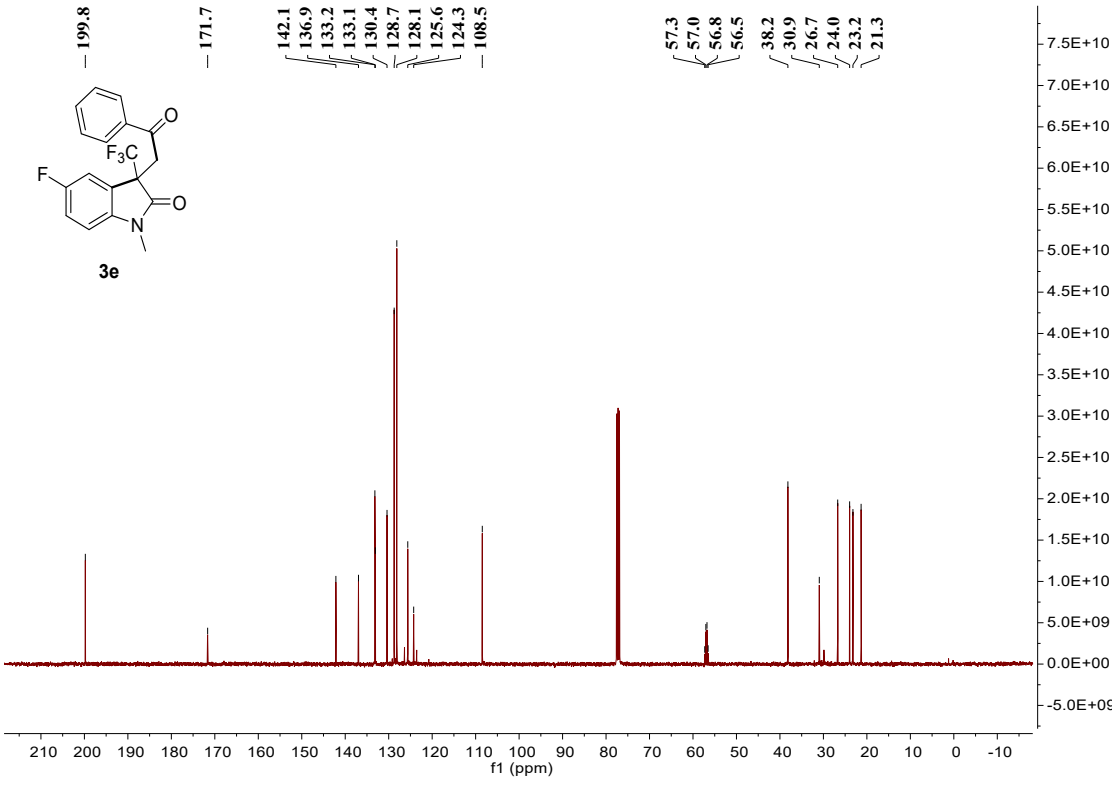
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3d**



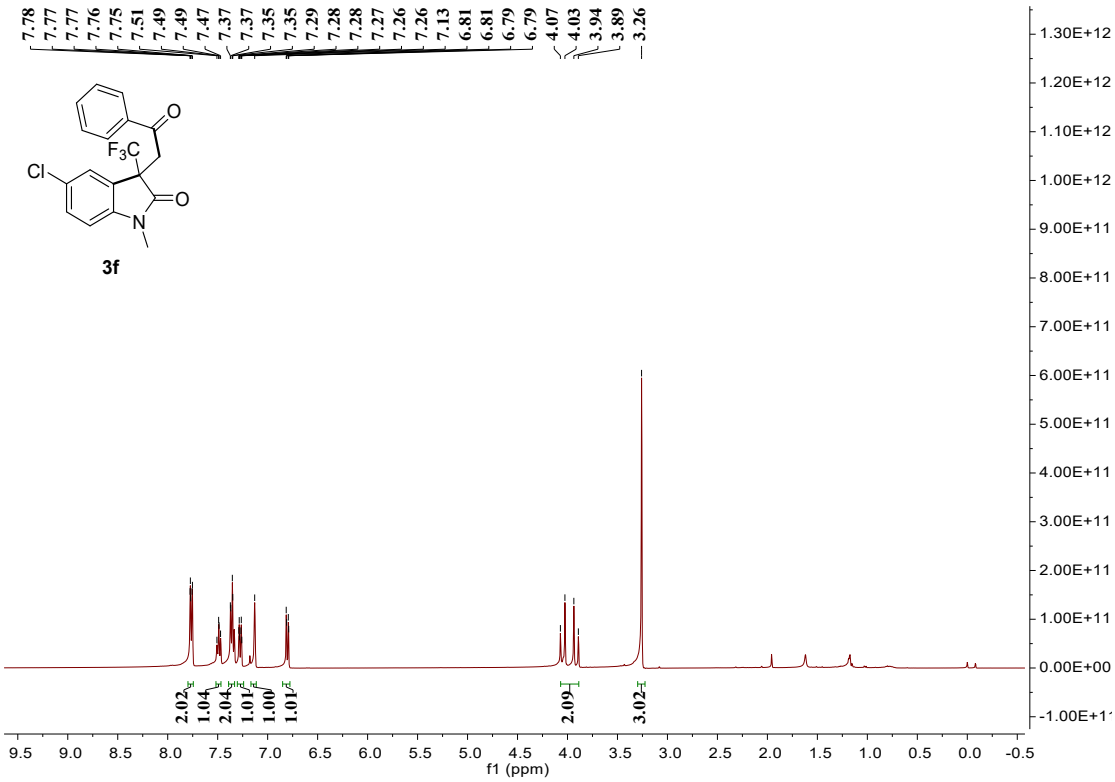
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3e**



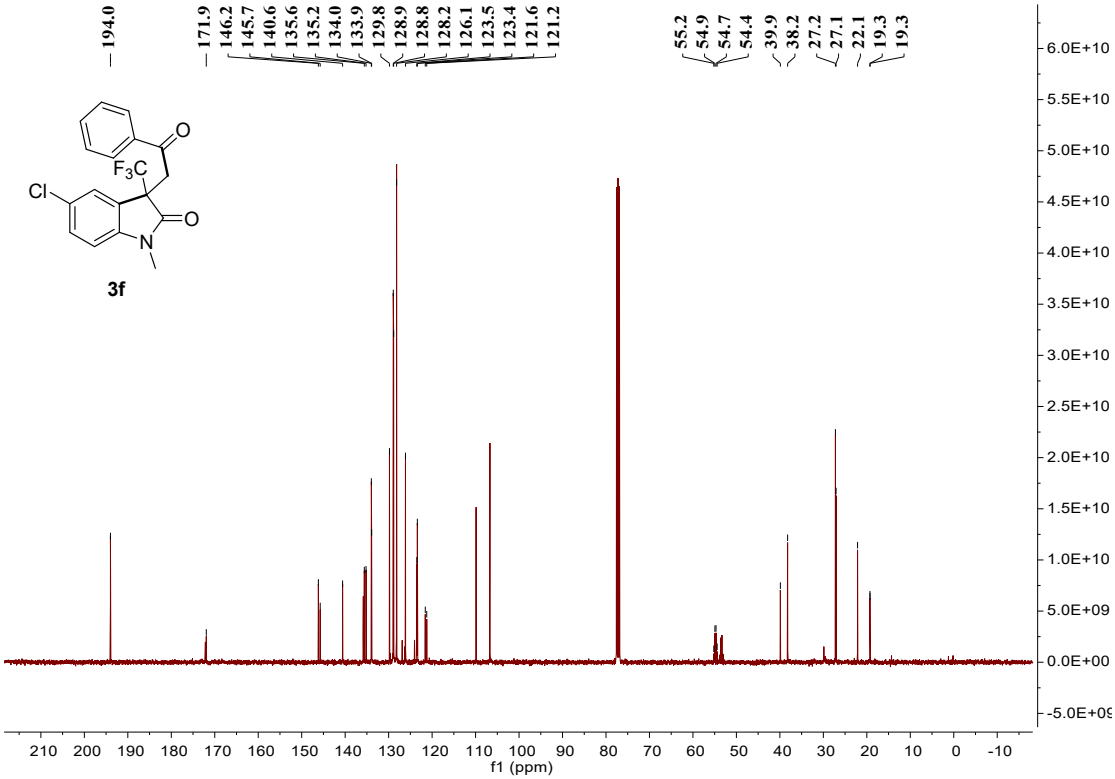
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3e**



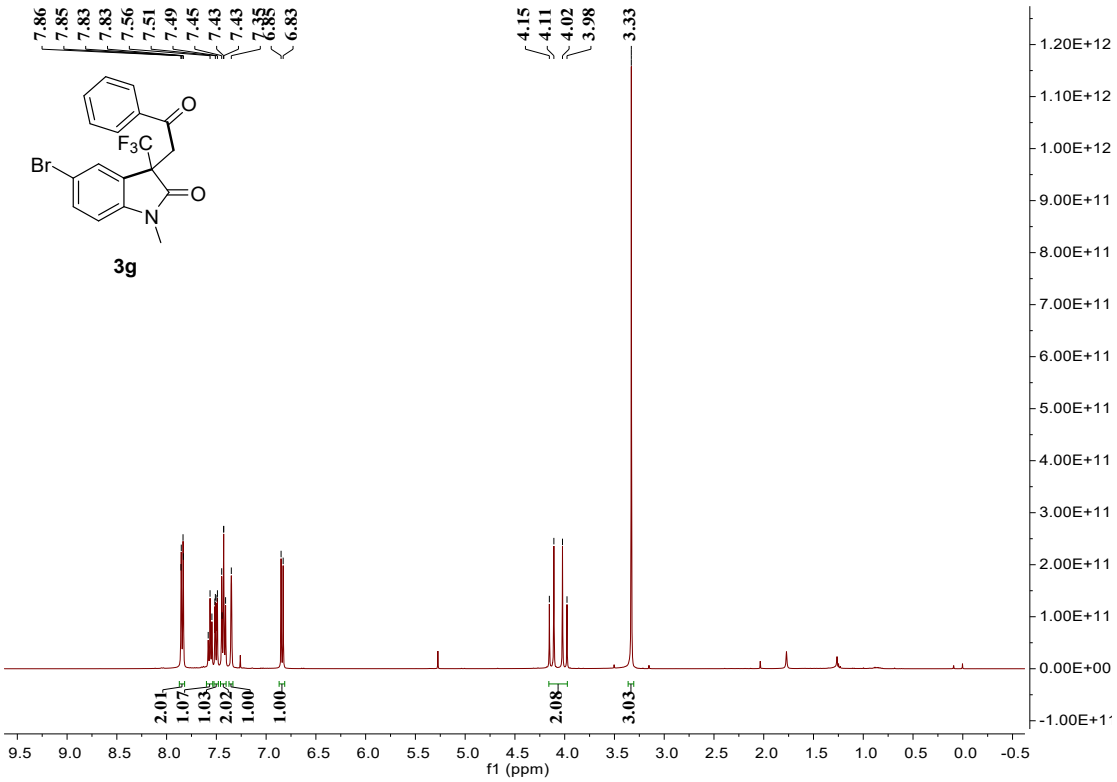
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3f**



