Design, Synthesis and Antifungal Activities of Novel Aromatic Carboxamides Containing Diphenylamine Scaffold

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Content

1. The physical data of compounds **1-29** in detail

*Data for Compound **1**.* Yield, 81 %; white solid; mp, 120.4-121.1 °C; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 9.51 (s, 1H, CONH), 8.40 (s, 1H, Ph-NH-Ph), 7.65 (s, 1H, Py-H), 7.39 (dd, *J* = 8.7, 6.4 Hz, 1H, Ph-H), 7.35 (t, $J_{H\text{-}F}$ = 54.1 Hz, 1H, CHF_2), 7.27 (t, *J* = 7.9 Hz, 2H, Ph-H), 7.07 (d, *J* = 7.7 Hz, 2H, Ph-H), 6.97 (dd, *J* = 11.2, 2.8 Hz, 1H, Ph-H), 6.91 (t, *J* = 7.3 Hz, 1H, Ph-H), 6.72 (td, *J* = 8.4, 2.8 Hz, 1H, Ph-H), 3.95 (s, 3H, NCH_3); ^{13}C NMR (100 MHz, DMSO) δ 161.02 (s, CONH), 160.81 (d, $J_{C\text{-}F}$ = 240.9 Hz, Ph-C), 145.46 (t, $J_{C\text{-}F}$ = 23.1 Hz, Py-C), 142.89 (s, Ph-C), 140.43 (d, $J_{C\text{-}F}$ = 10.7 Hz, Ph-C), 133.57 (s, Py-C), 129.69 (s, Ph-C), 129.23 (d, $J_{C\text{-}F}$ = 10.1 Hz, Ph-C), 123.34 (d, $J_{C\text{-}F}$ = 2.5 Hz, Ph-C), 121.53 (s, Ph-C), 118.92 (s, Ph-C), 116.57 (t, $J_{C\text{-}F}$ = 3.7 Hz, Py-C), 110.16 (t, $J_{\text{C-F}}$ = 234.5 Hz, CHF_2), 106.87 (d, $J_{C\text{-}F}$ = 22.5 Hz, Ph-C), 103.89 (d, $J_{C\text{-}F}$ = 25.6 Hz, Ph-C), 39.87 (s, NCH_3); ESI-HRMS:m/z [M+Na]$^+$calcd. for [$C_{18}H_{15}F_3N_4NaO$]: 383.1096; found: 383.1086.

*Data for Compound **2**.* Yield, 70 %; white solid; mp, 141.8-142.3 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.02 (s, 1H, CONH), 8.41 (s, 1H, Ph-NH-Ph), 7.42 (dd, *J* = 8.0, 1.4 Hz, 1H, Py-H), 7.38 (dd, *J* = 7.9, 5.3 Hz, 2H, Ph-H), 7.34 (t, $J_{H\text{-}F}$ =54.2 Hz, 1H, CHF_2), 7.23 – 7.17 (m, 1H, Ph-H), 7.11 (dd, *J* = 8.2, 1.4 Hz, 1H, Ph-H), 7.00 (dd, *J* = 10.7, 2.8 Hz, 1H, Ph-H), 6.94 – 6.87 (m, 2H, Ph-H), 3.96 (s, 3H, NCH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.17 (s, CONH), 160.92 (d, $J_{C\text{-}F}$ = 242.1 Hz, Ph-C), 145.56 (t, $J_{C\text{-}F}$ = 23.3 Hz, Py-C), 140.05 (s, Ph-C), 139.17 (d, $J_{C\text{-}F}$ = 10.7 Hz, Ph-C), 133.68 (s, Py-C), 130.36 (s, Ph-C), 128.69 (d, $J_{C\text{-}F}$ = 10.1 Hz, Ph-C), 128.45 (s, Ph-C), 125.36 (d, $J_{C\text{-}F}$ = 2.7 Hz, Ph-C), 122.63 (s, Ph-C), 122.11 (s, Ph-C), 117.98 (s, Ph-C), 115.78 (t, $J_{C\text{-}F}$ = 3.5 Hz, Py-C), 109.98 (t, $J_{C\text{-}F}$ = 234.5 Hz, CHF_2), 109.35 (d, $J_{C\text{-}F}$ = 22.5 Hz, Ph-C), 107.73 (d, *J* = 3.0 Hz, Ph-C), 39.93 (s, NCH_3); ESI-HRMS:m/z [M+Na]$^+$calcd. for [$C_{18}H_{14}ClF_3N_4NaO$]: 417.0706; found: 417.0693.

*Data for Compound **3**.* Yield, 59 %; white solid; mp, 121.6-122.3 °C; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 9.49 (s, 1H, CONH), 8.36 (s, 1H, Ph-NH-Ph), 8.00 (s, 1H, Py-H), 7.47 – 7.43 (m, 1H, Ph-H)), 7.41 (d, *J* = 8.8 Hz, 1H, Ph-H), 7.33 (t, $J_{H\text{-}F}$ = 57.5 Hz, 1H, CHF_2), 7.13 (d, *J* = 2.6 Hz, 1H, Ph-H), 7.08 (dd, *J* = 10.6, 2.8 Hz, 1H, Ph-H)), 6.98 (dd, *J* = 8.8, 2.7 Hz, 1H, Ph-H)), 6.86 (td, *J* = 8.4, 2.9 Hz, 1H, Ph-H)), 3.95 (s, 3H, NCH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.90 (s, CONH), 160.56 (d, J = 241.9 Hz, Ph-C), 145.46 (t, J_{C-F} = 23.2 Hz, Py-C), 144.08 (s, Ph-C), 138.40 (d, J_{C-F} = 10.7 Hz), 133.52 (s, Py-C), 131.80 (s, Ph-C), 131.22 (s, Ph-C), 129.36 (d, J_{C-F} = 9.8 Hz, Ph-C), 125.16 (d, J_{C-F} = 2.6 Hz, Ph-C), 121.38 (s), 118.51 (s), 117.19 (s), 116.46 (t, J_{C-F} = 3.5 Hz, Py-C), 110.11 (t, J_{C-F} = 234.5 Hz, CHF_2), 109.09 (d, J_{C-F} = 22.4 Hz, Ph-C), 106.78 (d, J_{C-F} = 25.1 Hz, Ph-C), 39.88 (s, NCH_3); ESI-HRMS:m/z $[M+Na]^+$calcd. for $[C_{18}H_{13}Cl_2F_3N_4NaO]$: 451.0316; found: 451.0310.

*Data for Compound **4**.* Yield, 73 %; light pink solid; mp, 145.5-150.1 °C; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 10.03 (s, 1H, CONH), 8.41 (s, 1H, Ph-NH-Ph), 7.54 (d, J = 2.4 Hz, 1H, Py-H), 7.47 (s, 1H, Ph-H), 7.40 (dd, J = 8.8, 6.1 Hz, 1H, Ph-H), 7.34 (t, J = 54.1 Hz, 1H, CHF_2), 7.24 (dd, J = 8.8, 2.4 Hz, 1H, Ph-H) , 7.08 – 7.04 (m, 2H, Ph-H), 6.95 (td, J = 8.4, 2.9 Hz, 1H, Ph-H), 3.96 (s, 3H, NCH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.16 (s, CONH), 160.86 (d, J_{C-F} = 242.5 Hz, Ph-C), 145.56 (t, J_{C-F} = 23.4 Hz, Py-C), 139.49 (s, Ph-C), 138.49 (d, J_{C-F} = 10.6 Hz, Ph-C), 133.71 (s, Py-C), 129.54 (s, Ph-C), 128.67 (d, J_{C-F} = 9.9 Hz, Ph-C), 128.40 (s, Ph-C), 125.86 (d, J_{C-F} = 2.8 Hz, Ph-C), 124.34 (s, Ph-C), 122.92 (s, Ph-C), 118.52 (s, Ph-C), 115.72 (t, J_{C-F} = 3.5 Hz， Py-C), 110.11 (d, J_{C-F} = 6.0 Hz, Ph-C), 110.03 (t, J_{C-F} = 234.7 Hz, CHF_2), 108.41 (d, J_{C-F} = 24.7 Hz, Ph-C), 39.93 (s, NCH_3); ESI-HRMS:m/z $[M+Na]^+$calcd. for $[C_{18}H_{13}Cl_2F_3N_4NaO]$: 451.0316; found: 451.0296.

*Data for Compound **5**.* Yield, 68 %; light yellow solid; mp, 186.3-189.4 °C; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 9.73 (s, 1H, CONH), 8.38 (s, 1H, Ph-NH-Ph), 7.61 (s, 1H, Py-H), 7.53 (dd, J = 10.9, 2.2 Hz, 1H, Ph-H), 7.41 (dd, J = 9.5, 6.2 Hz, 1H, Ph-H), 7.32 (t, J = 54.1 Hz, 1H, CHF_2), 7.26 (dd, J = 8.6, 1.2 Hz, 1H, Ph-H),7.06 (t, J = 8.8 Hz, 1H, Ph-H), 6.87 – 6.78 (m, 2H, Ph-H), 3.95 (s, 3H, NCH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.00 (s, CONH), 160.79 (d, J_{C-F} = 241.6 Hz, Ph-C), 153.76 (d, J_{C-F} = 247.7 Hz, Ph-C), 145.46 (t, J_{C-F} = 23.3 Hz, Py-C), 139.12 (d, J_{C-F} = 10.4 Hz, Ph-C), 133.61 (s, Py-C), 130.74 (d, J_{C-F} = 11.2 Hz, Ph-C), 128.86 (d, J_{C-F} = 9.7 Hz, Ph-C), 128.21 (d, J_{C-F} = 3.3 Hz, Ph-C), 124.38 (d, J_{C-F} = 2.6 Hz, Ph-C), 121.82 (d, J_{C-F} = 2.9 Hz, Ph-C), 119.55 (d, J_{C-F} = 22.6 Hz, Ph-C), 116.20 (t, J_{C-F} = 3.5 Hz, Py-C), 112.27 (d, J_{C-F} = 9.0 Hz, Ph-C), 110.12 (t, J_{C-F} = 234.6 Hz, Ph-C), 108.42 (d, J_{C-F} =

22.4 Hz, Ph-C), 105.90 (d, J_{C-F} = 24.7 Hz, Ph-C), 39.89 (s, NCH_3); ESI-HRMS:m/z $[M+Na]^+$calcd. for [$C_{18}H_{13}BrClF_3N_4NaO$]: 494.9811; found: 494.9801.

*Data for Compound **6**.* Yield, 70 %; pink solid; mp, 136.1-137.8 °C; ^1H NMR (400 MHz, DMSO-*d6*) δ 9.48 (s, 1H, CONH), 8.39 (s, 1H, Ph-H), 7.75 (s, 1H, Py-H), 7.39 (dd, J = 8.6, 6.4 Hz, 1H, Ph-H), 7.33 (t, J_{H-F} = 57.7 Hz, 1H, CHF_2), 7.21 (d, J = 8.2 Hz, 1H, Ph-H), 7.05 (d, J = 2.0 Hz, 1H, Ph-H), 7.00 – 6.92 (m, 2H, Ph-H), 6.75 (td, J = 8.5, 2.7 Hz, 1H, Ph-H), 3.95 (s, 3H, NCH_3), 2.24 (s, 3H, $PhCH_3$); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 160.99 (s, CONH), 160.76 (d, J_{C-F} = 241.3 Hz, Ph-C), 145.46 (t, J_{C-F} = 23.0 Hz, Py-C), 142.46 (s, Ph-C), 139.91 (d, J_{C-F} = 10.7 Hz, Ph-C), 133.95 (s, Ph-C), 133.54 (s, Py-C), 131.99 (s, Ph-C), 129.43 (d, J_{C-F} = 10.2 Hz, Ph-C), 127.58 (s, Ph-C), 123.72 (d, J_{C-F} = 2.4 Hz, Ph-C), 118.73 (s, Ph-C), 117.20 (s, Ph-C), 116.55 (t, J_{C-F} = 3.4 Hz, Py-C), 110.12 (t, J_{C-F} = 234.4 Hz, CHF_2), 107.48 (d, J_{C-F} = 22.4 Hz, Ph-C), 104.54 (d, J_{C-F} = 25.5 Hz, Ph-C), 39.88 (s, NCH_3), 19.19 (s, $PhCH_3$); ESI-HRMS:m/z $[M+Na]^+$calcd. for [$C_{19}H_{16}ClF_3N_4NaO$]: 431.0862; found: 431.0852.

Data for Compound 7. Yield, 63 %; light pink solid; mp, 130.1-131.7 °C; ^1H NMR (400 MHz, DMSO-*d6*) δ 9.53 (s, 1H, CONH), 8.39 (s, 1H, Ph-NH-Ph), 7.90 (s, 1H, Py-H), 7.45 (dd, J = 9.5, 3.2 Hz, 1H, Ph-H), 7.32 (t, J = 44.6 Hz, 1H, CHF_2), 7.24 (dd, J = 15.2, 8.1 Hz, 1H, Ph-H), 7.08 (dd, J = 10.8, 2.8 Hz, 1H, Ph-H), 6.88 – 6.80 (m, 2H, Ph-H), 6.77 (dt, J = 11.7, 2.3 Hz, 1H Ph-H), 6.64 (td, J = 8.4, 2.1 Hz, 1H Ph-H), 3.95 (s, 3H, NCH_3); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 163.43 (d, J = 241.6 Hz, Ph-C), 160.96 (s, CONH), 160.59 (d, J_{C-F} = 241.5 Hz, Ph-C), 145.68 (s, Ph-C), 145.42 (t, J_{C-F} = 17.8 Hz, Py-C), 138.95 (d, J_{C-F} = 10.7 Hz), 133.54 (s, Py-C), 131.13 (d, J_{C-F} = 10.0 Hz), 129.26 (d, J_{C-F} = 9.9 Hz), 124.61 (d, J_{C-F} = 2.6 Hz), 116.49 (t, J_{C-F} = 3.6 Hz, Py-C), 113.40 (d, J_{C-F} = 2.1 Hz, Ph-C), 110.13 (t, J_{C-F} = 234.5 Hz, CHF_2), 108.41 (d, J_{C-F} = 22.4 Hz, Ph-C), 107.03 (d, J_{C-F} = 21.2 Hz, Ph-C), 105.99 (d, J_{C-F} = 25.3 Hz, Ph-C), 104.15 (d, J_{C-F} = 24.8 Hz, Ph-C), 39.88 (s, NCH_3); ESI-HRMS:m/z $[M+Na]^+$ calcd. for [$C_{18}H_{14}BrF_3N_4NaO$]: 463.0180; found: 463.0169.

*Data for Compound **8**.* Yield, 75 %; light red solid; mp, 108.1-109.3 °C; ^1H NMR (400 MHz, DMSO-*d6*) δ 9.75 (s, 1H, CONH), 8.35 (s, 1H, Ph-NH-Ph), 7.38 (dd, J = 8.8, 6.2 Hz, 1H, Py-H), 7.33 (t, J = 54.1 Hz, 1H, CHF_2), 7.24 (s, 1H, Ph-H), 7.13 (d, J

= 7.9 Hz, 1H, Ph-H), 7.07 – 6.99 (m, 2H, Ph-H), 6.82 (td, *J* = 8.4, 2.9 Hz, 1H, Ph-H), 6.72 (dd, *J* = 10.7, 2.8 Hz, 1H, Ph-H), 3.94 (s, 3H, NCH_3), 2.13 (s, 3H, $PhCH_3$); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.01 (s, CONH), 160.97 (d, J_{C-F} = 241.6 Hz, Ph-C), 145.47 (t, J_{C-F} = 22.2 Hz, Py-C), 143.26 (s, Ph-C), 140.28 (d, J_{C-F} = 10.6 Hz, Ph-C), 133.64 (s, Py-C), 133.02 (s, Ph-C), 128.90 (d, J_{C-F} = 9.8 Hz, Ph-C), 128.10 (s, Ph-C), 124.59 (s, Ph-C), 124.35 (d, J_{C-F} = 2.6 Hz, Ph-C), 121.13 (s, Ph-C), 119.37 (s, Ph-C), 116.06 (t, J_{C-F} = 3.5 Hz, Py-C), 110.15 (t, J_{C-F} = 234.6 Hz, CHF_2), 108.11 (d, J_{C-F} = 22.4 Hz, Ph-C), 106.14 (d, J_{C-F} = 25.1 Hz, Ph-C), 39.89 (s, NCH_3), 17.72 (s, $PhCH_3$); ESI-HRMS:m/z $[M+Na]^+$calcd. for [$C_{19}H_{16}BrF_3N_4NaO$]: 477.0337; found: 477.0338.

*Data for Compound **9***. Yield, 72 %; white solid; mp, 155.1-156.4 °C; ^1H NMR (400 MHz, DMSO-*d6*) δ 9.70 (s, 1H, CONH), 8.36 (s, 1H, Ph-NH-Ph), 7.34 (dd, *J* = 9.3, 5.5 Hz, 2H, Py-H, Ph-H),7.32 (t, J_{H-F} = 54.1 Hz, 1H, CHF_2),7.28 (dd, *J* = 7.8, 1.1 Hz, 1H, Ph-H), 7.07 (t, *J* = 7.9 Hz, 1H, Ph-H), 7.01 (dd, *J* = 8.0, 1.0 Hz, 1H, Ph-H), 6.72 (td, *J* = 8.4, 2.9 Hz, 1H, Ph-H), 6.50 (dd, *J* = 11.0, 2.8 Hz, 1H, Ph-H), 3.95 (s, 3H, NCH_3), 2.26 (s, 3H, $PhCH_3$); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 161.15 (d, J_{C-F} = 241.2 Hz, Ph-C), 161.09 (s, CONH), 145.47 (t, J_{C-F} = 23.3 Hz, Py-C), 142.70 (s, Ph-C), 141.67 (d, J_{C-F} = 10.7 Hz, Ph-C), 133.64 (s, Py-C), 130.01 (s, Ph-C), 129.01 (d, J_{C-F} = 9.9 Hz, Ph-C), 128.44 (s, Ph-C), 127.08 (s, Ph-C), 125.88 (s, Ph-C), 123.11 (d, J_{C-F} = 2.5 Hz, Ph-C), 120.86 (s, Ph-C), 116.22 (t, J_{C-F} = 3.6 Hz, Py-C), 110.17 (t, J_{C-F} = 234.5 Hz, CHF_2), 106.87 (d, J_{C-F} = 22.4 Hz, Ph-C), 104.35 (d, J_{C-F} = 25.5 Hz, Ph-C), 39.88 (s, NCH_3), 18.28 (s, $PhCH_3$); ESI-HRMS:m/z $[M+Na]^+$calcd. for [$C_{19}H_{16}BrF_3N_4NaO$]: 477.0337; found: 477.0333.

*Data for Compound **10***. Yield, 79 %; off-white solid; mp, 149.2-150.1 °C; ^1H NMR (400 MHz, DMSO-*d6*) δ 9.49 (s, 1H, CONH), 8.40 (s, 1H, Ph-NH-Ph), 7.66 (s, 1H, Py-H), 7.39 (dd, *J* = 8.7, 6.4 Hz, 1H, Ph-H), 7.34 (t, J_{H-F} = 54.1 Hz, 1H, CHF_2), 7.16 (t, *J* = 8.1 Hz, 1H, Ph-H), 7.01 (dd, *J* = 11.1, 2.8 Hz, 1H, Ph-H), 6.74 (td, *J* = 8.4, 2.9 Hz, 1H, Ph-H), 6.65 (dd, *J* = 8.0, 1.4 Hz, 1H, Ph-H), 6.57 (t, *J* = 2.2 Hz, 1H, Ph-H), 6.48 (dd, *J* = 8.1, 2.0 Hz, 1H, Ph-H), 3.95 (s, 3H, NCH_3), 3.70 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 161.47 (d, J_{C-F} = 91.7 Hz, Ph-C), 160.67 (s, CONH), 159.53 (s), 145.46 (t, J_{C-F} = 23.0 Hz, Py-C), 144.32 (s, Ph-C), 140.08 (d, J_{C-F}

= 10.7 Hz, Ph-C), 133.56 (s, Py-C), 130.42 (s, Ph-C), 129.19 (d, J_{C-F} = 10.0 Hz, Ph-C), 123.67 (d, J_{C-F} = 2.4 Hz, Ph-C), 116.56 (t, J_{C-F} = 3.6 Hz, Py-C), 110.90 (s, Ph-C), 110.15 (t, J_{C-F} = 234.5 Hz, Ph-C), 107.22 (d, J_{C-F} = 22.6 Hz, Ph-C), 106.97 (s, Ph-C), 104.63 (d, J_{C-F} = 25.7 Hz, Ph-C), 104.33 (s, Ph-C), 55.38 (s, OCH_3), 39.87 (s, NCH_3); ESI-HRMS:m/z $[M+Na]^+$calcd. for $[C_{19}H_{17}F_3N_4NaO_2]$: 413.1201; found: 413.1212.

*Data for Compound **11***. Yield, 69 %; light white solid; mp, 191.7-192.4°C; ^1H NMR (400 MHz, DMSO-*d6*) δ 9.47 (s, 1H, CONH), 8.37 (s, 1H, Ph-NH-Ph), 7.83 (s, 1H, Py-H), 7.44 (dd, *J* = 8.8, 6.3 Hz, 1H, Ph-H), 7.34 (t, J_{H-F} = 54.1 Hz, 1H, CHF_2), 7.33 (t, *J* = 1.7 Hz, 1H, Ph-H), 7.19 (dt, *J* = 7.1, 1.5 Hz, 1H, Ph-H), 7.07 – 7.00 (m, 3H, Ph-H), 6.81 (td, *J* = 8.4, 2.9 Hz, 1H, Ph-H), 3.95 (s, 3H, NCH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.93 (s, CONH), 160.60 (d, J_{C-F} = 241.6 Hz, Ph-C), 145.46 (t, J_{C-F} = 23.0 Hz, Py-H), 145.07 (s, Ph-C), 139.00 (d, J_{C-F} = 10.7 Hz, Ph-C), 133.54 (s, Py-C), 131.49 (s, Ph-C), 129.33 (d, J_{C-F} = 9.9 Hz, Ph-C), 129.21 (s, Ph-C), 126.17 (s, Ph-C), 124.53 (d, J_{C-F} = 2.6 Hz, Ph-C), 116.73 (s, Ph-C), 116.53 (t, J_{C-F} = 3.6 Hz, Ph-C), 110.13 (t, J_{C-F} = 234.5 Hz, CHF_2), 108.28 (d, J_{C-F} = 22.4 Hz, Ph-C), 105.71 (d, J_{C-F} = 25.3 Hz, Ph-C), 95.63 (s, Ph-C), 39.89 (s, NCH_3); ESI-HRMS:m/z $[M+Na]^+$calcd. for $[C_{18}H_{14}F_3IN_4NaO]$: 509.0062; found: 509.0074.

