Supplementary Material

Synthesis, *In vitro* anticancer activity and molecular docking studies on some new phenylmorpholine linked aminotetrazoles and aryl tetrazoles

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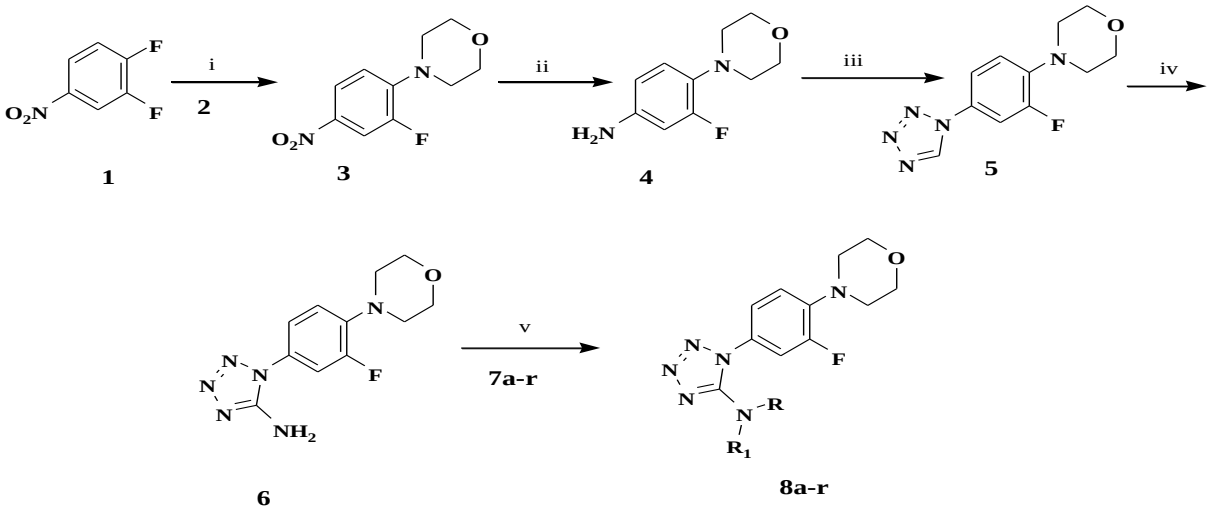
DETAILED EXPERIMENTAL SECTION

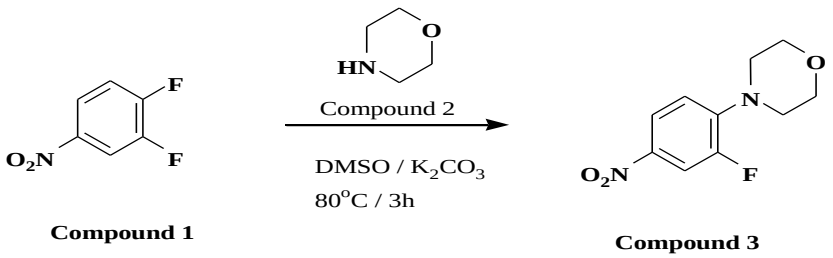
section-1



Detailed Experimental work

Chemistry of Synthesized Compounds

Preparation of 4-(2-Fluoro-4-nitrophenyl)morpholine (3):



To a stirred solution of 3,4-difluoronitrobenzene **1** (40 g, 251.4 mmol) in DMSO (400 mL) was added K_2CO_3 (44.4 g, 321.6 mmol) and morpholine **2** (24 g, 276.6 mmol) and heated to 80 °C for 3 hours. The reaction mixture was cooled to room temperature and diluted with water (400 mL) and extracted with ethyl acetate (3 X 400 mL). The organic layer was separated and washed with brine solution (300 mL), dried over Na_2SO_4, filtered and concentrated *in vaccuo* to afford 4-(2-fluoro-4-nitrophenyl)morpholine **3**(Fig. 1) (48 g, yield:84%)as a off white solid.

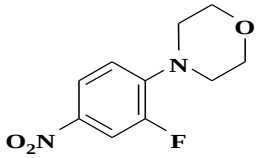
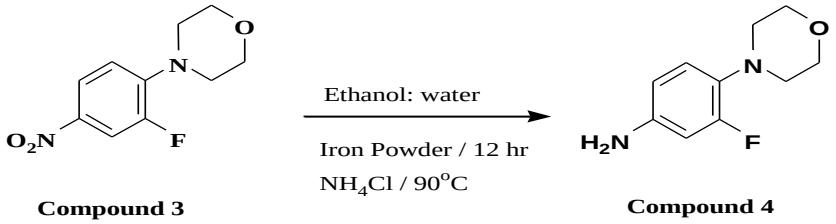


Figure 1: Structure of compound 3

Analytical data: Molecular formula: $C_{10}H_{11}FN_2O_3$; M.P: 112-114 °C; ^{1}H NMR **(**Fig.1) (400 MHz, $CDCl_3$) δ: 8.01-7.93(m, 1H), 7.92 (d, J = 2.8 Hz, 1H), 6.92 (t, J = 8.8 Hz, 1H), 4.01 (t, J = 4.8 Hz, 4H), 3.20 (t, J = 4.8 Hz, 4H); ^{13}C NMR **(**Fig.2) (100 MHz, $CDCl_3$) δ:154.3, 151.8, 145.4, 120.9, 116.8, 112.6, 66.5 (2C), 49.8 (2C); IR (KBr, cm^{-1})**(**Fig.3): 3432, 2925, 1739, 1604, 1242, 1050; HRMS (ESI) **(**Fig.4): calc.for $C_{10}H_{12}N_2O_3F$ $(M+H)^+$: 227.0832 found 227.0844.

Preparation of 3-fluoro-4-morpholinoaniline (4):



To a stirred solution of 4-(2-fluoro-4-nitrophenyl)morpholine **3** (40 g, 177 mmol) in ethanol (360 mL) and water (40 mL) was added iron powder (94.16 g, 1681.47 mmol) and ammonium chloride (4.74 g,88.48 mmol) and heated to 90 °C for 12 hours. The reaction mixture was cooled to room temperature and filtered through celite bed and washed with ethyl acetate, the organic layer was washed with water (400 mL) followed by brine (400 mL) solution. The organic layer was separated, dried over Na_2SO_4 and concentrated *in vacuo* to afford 3-fluoro-4-morpholinoaniline **4**(Figure. 2)Pale brown solid (29.88g,Yield: 86%)

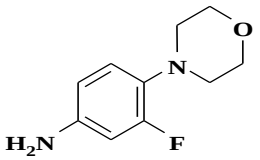
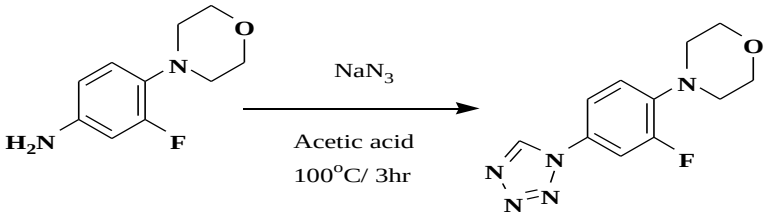


Figure.2: Structure of compound 4

Analytical data: Molecular formula: $C_{10}H_{13}FN_2O$; M.P: 125-127°C;*Anal*. Calc. for$C_{10}H_{13}FN_2O$ (196): Found C, 61.23; H, 6.70; F, 9.69; N, 14.28; O, 8.16%; Calc: C, 61.21; H, 6.68; F, 9.68; N, 14.28; O, 8.15 %;^{1}H NMR(Fig. 5) (400 MHz, $CDCl_3$) δ:6.81 (t, J = 8.4 Hz, 1H), 6.45-6.39 (m, 2H), 3.85 (t, J = 4.8 Hz, 4H), 3.54 (brs, 2H), 2.96 (t, J = 4.8 Hz, 4H); ^{13}C NMR (Fig. 6) (100 MHz, DMSO) δ: 156, 153.5, 150.1, 142.4, 125.2, 119.9,112.6, 77.3, 66.5, 49.8; ESI-MS**(**Fig.7): *m/z*197.2 $[M+H]^+$, +ve ion mode.

Preparation of 4-(2-fluoro-4-(1H-tetrazol-1-yl)phenyl)morpholine (5):



Compound 4 **Compound 5**

To a stirred solution of 3-fluoro-4-morpholinoaniline **4**(20 g, 102.04 mmol) in acetic acid (100 mL) was added triethylorthoformate (24 g, 163.26 mmol) and NaN_3 (9.8 g, 153.06 mmol) and heated to 100 °C for 3 hours. The reaction mixture was cooled to room temperature and diluted with water (200 mL) and extracted with ethyl acetate (3 X 200 mL). The organic layer was washed with water (200 mL) followed by brine solution (150 mL), separated and dried over Na_2SO_4 filtered and concentrated *in* vacuo to afford 4-(2-fluoro-4-(1H-tetrazol-1-yl)phenyl)morpholine **5** (Figure. 3) Off white solid (22.2 g, Yield: 87%)

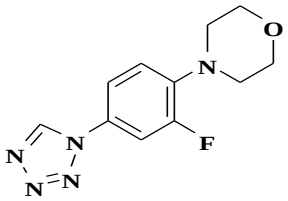
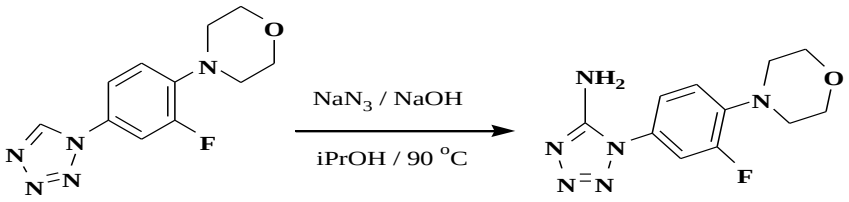


Figure 3: Structure of compound 5

Analytical data: Molecular formula:$C_{11}H_{12}FN_5O$; M.P: 161-163 °C; ^{1}H NMR (Fig.8) (400 MHz, $CDCl_3$) δ: 8.90 (s, 1H), 7.47-7.39 (m, 2H), 7.07 (m, 1H), 3.90 (t, J = 6.4 Hz, 4H), 3.17 (t, J = 6.4 Hz, 4H); ^{13}C NMR (Fig.9) (100 MHz, $CDCl_3$) δ:155.4, 142.1, 140.6, 127.5, 119.7, 117.6, 110.0, 65.9 ,50.1; HRMS (ESI) (Fig.10): calcd for $C_{11}H_{13}N_5OF$ $(M+H)^+$: 250.1104 found 250.1105.

Preparation of 1-(3-fluoro-4-morpholinophenyl)-1H-tetrazol-5-amine(6):



Compound 5 **Compound 6**

A stirred mixture of 4-(2-fluoro-4-(1H-tetrazol-1-yl)phenyl)morpholine 5 (16 g, 64.24 mmol), NaN_3 (6.2 g, 96.38 mmol), NaOH (3.8 g, 96.38 mmol) and Et_3N (12.8 g, 128.5 mmol) in *i*-PrOH (30 mL) was treated with DMSO (70 mL). The reaction mixture was stirred at room temperature until the gas evolution ceased (2 hours) and then was treated with glacial AcOH (11.4 g, 193.2 mmol).The resulting suspension was stirred at 90 °C for 2 hours. Cooled and diluted with water (200 mL). The precipitate was separated by filtration, washed with water and dried in vacuo at 50 °C to afford 1-(3-fluoro-4-morpholinophenyl)-1H-tetrazol-5-amine 6 (Figure. 4) White solid (14.0 g, Yield: 83%).

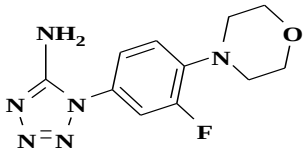
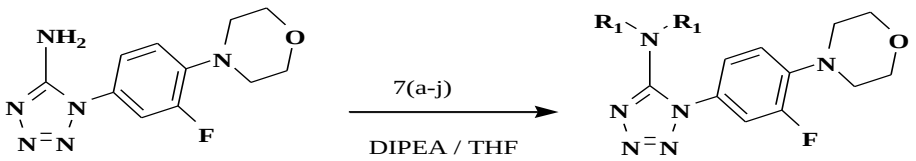


Figure 4: Structure of compound 6

Analytical data: Molecular formula:$C_{11}H_{13}FN_6O$; M.P: 207-209 °C; 1H NMR(Fig.11) (400 MHz, CDCl3) δ: 7.27-7.24 (m, 2H), 7.07 (t, J = 8.8 Hz, 1H), 4.80 (brs, 2H), 3.89 (t, J = 4.8 Hz, 4H), 3.17 (t, J = 4.8 Hz, 4H); 13C NMR(Fig.12) (100 MHz, CDCl3) δ:153.8, 120.1, 120.1, 119.3, 112.8 (2C), 77.3 (3C), 66.7, 50.4 (2C); IR (KBr, cm−1)(Fig.13): 3340, 3154, 2836, 1664, 1522, 1233, 1120; HRMS (ESI)(Fig.14): calcd for $C_{11}H_{14}N_6OF$ (M+H)+: 265.1213 found 265.1228.

Series-I:

General procedure for Compound 8a-8j (diacetylation):



Compound 6 **Compound 8 (a-j)**

To a solution of 1-(3-fluoro-4-morpholinophenyl)-1*H*-tetrazol-5-amine **6** (150 mg, 0.56 mmol) was dissolved in THF (10 mL), cooled to 0 °C and added DIPEA (20 mg, 1.7 mmol) followed by acid chlorides **(7a-7j)**,(1.12 mmol)The reaction mixture was stirred at room temperature for 2-6 hrand quenched with water and extracted with ethyl acetate (3 X10 mL). The combined organic layer was washed with brine solution (10 mL) and dried over Na_2SO_4 and concentration invacuo to afford respective amide derivatives **8a-8j.**

***N*1-Acetyl-*N*1-[1-(3-fluoro-4-morpholinophenyl)-1*H*-1,2,3,4-tetraazol-5-yl]acetamide(8a):**

Following the general procedure, compound **8a** was prepared by dissolving 1-(3-fluoro-4-morpholinophenyl)-1*H*-tetrazol-5-amine **6** (150 mg, 0.56 mmol) in THF (10 mL), cooled to 0 °C and added DIPEA (20 mg, 1.7 mmol) followed by acetyl chloride **7a** (88.6 mg, 1.136 mmol)stirred for 2 h. The corresponding amide derivative **8a** was afforded as an off white solid (Figure. 5) (180.2 mg, 91%)

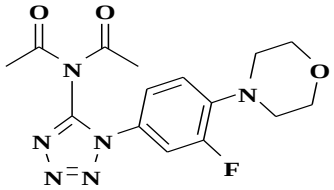


Figure.5: Structure of compound 8a

Analytical data: Molecular formula:$C_{15}H_{17}FN_6O_3$; M.P: 275 ^oC;^1H NMR(Fig.15) (400 MHz, $CDCl_3$) δ: 7.17-7.12 (m, 2H), 7.02 (t, J = 8.8 Hz, 1H), 3.88 (t, J = 4.8 Hz, 4H), 3.19 (t, J = 4.8 Hz, 4H), 2.30 (s, 6H); ^{13}C NMR(Fig.16) (100 MHz, $CDCl_3$) δ:170.3 (2C), 156.0, 153.5, 142.4, 125.2, 120.0, 119.0, 112.6, 66.6 (2C), 50.2 (2C), 25.7 (2C); IR (KBr, cm^{-1}) (Fig.17): 3454, 2927, 1740, 1513, 1209, 1024; HRMS (ESI) (Fig.18): calcd for $C_{15}H_{18}N_6O_3F$ $(M+H)^+$: 349.1424 found 349.1422.

***N*-[1-(3-Fluoro-4-morpholinophenyl)-1*H*-tetrazol-5-yl]-*N*-propionylpropanamide (8b):**

Following the general procedure, compound **8b** prepared by dissolving 1-(3-fluoro-4-morpholinophenyl)-1*H*-tetrazol-5-amine **6** (150 mg, 0.56 mmol) in THF (10 mL), cooled to 0 °C

and added DIPEA (220.3 mg, 1.7 mmol) followed bypropionyl chloride **7b** (105.1mg, 1.136 mmol) for 2 h. The correspondingamide derivatives **8b** (Figure. 6) (192 mg, 90%) as anPale yellow solid.

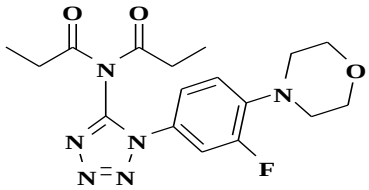


Figure 6: Structure of compound 8b

Analytical data: Molecular formula: $C_{17}H_{21}FN_6O_3$ M.P: 158-160 °C; ^{1}H NMR(Fig. 19) (400 MHz, $CDCl_3$) δ: 7.17-7.10 (m, 2H), 7.01 (t, J = 8.8 Hz, 1H), 3.88 (t, J = 4.8 Hz, 4H), 3.18 (t, J = 4.8 Hz, 4H), 2.54 (q, J = 7.2 Hz, 4H), 1.10 (t, J = 7.2 Hz, 6H); ^{13}C NMR (Fig. 20) (100 MHz, $CDCl_3$) δ:174.2 (2C), 150.0, 125.4, 119.9 (2C), 118.9 (2C), 112.7, 66.6 (2C), 50.2 (2C), 31.3 (2C), 8.3 (2C); IR (KBr, cm^{-1}) (Fig. 21): 3448, 2922, 2858, 1738, 1518, 1450, 1128; HRMS (ESI) (Fig.22): calcd for $C_{17}H_{21}FN_6O_3$ $(M+H)^+$: 377.1737 found 377.2128

N-[1-(3-Fluoro-4-morpholinophenyl)-1H-tetrazol-5-yl]isobutyramide(8c):

Following the general procedure, compound **8c** prepared by dissolving 1-(3-fluoro-4-morpholinophenyl)-1H-tetrazol-5-amine **6** (150 mg, 0.56 mmol) in THF (10 mL), cooled to 0 °C and added DIPEA (220.3 mg, 1.7 mmol) followed byisobutyryl chloride **7c**(105.1mg, 1.136 mmol) for2 h.The corresponding amide derivatives **8c**(Figure. 7) (175 mg, 82%)was afforded as anpale brown solid.

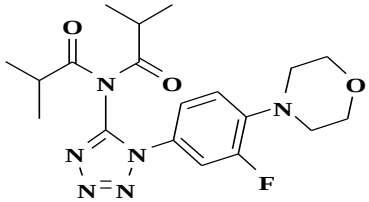


Figure 7: Structure of compound 8c

Analytical data: Molecular formula: $C_{19}H_{25}FN_6O_3$;M.P:.191-193 °C;*Anal*. Calc. for $C_{19}H_{25}FN_6O_3$ (404): Found C, 56.43; H, 6.24; F, 4.72; N, 20.76; O, 11.88%; Calc: C, 56.42; H, 6.23; F, 4.70; N, 20.78; O, 11.87%;^{1}H NMR (Fig.23) (400 MHz, $CDCl_3$) δ: 7.28-7.23 (m, 2H), 7.01 (t, J = 8.8 Hz, 1H), 3.88 (t, J = 4.8 Hz, 4H), 3.17 (t, J = 4.8 Hz, 4H), 2.81 (brs, 1H), 2.60-2.57 (m, 1H), 1.2 (d, J = 4.8 Hz, 12H); ^{13}C NMR (Fig. 24) (100 MHz, $CDCl_3$) δ:175.7, 156.0,

153.5, 149.2, 141.3, 119.5, 118.6, 112.0, 66.7 (2C), 50.4 (2C), 35.4 (2C), 18.8; IR (KBr, cm^{-1}) (Fig. 25): 3446, 3180, 2968, 2934, 1724, 1551, 1519, 1257, 1125; ESI-MS (Fig. 26): *m/z*405.4$[M+H]^+$, +ve ion mode.

***N*-(Cyclopropanecarbonyl)-*N*-[1-(3-fluoro-4-morpholinophenyl)-1*H*-tetrazol-5-yl]cyclopropanecarboxamide (8d)**:

Following the general procedure, compound **8d**was prepared dissolving 1-(3-fluoro-4-morpholinophenyl)-1*H*-tetrazol-5-amine **6** (150 mg, 0.56 mmol) in THF (10 mL), cooled to 0 °C and added DIPEA (220.3 mg, 1.7 mmol) followed by cyclopropanecarbonyl chloride **7d**(118.7 mg, 1.136 mmol)for 2 h.The corresponding amide derivatives **8d**(Figure. 8)(213.6 mg, 94%) was afforded as an off white solid.

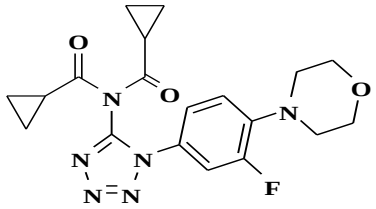


Figure 8: Structure of compound 8d

Analytical data: Molecular formula:$C_{19}H_{22}N_6O_3$; M.P: 103-105 °C;^{1}H NMR(Fig. 27) (400 MHz, $CDCl_3$) δ: 7.21-7.15 (m, 2H), 7.01 (t, J = 8.8 Hz, 1H), 3.89 (t, J = 4.8 Hz, 4H), 3.18 (t, J = 4.8 Hz, 4H), 1.98 (m, 2H), 1.25-1.07 (m, 4H), 1.06-0.96 (m, 4H); ^{13}C NMR(Fig. 28)(100 MHz, $CDCl_3$) δ:174.7 (2C),153.4, 150.2, 142.2, 125.6, 120.0, 118.8, 112.8, 66.6 (2C), 50.2 (2C), 15.6 (2C), 11.8 (4C); IR (KBr, cm^{-1})(Fig. 29): 3445, 2962, 2890, 2856, 1730, 1699, 1580, 1449, 1382, 1302, 1161, 1928; HRMS (ESI) (Fig. 30): calcd for $C_{19}H_{22}N_6O_3$ $(M+H)^+$: 401.1737 found 401.1766.

***N*1-[1-(3-Fluoro-4-morpholinophenyl)-1*H*-tetrazol-5-yl]-*N*1-(3-methylbutanoyl)-3-methylbutanamide (8e)**:

Following the general procedure, compound **8e** prepared by dissolving1-(3-fluoro-4-morpholinophenyl)-1*H*-tetrazol-5-amine **6** (150 mg, 0.56 mmol) in THF (10 mL), cooled to 0 °C and added DIPEA (220.3 mg, 1.7 mmol) followed by 3-methylbutanoyl chloride **7e** (137mg, 1.136 mmol)for 2 h. The corresponding amide derivatives **8e** (Figure. 9) (223 mg, 91%)was afforded as anPale brown thick liquid.

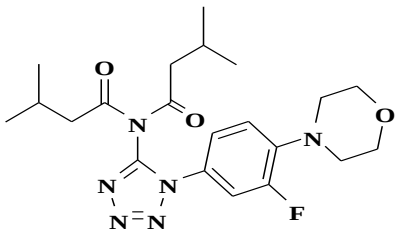


Figure 9: Structure of compound 8e

Analytical data: Molecular formula: $C_{21}H_{29}FN_6O_3$; M.P: NA; *Anal*. Calc. for$C_{21}H_{29}FN_6O_3$ (432):Found C, 58.34; H, 6.78; F, 4.37; N, 19.42; O, 11.14%; Calc: C, 58.32; H, 6.76; F, 4.39; N, 19.43; O, 11.10%;^{1}H NMR (Fig. 31) (400 MHz, $CDCl_3$) δ: 7.17-7.11 (m, 2H), 7.01 (t, J = 8.8 Hz, 1H), 3.88 (t, J = 4.8 Hz, 4H), 3.18 (t, J = 4.8 Hz, 4H), 2.40 (d, J = 6.4 Hz, 2H), 2.16-2.09 (m, 2H), 0.89 (d, J = 6.8 Hz, 12H); ^{13}C NMR (Fig. 32)(100 MHz, $CDCl_3$) δ:172.8 (2C), 156.0, 150.1, 142.3, 125.5, 120.1, 118.9, 112.7, 66.6 (2C), 50.2 (2C), 46.4 (2C), 24.8 (2C), 22.2 (4C); IR (KBr, cm^{-1})(Fig. 33): 3444, 1634, 1275, 1260, 1122; ESI MS(Fig. 34) : m/z 433.44 $(M+H)^+$, +ve ion mode.

.*N*-(3,3-Dimethylbutanoyl)-*N*-[1-(3-fluoro-4-morpholinophenyl)-1*H*--tetrazol-5-yl]-3,3-dimethylbutanamide (8f):

Following the general procedure, compound **8f** prepared treatment of 1-(3-fluoro-4-morpholinophenyl)-1*H*-tetrazol-5-amine **6** (150 mg, 0.56 mmol) was dissolved in THF (10 mL), cooled to 0 °C and added DIPEA (220.3 mg, 1.7 mmol) followed by 3,3-dimethyl butyryl chloride **7f** (152.9mg, 1.136 mmol)for 2 h. The corresponding amide derivatives **8f** (Figure. 10) (232.6 mg, 89%) as anPale yellow solid.

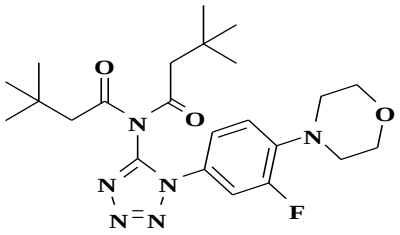


Figure 10: Structure of compound 8f

Analytical data: Molecular formula:$C_{23}H_{34}N_6O_3F$; M.P:138-140 °C; ^{1}H NMR (Fig. 35) (400 MHz, $CDCl_3$) δ: 7.18-7.13 (m, 2H), 7.01 (t, J = 8.8, 1H), 3.88 (t, J = 4.8 Hz, 4H), 3.17 (t, J = 4.8 Hz, 4H), 2.41 (s, 4H), 0.98 (s, 18H); ^{13}C NMR (Fig. 36) (100 MHz, $CDCl_3$) δ:172.3 (2C), 156.0,

150.4, 142.4, 125.5, 120.2, 118.9, 112.94, 66.6 (2C), 50.2 (2C), 49.4 (2C), 29.6 (6C); IR (KBr, cm^{-1})(Fig. 37): 3446, 2925, 1744, 1629, 1519, 1056; HRMS (ESI)(Fig. 38): calcd for $C_{23}H_{34}N_6O_3F$ $(M+H)^+$: 461.2676 found 461.2715.

N-(1-(3-fluoro-4-morpholinophenyl)-1*H*-tetrazol-5-yl)-N-(pivaloyl)pivalamide (8g):

Following the general procedure, compound **8g** prepared by dissolving1-(3-fluoro-4-morpholinophenyl)-1*H*-tetrazol-5-amine **6** (150 mg, 0.56 mmol) was dissolved in THF (10 mL), cooled to 0 °C and added DIPEA (220.3 mg, 1.7 mmol) followed by trimethylacetyl chloride **7g** (137mg, 1.136 mmol) for 2 h afforded the product corresponding amide derivatives **8g** (Figure. 11) (201.3 mg, 82%) as a pale yellow liquid.

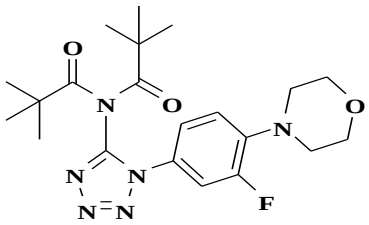


Figure 11: Structure of compound 8g

Analytical data: Molecular formula: $C_{21}H_{29}FN_6O_3$; M.P: NA °C;*Anal*. Calc. for$C_{21}H_{29}FN_6O_3$ (432):Found C, 58.34; H, 6.77; F, 4.38; N, 19.42; O, 11.12%; Calc: C, 58.32; H, 6.76; F, 4.39; N, 19.43; O, 11.10%; ^{1}H NMR(Fig. 39) (400 MHz, DMSO-d_6) δ: 7.43 (d, 1H), 7.34 (m, 1H), 7.23 (m, 1H),3.76 (m, 4H), 3.12 (m, 4H), 1.15 (s, 18H); ^{13}C NMR (Fig. 40) (400 MHz, DMSO-d_6) δ:179.3, 177.5, 155.0, 152.6, 149.5, 140.9 (2C),126.8, 126.7, 120.2, 119.3 (2C), 112.0 (2C), 66.9, 50.2 (2C), 40.1, 39.9 (5C), 38.9 (3C), 27.0 (2C); IR (KBr, cm^{-1}) (Fig. 41): 3446, 2971, 1705, 1521, 1274, 1261,1119; ESI-MS (Fig. 42): *m/z* 433.42 $[M+H]^+$, +ve ion mode.

***N*-[1-(3-Fluoro-4-morpholinophenyl)-1*H*-tetrazol-5-yl]N-Di-(4-(trifluoromethyl)benzamide (8h):**

Following the general procedure, compound **8h** prepared treatment of 1-(3-fluoro-4-morpholinophenyl)-1*H*-tetrazol-5-amine **6** (150 mg, 0.56 mmol) was dissolved in THF (10 mL), cooled to 0 °C and added DIPEA (220.3 mg, 1.7 mmol) followed by4-(trifluoromethyl)benzoyl chloride**7h** (237 mg, 1.136 mmol)for 2 h afforded the product corresponding amide derivatives **8h**(Figure. 12) (220.3 mg, 64%) as white solid.

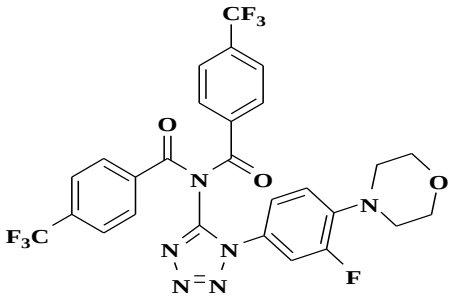


Figure 12: Structure of compound 8h

Analytical data: Molecular formula: $C_{27}H_{19}F_7N_6O_3$; M.P:138-141°C;*Anal*. Calc. for$C_{27}H_{19}F_7N_6O_3$ (608):Found C, 53.31; H, 3.16; F, 21.83; N, 13.84; O, 7.88%; Calc: CC, 53.30; H, 3.15; F, 21.86; N, 13.81; O, 7.89%; 1H NMR (Fig. 43) (400 MHz, DMSO- d_6) δ:7.83-7,87 (m, 2H), 7.66-7.81 (m, 6H), 7.46-7.41 (m, 1H), 7.27-7.21(m, 2H), 3.85 (t, J = 4.8 Hz, 4H), 3.11 (t, J = 4.8 Hz, 4H); 13C NMR (Fig.44)(400 MHz, CDCl3) δ:166.8 155.3, 152.8, 149, 142.4, 132.7, 132.6, 130.5, 127.3, 126.9, 126.6, 124.3(2C), 121.6 (2C), 119.6, 113.3 (2C), 65.9, 49.9,40.1, 39.9 (5C), 38.8; IR (KBr, cm^{-1}) (Fig. 45): 3439, 3080,2979,1752,1731, 1518, 1490, 1312, 1271, 1236, 1114;ESI-MS (Fig. 46): *m/z*609.70$[M+H]^+$, +ve ion mode.

N-(1-(3-fluoro-4-morpholinophenyl)-1*H*-tetrazol-5-yl)-Benzoylbenzamide (8i):

Following the general procedure, compound **8i** prepared treatment of 1-(3-fluoro-4-morpholinophenyl)-1*H*-tetrazol-5-amine **6** (150 mg, 0.56 mmol) was dissolved in THF (10 mL), cooled to 0 °C and added DIPEA (220.3 mg, 1.7 mmol) followed bybenzoyl chloride**7i** (160 mg, 1.136 mmol)for 2 h afforded the product corresponding amide derivatives **8i**(Figure. 13) (206.3 mg, 77%) as off white solid.

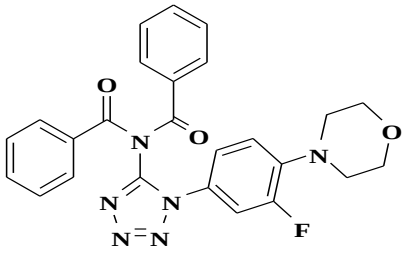


Figure 13: Structure of compound 8i

Analytical data: Molecular formula: $C_{25}H_{21}FN_6O_3$; M.P:101-104°C;*Anal*. Calc. for$C_{25}H_{21}FN_6O_3$ (472):Found C, 63.55; H, 4.48; F, 4.02; N, 17.79; O, 10.16%; Calc: C, 63.55; H, 4.48; F, 4.02; N, 17.79; O, 10.16%; 1H NMR (Fig. 47) (400 MHz, $CDCl_3$) δ: 8.17-8.08 (m,

1H), 7.68-7.63 (m,4H), 7.58-7.54(m, 3H), 7.37-7.34(m, 4H), 7.13-7.12(m, 1H), 6.95-6.92 (m, 2H), 3.92-3.85 (m, 4H), 3.20-3.12(m, 5H);^{13}C NMR (Fig.48) (400 MHz, CDCl3) δ:166.8 155.3, 152.8, 149, 142.4, 132.7, 132.6, 130.5,127.3, 126.9, 126.6, 124.3(2C), 121.6 (2C), 119.6, 113.3 (2C), 65.9, 49.9,40.1, 39.9 (5C), 38.8; IR (KBr, cm−1)(Fig.49): 3444, 2925,1706, 1519, 1275, 1261, 1116;ESI-MS (Fig.50): *m/z*473.21$[M+H]^+$, +ve ion mode.

2-Fluoro-*N*-[1-(3-fluoro-4-morpholinophenyl)-1*H*-tetrazol-5-yl]-N-(2-fluoro-6-methoxybenzoyl)6-methoxybenzamide (8j):

Following the general procedure, compound **8j** prepared treatment of 1-(3-fluoro-4-morpholinophenyl)-1*H*-tetrazol-5-amine **6** (150 mg, 0.56 mmol) was dissolved in THF (10 mL), cooled to 0 °C and added DIPEA (220.3 mg, 1.7 mmol) followed bybenzoyl chloride **7j** (218mg, 1.12 mmol)for 2 h afforded the product corresponding amide derivatives **8j**(Figure. 14)(280.5 mg, 87%) as an off white solid.

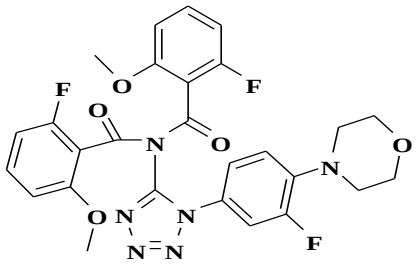
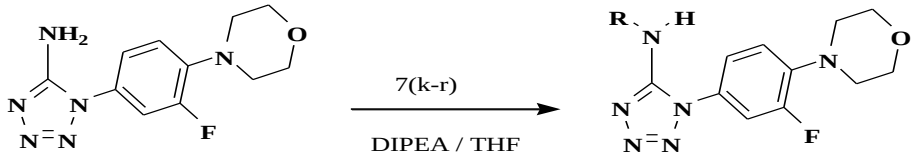


Figure 14: Structure of compound 8j

Analytical data: Molecular formula: $C_{19}H_{18}F_2N_6O_3$; M.P: 239-241°C;*Anal*. Calc. for$C_{19}H_{18}F_2N_6O_3$ (568):Found C, 57.05; H, 4.07; F, 10.04; N, 14.79; O, 14.08%; Calc: C, 57.04; H, 4.08; F, 10.03; N, 14.78; O, 14.07%;^{1}H NMR (Fig. 51) (400 MHz, $CDCl_3$) *δ*: 7.38-7.35 (m, 2H), 7.19-7.13 (m, 2H), 7.04 (t, *J* = 8.8 Hz, 1H), 6.51 (t, *J* = 9.8 Hz, 2H), 6.44 (d, *J* = 8.4 Hz, 2H), 3.89 (t, *J* = 4.8 Hz, 4H), 3.74 (s, 6H), 3.16 (t, *J* = 4.8 Hz, 4H); ^{13}C NMR (Fig. 52)(100 MHz, $CDCl_3$) *δ*:163.3 (2C), 161.4, 158.8, 157.5, 155.7, 153.2, 149.3, 141.8, 133.6; 126.3, 121.4, 118.5, 113.4, 107.9, 66.7 (2C), 56.0 (2C), 50.4 (2C); IR (KBr, cm^{-1})(Fig. 53): 3415, 2845, 1731, 1703, 1617, 1476, 1233, 1087; ESI MS(Fig. 54) : *m*/*z* 569.43 $(M+H)^+$.

General procedure for Compound 8k-8r(acetylation):



Compound 6 **Compound 8 (k-r)**

To a solution of 1-(3-fluoro-4-morpholinophenyl)-1H-tetrazol-5-amine **6** (150 mg, 0.56 mmol) was dissolved in THF (10 mL), cooled to 0 °C and added DIPEA (20 mg, 1.7 mmol) followed by acid chlorides **(7k-7r)**,(0.616 mmol)The reaction mixture was stirred at room temperature for 2-6 hr and quenched with water and extracted with ethyl acetate (3x10 mL). The combined organic layer was washed with brine solution (10 mL) and dried over Na_2SO_4 and concentration invacuo to afford respective amide derivatives **8k-8r.**

***N*-[1-(3-Fluoro-4-morpholinophenyl)-1*H*-tetrazol-5-yl]benzamide (8k):**

Following the general procedure, compound **8k** prepared treatment of 1-(3-fluoro-4-morpholinophenyl)-1*H*-tetrazol-5-amine **6** (150 mg, 0.56 mmol) was dissolved in THF (10 mL), cooled to 0 °C and added DIPEA (220.3 mg, 1.7 mmol) followed bybenzoyl chloride**7k** (160mg, 0.616 mmol)for 2 h afforded the product corresponding amide derivatives **8k**(Figure. 15)(177.7 mg, 85%) as a pale pink solid.

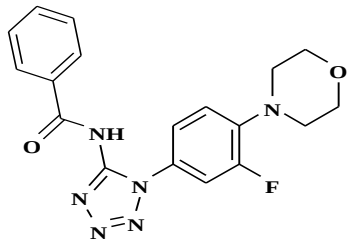


Figure 15 : Structure of compound 8j

Analytical data: Molecular formula:$C_{18}H_{17}FN_6O_2$; M.P: 257-259 °C; ^{1}H NMR(Fig. 55) (400 MHz, $CDCl_3$) δ:11.02 (brs, 1H), 8.07 (d, J = 7.2 Hz, 2H), 7.64 (t, J = 7.6 Hz, 1H), 7.53 (t, J = 7.6 Hz, 2H), 7.37-7.31 (m, 2H), 6.98 (t, J = 8.8 Hz, 1H), 3.86 (t, J = 4.8 Hz, 4H), 3.14 (t, J = 4.8 Hz, 4H);13C NMR (Fig.56) (400 MHz, CDCl3) δ:166.8 155.3, 152.8, 149, 142.4, 132.7, 132.6,

130.5,127.3, 126.9, 126.6, 124.3(2C), 121.6 (2C), 119.6, 113.3 (2C), 65.9, 49.9,40.1, 39.9 (5C), 38.8; IR (KBr, cm^{-1})(Fig. 57): 3270, 3081, 2921, 2839, 1691, 1546, 1265, 1103; HRMS (ESI)(Fig. 58): calcd for $C_{18}H_{18}N_6O_2F$ $(M+H)^+$: 369.1475 found 369.1440.

_N_-[1-(3-Fluoro-4-morpholinophenyl)-1_H_-tetrazol-5-yl]-2-methoxy-_N_-(2-methoxybenzoyl)benzamide (8l):

Following the general procedure, compound **8l** prepared treatment of 1-(3-fluoro-4-morpholinophenyl)-1*H*-tetrazol-5-amine **6** (150 mg, 0.56 mmol) was dissolved in THF (10 mL), cooled to 0 °C and added DIPEA (220.3 mg, 1.7 mmol) followed by benzoyl chloride**7l** (160mg, 0.616 mmol) for 2 h afforded the product corresponding amide derivatives **8l** (Figure. 16) (208 mg, 92%) as an off white solid.

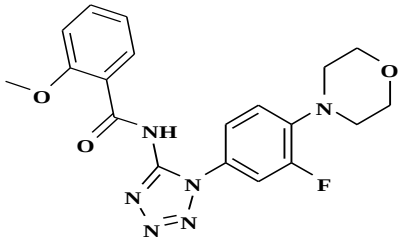


Figure 16: Structure of compound 8l

Analytical data: Molecular formula: $C_{19}H_{19}FN_6O_3$; M.P: 196-198°C; *Anal*. Calc. for $C_{19}H_{19}FN_6O_3$ (398):Found C, 57.29; H, 4.83; F, 4.78; N, 21.10; O, 12.07%; Calc: C, 57.28; H, 4.81; F, 4.77; N, 21.09; O, 12.05%; ^{1}H NMR (Fig. 59) (400 MHz, $CDCl_3$) δ: 7.52-7.42 (m, 4H), 7.31-7.27 (m, 2H), 6.99 (t, J = 9.2 Hz, 1H), 6.88-6.85 (m, 2H), 6.59 (d, J = 8.4 Hz, 2H), 3.85 (t, J = 4.8 Hz, 4H), 3.71 (s, 6H), 3.11 (t, J = 4.8 Hz, 4H); ^{13}C NMR(Fig. 60) (400 MHz, $CDCl_3$) δ:168.1 (2C), 156.6 (2C), 150.3, 141.5, 134.3 (2C), 131.3 (2C), 126.8 (2C), 126.7 (2C), 122.1, 120.6, 118.6, 112.3 (3C), 66.7 (2C), 55.2 (2C), 50.4 (2C); IR (KBr, cm^{-1})(Fig. 61): 3436, 2958, 2943, 1698, 1664, 1510, 1490, 1341, 1293, 1253, 1114; ESI-MS (Fig.62): *m/z*399.12$[M+H]^+$, +ve ion mode.

2,6-Difluoro_N_-[1-(3-Fluoro-4-morpholinophenyl)-1_H_-tetrazol-5-yl]-benzamide (8m):

Following the general procedure, compound **8m** prepared treatment of 1-(3-fluoro-4-morpholinophenyl)-1*H*-tetrazol-5-amine **6** (150 mg, 0.56 mmol) was dissolved in THF (10 mL), cooled to 0 °C and added DIPEA (220.3 mg, 1.7 mmol) followed by benzoyl chloride **7m**

(108.7mg, 0.616 mmol) for 2 h afforded the product corresponding amide derivatives **8m** (Figure 17) (221 mg, 90%) as an off white solid.

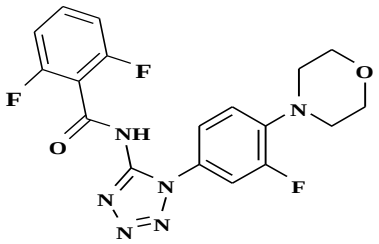


Figure 17: Structure of compound 8m

Analytical data: Molecular formula: $C_{18}H_{15}F_3N_6O_2$; M.P: 214-216 °C; *Anal*. Calc. for $C_{18}H_{15}F_3N_6O_2$ (404): Found C, 53.48; H, 3.75; F, 14.12; N, 20.79; O, 7.93%; Calc: C, 53.47; H, 3.74; F, 14.10; N, 20.78; O, 7.91%;^{1}H NMR(Fig. 63) (400 MHz, $CDCl_3$) δ: 7.51-7.21 (m, 3H), 7.00-6.88 (m, 3H), 3.87 (t, J = 4.8 Hz, 4H), 3.15 (t, J = 4.8 Hz, 4H);^{13}C NMR (Fig. 64)(100 MHz, $CDCl_3$) δ:179.3, 177.5, 155.0,52.6, 149.5, 140.9 (2C), 126.8 (2C), 120.2(2C), 119.3 (2C), 112.1(2C),65.9, 50.1 (2C), 40.1, 39.9 (5C), 38.7 (3C); IR (KBr, cm^{-1})(Fig. 65): 3437, 3177, 2955, 2836, 1723, 1567, 1246, 1125, 1010; ESI-MS (Fig.66): *m/z*405.33$[M+H]^+$, +ve ion mode.

N-(1-(3-fluoro-4-morpholinophenyl)-1*H*-tetrazol-5-yl)-4-(trifluoromethyl)benzamide (8n):

Following the general procedure, compound **8n** prepared treatment of 1-(3-fluoro-4-morpholinophenyl)-1*H*-tetrazol-5-amine **6** (150 mg, 0.56 mmol) was dissolved in THF (10 mL), cooled to 0 °C and added DIPEA (220.3 mg, 1.7 mmol) followed bybenzoyl chloride**7n** (208.4mg, 0.616 mmol)for 2 h afforded the product corresponding amide derivatives **8n** (Figure. 18) (215.5 mg, 87%) as a light brown solid.

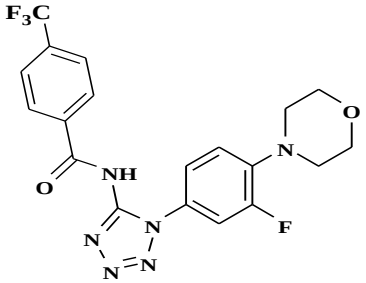


Figure 18: Structure of compound 8n

Analytical data: Molecular formula: $C_{19}H_{16}F_4N_6O_2$; M.P:202-204°C;*Anal*. Calc. for$C_{19}H_{16}F_4N_6O_2$ (436):Found C, 52.33; H, 3.71; F, 17.43; N, 19.27; O, 7.34%; Calc: C, 52.30; H, 3.70; F, 17.42; N, 19.26; O, 7.33%;^{1}H NMR (Fig. 67) (400 MHz, DMSO-d_6) δ: 7.85-7.67 (m, 4H), 7.63-7.59 (m, 1H), 7.47-7.45(m, 1H), 7.24-7.19 (m, 1H), 3.76-3.74(m, 4H), 3.10-3.07(m, 4H);^{13}C NMR (Fig. 68) (100 MHz, $CDCl_3$) δ:166.8 155.3, 152.8, 149, 142.4, 132.7, 132.6, 130.5,127.3, 126.9, 126.6, 124.3(2C), 121.6 (2C), 119.6, 113.3 (2C), 65.9, 49.9,40.1, 39.9 (5C), 38.8; IR (KBr, cm−1)(Fig.69):3455, 3179, 2921,2898, 2860, 1677, 1523, 1454, 1380, 1318,1274,1257; ESI-MS (Fig.70): *m/z*437.25$[M+H]^+$, +ve ion mode.

_N_-(1-(3-fluoro-4-morpholinophenyl)-1_H_-tetrazol-5-yl)cyclohexanecarboxamide (8o):

Following the general procedure, compound **8o** prepared treatment of 1-(3-fluoro-4-morpholinophenyl)-1*H*-tetrazol-5-amine **6** (150 mg, 0.56 mmol) was dissolved in THF (10 mL), cooled to 0 °C and added DIPEA (220.3 mg, 1.7 mmol) followed cyclohexane carboxylic acid chloride **7o** (90.3mg, 0.616 mmol)for 2 h afforded the product corresponding amide derivatives **8o** (Figure. 19) (180.6 mg, 85%) as aoff white solid.

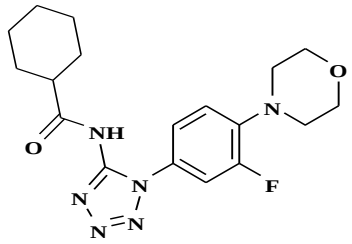


Figure 19: Structure of compound 8o

Analytical data: Molecular formula: $C_{18}H_{23}FN_6O_2$; M.P:201-205°C;*Anal*. Calc. for$C_{18}H_{23}FN_6O_2$ (374): Found C, 57.73; H, 6.20; F, 5.08; N, 22.47; O, 8.56%; Calc: C, 57.74; H, 6.19; F, 5.07; N, 22.45; O, 8.55%;^{1}H NMR(Fig. 71) (400 MHz, DMSO-d_6) δ:7.54-7.34 (m, 2H), 7.01 (t, J = 8.8, 1H),3.88 (t, J = 4.8 Hz, 4H), 3.17 (t, J = 4.8 Hz, 4H), 2.45-2.37 (m, 1H), 1.79-1.48 (m, 5H), 1.35-1.04(m, 5H); ^{13}C NMR (Fig. 72)(100 MHz, $CDCl_3$) δ: 174.8, 155, 152.4, 149.2, 140.8, 127 (2C), 120.4, 119.2, 112.3(2C), 66, 50.1, 43.3, 40.1 (2C), 28.4, 25.1 (2C); IR (KBr, cm−1)(Fig.73): 3446, 3220, 3036, 2928, 2855, 1728, 1551, 1448, 1303, 12568, 1258;ESI-MS (Fig.74): *m/z*375.27$[M+H]^+$, +ve ion mode.

N-(1-(3-fluoro-4-morpholinophenyl)-1_H_-tetrazol-5-yl)-3-phenylpropanamide (8p):

Following the general procedure, compound **8p** prepared treatment of 1-(3-fluoro-4-morpholinophenyl)-1*H*-tetrazol-5-amine **6** (150 mg, 0.56 mmol) was dissolved in THF (10 mL), cooled to 0 °C and added DIPEA (220.3 mg, 1.7 mmol) followed 3-Phenylpropionyl chloride **7p** (103.9mg, 0.616 mmol)for 2 h afforded the product corresponding amide derivatives **8p**(Figure. 20)(207 mg, 92%) as aoff white solid.

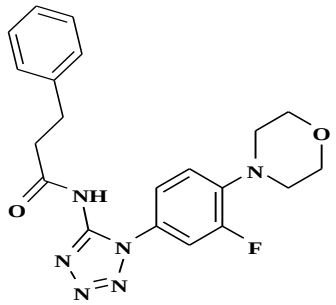


Figure 20: Structure of compound 8p

Analytical data: Molecular formula: $C_{20}H_{21}FN_6O_2$; M.P: 180-183°C;*Anal*. Calc. for $C_{20}H_{21}FN_6O_2$ (396): Found C, 60.61; H, 5.33; F, 4.78; N, 21.22; O, 8.06%; Calc: C, 60.60; H, 5.34; F, 4.79; N, 21.20; O, 8.07%; ^{1}H NMR(Fig. 75) (400 MHz, DMSO-*d6*) δ: 7.28-7.24 (m, 2H), 7.19-7.11 (m, 5H), 6.98-6.93(m, 1H), 3.90-3.85(m, 4H), 3.19-3.16(m, 4H), 2.98-2.93 (m, 4H); 13C NMR (Fig. 76) (100 MHz, $CDCl_3$) δ: 148.8, 139.6, 128.5, 128.4, 126.3, 119.9, 118.7, 112.5, 66.7, 50.3, 37.6, 30.5; IR (KBr, cm^{-1}) (Fig.77): 3405, 317,2963, 2928, 2864, 1959, 1705, 1558, 1520, 1452, 1380,1355 1258, 1122; ESI-MS (Fig.78): *m/z*397.26$[M+H]^+$, +ve ion mode.

2,3-difluoro-N-(1-(3-fluoro-4-morpholinophenyl)-1H-tetrazol-5-yl)-4-methylbenzamide (8q):

Following the general procedure, compound **8q** prepared treatment of 1-(3-fluoro-4-morpholinophenyl)-1*H*-tetrazol-5-amine **6** (150 mg, 0.56 mmol) was dissolved in THF (10 mL), cooled to 0 °C and added DIPEA (220.3 mg, 1.7 mmol) followed 2,3-difluoro-4-methylbenzoyl chloride **7q** (117.4mg, 0.616 mmol)for 2 h afforded the product corresponding amide derivatives **8q** (**Figure. 21**)(216 mg, 91%) as an off white solid.

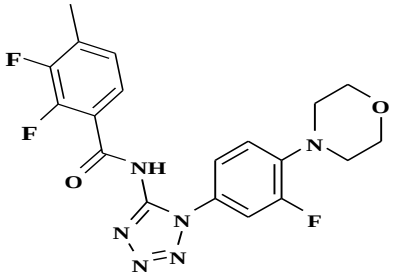


Figure 21: Structure of compound 8q

Analytical data: Molecular formula: $C_{19}H_{17}F_3N_6O_2$; M.P:112-115°C;*Anal*. Calc. for$C_{19}H_{17}F_3N_6O_2$ (418): Found C, 54.56; H, 4.11; F, 13.63; N, 20.07; O, 7.66%; Calc: C, 54.55; H, 4.10; F, 13.62; N, 20.09; O, 7.65%; ^{1}H NMR(Fig. 79) (400 MHz, DMSO-d_6) δ: 7.62 (m, 1H), 7.44-7.36 (m, 2H), 7.34-7.16 (m, 2H),3.90-3.85(m, 4H), 3.19-3.16(m, 4H), 2.34 (s,3H); 13C NMR (Fig. 80) (100 MHz, $CDCl_3$) δ: 162.3, 155, 152.6, 149.1, 140.9 (2C), 131.3 (2C), 126.6 (3C), 124.3, 121.1, 120.3, 119.2, 112.3 (2C), 65.9, 50, 44.5, 40.1, 39.9 (5C), 38.8, 14.1; IR (KBr, cm^{-1})(Fig.81): 3181, 2969, 2864, 1967, 1705, 1634, 1565, 1453, 1270, 1121, 1077; ESI-MS (Fig.82): *m/z*419.22$[M+H]^+$, +ve ion mode.

2-chloro-4-fluoro-N-(1-(3-fluoro-4-morpholinophenyl)-1*H*-tetrazol-5-yl)benzamide (8r):

Following the general procedure, compound **8r** prepared treatment of 1-(3-fluoro-4-morpholinophenyl)-1*H*-tetrazol-5-amine **6** (150 mg, 0.56 mmol) was dissolved in THF (10 mL), cooled to 0 °C and added DIPEA (220.3 mg, 1.7 mmol) followed 2-chloro-4-fluorobenzoyl chloride **7r** (118.8mg, 0.616 mmol)for 2 h afforded the product corresponding amide derivatives **8r** (**Figure. 22**) (210 mg, 88%) as a pale brown solid.

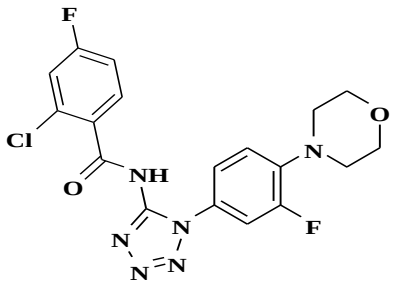
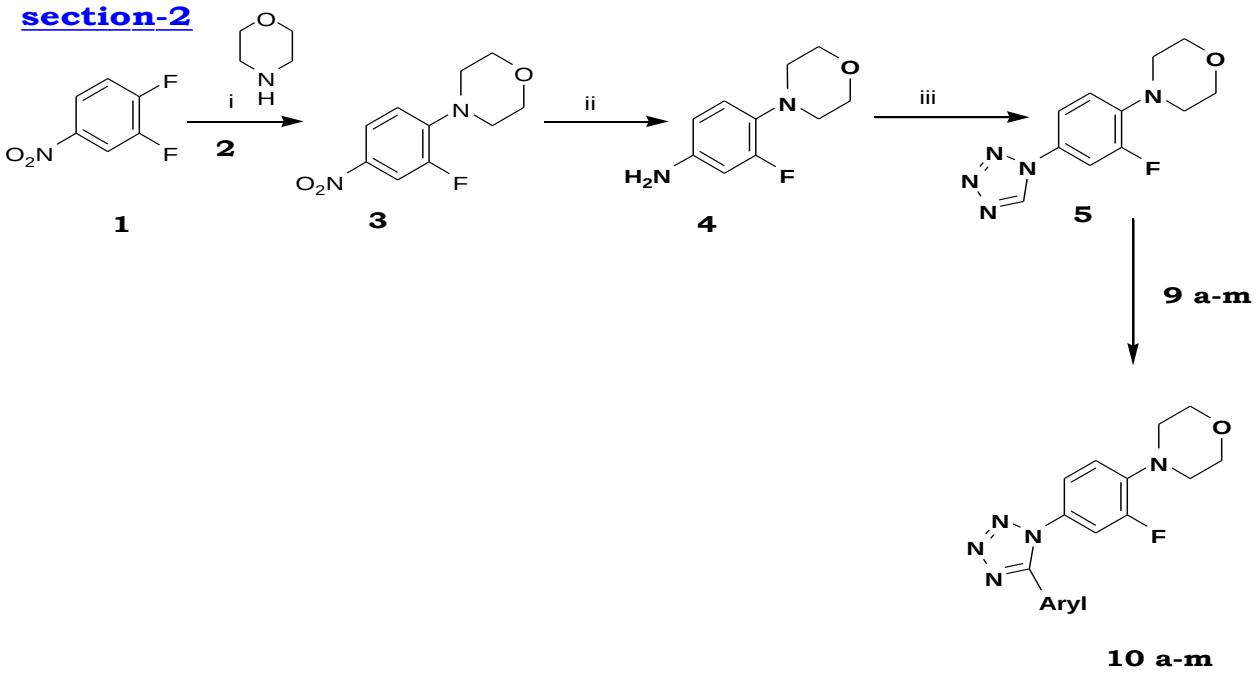


Figure 22: Structure of compound 8r

Analytical data: Molecular formula: $C_{18}H_{15}ClF_2N_6O_2$; M.P:172-175°C; *Anal*. Calc. for$C_{18}H_{15}ClF_2N_6O_2$ (421):Found C, 51.39; H, 3.58; Cl, 8.44; F, 9.04; N, 19.98; O, 7.62%; Calc: C, 51.38; H, 3.59; Cl, 8.43; F, 9.03; N, 19.97; O, 7.60%;^{1}H NMR(Fig. 83) (400 MHz, DMSO-

d6) δ: 712.16 (s, br, 1H), 7.88-7.19 (m, 6H), 3.76-3.74(m, 4H), 3.10-3.08(m, 4H);13C NMR (Fig. 84) (100 MHz, CDCl3) δ: 165.7, 164.5, 164.0, 161.8, 161.5, 155.1, 152.6, 148.9, 141.0, 133.6, 133.1, 131.8, 131.3, 126.8, 121.0, 119.2, 118.2, 117.9, 117.6, 117.4, 114.6, 112.9, 112.6; IR (KBr, cm^{-1}) (Fig.85): 3736, 3256, 3083, 2845, 2561, 1684, 1522, 1445, 1306, 1262, 1109,1095; ESI-MS (Fig.86): *m/z*421.21$[M+H]^+$, +ve ion mode.



