# Rh(III)-Catalyzed Tandem Annulative Redox-Neutral Arylation/Amidation of Aromatic Tethered Alkenes

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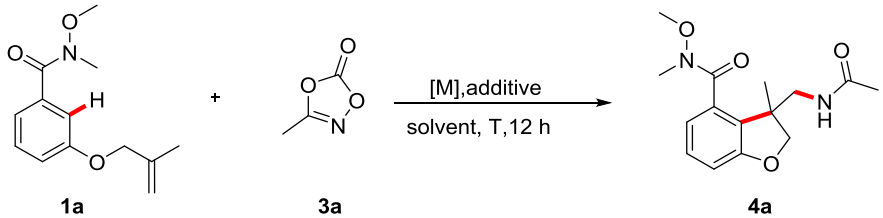
## General Information

Unless otherwise noted, all reactions were carried out under an $N_2$ atmosphere in sealed tube with magnetic stirring and all reagents were purchased from commercial suppliers with the highest purity grade, and used directly without further purification. General Methods $^{1}H$ NMR and $^{13}C$ NMR spectra were determined with BRUKER AVANCE II 400M or BRUKER AVANCE III 500M or AVANCE III 600 NMR spectrometer with $CDCl_3$ or $CD_3OD$ as solvent and tetramethylsilane (TMS) as internal standard. Chemical shifts were reported in ppm from internal TMS (δ). All coupling constants (*J* values) were reported in hertz (Hz). Reactions were monitored by thin-layer chromatography. High resolution ESI mass analysis was performed by Agilent 1290-6545 UHPLC-QTOF high resolution mass spectrometer. Column chromatography was performed on silica gel (200-300 mesh) manufactured by Qingdao Haiyang Chemical Group Co. (China).

## Table S1 and S2. Optimization studies.

**Table S1.** Conditions screening and optimization of the tandem annulative arylation/amidation reaction of aromatic tethered alkenes[a]



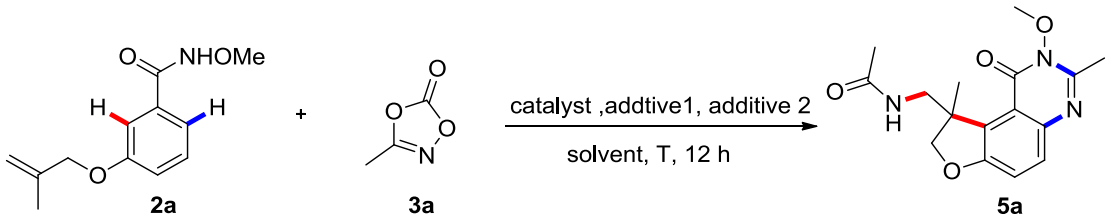

**1a** **3a** **4a**

| entry | catalyst | additive 1 | additive 2 | T[℃] | solvent | yield of **4a** (%) |
|---|---|---|---|---|---|---|
| 1 | $[Cp^*RhCl_2]_2$ | $AgSbF_6$ | HOAc | 70 | DCE | <5 |
| 2 | $[Cp^*RhCl_2]_2$ | $AgSbF_6$ | - | 70 | DCE | 89 |
| 3 | $Ru_3(CO)_{12}$ | $AgSbF_6$ | - | 70 | DCE | 0 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 4 | $[Ru(p\text{-}cymene)Cl_2]_2$ | $AgSbF_6$ | - | 70 | DCE | 0 |
| 5 | $Cp^*Co(CO)I_2$ | $AgSbF_6$ | - | 70 | DCE | 0 |
| 6 | $[Cp^*IrCl_2]_2$ | $AgSbF_6$ | - | 70 | DCE | 0 |
| 7 | $[Cp^*RhCl_2]_2$ | $AgSbF_6$ | - | 50 | DCE | 70 |
| 8 | $[Cp^*RhCl_2]_2$ | $AgSbF_6$ | - | 90 | DCE | 69 |
| 9 | $[Cp^*RhCl_2]_2$ | $AgSbF_6$ | - | 70 | MeOH | 21 |
| 10 | $[Cp^*RhCl_2]_2$ | $AgSbF_6$ | - | 70 | acetone | 43 |
| 11 | $[Cp^*RhCl_2]_2$ | $AgSbF_6$ | - | 70 | 1,4-dioxane | 66 |
| 12 | - | $AgSbF_6$ | - | 70 | DCE | 0 |

[a] Conditions: 1a (0.10 mmol), 3a (0.12 mmol), catalyst (5 mol%), additive 1 (20 mol%), additive 2 (20 mol%) in solvent (1 mL) for 12 h. Yield isolated by column chromatography.

**Table S2.** Conditions optimizations of the reaction for synthesis of **5a** [a]



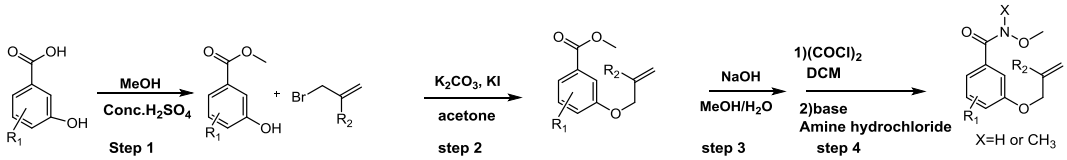

| entry | catalyst | **3a** (equiv) | additive 1 | additive 2 | T[℃] | Solvent | Yield of 5a (%) |
|---|---|---|---|---|---|---|---|
| 1 | $[Cp^*RhCl_2]_2$ | 2.5 | $AgSbF_6$ | $Cu(OAc)_2$ | 70 | DCE | 74 |
| 2 | $[Cp^*RhCl_2]_2$ | 3 | $AgSbF_6$ | $Cu(OAc)_2$ | 70 | DCE | 87 |
| 3 | $[Cp^*RhCl_2]_2$ | 4 | $AgSbF_6$ | $Cu(OAc)_2$ | 70 | DCE | 85 |
| 4 | $[Cp^*Ir\ Cl_2]_2$ | 3 | $AgSbF_6$ | $Cu(OAc)_2$ | 70 | DCE | 0 |
| 5 | $Ru_3(CO)_{12}$ | 3 | $AgSbF_6$ | $Cu(OAc)_2$ | 70 | DCE | 0 |
| 6 | $[Ru(p\text{-}cymene)Cl_2]_2$ | 3 | $AgSbF_6$ | $Cu(OAc)_2$ | 70 | DCE | 0 |
| 7 | $CoCp^*(CO)I_2$ | 3 | $AgSbF_6$ | $Cu(OAc)_2$ | 70 | DCE | 0 |
| 8 | $[Cp^*RhCl_2]_2$ | 3 | $AgSbF_6$ | LiOAc | 70 | DCE | 93 |
| 9 | $[Cp^*RhCl_2]_2$ | 3 | $AgSbF_6$ | NaOAc | 70 | DCE | 89 |
| 10 | $[Cp^*RhCl_2]_2$ | 3 | $AgSbF_6$ | KOAc | 70 | DCE | 86 |
| 11 | $[Cp^*RhCl_2]_2$ | 3 | $AgSbF_6$ | CsOAc | 70 | DCE | 79 |
| 12 | $[Cp^*RhCl_2]_2$ | 3 | $AgSbF_6$ | / | 70 | DCE | 50 |
| 13 | $[Cp^*RhCl_2]_2$ | 3 | $AgSbF_6$ | LiOAc | 70 | MeOH | 56 |
| 14 | $[Cp^*RhCl_2]_2$ | 3 | $AgSbF_6$ | LiOAc | 70 | Acetone | 81 |
| 15 | $[Cp^*RhCl_2]_2$ | 3 | $AgSbF_6$ | LiOAc | 70 | Dioxane | 88 |
| 16 | - | 3 | $AgSbF_6$ | LiOAc | 70 | DCE | 0 |

[a] Conditions: **2a** (0.10 mmol), **3a**, catalyst (5 mol %), additive 1 (20 mol %), additive 2 (20

mol %) in solvent (1 mL) for 12 h. Yield analyzed by column chromatography.

## Experimental Procedures and Characterizations

Substrates **1** and **2** were readily prepared according to the known method [1-3]:




Take synthesis of substrates **1a** for example:

**Step 1**: To a solution of 3-hydroxybenzoic acid (1.00 g, 7.24 mmol) in MeOH (30 mL), concentrated $H_2SO_4$ (0.5 mL) was added and then stir the solution under reflux overnight. After the solvent was evaporated and ice water was carefully poured into the residue. the reaction mixture was extracted with ethyl acetate for three times. The combined organic layers were washed by water and NaCl saturated solution then were dried over $MgSO_4$, filtered, concentrated under reduced pressure without further purification. There was thus obtained methyl 3-hydroxybenzoate, white solid, 0.95 g.

**Step 2**: To a solution of methyl 3-hydroxybenzoate (0.95 g, 6.25 mmol, 1.0 equiv), and potassium carbonate (2.59 g, 18.75 mmol, 3.0 equiv), potassium iodide (311.3 mg, 1.9 mmol, 0.3 equiv) in acetone (40 mL), 3-bromo-2-methylpropene (1.01 g, 7.5mmol, 1.2 equiv) was added and the mixture was stired under reflux for 6 hours. The mixture was filtered and the solvent was evaporated. The residue was purified by column chromatography on silica gel, and elution with petroleum ether/ethyl acetate (4:1) to obtain methyl 3-((2-methylallyl)oxy)benzoate, oil, 1.07 g.

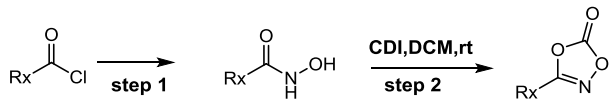
**Step3**: To a solution of methyl 3-allyloxybenzoate (1.07 g, 5.20 mmol, 1.0 equiv) in MeOH (20 mL) and $H_2O$ (20 mL), NaOH (416 mg, 10.4 mmol, 2.0 equiv) was added and the reaction mixture was refluxed for 3 h. The reaction mixture was concentrated to remove MeOH and the aqueous layer was acidified with 10% HCl to pH = 2. The reaction mixture was extracted with ethyl acetate for three times and combined organic layers were washed by water and NaCl saturated solution and then were dried over $MgSO_4$, filtered, concentrated under reduced pressure without further purification. There was thus obtained 3-((2-methylallyl)oxy)benzoic acid, white solid,

0.86g.

**Step 4**: 1) To a solution of 3-((2-methylallyl)oxy)benzoic acid (0.86 g, 4.5 mmol, 1.0 equiv) in dry $CH_2Cl_2$ (20 mL) was added oxalyl chloride (6.75 mmol, 1.5 equiv) at 0 ℃ under argon followed by the addition of a catalytic amount of DMF (2 drops). The reaction was then stirred for 0.5h at rt. The solvent was removed under reduced pressure to afford the crude acid chloride, which was directly engaged in the next step.

2)To a stirred suspension of the crude acid chloride in dry DCM (20 mL) at 0 ℃ was slowly added triethylamine (1.73 mL, 13.5 mmol, 3.0 equiv). N, O-Dimethylhydroxylamine hydrochloride (658 mg, 6.75 mmol,1.5 equiv) then was added slowly to the solution. The solution was allowed to warm to room temperature and stirred for 1 hour. the reaction mixture was extracted with ethyl acetate for three times. The combined organic layers were washed by water and NaCl saturated solution then were dried over $MgSO_4$, filtered, concentrated under reduced pressure. The residue was purified by column chromatography column chromatography on silica gel, and elution with petroleum ether/ethyl acetate (4:1) to obtain substrate **1a**, colorless oil, 0.84 g.

Substrates **3** were generated according to the following route[4-7]:

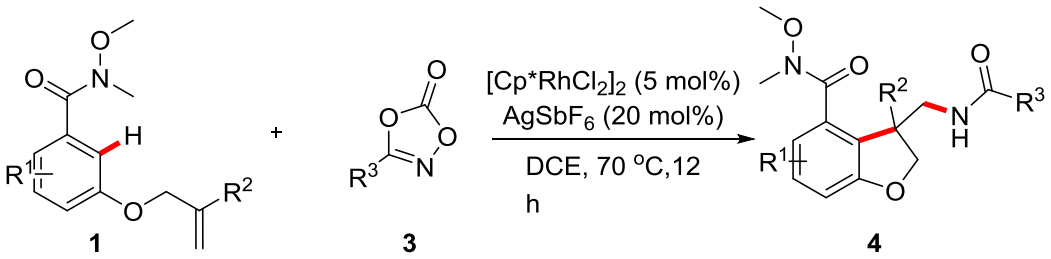



**Step1**: Methoxylamine hydrochloride (1.1 equiv) was added to a biphasic mixture of $K_2CO_3$ (2.0 equiv) in $Et_2O$ and $H_2O$ (v/v = 8:1). The mixture was cooled to 0 ℃, where upon the acid chloride (1.0 equiv) was added dropwise as a solution in $Et_2O$ (5 mL) over 0.5 h. The reaction was allowed to warm to room temperature overnight. After the separation of the organic layer, the aqueous layer was extracted with EtOAc. The combined organic layers were dried over $MgSO_4$, filtered and concentrated without further purification.

**Step 2**: To a stirred solution of hydoxamic acid (1.0 equiv) in dry dichloromethane was added 1,1′-carbonyldiimidazole (1.0 equiv) in one portion at room temperature.

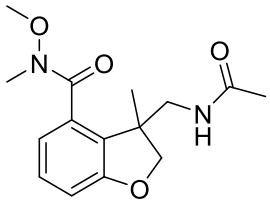
After stirring for 30 min, the reaction mixture was quenched with 1N HCl, extracted with dichloromethane three times and dried over magnesium sulfate. The solvent was removed under reduced pressure and the crude material was purified by column chromatography on silica to afford substrates **3**.

**Synthesis of 4:**



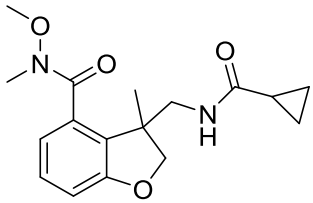

To an oven-dried 15 mL Schlenk tube equipped with a stir bar were added substrate **1** (0.1 mmol), **3** (0.12 mmol), $[Cp^*RhCl_2]_2$ (5 mol%), $AgSbF_6$ (20 mol%) and DCE (1 mL). The tube was sealed and the reaction was stirred at 70 ℃ for 12 h. The reaction mixture was cooled to room temperature and diluted with $CH_2Cl_2$ (5 mL) and filtered through a short pad silica gel washing with $CH_2Cl_2$ (20 mL). The filtrate was concentrated and then purified by column chromatography on silica gel to yield the desired product.

3-(acetamidomethyl)-N-methoxy-N,3-dimethyl-2,3-dihydrobenzofuran-4-carboxamide (**4a**)



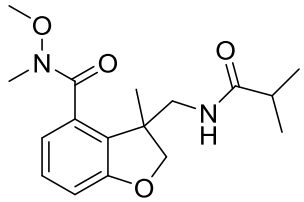
Colorless oil in 89% yield; **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.17 (t, *J* = 7.8 Hz, 1H), 6.87 – 6.81 (d, 7.8 Hz,1H), 6.78 (d, *J* = 7.8 Hz, 1H), 5.67 (m, 1H), 4.38 (d, *J* = 8.8 Hz, 1H), 4.14 (d, *J* = 8.8 Hz, 1H),3.80 – 3.13 (m, 8H), 1.89 (s, 3H), 1.27 (s, 3H); **$^{13}$C NMR** (151 MHz, Chloroform-*d*) δ 170.2, 160.5, 131.2, 128.1, 117.9, 110.9, 81.0, 60.9, 47.3, 45.3, 45.1, 32.1, 22.7, 21.9; **HRMS** (ESI) Calcd for $C_{15}H_{21}N_2O_4$ $[M+H]^+$ 293.1496, found 293.1503.

3-(cyclopropanecarboxamidomethyl)-N-methoxy-N,3-dimethyl-2,3-dihydrobenzofuran-4-carboxamide (**4b**)



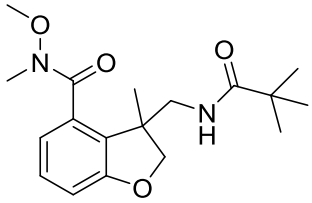
Colorless oil in 70% yield; **$^{1}$H NMR** (400 MHz, Chloroform-*d*) δ 7.18 (t, *J* = 7.9 Hz, 1H), 6.85 (d, *J* = 7.9, Hz, 1H), 6.78 (d, *J* = 7.9, Hz, 1H), 4.37 (d, *J* = 8.8 Hz, 1H), 4.14 (d, *J* = 8.8 Hz, 1H), 3.87 – 3.11 (m, 8H), 1.33 (m, 1H), 1.29 (s, 3H), 0.88 – 0.84 (m, 2H), 0.64 (m, 2H); **$^{13}$C NMR** (151 MHz, Chloroform-*d*) δ 174.2, 161.0, 131.7, 128.6, 118.4, 111.3, 81.4, 61.3, 47.9, 45.7, 22.5, 14.7, 7.1, 7.0; **HRMS** (ESI) Calcd for $C_{17}H_{23}N_2O_4$ $[M+H]^+$ 319.1652, found 319.1653.

3-(isobutyramidomethyl)-N-methoxy-N,3-dimethyl-2,3-dihydrobenzofuran-4-carboxamide (**4c**)



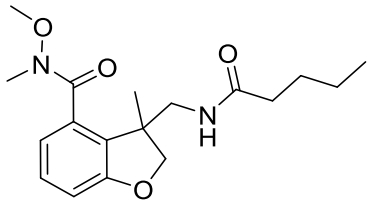
Colorless oil in 80% yield; **$^{1}$H NMR** (400 MHz, Chloroform-*d*) δ 7.18 (t, *J* = 7.8 Hz, 1H), 6.84 (d, *J* = 7.8 Hz, 1H), 6.79 (d, *J* = 7.8 Hz, 1H), 6.64 (brs, 1H), 4.42 (d, *J* = 8.9 Hz, 1H), 4.15 (d, *J* = 8.9 Hz, 1H), 3.76 (dd, *J* = 13.9, 7.8 Hz, 1H), 3.55 (s, 3H), 3.28 (s, 3H), 3.19 (m, 1H), 2.29 (m, 1H), 1.29 (s, 3H), 1.02 (dd, *J* = 10.3, 6.9 Hz, 6H); **$^{13}$C NMR** (126 MHz, Chloroform-*d*) δ 178.1, 161.1, 131.7, 128.7, 118.4, 111.3, 81.6, 61.2, 48.0, 45.6, 35.5, 22.7, 19.6, 19.3; **HRMS** (ESI) Calcd for $C_{17}H_{25}N_2O_4$ $[M+H]^+$ 321.1809, found 321.1808.

N-methoxy-N,3-dimethyl-3-(pivalamidomethyl)-2,3-dihydrobenzofuran-4-carboxamide (**4d**)



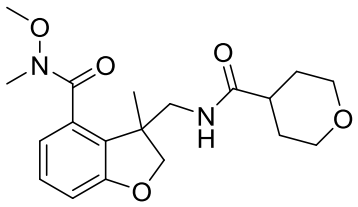
Colorless oil in 78% yield; **$^{1}$H NMR** (400 MHz, Chloroform-*d*) δ 7.17 (t, *J* = 7.8 Hz, 1H), 6.83 (d, *J* = 7.8 Hz,1H), 6.79 (d, *J* = 7.8 Hz,1H), 6.54 (s, 1H),4.44 (d, *J* = 9.0 Hz, 1H), 4.15 (d, *J* = 9.0 Hz, 1H), 3.88 (dd, *J* = 13.9, 8.8 Hz, 1H), 3.56 (s, 3H), 3.33 (s, 3H), 3.08 (d, J = 13.8 Hz, 1H), 1.29 (s, 3H), 1.02 (s, 9H); **$^{13}$C NMR** (126 MHz, Chloroform-*d*) δ 179.2, 161.2, 131.7, 128.7, 118.2, 111.1, 81.5, 61.3, 48.5, 45.4, 38.7, 32.5, 27.3, 23.7; **HRMS** (ESI) Calcd for $C_{18}H_{27}N_2O_4$ $[M+H]^+$335.1965, found 335.1967.

N-methoxy-N,3-dimethyl-3-(pentanamidomethyl)-2,3-dihydrobenzofuran-4-carboxa mide (**4e**)



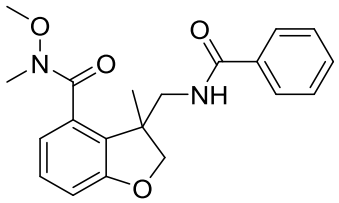
Colorless oil in 81% yield; **$^{1}$H NMR** (400 MHz, Chloroform-*d*) δ 7.19 (t, *J* = 7.8 Hz, 1H), 6.91 – 6.69 (m, 3H), 4.41 (d, *J* = 8.9 Hz, 1H), 4.16 (d, *J* = 8.9 Hz, 1H), 3.98 – 3.07 (m, 8H), 2.14 (td, *J* = 7.5, 2.6 Hz, 2H), 1.57 – 1.36 (m, 2H), 1.29 (s, 3H), 1.22 (m, 2H), 0.84 (t, *J* = 7.3 Hz, 3H); **$^{13}$C NMR** (151 MHz, Chloroform-*d*) δ 173.8,171.0, 161.0, 131.6, 128.5, 118.2, 111.1, 81.4, 61.3, 47.9, 45.4, 36.3, 32.5, 27.7, 22.6, 22.1, 13.7; **HRMS** (ESI) Calcd for $C_{18}H_{27}N_2O_4$ $[M+H]^+$ 335.1965, found 335.1961.

N-methoxy-N,3-dimethyl-3-((tetrahydro-2H-pyran-4-carboxamido)methyl)-2,3-dihyd robenzofuran-4-carboxamide (**4f**)



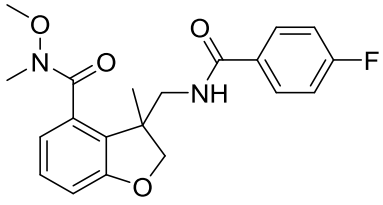
White solid in 62 % yield; **$^{1}$H NMR** (400 MHz, Chloroform-*d*) δ 7.20 (t, *J* = 7.8 Hz, 1H), 7.01 – 6.73 (m, 3H), 4.41 (d, *J* = 8.9 Hz, 1H), 4.17 (d, *J* = 8.9 Hz, 1H), 4.08 – 3.04 (m, 12H), 2.33 (m, 1H), 1.75 – 1.54 (m, 4H), 1.29 (s, 3H); **$^{13}$C NMR** (151 MHz, Chloroform-*d*) δ 174.9, 170.9, 160.9, 131.6, 128.5, 118.3, 111.1, 81.4, 67.1, 67.1, 61.3, 48.0, 45.4, 41.9, 32.4, 29.1, 28.9, 22.6; **HRMS** (ESI) Calcd for $C_{19}H_{27}N_2O_5$ $[M+H]^+$ 363.1914, found 363.1919.

3-(benzamidomethyl)-N-methoxy-N,3-dimethyl-2,3-dihydrobenzofuran-4-carboxamide (**4g**)




Colorless oil in 64% yield; **$^{1}$H NMR** (400 MHz, Chloroform-*d*) δ 7.69 (d, *J* = 7.6 Hz, 2H), 7.60 – 7.37 (m, 2H), 7.33 (m, 2H), 7.18 (t, *J* = 7.8 Hz, 1H), 6.86 – 6.82 (m, 1H), 6.81 (m, 1H), 4.50 (d, *J* = 8.9 Hz, 1H), 4.22 (d, *J* = 8.8 Hz, 1H), 4.03 (dd, *J* = 14.0, 8.0 Hz, 1H), 3.89 – 3.07 (m, 7H), 1.34 (s, 3H); **$^{13}$C NMR** (126 MHz, Chloroform-*d*) δ 167.7, 161.1, 134.4, 131.7, 131.3, 128.4, 127.1, 118.3, 111.4, 81.4, 61.4, 48.3, 45.5, 32.6, 23.5; **HRMS** (ESI) Calcd for $C_{20}H_{23}N_2O_4$ $[M+H]^+$355.1652, found 355.1650.

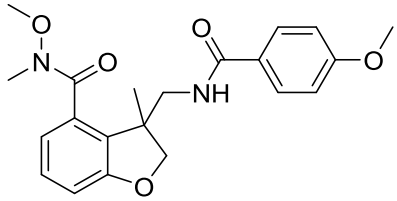
3-((4-fluorobenzamido)methyl)-N-methoxy-N,3-dimethyl-2,3-dihydrobenzofuran-4-carboxamide (**4h**)




Yellow oil in 58% yield; **$^{1}$H NMR** (400 MHz, Chloroform-*d*) δ 7.78 – 7.68 (m, 2H), 7.58 (s, 1H), 7.17 (t, *J* = 7.8 Hz, 1H), 7.06 – 6.95 (m, 2H), 6.83 (m, 2H), 4.47 (d, *J* = 8.9 Hz, 1H), 4.21 (d, *J* = 8.9 Hz, 1H), 3.97 (dd, *J* = 14.0, 7.6 Hz, 1H), 3.89 – 3.08 (m, 7H), 1.33 (s, 3H); **$^{13}$C NMR** (126 MHz, Chloroform-*d*) δ 171.2, 166.7, 164.6 (d,

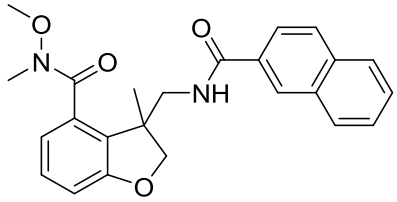
$J_{C\text{-}F}$ = 251.1 Hz), 161.1, 131.5, 130.6, 129.5 (d, $J_{C\text{-}F}$ = 8.9 Hz), 128.6, 118.4, 115.3 (d, $J_{C\text{-}F}$ = 21.8 Hz), 111.4, 81.6, 61.4, 48.2, 45.8, 32.5, 22.9; **$^{19}$F NMR** (471 MHz, Chloroform-*d*) δ -108.9; **HRMS** (ESI) Calcd for $C_{20}H_{22}FN_2O_4$ $[M+H]^+$373.1558, found 373.1569.

N-methoxy-3-((4-methoxybenzamido)methyl)-N,3-dimethyl-2,3-dihydrobenzofuran-4-carboxamide (**4i**)



Colorless oil in 54% yield; **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.66 (d, *J* = 8.3 Hz, 2H), 7.45 – 7.27 (m, 1H), 7.17 (t, *J* = 7.8 Hz, 1H), 6.83 (dd, *J* = 8.7, 2.0 Hz, 4H), 4.49 (d, *J* = 8.9 Hz, 1H), 4.21 (d, *J* = 8.9 Hz, 1H), 4.01 (dd, *J* = 14.1, 8.0 Hz, 1H), 3.77 (s, 3H), 3.59 – 3.30 (m, 7H) , 1.34 (s, 3H); **$^{13}$C NMR** (125 MHz, Chloroform-*d*) δ 167.2, 162.0, 161.1, 128.9, 128.6, 126.8, 118.3, 113.5, 111.3, 81.4, 61.4, 55.3, 48.4, 45.4, 32.6, 23.5. **HRMS** (ESI) Calcd for $C_{21}H_{23}N_2O_5$ $[M-H]^-$ 383.1612, found 383.1606.

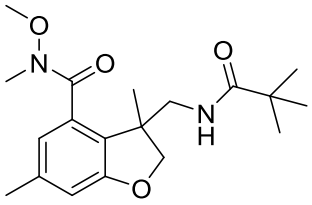
3-((2-naphthamido)methyl)-N-methoxy-N,3-dimethyl-2,3-dihydrobenzofuran-4-carboxamide (**4j**)



Colorless oil in 42% yield; **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 8.23 (s, 1H), 7.89 – 7.72 (m, 4H), 7.63 (s, 1H), 7.48 (tt, *J* = 7.0, 5.3 Hz, 2H), 7.20 (t, *J* = 7.8 Hz, 1H), 6.85 (d, *J* = 8.0 Hz, 2H), 4.57 (d, *J* = 8.9 Hz, 1H), 4.26 (d, *J* = 8.9 Hz, 1H), 4.09 (dd, *J* = 14.0, 7.9 Hz, 1H), 4.01 – 3.08 (m, 7H), 1.39 (s, 3H); **$^{13}$C NMR** (126 MHz, Chloroform-*d*) δ 167.8, 161.1, 134.7, 132.6, 131.7, 129.0 , 128.7, 128.2, 127.7, 127.6, 127.5, 126.5, 123.8, 118.4, 111.4, 81.6, 61.4, 48.4, 45.9, 32.6, 23.3. **HRMS** (ESI)

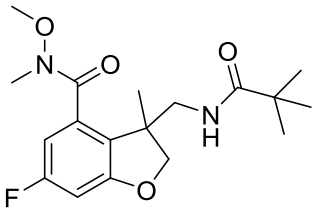
Calcd for $C_{24}H_{23}N_2O_4$ $[M-H]^-$ 403.1663, found 403.1653.

N-methoxy-N,3,6-trimethyl-3-(pivalamidomethyl)-2,3-dihydrobenzofuran-4-carboxa mide (**4k**)



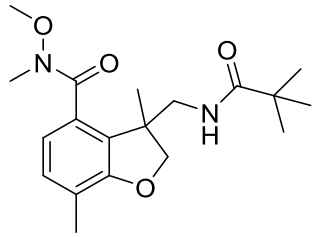
White solid in 79% yield; **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 6.61 (s, 1H), 6.57 (s, 1H), 4.39 (d, *J* = 8.9 Hz, 1H), 4.10 (d, *J* = 8.9 Hz, 1H), 3.82 (dd, *J* = 13.9, 8.7 Hz, 1H), 3.58 (s, 3H), 3.27 (s, 3H), 3.04 (m, 1H), 2.28 (s, 3H), 1.24 (s, 3H), 1.03 (s, 9H); **$^{13}$C NMR** (151 MHz, Chloroform-*d*) δ 178.8, 171.0, 161.3, 138.9, 131.3, 125.2, 118.7, 111.6, 81.5, 61.2, 48.1, 45.0, 38.6, 32.4, 27.3, 23.8, 21.3; **HRMS** (ESI) Calcd for $C_{19}H_{29}N_2O_4$ $[M+H]^+$ 349.2122, found 349.2122.

6-fluoro-N-methoxy-N,3-dimethyl-3-(pivalamidomethyl)-2,3-dihydrobenzofuran-4-ca rboxamide(**4l**)



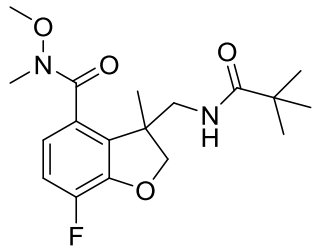
White solid in 72% yield; **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 6.52 (ddd, *J* = 9.7, 5.8, 3.9 Hz, 2H), 6.44 (m, 1H), 4.52 (d, *J* = 9.0 Hz, 1H), 4.19 (d, *J* = 9.0 Hz, 1H), 3.87 (dd, *J* = 14.0, 8.8, Hz, 1H), 3.60 (s, 3H), 3.32 (s, 3H), 3.03 (d, *J* = 14.0 Hz, 1H), 1.28 (s, 3H), 1.04 (s, 9H); **$^{13}$C NMR** (126 MHz, Chloroform-*d*) δ 178.4, 169.2, 162.1(d, $J_{C-F}$ = 204.8 Hz), 161.3, 131.8, 123.7, 104.5(d, $J_{C-F}$ = 25.2 Hz) , 98.8(d), 82.1, 61.0, 47.7, 44.6, 38.2, 32.0, 26.9, 23.4; **$^{19}$F NMR** (471 MHz, Chloroform-*d*) δ -112.5. **HRMS** (ESI) Calcd for $C_{18}H_{26}FN_2O_4$ $[M+H]^+$ 353.1871, found 353.1876.

N-methoxy-N,3,7-trimethyl-3-(pivalamidomethyl)-2,3-dihydrobenzofuran-4-carboxa mide (**4m**)



20 mol% AgOAc was added and this reaction was carried out at 90 $^{o}$C. White solid in 47% yield; **$^{1}$H NMR** (400 MHz, Chloroform-*d*) δ 6.96 (d, *J* = 7.7Hz, 1H), 6.68 (d, *J* = 7.7 Hz, 1H), 6.48 (dd, *J* = 8.7, 4.1 Hz, 1H), 4.44 (d, *J* = 8.9 Hz, 1H), 4.11 (d, *J* = 8.9 Hz, 1H), 3.83 (dd, *J* = 13.8, 8.7 Hz, 1H), 3.61 (s, 3H), 3.26 (s, 3H), 3.08 (dd, *J* = 13.9, 4.1 Hz, 1H), 2.16 (s, 3H), 1.26 (s, 3H), 0.99 (s, 9H); **$^{13}$C NMR** (151 MHz, Chloroform-*d*) δ 178.3, 158.9, 129.2, 128.5, 127.0, 121.1, 117.7, 80.9, 60.7, 48.2, 45.1, 38.1, 32.2, 26.9, 23.0, 14.7; **HRMS** (ESI) Calcd for $C_{19}H_{29}N_2O_4$ $[M+H]^+$ 349.2122, found 349.2122.

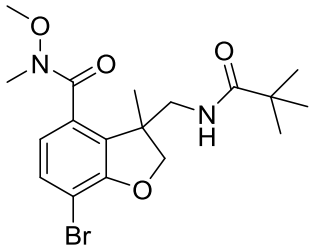
7-fluoro-N-methoxy-N,3-dimethyl-3-(pivalamidomethyl)-2,3-dihydrobenzofuran-4-ca rboxamide (**4n**)



20 mol% AgOAc was added and this reaction was carried out at 90 $^{o}$C. White solid in 69% yield; **$^{1}$H NMR** (400 MHz, Chloroform-*d*) δ 6.98 (dd, *J* = 10.0, 8.4 Hz, 1H), 6.76 (dd, *J* = 8.4, 4.1 Hz, 1H), 6.53 (dd, *J* = 8.8, 4.2 Hz, 1H), 4.57 (d, *J* = 9.0 Hz, 1H), 4.25 (d, *J* = 9.0 Hz, 1H), 3.90 (dd, *J* = 14.1, 8.8 Hz, 1H), 3.61 (s, 3H), 3.30 (s, 3H), 3.09 (dd, *J* = 14.1, 4.2 Hz, 1H), 1.31 (s, 3H), 1.04 (s, 9H); **$^{13}$C NMR** (151 MHz, Chloroform-*d*) δ 178.5, 147.7 (d, $J_{C-F}$ = 208.7 Hz), 147.4, 132.1, 126.8, 123.2 (d, $J_{C-F}$ = 61.1 Hz), 118.5, 115.3, 82.3, 60.8, 49.1, 44.4, 38.2, 31.2, 26.9, 23.2; **$^{19}$F NMR** (471

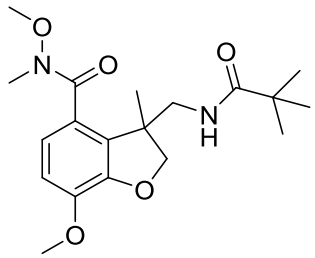
MHz, Chloroform-*d*) δ -136.8. **HRMS** (ESI) Calcd for $C_{18}H_{26}FN_2O_4$ $[M+H]^+$353.1871, found 353.1879.

7-bromo-N-methoxy-N,3-dimethyl-3-(pivalamidomethyl)-2,3-dihydrobenzofuran-4-carboxamide (**4o**)




Yellow solid in 78% yield; **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.33 (d, *J* = 8.1 Hz, 1H), 6.68 (d, *J* = 8.1 Hz, 1H), 6.39 (m, 1H), 4.55 (d, *J* = 9.0 Hz, 1H), 4.22 (d, *J* = 9.0 Hz, 1H), 3.87 (dd, *J* = 14.0, 8.8 Hz, 1H), 3.54 (s, 3H), 3.29 (s, 3H), 3.06 (d, *J* = 14.0 Hz, 1H), 1.28 (s, 3H), 1.02 (s, 9H); **$^{13}$C NMR** (151 MHz, Chloroform-d) δ 178.9, 169.9, 158.2, 131.6, 130.9, 129.8, 119.4, 104.2, 81.7, 61.4, 49.8, 45.2, 38.6, 32.5, 27.3, 23.4; **HRMS** (ESI) Calcd for $C_{18}H_{26}B_rN_2O_4$ $[M+H]^+$ 413.1070, found 413.1072.

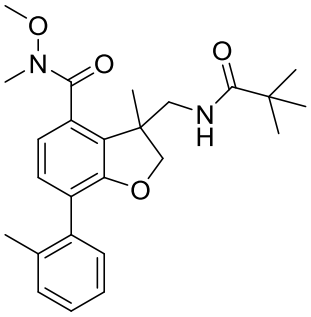
N,7-dimethoxy-N,3-dimethyl-3-(pivalamidomethyl)-2,3-dihydrobenzofuran-4-carboxamide (**4p**)




White solid in 63% yield; **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 6.82 – 6.72 (m, 2H), 6.64 (m, 1H), 4.47 (d, *J* = 9.0 Hz, 1H), 4.19 (d, *J* = 9.0 Hz, 1H), 3.86 (m, 4H), 3.62 (s, 3H), 3.27 (s, 3H), 3.11 (dd, *J* = 13.9, 4.1 Hz, 1H), 1.27 (s, 3H), 1.02 (s, 9H); **$^{13}$C NMR** (126 MHz, Chloroform-*d*) δ 178.4, 148.9, 145.2, 129.5, 123.1, 119.1, 110.6,

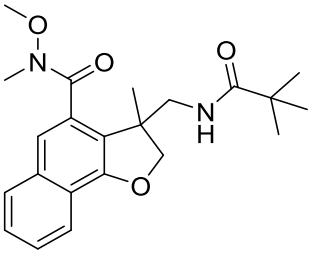
81.6, 60.7, 55.5, 48.8, 44.4, 38.2, 26.9, 23.3; **HRMS** (ESI) Calcd for $C_{19}H_{29}N_2O_5$ $[M+H]^+$ 365.1998, found 365.2014.

N-methoxy-N,3-dimethyl-3-(pivalamidomethyl)-7-(o-tolyl)-2,3-dihydrobenzofuran-4-carboxamide (**4q**)



White solid in 87% yield; **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.24 – 7.19 (m, 4H), 7.10 (d, *J* = 7.7 Hz, 1H), 6.87 (d, *J* = 7.7 Hz, 1H), 4.43 (d, *J* = 9.0 Hz, 1H), 4.17 (d, *J* = 9.0 Hz, 1H), 3.91 (dd, *J* = 14.0, 8.7 Hz, 1H),3.69 (s, 3H), 3.35 (s, 3H), 3.12 (d, *J* = 14.0 Hz, 1H), 2.18 (s, 3H), 1.34 (s, 3H), 1.06 (s, 9H); **$^{13}$C NMR** (126 MHz, Chloroform-*d*) δ 178.8, 158.2, 136.4, 130.7, 130.1, 129.8, 127.9, 125.7, 118.2, 81.2, 61.3, 48.8, 44.8, 38.6, 27.4, 24.3, 19.9; **HRMS** (ESI) Calcd for $C_{25}H_{33}N_2O_4$ $[M+H]^+$ 425.2435, found 425.2440.

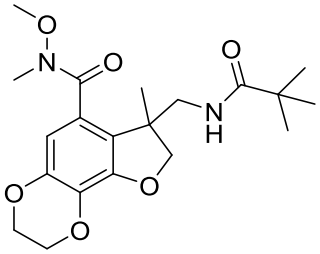
N-methoxy-N,3-dimethyl-3-(pivalamidomethyl)-2,3-dihydronaphtho[1,2-b]furan-4-carboxamide (**4r**)



Yellow solid in 83% yield; **$^1$H NMR** (400 MHz, Chloroform-d) δ 8.01 – 7.93 (m, 1H), 7.85 – 7.76 (m, 1H), 7.53 – 7.44 (m, 2H), 7.33 (s, 1H), 6.47 (m, 1H), 4.69 (d, J = 8.9 Hz, 1H), 4.36 (dd, J = 8.9, 1.2 Hz, 1H), 3.97 (dd, J = 14.0, 9.0 Hz, 1H), 3.65 (s, 3H), 3.35 (s, 3H), 3.16 (dd, J = 13.8, 3.9 Hz, 1H), 1.36 (s, 3H), 0.95 (s, 9H); **$^{13}$C NMR** (126 MHz, Chloroform-d) δ 178.9, 157.1, 133.4, 129.3, 127.9, 126.9, 126.4,

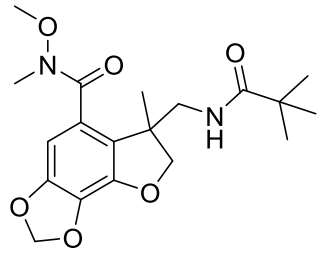
121.8, 121.0, 120.8, 117.8, 82.3, 61.3, 49.5, 45.4, 45.2, 38.6, 27.3, 24.1; **HRMS** (ESI) Calcd for $C_{22}H2_{29}\ N_2O_4$ $[M+H]^+$ 385.2122, found 385.2129.

N-methoxy-N,7-dimethyl-7-(pivalamidomethyl)-2,3,7,8-tetrahydro-[1,4]dioxino[2,3-g ]benzofuran-6-carboxamide (**4s**)



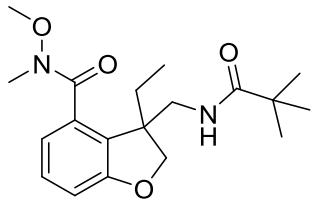
White solid in 86% yield; **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 6.66 (s, 1H), 6.37 (s, 1H), 4.48 (d, *J* = 8.9 Hz, 1H), 4.33 – 4.23 (m, 4H), 4.20 (d, *J* = 8.9 Hz, 1H), 3.82 (dd, *J* = 13.9, 8.6 Hz, 1H), 3.65 (s, 3H), 3.26 (s, 3H), 3.06 (dd, *J* = 13.9, 4.2 Hz, 1H), 1.24 (s, 3H), 1.05 (s, 9H);**$^{13}$C NMR** (151 MHz, Chloroform-*d*) δ 178.5, 148.8, 143.1, 129.9，129.4, 122.4, 121.8, 107.2, 82.6, 64.0, 64.0, 60.7, 50.2, 48.4, 44.5, 38.2, 26.9, 23.3; **HRMS** (ESI) Calcd for $C_{20}H_{29}N_2O_6$ $[M+H]^+$ 393.2020, found 393.2030.

N-methoxy-N,6-dimethyl-6-(pivalamidomethyl)-6,7-dihydro-[1,3]dioxolo[4,5-g]benz ofuran-5-carboxamide (**4t**)



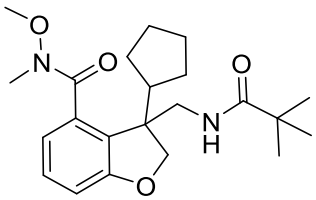
White solid in 74% yield; **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 6.63 (s, 1H), 6.35 (s, 1H), 5.96 (q, *J* = 1.4 Hz, 2H), 4.48 (d, *J* = 8.9 Hz, 1H), 4.19 (d, *J* = 8.9 Hz, 1H), 3.83 (dd, *J* = 14.0, 8.7 Hz, 1H), 3.64 (s, 3H), 3.26 (s, 3H), 3.06 (dd, *J* = 14.0, 4.2 Hz, 1H), 1.25 (s, 3H), 1.05 (s, 9H); **$^{13}$C NMR** (151 MHz, Chloroform-*d*) δ 178.5, 148.4, 142.9, 130.8, 125.3, 123.5, 101.6, 99.1, 82.8, 60.8, 48.2, 44.4, 38.2, 27.0, 23.2; **HRMS** (ESI) Calcd for $C_{19}H_{27}N_2O_6$ $[M+H]^+$ 379.1864, found 379.1871.

3-ethyl-N-methoxy-N-methyl-3-(pivalamidomethyl)-2,3-dihydrobenzofuran-4-carbox amide (**4u**)



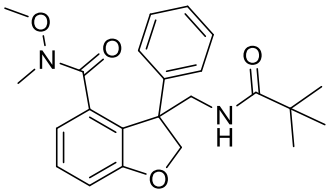
Colorless oil in 73% yield; **$^{1}$H NMR** (400 MHz, Chloroform-*d*) δ 7.17 (t, *J* = 7.8 Hz, 1H), 6.79 (t, *J* = 9.2 Hz, 2H), 6.53 (m, 1H),4.40 (d, *J* = 9.2 Hz, 1H), 4.32 (d, *J* = 9.2 Hz, 1H), 3.95 (dd, *J* = 13.9, 9.2 Hz, 1H), 3.67 – 2.89 (m, 7H), 1.59 (q, *J* = 7.4 Hz, 2H), 0.99 (s, 9H), 0.79 (t, *J* = 7.4 Hz, 3H); **$^{13}$C NMR** (126 MHz, Chloroform-*d*) δ 178.8, 161.8, 131.9, 128.7, 126.5, 118.0, 110.8, 78.5, 61.2, 53.1, 44.1, 38.6, 30.5, 27.3, 8.4; **HRMS** (ESI) Calcd for $C_{19}H_{29}N_2O_4$ $[M+H]^+$ 349.2122, found 349.2116.

3-cyclopentyl-N-methoxy-N-methyl-3-(pivalamidomethyl)-2,3-dihydrobenzofuran-4-carboxamide (**4v**)



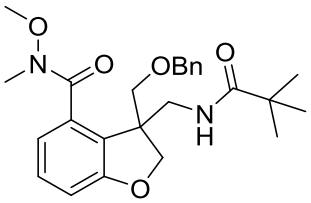
Colorless oil in 54% yield; **$^{1}$H NMR** (400 MHz, Chloroform-*d*) δ 7.16 (t, *J* = 7.8 Hz, 1H), 6.84 – 6.74 (m, 2H), 6.54 (s, 1H), 4.42 (d, *J* = 8.4 Hz, 2H), 4.02 (dd, *J* = 13.8, 9.5 Hz, 1H), 3.73 – 2.85 (m, 7H), 2.10 (m, 1H), 1.69 – 1.10 (m, 8H), 0.97 (s, 9H); **$^{13}$C NMR** (126 MHz, Chloroform-*d*) δ 178.7, 161.7, 128.5, 117.8, 110.7, 75.7, 61.2, 55.7, 47.1, 44.7, 38.6, 32.6, 28.1, 27.5, 27.3, 25.7, 24.9; **HRMS** (ESI) Calcd for $C_{22}H_{33}N_2O_4$ $[M+H]^+$ 389.2435, found 389.2438.

3-cyclopentyl-N-methoxy-N-methyl-3-(pivalamidomethyl)-2,3-dihydrobenzofuran-4-carboxamide (**4w**)



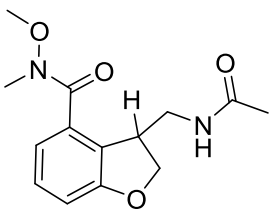
Yellow oil in 63% yield; **$^{1}$H NMR** (400 MHz, Chloroform-*d*) δ 7.38 – 7.16 (m, 6H), 6.95 – 6.70 (m, 3H), 4.73 (s, 1H), 4.49 (d, *J* = 9.1 Hz, 1H), 4.35 (s, 1H), 3.86 (dd, *J* = 13.5, 4.2 Hz, 1H), 3.36 (s, 3H), 2.77 (d, *J* = 78.6 Hz, 3H), 1.05 (s, 9H).; **$^{13}$C NMR** (126 MHz, Chloroform-*d*) δ 179.3, 161.8, 158.8, 142.7, 138.2, 132.1, 129.6, 128.5, 127.1, 126.7, 126.0, 118.8, 115.1, 111.5, 84.4, 70.0, 60.4, 55.8, 43.9, 38.7, 27.4; **HRMS** (ESI) Calcd for $C_{23}H_{29}N_2O_4$ $[M+H]^+$ 397.2122, found 397.2119.

