Supporting Information *for*

Synthesis of 4-trifluoromethyl 2-pyrones and pyridones through Brønsted base catalyzed Pechmann type reaction with cyclic 1,3-diones

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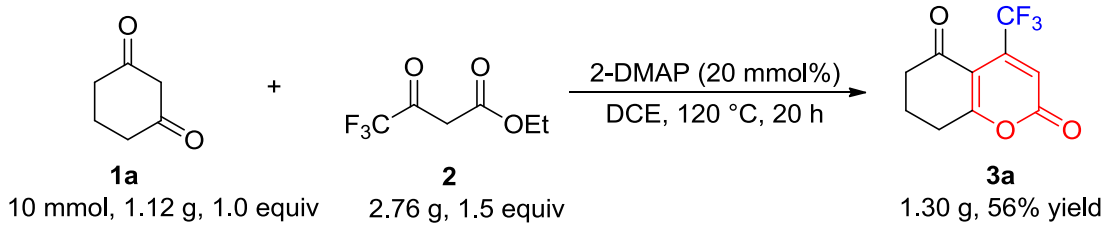
Procedure for gram scale reaction for synthesis of 4-(trifluoromethyl)-7,8-dihydro-2H-chromene-2,5(6*H*)-dione (3a)



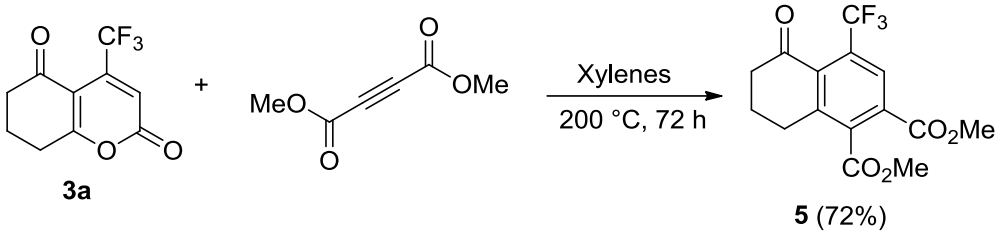
1a
10 mmol, 1.12 g, 1.0 equiv

2
2.76 g, 1.5 equiv

3a
1.30 g, 56% yield

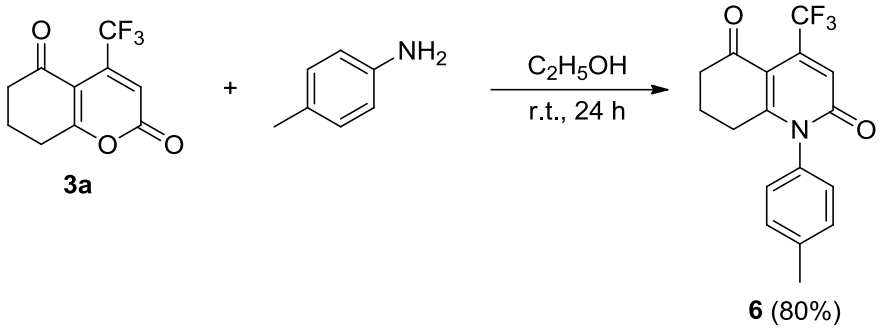
In a glove box filled with nitrogen, to an oven-dried 25 mL pressure tube equipped with a stir bar were added 1,3-cyclohexanedione (10 mmol, 1.12 g, 1.0 equiv), ethyl 4,4,4-trifluoroacetoacetate (15 mmol, 2.76 g, 1.50 equiv), 2-dimethylaminopyridine (2 mmol, 0.24 g, 0.20 equiv), and 1,2-bichloroethane (10 mL). The tube was sealed with Teflon screw cap and the solution was stirred at 120 °C for 20 h. The reaction mixture was cooled to room temperature, diluted with ethyl acetate, washed with saturated ammonium chloride solution (3 × 60 mL) and water (60 mL), dried over Mg_2SO_4, and filtered. The residue obtained was purified by flash column chromatography over silica gel with *n*-pentane/dichloromethane (1:1) to give 1.30 g of product **3a** (56% yield).

Procedure for the synthesis of compound 5



In a glove box filled with nitrogen, to an oven-dried 5 mL pressure tube equipped with a stir bar were added 4-(trifluoromethyl)-7,8-dihydro-2*H*-chromene-2,5(6*H*)-dione **3a** (47 mg, 0.20 mmol, 1.0 equiv), dimethyl acetylenedicarboxylate (142 mg, 1.0 mmol, 5.0 equiv), and xylene (0.20 mL). The tube was sealed with Teflon screw cap and the solution was stirred at 200 °C for 72 h. The reaction mixture was cooled to room temperature and was filtered through a layer of Celite, eluted with dichloromethane. The solvent was removed by rotary evaporation and the resulting product was purified by column chromatography on silica gel with *n*-pentane/dichloromethane to give product **5** (48 mg, 0.14 mol, 72% yield).

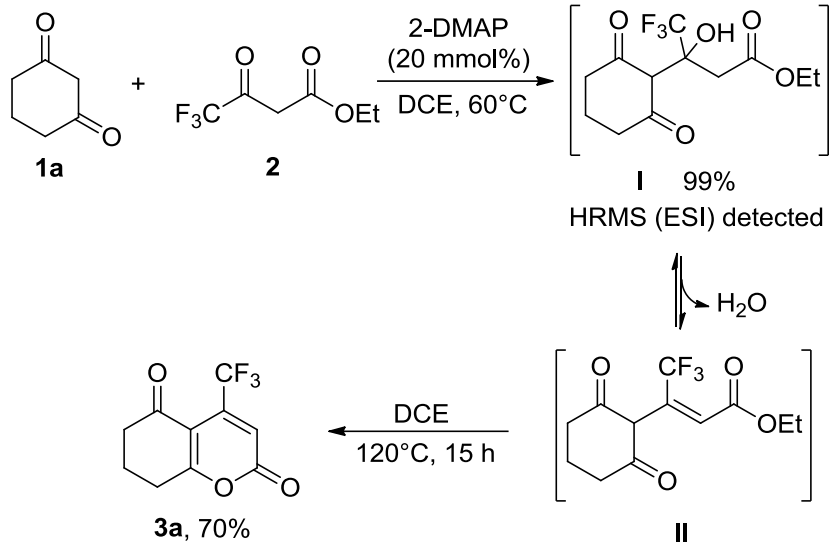
Procedure for the synthesis of compound 6



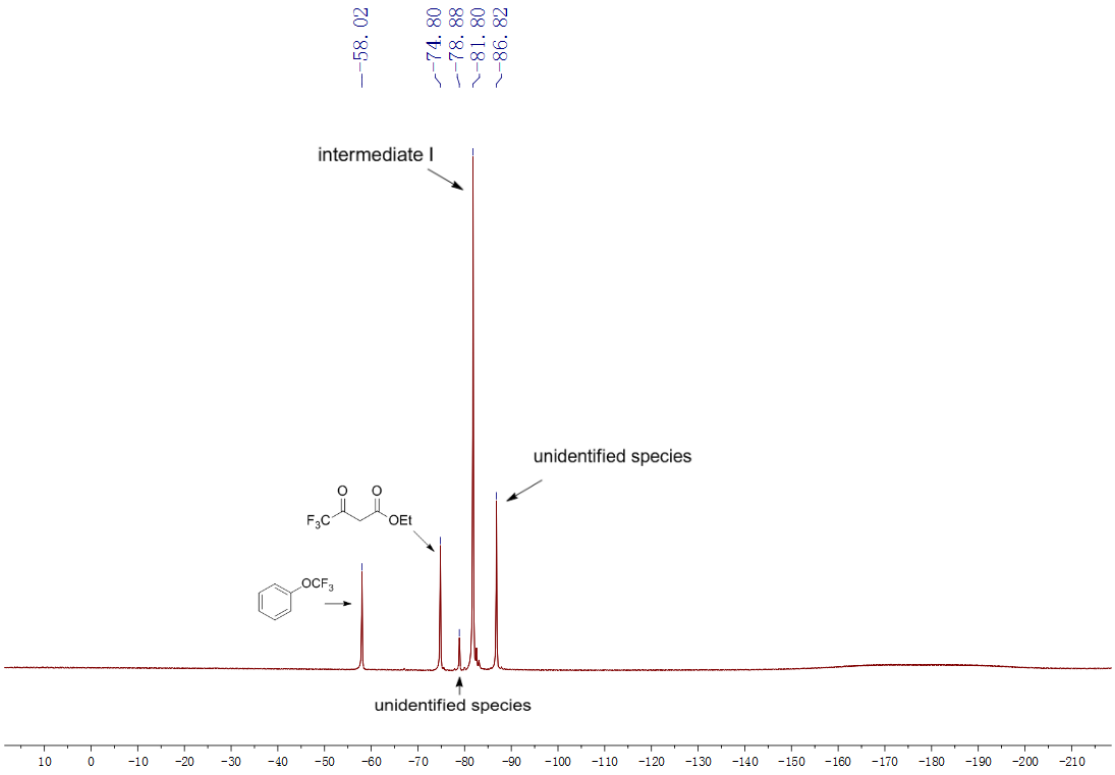
Under atmospheric conditions, a scintillation vial equipped with a stir bar were added 4-(trifluoromethyl)-7,8-dihydro-2*H*-chromene-2,5(6*H*)-dione **3a** (47 mg, 0.20 mmol, 1.0 equiv), *p*-toluidine (26 mg, 0.24 mmol, 1.2 equiv), and C_2H_5OH (1.0 mL). The tube was sealed with Teflon screw cap and the solution was stirred at room temperature for 24 h. The reaction mixture was filtered through a layer of Celite, eluted with dichloromethane. The solvent was removed by rotary evaporation and the resulting product was purified by column chromatography on silica gel with *n*-pentane/dichloromethane to give product **6** (51 mg, 0.16 mmol, 80% yield).

Mechanism exploratory experiments

(1).

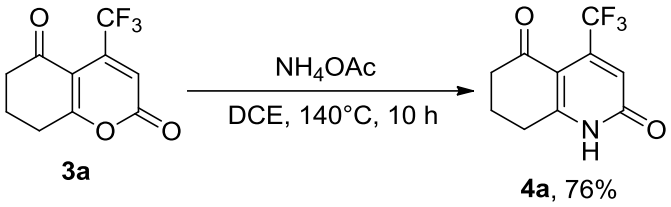


In a glove box filled with nitrogen, to an oven-dried 5 mL pressure tube equipped with a stir bar were added 1,3-cyclohexanedione (33.6 mg, 0.30 mmol, 1.0 equiv), ethyl 4,4,4-trifluoroacetoacetate (82.8 mg, 0.45 mmol, 1.5 equiv), 2-dimethylaminopyridine (7.3 mg, 0.060 mmol, 0.20 equiv), and 1,2-bichloroethane (1.0 mL). The tube was sealed with Teflon screw cap and the solution was stirred at 60 °C in oil bath for 10 h. The reaction mixture was cooled to room temperature, and then 10μL (trifluoromethoxy)benzene was added as an internal standard. The filtrate was analyzed by ^{19}F NMR and HRMS (ESI). The yield of the intermediate **I** was calculated to be 99%.



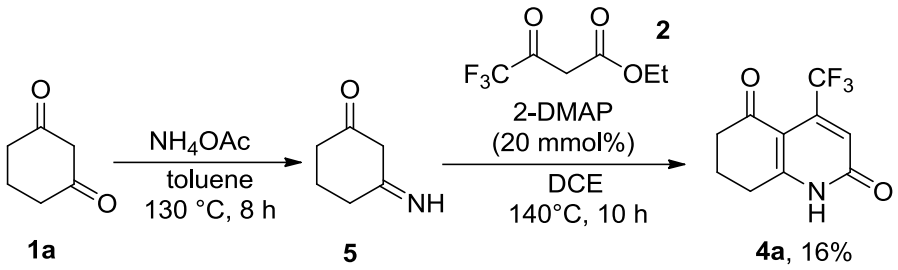
The reaction mixture was further stirred at 120 °C in oil bath for 10 h, and was cooled to room temperature. The resulting mixture was filtered through a layer of Celite. The filtrate was analyzed by ^{19}F NMR and GC-MS. The yield of the **3a** was calculated to be 70%.

(2).

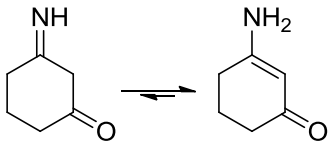


In a glove box filled with nitrogen, to an oven-dried 5 mL pressure tube equipped with a stir bar were added 4-(trifluoromethyl)-7,8-dihydro-2*H*-chromene-2,5(6*H*)-dione **3a** (23.2 mg, 0.10 mmol, 1.0 equiv), NH_4OAc (23.1 mg, 0.30 mmol, 3.0 equiv), and 1,2-bichloroethane (1.0 mL). The tube was sealed with Teflon screw cap and the solution was stirred at 140 °C in oil bath for 10 h. The reaction mixture was cooled to room temperature, and then 10μL (trifluoromethoxy)benzene was added as an internal standard. The resulting mixture was filtered through a layer of Celite. The filtrate was analyzed by ^{19}F NMR and GC-MS. The yield of the 4-(trifluoromethyl)-7,8-dihydroquinoline-2,5(1*H*,6*H*)-dione **4a** was calculated to be 76%.

(3).



Under nitrogen atmospheric conditions, a scintillation vial equipped with a stir bar were added 1,3-cyclohexanedione (224 mg, 2.0 mmol, 1.0 equiv), NH_4OAc (154 mg, 2.0 mmol, 1.0 equiv), and dry toluene (6.0 mL). The tube was sealed with Teflon screw cap and the solution was stirred at 130 °C for 8 h. The reaction mixture was cooled to room temperature for two hours. The upper layer of toluene solution was separated and the lower layer was extracted with ethyl acetate, and dried. The solvent was removed by rotary evaporation and the resulting crude product was recrystallized by ethyl acetate to give 3-iminocyclohexanone **5**.



3-iminocyclohexanone (5)

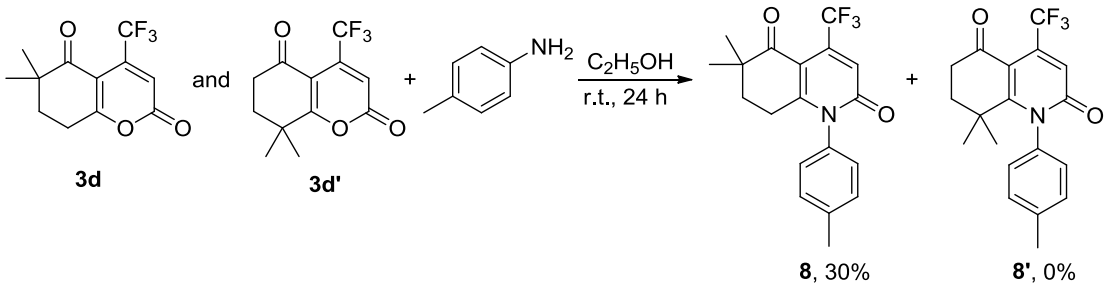
Obtained as a reddish-brown solid in 45% yield (100 mg). M.p.: 108.6-109.2 °C. R_f (dichloromethane : methanol 1:1) = 0.37. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.55 (br, s, 2H), 5.25 (s, 1H), 2.36 (t, J = 5.3 Hz, 2H), 2.26 (t, J = 5.7 Hz, 2H), 2.03 – 1.86 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.1 (s), 167.1 (s), 99.7 (s), 35.7 (s), 28.7 (s), 21.7 (s). IR (ATR): ν 3319, 3121, 2939, 1673, 1522, 1378, 1249, 1186, 825, 645 cm^{-1}. GC-MS (EI) for C_6H_9NO m/z: $[M]^+$: 111.07.

In a glove box filled with nitrogen, to an oven-dried 5 mL pressure tube equipped with a stir bar were added 3-iminocyclohexanone **5** (22.2 mg, 0.20 mmol, 1.0 equiv), ethyl 4,4,4-trifluoroacetoacetate (55.2 mg, 0.30 mmol, 1.5 equiv),

2-dimethylaminopyridine (4.9 mg, 0.04 mmol, 0.2 equiv), and 1,2-bichloroethane (1.0 mL). The tube was sealed with Teflon screw cap and the solution was stirred at 140 °C in oil bath for 10 h. The reaction mixture was cooled to room temperature, and then 10μL (trifluoromethoxy)benzene was added as an internal standard. The resulting mixture was filtered through a layer of Celite. The filtrate was analyzed by ^{19}F NMR and GC-MS. The yield of the **4a** was calculated to be 16%.

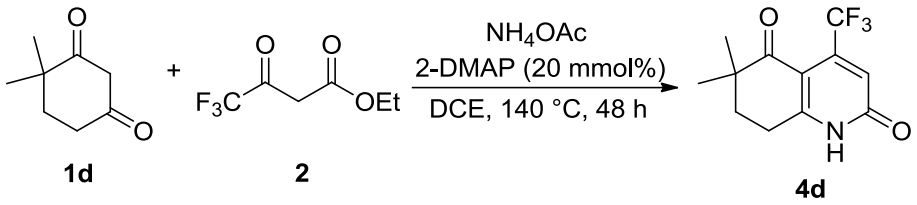
(4)

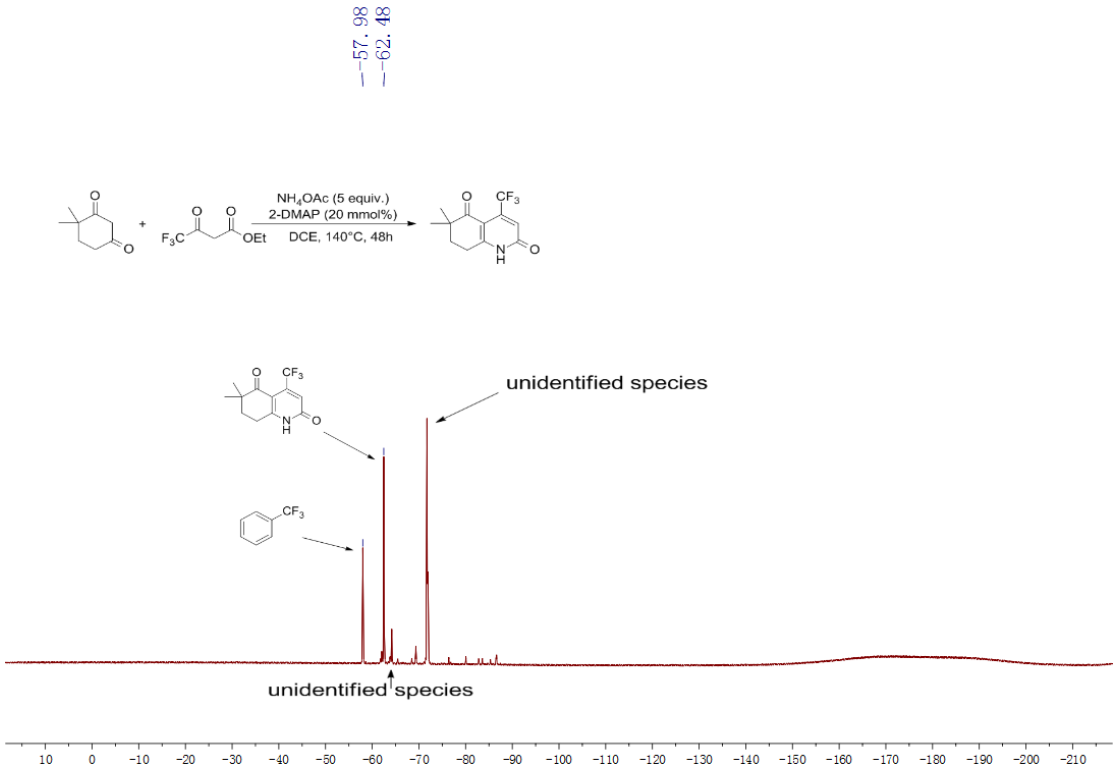
Reaction of two isomers 3d and 3d′ with *p*-toluidine



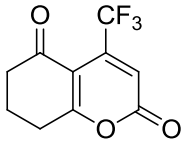
Under atmospheric conditions, a scintillation vial equipped with a stir bar were added a mixture containing two regioisomers **3d** and **3d′** (1:3 ratio) (52 mg, 0.20 mmol, 1.0 equiv), *p*-toluidine (26 mg, 0.24 mmol, 1.2 equiv), and C_2H_5OH (1.0 mL). The tube was sealed with Teflon screw cap and the solution was stirred at room temperature for 24 h. The reaction mixture was filtered through a layer of Celite, eluted with dichloromethane. The solvent was removed by rotary evaporation and the resulting product was purified by column chromatography on silica gel with *n*-pentane/dichloromethane to give product **8** as single regioisomer (21 mg, 0.06 mmol, 30% yield).

The ^{19}F NMR of the crude reaction mixture of the reaction of 1d with 2



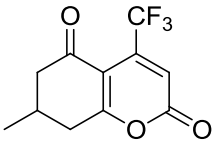


Data for compounds 3–6



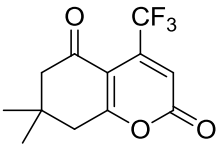
4-(Trifluoromethyl)-7,8-dihydro-2*H*-chromene-2,5(6*H*)-dione (3a)

Obtained as a light yellow solid in 99% yield (70 mg). Mp: 78.2-79.5 °C. R_f (*n*-pentane:dichloromethane 1:2) = 0.36. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.67 (s, 1H), 2.94 (t, *J* = 6.2 Hz, 2H), 2.62 (t, *J* = 6.2 Hz, 2H), 2.23 – 2.10 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$): δ -63.6 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$): δ 190.8 (s), 176.2 (d, *J* = 1.3 Hz), 158.0 (s), 141.6 (q, *J* = 35.1 Hz), 120.8 (q, *J* = 275.1 Hz), 115.0 (q, *J* = 7.3 Hz), 111.3 (s), 38.0 (s), 29.2 (s), 19.4 (s). IR (ATR): ν 3082, 2971, 1749, 1687, 1629, 1460, 1276, 1236, 1138, 1019 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{10}H_8F_3O_3$ $[M+H]^+$: 233.0420; found: 233.0416.



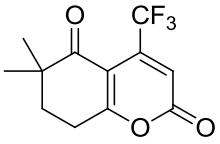
7-Methyl-4-(trifluoromethyl)-7,8-dihydro-2*H*-chromene-2,5(6*H*)-dione(3b)

Obtained as a white solid in 99% yield (74 mg). Mp: 131.3-133.0 °C. R_f (*n*-pentane:dichloromethane 1:2) = 0.44. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.64 (s, 1H), 2.05 – 2.86 (m, 1H), 2.79 – 2.56 (m, 2H), 2.51 – 2.22 (m, 2H), 1.25 – 1.05 (m, 3H). ^{19}F NMR (376 MHz, $CDCl_3$): δ -63.6 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$): δ 190.7 (s), 175.6 (s), 158.1 (s), 141.6 (q, *J* = 35.1 Hz), 120.8 (q, *J* = 275.2 Hz), 115.0 (q, *J* = 7.4 Hz), 110.9 (s), 46.2 (s), 37.0 (s), 27.2 (s), 20.5 (s). IR (ATR): ν 3088, 2959, 2930, 1750, 1686, 1545, 1457, 1279, 1144, 1029 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{11}H_{10}F_3O_3$ $[M+H]^+$: 247.0577; found: 247.0571.