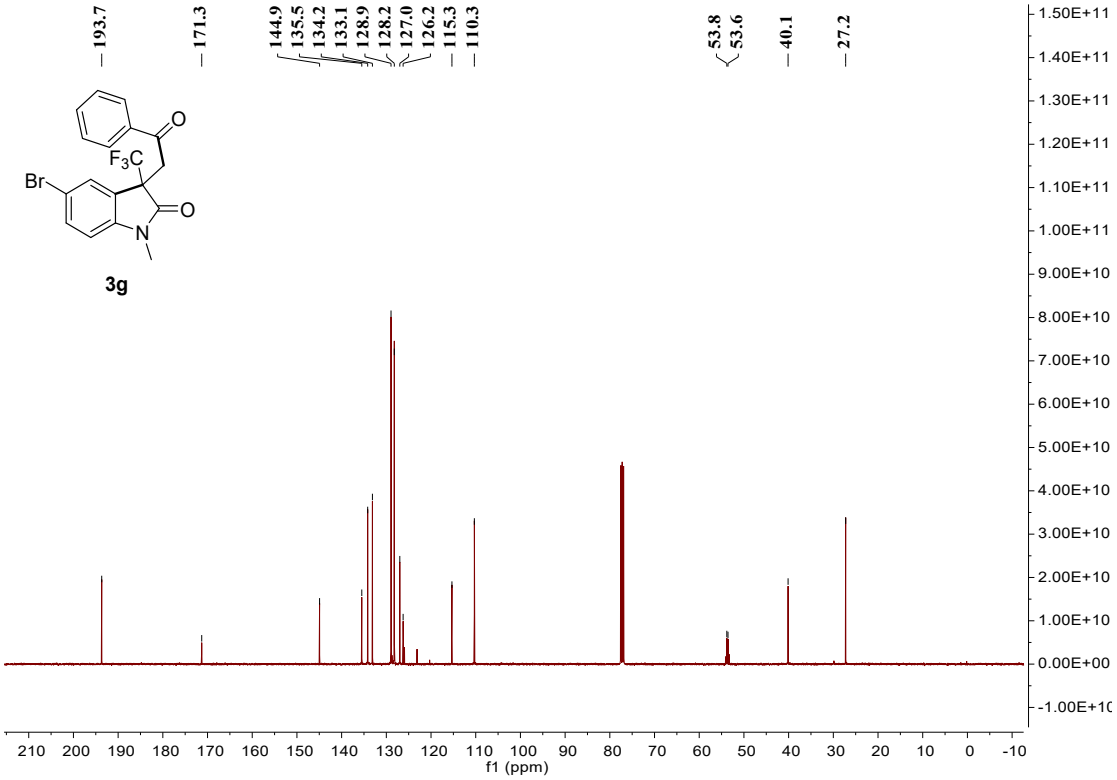
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3f**



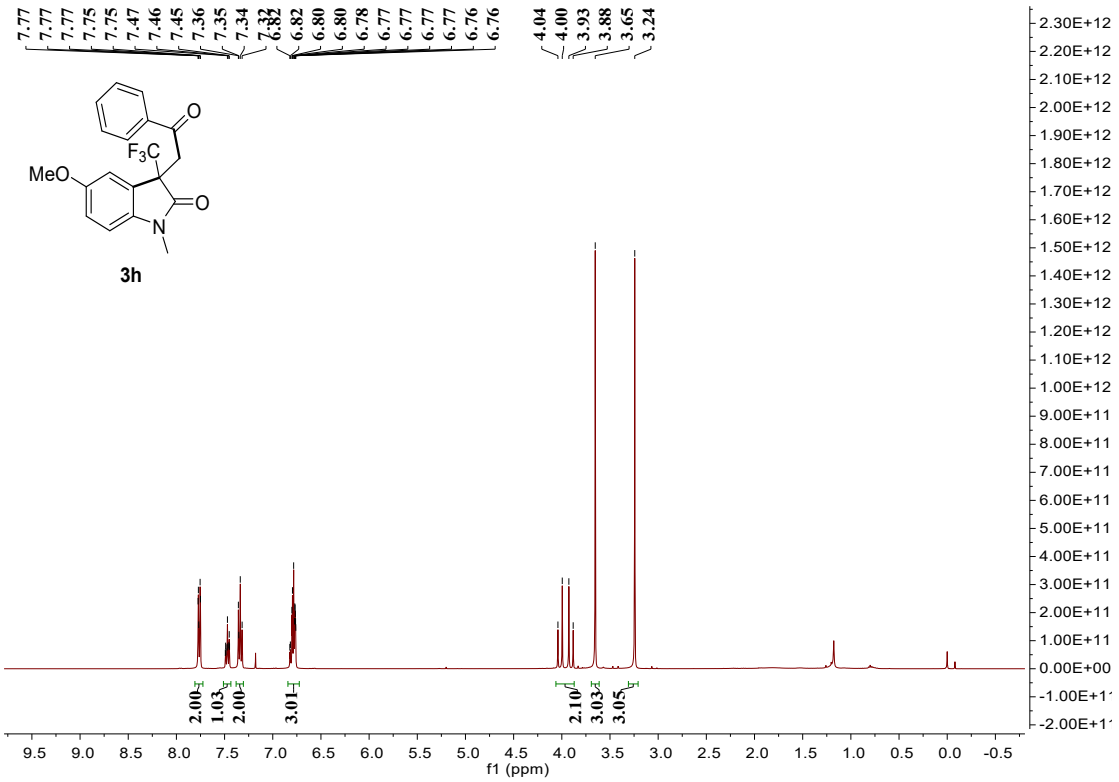
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3g**



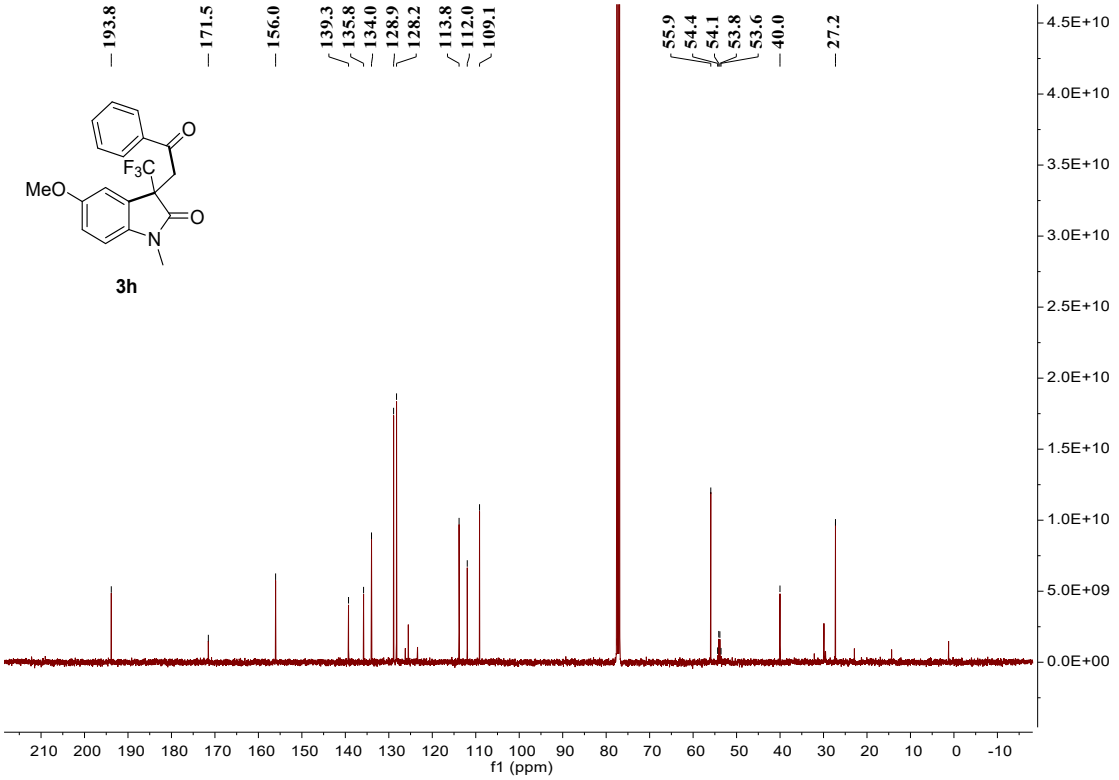
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3g**



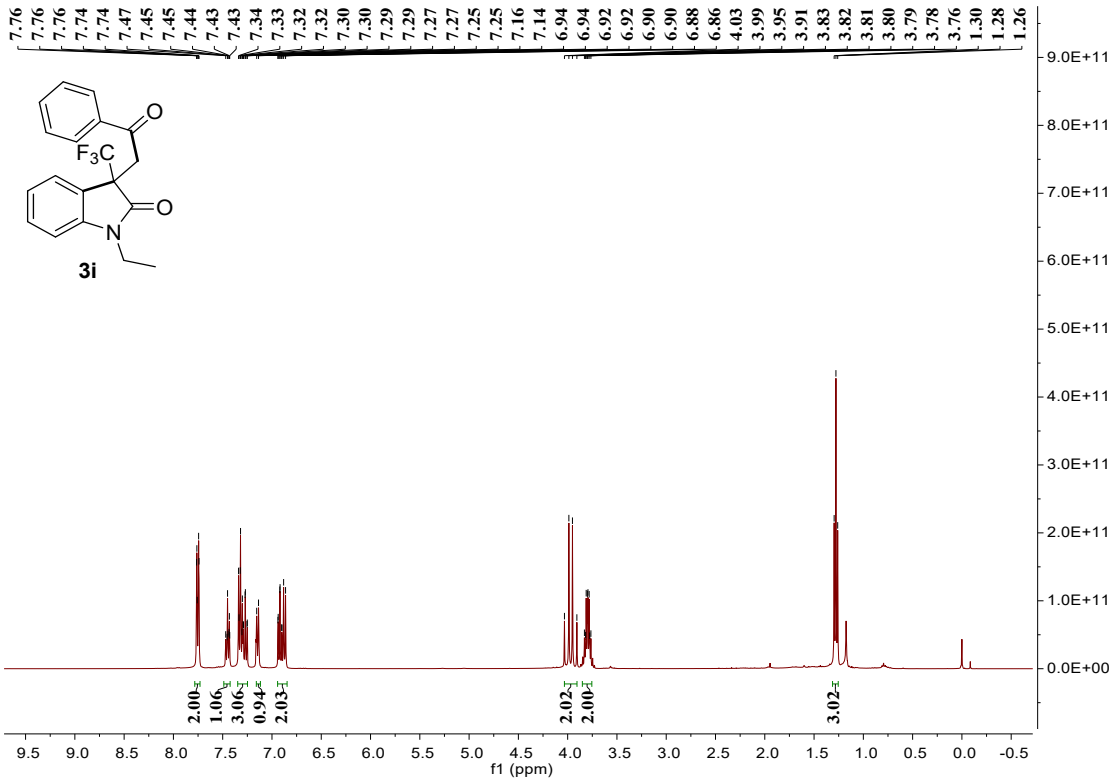
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3h**