3-((benzyloxy)methyl)-N-methoxy-N-methyl-3-(pivalamidomethyl)-2,3-dihydrobenz ofuran-4-carboxamide (**4x**)



Yellow oil in 82% yield; **$^{1}$H NMR** (400 MHz, Chloroform-d) δ 7.49 – 7.04 (m, 6H), 6.94 – 6.65 (m, 2H), 4.53 – 4.46 (m, 3H), 4.37 (d, J = 9.2 Hz, 1H), 4.02 – 3.02 (m, 10H), 0.97 (s, 9H); **$^{13}$C NMR** (126 MHz, Chloroform-*d*) δ 178.8, 161.7, 137.7, 132.4, 129.0, 128.4, 127.8, 125.1, 118.4, 111.3, 77.6, 74.2, 73.6, 61.0, 53.2, 42.4, 38.6, 27.3; **HRMS** (ESI) Calcd for $C_{25}H_{33}N_2O_5$ $[M+H]^+$ 441.2384, found 441.2384.

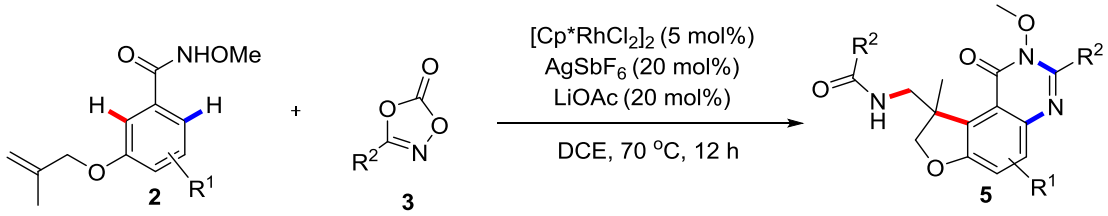
3-(acetamidomethyl)-N-methoxy-N-methyl-2,3-dihydrobenzofuran-4-carboxamide (**4y**)



Colorless oil in 40% yield; **$^{1}$H NMR** (400 MHz, Chloroform-*d*) δ 7.19 (t, *J* = 7.8 Hz, 1H), 6.92 (d, *J* = 7.6 Hz, 1H), 6.86 (d, *J* = 8.0 Hz, 1H), 6.25 (s, 1H), 4.56 (t, *J* =

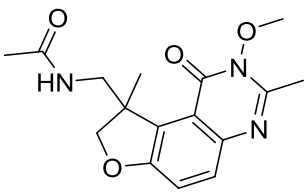
8.9 Hz, 1H), 4.38 (dd, *J* = 9.2, 4.6 Hz, 1H), 3.72 (dd, *J* = 9.1, 5.0 Hz, 1H), 3.55 (s, 3H), 3.45 (t, *J* = 5.6 Hz, 2H), 3.32 (s, 3H), 1.92 (s, 3H); **$^{13}$C NMR** (126 MHz, Chloroform-*d*) δ 171.1, 160.2, 131.1, 129.5, 128.6, 125.7, 118.7, 111.2, 75.0, 61.0, 42.0, 41.5, 26.8, 22.6; **HRMS** (ESI) Calcd for $C_{14}H_{19}N_2O_4$ $[M+H]^+$ 279.1339, found 279.1340.

Unless otherwise stated, reactions were performed in accordance with the conditions shown in **table S2** of **entry 8** to synthesis product (**5a** – **5t**):



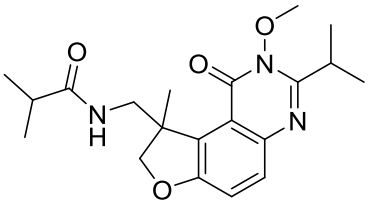

To an oven-dried 15 mL Schlenk tube equipped with a stir bar were added Substrate **2** (0.1 mmol), **3** (0.30 mmol), $[Cp^*RhCl_2]_2$ (5 mol %), $AgSbF_6$ (20 mol %), LiOAc (20 mol %) and DCE (1mL). The tube was sealed and the reaction was stirred for 12 h at 70 ℃. The reaction mixture was cooled to room temperature and diluted with $CH_2Cl_2$ (5 mL) and filtered through a short pad silica gel washing with $CH_2Cl_2$ (20 mL). The filtrate was concentrated and then purified by column chromatography on silica gel (DCM/MeOH) to yield the desired product. Some of the product compounds (**5h, 5i, 5j, 5k, 5m, 5o**) specially noted were further purified by C18 reverse phase preparative HPLC column(Agilent ZORBAX SB-C18 reversed-phase column (250 mm × 4.60 mm, 5 μm) with $H_2O$ (containing 0.1% TFA) and MeCN (containing 0.1% TFA) as eluents and they were obtained as a TFA salt. Conditions were as follows: flow rate = 18 mL/min, $CH_3CN/H_2O$ eluent (containing 0.1% trifluoroacetic acid); gradient, 20 % $CH_3CN$ to 60 % $CH_3CN$; 20 min; monitored by UV absorption at 210 and 254 nm.

N-((2-methoxy-3,9-dimethyl-1-oxo-1,2,8,9-tetrahydrofuro[3,2-f]quinazolin-9-yl)methyl)acetamide (**5a**)



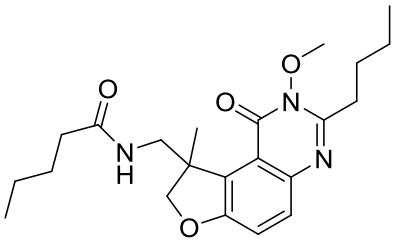
White solid in 93% yield; **$^{1}$H NMR** (400 MHz, Chloroform-*d*) δ 7.15 (d, *J* = 8.8 Hz, 1H), 7.03 (d, *J* = 8.8 Hz, 1H), 6.69 (dd, J = 8.2, 4.3 Hz, 1H), 4.57 (d, *J* = 9.0 Hz, 1H), 4.19 (d, *J* = 9.0 Hz, 1H), 4.01 (s, 3H), 3.93 (dd, *J* = 13.8, 4.3 Hz, 1H), 3.80 (dd, *J* = 13.8, 8.2 Hz, 1H), 2.46 (s, 3H), 1.82 (s, 3H), 1.47 (s, 3H); **$^{13}$C NMR** (126 MHz, Chloroform-*d*) δ 170.3, 159.5, 156.1, 149.6, 141.6, 128.4, 128.2, 119.9, 117.6, 82.1, 63.5, 49.0, 45.1, 23.6, 22.6, 18.7; **HRMS** (ESI) Calcd for $C_{16}H_{20}N_3O_4$ $[M+H]^+$ 318.1448, found 318.1455.

N-((3-isopropyl-2-methoxy-9-methyl-1-oxo-1,2,8,9-tetrahydrofuro[3,2-f]quinazolin-9-yl)methyl)isobutyramide (**5b**)



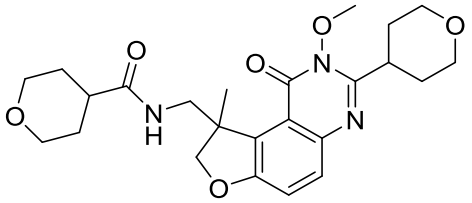
White solid in 63% yield; **$^{1}$H NMR** (400 MHz, Chloroform-*d*) δ 7.55 (d, *J* = 8.8 Hz, 1H), 7.19 (d, *J* = 8.8 Hz, 1H), 5.69 (dd, *J* = 7.9, 4.9 Hz,, 1H), 4.60 (d, *J* = 9 .0 Hz, 1H), 4.23 (d, *J* = 9.0 Hz, 1H), 4.07 (s, 3H), 3.89 (dd, *J* = 13.7, 4.9 Hz, 1H), 3.80 (dd, *J* = 13.7, 7.9 Hz, 1H), 3.27 (h, *J* = 6.8 Hz, 1H), 2.14 (h, *J* = 6.9 Hz, 1H), 1.55 (s, 3H), 1.33 (dd, *J* = 6.8, 2.6 Hz, 6H), 0.97 (dd, *J* = 9.8, 6.9 Hz, 6H); **$^{13}$C NMR** (126 MHz, Chloroform-*d*) δ 176.9, 159.5, 156.7,156.4, 142.3, 129.6, 127.8, 119.8, 117.5, 82.6, 64.0, 49.0, 45.3, 35.2, 29.6, 23.3, 20.2, 19.3, 18.9; **HRMS** (ESI) Calcd for $C_{20}H_{28}N_3O_4$ $[M+H]^+$ 374.2074, found 374.2079.

N-((3-butyl-2-methoxy-9-methyl-1-oxo-1,2,8,9-tetrahydrofuro[3,2-f]quinazolin-9-yl)methyl)pentanamide (**5c**)



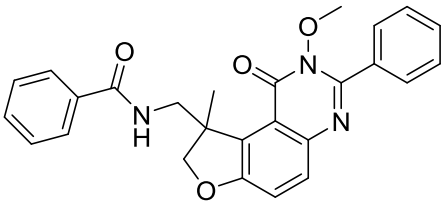
White solid in 78% yield; **$^{1}$H NMR** (400 MHz, Chloroform-*d*) δ 7.50 (d, *J* = 8.8 Hz, 1H), 7.18 (d, *J* = 8.8 Hz, 1H), 4.61 (d, *J* = 9.0 Hz, 1H), 4.23 (d, *J* = 9.0 Hz, 1H), 4.07 (s, 3H), 3.91 (d, *J* = 13.7 Hz, 1H), 3.80 (d, *J* = 13.7 Hz, 1H), 2.85 – 2.71 (m, 2H), 2.00 (m,2H), 1.87 – 1.71 (m, 2H), 1.54 (s, 3H), 1.44 (m, 4H), 1.21 – 1.14 (m, 2H), 0.95 (t, *J* = 7.3 Hz, 3H), 0.78 (t, *J* = 7.3 Hz, 3H); **$^{13}$C NMR** (126 MHz, Chloroform-*d*) δ 173.0, 159.5, 156.5, 152.5, 142.2, 129.3, 128.0, 119.8, 117.6, 82.5, 63.7, 49.0, 45.3, 36.0, 31.5, 28.3, 27.4, 23.4, 22.0, 21.7, 13.4, 13.3; **HRMS** (ESI) Calcd for $C_{22}H_{32}N_3O_4$ $[M+H]^+$ 402.2387, found 402.2392.

N-((2-methoxy-9-methyl-1-oxo-3-(tetrahydro-2H-pyran-4-yl)-1,2,8,9-tetrahydrofuro[3,2-f]quinazolin-9-yl)methyl)tetrahydro-2H-pyran-4-carboxamide (**5d**)



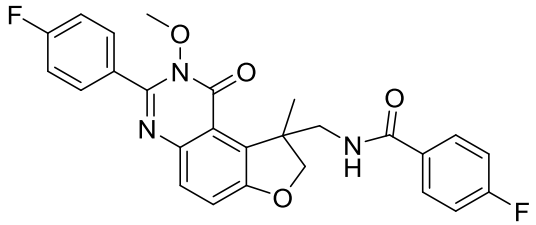
White solid in 47% yield; **$^{1}$H NMR** (400 MHz, Chloroform-*d*) δ 7.63 (d, *J* = 8.7 Hz, 1H), 7.28 (m, 1H), 6.01 (t, *J* = 6.3 Hz, 1H), 4.62 (d, *J* = 9.1 Hz, 1H), 4.30 (d, *J* = 9.1 Hz, 1H), 4.15 (m, 5H), 4.02 – 3.91 (m, 3H), 3.82 (dd, *J* = 13.7, 7.5 Hz, 1H), 3.61 (td, *J* = 11.8, 2.2 Hz, 2H), 3.42 – 3.27 (m, 2H), 3.23 (m, 1H), 2.32 – 2.18 (m, 1H), 2.17 – 2.01 (m, 2H), 1.92 (t, *J* = 13.7 Hz, 2H), 1.62 (m, 7H); **$^{13}$C NMR** (126 MHz, Chloroform-*d*) δ 174.9, 159.7, 156.7, 153.7, 142.2, 129.9, 127.7, 119.8, 117.8, 82.7, 67.1, 66.7, 64.2, 48.8, 45.9, 41.8, 36.7, 29.9, 28.8, 28.6, 23.1; **HRMS** (ESI) Calcd for $C_{24}H_{32}N_3O_6$ $[M+H]^+$ 458.2286, found 458.2287.

N-((2-methoxy-9-methyl-1-oxo-3-phenyl-1,2,8,9-tetrahydrofuro[3,2-f]quinazolin-9-yl)methyl)benzamide (**5e**)



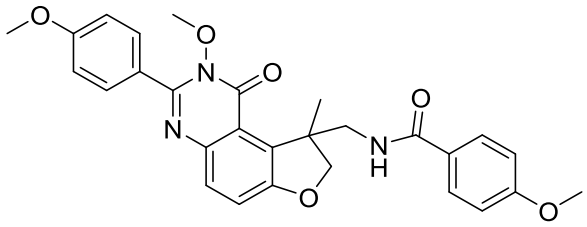
White solid in 40% yield; **$^{1}$H NMR** (400 MHz, Chloroform-*d*) δ 7.89 – 7.83 (m, 2H), 7.76 (d, *J* = 8.8 Hz, 1H), 7.65 – 7.61 (m, 2H), 7.59 – 7.50 (m, 3H), 7.49 – 7.45 (m, 1H), 7.39 – 7.34 (m, 3H), 7.19 (m, 1H), 4.76 (d, *J* = 9.2 Hz, 1H), 4.40 (d, *J* = 9.2 Hz, 1H), 4.20 (dd, *J* = 13.8, 5.3Hz, 1H), 3.98 (dd, *J* = 13.8, 6.7 Hz, 1H), 3.72 (s, 3H), 1.74 (s, 3H); **$^{13}$C NMR** (150 MHz, Chloroform-*d*) δ 169.2, 160.5, 156.6, 150.6, 140.8, 133.3, 131.5, 131.0, 129.6, 129.2, 128.9, 128.5，128.2, 128.0, 126.5, 119.6，118.7, 83.0, 63.8, 48.6, 47.3, 22.7; **HRMS** (ESI) Calcd for $C_{26}H_{24}N_3O_4$ $[M+H]^+$ 442.1761, found 442.1768.

4-fluoro-N-((3-(4-fluorophenyl)-2-methoxy-9-methyl-1-oxo-1,2,8,9-tetrahydrofuro[3,2-f]quinazolin-9-yl)methyl)benzamide (**5f**)



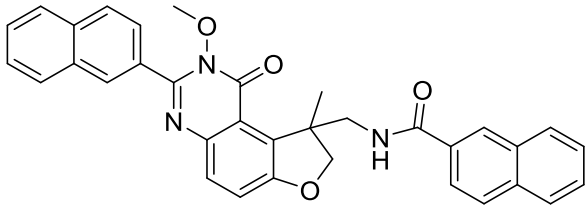
Yellow oil in 37% yield; **$^{1}$H NMR** (400 MHz, Chloroform-*d*) δ 7.97 – 7.89 (m, 2H), 7.72 – 7.63 (m, 3H), 7.31 (d, *J* = 8.8 Hz, 1H), 7.20 (t, *J* = 8.6 Hz, 2H), 7.02 (t, *J* = 8.6 Hz, 2H), 6.94 – 6.87 (m, 1H), 4.73 (d, *J* = 9.0 Hz, 1H), 4.36 (d, *J* = 9.0 Hz, 1H), 4.13 – 3.95 (m, 2H), 3.74 (s, 3H), 1.71 (s, 3H); **$^{13}$C NMR** (125 MHz, Chloroform-*d*) δ 167.0, 164.6 (d, $J_{C\text{-}F}$ = 251.7 Hz), 164.2 (d, $J_{C\text{-}F}$ = 252.2 Hz), 160.6, 157.3, 148.9, 142.8, 131.7 (d, $J_{C\text{-}F}$ = 8.7 Hz), 130.9, 129.3(d, $J_{C\text{-}F}$ = 8.8 Hz), 128.9, 127.8 (d, $J_{C\text{-}F}$ = 3.4 Hz), 120.5, 118.7, 115.6 (d, $J_{C\text{-}F}$ = 21.6 Hz), 115.5(d, $J_{C\text{-}F}$ = 21.6 Hz), 83.5, 64.0, 49.2, 47.5, 23.3; **$^{19}$F NMR** (471 MHz, Chloroform-*d*) δ -108.5, -108.6. **HRMS** (ESI) Calcd for $C_{26}H_{20}F_2N_3O_4$ $[M-H]^-$ 476,1427, found 476.1419.

4-methoxy-N-((2-methoxy-3-(4-methoxyphenyl)-9-methyl-1-oxo-1,2,8,9-tetrahydrofuro[3,2-f]quinazolin-9-yl)methyl)benzamide (**5g**)



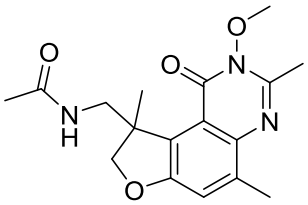
Colorless oil in 36 % yield; **$^{1}$H NMR** (400 MHz, Chloroform-*d*) δ 7.99 – 7.84 (m, 2H), 7.68 (d, *J* = 8.7 Hz, 1H), 7.61 (d, *J* = 8.8 Hz, 1H), 7.29 (d, *J* = 8.8 Hz, 1H), 7.01 (d, *J* = 8.9 Hz, 1H), 6.84 (d, *J* = 8.8 Hz, 1H), 6.73 (t, *J* = 6.1 Hz, 1H), 4.74 (d, *J* = 9.0 Hz, 1H), 4.35 (d, *J* = 9.0 Hz, 1H), 4.14 – 4.00 (m, 2H), 3.89 (s, 3H), 3.79 (s, 3H), 3.74 (s, 3H), 1.70 (s, 3H); **$^{13}$C NMR** (125 MHz, Chloroform-*d*) δ 167.5, 162.0, 161.6, 160.3, 157.4, 143.0, 131.2, 130.6, 128.8, 128.7, 124.0, 120.2, 118.5, 113.8, 113.6, 83.4, 63.8, 55.4, 55.4, 49.3, 47.1, 23.5; **HRMS** (ESI) Calcd for $C_{28}H_{26}N_3O_6$ $[M-H]^-$ 500.1827, found 500.1818.

N-((2-methoxy-9-methyl-3-(naphthalen-2-yl)-1-oxo-1,2,8,9-tetrahydrofuro[3,2-f]quinazolin-9-yl)methyl)-2-naphthamide (**5h**)



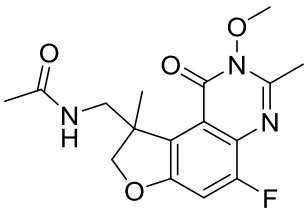
Colorless oil in 36 % yield;**$^{1}$H NMR** (400 MHz, Chloroform-*d*) δ 8.43 (s, 1H), 8.18 (s, 1H), 7.98 – 7.90 (m, 4H), 7.88 – 7.72 (m, 5H), 7.62 – 7.47 (m, 4H), 7.35 (d, *J* = 8.8 Hz, 1H), 7.09 (t, *J* = 5.5 Hz, 1H), 4.83 (d, *J* = 9.0 Hz, 1H), 4.42 (d, *J* = 9.0 Hz, 1H), 4.16 (m, 2H), 3.70 (s, 3H), 1.78 (s, 3H); **$^{13}$C NMR** (125 MHz, Chloroform-*d*) δ 168.3, 160.8, 134.8, 132.8, 132.7 132.1, 131.0, 130.0, 129.3, 129.1, 129.0, 129.0, 128.5, 128.1, 127.9, 127.8, 127.8, 127.7, 127.5, 126.8, 126.8, 126.0, 123.8, 118.8, 83.7, 64.2, 49.5, 47.6, 23.6; **HRMS** (ESI) Calcd for $C_{34}H_{28}N_3O_4$ $[M+H]^+$ 542.2074, found 542.2076.

N-((2-methoxy-3,5,9-trimethyl-1-oxo-1,2,8,9-tetrahydrofuro[3,2-f]quinazolin-9-yl)methyl)acetamide (**5i**)



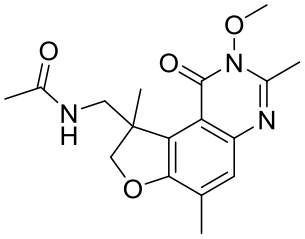
White solid in 65% yield; **$^{1}$H NMR** (400 MHz, Chloroform-*d*) δ 7.10 (d, *J* = 1.2 Hz, 1H), 5.89 (dd, *J* = 7.8, 4.6 Hz,, 1H)4.54 (d, *J* = 9.0 Hz, 1H), 4.21 (d, *J* = 9.0, 1H), 4.08 (s, 3H), 3.89 (dd, *J* = 13.6, 4.6 Hz, 1H), 3.78 (dd, *J* = 13.6, 7.8, 1H), 2.59 (d, *J* = 1.2Hz, 3H), 2.52 (s, 3H), 1.83 (s, 3H); **$^{13}$C NMR** (126 MHz, Chloroform-*d*) δ 170.1, 159.1, 156.8, 148.0, 140.7, 138.1, 125.2, 120.0, 118.3, 82.2, 63.4, 48.7, 45.8, 23.4, 22.8, 19.2, 17.9; **HRMS** (ESI) Calcd for $C_{17}H_{22}N_3O_4$ $[M+H]^+$ 332.1605, found 332.1603.

N-((5-fluoro-2-methoxy-3,9-dimethyl-1-oxo-1,2,8,9-tetrahydrofuro[3,2-f]quinazolin-9-yl)methyl)acetamide (**5j**)



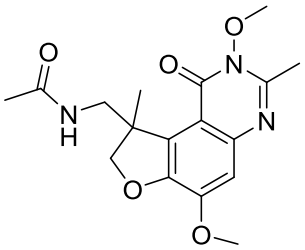
White solid in 82% yield; **$^{1}$H NMR** (400 MHz, Chloroform-*d*) δ 6.92 (d, *J* = 10.0 Hz, 1H), 6.32 (dd, *J* = 8.5, 4.5 Hz, 1H), 4.65 (d, *J* = 9.0 Hz, 1H), 4.27 (d, *J* = 9.0 Hz, 1H), 4.08 (s, 3H), 3.95 (dd, *J* = 13.8, 4.5 Hz, 1H), 3.85 (dd, *J* = 13.8, 8.5 Hz, 1H), 2.57 (s, 3H), 1.89 (s, 3H), 1.52 (s, 3H); **$^{13}$C NMR** (126 MHz, Chloroform-*d*) δ 170.5, 159.6 (d, J = 11.9 Hz), 157.1 (d, J = 255.3 Hz), 155.5, 150.2, 130.6 (d, J = 11.5 Hz), 123.7 (d, J = 4.0 Hz), 120.7, 104.2 (d, J = 23.2 Hz), 82.5, 63.6, 48.7, 45.1, 23.7, 22.7, 18.9; **$^{19}$F NMR** (471 MHz, Chloroform-*d*) δ -119.9; **HRMS** (ESI) Calcd for $C_{16}H_{19}FN_3O_4$ $[M+H]^+$ 336.1354, found 336.1353.

N-((2-methoxy-3,6,9-trimethyl-1-oxo-1,2,8,9-tetrahydrofuro[3,2-f]quinazolin-9-yl)methyl)acetamide (**5k**)



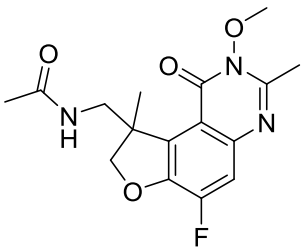
White solid in 45% yield; **$^{1}$H NMR** (400 MHz, Chloroform-*d*) δ 7.43 (s, 1H), 6.50 (dd, *J* = 7.3, 5.2 Hz, 1H), 4.61 (d, *J* = 9.2 Hz, 1H), 4.31 (d, *J* = 9.2 Hz, 1H), 4.14 (s, 3H), 4.02 (dd, *J* = 13.8, 5.2 Hz, 1H), 3.72 (dd, *J* = 13.8, 7.3 Hz, 1H), 2.71 (s, 3H), 2.33 (s, 3H), 1.90 (s, 3H), 1.57 (s, 3H); **$^{13}$C NMR** (126 MHz, Chloroform-*d*) δ 170.0, 158.5, 156.4, 149.5, 142.0, 129.3, 128.8, 126.9, 117.7, 82.1, 63.5, 49.0, 45.6, 45.4, 23.5, 22.8, 18.9, 15.7; **HRMS** (ESI) Calcd for $C_{17}H_{22}N_3O_4$ $[M+H]^+$ 332.1615, found 332.1613.

N-((2,6-dimethoxy-3,9-dimethyl-1-oxo-1,2,8,9-tetrahydrofuro[3,2-f]quinazolin-9-yl)methyl)acetamide (**5l**)



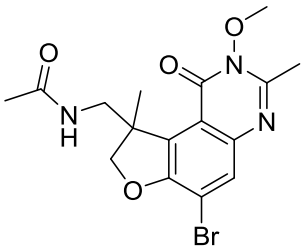
White solid in 80% yield; **$^{1}$H NMR** (400 MHz, Chloroform-*d*) δ 7.37 (s, 1H), 7.14 (m, 1H), 4.75 (d, *J* = 9.3 Hz, 1H), 4.39 (d, *J* = 9.3 Hz, 1H), 4.19 (m, 4H), 3.93 (s, 3H), 3.57 (dd, *J* = 14.2, 6.1 Hz, 1H), 2.86 (s, 3H), 1.87 (s, 3H), 1.59 (s, 3H); **$^{13}$C NMR** (151 MHz, Chloroform-*d*) δ 172.6, 159.3(q, *J* = 40 Hz, $CF_3COOH$), 155.2, 153.7, 151.1, 150.6, 136.1, 129.5, 114.8(q, *J* = 286.9 Hz, $CF_3COOH$), 111.6, 103.4, 82.7, 64.7, 56.2, 49.5, 45.5, 23.4, 21.7, 16.0; **HRMS** (ESI) Calcd for $C_{17}H_{22}N_3O_5$ $[M+H]^+$ 348.1554, found 348.1563.

N-((6-fluoro-2-methoxy-3,9-dimethyl-1-oxo-1,2,8,9-tetrahydrofuro[3,2-f]quinazolin-9-yl)methyl)acetamide (**5m**)



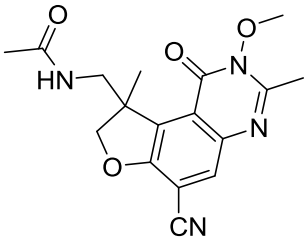
White solid in 92% yield; **$^{1}$H NMR** (400 MHz, Chloroform-*d*) δ 7.09 (d, *J* = 10.6 Hz, 1H), 6.34 – 6.18 (dd, *J* = 8.1, 4.8 Hz, 1H), 4.72 (d, *J* = 9.1 Hz, 1H), 4.35 (d, *J* = 9.1 Hz, 1H), 4.06 (s, 3H), 3.97 (dd, *J* = 13.9, 4.8 Hz, 1H), .82 (dd, *J* = 13.8, 8.1 Hz, 1H), 2.53 (s, 3H), 1.86 (s, 3H), 1.54 (s, 3H); **$^{13}$C NMR** (151 MHz, Chloroform-*d*) δ 173.7, 159.7(q, *J* = 40 Hz, $CF_3COOH$), 156.2, 153.2, 151.7(d, *J* = 262.0 Hz), 149.1(d, *J* = 10.6 Hz), 135.7(d, *J* = 10.6 Hz), 133.5, 115.6, (d, *J* = 61.9 Hz), 113.9, 109.9(d, *J* = 19.6 Hz), 83.3, 64.5, 49.7, 45.9, 22.8, 21.2, 16.3; **$^{19}$F NMR** (471 MHz, Chloroform-*d*) δ -125.7. **HRMS** (ESI) Calcd for $C_{16}H_{19}FN_3O_4$ $[M+H]^+$ 336.1354, found 336.1360.

N-((6-bromo-2-methoxy-3,9-dimethyl-1-oxo-1,2,8,9-tetrahydrofuro[3,2-f]quinazolin-9-yl)methyl)acetamide (**5n**)



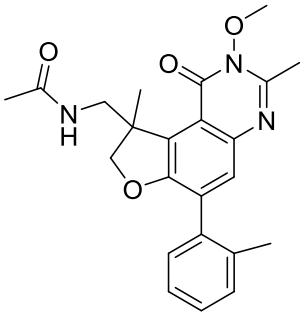
Yellow solid in 82% yield; **$^{1}$H NMR** (400 MHz, Chloroform-*d*) δ 7.90 (s, 1H), 7.29 (dd, *J* = 6.7 Hz, 6,3Hz,1H), 4.77 (d, *J* = 9.6 Hz, 1H), 4.42 (d, *J* = 9.6 Hz, 1H), 4.37 (dd, *J* = 14.0, 6.7 Hz, 1H), 4.17 (s, 3H), 3.43 (dd, *J* = 14.0, 6.3 Hz, 1H), 2.82 (s, 3H), 1.87 (s, 3H) , 1.62 (s, 3H); **$^{13}$C NMR** (151 MHz, Chloroform-*d*) δ 173.7, 159.7(q, *J* = 40 Hz, $CF_3COOH$), 158.2, 156.1, 154.1, 134.5, 130.2, 126.3, 118.0, 114.8(q, *J* = 286.9 Hz, $CF_3COOH$), 113.4, 82.2, 64.5, 50.3, 45.9, 23.0, 21.2, 16.3; **HRMS** (ESI) Calcd for $C_{16}H_{19}BrN_3O_4$ $[M+H]^+$ 396.0553, found 396.0553.

N-((6-cyano-2-methoxy-3,9-dimethyl-1-oxo-1,2,8,9-tetrahydrofuro[3,2-f]quinazolin-9-yl)methyl)acetamide (**5o**)



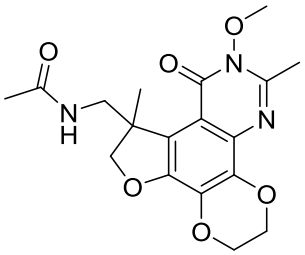
White solid in 44% yield; **$^{1}$H NMR** (400 MHz, Chloroform-*d*) δ 7.74 (s, 1H), 5.88 (dd, *J* = 7.5 Hz, 5.7 Hz, 1H), 4.79 (d, *J* = 9.2 Hz, 1H), 4.41 (d, *J* = 9.2 Hz, 1H), 4.10 (s, 3H), 4.06 (dd, *J* = 14.0, 5.7 Hz, 1H), 3.73 (dd, *J* = 13.9, 7.5 Hz, 1H), 2.58 (s, 3H), 1.85 (s, 3H), 1.57 (s, 3H); **$^{13}$C NMR** (126 MHz, Chloroform-*d*) δ 170.7, 160.1, 156.0, 151.8, 141.8, 132.9, 131.4, 124.2, 114.2, 101.7, 84.0, 64.1, 50.0, 45.6, 23.7, 23.2, 19.5; **HRMS** (ESI) Calcd for $C_{17}H_{19}N_4O_4$ $[M+H]^+$ 343.1401, found 343.1403.

N-((2-methoxy-3,9-dimethyl-1-oxo-6-(o-tolyl)-1,2,8,9-tetrahydrofuro[3,2-f]quinazolin-9-yl)methyl)acetamide (**5p**)



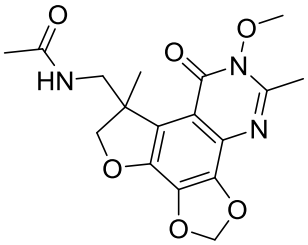
White solid in 47% yield; **$^{1}$H NMR** (400 MHz, Chloroform-*d*) δ 7.57 (s, 1H), 7.33 – 7.17 (m, 4H), 6.98 (dd, *J* = 5.9 Hz, 6.8Hz,1H), 4.64 (d, *J* = 9.3 Hz, 1H), 4.26 (d, *J* = 9.3 Hz, 1H), 4.18 (dd, *J* =13.8 Hz, 5.9 Hz, 1H), 4.15 (s, 3H), 3.59 (dd, *J* = 13.8, 6.8 Hz, 1H), 2.73 (s, 3H), 2.16 (s, 3H), 1.84 (s, 3H), 1.63 (s, 3H); **$^{13}$C NMR** (151 MHz, Chloroform-*d*) δ 172.2, 159.7(q, *J* = 40 Hz, $CF_3COOH$), 158.1, 155.1, 153.4, 137.1, 135.7, 134.2, 133.3, 129.8, 129.1, 129.0, 128.4, 126.1, 125.5, 118.2, 115.0(q, *J* = 286.9 Hz, $CF_3COOH$), 82.2, 64.2, 48.9, 46.2, 23.0, 21.8, 19.2, 17.1; **HRMS** (ESI) Calcd for $C_{23}H_{26}N_3O_4$ $[M+H]^+$ 408.1918, found 408.1925.

N-((3-methoxy-2,5-dimethyl-4-oxo-3,4,5,6,9,10-hexahydro-[1,4]dioxino[2,3-h]furo[3,2-f]quinazolin-5-yl)methyl)acetamide (**5q**)



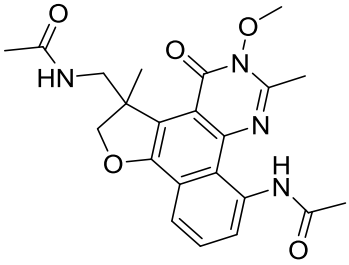
White solid in 85% yield; **$^{1}$H NMR** (400 MHz, Chloroform-*d*) δ 4.65 (d, *J* = 9.0 Hz, 1H), 4.49 – 4.37 (m, 4H), 4.34 (d, *J* = 9.0 Hz, 1H), 4.08 (s, 3H), 3.95 (d, *J* = 13.7 Hz, 1H), 3.84 (d, *J* = 13.8 Hz, 1H), 2.62 (s, 3H), 1.90 (s, 3H), 1.53 (s, 3H); **$^{13}$C NMR** (126 MHz, Chloroform-*d*) δ 170.1, 156.0, 150.0, 148.8, 137.7, 134.0, 133.0, 120.3, 112.8, 83.0, 64.2, 64.2, 63.6, 49.1, 45.3, 23.9, 22.8, 19.2; **HRMS** (ESI) Calcd for $C_{18}H_{22}N_3O_6$ $[M+H]^+$ 376.1503, found 376.1496.

N-((6-methoxy-5,8-dimethyl-7-oxo-6,7,8,9-tetrahydro-[1,3]dioxolo[4,5-h]furo[3,2-f]quinazolin-8-yl)methyl)acetamide (**5r**)



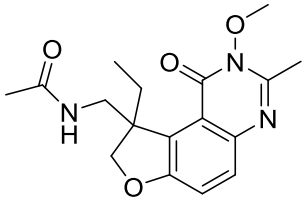
White solid in 90% yield; **$^{1}$H NMR** (400 MHz, Chloroform-*d*) δ 7.50 (dd,8.2 Hz, 4.5 Hz,1H), 6.21 (d, *J* = 1.3 Hz, 1H), 6.15 (d, *J* = 1.3 Hz, 1H), 4.67 (d, *J* = 9.3 Hz, 1H), 4.39 (d, *J* = 9.3 Hz, 1H), 4.18 (dd, *J* = 13.9, 4.5 Hz, 1H), 4.09 (s, 3H), 3.79 (dd, *J* = 13.9, 8.2 Hz, 1H), 2.62 (s, 3H), 2.04 (s, 3H), 1.54 (s, 3H); **$^{13}$C NMR** (151 MHz, Chloroform-*d*) δ 173.9, 159.2(q, *J* = 40 Hz, $CF_3COOH$), 154.9, 152.8, 144.1, 141.5, 136.2, 126.4, 123.6, 114.6(q, *J* = 286.9 Hz, $CF_3COOH$), 112.9, 104.0, 83.3, 64.1, 48.9, 45.7, 23.6, 21.5, 17.5; **HRMS** (ESI) Calcd for $C_{17}H_{20}N_3O_6$ $[M+H]^+$ 362.1347, found 362.1352.

N-((11-acetamido-3-methoxy-2,5-dimethyl-4-oxo-3,4,5,6-tetrahydrobenzo[h]furo[3,2-f]quinazolin-5-yl)methyl)acetamide (**5s**)



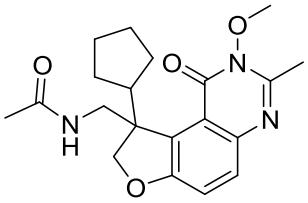
Yellow solid in 65 % yield; **$^{1}$H NMR** (400 MHz, Chloroform-*d*) δ 13.99 (s, 1H), 8.80 (d, *J* = 8.0 Hz, 1H), 7.79 (d, *J* = 8.0, 1.3 Hz, 1H), 7.62 (t, *J* = 8.0 Hz, 1H), 6.65 (dd, *J* = 7.5, 5.2 Hz, 1H), 4.74 (d, *J* = 9.1 Hz, 1H), 4.44 (d, *J* = 9.1 Hz, 1H), 4.22 (s, 3H), 4.17 (dd, *J* = 14.1, 5.2 Hz, 1H), 3.79 (dd, *J* = 14,1, 7.5 Hz, 1H), 2.70 (s, 3H), 2.13 (s, 3H), 1.90 (s, 3H), 1.63 (s, 3H); **$^{13}$C NMR** (151 MHz, Chloroform-*d*) δ 172.3, 168.6, 156.3, 156.0, 148.1, 141.3, 138.1, 129.6, 124.8, 118.5, 118.3, 118.1, 117.5, 116.6, 82.2, 63.9, 49.5, 46.6, 24.9, 24.0, 22.1, 19.4; **HRMS** (ESI) Calcd for $C_{22}H_{25}N_4O_5$ $[M+H]^+$ 425.1819, found 425.1830.

N-((9-ethyl-2-methoxy-3-methyl-1-oxo-1,2,8,9-tetrahydrofuro[3,2-f]quinazolin-9-yl) methyl)acetamide (**5t**)



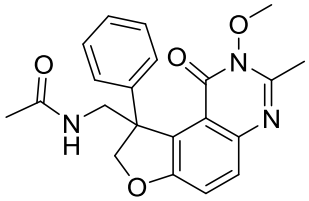
Colorless oil in 91% yield; **$^{1}$H NMR** (400 MHz, Chloroform-*d*) δ 7.30 (d, *J* = 8.8 Hz, 1H), 7.11 (d, *J* = 8.8 Hz, 1H), 6.34 (dd, *J* = 8.2, 4.2 Hz, 1H), 4.53 (d, *J* = 9.2 Hz, 1H), 4.40 (d, *J* = 9.2 Hz, 1H), 4.06 (s, 3H), 3.95 (dd, *J* = 13.7, 4.2 Hz, 1H), 3.85 (dd, *J* = 13.7, 8.2 Hz, 1H), 2.53 (s, 3H), 2.26 (qd, *J* = 14.0, 7.4 Hz, 1H), 1.64 (qd, *J* = 14.0, 7.4 Hz, 1H), 0.67 (t, *J* = 7.4 Hz, 3H); **$^{13}$C NMR** (126 MHz, Chloroform-*d*) δ 170.7, 160.8, 156.8, 150.0, 142.2, 129.3, 126.3, 120.7, 118.1, 79.7, 64.0, 53.9, 45.4, 28.7, 23.2, 19.3, 8.8; **HRMS** (ESI) Calcd for $C_{17}H_{22}N_3O_4$ $[M+H]^+$ 332.1605, found 332.1610.

N-((9-cyclopentyl-2-methoxy-3-methyl-1-oxo-1,2,8,9-tetrahydrofuro[3,2-f]quinazolin-9-yl)methyl)acetamide (**5u**)



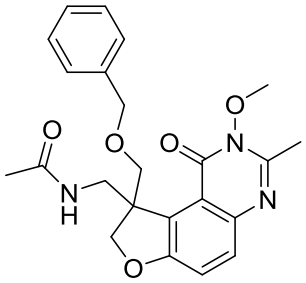
Colorless oil in 63 % yield; **$^{1}$H NMR** (400 MHz, Chloroform-*d*) δ 7.42 (d, *J* = 8.7 Hz, 1H), 7.16 (d, *J* = 8.7 Hz, 1H), 5.99 – 5.81 (m, 1H), 4.54 (d, *J* = 9.5 Hz, 1H), 4.46 (d, *J* = 9.5 Hz, 1H), 4.10 (s, 3H), 4.06 (dd, *J* = 13.7, 3.7 Hz, 1H), 3.93 (dd, *J* = 13.7, 8.8 Hz, 1H), 3.10 – 2.94 (m, 1H), 2.58 (s, 3H), 1.83 (s, 3H), 1.69 – 1.32 (m, 5H), 1.26 – 1.17 (m, 1H), 1.12 – 1.04 (m, 2H); **$^{13}$C NMR** (126 MHz, Chloroform-*d*) δ 170.0, 160.0, 156.6, 149.4, 142.0, 129.0, 126.9, 119.9, 117.7, 63.5, 55.7, 44.7, 43.6, 27.8, 26.9, 25.3, 24.4, 22.8, 18.9; **HRMS** (ESI) Calcd for $C_{20}H_{26}N_3O_4$ $[M+H]^+$ 372.1918, found 372.1923.

N-((2-methoxy-3-methyl-1-oxo-9-phenyl-1,2,8,9-tetrahydrofuro[3,2-f]quinazolin-9-yl)methyl)acetamide (**5v**)



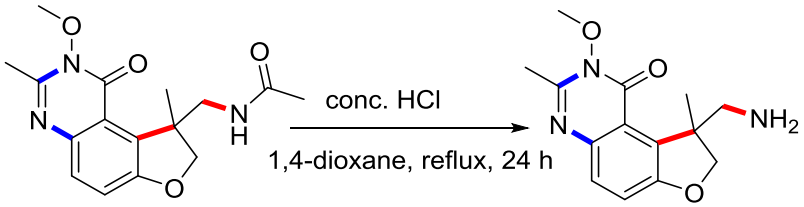
Yellow solid in 85% yield; **$^{1}$H NMR** (400 MHz, Chloroform-*d*) δ 7.62 (d, *J* = 8.8 Hz, 1H), 7.36 (d, *J* = 8.7 Hz, 1H), 7.30 – 7.27 (m, 1H), 7.23 – 7.13 (m, 3H), 6.69 (s, 1H), 4.74 (d, *J* = 9.2 Hz, 1H), 4.51 (d, *J* = 9.1 Hz, 1H), 4.41 – 4.26 (m, 2H), 3.86 (s, 3H), 2.57 (s, 3H), 1.85 (s, 3H); **$^{13}$C NMR** (126 MHz, Chloroform-*d*) δ 170.7, 160.7, 150.5, 143.5, 143.0, 130.2, 128.5, 127.2, 126.7, 125.9, 118.6, 85.6, 63.8, 56.5, 45.2, 23.3, 19.5; **HRMS** (ESI) Calcd for $C_{21}H_{22}N_3O_4$ $[M+H]^+$ 380.1605, found 380.1614.

N-((9-((benzyloxy)methyl)-2-methoxy-3-methyl-1-oxo-1,2,8,9-tetrahydrofuro[3,2-f]quinazolin-9-yl)methyl)acetamide (**5w**)



Yellow oil in 94% yield; **$^{1}$H NMR** (400 MHz, Chloroform-*d*) δ 7.49 (d, *J* = 8.8 Hz, 1H), 7.30 – 728 (m, 2H), 7.26 – 7.17 (m, 4H), 6.24 (t, *J* = 6.0 Hz, 1H), 4.75 (d, *J* = 9.3 Hz, 1H), 4.60 – 4.54 (m, 2H), 4.42 (d, *J* = 12.0 Hz, 1H), 4.23 (d, *J* = 8.8 Hz, 1H), 4.06 (s, 1H), 4.04 (s, 3H), 3.98 (dd, *J* = 13.6, 6.0 Hz, 1H), 3.84 (d, *J* = 8.8 Hz, 1H), 2.58 (s, 3H), 1.83 (s, 3H); **$^{13}$C NMR** (126 MHz, Chloroform-*d*) δ 170.4, 160.6, 156.9, 149.9, 142.4, 138.0, 130.0, 128.4, 127.7, 127.5, 124.6, 118.4, 79.1, 73.9, 73.4, 64.0 , 53.6, 44.0, 23.3; **HRMS** (ESI) Calcd for $C_{23}H_{26}N_3O_5$ $[M+H]^+$ 424.1867, found 424.1869.

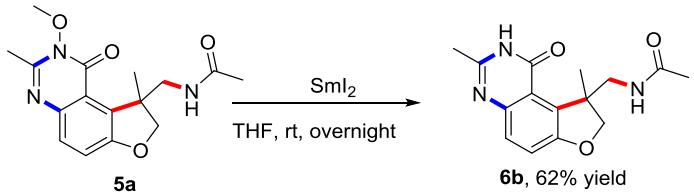
**Synthesis of compound 6a and 6b:**




**5a** **6a**, 79% yield

Compound **5a** (31.7 mg, 0.1 mmol) was added to a round-bottomed flask and dissolved in 1,4-dioxane (3 mL), Then concentrated HCl (1.5 mL) was added slowly and the reaction mixture refluxed for 24 h. The mixture was basified with $Na_2CO_3$ and the amine product was extracted with EA several times. Combined organic layers were washed by water and NaCl saturated solution, then were dried over $MgSO_4$, filtered, concentrated under reduced pressure. The residue was purified by flash column chromatography (DCM/MeOH) to afford **6a** as yellow oil in 79% yield; **$^{1}$H**

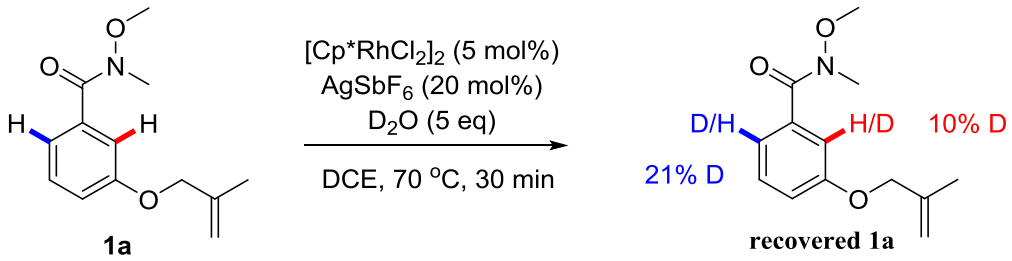
**NMR** (400 MHz, DMSO-$d_6$) δ 8.07 (s, 2H), 7.55 (d, *J* = 8.7 Hz, 1H), 7.37 (d, *J* = 8.7 Hz, 1H), 4.84 (d, *J* = 9.5 Hz, 1H), 4.34 (d, *J* = 9.4 Hz, 1H), 4.03 (s, 3H), 3.75 – 3.67 (m, 1H), 3.26 (m, 1H), 1.49 (s, 3H).; **$^{13}$C NMR** (150 MHz, Methanol-d4) δ 160.3, 156.9, 152.2, 141.6, 129.1, 125.4, 120.4, 118.4, 81.3, 63.5, 46.9, 45.6, 23.3, 17.7; **HRMS** (ESI) Calcd for $C_{14}H_{18}N_3O_3$ $[M+H]^+$ 276.1343, found 276.1348.




**5a** **6b**, 62% yield

Compound **5a** (31.7 mg, 0.1 mmol) was added to a round-bottomed flask and dissolved in dry THF (5 mL). Then $SmI_2$ solution (0.1 M in THF, 2.0 mL, 0.2 mmol) was added slowly via a syringe and the reaction mixture was stirred at room temperature overnight. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography (DCM/MeOH) to afford **6b** as yellow oil in 62% yield; **$^1$H NMR** (400 MHz, Methanol-$d_4$) δ 7.56 (d, *J* = 8.8 Hz, 1H), 7.38 (d, *J* = 8.8 Hz, 1H), 4.72 (d, *J* = 9.2 Hz, 1H), 4.31 (d, *J* = 9.2 Hz, 1H), 4.14 (d, *J* = 13.6 Hz, 1H), 3.48 (d, *J* = 13.6 Hz, 1H), 2.68 (s, 3H), 1.76 (s, 3H), 1.60 (s, 3H); **$^{13}$C NMR** (151 MHz, Methanol-d4) δ 161.7, 158.2, 156.9, 133.5, 130.9, 121.2, 118.4, 118.3, 82.3, 49.4, 45.0, 22.3, 21.0, 16.7; **HRMS** (ESI) Calcd for $C_{15}H_{18}N_3O_3$ $[M+H]^+$ 288.1343, found 288.1341.