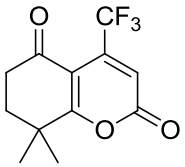
7,7-Dimethyl-4-(trifluoromethyl)-7,8-dihydro-2*H*-chromene-2,5(6*H*)-dione (3c)

Obtained as a white solid in 99% yield (78 mg). Mp: 109.8-111.6 °C. R_f (*n*-pentane:dichloromethane 1:2) = 0.44. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.63 (s, 1H), 2.78 (s, 2H), 2.47 (s, 2H), 1.14 (s, 6H). ^{19}F NMR (376 MHz, $CDCl_3$): δ -63.6 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$): δ 190.8 (s), 174.7 (s), 158.3 (s), 141.4 (q, *J* = 35.4 Hz), 120.8 (q, *J* = 275.1 Hz), 114.8 (q, *J* = 7.4 Hz), 110.4 (s), 51.9 (s), 42.7 (s), 31.7 (s), 27.9 (s). IR (ATR): ν 3102, 2965, 1756, 1679, 1550, 1471, 1400, 1278, 1129, 1047 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{12}H_{12}F_3O_3$ $[M+H]^+$: 261.0739; found: 261.0746.



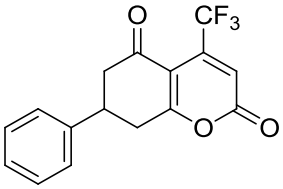
6,6-Dimethyl-4-(trifluoromethyl)-7,8-dihydro-2*H*-chromene-2,5(6*H*)-dione (3d)

and



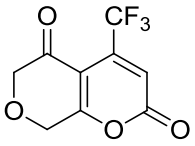
8,8-Dimethyl-4-(trifluoromethyl)-7,8-dihydro-2*H*-chromene-2,5(6*H*)-dione (3d′)

Obtained as a light red solid mixture in 99% yield (78 mg) with **3d**:**3d′** ratio 3:1. ^{1}H NMR (400 MHz, $CDCl_3$) **3d** + **3d′**: δ 6.67 (s), 6.65 (s), 2.93 (t, *J* = 6.0 Hz), 2.65 (t, *J* = 6.4 Hz), 2.32 – 2.12 (m), 2.07 – 1.88 (m), 1.45 (s), 1.21 (s). ^{19}F NMR (376 MHz, $CDCl_3$) **3d′**: δ -63.1 (s, 3F), **3d**: -63.5 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) **3d** + **3d′**: δ 196.1 (s), 191.0 (s), 180.9 (s), 174.0 (s), 158.2 (s), 142.3 (q, *J* = 35.0 Hz), 141.9 (q, *J* = 35.0 Hz), 120.9 (q, *J* = 275.1 Hz), 115.3 (q, *J* = 7.4 Hz), 115.1 (q, *J* = 7.3 Hz), 110.0 (s), 109.9 (s), 41.7 (s), 36.9 (s), 34.9 (s), 34.3 (s), 32.6 (s), 26.2 (s), 26.0 (s), 24.0 (s). IR (ATR) **3d** + **3d′**: ν 2969, 2924, 1744, 1689, 1552, 1474, 1401, 1316, 1154, 1074, 1039 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{12}H_{12}F_3O_3$ $[M+H]^+$: 261.0733; found **3d** + **3d′**: 261.0728, 261.0729.



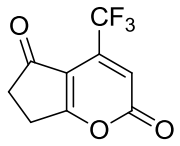
7-Phenyl-4-(trifluoromethyl)-7,8-dihydro-2*H*-chromene-2,5(6*H*)-dione (3e)

Obtained as a light yellow solid in 99% yield (92 mg). Mp: 138.2-140.1 °C. R_f (*n*-pentane:dichloromethane 1:2) = 0.44. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 (t, *J* = 7.1 Hz, 2H), 7.35 (d, *J* = 7.0 Hz, 1H), 7.29 (d, *J* = 7.1 Hz, 2H), 6.71 (s, 1H), 3.65 – 3.45 (m, 1H), 3.17 (d, *J* = 7.8 Hz, 2H), 3.02 – 2.60 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$): δ -63.5 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$): δ 190.0 (s), 175.2 (s), 157.9 (s), 141.5 (q, *J* = 35.3 Hz), 140.7 (s), 129.2 (s), 127.8 (s), 126.5 (s), 120.9 (q, *J* = 275.2 Hz), 115.3 (q, *J* = 7.4 Hz), 111.1 (s), 45.1 (s), 37.4 (s), 36.7 (s). IR (ATR): ν 3111, 3037, 2919, 1755, 1683, 1547, 1499, 1398, 1267, 1134, 1045 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{16}H_{12}F_3O_3$ $[M+H]^+$: 309.0739; found: 309.0749.



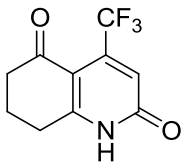
4-(Trifluoromethyl)pyrano[3,4-*b*]pyran-2,5(6*H*,8*H*)-dione (3f)

Obtained as a brown solid in 43% yield (30 mg). Mp: 119.0-120.5 °C. R_f (*n*-pentane:dichloromethane 1:2) = 0.36. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.75 (s, 1H), 4.73 (s, 2H), 4.32 (s, 2H). ^{19}F NMR (376 MHz, $CDCl_3$): δ -64.5 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$): δ 186.2 (s), 173.1 (s), 156.5 (s), 140.7 (q, *J* = 36.4 Hz), 120.4 (q, *J* = 275.3 Hz), 115.6 (q, *J* = 7.1 Hz), 108.9 (s), 72.3 (s), 65.2 (s). IR (ATR): ν 3107, 2992, 2921, 1770, 1699, 1559, 1412, 1271, 1138, 1055 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_9H_6F_3O_4$ $[M+H]^+$: 235.0218; found: 235.0223.



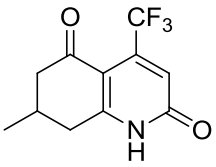
4-(Trifluoromethyl)-6,7-dihydrocyclopenta[*b*]pyran-2,5-dione (3g)

Obtained as a light yellow solid powder in 84% yield (55 mg). Mp: 98.5-100.2 °C. R_f (*n*-pentane:dichloromethane 1:2) = 0.28. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.60 (s, 1H), 3.17 – 3.01 (m, 2H), 2.85 – 2.72 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$): δ -66.3 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$): δ 194.2 (s), 187.4 (s), 158.9 (s), 139.5 (q, J = 37.2 Hz), 120.1 (q, J = 275.1 Hz), 112.7 (s), 112.6 (q, J = 6.1 Hz), 34.4 (s), 26.3 (s). IR (ATR): ν 3095, 2923, 1757, 1714, 1575, 1482, 1278, 1140, 1030 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_9H_6F_3O_3$ $[M+H]^+$: 219.0264; found: 219.0259.



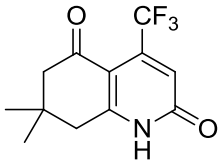
4-(Trifluoromethyl)-7,8-dihydroquinoline-2,5(1*H*,6*H*)-dione (4a)

Obtained as a white solid in 78% yield (54 mg). Mp: 209.5-211.2 °C. R_f (*n*-pentane:ethyl acetate 1:4) = 0.30. ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.63 (br, 1H), 6.67 (s, 1H), 2.87 (t, *J* = 5.5 Hz, 2H), 2.48 (t, *J* = 6.1 Hz, 2H), 2.12 – 1.82 (m, 2H). ^{19}F NMR (376 MHz, DMSO-d_6): δ -61.2 (s, 3F). ^{13}C NMR (101 MHz, DMSO-d_6): δ 191.6 (s), 161.5 (s), 161.0 (s), 138.6 (q, *J* = 33.0 Hz), 122.6 (q, *J* = 274.6 Hz), 119.2 (q, *J* = 7.0 Hz), 109.3 (s), 38.6 (s), 28.2 (s), 20.5 (s). IR (ATR): ν 3447, 2987, 1749, 1698, 1557, 1477, 1407, 1279, 1165, 1025, 1007, 821 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{10}H_9F_3NO_2$ $[M+H]^+$: 232.0580; found: 232.0574.



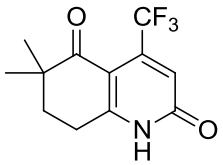
7-Methyl-4-(trifluoromethyl)-7,8-dihydroquinoline-2,5(1*H*,6*H*)-dione (4b)

Obtained as a white solid powder in 91% yield (67 mg). Mp: 214.2-215.7 °C. R_f (*n*-pentane:ethyl acetate 1:2) = 0.40. ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.65 (br, 1H), 6.67 (s, 1H), 2.88 (d, *J* = 17.9 Hz, 1H), 2.71 – 2.39 (m, 2H), 2.36 – 2.19 (m, 2H), 1.04 (d, *J* = 4.5 Hz, 3H). ^{19}F NMR (376 MHz, DMSO-d_6): δ -61.2 (s, 3F). ^{13}C NMR (101 MHz, DMSO-d_6): δ 191.6 (s), 161.6 (s), 160.3 (s), 138.4 (q, *J* = 33.0 Hz), 122.6 (q, *J* = 274.5 Hz), 119.1 (q, *J* = 7.5 Hz), 109.0 (s), 46.6 (s), 35.8 (s), 27.9 (s), 20.8 (s). IR (ATR): ν 3072, 2924, 1693, 1648, 1558, 1475, 1283, 1140, 1046, 888 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{11}H_{11}F_3NO_2$ $[M+H]^+$: 246.0736; found: 246.0731.



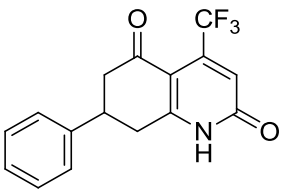
7,7-Dimethyl-4-(trifluoromethyl)-7,8-dihydroquinoline-2,5(1*H*,6*H*)-dione (4c)

Obtained as a light yellow solid powder in 82% yield (64 mg). Mp: 195.0-196.2 °C. R_f (*n*-pentane:ethyl acetate 1:2) = 0.43. ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.65 (br, 1H), 6.67 (s, 1H), 2.79 (s, 2H), 2.40 (s, 2H), 1.02 (s, 6H). ^{19}F NMR (376 MHz, DMSO-d_6): δ -61.3 (s, 3F). ^{13}C NMR (101 MHz, DMSO-d_6): δ 191.5 (s), 161.8 (s), 159.1 (s), 138.2 (q, J = 32.7 Hz), 122.6 (q, J = 274.2 Hz), 119.0 (q, J = 6.8 Hz), 108.5 (s), 52.1 (s), 41.3 (s), 32.2 (s), 27.8 (s). IR (ATR): ν 3079, 2945, 1689, 1655, 1605, 1477, 1284, 1124, 1041, 880 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{12}H_{13}F_3NO_2$ $[M+H]^+$: 260.0893; found: 260.0887.



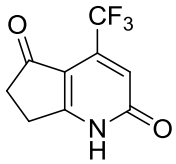
8,8-Dimethyl-4-(trifluoromethyl)-7,8-dihydroquinoline-2,5(1*H*,6*H*)-dione (4d)

Obtained as a yellow solid powder in 47% yield (37 mg). Mp: 196.5-198.0 °C. R_f (*n*-pentane:ethyl acetate 1:2) = 0.40. ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.57 (br, 1H), 6.66 (s, 1H), 2.88 (t, J = 6.0 Hz, 2H), 1.87 (t, J = 6.0 Hz, 2H), 1.08 (s, 6H). ^{19}F NMR (376 MHz, DMSO-d_6): δ -61.1 (s, 3F). ^{13}C NMR (101 MHz, DMSO-d_6): δ 196.8 (s), 161.6 (s), 159.2 (s), 139.1 (q, J = 33.0 Hz), 122.7 (q, J = 274.6 Hz), 119.5 (q, J = 6.9 Hz), 108.1 (s), 41.6 (s), 33.5 (s), 24.7 (s). IR (ATR): ν 2976, 2920, 2850, 1672, 1614, 1558, 1475, 1236, 1156, 1051, 880, 842 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{12}H_{13}F_3NO_2$ $[M+H]^+$: 260.0893; found: 260.0887.



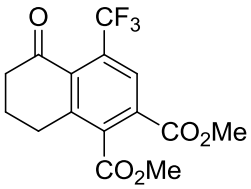
7-Phenyl-4-(trifluoromethyl)-7,8-dihydroquinoline-2,5(1*H*,6*H*)-dione (4e)

Obtained as a white solid in 50% yield (46 mg). Mp: 230.6-232.4 °C. R_f (*n*-pentane:ethyl acetate 1:2) = 0.59. ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.73 (br, 1H), 7.43 – 7.33 (m, 4H), 7.32 – 7.24 (m, 1H), 6.73 (s, 1H), 3.51 (t, *J* = 12.6 Hz, 1H), 3.27 – 3.15 (m, 1H), 3.03 (d, *J* = 17.1 Hz, 1H), 2.90 (t, *J* = 16.0 Hz, 1H), 2.64 (d, *J* = 15.1 Hz, 1H). ^{19}F NMR (376 MHz, DMSO-d_6): δ -61.2 (s, 3F). ^{13}C NMR (101 MHz, DMSO-d_6): δ 190.5 (s), 161.2 (s), 159.7 (s), 142.5 (s), 138.0 (q, *J* = 33.3 Hz), 128.7 (s), 127.0 (s), 126.8 (s), 122.2 (q, *J* = 275.0 Hz), 118.9 (q, *J* = 6.8 Hz), 108.5 (s), 45.1 (s), 37.5 (s), 34.9 (s). IR (ATR): ν 2921, 2850, 1659, 1604, 1560, 1478, 1269, 1148, 1123, 1016, 888 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{16}H_{13}F_3NO_2$ $[M+H]^+$: 308.0893; found: 308.0887.



4-(Trifluoromethyl)-6,7-dihydro-1*H*-cyclopenta[*b*]pyridine-2,5-dione (4g)

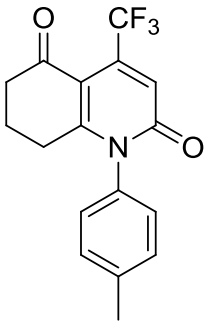
Obtained as a brown solid in 50% yield (33 mg). Mp: 191.9-193.3 °C. R_f (*n*-pentane:ethyl acetate 1:4) = 0.30. ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.07 (br, 1H), 6.64 (s, 1H), 2.96 (t, *J* = 4.0 Hz, 2H), 2.58 (t, *J* = 4.0 Hz, 2H). ^{19}F NMR (376 MHz, DMSO-d_6): δ -63.9 (s, 3F). ^{13}C NMR (101 MHz, DMSO-d_6): δ 196.5 (s), 172.3 (s), 163.0 (s), 135.5 (q, *J* = 34.9 Hz), 123.2 (q, *J* = 275.7 Hz), 117.8 (q, *J* = 5.6 Hz), 111.1 (s), 35.2 (s), 24.9 (s). IR (ATR): ν 3217, 3068, 2921, 1668, 1571, 1505, 1490, 1256, 1120, 1038, 888, 840 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_9H_6F_3NO_2$ $[M]^+$: 217.0345; found: 217.0303.



Dimethyl

5-oxo-4-(trifluoromethyl)-5,6,7,8-tetrahydronaphthalene-1,2-dicarboxylate (6)

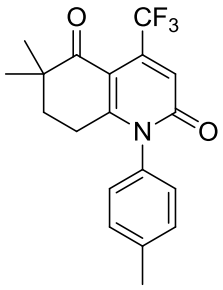
Obtained as a yellow solid in 72% yield (48 mg). Mp: 110.0-111.5 °C. R_f (dichloromethane) = 0.67. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.34 (s, 1H), 4.01 (d, *J* = 1.0 Hz, 3H), 3.98 (d, *J* = 1.0 Hz, 3H), 2.96 (t, *J* = 5.7 Hz, 2H), 2.80 (t, *J* = 6.3 Hz, 2H), 2.19 (dt, *J* = 12.0 5.6 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$): δ -59.2 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$): δ 195.9 (s), 167.8 (s), 164.2 (s), 143.4 (s), 138.8 (d, *J* = 0.9 Hz), 135.9 (d, *J* = 0.7 Hz), 130.4 (q, *J* = 33.3 Hz), 130.1 (s), 127.4 (q, *J* = 6.9 Hz), 122.7 (q, *J* = 274.2 Hz), 53.2 (s), 53.1 (s), 39.4 (s), 27.1 (s), 22.0 (s). IR (ATR): ν 3079, 2978, 2948, 2920, 2870, 1735, 1689, 1597, 1561, 1440, 1425, 1234, 1158, 1005, 904, 807, 751, 716, 690 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{15}H_{14}F_3O_5$ $[M+H]^+$: 331.0793; found: 331.0774.



1-(*p*-Tolyl)-4-(trifluoromethyl)-7,8-dihydroquinoline-2,5(1*H*,6*H*)-dione (7)

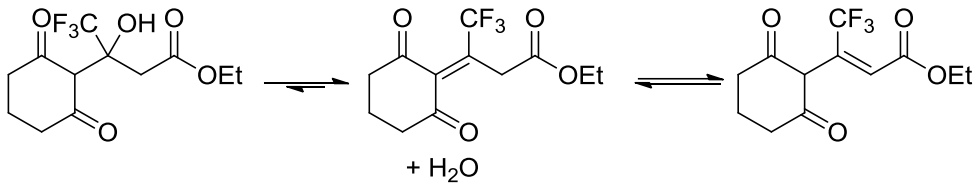
Obtained as a white solid in 80% yield (51 mg). Mp: 175.0-176.2 °C. R_f (dichloromethane) = 0.58. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, *J* = 7.2 Hz, 2H), 7.09 (d, *J* = 7.2 Hz, 2H), 7.04 (s, 1H), 2.63 – 2.49 (m, 4H), 2.47 (s, 3H), 2.02 (dt, *J* = 11.2, 5.5 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$): δ -62.1 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$): δ 191.7 (s), 161.7 (s), 159.4 (s), 140.1 (s), 139.1 (q, *J* = 33.8 Hz), 134.2 (s),

131.0 (s), 127.1 (s), 122.0 (q, J = 275.2 Hz), 120.3 (q, J = 7.1 Hz), 111.8 (s), 37.9 (s), 30.3 (s), 21.3 (s), 20.7 (s). IR (ATR): ν 3005, 2957, 2920, 2849, 1727, 1705, 1549, 1458, 1360, 1265, 1129, 1085, 786 cm^{-1}. HRMS (ESI) m/z: calcd. for $C_{17}H_{15}F_3NO_2$ $[M+H]^+$: 322.1055; found: 322.1039.



6,6-Dimethyl-1-(*p*-tolyl)-4-(trifluoromethyl)-7,8-dihydroquinoline-2,5(1*H*,6*H*)-dione (8)

Obtained as a white solid in 30% yield (21 mg). Mp: 205.1-205.9 °C. R_f (dichloromethane) = 0.35. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, J = 7.3 Hz, 2H), 7.10 (s, 1H), 7.07 (d, J = 7.3 Hz, 2H), 2.51 (t, J = 5.8 Hz, 2H), 2.47 (s, 3H), 1.85 (t, J = 5.6 Hz, 2H), 1.21 (s, 6H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.0 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.3 (s), 161.8 (s), 157.5 (s), 140.1 (s), 139.7 (q, J = 33.8 Hz), 134.1 (s), 131.0 (s), 127.1 (s), 122.1 (q, J = 274.9 Hz), 120.5 (q, J = 7.2 Hz), 110.6 (s), 41.0 (s), 34.0 (s), 26.8 (s), 24.2 (s), 21.3 (s). IR (ATR): ν 3046, 2982, 2926, 2869, 1665, 1520, 1429, 1413, 1279, 1258, 1138, 1106, 878, 815, 497 cm^{-1}. GC-MS (EI) for $C_{19}H_{18}F_3NO_2$ m/z: $[M]^+$: 349.50.



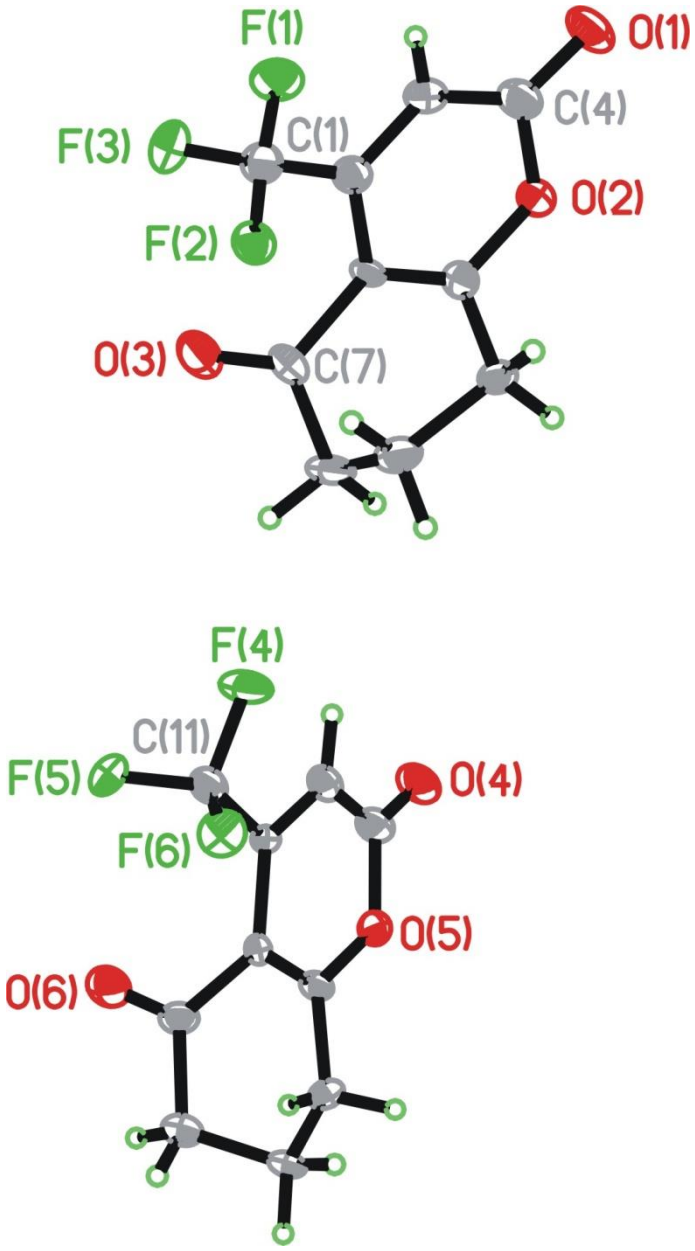
Intermediate (I)

Obtained as an oil liquid in 98% yield (20 mg). R_f (dichloromethane : ethyl acetate = 1:2) = 0.42. ^{1}H NMR (400 MHz, C_6D_6) δ 3.87 (d, *J* = 17.2 Hz, 1H), 3.75 (t, *J* = 6.7 Hz, 2H), 3.20 (d, *J* = 17.2 Hz, 1H), 1.97 (dt, *J* = 24.4, 4.2 Hz, 4H), 1.25 – 1.14 (m, 2H), 0.80 (t, *J* = 7.1 Hz, 3H). ^{19}F NMR (376 MHz, C_6D_6) δ -81.1 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.5 (s), 124.9 (q, *J* = 286.3 Hz), 107.7 (s), 77.9 (q, *J* = 31.2 Hz), 61.8 (s), 36.6 (s), 19.8 (s), 13.9 (s). HRMS (ESI) m/z: calcd. for $C_{12}H_{16}F_3O_5$ $[M+H]^+$: 297.0944; found: 297.0933.