General procedure for Preparation of Compounds10a-10m(Direct Arylation of 4-(2-fluoro-4-(1*H*-tetrazol-1-yl)phenyl)morpholine):

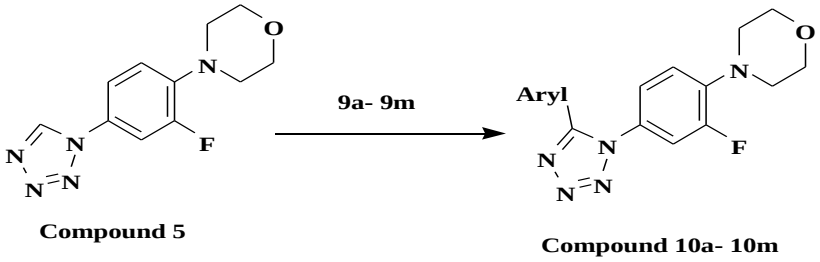


Figure 23: Structure of compound 10a-10m

A suspension of 4-(2-fluoro-4-(1*H*-tetrazol-1-yl)phenyl)morpholine **5** (1.00 mmol), the appropriate aryl iodide **9a-9m** (1.00 mmol), cesium carbonate (1.10 mmol), copper(I) iodide (1.00 mmol), palladium(II) acetate (0.05 mmol), and tris(2-furyl)-phosphine (0.10 mmol) in dry

acetonitrile (6 mL) was heated at 40 °C under argon atmosphere for 4 -8 h. The resulting mixture was diluted with ethyl acetate (40 mL) and filtered quickly through Celite, then the solvents were removed under reduced pressure. The residue was purified by column chromatography (hexane:ethyl acetate) to afford the title compounds**10a-10m** (76-88%).

4-(2-fluoro-4-(5-phenyl-1*H*-tetrazol-1-yl)phenyl)morpholine (10a):

A suspension of 4-(2-fluoro-4-(1*H*-tetrazol-1-yl)phenyl)morpholine**5** (249 mg, 1.00 mmol), iodobenzene **9a**(204 mg, 1.00 mmol), cesium carbonate (357.5mg, 1.10 mmol), copper(I) iodide (190 mg, 1.00 mmol), palladium(II) acetate (11.2 mg, 0.05 mmol), and tris(2-furyl)-phosphine (23.2 mg, 0.10 mmol) in dry acetonitrile (6 mL) was heated at 40 °C under argon atmosphere for 4 h. The resultingmixture was diluted with ethyl acetate (40 mL) and filtered quickly through celite, then the solvents were removed under reduced pressure. The residue was purified by column chromatography (hexane:ethyl acetate 9:1) to obtained compound **10a**(Figure. 24) (285 mg, 87%) as a off white solid.

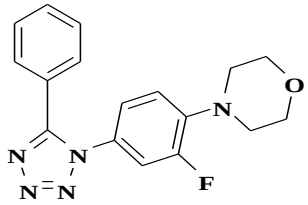


Figure 24: Structure of compound 10a

Analytical data: Molecular formula: $C_{17}H_{16}FN_5O$; M.P:148-151°C; *Anal*. Calc. for$C_{17}H_{16}FN_5O$ (325): Found C, 62.77; H, 4.96; F, 5.86; N, 21.56; O, 4.94%; Calc: C, 62.76; H, 4.96; F, 5.84; N, 21.53; O, 4.92%;^{1}H-NMR(Fig. 87) (400 MHz, DMSO-d6) δ: 7.59-7.41(m, 5H), 7.15-7.10(m, 2H), 6.99-6.97(m, 1H), 3.90-3.87(m, 4H), 3.19-3.17(m, 4H); ^{13}C-NMR (Fig. 88) (100 MHz, $CDCl_3$) δ: 155.9,153.4, 141.7, 141.6, 131.3, 129.0, 128.8, 127.8, 127.7, 123.4, 121.6, 118.8, 113.9, 113.7, 66.7, 50.3; IR (KBr, cm^{-1}) (Fig.89):3733, 3443, 3065, 2955, 2854, 1615, 1516, 1460, 1378, 1348, 1302, 1233,1107; ESI-MS (Fig.90): *m/z*326.26$[M+H]^+$, +ve ion mode.

4-(2-fluoro-4-(5-o-tolyl-1*H*-tetrazol-1-yl)phenyl)morpholine (10b):

A suspension of 4-(2-fluoro-4-(1*H*-tetrazol-1-yl)phenyl)morpholine**5** (249 mg, 1.00 mmol), 2-iodotoluene **9b** (218 mg, 1.00 mmol), cesium carbonate (357.5 mg, 1.10 mmol), copper(I)

iodide (190 mg, 1.00 mmol), palladium(II) acetate (11.2 mg, 0.05 mmol), and tris(2-furyl)-phosphine (23.2 mg, 0.10 mmol) in dry acetonitrile (6 mL) washeated at 40 °C under argon atmosphere for 4 h. The resulting mixture was diluted with ethyl acetate (40 mL) and filtered quickly through Celite, then the solvents were removedunder reduced pressure. The residue was purified by column chromatography (hexane:ethyl acetate 9:4) to obtainedcompound **10b**(Figure. 25) (294 mg, 86%) as a light brown solid.

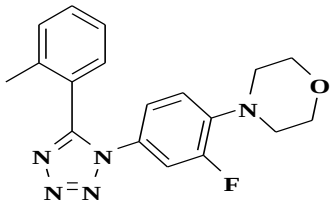


Figure 25: Structure of compound 10b

Analytical data: Molecular formula:$C_{18}H_{18}FN_5O$; M.P: 98-101°C;*Anal*. Calc. for$C_{18}H_{18}FN_5O$ (339):Found C, 63.71; H, 5.33; F, 5.62; N, 20.65; O, 4.72%; Calc: C, 63.70; H, 5.35; F, 5.60; N, 20.64; O, 4.71%;^{1}H NMR(Fig. 91) (400 MHz, $CDCl_3$) δ: 7.45-7.41(m, 1H), 7.32-7.30(m, 3H), 7.09-7.05(m, 1H), 7.00-6.98(m, 1H), 6.91-6.86(m, 1H), 3.86-3.83(m, 4H), 3.13-3.10(m, 4H), 2.12 (s, 3H); 13C NMR (Fig. 92) (100 MHz, $CDCl_3$) δ: 155.8, 153.3, 153.2, 141.0, 137.7, 131.1, 130.9, 130.0, 127.7, 127.6, 126.2, 123.6, 119.7, 118.6, 112.3, 112.1, 66.6, 50.3, 19.6;IR (KBr, cm−1) (Fig.93): 3874, 3732, 3440, 3061, 2957, 2921, 2855, 1957, 1613, 1515,1381, 1255, 1112 ; ESI-MS (Fig.94): *m/z*340.24$[M+H]^+$, +ve ion mode.

4-(2-fluoro-4-(5-m-tolyl-1*H*-tetrazol-1-yl)phenyl)morpholine (10c):

A suspension of 4-(2-fluoro-4-(1*H*-tetrazol-1-yl)phenyl)morpholine**5** (249 mg, 1.00 mmol), 3-iodotoluene **9c** (218 mg, 1.00 mmol), cesium carbonate (357.5 mg, 1.10 mmol), copper(I) iodide (190 mg, 1.00 mmol), palladium(II) acetate (11.2 mg, 0.05 mmol), and tris(2-furyl)-phosphine (23.2 mg, 0.10 mmol) in dry acetonitrile (6 mL) washeated at 40 °C under argon atmosphere for 4 h. The resulting mixture was diluted with ethyl acetate (40 mL) and filtered quickly through Celite, then the solvents were removed under reduced pressure. The residue was purified by column chromatography (hexane:ethyl acetate 9:4) to obtained compound **10c**(Figure. 26) (281 mg, 83%) as a light brown solid.

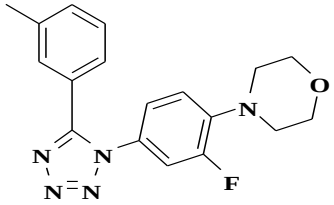


Figure 26: Structure of compound 10c

Analytical data: Molecular formula: $C_{18}H_{18}FN_5O$; M.P: 101-104°C;*Anal*. Calc. for$C_{18}H_{18}FN_5O$ (339):Found C, 63.71; H, 5.33; F, 5.62; N, 20.65; O, 4.73%; Calc: C, 63.70; H, 5.35; F, 5.60; N, 20.64; O, 4.71%; ^{1}H NMR(Fig. 95) (400 MHz, $CDCl_3$) δ: 7.53(s, 1H), 7.32-7.21(m, 3H), 7.14-7.10(m, 2H), 6.99-6.97(m, 1H), 3.90-3.88(m, 4H), 3.19-3.17(m, 4H), 2.36(s, 3H); 13C NMR (Fig. 96) (100 MHz, $CDCl_3$) δ: 155.9, 153.5, 153.4, 141.6, 141.5, 139.0, 132.0, 129.5, 128.7, 127.8, 125.6, 121.5, 118.7, 113.8, 113.6, 66.6, 50.3;IR (KBr, cm−1) (Fig.97):3735, 3446, 3041, 2962, 2860, 2837, 1813, 1614, 1575, 1512, 1453, 1377, 1304, 1237, 1166, 1117; ESI-MS (Fig.98): *m/z*340.0$[M+H]^+$, +ve ion mode.

4-(2-fluoro-4-(5-p-tolyl-1*H*-tetrazol-1-yl)phenyl)morpholine (10d):

A suspension of 4-(2-fluoro-4-(1*H*-tetrazol-1-yl)phenyl)morpholine**5** (249 mg, 1.00 mmol), 4-iodotoluene **9d** (218 mg, 1.00 mmol), cesium carbonate (357.5 mg, 1.10 mmol), copper(I) iodide (190 mg, 1.00 mmol), palladium(II) acetate (11.2 mg, 0.05 mmol), and tris(2-furyl)-phosphine (23.2 mg, 0.10 mmol) in dry acetonitrile (6 mL) was heated at 40 °C under argon atmosphere for 4 h. The resulting mixture was diluted with ethyl acetate (40 mL) and filtered quickly through Celite, then the solvents were removed under reduced pressure. The residue was purified by column chromatography (hexane:ethyl acetate 9:4) to obtained compound **10d** (Figure. 27) (284 mg, 84%) as a light brown solid.

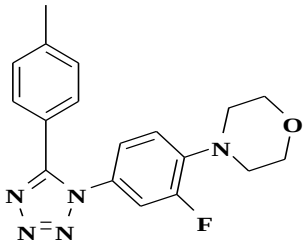


Figure 27: Structure of compound 10d

Analytical data: Molecular formula: $C_{18}H_{18}FN_5O$; M.P: 149-151°C;*Anal*. Calc. for$C_{18}H_{18}FN_5O$ (339):Found C, 63.69; H, 5.34; F, 5.65; N, 20.63; O, 4.70%; Calc: C, 63.70; H, 5.35; F, 5.60; N, 20.64; O, 4.71%; ^{1}H NMR(Fig. 99) (400 MHz, DMSO-d6) δ: 7.59(m, 1H), 7.48-7.41(m, 2H), 7.38-7.31 (m, 3H), 7.14-7.10(m, 1H), 3.90-3.88(m, 4H), 3.19-3.17(m, 4H), 2.36(s, 3H); 13C NMR (Fig. 100) (100 MHz, $CDCl_3$) δ: 154.9, 153.6, 152.4, 141.3, 141.2, 129.4, 128.6, 127.2, 127.1, 122.9, 120.4, 119.2, 119.1, 114.6, 114.4, 65.9, 49.9, 20.8;IR (KBr, cm−1) (Fig.101): 3735, 3445, 2962, 2917, 1614, 1520, 1450, 1376, 1342, 1256, 1120; ESI-MS (Fig.102): *m/z*340.31$[M+H]^+$, +ve ion mode.

4-(4-(5-(2-ethylphenyl)-1*H*-tetrazol-1-yl)-2-fluorophenyl)morpholine (10e):

A suspension of 4-(2-fluoro-4-(1*H*-tetrazol-1-yl)phenyl)morpholine**5** (249 mg, 1.00 mmol), 1-ethyl-2-iodobenzene **9e** (232 mg, 1.00 mmol), cesium carbonate (357.5 mg, 1.10 mmol), copper(I) iodide (190 mg, 1.00 mmol), palladium(II) acetate (11.2 mg, 0.05 mmol), and tris(2-furyl)-phosphine (23.2 mg, 0.10 mmol) in dry acetonitrile (6 mL) washeated at 40 °C under argon atmosphere for 4 h. The resulting mixture was diluted with ethyl acetate (40 mL) and filtered quickly through celite, then the solvents were removedunder reduced pressure. The residue was purified by column chromatography (hexane:ethyl acetate 9:1) to obtained compound **10e** (Figure. 28) (286 mg, 81%) as a colourless liquid.

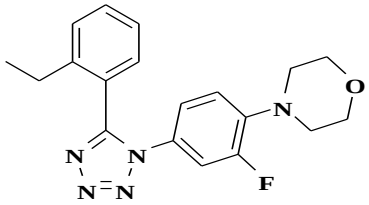


Figure 28: Structure of compound 10e

Analytical data: Molecular formula: $C_{19}H_{20}FN_5O$; M.P: NA ;*Anal*. Calc. for$C_{19}H_{20}FN_5O$ (353): Found C, 64.55; H, 5.72; F, 5.39; N, 19.81; O, 4.52%; Calc: C, 64.57; H, 5.70; F, 5.38; N, 19.82; O, 4.53%; ^{1}H NMR(Fig. 103) (400 MHz, DMSO-d6) δ: 7.45-7.44(m, 1H), 7.44-7.43(m, 1H), 7.35-7.34(m, 1H), 7.20-7.19(m, 1H), 7.15-7.13(m, 1H), 7.00-6.98 (m, 1H), 6.95-6.93(m, 1H), 3.85-3.80(m, 4H), 3.10-3.08(m, 4H), 2.45-2.43(m, 2H), 1.05-1.03(m, 3H); 13C NMR (Fig. 104) (100 MHz, $CDCl_3$) δ: 155.8, 153.4, 153.1, 143.9, 141.1, 141.0, 131.3, 130.1, 129.4, 127.8,

127.7, 126.2, 123.0, 119.8, 118.6, 112.5, 112.2, 66.7, 50.3, 26.2, 14.9;IR (KBr, cm−1) (Fig.105):3443, 2967, 2855, 1516, 1450, 1378, 1275, 1261, 1118; ESI-MS (Fig.106): *m/z*364.0$[M+H]^+$, +ve ion mode.

4-(4-(5-(4-ethylphenyl)-1*H*-tetrazol-1-yl)-2-fluorophenyl)morpholine (10f):

A suspension of 4-(2-fluoro-4-(1*H*-tetrazol-1-yl)phenyl)morpholine**5** (249 mg, 1.00 mmol), 1-Ethyl-4-iodobenzene **9f** (232 mg, 1.00 mmol), cesium carbonate (357.5 mg, 1.10 mmol), copper(I) iodide (190 mg, 1.00 mmol), palladium(II) acetate (11.2 mg, 0.05 mmol), and tris(2-furyl)-phosphine (23.2 mg, 0.10 mmol) in dry acetonitrile (6 mL) was heated at 40 °C under argon atmosphere for 4 h. The resulting mixture was diluted with ethyl acetate (40 mL) and filtered quickly through celite, then the solvents were removed under reduced pressure. The residue was purified by column chromatography (hexane:ethyl acetate 9:3) to obtained compound **10f**(Figure. 29) (275 mg,78%) as an off white solid.

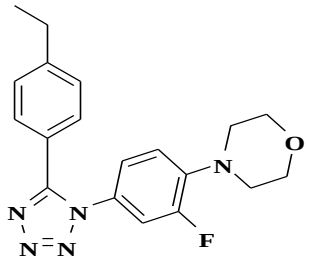


Figure 29: Structure of compound 10f

Analytical data: Molecular formula:$C_{19}H_{20}FN_5O$; M.P: 118-120°C;*Anal*. Calc. for$C_{19}H_{20}FN_5O$ (353):Found C, 64.56; H, 5.71; F, 5.37; N, 19.80; O, 4.54%; Calc: C, 64.57; H, 5.70; F, 5.38; N, 19.82; O, 4.53%;^{1}H NMR(Fig. 107) (400 MHz, $CDCl_3$) δ: 7.50-7.48(m, 2H), 7.26-7.24(m, 2H), 7.14-7.11(m, 2H), 7.02-6.98(m, 1H), 3.90-3.88(m, 4H), 3.20-3.17(m, 4H), 2.72-2.66(m, 2H), 1.27-1.23(m, 3H); 13C NMR (Fig. 108(100 MHz, $CDCl_3$) δ: 156.0, 153.5, 148.0, 141.7, 128.7, 128.5, 128.0, 127.9, 121.7, 120.6, 118.7, 114.0, 113.8, 66.7, 50.4, 28.7, 14.9;IR (KBr, cm−1) (Fig.109): 3077, 3032, 2960, 2861, 1676, 1613, 1522,1470,1488, 154, 1121; ESI-MS (Fig.110): *m/z*354.20$[M+H]^+$, +ve ion mode.

4-(2-fluoro-4-(5-(2-methoxyphenyl)-1*H*-tetrazol-1-yl)phenyl)morpholine (10g):

A suspension of 4-(2-fluoro-4-(1*H*-tetrazol-1-yl)phenyl)morpholine**5** (249 mg, 1.00 mmol),

2-iodoanisole **9g** (234 mg, 1.00 mmol), cesium carbonate (357.5 mg, 1.10 mmol), copper(I) iodide (190 mg, 1.00 mmol), palladium(II) acetate (11.2 mg, 0.05 mmol), and tris(2-furyl)-phosphine (23.2 mg, 0.10 mmol) in dry acetonitrile (6 mL) washeated at 40 °C under argon atmosphere for 4 h. The resulting mixture was diluted with ethyl acetate (40 mL) and filteredquickly through celite, then the solvents were removed under reduced pressure. The residue was purified by column chromatography (hexane:ethyl acetate 9:3) to obtained compound **10g**(Figure. 30) (284 mg, 80%) as a brown colour solid.

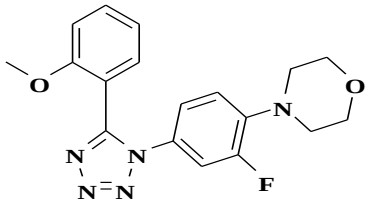


Figure 30: Structure of compound 10g

Analytical data: Molecular formula: $C_{18}H_{18}FN_5O_2$; M.P: 123-125°C;*Anal*. Calc. for$C_{18}H_{18}FN_5O_2$ (355):Found C, 60.83; H, 5.12; F, 5.38; N, 19.72; O, 9.03%; Calc: C, 60.84; H, 5.11; F, 5.35; N, 19.71; O, 9.00%;^{1}H NMR (Fig. 111) (400 MHz, $CDCl_3$) δ: 7.59-7.50(m, 2H), 7.11-6.88(m, 5H), 3.86(s, 4H), 3.44(s, 4H), 3.11(s, 4H); 13C NMR (Fig. 112) (100 MHz, $CDCl_3$) δ: 156.5, 155.8, 153.3, 151.9, 140.9, 140.8, 133.1, 131.4, 129.1, 129.0, 121.1, 119.3, 118.3, 113.1, 112.0, 111.8, 111.3, 66.6, 55.0, 50.4;IR (KBr, cm^{-1}) (Fig.113): 3556, 3468, 3069, 2958, 2842, 2230, 2069, 1604, 1582, 1518, 1250, 1115; ESI-MS (Fig.114): *m/z*356.0$[M+H]^+$, +ve ion mode.

4-(2-fluoro-4-(5-(3-methoxyphenyl)-1*H*-tetrazol-1-yl)phenyl)morpholine (10h):

A suspension of 4-(2-fluoro-4-(1*H*-tetrazol-1-yl)phenyl)morpholine**5** (249 mg, 1.00 mmol), 3-iodoanisole **9h** (234 mg, 1.00 mmol), cesium carbonate (357.5 mg, 1.10 mmol), copper(I) iodide (190 mg, 1.00 mmol), palladium(II) acetate (11.2 mg, 0.05 mmol), and tris(2-furyl)-phosphine (23.2 mg, 0.10 mmol) in dry acetonitrile (6 mL) was heated at 40 °C under argon atmosphere for 4 h. The resultingmixture was diluted with ethyl acetate (40 mL) and filtered quickly through celite, then the solvents were removed under reduced pressure. The residue was purified by column chromatography (hexane:ethyl acetate 9:3) to obtained compound **10h**(Figure. 31) (298 mg, 84%) as a light brown solid.

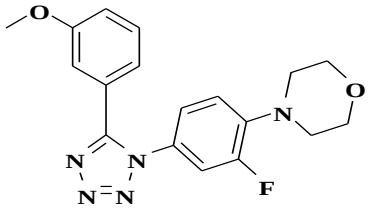


Figure 31: Structure of compound 10h

Analytical data: Molecular formula: $C_{18}H_{18}FN_5O_2$; M.P: 110-114°C;*Anal*. Calc. for$C_{18}H_{18}FN_5O_2$ (355):Found C, 60.85; H, 5.13; F, 5.36; N, 19.73; O, 9.02%; Calc: C, 60.84; H, 5.11; F, 5.35; N, 19.71; O, 9.00%;^{1}H NMR(Fig. 115) (400 MHz, $CDCl_3$) δ: 7.33-7.27(m, 1H), 7.20-7.12(m, 3H), 7.05-6.98(m, 3H), 3.90-3.88(m, 4H), 3.79(s, 3H), 3.19-3.17(m, 4H); ^{13}C NMR (Fig. 116) (100 MHz, $CDCl_3$) δ: 159.7, 155.9, 153.4, 153.3, 141.7, 141.6, 130.0, 127.7, 124.4, 121.6, 120.9, 118.7, 117.4, 113.7, 66.7, 55.3, 50.3; IR (KBr, cm^{-1}) (Fig.117): 3444, 3070, 2898, 2861, 2231, 1615, 1582, 1514, 1483, 1236, 1115, 1048; ESI-MS (Fig.118): *m/z*356.0$[M+H]^+$, +ve ion mode.

4-(2-fluoro-4-(5-(4-methoxyphenyl)-1*H*-tetrazol-1-yl)phenyl)morpholine (10i):

A suspension of 4-(2-fluoro-4-(1*H*-tetrazol-1-yl)phenyl)morpholine**5** (249 mg, 1.00 mmol), 4-iodoanisole **9i** (234 mg, 1.00 mmol), cesium carbonate (357.5 mg, 1.10 mmol), copper(I) iodide (190 mg, 1.00 mmol), palladium(II) acetate (11.2 mg, 0.05 mmol), and tris(2-furyl)-phosphine (23.2 mg, 0.10 mmol) in dry acetonitrile (6 mL) was heated at 40 °C under argon atmosphere for 4 h. The resulting mixture was diluted with ethyl acetate (40 mL) and filtered quickly through celite, then the solvents were removed under reduced pressure. The residue was purified by column chromatography (hexane:ethyl acetate 9:3) to obtained compound **10i** (Figure. 32) (287 mg, 81%) as an off white solid.

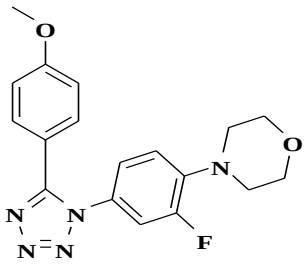


Figure 32: Structure of compound 10i

Analytical data: Molecular formula: $C_{18}H_{18}FN_5O_2$; M.P: 154-156°C; *Anal*. Calc. for $C_{18}H_{18}FN_5O_2$ (355):Found C, 60.86; H, 5.14; F, 5.33; N, 19.72; O, 9.03%; Calc: C, 60.84; H, 5.11; F, 5.35; N, 19.71; O, 9.00%;^{1}H NMR(Fig. 119) (400 MHz, $CDCl_3$) δ: 7.59-7.51(m, 2H), 7.14-7.11(m, 2H), 7.06-7.01 (m, 1H), 6.93-6.91(m, 2H), 3.90-3.84(m, 7H), 3.20-3.18(m, 4H); ^{13}C NMR (Fig. 120) (100 MHz, $CDCl_3$) δ: 161.8, 155.9, 153.5, 145.8, 141.6, 130.3, 128.0, 127.9, 121.7, 118.8, 115.4, 114.4, 113.8, 112.0, 66.7, 55.3, 50.3;IR (KBr, cm^{-1}) (Fig.121): 3445, 3082, 2920, 2861, 2567, 2228, 2055, 1725, 1236, 1612, 1257, 1117, 1030; ESI-MS (Fig.122): *m/z*356.33$[M+H]^+$, +ve ion mode.

4-(2-fluoro-4-(5-(2,4-dimethoxyphenyl)-1*H*-tetrazol-1-yl)phenyl)morpholine (10j):

A suspension of 4-(2-fluoro-4-(1*H*-tetrazol-1-yl)phenyl)morpholine**5** (249 mg, 1.00 mmol), 2,4-dimethoxyiodobenzene **9j** (264 mg, 1.00 mmol), cesium carbonate (357.5 mg, 1.10 mmol), copper(I) iodide (190 mg, 1.00 mmol), palladium(II) acetate (11.2 mg, 0.05 mmol), and tris(2-furyl)-phosphine (23.2 mg, 0.10 mmol) in dry acetonitrile (6 mL) washeated at 40 °C under argon atmosphere for 4 h. The resulting mixture was diluted with ethyl acetate (40 mL) and filtered quickly through celite, then the solvents were removed under reduced pressure. The residue was purified by column chromatography (hexane:ethyl acetate 9:3) to obtained compound **10j** (Figure. 33) (308 mg, 80%) as a light brown solid.

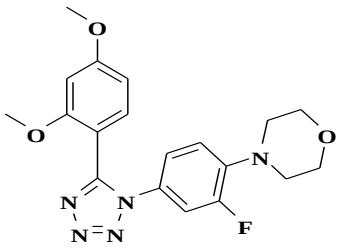


Figure 33: Structure of compound 10j

Analytical data: Molecular formula: $C_{19}H_{20}FN_5O_3$; M.P: 104-106°C; *Anal*. Calc. for$C_{19}H_{20}FN_5O_3$ (385):Found C, 59.23; H, 5.24; F, 4.91; N, 18.18; O, 12.46%; Calc: C, 59.21; H, 5.23; F, 4.93; N, 18.17; O, 12.45%; ^{1}H NMR (Fig. 123) (400 MHz, $CDCl_3$) δ: 7.52-7.50(m, 1H), 7.12-7.08 (m, 1), 7.04-7.03(m, 1H), 6.93-6.89 (m, 1H), 6.64-6.62(m, 1H), 6.40-6.38 (m, 1H), 3.87 (s, 4H), 3.40 (s, 3H), 3.12-3.10 (m, 4H); 13C NMR (Fig. 124) (100 MHz, $CDCl_3$) δ: 163.7, 157.8, 155.8, 153.3, 151.9, 140.7, 132.3, 129.4, 119.3, 118.3, 112.0, 111.7, 105.5, 98.9,

66.6, 55.5, 50.4;IR (KBr, cm^{-1}) (Fig.125): 3446, 3083, 2920, 2851, 2567, 2227, 1611, 1519, 1467, 1257, 1116, 1043; ESI-MS (Fig.126): *m/z*386.0$[M+H]^+$, +ve ion mode.

4-(2-fluoro-4-(5-(3,4,5-trimethoxyphenyl)-1*H*-tetrazol-1-yl)phenyl)morpholine (10k):

A suspension of 4-(2-fluoro-4-(1*H*-tetrazol-1-yl)phenyl)morpholine **5** (249 mg, 1.00 mmol), 3,4,5-Trimethoxyiodobenzene **9k** (294 mg, 1.00 mmol), cesium carbonate (357.5 mg, 1.10 mmol), copper(I) iodide (190 mg, 1.00 mmol),palladium(II) acetate (11.2 mg, 0.05 mmol), and tris(2-furyl)-phosphine (23.2 mg, 0.10 mmol) in dry acetonitrile (6 mL) was heated at 40 °C under argon atmosphere for 4 h. The resulting mixture was diluted with ethyl acetate (40 mL) and filtered quickly through Celite, then the solvents were removed under reduced pressure. The residue was purified by column chromatography (hexane:ethyl acetate 9:5) to obtained compound **10k**(Figure. 34) (352 mg, 85%) as a pale yellow solid.

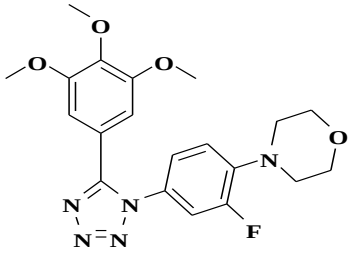


Figure 34: Structure of compound 10k

Analytical data: Molecular formula: $C_{20}H_{22}FN_5O_4$; M.P: 130-132°C; *Anal*. Calc. for$C_{20}H_{22}FN_5O_4$ (415):Found C, 57.81; H, 5.36; F, 4.56; N, 16.84; O, 15.43%; Calc: C, 57.82; H, 5.34; F, 4.57; N, 16.86; O, 15.41%;^{1}H NMR(Fig. 127) (400 MHz, $CDCl_3$) δ: 7.21-7.15(m, 2H), 7.06-7.01(m, 1H), 6.80 (s, 2H), 3.90-3.89(m, 7H), 3.72(s, 5H), 3.17-3.15(m, 4H); 13C NMR (Fig. 128) (100 MHz, $CDCl_3$) δ: 156.0, 153.5, 153.3, 141.9, 141.8, 140.6, 127.9, 122.0, 118.7, 118.1, 114.3, 106.3, 66.6, 60.9, 56.1, 50.4;IR (KBr, cm^{-1}) (Fig.129): 3446, 3083, 2920, 2851, 2567, 2227, 1611, 1519, 1467, 1257, 1116, 1043; ESI-MS (Fig.130): *m/z*416.0$[M+H]^+$, +ve ion mode.

1-(3-(1-(3-fluoro-4-morpholinophenyl)-1*H*-tetrazol-5-yl)phenyl)ethanone (10l):

A suspension of 4-(2-fluoro-4-(1*H*-tetrazol-1-yl)phenyl)morpholine**5** (249 mg, 1.00 mmol),1-(2-iodophenyl)ethanone **9l** (246 mg, 1.00 mmol), cesium carbonate (357.5 mg, 1.10 mmol), copper(I) iodide (190 mg, 1.00 mmol), palladium(II) acetate (11.2 mg, 0.05 mmol), and tris(2-

furyl)-phosphine (23.2 mg, 0.10 mmol) in dry acetonitrile (6 mL) washeated at 40 °C under argon atmosphere for 4 h. The resultingmixture was diluted with ethyl acetate (40 mL) and filtered quickly through celite, then the solvents were removedunder reduced pressure. The residue was purified by columnchromatography (hexane:ethyl acetate 9:2) to obtainedcompound **10l**(Figure. 35) (286 mg, 85%) as a pale yellow solid.

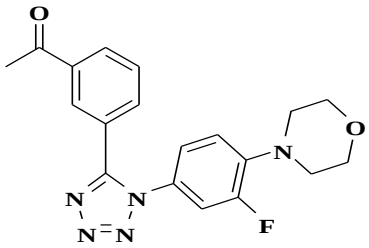


Figure 35: Structure of compound 10l

Analytical data: Molecular formula: $C_{19}H_{18}FN_5O_2$; M.P: 157-159°C;*Anal*. Calc. for$C_{19}H_{18}FN_5O_2$ (367):Found C, 62.13; H, 4.54; F, 5.18; N, 19.03; O, 8.73%; Calc: C, 62.12; H, 4.94; F, 5.17; N, 19.06; O, 8.71%; ^{1}H NMR (Fig. 131) (400 MHz, $CDCl_3$) δ: 8.21 (s, 1H), 8.05-8.04(m, 1H), 7.75-7.73(m, 1H), 7.58-7.56(m, 1H), 7.18-7.16(m, 2H), 7.01-6.98(m, 1H), 3.95-3.93(m, 4H), 3.21-3.19(m, 4H), 2.58-2.56(m, 3H); ^{13}C NMR (Fig. 132) (100 MHz, $CDCl_3$) δ: 196.4, 156.0, 153.5, 152.8, 142.0, 137.7, 132.8, 130.8, 129.5, 128.8, 127.4, 124.1, 121.7, 118.9, 114.0, 113.8, 66.7, 50.3, 26.5;IR (KBr, cm^{-1}) (Fig.133): 3451, 3064, 2944, 2831, 2695, 1693, 1608, 1579, 1508, 1446, 1248, 1117; ESI-MS (Fig.134): *m/z*368.0$[M+H]^+$, +ve ion mode.

4-(2-fluoro-4-(5-(2-fluorophenyl)-1*H*-tetrazol-1-yl)phenyl)morpholine (10m):

A suspension of 4-(2-fluoro-4-(1*H*-tetrazol-1-yl)phenyl)morpholine**5** (249 mg, 1.00 mmol), 1-Fluro-2-iodobenzene **9m** (222 mg, 1.00 mmol), cesium carbonate (357.5 mg, 1.10 mmol), copper(I) iodide (190 mg, 1.00 mmol), palladium(II) acetate (11.2 mg, 0.05 mmol), and tris(2-furyl)-phosphine (23.2 mg, 0.10 mmol) in dry acetonitrile (6 mL) was heated at 40 °C under argon atmosphere for 4 h. The resulting mixture was diluted with ethyl acetate (40 mL) and filtered quickly through celite, then the solvents were removed under reduced pressure. The residue was purified by column chromatography (hexane:ethyl acetate 9:1) to obtained compound **10m**(Figure. 36) (295 mg, 86%) as a pale yellow solid.

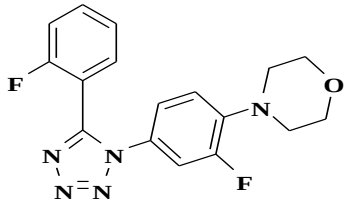


Figure 36: Structure of compound 10m

Analytical data: Molecular formula:$C_{17}H_{15}F_2N_5O$; M.P: 124-126°C;*Anal*. Calc. for$C_{17}H_{15}F_2N_5O$ (343): Found C, 59.48; H, 4.42; F, 11.09; N, 20.43; O, 4.64%; Calc: C, 59.47; H, 4.40; F, 11.07; N, 20.40; O, 4.66 %;^{1}H NMR(Fig. 135) (400 MHz, $CDCl_3$) δ: 7.67-7.64(m, 1H), 7.58-7.56(m, 1H), 7.35-7.32(m, 1H), 7.15-7.04(m, 3H), 6.95-6.91(m, 1H), 3.86(s, 4H), 3.14(s, 4H); 13C NMR (Fig. 136) (100 MHz, $CDCl_3$) δ: 160.6, 158.1, 155.8, 153.4, 149.9, 141.4, 133.7, 131.5, 127.8, 125.0, 124.9, 120.0, 119.9, 118.6, 118.5, 116.6, 112.6, 112.3, 66.6, 654.7, 50.3, 50.2, 15.2;IR (KBr, cm^{-1}) (Fig.137): 3735, 3446, 3041, 2944, 2860, 2837, 1813, 1614, 1575, 1512, 1237,1117; ESI-MS (Fig.138): *m/z*344.0$[M+H]^+$, +ve ion mode.

SPECTRAS OF SYNTHESIZED COMPOUNDS

Analytical Spectra's of Compound 3

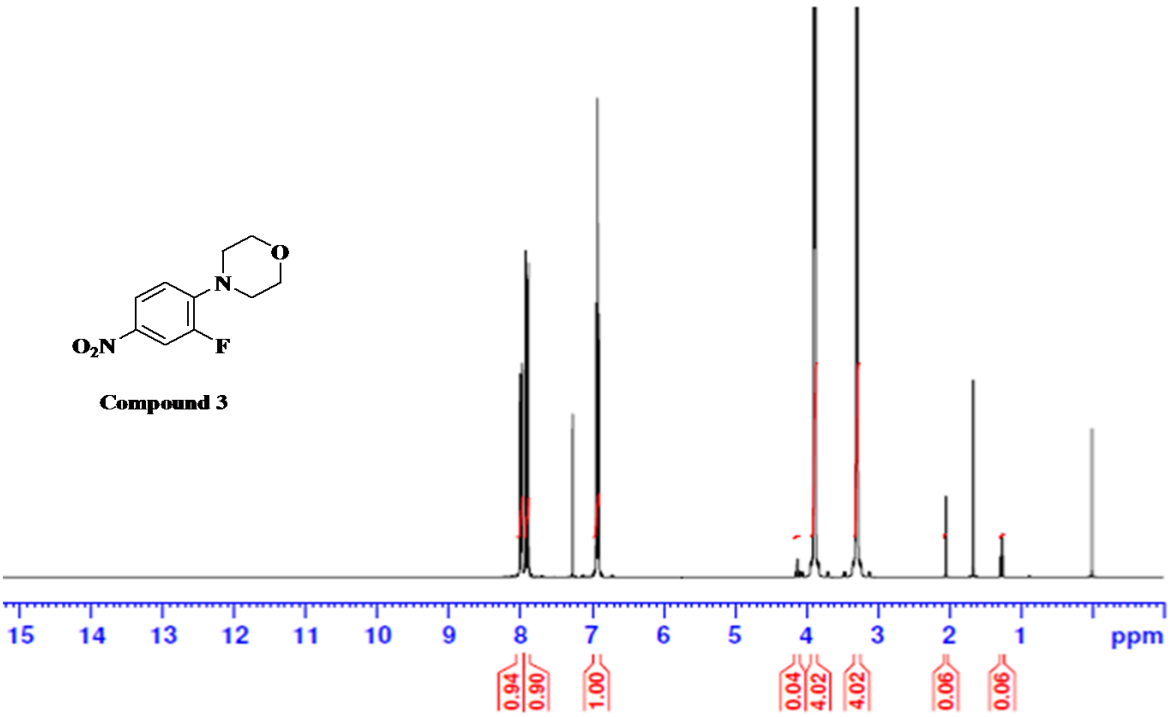


Figure 1.^{1}H NMR Spectra of Compound 3

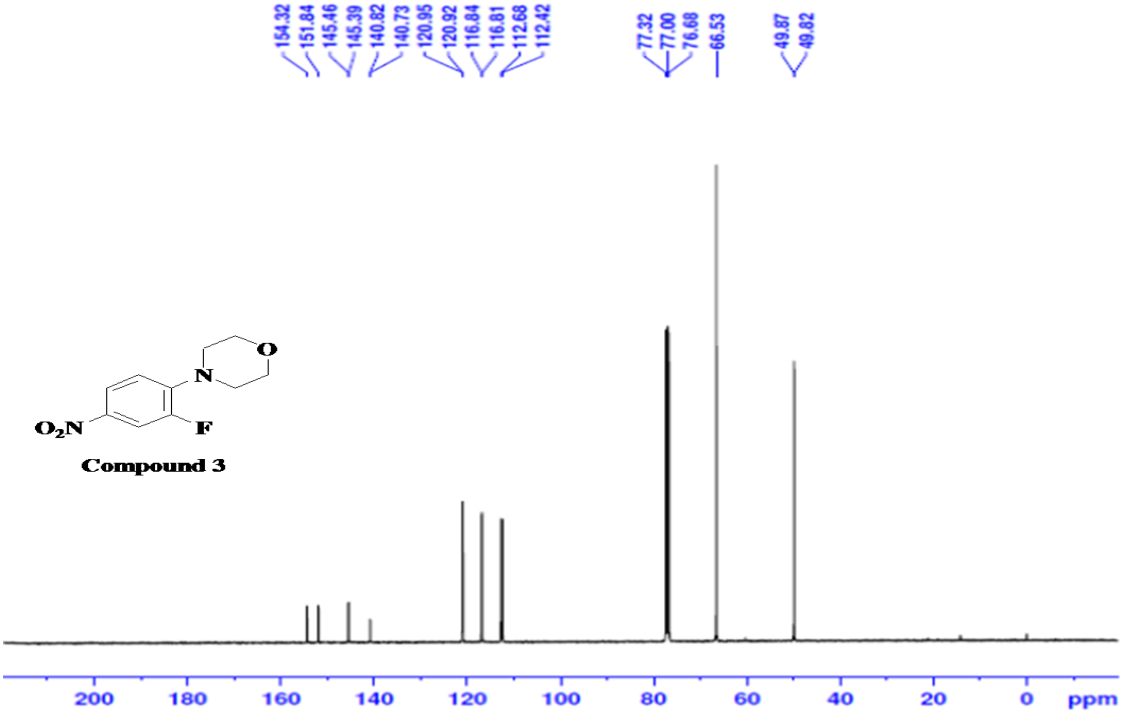


Figure 2.^{13}C NMR Spectra of Compound 3

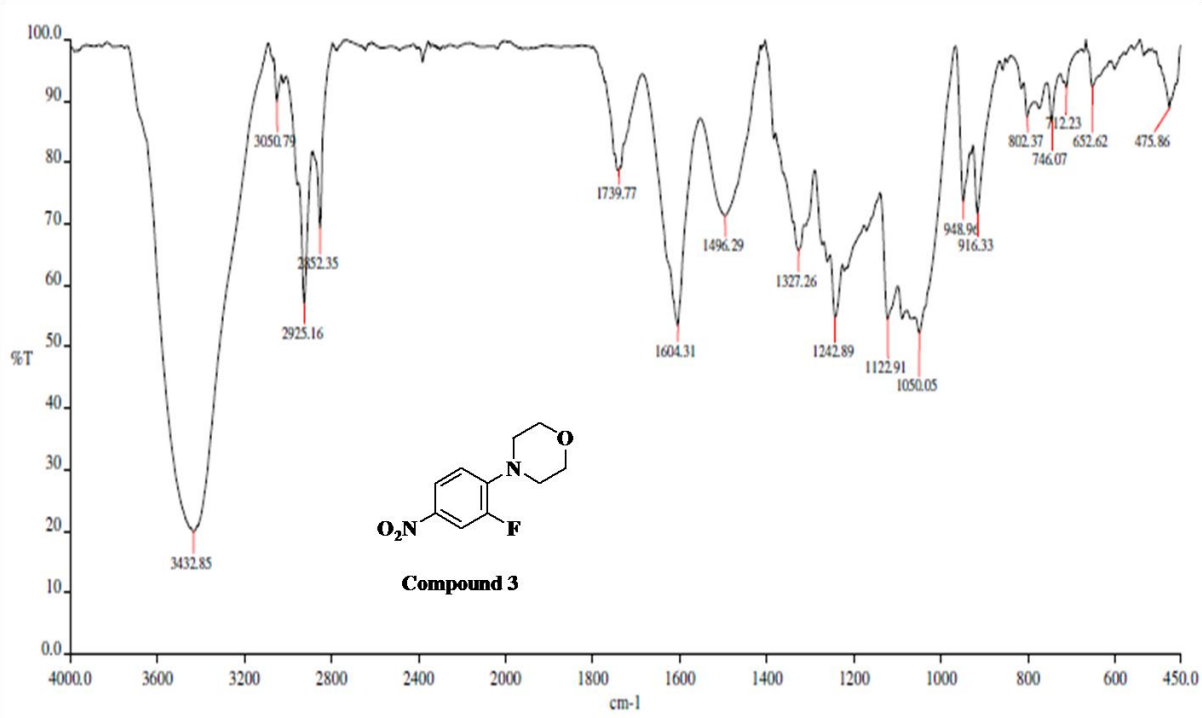
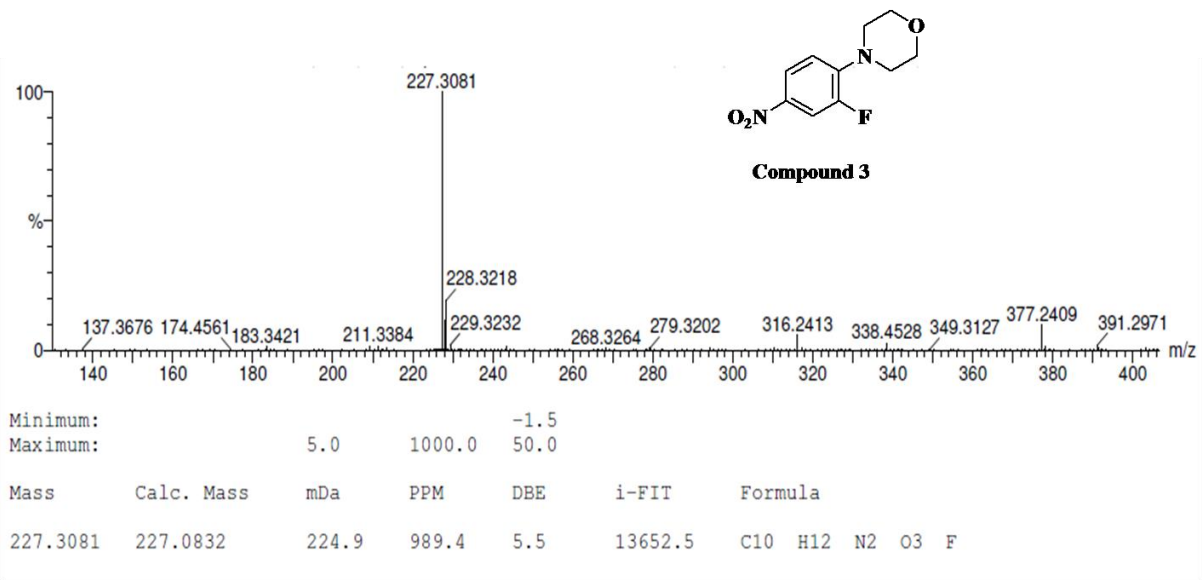


Figure 3. FT-IR Spectra of Compound 3



Minimum:				-1.5		
Maximum:		5.0	1000.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
227.3081	227.0832	224.9	989.4	5.5	13652.5	C10 H12 N2 O3 F

Figure.4. HRMS Spectra of Compound 3

Analytical data of Compound 4

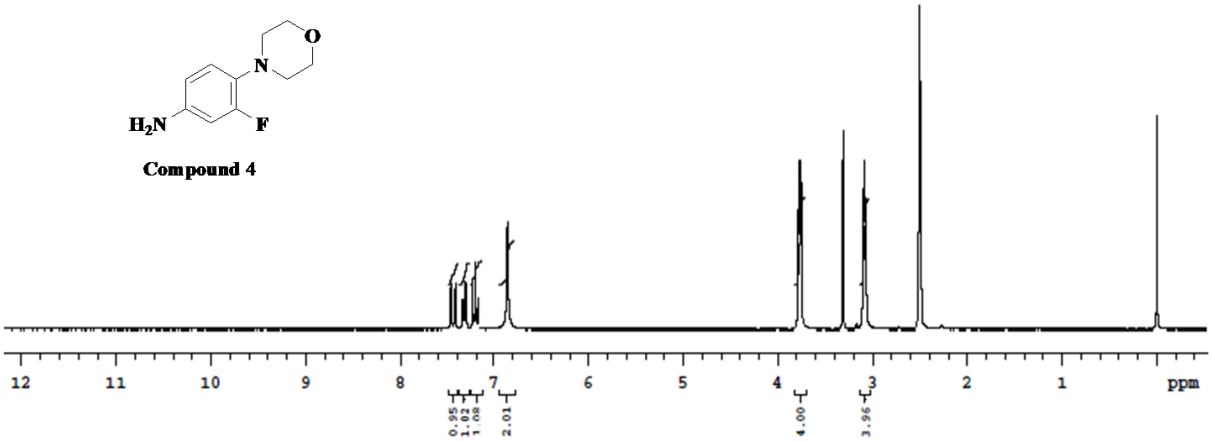


Figure 5. ^{1}H NMR Spectra of Compound 4

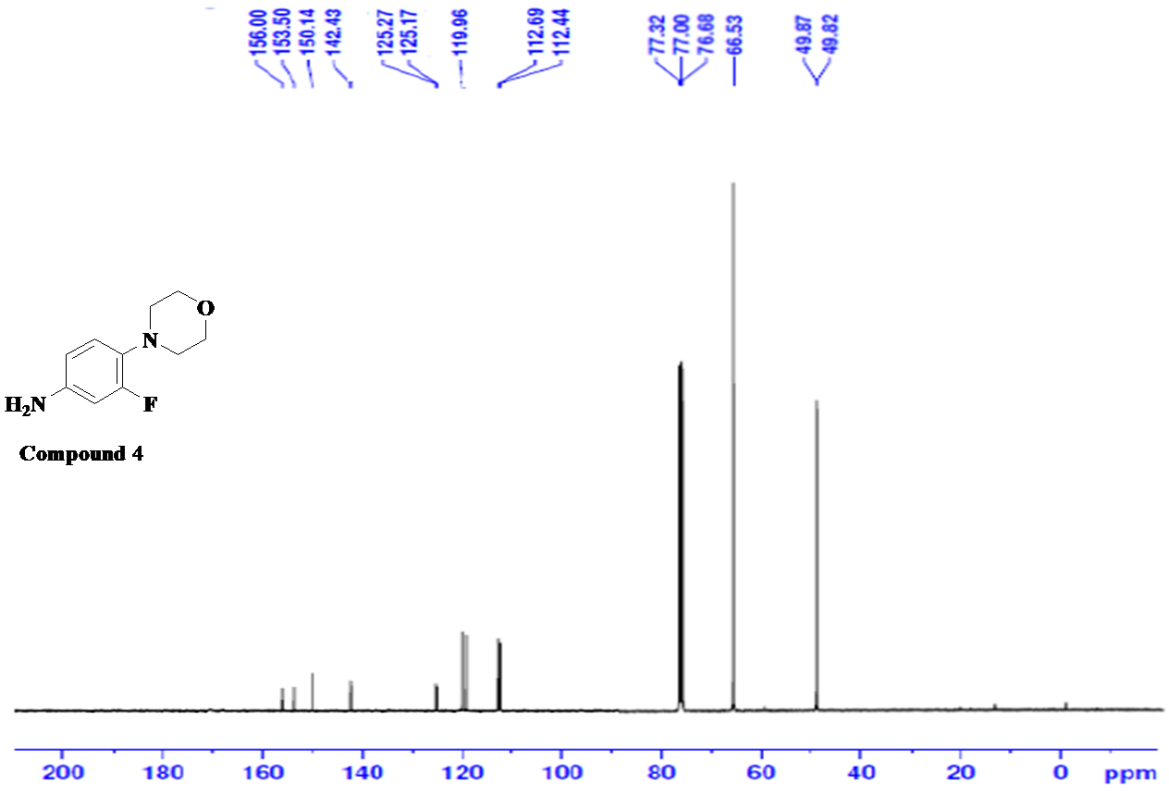


Figure 6.^{13}C NMR Spectra of Compound 4

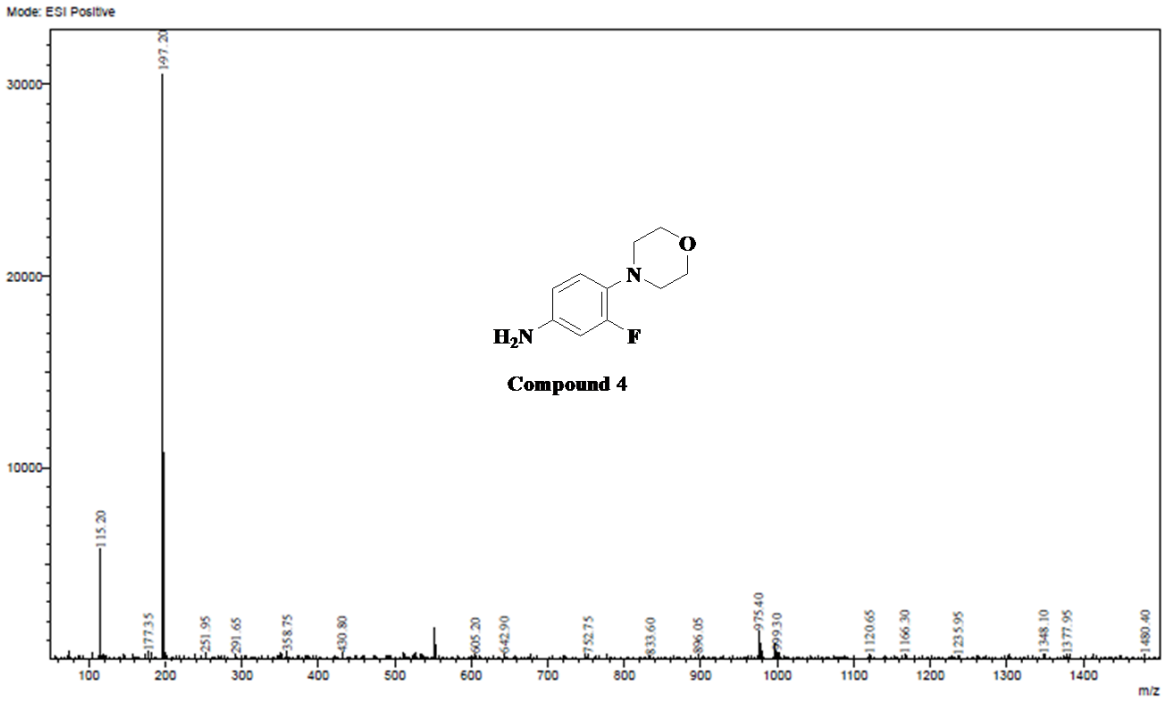


Figure 7. ESI-MS Spectra of Compound 4

Analytical data of Compound 5

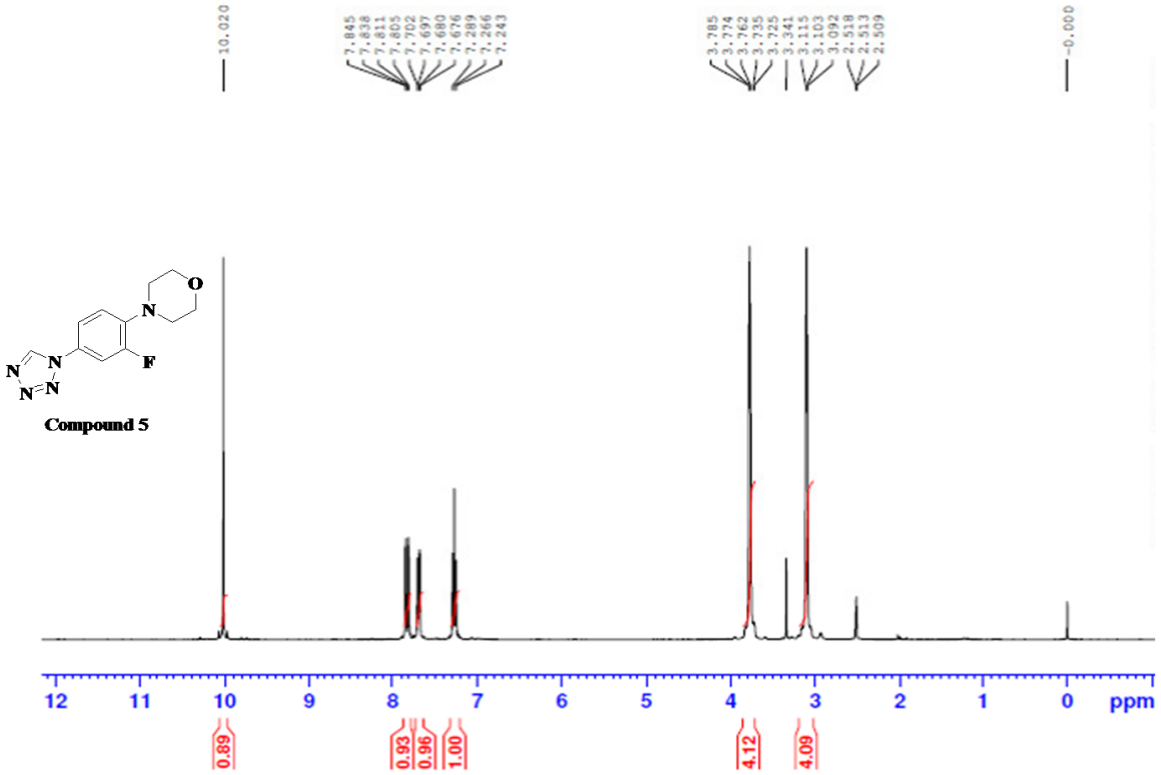


Figure 8.^{1}H NMR Spectra of Compound 5

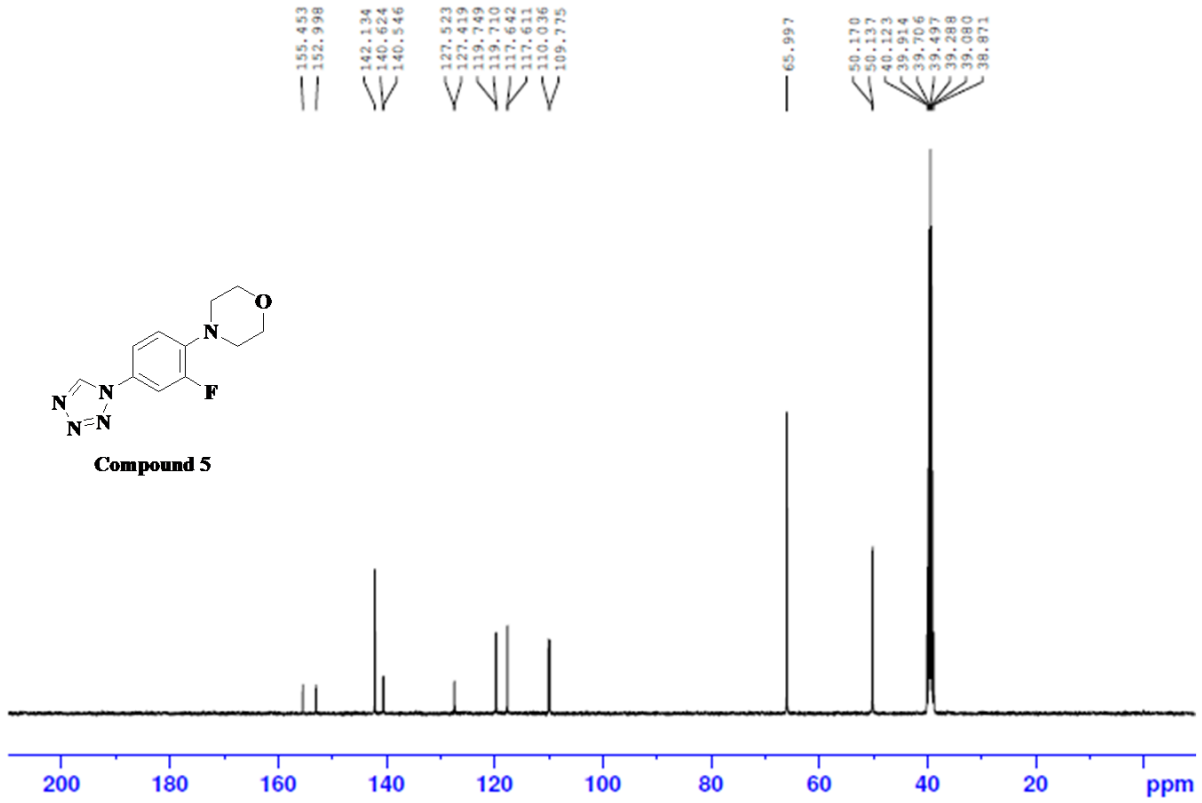
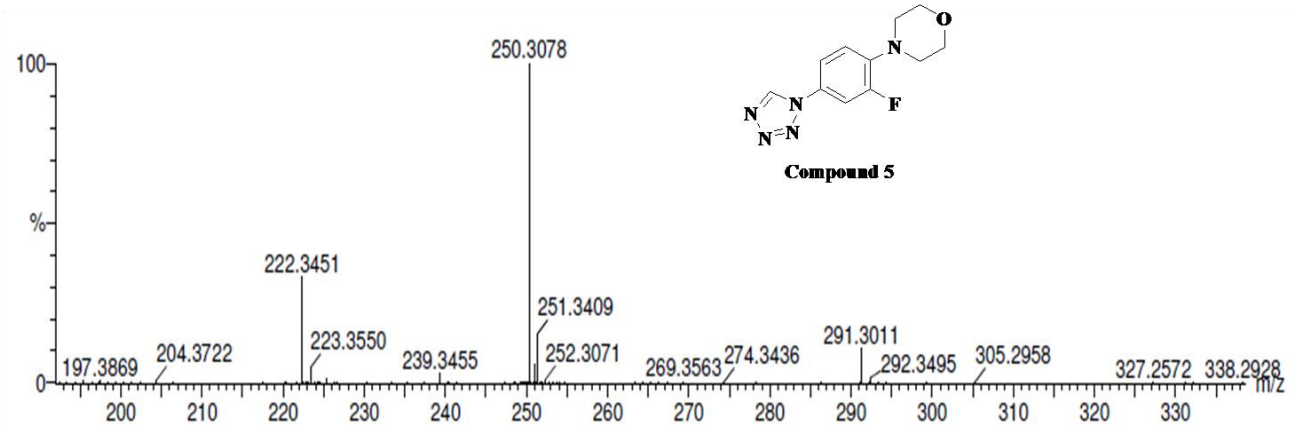