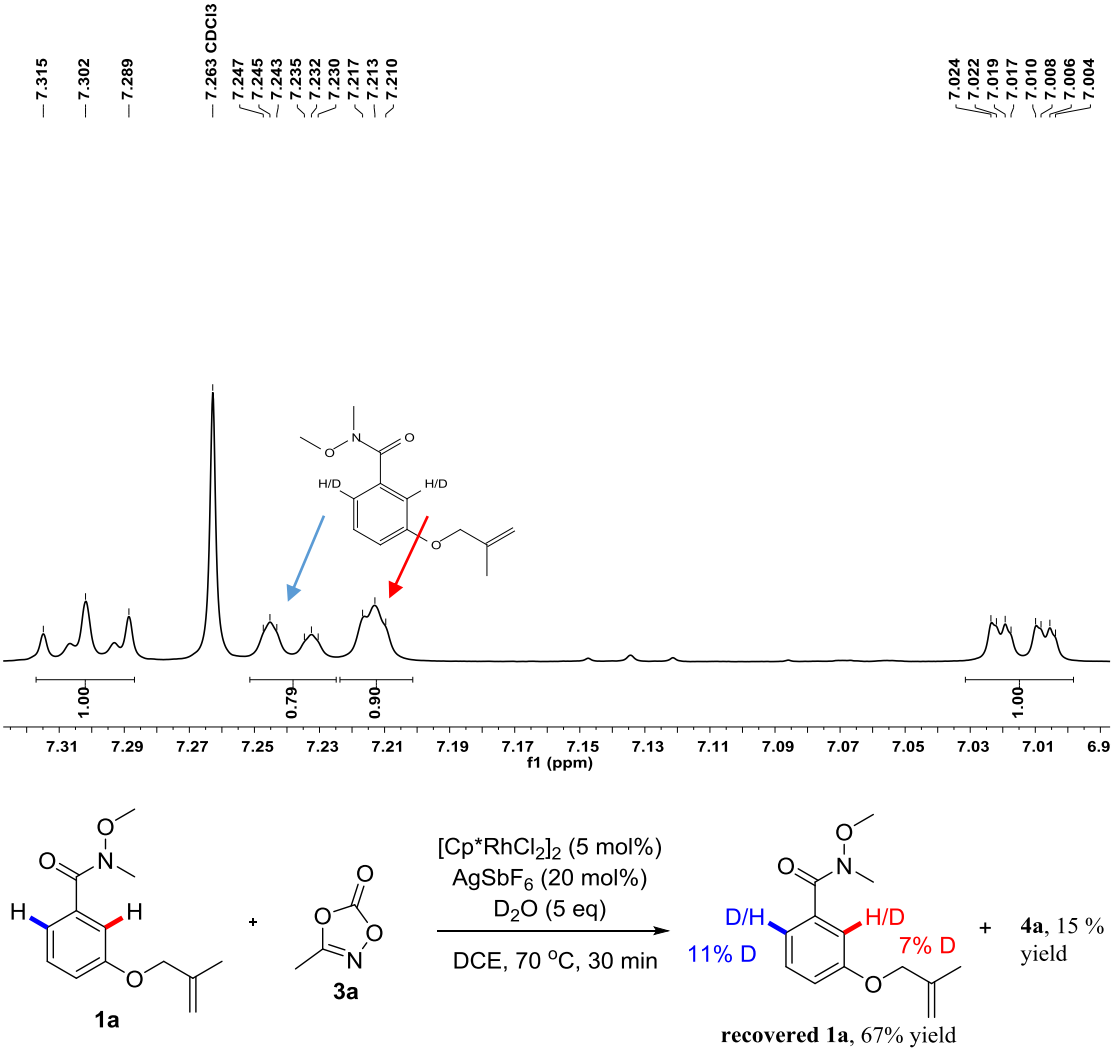
## Mechanistic Studies:




**1a** **recovered 1a**

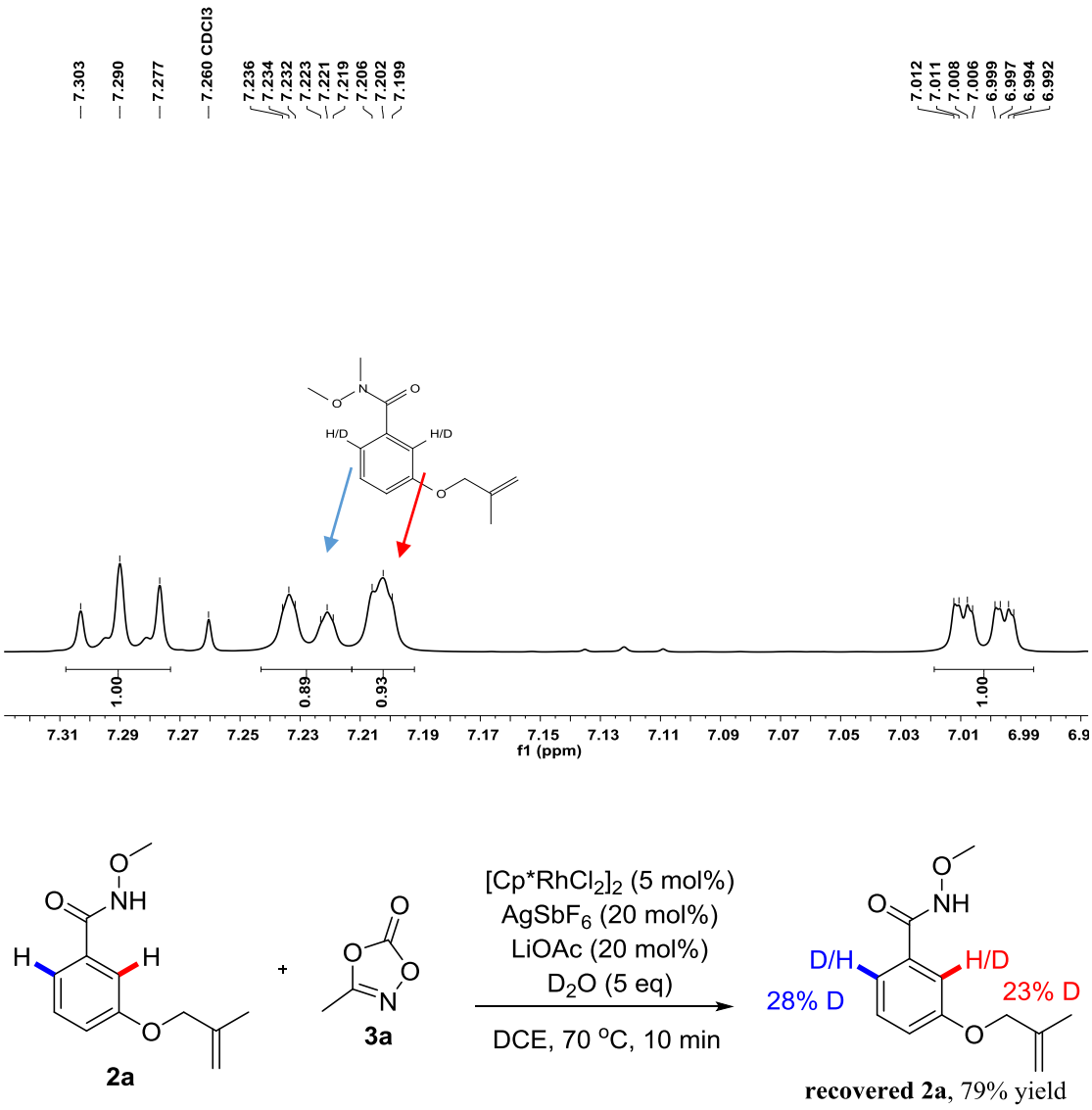
To an oven-dried 15 mL Schlenk tube equipped with a stir bar were added substrate **1a** (0.1 mmol), $[Cp^*RhCl_2]_2$ (5 mol%), $AgSbF_6$ (20 mol%), DCE (1 mL) and $D_2O$ (0.5 mmol) under a positive stream of argon. The tube was sealed and the

reaction was stirred for 0.5 h at 70 ℃. The reaction mixture was cooled to room temperature and diluted with $CH_2Cl_2$ (5 mL) and filtered through a short pad silica gel washing with $CH_2Cl_2$ (20 mL). The filtrate was concentrated and then purified by column chromatography on silica gel (PE/EA = 4:1) to recover substrate **1a**. The ratio of deuterium-hydrogen exchange could be clearly determined in $^1$H NMR spectrum.



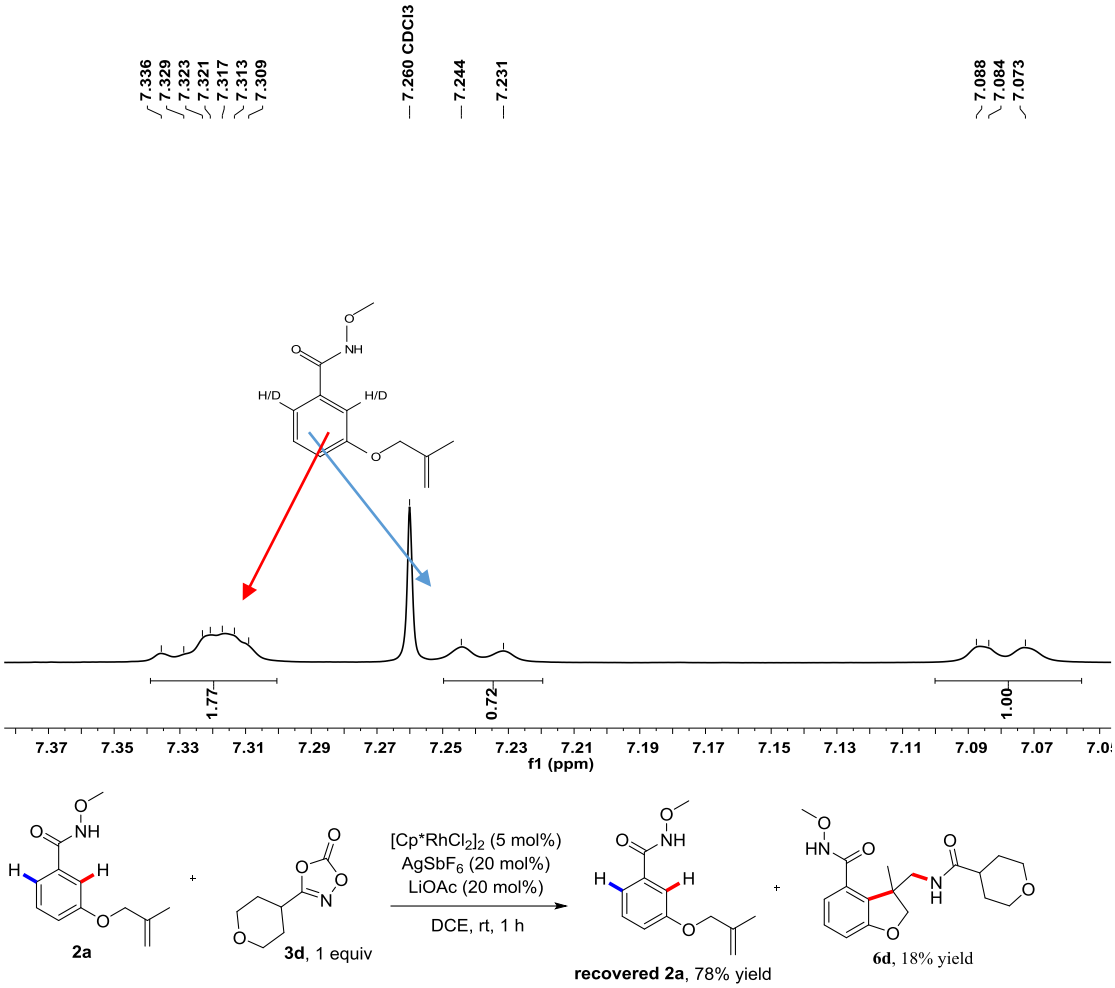

To an oven-dried 15 mL Schlenk tube equipped with a stir bar were added substrate **1a** (0.1 mmol), **3a** (0.12 mmol), $[Cp^*RhCl_2]_2$ (5 mol%), $AgSbF_6$ (20 mol%), DCE (1 mL) and $D_2O$ (0.5 mmol) under a positive stream of argon. The tube was sealed and the reaction was stirred for 0.5 h at 70 ℃. The reaction mixture was cooled to room temperature and diluted with $CH_2Cl_2$ (5 mL) and filtered through a short pad silica gel washing with $CH_2Cl_2$ (20 mL). The filtrate was concentrated and then purified by column chromatography on silica gel to recover substrate **1a** and yield the

product **4a**. The ratio of deuterium-hydrogen exchange could be clearly determined in $^1$H NMR spectrum.



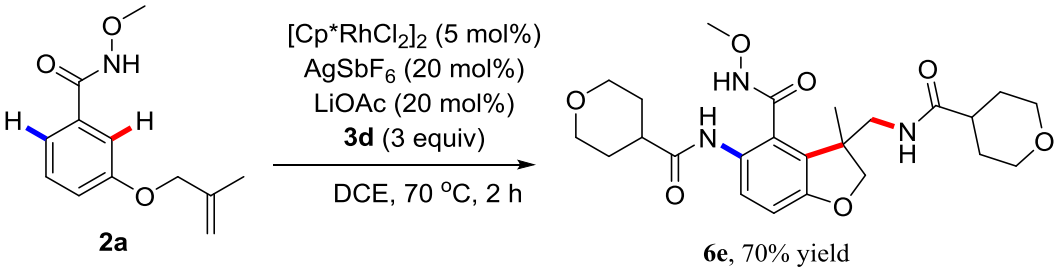

To an oven-dried 15 mL Schlenk tube equipped with a stir bar were added Substrate **2a** (0.1 mmol), **3a** (0.3 mmol), $[Cp^*RhCl_2]_2$ (5 mol%), LiOAc (20 mol%), $AgSbF_6$ (20 mol%), DCE (1 mL) and $D_2O$ (0.5 mmol) under a positive stream of argon. The tube was sealed and the reaction was stirred for 10 minutes at room temperature. The reaction mixture was diluted with $CH_2Cl_2$ (5 mL) and filtered through a short pad silica gel washing with $CH_2Cl_2$ (20 mL). The filtrate was

concentrated and then purified by column chromatography on silica gel to recover **2a**. The ratio of deuterium-hydrogen exchange could be clearly determined in 1H NMR spectrum.




To an oven-dried 15 mL Schlenk tube equipped with a stir bar were added substrate **2a** (0.1 mmol), **3d** (0.1 mmol), $[Cp^*RhCl_2]_2$ (5 mol%), $AgSbF_6$ (20 mol%), LiOAc (20 mol%), DCE (1 mL) under a positive stream of argon. The tube was sealed and the reaction was stirred 1 h at room temperature. The reaction mixture was diluted with $CH_2Cl_2$ (5 mL) and filtered through a short pad silica gel washing with $CH_2Cl_2$ (20 mL). The filtrate was concentrated and then purified by column chromatography on silica gel to recover **2a** and afford product **6d** as colorless oil in 18% yield; **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 10.45 (s, 1H), 7.16 (t, *J* = 7.8 Hz, 1H), 6.88 (d, *J* = 7.8, Hz, 1H), 6.84 (d, *J* = 7.8, Hz, 1H), 6.70 (m, 1H), 4.43 (d, *J* = 9.1 Hz, 1H), 4.15 (d, *J* = 9.1 Hz, 1H), 3.97 – 3.80 (m, 6H), 3.27 (m, 3H), 2.16 (m, 1H), 1.60 – 1.35 (m, 7H); **$^{13}$C NMR** (126 MHz, Chloroform-*d*) δ 177.0, 168.0, 162.5,

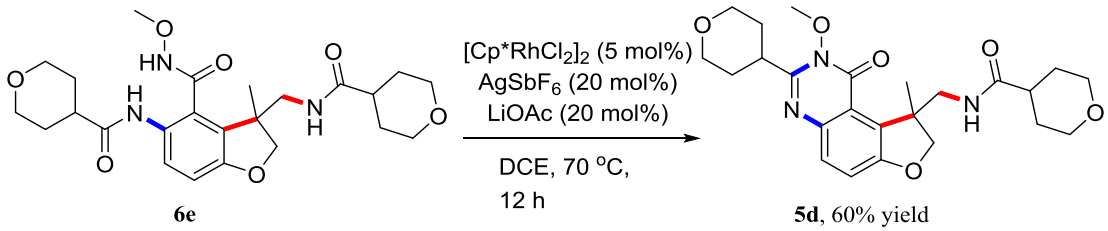
132.7, 130.7, 129.8, 121.8, 113.6, 84.0, 78.7, 68.5, 65.8, 49.7, 49.1, 43.4, 30.4, 30.2, 23.0; **HRMS** (ESI) Calcd for $C_{18}H_{25}N_2O_5$ $[M+H]^+$ 349.1758, found 349.1751.




**2a**

**6e**, 70% yield

To an oven-dried 15 mL Schlenk tube equipped with a stir bar were added substrate **2a** (0.1 mmol), **3d** (0.3 mmol), $[Cp^*RhCl_2]_2$ (5 mol%), $AgSbF_6$ (20 mol%), LiOAc (20 mol%), DCE (1 mL) under a positive stream of argon. The tube was sealed and the reaction was stirred 2 h at 70 ℃. The reaction mixture was cooled to room temperature and diluted with $CH_2Cl_2$ (5 mL) and filtered through a short pad silica gel washing with $CH_2Cl_2$ (20 mL). The filtrate was concentrated and then purified by column chromatography on silica gel to afford product **6e** as colorless oil in 70% yield; **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 11.61 (s, 1H), 8.06 (s, 1H), 7.71 (d, *J* = 8.7 Hz, 1H), 6.77 (d, *J* = 8.7 Hz, 1H), 6.52 (s, 1H), 4.42 (d, *J* = 9.2 Hz, 1H), 4.14 (d, *J* = 9.1 Hz, 1H), 4.01 (m, 3H), 3.90 (m, 5H), 3.53 – 3.33 (m, 2H), 3.33 – 3.18 (m, 2H), 3.13 (dd, *J* = 14.3, 4.6 Hz, 1H), 2.54 – 2.38 (m, 1H), 2.22 – 2.14 (m, 1H), 1.82 (m, 4H), 1.60 – 1.32 (m, 7H); **$^{13}$C NMR** (126 MHz, Chloroform-*d*) δ 176.1, 173.5, 164.3, 158.0, 128.8, 127.9, 125.3, 111.59 , 83.2 , 67.2, 67.0, 67, 64.1, 49.2, 47.9, 42.7, 42.1, 29.10, 29.1, 29.0, 28.7, 21.2; **HRMS** (ESI) Calcd for $C_{24}H_{34}N_3O_7$ $[M+H]^+$ 476.2391, found 476.2393.




**6e**

**5d**, 60% yield

To an oven-dried 15 mL Schlenk tube equipped with a stir bar were added

Substrate **6e** (0.05 mmol), $[Cp^*RhCl_2]_2$ (5 mol%), $AgSbF_6$ (20 mol%), LiOAc (20 mol%), DCE (0.5 mL) under a positive stream of argon. The tube was sealed and the reaction was stirred 12 h at 70 ℃. The reaction mixture was cooled to room temperature and diluted with $CH_2Cl_2$ (5 mL) and filtered through a short pad silica gel washing with $CH_2Cl_2$ (20 mL). The filtrate was concentrated and then purified by column chromatography on silica gel to yield the product **5d** in 60% yield.

**Reference:**


[1] R. K. Thalji, K. A. Ahrendt, R. G. Bergman and J. A. Ellman, *J. Org. Chem.*, 2005, **70**, 6775.

[2] Z. Shi, M. Boultadakis-Arapinis, D. C. Koester and F. Glorius, *Chem. Commun*., 2014, **50**, 2650.

[3] Z. Guan, S. Chen, Y. Huang and H. Yao, *Org. Lett*., 2019, **21**, 3959.

[4] Y. Park, K. T. Park, J. G. Kim and S. Chang, *J. Am. Chem. Soc.*, 2015, **137**, 4534.

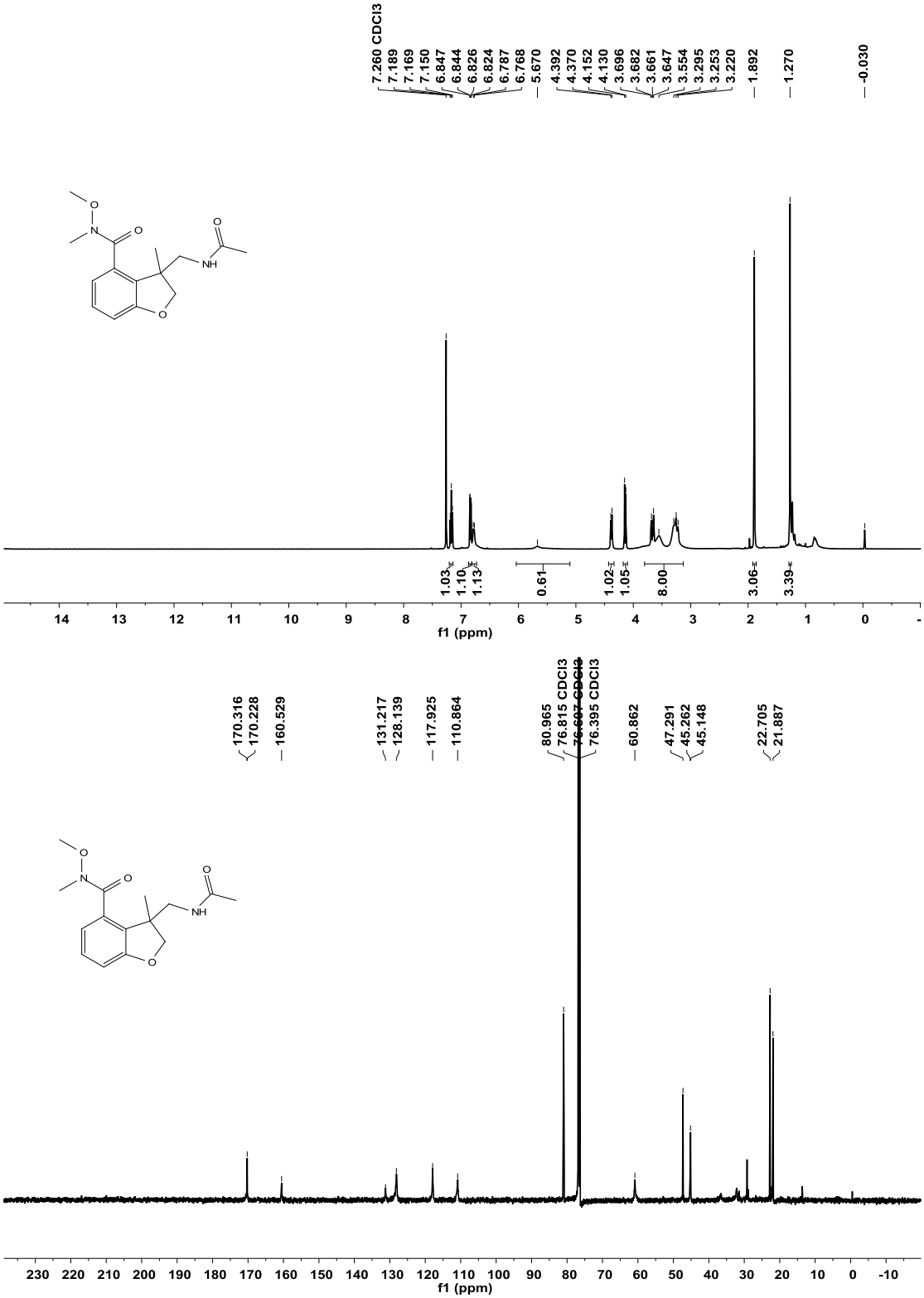
[5] J. Park and S. Chang, *Angew. Chem. Int. Ed.*, 2015, **54,** 14103.

[6] S. Y. Hong, Y. Park, Y. Hwang, Y. B. Kim, M.-H. Baik and S. Chang, *Science*., 2018, **359**, 1016.

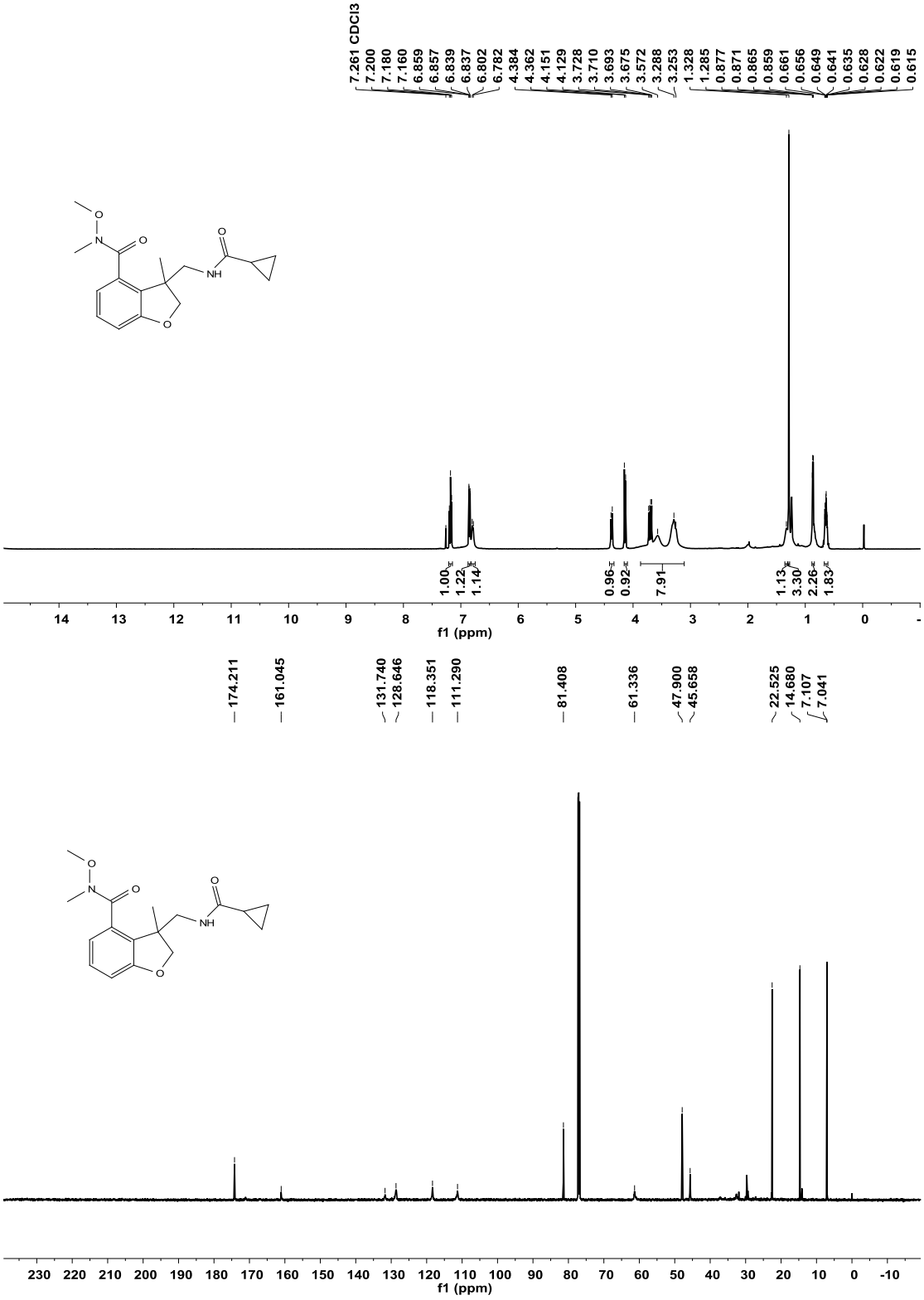
[7] T. Pinkert, T. Wegner, S. Mondal and F. Glorius, *Angew. Chem. Int. Ed.*, 2019, **58**, 15041.

# $^{1}$H and $^{13}$C NMR Spectra of Compounds:

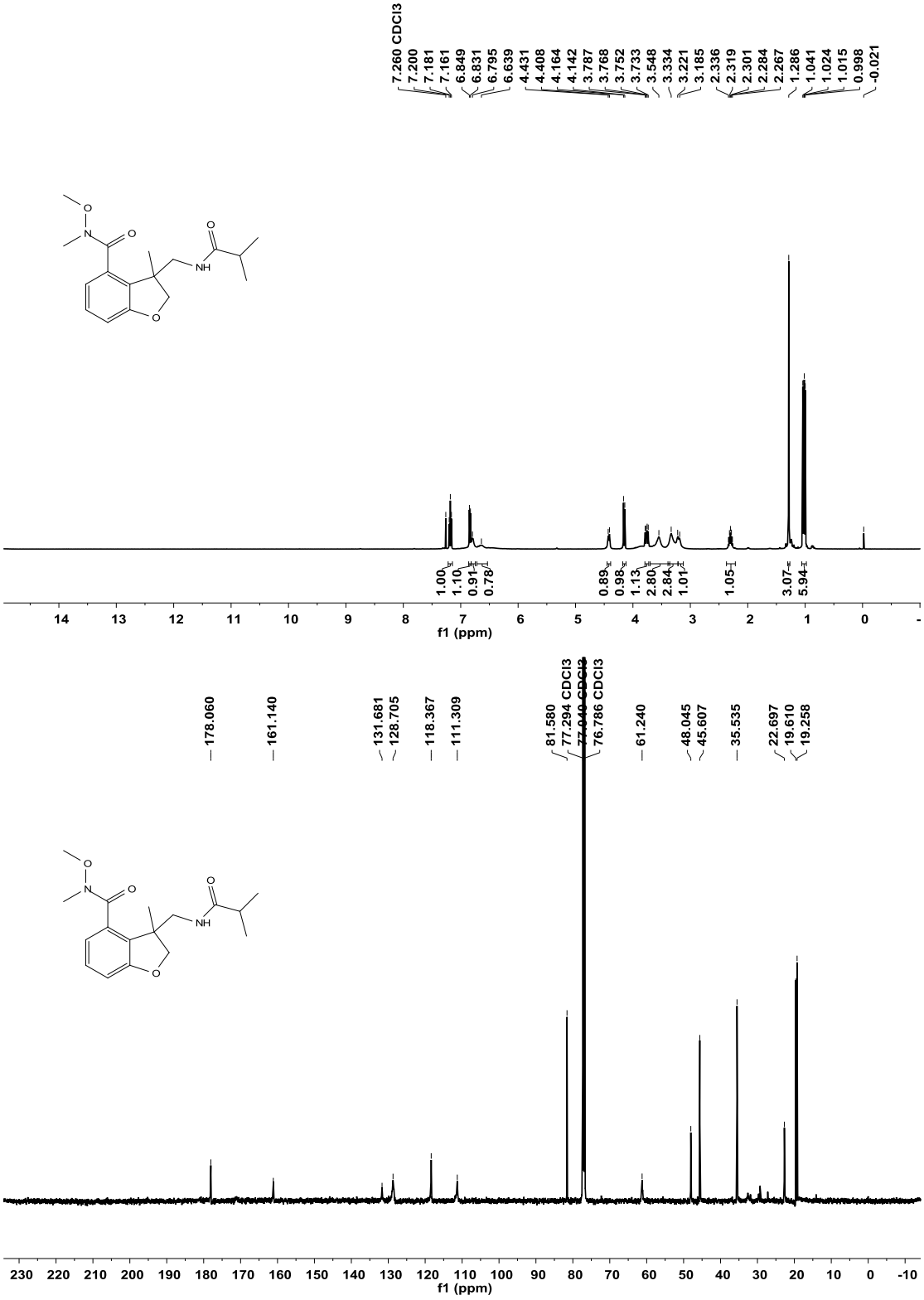
$^{1}$H and $^{13}$C NMR Spectra of Compound **4a:**



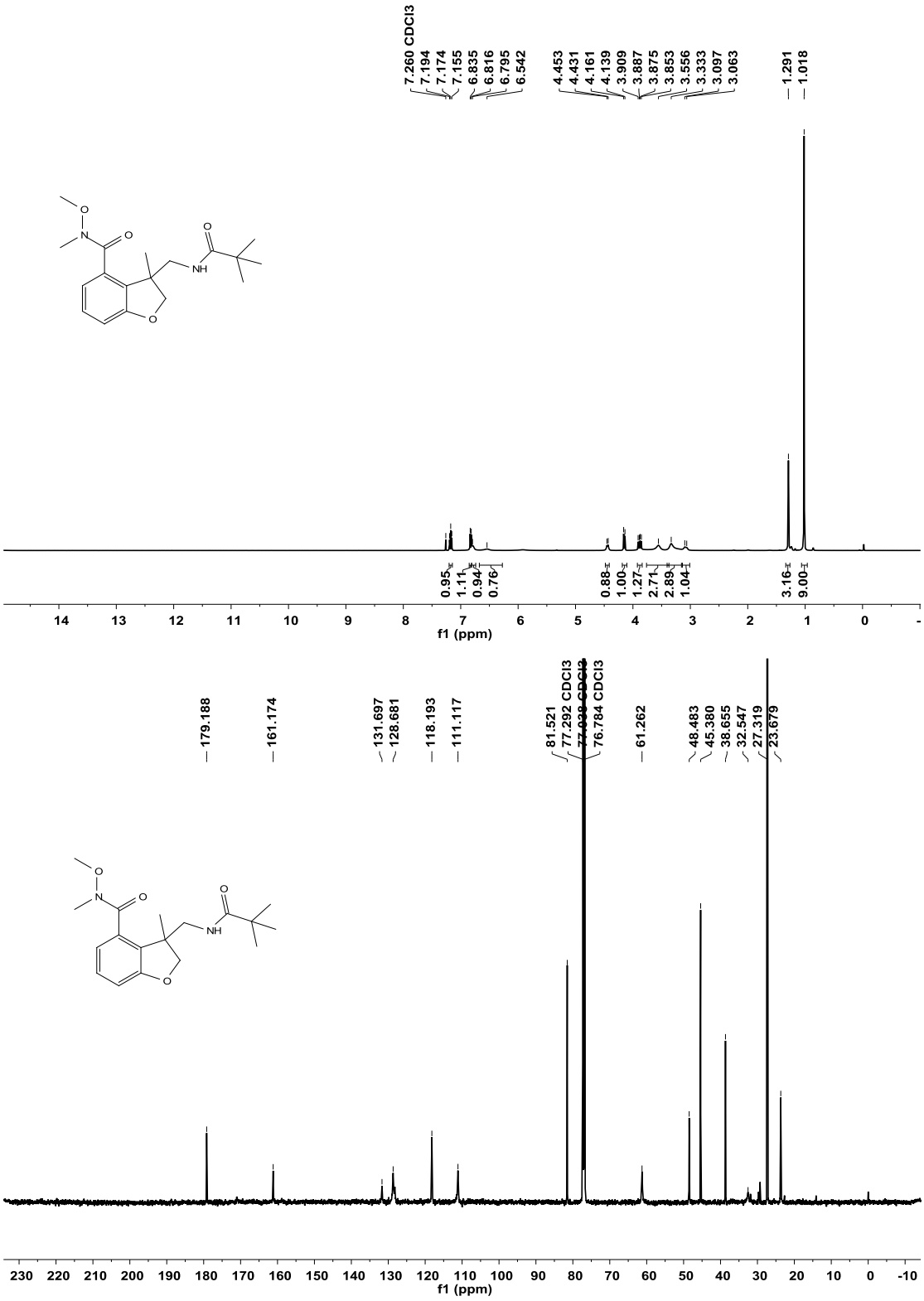
$^{1}H$ and $^{13}C$ NMR Spectra of Compound **4b:**



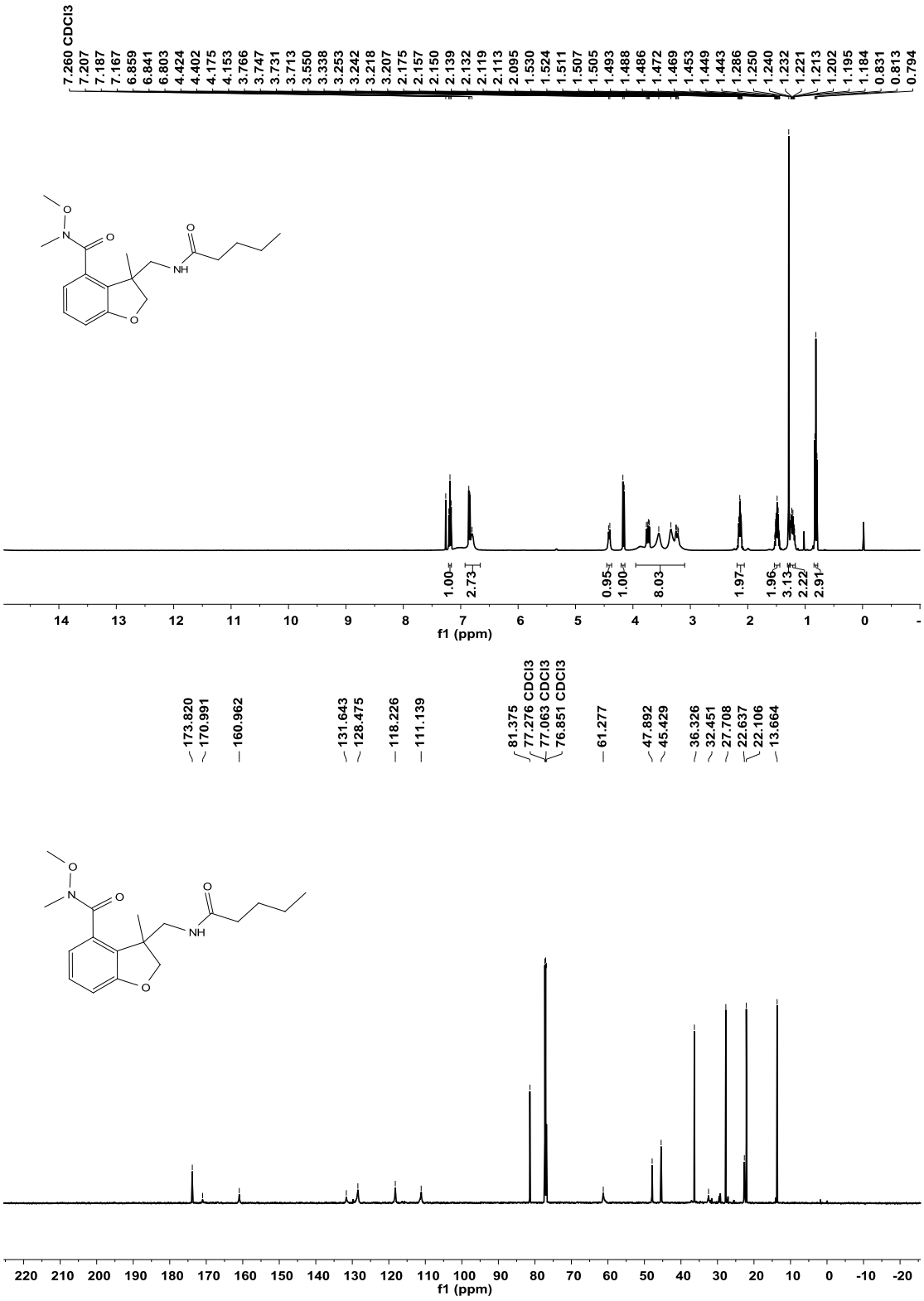
$^{1}H$ and $^{13}C$ NMR Spectra of Compound **4c:**



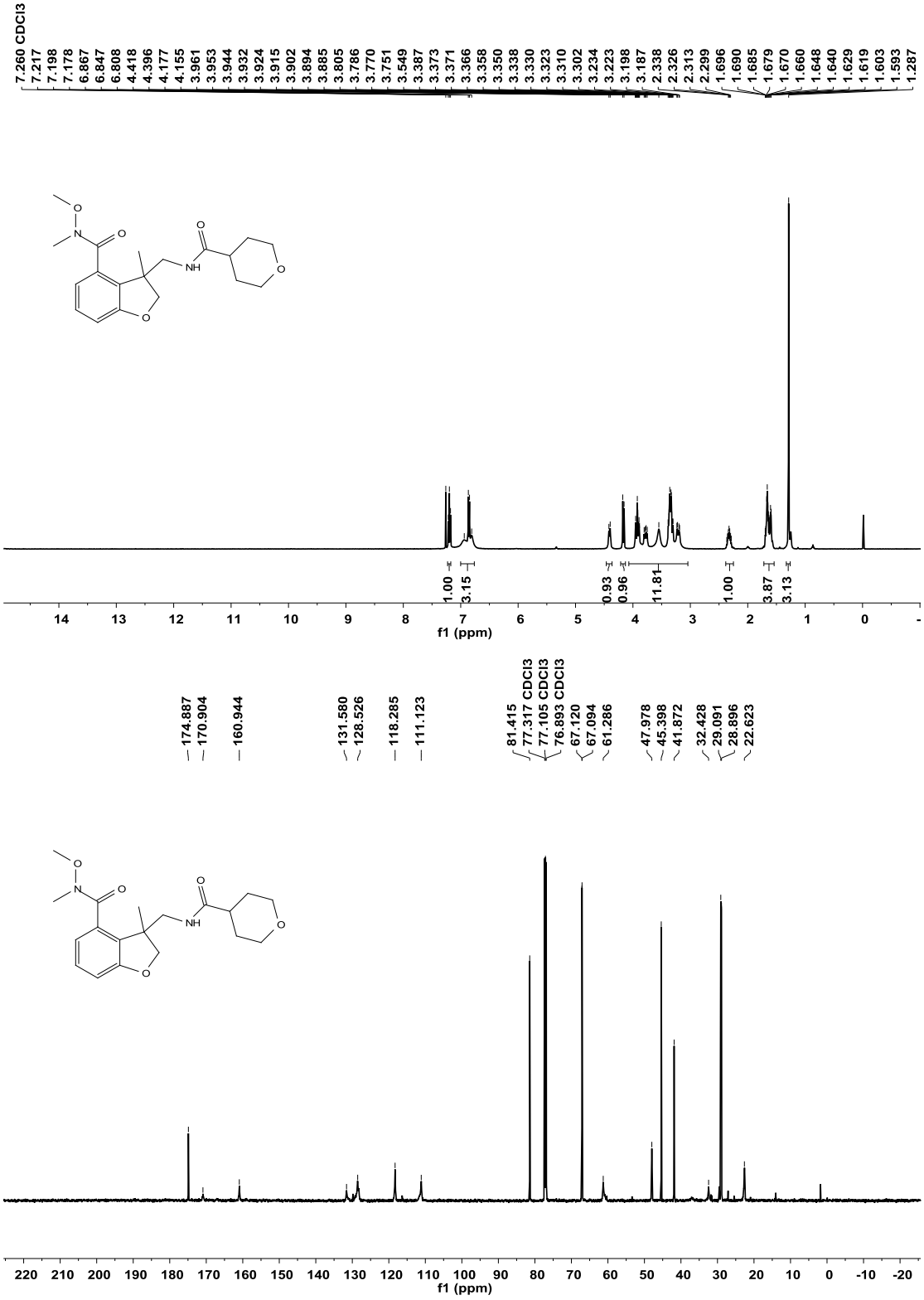
$^{1}H$ and $^{13}C$ NMR Spectra of Compound **4d:**



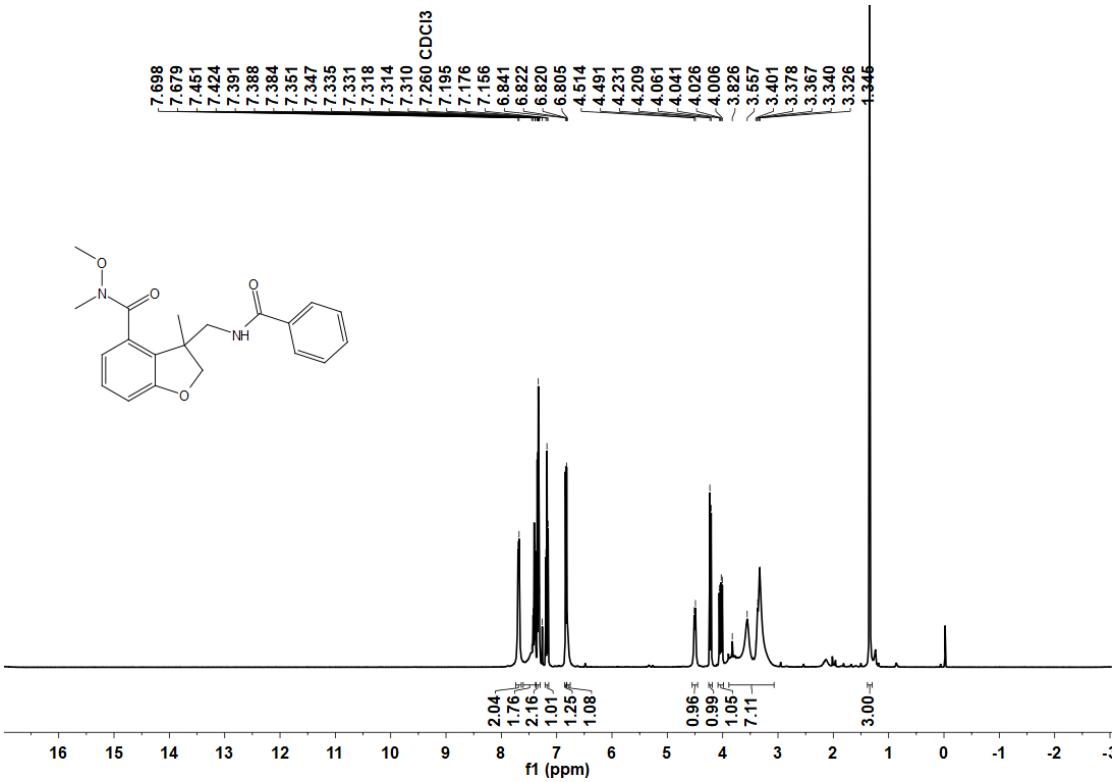
$^{1}$H and $^{13}$C NMR Spectra of Compound **4e:**