*Data for Compound **12***. Yield, 70 %; pink solid; mp, 139.8-134.6 °C; ^1H NMR (400 MHz, DMSO-*d6*) δ 9.54 (s, 1H, CONH), 8.36 (d, *J* = 20.9 Hz, 1H, Ph-NH-Ph), 8.15 (s, 1H, Py-H), 7.48 (dd, *J* = 9.8, 3.6 Hz, 1H, Ph-H), 7.34 (t, J_{H-F} = 63.9 Hz, 1H, CHF_2) , 7.16 (dd, *J* = 10.5, 2.8 Hz, 1H, Ph-H), 6.92 (td, *J* = 8.5, 2.9 Hz, 1H, Ph-H), 6.61 – 6.52 (m, 3H, Ph-H), 3.95 (s, 3H, NCH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.08 (d, J_{C-F} = 16.6 Hz, Ph-C), 162.69 (d, J_{C-F} = 16.7 Hz, Ph-C), 161.11 (d, J_{C-F} = 241.1 Hz, Ph-C), 161.09 (s, CONH), 160.44 (d, J_{C-F} = 242.3 Hz, Ph-C), 146.99 (t, J_{C-F} = 13.7 Hz, Ph-C), 145.45 (t, J_{C-F} = 23.3 Hz, Py-C), 137.65 (d, J_{C-F} = 10.7 Hz), 133.53 (s, Py-C), 129.29 (d, J_{C-F} = 9.8 Hz), 125.82 (d, J_{C-F} = 2.7 Hz), 116.41 (t, J_{C-F} = 3.6 Hz, Py-C), 110.04 (d, J_{C-F} = 12.6 Hz, CHF_2), 109.99 (t, J_{C-F} = 234.4 Hz, Ph-C), 108.02 (d, J_{C-F} = 24.9 Hz, Ph-C), 101.03 – 97.65 (m, Ph-C), 94.84 (t, J_{C-F} = 26.4 Hz, Ph-C), 39.89 (s, NCH_3); ESI-HRMS:m/z $[M+Na]^+$calcd. for $[C_{18}H_{13}F_5N_4NaO]$: 419.0907;

found: 419.0903.

*Data for Compound **13***. Yield, 70 %; white solid; mp, 179.5-180.6 °C; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 9.53 (s, 1H, CONH), 8.35 (s, 1H, Ph-NH-Ph), 8.08 (s, 1H, Py-H), 7.45 (d, J = 7.9 Hz, 1H, Ph-H), 7.39 (t, J = 7.8 Hz, 1H, Ph-H), 7.33 (t, J_{H-F} = 57.7 Hz, 1H, CHF_2, Ph-H), 7.29 (d, J = 8.4 Hz, 2H, Ph-H), 7.23 (d, J = 7.5 Hz, 1H, Ph-H), 7.11 (dd, J = 10.6, 2.8 Hz, 1H, Ph-H), 6.88 (td, J = 8.5, 2.8 Hz, 1H, Ph-H), 3.94 (s, 3H, NCH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.89 (s, CONH), 160.59 (d, J_{C-F} = 242.1 Hz, Ph-C), 145.46 (t, J_{C-F} = 23.2 Hz, Py-C), 144.60 (s, Ph-C), 138.27 (d, J_{C-F} = 10.7 Hz, Ph-C), 133.48 (s, Py-C), 130.84 (s, Ph-C), 129.42 (d, J_{C-F} = 9.8 Hz, Ph-C), 125.21 (d, J_{C-F} = 2.6 Hz, Ph-C), 123.66 (s, Ph-C), 121.60 (s, Ph-C), 119.60 (s, Ph-C), 119.38 (s, Ph-C), 116.42 (t, J_{C-F} = 3.5 Hz, Py-C), 112.34 (s, Ph-C), 110.09 (t, J_{C-F} = 234.5 Hz, Ph-C), 109.20 (d, J_{C-F} = 22.4 Hz, Ph-C), 106.87 (d, J_{C-F} = 25.0 Hz, Ph-C), 39.88 (s, NCH_3); ESI-HRMS:m/z $[M+Na]^+$calcd. for [$C_{19}H_{14}F_3N_5NaO$]: 408.1048; found: 408.1050.

*Data for Compound **14***. Yield, 66 %; light grey solid; mp, 158.1-158.9 °C; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 9.51 (s, 1H, CONH), 8.37 (s, 1H, Ph-NH-Ph), 8.02 (s, 1H, Py-H), 7.45 (d, J = 8.9 Hz, 1H, Ph-H), 7.33 (dd, J = 65.0, 48.7 Hz, 1H, CHF_2), 7.33 (s, 1H, Ph-H), 7.08 (dd, J = 10.7, 2.6 Hz, 1H, Ph-H), 7.02 (d, J = 8.1 Hz, 1H, Ph-H), 6.91 (s, 1H, Ph-H), 6.84 (td, J = 8.5, 2.6 Hz, 1H, Ph-H), 6.79 (d, J = 8.0 Hz, 1H, Ph-H), 3.94 (s, 3H, NCH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.94 (s, CONH), 160.53 (d, J_{C-F} = 241.8 Hz, Ph-C), 149.68 (d, J_{C-F} = 1.5 Hz, Ph-C), 145.46 (t, J_{C-F} = 23.2 Hz, Py-C), 138.64 (d, J_{C-F} = 10.5 Hz, Ph-C), 133.51 (s, Py-C), 131.17 (s, Ph-C), 129.36 (d, J_{C-F} = 10.0 Hz, Ph-C), 124.86 (d, J_{C-F} = 2.4 Hz, Ph-C), 121.82 (s, Ph-C), 119.28 (s, Ph-C), 116.49 (t, J_{C-F} = 3.4 Hz, Py-C), 115.89 (s, Ph-C), 112.30 (s, Ph-C), 110.11 (t, J_{C-F} = 234.3 Hz, CHF_2), 109.50(s, Ph-C), 108.71 (d, J_{C-F} = 22.4 Hz, Ph-C), 106.19 (d, J_{C-F} = 25.2 Hz, Ph-C), 39.87 (s, NCH_3); ESI-HRMS:m/z $[M+Na]^+$calcd. for [$C_{19}H_{14}F_6N_4NaO_2$]: 467.0919; found: 467.0920.

*Data for Compound **15***. Yield, 76 %; light pink solid; mp, 136.5-137.9 °C; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 9.48 (s, 1H, CONH), 8.36 (s, 1H, Ph-H), 7.71 (s, 1H, Py-H), 7.55 (dd, J = 7.9, 1.3 Hz, 1H, Ph-H), 7.31 (t, J = 63.4 Hz, 1H, CHF_2), 7.07 (td, *J* = 7.8, 1.3 Hz, 1H, Ph-H), 6.85 (t, *J* = 2.0 Hz, 1H, Ph-H), 6.84 – 6.80 (m, 1H, Ph-H), 6.76 (dd, *J* = 7.9, 1.2 Hz, 1H, Ph-H), 3.93 (s, 3H, NCH_3); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 160.67 (s, CONH), 146.61 (s, Ph-C), 145.35 (t, J_{C-F} = 23.4 Hz, Py-C), 135.94 (s, Ph-C), 133.98 (s, Py-C), 133.60 (s, Ph-C), 131.02 (s, Ph-C), 130.09 (s, Ph-C), 126.91 (s, Ph-C), 126.52 (s, Ph-C), 123.23 (s, Ph-C), 121.93 (s, Ph-C), 118.87 (s, Ph-C), 116.51 (t, J_{C-F} = 3.5 Hz, Py-C), 115.39 (s, Ph-C), 114.52 (s, Ph-C), 110.19 (t, J_{C-F} = 234.4 Hz, CHF_2), 39.87 (s, NCH_3); ESI-HRMS:m/z $[M+Na]^+$calcd. for $[C_{18}H_{12}F_6N_4NaO]$: 437.0813; found: 437.0795;

*Data for Compound **16**.* Yield, 72 %; pink solid; mp, 146.1-147.3 °C; ^1H NMR (400 MHz, DMSO-*d6*) δ 9.90 (s, 1H, CONH), 9.09 (d, *J* = 1.6 Hz, 1H, Py-H), 8.74 (dd, *J* = 4.8, 1.5 Hz, 1H, Py-H), 8.27 (d, *J* = 7.9 Hz, 1H, Py-H), 7.85 (s, 1H, Ph-NH-Ph), 7.54 (dd, *J* = 7.9, 4.8 Hz, 1H, Py-H), 7.43 (dd, *J* = 8.7, 6.4 Hz, 1H, Ph-H), 7.21 (d, *J* = 8.3 Hz, 1H, Ph-H), 7.06 (d, *J* = 2.2 Hz, 1H, Ph-H), 6.98 (dd, *J* = 17.1, 2.5 Hz, 1H, Ph-H), 6.98 (t, *J* = 2.3 Hz, 1H, Ph-H), 6.77 (td, *J* = 8.4, 2.8 Hz, 1H, Ph-H), 2.23 (s, 3H, $PhCH_3$); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.95 (s, CONH), 161.02 (d, J_{C-F} = 241.4 Hz, Ph-C), 152.44 (s, Py-C), 149.42 (s, Py-C), 142.38 (s, Ph-C), 140.38 (d, J_{C-F} = 10.8 Hz, Ph-C), 136.00 (s, Py-C), 133.93 (s, Ph-C), 131.95 (s, Py-C), 130.53 (s, Ph-C), 129.89 (d, J_{C-F} = 9.9 Hz, Ph-C), 127.66 (s, Py-C), 123.76 (s, Ph-C), 123.72 (s, Ph-C), 118.92 (s, Ph-C), 117.41 (s, Ph-C), 107.34 (d, J_{C-F} = 22.6 Hz, Ph-C), 104.42 (d, J_{C-F} = 25.8 Hz, Ph-C), 19.18 (s, $PhCH_3$); ESI-HRMS: m/z $[M+Na]^+$ calcd. for $[C_{19}H_{15}ClFN_3NaO]$: 378.0785, found 378.0767.

*Data for Compound **17**.* Yield, 71 %; gray solid; mp, 132.1-133.3 °C; ^1H NMR (400 MHz, DMSO-*d6*) δ 9.96 (s, 1H, CONH), 8.76 (d, *J* = 6.0 Hz, 2H, Py-H), 7.85 (d, *J* = 1.6 Hz, 2H, Py-H), 7.84 (s, 1H, Ph-NH-Ph), 7.41 (dd, *J* = 8.7, 6.3 Hz, 1H, Ph-H), 7.21 (d, *J* = 8.3 Hz, 1H, Ph-H), 7.05 (d, *J* = 2.2 Hz, 1H, Ph-H), 7.01 – 6.94 (m, 2H, Ph-H), 6.77 (td, *J* = 8.4, 2.8 Hz, 1H, Ph-H), 2.23 (s, 3H, $PhCH_3$); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.82 (s, CONH), 161.11 (d, J_{C-F} = 241.6 Hz, Ph-C), 150.55 (s, Py-C), 142.32 (s, Ph-C), 141.92 (s, Py-C), 140.47 (d, J_{C-F} = 10.9 Hz, Ph-C), 133.93 (s, Ph-C), 131.96 (s, Ph-C), 129.93 (d, J_{C-F} = 10.1 Hz, Ph-C), 127.73 (s, Ph-C), 123.46 (d, J_{C-F} = 2.4 Hz, Ph-C), 122.21 (s, Py-C), 118.98 (s, Ph-C), 117.46 (s, Ph-C), 107.34

(d, $J_{C\text{-}F}$ = 22.5 Hz, Ph-C), 104.37 (d, $J_{C\text{-}F}$ = 25.8 Hz, Ph-C), 19.19 (s, $PhCH_3$); ESI-HRMS: m/z $[M+Na]^+$ calcd. for $[C_{19}H_{15}ClFN_3NaO]$: 378.0785, found 378.0761

*Data for Compound **18***. Yield, 75 %; pink solid; mp, 159.0-160.1 °C; ^1H NMR (400 MHz, DMSO-*d6*) δ 10.03 (s, 1H, CONH), 8.51 (dd, *J* = 4.8, 1.9 Hz, 1H, Py-H), 8.01 (dd, *J* = 7.5, 1.9 Hz, 1H, Py-H), 7.65 (s, 1H, Ph-NH-Ph), 7.57 (dd, *J* = 7.5, 4.9 Hz, 1H, Py-H), 7.54 (dd, *J* = 6.2, 3.5 Hz, 1H, Ph-H), 7.22 (d, *J* = 8.3 Hz, 1H, Ph-H), 7.00 (dd, *J* = 10.0, 2.5 Hz, 2H, Ph-H), 6.91 (dd, *J* = 8.2, 2.3 Hz, 1H, Ph-H), 6.84 (td, J = 8.4, 2.8 Hz, 1H, Ph-H), 2.25 (s, 3H, $PhCH_3$); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.70 (s, CONH), 160.77 (d, $J_{C\text{-}F}$ = 241.8 Hz, Ph-C), 150.94 (s, Py-C), 147.24 (s, Py-C), 142.66 (s, Ph-C), 139.10 (d, $J_{C\text{-}F}$ = 10.7 Hz, Ph-C), 138.81 (s, Py-C), 134.03 (s, Ph-C), 133.23 (s, Py-C), 132.10 (s, Ph-C), 128.42 (d, $J_{C\text{-}F}$ = 10.1 Hz, Ph-C), 127.48 (s, Py-C), 124.22 (d, $J_{C\text{-}F}$ = 2.6 Hz, Ph-C), 123.40 (s, Ph-C), 118.18 (s, Ph-C), 116.85 (s, Ph-C), 108.20 (d, $J_{C\text{-}F}$ = 22.5 Hz, Ph-C), 105.71 (d, $J_{C\text{-}F}$ = 25.2 Hz, Ph-C), 19.18 (s, NCH_3); ESI-HRMS: m/z $[M+Na]^+$ calcd. for $[C_{19}H_{14}Cl_2FN_3NaO]$: 412.0396, found 412.0394.

*Data for Compound **19***. Yield, 69 %; light red solid; mp, 149.1-150.9 °C; ^1H NMR (400 MHz, DMSO-*d6*) δ 9.70 (s, 1H, CONH), 7.95 (s, 1H, Ph-NH-Ph), 7.94 (s, 1H), 7.78 (s, 1H), 7.57 (t, *J* = 7.3 Hz, 1H), 7.51 (d, *J* = 7.7 Hz, 2H), 7.45 (dd, *J* = 8.7, 6.4 Hz, 1H), 7.20 (d, *J* = 8.3 Hz, 1H), 7.04 (d, *J* = 2.2 Hz, 1H), 6.99 (dd, *J* = 11.0, 2.8 Hz, 1H), 6.94 (dd, *J* = 8.2, 2.3 Hz, 1H), 6.78 (td, *J* = 8.4, 2.8 Hz, 1H), 2.23 (s, 3H, $PhCH_3$); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 166.29 (s, CONH), 160.77 (d, $J_{C\text{-}F}$ = 241.1 Hz), 142.60 (s), 140.01 (d, $J_{C\text{-}F}$ = 10.8 Hz), 134.88 (s), 133.96 (s), 131.99 (s), 129.48 (d, $J_{C\text{-}F}$ = 10.2 Hz), 128.69 (s), 128.29 (s), 127.47 (s), 124.60 (d, $J_{C\text{-}F}$ = 2.6 Hz), 118.60 (s), 117.14 (s), 107.61 (d, $J_{C\text{-}F}$ = 22.6 Hz), 104.82 (d, $J_{C\text{-}F}$ = 25.4 Hz), 19.18 (s, NCH_3); ESI-HRMS: m/z $[M+Na]^+$ calcd. for $[C_{20}H_{16}ClFN_2NaO]$: 377.0833, found 377.0806

*Data for Compound **20***. Yield, 83%; light red solid; mp, 159.4-161.2 °C; ^1H NMR (400 MHz, DMSO-*d6*) δ 9.89 (s, 1H, CONH), 7.61 (s, 1H, Ph-NH-Ph), 7.59 – 7.52 (m, 3H), 7.49 (td, *J* = 7.7, 1.7 Hz, 1H), 7.42 (td, *J* = 7.4, 1.2 Hz, 1H), 7.22 (d, *J* = 8.3 Hz, 1H), 7.04 – 6.98 (m, 2H), 6.89 (dd, *J* = 8.2, 2.3 Hz, 1H), 6.84 (td, *J* = 8.5, 2.8 Hz, 1H), 2.25 (s, 3H, $PhCH_3$); ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.92 (s, CONH), 160.66 (d, J_{C-F} = 241.7 Hz), 142.74 (s), 138.91 (d, J_{C-F} = 10.6 Hz), 136.87 (s), 134.06 (s), 132.12 (s), 131.62 (s), 130.66 (s), 130.13 (s), 129.61 (s), 128.37 (d, J_{C-F} = 9.9 Hz), 127.52 (s), 127.37 (s), 124.63 (d, J_{C-F} = 2.5 Hz), 117.97 (s), 116.72 (s), 108.26 (d, J_{C-F} = 22.5 Hz), 105.86 (d, J_{C-F} = 25.2 Hz), 19.18 (s, $PhCH_3$); ESI-HRMS: m/z $[M+Na]^+$ calcd. for $[C_{20}H_{15}Cl_2FN_2NaO]$: 411.0443, found 411.0427

*Data for Compound **21***. Yield, 72 %; light pink solid; mp, 172.1-173.4 °C; ^1H NMR (400 MHz, DMSO-*d6*) δ 9.86 (s, 1H, CONH), 7.92 (d, J_{C-F} = 7.9 Hz, 1H), 7.59 (s, 1H, Ph-NH-Ph), 7.57 – 7.55 (m, 1H), 7.49-7.43 (m, 2H), 7.21 (ddd, *J* = 9.2, 5.8, 3.7 Hz, 2H), 7.05 – 6.97 (m, 2H), 6.92 (dd, *J* = 8.2, 2.3 Hz, 1H), 6.84 (td, *J* = 8.4, 2.8 Hz, 1H), 2.25 (s, 3H, $PhCH_3$)； ^{13}C NMR (100 MHz, DMSO-d_6) δ 168.58 (s, CONH), 160.72 (d, *J* = 241.7 Hz), 142.90 (s), 142.58 (s), 139.52 (s), 139.08 (d, J_{C-F} = 10.6 Hz), 134.06 (s), 132.14 (s), 131.56 (s), 128.74 (s), 128.43 (s), 128.36 (s), 127.50 (s), 124.35 (d, J_{C-F} = 2.6 Hz), 118.16 (s), 116.96 (s), 108.02 (d, J_{C-F} = 22.5 Hz), 105.43 (d, J_{C-F} = 25.4 Hz), 94.34 (s), 19.20 (s, $PhCH_3$); ESI-HRMS: m/z $[M+Na]^+$ calcd. for $[C_{20}H_{15}ClFIN_2NaO]$: 502.9799, found 502.9784.

*Data for Compound **22***. Yield, 70 %; brown solid; mp, 201.8-203.1 °C; ^1H NMR (400 MHz, DMSO-*d6*) δ 9.62 (s, 1H, CONH), 7.67 (s, 1H, Ph-NH-Ph), 7.56 (dd, *J* = 8.7, 6.4 Hz, 1H), 7.44 (d, *J* = 7.4 Hz, 1H), 7.36 (t, *J* = 7.2 Hz, 1H), 7.29 – 7.24 (m, 2H), 7.20 (d, *J* = 8.3 Hz, 1H), 6.99 (d, *J* = 2.1 Hz, 2H), 6.88 (dd, *J* = 8.2, 2.3 Hz, 1H), 6.83 (td, *J* = 8.5, 2.7 Hz, 1H), 2.38 (s, 3H, $PhCH_3$), 2.24 (s, 3H, $PhCH_3$); ^{13}C NMR (100 MHz, DMSO-d_6) δ 168.65 (s, CONH), 160.51 (d, J_{C-F} = 241.2 Hz), 142.94 (s), 138.91 (d, J_{C-F} = 10.5 Hz), 136.97 (s), 136.17 (s), 134.05 (s), 132.09 (s), 131.00 (s), 130.18 (s), 128.47 (d, J_{C-F} = 10.1 Hz), 127.91 (s), 127.19 (s), 125.92 (s), 125.36 (d, J_{C-F} = 2.1 Hz), 117.83 (s), 116.60 (s), 108.32 (d, J_{C-F} = 22.5 Hz), 106.06 (d, J_{C-F} = 25.0 Hz), 19.91 (s, $PhCH_3$), 19.16 (s, $PhCH_3$); ESI-HRMS: m/z $[M+Na]^+$ calcd. for $[C_{21}H_{18}ClFN_2NaO]$: 391.0989, found 391.0969.

*Data for Compound **23***. Yield, 67 %; light gray solid; mp, 180.4-181.5 °C; ^1H NMR (400 MHz, DMSO-*d6*) δ 9.97 (s, 1H, CONH), 7.83 (d, *J* = 7.6 Hz, 1H), 7.74 (t, *J* = 7.1 Hz, 1H), 7.70 (d, *J* = 7.4 Hz, 1H), 7.65 (d, *J* = 7.8 Hz, 1H), 7.61 (s, 1H, Ph-NH-Ph), 7.49 (dd, J = 8.8, 6.3 Hz, 1H), 7.23 (d, J = 8.3 Hz, 1H), 7.04 – 6.97 (m, 2H), 6.90 (dd, J = 8.2, 2.3 Hz, 1H), 6.84 (td, J = 8.4, 2.8 Hz, 1H), 2.26 (s, 3H, $PhCH_3$); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 166.67 (s, CONH), 160.74 (d, $J_{C\text{-}F}$ = 241.6 Hz), 142.72 (s), 139.12 (d, $J_{C\text{-}F}$ = 10.6 Hz), 136.34 (d, $J_{C\text{-}F}$ = 2.2 Hz), 134.06 (s), 132.83 (s), 132.12 (s), 130.54 (s), 129.13 (s), 128.41 (d, $J_{C\text{-}F}$ = 10.1 Hz), 127.42 (s), 126.89 – 126.54 (m), 124.87 (dd, $J_{C\text{-}F}$ = 231.7, 113.1 Hz, $PhCF_3$), 124.48 (d, $J_{C\text{-}F}$ = 2.7 Hz), 118.05 (s), 116.76 (s), 108.25 (d, $J_{C\text{-}F}$ = 22.6 Hz), 105.77 (d, $J_{C\text{-}F}$ = 25.4 Hz), 19.17 (s, $PhCH_3$); ESI-HRMS: m/z $[M+Na]^+$ calcd. for $[C_{21}H_{15}ClF_4N_2NaO]$: 445.0707, found 445.0698.