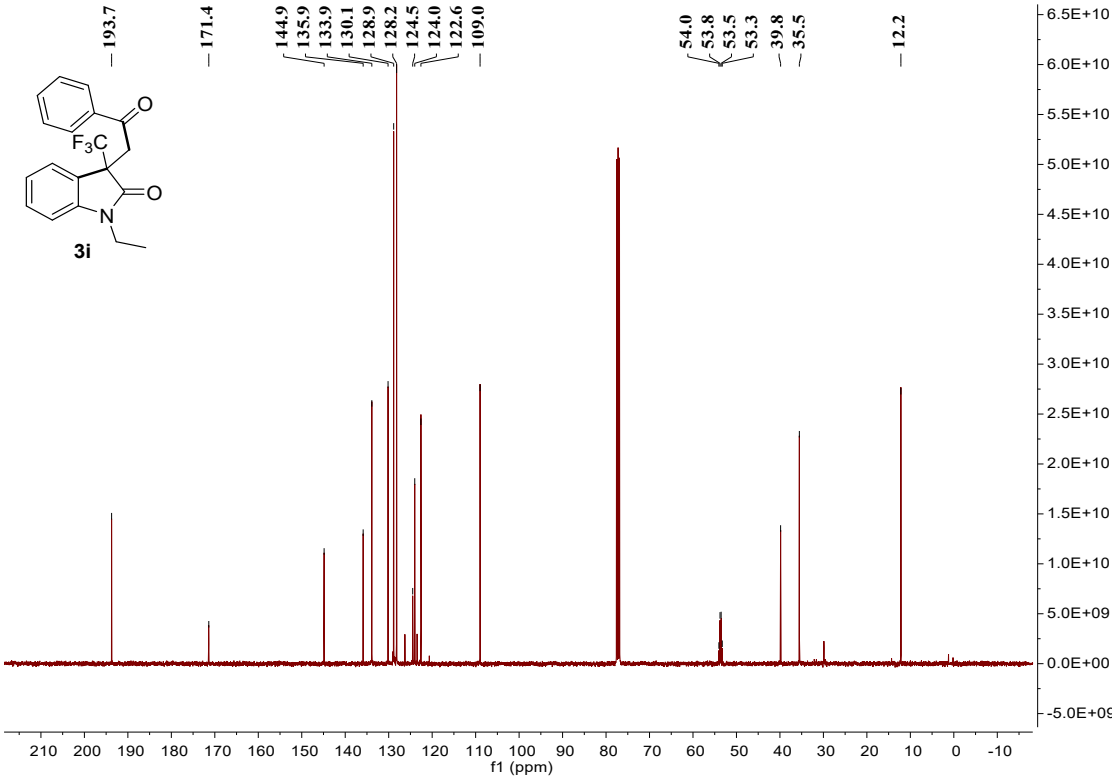
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3h**



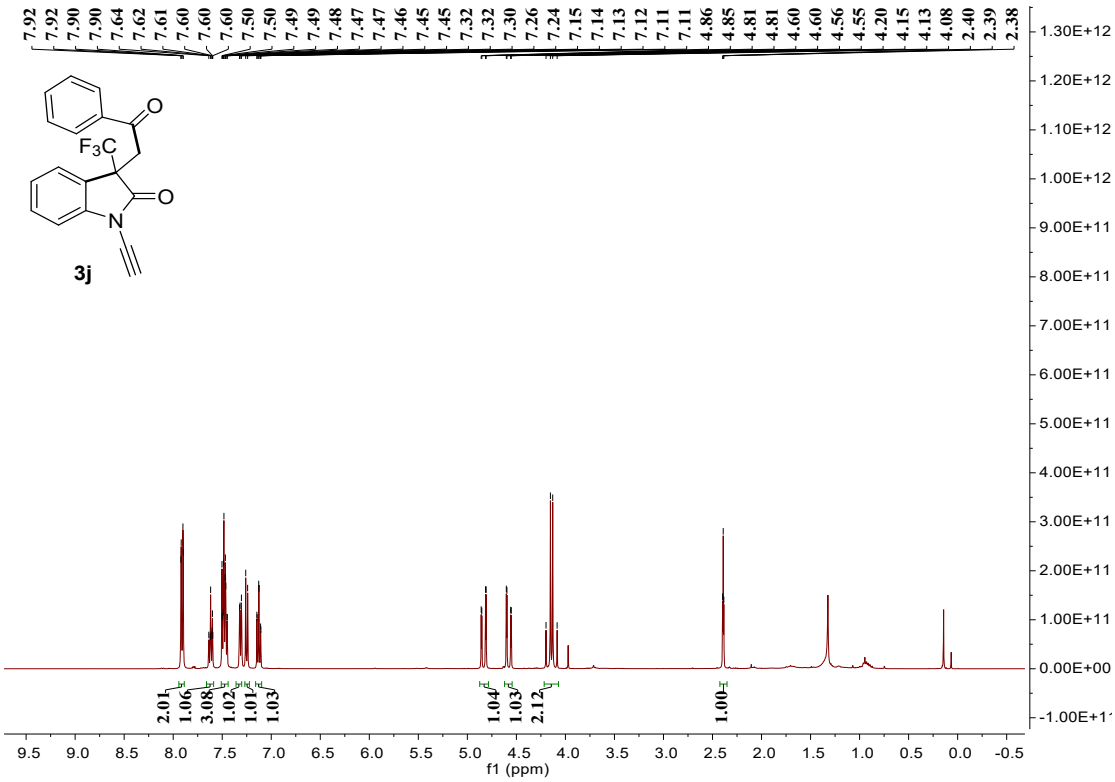
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3i**



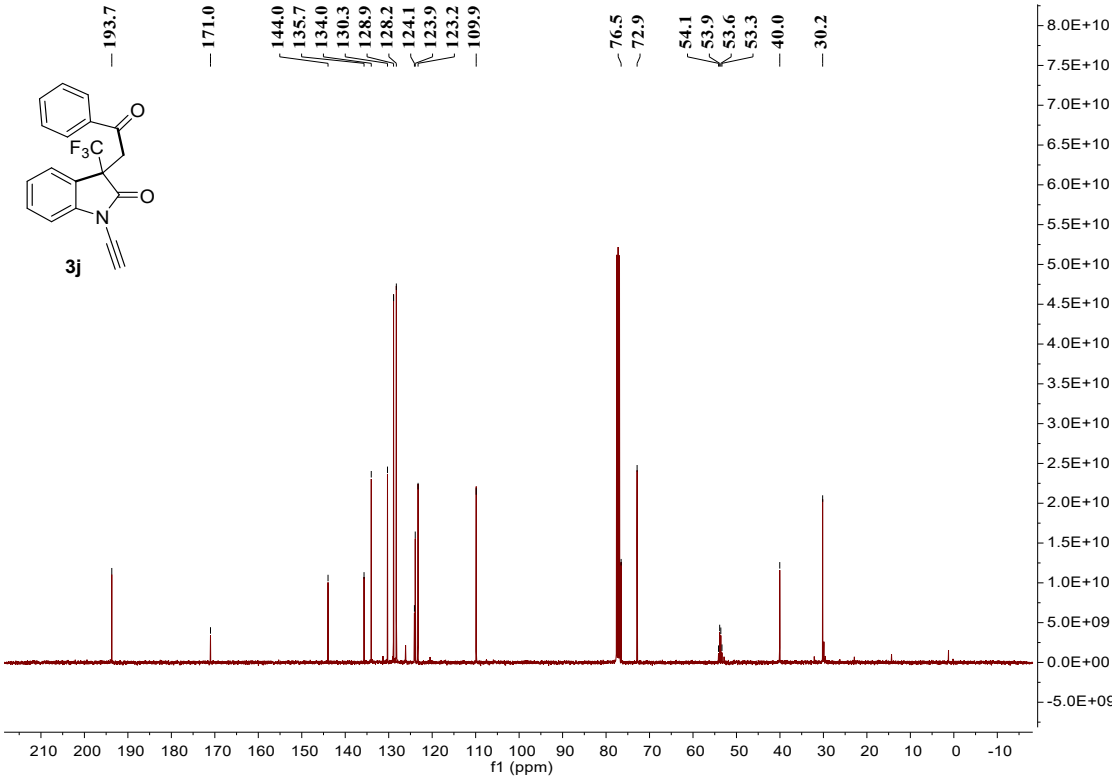
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3i**



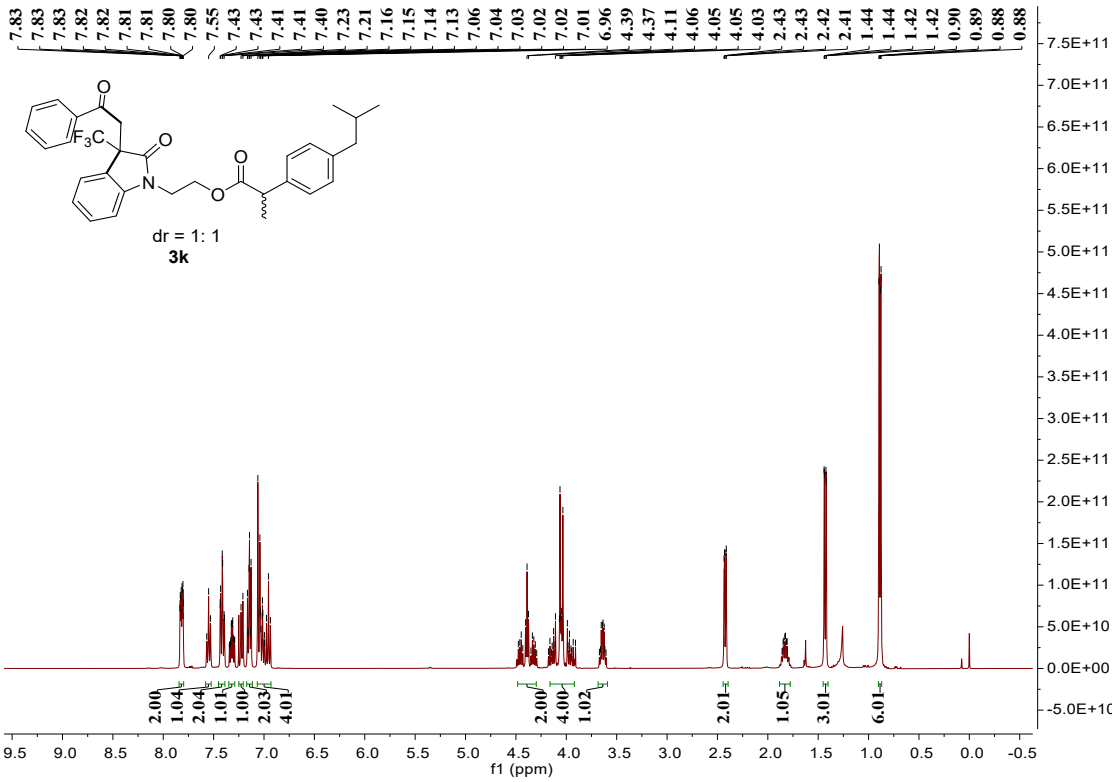
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3j**