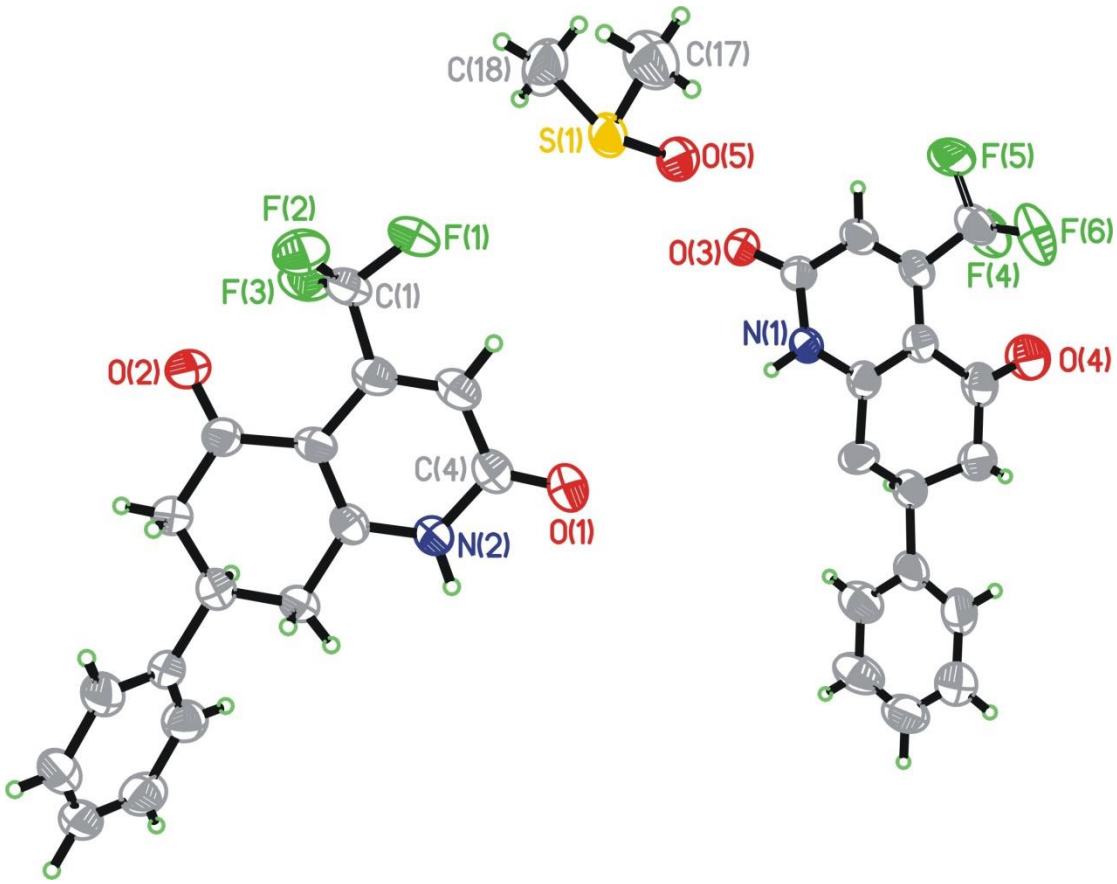
Crystal structure analyses

The suitable crystals of **3a** (CCDC 1872006), and **4e** (CCDC 1870545) were mounted on quartz fibers and X-ray data collected on a Bruker AXS APEX diffractometer, equipped with a CCD detector at -50 ºC, using MoKα radiation (λ 0.71073 Å). The data was corrected for Lorentz and polarisation effect with the **SMART** suite of programs and for absorption effects with SADABS.[1] Structure solution and refinement were carried out with the SHELXTL suite of programs.[1] The structure was solved by direct methods to locate the heavy atoms, followed by difference maps for the light non-hydrogen atoms.

ORTEP diagrams



ORTEP diagram of compound 3a. Thermal ellipsoids are drawn at 40% probability



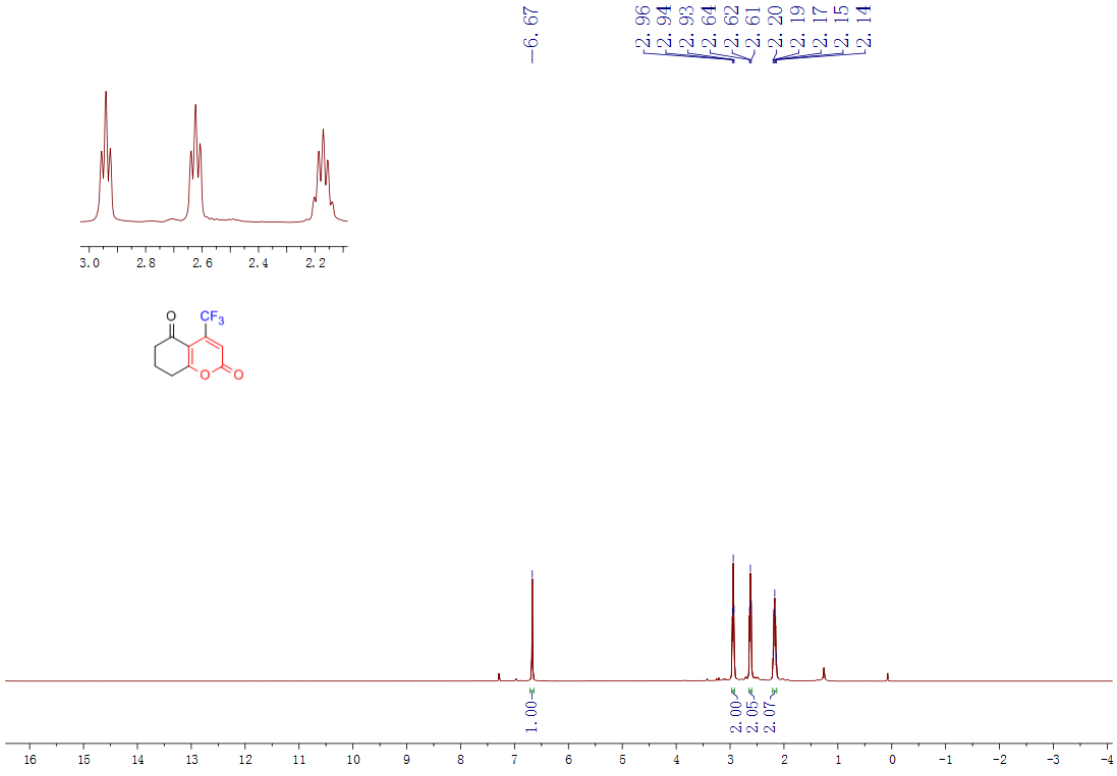
ORTEP diagram of compound 4e·DMSO. Thermal ellipsoids are drawn at 40% probability

References

1. SHELXTL version 5.03; Bruker Analytical X-ray Systems, Madison, WI, 1997.

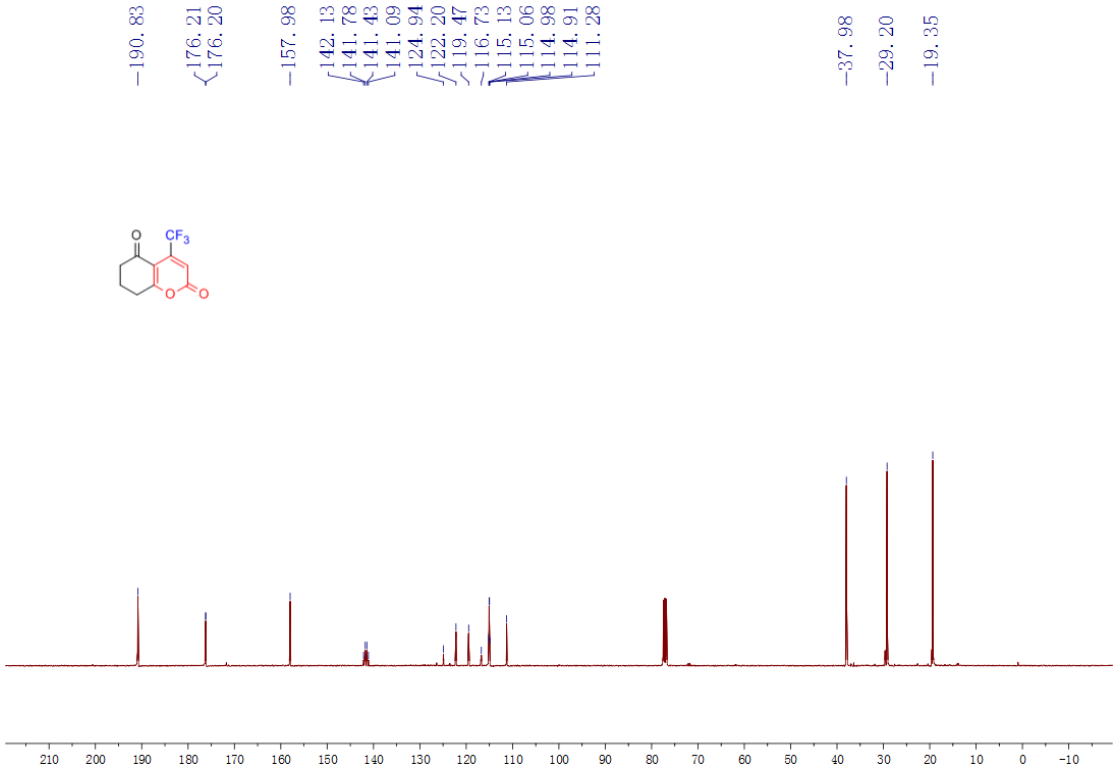
Copies of ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra

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

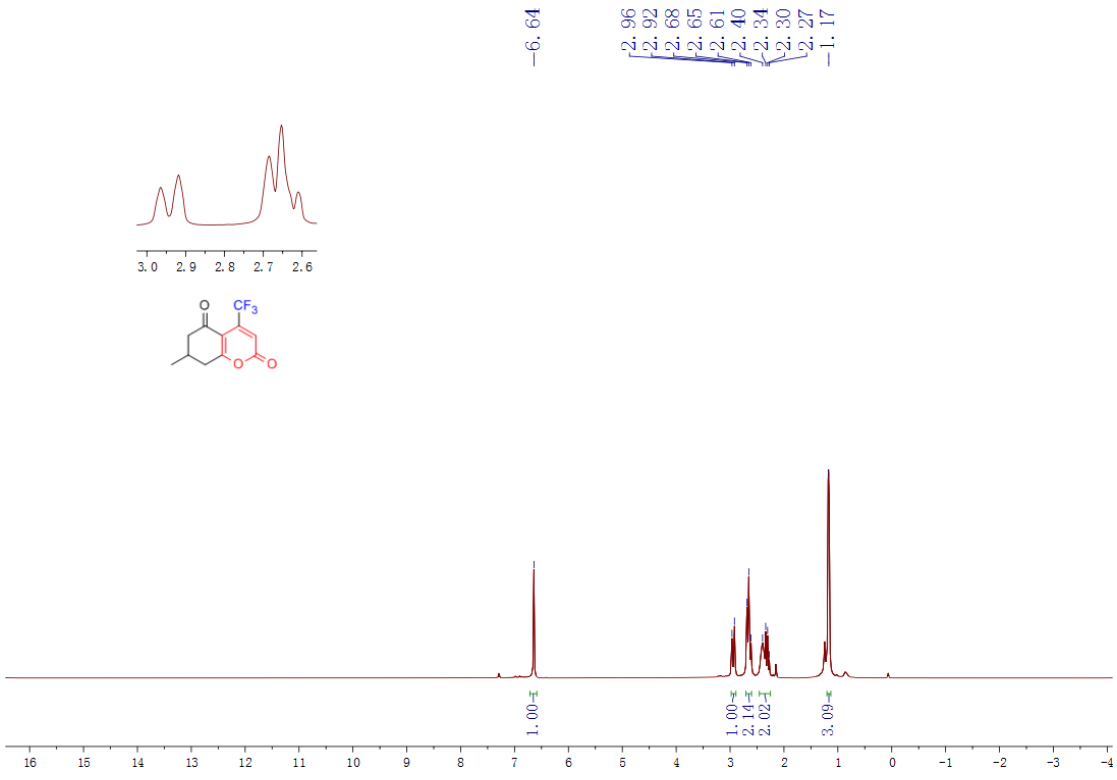


^{19}F NMR spectrum of **3a** in $CDCl_3$

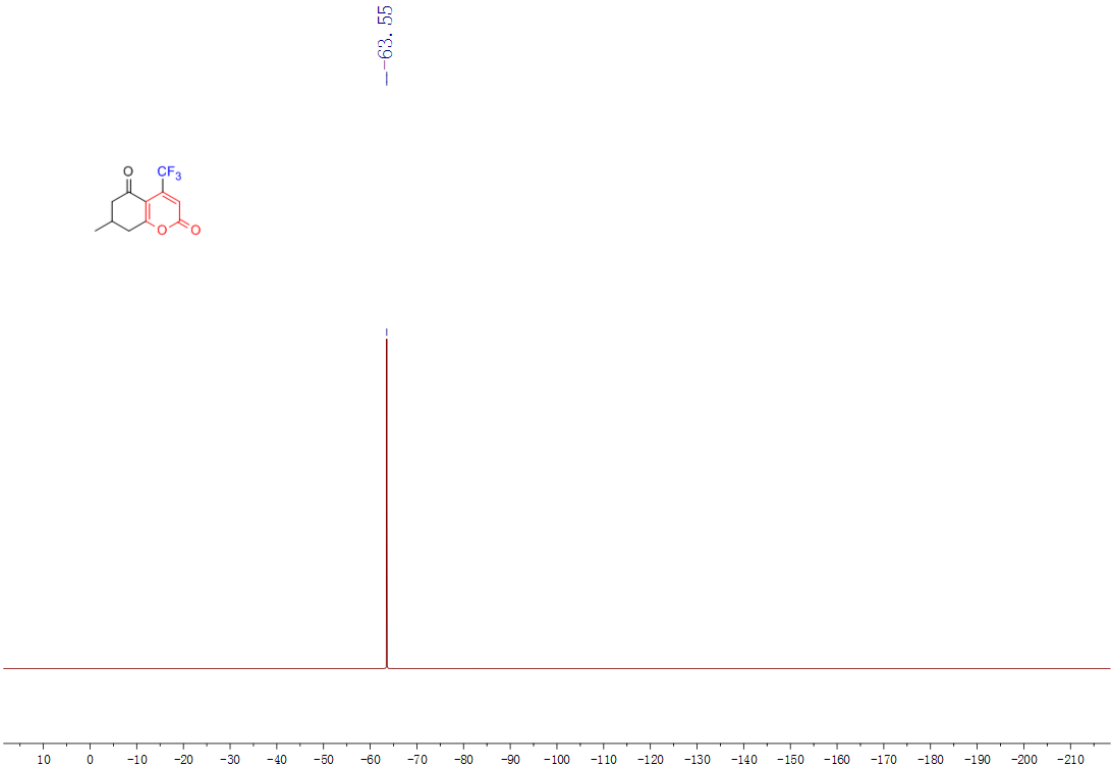
^{13}C NMR spectrum of **3a** in $CDCl_3$



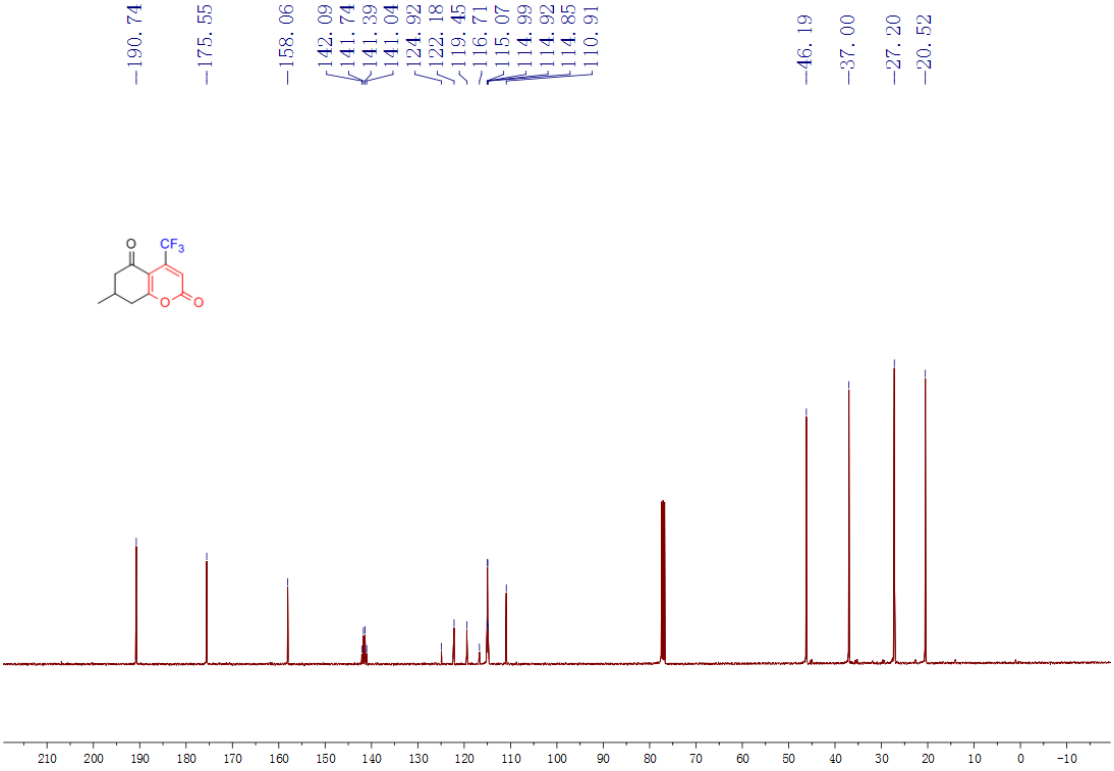
^{1}H NMR spectrum of **3b** in $CDCl_3$



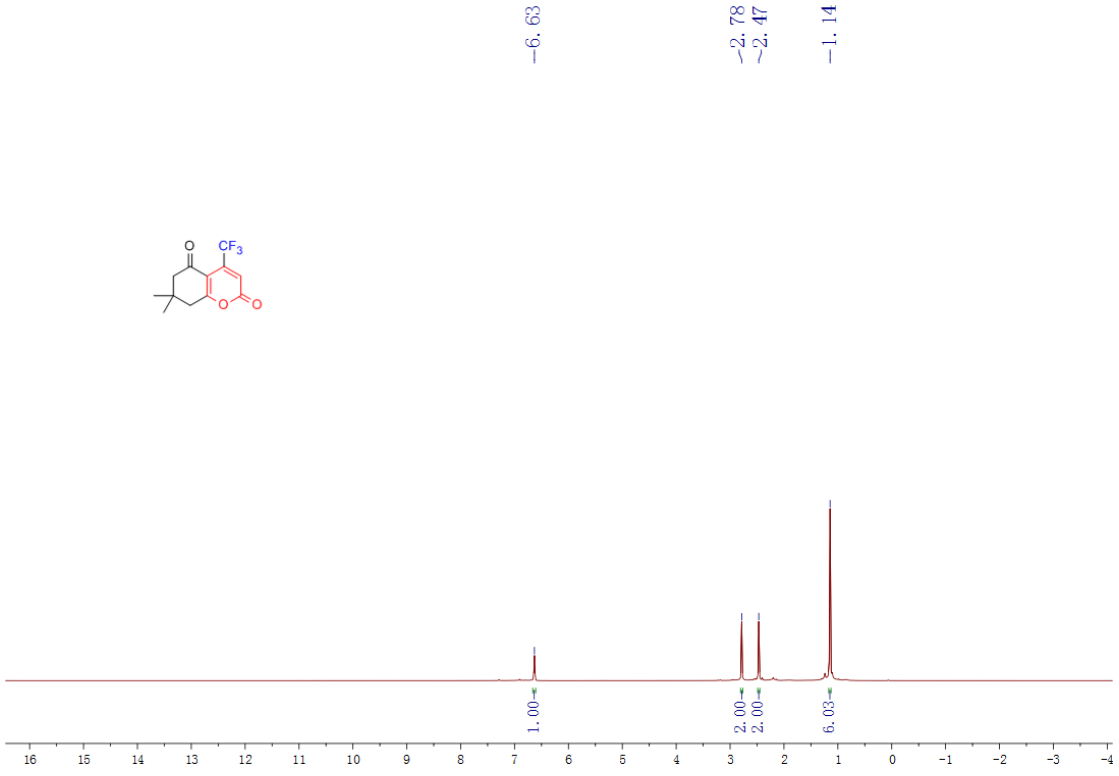
^{19}F NMR spectrum of **3b** in $CDCl_3$



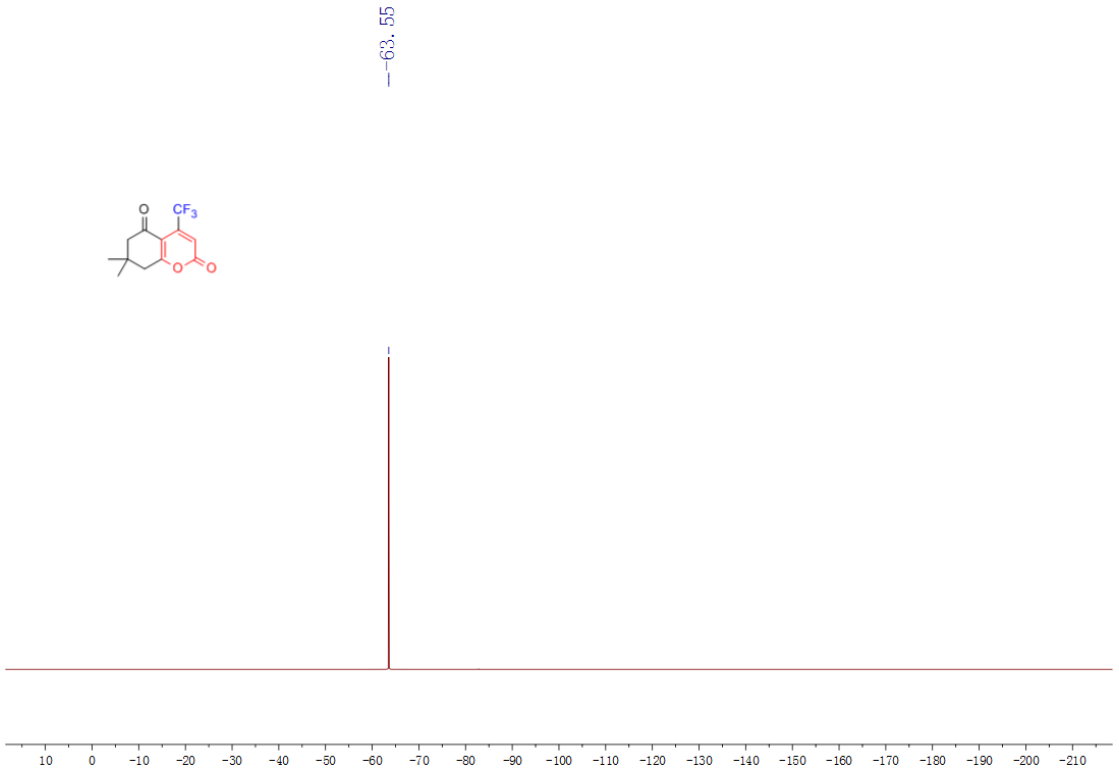
^{13}C NMR spectrum of **3b** in $CDCl_3$