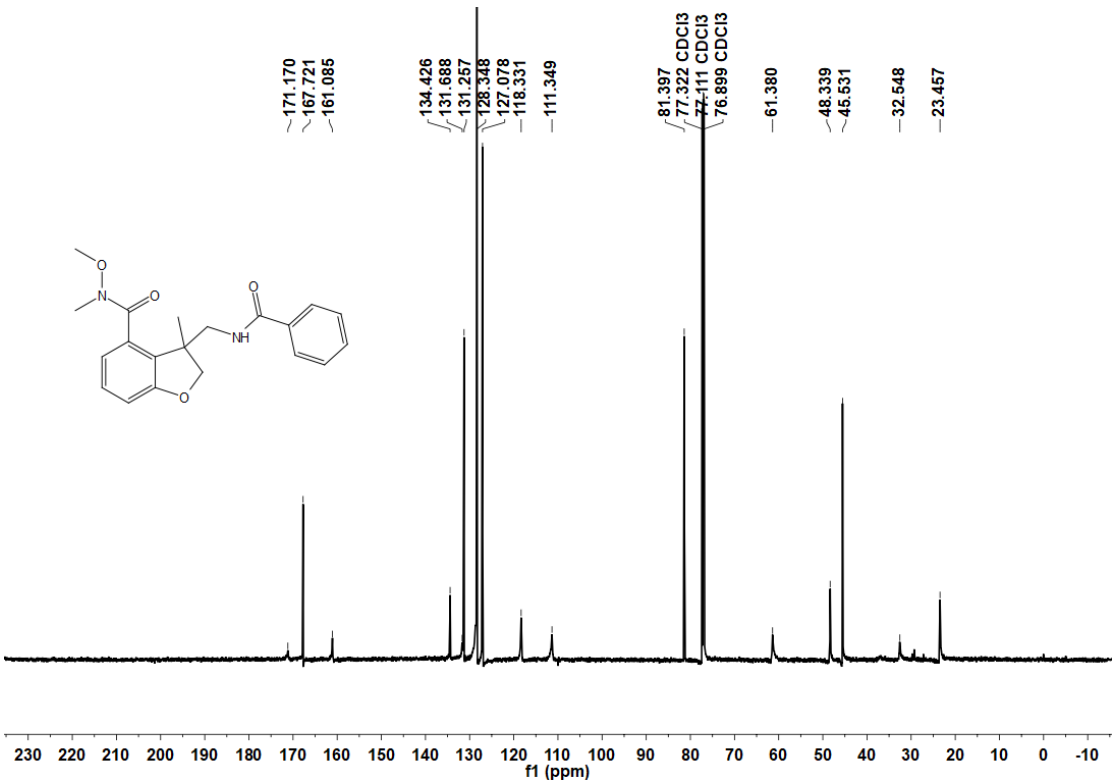


$^{1}H$ and $^{13}C$ NMR Spectra of Compound **4f:**

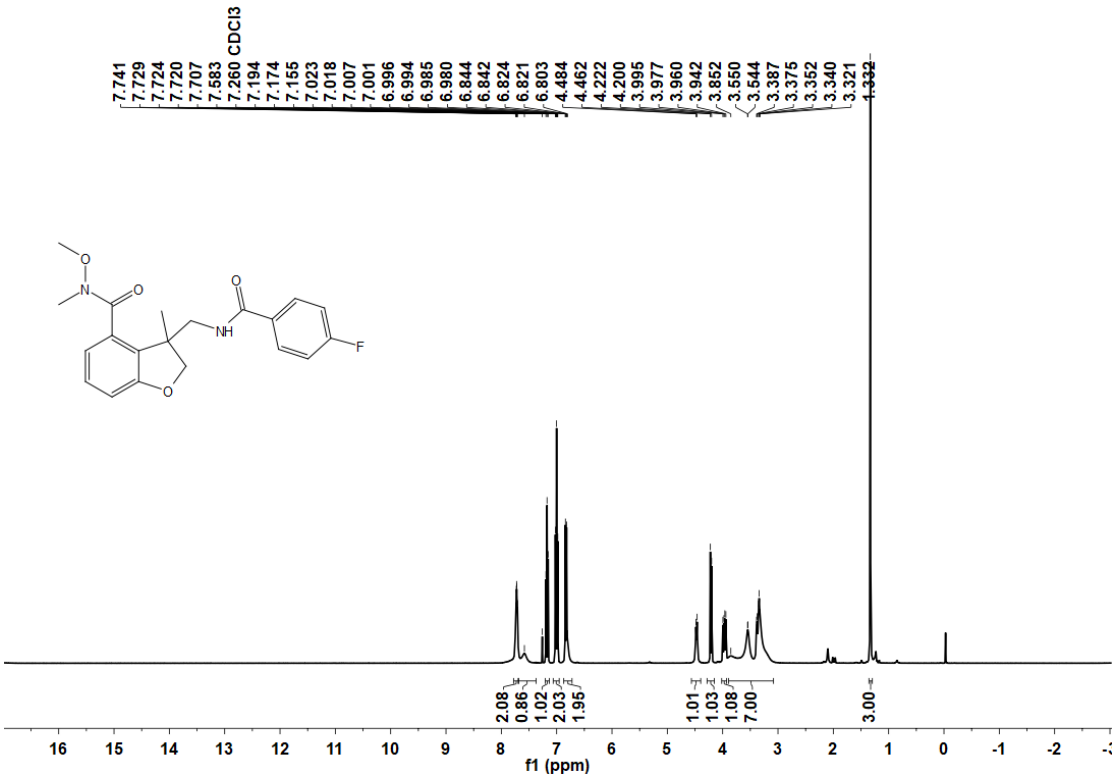


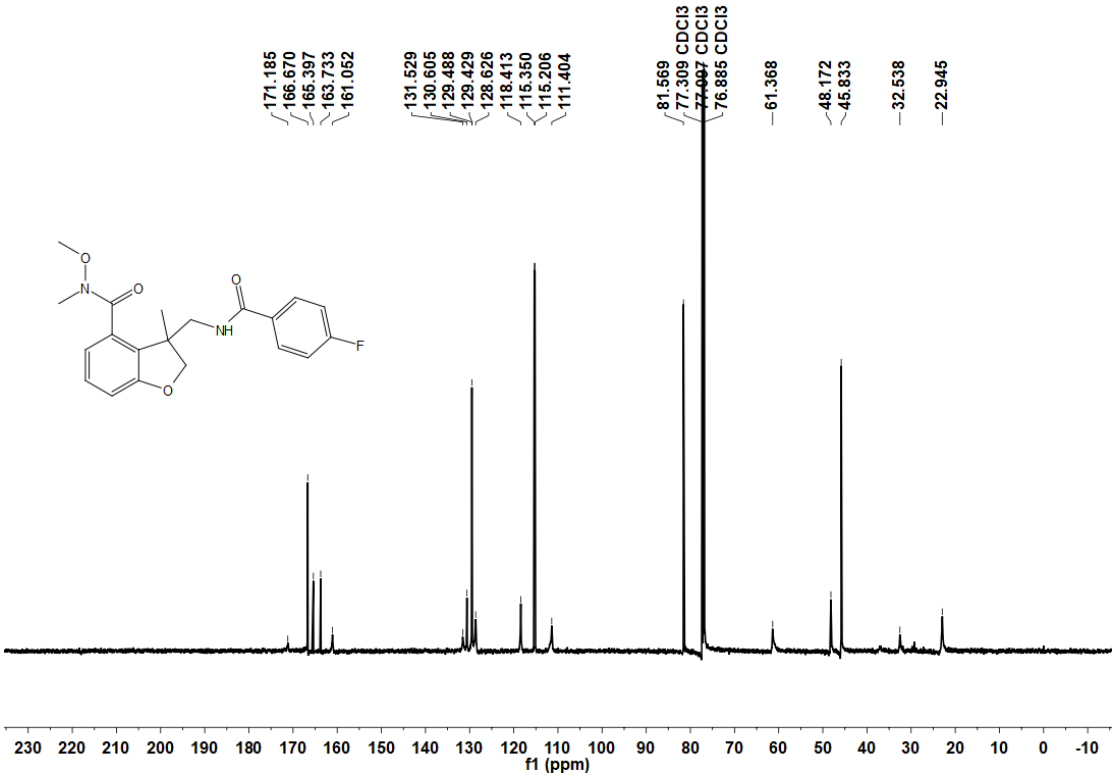
$^{1}H$ and $^{13}C$ NMR Spectra of Compound **4g:**

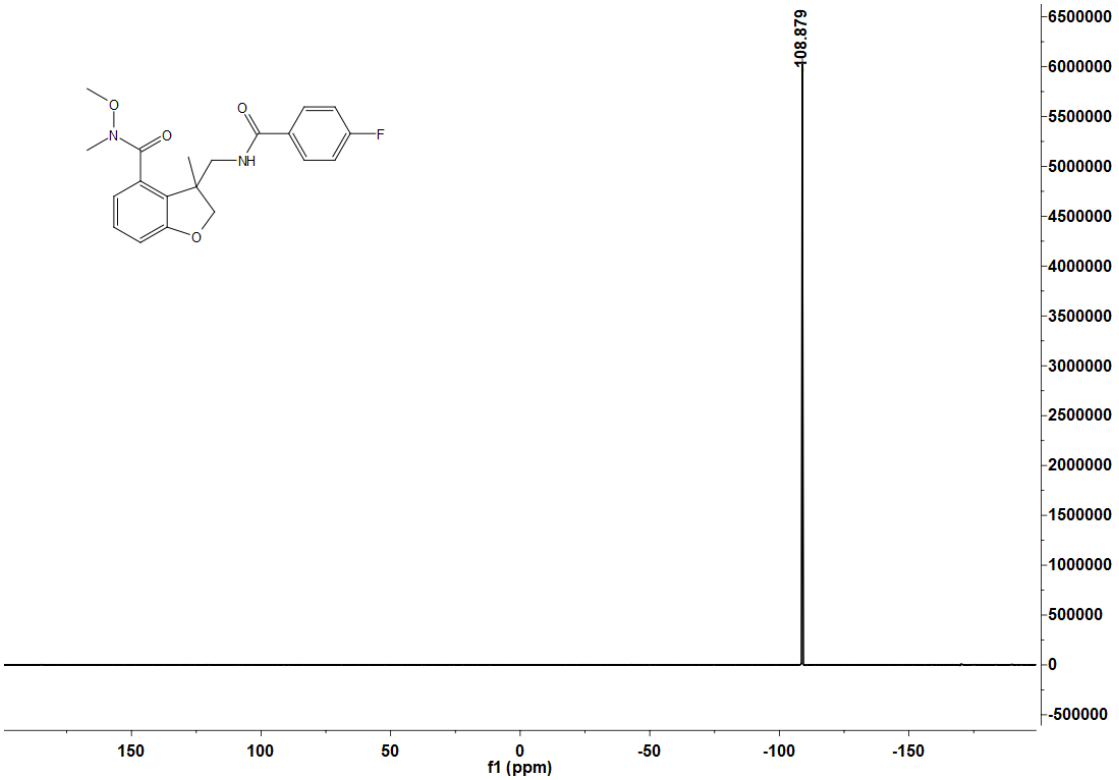


$^{1}H$ , $^{13}C$ and $^{19}F$ NMR Spectra of Compound **4h:**

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50
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f1 (ppm)
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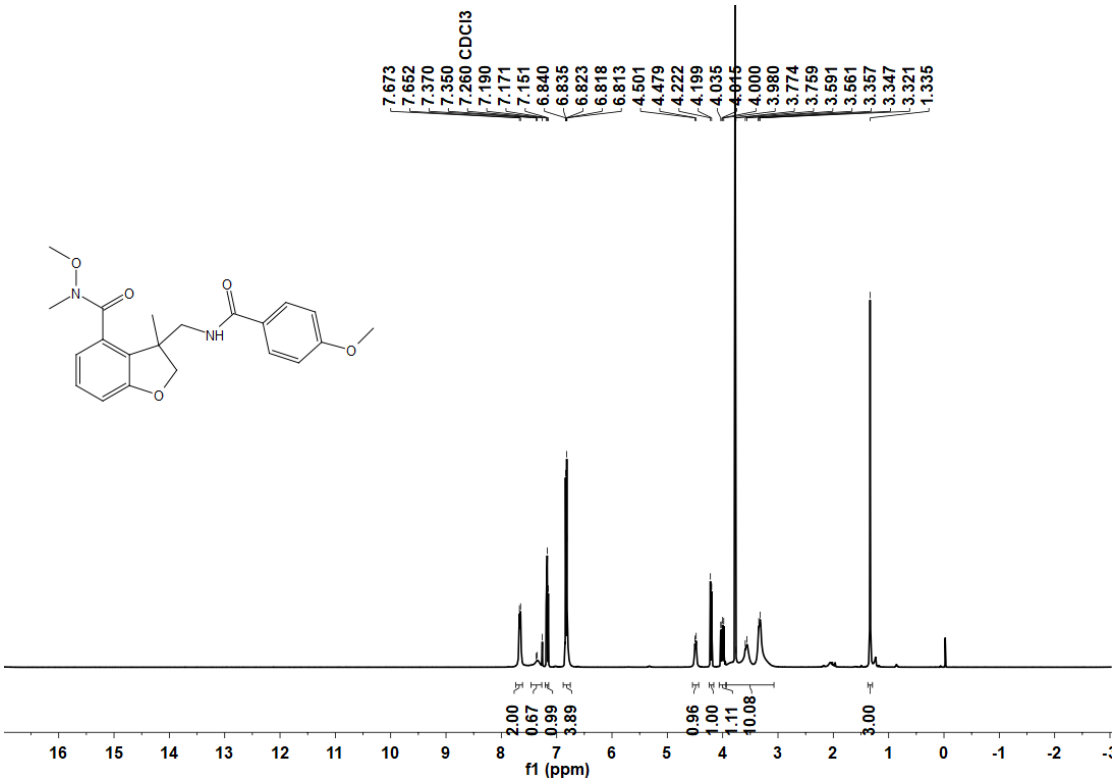
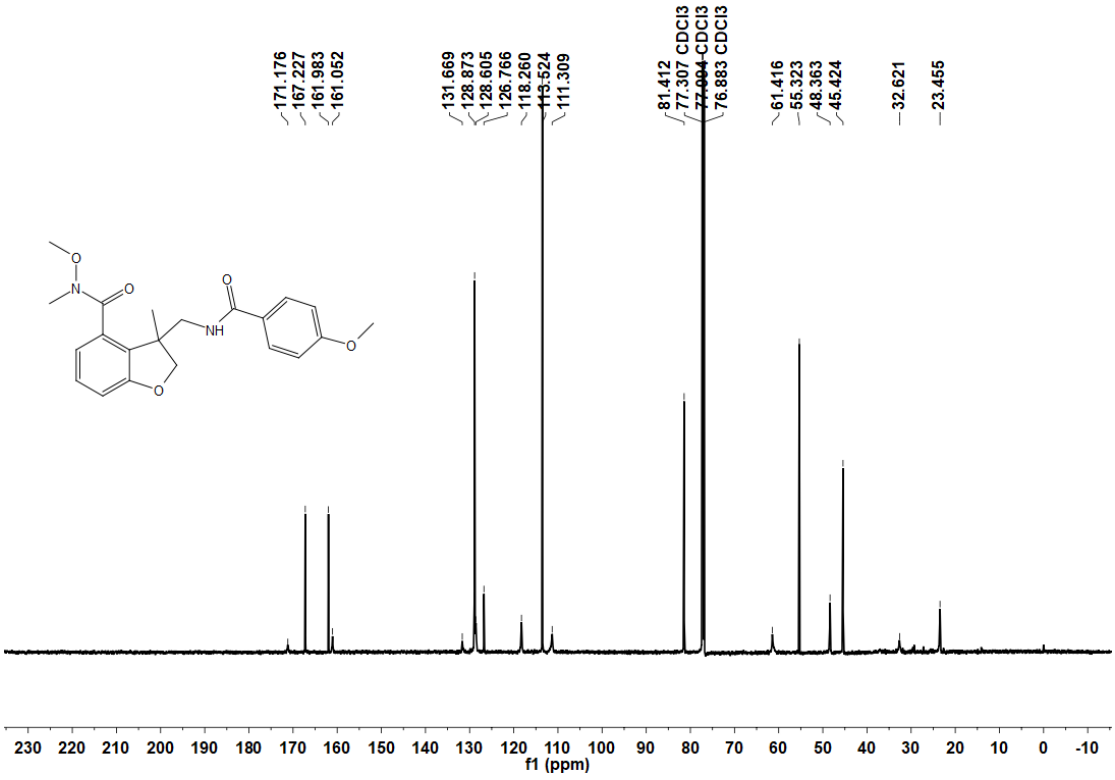
O
O
NH
O
F

$^{1}H$ and $^{13}C$ NMR Spectra of Compound **4i:**



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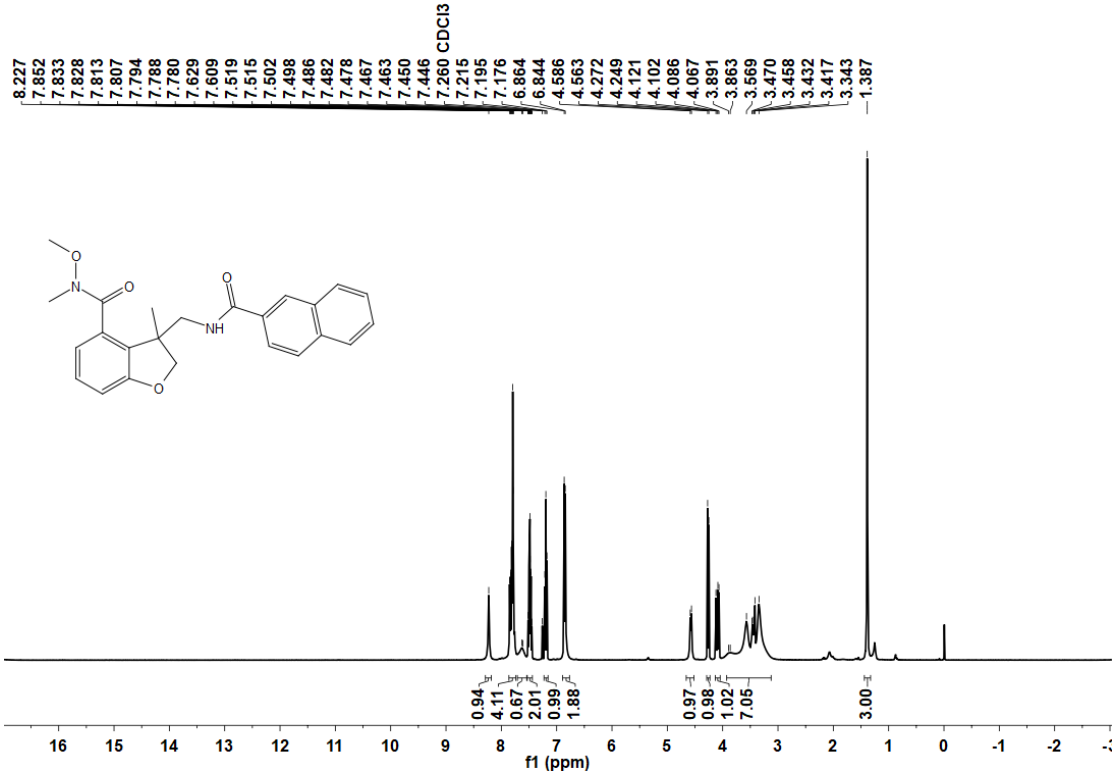
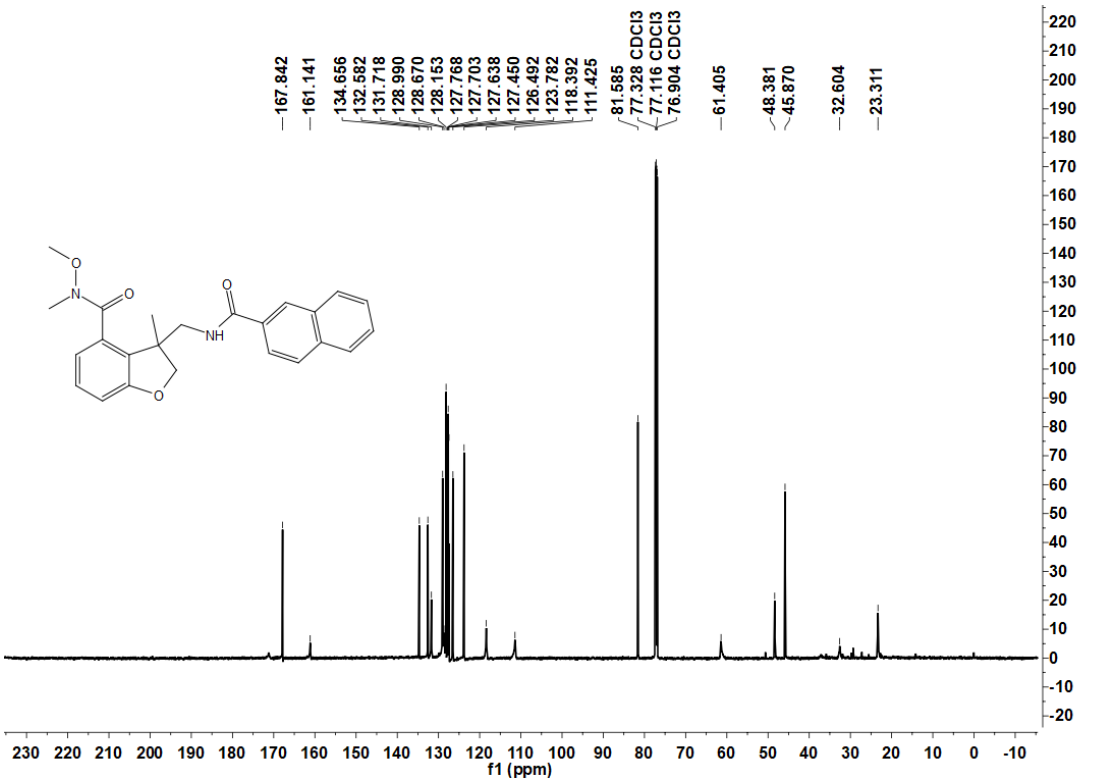
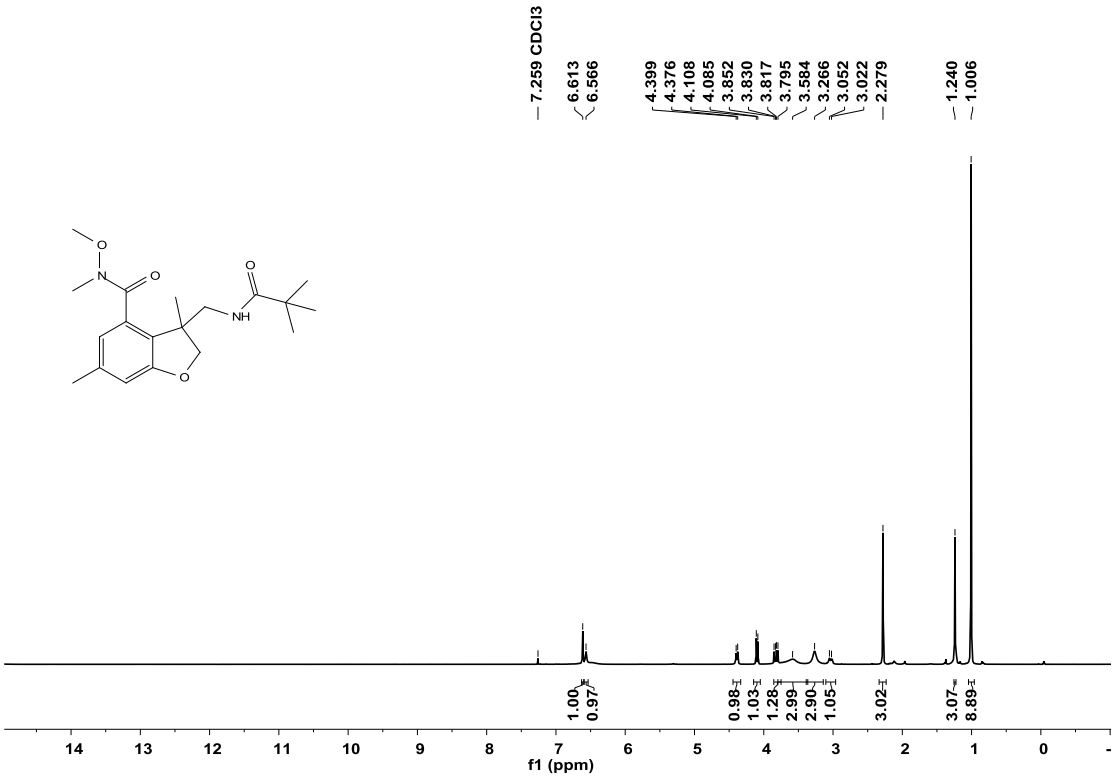
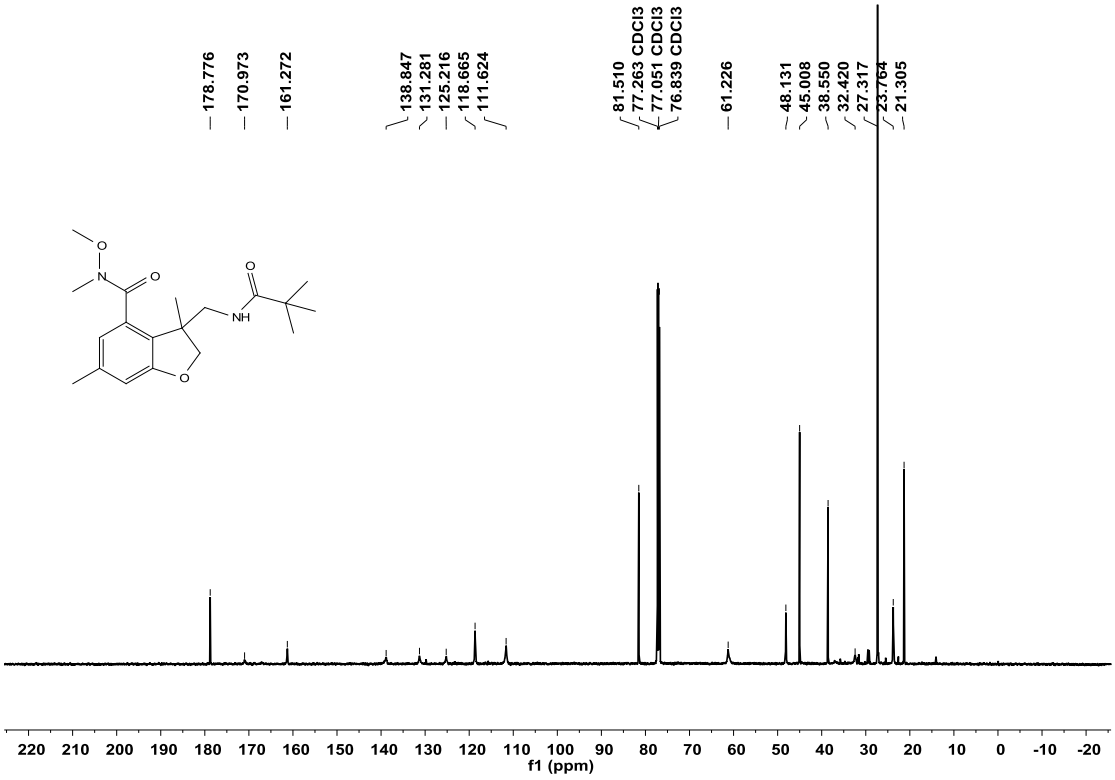


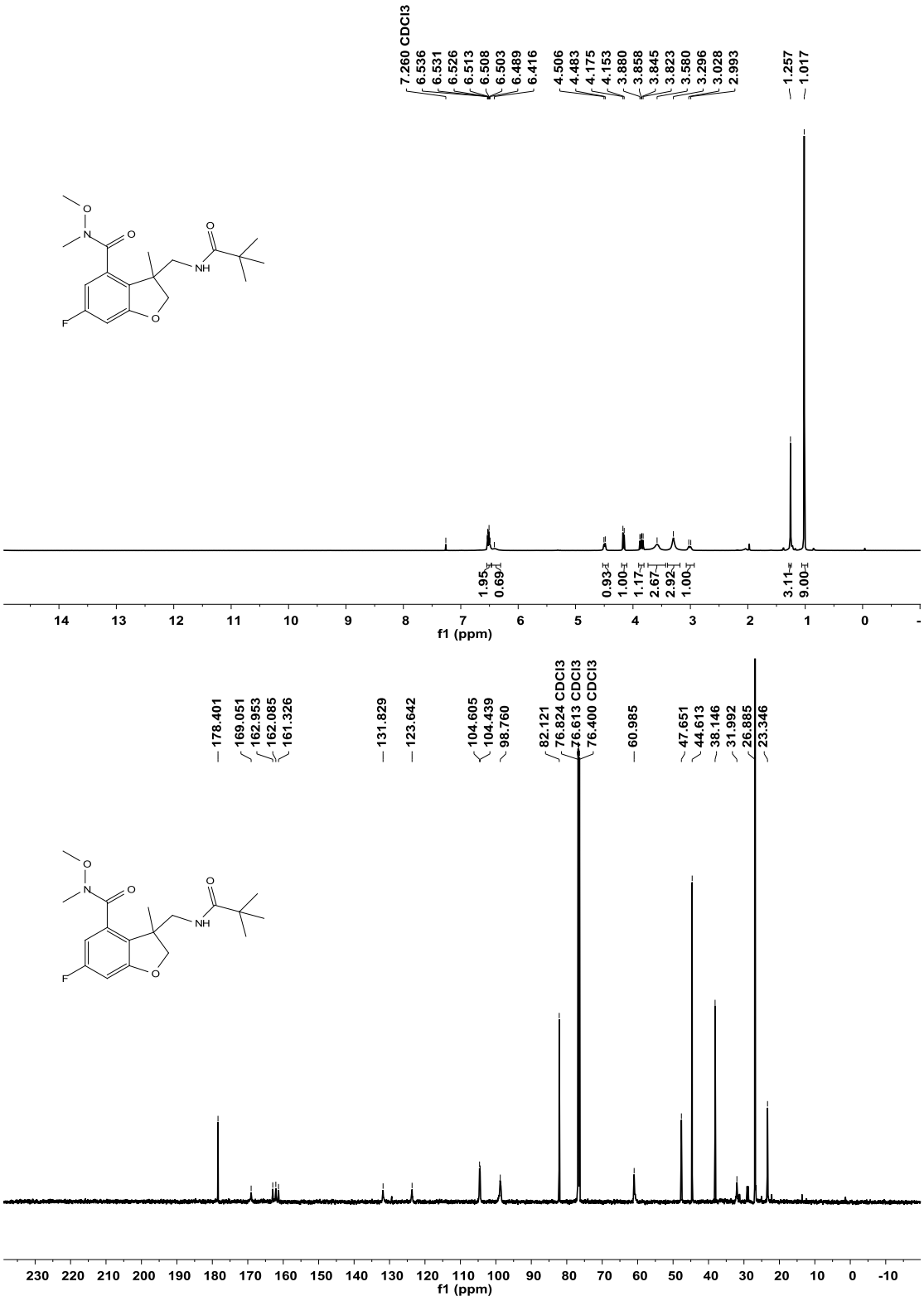



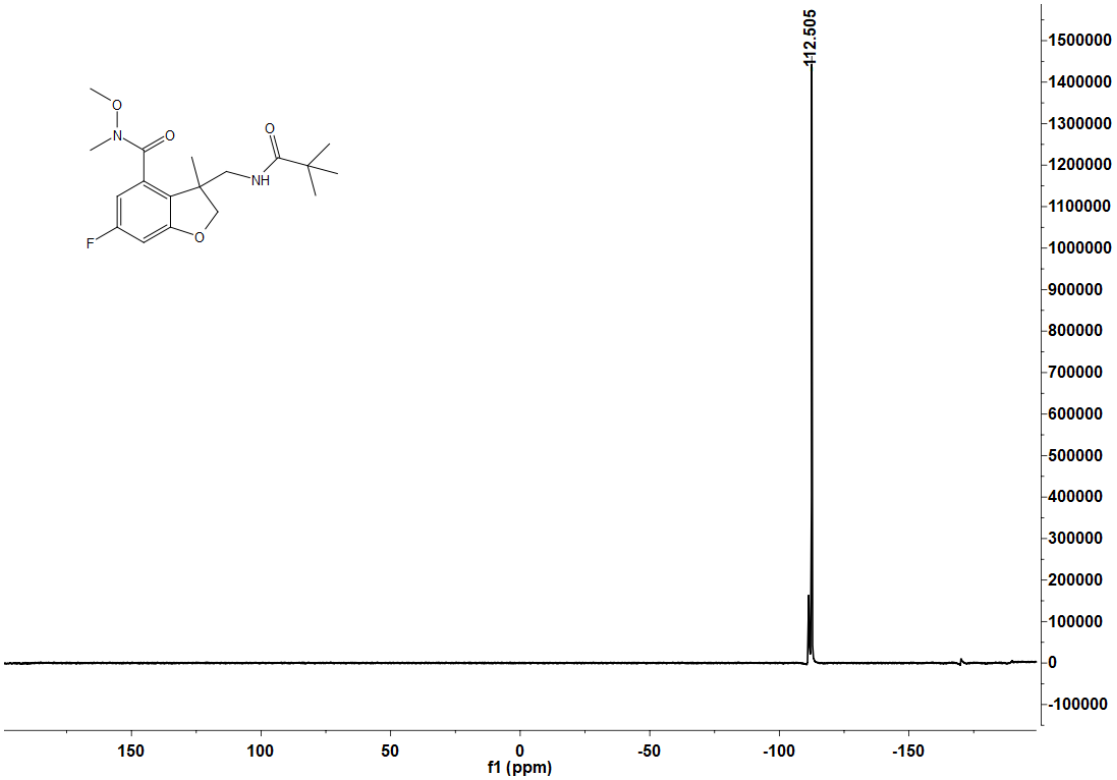
$^{1}H$ and $^{13}C$ NMR Spectra of Compound **4k:**



$^{1}H$ , $^{13}C$ and $^{19}F$ NMR Spectra of Compound **4l:**

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f1 (ppm)
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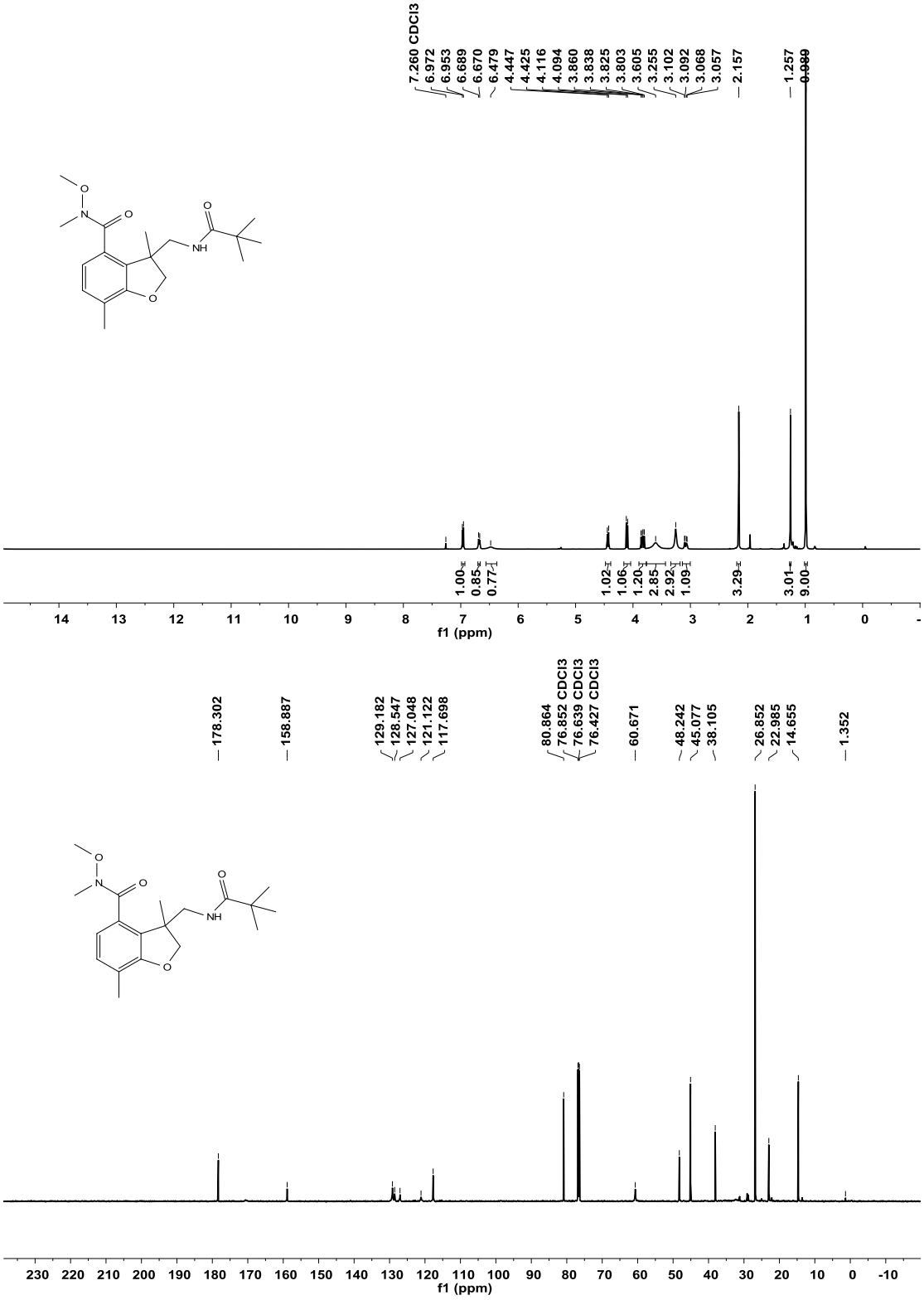
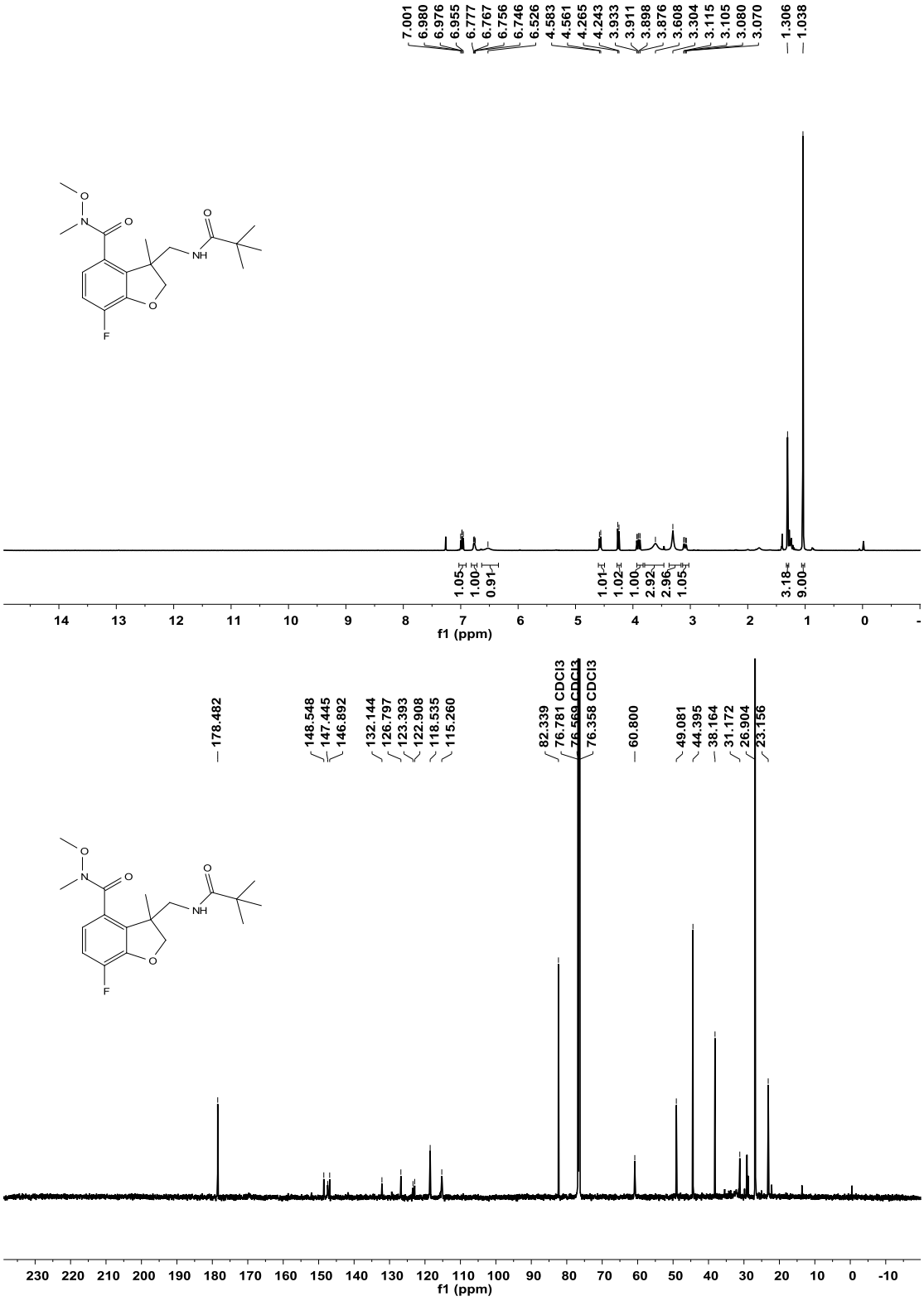
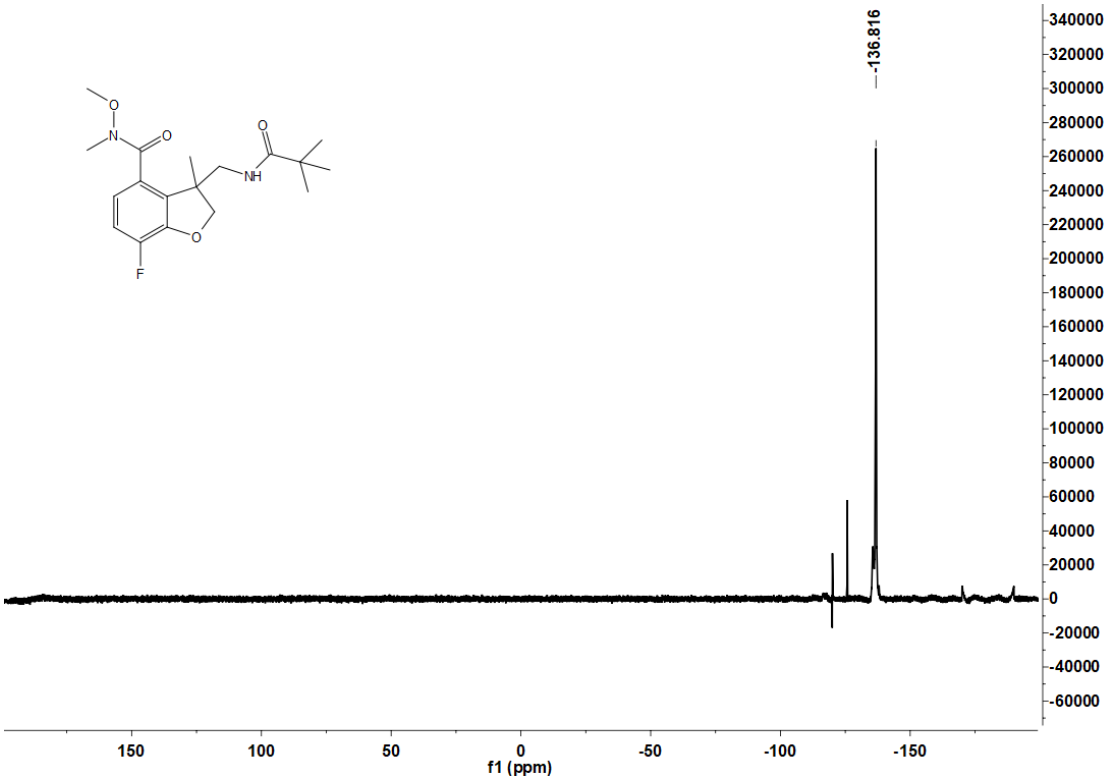
N
O
O
NH
F
O

$^{1}H$ and $^{13}C$ NMR Spectra of Compound **4m:**



$^{1}H$ , $^{13}C$ and $^{19}F$ NMR Spectra of Compound **4n:**

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40000
20000
0
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-40000
-60000
150
100
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f1 (ppm)
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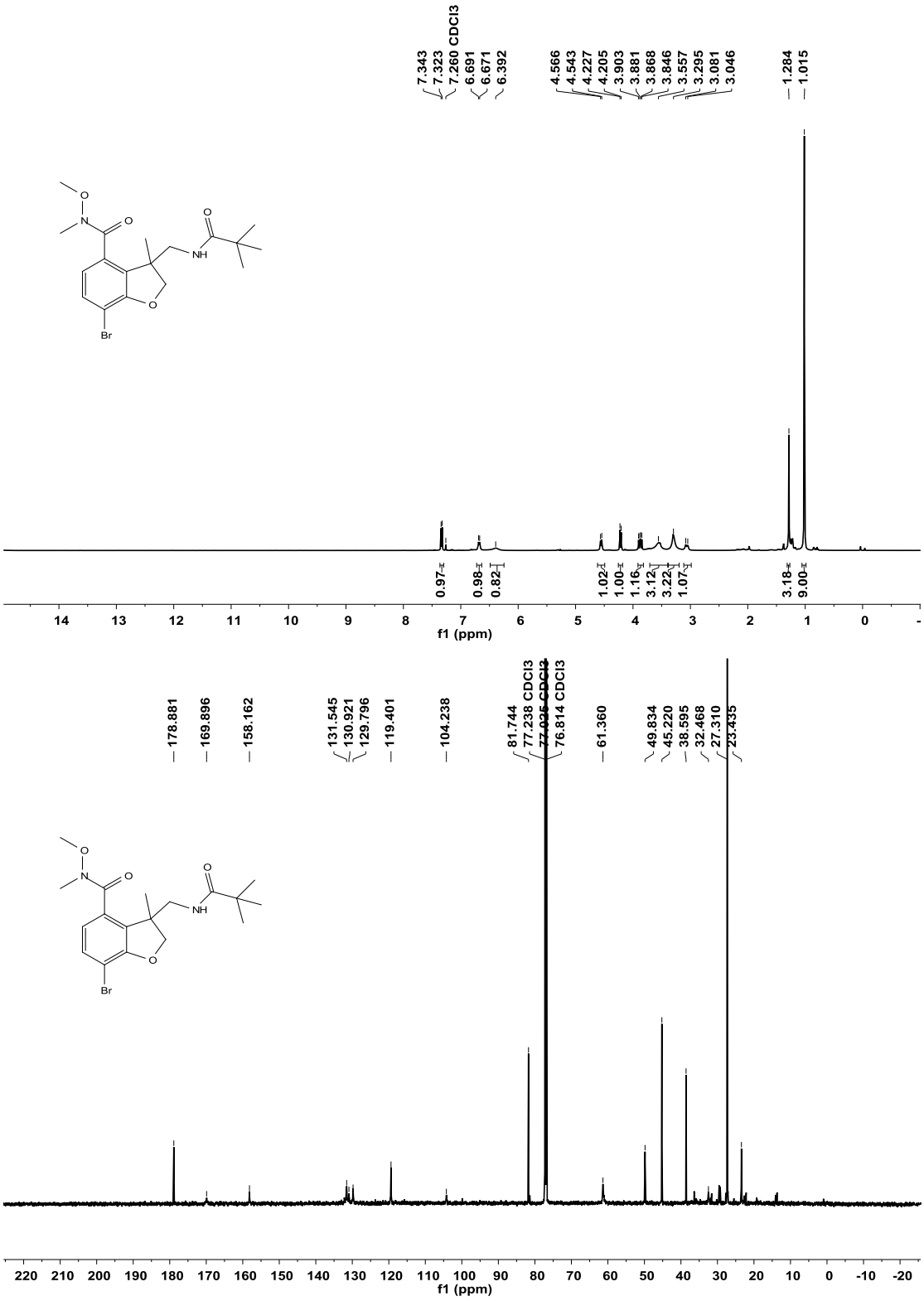
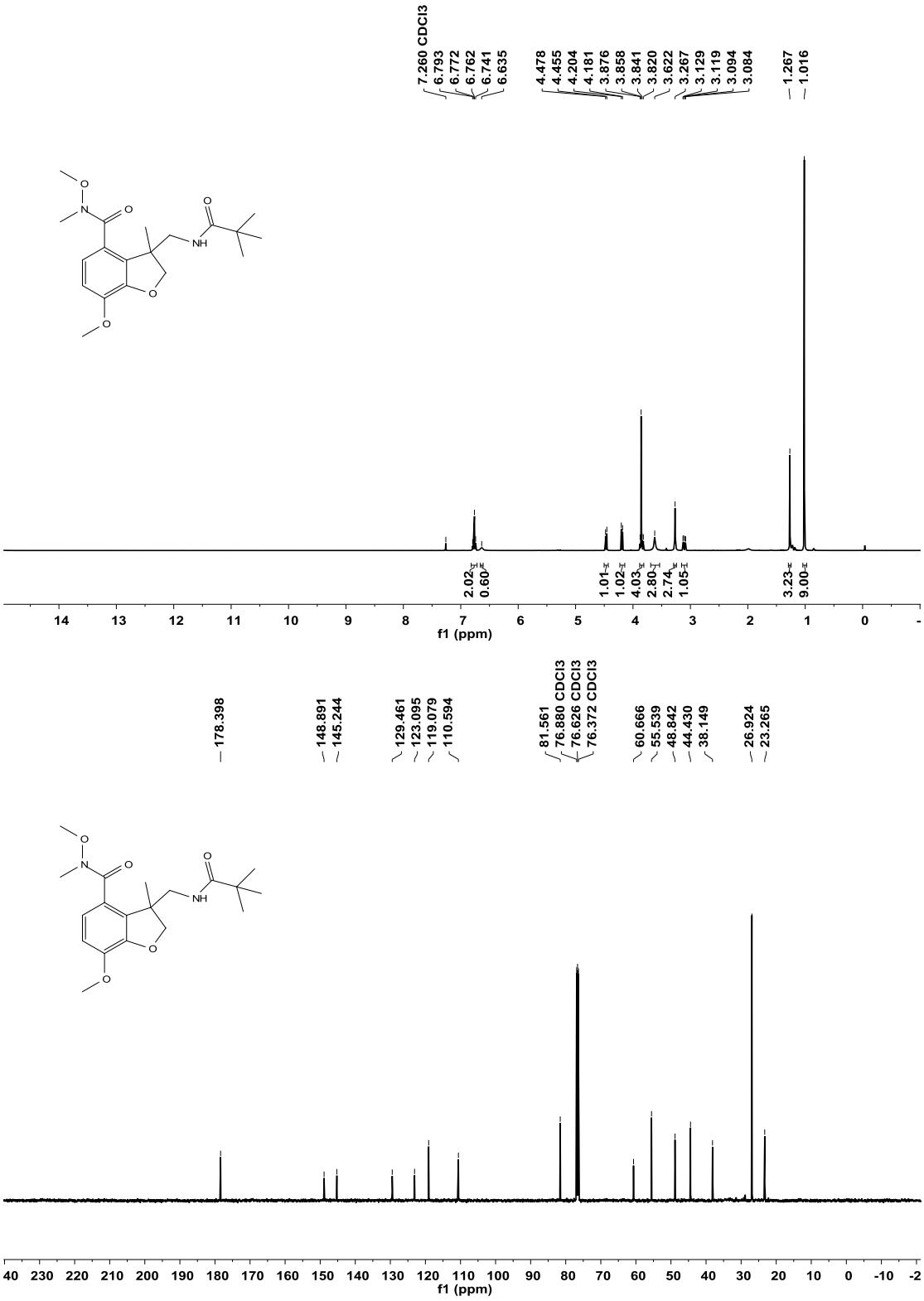
N
O
O
NH
O
F

