Supplementary Material

Synthesis, \textit{In vitro} anticancer activity and molecular docking studies on some new phenylmorpholine linked aminotetrazoles and aryl tetrazoles

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Table of Contents

Detailed Experimental work ..................................................................................................................S2

Spectra of compounds 3, 4, 5, 6, 8a-8r, 10a-m ........................................................................S31
**Detailed Experimental Section**

![Chemical structures and reaction arrows]

**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$_2$CO$_3$ (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$_2$SO$_4$, filtered and concentrated *in vacuo* 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\textsubscript{10}H\textsubscript{11}FN\textsubscript{2}O\textsubscript{3}; M.P: 112-114 °C; \textsuperscript{1}H NMR (Fig.1) (400 MHz, CDCl\textsubscript{3}) \delta: 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); \textsuperscript{13}C NMR (Fig.2) (100 MHz, CDCl\textsubscript{3}) \delta:154.3, 151.8, 145.4, 120.9, 116.8, 112.6, 66.5 (2C), 49.8 (2C); IR (KBr, cm\textsuperscript{-1})(Fig.3): 3432, 2925, 1739, 1604, 1242, 1050; HRMS (ESI) (Fig.4): calc.for C\textsubscript{10}H\textsubscript{12}N\textsubscript{2}O\textsubscript{3}F (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\textsubscript{2}SO\textsubscript{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_{2}O; M.P: 125-127°C; Anal. Calc. for C_{10}H_{13}FN_{2}O (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%; ^1H 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); ^13C 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):

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_{5}O; M.P: 161-163 °C; ^1H 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); ^13C 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_{12}N_{5}OF (M+H)^+: 250.1104 found 250.1105.
Preparation of 1-(3-fluoro-4-morpholinophenyl)-1H-tetrazol-5-amine(6):

\[
\begin{align*}
\text{Compound 5} & \quad \text{NaN}_3 / \text{NaOH} \quad \text{iPrOH} / 90 ^\circ \text{C} \\
\text{Compound 6} & 
\end{align*}
\]

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\(_3\)N (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%).

\[
\begin{align*}
\text{NH}_2 & \\
\text{F} & \\
\text{N} & \\
\text{N} & \\
\text{O} & \\
\text{N} & \\
\text{N} & \\
\text{F} & \\
\end{align*}
\]

**Figure 4: Structure of compound 6**

**Analytical data:** Molecular formula:C\(_{11}\)H\(_{13}\)FN\(_6\)O; M.P: 207-209 °C; 1H NMR(Fig.11) (400 MHz, CDCl\(_3\)) \(\delta\): 7.27-7.24 (m, 2H), 7.07 (t, \(J = 8.8 \text{ Hz}\), 1H), 4.80 (brs, 2H), 3.89 (t, \(J = 4.8 \text{ Hz}\), 4H), 3.17 (t, \(J = 4.8 \text{ Hz}\), 4H); 13C NMR(Fig.12) (100 MHz, CDCl\(_3\)) \(\delta\):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\(_6\)OF (M+H)+: 265.1213 found 265.1228.

**Series-I:**

**General procedure for Compound 8a-8j (diacetylation):**
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 (7a-7j) (1.12 mmol). The reaction mixture was stirred at room temperature for 2-6 h and then quenched with water and extracted with ethyl acetate (3 x 10 mL). The combined organic layer was washed with brine solution (10 mL) and dried over Na₂SO₄ and concentration in vacuo to afford respective amide derivatives 8a-8j.

**N1-Acetyl-N1-[1-(3-fluoro-4-morpholinophenyl)-1H-1,2,3,4-tetraazol-5-yl]acetamide (8a):**

Following the general procedure, compound 8a was 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 (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: C₁₅H₁₇FN₆O₃; M.P: 275 °C; ¹H NMR (Fig.15) (400 MHz, CDCl₃) 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); ¹³C NMR (Fig.16) (100 MHz, CDCl₃) 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 C₁₅H₁₈N₆O₃F (M+H)⁺: 349.1424 found 349.1422.