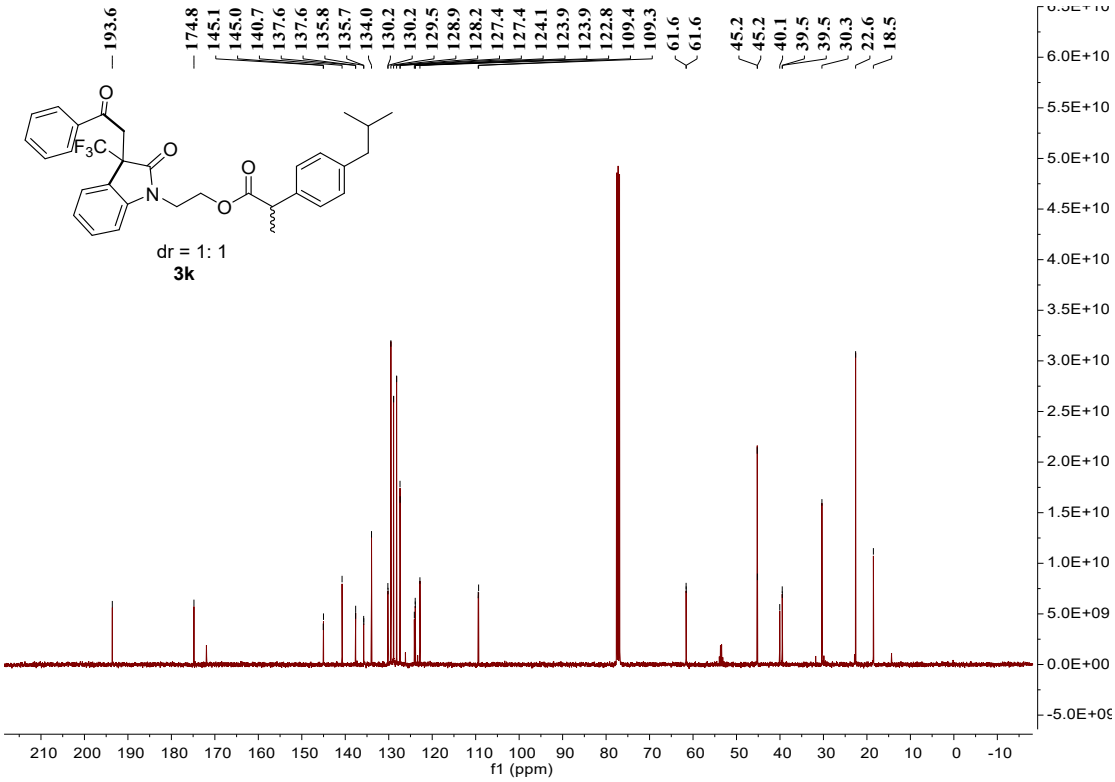
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3j**



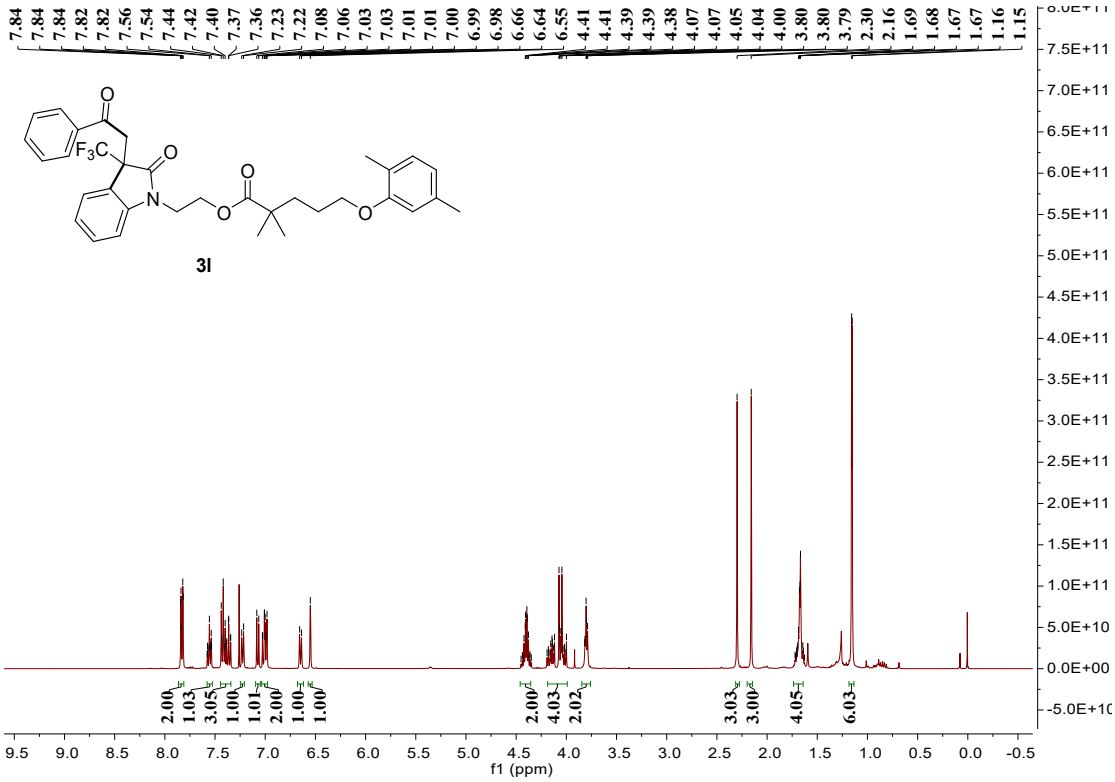
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3k**



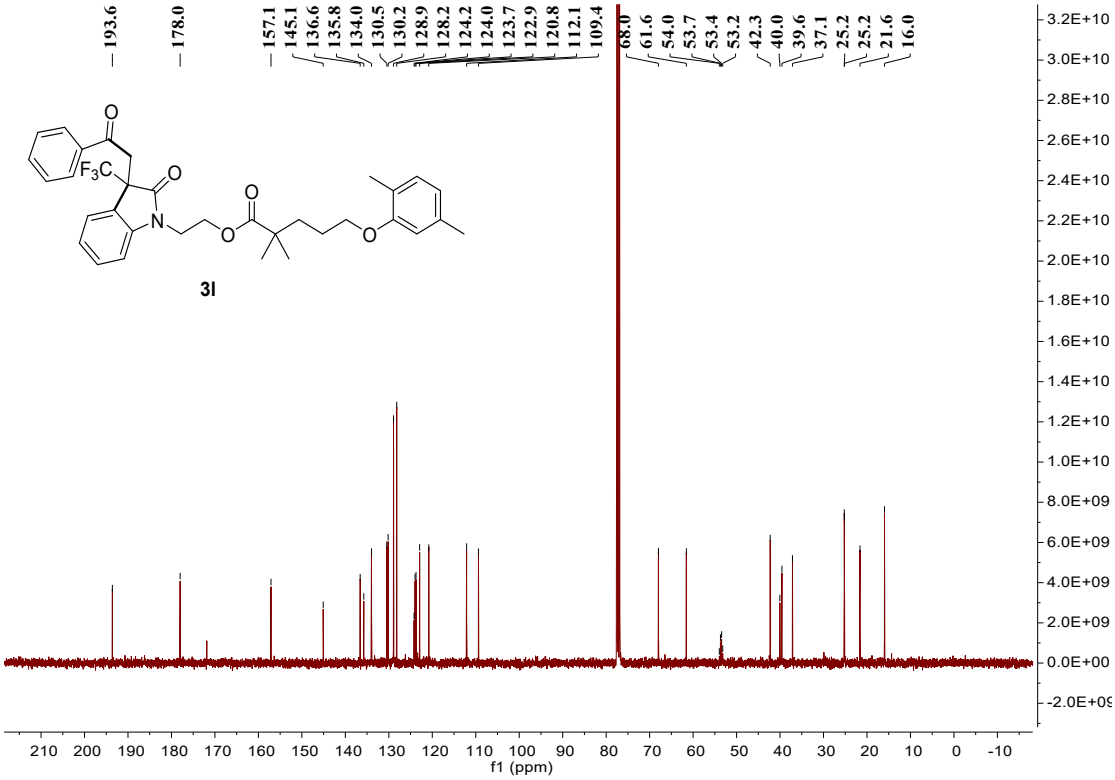
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3k**



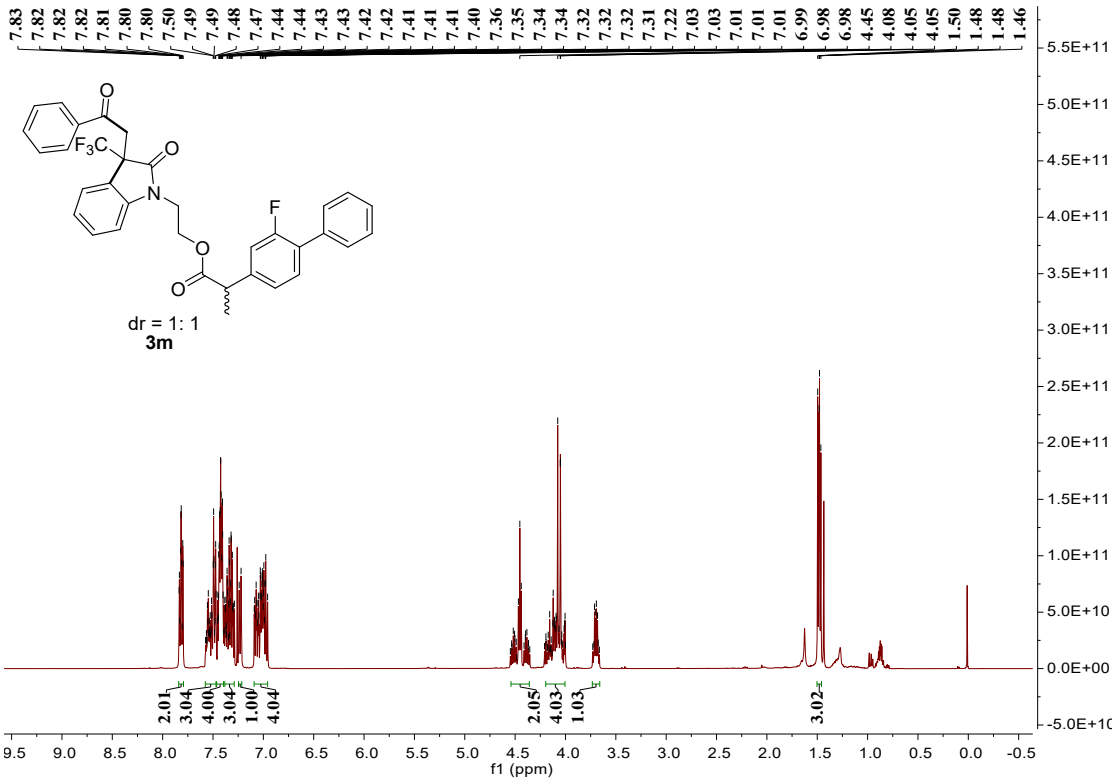
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3l**