Data for Compound ***24***. Yield, 70 %; white solid; mp, 137.0-138.5 °C; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 9.56 (s, 1H, CONH), 7.91 (d, J = 1.0 Hz, 1H, Fu-H), 7.81 (s, 1H, Ph-NH-Ph), 7.45 (dd, J = 8.8, 6.3 Hz, 1H, Ph-H), 7.27 (d, J = 3.4 Hz, 1H, Fu-H), 7.21 (d, J = 8.3 Hz, 1H, Ph-H), 7.04 (d, J = 2.2 Hz, 1H, Ph-H), 6.98 (dd, J = 11.0, 2.8 Hz, 1H, Fu-H), 6.94 (dd, J = 8.2, 2.3 Hz, 1H, Ph-H), 6.77 (td, J = 8.4, 2.9 Hz, 1H, Ph-H), 6.68 (dd, J = 3.5, 1.7 Hz, 1H, Ph-H), 2.24 (s, 3H, $PhCH_3$); ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.77 (d, $J_{C\text{-}F}$ = 241.4 Hz), 157.30 (s, CONH), 148.08 (s, Fu-C), 145.94 (s, Ph-C), 142.67 (s, Fu-C), 139.88 (d, $J_{C\text{-}F}$ = 10.6 Hz, Ph-C), 133.98 (s, Ph-C), 132.04 (s, Ph-C), 129.07 (d, $J_{C\text{-}F}$ = 10.3 Hz, Ph-C), 127.51 (s, Ph-C), 123.91 (d, $J_{C\text{-}F}$ = 2.5 Hz, Ph-C), 118.56 (s, Ph-C), 117.10 (s, Ph-C), 115.10 (s, Fu-C), 112.56 (s, Fu-C), 107.76 (d, $J_{C\text{-}F}$ = 22.5 Hz, Ph-C), 104.92 (d, $J_{C\text{-}F}$ = 25.5 Hz, Ph-C), 19.19 (s, $PhCH_3$); ESI-HRMS: m/z $[M+Na]^+$ calcd. for $[C_{18}H_{14}ClFN_2NaO_2]$: 367.0626, found 367.0590

Data for Compound ***25***. Yield, 72 %; light pink; mp, 150.2-152.1 °C; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 9.46 (s, 1H, CONH), 8.32 (s, 1H, Ph-NH-Ph), 7.77 (d, J = 1.5 Hz, 2H, Fu-H), 7.38 (dd, J = 8.7, 6.4 Hz, 1H, Ph-H), 7.20 (d, J = 8.3 Hz, 1H, Fu-H), 7.06 (d, J = 2.2 Hz, 1H, Ph-H), 7.01 – 6.92 (m, 3H, Ph-H), 6.76 (td, J = 8.4, 2.8 Hz, 1H, Ph-H), 2.24 (s, 3H, $PhCH_3$); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.57 (s, CONH), 160.81 (d, $J_{C\text{-}F}$ = 241.4 Hz, Ph-C), 146.39 (s, Fu-C), 144.44 (s, Ph-C), 142.46 (s, Fu-C), 140.09 (d, $J_{C\text{-}F}$ = 10.7 Hz, Ph-C), 133.96 (s, Ph-C), 132.00 (s, Ph-C), 129.56 (d, $J_{C\text{-}F}$ = 10.1 Hz, Ph-C), 127.56 (s, Ph-C), 123.88 (d, $J_{C\text{-}F}$ = 2.6 Hz, Ph-C), 123.22 (s, Fu-C), 118.71 (s, Ph-C), 117.21 (s, Ph-C), 109.91 (s, Fu-C), 107.47 (d, $J_{C\text{-}F}$

= 22.5 Hz, Ph-C), 104.50 (d, J_{C-F} = 25.6 Hz, Ph-C), 19.19 (s, $PhCH_3$); ESI-HRMS: m/z $[M+Na]^+$ calcd. for $[C_{18}H_{14}ClFN_2NaO_2]$: 367.0626, found 367.0613.

*Data for Compound **26***. Yield, 68 %; white solid; mp, 147.0-148.3 °C; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 9.24 (s, 1H, CONH), 7.73 (s, 1H, Ph-NH-Ph), 7.56 (d, *J* = 2.0 Hz, 1H, Ph-H), 7.39 (dd, *J* = 8.7, 6.4 Hz, 1H, Ph-H), 7.20 (d, *J* = 8.3 Hz, 1H, Fu-H), 7.03 (d, *J* = 2.2 Hz, 1H, Fu-H), 6.96 (ddd, *J* = 10.5, 9.7, 2.6 Hz, 3H, Ph-H), 6.76 (td, *J* = 8.4, 2.8 Hz, 1H, Ph-H), 2.53 (s, 3H, $FuCH_3$), 2.24 (s, 3H, $PhCH_3$); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 162.76 (s, CONH), 160.71 (d, J_{C-F} = 241.2 Hz, Ph-C), 157.17 (s, Fu-C), 142.59 (s, PH-C), 141.06 (s, Fu-C), 139.94 (d, J_{C-F} = 10.6 Hz, Ph-C), 133.97 (s, Ph-C), 132.00 (s, Ph-C), 129.48 (d, J_{C-F} = 10.1 Hz, Ph-C), 127.43 (s, Ph-C), 124.35 (d, J_{C-F} = 2.6 Hz, Ph-C), 118.48 (s, Ph-C), 117.07 (s, Ph-C), 116.31 (s, Fu-C), 110.17 (s, Fu-C), 107.62 (d, J_{C-F} = 22.4 Hz, Ph-C), 104.82 (d, J_{C-F} = 25.6 Hz, Ph-C), 19.18 (s, $PhCH_3$), 13.79 (s, $FuCH_3$); ESI-HRMS: m/z $[M+Na]^+$ calcd. for $[C_{19}H_{16}ClFN_2NaO_2]$: 381.0782, found 381.0754

*Data for Compound **27***. Yield, 77 %; light red solid; mp, 172.1-173.6 °C; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 9.73 (s, 1H, CONH), 7.93 (d, *J* = 3.3 Hz, 1H, Fu-H), 7.83 (s, 1H, Ph-NH-Ph), 7.82 (d, *J* = 1.0 Hz, 1H, Fu-H), 7.38 (dd, *J* = 8.8, 6.3 Hz, 1H, Ph-H), 7.22 – 7.18 (m, 1H, Fu-H), 7.19 (d, *J* = 0.8 Hz, 1H, Ph-H), 7.07 (d, *J* = 2.2 Hz, 1H, Ph-H), 6.97 (ddd, *J* = 6.6, 5.3, 2.6 Hz, 2H, Ph-H), 6.76 (td, *J* = 8.4, 2.8 Hz, 1H, Ph-H), 2.24 (s, 3H, $PhCH_3$); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.03 (s, CONH), 160.91 (d, J_{C-F} = 241.3 Hz, Ph-C), 142.46 (s, Ph-C), 140.33 (d, J_{C-F} = 10.7 Hz, Ph-C), 140.20 (s, Th-C), 133.96 (s, Ph-C), 131.96 (d, J_{C-F} = 6.3 Hz, Ph-C), 129.81 (s, Th-C), 129.73 (s), 128.40 (s, Th-C), 127.59 (s, Th-C), 123.78 (d, J_{C-F} = 2.4 Hz, Ph-C), 118.80 (s, Ph-C), 117.28 (s, Ph-C), 107.43 (d, J_{C-F} = 22.6 Hz, Ph-C), 104.41 (d, J_{C-F} = 25.8 Hz, Ph-C), 19.19 (s, $PhCH_3$); ESI-HRMS: m/z $[M+Na]^+$ calcd. for $[C_{18}H_{14}ClFN_2NaOS]$: 383.0397, found 393.0377.

*Data for Compound **28***. Yield, 70 %; grayish white solid; mp, 157.8-159.1 °C; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 9.58 (s, 1H, CONH), 8.29 (s, 1H, Ph-NH-Ph), 7.81 (s, 1H, Th-H), 7.64 – 7.57 (m, 2H, Th-H), 7.40 (dd, *J* = 8.6, 6.4 Hz, 1H, Ph-H), 7.20 (d, *J* = 8.3 Hz, 1H, Ph-H), 7.06 (d, *J* = 2.0 Hz, 1H, Ph-H), 7.01 – 6.93 (m, 2H, Ph-H), 6.76

(td, J = 8.4, 2.8 Hz, 1H, Ph-H), 2.23 (s, 3H, $PhCH_3$); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 161.90 (s, CONH), 160.78 (d, $J_{C\text{-}F}$ = 241.2 Hz, Ph-C), 142.52 (s, Ph-C), 140.10 (d, $J_{C\text{-}F}$ = 10.7 Hz, Ph-C), 138.04 (s, Th-C), 133.96 (s, Ph-C), 132.00 (s, Ph-C), 130.25 (s, Ph-C), 129.56 (d, $J_{C\text{-}F}$ = 10.3 Hz, Ph-C), 127.80 (s, Th-C), 127.52 (s, Th-C), 127.10 (s, Th-C), 124.17 (d, $J_{C\text{-}F}$ = 2.7 Hz, Ph-C), 118.68 (s, Ph-C), 117.19 (s, Ph-C), 107.47 (d, $J_{C\text{-}F}$ = 22.4 Hz, Ph-C), 104.51 (d, $J_{C\text{-}F}$ = 25.5 Hz, Ph-C), 19.19 (s, $PhCH_3$); ESI-HRMS: m/z $[M+Na]^+$ calcd. for $[C_{18}H_{14}ClFN_2NaOS]$: 383.0397, found 383.0364

*Data for Compound **29***. Yield, 73 %; white solid; mp, 160.4-161.3 °C; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 10.16 (s, 1H, CONH), 7.78 (s, 1H, Ph-NH-Ph), 7.42 (dd, J = 8.6, 6.4 Hz, 1H, Ph-H), 7.22 (d, J = 8.3 Hz, 1H, Ph-H), 7.03 – 6.95 (m, 2H, Ph-H), 6.88 (dd, J = 8.2, 1.7 Hz, 1H, Ph-H), 6.82 (td, J = 8.5, 2.5 Hz, 1H, Ph-H), 2.73 (s, 3H, $ThCH_3$), 2.26 (s, 3H, $PhCH_3$); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 168.16 (s, CONH), 161.01 (d, $J_{C\text{-}F}$ = 242.5 Hz, Ph-C), 158.51 (s, Ph-C), 142.56 (s, Th-C), 139.42 (d, $J_{C\text{-}F}$ = 9.9 Hz, Th-C), 134.71 (s, Ph-C), 134.02 (s, Ph-C), 132.06 (s, Th-C), 128.83 (d, $J_{C\text{-}F}$ = 10.2 Hz, Ph-C), 127.48 (s, Ph-C), 123.80 (d, J = 2.4 Hz, Ph-C), 122.15 (s, Ph-C), 119.45 (s, Ph-C), 118.10 (s, Ph-C), 116.76 (s, Ph-C), 108.20 (d, $J_{C\text{-}F}$ = 22.6 Hz, Ph-C), 105.75 (d, $J_{C\text{-}F}$ = 24.8 Hz, Ph-C), 19.19 (s, $PhCH_3$), 19.07 (s, $ThCH_3$); ESI-HRMS: m/z $[M+Na]^+$ calcd. for $[C_{19}H_{14}ClF_4N_3NaOS]$: 466.0380, found 466.0365.

2. Biological Assay

In vitro antifungal activities of the target compounds

The tested compounds were dissolved in acetone to prepare a 10 mg/mL stock solution before mixing with PDA. The media containing compounds at a concentration of 20 mg/L were then poured into sterilized Petri dishes for primary screening. After 24-72 h at 28 °C, the colony diameter of each strain was measured. Percentage inhibition rate was calculated as (C-A)/(C-B) × 100 %, where A represents the colony diameter in the Petri dishes with tested compounds, B represents the diameter of mycelial disc and C is the mean colony diameter in control Petri dishes. The commercial fungicide bixafen and thifluzamide was employed as the positive control. Each treatment was performed three times. The inhibition rate of the potent compounds was further tested and the corresponding EC_{50} values were calculated by using Data Processing System (DPS, v17.0).

Assay of SDH's inhibitory activity

Isolation of R. solani. Cultures were inoculated at 0.05 OD_{600} nm and grown on a reciprocal shaker (180 rpm, 25 °C) for 5 days in Sabouraud maltose broth (SMB) medium. Cells were harvested by vacuum filtration and disrupted in liquid nitrogen using a mortar and pestle. The resultant powder was resuspended to 10 % w/v in mitochondrial extraction buffer (10 mM KH_2PO_4, pH 7.2, 10 mM KCl, 10 mM $MgCl_2$, 0.5 M sucrose, 0.2 mM EDTA, 2 mM PMSF). The extract was clarified by centrifugation (5000 g, 4 °C for 10 min, 2 times), and intact mitochondria were then pelleted at 10000 g for 20 min at 4 °C and resuspended in the same buffer. Mitochondrial suspensions were brought to a concentration of 10 mg/mL and stored at -80 °C until use. SDH activity was found to remain stable for months.

Activity inhibition of Succinate: Ubiquinone/DCPIP. Mitochondrial suspensions were diluted 1/20 in extraction buffer and preactivated at 30 °C for 30 min in the presence of 10 mM succinate. Succinate: ubiquinone/DCPIP activity inhibition measurements were performed by adding 10 μL of preactivated mitochondria to 200 μL of assay buffer (50 mM phosphate-sodium, pH 7.2, 250 mM sucrose, 3 mM NaN_3, 10 mM succinate) supplemented with 140 μM dichloro-phenolindophenol (DCPIP) and 1 mM 2,3-dimethoxy-5-methyl-1,4-benzoquinone (Q_0). Inhibitor concentrations ranged between 0.0050 and 15 mg/L, with uniform 5 × dilution factor steps (six inhibitor concentrations + DMSO control). A total of 96 well plates were pre-equilibrated at reaction temperature (30 °C) for 10 min before the reactions were started by the addition of 10 μL of preactivated R. solani mitochondrial suspension. DCPIP reduction was conducted at 30 °C and monitored at 595 nm. Calculated absorbance slopes (OD/h) were used for half-inhibitory concentration (IC_{50}) calculations using Data Processing System (DPS, v17.0).

*In vivo pot tests for the target compounds **6**, **9** and **15** against R. solani.*

The *in vivo* antifungal activities of **6**, **9** and **15** against *R. solani* were tested according to the procedure described previously.[25] Rice plants were grown under greenhouse conditions (Relative Humidity = 70-80 %, Temperature = 24-26 °C, Light Intensity ≥ 2000 lux) in plastic planting pots. The tested compounds dissolved in acetone/distilled water containing Tween-80 (0.05 %) at the given concentration were sprayed over the plant and subsequently cultivated for 24 h. The blank control groups and the treated rice seedlings at the third-leaf stage were inoculated with strain *R. solani*, then the symptoms were examined five days later. Pots were arranged as a randomized complete block with three replicates per treatment. The inhibition percentage was expressed as the mean of values obtained in three independent experiments. The results are listed in Table 6, and bixafen and thifluzamide were used as a control. The corresponding EC_{50} values were calculated by using Data Processing System (DPS, v17.0).

*In vivo pot tests for the target compounds **6**, **9** and **15** against R. solani.*

Rice plants were grown under greenhouse conditions (Relative Humidity = 70-80 %, Temperature = 24-26 °C, Light Intensity ≥ 2000 lux) in plastic planting pots. The tested compounds dissolved in acetone/distilled water containing Tween-80 (0.05 %) at the given concentration were sprayed over the plant and subsequently cultivated for 24 h. The blank control groups and the treated rice seedlings at the third-leaf stage were inoculated with strain *R. solani*, then the symptoms were examined five days later. Pots were arranged as a randomized complete block with three replicates per treatment.

*Field trials for compound **6** in controlling rice sheath blight.*

Field trials were conducted in Chengdu, Sichuan Province, China (N30° 29′ 13.57″, E103° 37′ 4.17″), to determine the potential control of rice sheath blight in summer rice in 2018. The field was divided into 15 plots and each plot had an area of 30 m^2 (5 m × 6 m). Each of the plots were separated by a 50 cm interval with untreated rice plants. The five treatments were treated as follows: (1-2) **6**: 200 g a.i ha^{-1}, 100 g a.i ha^{-1}; (3-4) thifluzamide: 200 g a.i ha^{-1}, 100 g a.i ha^{-1}; (5) no treatment control (CK). Each treatment took up in three plots and was distributed randomly in each field. Fungicides were sprayed upon initiation of disease on August 4, 2018 for the first time and the second application was carried out seven days later. The relative control effects were assessed on the 7th and 21th day of foliar application of **6** and thifluzamide. No other fungicides were applied to the experimental plots. Visual disease assessment was made on the 7th day after the first spraying of fungicides and 14th day after the second spraying of fungicides.

The disease severity was scored by using the following scale:

0: no symptoms;

1: lesions limited to lower 1/4 of leaf sheath area;

3: lesions present on lower 1/2 of leaf sheath area;

5: lesions present on more than 1/2 of leaf sheath area, with slight infection on lower (3rd or 4th) leaves;

7: lesions present on more than 3/4 of leaf sheath, with severe infection on upper leaves (flag and 2nd leaf);

9: lesions reaching top of tillers, with severe infection on all leaves and some plants killed.

Disease severity and the control control efficacy were calculated as follows:

Disease severity = [Σ (The number of diseased plants in this index × Disease index)/(Total number of plants investigated × The highest disease index)]×100 %.

Control efficacy = [(Disease severity of control−Disease severity of treated group)/Disease severity of control] ×100 %.

3. Homology modeling and molecular docking

Homology modeling

The NCBI protein database (http://www.ncbi.nlm.nih.gov/protein/) was used to search the SDH amino acid sequence of *R. solani*. The employed protein sequence was CUA72490.1, CUA71217.1, CUA73421.1 and CUA73959.1 reported by Wibberg. The BLAST server (http://blast.ncbi.nlm.nih.gov) was used to search a template for the chain. We applied SDH from avian (PDB ID:1YQ3) as the template, and the homology of amino acid sequence was aligned. Homology modeling of SDH from *R. solani* was carried out using MODELER 9.15 (http://salilab. org/modeller/).

Molecular docking

Molecular docking studies were performed to investigate the binding mode between compound and the SDH by using Autodockvina 1.1.2.[28] The 3D structure of the compounds were drawn by ChemBioDraw Ultra 14.0 and ChemBio3D Ultra 14.0 softwares and minimized by MM2 using ChemBio3D Ultra 14.0 software. The AutoDockTools 1.5.6 package was employed to generate the docking input files.[29,30] The ligand was prepared for docking by merging non-polar hydrogen atoms and defining rotatable bonds. The search grid of SDH was identified as center_x: 86.459, center_y: 65.6, and center_z: 85.537 with dimensions size_x: 15, size_y: 15, and size_z: 15. The value of exhaustiveness was set to 20. For Vina docking, the default parameters were used if it was not mentioned. The best-scoring pose as judged by the Vina docking score was chosen and visually analyzed using PyMoL 1.7.6 software (http://www.pymol.org/). In addition, residues of amino acids that were close to compound within 4 Å were selected as the binding site.

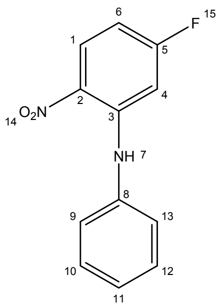
4. *In vivo* fungicidal activities of titled compounds against *R.solani*

Compd.	Dosage (mg/ L)	Fungicidal activity (%)	Compd.	Dosage (mg/L)	Fungicidal activity (%)
6	20	95	**9**	20	95
	10	80		10	85
	5	70		5	75
	2.5	60		2.5	55
	1.25	40		1.25	30
15	20	90	**bixafen**	20	80
	10	75		10	75
	5	35		5	60
	2.5	15		2.5	40

	1.25	5		1.25	25
thifluzamide	20	100			
	10	95			
	5	85			
	2.5	75			
	1.25	40			

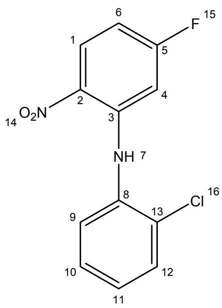
5. Structural characterization of intermediate compounds c and d

5-fluoro-2-nitro-*N*-phenylaniline(**c1**)



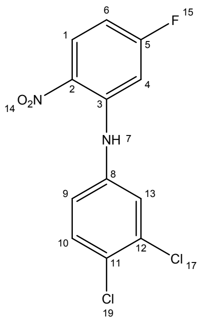
Yield, 81 %; yellow solid; mp, 84.5-86.1 °C; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 9.61 (s, 1H, Ph-NH-Ph), 8.24 (dd, *J* = 9.4, 6.2 Hz, 1H, C_1-H), 7.47 (t, *J* = 7.8 Hz, 2H, C_{10}-H, C_{12}-H), 7.37 (d, *J* = 7.5 Hz, 2H, C_9-H, C_{13}-H), 7.28 (t, *J* = 7.3 Hz, 1H, C_{11}-H), 6.80 – 6.67 (m, 2H, C_6-H, C_4-H); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 166.69 (d, $J_{C\text{-}F}$ = 253.2 Hz, C_5), 145.16 (d, $J_{C\text{-}F}$ = 13.1 Hz, C_3), 138.95 (s, C_8), 130.52 (s, C_2), 130.36 (d, $J_{C\text{-}F}$ = 12.4 Hz, C_1), 130.16 (s, C_{10}, C_{12}), 126.26 (s, C_{11}), 125.05 (s, C_9, C_{13}), 106.36 (d, $J_{C\text{-}F}$ = 24.8 Hz, C_6), 101.95 (d, $J_{C\text{-}F}$ = 27.9 Hz, C_4); ESI-HRMS:m/z [M-H]$^-$ calcd. for [$C_{12}H_8FN_2O_2$]: 231.0575; found: 231.0568.

N-(2-chlorophenyl)-5-fluoro-2-nitroaniline(**c2**)



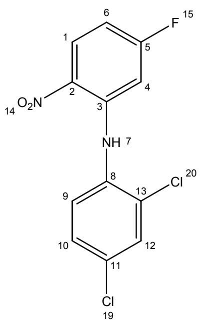
Yield, 83 %; light red solid; mp, 72.1-73.2 °C; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 9.65 (s, 1H, Ph-NH-Ph), 8.28 (dd, *J* = 9.5, 6.1 Hz, 1H, C_1-H), 7.66 (dd, *J* = 8.0, 1.4 Hz, 1H, C_{12}-H), 7.57 (dd, *J* = 7.9, 1.4 Hz, 1H, C_9-H), 7.47 (td, *J* = 7.7, 1.4 Hz, 1H, C_{10}-H), 7.36 (td, *J* = 7.8, 1.5 Hz, 1H, C_{11}-H), 6.84 – 6.70 (m, 1H, C_6-H), 6.51 (dd, *J* = 11.5, 2.7 Hz, 1H, C_4-H); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 166.80 (d, $J_{C\text{-}F}$ = 253.7 Hz, C_5), 144.58 (d, $J_{C\text{-}F}$ = 13.1 Hz, C_3), 135.95 (s, C_8), 130.86 (s, C_2), 130.56 (s, C_{12}), 130.38 (d, $J_{C\text{-}F}$ = 12.3 Hz, C_1), 129.86 (s, C_{10}), 129.01 (s, C_{13}), 128.40 (s, C_9), 127.83 (s, C_{11}), 106.78 (d, $J_{C\text{-}F}$ = 24.7 Hz, C_6), 102.09 (d, $J_{C\text{-}F}$ = 27.9 Hz, C_4); ESI-HRMS:m/z [M-H]$^-$ calcd. for [$C_{12}H_7ClFN_2O_2$]: 265.0186; found: 265.0179.