Figure 9.^{13}C NMR Spectra of Compound 5



Minimum:				-1.5		
Maximum:		5.0	1000.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
250.3078	250.1104	197.4	788.6	7.5	8708.5	C11 H13 N5 O F

Figure 10. HRMS Spectra of Compound 5

Analytical data of Compound 6

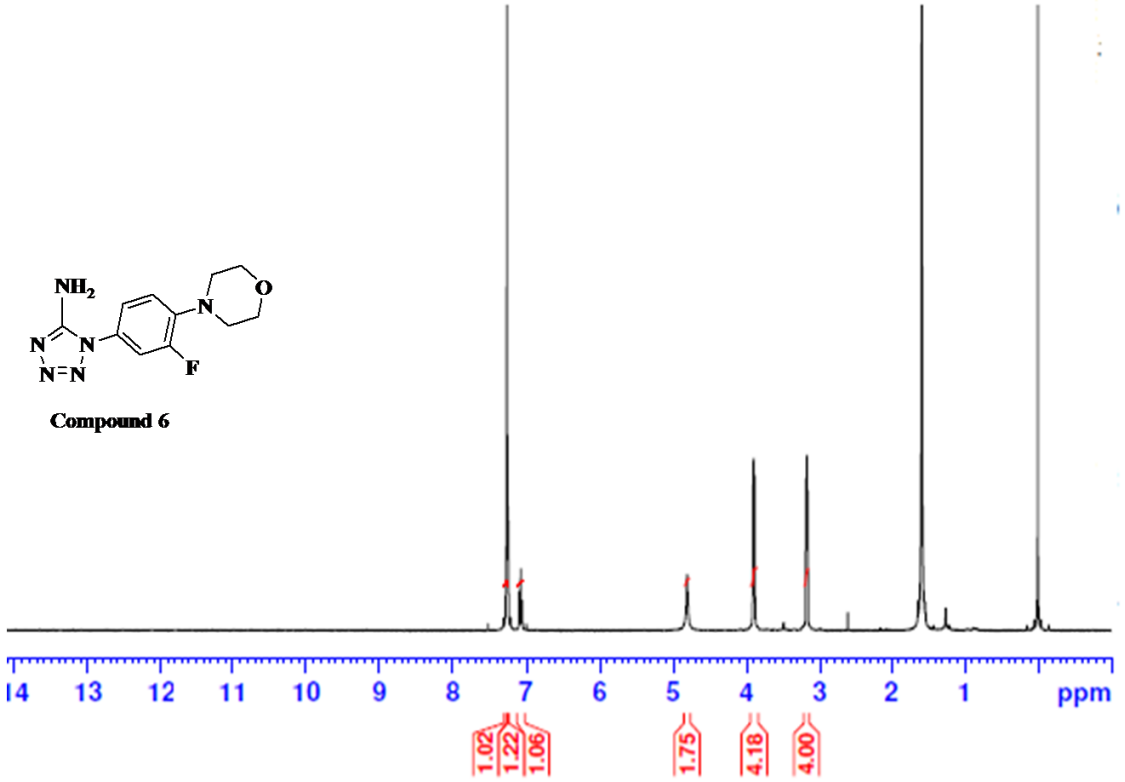


Figure 11.^{1}H NMR Spectra of Compound 6

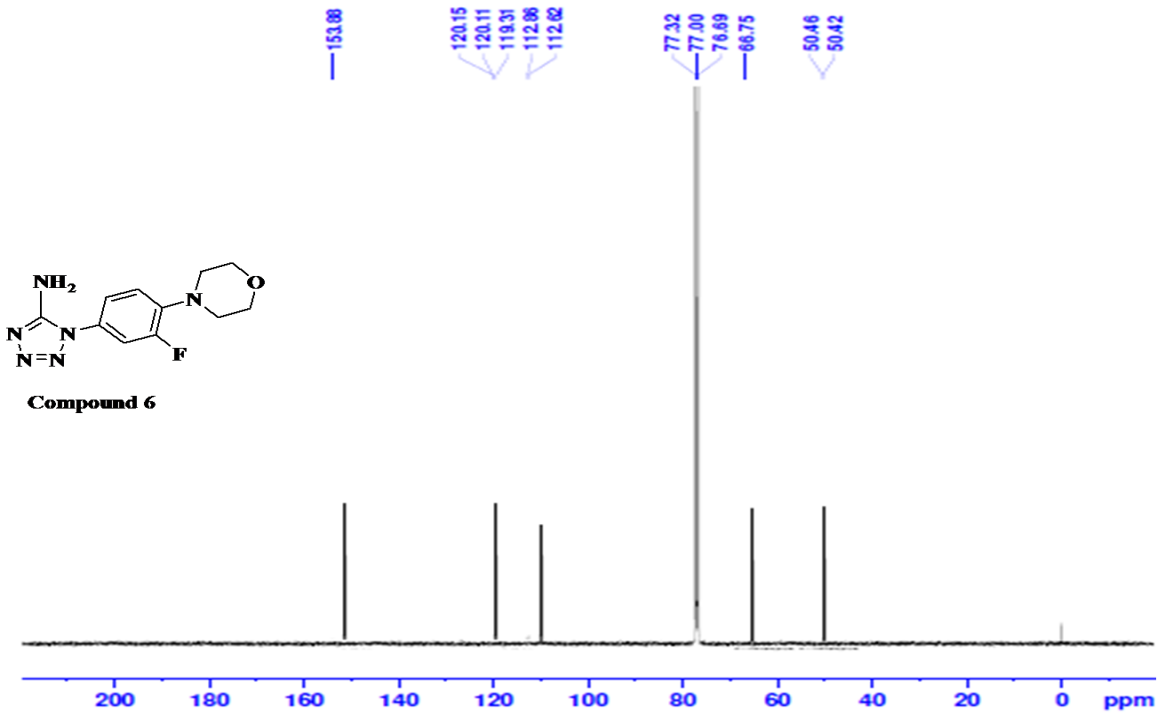


Figure 12.^{13}C NMR Spectra of Compound 6

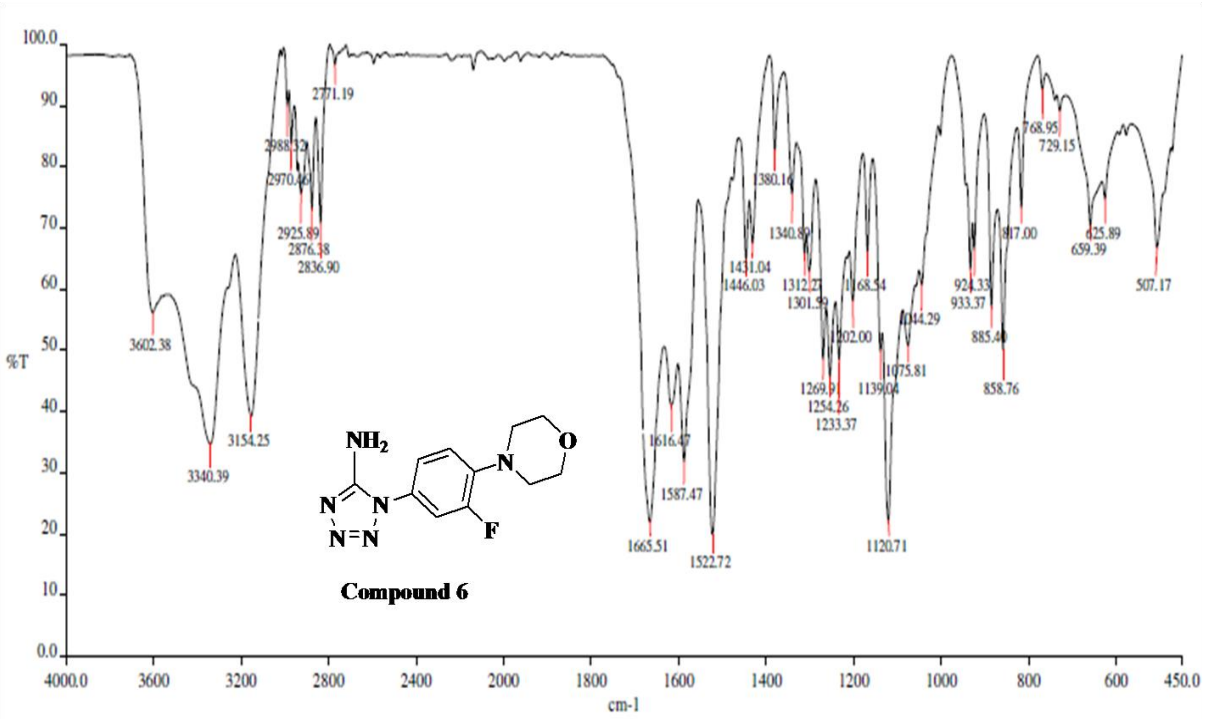
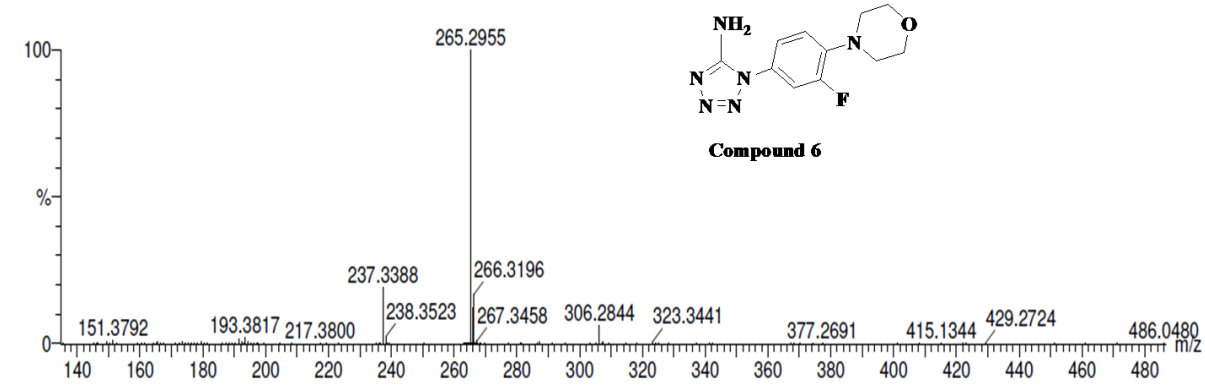


Figure 13. FT-IR Spectra of Compound 6



Minimum: -1.5
Maximum: 5.0 1000.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
265.2955	265.1213	174.2	656.6	7.5	8295.3	C11 H14 N6 O F

Figure 14. HRMS Spectra of Compound 6

Analytical data of Compound 8a

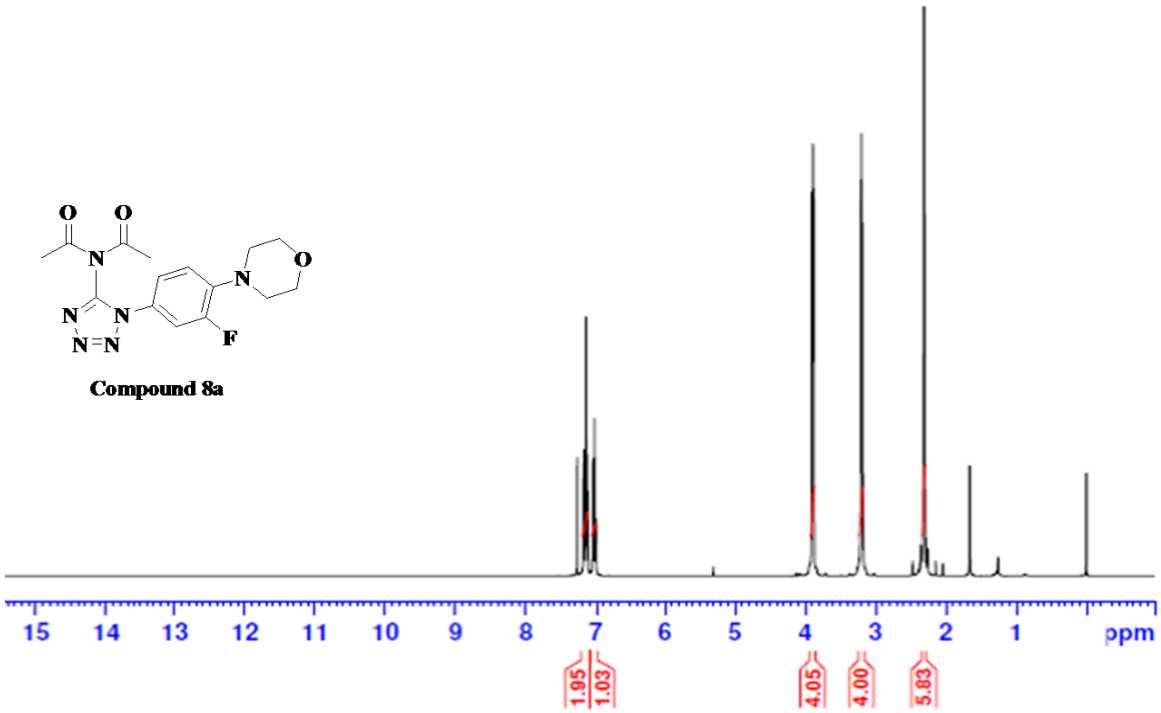


Figure 15.^{1}H NMR Spectra of Compound 8a

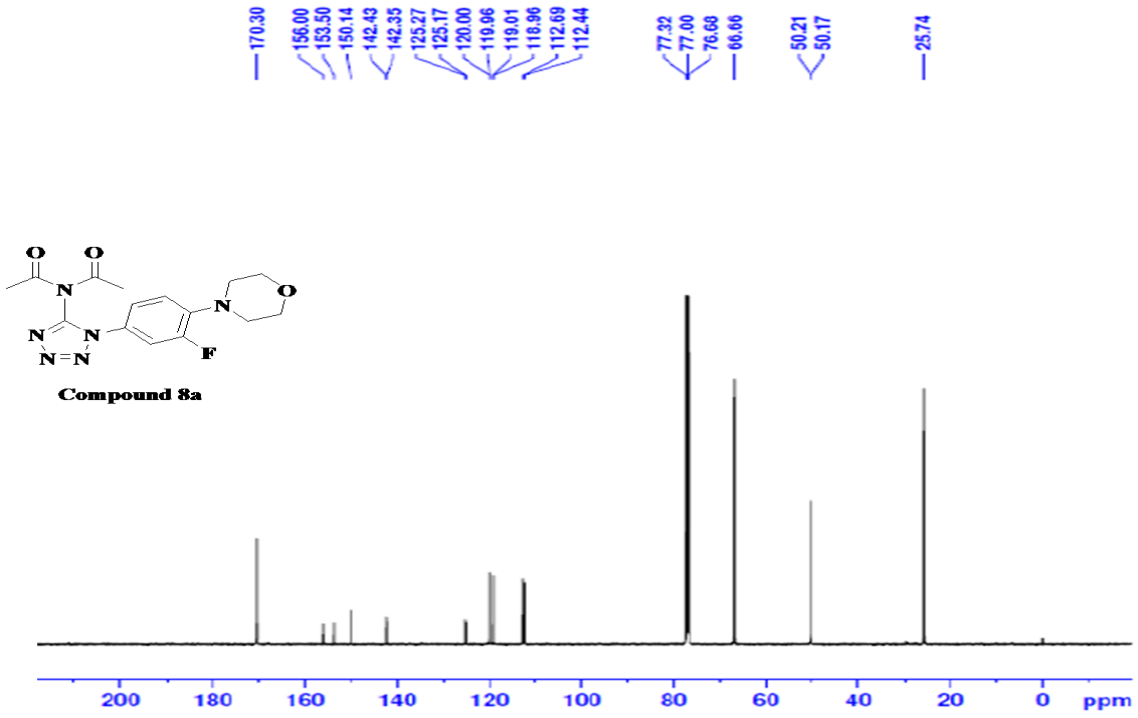


Figure 16.^{13}C NMR Spectra of Compound 8a

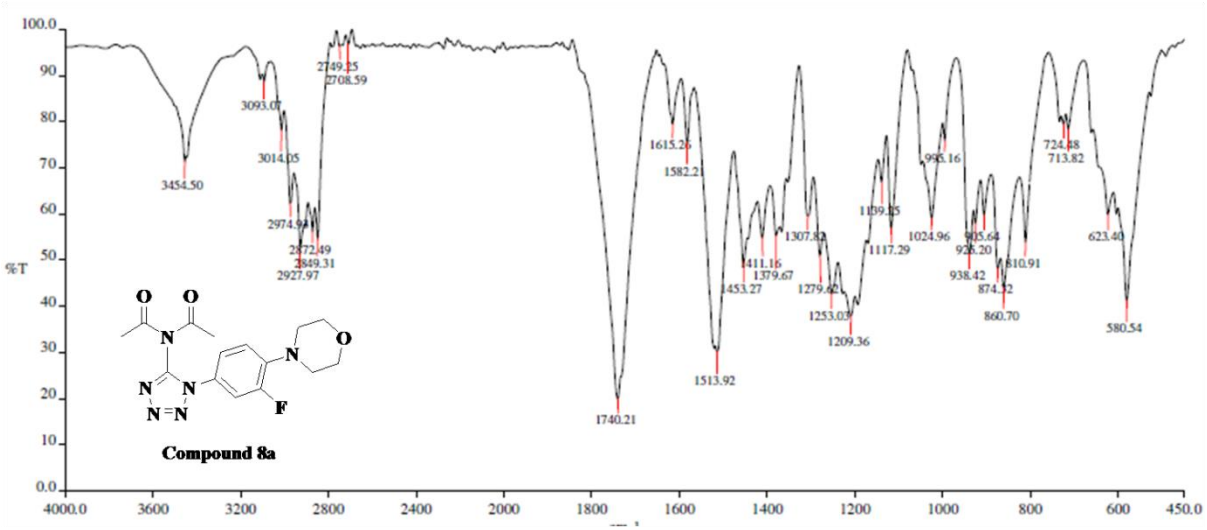
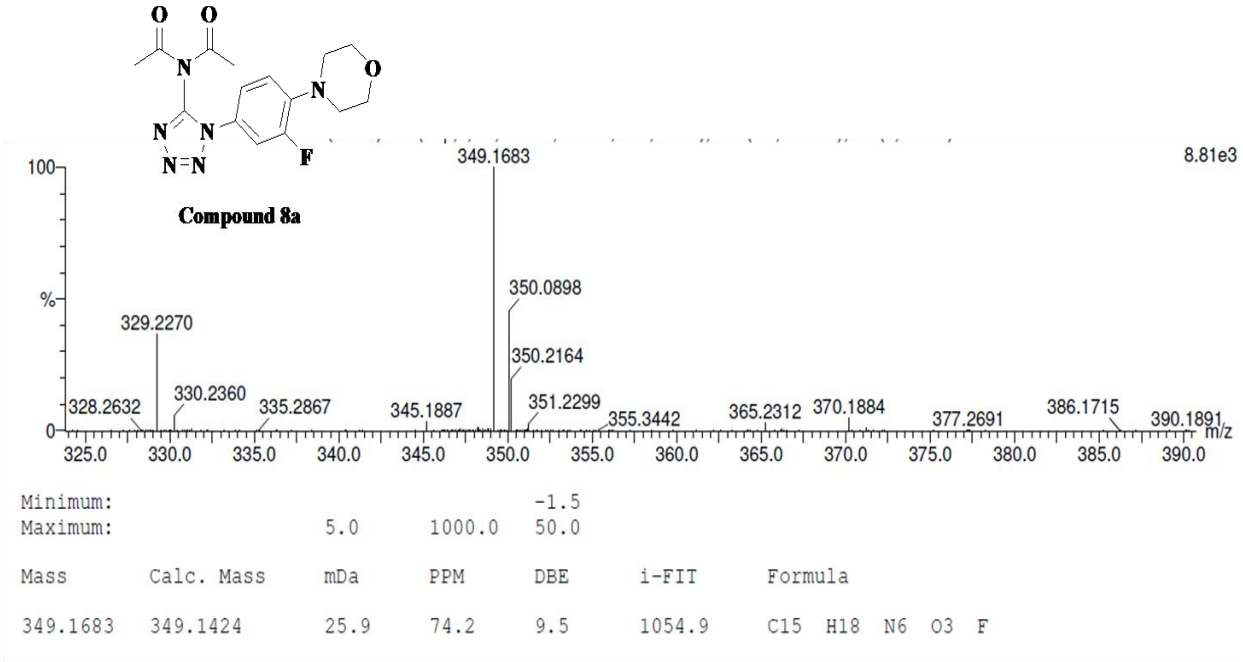


Figure 17. FT-IR Spectra of Compound 8a



Minimum:				-1.5		
Maximum:		5.0	1000.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
349.1683	349.1424	25.9	74.2	9.5	1054.9	C15 H18 N6 O3 F

Figure 18. HRMS Spectra of Compound 8a

Analytical data of Compound 8b

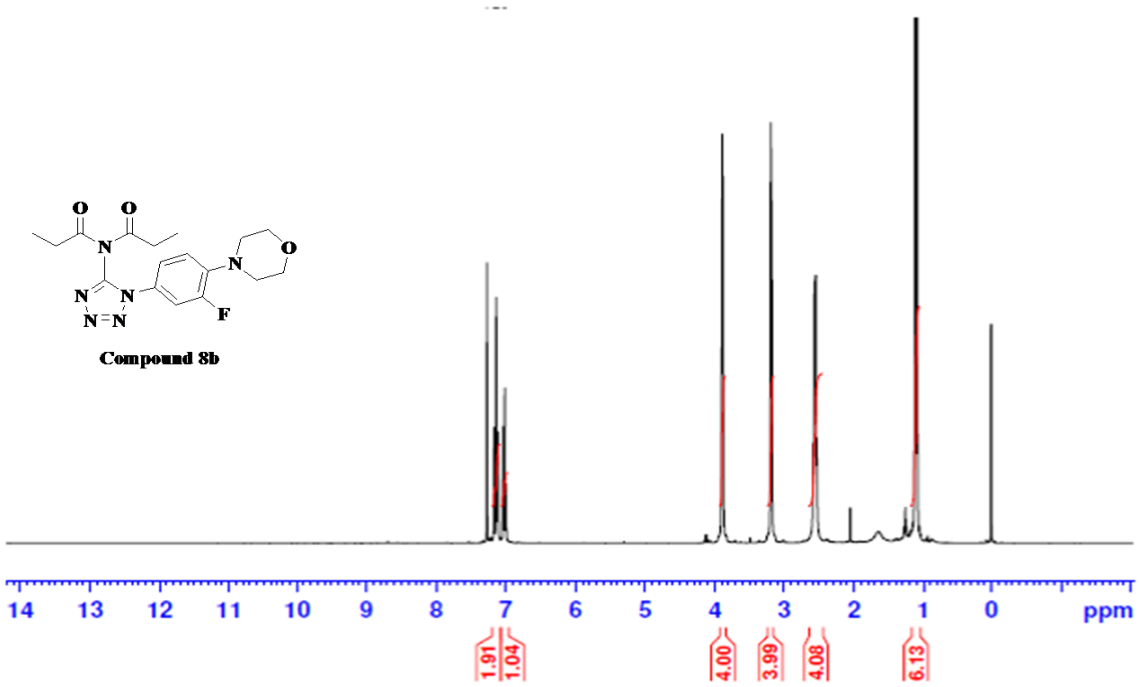


Figure 19.^{1}H NMR Spectra of Compound 8b

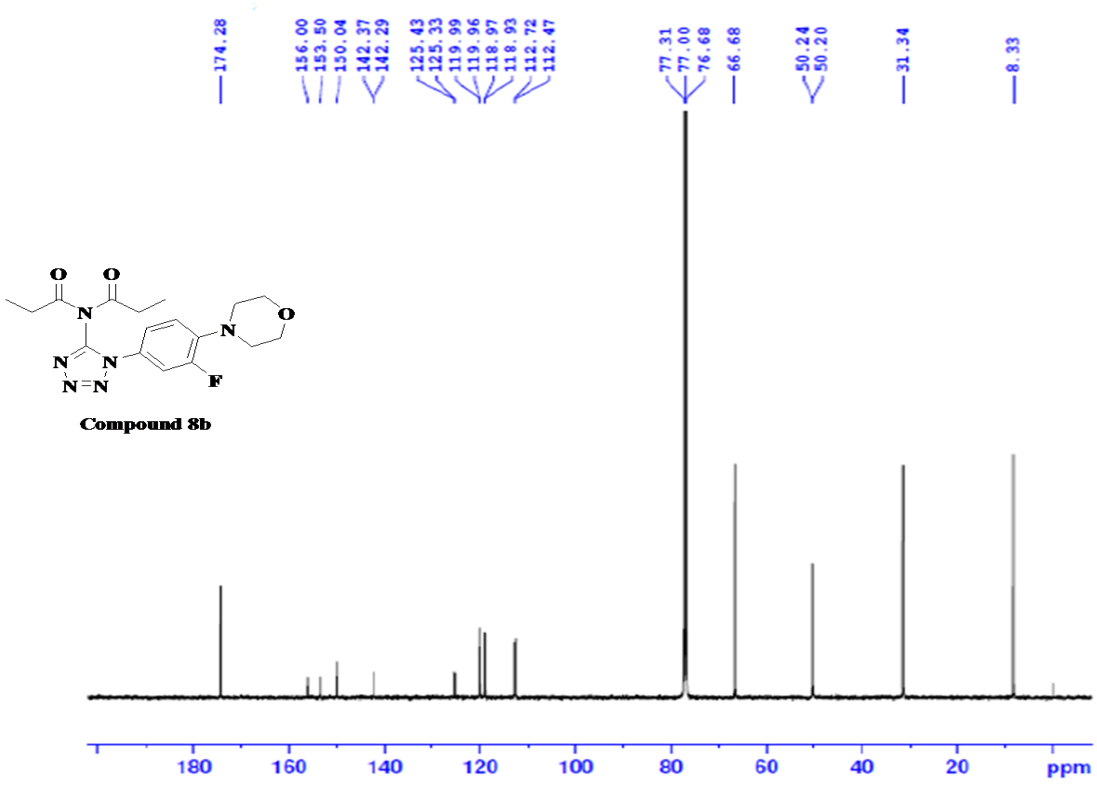


Figure 20.^{13}C NMR Spectra of Compound 8b

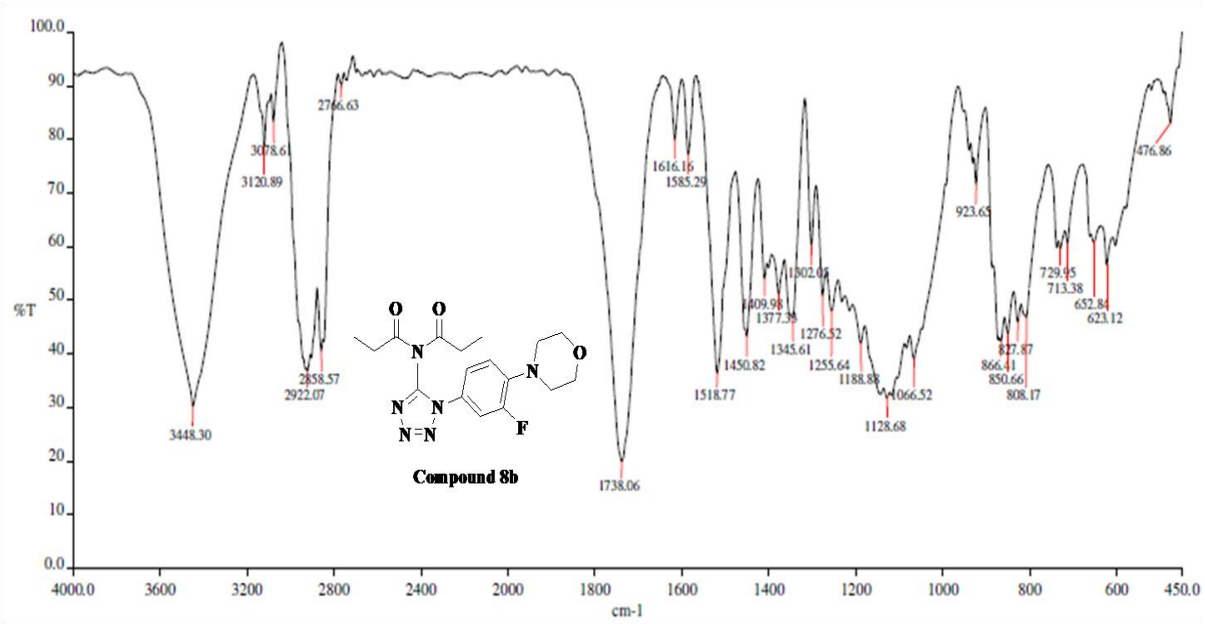
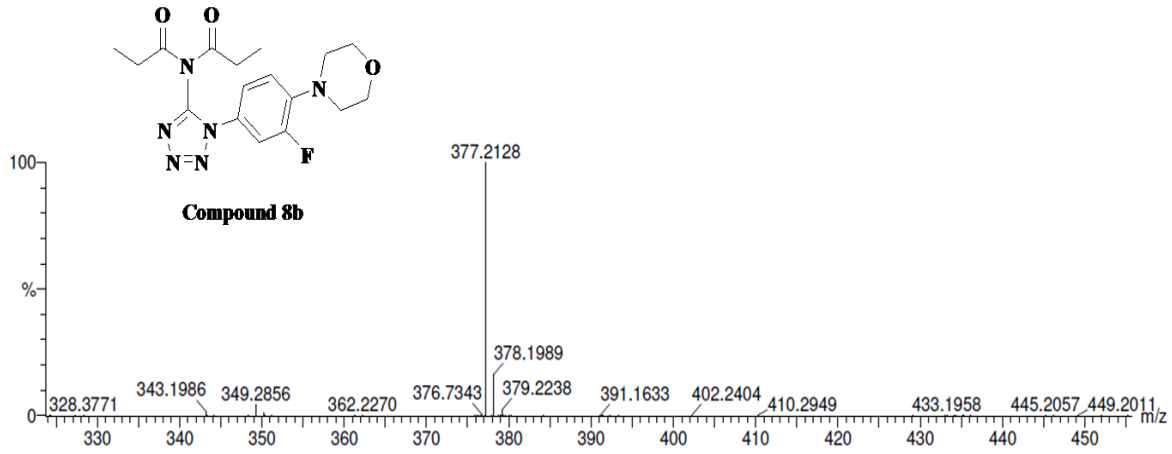


Figure 21. FT-IR Spectra of Compound 8b



Minimum:				-1.5		
Maximum:		5.0	1000.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
377.2128	377.1737	39.1	103.7	9.5	78.6	C17 H22 N6 O3 F

Figure 22. HRMS Spectra of Compound 8b

Analytical data of Compound 8c

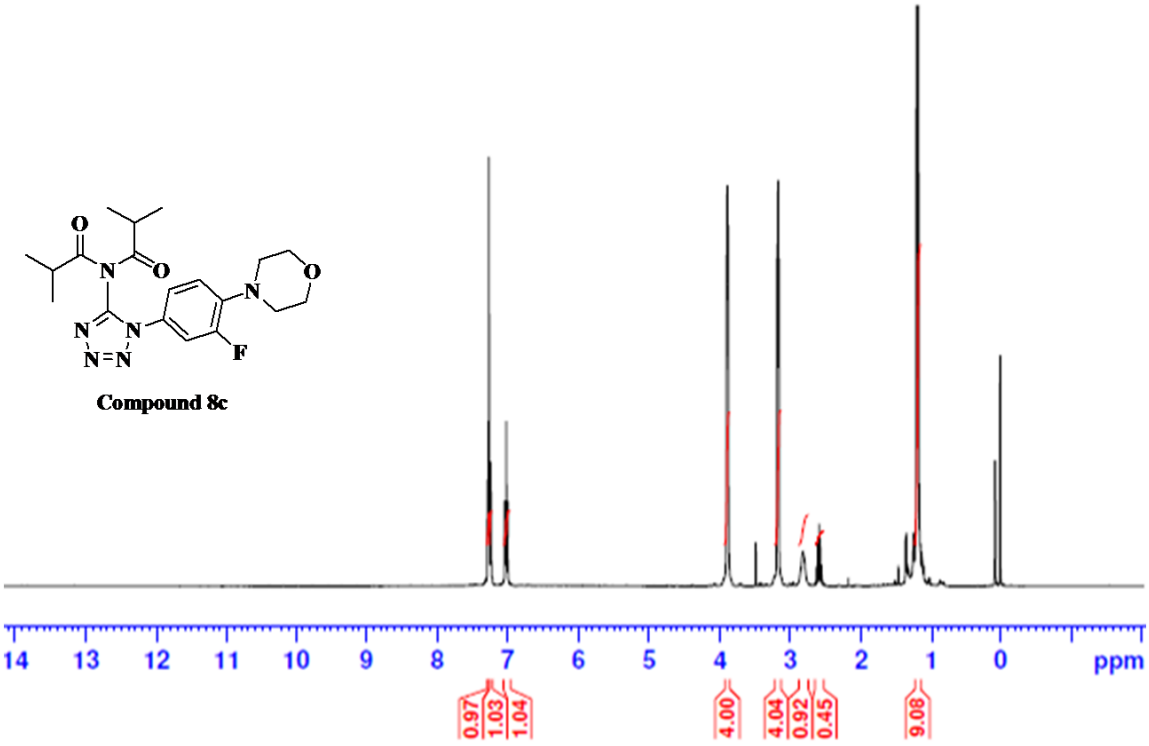


Figure 23.^{1}H NMR Spectra of Compound 8c

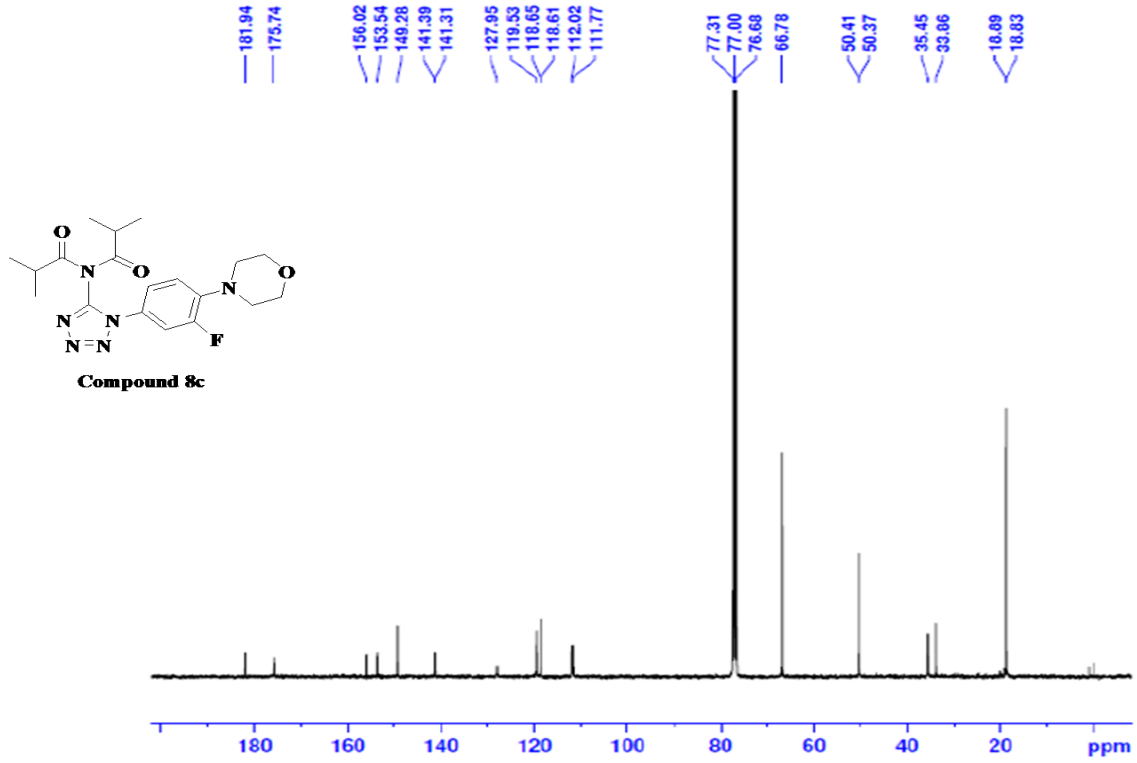


Figure 24.^{13}C NMR Spectra of Compound 8c

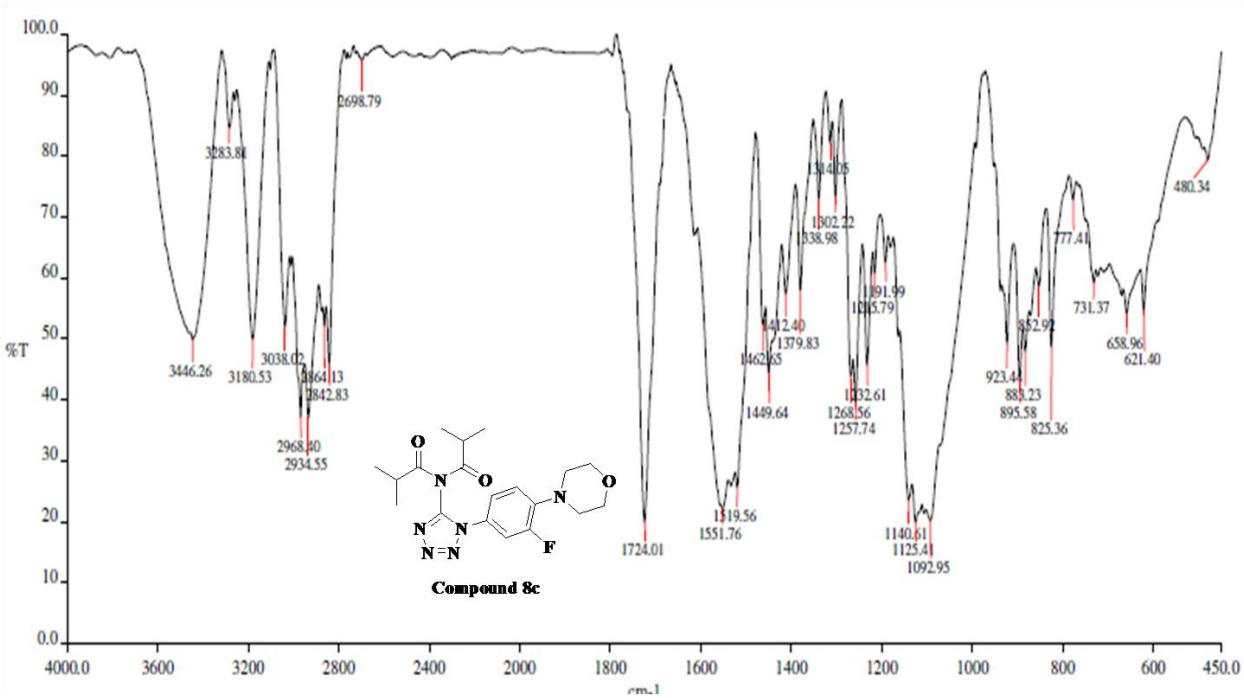


Figure 25. FT-IR Spectra of Compound 8c

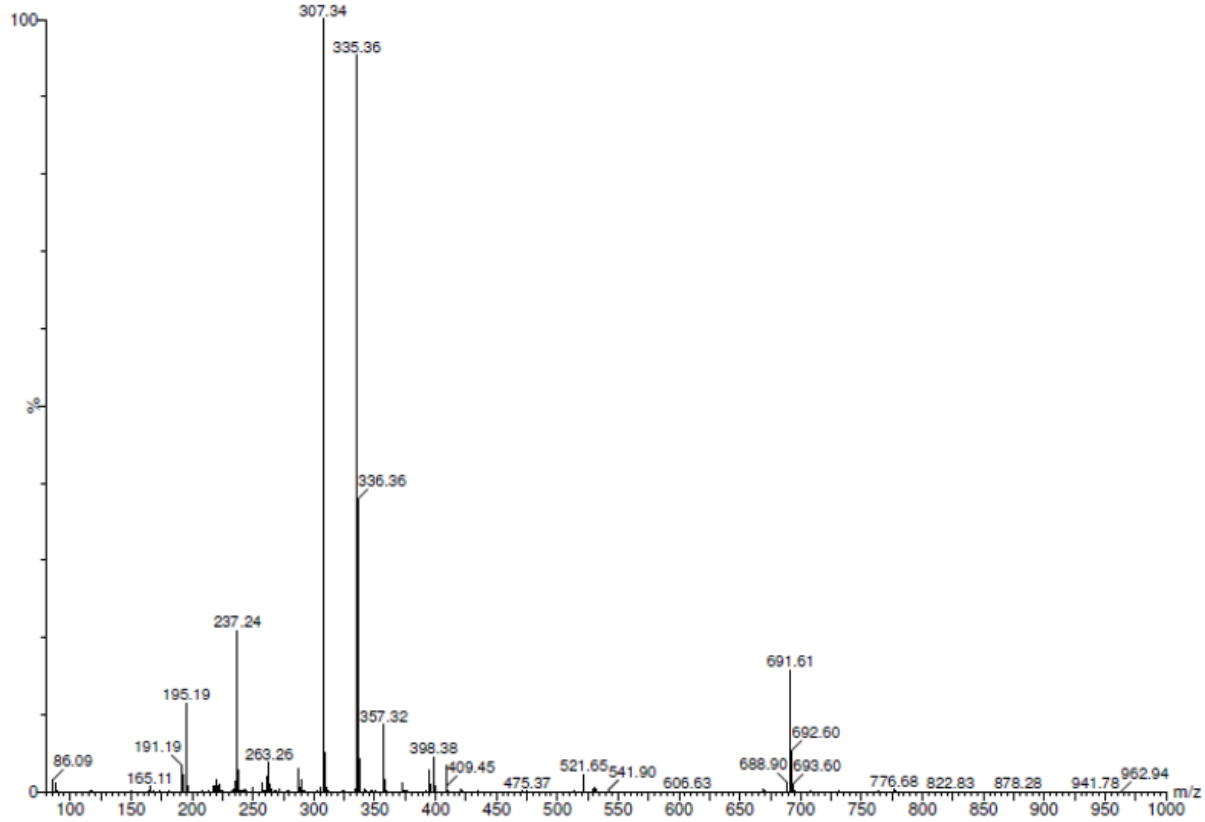


Figure 26. ESI-MS Spectra of Compound 8c

Analytical data of Compound 8d

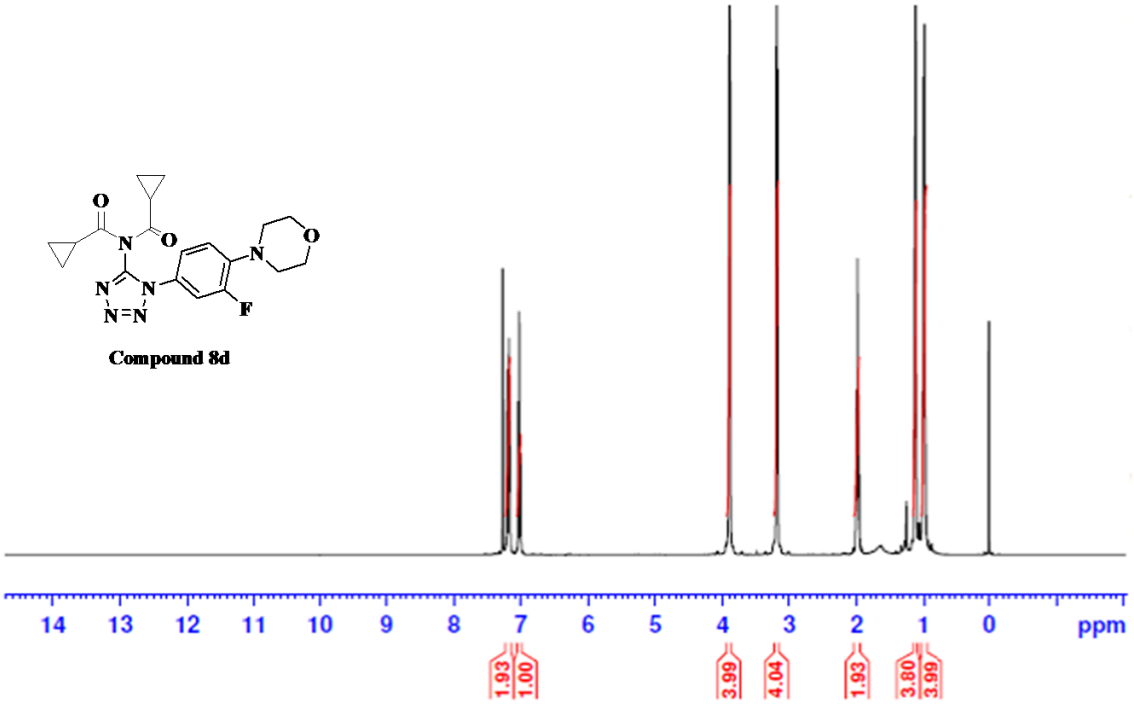


Figure 27.^{1}H NMR Spectra of Compound 8d

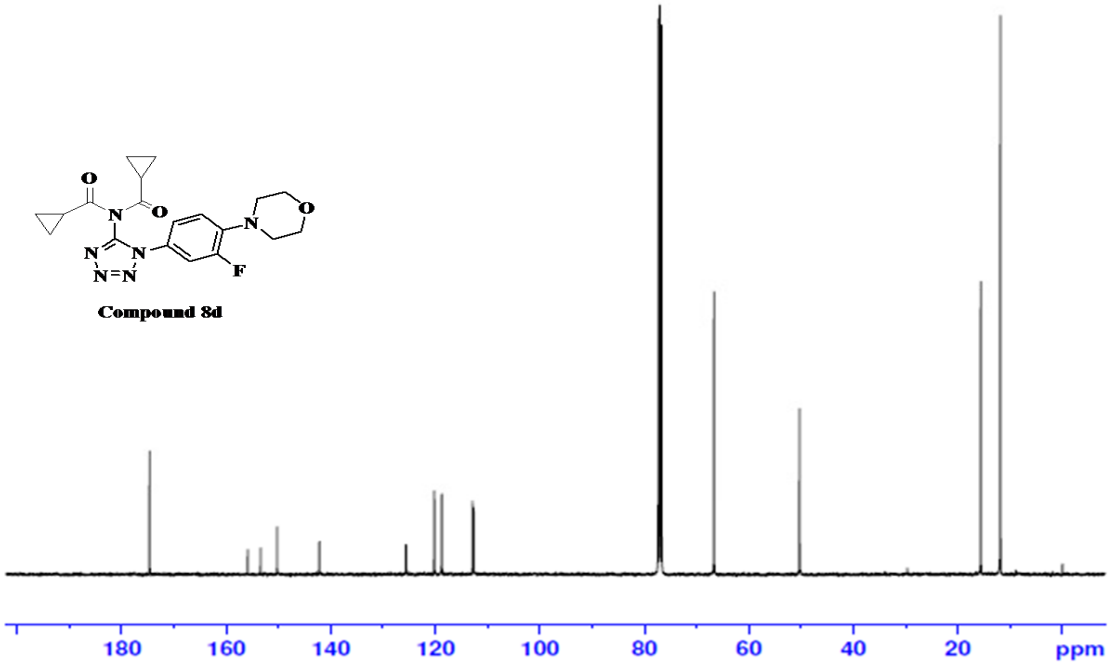


Figure 28.^{13}C NMR Spectra of Compound 8d

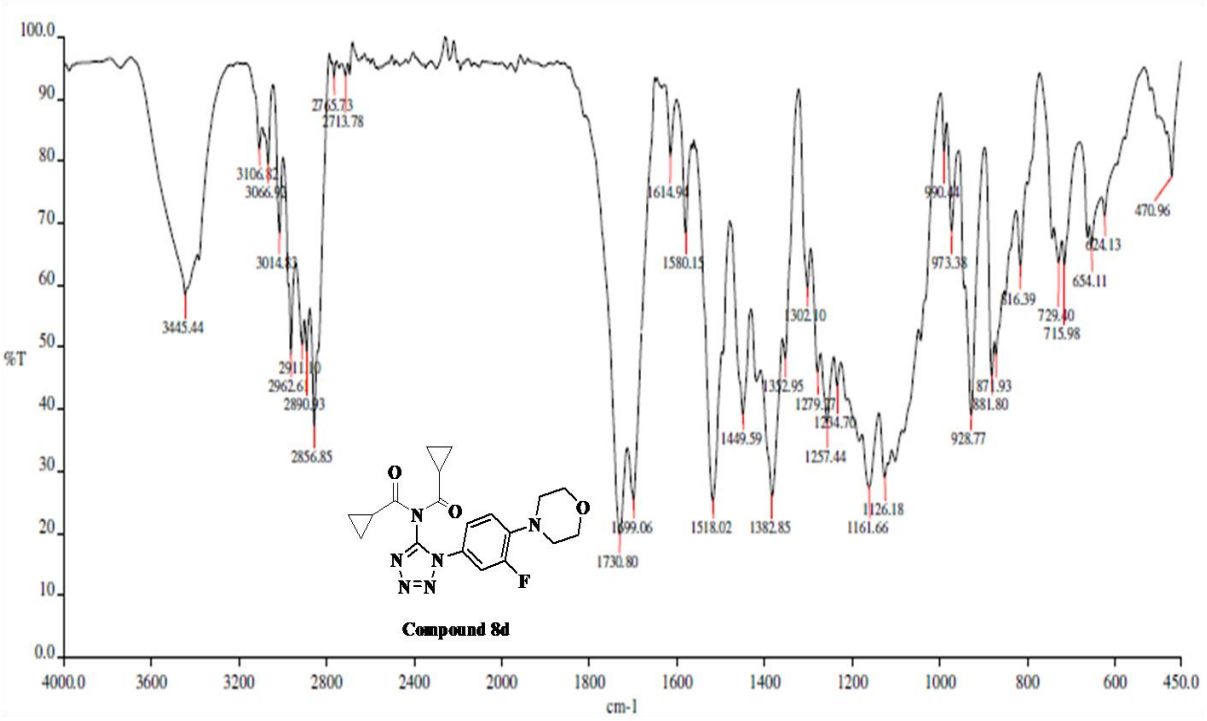
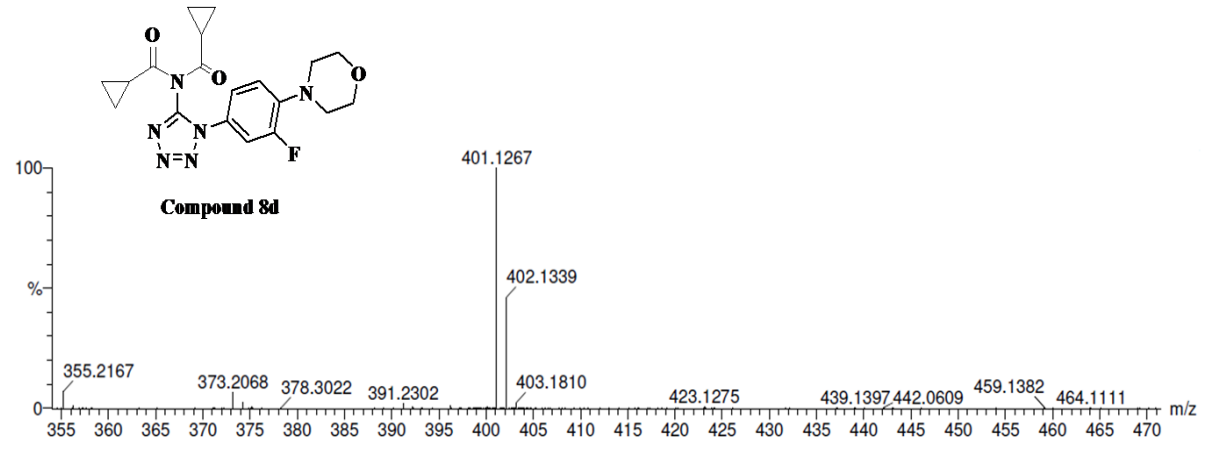


Figure 29. FT-IR Spectra of Compound 8d



Minimum:				-1.5		
Maximum:		5.0	1000.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
401.1267	401.1737	-47.0	-117.2	11.5	753.8	C19 H22 N6 O3 F