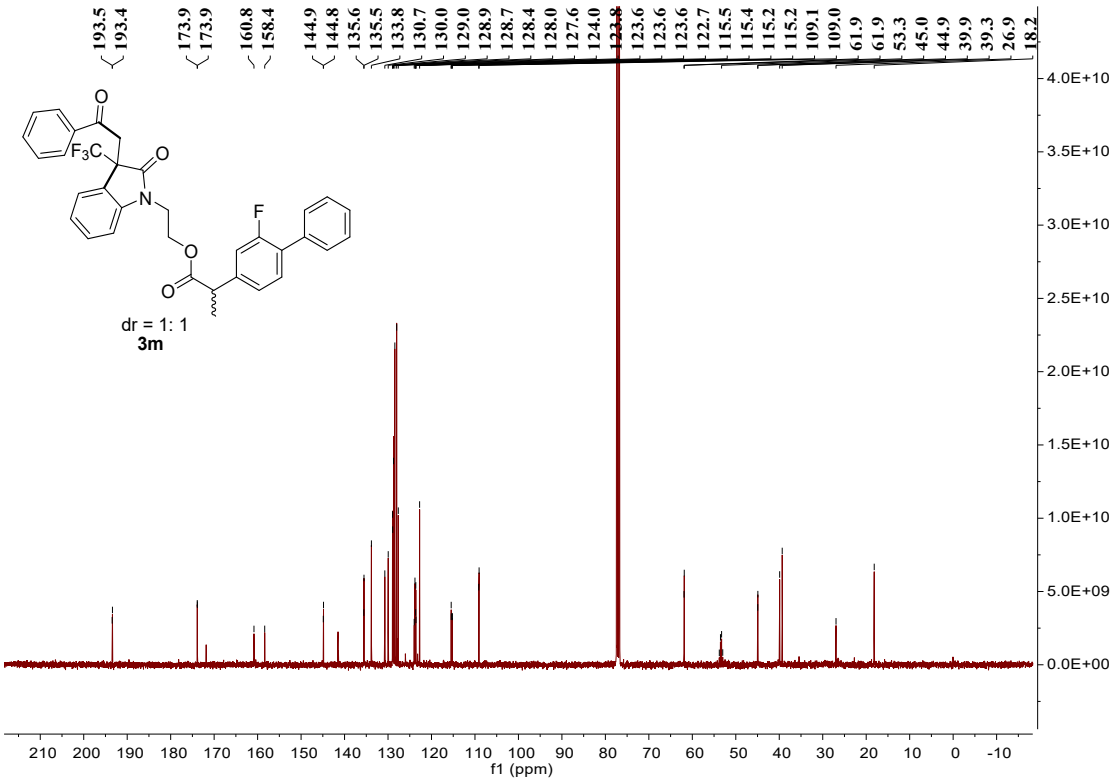
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3l**



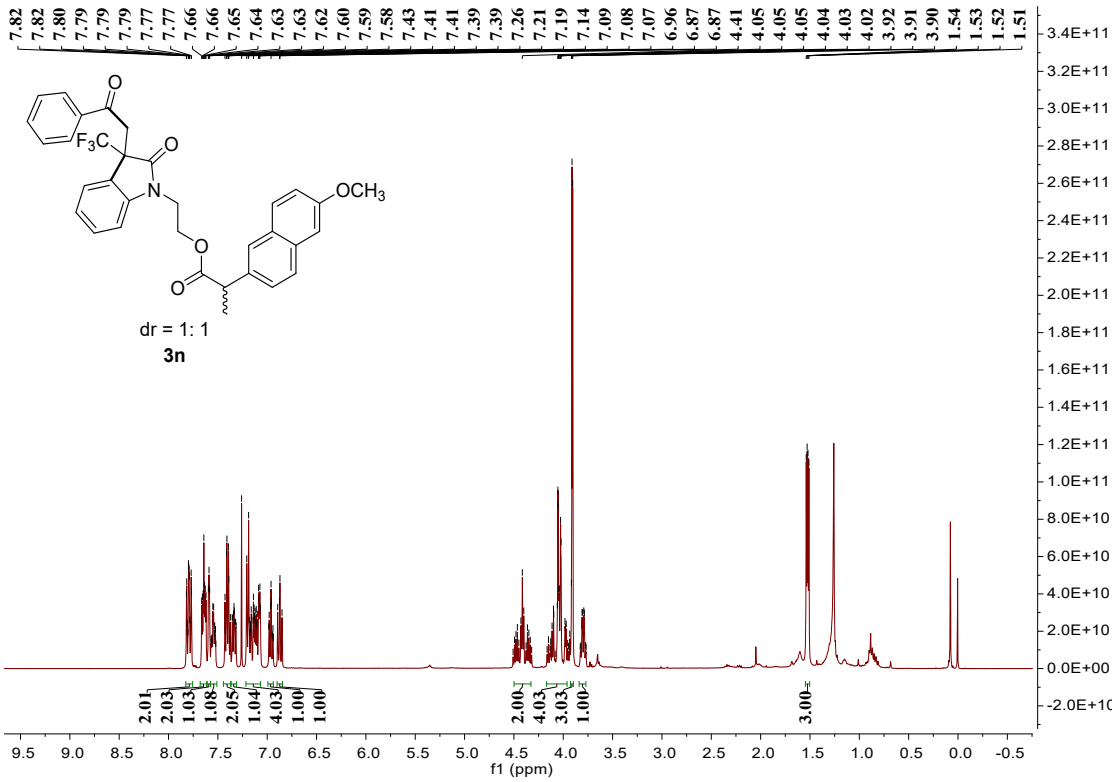
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3m**



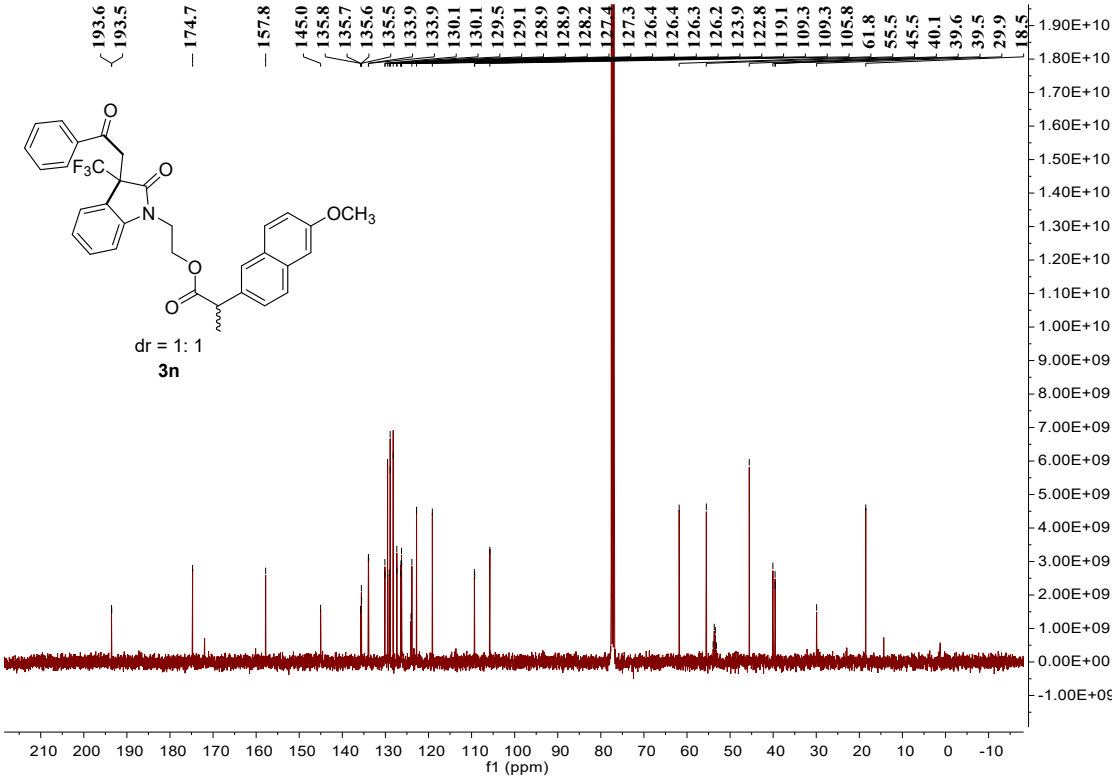
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3m**



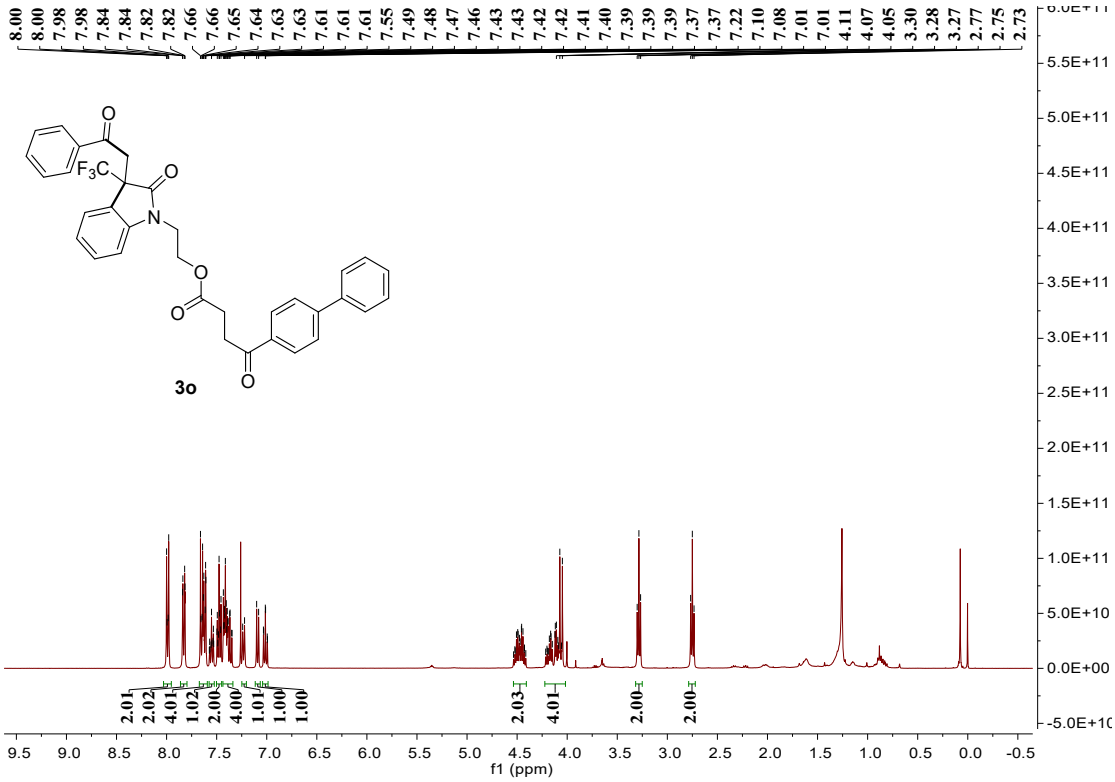
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3n**