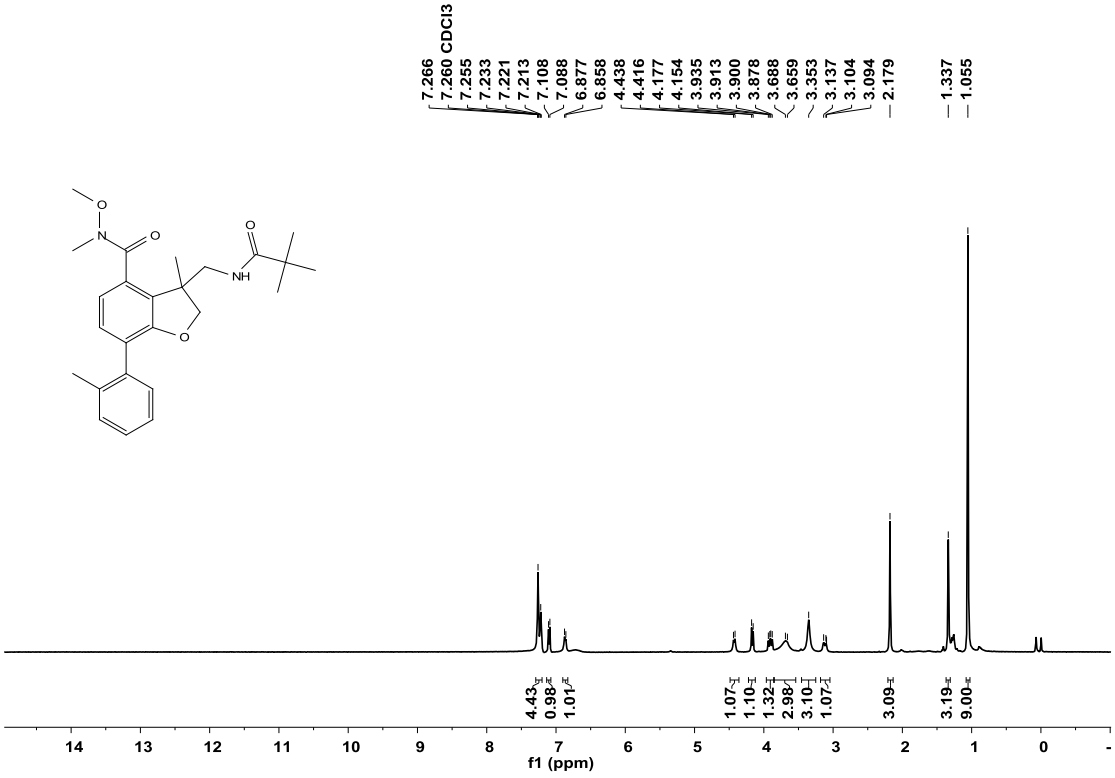
$^{1}$H and $^{13}$C NMR Spectra of Compound **4o:**

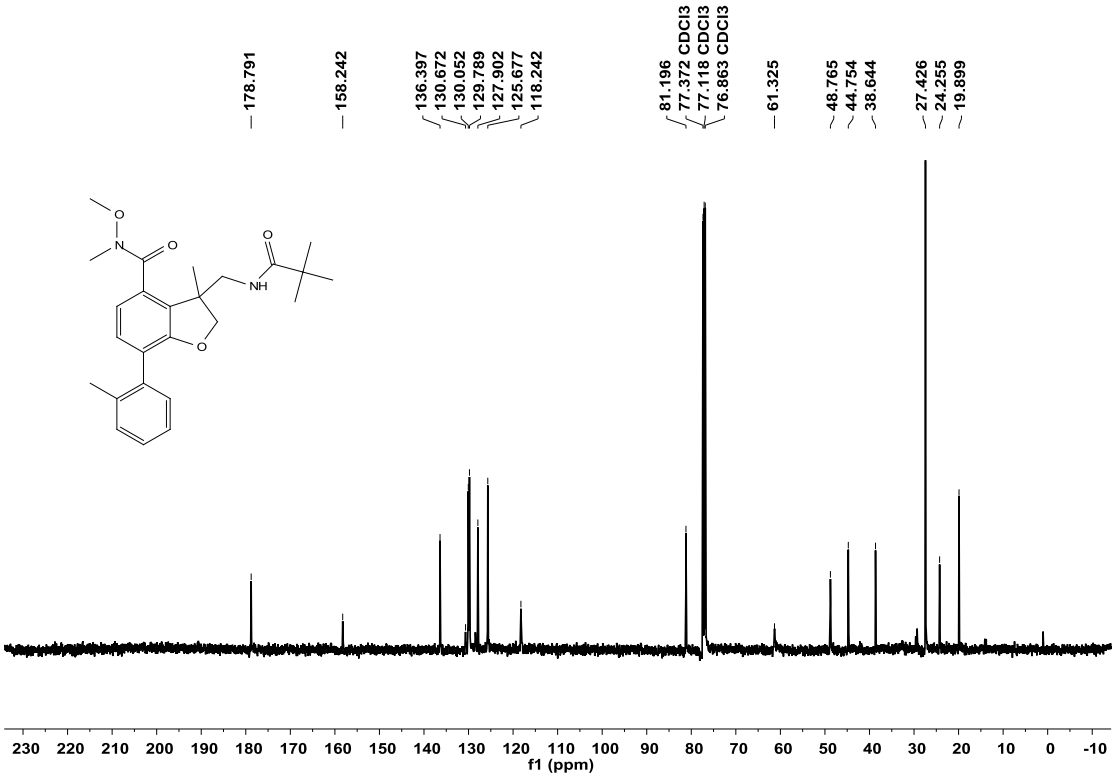


$^{1}H$ and $^{13}C$ NMR Spectra of Compound **4p:**

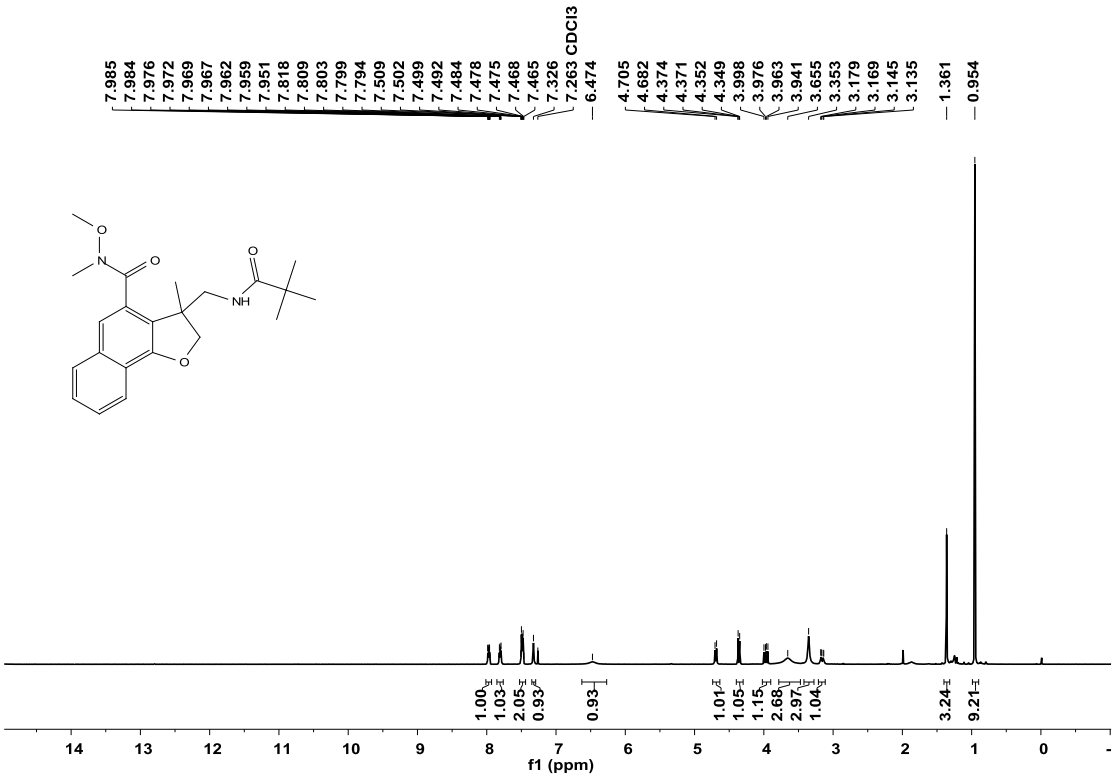


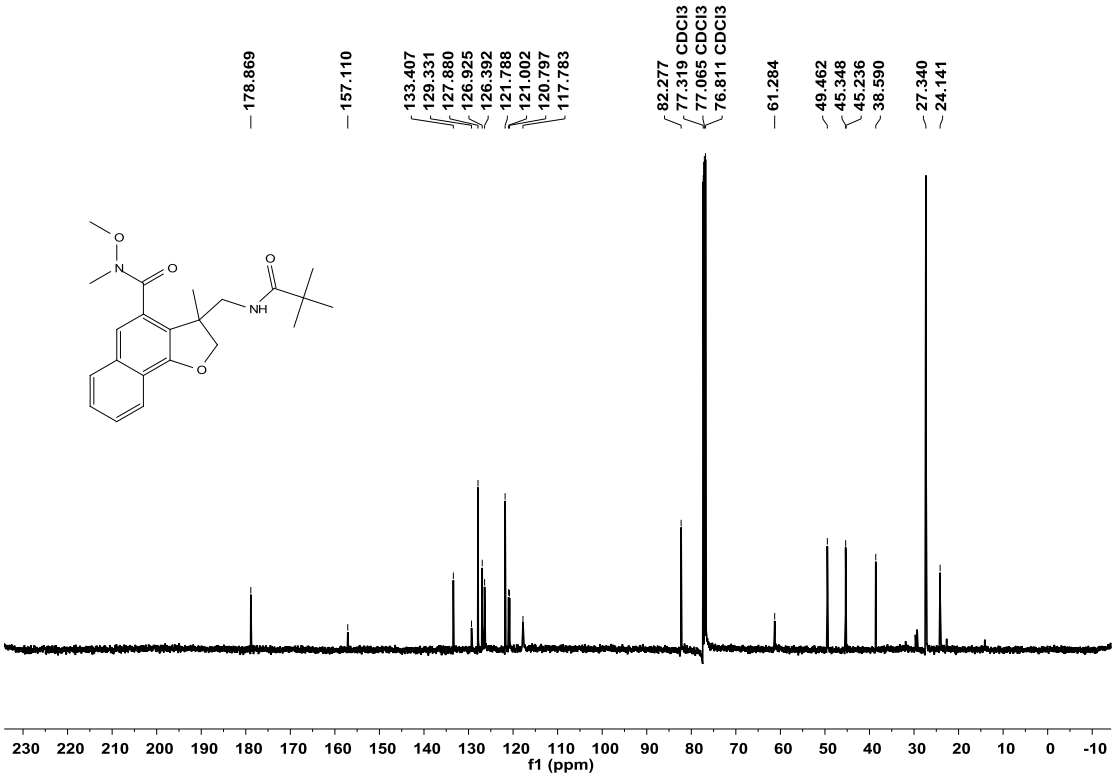
$^{1}H$ and $^{13}C$ NMR Spectra of Compound **4q:**



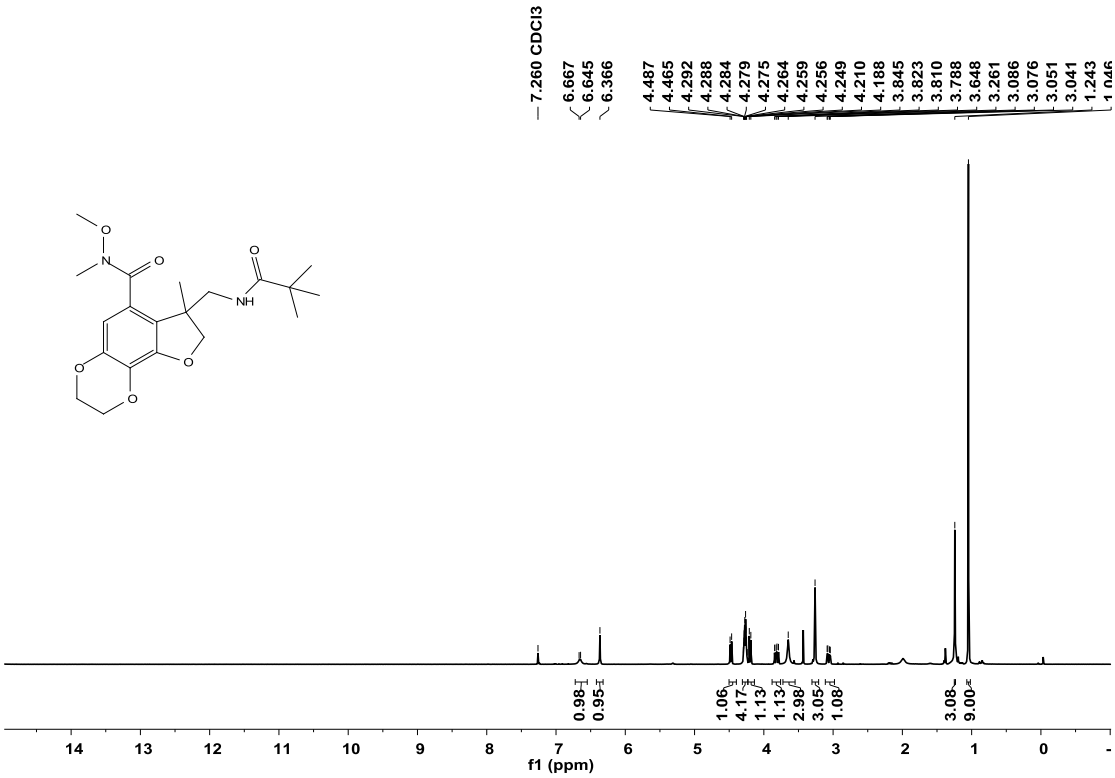



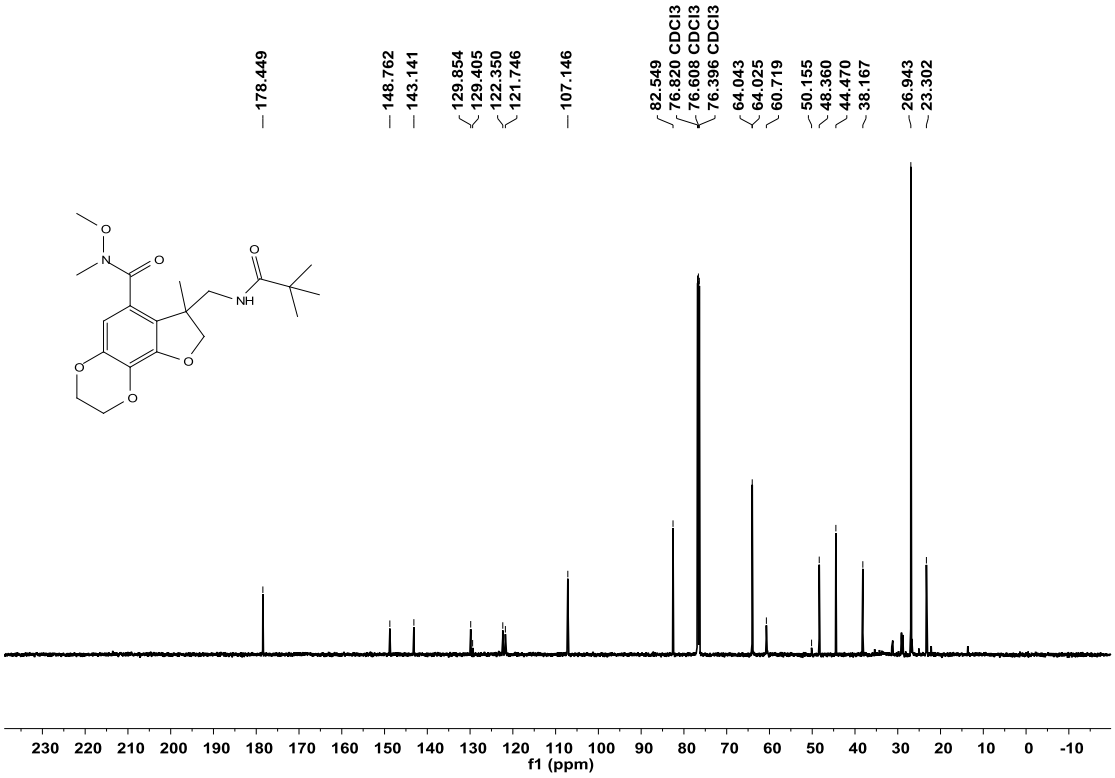
$^{1}H$ and $^{13}C$ NMR Spectra of Compound **4r:**



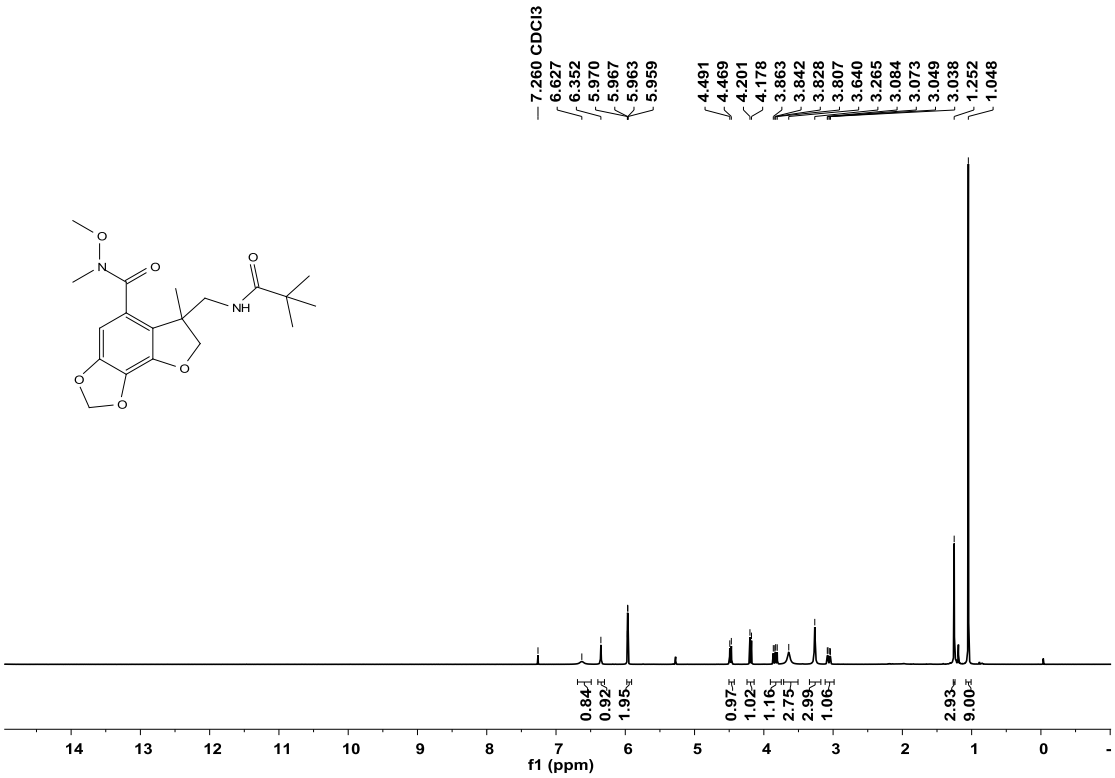



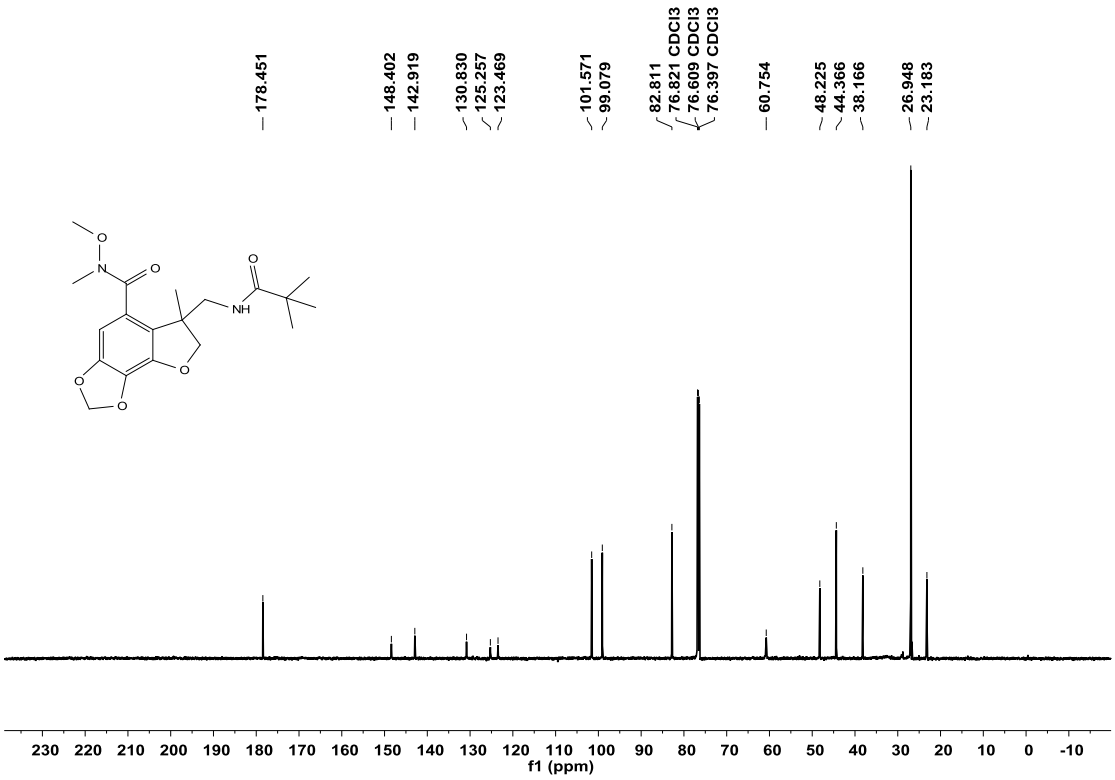
$^{1}$H and $^{13}$C NMR Spectra of Compound **4s:**



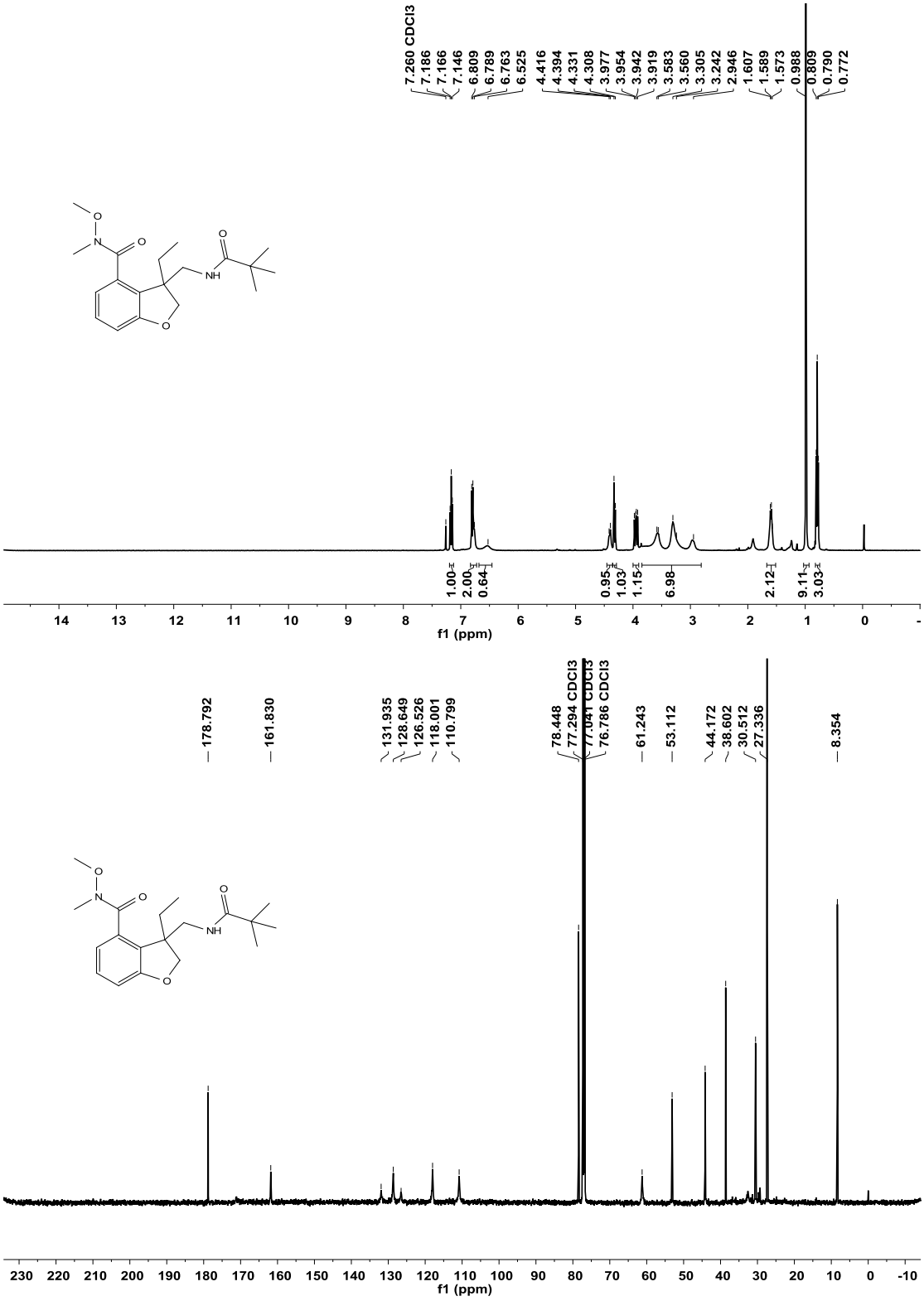



$^{1}H$ and $^{13}C$ NMR Spectra of Compound **4t:**

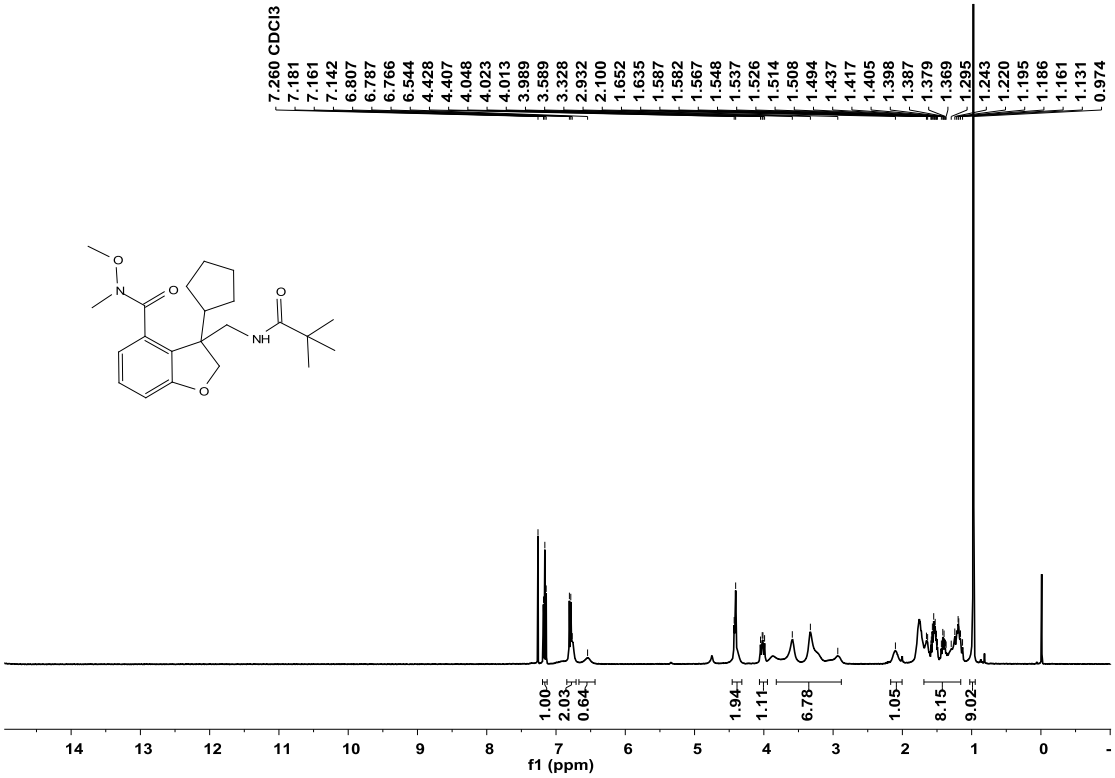


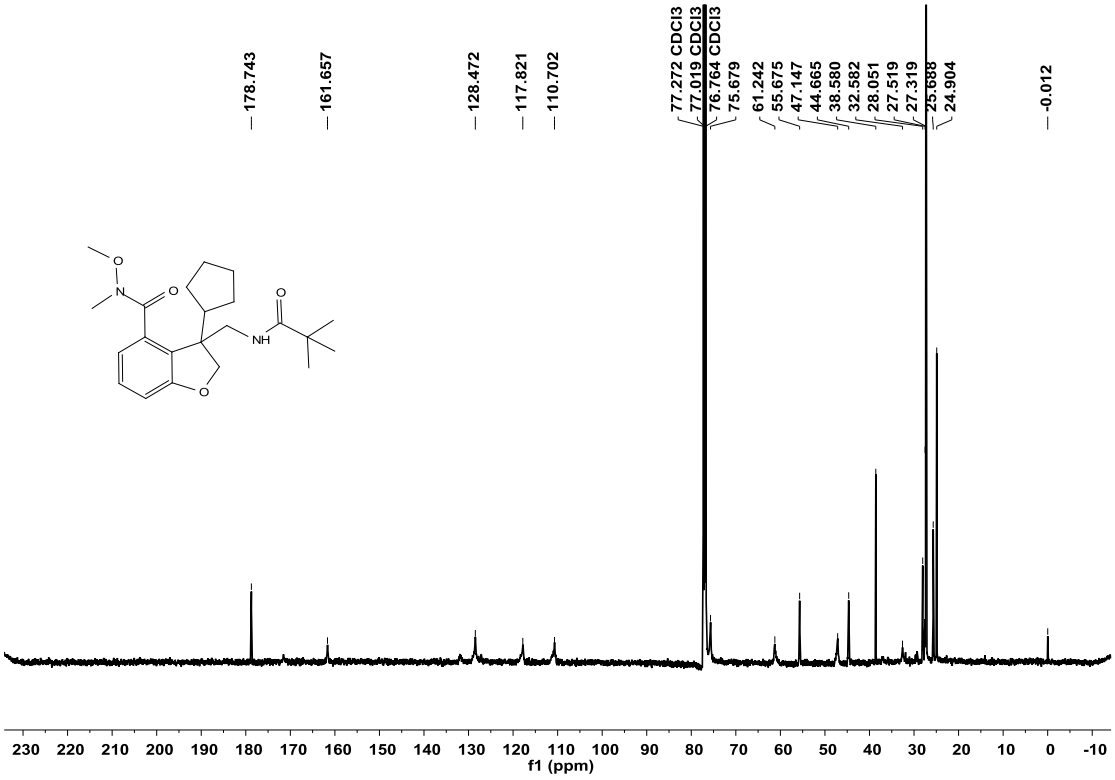



$^{1}H$ and $^{13}C$ NMR Spectra of Compound **4u:**

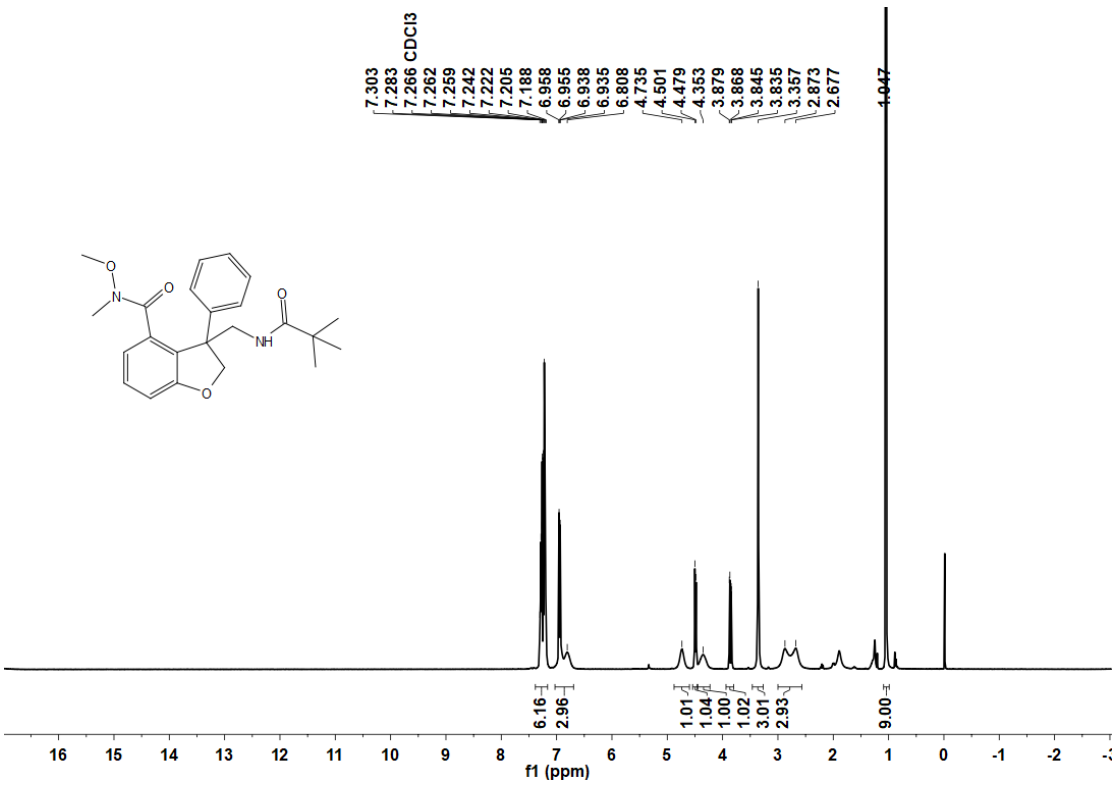


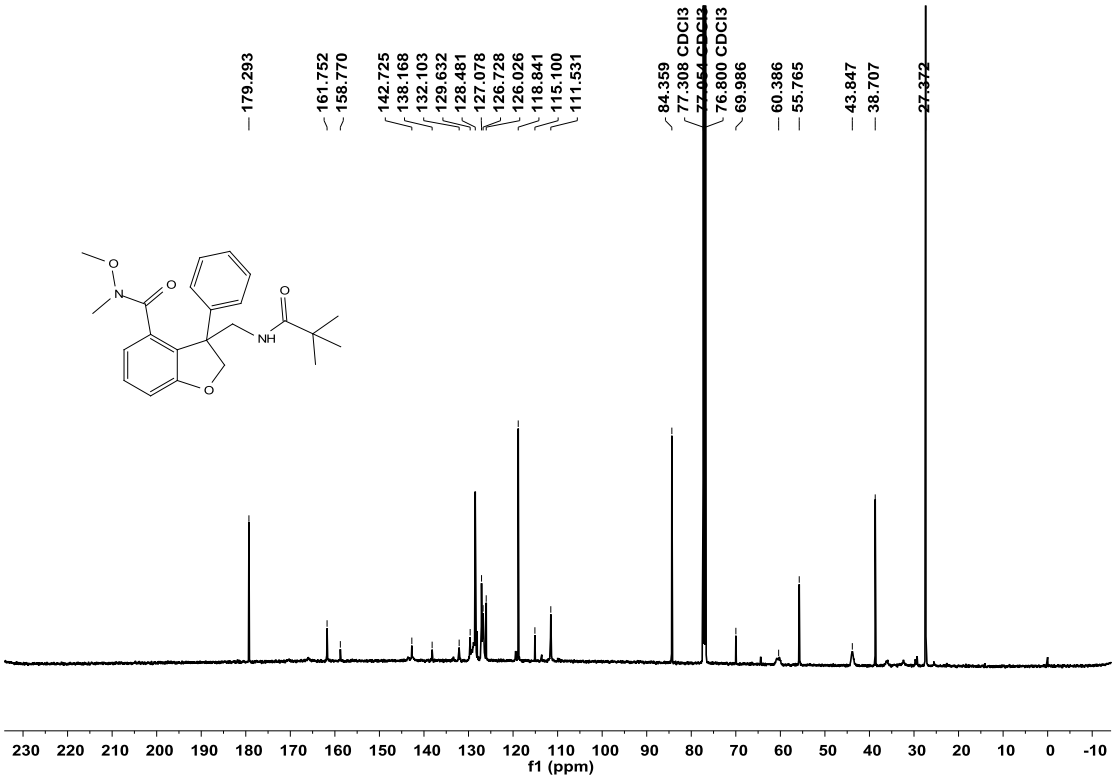
$^{1}H$ and $^{13}C$ NMR Spectra of Compound **4v:**



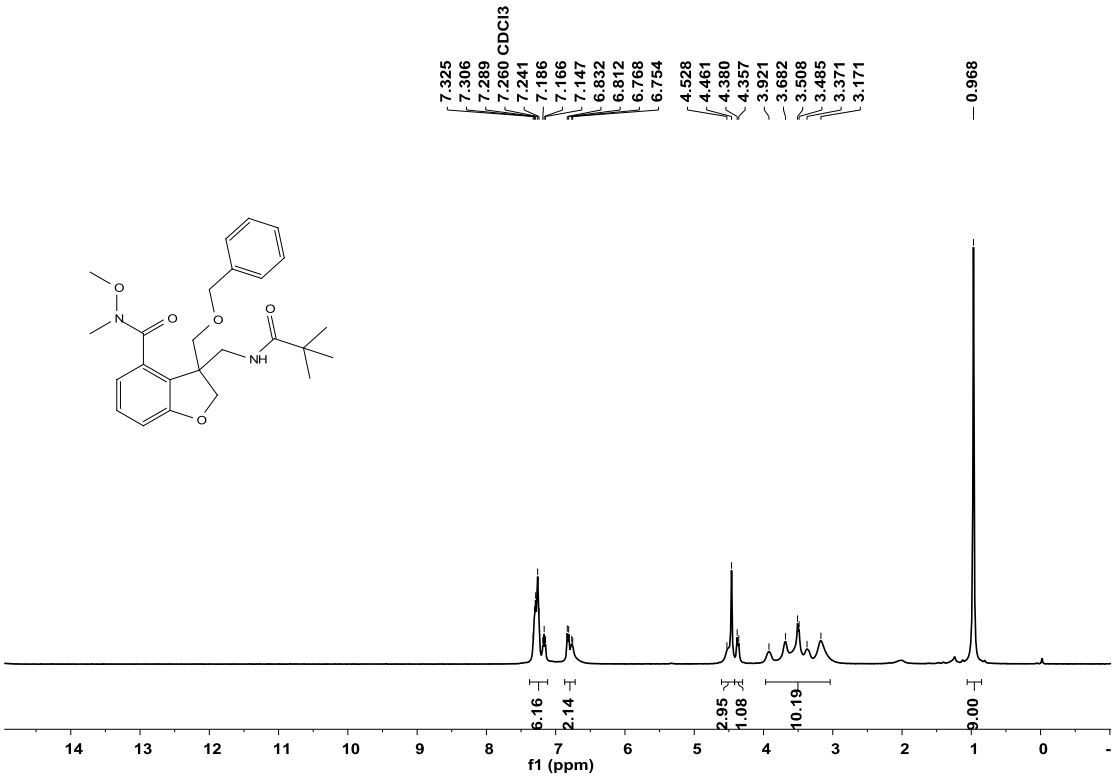



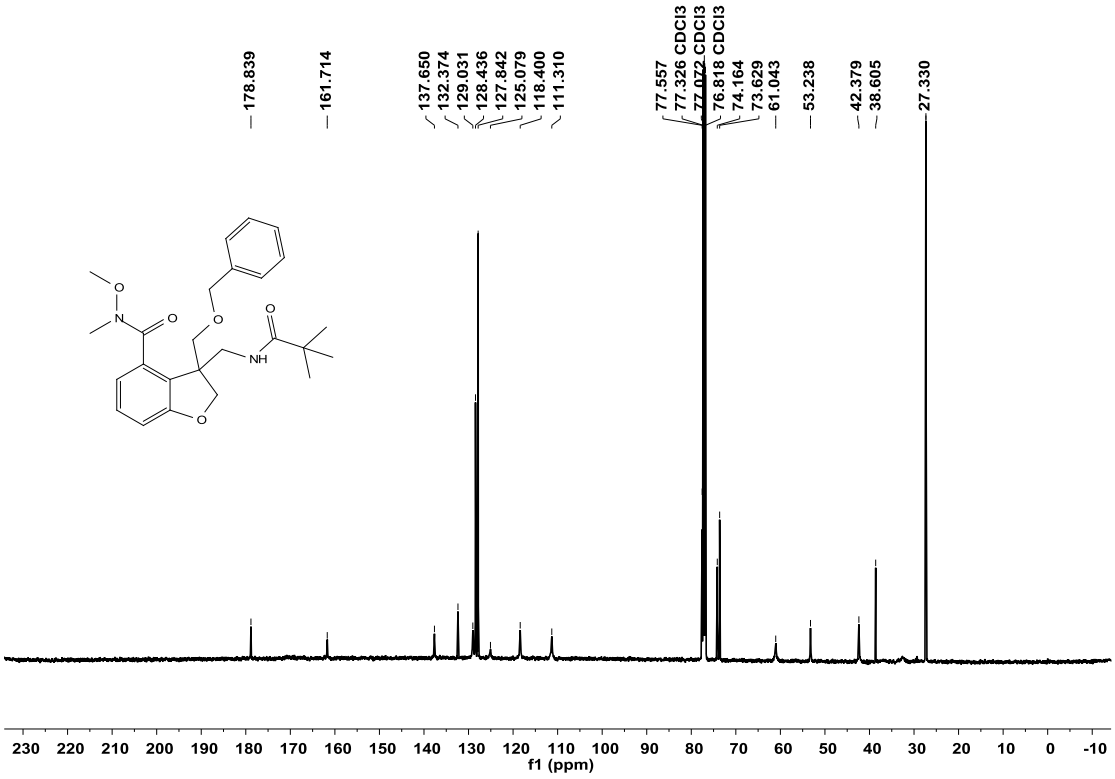
$^{1}$H and $^{13}$C NMR Spectra of Compound **4w:**



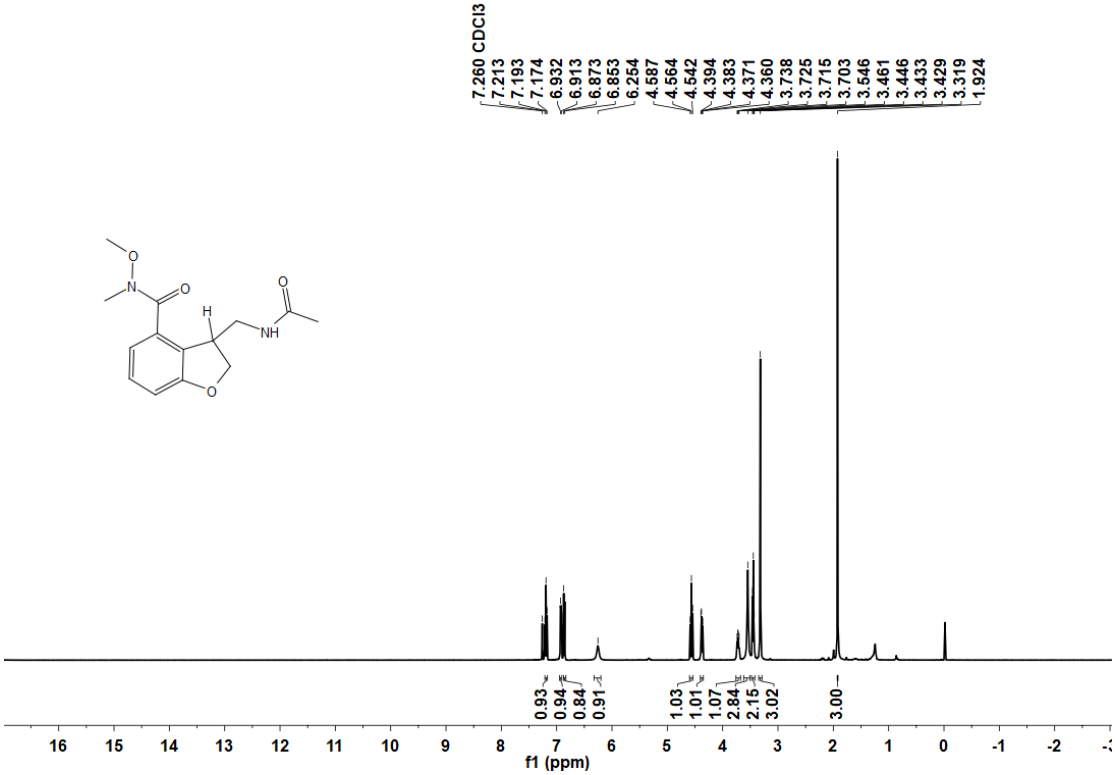



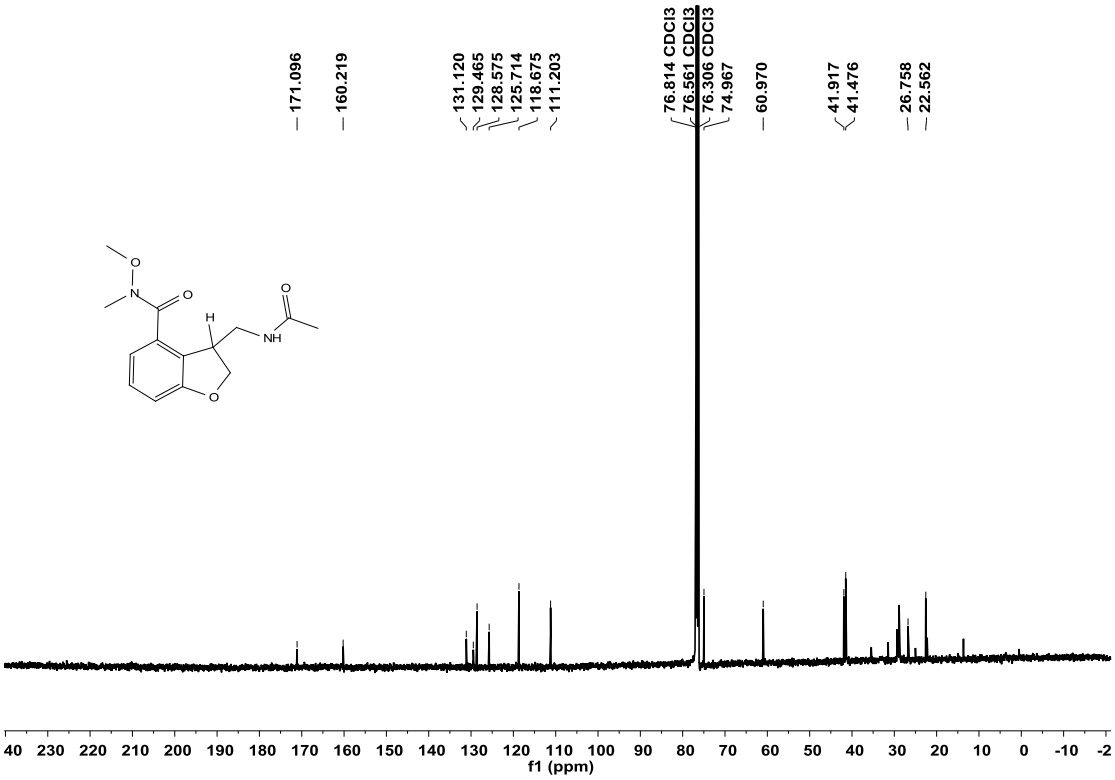
$^{1}H$ and $^{13}C$ NMR Spectra of Compound **4x:**