Figure 30. HRMS Spectra of Compound 8d

Analytical data of Compound 8e

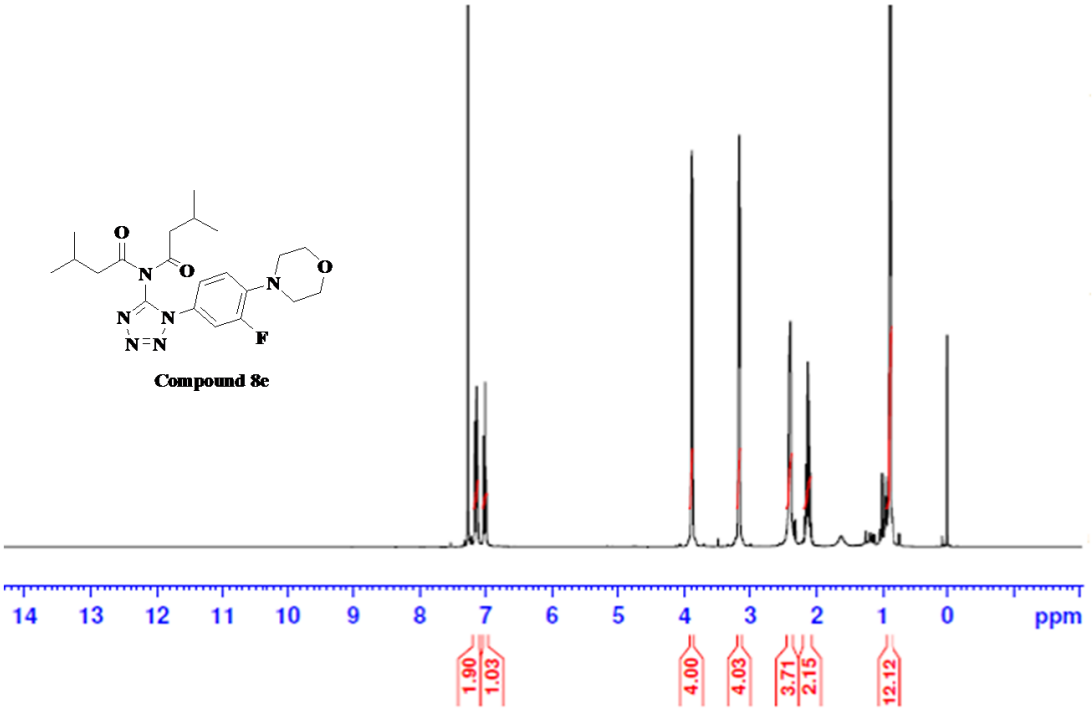


Figure 31.^{1}H NMR Spectra of Compound 8e

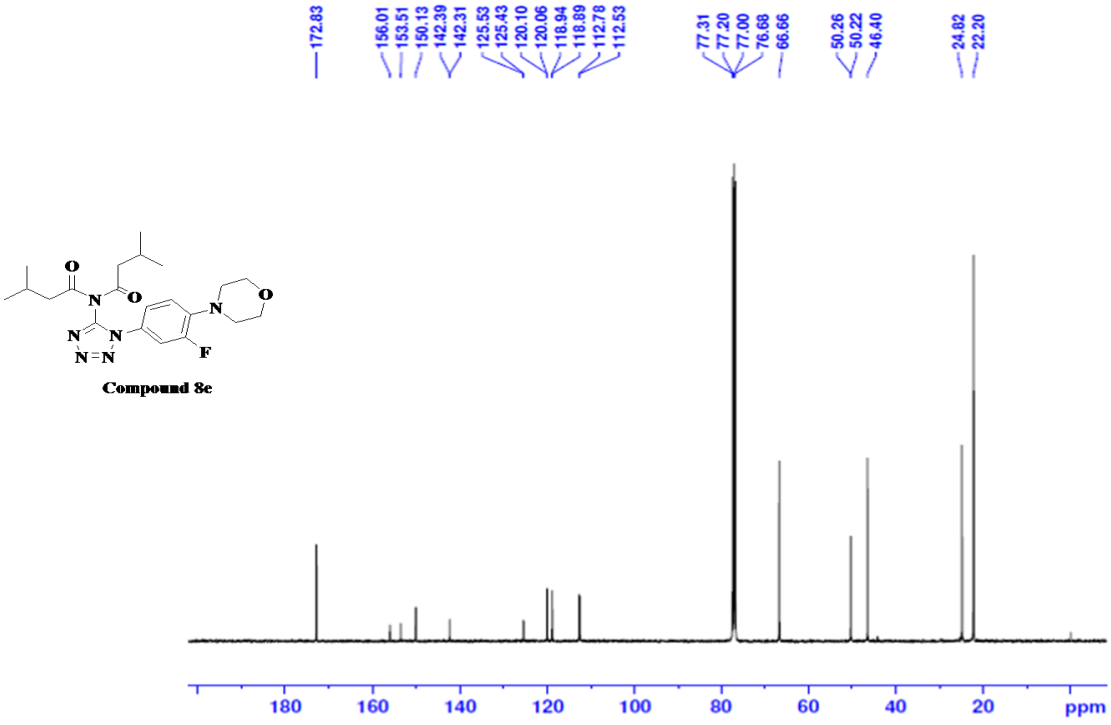


Figure 32.^{13}C NMR Spectra of Compound 8e

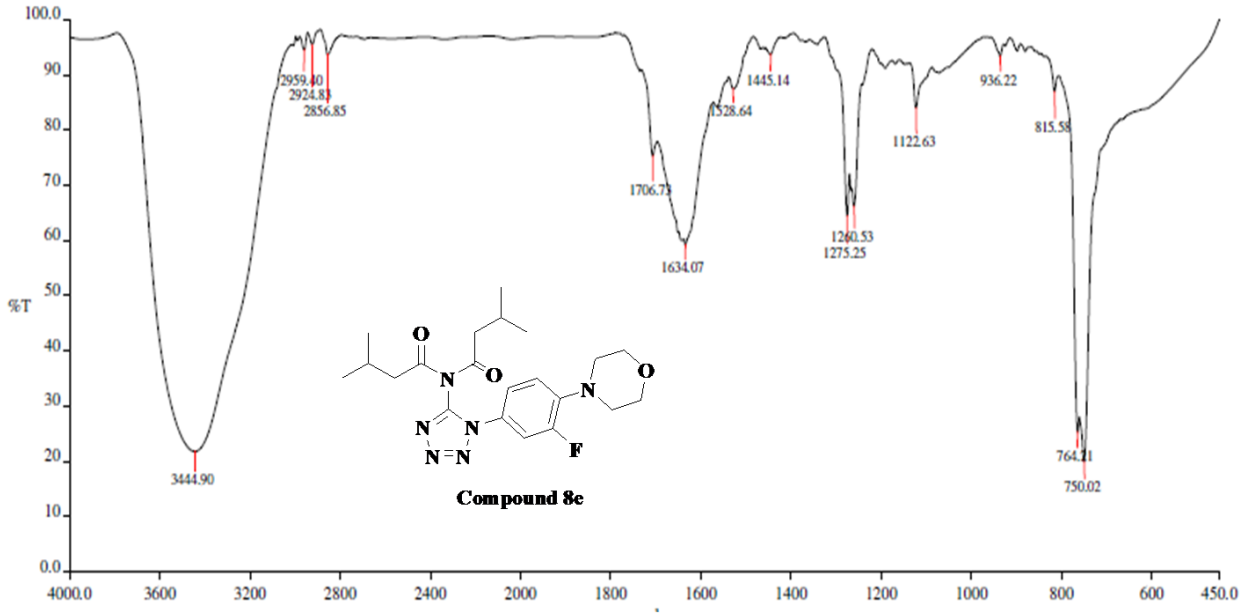


Figure 33. FT-IR Spectra of Compound 8e

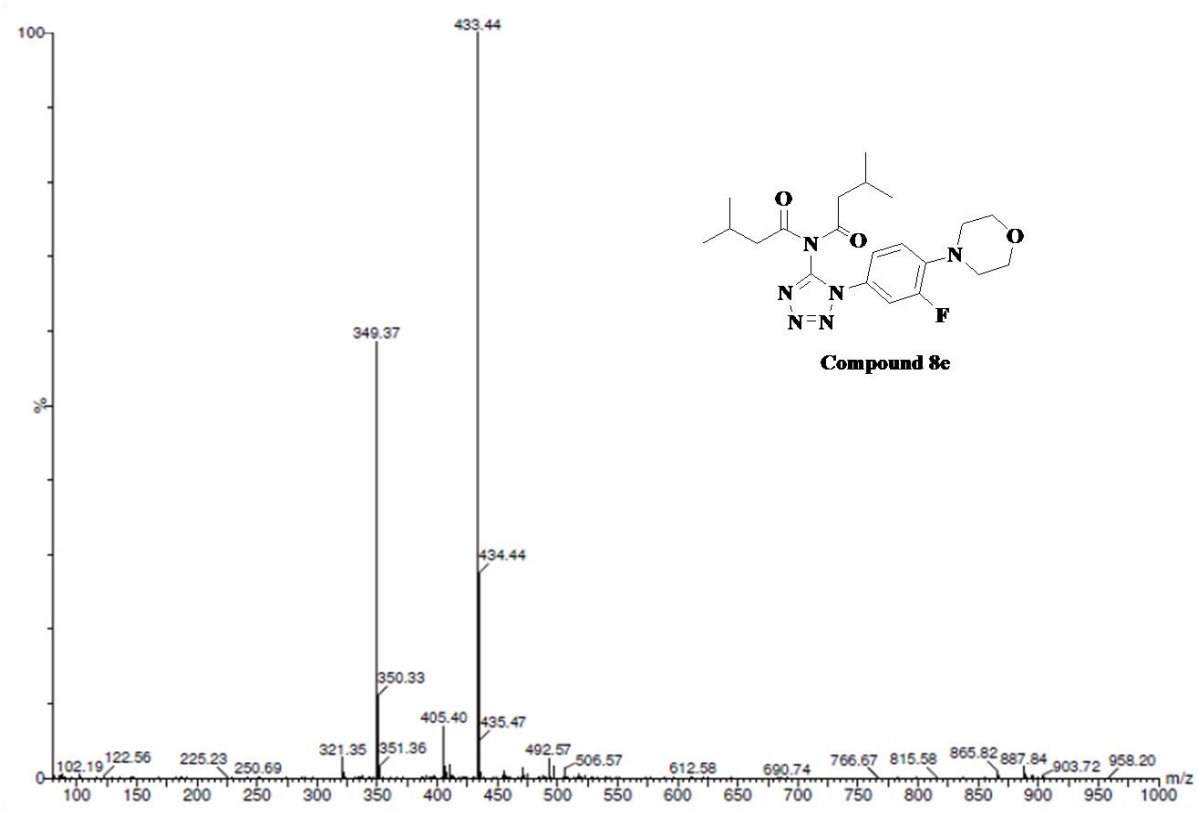


Figure 34. ESI-MS Spectra of Compound 8e

Analytical data of Compound 8f

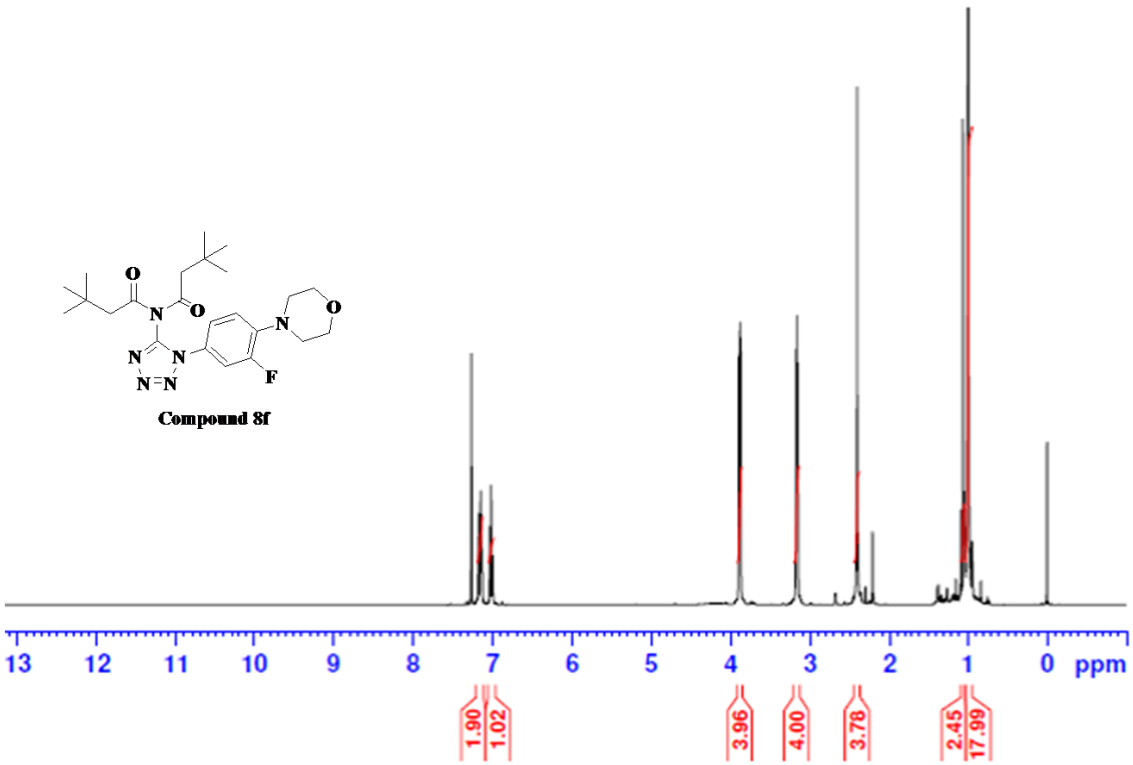


Figure 35.^{1}H NMR Spectra of Compound 8f

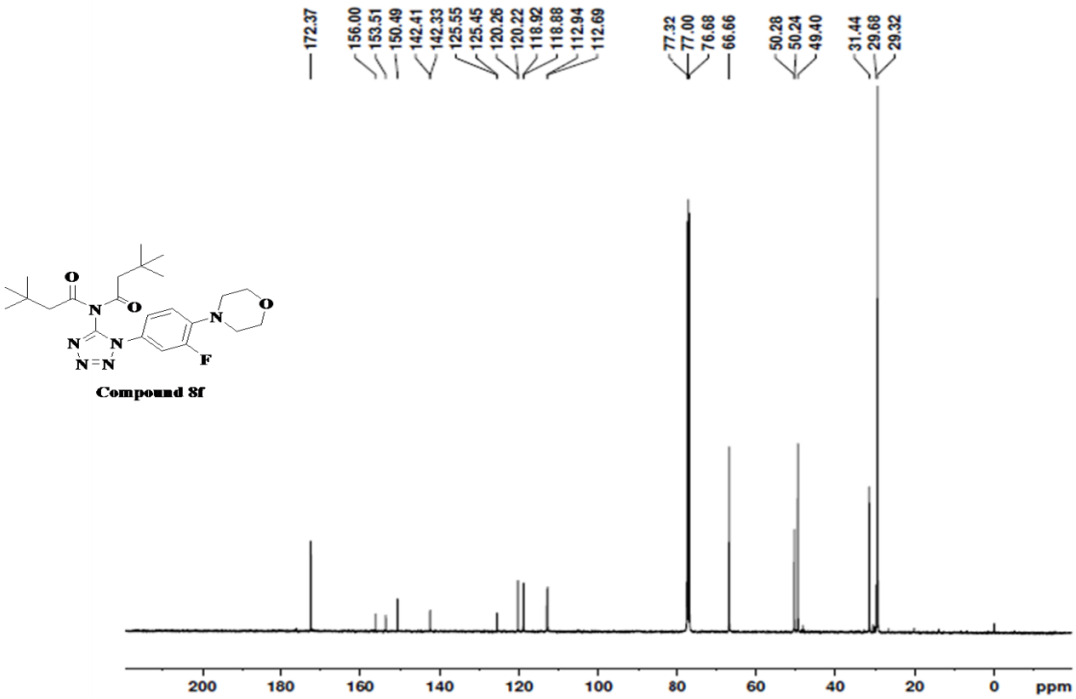


Figure 36.^{13}C NMR Spectra of Compound 8f

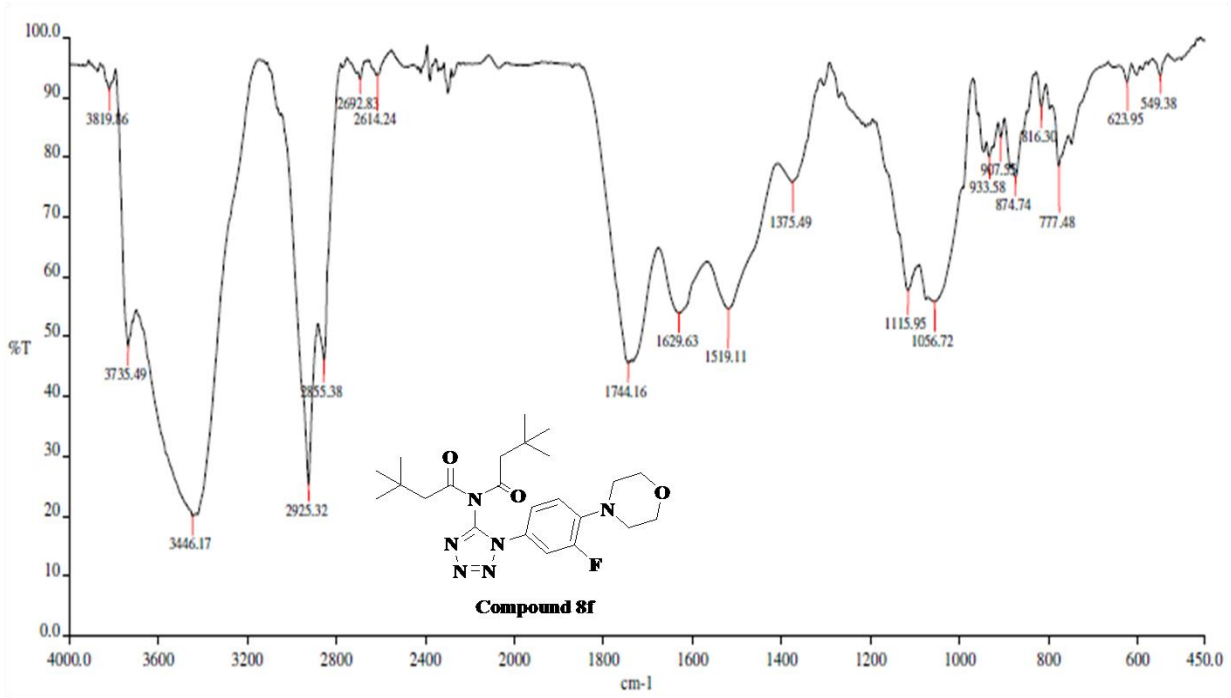
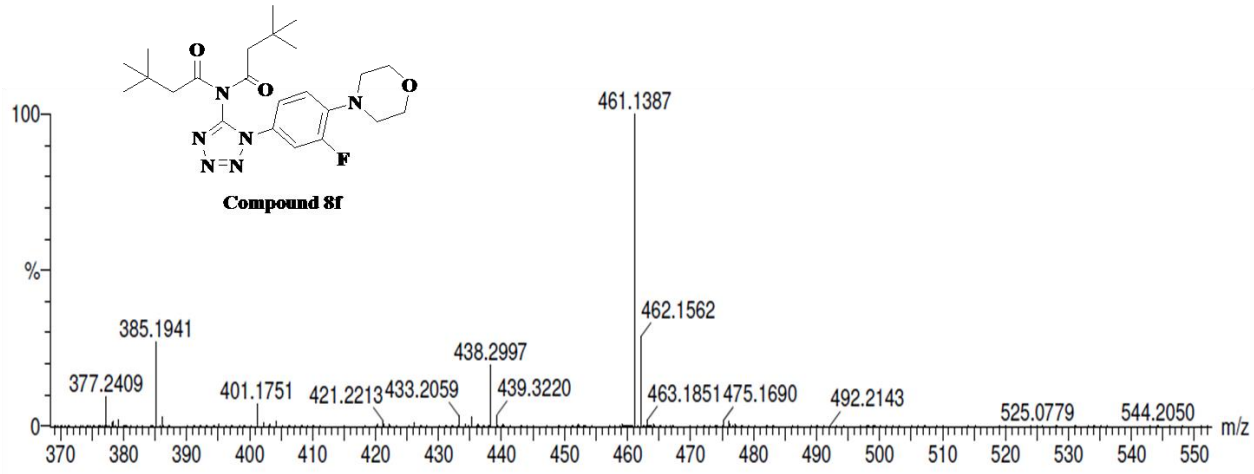


Figure 37. FT-IR Spectra of Compound 8f



Minimum:				-1.5		
Maximum:		5.0	1000.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
461.1387	461.2676	-128.9	-279.5	9.5	1418.2	C23 H34 N6 O3 F