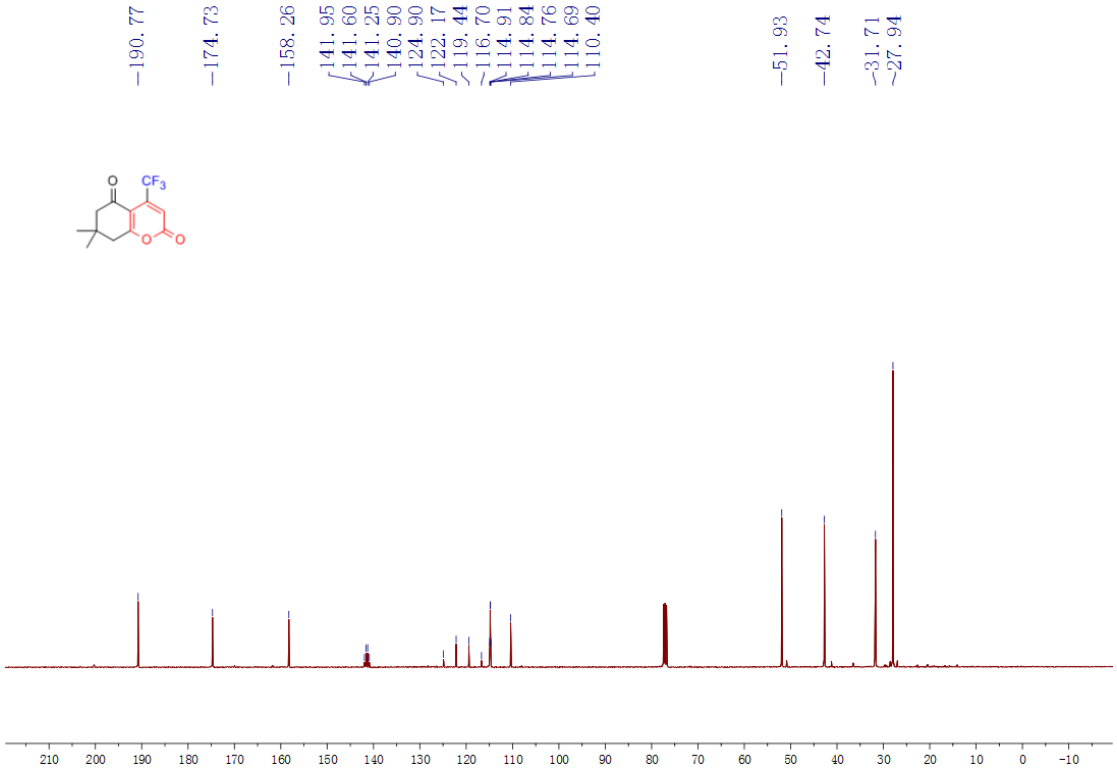
^{1}H NMR spectrum of **3c** in $CDCl_3$



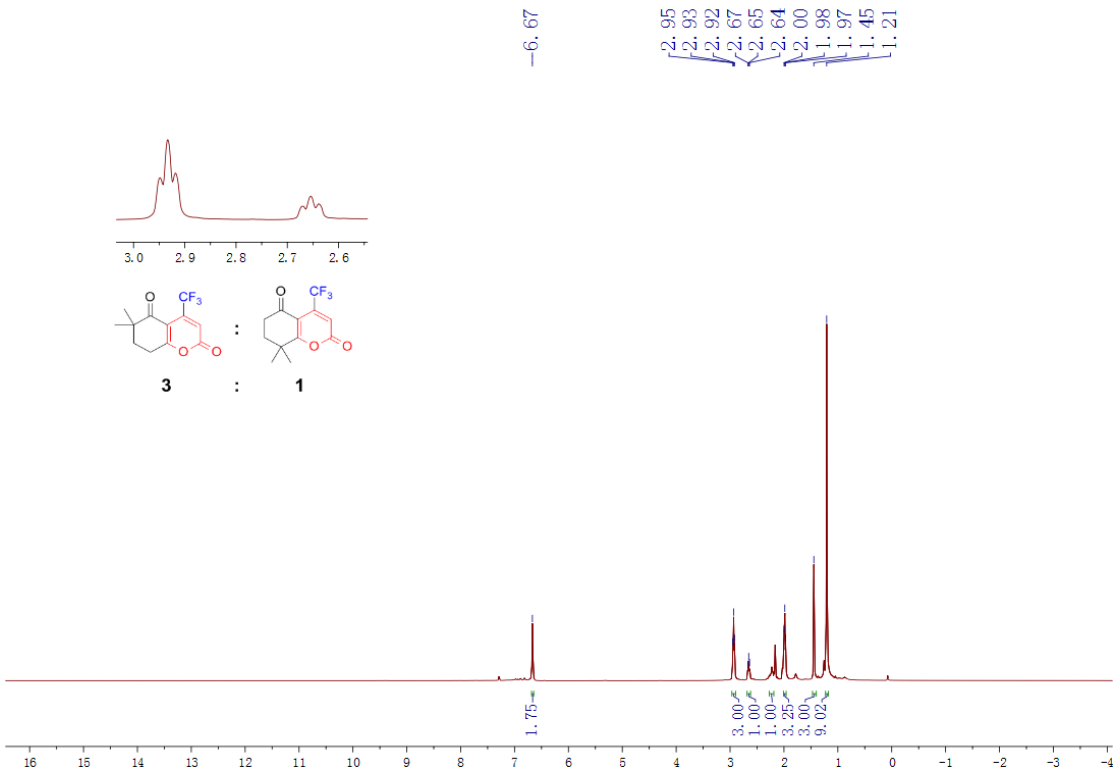
^{19}F NMR spectrum of **3c** in $CDCl_3$



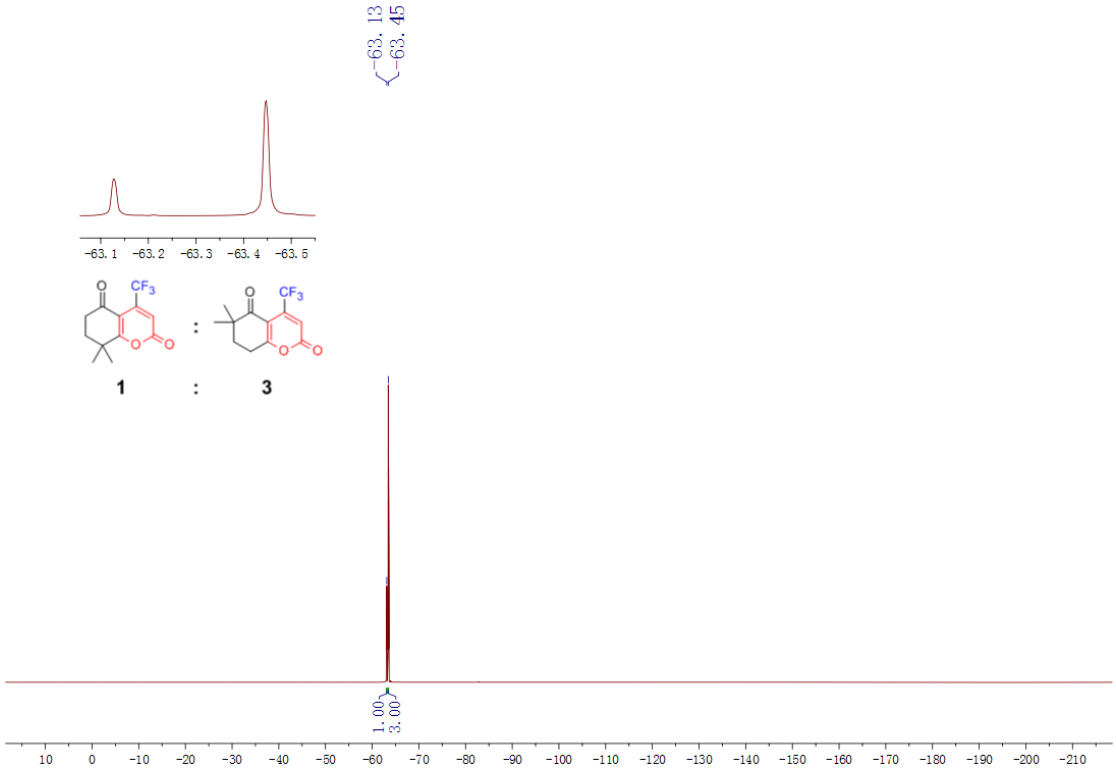
^{13}C NMR spectrum of **3c** in $CDCl_3$



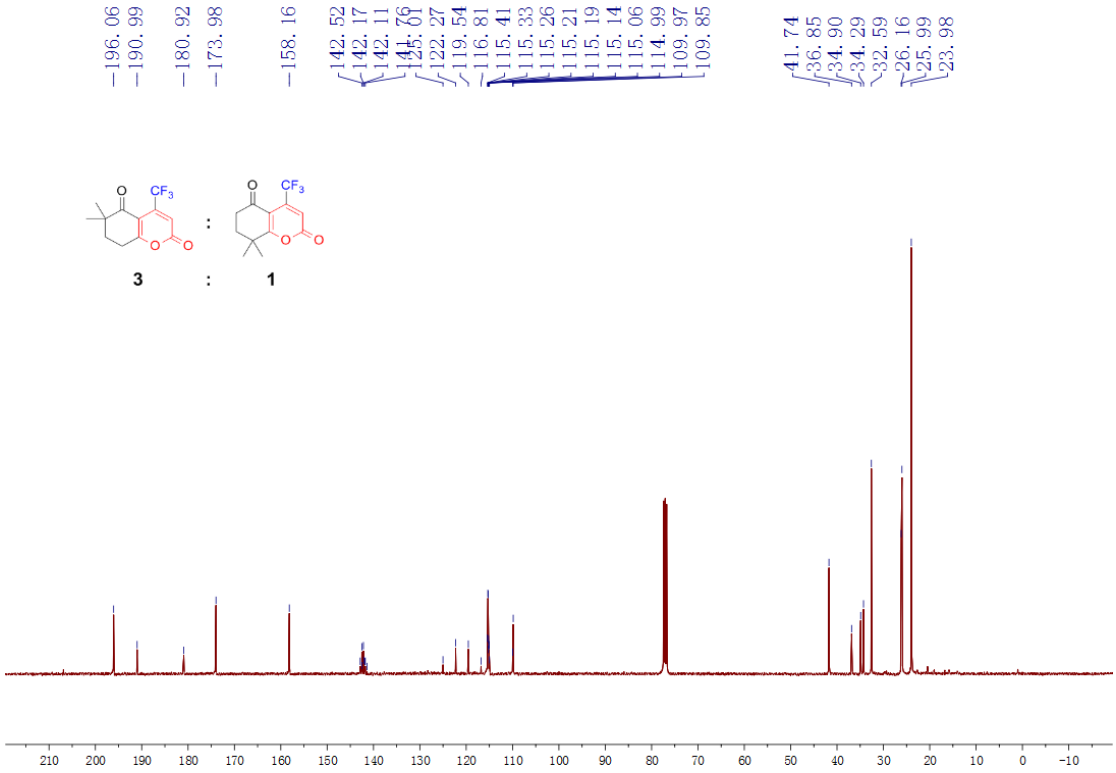
^{1}H NMR spectrum of **3d** in $CDCl_3$



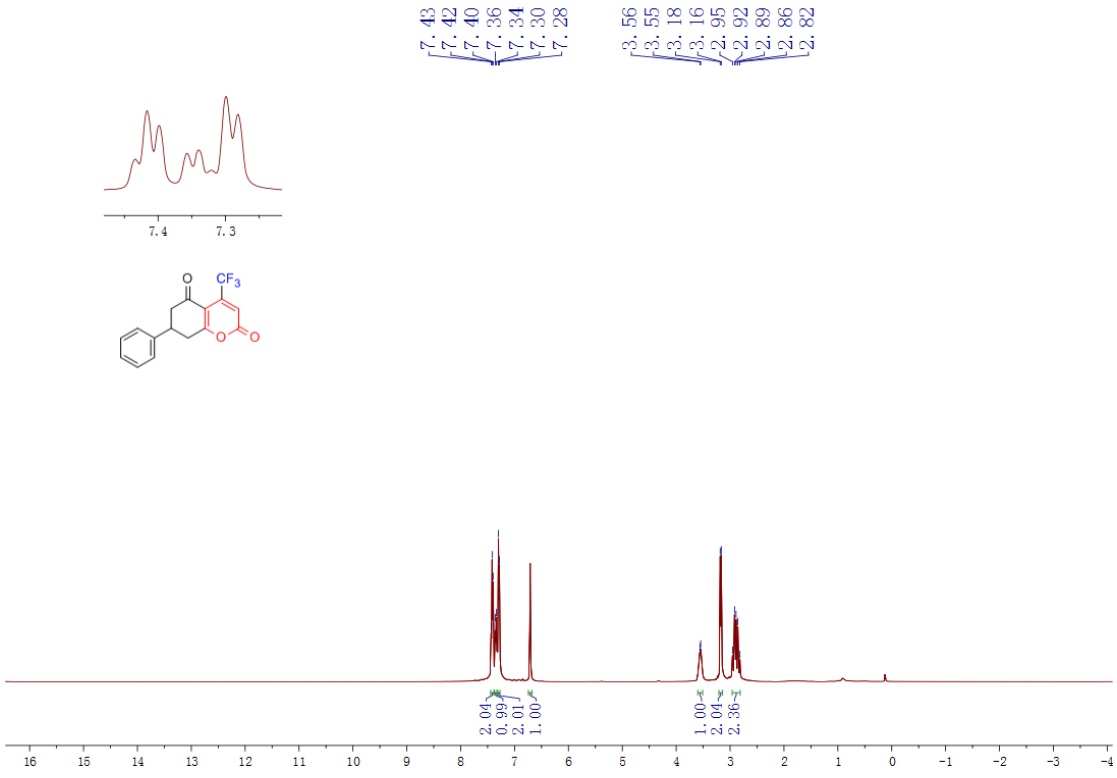
^{19}F NMR spectrum of **3d** in $CDCl_3$



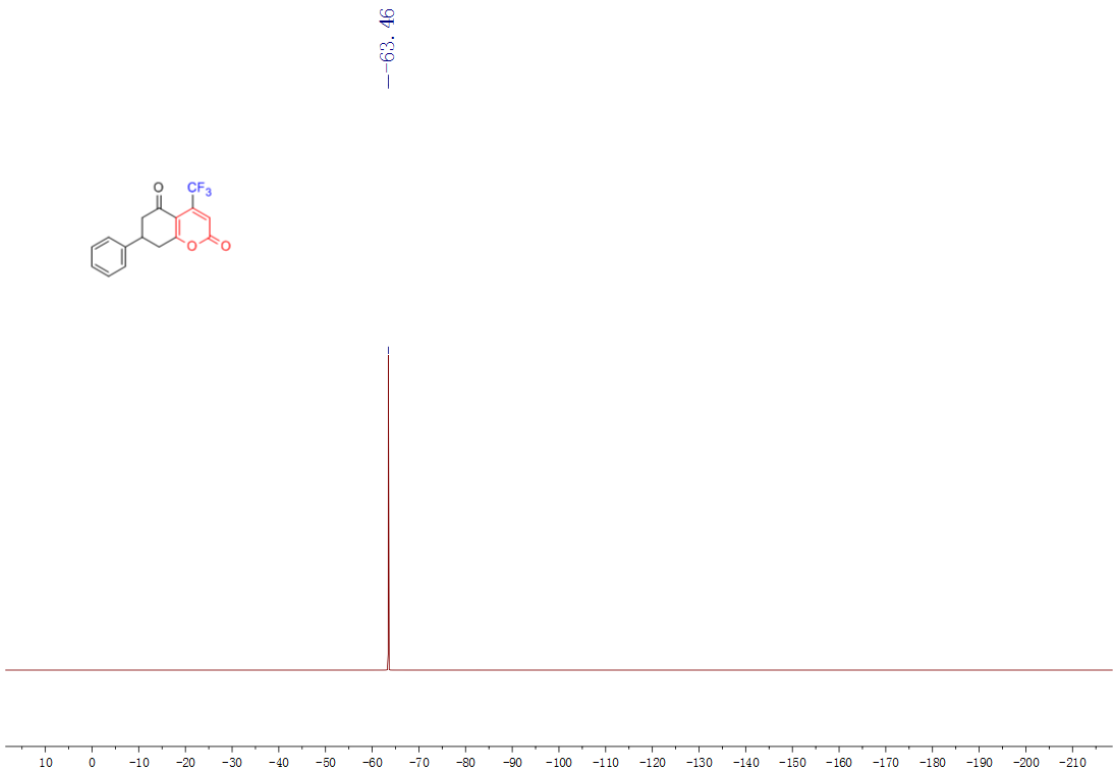
^{13}C NMR spectrum of **3d** in $CDCl_3$



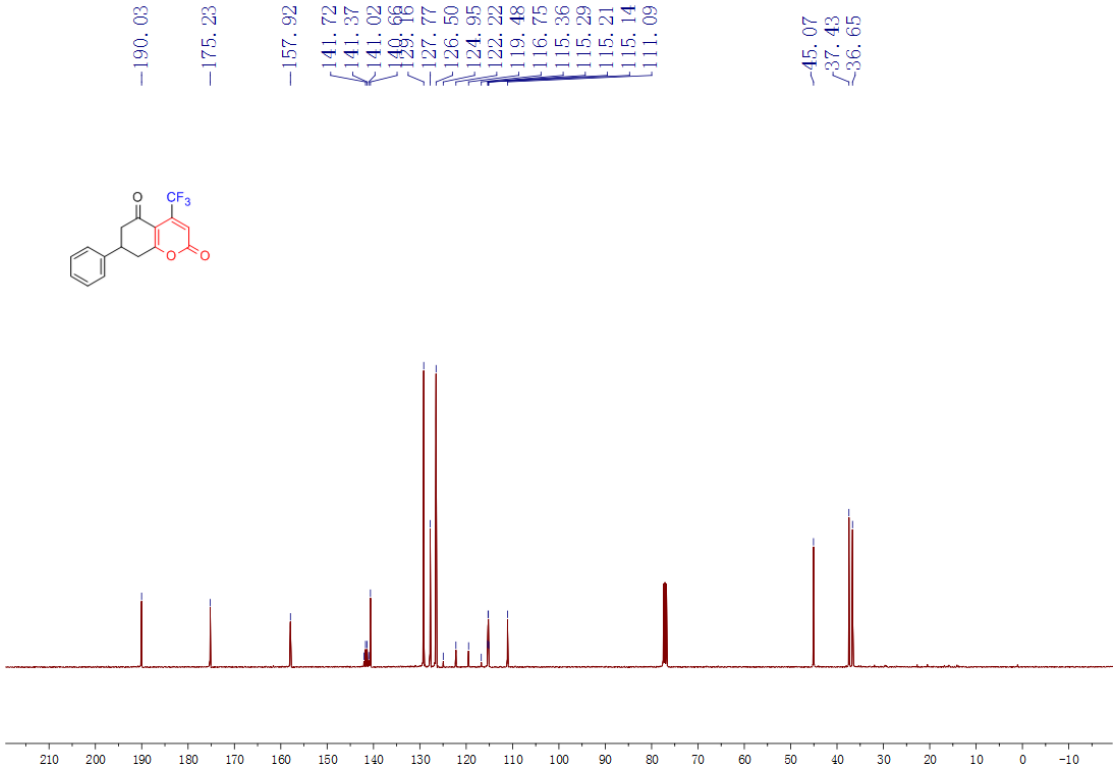
^{1}H NMR spectrum of **3e** in $CDCl_3$



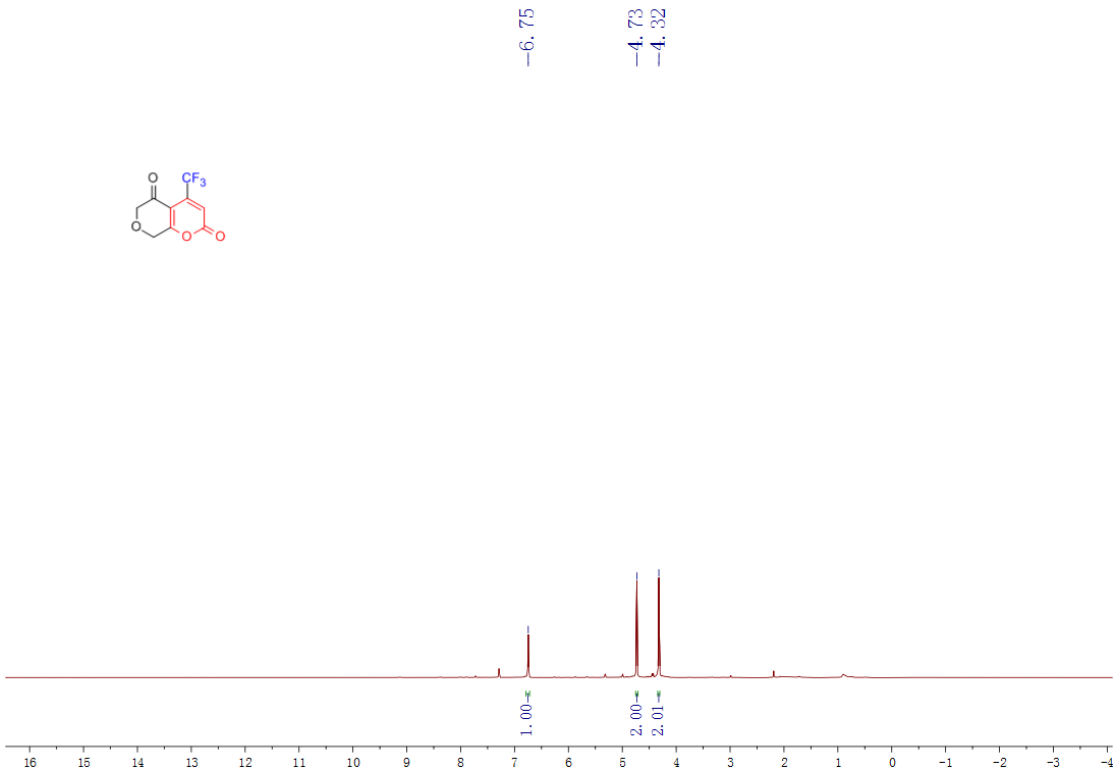
^{19}F NMR spectrum of **3e** in $CDCl_3$



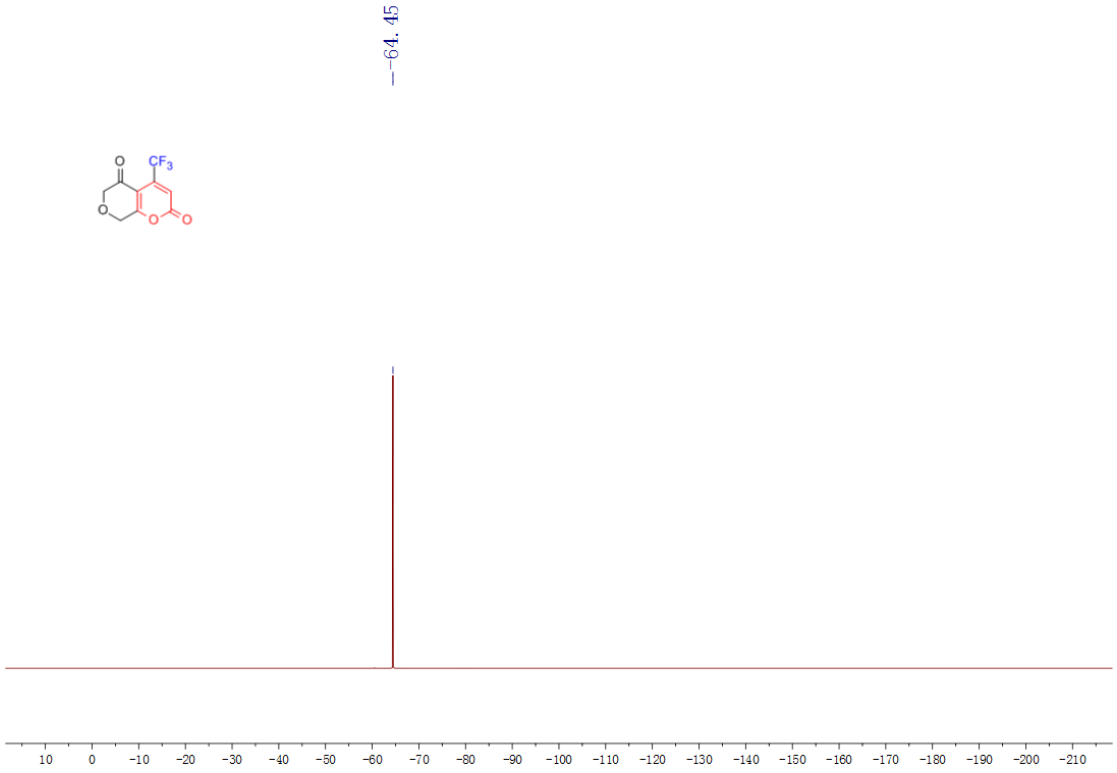
^{13}C NMR spectrum of **3e** in $CDCl_3$