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

Following the general procedure, compound 8b 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 by propionyl chloride 7b (105.1 mg, 1.136 mmol) for 2 h. The corresponding amide derivatives 8b (Figure. 6) (192 mg, 90%) as an pale yellow solid.

Figure 6: Structure of compound 8b

**Analytical data:** Molecular formula: C\(_{17}\)H\(_{21}\)F\(_n\)N\(_6\)O\(_3\) M.P: 158-160 °C; \(^1\)H NMR(Fig. 19) (400 MHz, CDCl\(_3\)) \(\delta\): 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); \(^1\)C NMR (Fig. 20) (100 MHz, CDCl\(_3\)) \(\delta\): 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\(_{21}\)F\(_n\)N\(_6\)O\(_3\) (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 by isobutyryl chloride 7c (105.1 mg, 1.136 mmol) for 2 h. The corresponding amide derivatives 8c (Figure. 7) (175 mg, 82%) was afforded as an pale brown solid.

Figure 7: Structure of compound 8c

**Analytical data:** Molecular formula: C\(_{19}\)H\(_{25}\)F\(_n\)N\(_6\)O\(_3\) M.P.: 191-193 °C; Anal. Calc. for C\(_{19}\)H\(_{25}\)F\(_n\)N\(_6\)O\(_3\) (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\(_3\)) \(\delta\): 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); \(^1\)C NMR (Fig. 24) (100 MHz, CDCl\(_3\)) \(\delta\): 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)-1H-tetrazol-5-yl]cyclopropanecarboxamide (8d):**

Following the general procedure, compound 8d was prepared 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 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\(_6\)O\(_3\); M.P: 103-105 °C; \(^1\)H NMR (Fig. 27) (400 MHz, CDCl\(_3\)) \(\delta\): 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\(_3\)) \(\delta\): 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\(_6\)O\(_3\) (M+H)\(^+\): 401.1737 found 401.1766.

**N1-[1-(3-Fluoro-4-morpholinophenyl)-1H-tetrazol-5-yl]-N1-(3-methylbutanoyl)-3-methylbutanamide (8e):**

Following the general procedure, compound 8e 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 by 3-methylbutanoyl chloride 7e (137 mg, 1.136 mmol) for 2 h. The corresponding amide derivatives 8e (Figure. 9) (223 mg, 91%) was afforded as an Pale brown thick liquid.
**Figure 9: Structure of compound 8e**

**Analytical data:** Molecular formula: C_{21}H_{29}F_6N_6O_3; M.P: NA; Anal. Calc. for C_{21}H_{29}F_6N_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%; ^1H 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); ^13C 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)-1H-tetrazol-5-yl]-3,3-dimethylbutanamide (8f):**

Following the general procedure, compound 8f prepared treatment 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 (220.3 mg, 1.7 mmol) followed by 3,3-dimethyl butyryl chloride 7f (152.9 mg, 1.136 mmol) for 2 h. The corresponding amide derivatives 8f (Figure. 10) (232.6 mg, 89%) as an Pale yellow solid.

**Figure 10: Structure of compound 8f**

**Analytical data:** Molecular formula: C_{23}H_{34}N_6O_3F; M.P: 138-140 °C; ^1H 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); ^13C 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\(_6\)O\(_3\)F (M+H\(^+\)): 461.2676 found 461.2715.

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

Following the general procedure, compound 8\(g\) prepared by dissolving 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 (220.3 mg, 1.7 mmol) followed by trimethylacetyl chloride 7\(g\) (137 mg, 1.136 mmol) for 2 h afforded the product corresponding amide derivatives 8\(g\) (Figure 11) (201.3 mg, 82%) as a pale yellow liquid.