Figure 38. HRMS Spectra of Compound 8f

Analytical data of Compound 8g

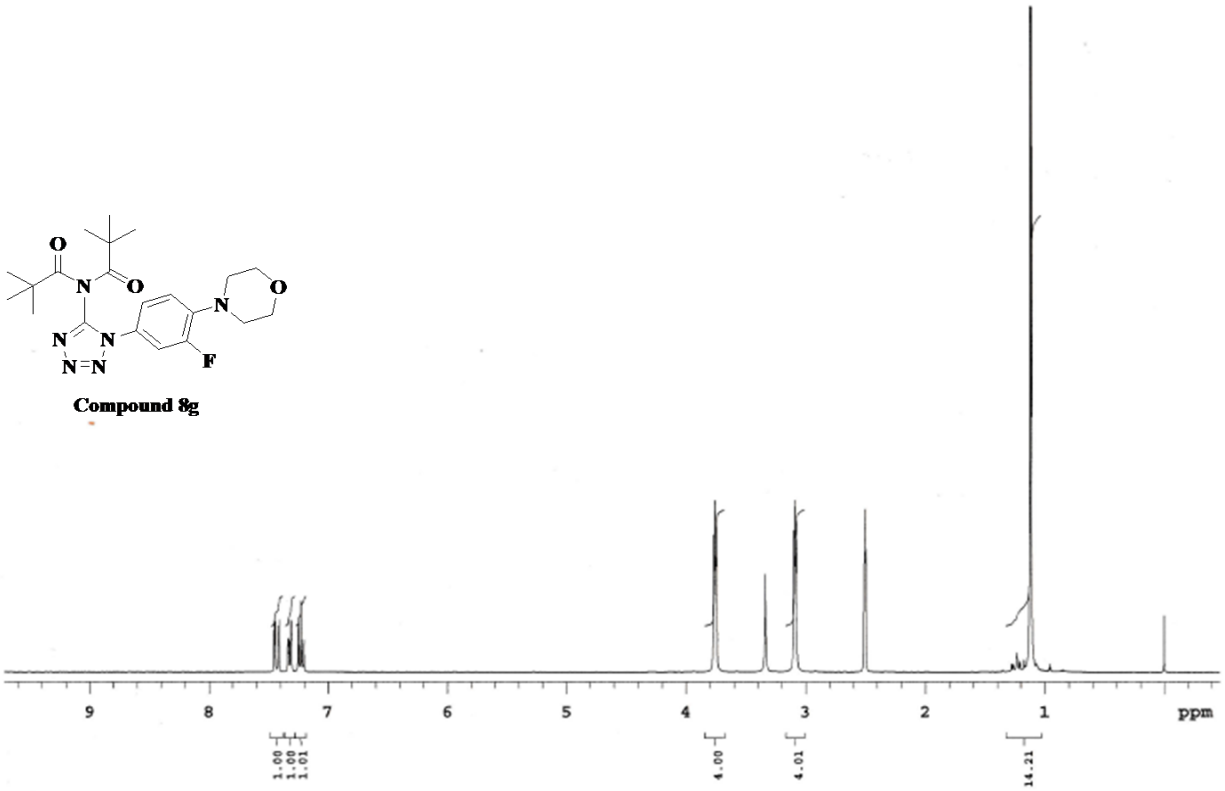


Figure 39.^{1}H NMR Spectra of Compound 8g

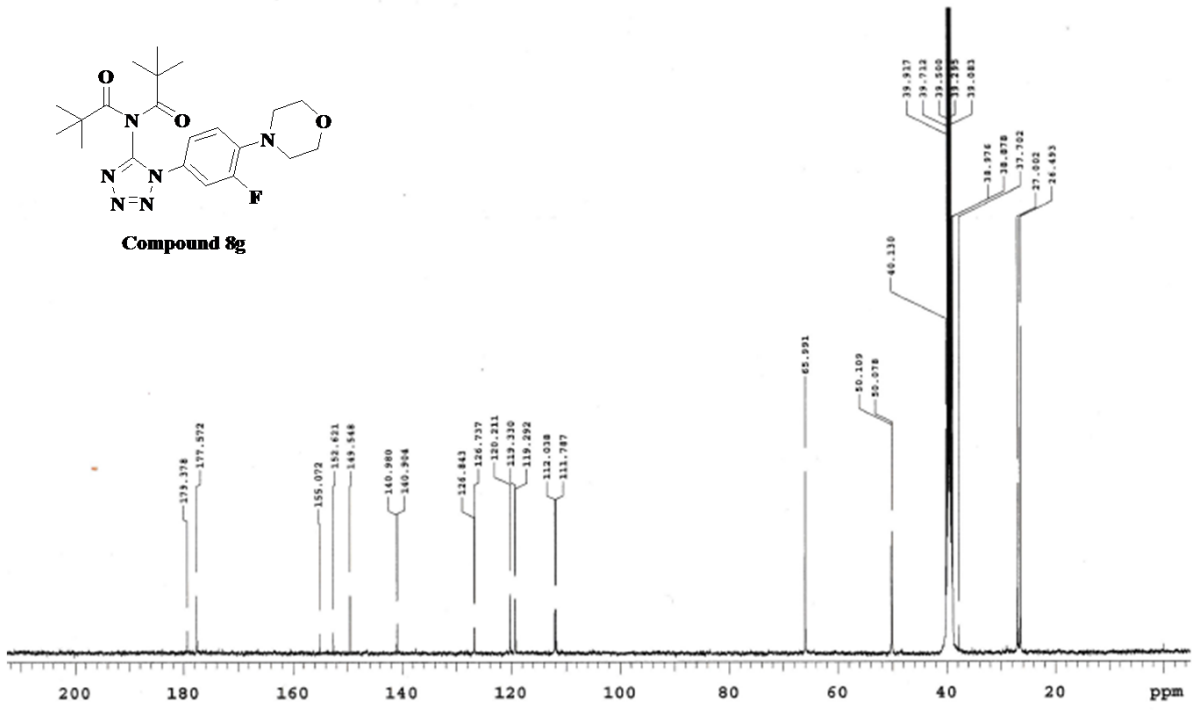


Figure 40.^{13}C NMR Spectra of Compound 8g

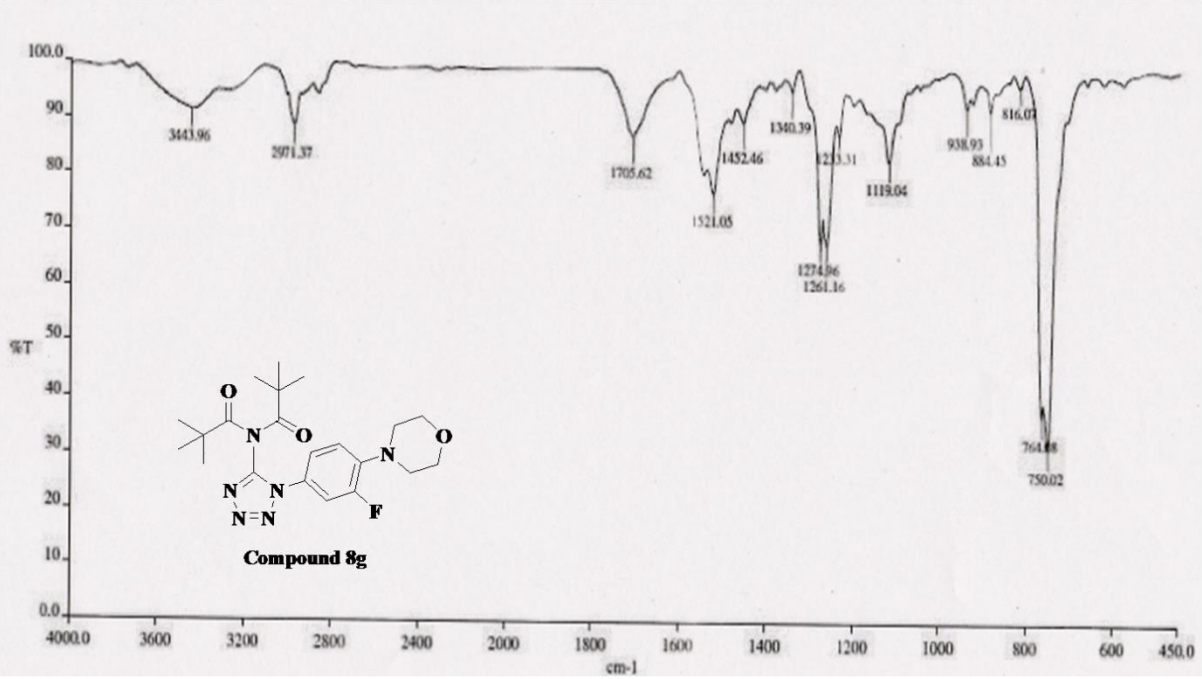


Figure 41. FT-IR Spectra of Compound 8g

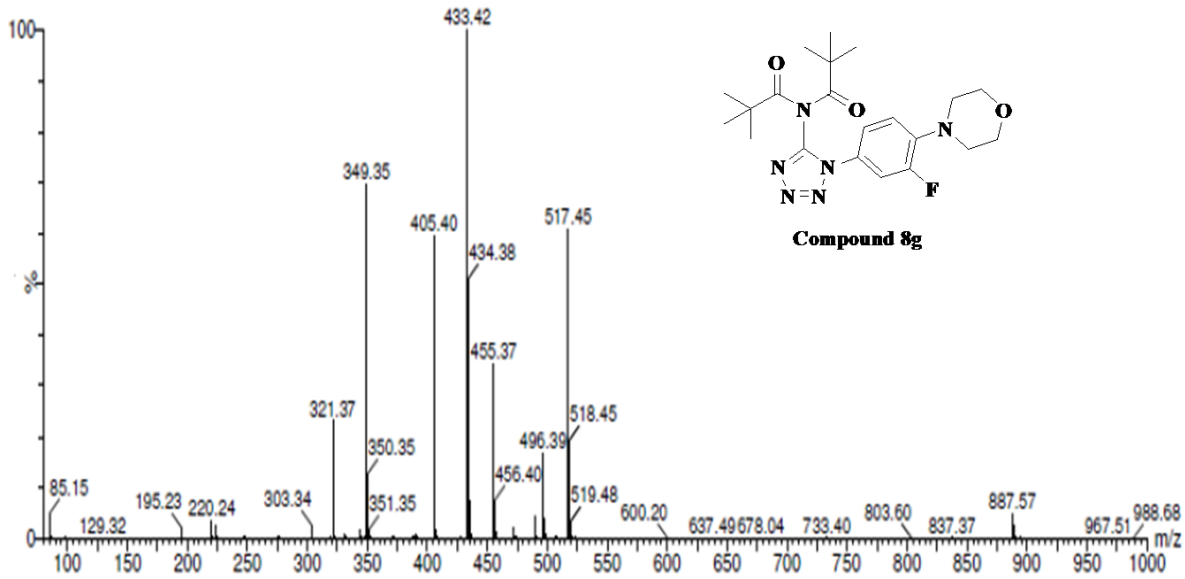


Figure 42. ESI-MS Spectra of Compound 8g

Analytical data of Compound 8h

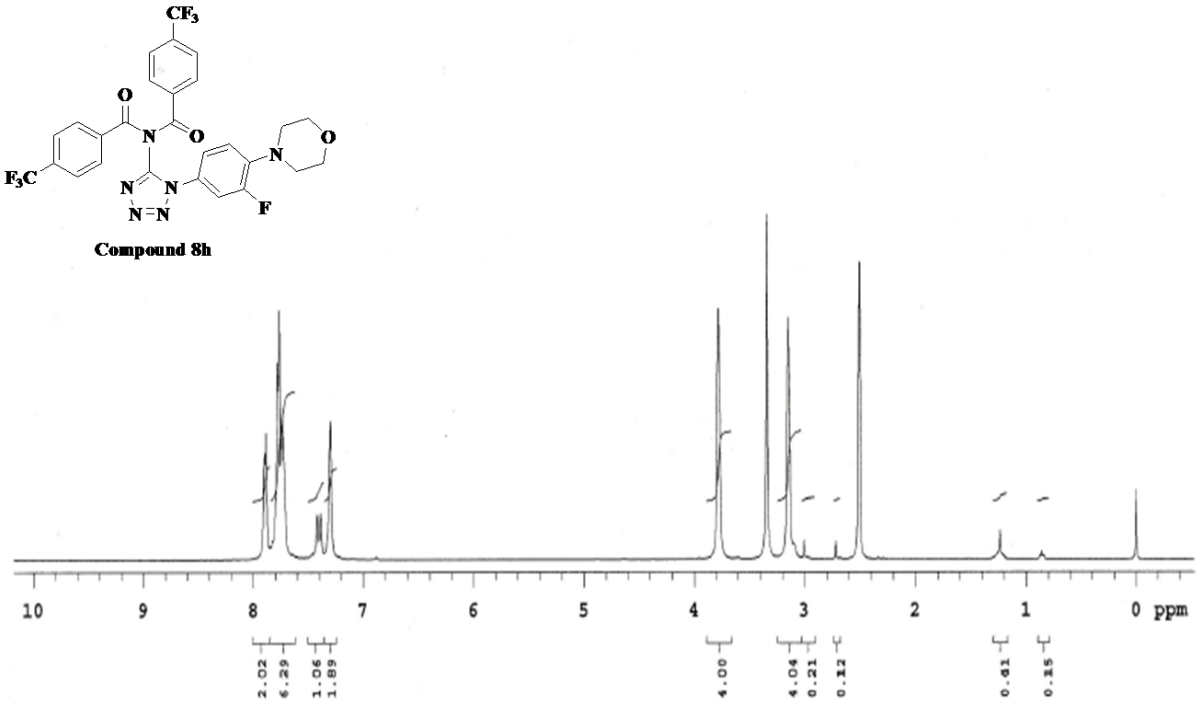


Figure 43.^{1}H NMR Spectra of Compound 8h

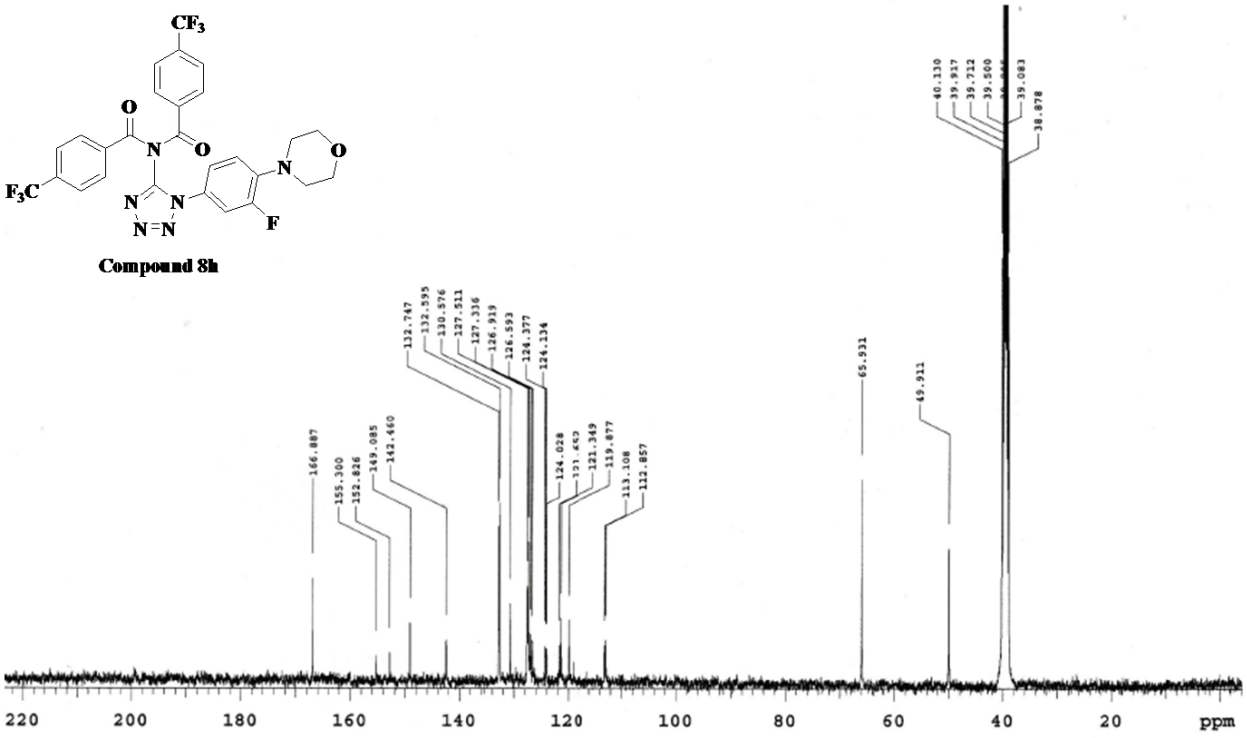


Figure 44.^{13}C NMR Spectra of Compound 8h

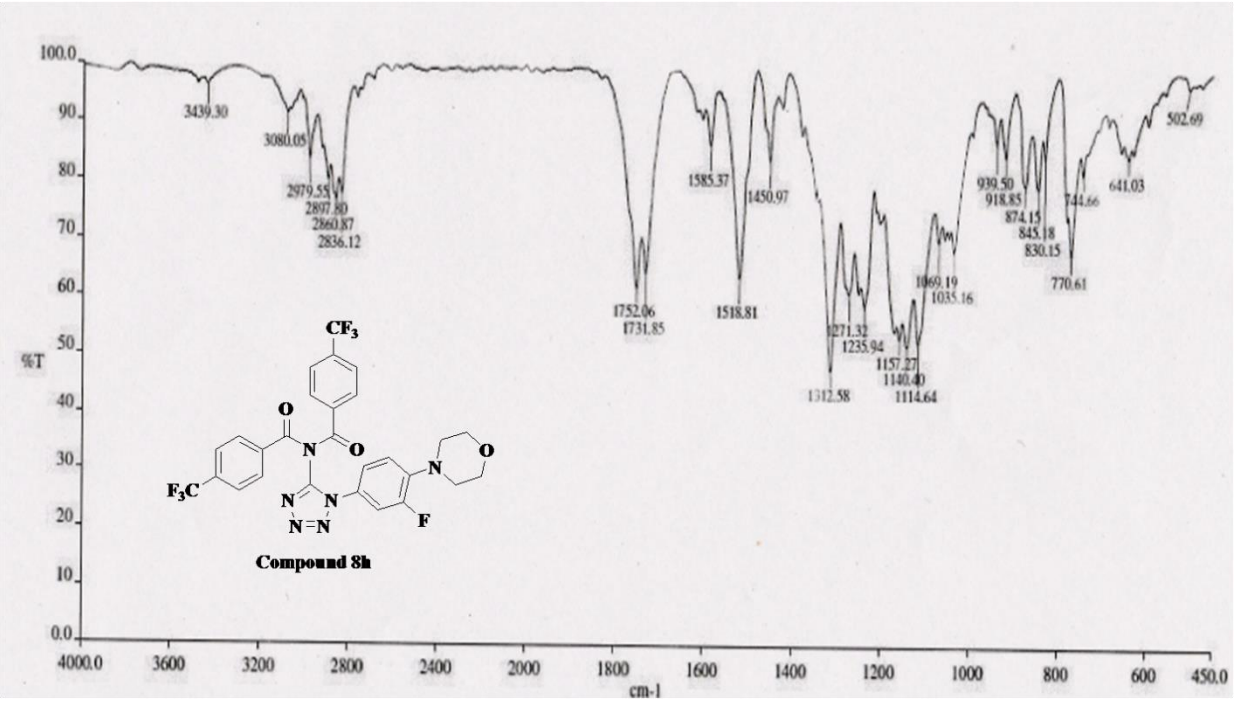


Figure 45. FT-IR Spectra of Compound 8h

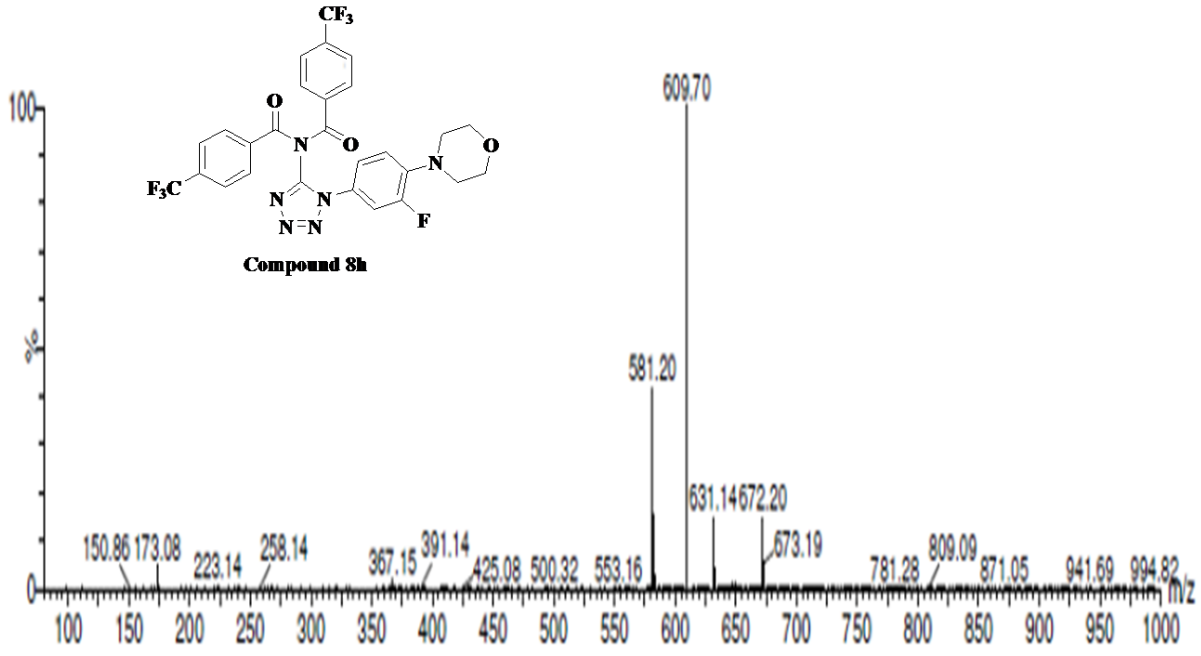


Figure 46. ESI-MS Spectra of Compound 8h

Analytical data of Compound 8i

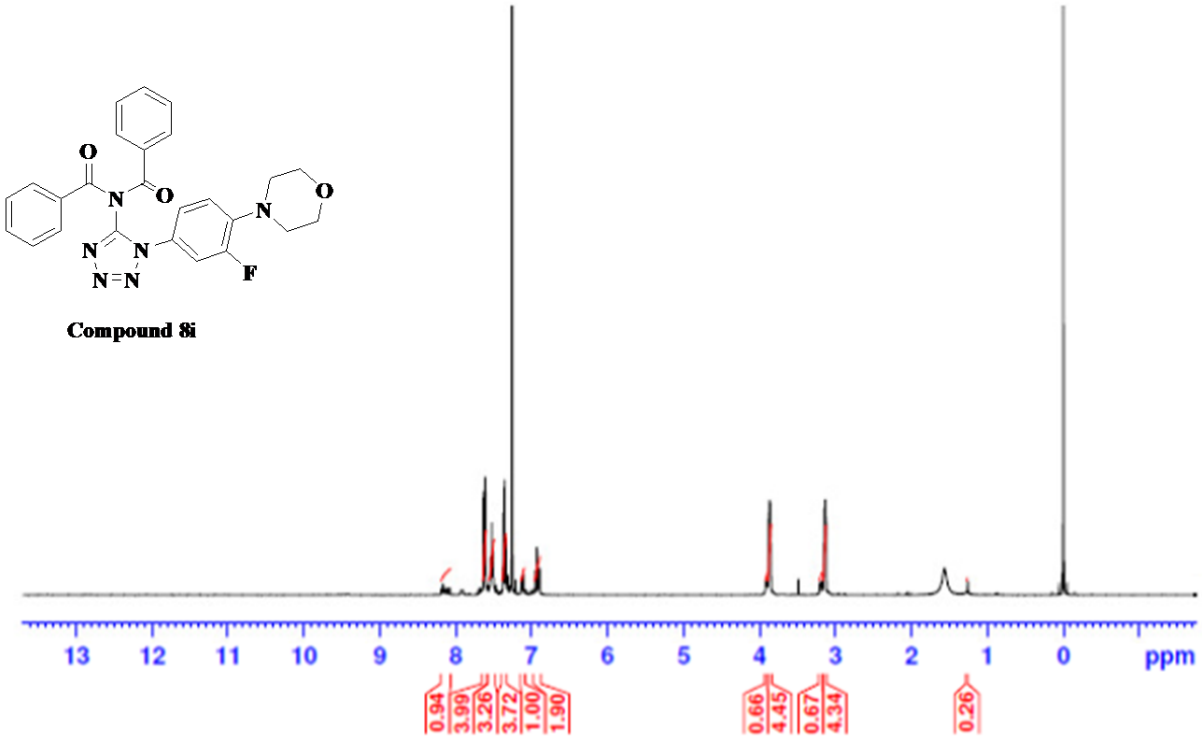


Figure 47.^{1}H NMR Spectra of Compound 8i

Figure 48.^{13}C NMR Spectra of Compound 8i

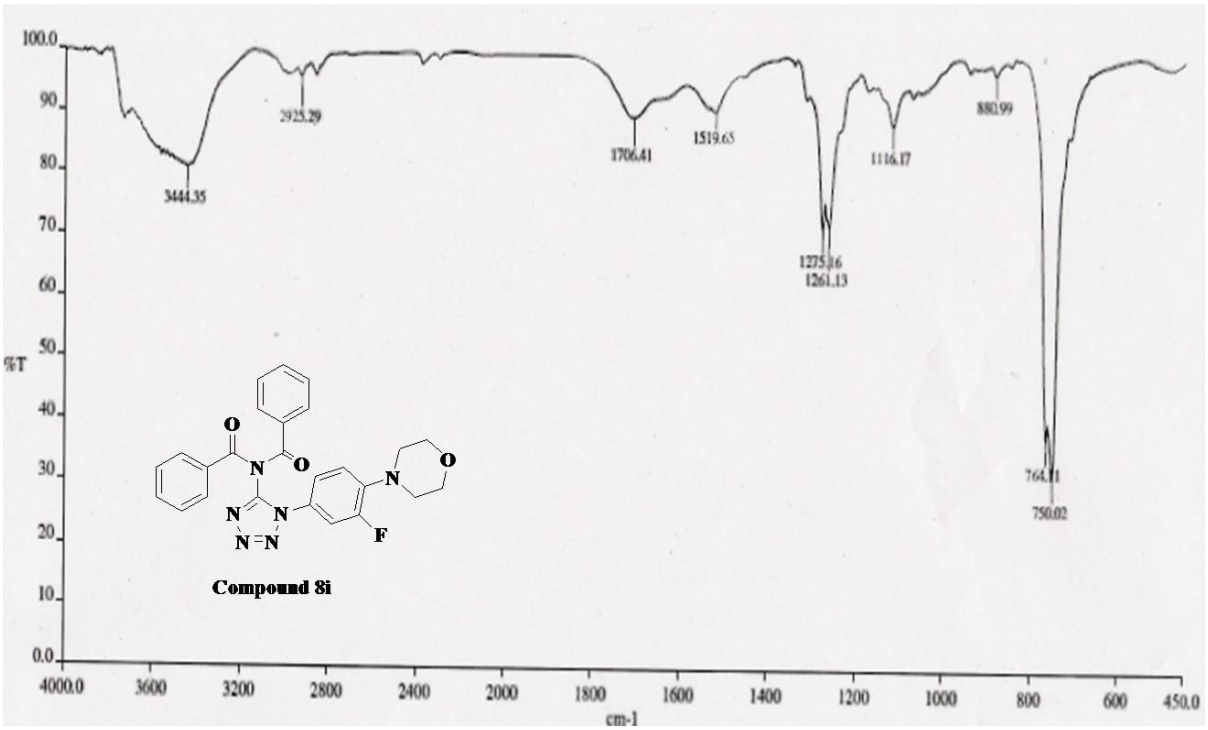


Figure 49. FT-IR Spectra of Compound 8i

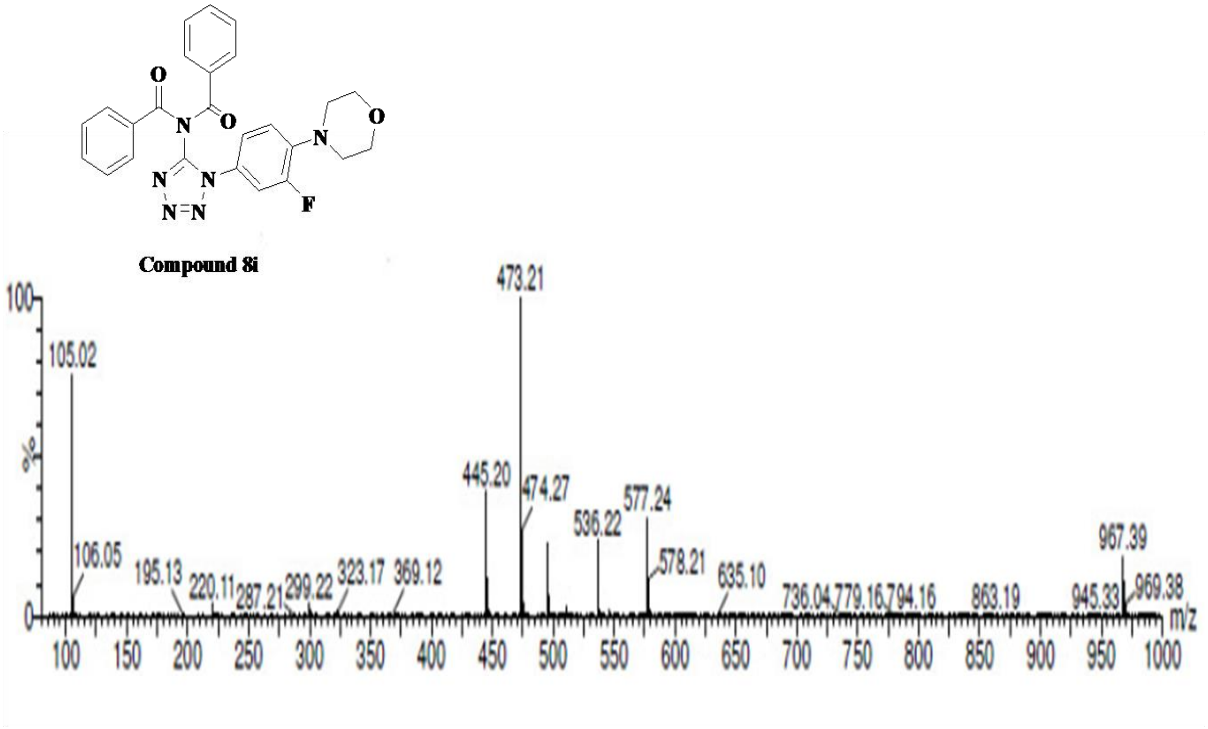


Figure 50. ESI-MS Spectra of Compound 8i

Analytical data of Compound 8j

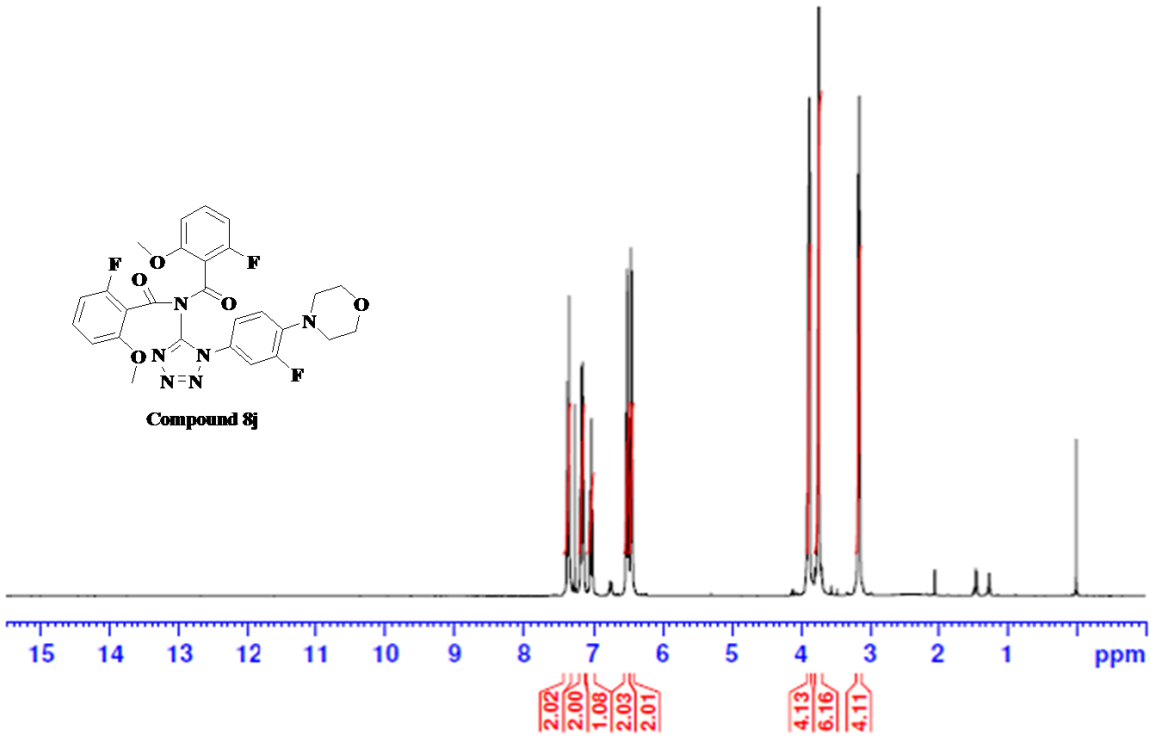


Figure 51.^{1}H NMR Spectra of Compound 8j

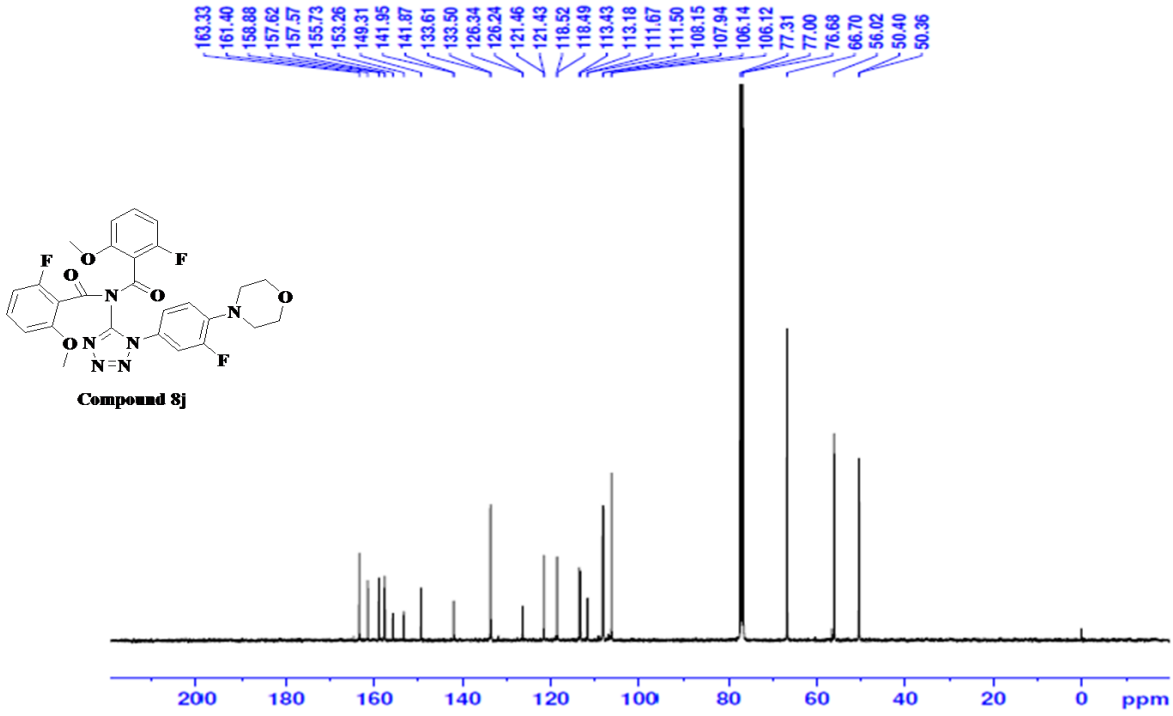


Figure 52.^{13}C NMR Spectra of Compound 8j

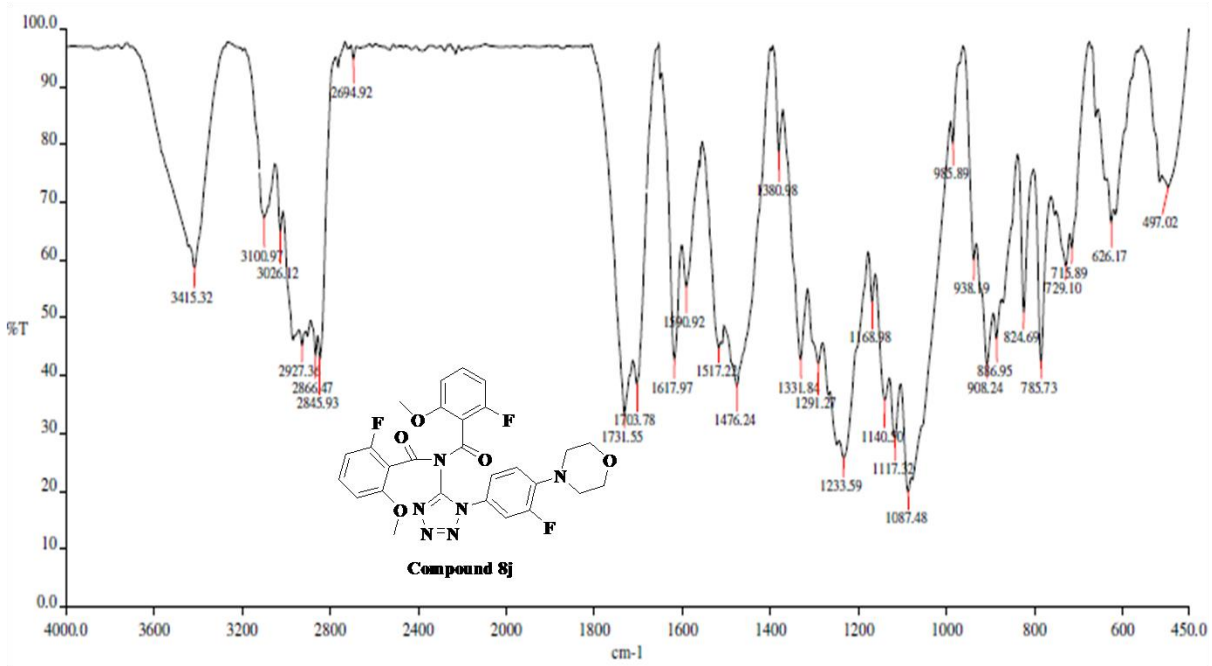


Figure 53. FT-IR Spectra of Compound 8j

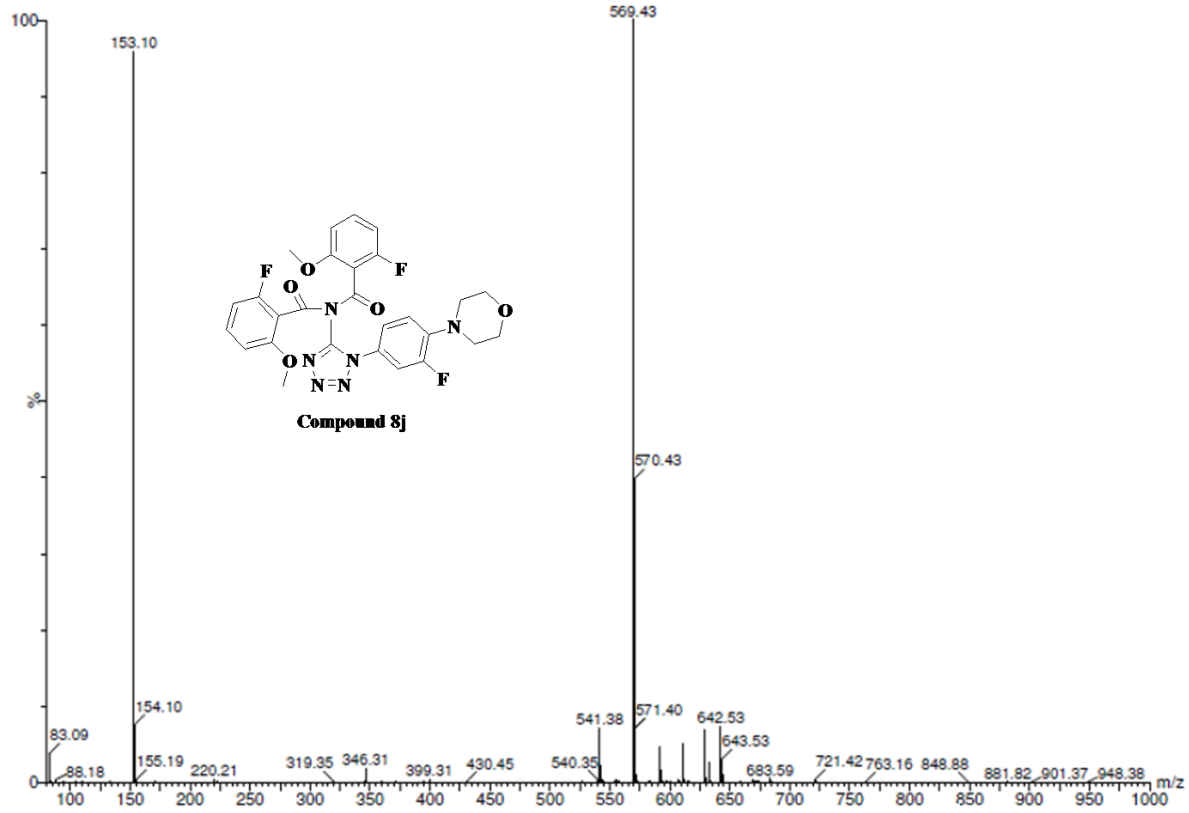


Figure 54. ESI-MS Spectra of Compound 8j

Analytical data of Compound 8k

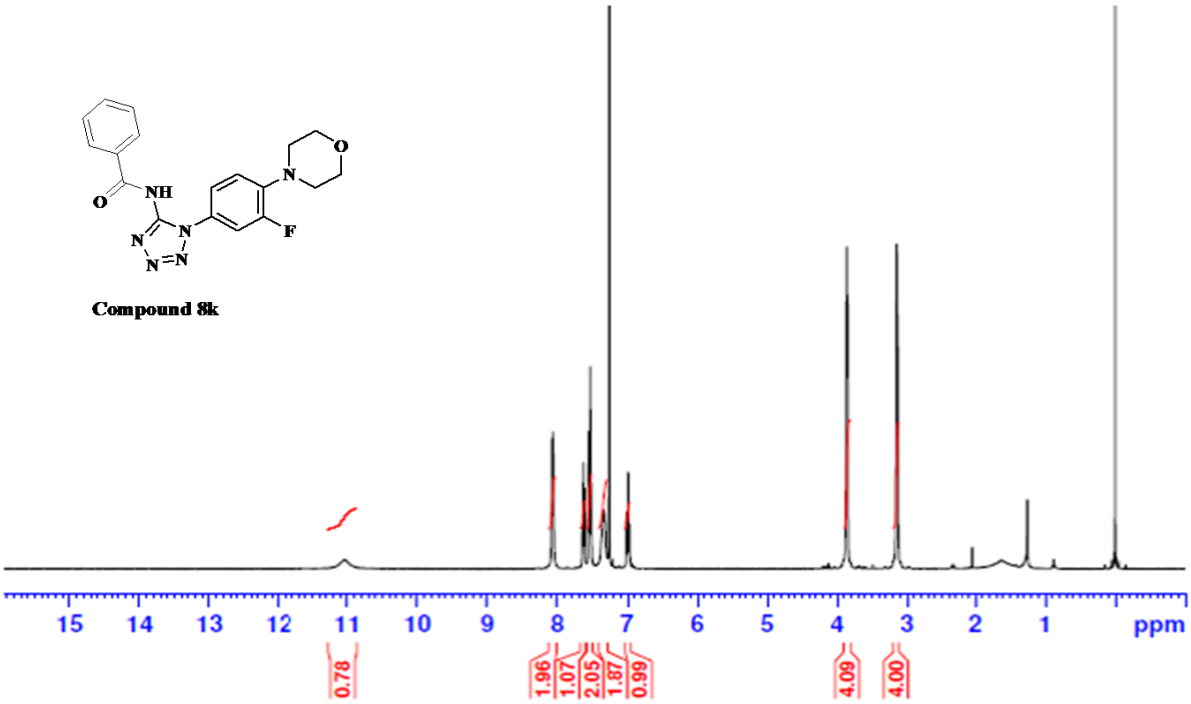


Figure 55.^{1}H NMR Spectra of Compound 8k

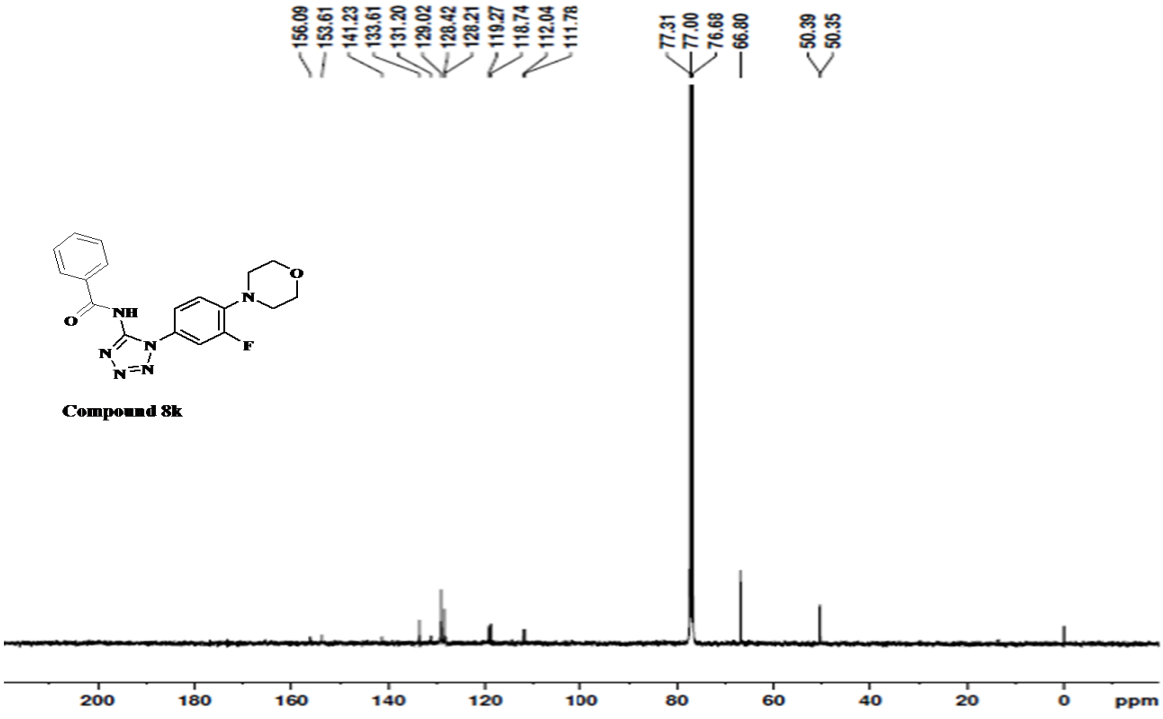


Figure 56.^{13}C NMR Spectra of Compound 8k

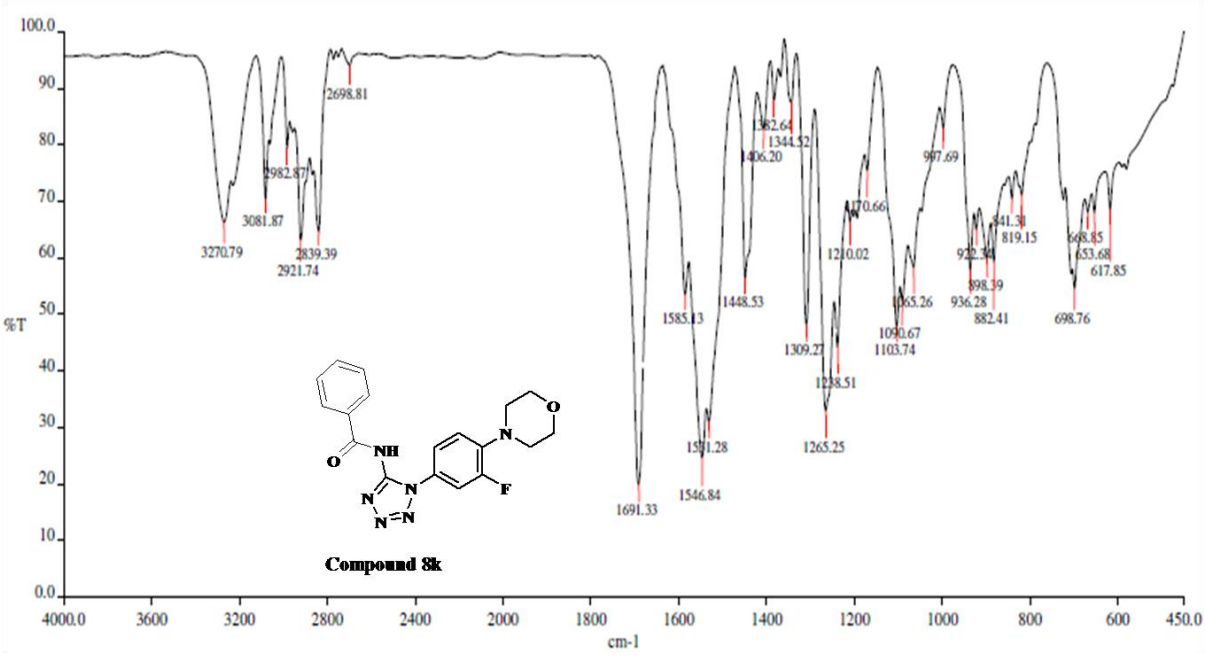
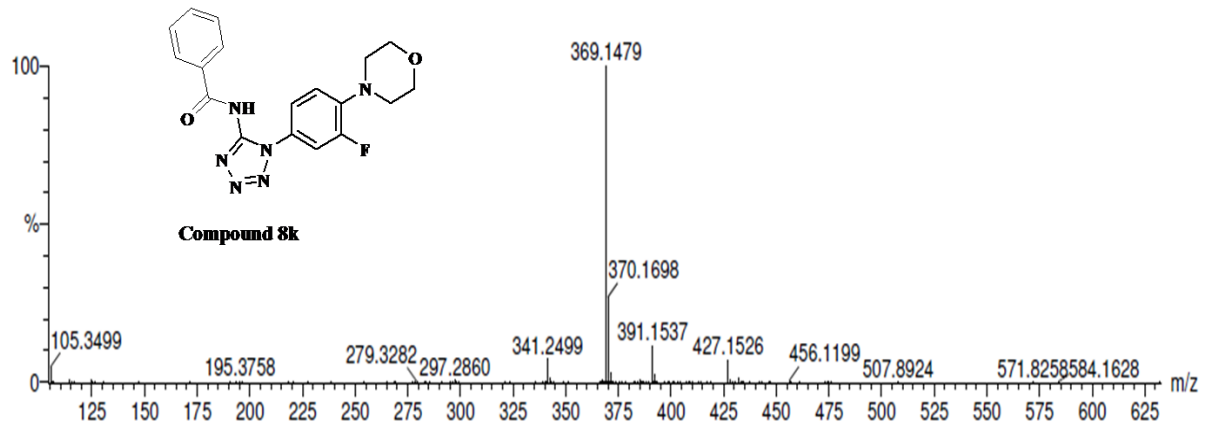


Figure 57. FT-IR Spectra of Compound 8k



Minimum:				-1.5		
Maximum:		5.0	1000.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
369.1479	369.1475	0.4	1.1	12.5	43.7	C18 H18 N6 O2 F