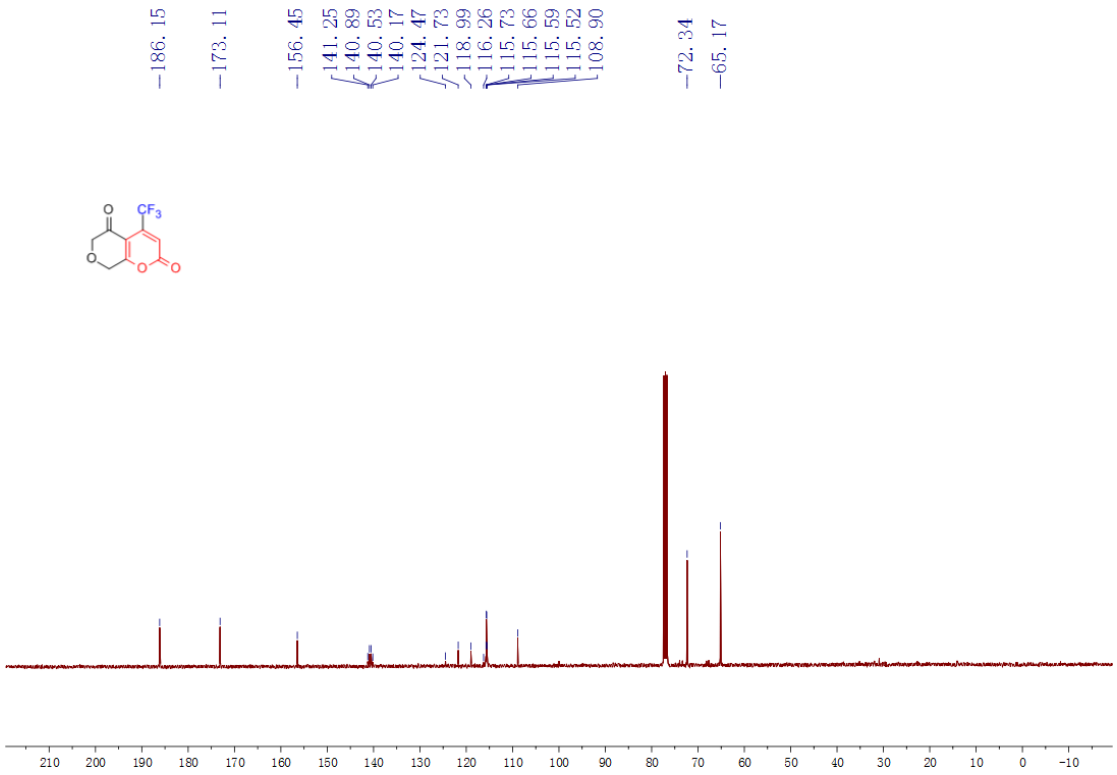
^{1}H NMR spectrum of **3f** in $CDCl_3$



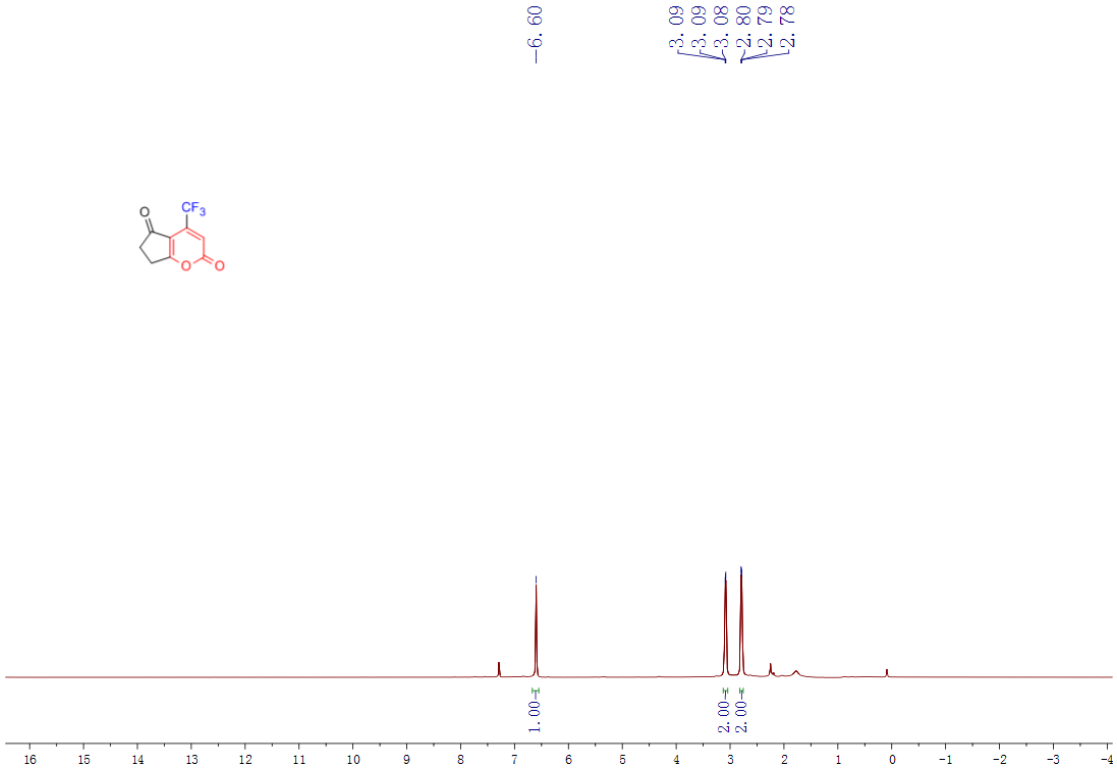
^{19}F NMR spectrum of **3f** in $CDCl_3$



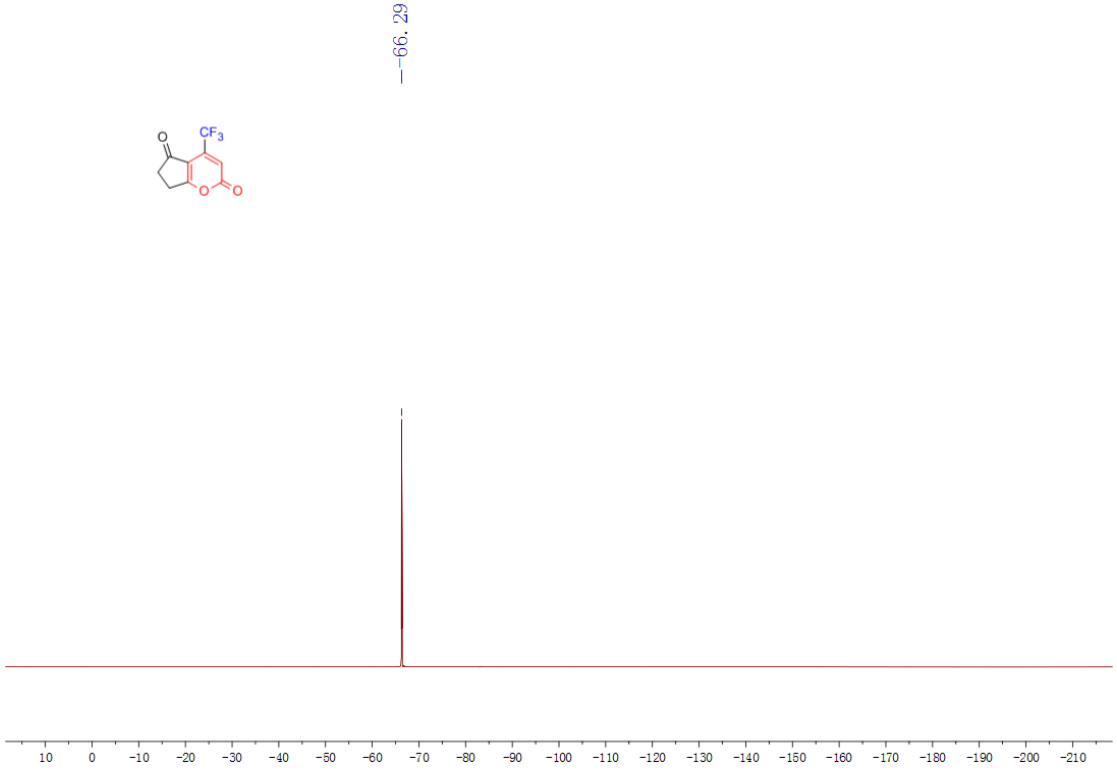
^{13}C NMR spectrum of **3f** in $CDCl_3$



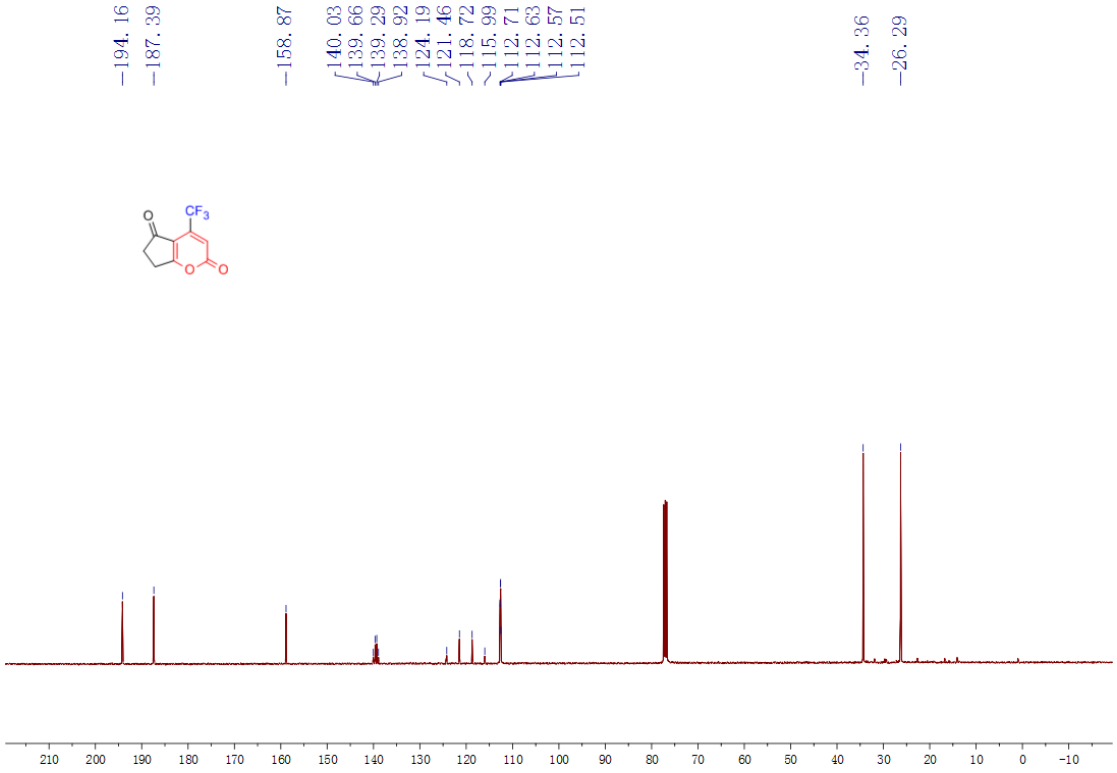
^{1}H NMR spectrum of **3g** in $CDCl_3$



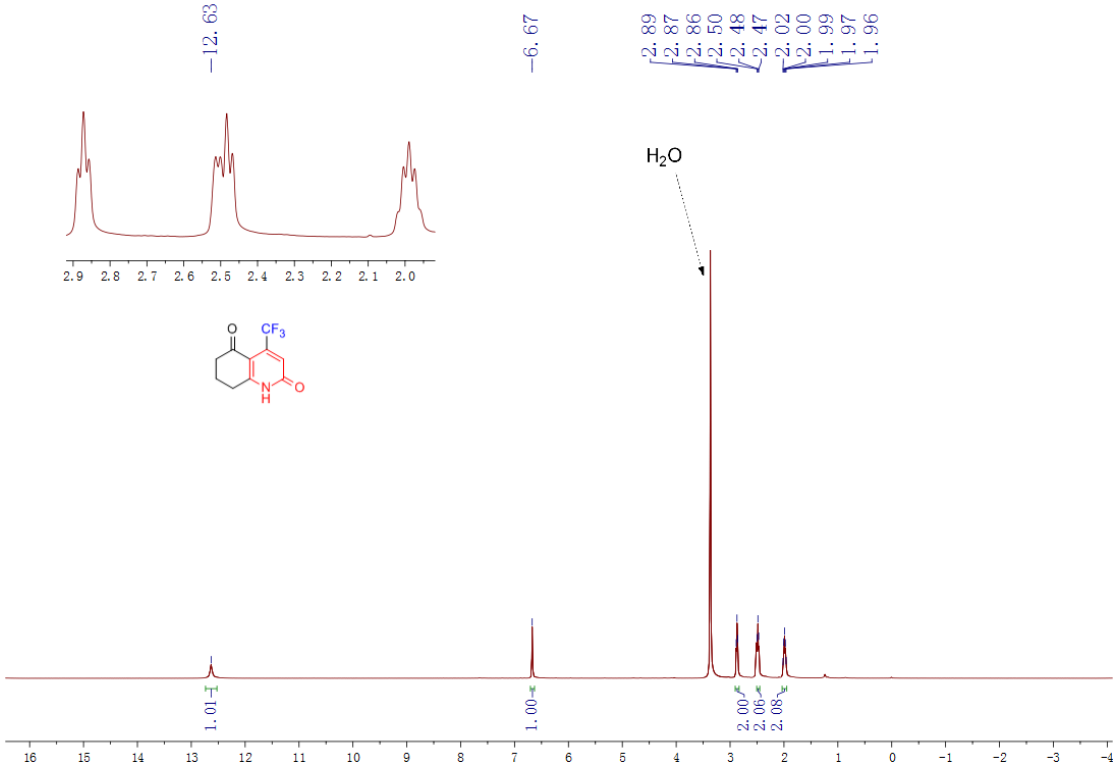
^{19}F NMR spectrum of **3g** in $CDCl_3$



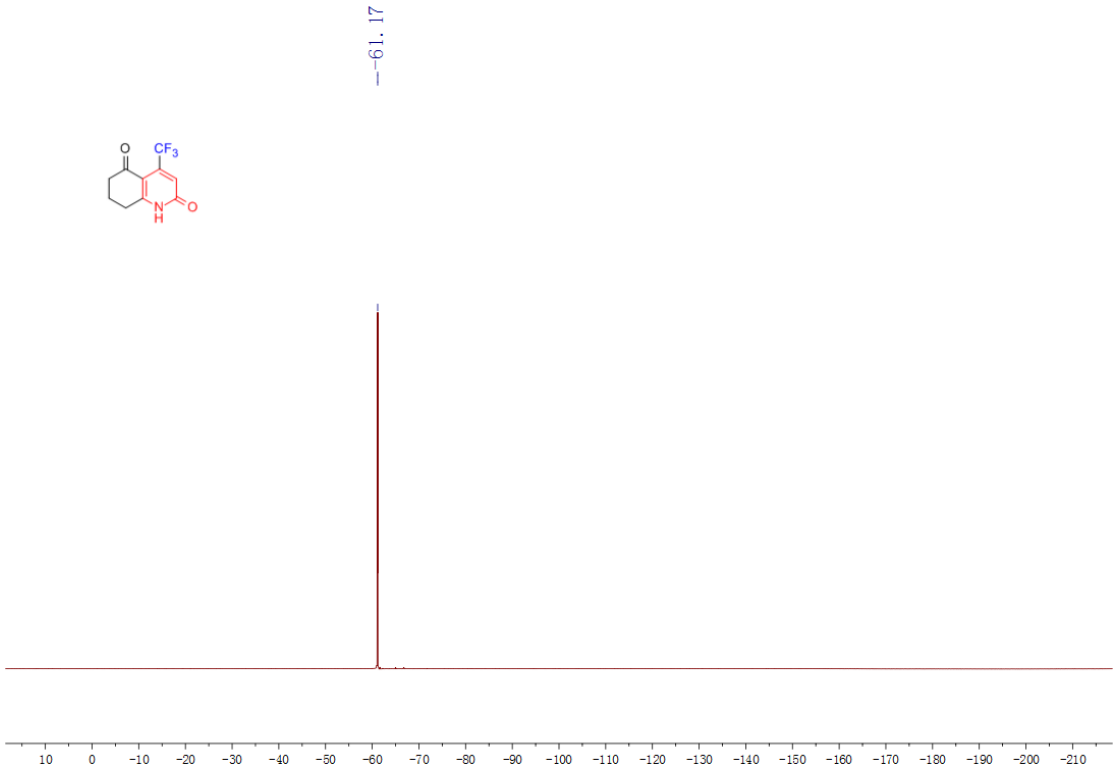
^{13}C NMR spectrum of **3g** in $CDCl_3$



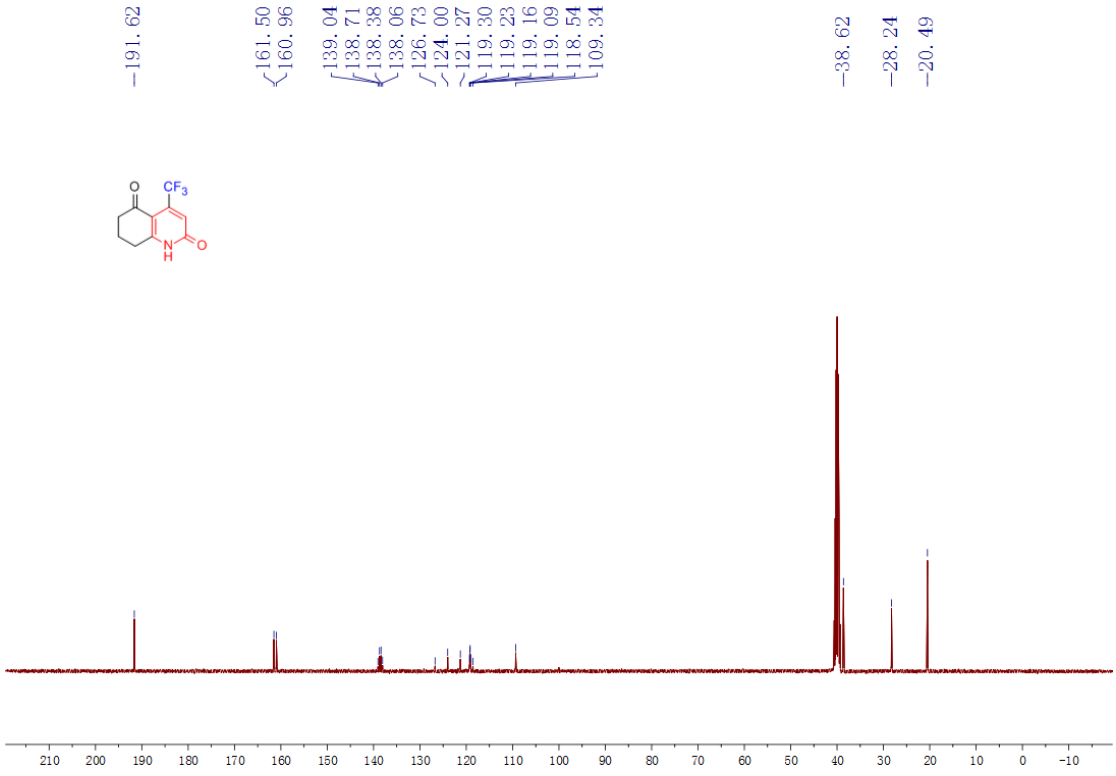
^{1}H NMR spectrum of **4a** in DMSO-d_6



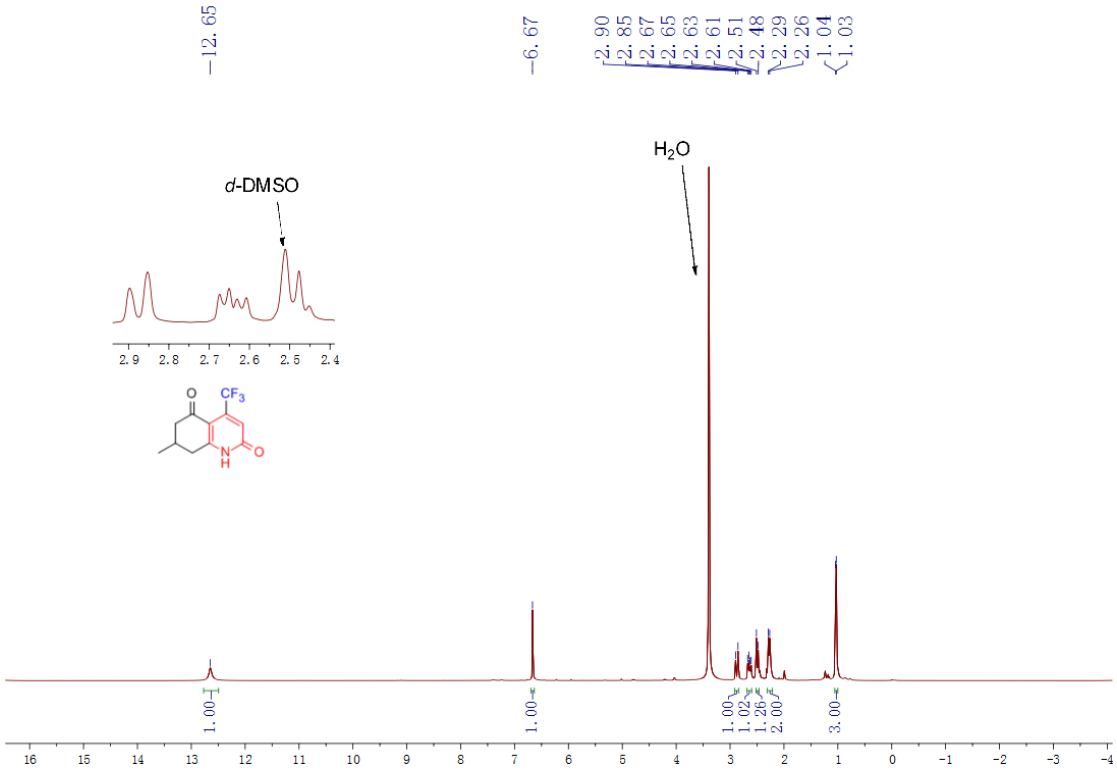
^{19}F NMR spectrum of **4a** in DMSO-d_6