N-(3,4-dichlorophenyl)-5-fluoro-2-nitroaniline(**c3**)



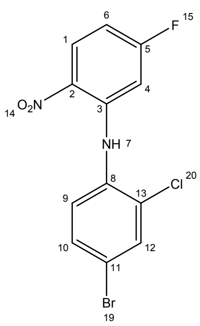
Yield, 79 %; yellow solid; mp, 178.0-178.6 °C; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 9.53 (s, 1H, Ph-NH-Ph), 8.24 (dd, *J* = 9.4, 6.1 Hz, 1H, C_1-H), 7.65 (d, 2.1 Hz, 2H, C_9-H, C_{10}-H), 7.37 (s, 1H, C_{13}-H), 7.09 – 6.75 (m, 2H, C_4-H, C_6-H); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 168.83 (d, J_{C-F} = 197.5 Hz, C_5), 157.25 (s, C_8), 139.86 (d, J_{C-F} = 30.8 Hz, C_3), 132.20 (s, C_{12}), 132.05 (s, C_{10}), 131.71 (d, J_{C-F} = 3.8 Hz, C_1), 130.22 (d, J_{C-F} = 13.1 Hz, C_2), 127.19 (s, C_{11}), 125.79 (s, C_{13}), 124.05 (s, C_9), 107.61 (d, J_{C-F} = 25.5 Hz, C_6), 103.66 (d, J_{C-F} = 26.8 Hz, C_4); ESI-HRMS:m/z $[M-H]^-$ calcd. for $[C_{12}H_6Cl_2FN_2O_2]$: 298.9796; found: 298.9792.

2,4-dichloro-*N*-(5-fluoro-2-nitrophenyl)aniline(**c4**)



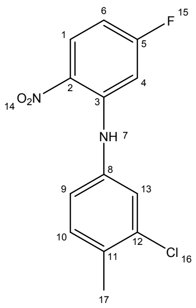
Yield, 69 %; yellow solid; mp, 83.0-83.6 °C; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 9.59 (s, 1H, Ph-NH-Ph), 8.27 (dd, *J* = 7.8, 4.5 Hz, 1H, C_1-H), 7.57 (d, *J* = 8.6 Hz, 1H, C_{12}-H), 7.06 (dd, *J* = 8.7, 2.4 Hz, 2H, C_9-H, C_{10}-H), 6.83 – 6.76 (m, 1H, C_6-H), 6.57 (dd, *J* = 11.4, 2.6 Hz, 1H, C_4-H); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 167.50 (d, J_{C-F} = 109.9 Hz, C_5), 144.27 (d, J_{C-F} = 13.1 Hz, C_3), 135.37 (s, C_8), 131.52 (s, C_{12}), 131.00 (s, C_{11}), 130.83 (s, C_{13}), 130.31 (d, J_{C-F} = 12.2 Hz, C_1), 129.23 (d, J_{C-F} = 2.0 Hz, C_2), 129.08 (s, C_{10}), 129.05 (s, C_9), 107.27 (d, J_{C-F} = 27.6 Hz, C_6), 102.52 (d, J_{C-F} = 30.7 Hz, C_4); ESI-HRMS:m/z $[M-H]^-$ calcd. for $[C_{12}H_6Cl_2FN_2O_2]$: 298.9796; found: 298.9789.

4-bromo-2-chloro-*N*-(5-fluoro-2-nitrophenyl)aniline(**c5**)



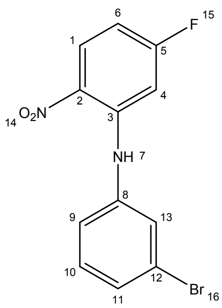
Yield, 87 %; yellow solid; mp, 81.3-81.8 °C; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 9.57 (s, 1H, Ph-NH-Ph), 8.27 (dd, *J* = 7.7, 4.6 Hz, 1H, C_1-H), 7.91 (d, *J* = 2.2 Hz, 1H, C_{12}-H), 7.64 (dd, *J* = 8.6, 2.2 Hz, 1H, C_{10}-H), 7.50 (d, *J* = 8.6 Hz, 1H, C_9-H), 6.82 – 6.77 (m, 1H, C_6-H), 6.60 (dd, *J* = 11.4, 2.6 Hz, 1H, C_4-H); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 165.68 (d, J_{C-F} = 256.8 Hz, C_5), 157.79 (s, C_8), 144.08 (d, J_{C-F} = 13.2 Hz, C_3), 135.78 (s, C_{12}), 132.99 (s, C_{10}), 131.97 (s, C_{13}), 131.03 (s, C_9), 129.18 (d, J_{C-F} = 9.7 Hz, C_1), 119.33 (s, C_{11}), 113.28 (d, J_{C-F} = 19.5 Hz, C_2), 107.40 (d, J_{C-F} = 2.9 Hz, C_6), 102.62 (d, J_{C-F} = 28.0 Hz, C_4); ESI-HRMS:m/z $[M-H]^-$ calcd. for $[C_{12}H_6BrClFN_2O_2]$: 344.9271; found: 344.9265.

N-(3-chloro-4-methylphenyl)-5-fluoro-2-nitroaniline(**c6**)



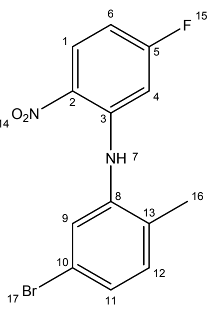
Yield, 90 %; yellow solid; mp, 142.1-142.5 °C; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 9.54 (s, 1H, Ph-NH-Ph), 8.23 (dd, *J* = 9.4, 6.1 Hz, 1H, C_1-H), 7.44 (d, *J* = 2.1 Hz, 1H, C_{13}-H), 7.41 (d, *J* = 8.2 Hz, 1H, C_9-H), 7.25 (dd, *J* = 8.1, 2.1 Hz, 1H, C_{10}-H), 6.96 – 6.52 (m, 2H, C_4-H, C_6-H), 2.34 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 166.64 (d, J_{C-F} = 253.4 Hz, C_5), 144.78 (d, J_{C-F} = 13.1 Hz, C_3), 138.34 (s, C_8), 134.25 (s, C_{12}), 133.11 (s, C_{10}), 132.37 (s, C_{13}), 130.89 (s, C_9), 130.29 (d, J_{C-F} = 12.3 Hz, C_1), 125.26 (s, C_2), 123.62 (s, C_{11}), 106.70 (d, J_{C-F} = 24.8 Hz, C_6), 102.43 (d, J_{C-F} = 27.8 Hz, C_4), 19.55 (s, CH_3); ESI-HRMS:m/z $[M-H]^-$ calcd. for $[C_{13}H_9ClFN_2O_2]$: 279.0342; found: 279.0334.

N-(3-bromophenyl)-5-fluoro-2-nitroaniline(**c7**)



Yield, 78 %; red solid; mp, 128.6-129.0 °C; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 9.55 (s, 1H, Ph-NH-Ph), 8.24 (dd, *J* = 9.4, 6.1 Hz, 1H, C_1-H), 7.58 (s, 1H, C_{13}-H), 7.47 – 7.25 (m, 3H, C_9-H, C_{10}-H, C_{11}-H), 6.88 (dd, *J* = 11.6, 2.7 Hz, 1H, C_4-H), 6.79 (ddd, *J* = 9.8, 7.4, 2.7 Hz, 1H, C_6-H); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 166.54 (d, J_{C-F} = 253.4 Hz, C_5), 144.02 (d, J_{C-F} = 13.0 Hz, C_3), 141.23 (s, C_8), 131.82 (s, C_{10}), 131.55 (d, J_{C-F} = 1.2 Hz, C_1), 130.27 (d, J_{C-F} = 12.2 Hz, C_3), 128.37 (s, C_{11}), 126.95 (s, C_{13}), 123.09 (s, C_{12}), 122.63 (s, C_9), 107.22 (d, J_{C-F} = 24.7 Hz, C_6), 103.05 (d, J_{C-F} = 27.7 Hz, C_4); ESI-HRMS:m/z $[M-H]^-$ calcd. for $[C_{12}H_7BrFN_2O_2]$: 308.9680; found: 308.9671.

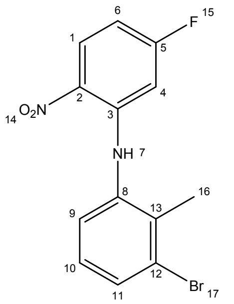
5-bromo-*N*-(5-fluoro-2-nitrophenyl)-2-methylaniline(**c8**)



Yield, 70 %; red solid; mp, 84.3-85.0 °C; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 9.52 (s, 1H, Ph-NH-Ph), 8.26 (dd, *J* = 9.5, 6.1 Hz, 1H, C_1-H), 7.52 (d, *J* = 1.9 Hz, 1H, C_{11}-H), 7.47 (dd, *J* = 8.2, 2.0 Hz, 1H, C_9-H), 7.36 (d, *J* = 8.2 Hz, 1H, C_{12}-H), 6.70 (ddd, *J* = 9.8, 7.5, 2.7 Hz, 1H, C_6-H), 6.26 (dd, *J* = 11.6, 2.7 Hz, 1H, C_4-H), 2.14 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 166.89 (d, J_{C-F} = 253.6 Hz, C_5), 145.63 (d, J_{C-F} = 13.1 Hz, C_3), 139.14 (s, C_8), 134.88 (s, C_{12}), 133.48 (s, C_{13}), 130.36 (d, J_{C-F} = 12.3 Hz, C_1), 130.35 (s, C_2), 130.12 (s, C_9), 130.01 (s, C_{11}), 119.39 (s, C_{10}), 106.05 (d, J_{C-F} = 24.8 Hz, C_6), 101.60 (d, J_{C-F}

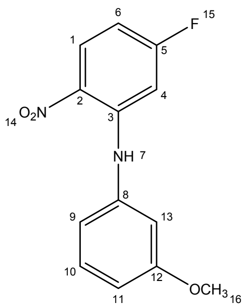
= 27.7 Hz, C_4), 17.50 (s, CH_3); ESI-HRMS:m/z $[M-H]^-$ calcd. for $[C_{13}H_9BrFN_2O_2]$: 322.9837; found: 322.9832.

3-bromo-*N*-(5-fluoro-2-nitrophenyl)-2-methylaniline(**c9**)



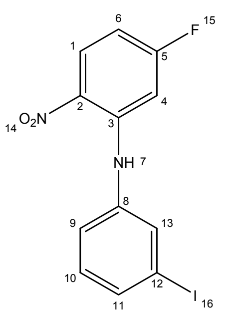
Yield, 77 %; yellow solid; mp, 93.8-95.2 °C; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 9.62 (s, 1H, Ph-NH-Ph), 8.26 (dd, *J* = 9.5, 6.1 Hz, 1H, C_1-H), 7.64 (d, *J* = 7.9 Hz, 1H, C_{11}-H), 7.35 (d, *J* = 7.6 Hz, 1H, C_9-H), 7.27 (t, *J* = 7.9 Hz, 1H, C_{10}-H), 6.69 (ddd, *J* = 9.7, 7.5, 2.6 Hz, 1H, C_6-H), 6.23 (dd, *J* = 11.7, 2.7 Hz, 1H, C_4-H), 2.20 (d, *J* = 48.1 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 166.89 (d, J_{C-F} = 253.6 Hz, C_5), 145.95 (d, J_{C-F} = 13.1 Hz, C_3), 138.91 (s, C_8), 135.63 (s, C_{13}), 131.72 (s, C_{10}), 130.37 (d, J_{C-F} = 12.4 Hz, C_1), 129.79 (s, C_2), 128.96 (s, C_{12}), 127.67 (s, C_{11}), 125.91 (s, C_9), 105.89 (d, J_{C-F} = 24.8 Hz, C_6), 101.49 (d, J_{C-F} = 27.8 Hz, C_4), 18.42 (s, CH_3); ESI-HRMS:m/z $[M-H]^-$ calcd. for $[C_{13}H_9BrFN_2O_2]$: 322.9837; found: 322.9833.

5-fluoro-*N*-(3-methoxyphenyl)-2-nitroaniline(**c10**)



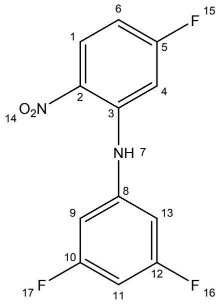
Yield, 78 %; yellow solid; mp, 105.1-105.5 °C; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 9.55 (s, 1H, Ph-NH-Ph), 8.24 (dd, *J* = 9.4, 6.2 Hz, 1H, C_1-H), 7.35 (dd, *J* = 10.8, 5.9 Hz, 1H, C_{13}-H), 6.95 (d, *J* = 6.5 Hz, 2H, C_9-H, C_{11}-H), 6.84 (d, *J* = 9.3 Hz, 2H, C_4-H, C_6-H), 6.73 (ddd, *J* = 9.9, 7.5, 2.6 Hz, 1H, C_{10}-H), 3.78 (s, 3H, C_{16}-H); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 166.66 (d, J_{C-F} = 253.1 Hz, C_5), 160.79 (s, C_{12}), 144.92 (d, J_{C-F} = 13.2 Hz, C_3), 140.19 (s, C_8), 130.84 (s, C_9), 130.68 (s, C_{10}), 130.29 (d, J_{C-F} = 12.4 Hz, C_1), 116.68 (s, C_2), 111.89 (s, C_{11}), 110.47 (s, C_{13}), 106.51 (d, J_{C-F} = 24.8 Hz, C_6), 102.36 (d, J_{C-F} = 27.8 Hz, C_4), 55.70 (s, OCH_3); ESI-HRMS:m/z $[M-H]^-$ calcd. for $[C_{13}H_{10}FN_2O_3]$: 308.9680; found: 261.0679.

5-fluoro-*N*-(3-iodophenyl)-2-nitroaniline(**c11**)



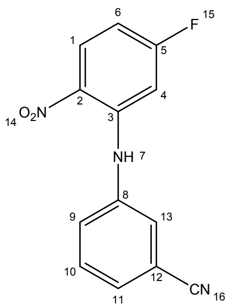
Yield, 76 %; yellow solid; mp, 84.4-85.1 °C; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 9.53 (s, 1H, Ph-NH-Ph), 8.23 (dd, *J* = 9.4, 6.1 Hz, 1H, C_1-H), 7.74 (t, *J* = 1.6 Hz, 1H, C_9-H), 7.59 (d, *J* = 7.9 Hz, 1H, C_{13}-H), 7.40 (dd, *J* = 8.0, 1.4 Hz, 1H, C_{10}-H), 7.22 (t, *J* = 7.9 Hz, 1H, C_{11}-H), 6.84 (dd, *J* = 11.6, 2.6 Hz, 1H, C_4-H), 6.77 (ddd, *J* = 9.9, 7.4, 2.7 Hz, 1H, C_6-H); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 166.55 (d, J_{C-F} = 253.3 Hz, C_5), 144.18 (d, J_{C-F} = 13.0 Hz, C_3), 140.90 (s, C_8), 134.37 (s, C_{11}), 132.87 (s, C_{10}), 131.82 (s, C_{13}), 131.34 (d, J_{C-F} = 0.9 Hz, C_1), 130.27 (d, J_{C-F} = 12.3 Hz, C_2), 123.68 (s, C_9), 107.05 (d, J_{C-F} = 24.7 Hz, C_6), 102.83 (d, J_{C-F} = 27.7 Hz, C_4), 95.70 (s, C_{12}); ESI-HRMS:m/z $[M-H]^-$ calcd. for $[C_{12}H_7FIN_2O_2]$: 356.9542; found: 356.9537.

N-(3,5-difluorophenyl)-5-fluoro-2-nitroaniline(**c12**)



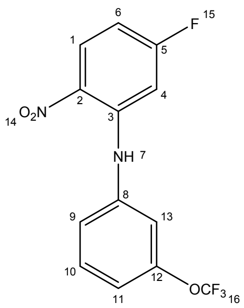
Yield, 79 %; yellow solid; mp, 124.3-124.7 °C; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 9.50 (s, 1H, Ph-NH-Ph), 8.24 (dd, *J* = 9.4, 6.1 Hz, 1H, C_1-H), 7.18 – 7.06 (m, 3H, C_4-H, C_9-H, C_{13}-H), 6.99 (tt, *J* = 9.4, 2.3 Hz, 1H, C_6-H), 6.88 (ddd, *J* = 9.8, 7.5, 2.7 Hz, 1H, C_{11}-H); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 166.39 (d, *J* = 253.7 Hz, C_5), 164.65 (d, J_{C-F} = 15.5 Hz, C_{10}), 162.21 (d, J_{C-F} = 15.6 Hz, C_{12}), 142.94 (t, J_{C-F} = 13.3 Hz, C_3), 142.47 (d, J_{C-F} = 12.9 Hz, C_8), 132.88 (d, J_{C-F} = 1.6 Hz, C_1), 130.11 (d, J_{C-F} = 12.1 Hz, C_2), 108.31 (d, J_{C-F} = 24.5 Hz, C_6), 105.86 (d, J_{C-F} = 28.0 Hz, C_4), 105.86 (d, J_{C-F} = 11.9 Hz, C_9), 104.70 (d, J_{C-F} = 27.5 Hz, C_{13}), 99.97 (t, J_{C-F} = 26.1 Hz, C_{11}); ESI-HRMS:m/z $[M-H]^-$ calcd. for $[C_{12}H_6F_3N_2O_2]$: 267.0387; found: 267.0382.

3-((5-fluoro-2-nitrophenyl)amino)benzonitrile(**c13**)



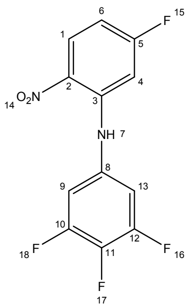
Yield, 67 %; yellow solid; mp, 160.3-161.0 °C; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 9.60 (s, 1H, Ph-NH-Ph), 8.25 (dd, *J* = 9.4, 6.1 Hz, 1H, C_1-H), 7.82 (s, 1H, C_{13}-H), 7.72 – 7.67 (m, 1H, C_9-H), 7.67 – 7.58 (m, 2H, C_{10}-H, C_{11}-H), 6.97 (dd, *J* = 11.5, 2.6 Hz, 1H, C_4-H), 6.83 (ddd, *J* = 9.8, 7.5, 2.6 Hz, 1H, C_6-H); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 166.56 (d, J_{C-F} = 253.6 Hz, C_5), 143.51 (d, J_{C-F} = 12.9 Hz, C_3), 140.68 (s, C_8), 131.96 (d, J_{C-F} = 1.2 Hz, C_1), 131.29 (s, C_{10}), 130.24 (d, J_{C-F} = 12.2 Hz, C_2), 128.79 (d, J_{C-F} = 20.9 Hz, C_9), 127.13 (s, C_{11}), 118.90 (s, C_{18}), 112.92 (s, C_{12}), 107.62 (d, J_{C-F} = 24.6 Hz, C_6), 103.44 (d, J_{C-F} = 27.7 Hz, C_4); ESI-HRMS:m/z $[M-H]^-$ calcd. for $[C_{13}H_7FN_3O_2]$: 256.0528; found: 256.0528.

5-fluoro-2-nitro-*N*-(3-(trifluoromethoxy)phenyl)aniline(**c14**)



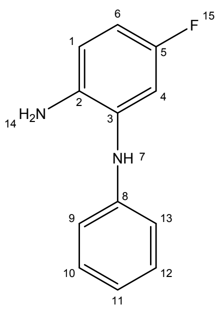
Yield, 85 %; yellow solid; mp, 61.5-62.3 °C; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 9.59 (s, 1H, Ph-NH-Ph), 8.25 (dd, *J* = 9.4, 6.1 Hz, 1H, C_1-H), 7.54 (t, *J* = 8.1 Hz, 1H, C_{10}-H), 7.41 (d, *J* = 7.9 Hz, 2H, C_9-H), 7.19 (d, *J* = 8.1 Hz, 1H, C_{11}-H), 6.94 (dd, *J* = 11.6, 2.6 Hz, 1H, C_4-H), 6.81 (ddd, *J* = 9.8, 7.4, 2.6 Hz, 1H, C_6-H); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 166.50 (d, J_{C-F} = 253.4 Hz, C_5), 149.53 (dd, J_{C-F} = 3.2, 1.5 Hz, C_{12}), 143.64 (d, J_{C-F} = 13.0 Hz, C_3), 141.44 (s, C_8), 131.91 (s, C_{11}), 131.60 (s, C_{10}), 130.26 (d, J_{C-F} = 12.2 Hz, C_1), 122.51 (s, C_2), 129.42 – 113.02 (m, OCF_3), 117.51 (s, C_9), 116.47 (s, C_{13}), 107.44 (d, J_{C-F} = 24.6 Hz, C_6), 103.24 (d, J_{C-F} = 27.8 Hz, C_4); ESI-HRMS:m/z [M-H]$^-$ calcd. for [$C_{13}H_7F_4N_2O_3$]: 315.0398; found: 315.0400.

3,4,5-trifluoro-*N*-(5-fluoro-2-nitrophenyl)aniline(**c15**)



Yield, 80 %; yellow solid; mp, 54.0-54.7 °C; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 9.43 (d, *J* = 43.0 Hz, 1H, Ph-NH-Ph), 8.35 – 8.09 (m, 1H, C_1-H), 7.41 – 7.33 (m, 2H, C_9-H, C_{13}-H), 7.03 (dd, *J* = 11.5, 2.6 Hz, 1H, C_4-H), 6.83 (ddd, *J* = 9.8, 7.5, 2.7 Hz, 1H, C_6-H); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 166.59 (d, J_{C-F} = 253.6 Hz, C_5), 152.30 (dd, J_{C-F} = 10.1, 5.5 Hz, C_{10}), 149.85 (dd, J_{C-F} = 10.4, 5.5 Hz, C_{12}), 143.52 (d, J_{C-F} = 13.0 Hz, C_3), 136.21 (td, J_{C-F} = 11.7, 4.1 Hz, C_8), 132.03 (d, J_{C-F} = 1.4 Hz, C_1), 130.11 (d, J_{C-F} = 12.2 Hz, C_2), 109.06 (m, C_{11}), 107.75 (d, J_{C-F} = 24.6 Hz, C_6), 103.84 (d, J_{C-F} = 27.7 Hz, C_4), 97.27 (dd, J_{C-F} = 22.9, 1.8 Hz, C_9, C_{13}); ESI-HRMS:m/z [M-H]$^-$ calcd. for [$C_{12}H_5F_4N_2O_2$]: 285.0293; found: 285.0286.