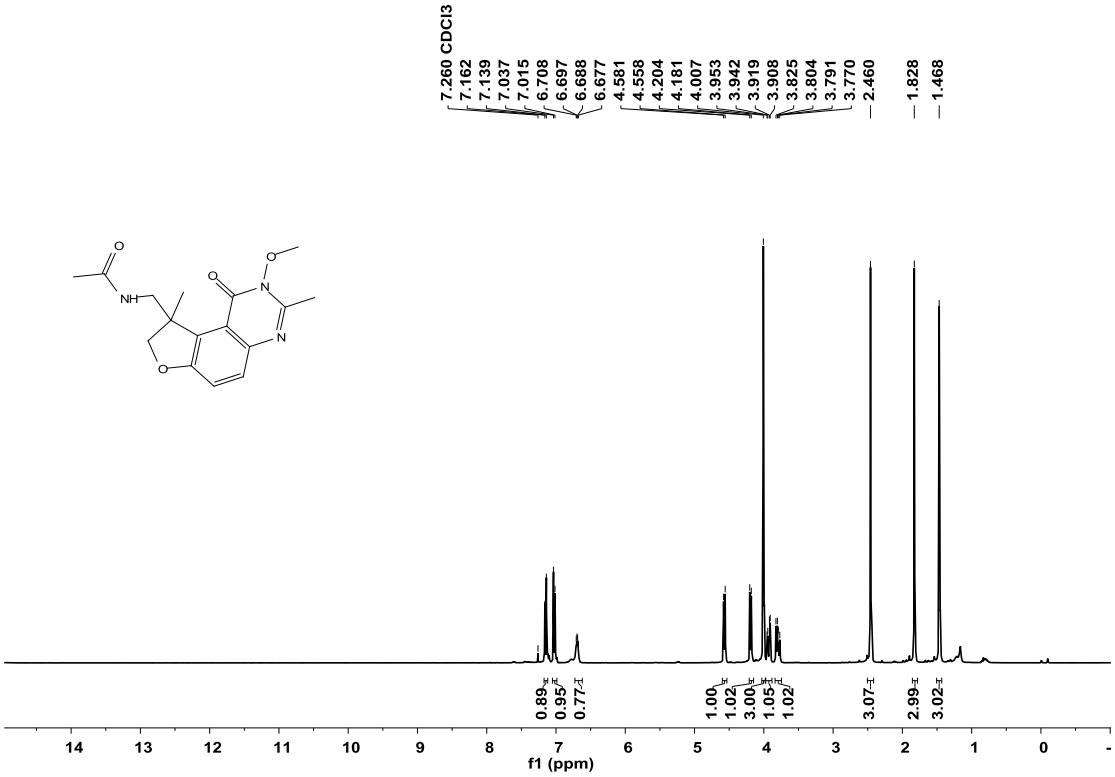



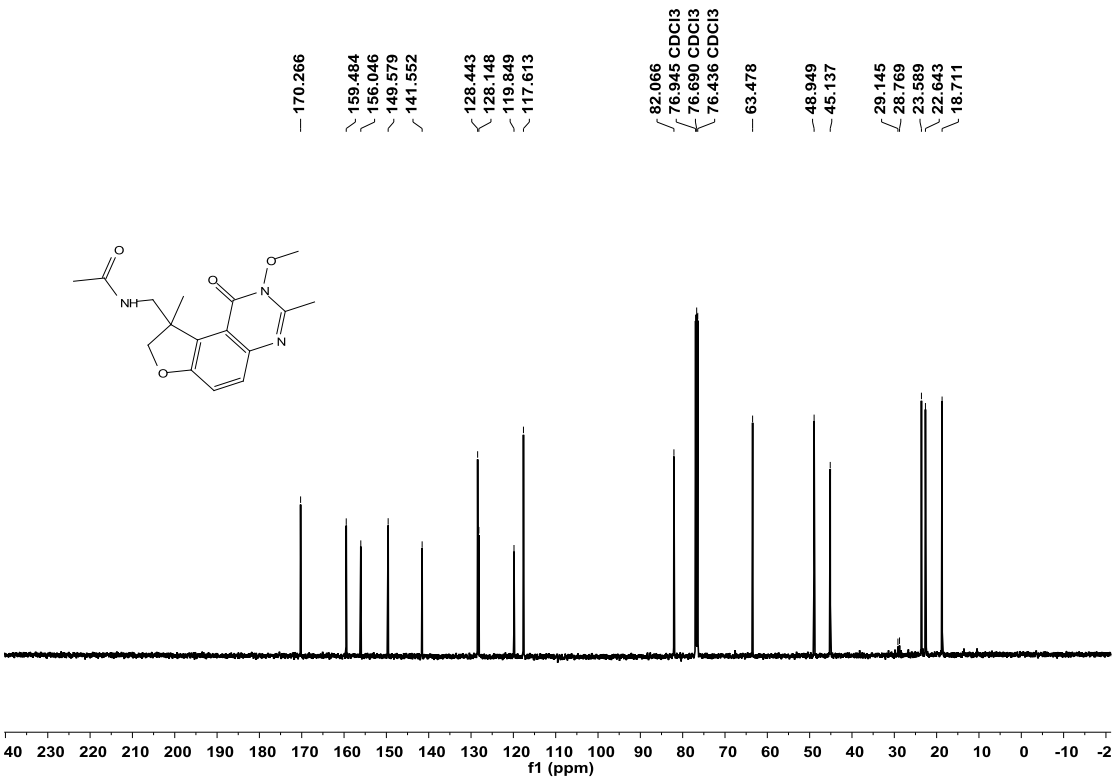
$^{1}H$ and $^{13}C$ NMR Spectra of Compound **4y:**



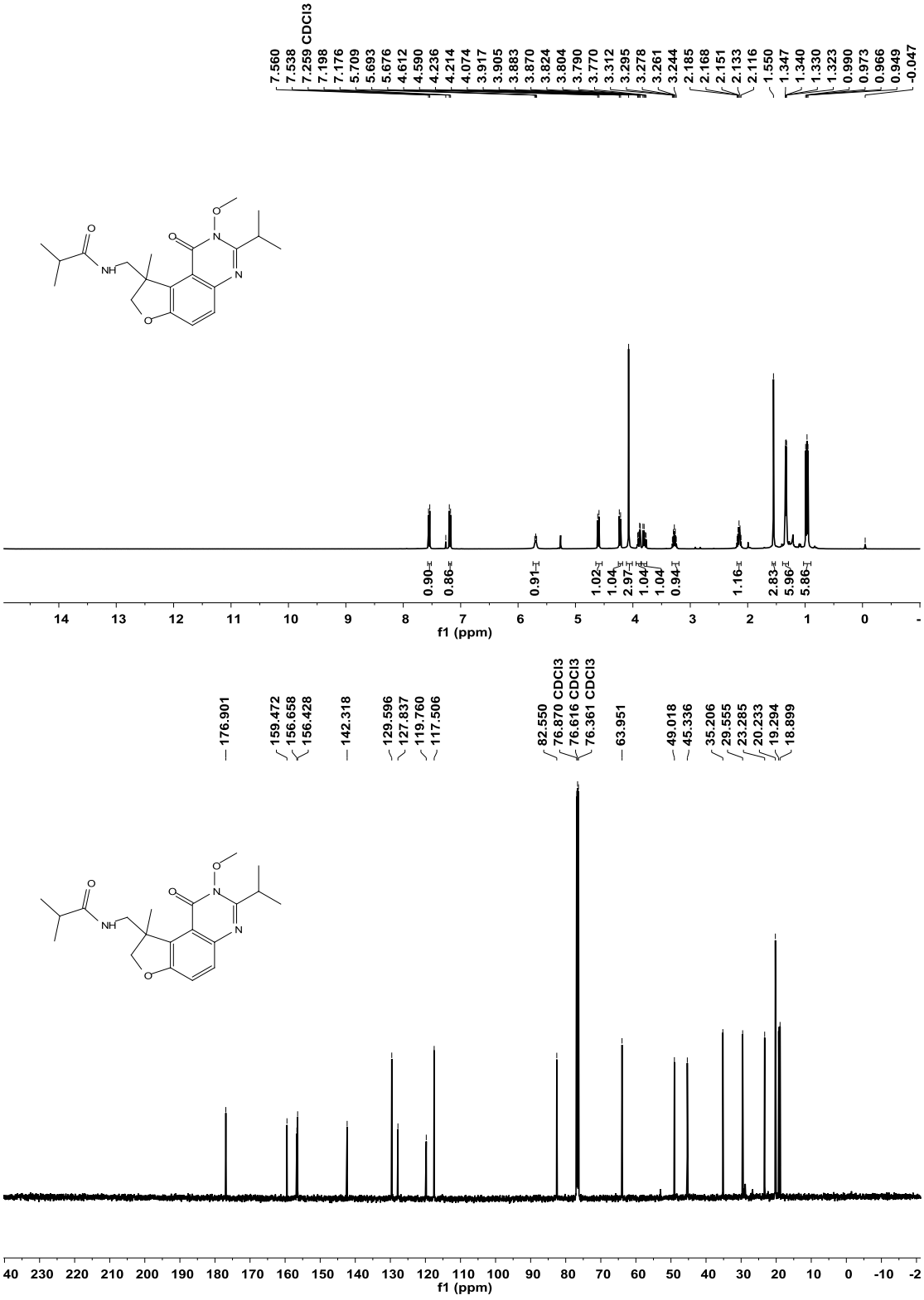



$^{1}H$ and $^{13}C$ NMR Spectra of Compound **5a:**

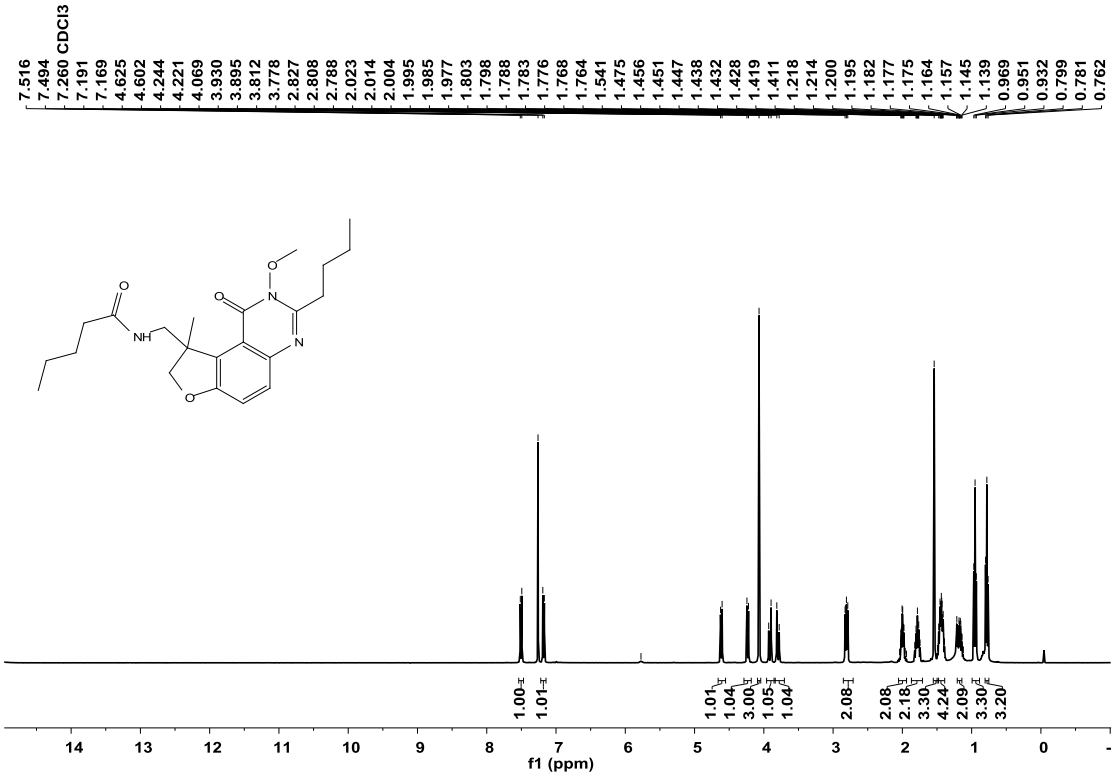


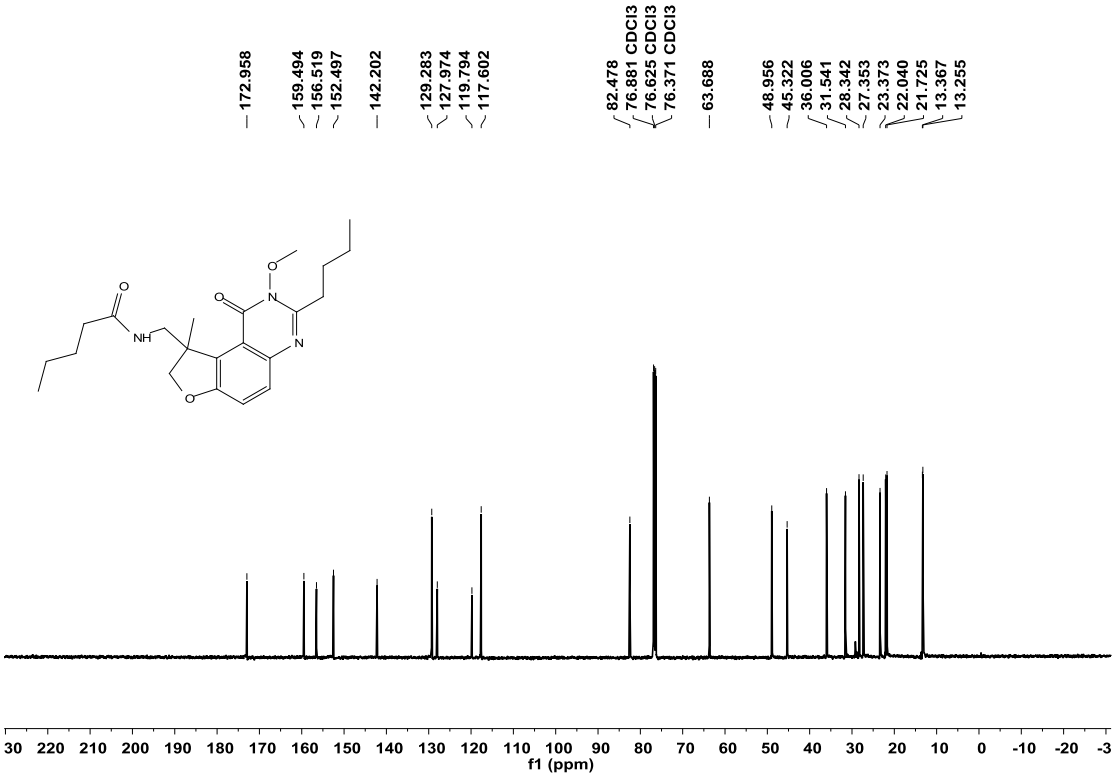



$^{1}H$ and $^{13}C$ NMR Spectra of Compound **5b:**

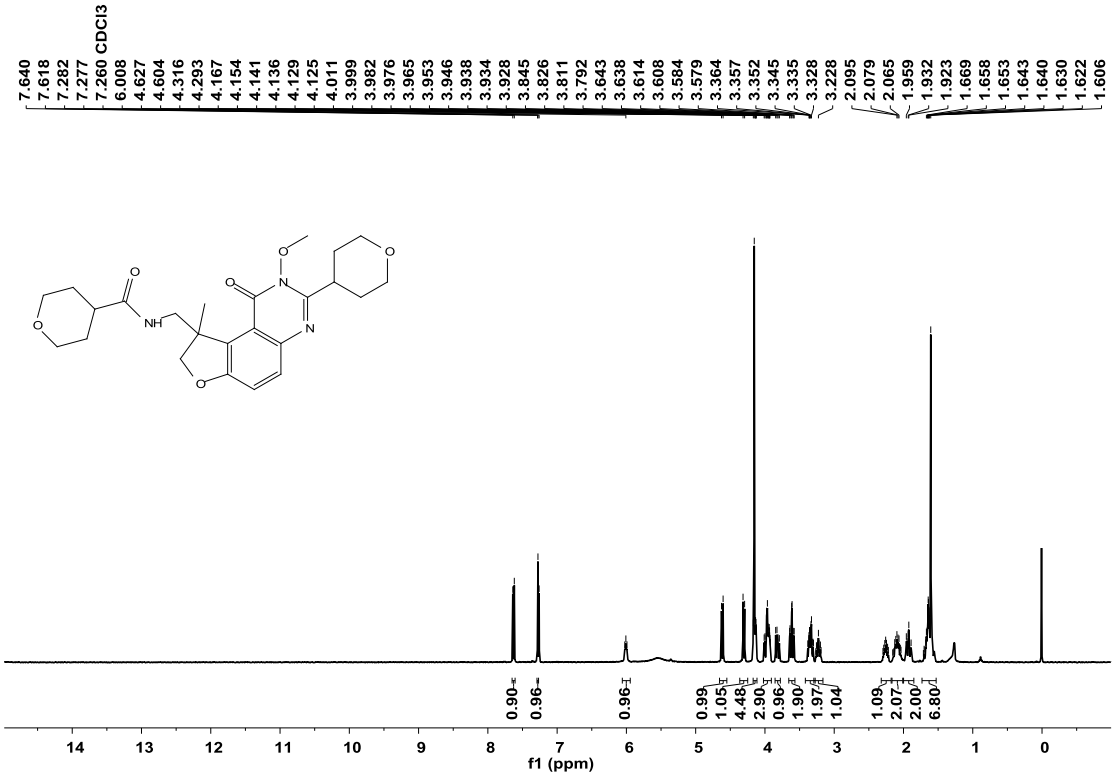


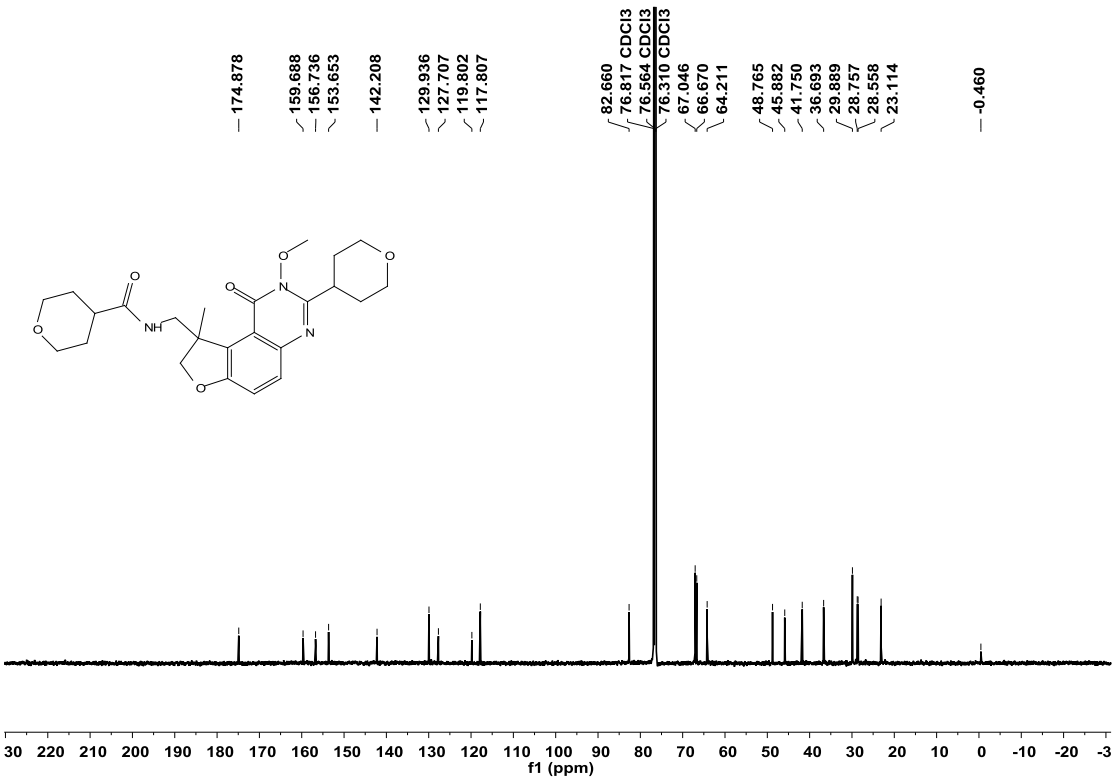
$^{1}H$ and $^{13}C$ NMR Spectra of Compound **5c:**



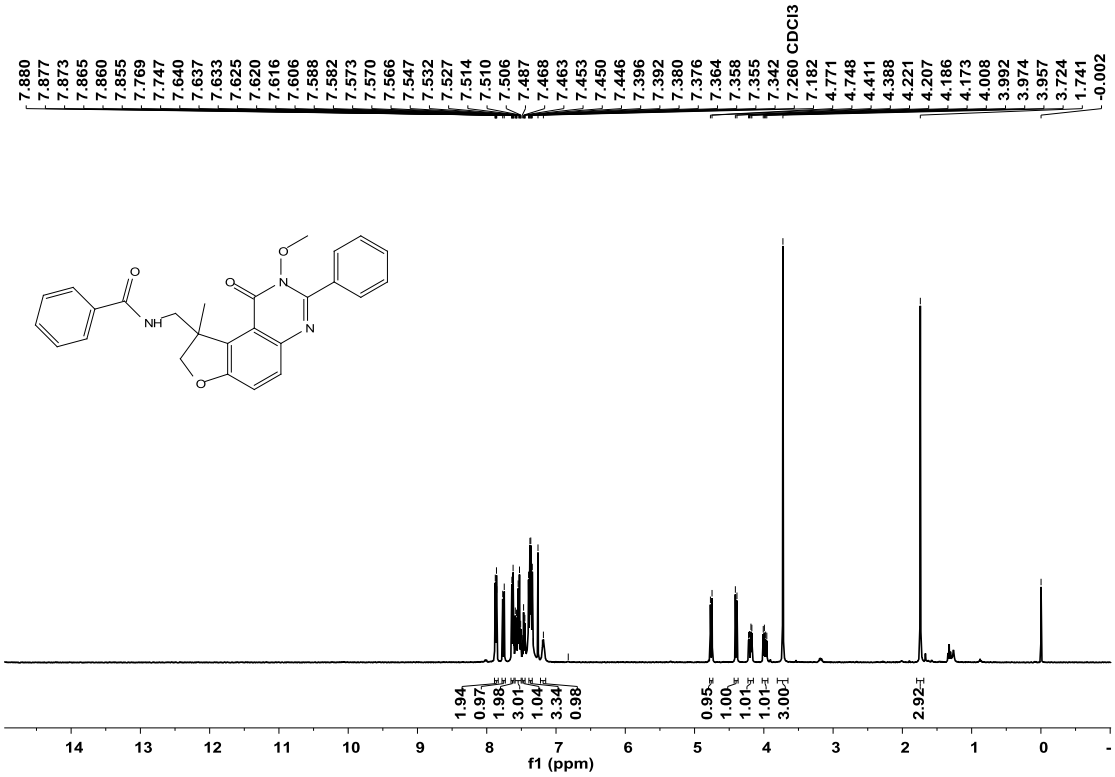



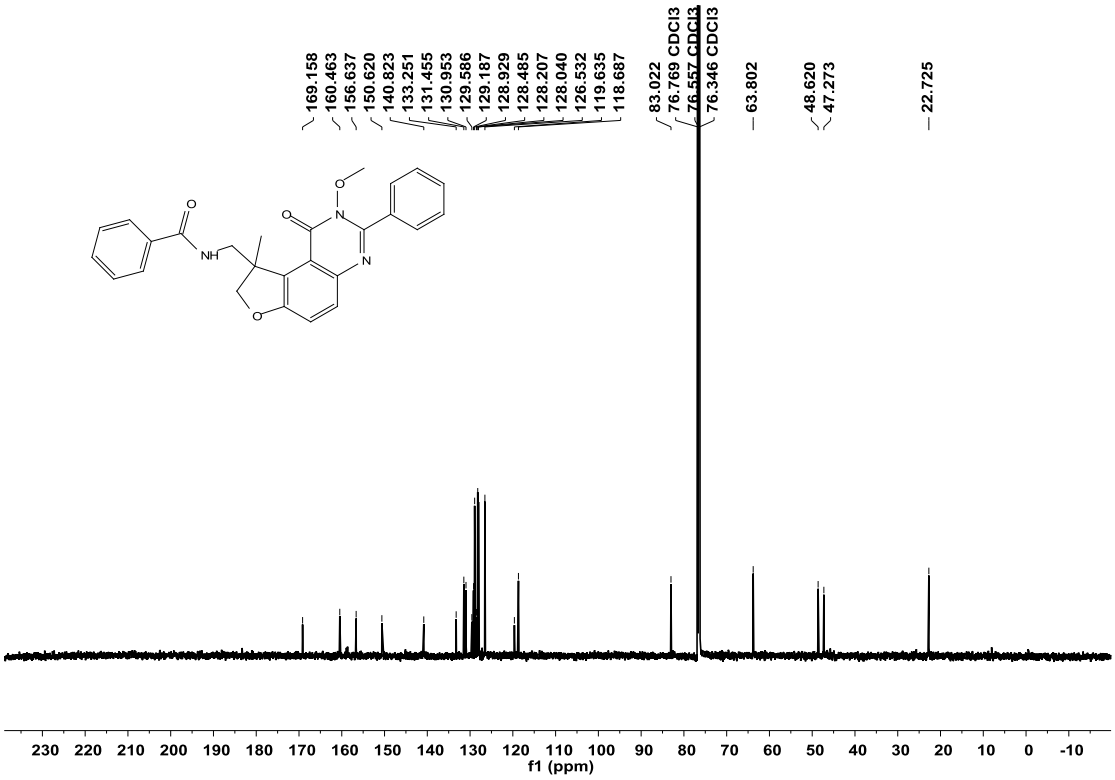
$^{1}H$ and $^{13}C$ NMR Spectra of Compound **5d:**



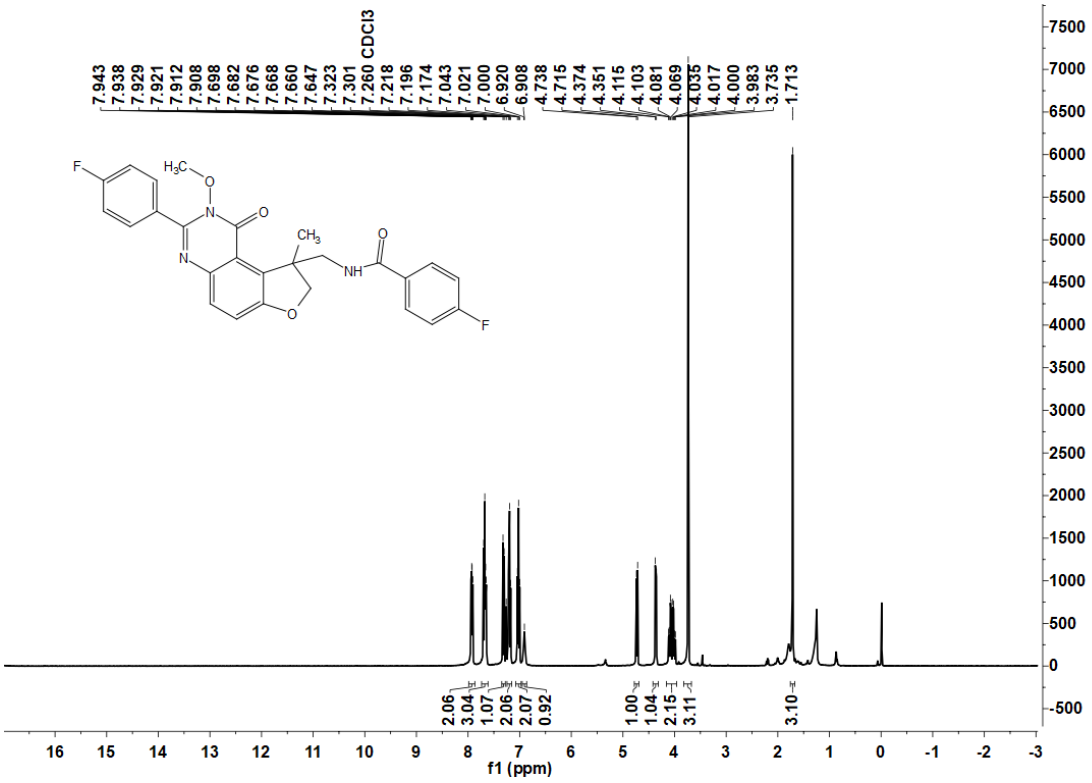



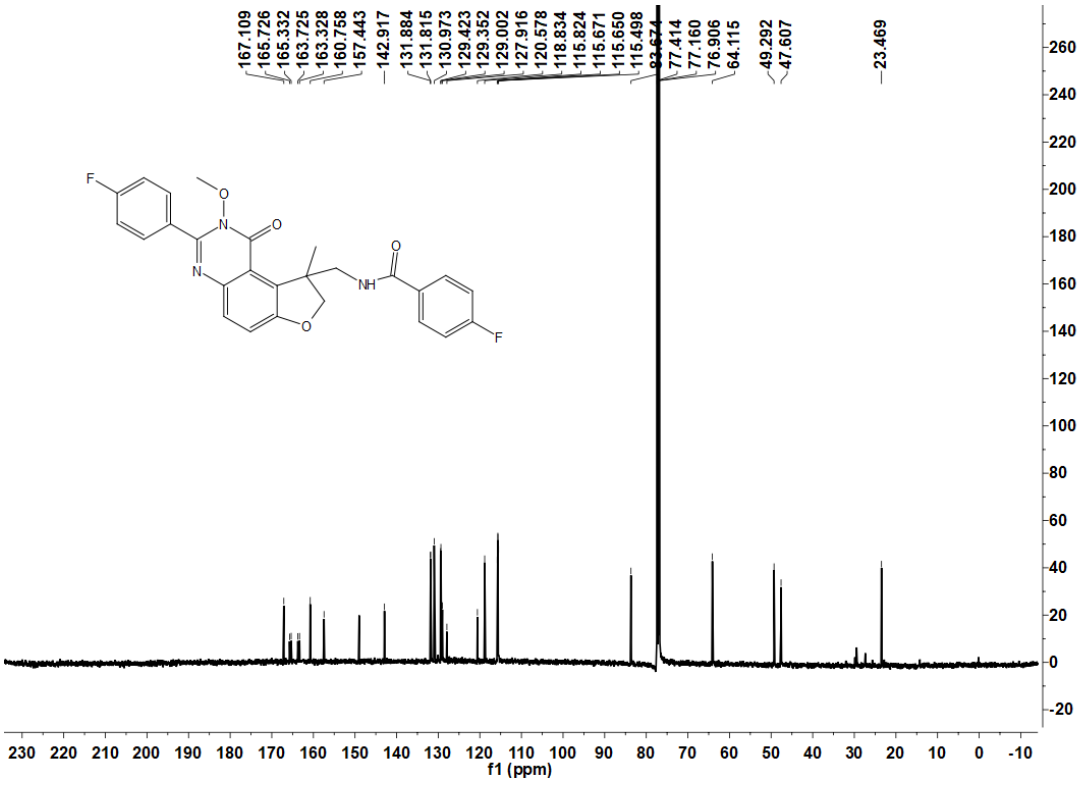
$^{1}H$ and $^{13}C$ NMR Spectra of Compound **5e:**

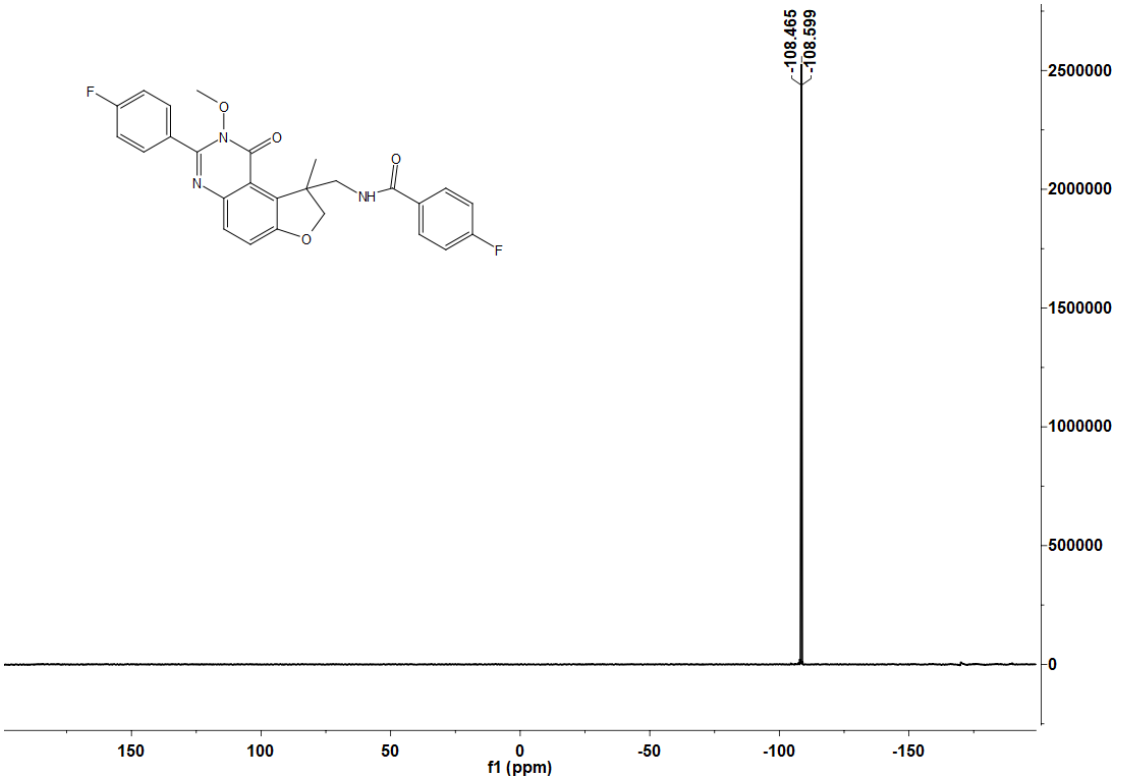


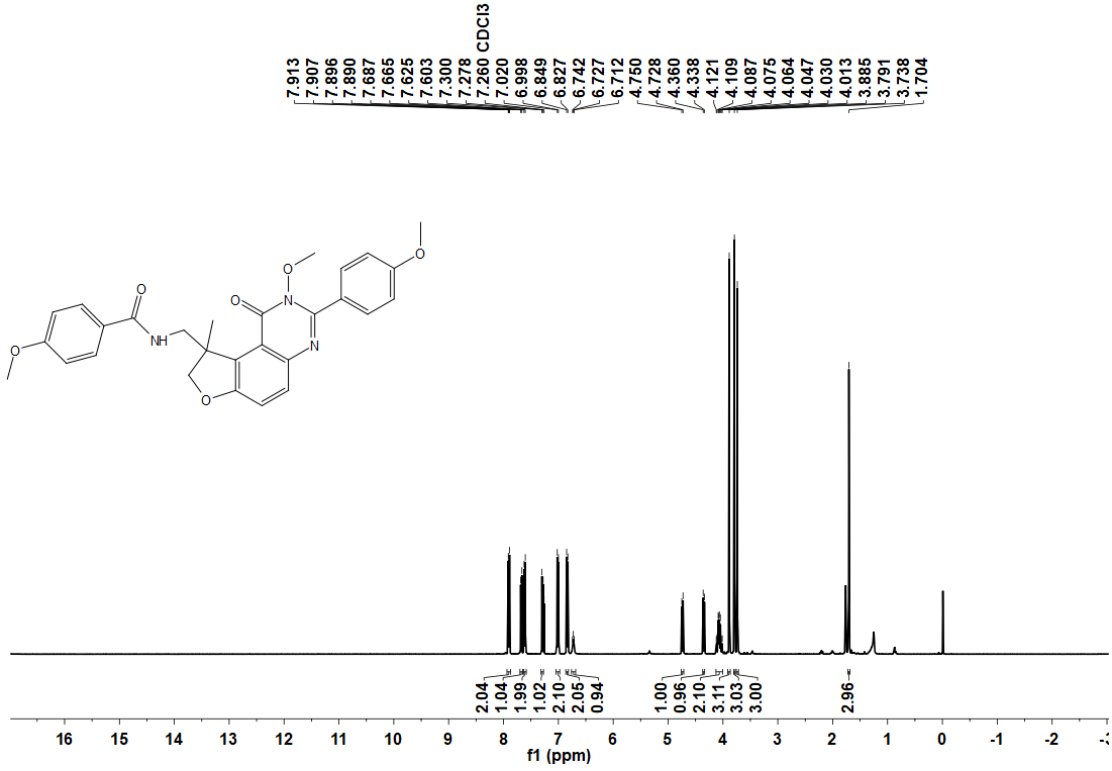
$^{1}H$ , $^{13}C$ and $^{19}F$ NMR Spectra of Compound **5f:**

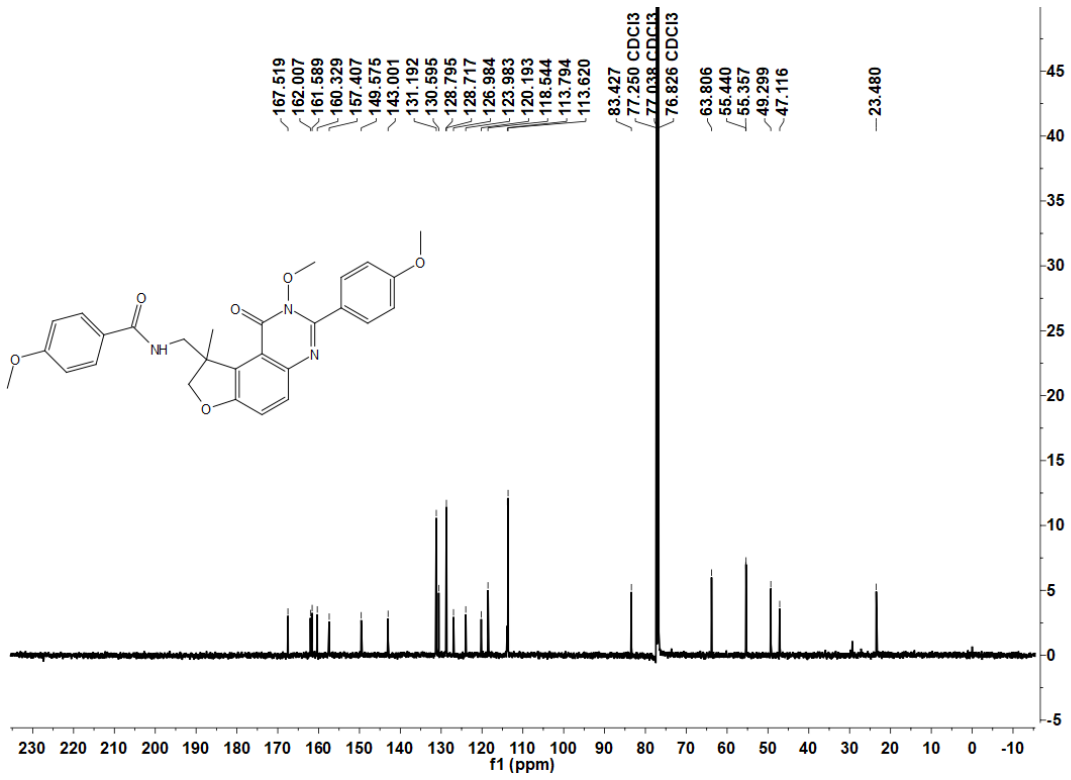


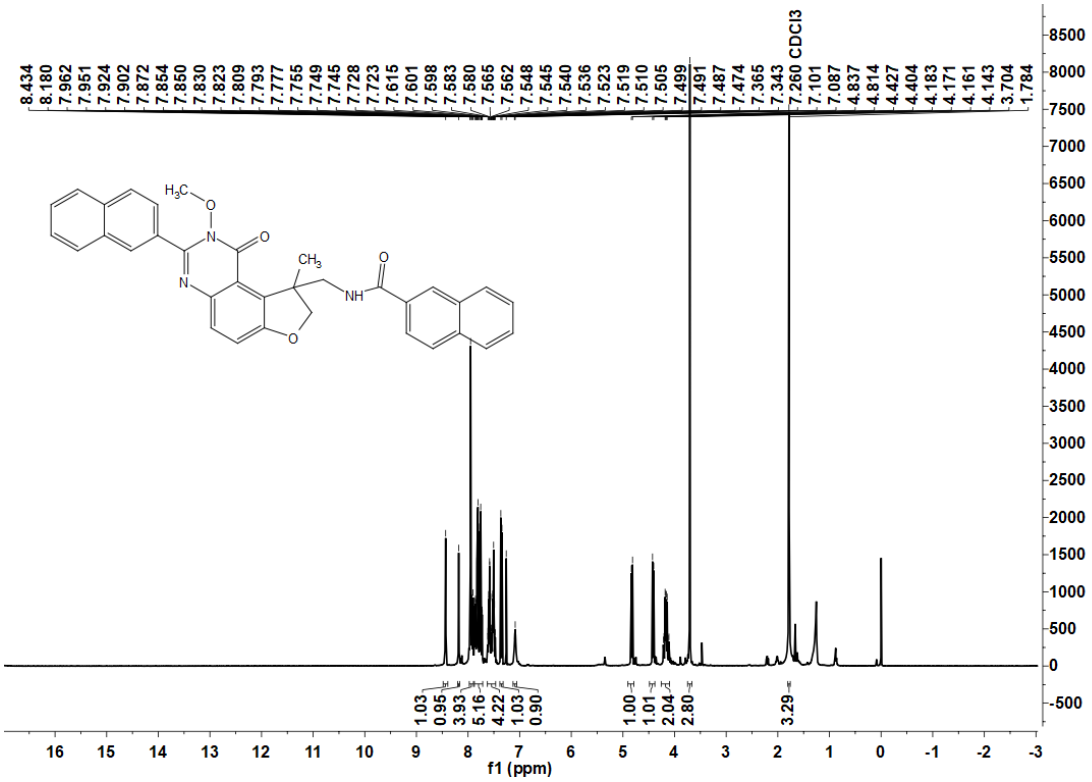

-108.465
-108.599
2500000
2000000
1500000
1000000
500000
0
150
100
50
0
-50
-100
-150
f1 (ppm)
F
O
N
O
N
O
NH
O
F

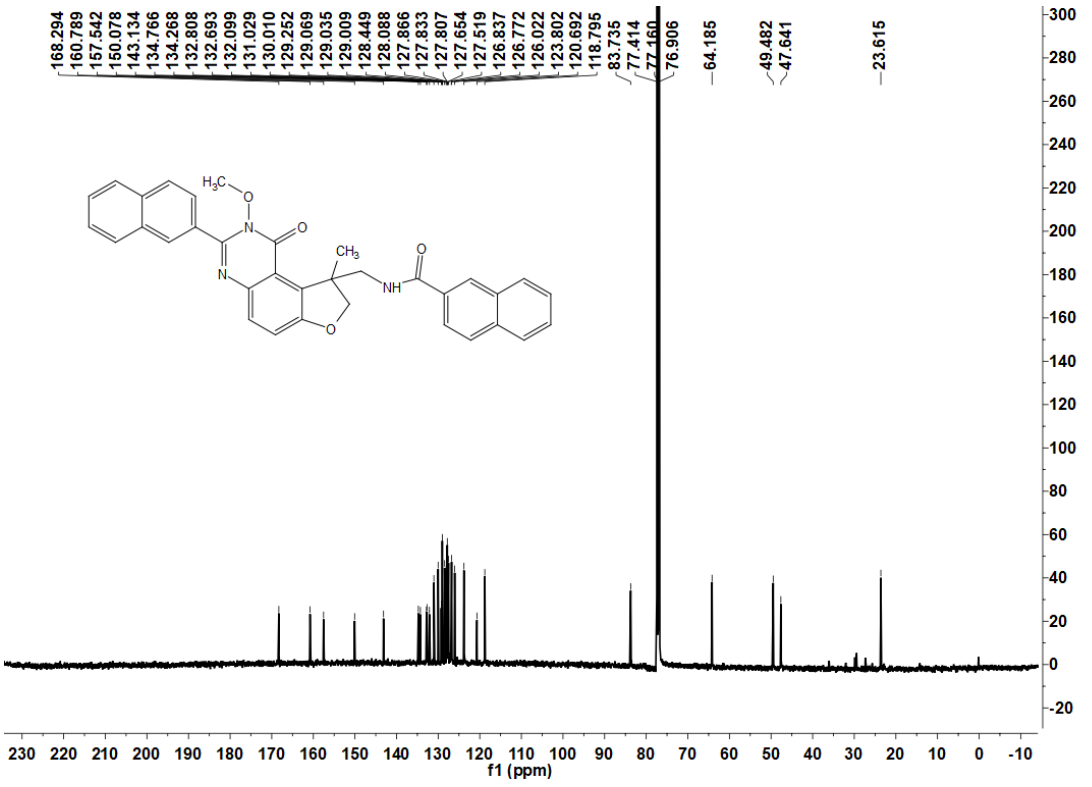
$^{1}H$ and $^{13}C$ NMR Spectra of Compound **5g:**