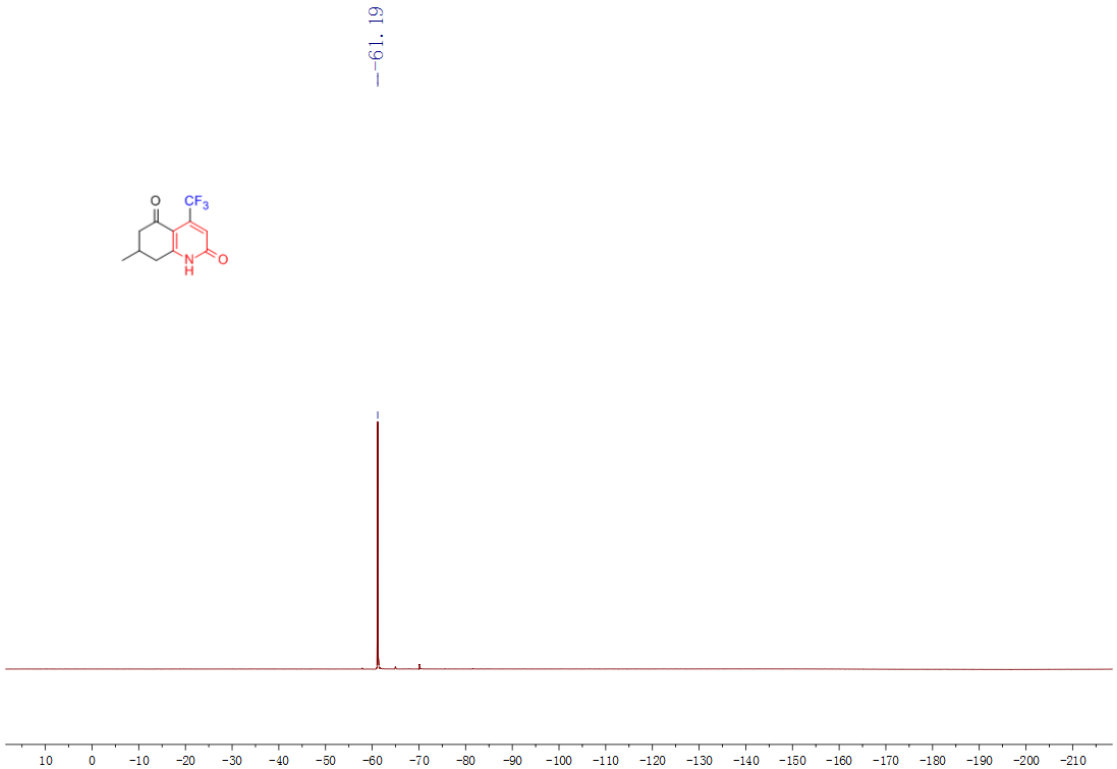
^{13}C NMR spectrum of **4a** in DMSO-d_6



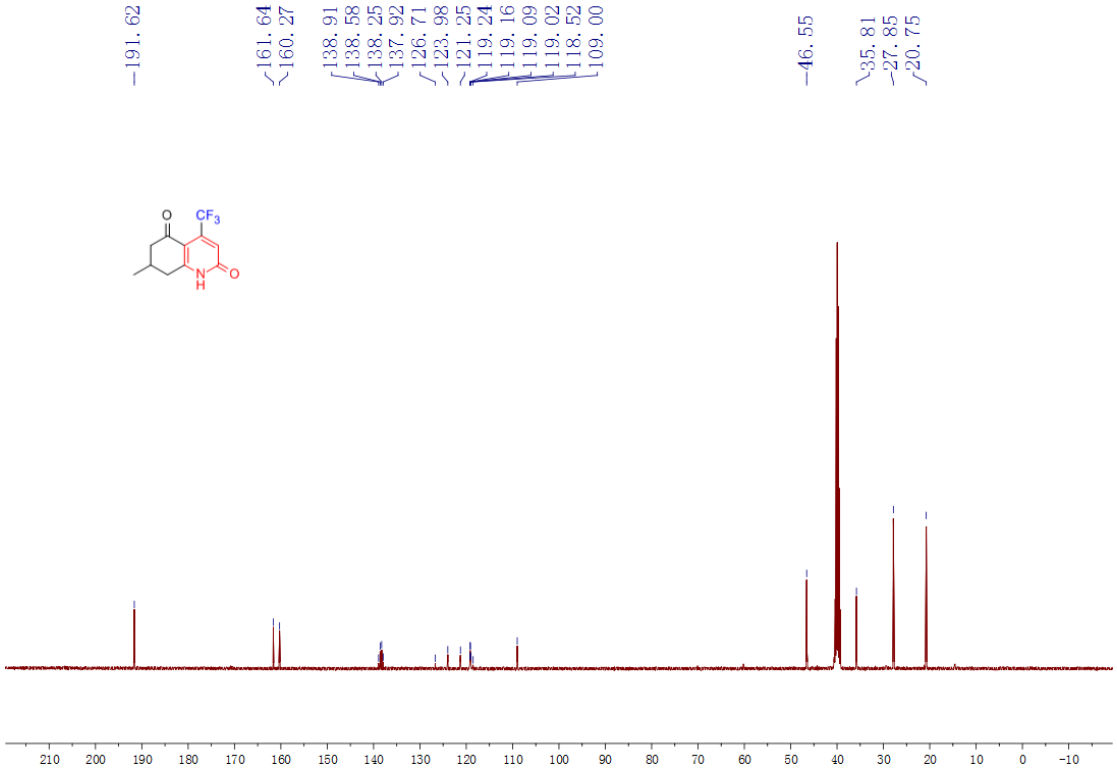
[1]H NMR spectrum of **4b** in DMSO-d_6



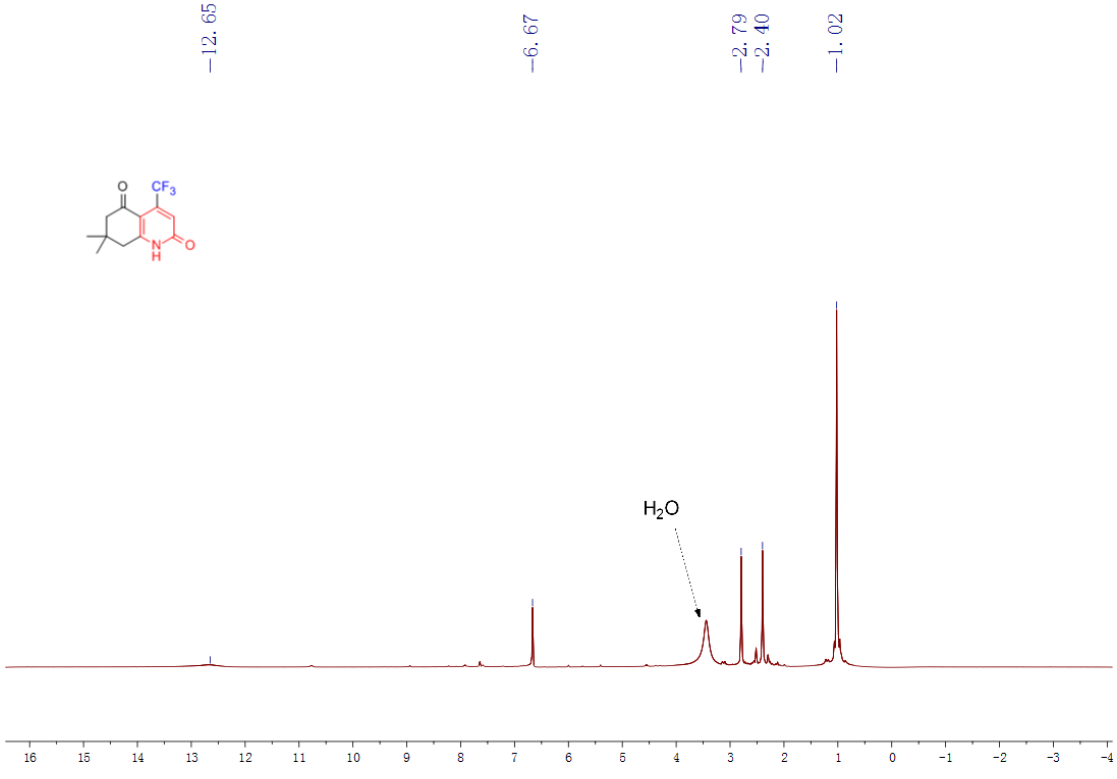
[19]F NMR spectrum of **4b** in DMSO-d_6



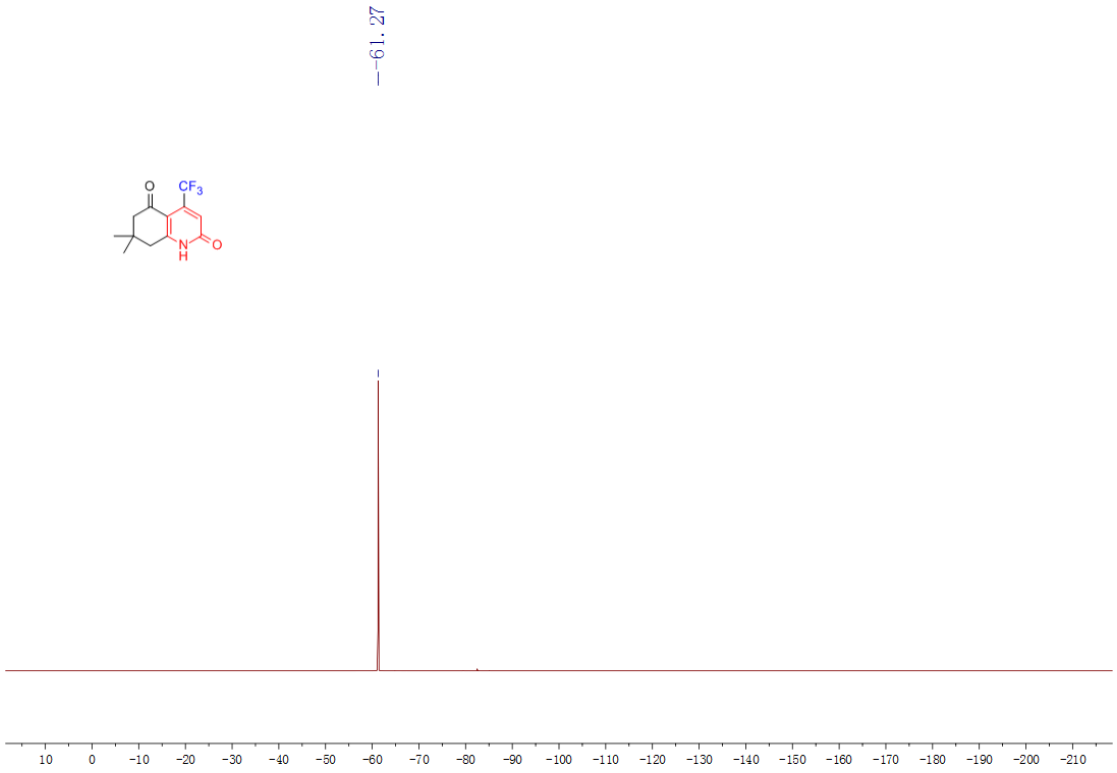
^{13}C NMR spectrum of **4b** in DMSO-d_6



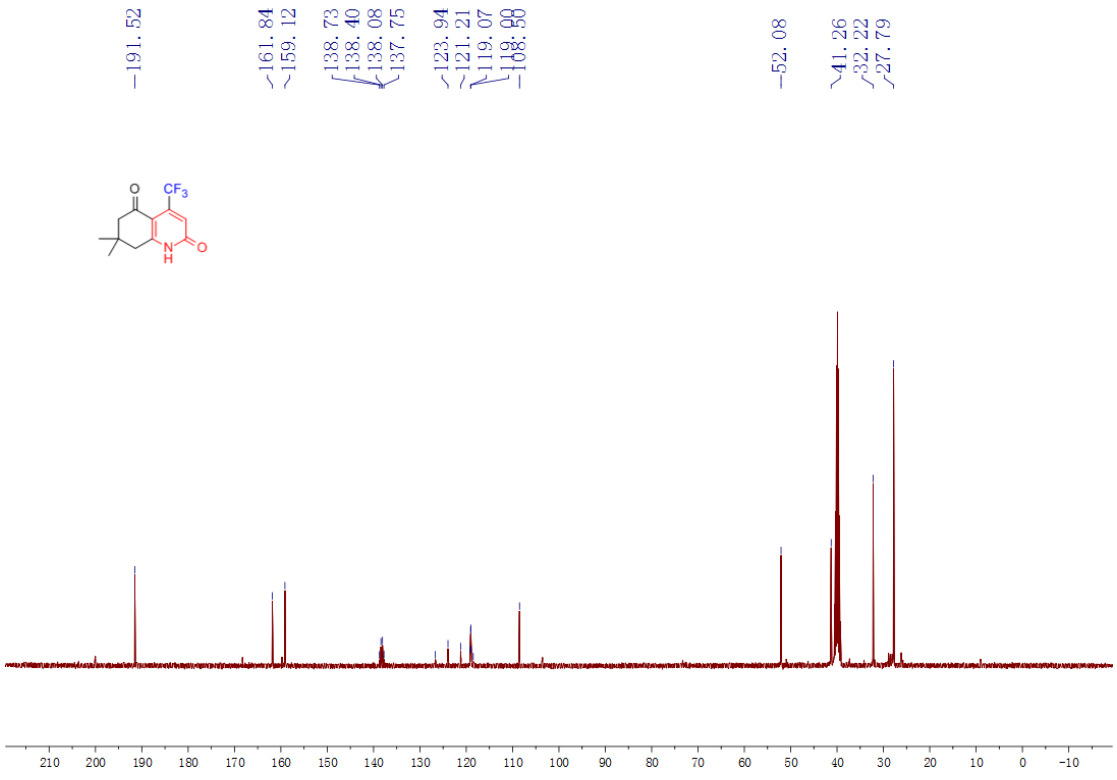
^{1}H NMR spectrum of **4c** in DMSO-d_6



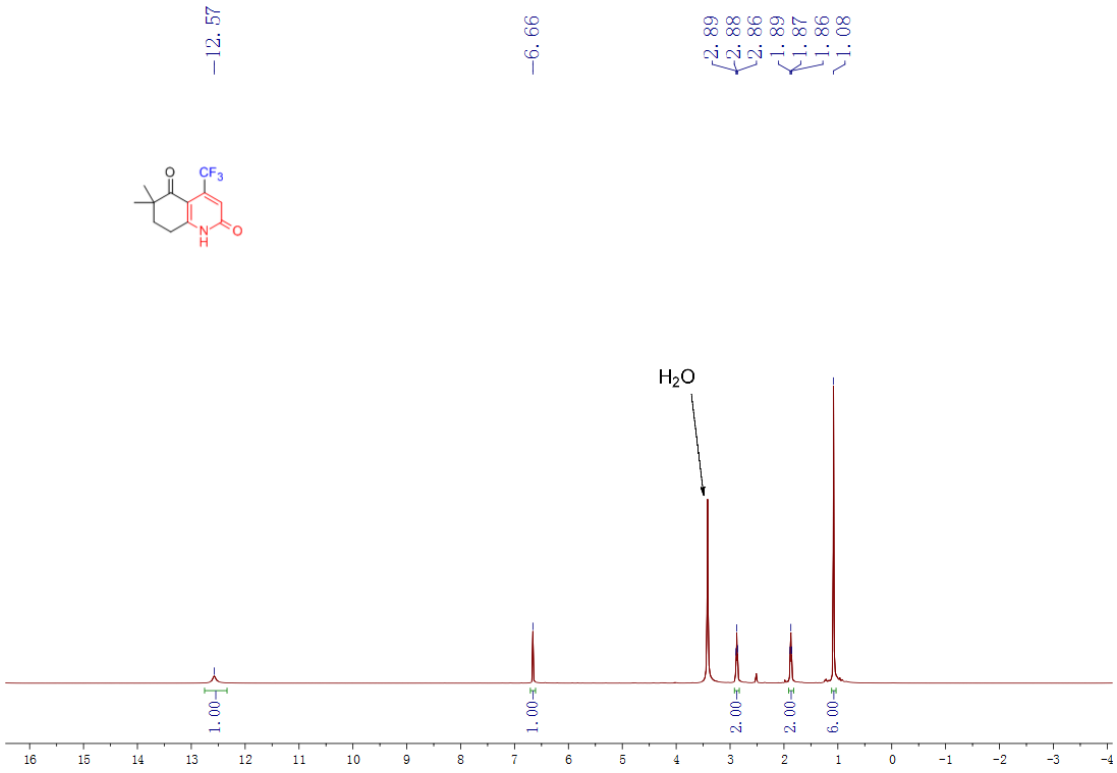
^{19}F NMR spectrum of **4c** in DMSO-d_6



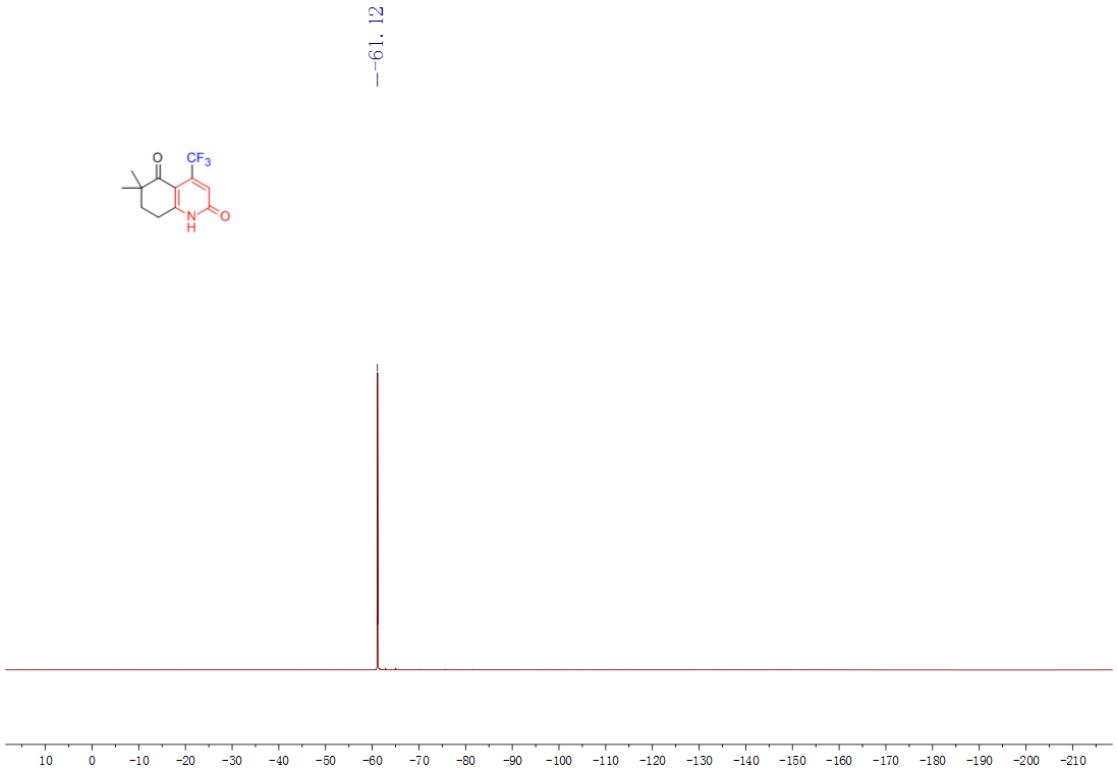
^{13}C NMR spectrum of **4c** in DMSO-d_6



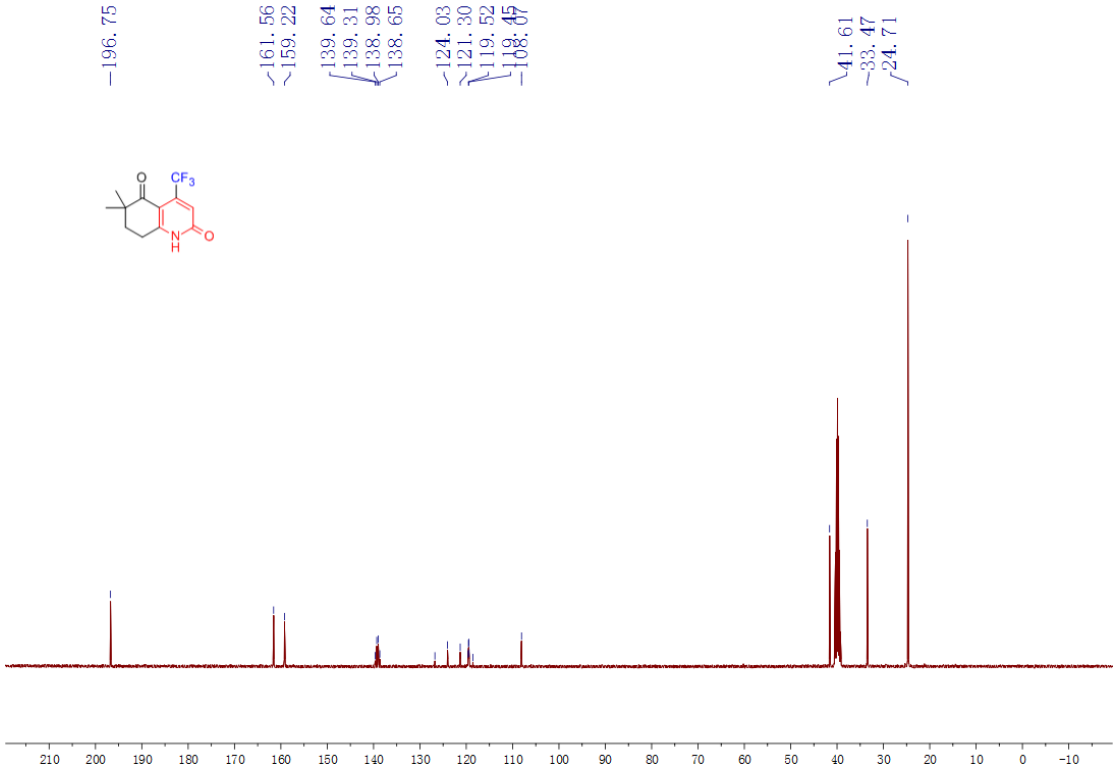
^{1}H NMR spectrum of **4d** in DMSO-d_6



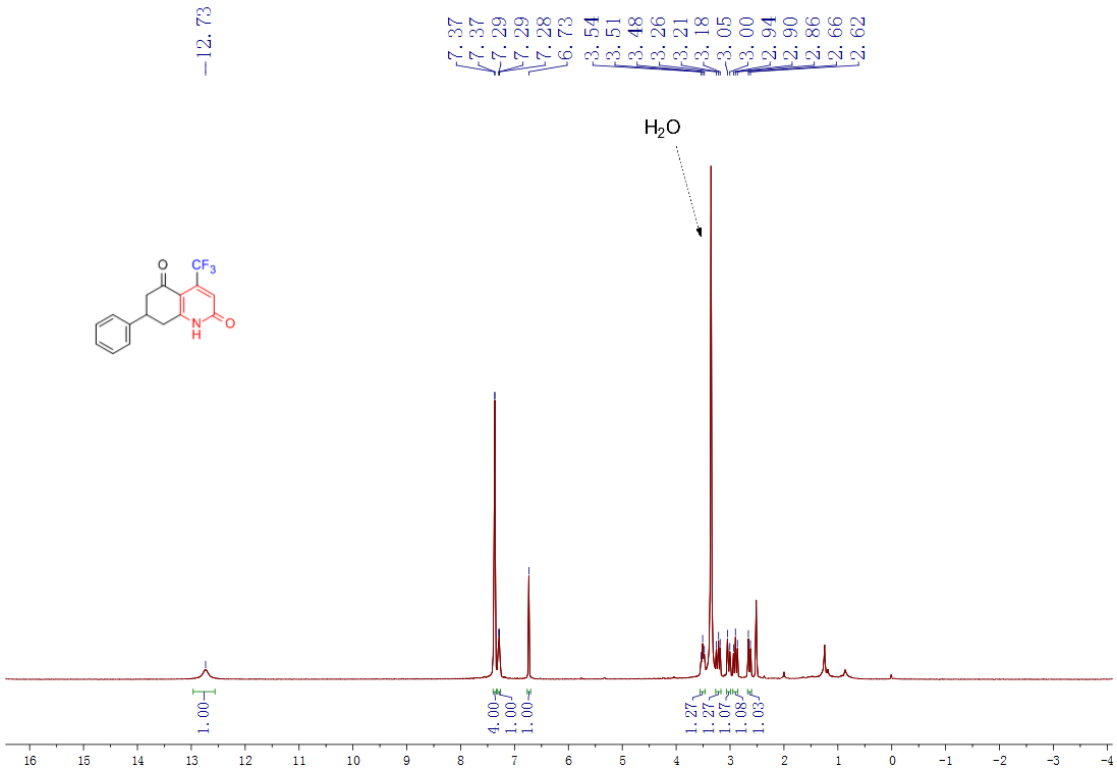
^{19}F NMR spectrum of **4d** in DMSO-d_6