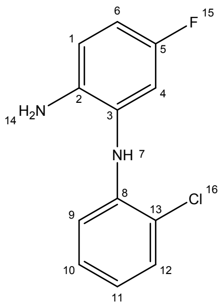
5-fluoro-*N^1*-phenylbenzene-1,2-diamine(**d1**)



Yield, 91 %; brown solid; mp, 70.0-70.4 °C; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 7.24 (s, 1H, Ph-NH-Ph), 7.18 (dd, *J* = 8.4, 7.4 Hz, 2H, C_{10}-H, C_{12}-H), 6.86 (dd, *J* = 8.5, 0.9 Hz, 2H, C_9-H, C_{13}-H), 6.80 (dd, *J* = 10.6, 2.9 Hz, 1H, C_1-H), 6.76 (t, *J* = 7.3 Hz, 1H, C_{11}-H),), 6.71 (dd, *J* = 8.7, 6.0 Hz, 1H, C_4-H),), 6.61 (td, *J* = 8.5, 2.9 Hz, 1H, C_6-H),), 4.64 (s, 2H, NH_2); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 154.83 (d, J_{C-F} = 231.3 Hz, C_5), 144.99 (s, C_8), 137.81 (d, J_{C-F} = 1.8 Hz, C_3), 129.79 (d, J_{C-F} = 9.4 Hz, C_1), 129.52 (s, C_{10}, C_{12}), 119.37 (s, C_{11}), 116.25 (s, C_9, C_{13}), 115.90 (d, J_{C-F} = 8.9 Hz, C_2), 109.27 (d, J_{C-F} =

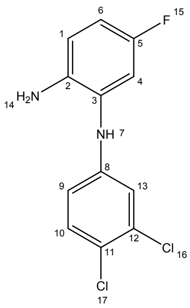
21.7 Hz, C_6), 107.55 (d, $J_{C\text{-}F}$ = 24.0 Hz, C_4); ESI-HRMS:m/z $[M\text{-}H]^-$ calcd. for $[C_{12}H_{10}FN_2]$: 201.0834; found: 201.0828.

N¹-(2-chlorophenyl)-5-fluorobenzene-1,2-diamine(**d2**)



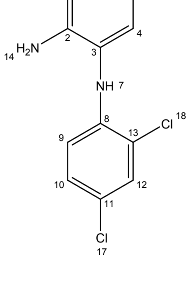
Yield, 86 %; brownish red solid; mp, 35.1-35.5 °C; ^1H NMR (400 MHz, DMSO-*d6*) δ 7.37 (dd, J = 7.9, 1.4 Hz, 1H, C_{12}-H), 7.18 – 7.06 (m, 1H, C_9-H), 6.87 (s, 1H, Ph-NH-Ph), 6.79 (td, J = 7.7, 1.4 Hz, 1H, C_6-H), 6.77 – 6.70 (m, 2H, C_{10}-H, C_{11}-H), 6.67 (dd, J = 8.2, 1.3 Hz, 1H, C_4-H), 4.69 (s, 2H, NH_2); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 154.76 (d, $J_{C\text{-}F}$ = 231.9 Hz, C_5), 141.65 (s, C_8), 139.27 (d, $J_{C\text{-}F}$ = 2.0 Hz, C_3), 130.03 (s, C_{12}), 128.35 (s, C_{10}), 128.24 (s, C_2), 121.24 (s, C_{13}), 120.41 (s, C_9), 116.75 (s, C_{11}), 116.25 (d, $J_{C\text{-}F}$ = 8.7 Hz, C_1), 111.20 (d, $J_{C\text{-}F}$ = 21.6 Hz, C_6), 110.45 (d, $J_{C\text{-}F}$ = 23.4 Hz, C_4); ESI-HRMS:m/z $[M\text{-}H]^-$ calcd. for $[C_{12}H_9ClFN_2]$: 235.0444; found: 235.0441.

N¹-(3,4-dichlorophenyl)-5-fluorobenzene-1,2-diamine(**d3**)



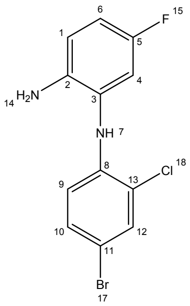
Yield, 90 %; brownish red solid; mp, 54.5-54.9 °C; ^1H NMR (400 MHz, DMSO-*d6*) δ 7.71 (s, 1H, Ph-NH-Ph), 7.35 (d, J = 8.8 Hz, 1H, C_1-H), 6.83 (dd, J = 6.2, 3.6 Hz, 2H, C_9-H, C_{10}-H), 6.75 (dd, J = 7.1, 1.5 Hz, 2H, C_6-H, C_{13}-H), 6.71 (dd, J = 8.8, 2.7 Hz, 1H, C_4-H), 4.72 (s, 2H, NH_2); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 154.46 (d, $J_{C\text{-}F}$ = 232.2 Hz, C_5), 146.14 (s, C_8), 139.70 (d, $J_{C\text{-}F}$ = 1.9 Hz, C_3), 131.66 (s, C_{12}), 131.11 (s, C_{10}), 127.14 (d, $J_{C\text{-}F}$ = 9.4 Hz, C_2), 119.19 (s, C_{11}), 116.21 (d, $J_{C\text{-}F}$ = 8.7 Hz, C_1), 115.86 (s, C_{13}), 115.12 (s, C_9), 111.82 (d, $J_{C\text{-}F}$ = 21.7 Hz, C_6), 110.68 (d, $J_{C\text{-}F}$ = 23.0 Hz, C_4); ESI-HRMS:m/z $[M\text{-}H]^-$ calcd. for $[C_{12}H_8Cl_2FN_2]$: 269.0054; found: 269.0047.

N¹-(2,4-dichlorophenyl)-5-fluorobenzene-1,2-diamine(**d4**)



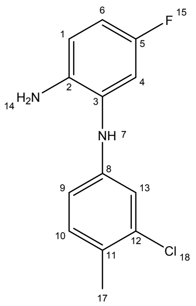
Yield, 83 %; off-white solid; mp, 75.3-75.9 °C; ^1H NMR (400 MHz, DMSO-*d6*) δ 7.48 (d, J = 2.4 Hz, 1H, C_{12}-H), 7.17 (dd, J = 8.8, 2.4 Hz, 1H, C_1-H), 7.07 (s, 1H, Ph-NH-Ph), 6.77 (m, 3H, C_9-H, C_{10}-H, C_6-H), 6.54 (d, J = 8.8 Hz, 1H, C_4-H), 4.70 (s, 2H, NH_2); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 154.58 (d, $J_{C\text{-}F}$ = 232.1 Hz, C_5), 141.15 (s, C_8), 140.00 (d, $J_{C\text{-}F}$ = 1.9 Hz, C_3), 129.14 (s, C_{12}), 128.15 (s, C_{13}), 127.22 (d, J_{C-F} = 9.4 Hz, C_2), 122.40 (s, C_{11}), 121.26 (s, C_{10}), 117.04 (s, C_9), 116.30 (d, J_{C-F} = 8.7 Hz, C_1), 112.14 (d, J_{C-F} = 21.7 Hz, C_6), 111.71 (d, J_{C-F} = 23.0 Hz, C_4); ESI-HRMS:m/z $[M-H]^-$ calcd. for $[C_{12}H_8Cl_2FN_2]$: 269.0054; found: 269.0043.

N^1-(4-bromo-2-chlorophenyl)-5-fluorobenzene-1,2-diamine(**d5**)



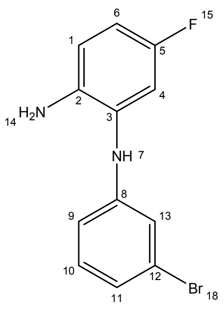
Yield, 86 %; creamy-white solid; mp, 92.0-92.3 °C; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 7.57 (d, J = 2.3 Hz, 1H, C_{12}-H), 7.28 (dd, J = 8.8, 2.3 Hz, 1H, C_1-H), 7.08 (s, 1H, Ph-NH-Ph), 6.83 – 6.72 (m, 3H, C_6-H, C_9-H, C_{10}-H), 6.47 (d, J = 8.8 Hz, 1H, C_4-H), 4.70 (s, 2H, NH_2); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 154.55 (d, J_{C-F} = 232.3 Hz, C_5), 141.56 (s, C_8), 140.13 (d, J_{C-F} = 1.9 Hz, C_3), 131.71 (s, C_{12}), 130.96 (s, C_{10}), 127.01 (d, J_{C-F} = 9.5 Hz, C_2), 121.46 (s, C_{13}), 117.35 (s, C_9), 116.31 (d, J_{C-F} = 8.7 Hz, C_1), 112.30 (d, J_{C-F} = 21.6 Hz, C_6), 111.93 (d, J_{C-F} = 22.9 Hz, C_4), 109.39 (s, C_{11}); ESI-HRMS:m/z $[M-H]^-$ calcd. for $[C_{12}H_8BrClFN_2]$: 314.9528; found: 314.9521.

N^1-(3-chloro-4-methylphenyl)-5-fluorobenzene-1,2-diamine(**d6**)



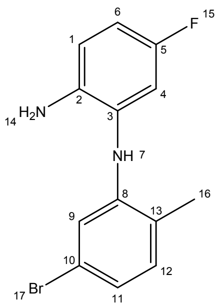
Yield, 92 %; light brown solid; mp, 80.8-81.1 °C; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 7.38 (s, 1H, Ph-NH-Ph), 7.12 (d, J = 8.3 Hz, 1H, C_1-H), 6.81 – 6.77 (m, 2H, C_9-H, C_{10}-H), 6.73 – 6.63 (m, 3H, C_4-H, C_6-H, C_{13}-H), 4.65 (s, 2H, NH_2), 2.21 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 154.67 (d, J_{C-F} = 231.8 Hz, C_5), 144.76 (s, C_8), 138.55 (d, J_{C-F} = 1.9 Hz, C_3), 133.91 (s, C_{12}), 131.89 (s, C_{10}), 128.79 (d, J_{C-F} = 9.4 Hz, C_2), 125.03 (s, C_{11}), 116.01 (d, J_{C-F} = 8.8 Hz, C_1), 115.65 (s, C_{13}), 114.65 (s, C_9), 110.30 (d, J_{C-F} = 21.7 Hz, C_6), 108.78 (d, J_{C-F} = 23.5 Hz, C_4), 19.05 (s, CH_3); ESI-HRMS:m/z $[M-H]^-$ calcd. for $[C_{13}H_{11}ClFN_2]$: 249.0600; found: 249.0594.

N^1-(3-bromophenyl)-5-fluorobenzene-1,2-diamine(**d7**)



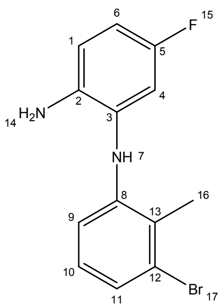
Yield, 84 %; brown red solid; mp, 53.0-53.3 °C; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 7.55 (s, 1H, Ph-NH-Ph), 7.10 (t, J = 8.2 Hz, 1H, C_1-H), 6.90 – 6.80 (m, 3H, C_9-H, C_{10}-H, C_{11}-H), 6.78 – 6.69 (m, 3H, C_4-H, C_6-H, C_{13}-H), 4.69 (s, 2H, NH_2);^{13}C NMR (100 MHz, DMSO-*d6*) δ 154.53 (d, J_{C-F} = 232.1 Hz, C_5), 147.54 (s, C_8), 139.40 (d, $J_{C\text{-}F}$ = 1.9 Hz, C_3), 131.32 (s, C_{10}), 127.73 (d, $J_{C\text{-}F}$ = 9.3 Hz, C_1), 122.61 (s, C_{11}), 120.96 (s, C_{13}), 117.32 (s, C_{12}), 116.13 (d, $J_{C\text{-}F}$ = 8.8 Hz, C_2), 113.98 (s, C_9), 111.30 (d, $J_{C\text{-}F}$ = 21.6 Hz, C_6), 110.19 (d, $J_{C\text{-}F}$ = 23.1 Hz, C_4); ESI-HRMS:m/z $[M-H]^-$ calcd. for $[C_{12}H_9BrFN_2]$: 280.9918; found: 280.9912.

N¹-(5-bromo-2-methylphenyl)-5-fluorobenzene-1,2-diamine(**d8**)



Yield, 89 %; off-white solid; mp, 90.6-91.0 °C; ^1H NMR (400 MHz, DMSO-*d6*) δ 7.04 (d, *J* = 8.0 Hz, 1H, C_{11}-H), 6.86 (dd, *J* = 7.9, 2.0 Hz, 1H, C_1-H), 6.78 (s, 1H, Ph-NH-Ph), 6.75 (d, *J* = 1.6 Hz, 1H, C_9-H), 6.74 – 6.72 (m, 1H, C_{12}-H), 6.69 – 6.64 (m, 1H, C_6-H), 6.50 (d, *J* = 2.0 Hz, 1H, C_4-H), 4.67 (s, 2H, NH_2), 2.18 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 154.63 (d, $J_{C\text{-}F}$ = 232.0 Hz, C_5), 145.48 (s, C_8), 139.59 (d, $J_{C\text{-}F}$ = 1.9 Hz, C_3), 132.48 (s, C_{12}), 128.37 (d, $J_{C\text{-}F}$ = 9.3 Hz, C_2), 125.01 (s, C_{13}), 121.70 (s, C_9), 119.53 (s, C_{11}), 117.10 (s, C_{10}), 115.96 (d, $J_{C\text{-}F}$ = 8.7 Hz, C_1), 111.38 (d, $J_{C\text{-}F}$ = 21.6 Hz, C_6), 111.08 (d, $J_{C\text{-}F}$ = 22.9 Hz, C_4), 17.91 (s, CH_3); ESI-HRMS:m/z $[M-H]^-$ calcd. for [C13H11BrFN2]: 295.0075; found: 295.0084.

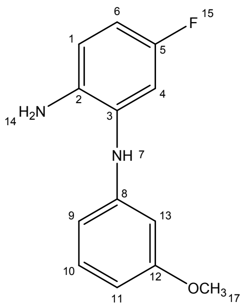
N¹-(3-bromo-2-methylphenyl)-5-fluorobenzene-1,2-diamine(**d9**)



Yield, 87 %; gray solid; mp, 102.0-102.8 °C; ^1H NMR (400 MHz, DMSO-*d6*) δ 7.09 (d, *J* = 7.6 Hz, 1H, C_1-H), 6.96 (t, *J* = 7.8 Hz, 1H, C_{10}-H), 6.81 (s, 1H, Ph-NH-Ph), 6.74 – 6.62 (m, 2H, C_4-H, C_6-H), 6.57 (d, *J* = 7.8 Hz, 1H, C_{11}-H), 6.52 (d, *J* = 10.2 Hz, 1H, C_9-H), 4.65 (s, 2H, NH_2), 2.30 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 154.84 (d, $J_{C\text{-}F}$ = 231.4 Hz, C_5), 144.94 (s, C_8), 138.38 (s, C_{13}), 129.89 (d, $J_{C\text{-}F}$ = 9.4 Hz, C_3), 128.16 (s, C_{13}), 126.26 (s, C_{10}), 125.66 (s, C_{12}), 124.14 (s, C_{11}), 116.36 (s, C_9), 115.81 (d, $J_{C\text{-}F}$ = 9.0 Hz, C_1), 110.06 (d, $J_{C\text{-}F}$ = 21.5 Hz, C_6), 109.15 (d, $J_{C\text{-}F}$ = 23.5 Hz, C_4), 18.10 (s, CH_3); ESI-HRMS:m/z $[M-H]^-$ calcd. for $[C_{13}H_{11}BrFN_2]$: 295.0075; found: 295.0072.

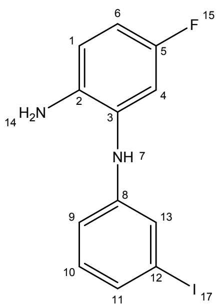
5-fluoro-*N¹*-(3-methoxyphenyl)benzene-1,2-diamine(**d10**)

Yield, 94 %; brownish red solid; mp, 66.4-66.7 °C; ^1H NMR (400 MHz, DMSO-*d6*) δ 7.26 (s, 1H s, 1H, Ph-NH-Ph), 7.08 (t, *J* = 8.1 Hz, 1H, C_{10}-H), 6.82 (dd, *J* = 10.6, 2.9 Hz, 1H, C_1-H), 6.71 (dd, *J* = 8.7, 6.0 Hz, 1H, C_9-H), 6.62 (td, *J* = 8.5, 2.9 Hz, 1H,



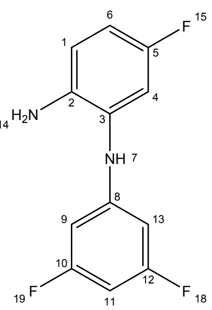
C_{11}-H), 6.44 (dd, *J* = 8.0, 1.6 Hz, 1H, C_6-H), 6.39 (t, *J* = 2.2 Hz, 1H, C_{13}-H), 6.34 (dd, *J* = 8.0, 2.2 Hz, 1H, C_4-H), 4.64 (s, 2H, NH_2), 3.68 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 160.69 (s, C_{12}), 154.77 (d, $J_{C\text{-}F}$ = 231.5 Hz, C_5), 146.47 (s, C_8), 138.08 (d, $J_{C\text{-}F}$ = 1.9 Hz, C_3), 130.26 (s, C_{10}), 129.43 (d, $J_{C\text{-}F}$ = 9.4 Hz, C_1), 115.96 (d, $J_{C\text{-}F}$ = 8.8 Hz, C_1), 109.64 (d, $J_{C\text{-}F}$ = 21.7 Hz, C_6), 108.63 (s, C_9), 108.26 (d, $J_{C\text{-}F}$ = 23.8 Hz, C_4), 104.70 (s, C_{11}), 101.86 (s, C_{13}), 55.24 (s, OCH_3); ESI-HRMS:m/z $[M\text{-}H]^-$ calcd. for $[C_{13}H_{12}FN_2O]$: 231.0939; found: 231.0933.

5-fluoro-*N¹*-(3-iodophenyl)benzene-1,2-diamine(**d11**)



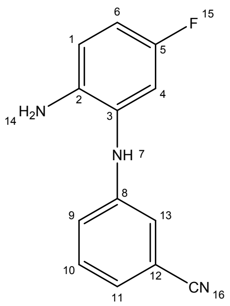
Yield, 87 %; brown red solid; mp, 58.5-58.7 °C; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 7.46 (s, 1H, Ph-NH-Ph), 7.08 – 7.03 (m, 2H, C_9-H, C_{11}-H), 6.94 (t, *J* = 7.9 Hz, 1H, C_{10}-H), 6.89 – 6.65 (m, 4H, C_1-H, C_4-H, C_6-H, C_{13}-H), 4.68 (s, 2H, NH_2); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 154.54 (d, $J_{C\text{-}F}$ = 232.0 Hz, C_5), 147.31 (s, C_8), 139.26 (d, $J_{C\text{-}F}$ = 1.9 Hz, C_3), 131.43 (s, C_{11}), 127.84 (d, $J_{C\text{-}F}$ = 9.3 Hz, C_2), 127.05 (s, C_{10}), 123.43 (s, C_{13}), 116.09 (d, $J_{C\text{-}F}$ = 8.8 Hz, C_1), 114.43 (s, C_9), 111.11 (d, $J_{C\text{-}F}$ = 21.7 Hz, C_6), 109.95 (d, $J_{C\text{-}F}$ = 23.2 Hz, C_4), 95.72 (s, C_{12}); ESI-HRMS:m/z $[M\text{-}H]^-$ calcd. for $[C_{12}H_9FIN_2]$: 326.9800; found: 326.9792.

N¹-(3,5-difluorophenyl)-5-fluorobenzene-1,2-diamine (**d12**)



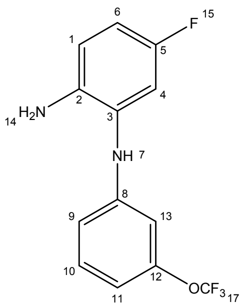
Yield, 88 %; brown red solid; mp, 78.0-78.5 °C; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 7.87 (s, 1H, Ph-NH-Ph), 6.86 (dd, *J* = 10.1, 1.8 Hz, 1H, C_1-H), 6.77 (dd, *J* = 7.3, 2.7 Hz, 2H, C_9-H, C_{13}-H), 6.42 (tt, *J* = 9.4, 2.2 Hz, 1H, C_{11}-H), 6.37 – 6.23 (m, 2H, C_6-H, C_{13}-H), 4.73 (s, 2H, NH_2); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 165.00 (d, $J_{C\text{-}F}$ = 16.3 Hz, C_{10}), 162.59 (d, $J_{C\text{-}F}$ = 16.4 Hz, C_{12}), 154.41 (d, $J_{C\text{-}F}$ = 232.4 Hz, C_5), 149.03 (t, $J_{C\text{-}F}$ = 13.6 Hz, C_8), 140.01 (d, $J_{C\text{-}F}$ = 2.0 Hz, C_3), 126.60 (d, $J_{C\text{-}F}$ = 9.3 Hz, C_2), 116.30 (d, $J_{C\text{-}F}$ = 8.7 Hz, C_1), 112.31 (d, $J_{C\text{-}F}$ = 21.7 Hz, C_6), 111.38 (d, $J_{C\text{-}F}$ = 22.9 Hz, C_4), 97.74 – 96.80 (m, C_9, C_{13}), 92.97 (t, $J_{C\text{-}F}$ = 26.5 Hz, C_{11}); ESI-HRMS:m/z $[M\text{-}H]^-$ calcd. for $[C_{12}H_8F_3N_2]$: 237.0645; found: 237.0640.