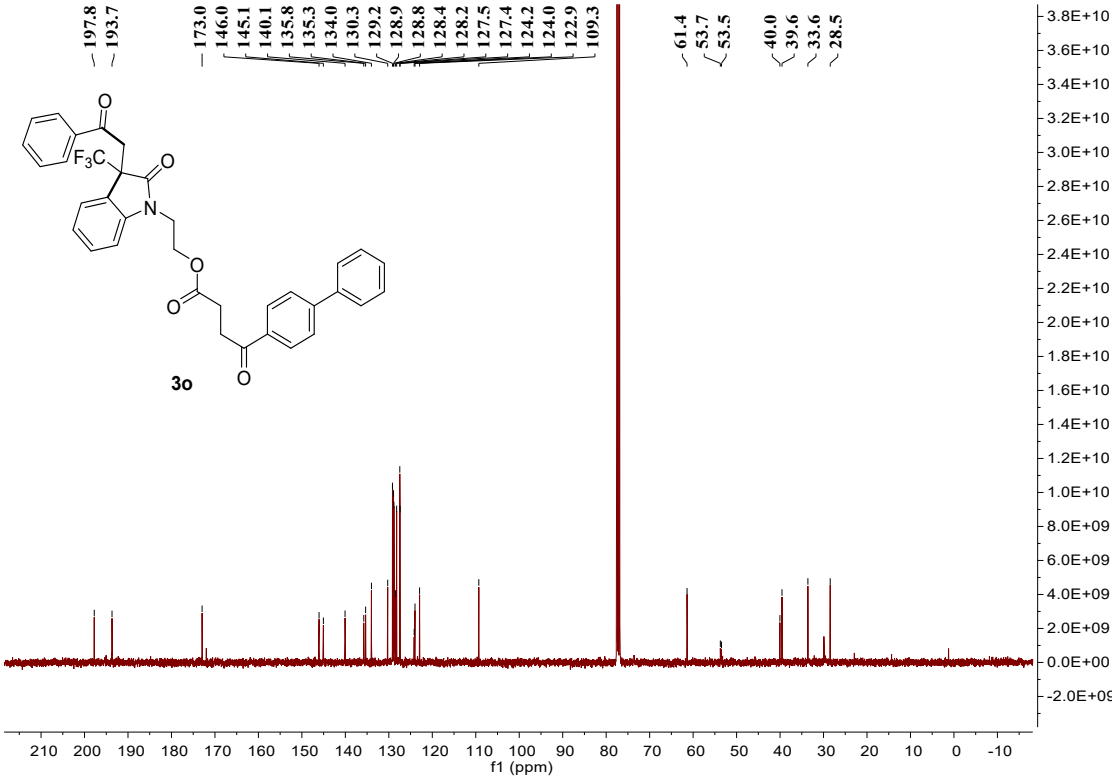
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3n**



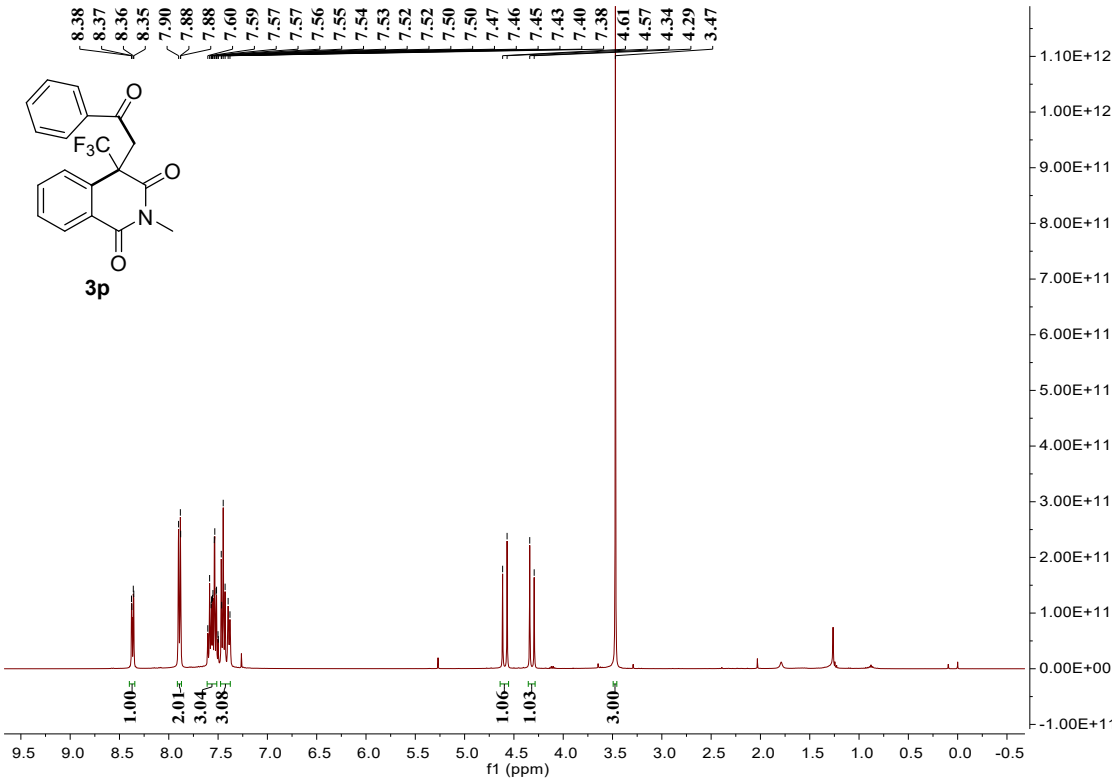
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3o**



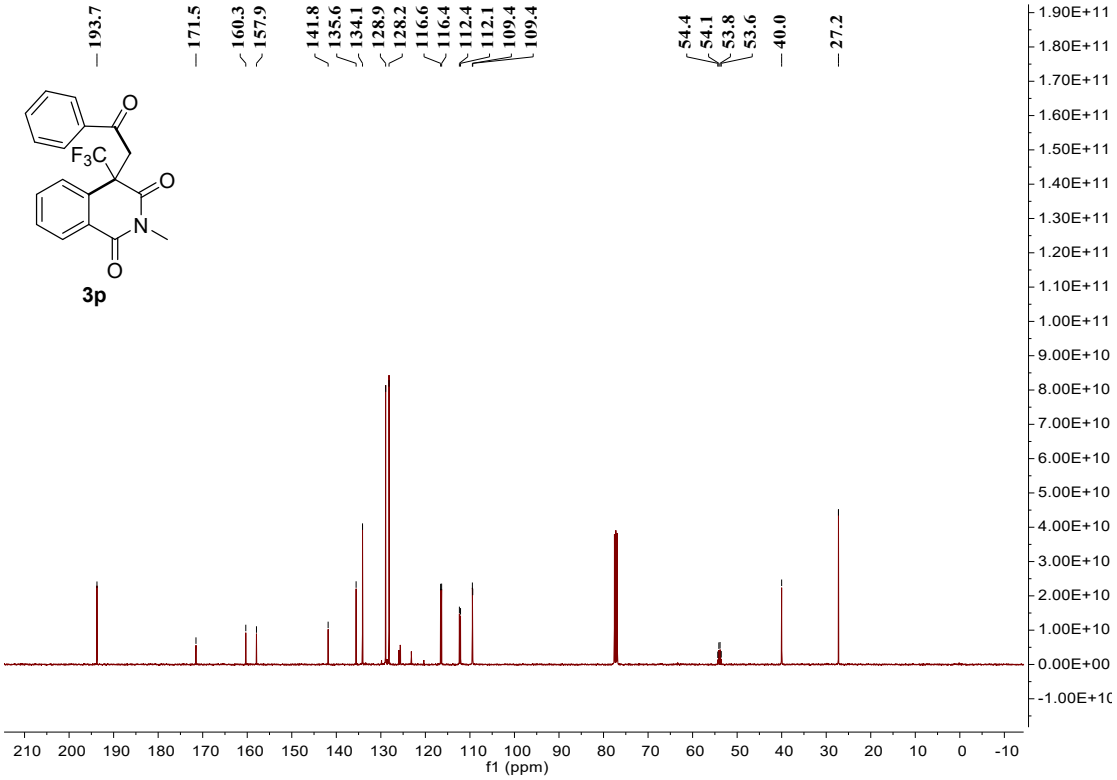
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3o**



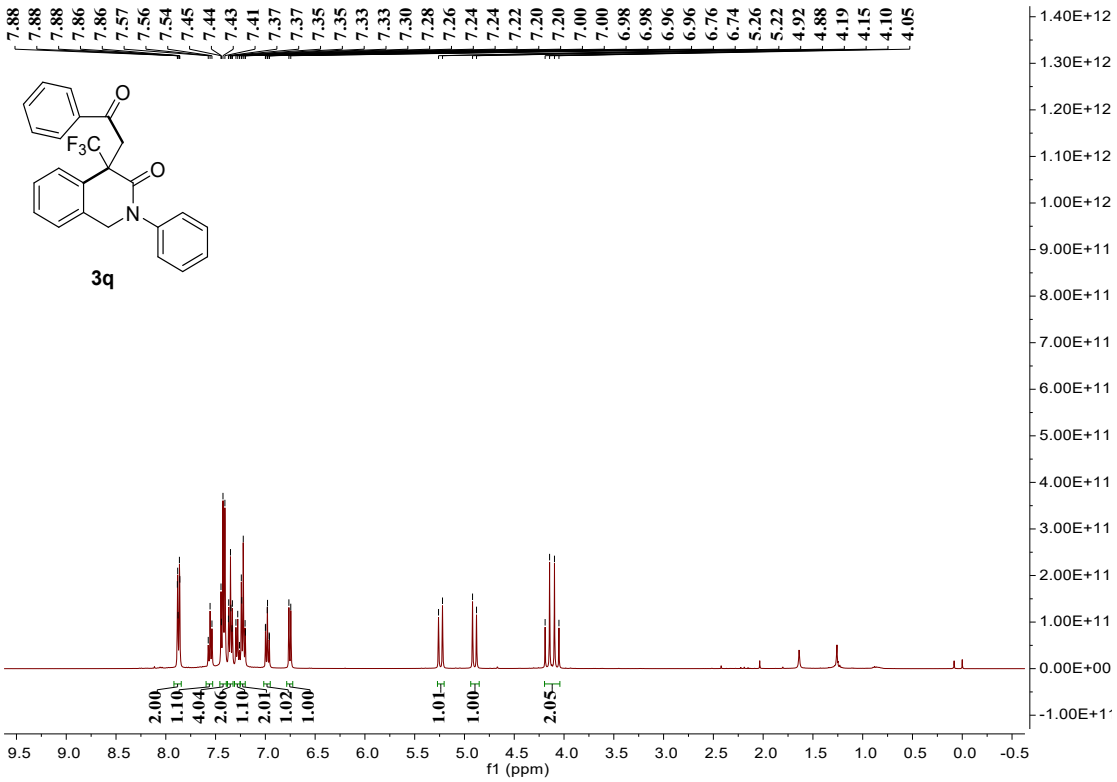
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3p**