![Structure of compound 8g](image)

**Figure 11: Structure of compound 8g**

**Analytical data:** Molecular formula: C\(_{21}\)H\(_{29}\)FN\(_6\)O\(_3\); M.P: NA °C; Anal. Calc. for C\(_{21}\)H\(_{29}\)FN\(_6\)O\(_3\) (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-\(d_6\)) \(\delta\): 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-\(d_6\)) \(\delta\): 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)-1H-tetrazol-5-yl]N-Di-(4-(trifluoromethyl)benzamide (8h):**

Following the general procedure, compound 8\(h\) prepared treatment 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 (220.3 mg, 1.7 mmol) followed by 4-(trifluoromethyl)benzoyl chloride 7\(h\) (237 mg, 1.136 mmol) for 2 h afforded the product corresponding amide derivatives 8\(h\) (Figure 12) (220.3 mg, 64%) as white solid.
Figure 12: Structure of compound 8h

**Analytical data:** Molecular formula: \( \text{C}_{27}\text{H}_{19}\text{F}_{7}\text{N}_{6}\text{O}_{3} \); M.P: 138-141°C; \textit{Anal.} Calc. for \( \text{C}_{27}\text{H}_{19}\text{F}_{7}\text{N}_{6}\text{O}_{3} \) (608): Found C, 53.31; H, 3.16; F, 21.83; N, 13.84; O, 7.88%; Calc: C, 53.30; H, 3.15; F, 21.86; N, 13.81; O, 7.89%; 1H NMR (Fig. 43) (400 MHz, DMSO-\( d_{6} \)) \( \delta \): 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, \( J = 4.8 \text{ Hz} \), 4H), 3.11 (t, \( J = 4.8 \text{ Hz} \), 4H); 13C NMR (Fig.44)(400 MHz, CDCl3) \( \delta \): 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)-1H-tetrazol-5-yl)-Benzoylbenzamide (8i):**

Following the general procedure, compound 8i prepared treatment 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 (220.3 mg, 1.7 mmol) followed benzoyl 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: \( \text{C}_{25}\text{H}_{21}\text{FN}_{6}\text{O}_{3} \); M.P: 101-104°C; \textit{Anal.} Calc. for \( \text{C}_{25}\text{H}_{21}\text{FN}_{6}\text{O}_{3} \) (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, CDCl3) \( \delta \): 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, CDCl$_3$) $\delta$: 166.8, 155.3, 152.8, 149.3, 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)-1H-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)-1H-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 7j (218 mg, 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](image)

**Analytical data:** Molecular formula: C$_{19}$H$_{18}$F$_2$N$_6$O$_3$; M.P: 239-241°C; Anal. Calc. for C$_{19}$H$_{18}$F$_2$N$_6$O$_3$ (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$_3$) $\delta$: 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$_3$) $\delta$: 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):**
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 Na₂SO₄ and concentration invacuo to afford respective amide derivatives 8k-8r.

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

Following the general procedure, compound 8k prepared treatment 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 (220.3 mg, 1.7 mmol) followed by benzoyl chloride 7k (160 mg, 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](image)

**Analytical data:** Molecular formula: C₁₈H₁₇FN₆O₂; M.P: 257-259 °C; 😮NMR(Fig. 55) (400 MHz, CDCl₃) 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 C₁₈H₁₈N₆O₂F (M+H)⁺: 369.1475 found 369.1440.

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

Following the general procedure, compound 8l prepared treatment 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 (220.3 mg, 1.7 mmol) followed by benzoyl chloride 7l (160 mg, 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](image)

**Analytical data:** Molecular formula: C₁₉H₁₉FN₆O₃; M.P: 196-198°C; Anal. Calc. for C₁₉H₁₉FN₆O₃ (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%; ¹H NMR (Fig. 59) (400 MHz, CDCl₃) 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); ¹³C NMR (Fig. 60) (400 MHz, CDCl₃) 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-DifluoroN-[1-(3-Fluoro-4-morpholinophenyl)-1H-tetrazol-5-yl]-benzamide (8m):