Figure 58. HRMS Spectra of Compound 8k

Analytical data of Compound 8l

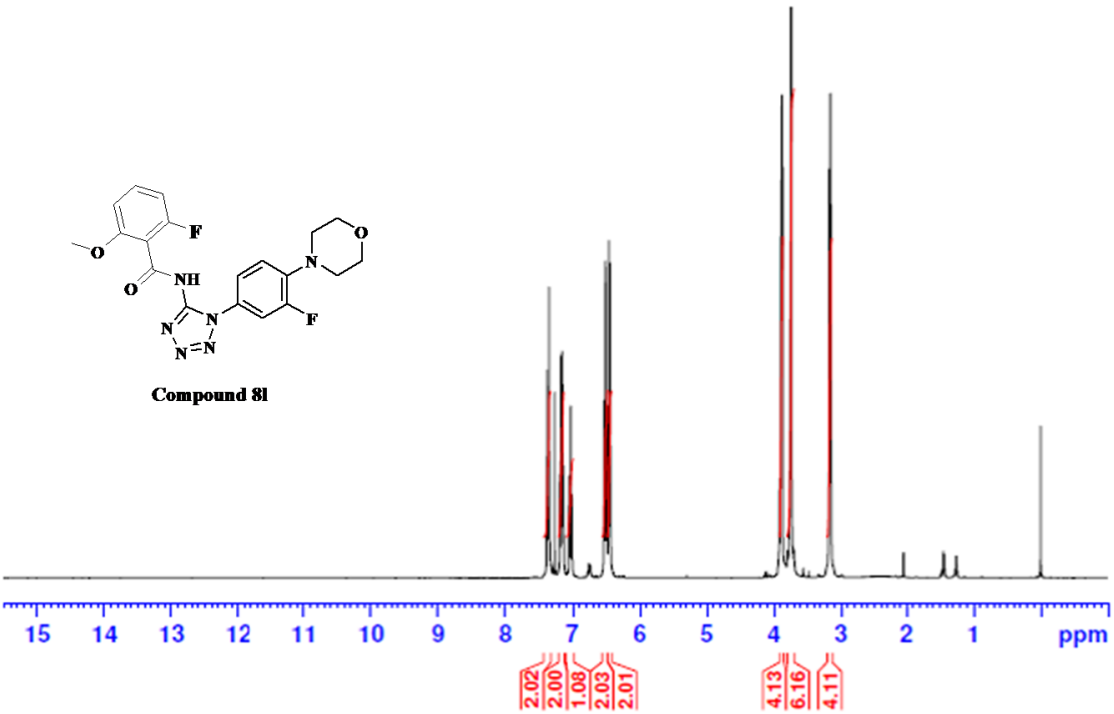


Figure 59.^{1}H NMR Spectra of Compound 8l

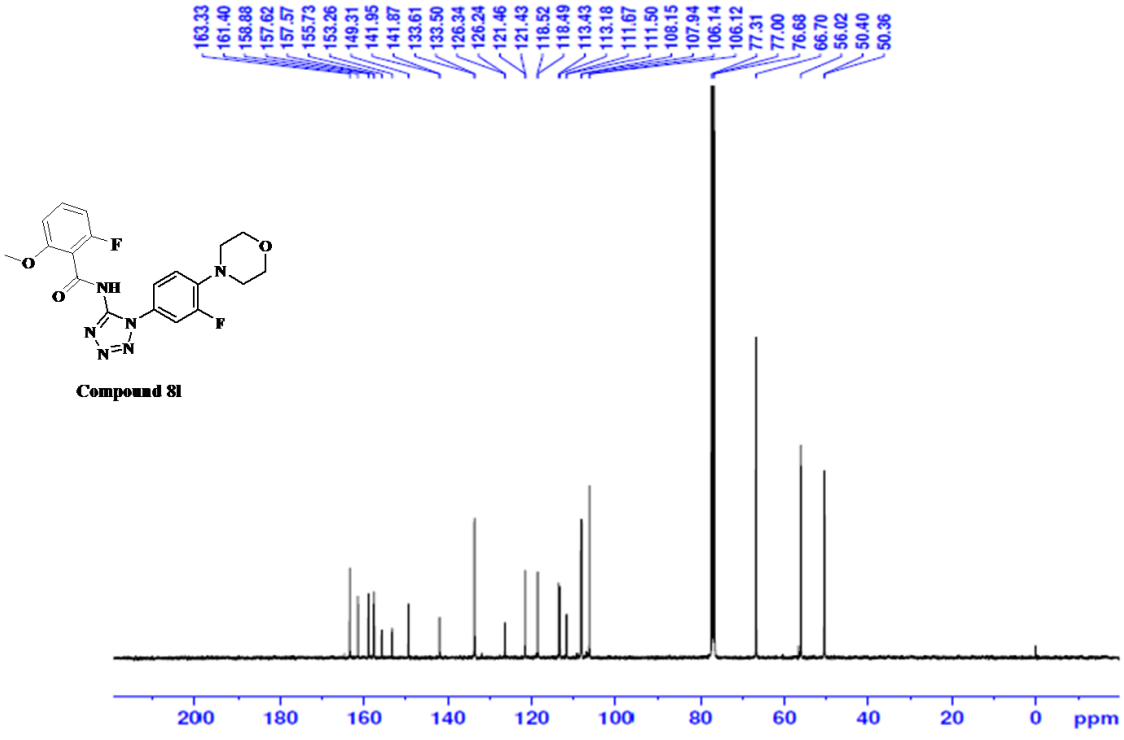


Figure 60.^{13}C NMR Spectra of Compound 8l

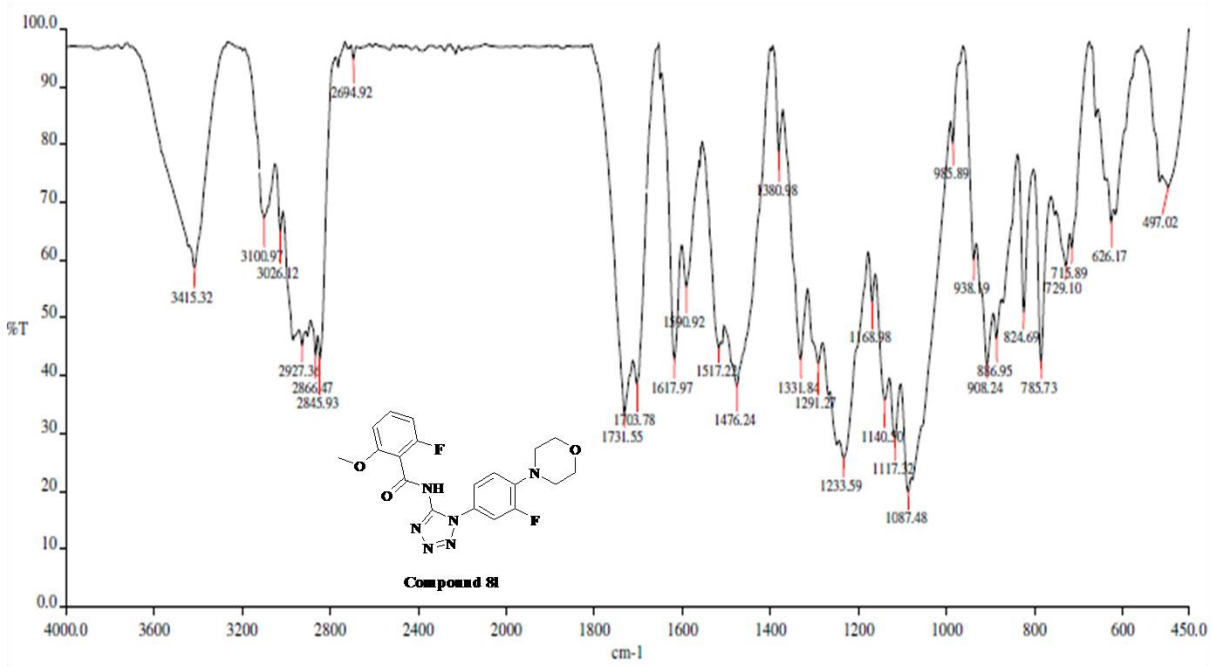


Figure 61. FT-IR Spectra of Compound 8l

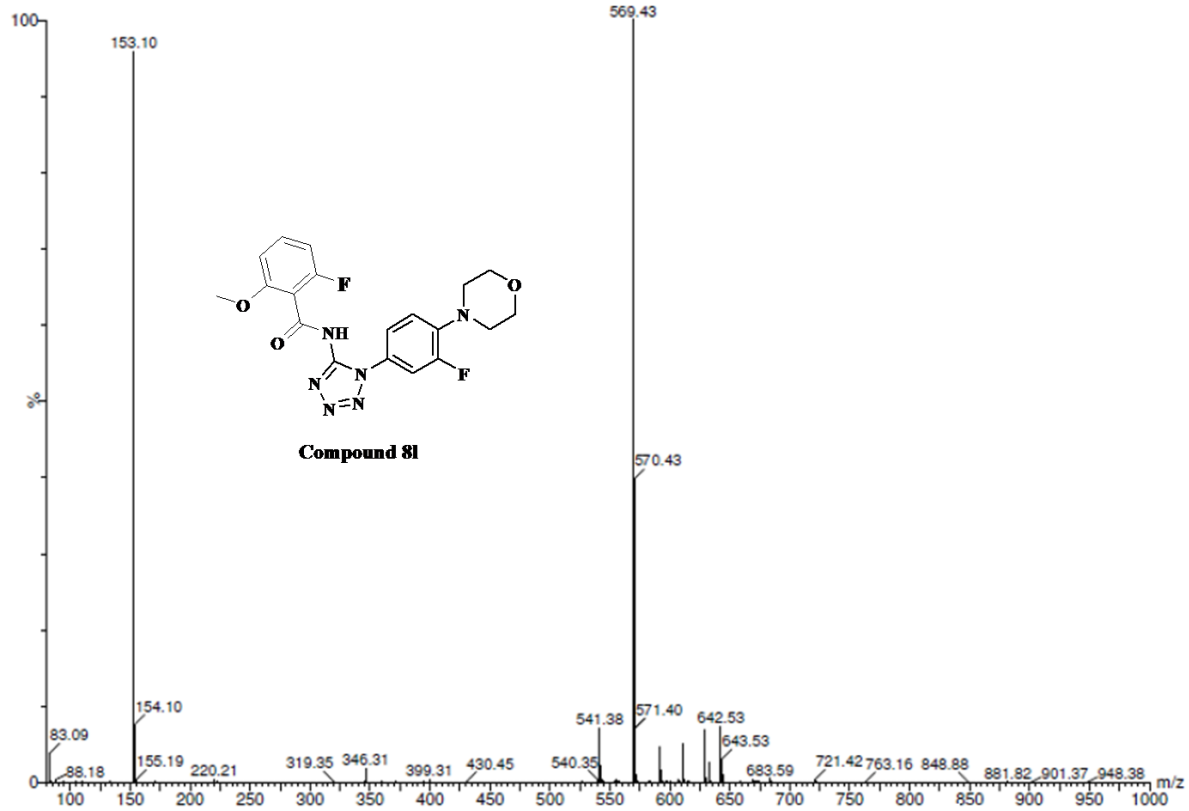


Figure 62. ESI-MS Spectra of Compound 8l

Analytical data of Compound 8m

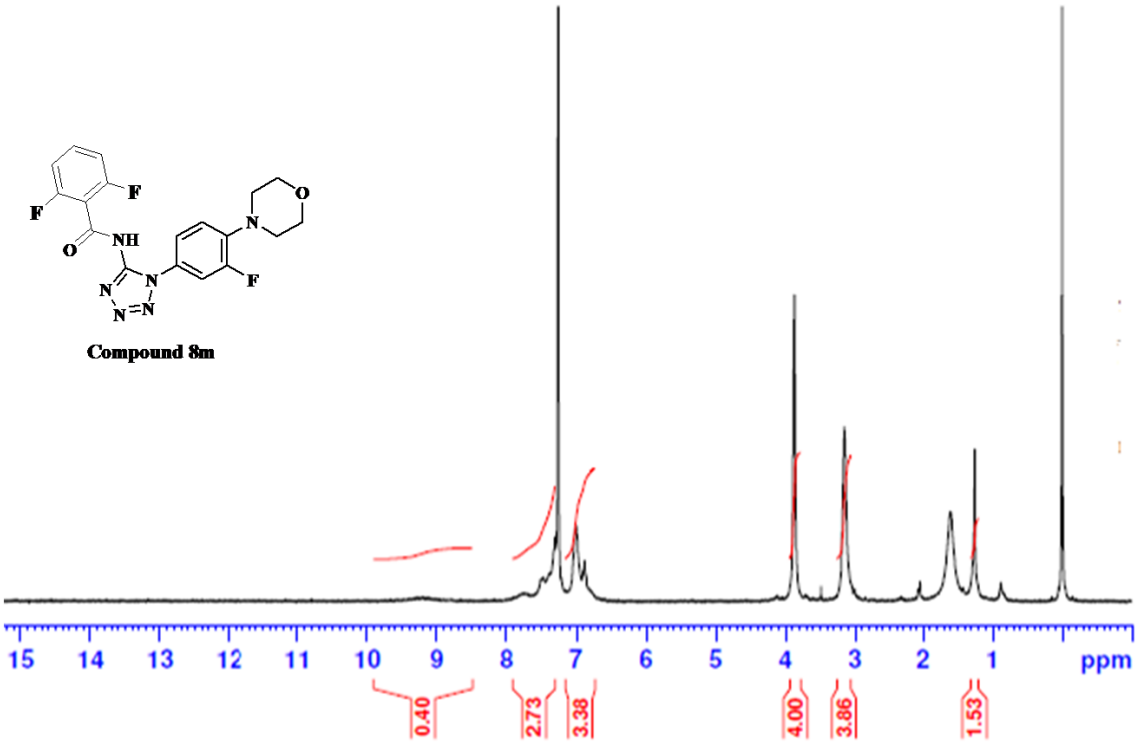


Figure 63.^{1}H NMR Spectra of Compound 8m

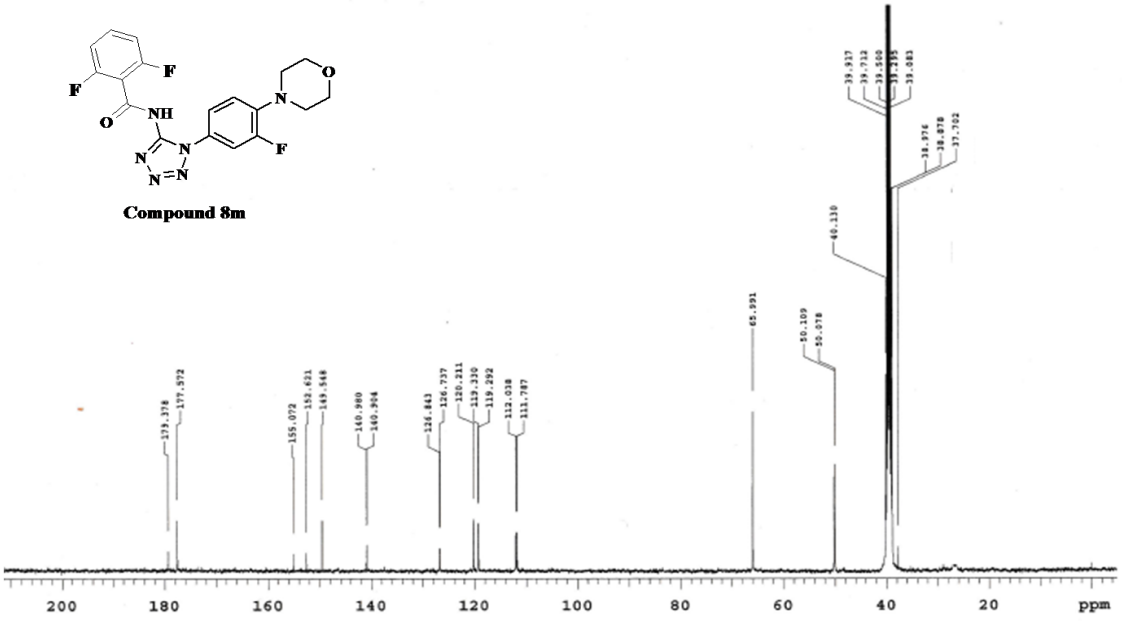


Figure 64.^{13}C NMR Spectra of Compound 8m

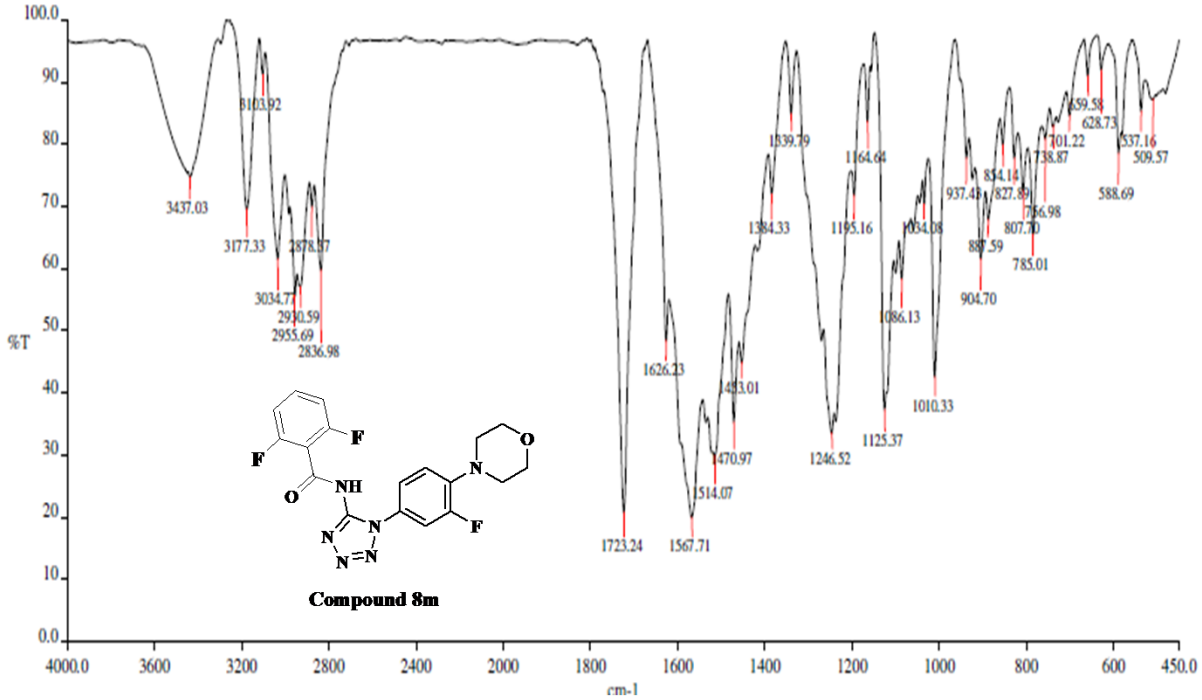


Figure 65. FT-IR Spectra of Compound 8m

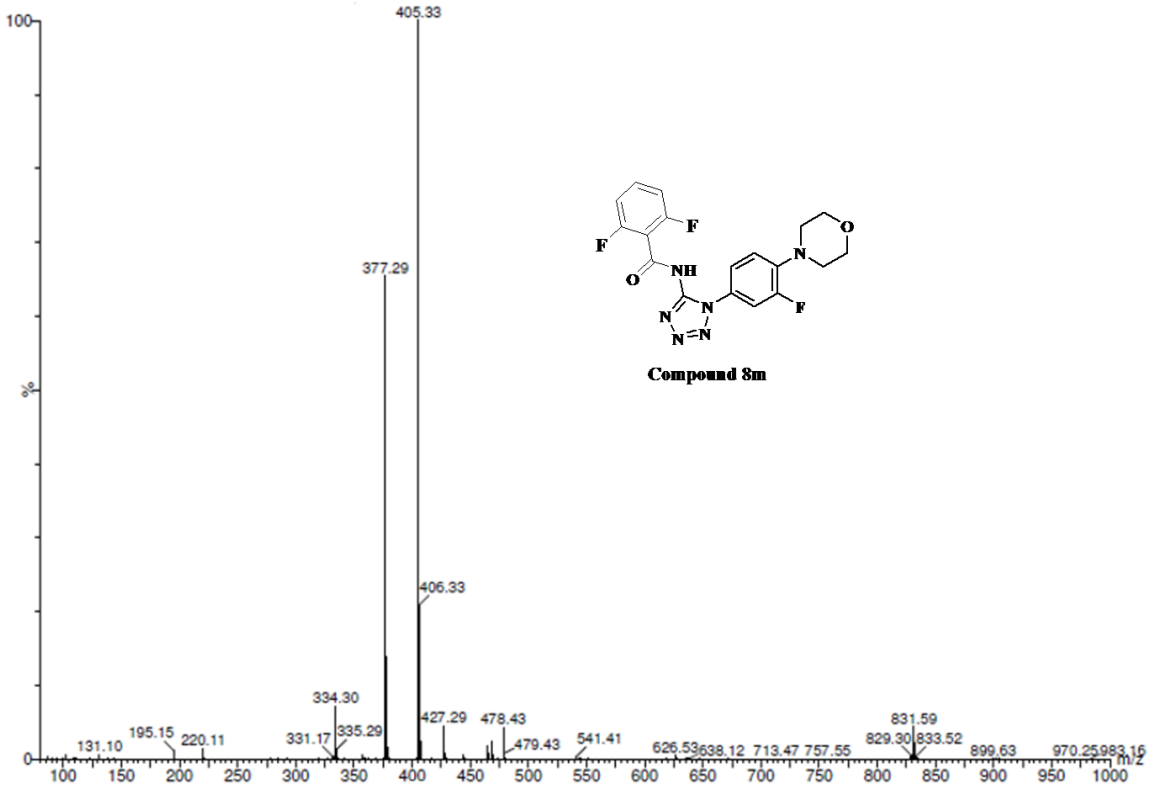


Figure 66. ESI-MS Spectra of Compound 8m

Analytical data of Compound 8n

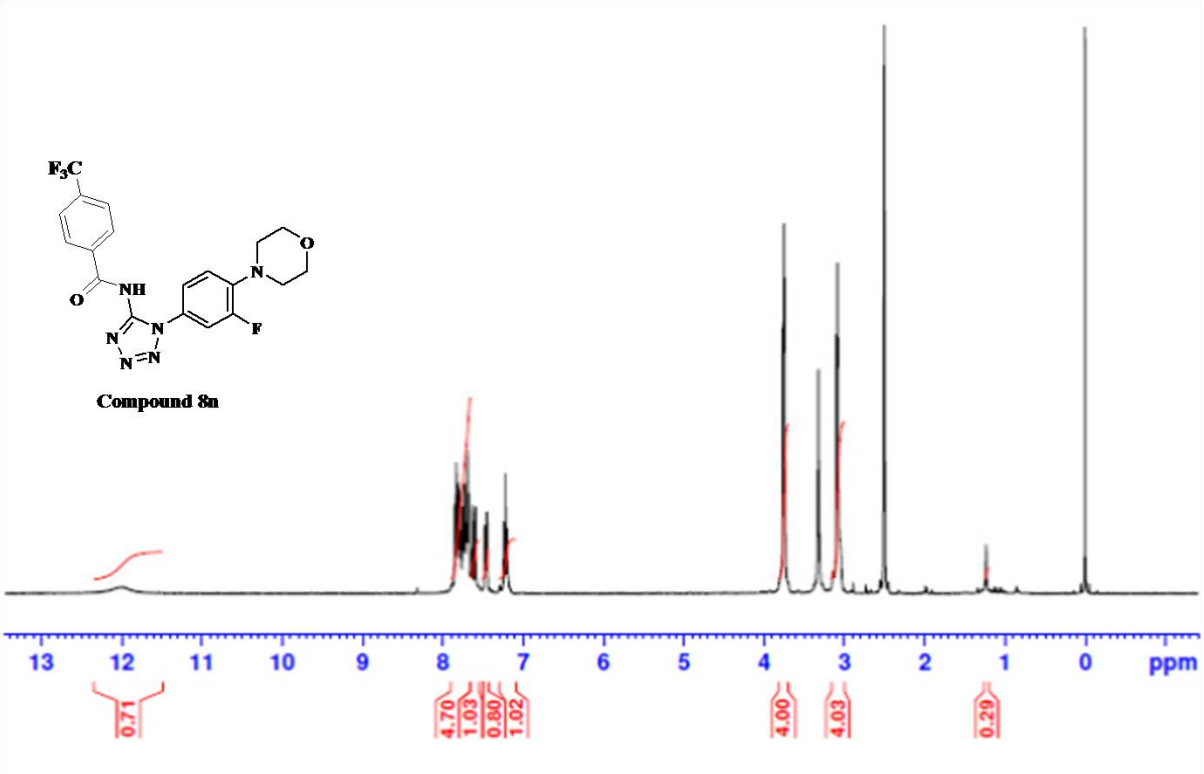


Figure 67.^{1}H NMR Spectra of Compound 8n

Fig.68.^{13}C NMR Spectra of Compound 8n

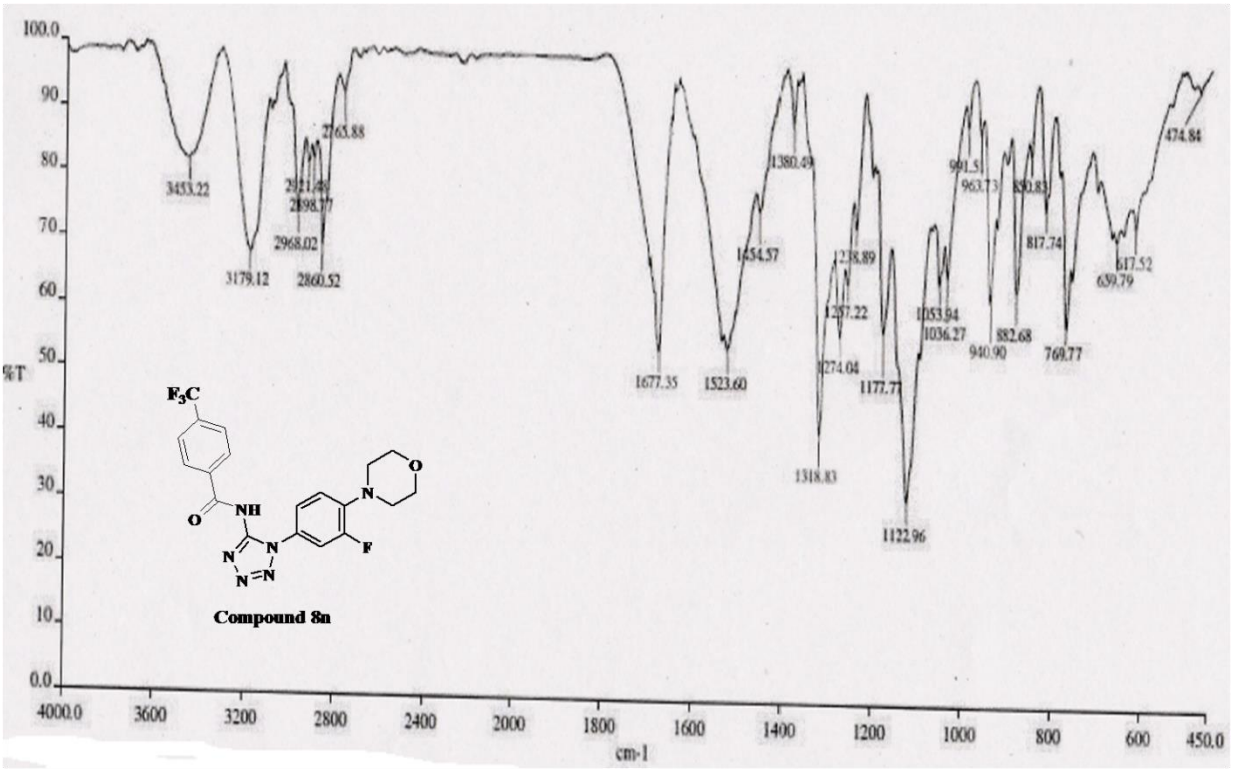


Fig.69. FT-IR Spectra of Compound 8n

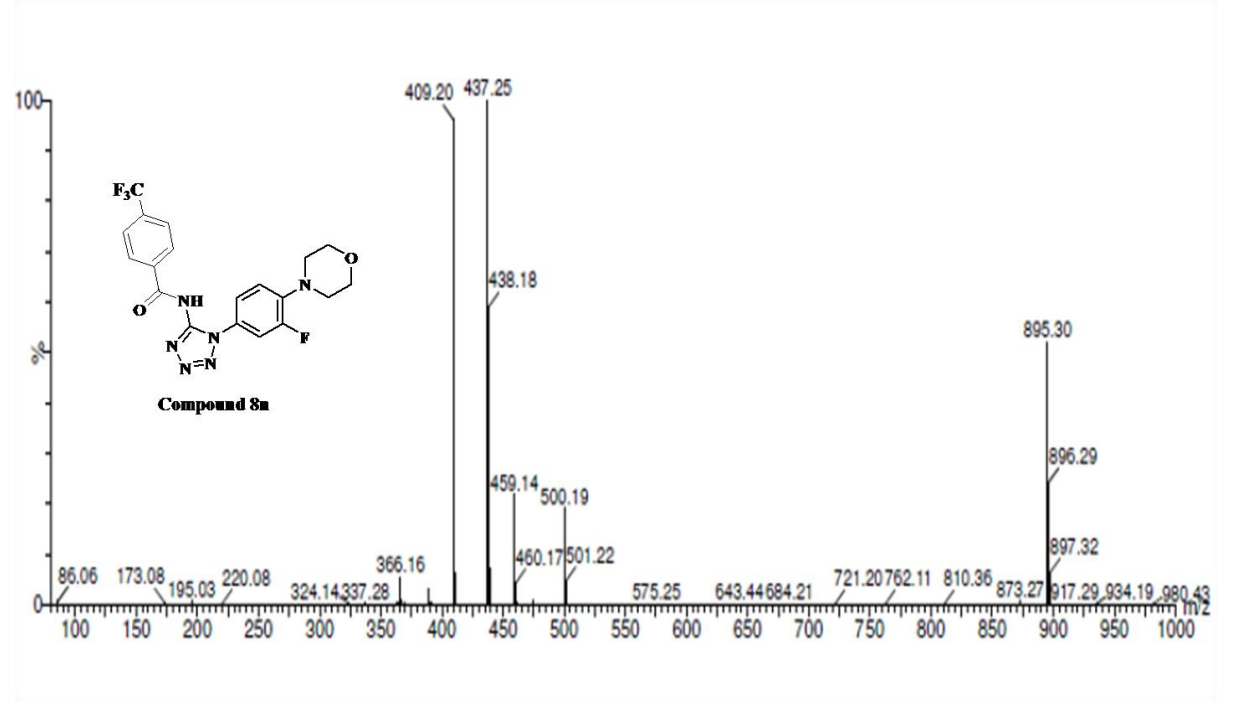


Figure 70. ESI-MS Spectra of Compound 8n

Analytical data of Compound 8o

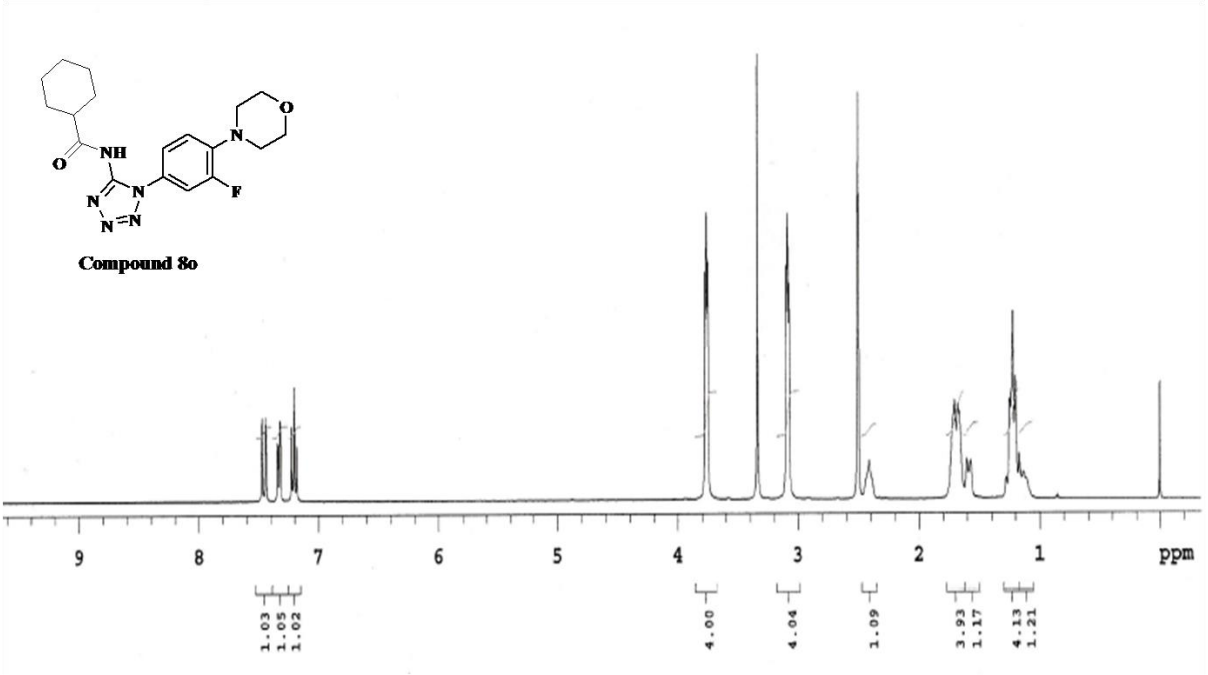


Figure 71.^{1}H NMR Spectra of Compound 8o

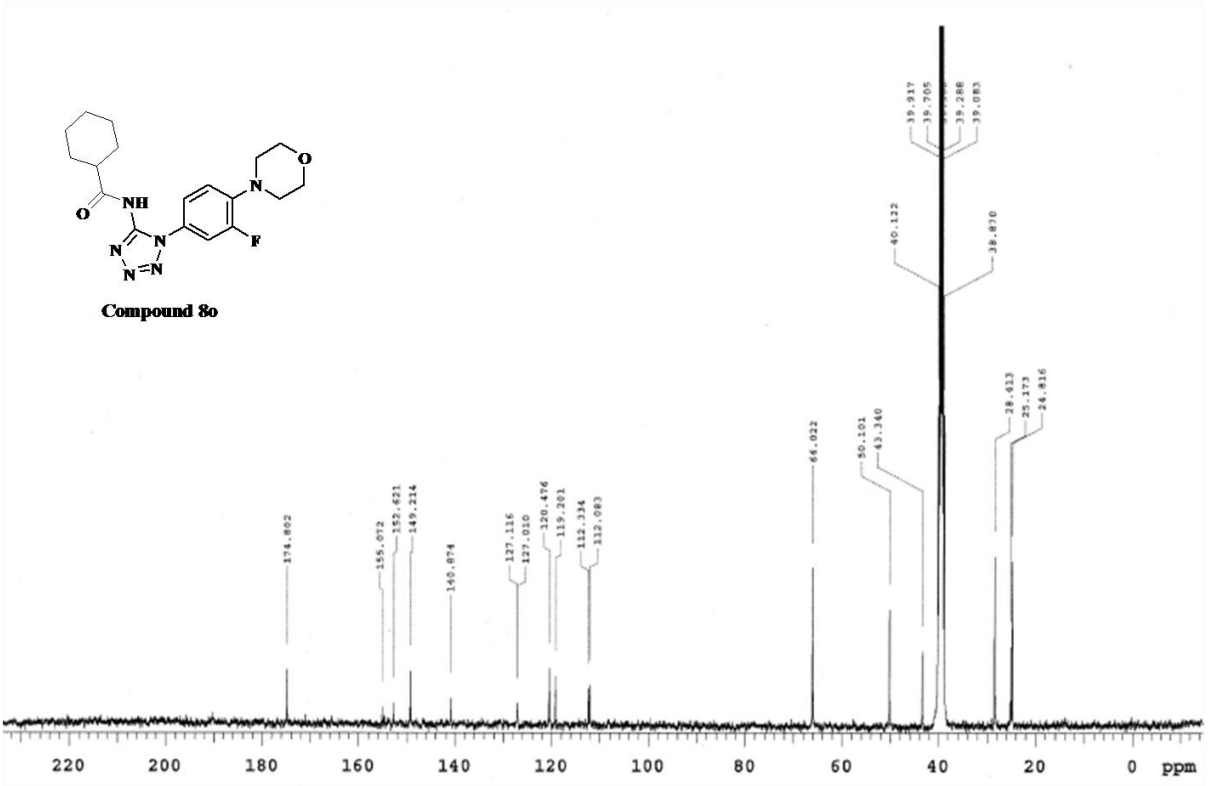


Figure 72.^{13}C NMR Spectra of Compound 8o

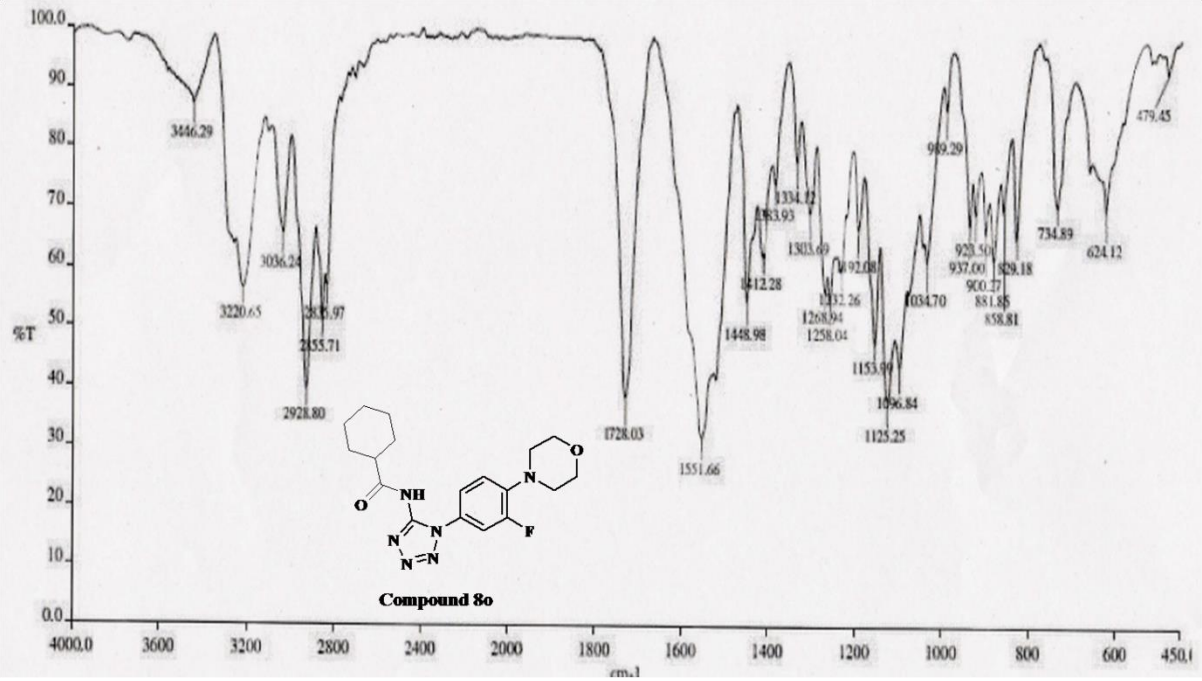


Figure 73. FT-IR Spectra of Compound 8o

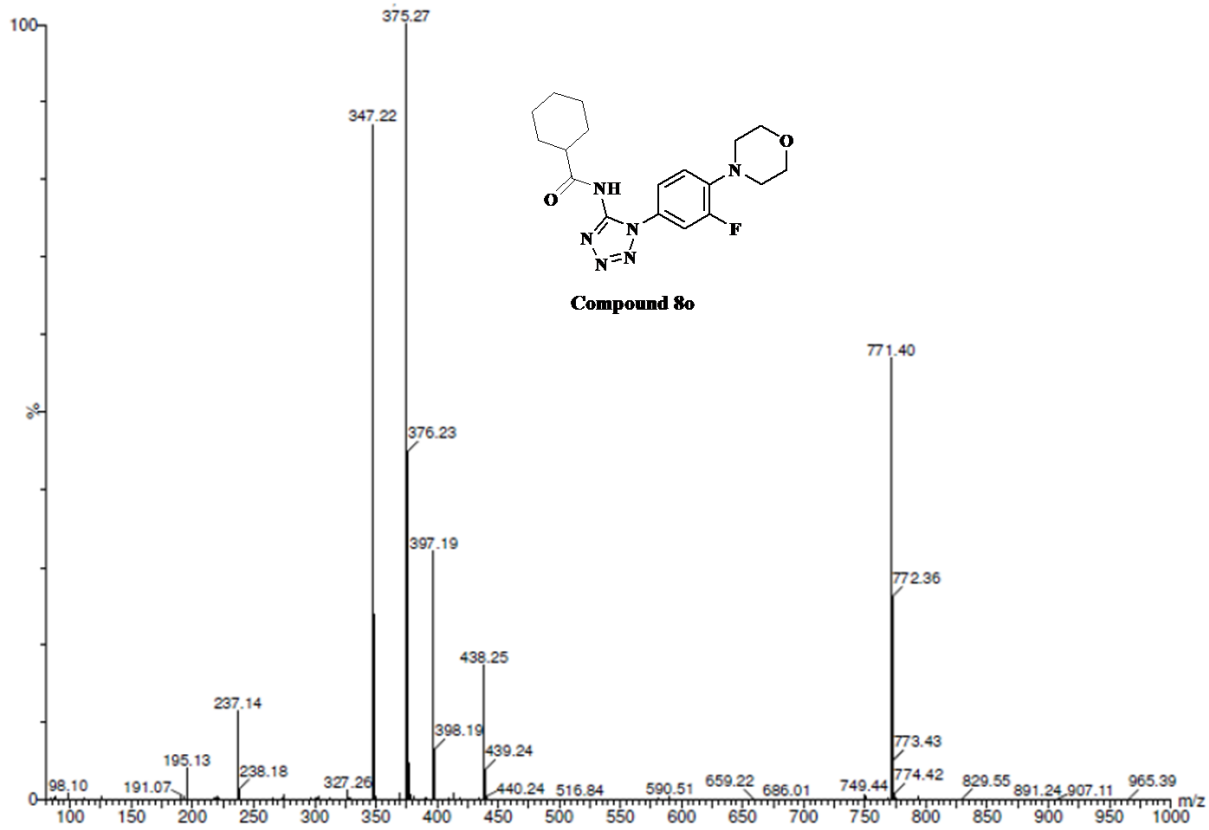


Figure 74. ESI-MS Spectra of Compound 8o

Analytical data of Compound 8p

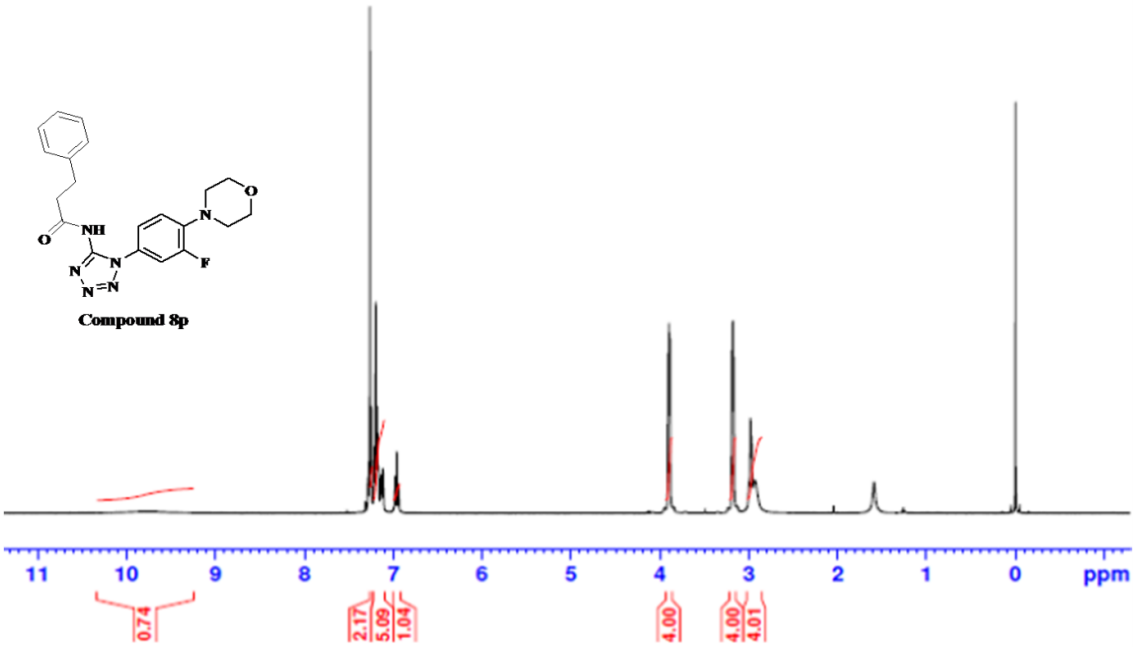


Figure 75.^{1}H NMR Spectra of Compound 8p

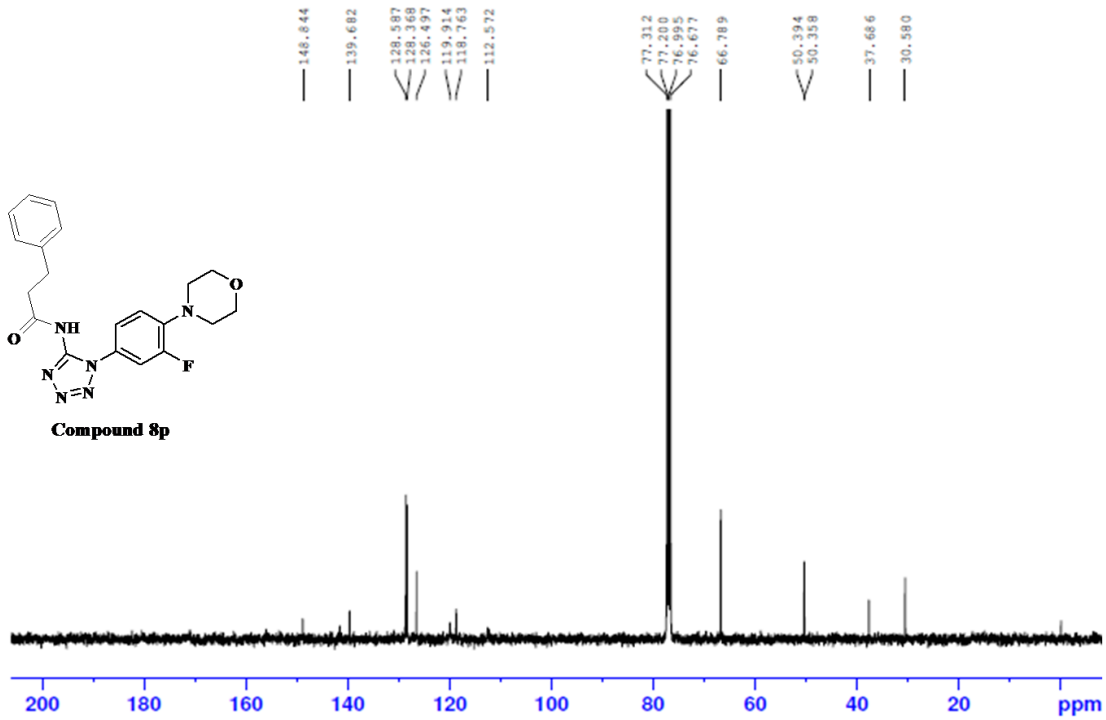


Figure 76.^{13}C NMR Spectra of Compound 8p

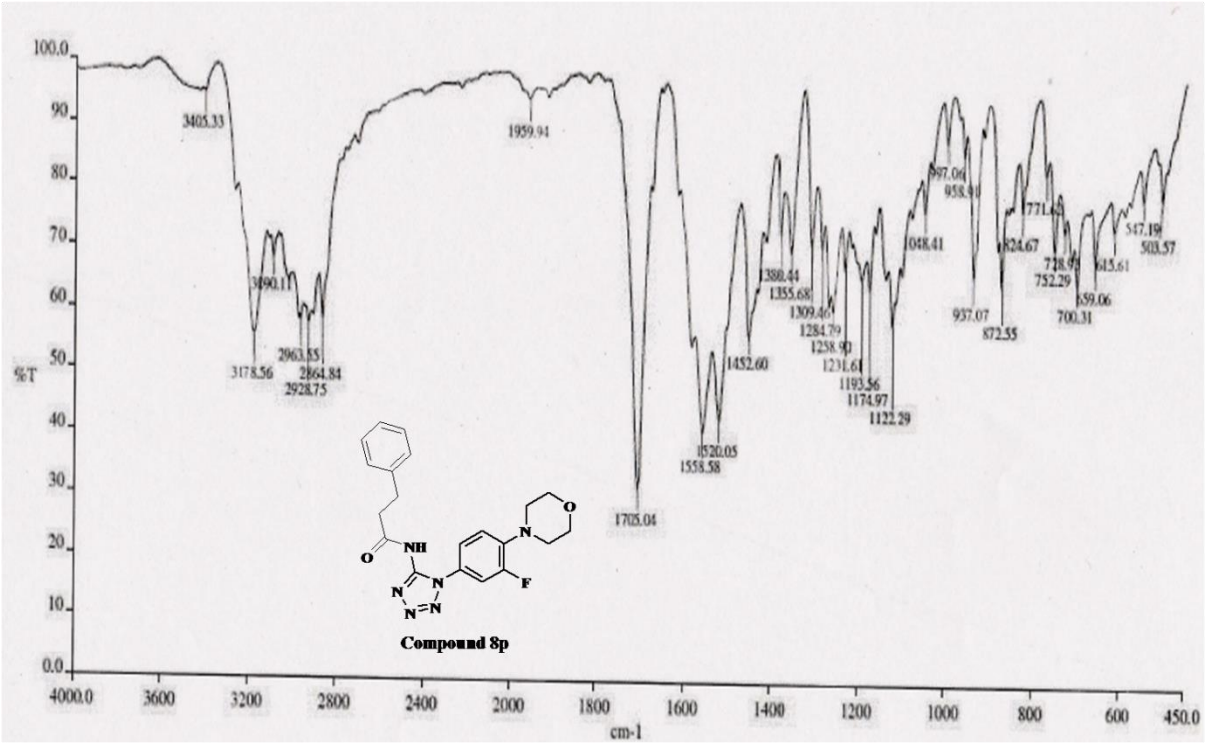


Figure 77. FT-IR Spectra of Compound 8p

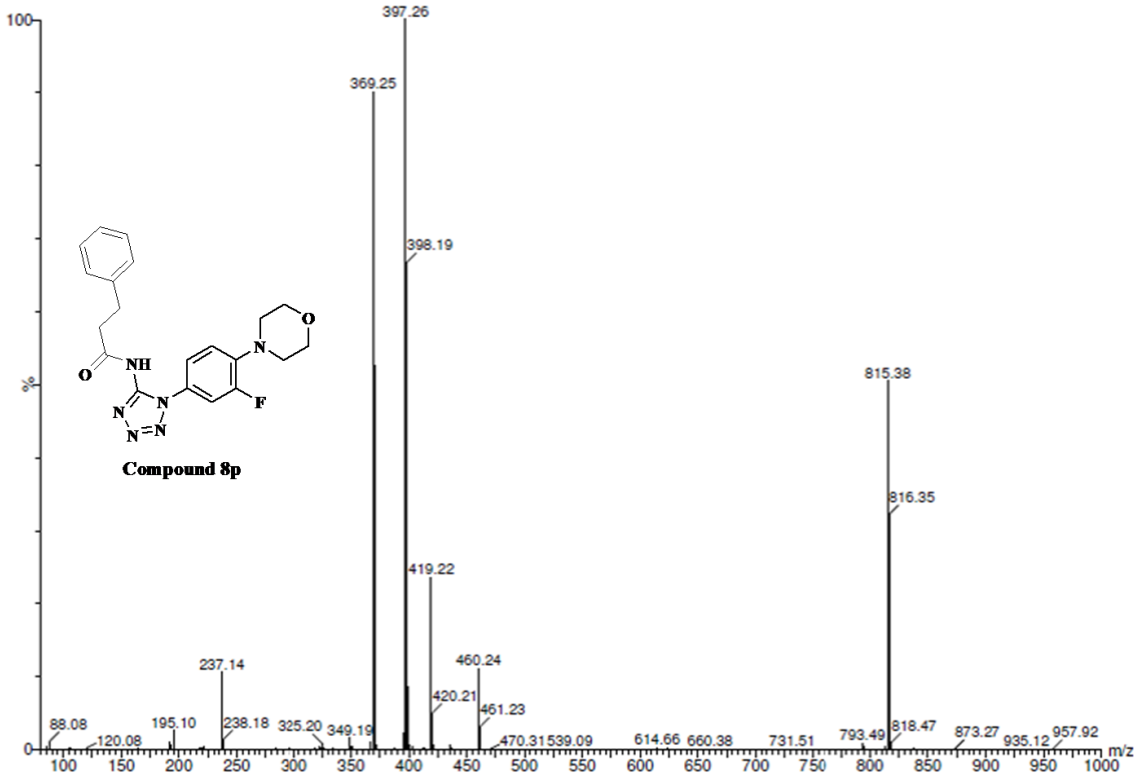


Figure 78. ESI-MS Spectra of Compound 8p

Analytical data of Compound 8q

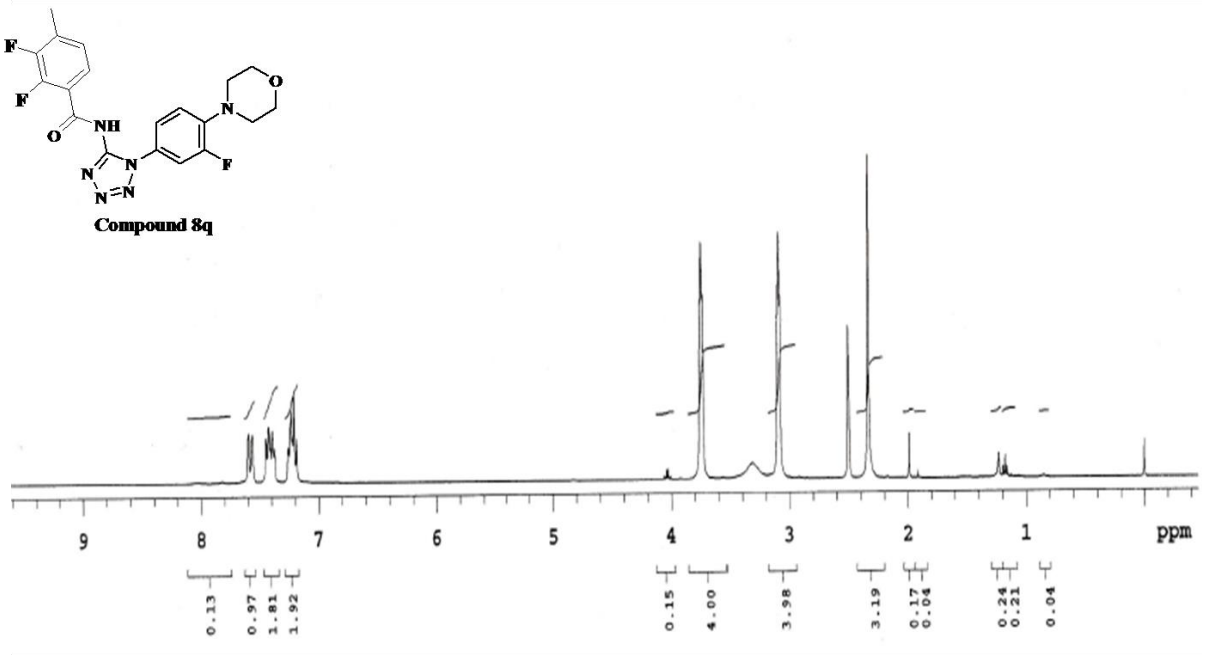


Figure 79.^{1}H NMR Spectra of Compound 8q

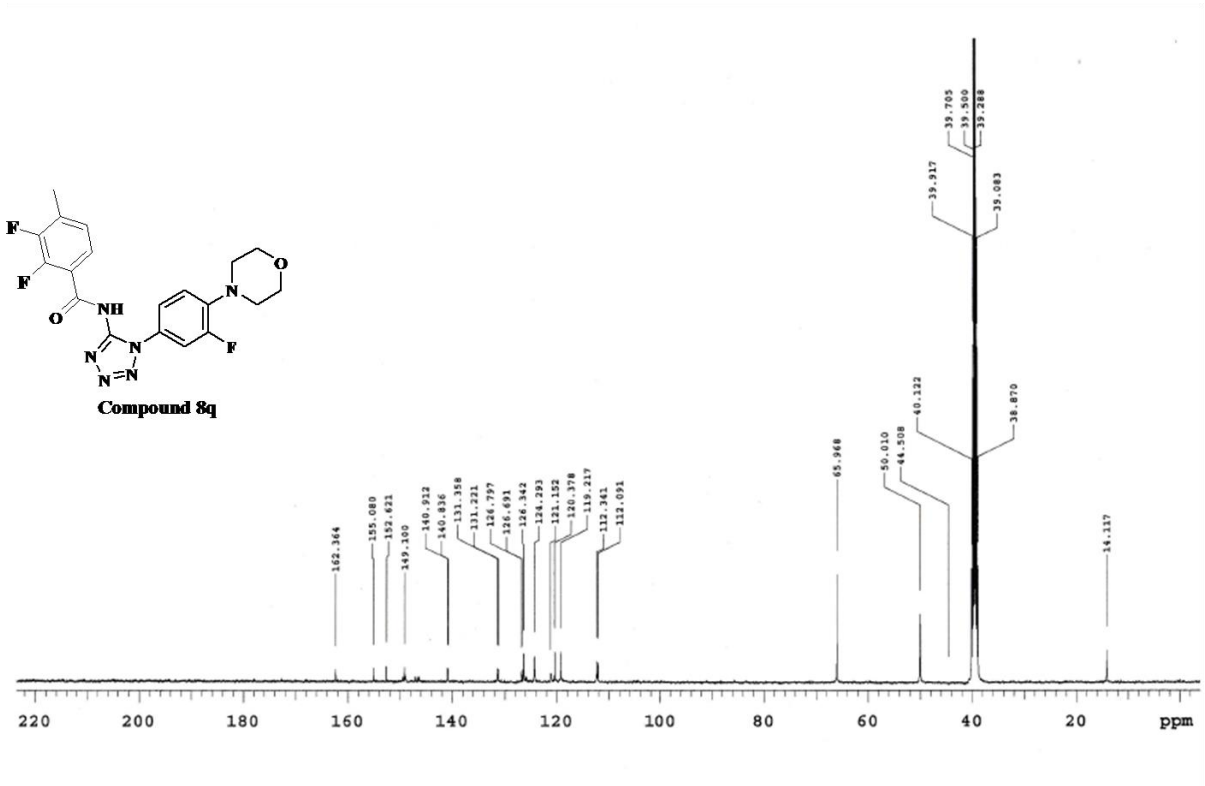


Figure 80.^{13}C NMR Spectra of Compound 8q

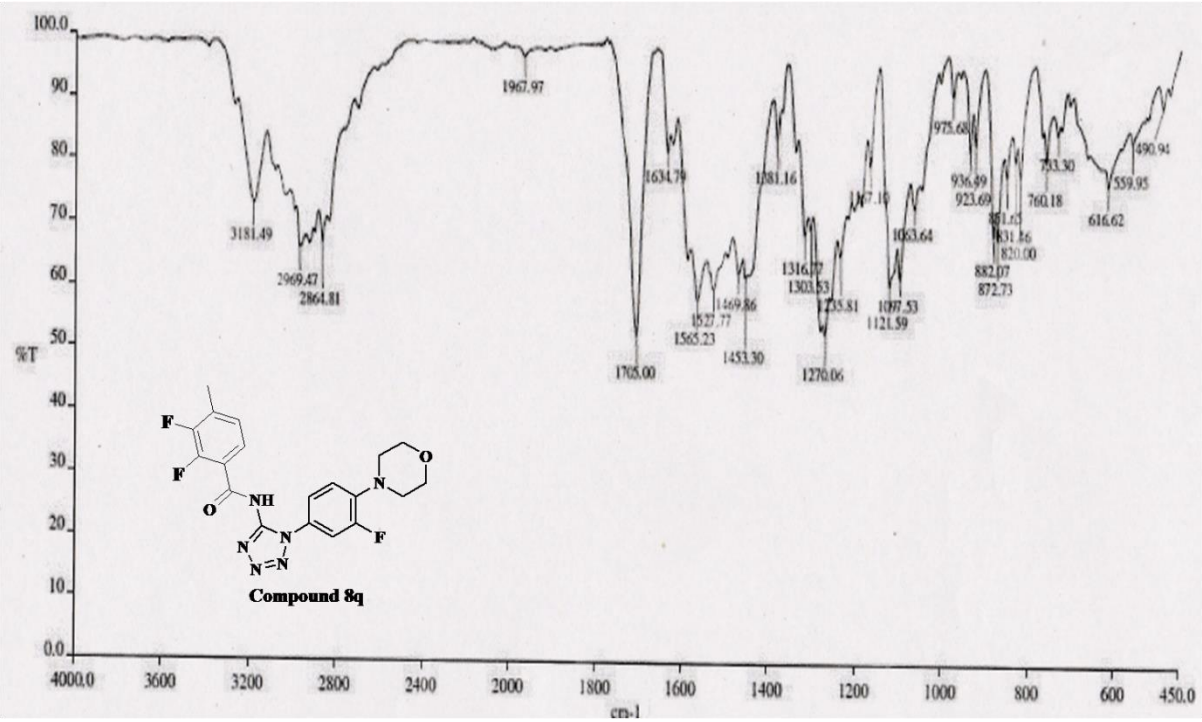


Figure 81. FT-IR Spectra of Compound 8q

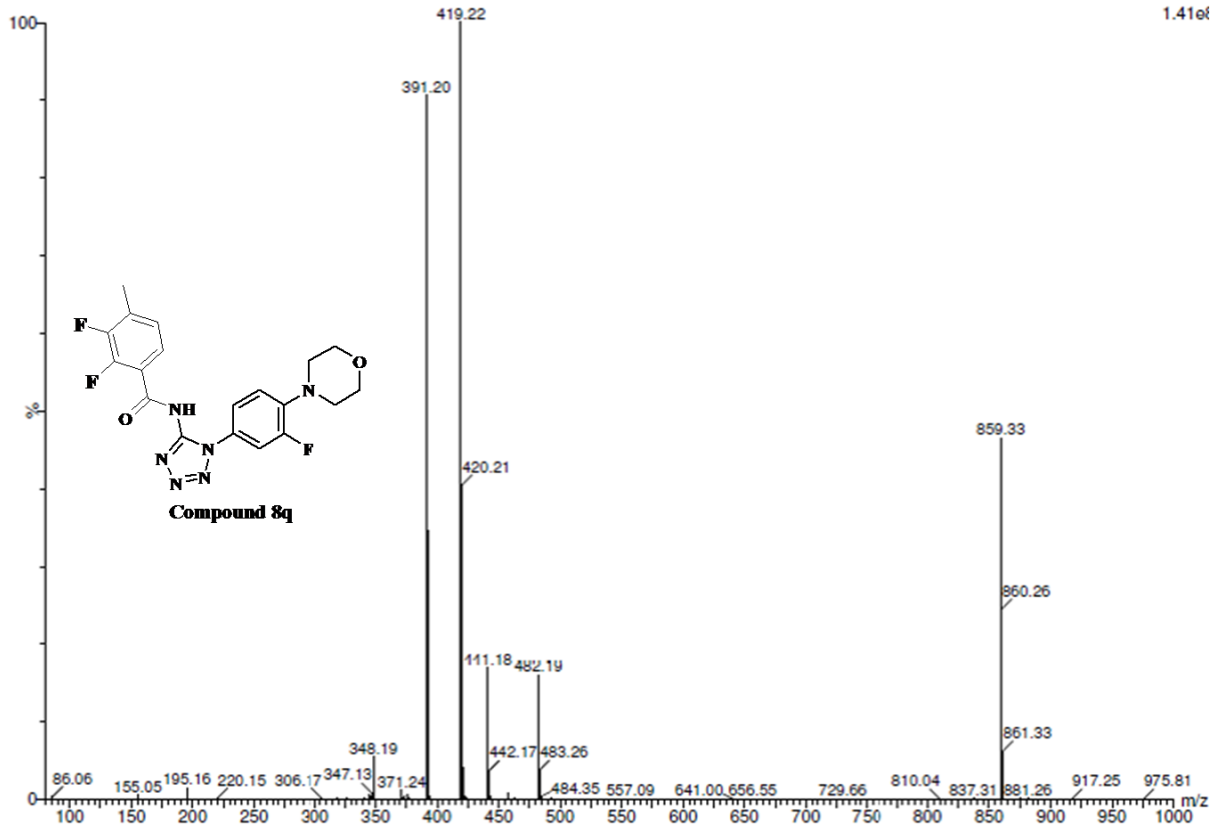


Figure 82. ESI-MS Spectra of Compound 8q

Analytical data of Compound 8r

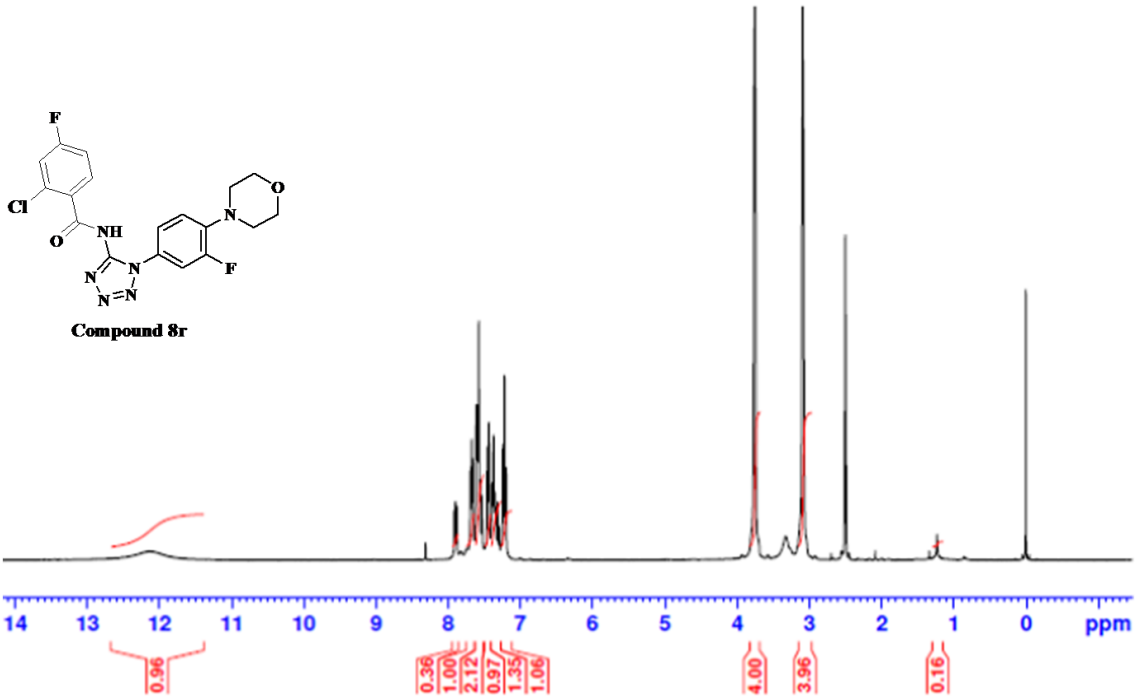


Figure 83.^{1}H NMR Spectra of Compound 8r

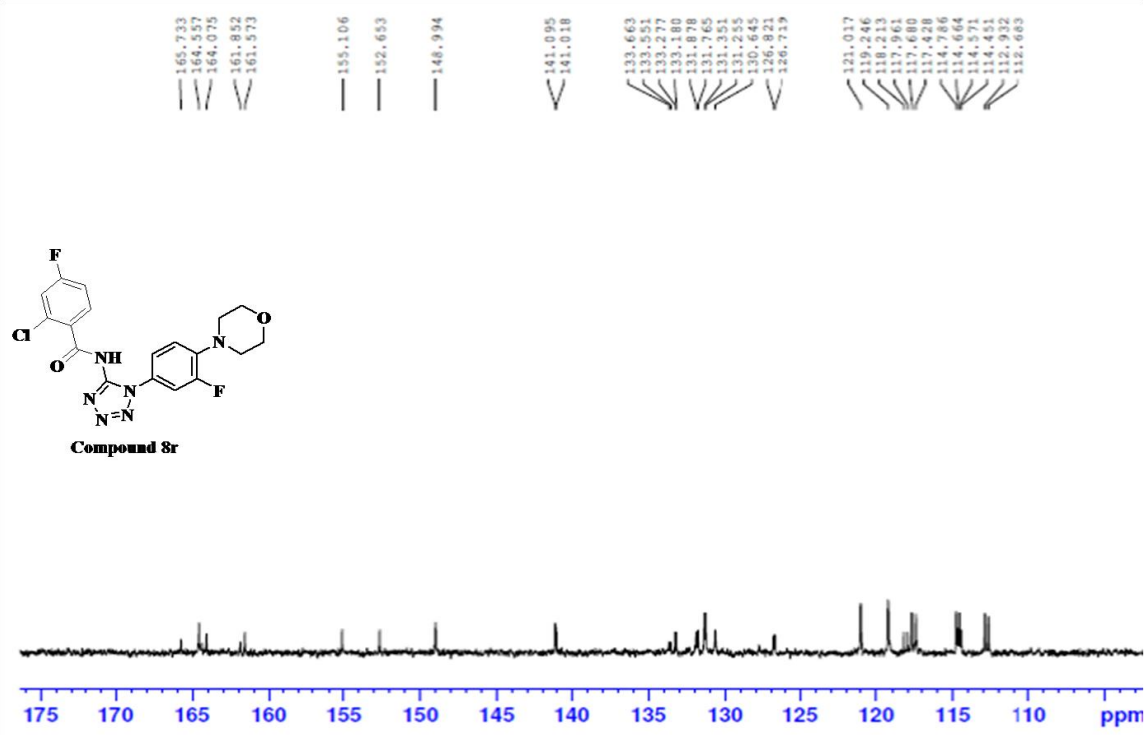


Figure 84.^{13}C NMR Spectra of Compound 8r

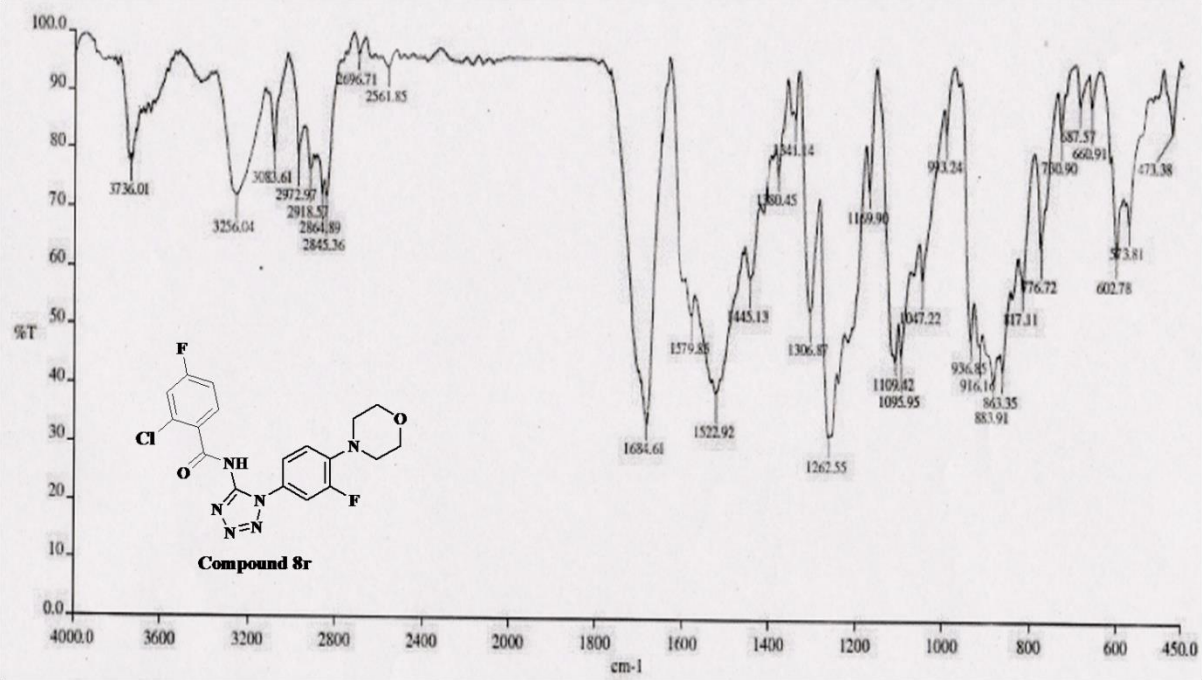


Figure 85. FT-IR Spectra of Compound 8r