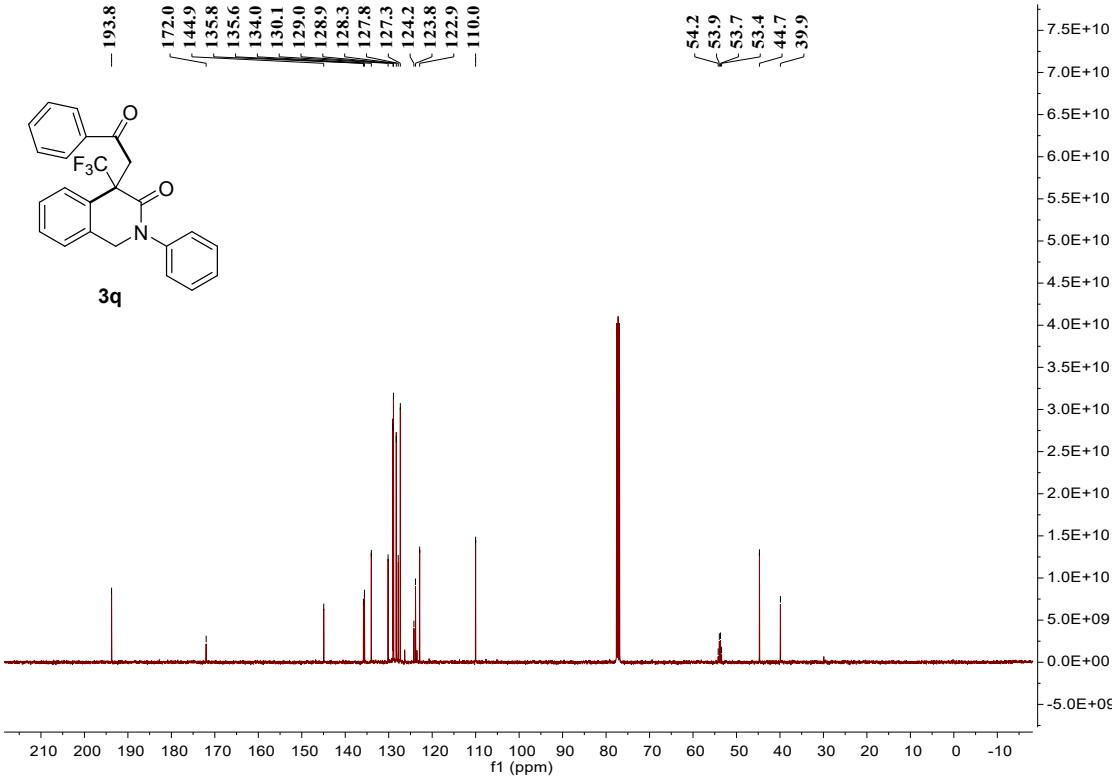
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3p**



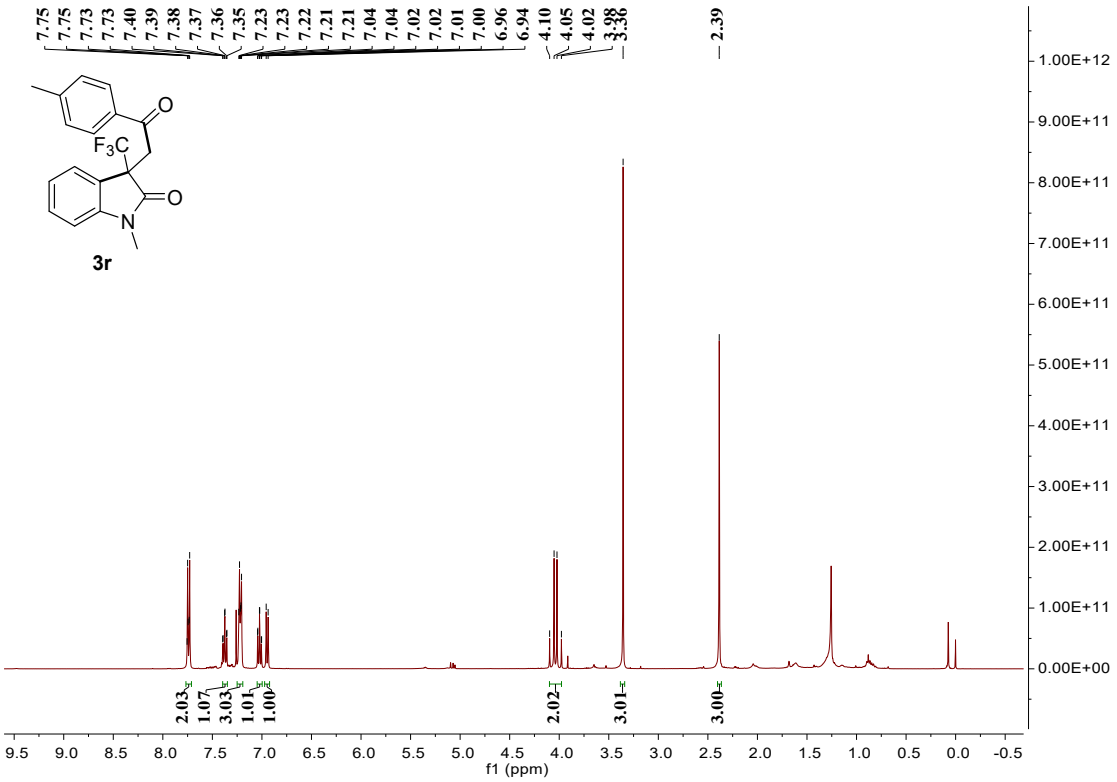
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3q**



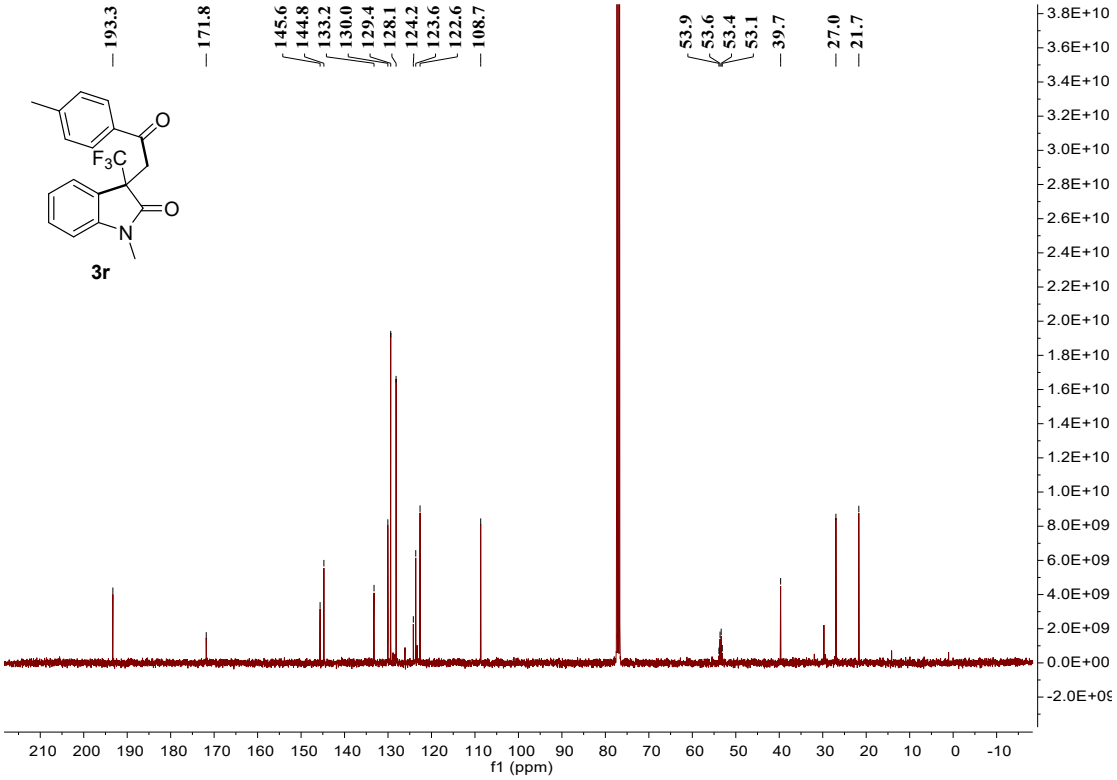
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3q**



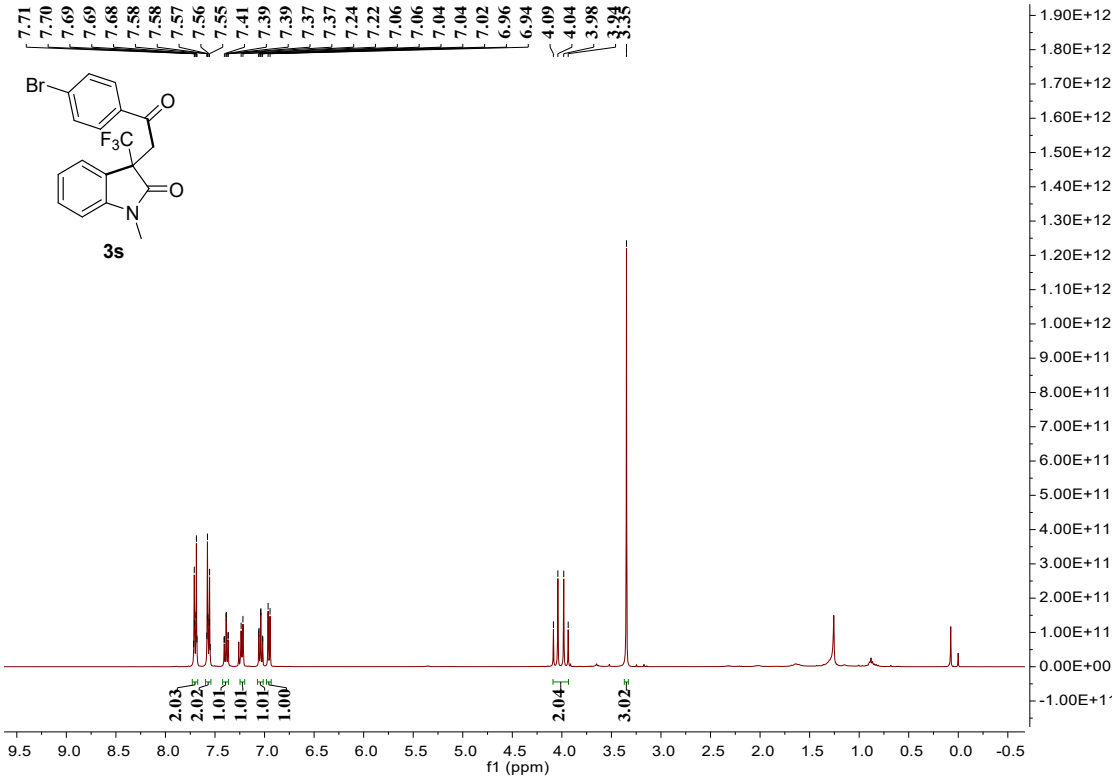
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3r**