Following the general procedure, compound 8m prepared treatment 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 (220.3 mg, 1.7 mmol) followed by benzoyl chloride 7m.
(108.7 mg, 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_{3}N_{6}O_{2}; M.P: 214-216 °C; *Anal. Calc.* for C_{18}H_{15}F_{3}N_{6}O_{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%; 1H 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); 13C 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)-1H-tetrazol-5-yl)-4-(trifluoromethyl)benzamide (8n):

Following the general procedure, compound 8n prepared treatment 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 (220.3 mg, 1.7 mmol) followed by benzoyl chloride 7n (208.4 mg, 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$_4$N$_6$O$_2$; M.P: 202-204°C; Anal. Calc. for C$_{19}$H$_{16}$F$_4$N$_6$O$_2$ (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-$_d_6$) $\delta$: 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$_3$) $\delta$: 166.8, 155.3, 152.8, 149.0, 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)-1H-tetrazol-5-yl)cyclohexanecarboxamide (8o):

Following the general procedure, compound 8o prepared treatment 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 (220.3 mg, 1.7 mmol) followed cyclohexane carboxylic acid chloride 7o (90.3 mg, 0.616 mmol) for 2 h afforded the product corresponding amide derivatives 8o (Figure 19) (180.6 mg, 85%) as a off white solid.

![Figure 19: Structure of compound 8o](image_url)

Analytical data: Molecular formula: C$_{18}$H$_{23}$FN$_6$O$_2$; M.P: 201-205°C; Anal. Calc. for C$_{18}$H$_{23}$FN$_6$O$_2$ (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-$_d_6$) $\delta$: 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$_3$) $\delta$: 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, 1258; ESI-MS (Fig.74): $m/z$ 375.27 [M+H]$^+$, +ve ion mode.

$N$-(1-(3-fluoro-4-morpholinophenyl)-1H-tetrazol-5-yl)-3-phenylpropanamide (8p):
Following the general procedure, compound 8p prepared treatment 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 (220.3 mg, 1.7 mmol) followed 3-Phenylpropionyl chloride 7p (103.9 mg, 0.616 mmol) for 2 h afforded the product corresponding amide derivatives 8p (Figure. 20) (207 mg, 92%) as an off white solid.

![Figure 20: Structure of compound 8p](image)

**Analytical data:** Molecular formula: C_{20}H_{21}FN_{6}O_{2}; M.P: 180-183°C; Anal. Calc. for C_{20}H_{21}FN_{6}O_{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%; 1H 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, CDCl3) 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, 3172, 2986, 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)-1H-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 (117.4 mg, 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_{3}N_{6}O_{2}; M.P: 112-115°C; Anal. Calc. for C_{19}H_{17}F_{3}N_{6}O_{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)-1H-tetrazol-5-yl)benzamide (8r):

Following the general procedure, compound 8r prepared treatment 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 (220.3 mg, 1.7 mmol) followed 2-chloro-4-fluorobenzoyl chloride 7r (118.8 mg, 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$_{2}$N$_{6}$O$_{2}$; M.P: 172-175°C; Anal. Calc. for C$_{18}$H$_{15}$ClF$_{2}$N$_{6}$O$_{2}$ (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 $\delta$: 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) $\delta$: 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 Compounds 10a-10m (Direct Arylation of 4-(2-fluoro-4-(1H-tetrazol-1-yl)phenyl)morpholine):**

A suspension of 4-(2-fluoro-4-(1H-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-1H-tetrazol-1-yl)phenyl)morpholine (10a):
A suspension of 4-(2-fluoro-4-(1H-tetrazol-1-yl)phenyl)morpholine 5 (249 mg, 1.00 mmol), iodobenzene 9a (204 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 10a (Figure. 24) (285 mg, 87%) as a off white solid.