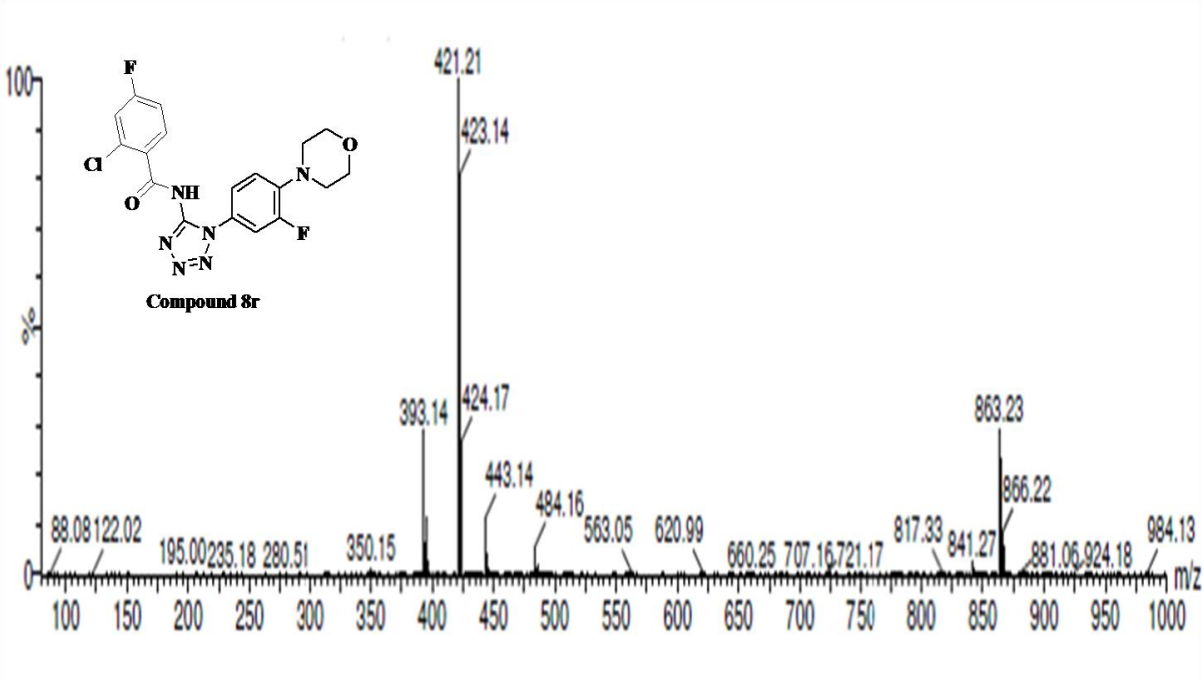


Figure 86. ESI-MS Spectra of Compound 8r

Analytical data of Compound 10a

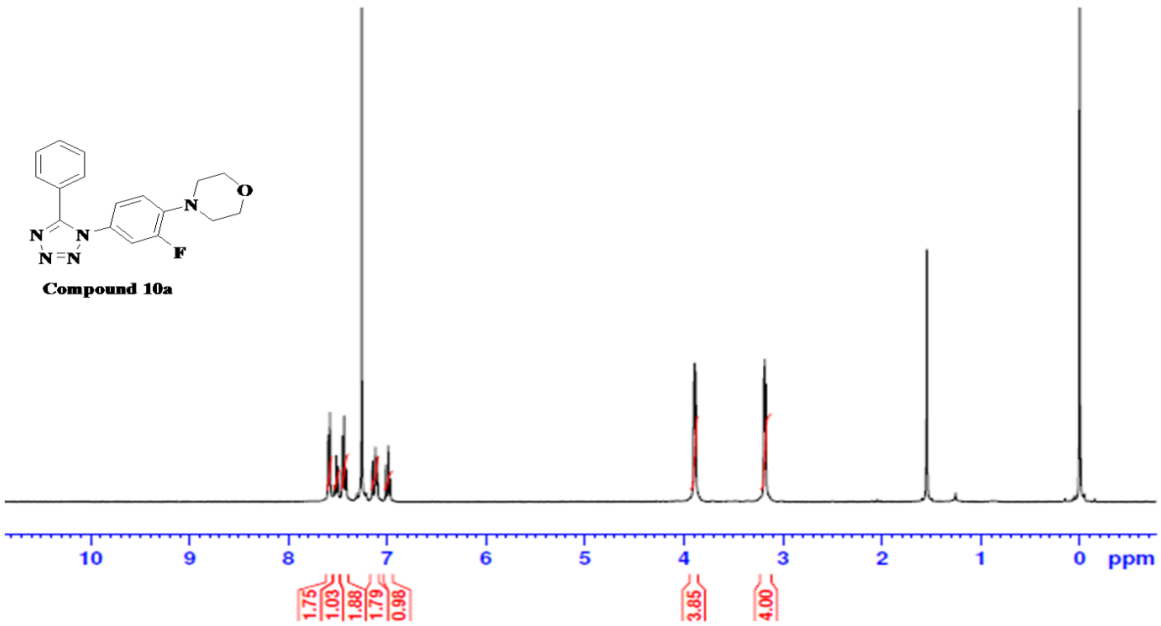


Figure 87.^{1}H NMR Spectra of Compound 10a

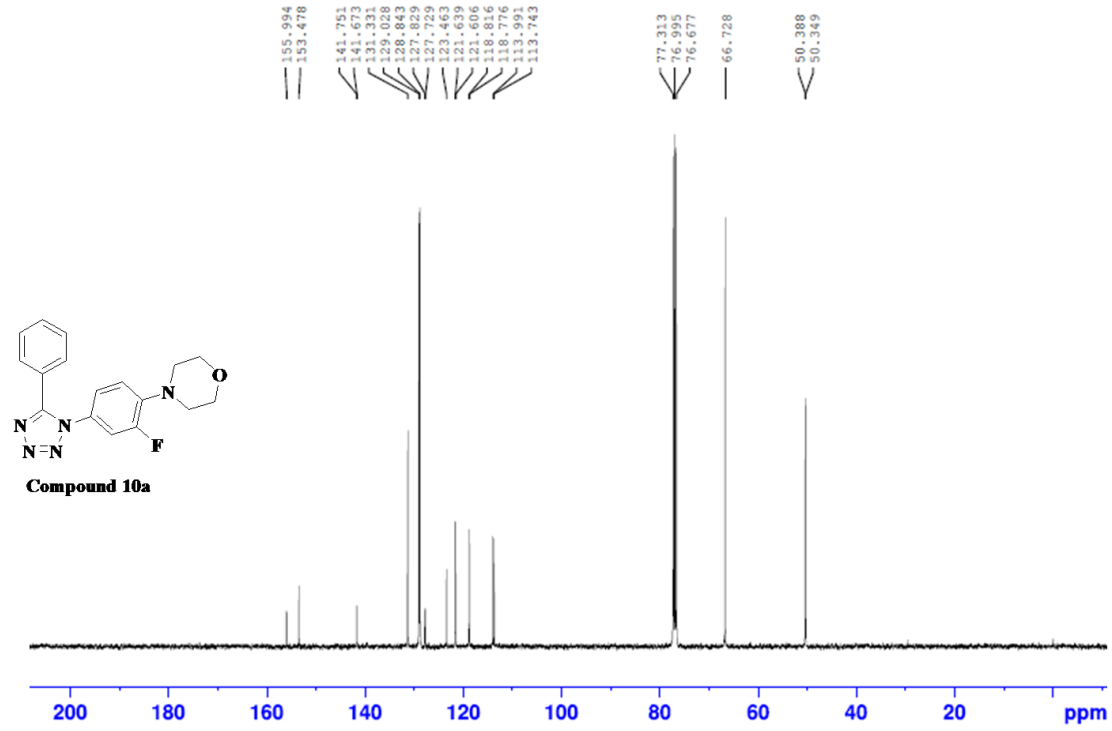


Figure 88.^{13}C NMR Spectra of Compound 10a

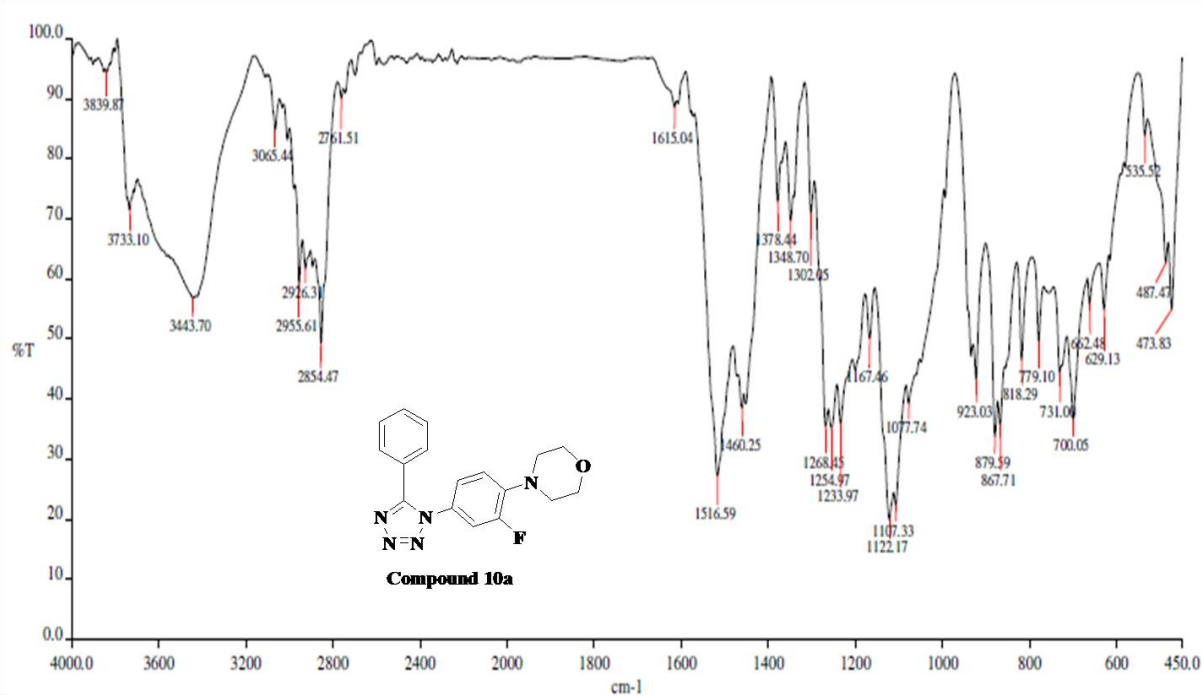


Figure 89. FT-IR Spectra of Compound 10a

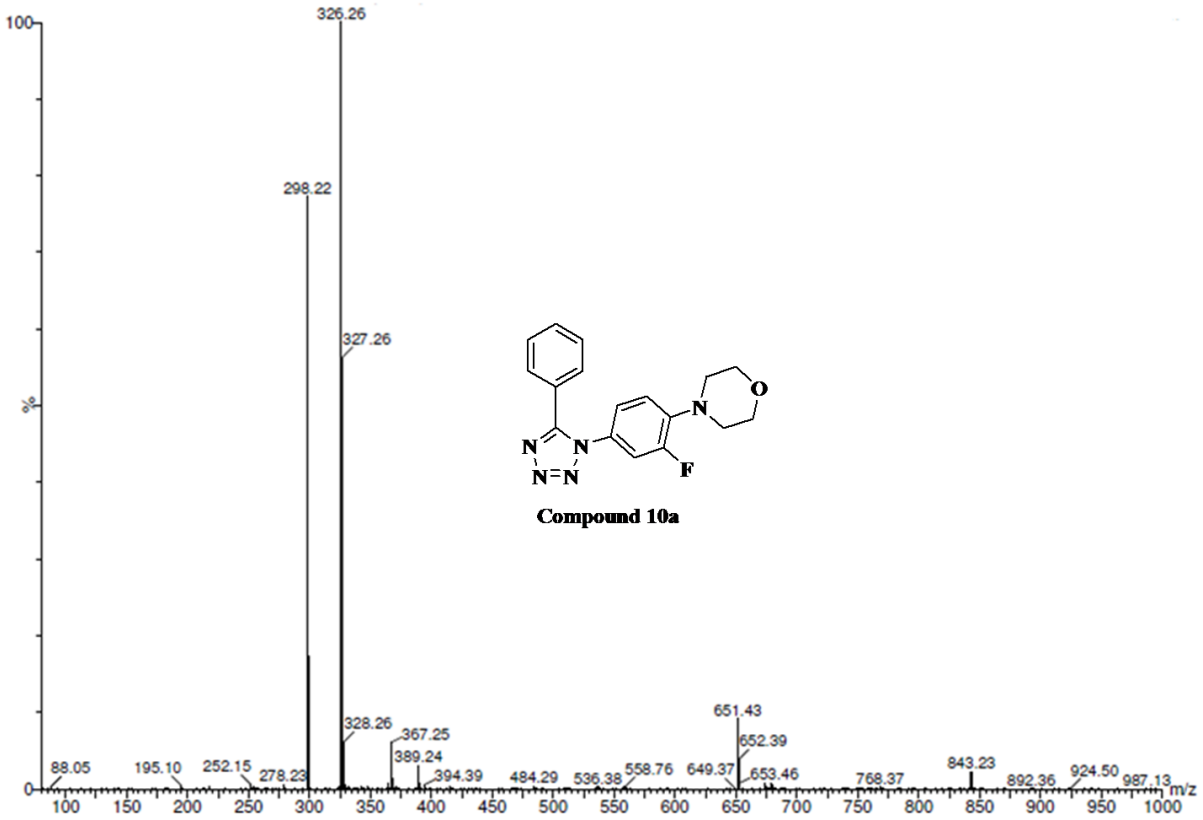


Figure 90. ESI-MS Spectra of Compound 10a

Analytical data of Compound 10b

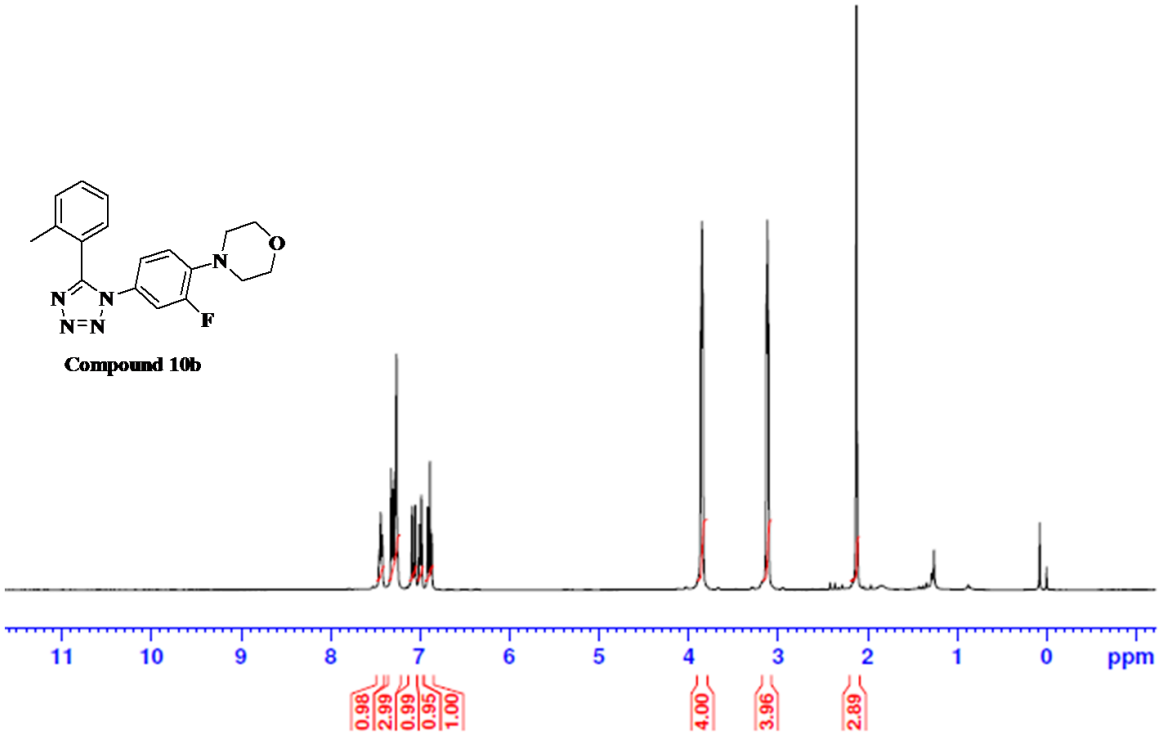


Figure 91.^{1}H NMR Spectra of Compound 10b

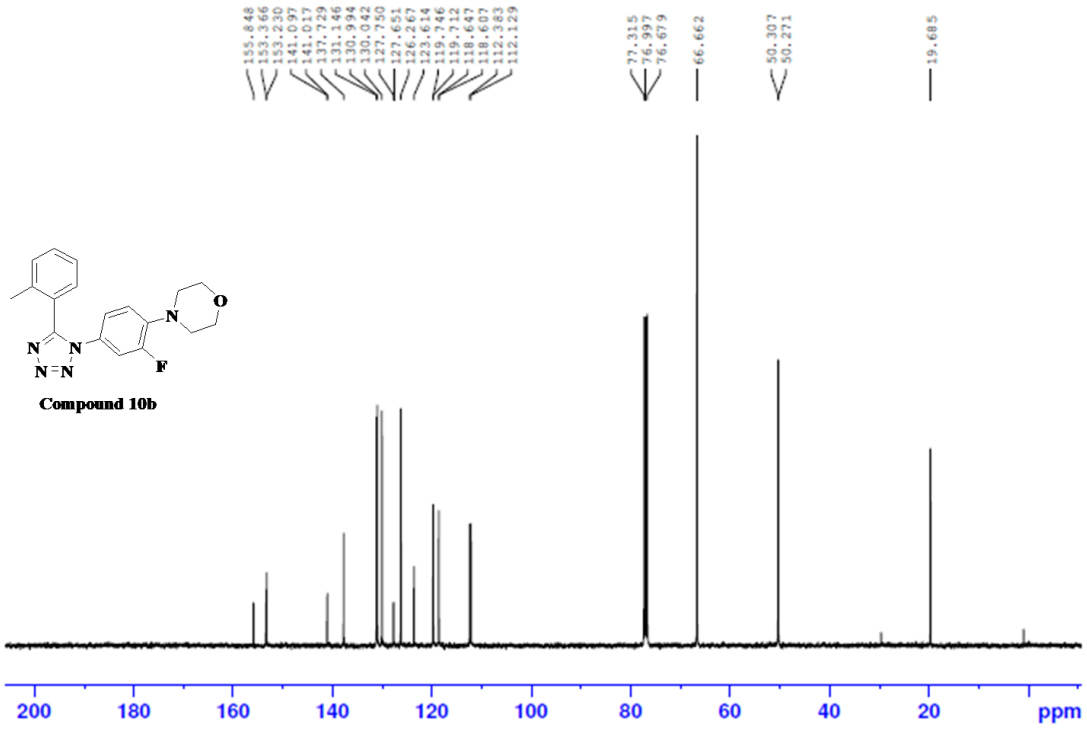


Figure 92.^{13}C NMR Spectra of Compound 10b

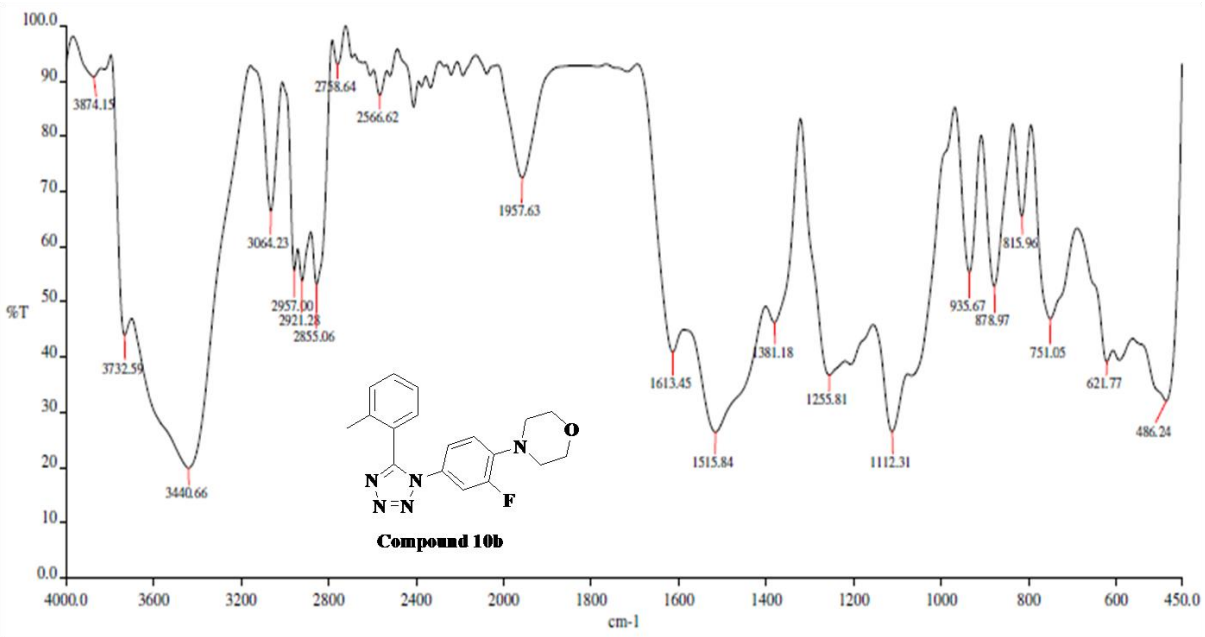


Figure 93. FT-IR Spectra of Compound 10b

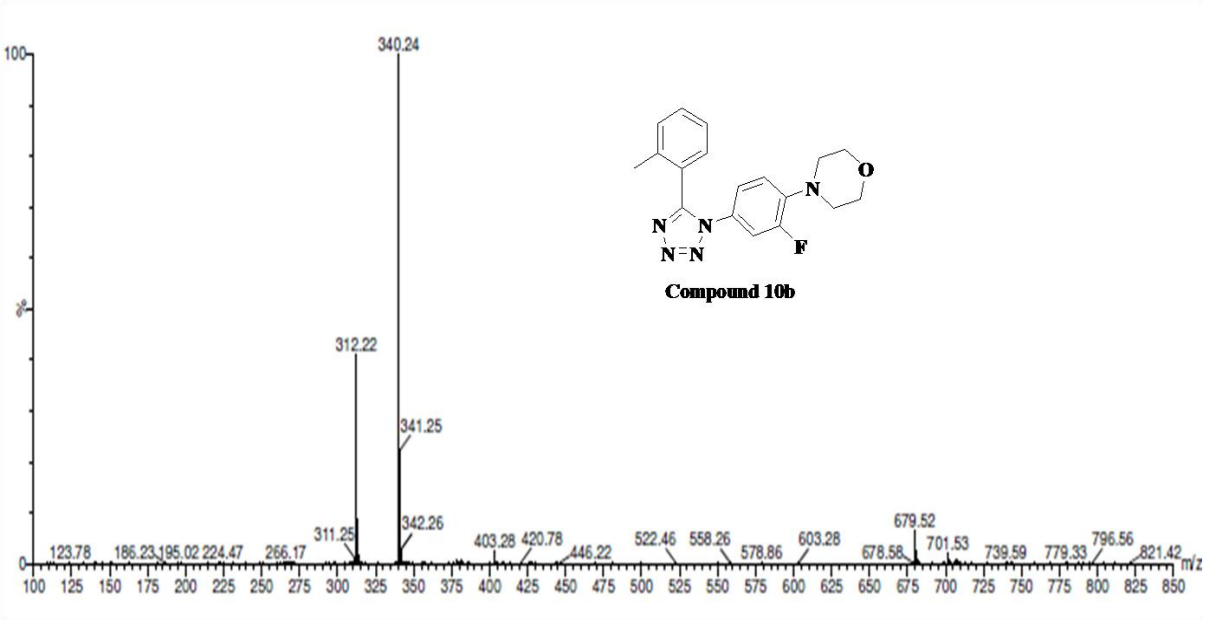


Figure 94. ESI-MS Spectra of Compound 10b

Analytical data of Compound 10c

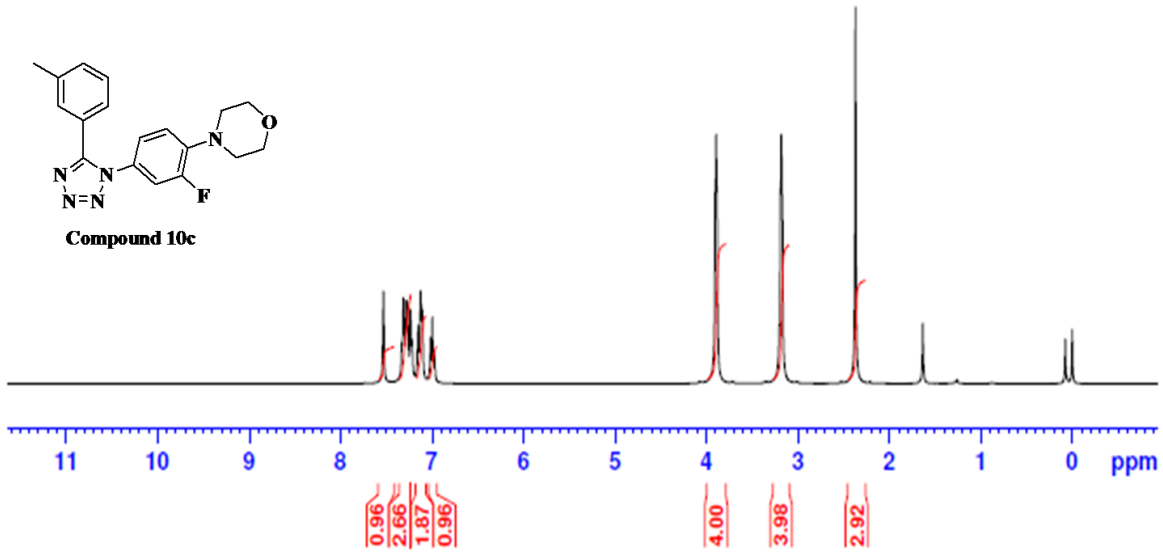


Figure 95.^{1}H NMR Spectra of Compound 10c

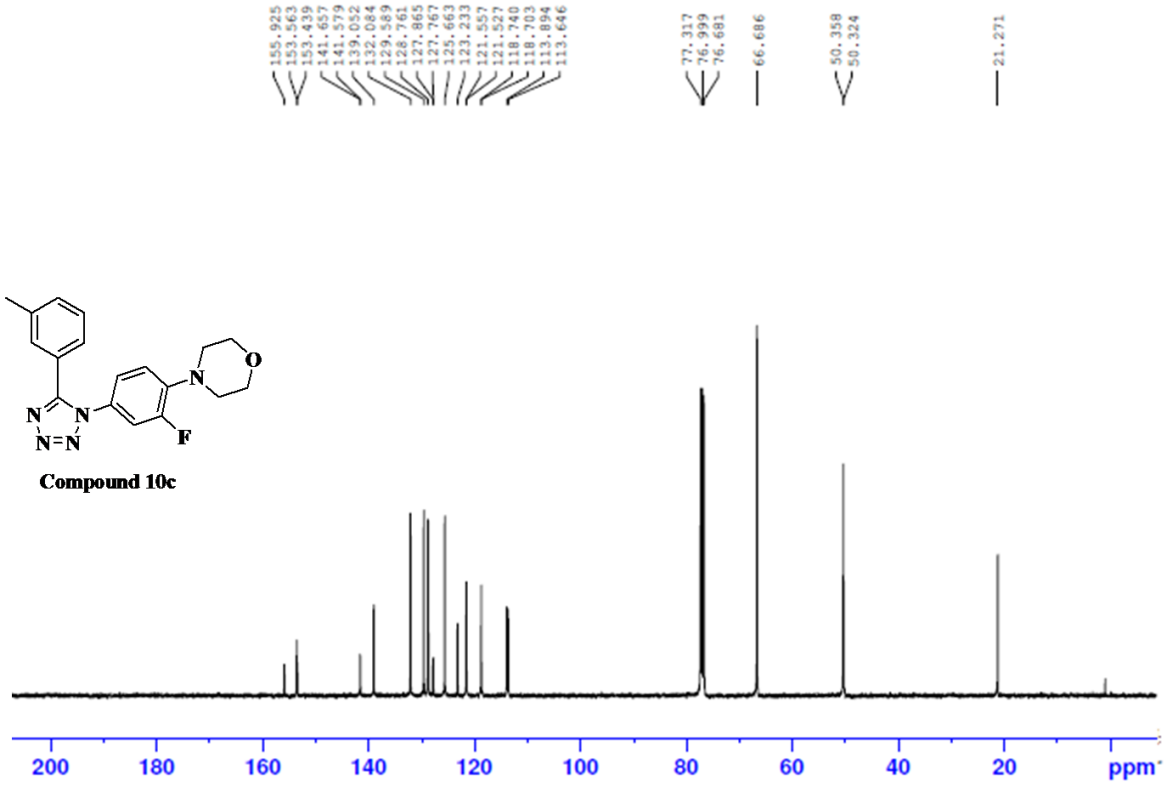


Figure.96.^{13}C NMR Spectra of Compound 10c

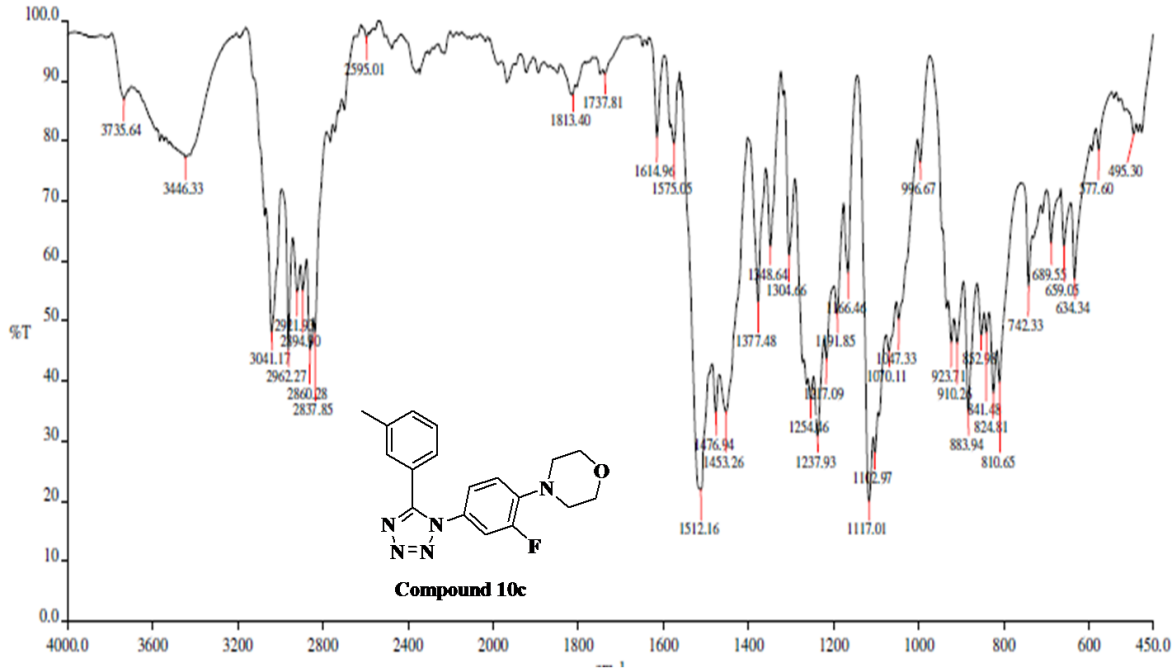


Figure 97. FT-IR Spectra of Compound 10c

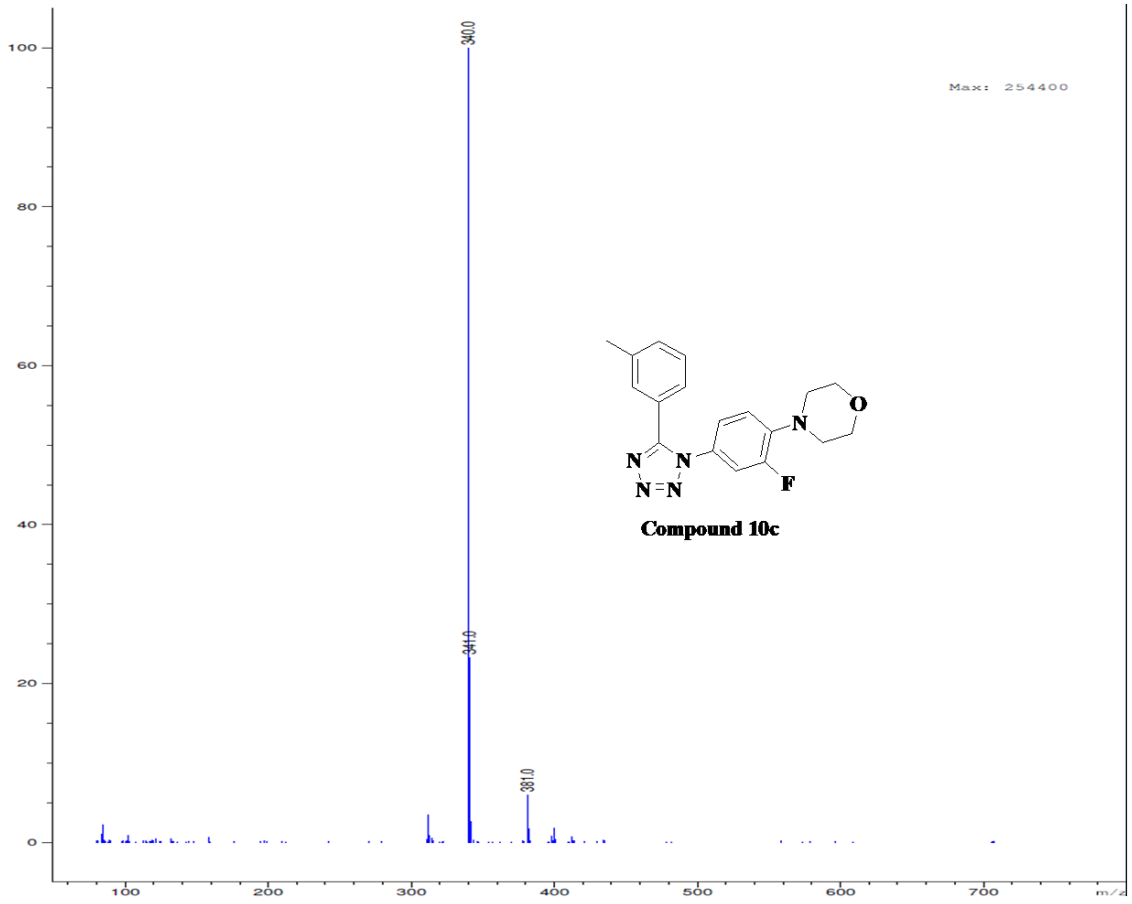


Figure 98. ESI-MS Spectra of Compound 10c

Analytical data of Compound 10d

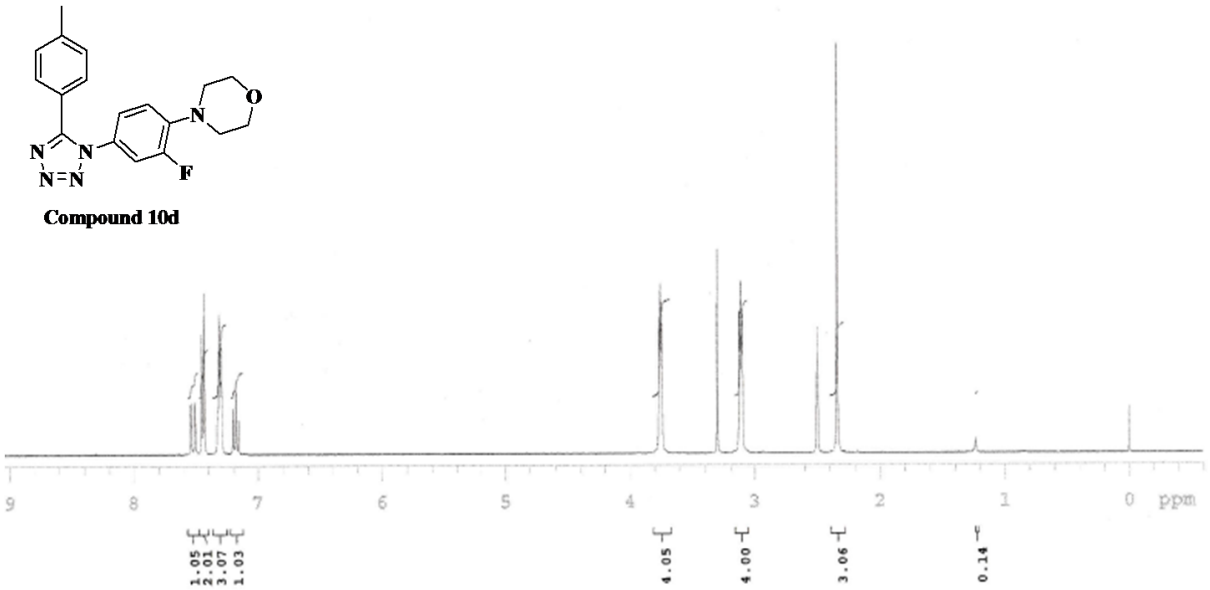


Figure 99.^{1}H NMR Spectra of Compound 10d

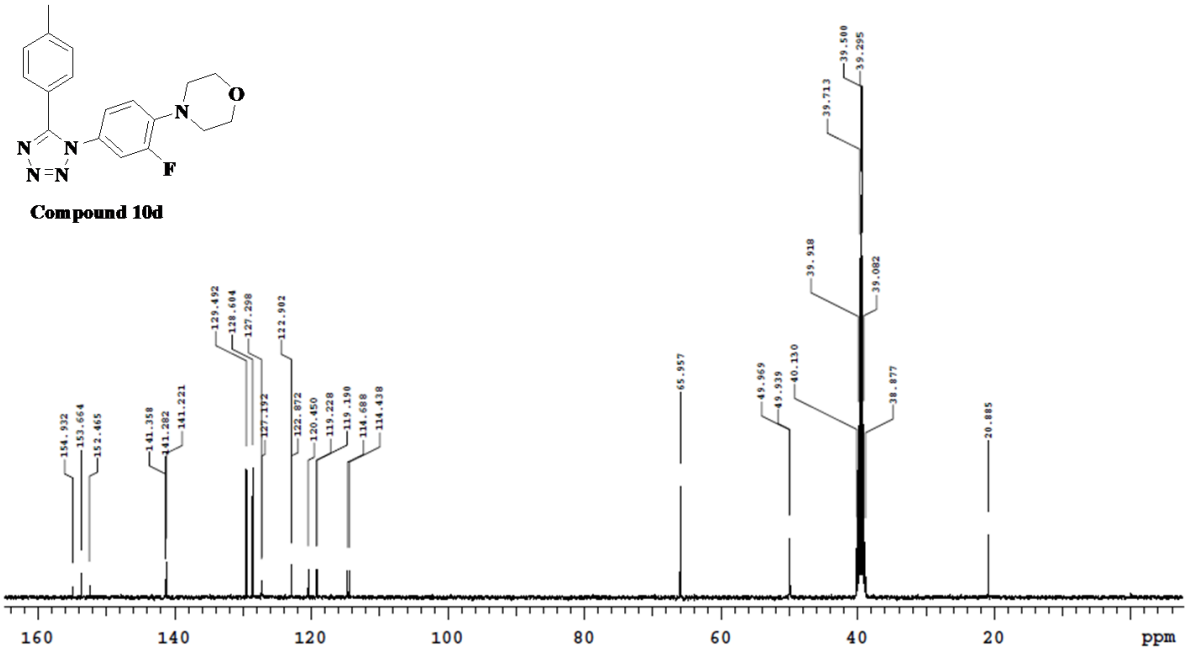


Figure 100.^{13}C NMR Spectra of Compound 10d

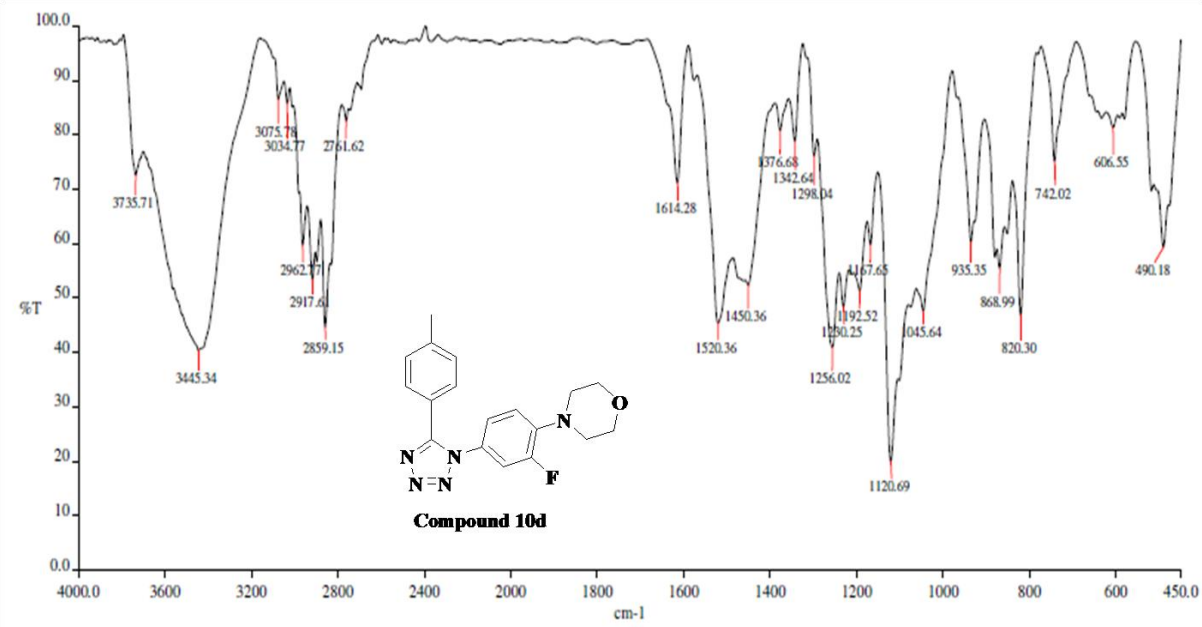


Figure 101. FT-IR Spectra of Compound 10d

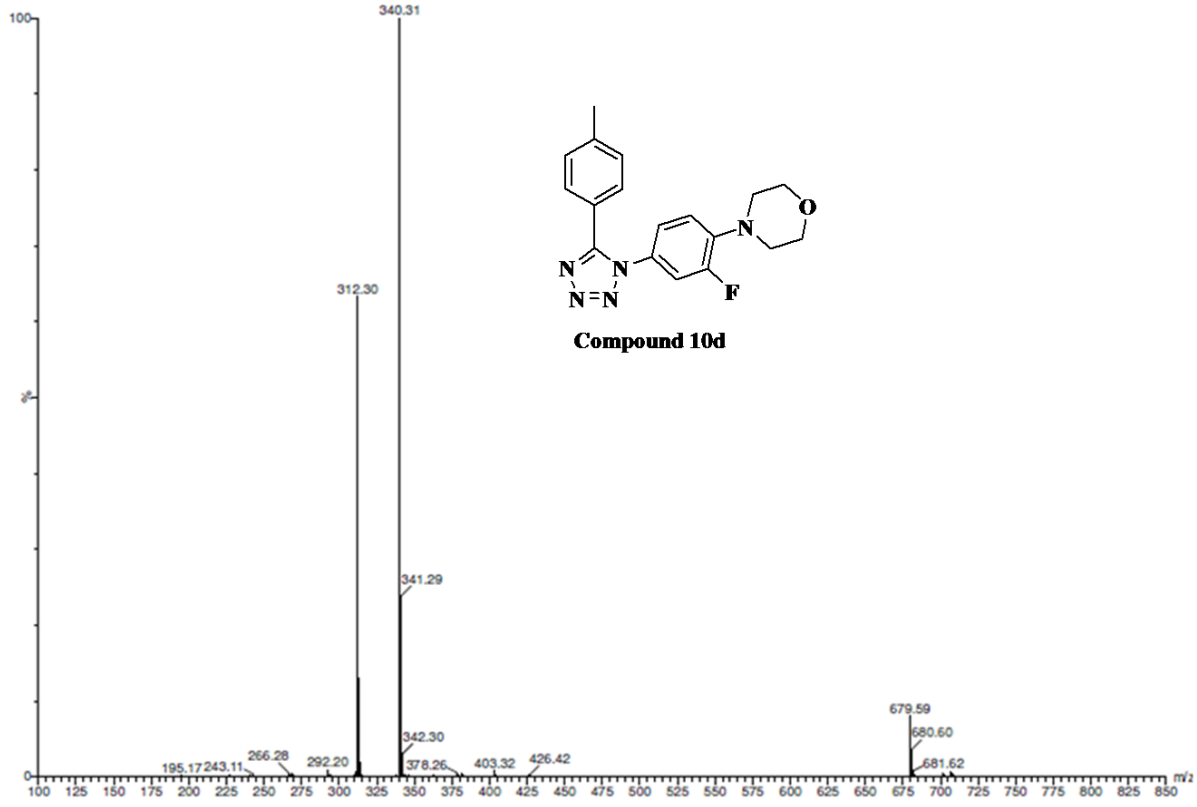


Figure 102. ESI-MS Spectra of Compound 10d

Analytical data of Compound 10e

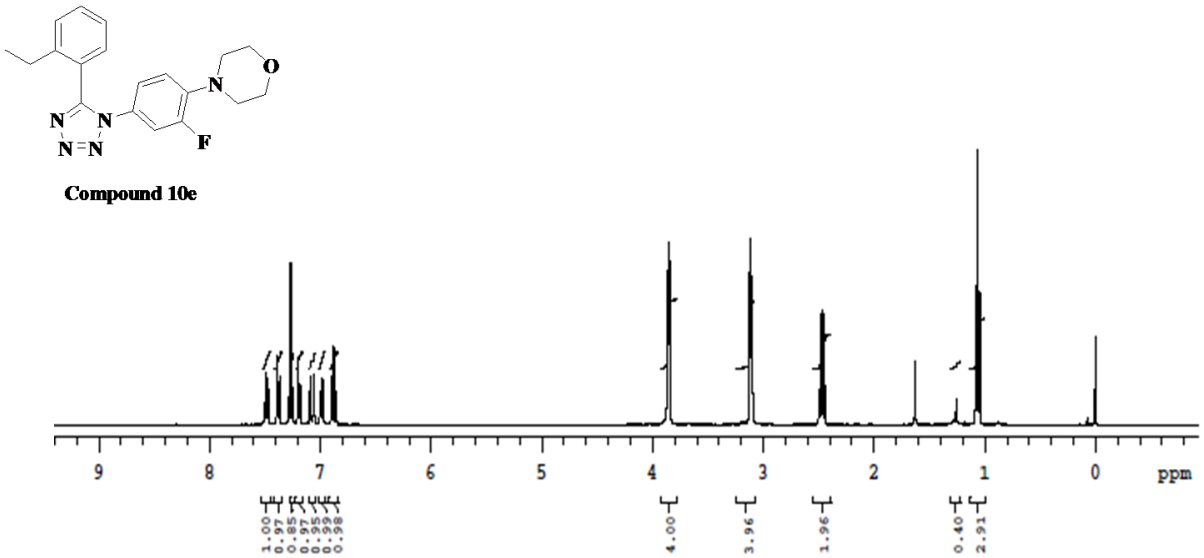


Figure 103.^{1}H NMR Spectra of Compound 10e

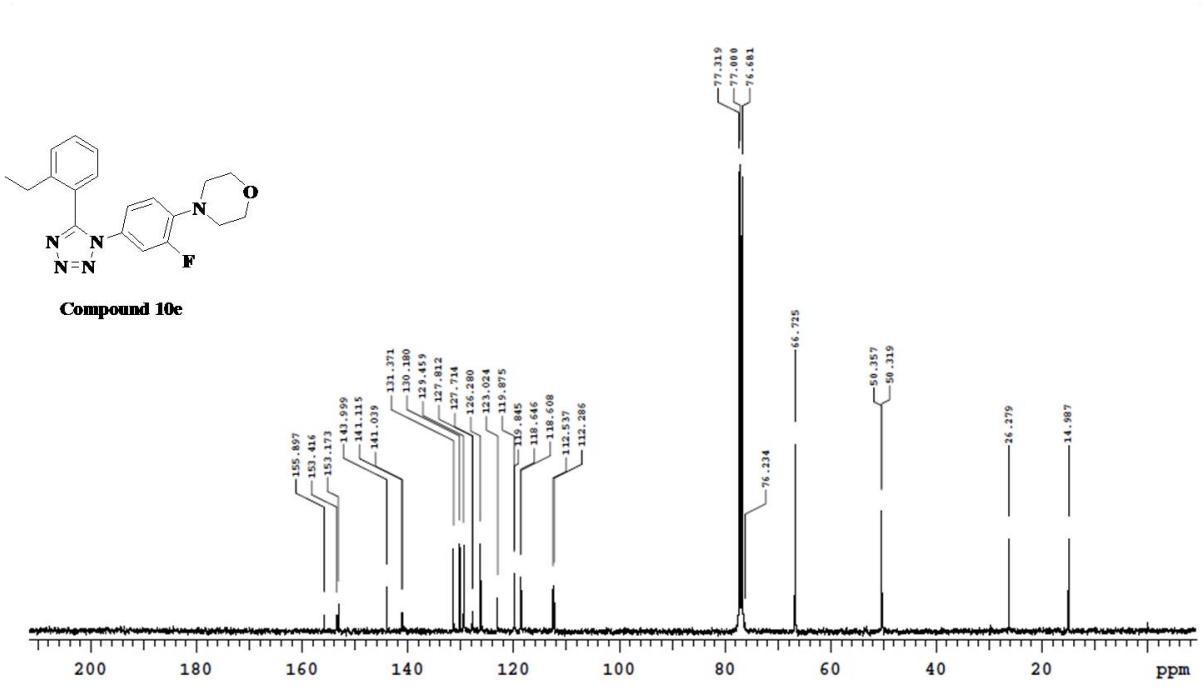


Figure 104.^{13}C NMR Spectra of Compound 10e

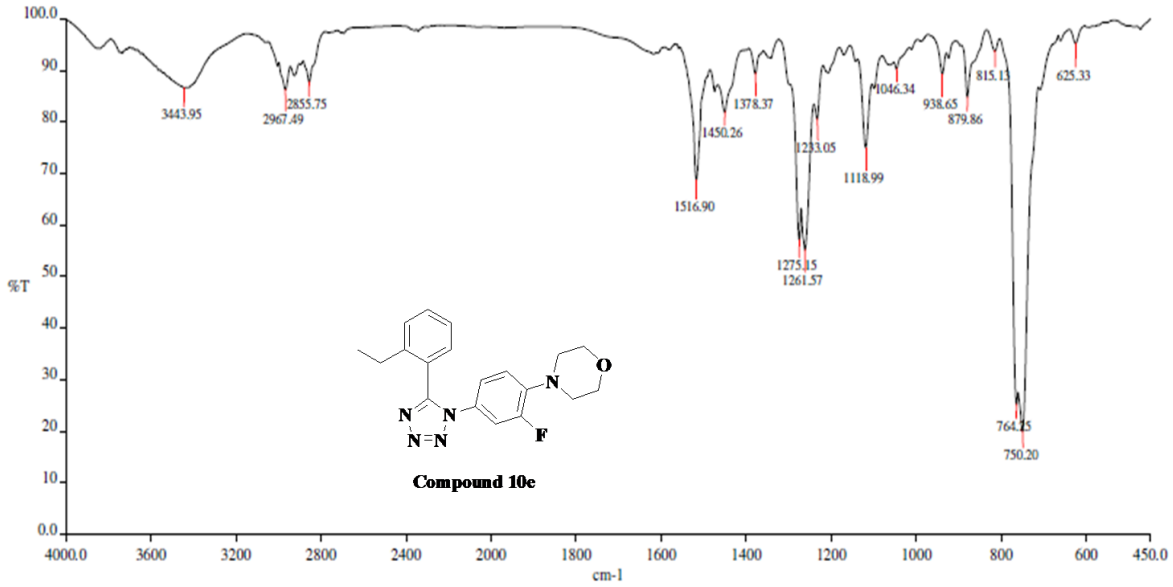


Figure 105. FT-IR Spectra of Compound 10e

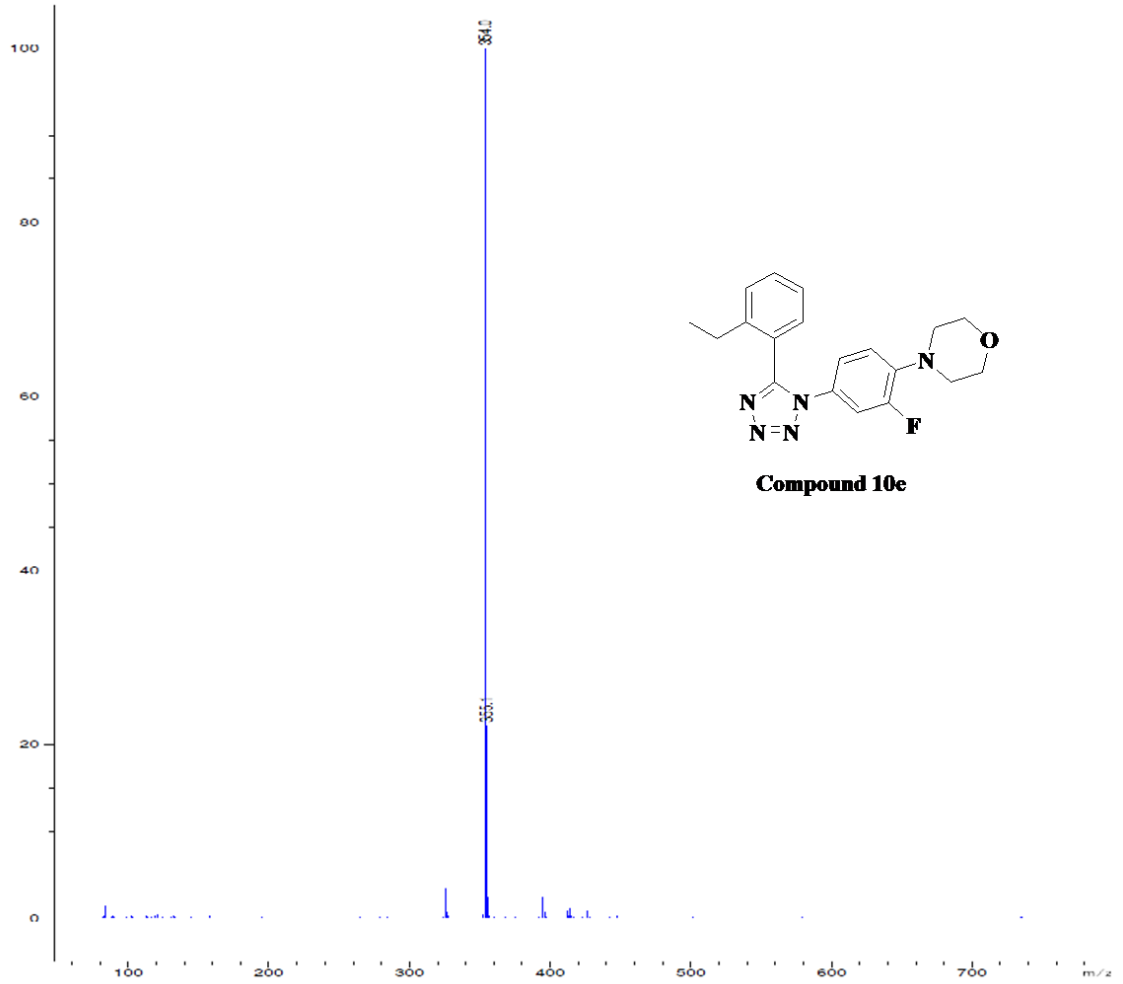


Figure 106. ESI-MS Spectra of Compound 10e

Analytical data of Compound 10f

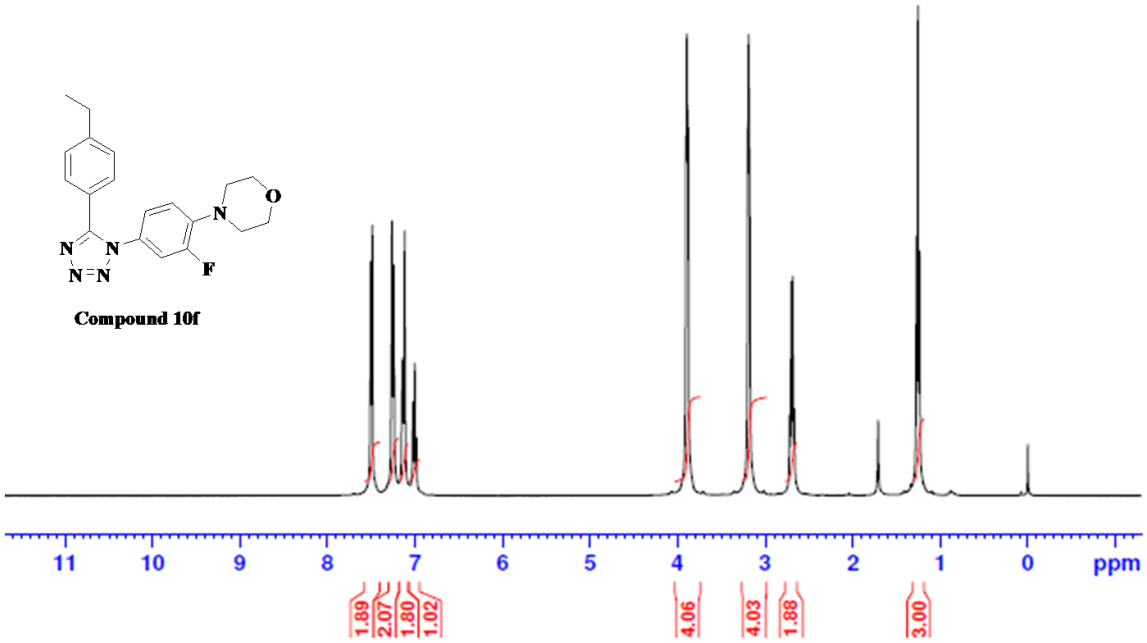


Figure 107. ^{1}H NMR Spectra of Compound 10f

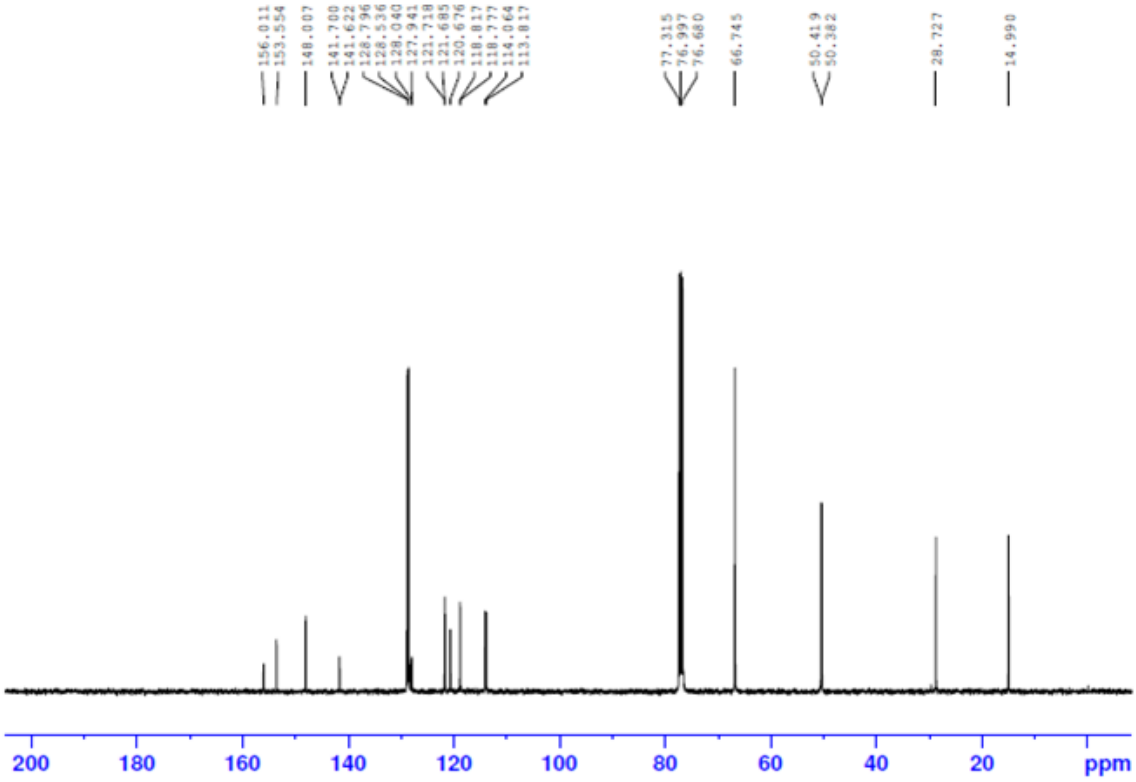


Figure 108. ^{13}C NMR Spectra of Compound 10f

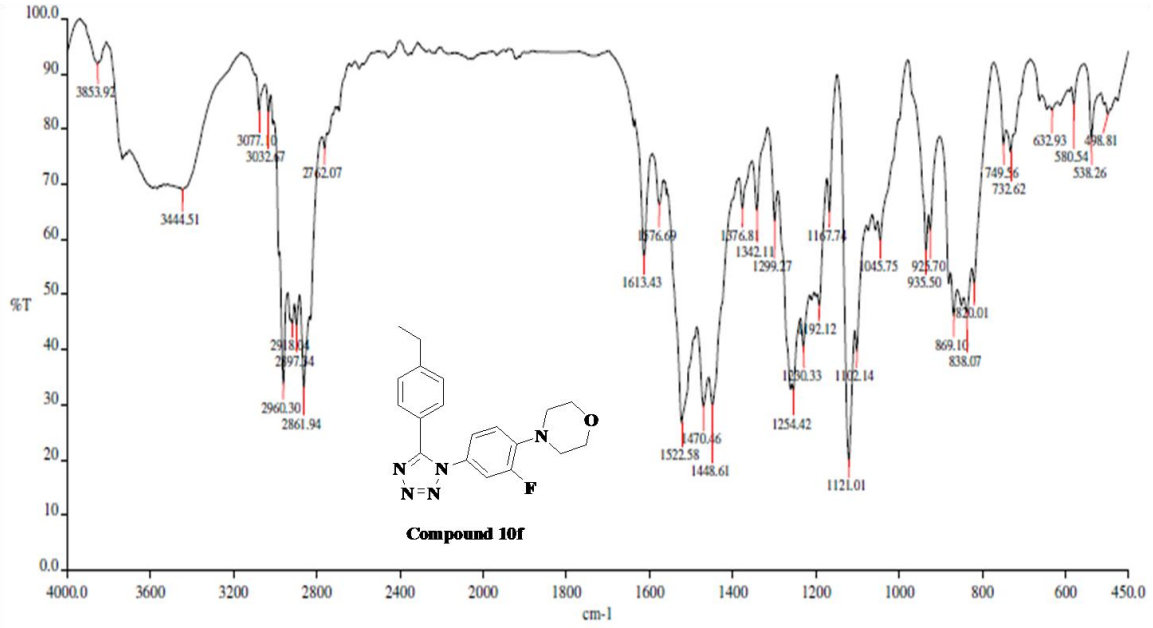


Figure 109. FT-IR Spectra of Compound 10f

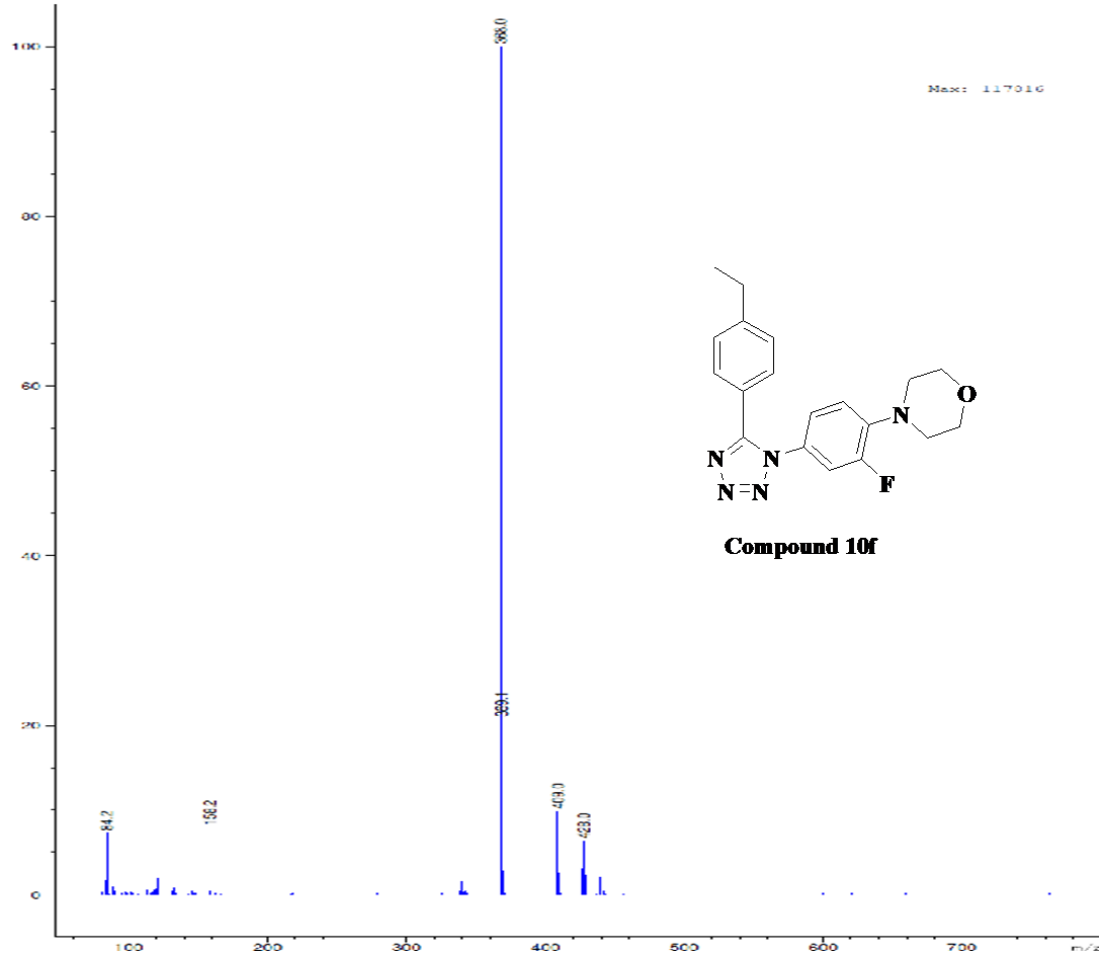


Figure 110. ESI-MS Spectra of Compound 10f

Analytical data of Compound 10g

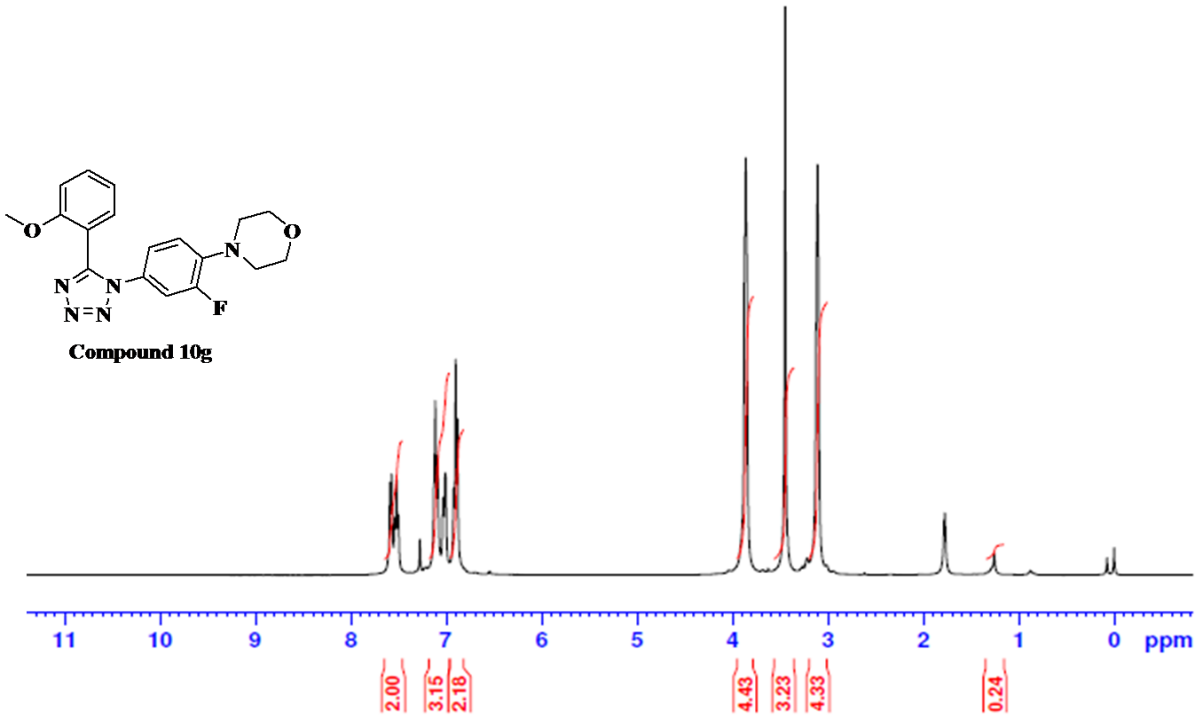


Figure 111.^{1}H NMR Spectra of Compound 10g

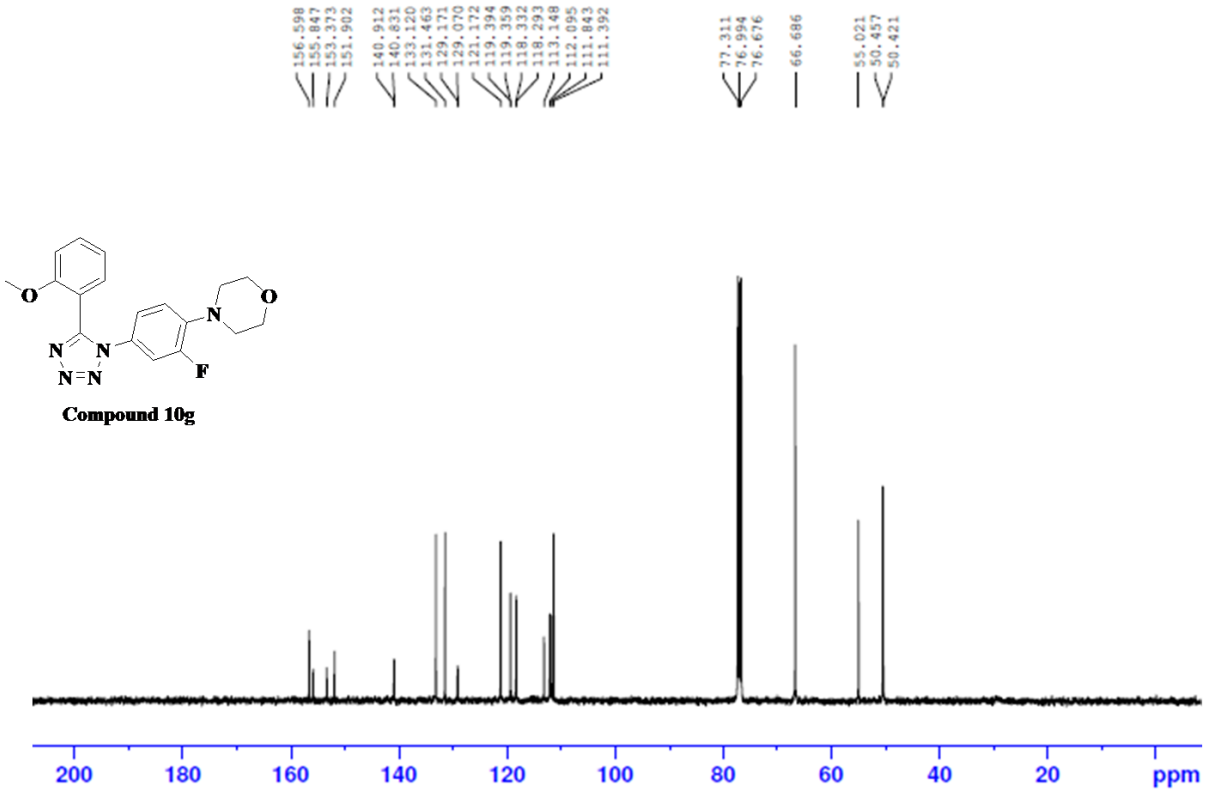