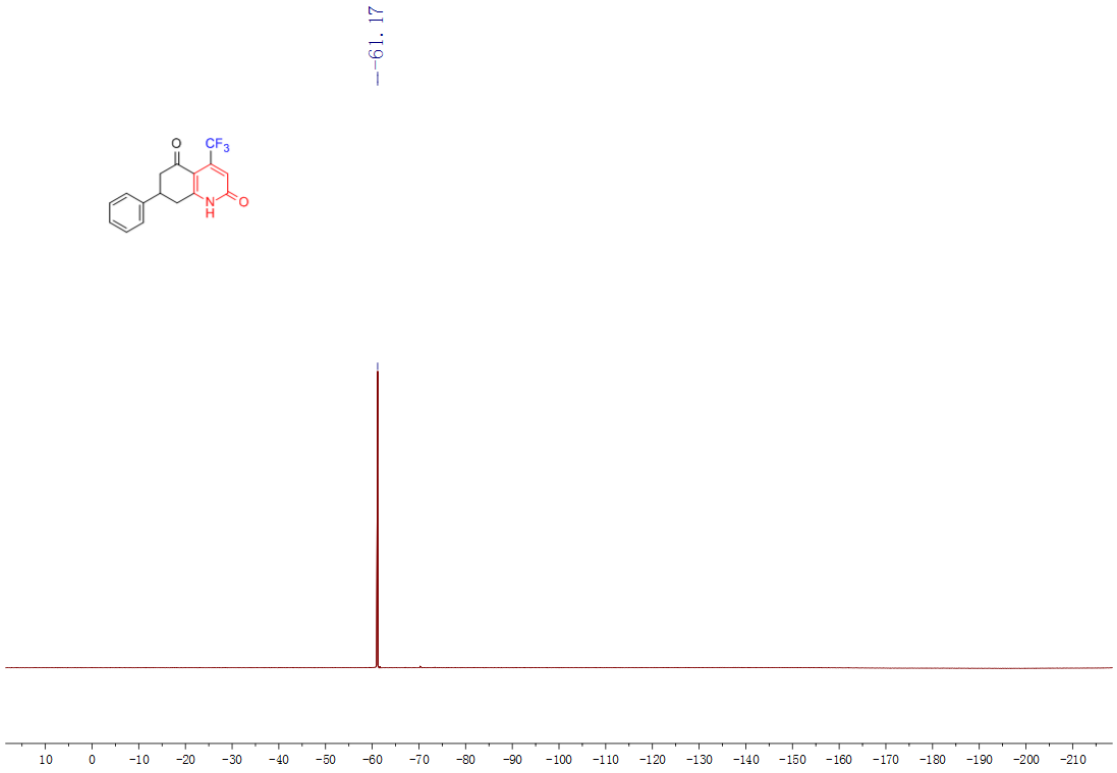
^{13}C NMR spectrum of **4d** in DMSO-d_6



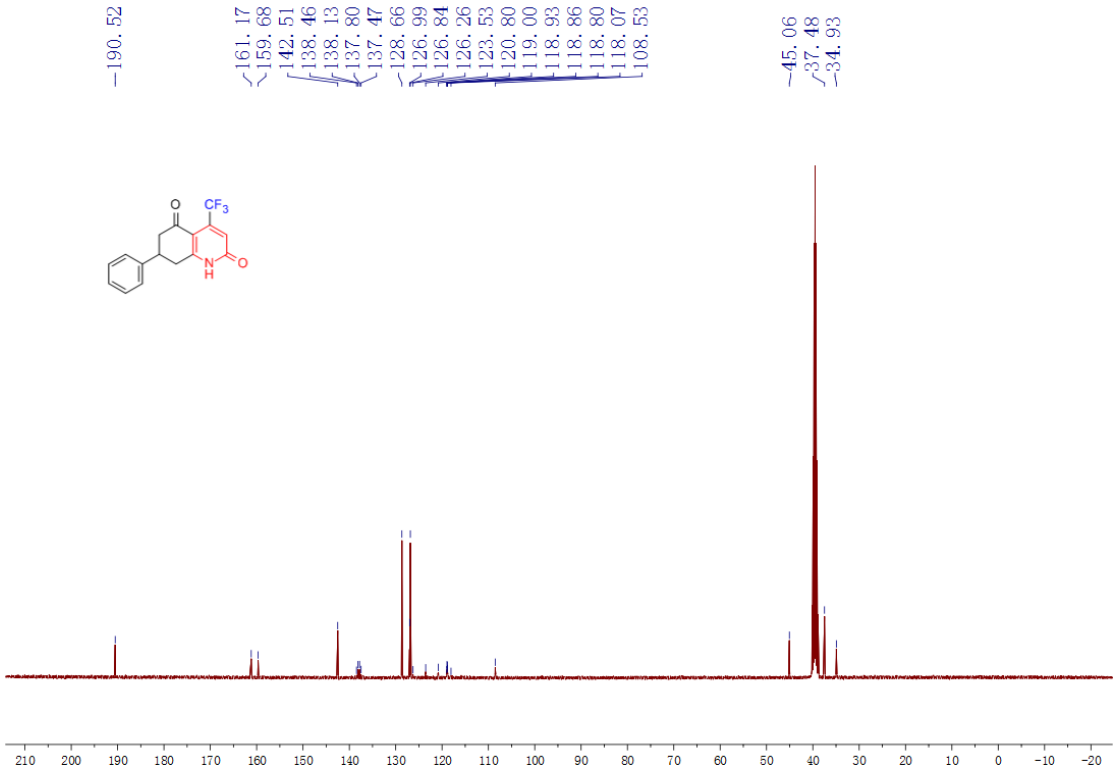
^{1}H NMR spectrum of **4e** in DMSO-d_6



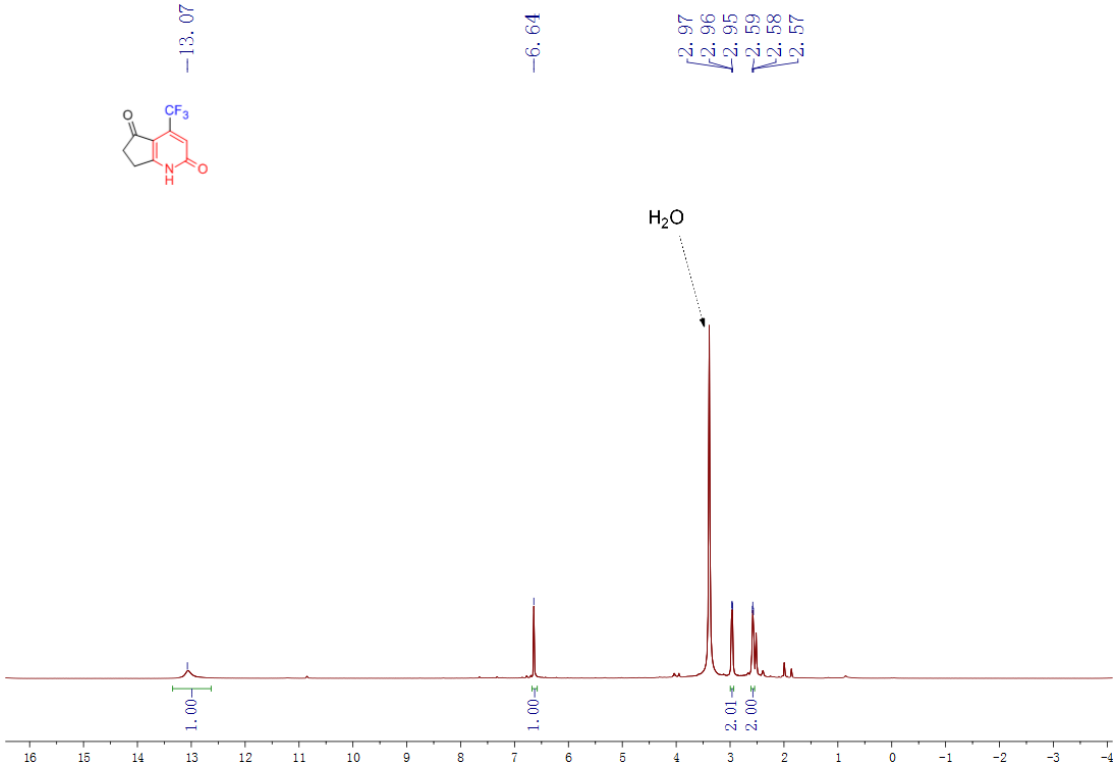
^{19}F NMR spectrum of **4e** in DMSO-d_6



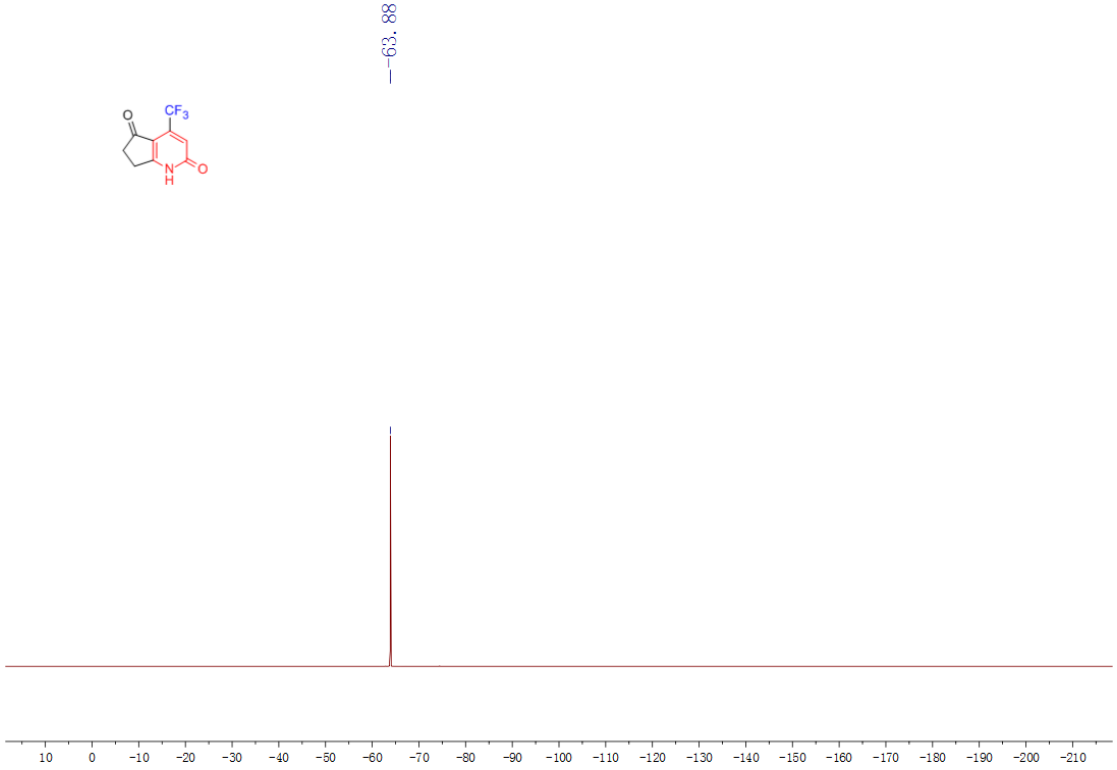
^{13}C NMR spectrum of **4e** in DMSO-d_6



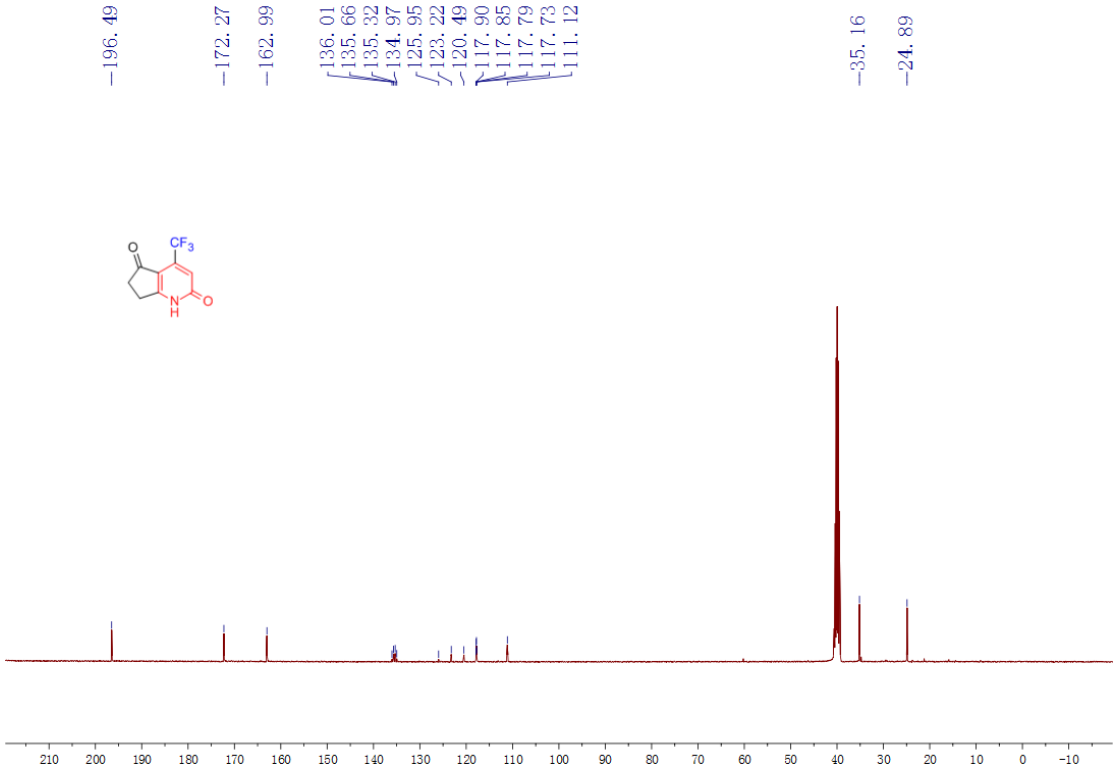
^{1}H NMR spectrum of **4g** in DMSO-d_6



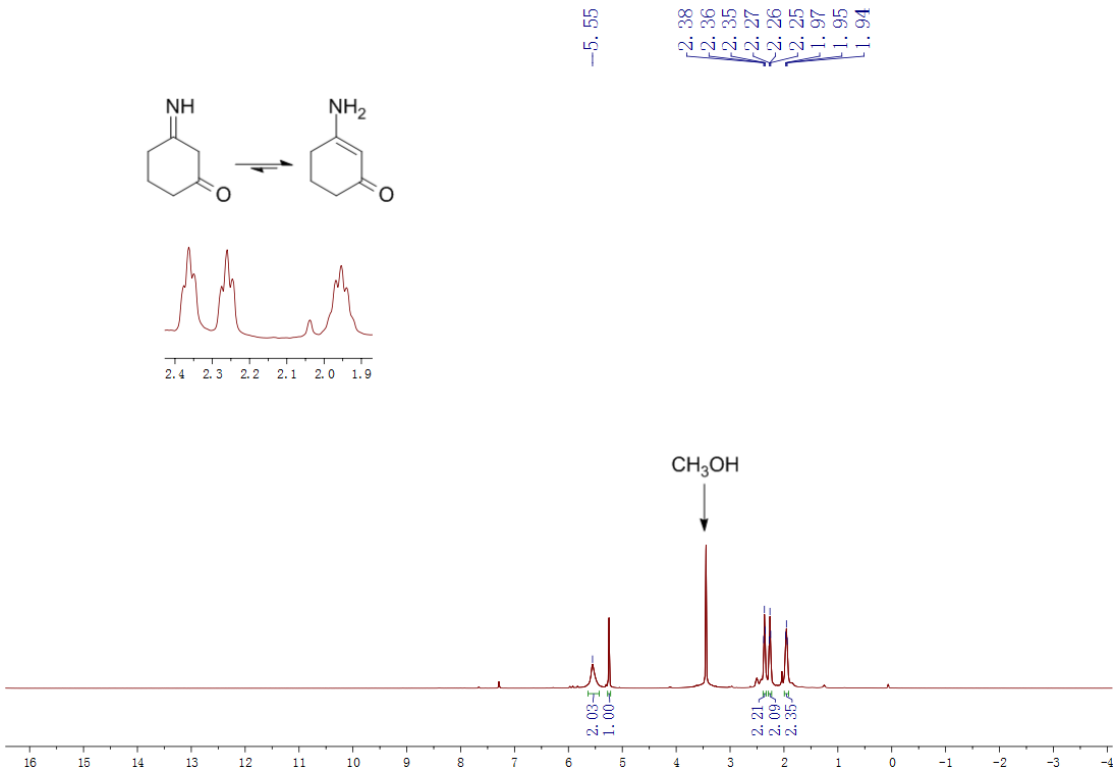
^{19}F NMR spectrum of **4g** in DMSO-d_6



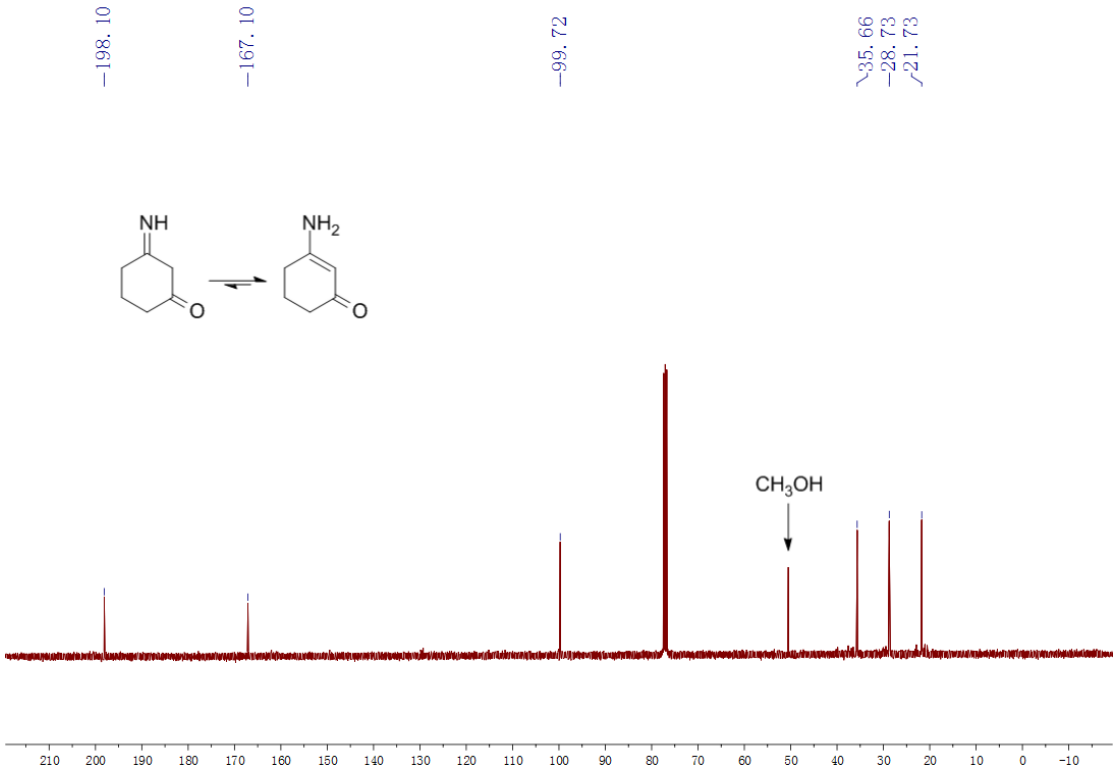
^{13}C NMR spectrum of **4g** in DMSO-d_6