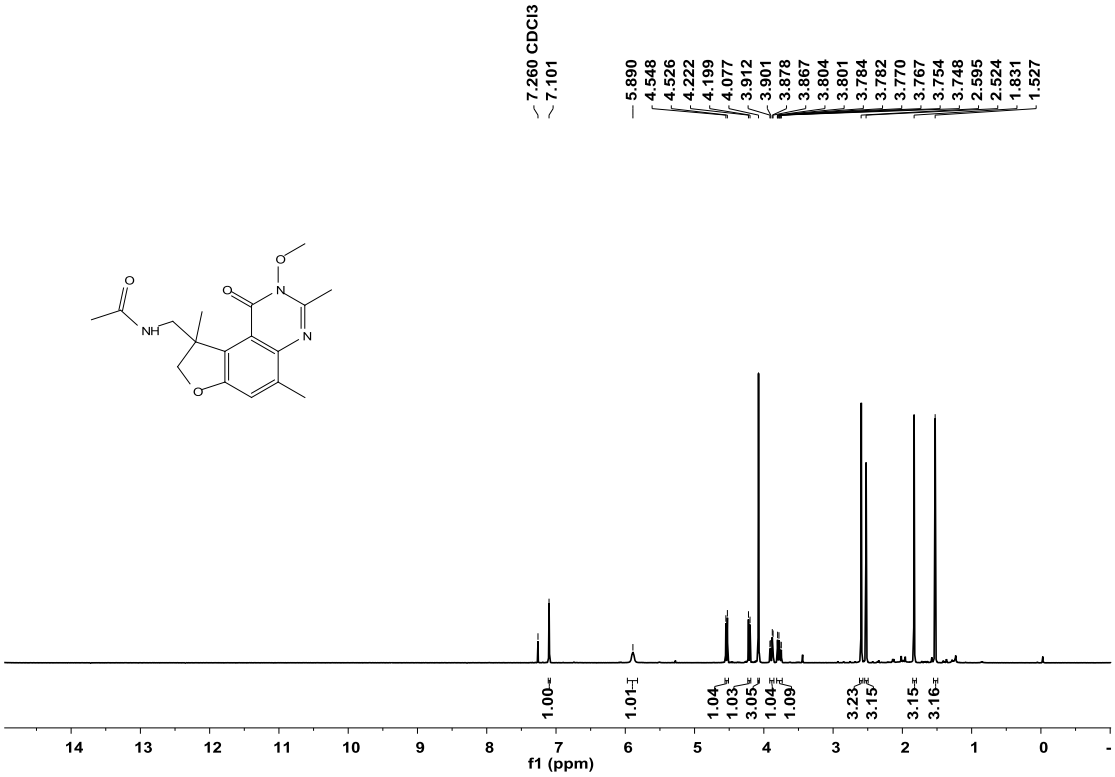



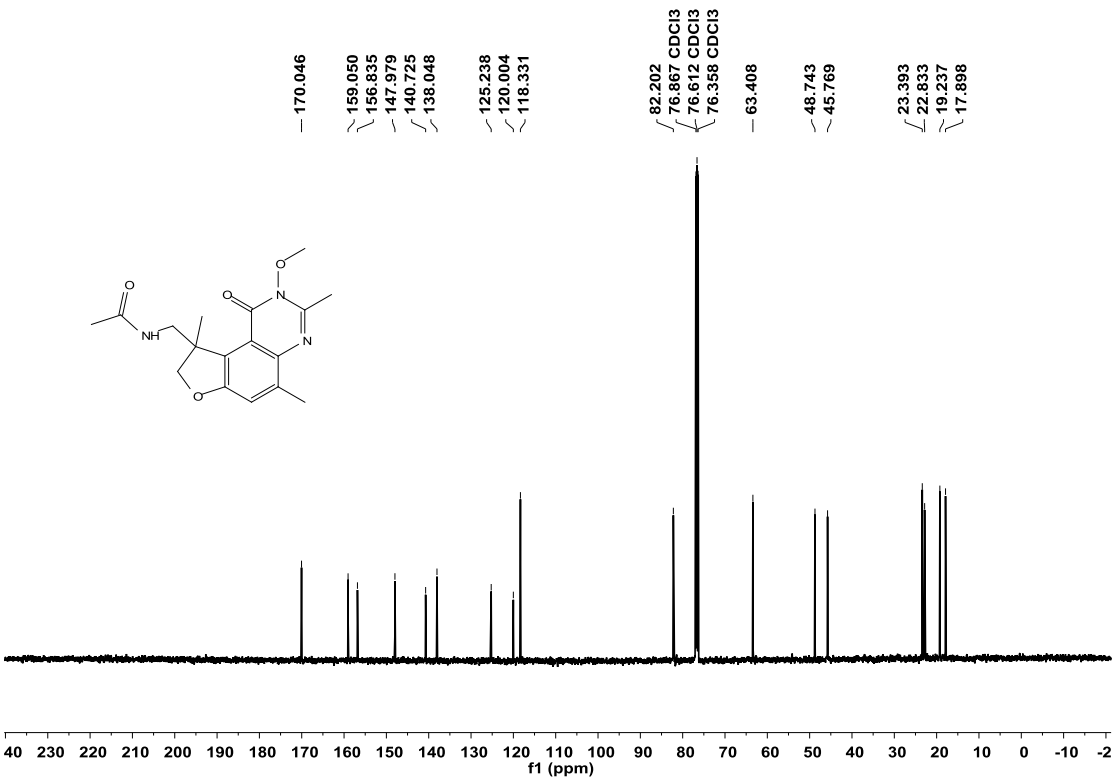
$^{1}H$ and $^{13}C$ NMR Spectra of Compound **5h:**



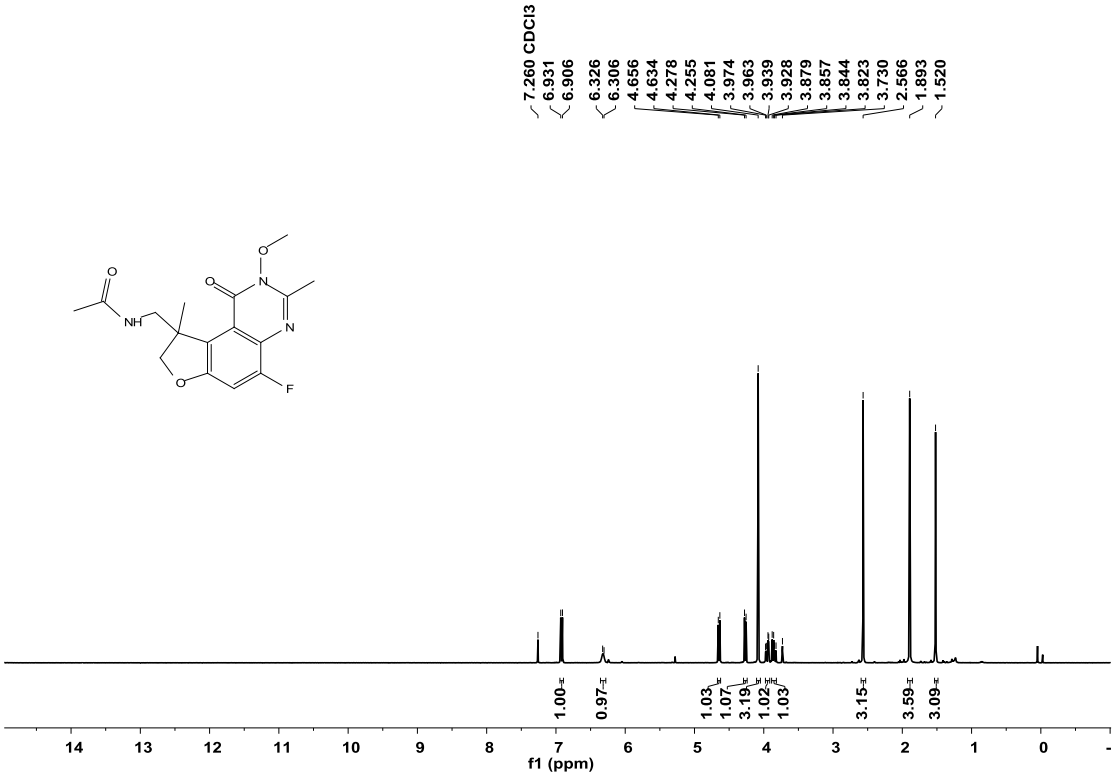



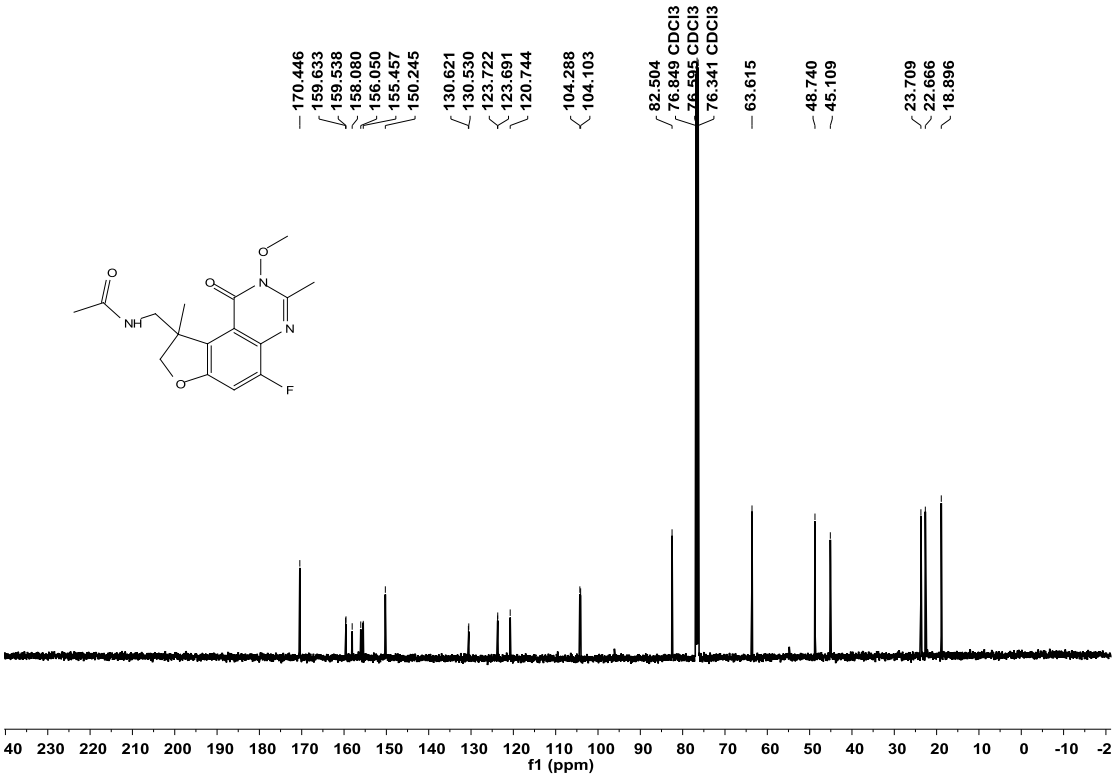
$^{1}$H and $^{13}$C NMR Spectra of Compound **5i:**

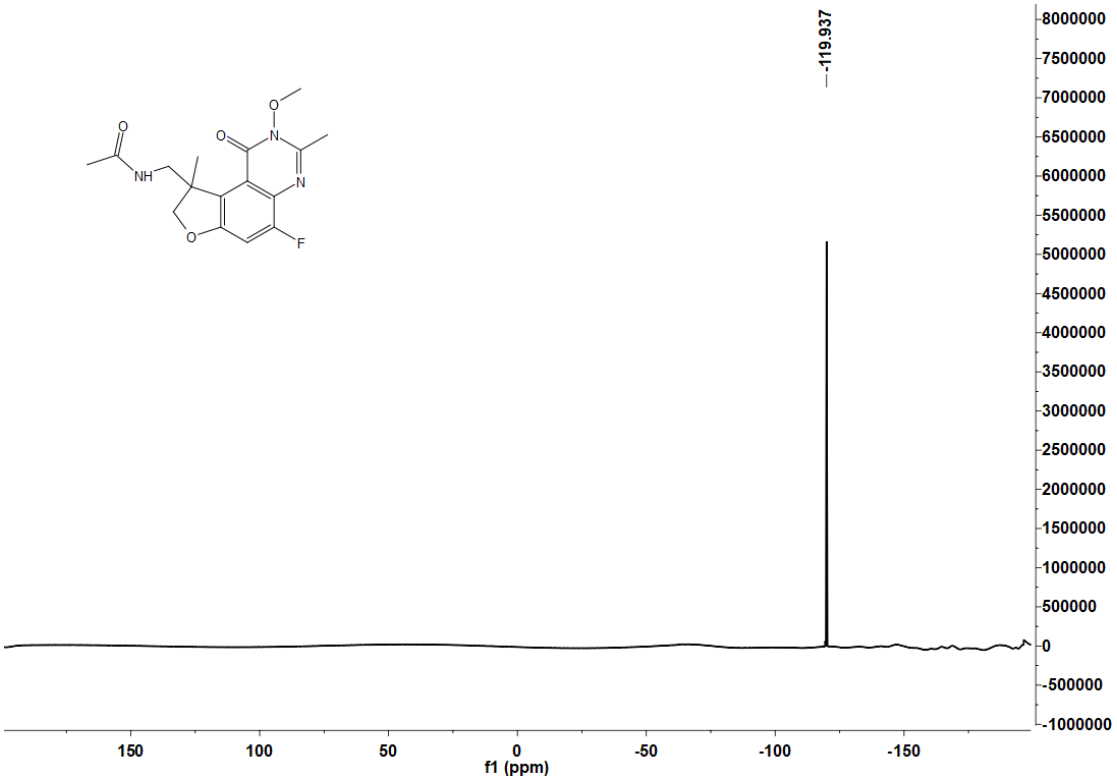


$^{1}H$ ,$^{13}C$ and $^{19}F$ NMR Spectra of Compound **5j:**

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8000000
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7000000
6500000
6000000
5500000
5000000
4500000
4000000
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3000000
2500000
2000000
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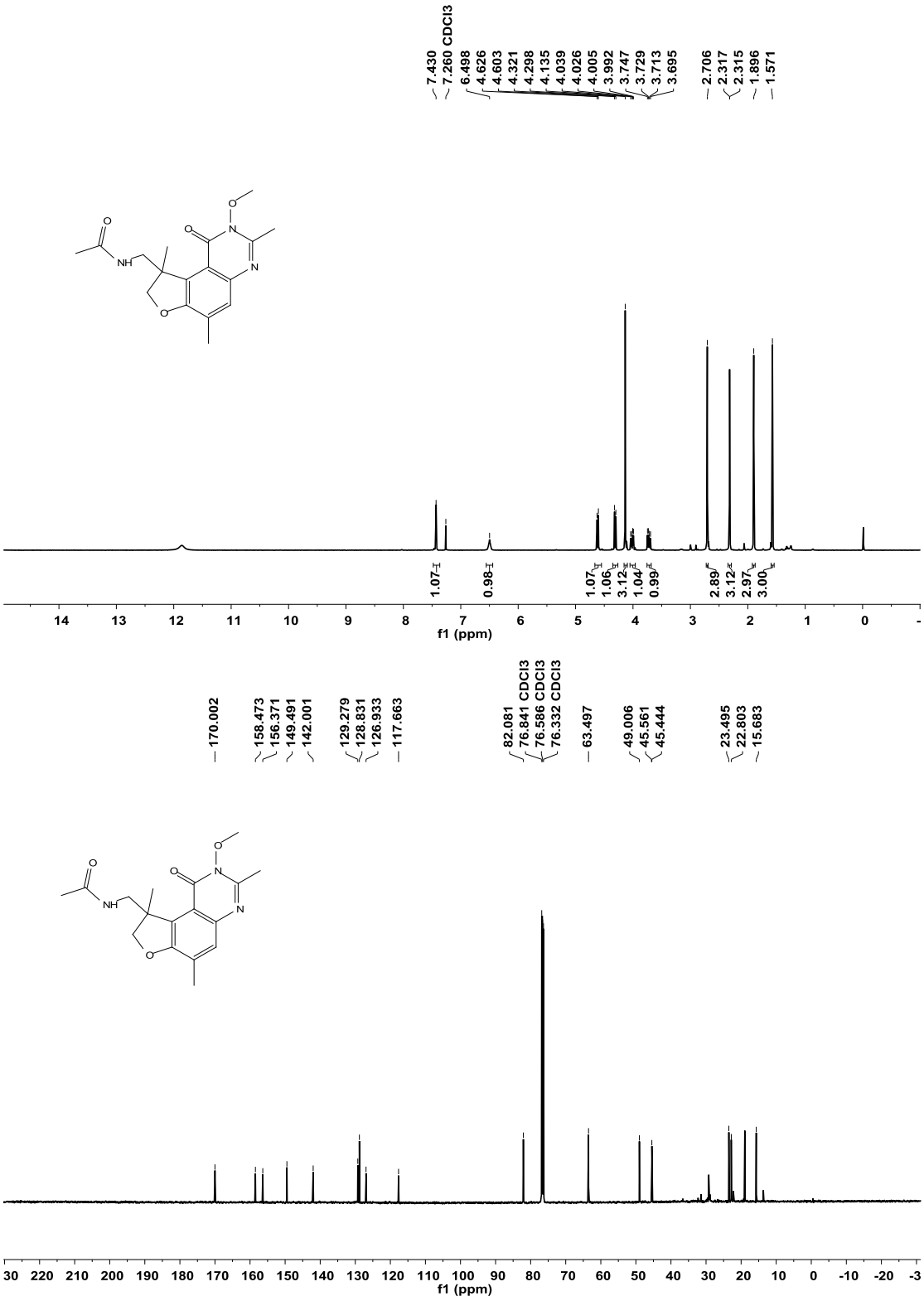
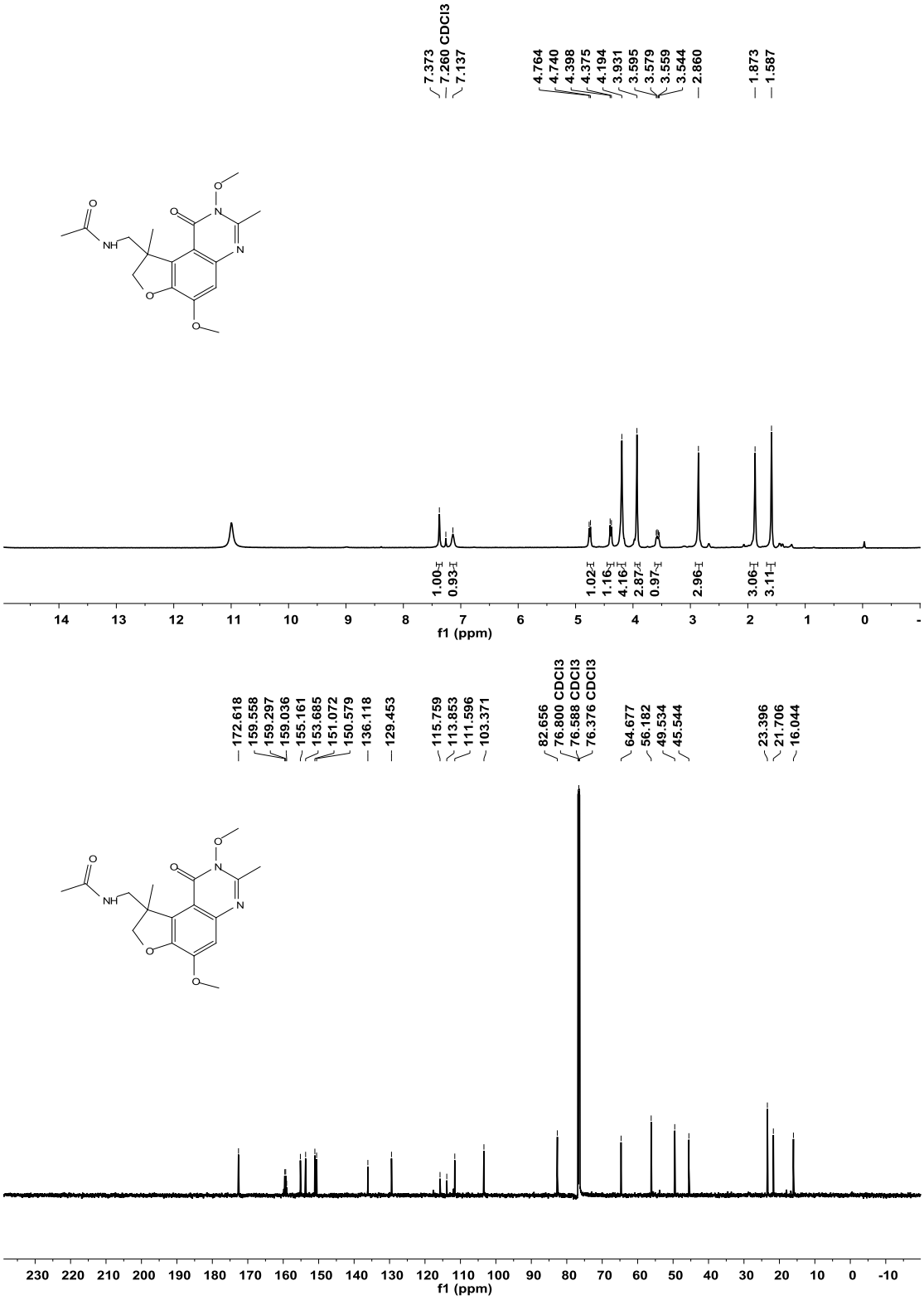
500000
0
-500000
-1000000
150
100
50
0
-50
-100
-150
f1 (ppm)
O
NH
O
N
O
N
F
O

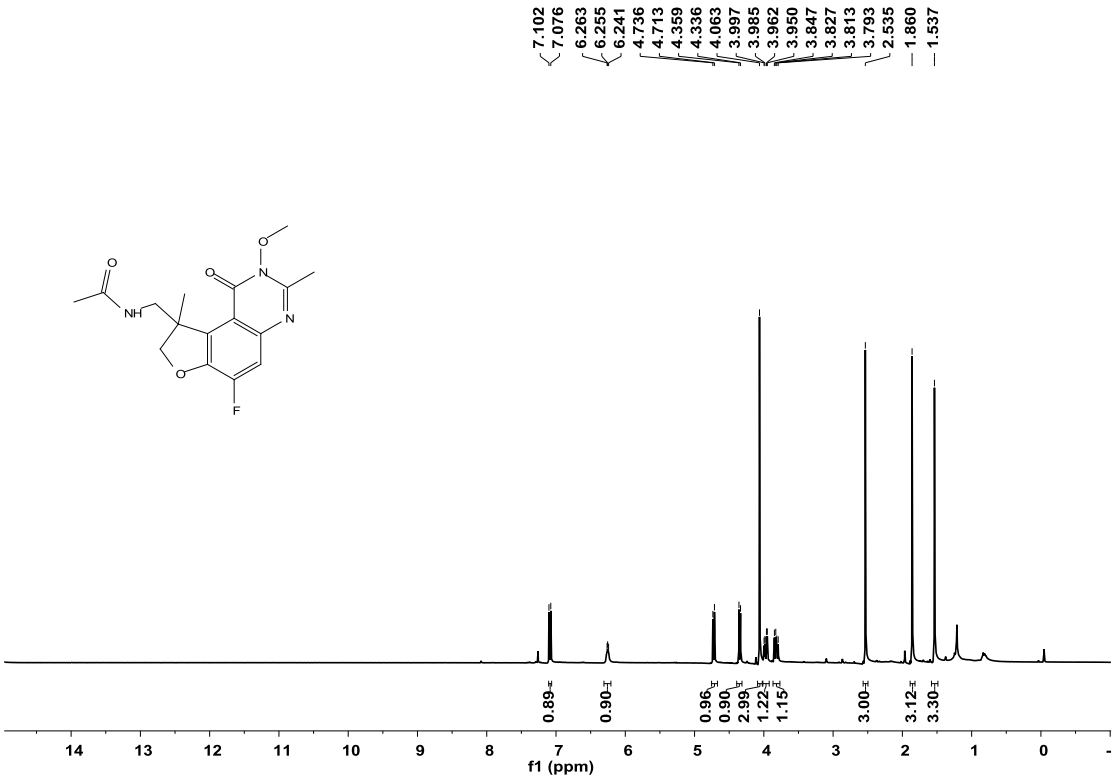
$^{1}H$ and $^{13}C$ NMR Spectra of Compound **5k:**

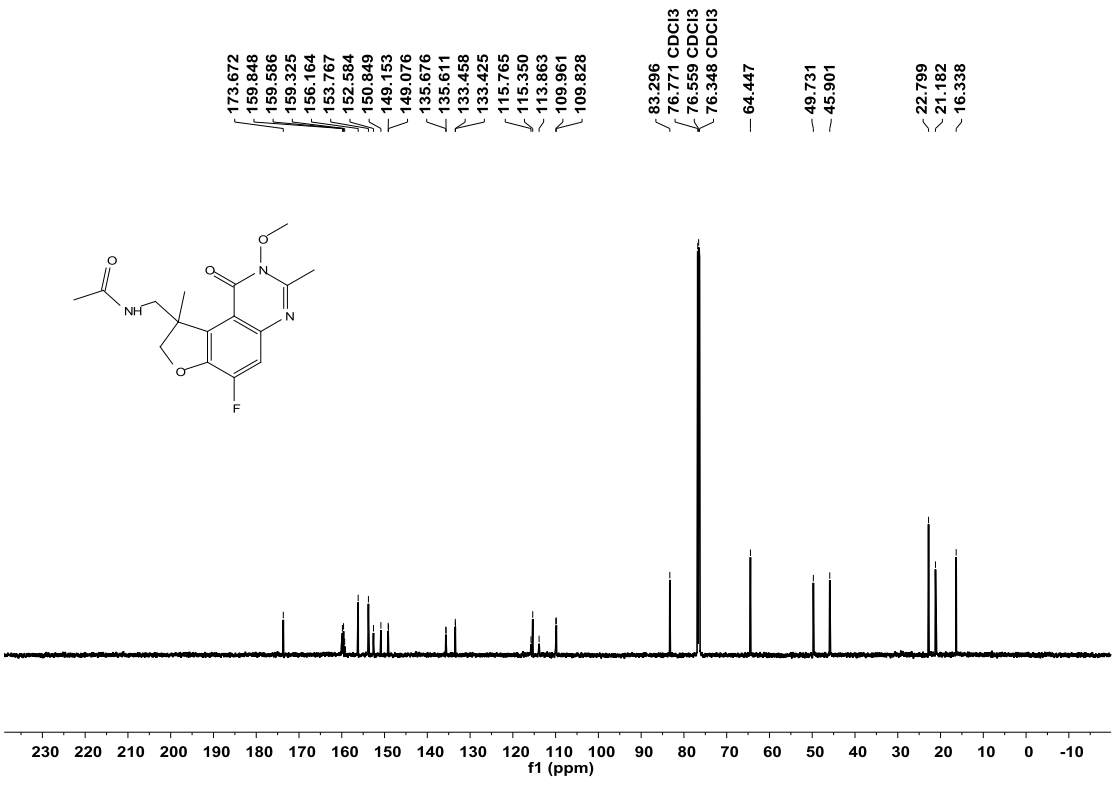


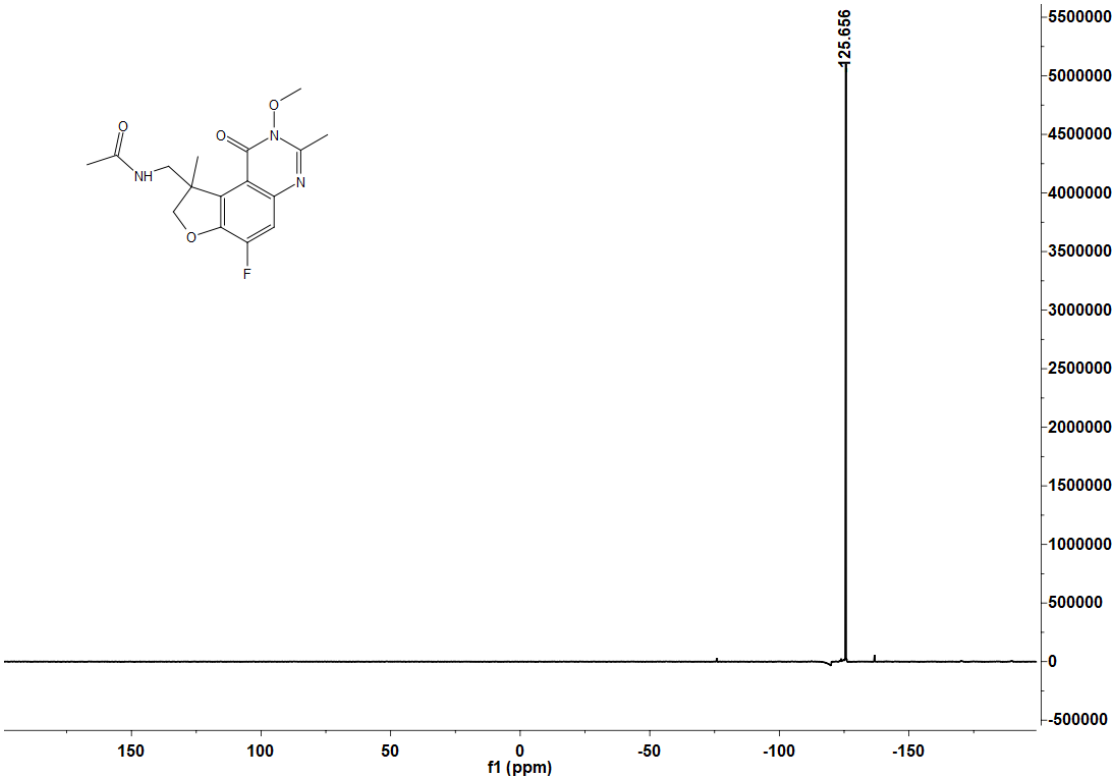
$^{1}H$ and $^{13}C$ NMR Spectra of Compound **5l:**



$^{1}H$ ,$^{13}C$ and $^{19}F$ NMR Spectra of Compound **5m:**




125.656
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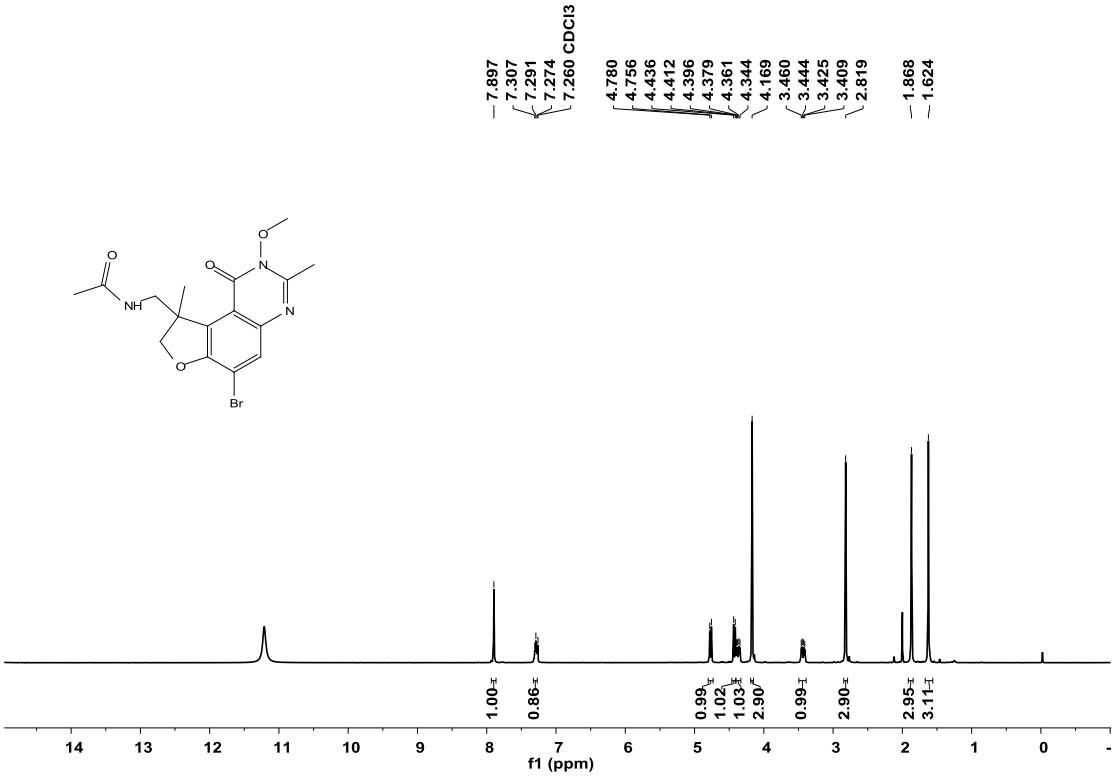
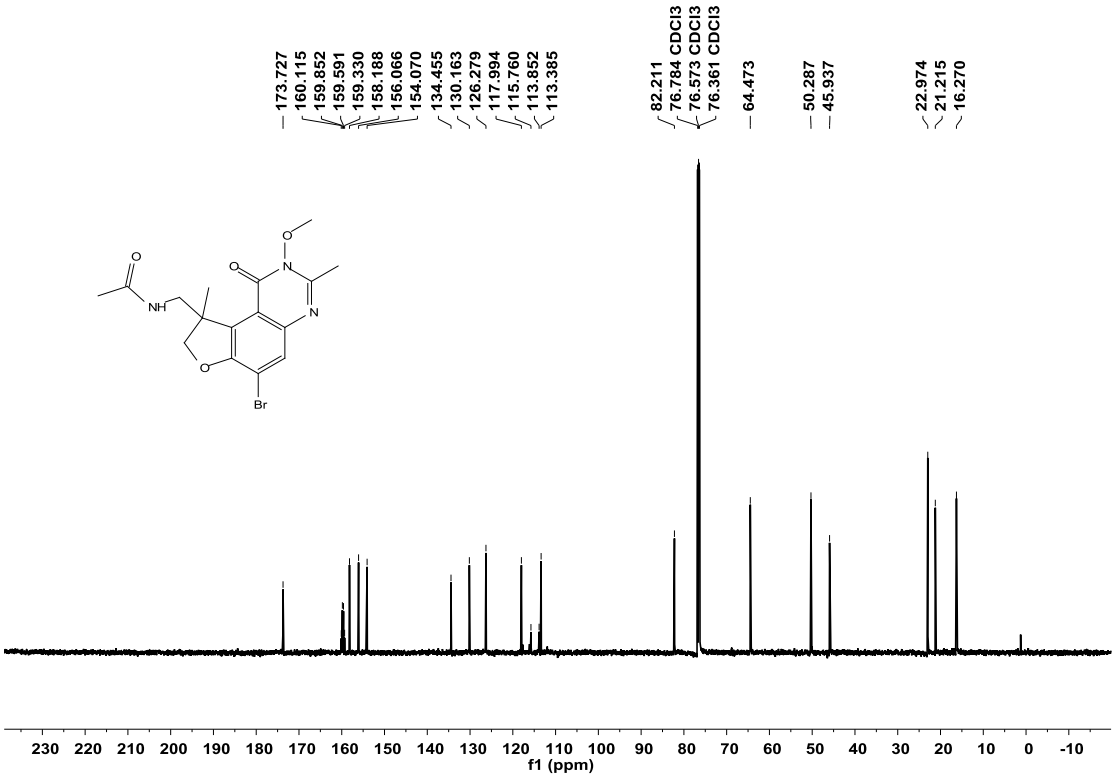
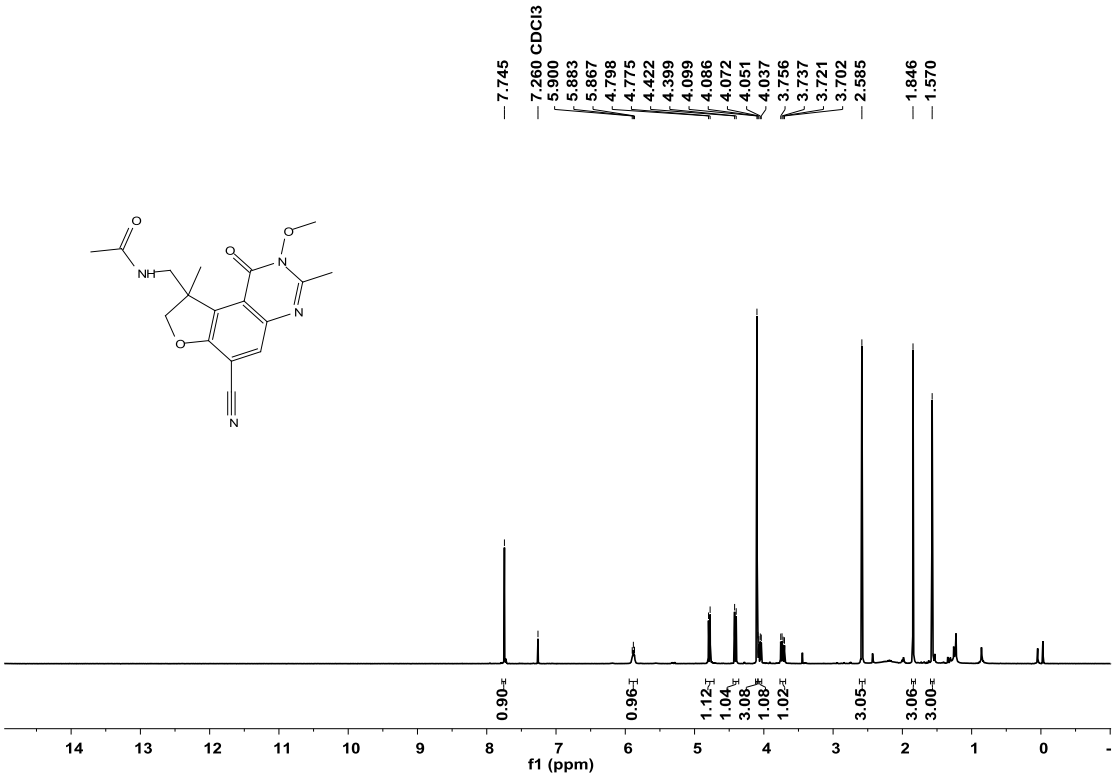
5000000
4500000
4000000
3500000
3000000
2500000
2000000
1500000
1000000
500000
0
-500000
150
100
50
0
-50
-100
-150
f1 (ppm)
O
NH
O
N
O
N
O
F

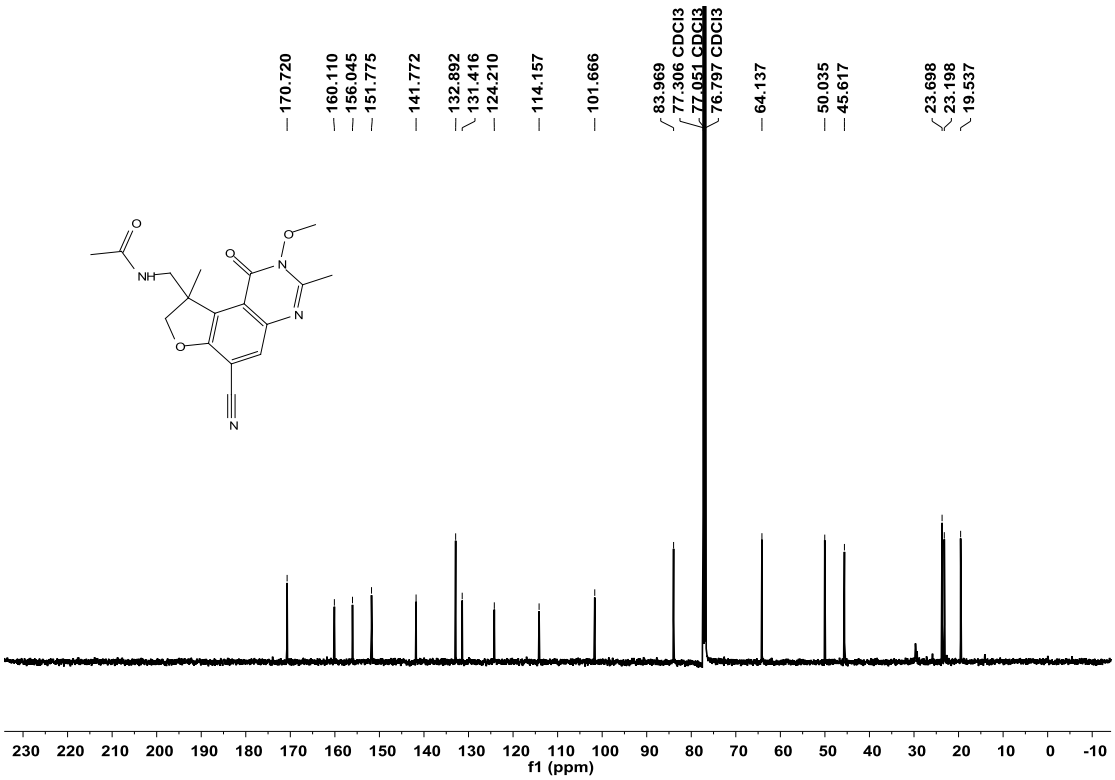
$^{1}H$ and $^{13}C$ NMR Spectra of Compound **5n:**



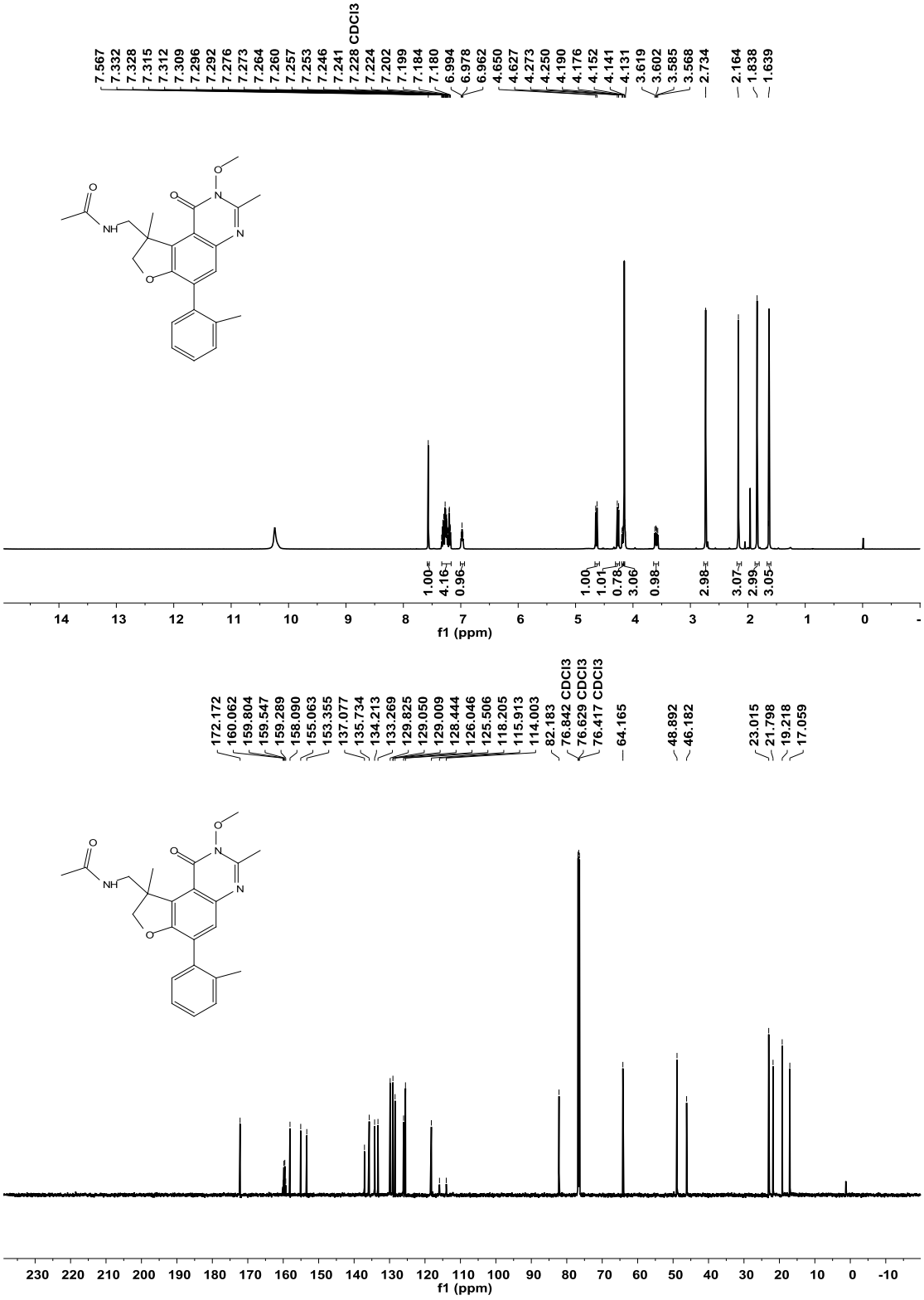



$^{1}H$ and $^{13}C$ NMR Spectra of Compound **5o:**

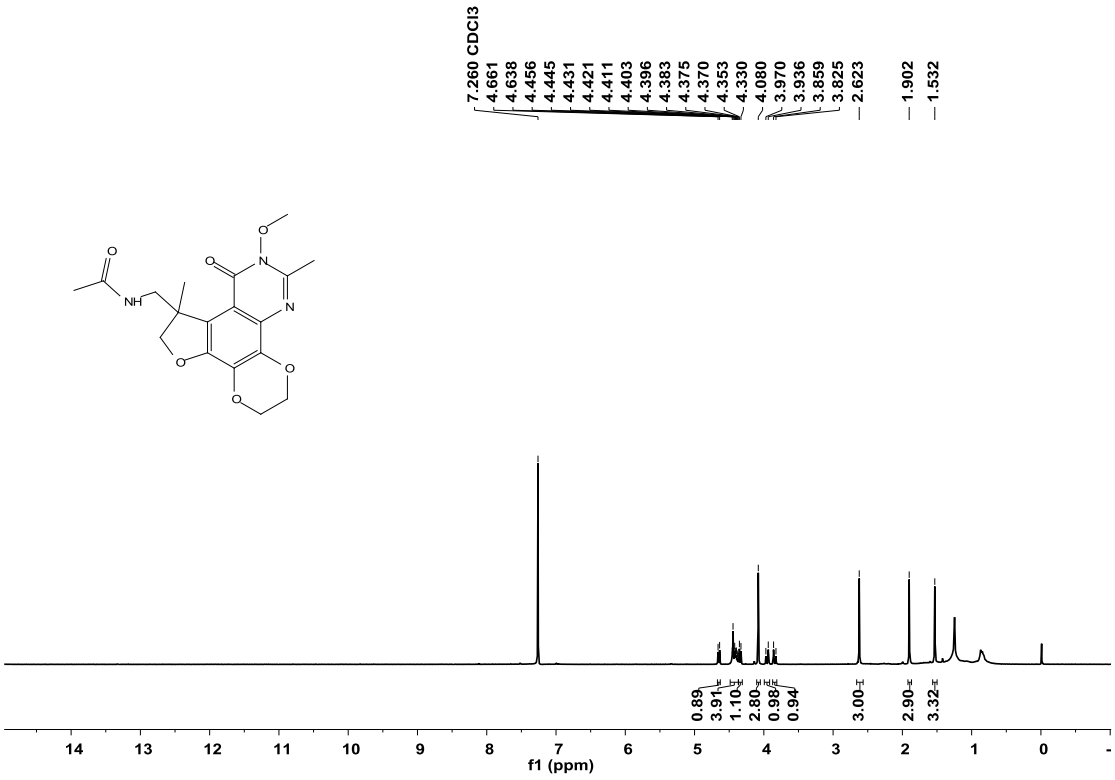


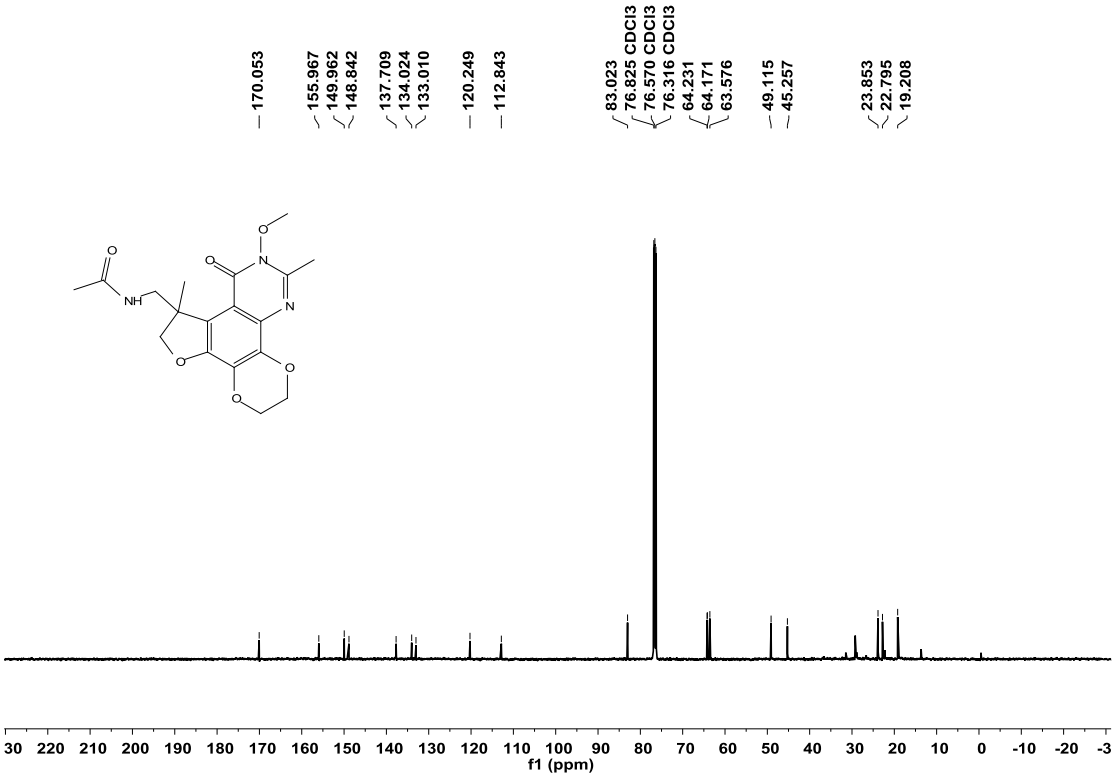



$^{1}H$ and $^{13}C$ NMR Spectra of Compound **5p:**

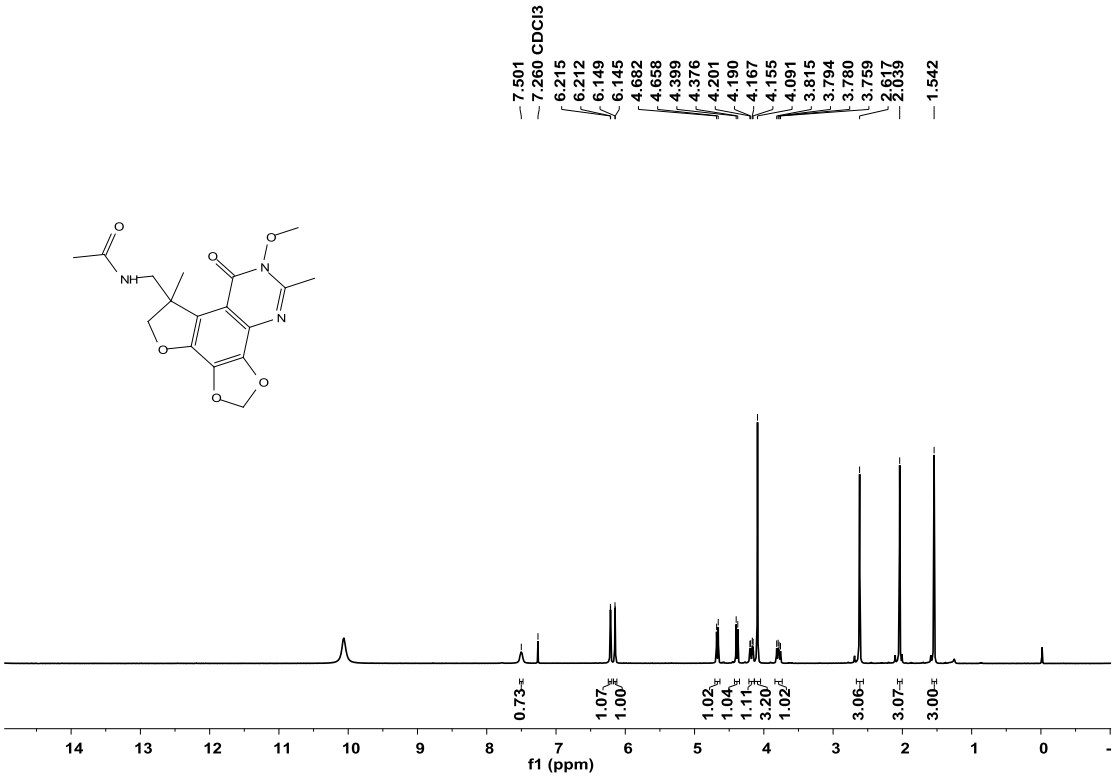


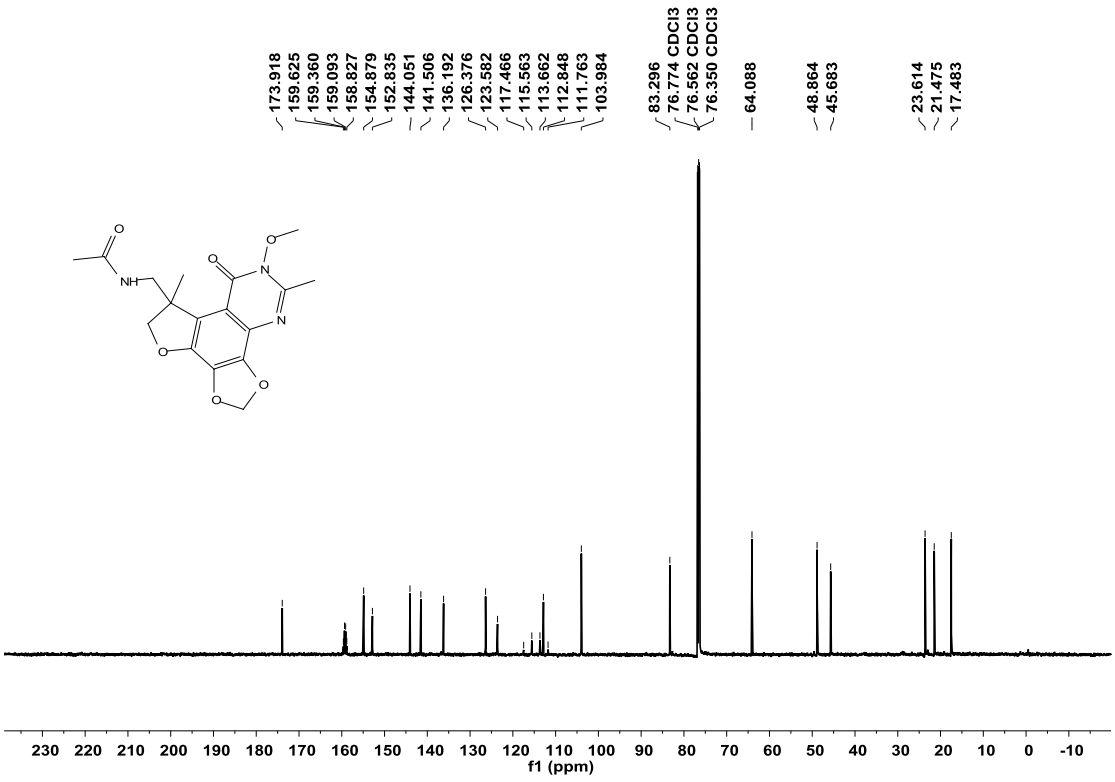
$^{1}$H and $^{13}$C NMR Spectra of Compound **5q:**