3-((2-amino-5-fluorophenyl)amino)benzonitrile (**d13**)



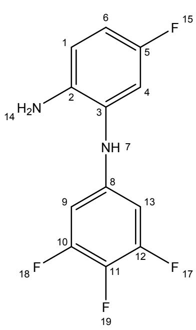
Yield, 78 %; gray solid; mp, 82.5-82.8 °C; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 7.77 (s, 1H, Ph-NH-Ph), 7.34 (t, *J* = 7.9 Hz, 1H, C_{10}-H), 7.11 (d, *J* = 7.6 Hz, 1H, C_1-H), 7.04 (dd, *J* = 8.3, 2.0 Hz, 1H, C_6-H), 6.97 (s, 1H, C_{13}-H), 6.85 (d, *J* = 9.9 Hz, 1H, C_9-H), 6.77 (d, *J* = 1.4 Hz, 1H, C_{11}-H), 6.76 (s, 1H, C_4-H), 4.71 (s, 2H, NH_2); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 154.50 (d, $J_{C\text{-}F}$ = 232.3 Hz, C_5), 146.56 (s, C_8), 139.70 (d, $J_{C\text{-}F}$ = 1.9 Hz, C_3), 130.73 (s, C_{10}), 127.07 (d, $J_{C\text{-}F}$ = 9.4 Hz, C_2), 121.70 (s, C_9), 119.71 (s, C_{11}), 119.57 (s, C_{13}), 117.17 (s, CN), 116.25 (d, $J_{C\text{-}F}$ = 8.7 Hz, C_1), 112.14 (s, C_{12}), 111.84 (d, $J_{C\text{-}F}$ = 21.7 Hz, C_6), 110.64 (d, $J_{C\text{-}F}$ = 23.0 Hz, C_4); ESI-HRMS:m/z $[M-H]^-$ calcd. for $[C_{13}H_9FN_3]$: 226.0786; found: 226.0781.

5-fluoro-*N^1*-(3-(trifluoromethoxy)phenyl)benzene-1,2-diamine(**d14**)



Yield, 77 %; brown liquid; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 7.68 (s, 1H, Ph-NH-Ph), 7.28 – 7.22 (m, 1H, C_{10}-H), 6.85 (dd, *J* = 10.2, 2.6 Hz, 1H, C_1-H), 6.80 – 6.67 (m, 3H, C_4-H, C_6-H, C_{13}-H), 6.64 (d, *J* = 6.9 Hz, 2H, C_9-H, C_{11}-H), 4.70 (s, 2H, NH_2); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 154.53 (d, $J_{C\text{-}F}$ = 232.1 Hz, C_5), 149.85 (d, $J_{C\text{-}F}$ = 1.6 Hz, C_{11}), 147.61 (s, C_8), 139.38 (d, $J_{C\text{-}F}$ = 1.9 Hz, C_3), 130.97 (s, C_{10}), 127.65 (d, $J_{C\text{-}F}$ = 9.4 Hz, C_2), 120.58 (q, $J_{C\text{-}F}$ = 255.8 Hz, OCF_3), 116.18 (d, $J_{C\text{-}F}$ = 8.7 Hz, C_1), 113.70 (s, C_9), 111.32 (d, $J_{C\text{-}F}$ = 21.7 Hz, C_6), 110.18 (s, C_9), 110.04 (d, $J_{C\text{-}F}$ = 18.2 Hz, C_4), 106.96 (s, C_{13}); ESI-HRMS:m/z $[M-H]^-$ calcd. for $[C_{13}H_9F_4N_2O]$: 285.0656; found: 285.0653.

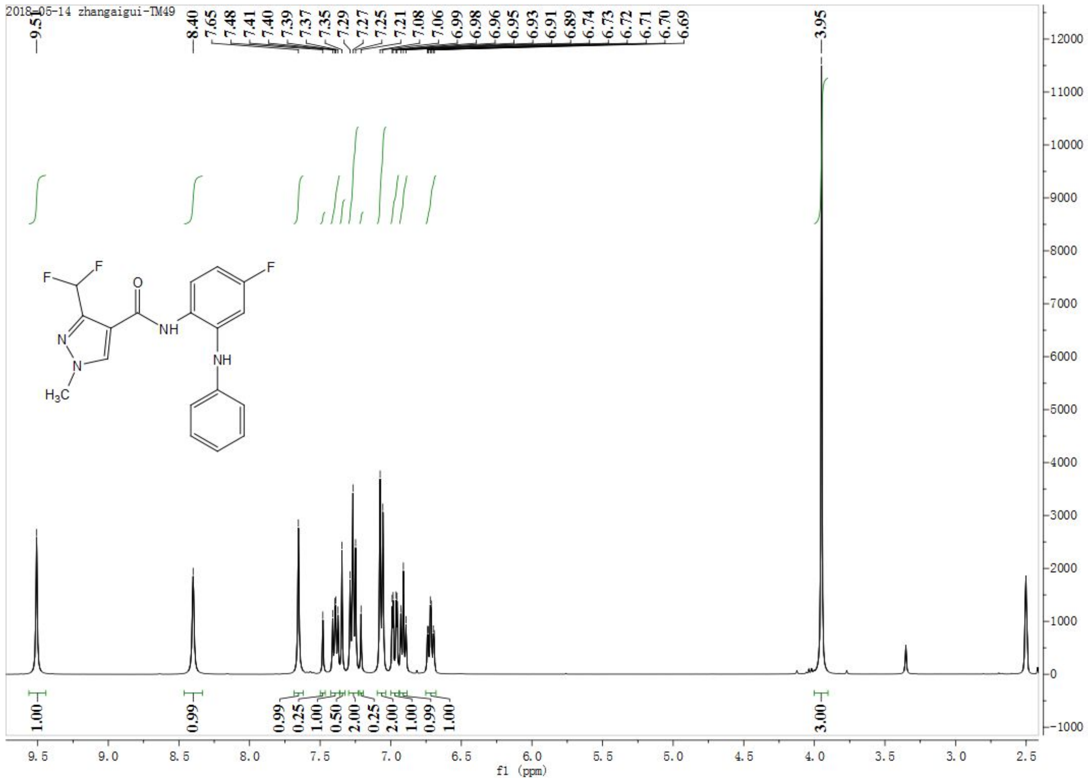
5-fluoro-*N^1*-(3,4,5-trifluorophenyl)benzene-1,2-diamine(**d15**)



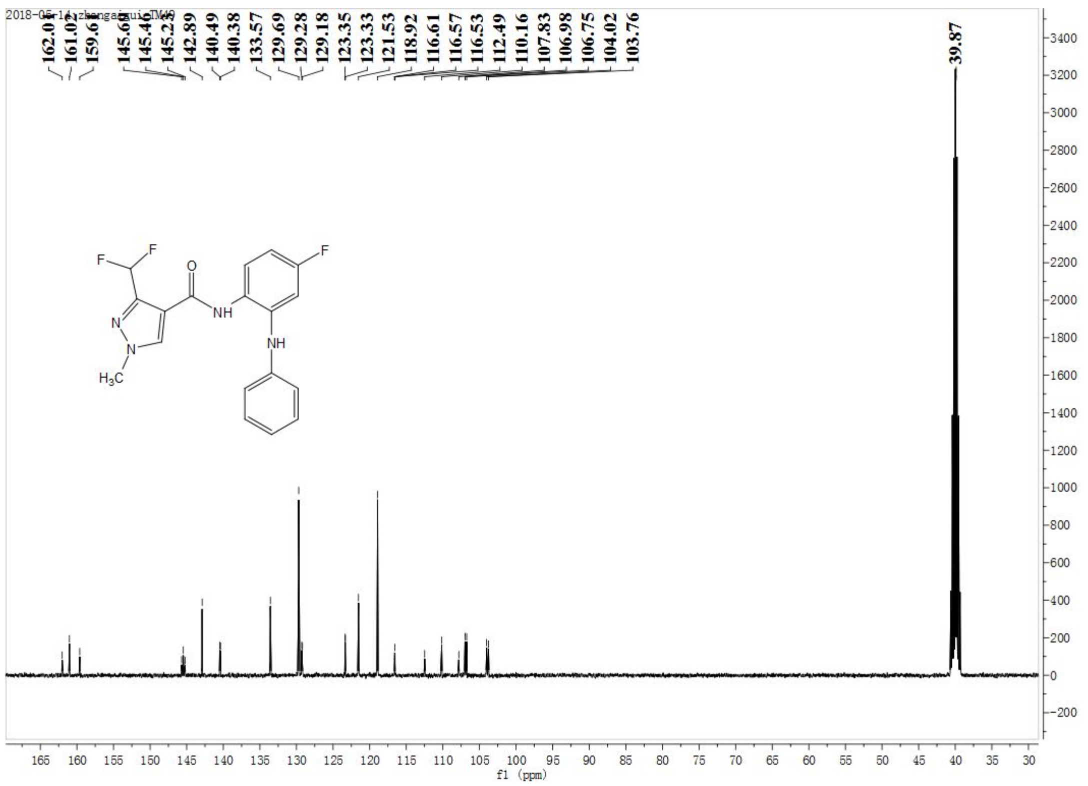
Yield, 80%; brown red; mp, 78.4-78.8 °C; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 7.74 (s, 1H, Ph-NH-Ph), 6.84 (d, *J* = 9.7 Hz, 1H, C_1-H), 6.80 – 6.69 (m, 2H, C_9-H, C_{13}-H), 6.46 (dd, *J* = 10.7, 6.0 Hz, 2H, C_4-H, C_6-H), 4.72 (s, 2H, NH_2); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 154.48 (d, $J_{C\text{-}F}$ = 232.3 Hz, C_5), 152.55 (dd, $J_{C\text{-}F}$ = 10.0, 6.1 Hz, C_{10}, C_{12}), 150.13 (dd, $J_{C\text{-}F}$ = 10.1, 6.1 Hz, C_8), 142.69 (td, $J_{C\text{-}F}$ = 11.5, 2.1 Hz, C_{11}), 139.77 (d, $J_{C\text{-}F}$ = 1.9 Hz, C_3), 126.87 (d,

$J_{C\text{-}F}$ = 9.4 Hz, C_2), 116.31 (d, $J_{C\text{-}F}$ = 8.7 Hz, C_1), 112.08 (d, $J_{C\text{-}F}$ = 21.7 Hz, C_6), 110.84 (d, $J_{C\text{-}F}$ = 23.1 Hz, C_4), 98.63 – 98.18 (m, C_9, C_{13}); ESI-HRMS:m/z $[M\text{-}H]^-$ calcd. for $[C_{12}H_7F_4N_2]$: 255.0551; found: 255.0538.

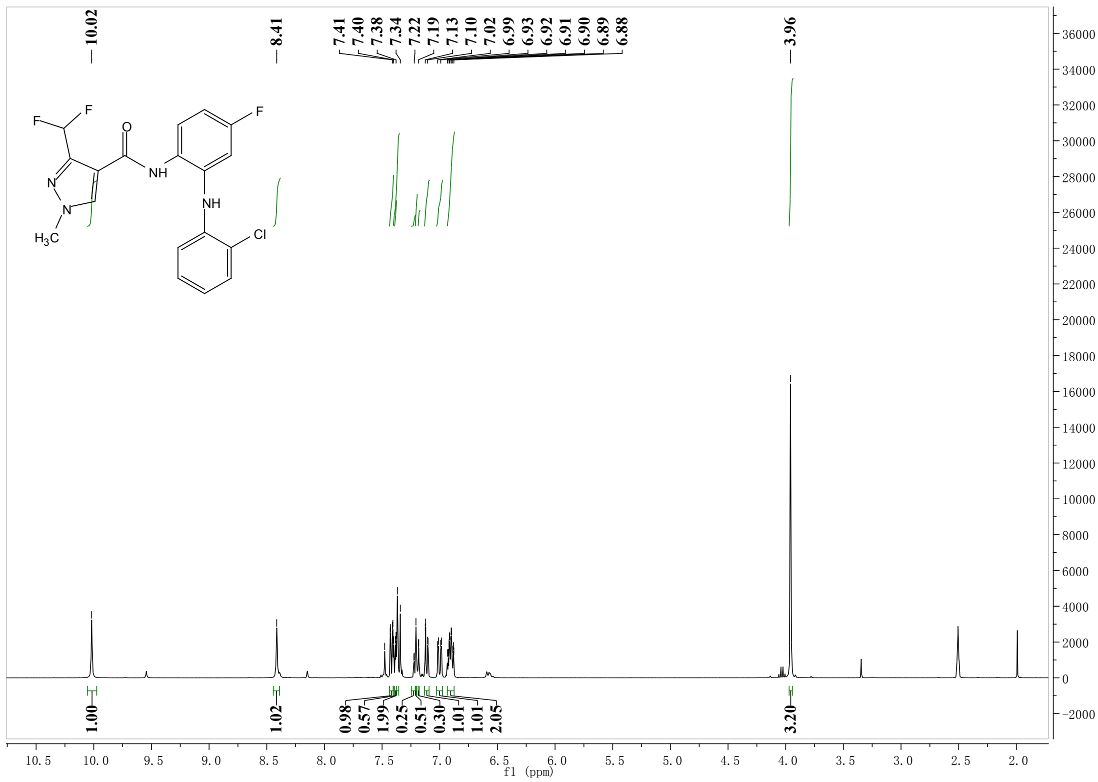
6. Spectrums of the representative compounds



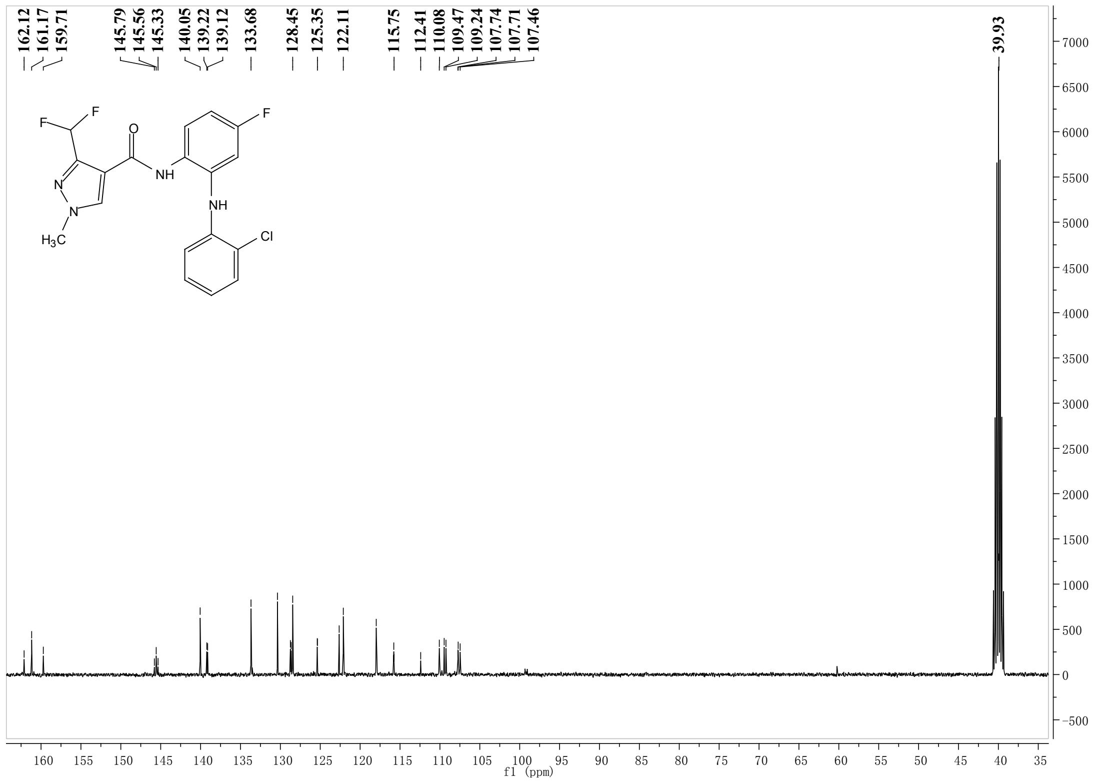
The ^{1}H NMR spectrogram of compound **1**



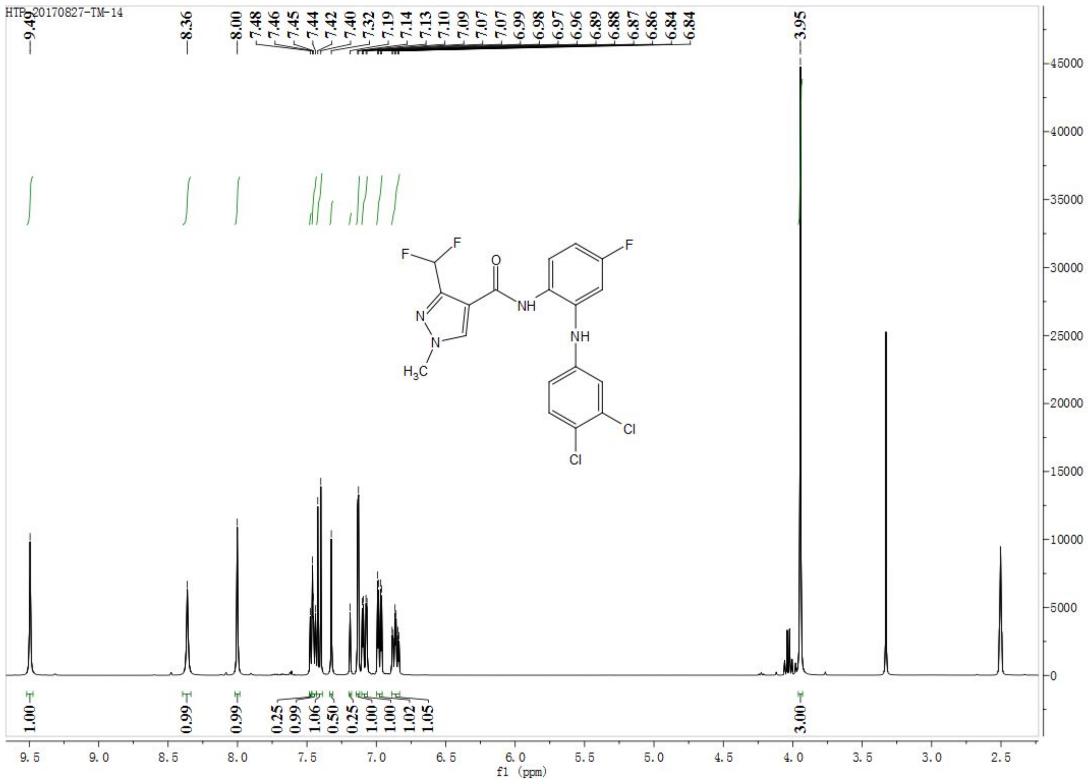
The ^{13}C NMR spectrogram of compound **1**



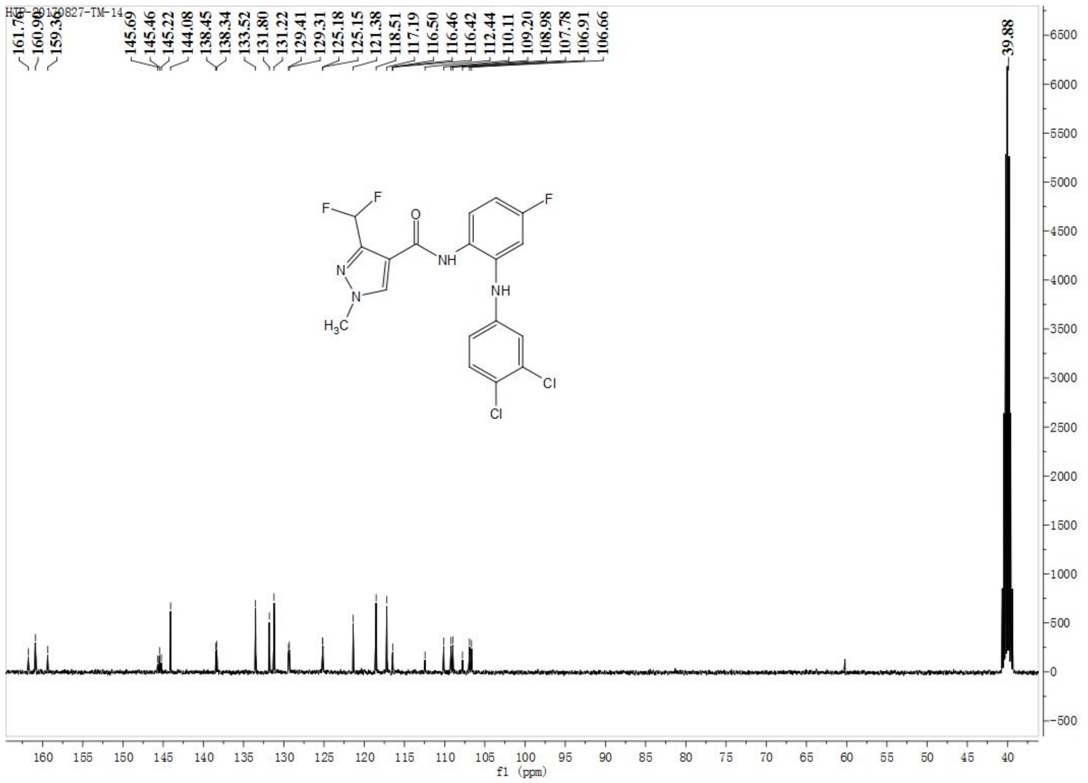
The ^{1}H NMR spectrogram of compound **2**



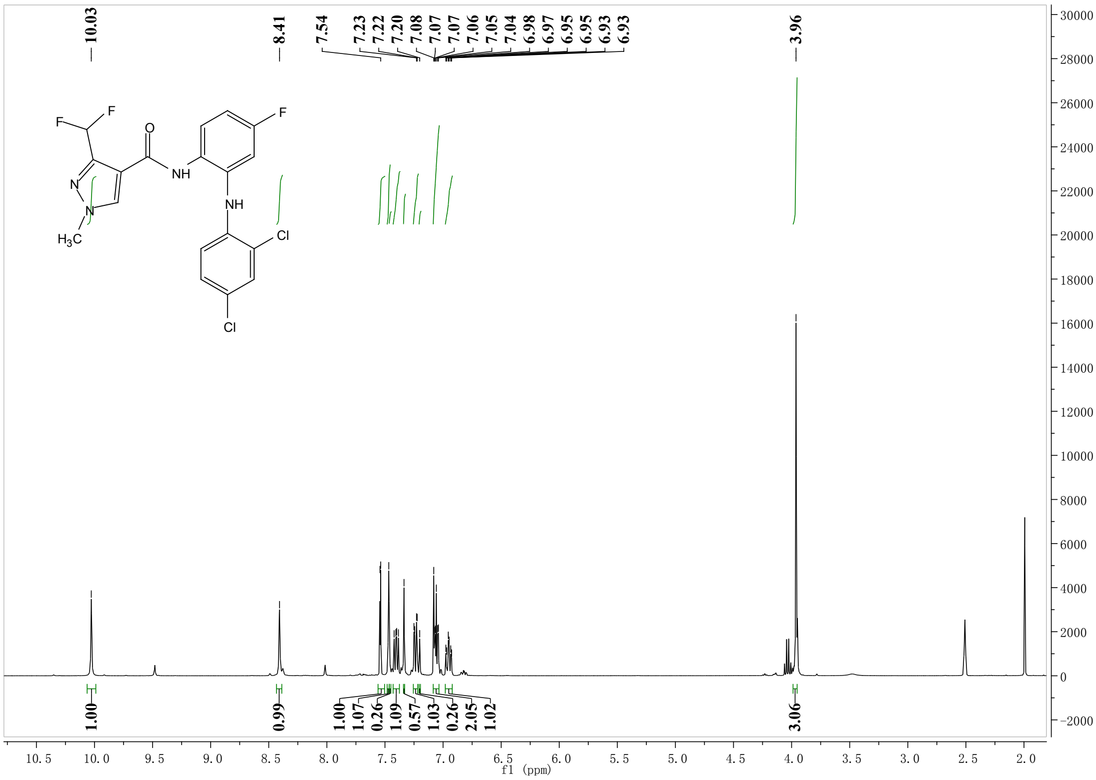
The ^{13}C NMR spectrogram of compound **2**