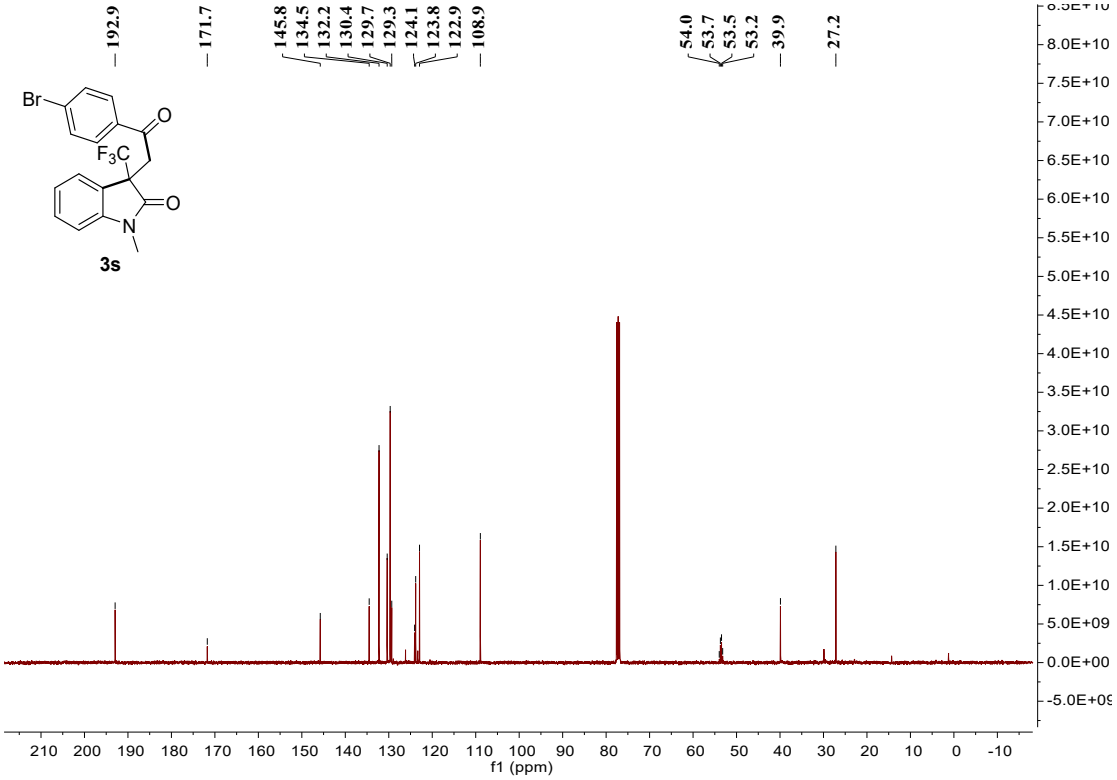
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3r**



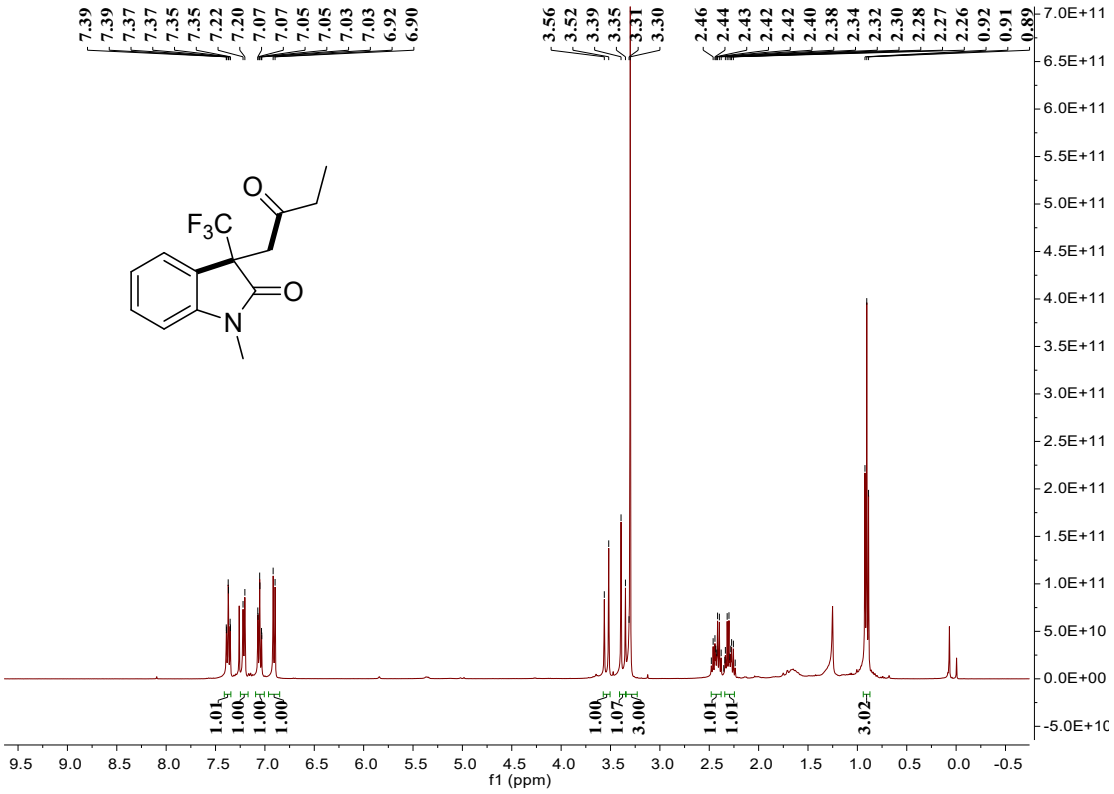
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3s**



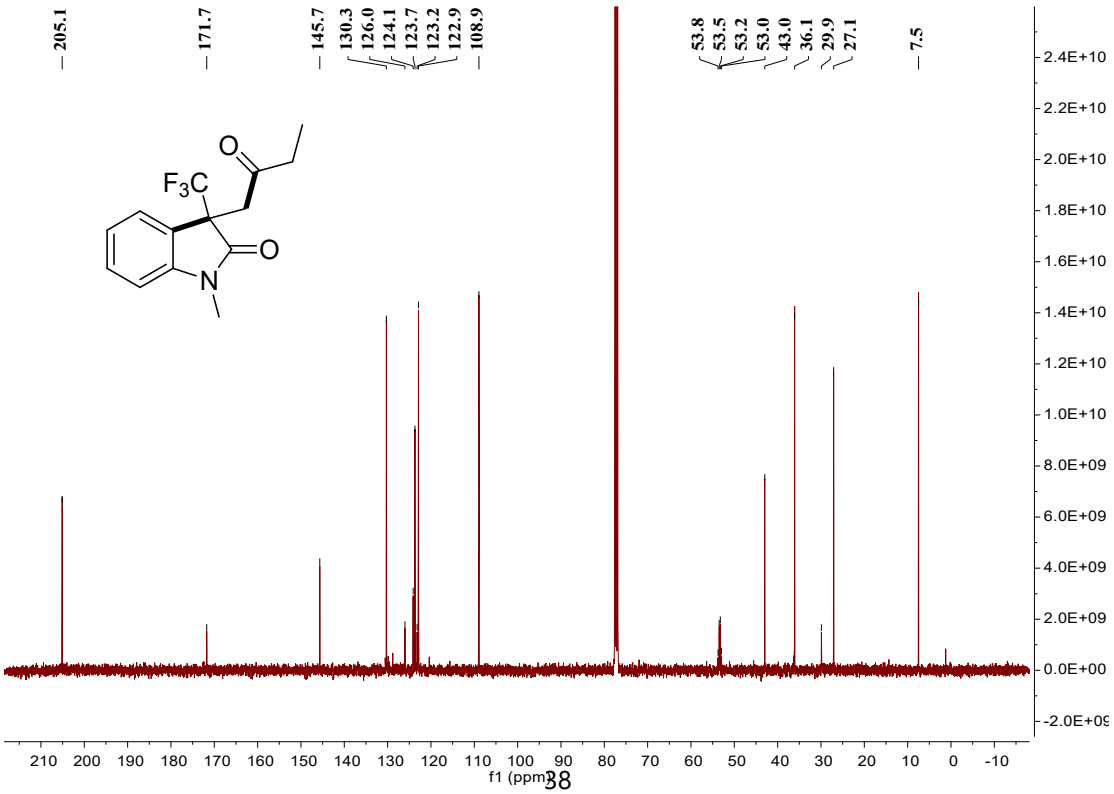
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3s**



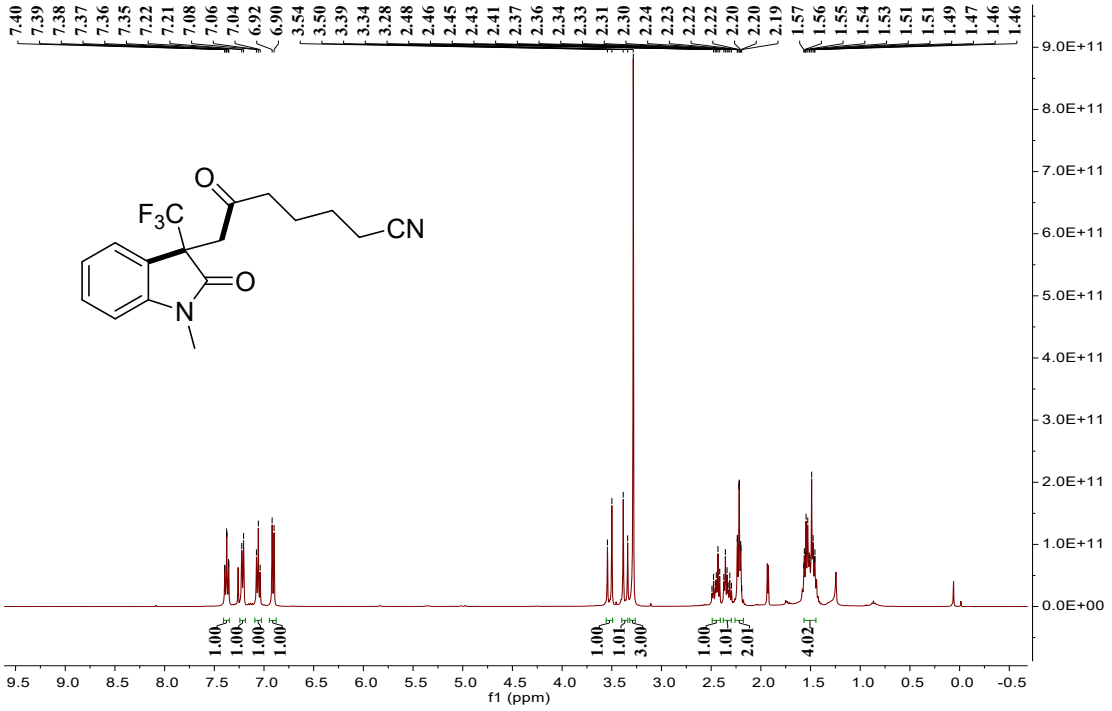
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3t**



^{13}C NMR (101 MHz, $CDCl_3$) of compound **3t**



^{1}H NMR (400 MHz, $CDCl_3$) of compound **3u**



^{13}C NMR (101 MHz, $CDCl_3$) of compound **3u**