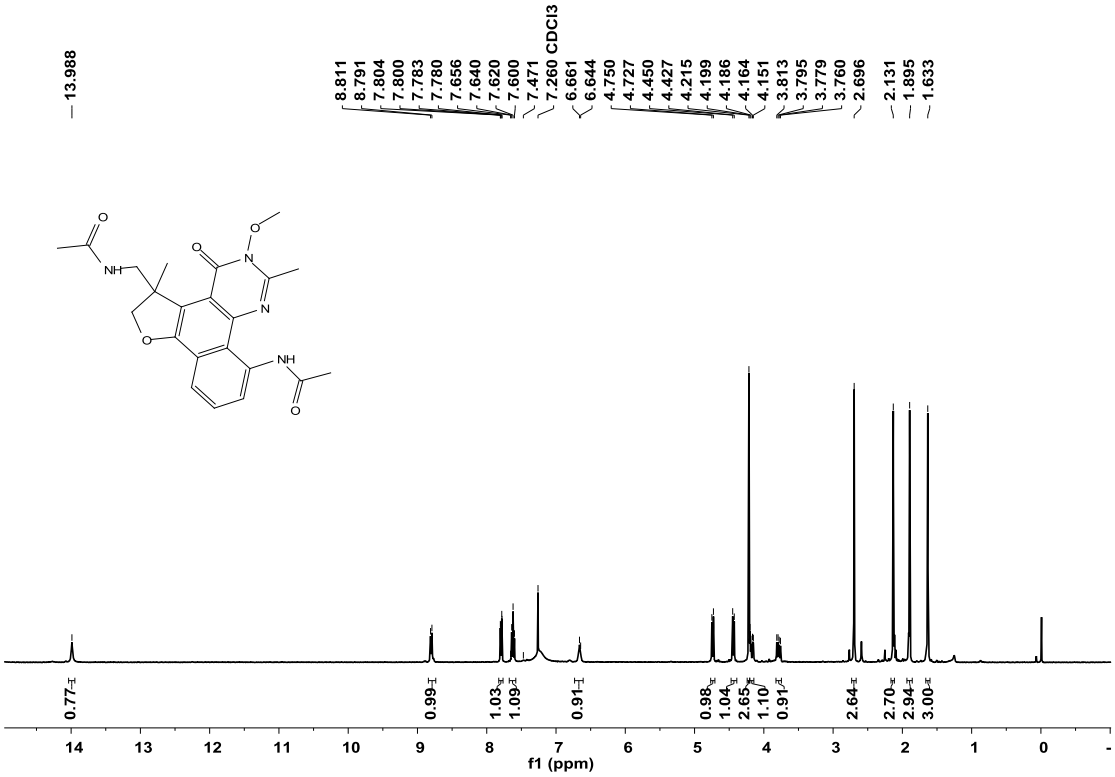



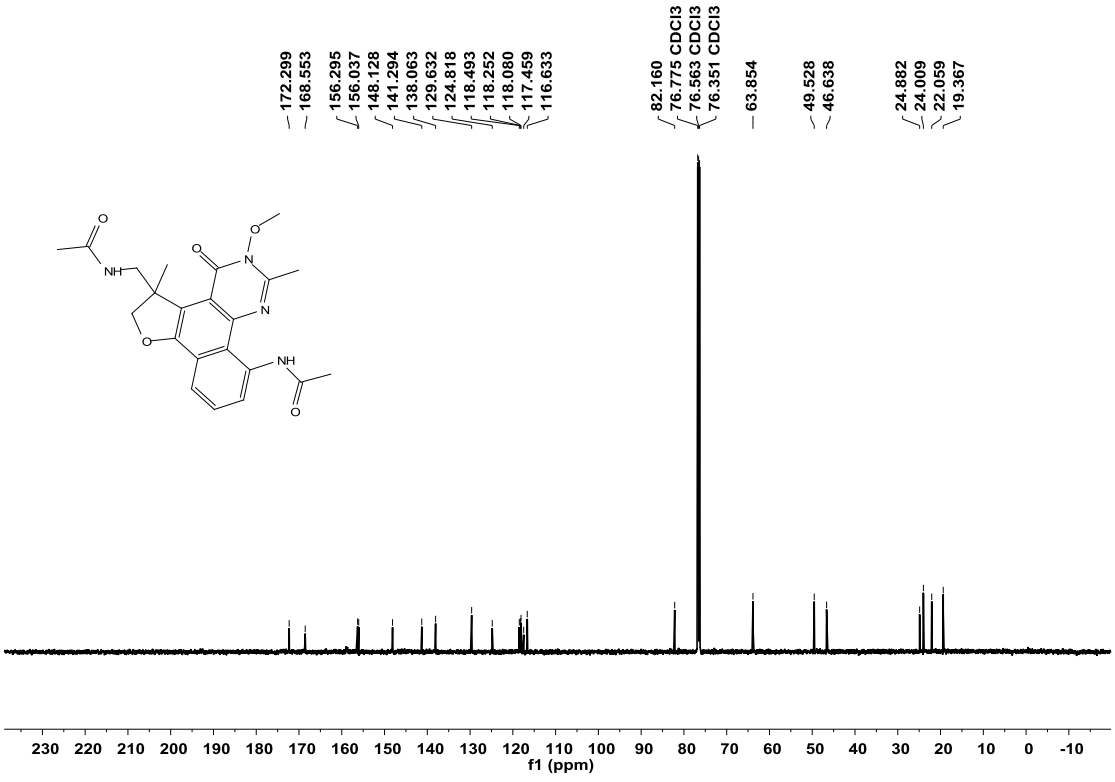
$^{1}$H and $^{13}$C NMR Spectra of Compound **5r:**



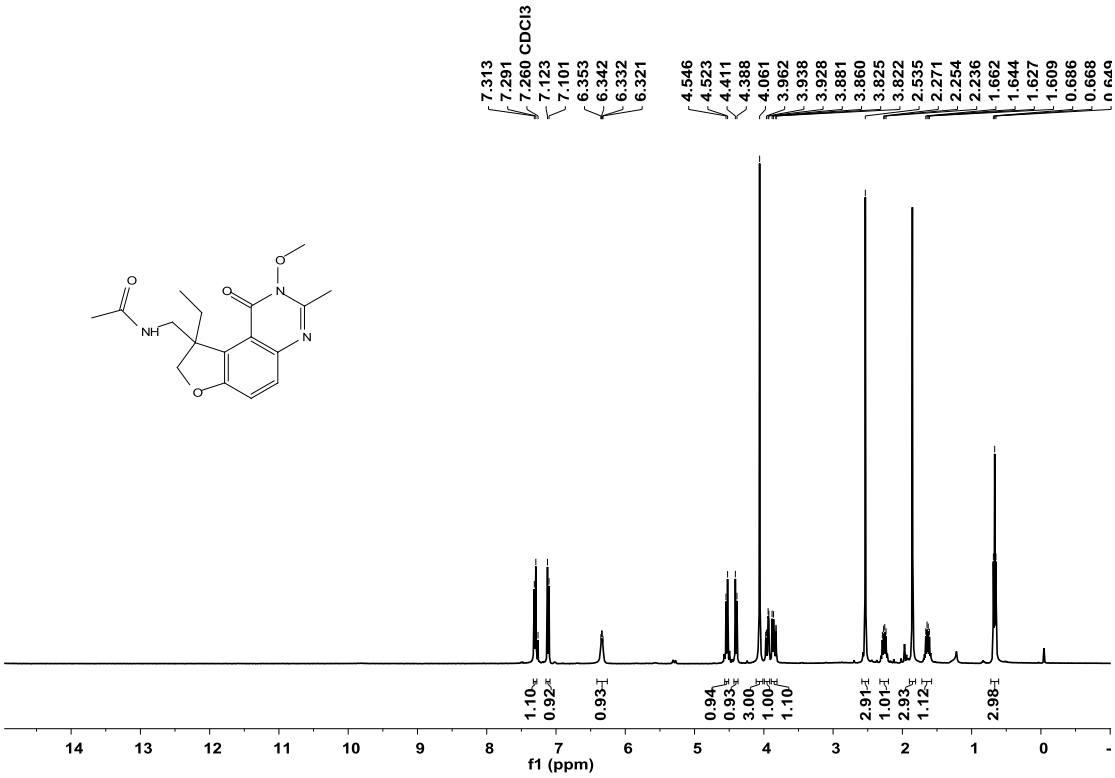



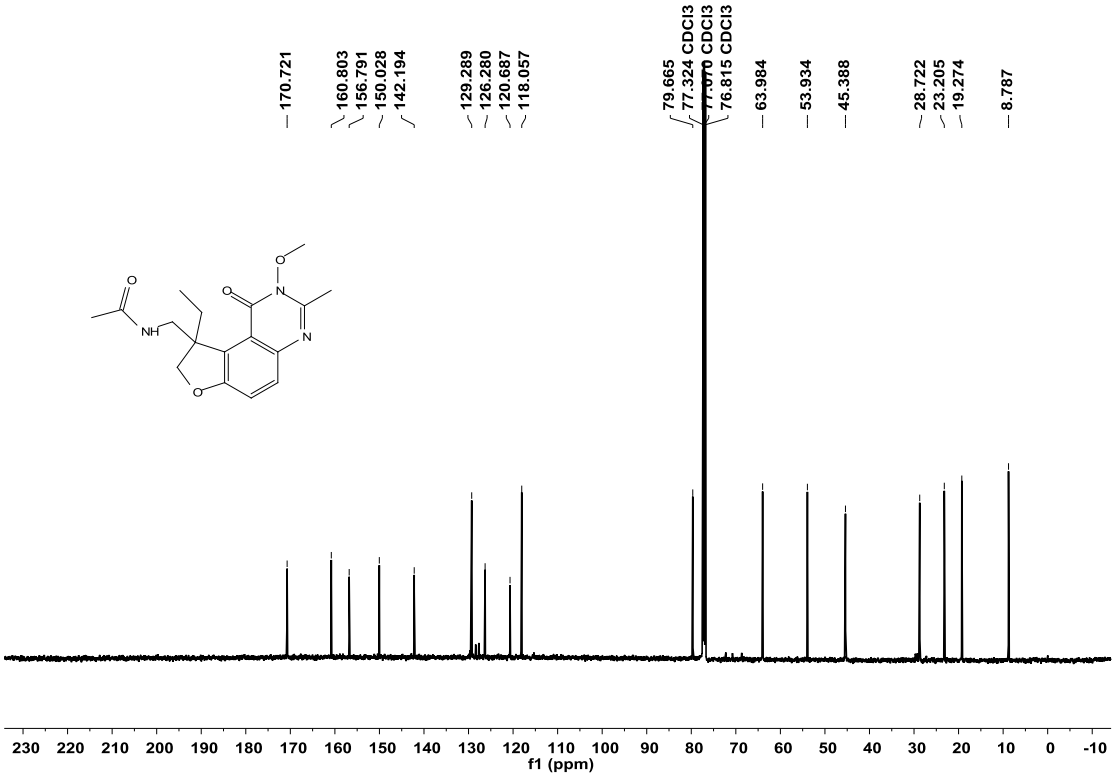
$^{1}H$ and $^{13}C$ NMR Spectra of Compound **5s:**



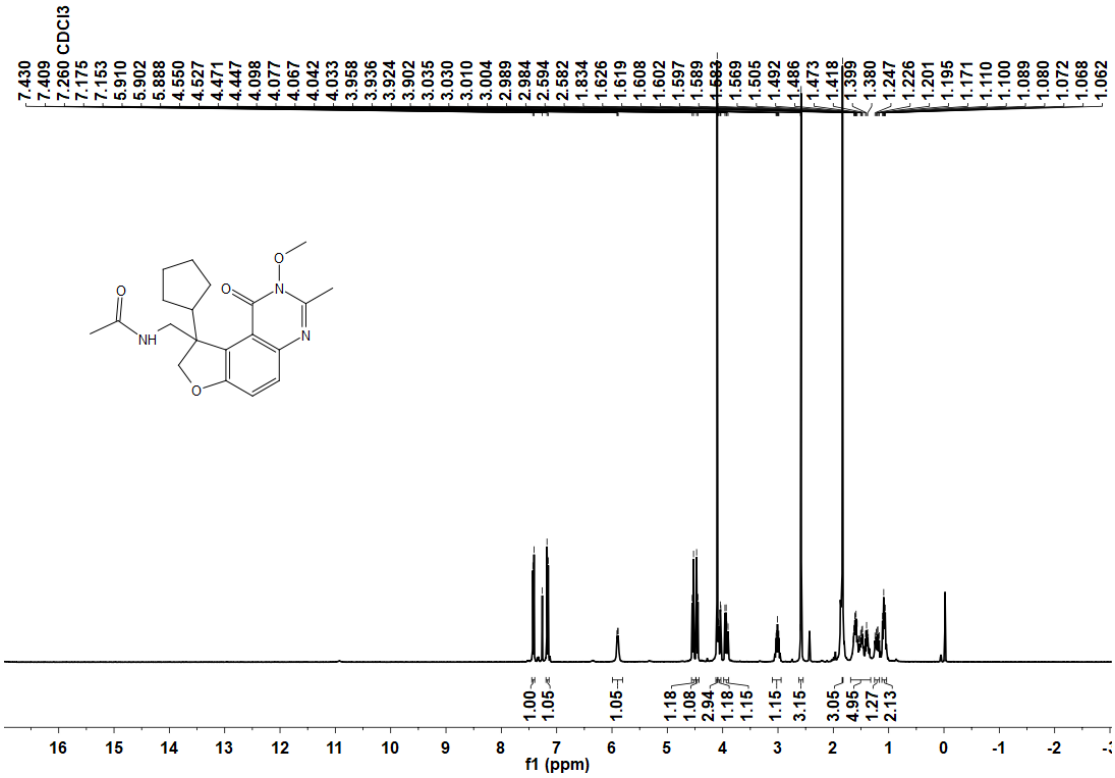



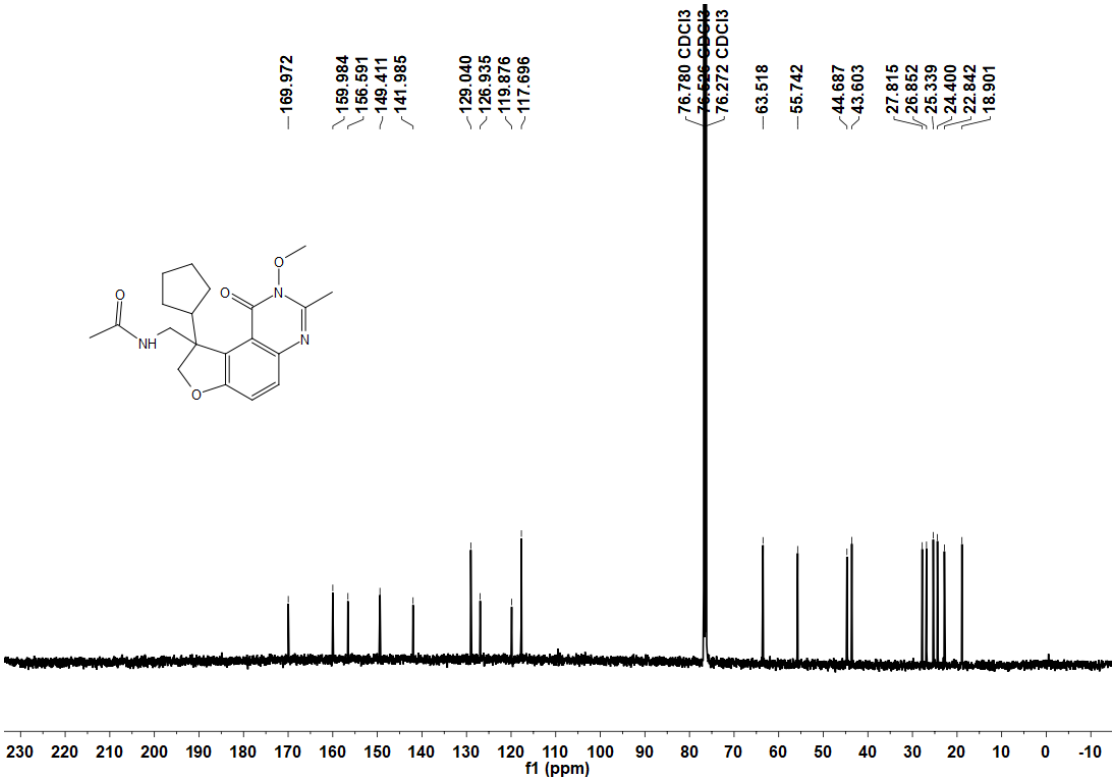
$^{1}H$ and $^{13}C$ NMR Spectra of Compound **5t:**



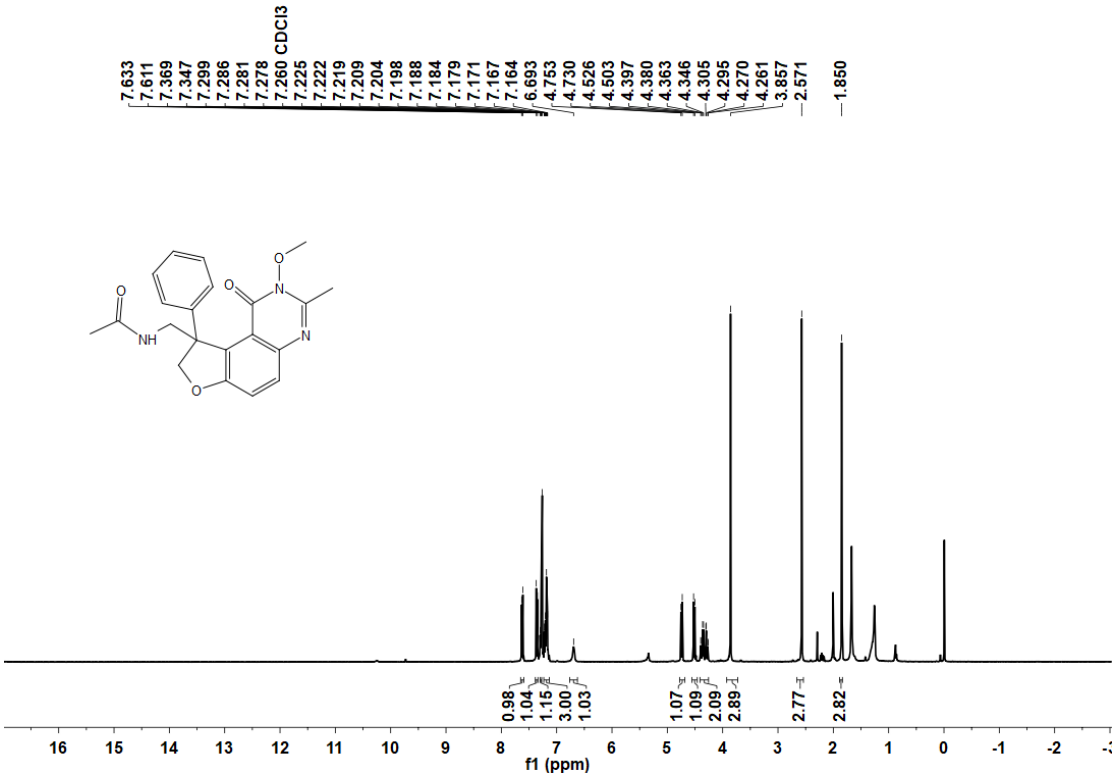



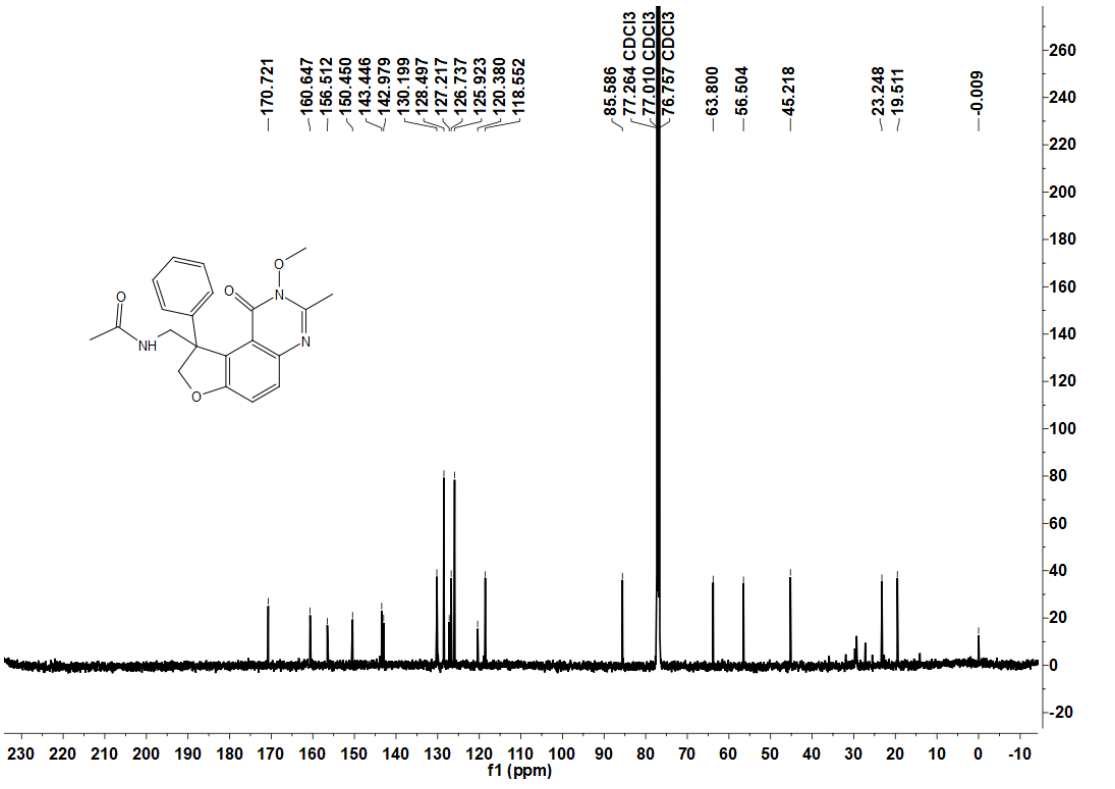
$^{1}$H and $^{13}$C NMR Spectra of Compound **5u:**



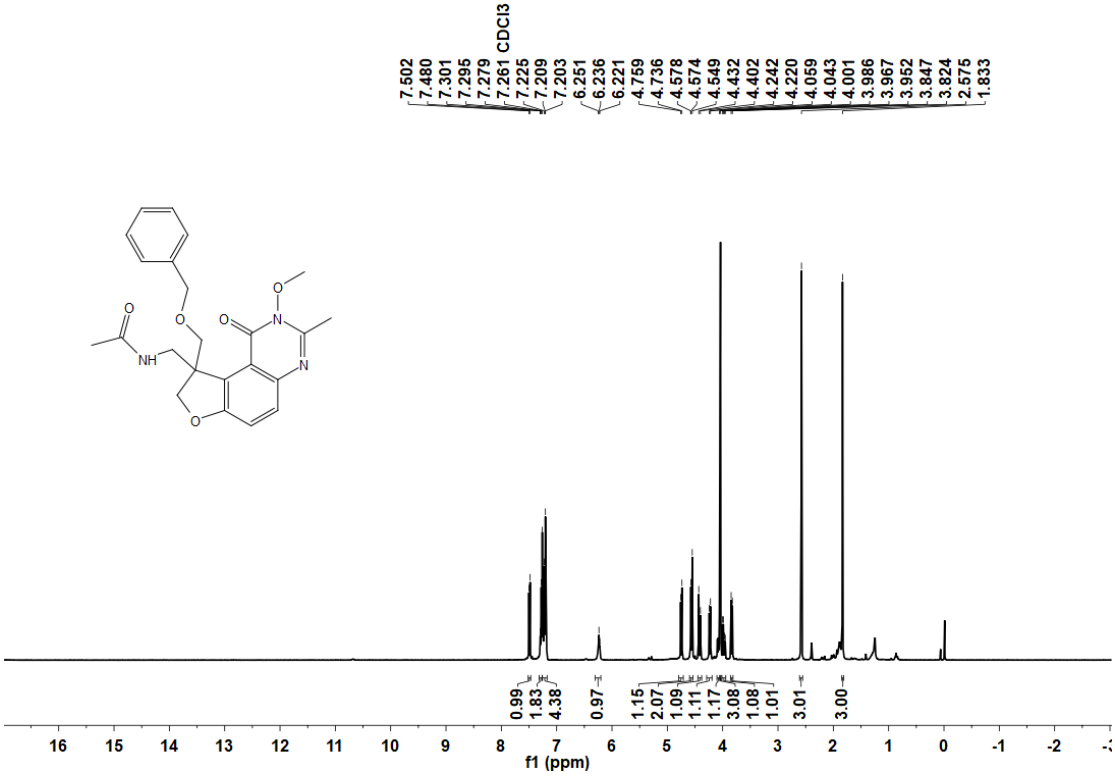



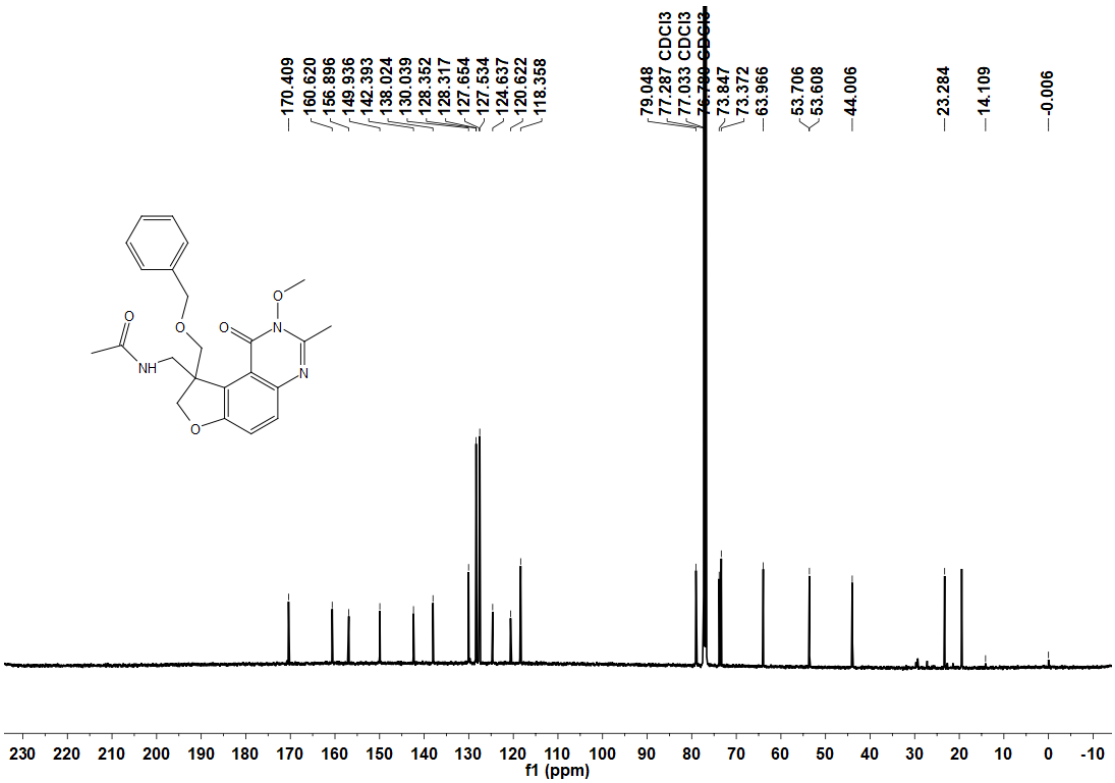
$^{1}$H and $^{13}$C NMR Spectra of Compound **5v:**



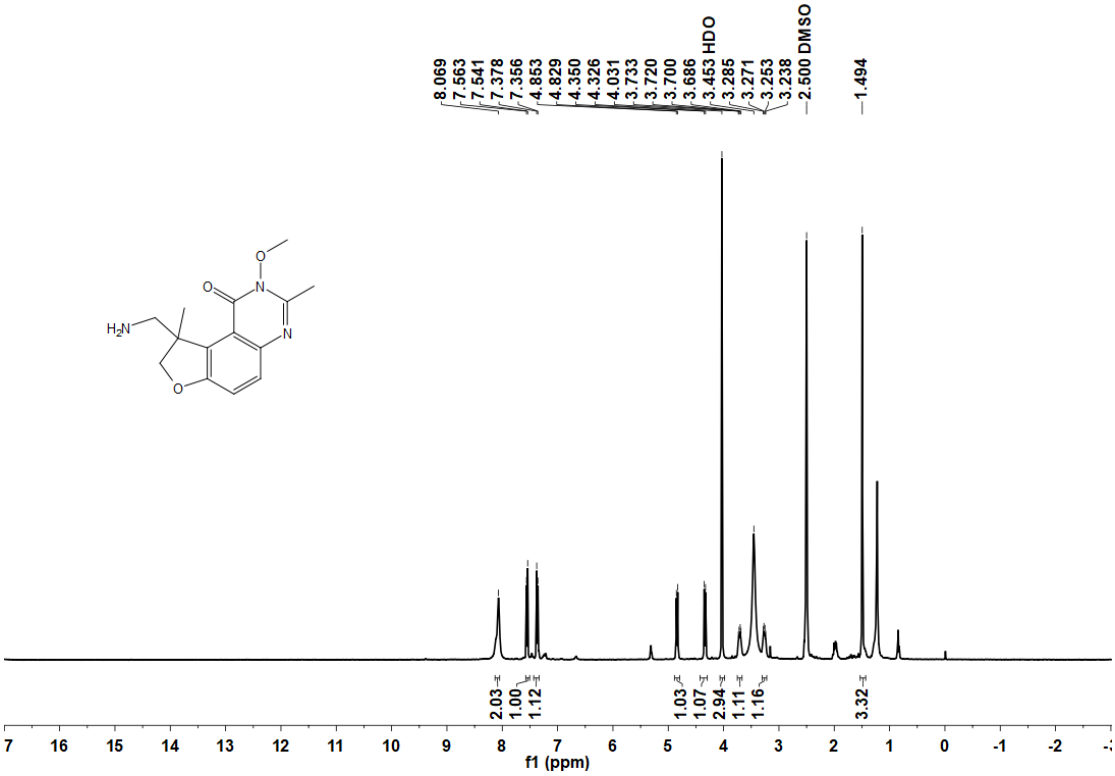



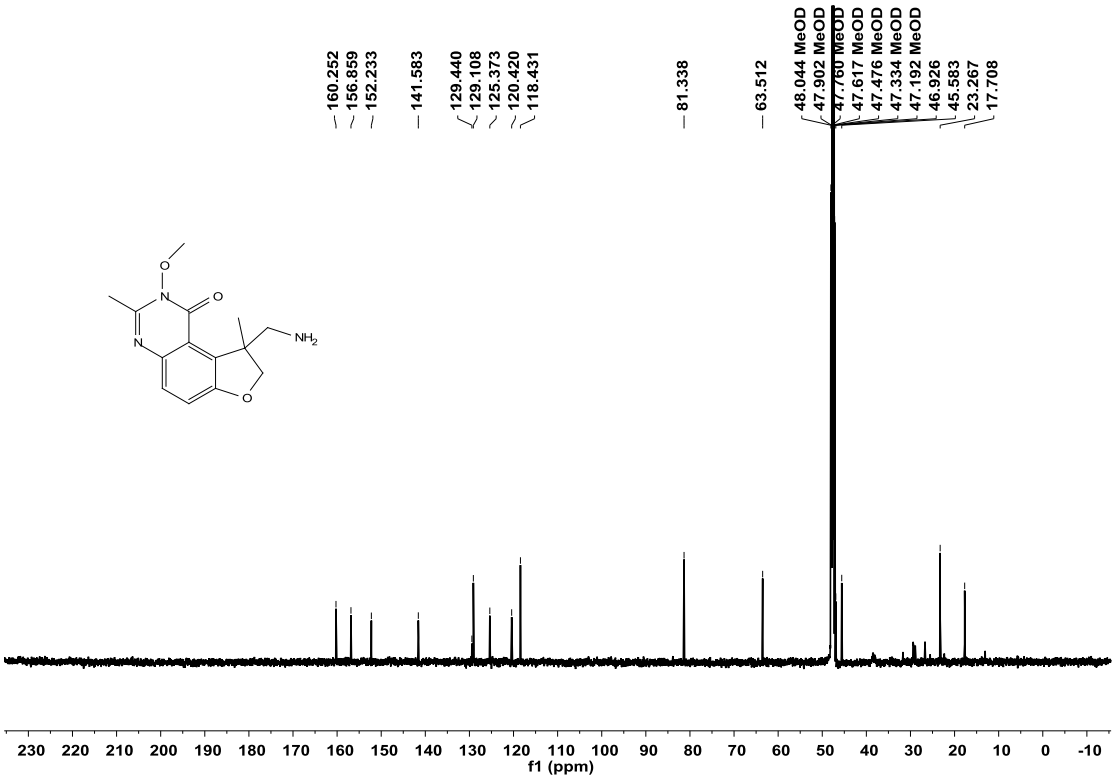
$^{1}$H and $^{13}$C NMR Spectra of Compound **5w:**



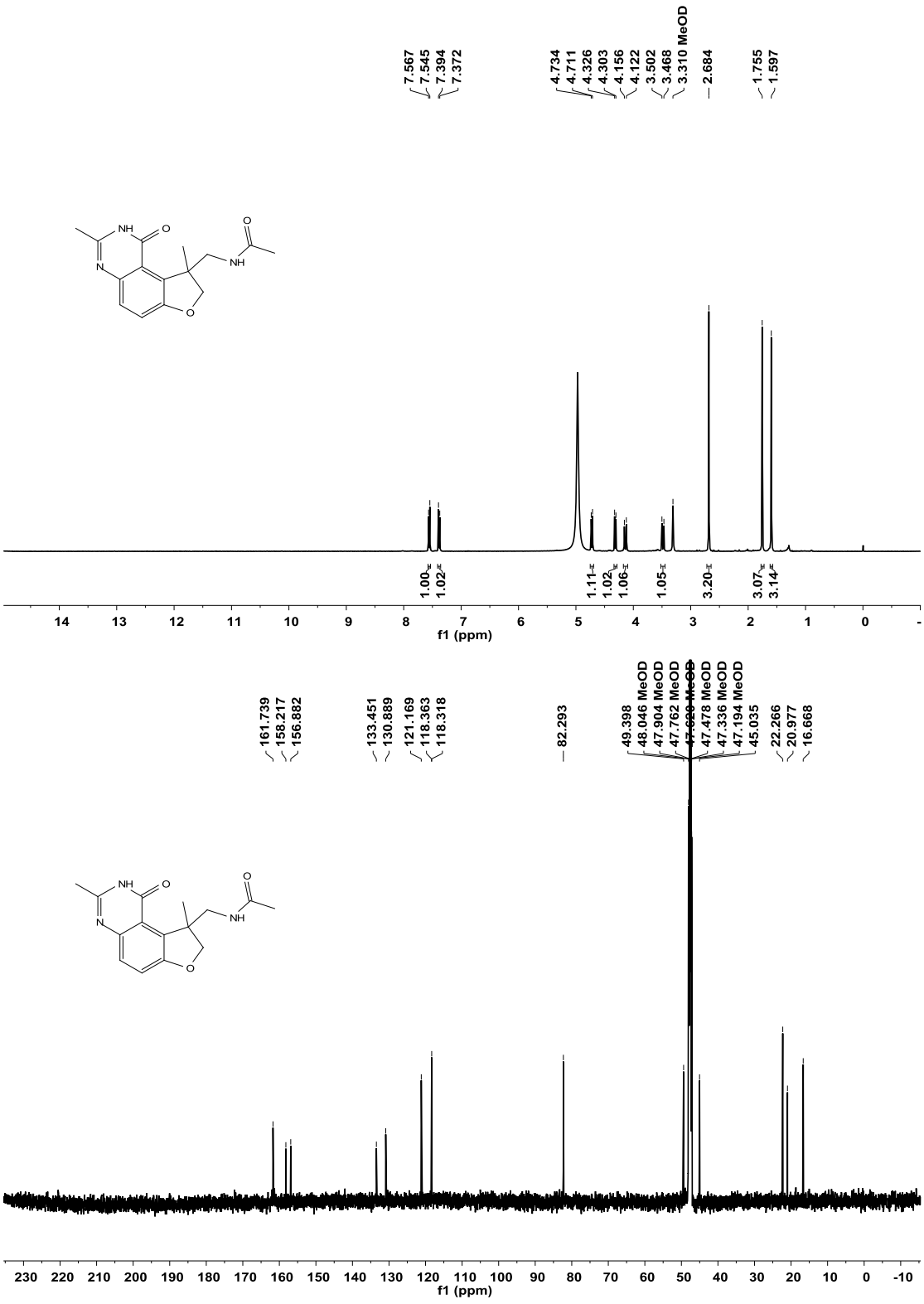



$^{1}H$ and $^{13}C$ NMR Spectra of Compound **6a:**

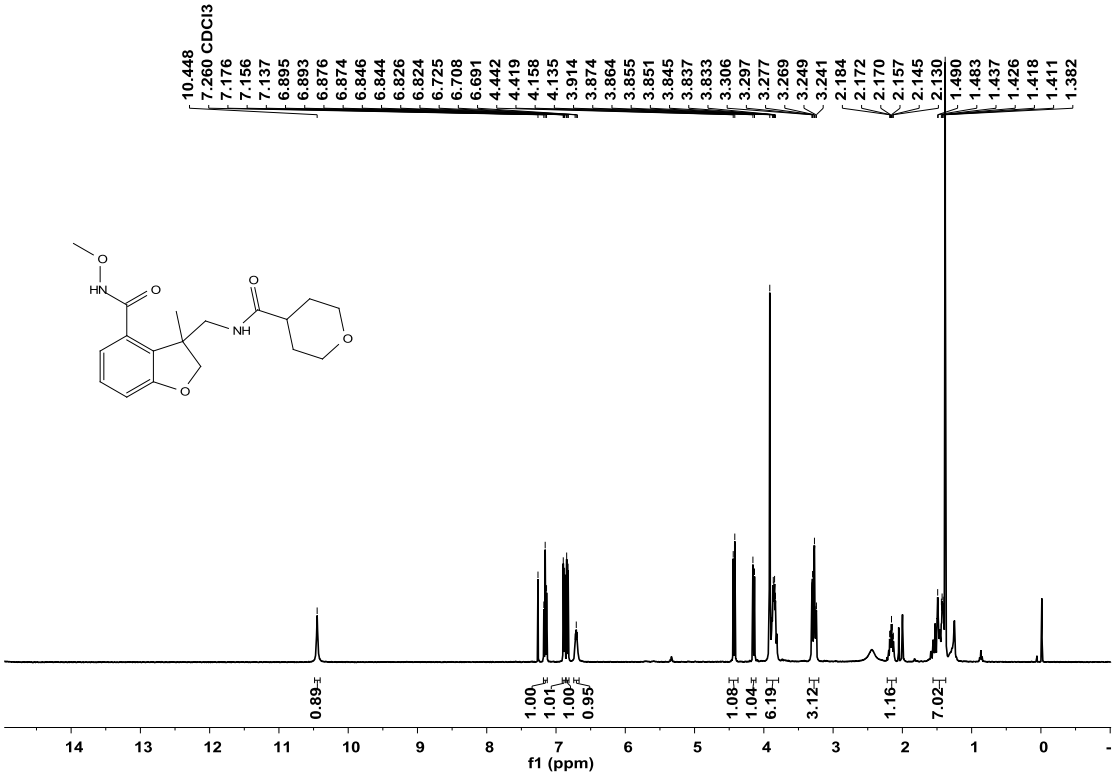


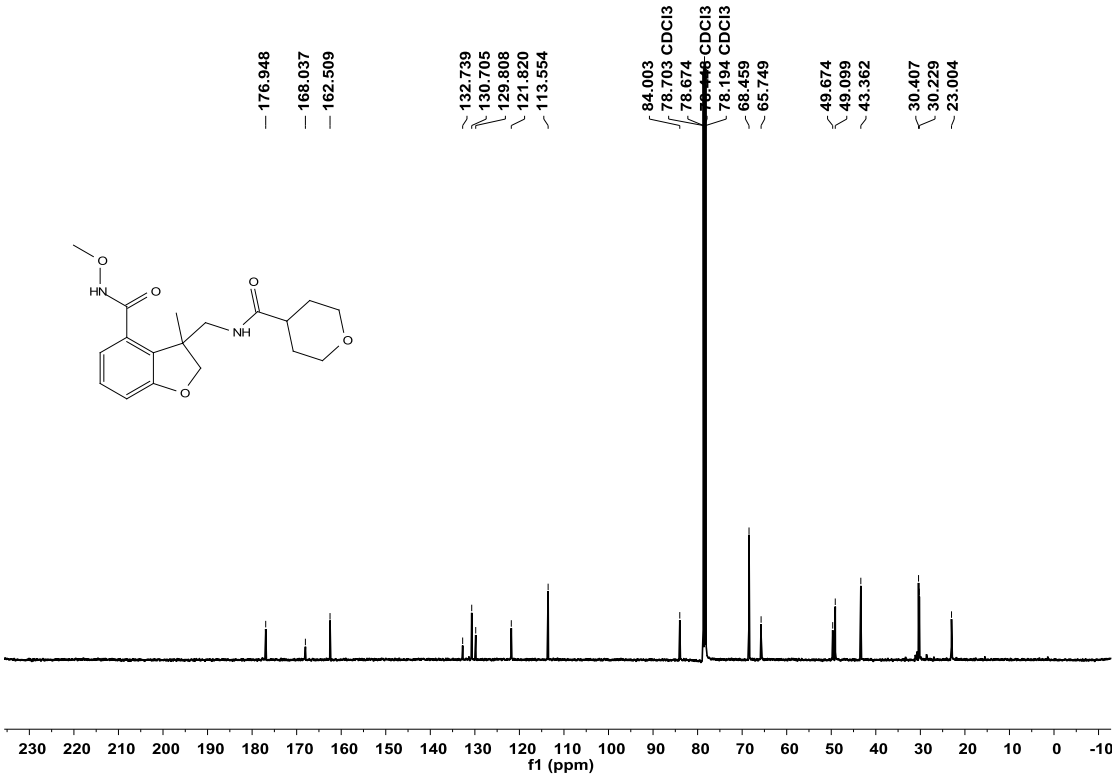



$^{1}H$ and $^{13}C$ NMR Spectra of Compound **6b:**



$^{1}H$ and $^{13}C$ NMR Spectra of Compound **6d:**



$^{1}H$ and $^{13}C$ NMR Spectra of Compound **6e:**