Figure 112.^{13}C NMR Spectra of Compound 10g

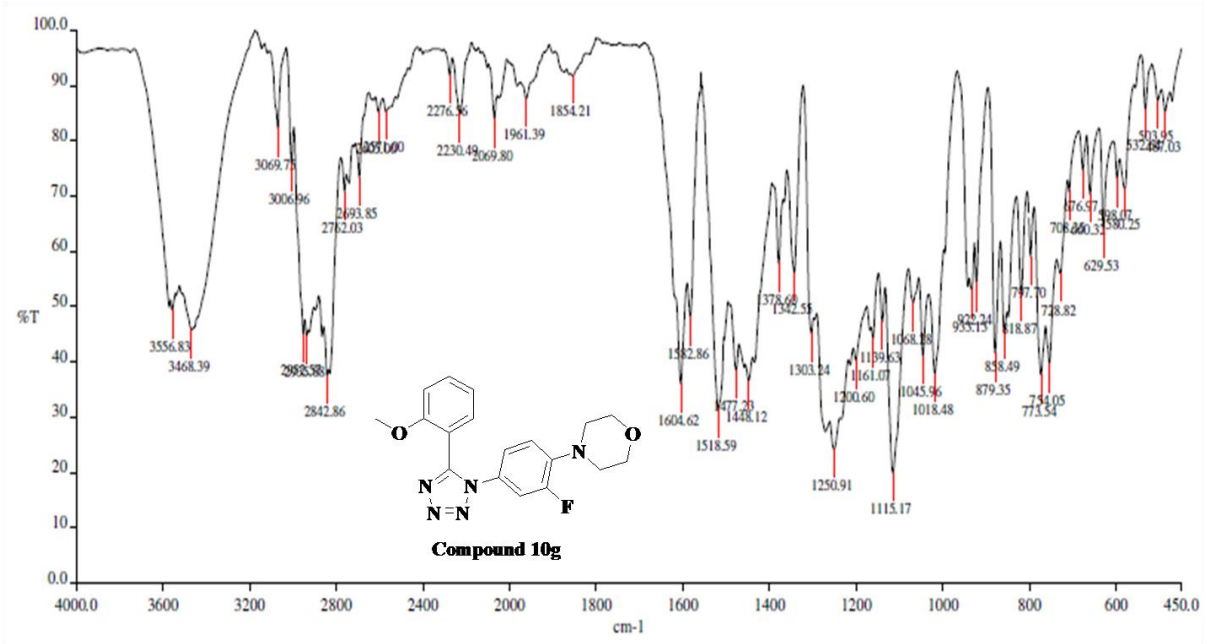


Figure 113. FT-IR Spectra of Compound 10g

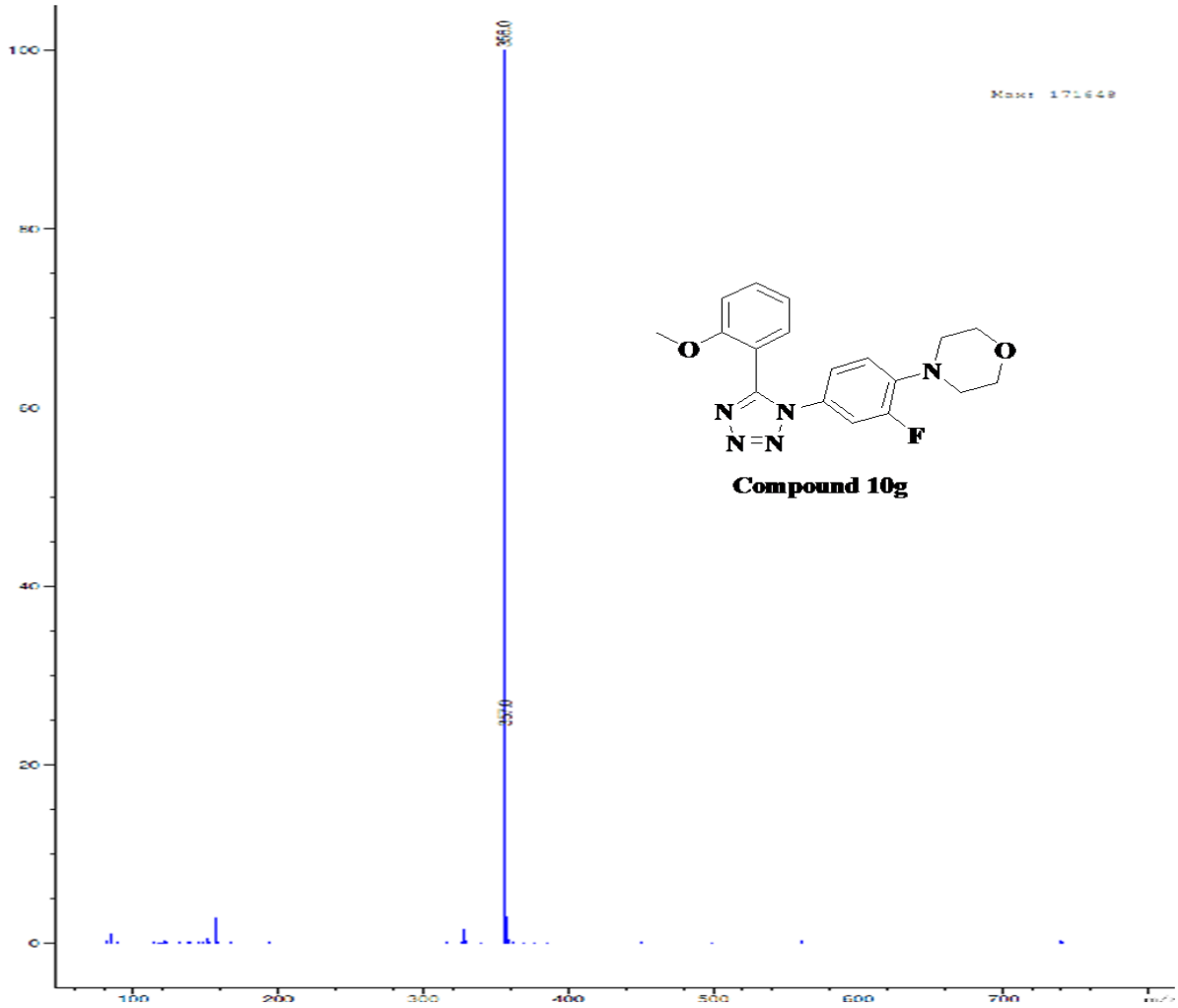


Figure 114. ESI-MS Spectra of Compound 10g

Analytical data of Compound 10h

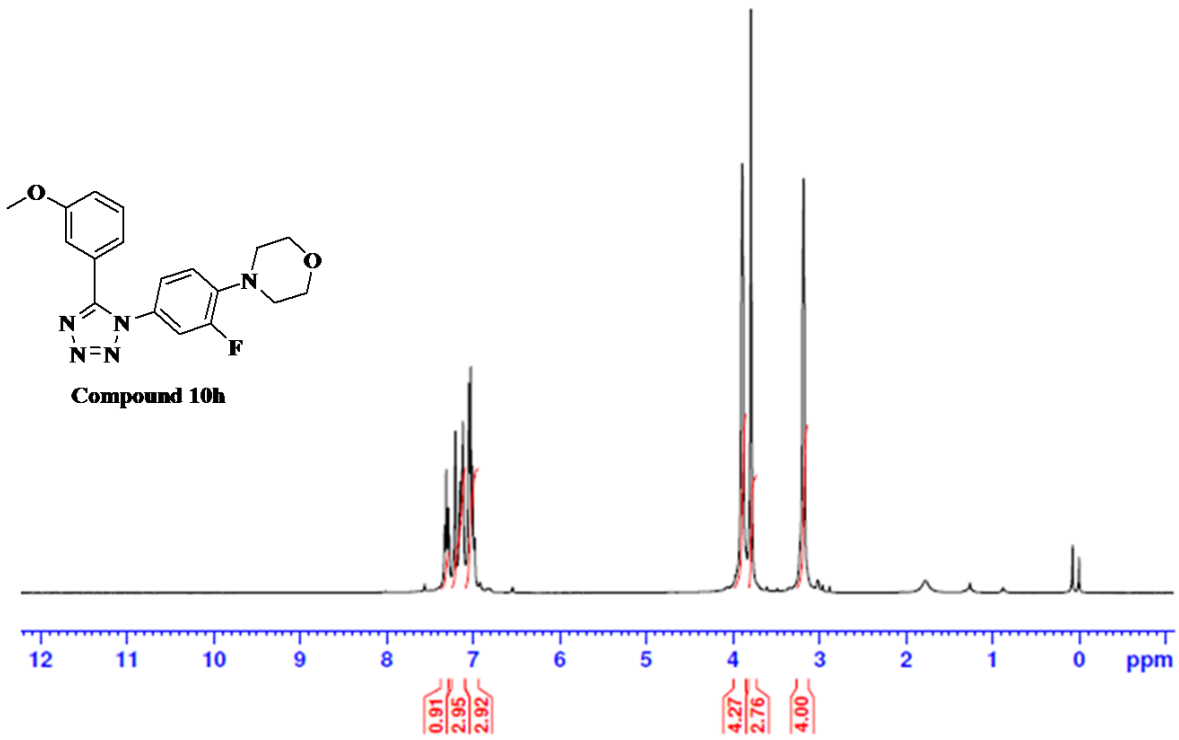


Figure 115.^{1}H NMR Spectra of Compound 10h

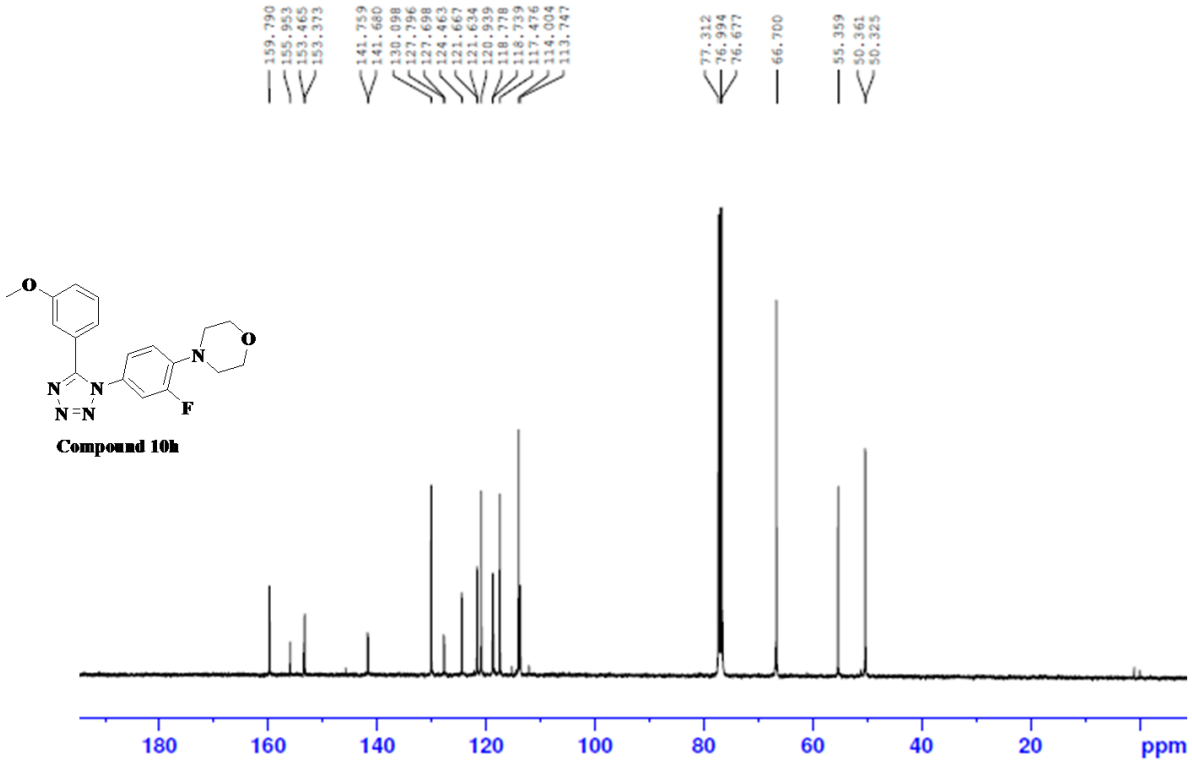


Figure 116.^{13}C NMR Spectra of Compound 10h

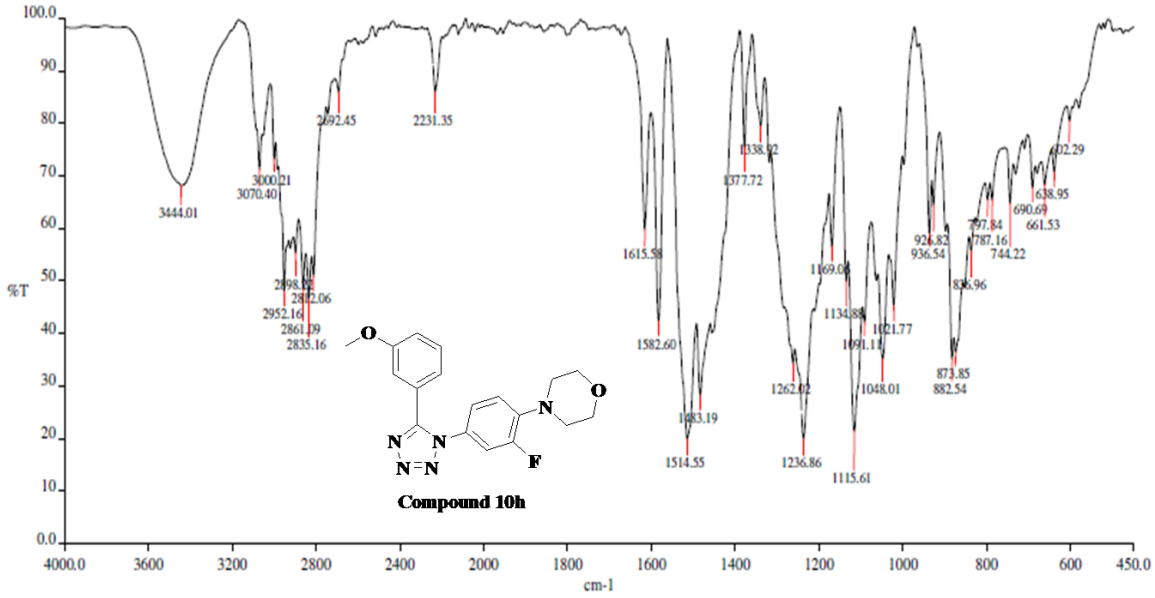


Figure 117. FT-IR Spectra of Compound 10h

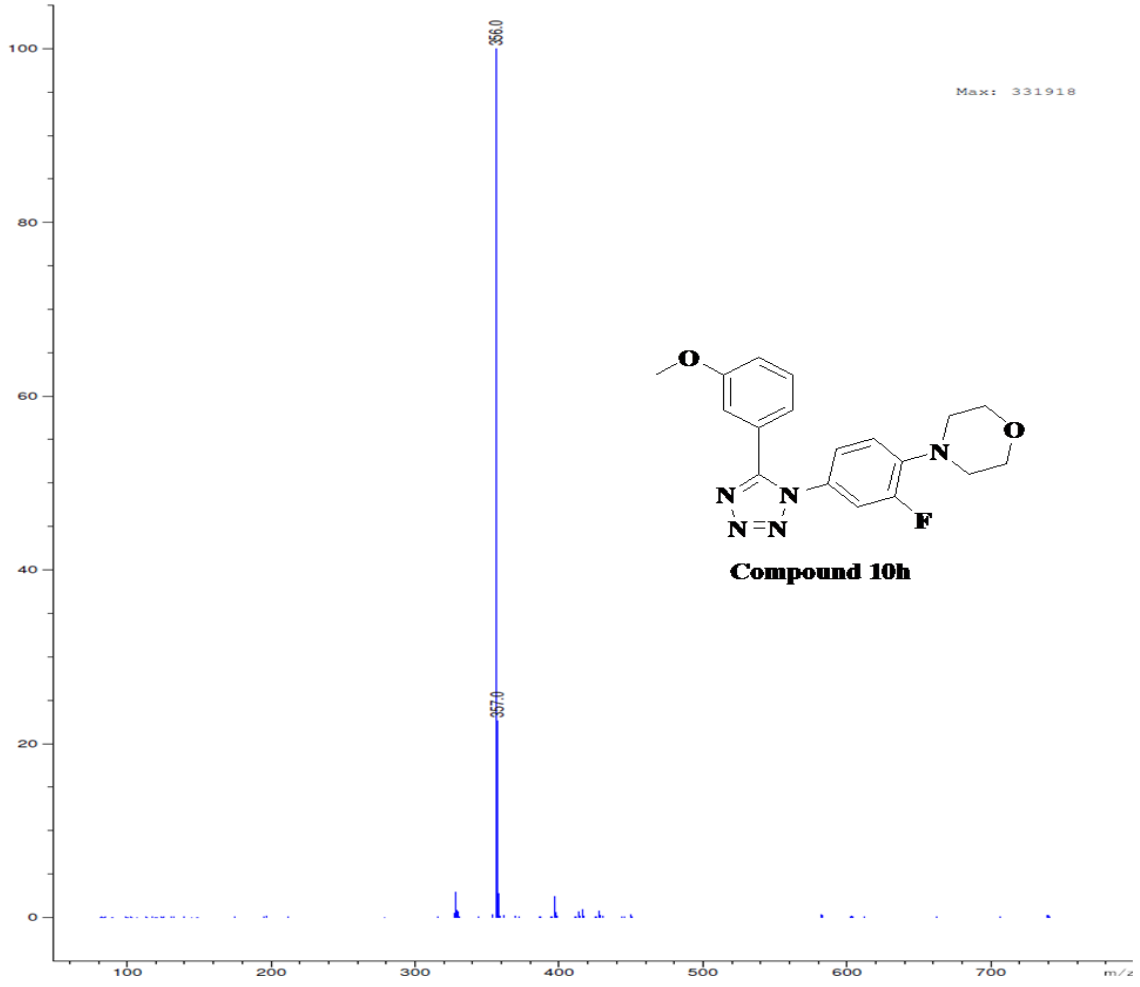


Figure 118. ESI-MS Spectra of Compound 10h

Analytical data of Compound 10i

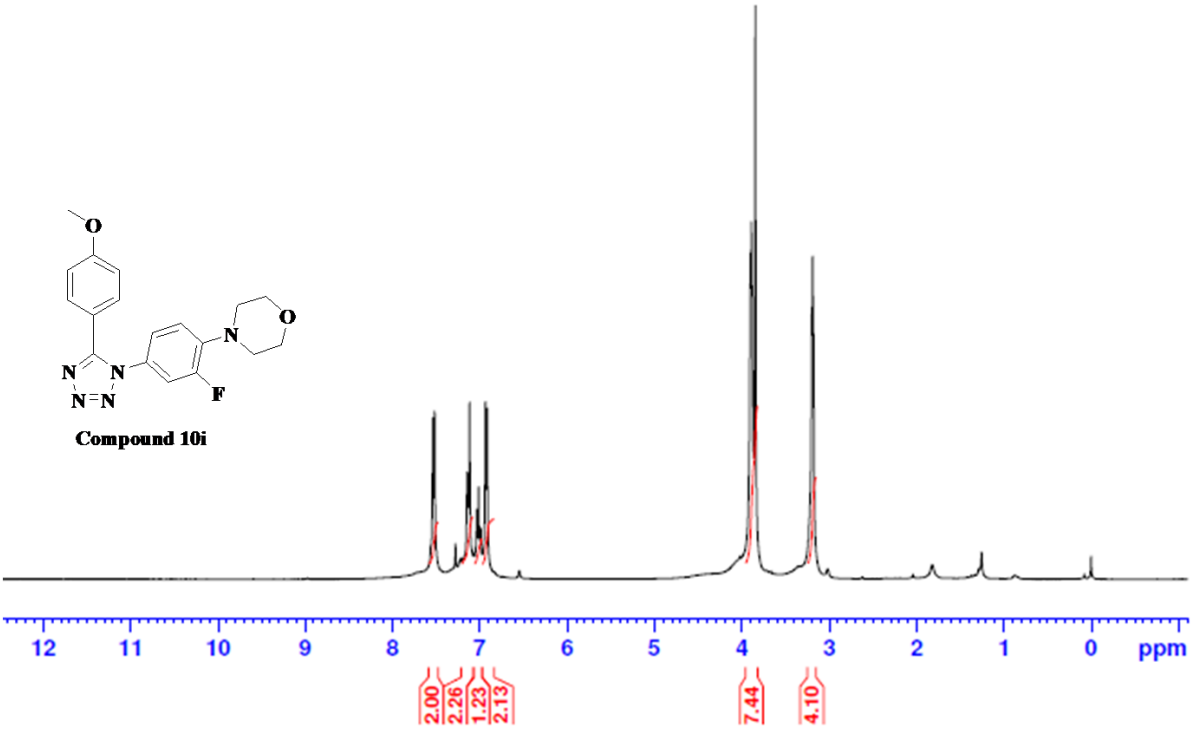


Figure 119.^{1}H NMR Spectra of Compound 10i

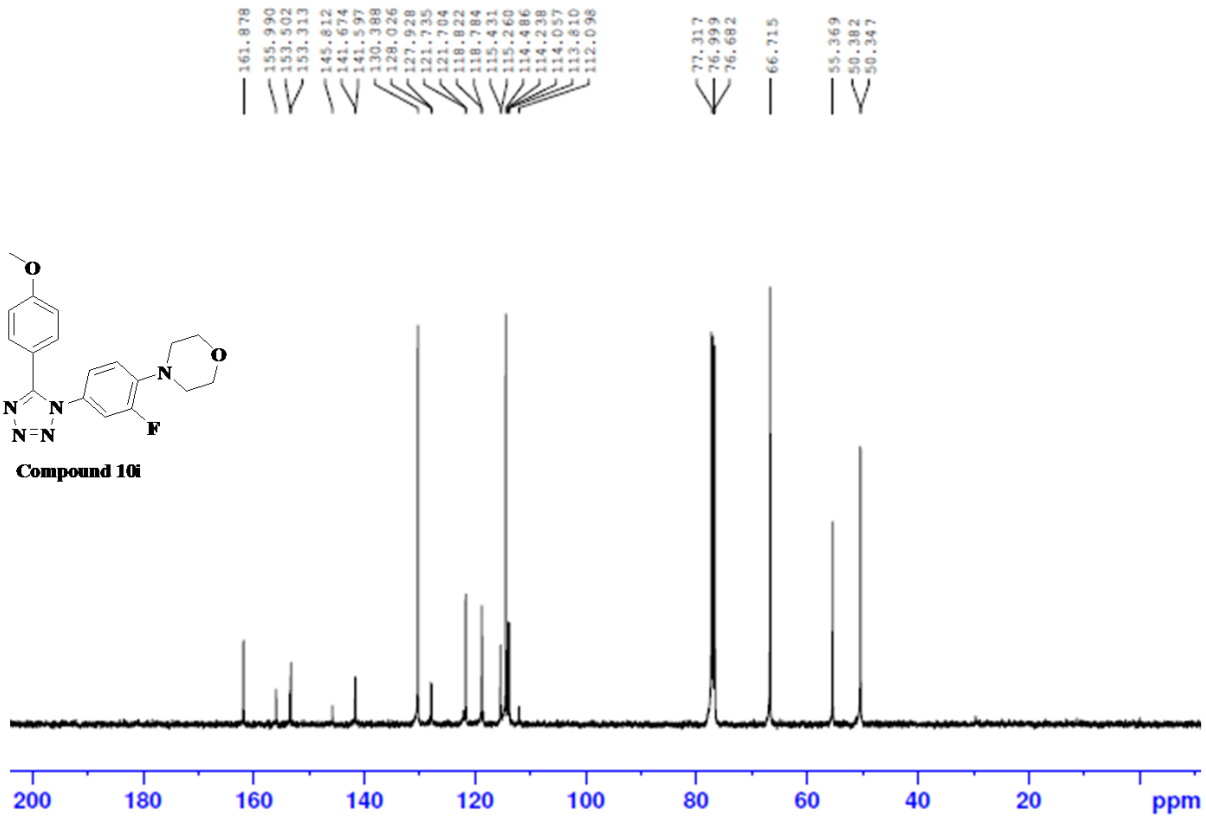


Figure 120.^{13}C NMR Spectra of Compound 10i

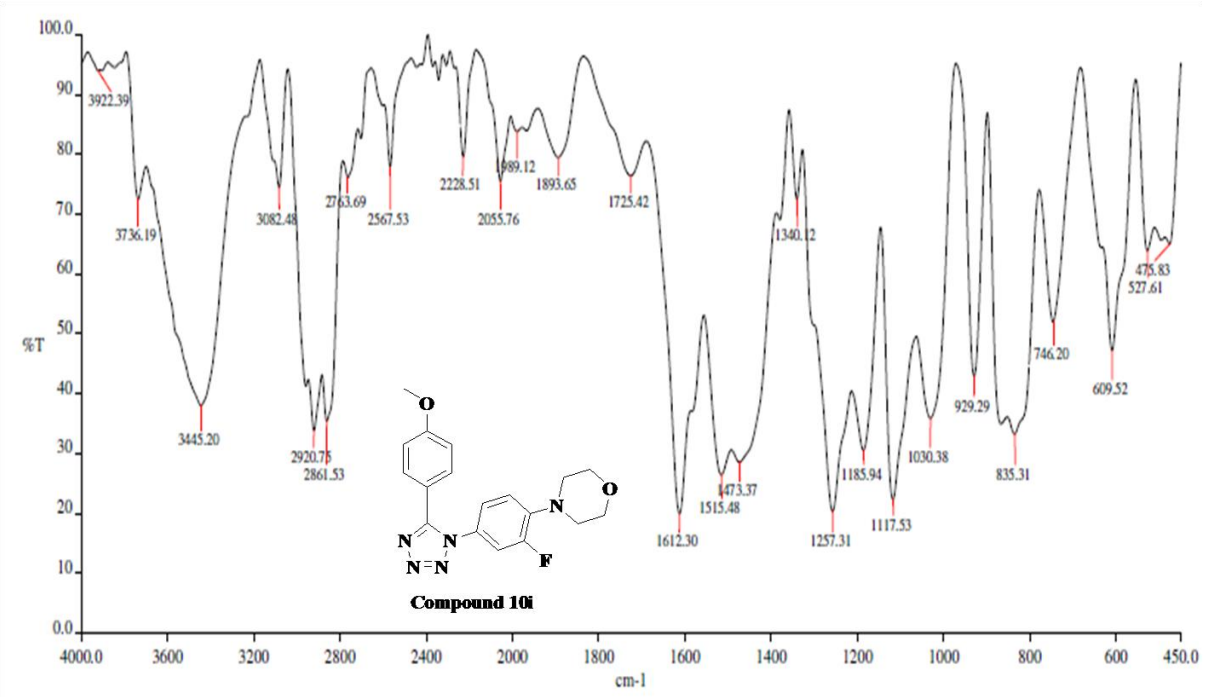


Figure 121. FT-IR Spectra of Compound 10i

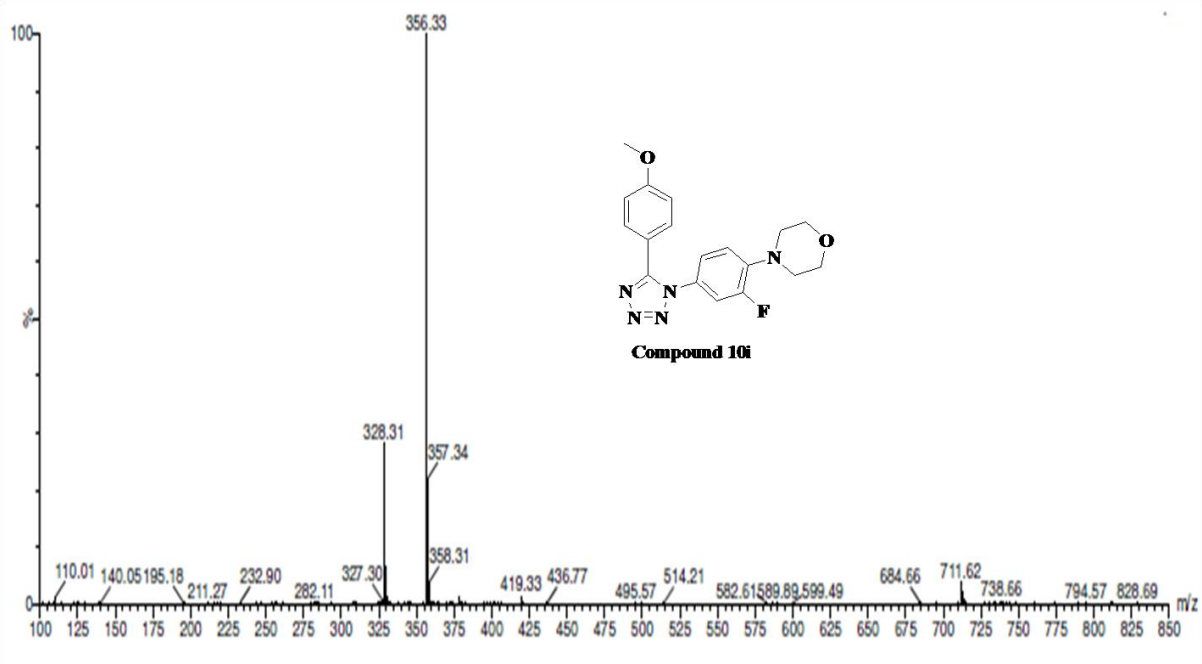


Figure 122. ESI-MS Spectra of Compound 10i

Analytical data of Compound 10j

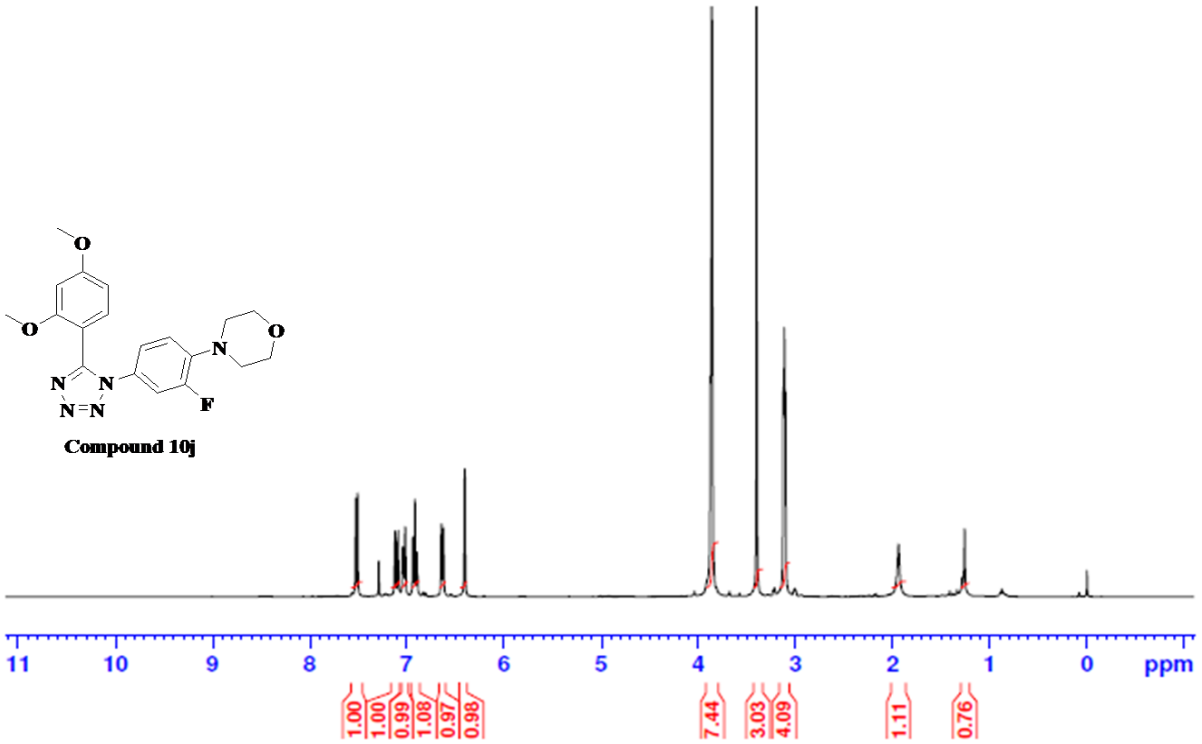


Figure 123.^{1}H NMR Spectra of Compound 10j

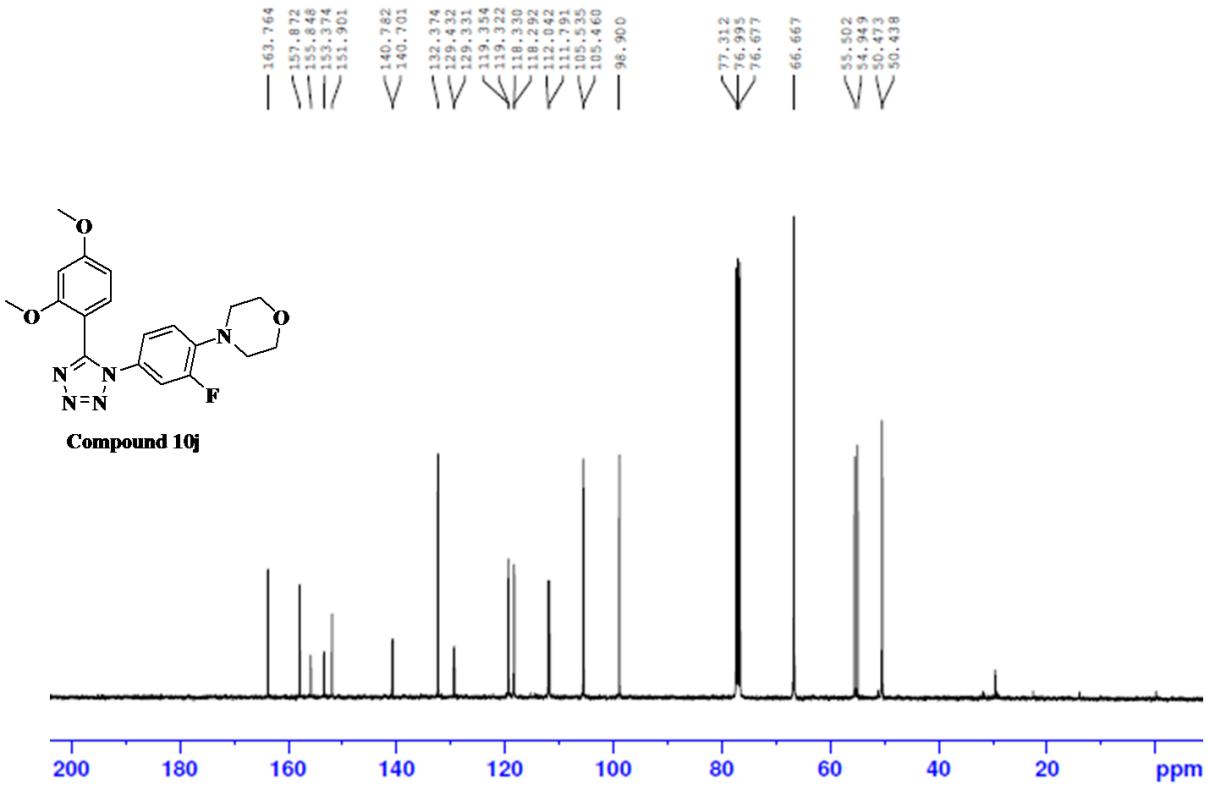


Figure 124.^{13}C NMR Spectra of Compound 10j

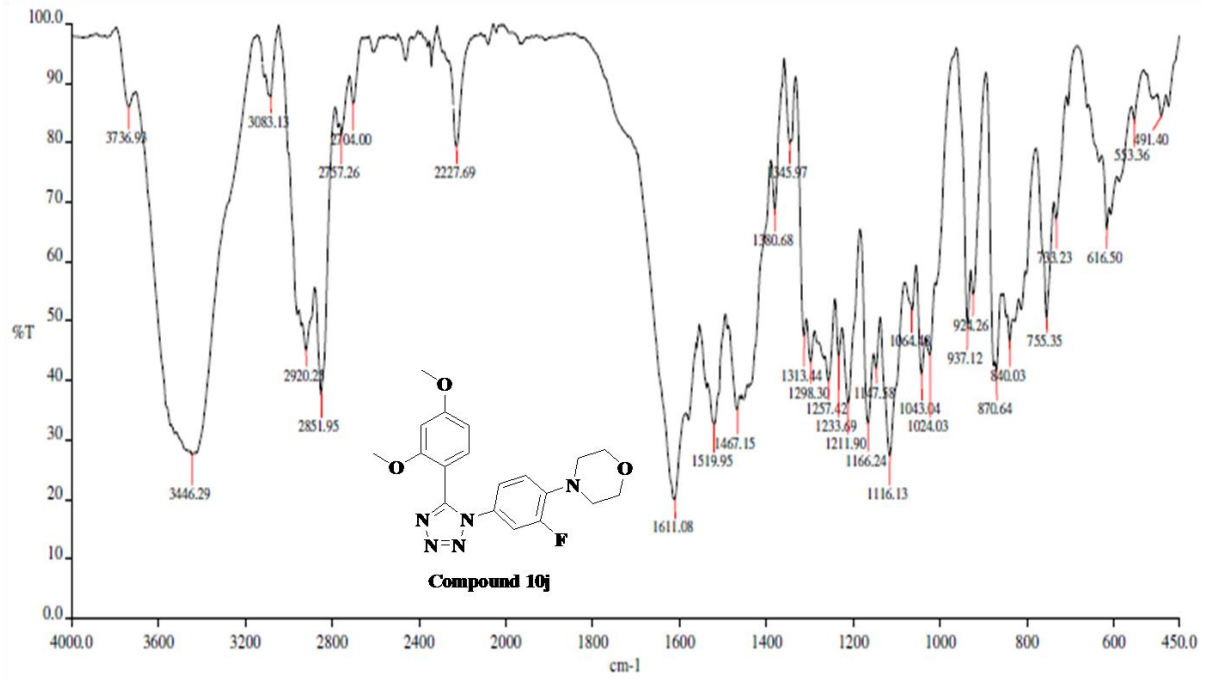


Figure 125. FT-IR Spectra of Compound 10j

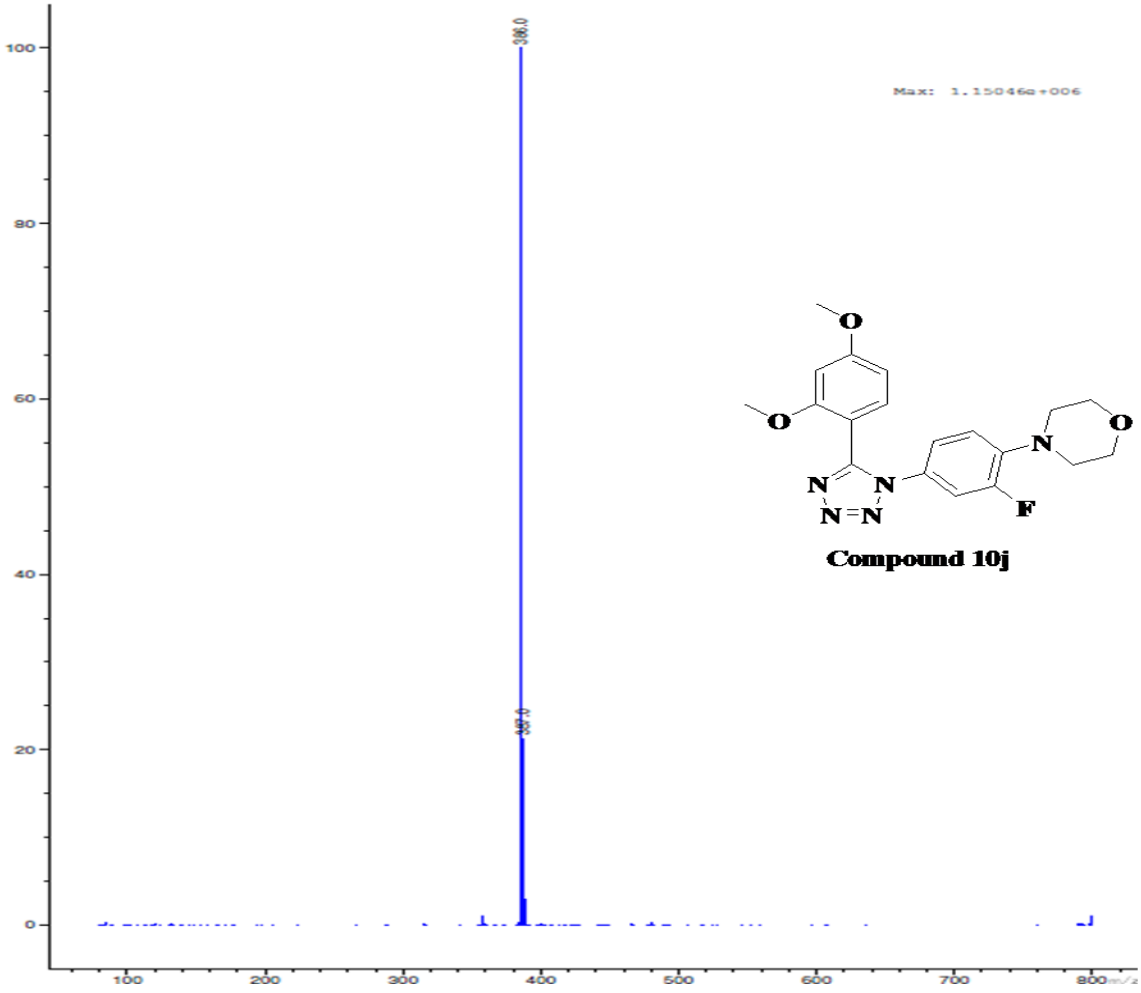


Figure 126. ESI-MS Spectra of Compound 10j

Analytical data of Compound 10k

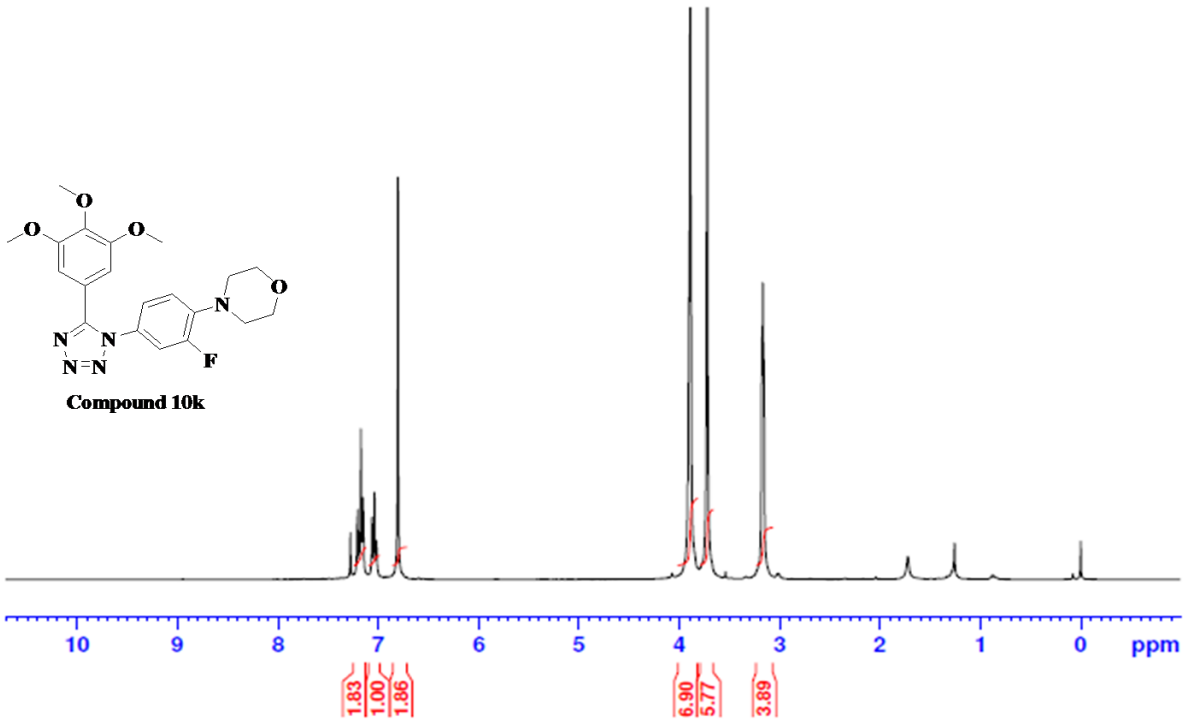


Figure 127.^{1}H NMR Spectra of Compound 10k

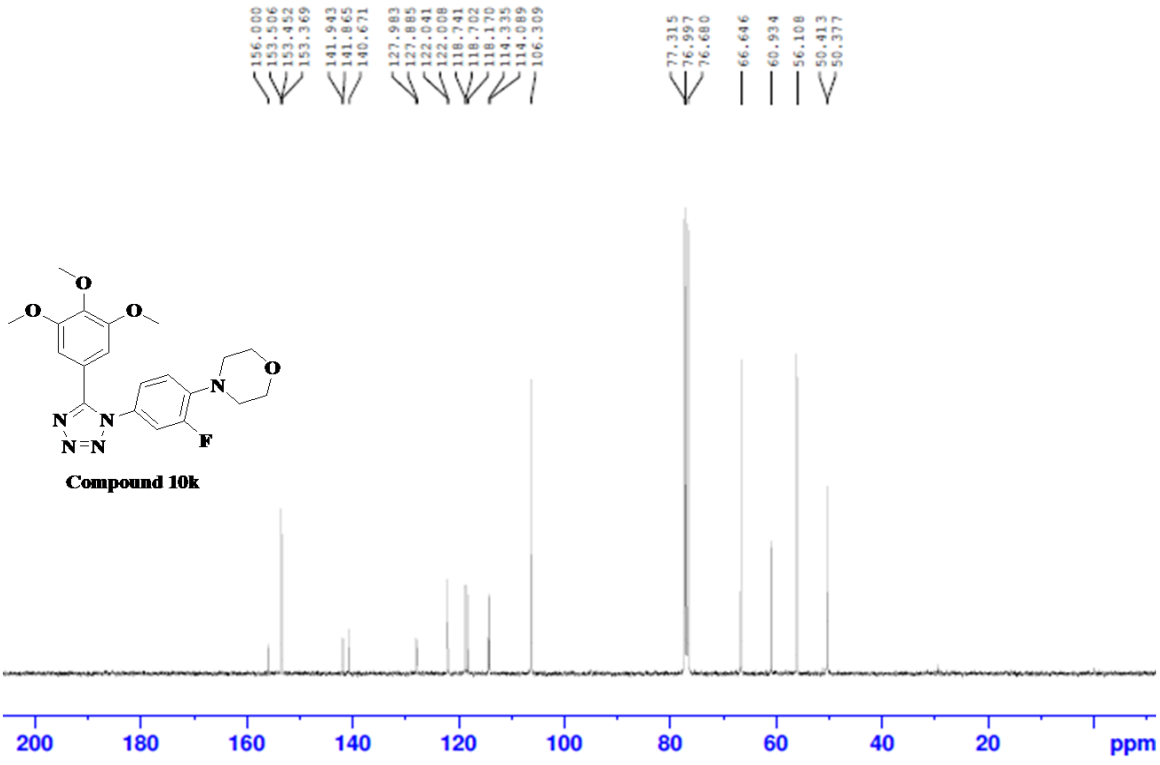


Figure 128.^{13}C NMR Spectra of Compound 10k

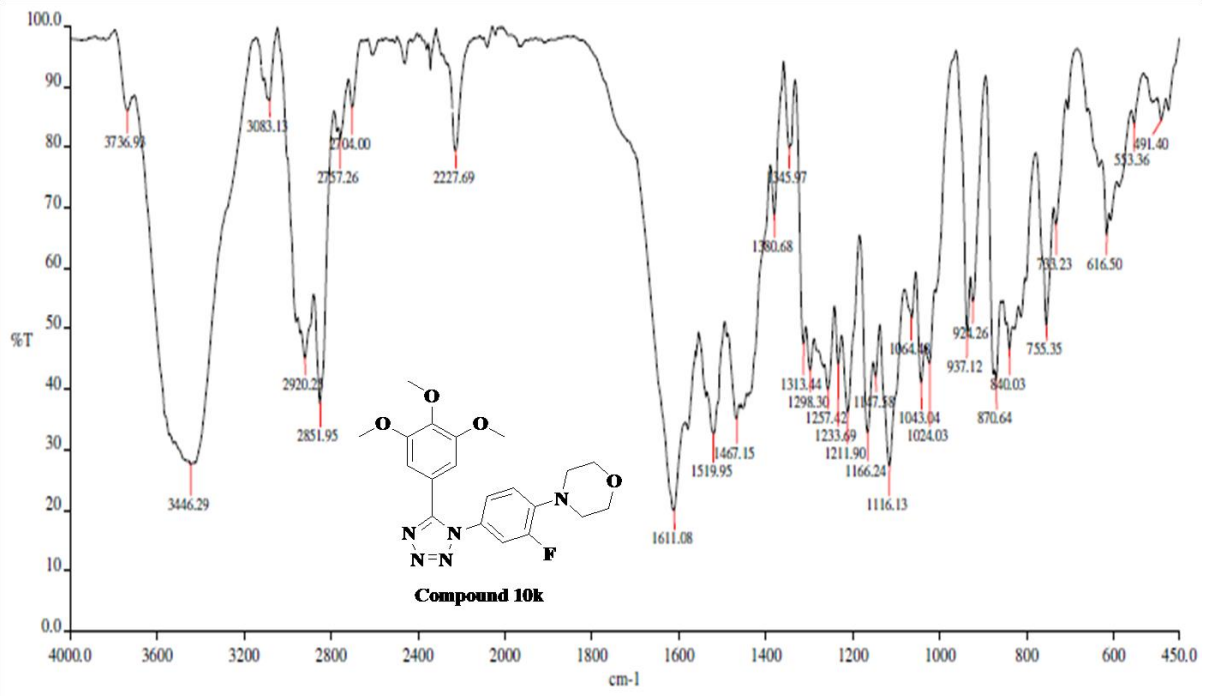


Figure 129. FT-IR Spectra of Compound 10k

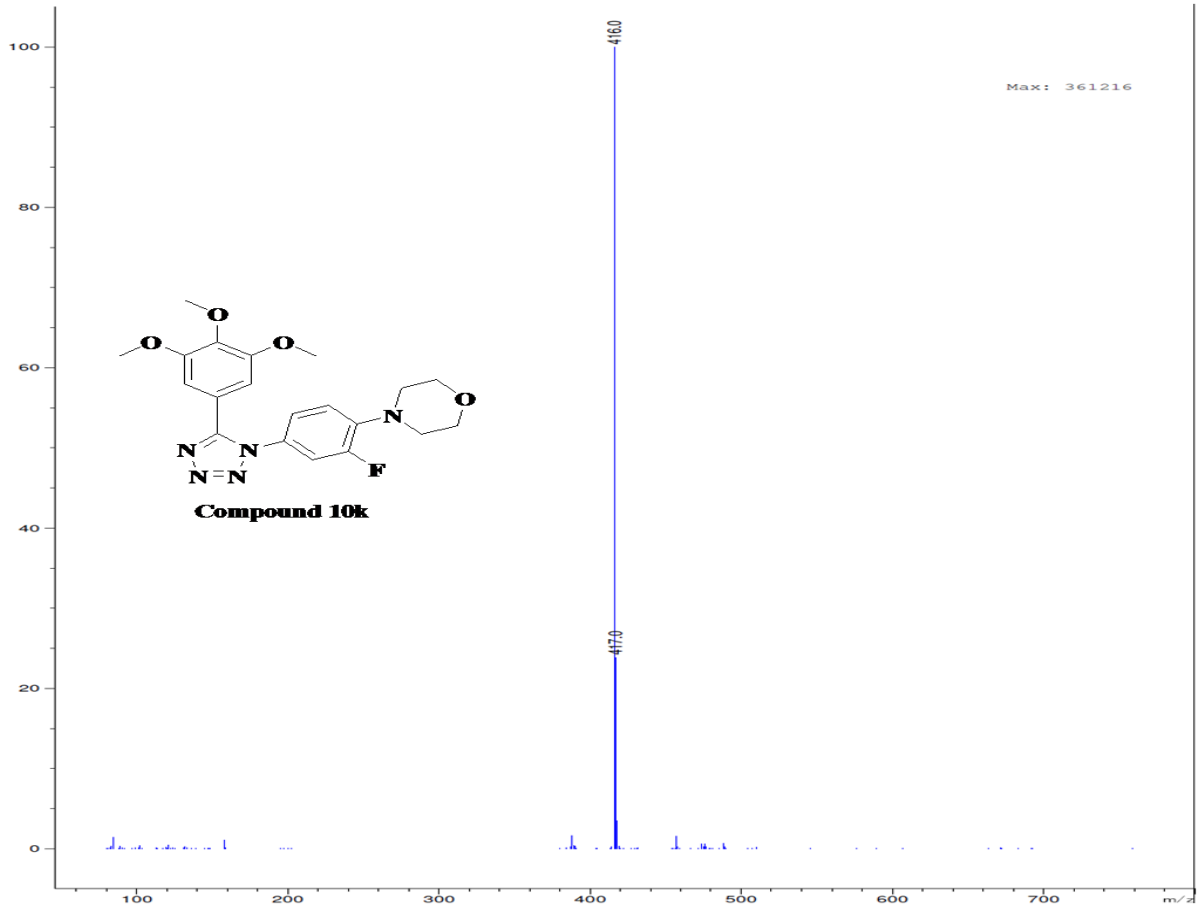


Figure 130. ESI-MS Spectra of Compound 10k

Analytical data of Compound 10l

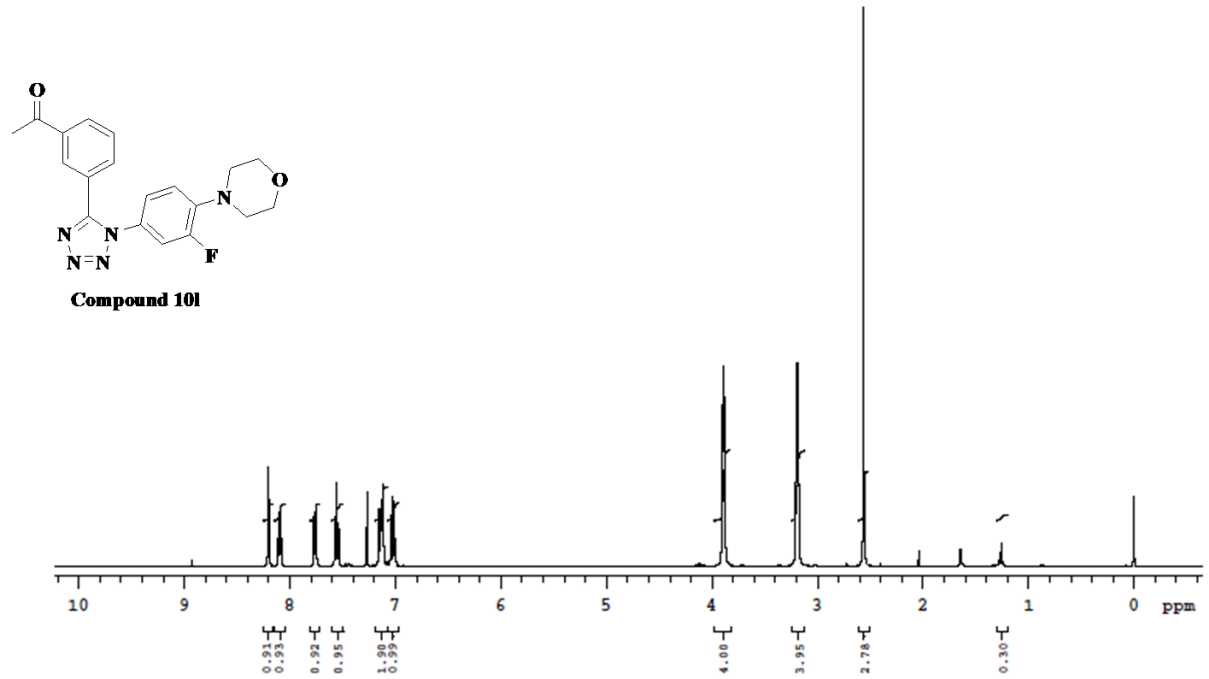


Figure 131.^{1}H NMR Spectra of Compound 10l

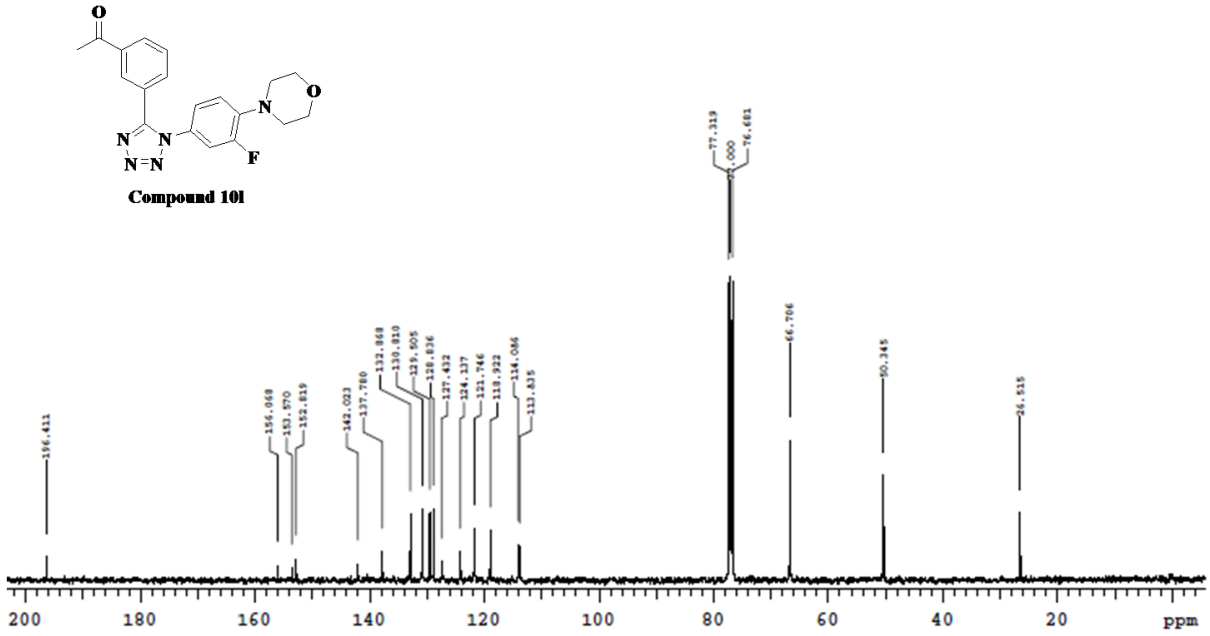


Figure 132.^{13}C NMR Spectra of Compound 10l

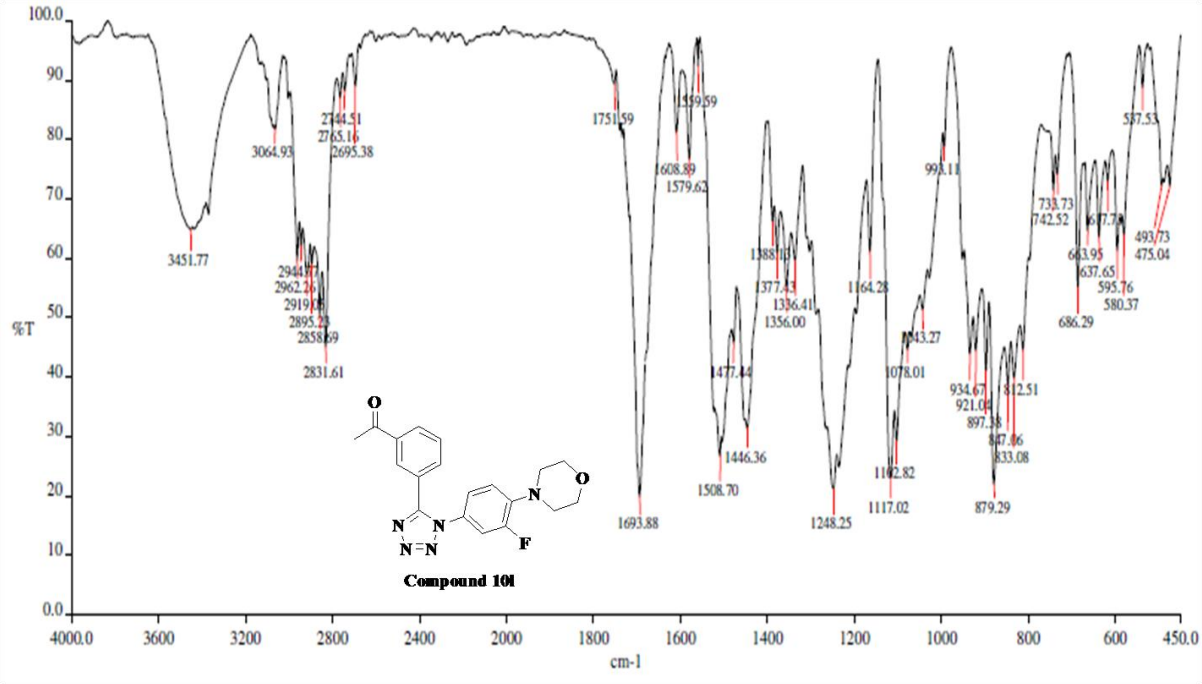


Figure 133. FT-IR Spectra of Compound 10l

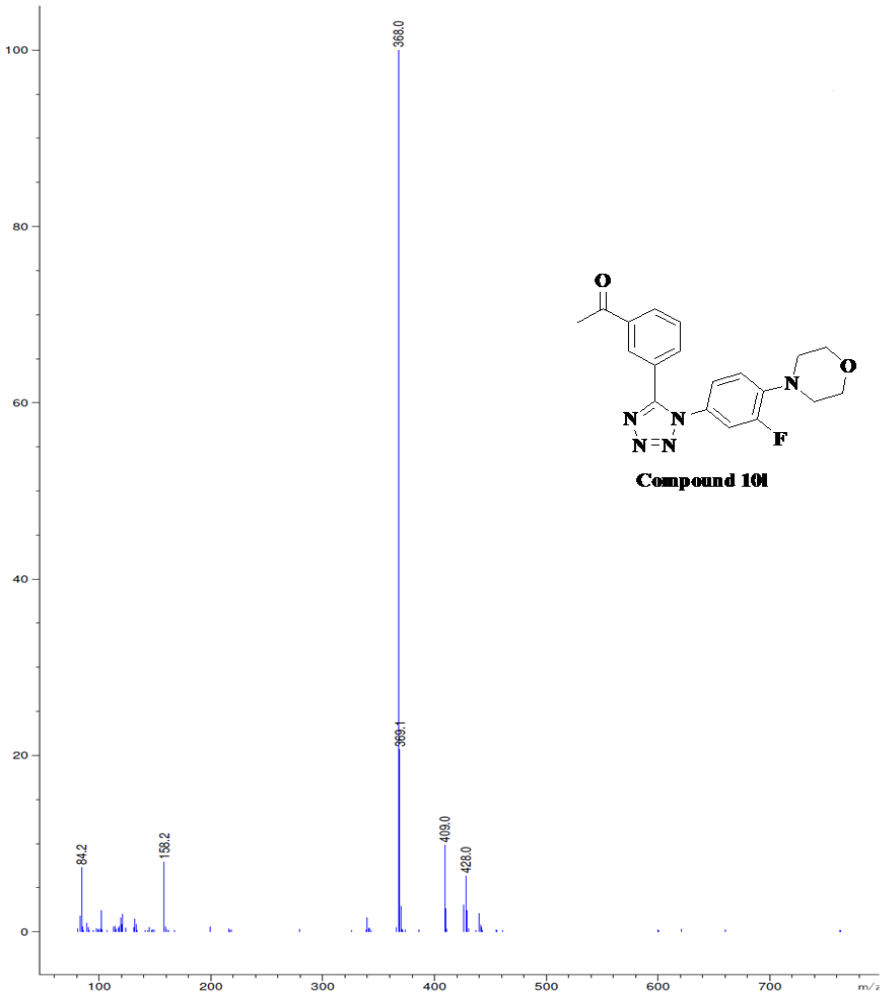


Figure 134. ESI-MS Spectra of Compound 10l

Analytical data of Compound 10m

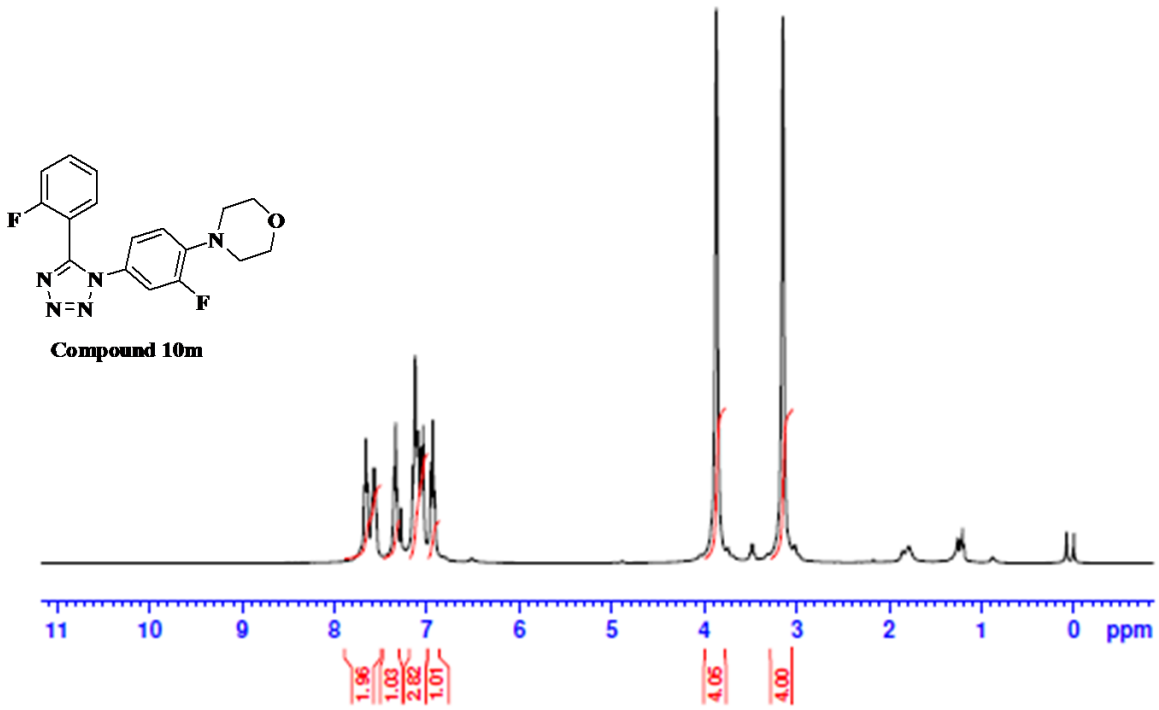


Figure 135.^{1}H NMR Spectra of Compound 10m

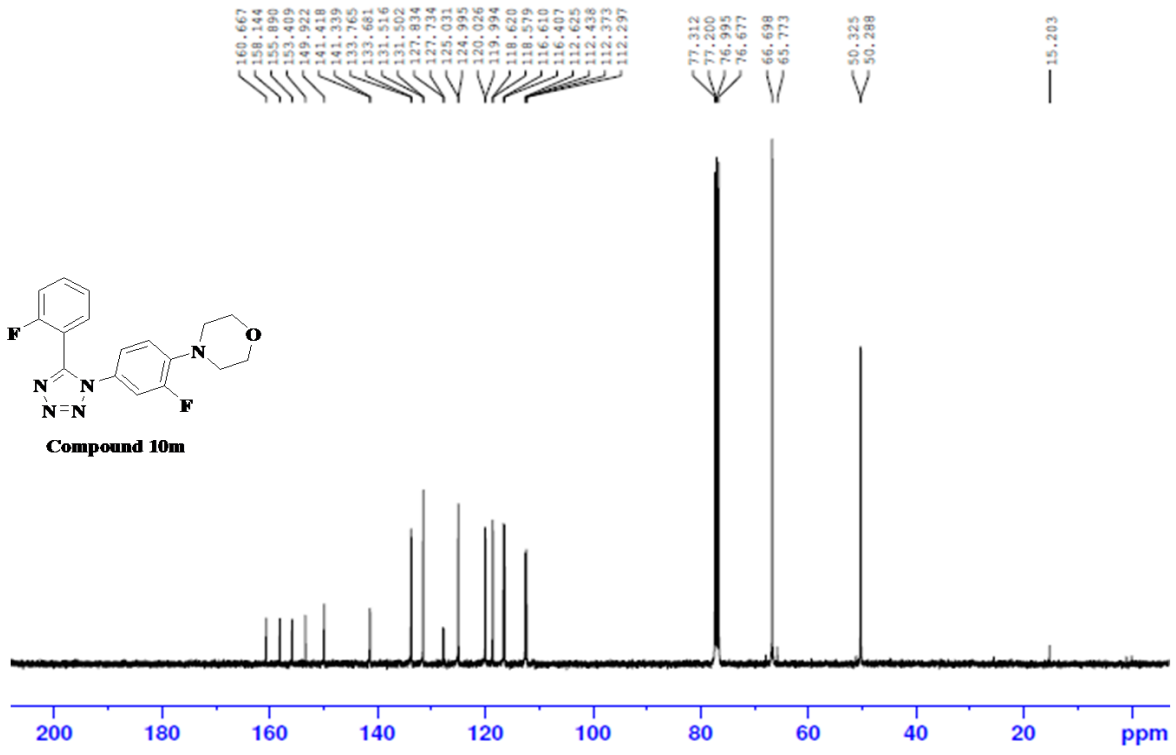


Figure 136.^{13}C NMR Spectra of Compound 10m

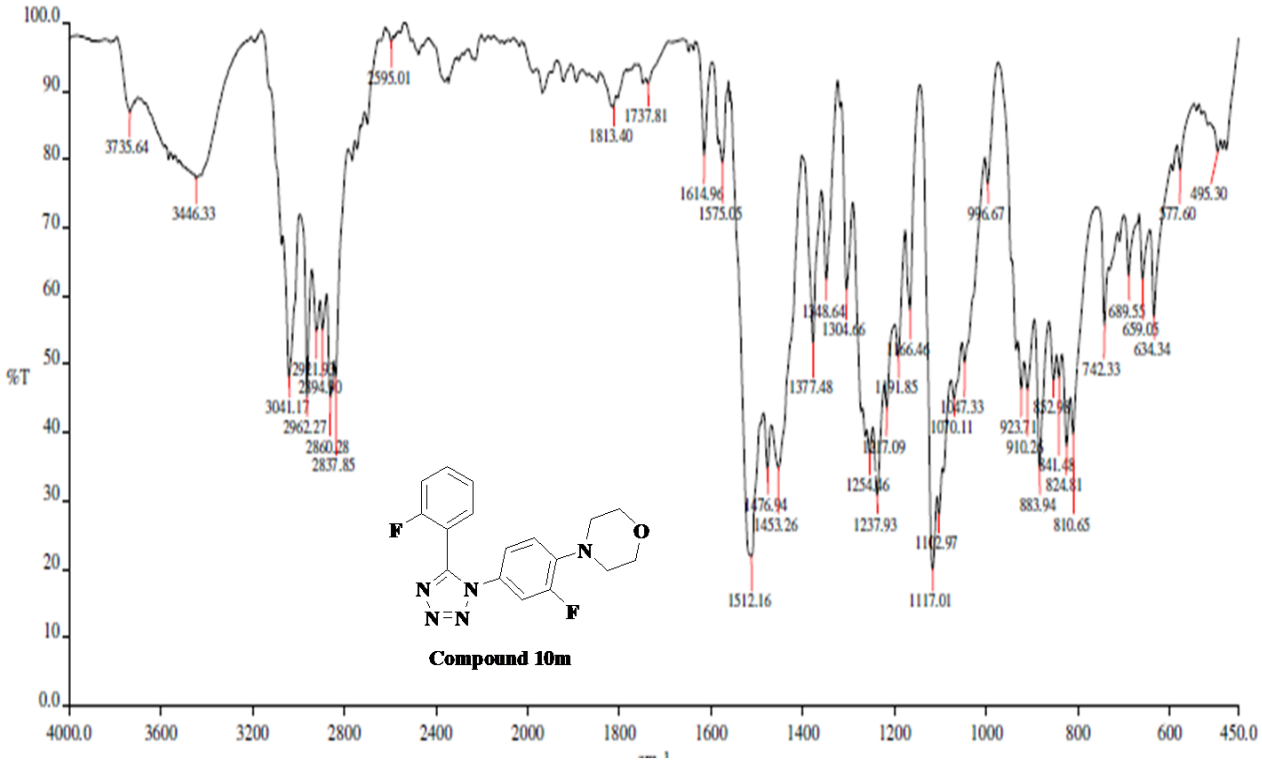


Figure 137. FT-IR Spectra of Compound 10m

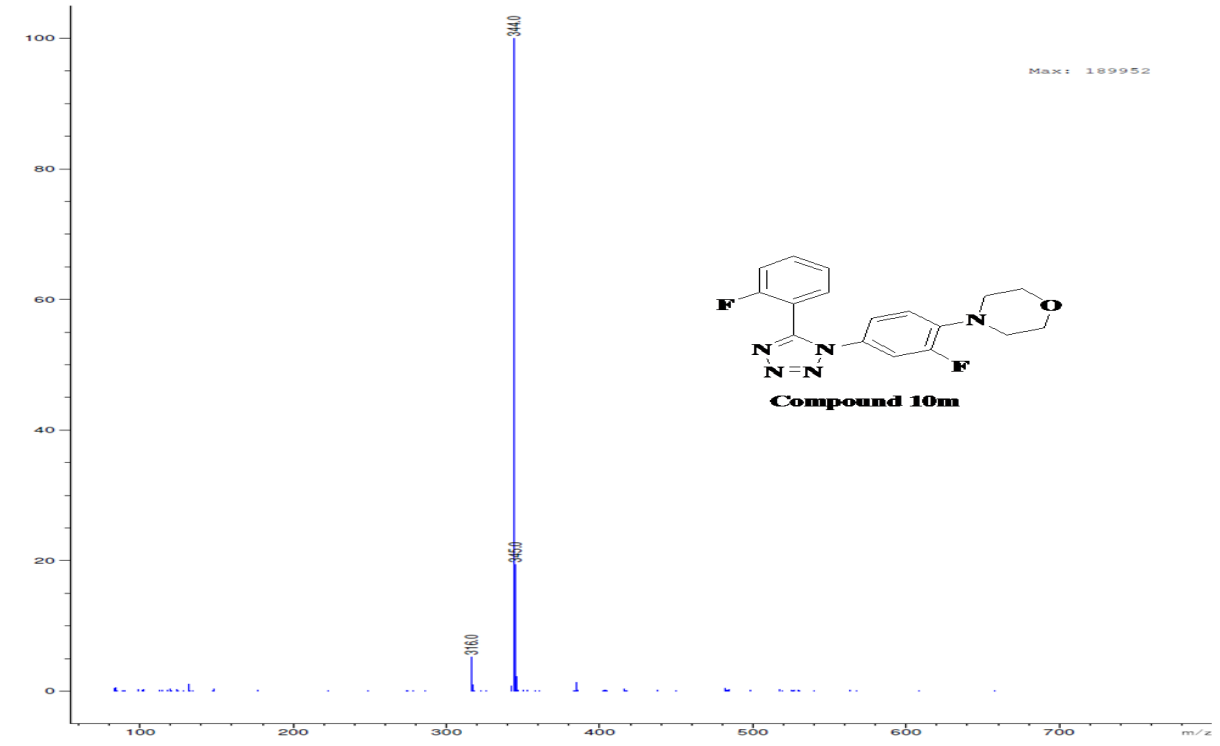


Figure 138. ESI-MS Spectra of Compound 10m