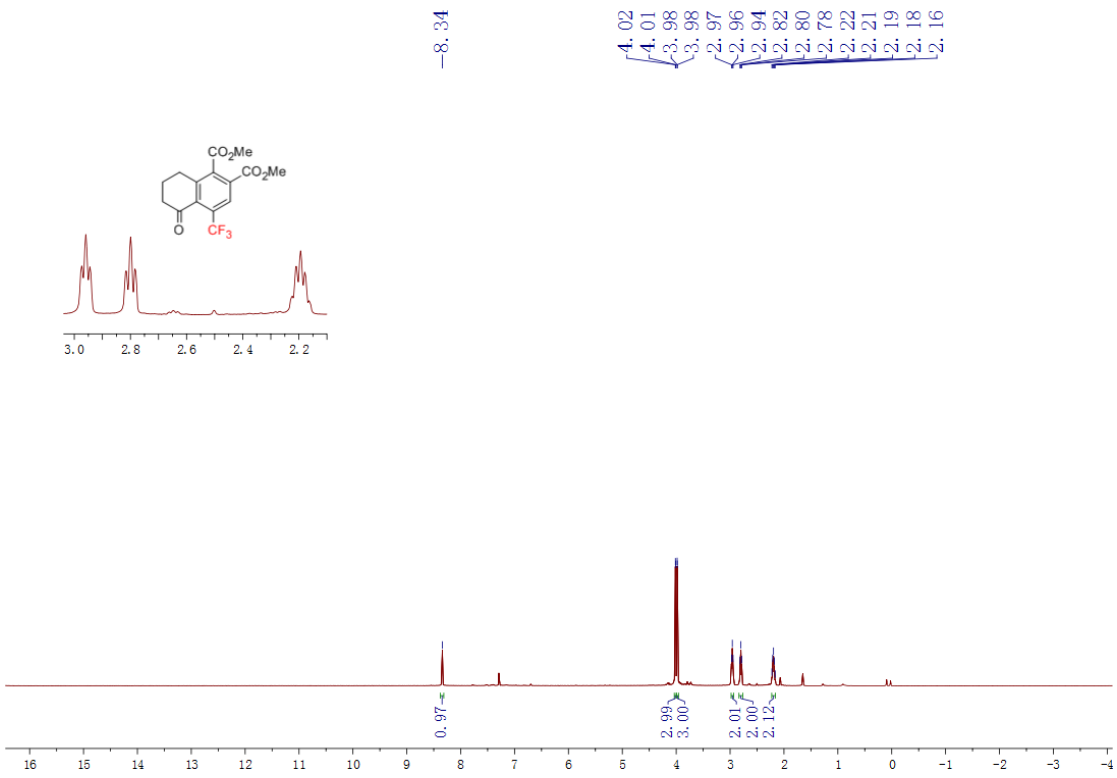
^{1}H NMR spectrum of **5** in $CDCl_3$



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

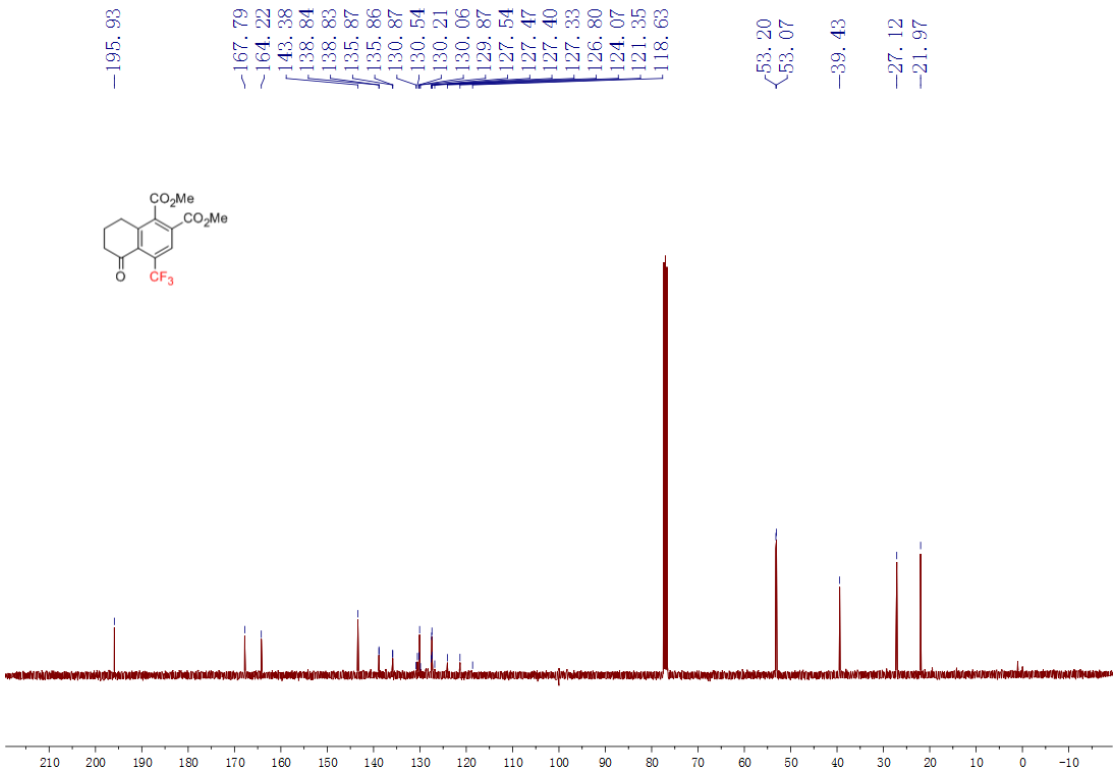


^{1}H NMR spectrum of **6** in $CDCl_3$

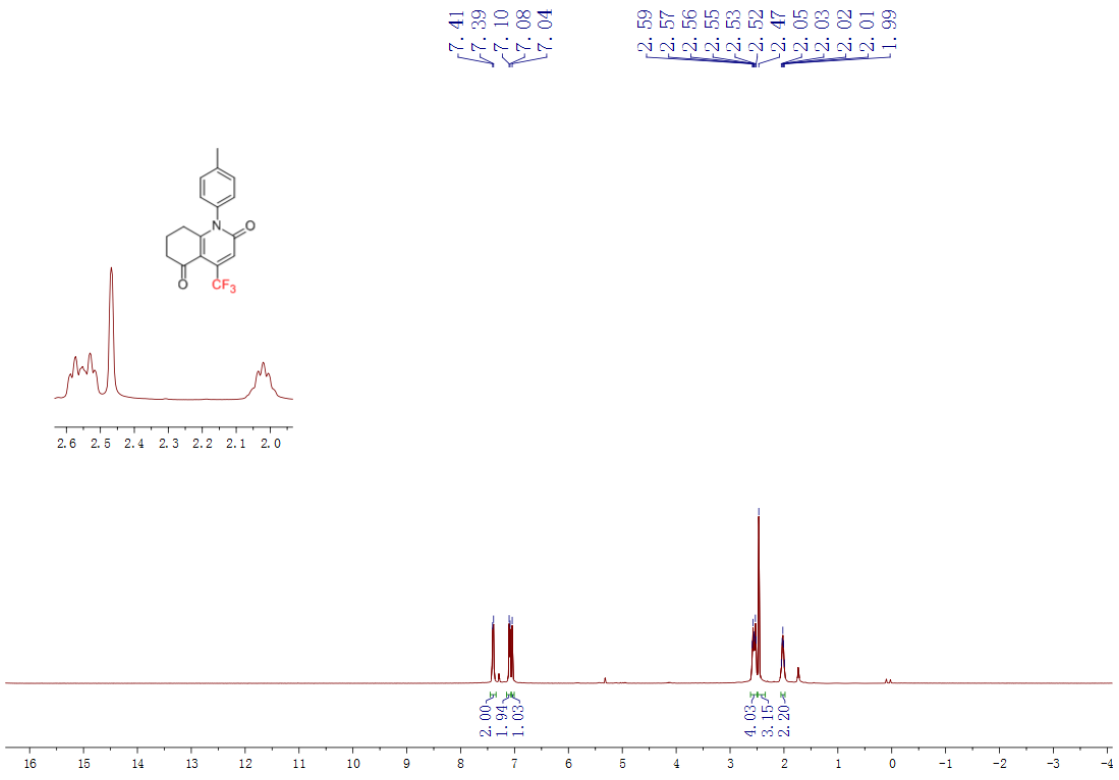


^{19}F NMR spectrum of **6** in $CDCl_3$

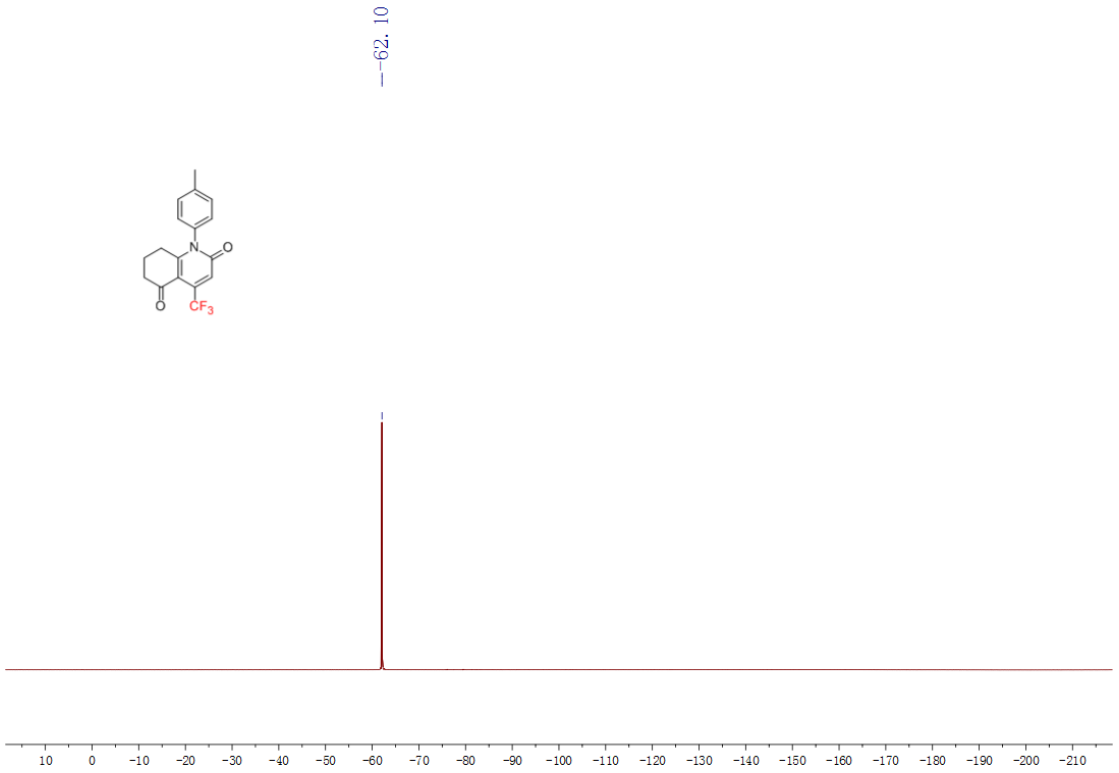
^{13}C NMR spectrum of **6** in $CDCl_3$



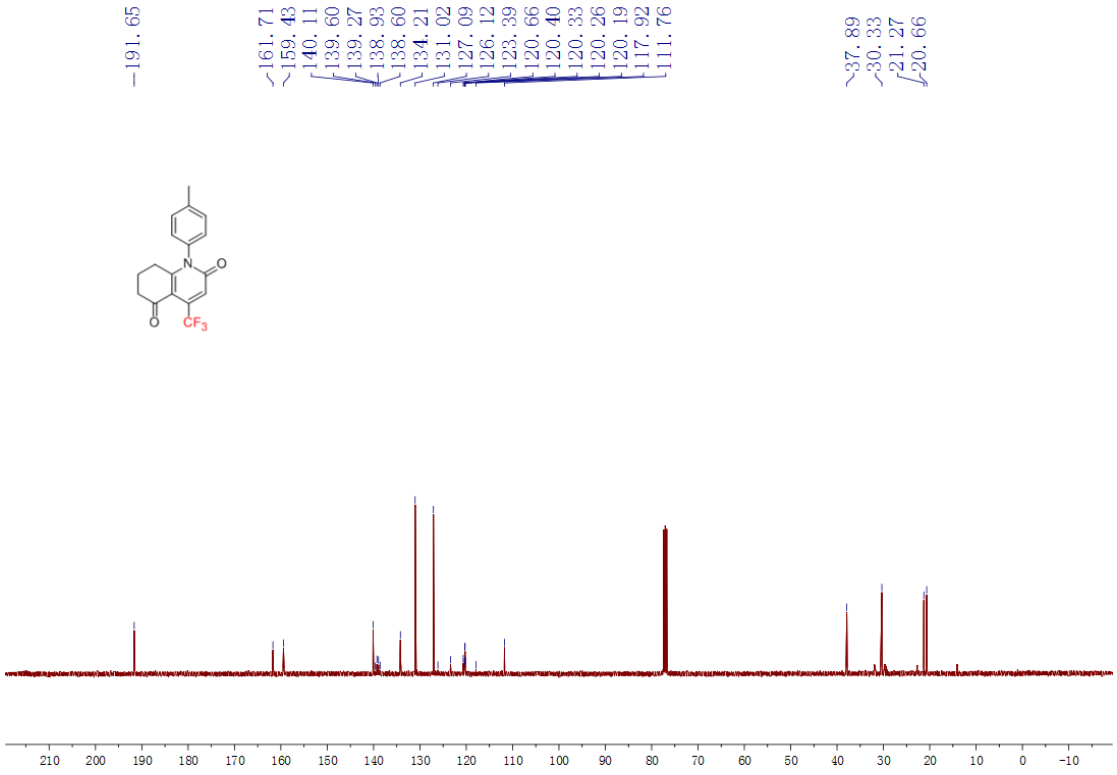
^{1}H NMR spectrum of **7** in $CDCl_3$



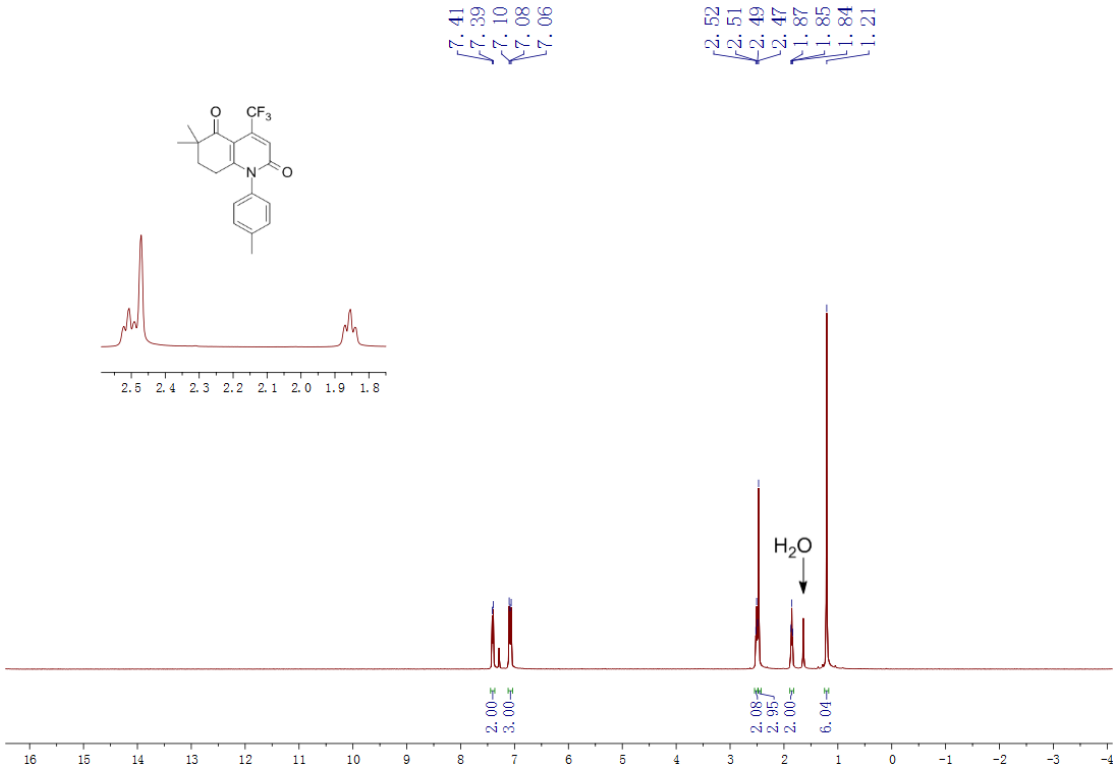
^{19}F NMR spectrum of **7** in $CDCl_3$



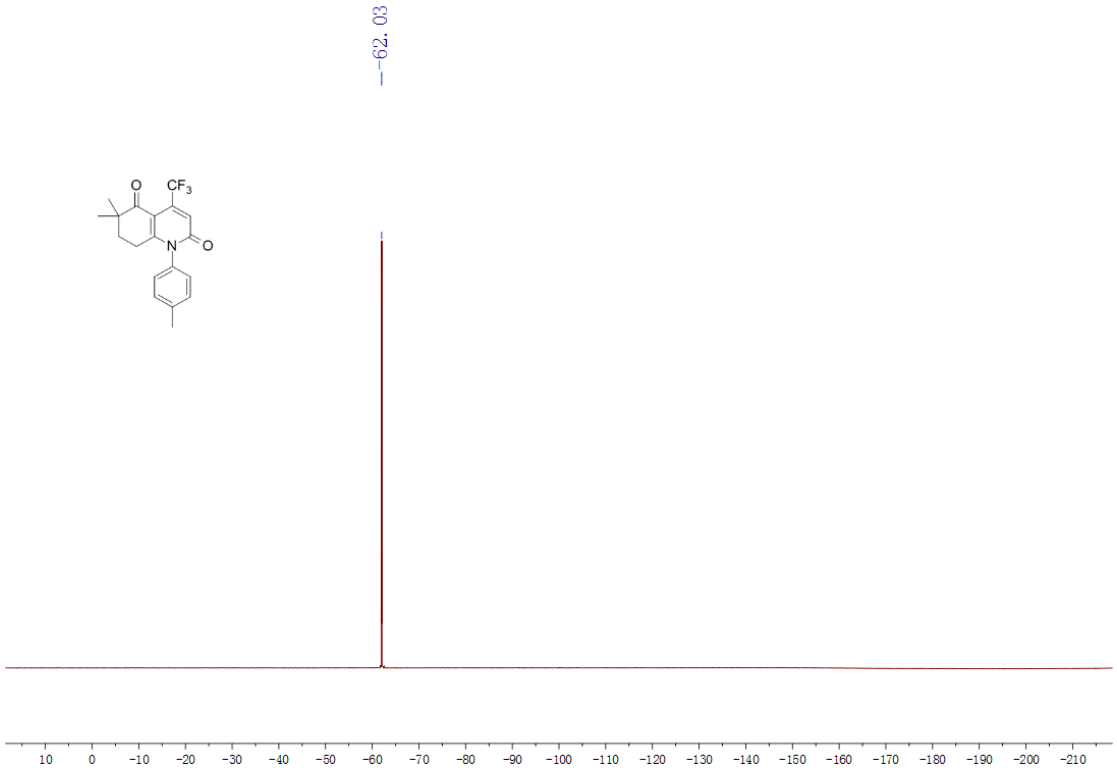
^{13}C NMR spectrum of **7** in $CDCl_3$



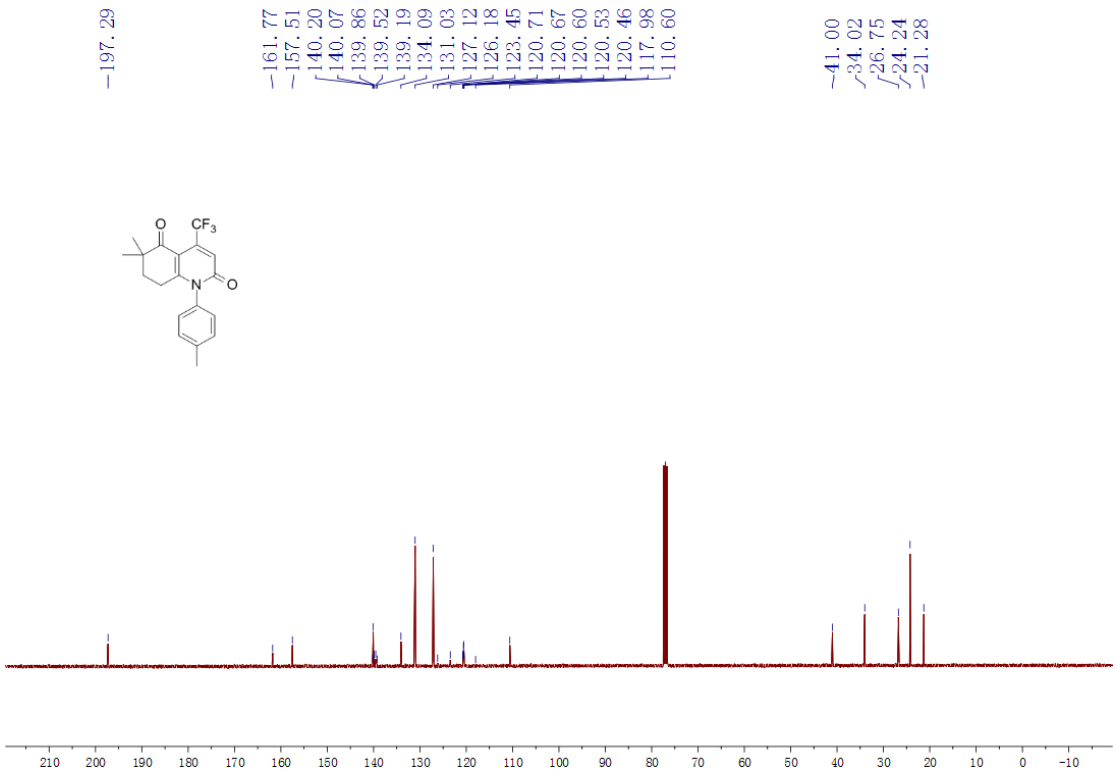
^{1}H NMR spectrum of **8** in $CDCl_3$



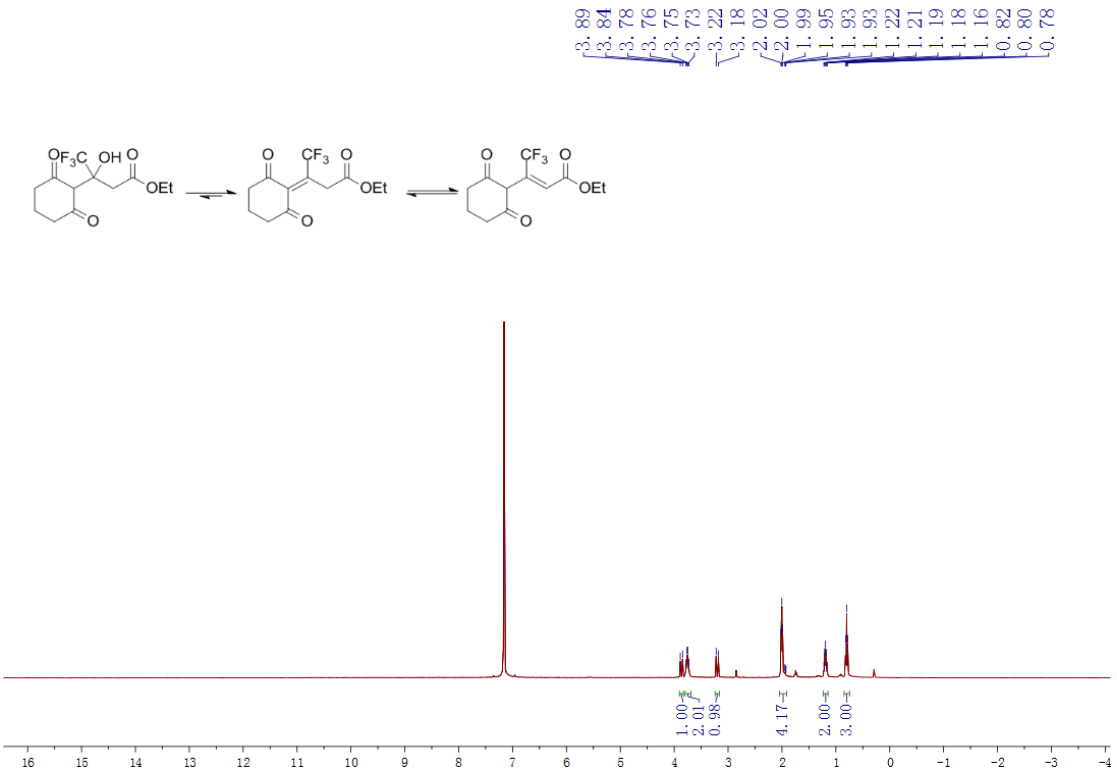
^{19}F NMR spectrum of **8** in $CDCl_3$



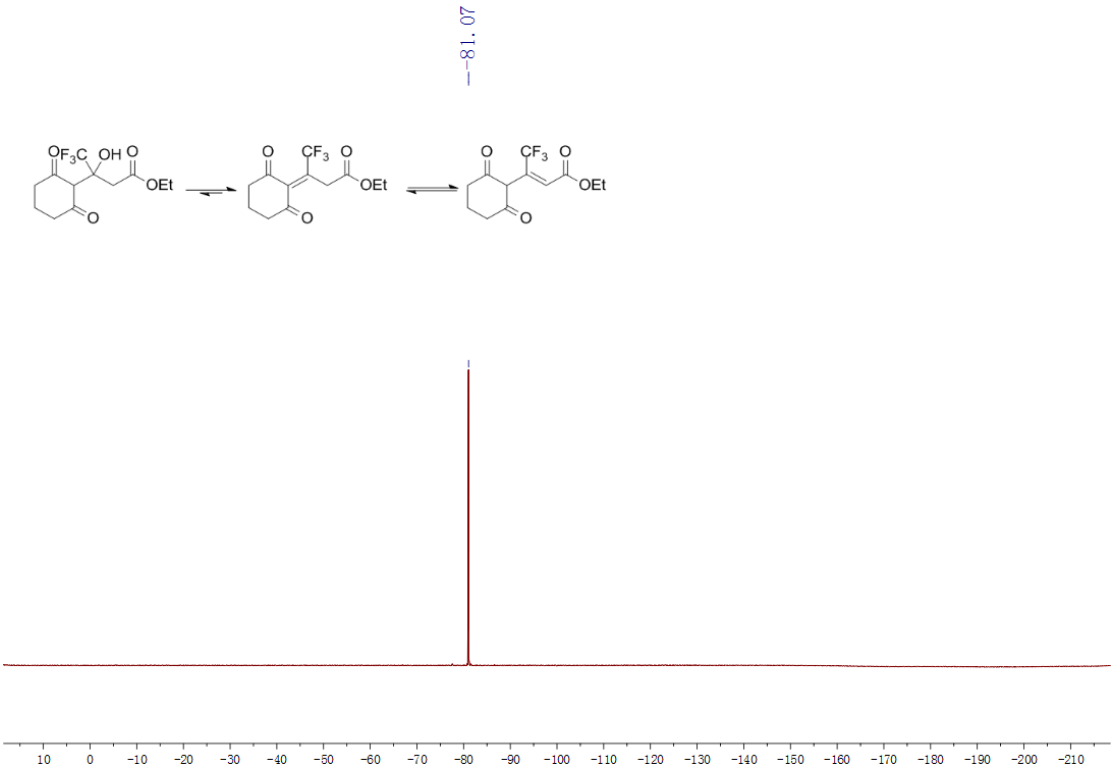
^{13}C NMR spectrum of **8** in $CDCl_3$



^{1}H NMR spectrum of intermediate (**I**) in C_6D_6



^{19}F NMR spectrum of intermediate (**I**) in C_6D_6



^{13}C NMR spectrum of intermediate (**I**) in C_6D_6