![Structure of compound 10a](image)

**Figure 24: Structure of compound 10a**

**Analytical data:** Molecular formula: C_{17}H_{16}FN_{5}O; M.P:148-151°C; Anal. Calc. for C_{17}H_{16}FN_{5}O (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%; \^1H-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); \^13C-NMR (Fig. 88) (100 MHz, CDCl\textsubscript{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\textsuperscript{-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-1H-tetrazol-1-yl)phenyl)morpholine (10b):
A suspension of 4-(2-fluoro-4-(1H-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) 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 obtain compound 10b (Figure. 25) (294 mg, 86%) as a light brown solid.

![Structure of compound 10b](image)

**Figure 25: Structure of compound 10b**

**Analytical data:** Molecular formula: C$_{18}$H$_{18}$FN$_{5}$O; M.P: 98-101°C; Anal. Calc. for C$_{18}$H$_{18}$FN$_{5}$O (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%; ¹H 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-1H-tetrazol-1-yl)phenyl)morpholine (10c):**

A suspension of 4-(2-fluoro-4-(1H-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) 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 obtain 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_{5}O; M.P: 101-104°C; Anal. Calc. for C_{18}H_{18}FN_{5}O (339): Found C, 63.7; 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%; ¹H NMR (Fig. 95) (400 MHz, CDCl₃) 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, CDCl₃) 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, 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-1H-tetrazol-1-yl)phenyl)morpholine (10d):

A suspension of 4-(2-fluoro-4-(1H-tetrazol-1-yl)phenyl)morpholine (249 mg, 1.00 mmol), 4-iodotoluene (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}F_{5}N_{5}O; M.P: 149-151°C; Anal. Calc. for C_{18}H_{18}F_{5}N_{5}O (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%; \textsuperscript{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); \textsuperscript{13}C NMR (Fig. 100) (100 MHz, CDCl\textsubscript{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\textsuperscript{-1}) (Fig. 101): 3735, 3445, 2962, 2917, 1614, 1520, 1450, 1376, 1342, 1256, 1120; ESI-MS (Fig. 102): m/z 340.31 [M+H]\textsuperscript{+}, +ve ion mode.

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

A suspension of 4-(2-fluoro-4-(1H-tetrazol-1-yl)phenyl)morpholine\textsuperscript{5} (249 mg, 1.00 mmol), 1-ethyl-2-iodobenzene \textsuperscript{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) 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 \textsuperscript{10e} (Figure. 28) (286 mg, 81%) as a colourless liquid.

![Figure 28: Structure of compound 10e](image)

Figure 28: Structure of compound 10e

Analytical data: Molecular formula: C_{19}H_{20}F_{5}N_{5}O; M.P: NA; Anal. Calc. for C_{19}H_{20}F_{5}N_{5}O (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%; \textsuperscript{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); \textsuperscript{13}C NMR (Fig. 104) (100 MHz, CDCl\textsubscript{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)-1H-tetrazol-1-yl)-2-fluorophenyl)morpholine (10f):

A suspension of 4-(2-fluoro-4-(1H-tetrazol-1-yl)phenyl)morpholine5 (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](image)

**Analytical data:** Molecular formula:C₁₉H₂₀FN₅O; M.P: 118-120°C; Anal. Calc. for C₁₉H₂₀FN₅O (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%; ¹H NMR(Fig. 107) (400 MHz, CDCl₃) 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, CDCl₃) 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)-1H-tetrazol-1-yl)phenyl)morpholine (10g):

A suspension of 4-(2-fluoro-4-(1H-tetrazol-1-yl)phenyl)morpholine5 (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) 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 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}F_{5}N_{5}O_{2}; M.P: 123-125°C; Anal. Calc. for C_{18}H_{18}F_{5}N_{5}O_{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%; ¹H NMR (Fig. 111) (400 MHz, CDCl₃) 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, CDCl₃) 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)-1H-tetrazol-1-yl)phenyl)morpholine (10h):

A suspension of 4-(2-fluoro-4-(1H-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 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 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_{5}O_{2}; M.P: 110-114°C; Anal. Calc. for C_{18}H_{18}FN_{5}O_{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 (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 (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)-1H-tetrazol-1-yl)phenyl)morpholine (10i):