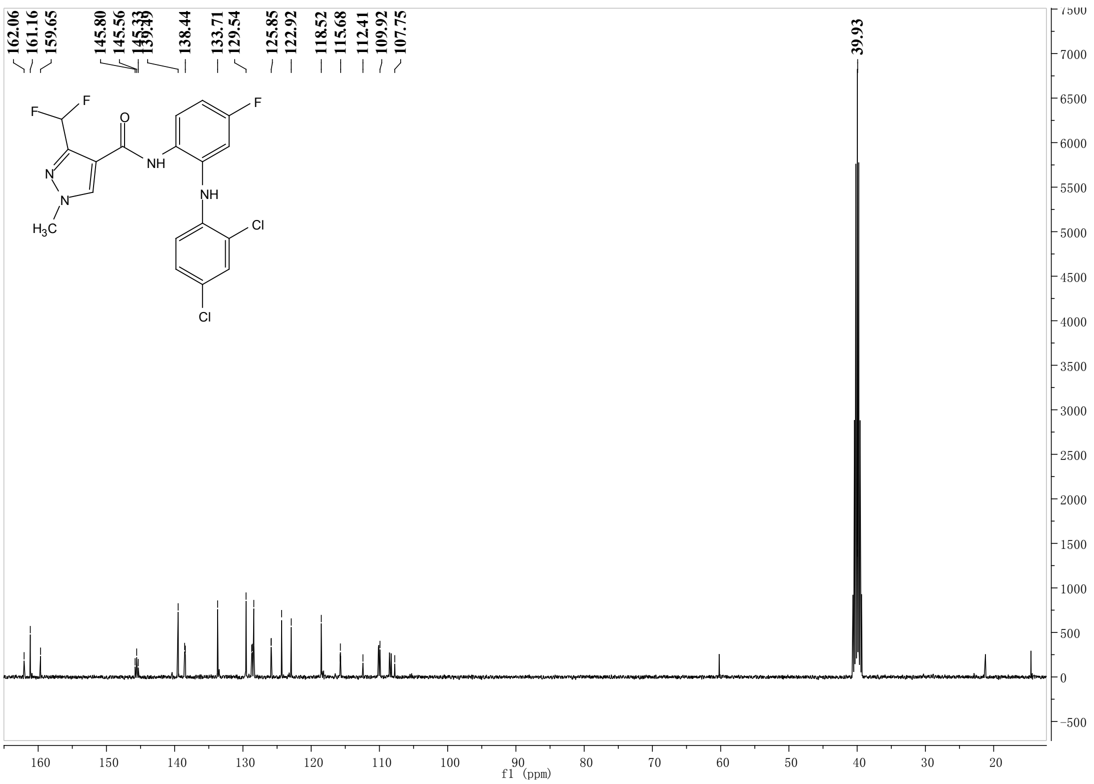
The ^{1}H NMR spectrogram of compound **3**



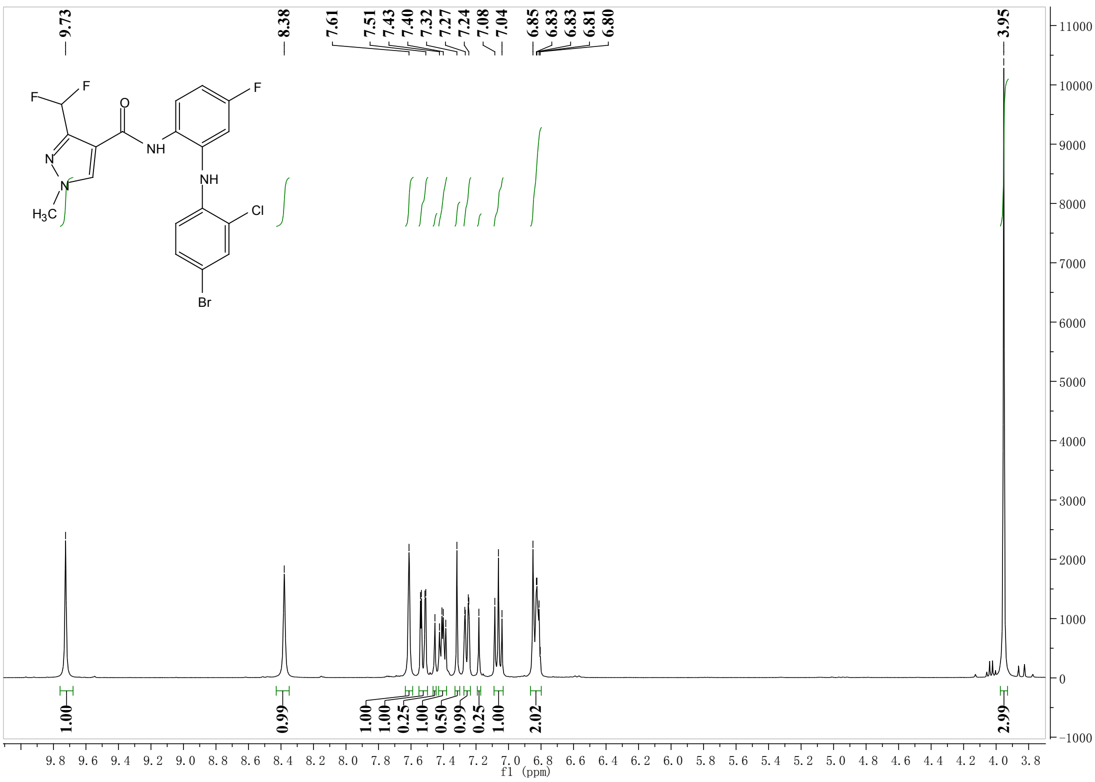
The ^{13}C NMR spectrogram of compound **3**



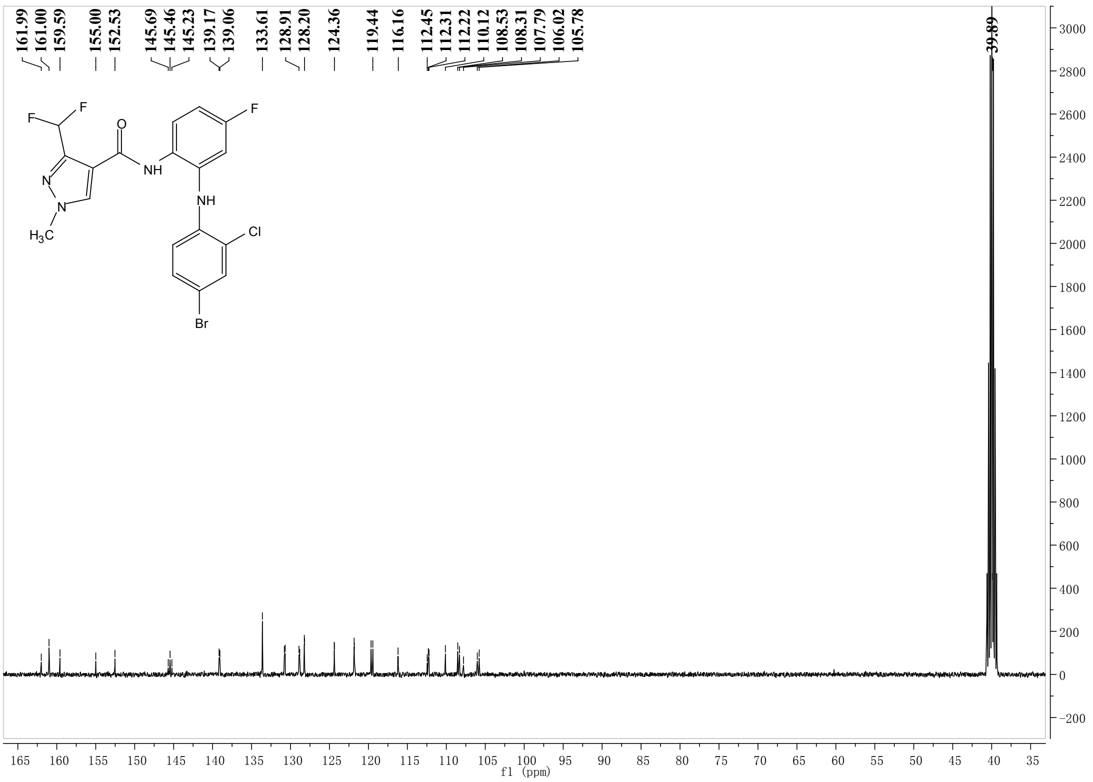
The [1]H NMR spectrogram of compound **4**



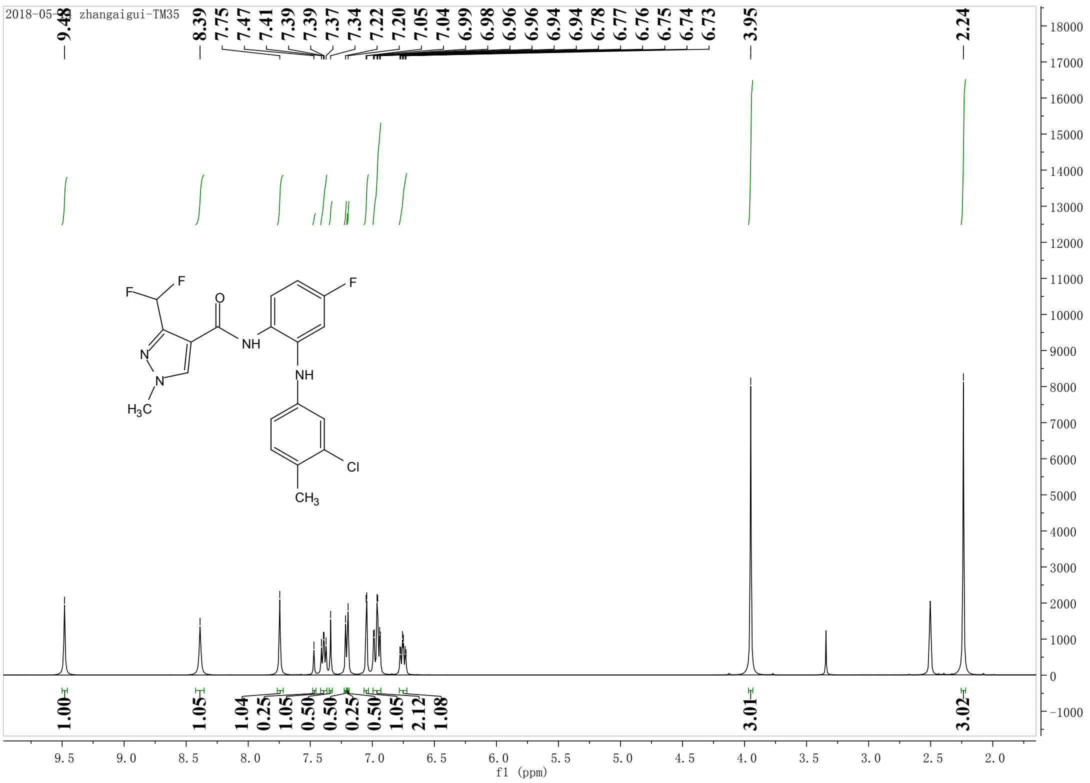
The [13]C NMR spectrogram of compound **4**



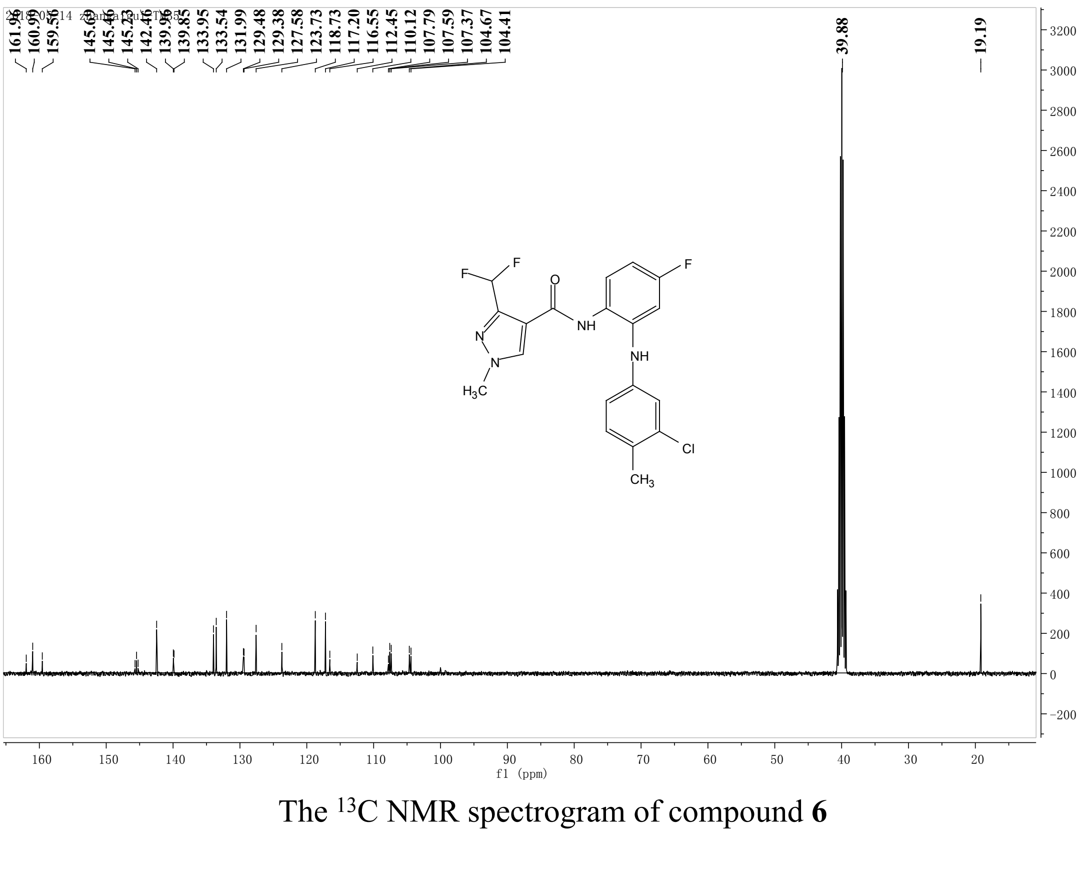
The ^{1}H NMR spectrogram of compound **5**



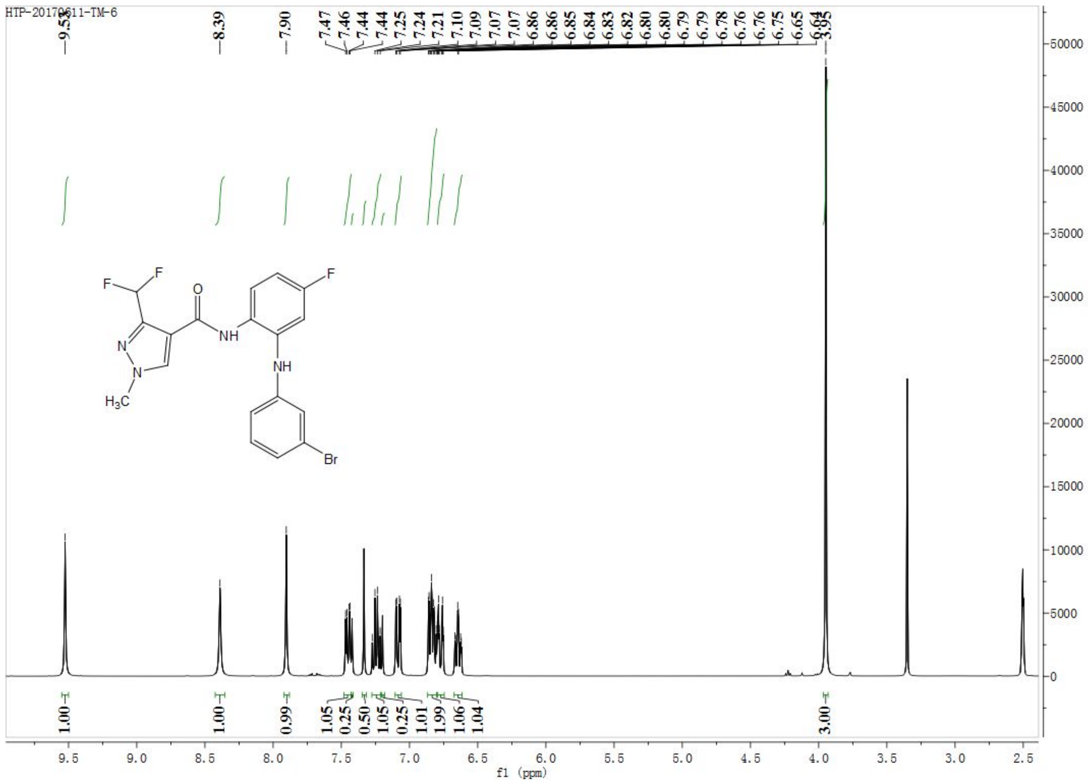
The ^{13}C NMR spectrogram of compound **5**



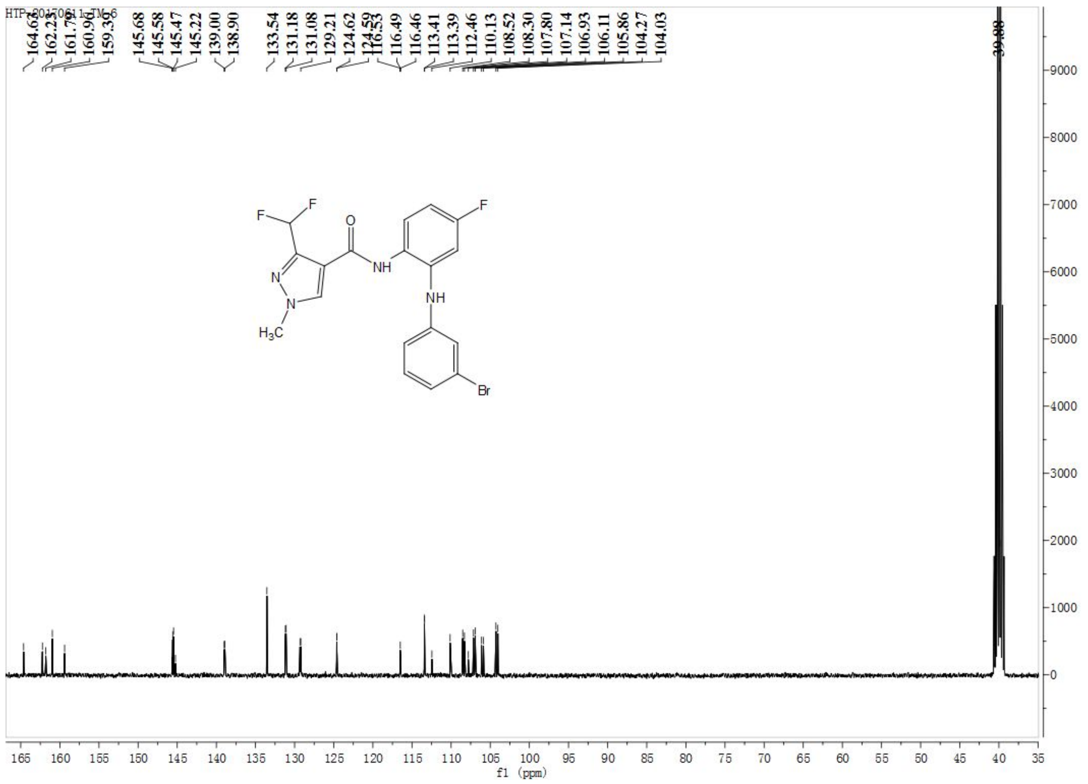
The ^{1}H NMR spectrogram of compound **6**



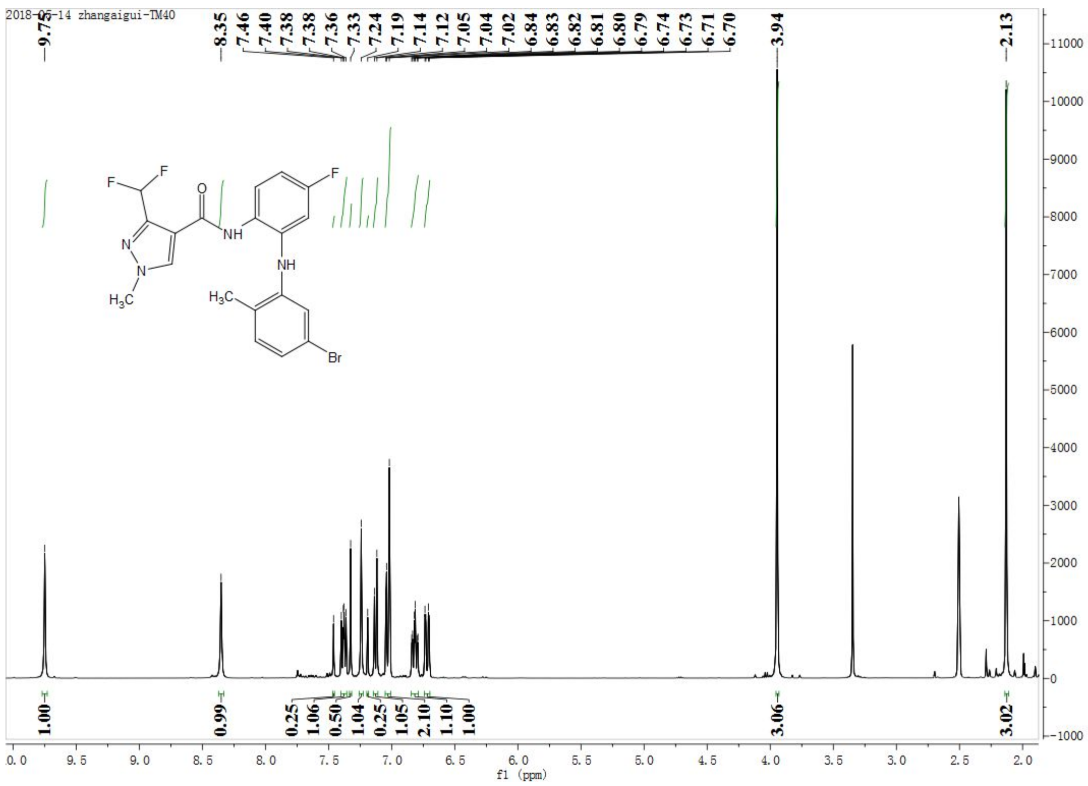
The ^{13}C NMR spectrogram of compound **6**