A suspension of 4-(2-fluoro-4-(1H-tetrazol-1-yl)phenyl)morpholine5 (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: \(\text{C}_{18}\text{H}_{18}\text{FN}_{5}\text{O}_{2}\); M.P: 154-156°C; \textit{Anal.} Calc. for \(\text{C}_{18}\text{H}_{18}\text{FN}_{5}\text{O}_{2}\) (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%; \(^1\text{H} \text{NMR} \) (Fig. 119) (400 MHz, CDCl\(_3\)) \(\delta\): 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); \(^{13}\text{C} \text{NMR} \) (Fig. 120) (100 MHz, CDCl\(_3\)) \(\delta\): 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): \(m/\zeta\) 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) 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 10j (Figure. 33) (308 mg, 80%) as a light brown solid.

![Figure 33: Structure of compound 10j](image_url)

Analytical data: Molecular formula: \(\text{C}_{19}\text{H}_{20}\text{FN}_{5}\text{O}_{3}\); M.P: 104-106°C; \textit{Anal.} Calc. for \(\text{C}_{19}\text{H}_{20}\text{FN}_{5}\text{O}_{3}\) (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%; \(^1\text{H} \text{NMR} \) (Fig. 123) (400 MHz, CDCl\(_3\)) \(\delta\): 7.52-7.50 (m, 1H), 7.12-7.08 (m, 1H), 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); \(^{13}\text{C} \text{NMR} \) (Fig. 124) (100 MHz, CDCl\(_3\)) \(\delta\): 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)-1H-tetrazol-1-yl)phenyl)morpholine (10k):

A suspension of 4-(2-fluoro-4-(1H-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](image)

**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\(_3\)) \(\delta\): 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\(_3\)) \(\delta\): 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)-1H-tetrazol-5-yl)phenyl)ethanone (10l):

A suspension of 4-(2-fluoro-4-(1H-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) 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 9:2) to obtained compound 10l (Figure 35) (286 mg, 85%) as a pale yellow solid.

![Figure 35: Structure of compound 10l](image)

**Analytical data:** Molecular formula: C_{19}H_{18}F_{5}N_{5}O_{2}; M.P: 157-159°C; Anal. Calc. for C_{19}H_{18}F_{5}N_{5}O_{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\(_3\)) \(\delta\): 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\(_3\)) \(\delta\): 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): \(m/\varepsilon\) 368.0 [M+H]\(^+\), +ve ion mode.

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

A suspension of 4-(2-fluoro-4-(1H-tetrazol-1-yl)phenyl)morpholine\(\text{5}\) (249 mg, 1.00 mmol), 1-Fluro-2-iodobenzene \(\text{9m}\) (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_{2}N_{5}O; M.P: 124-126^\circ C; Anal. Calc. for C_{17}H_{15}F_{2}N_{5}O (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%; \textsuperscript{1}H NMR (Fig. 135) (400 MHz, CDCl\textsubscript{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); \textsuperscript{13}C NMR (Fig. 136) (100 MHz, CDCl\textsubscript{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\textsuperscript{-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]\textsuperscript{+}, +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

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

Figure 10. HRMS Spectra of Compound 5
Analytical data of Compound 6

![1H NMR Spectra of Compound 6](image1)

Figure 11. 1H NMR Spectra of Compound 6

![13C NMR Spectra of Compound 6](image2)

Figure 12. 13C NMR Spectra of Compound 6
Figure 13. FT-IR Spectra of Compound 6

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

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

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

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

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

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 80**

![Figure 71. $^1$H NMR Spectra of Compound 80](image1)

**Figure 71. $^1$H NMR Spectra of Compound 80**

![Figure 72. $^{13}$C NMR Spectra of Compound 80](image2)

**Figure 72. $^{13}$C NMR Spectra of Compound 80**
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