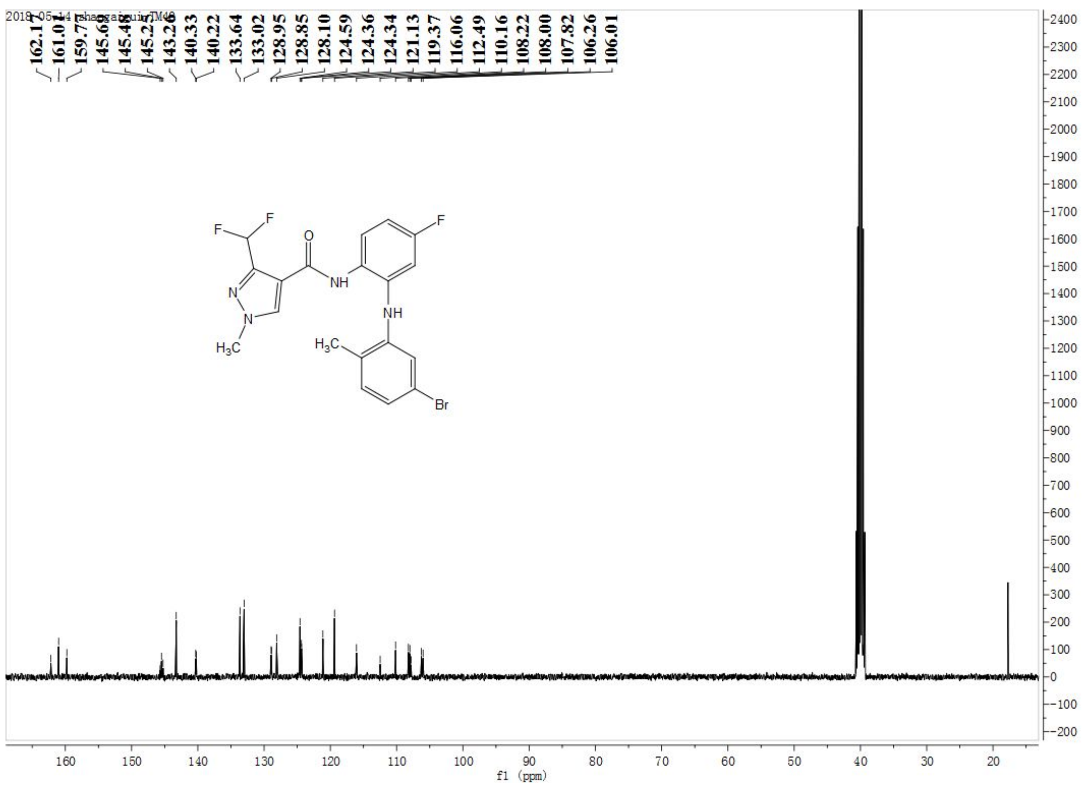
The ^{1}H NMR spectrogram of compound **7**



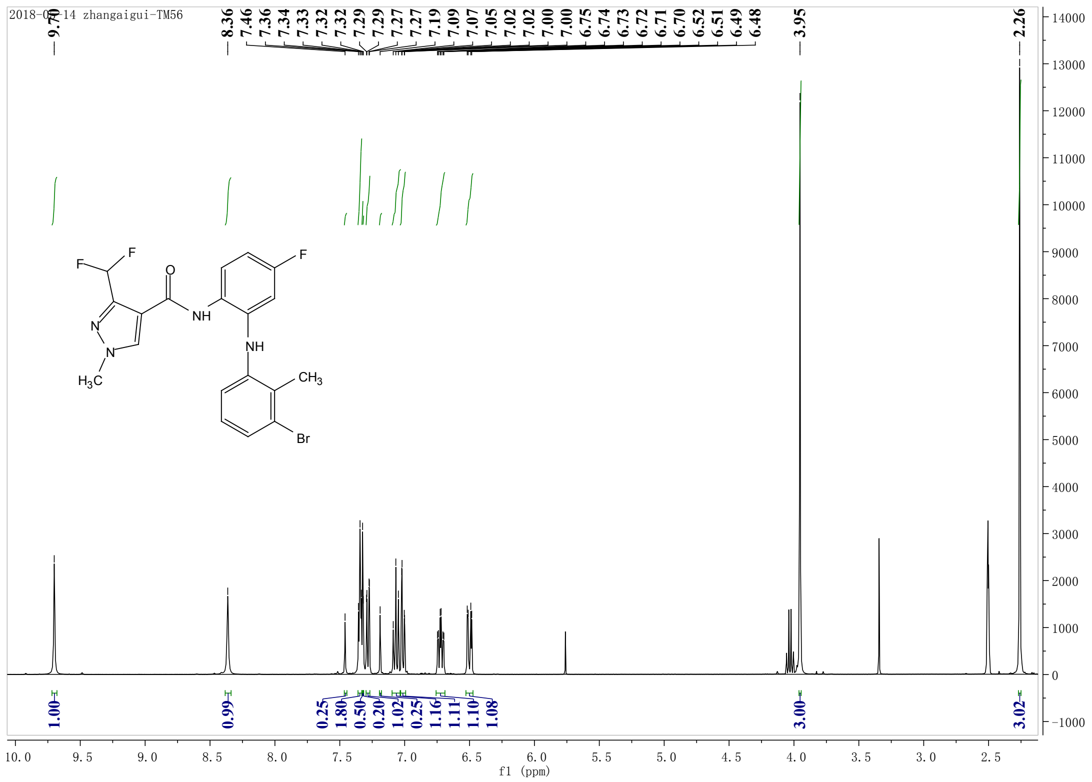
The ^{13}C NMR spectrogram of compound **7**



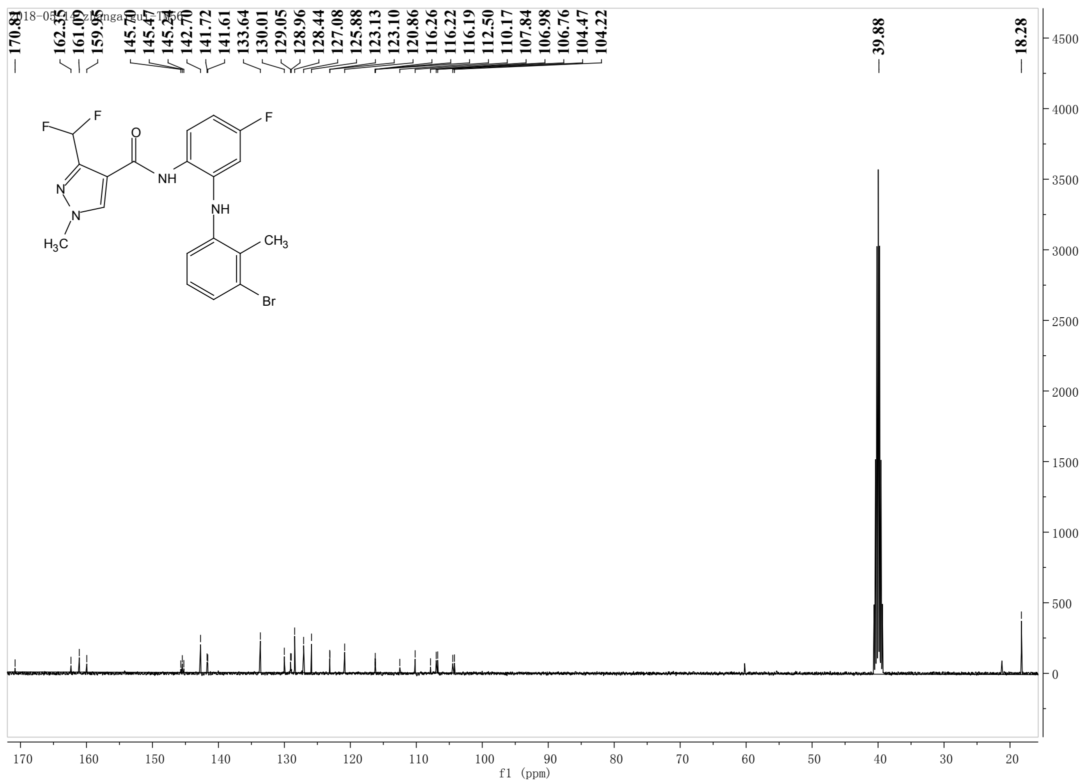
The [1]H NMR spectrogram of compound **8**



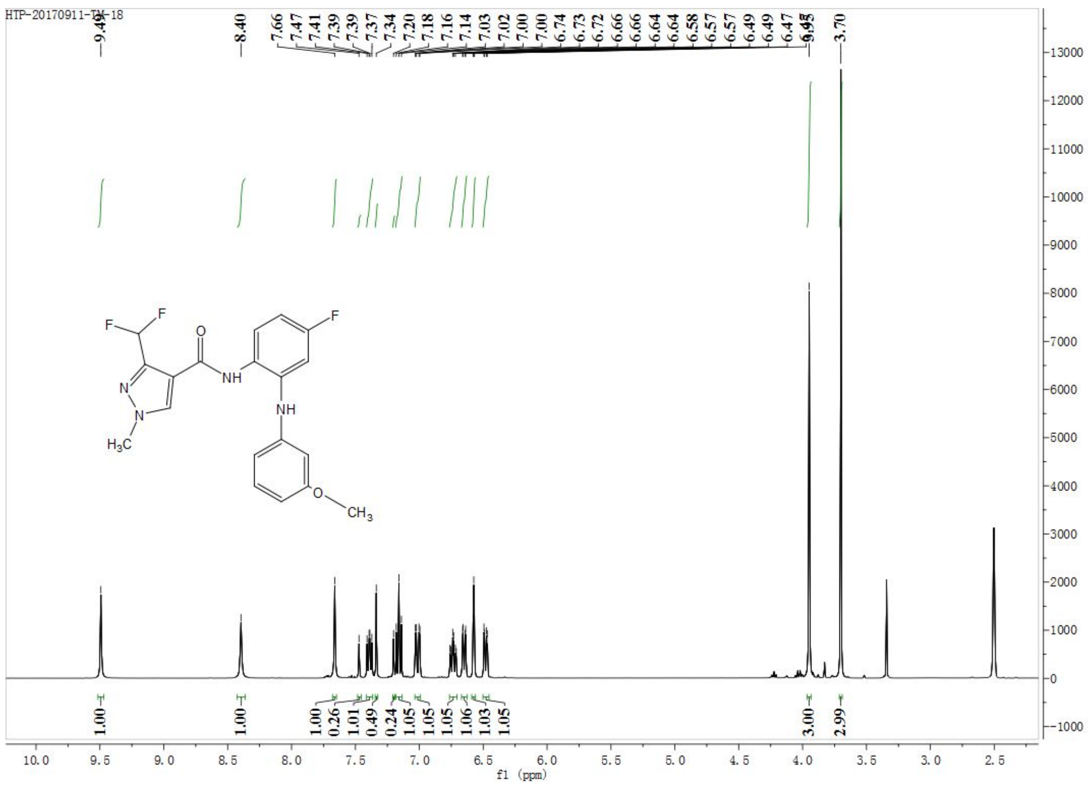
The [13]C NMR spectrogram of compound **8**



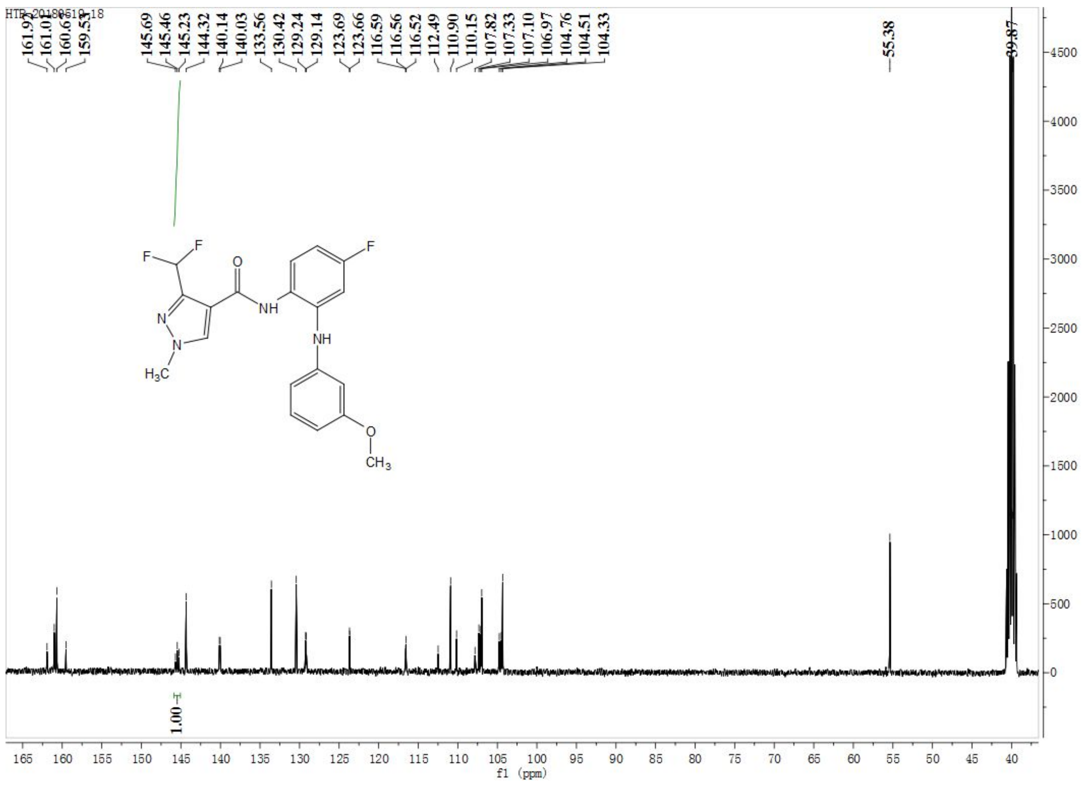
The ^{1}H NMR spectrogram of compound **9**



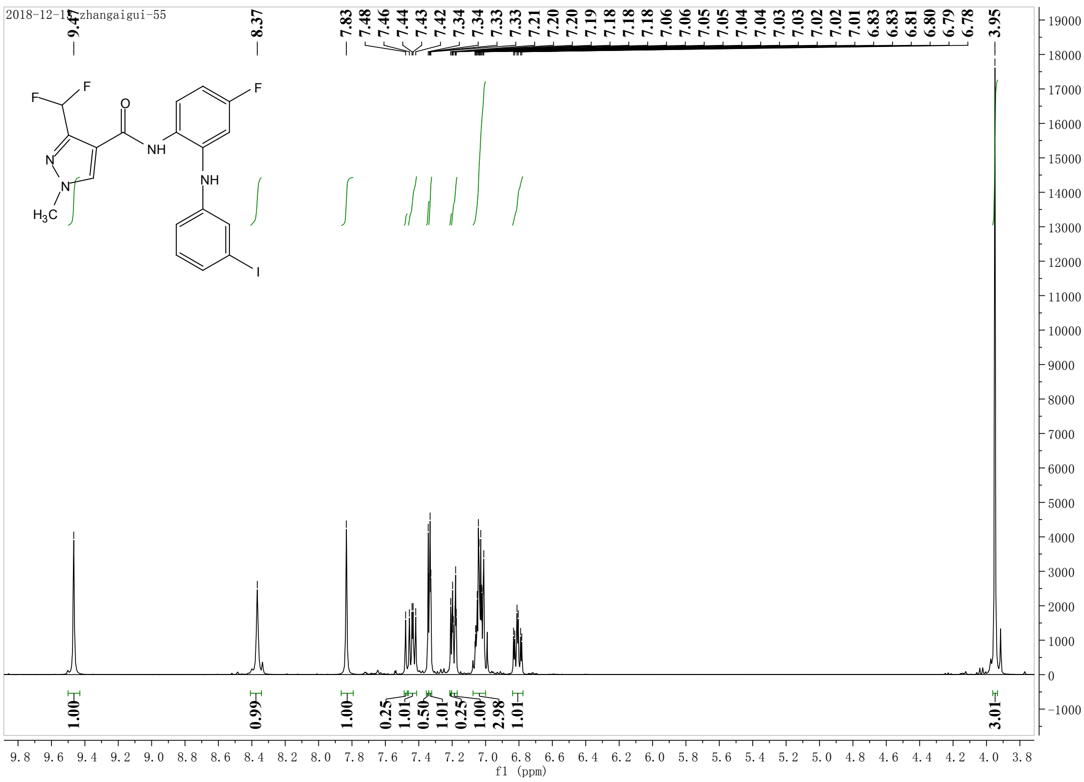
The ^{13}C NMR spectrogram of compound **9**



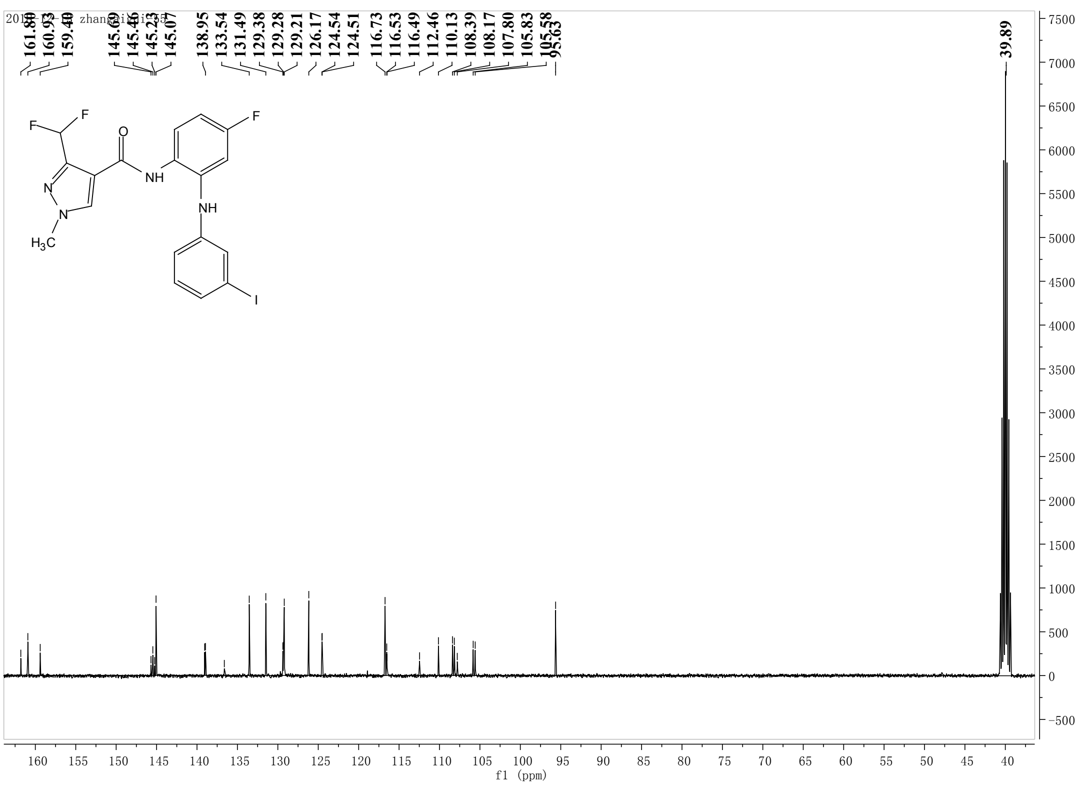
The ^{1}H NMR spectrogram of compound **10**



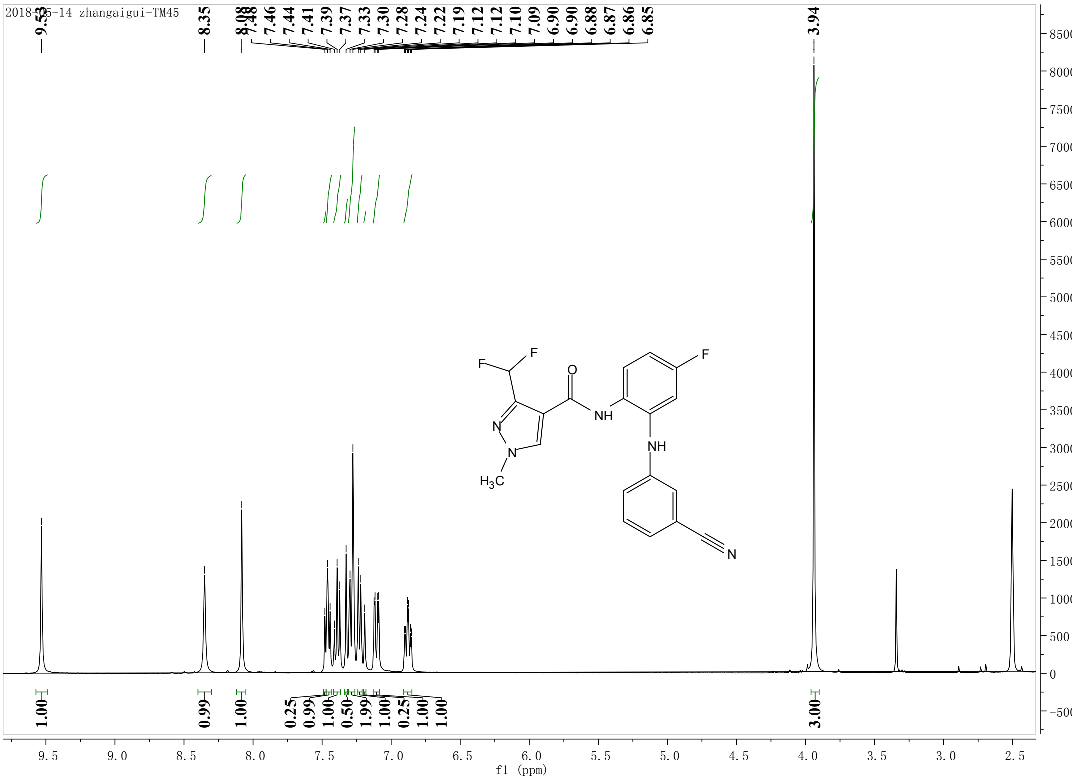
The ^{13}C NMR spectrogram of compound **10**



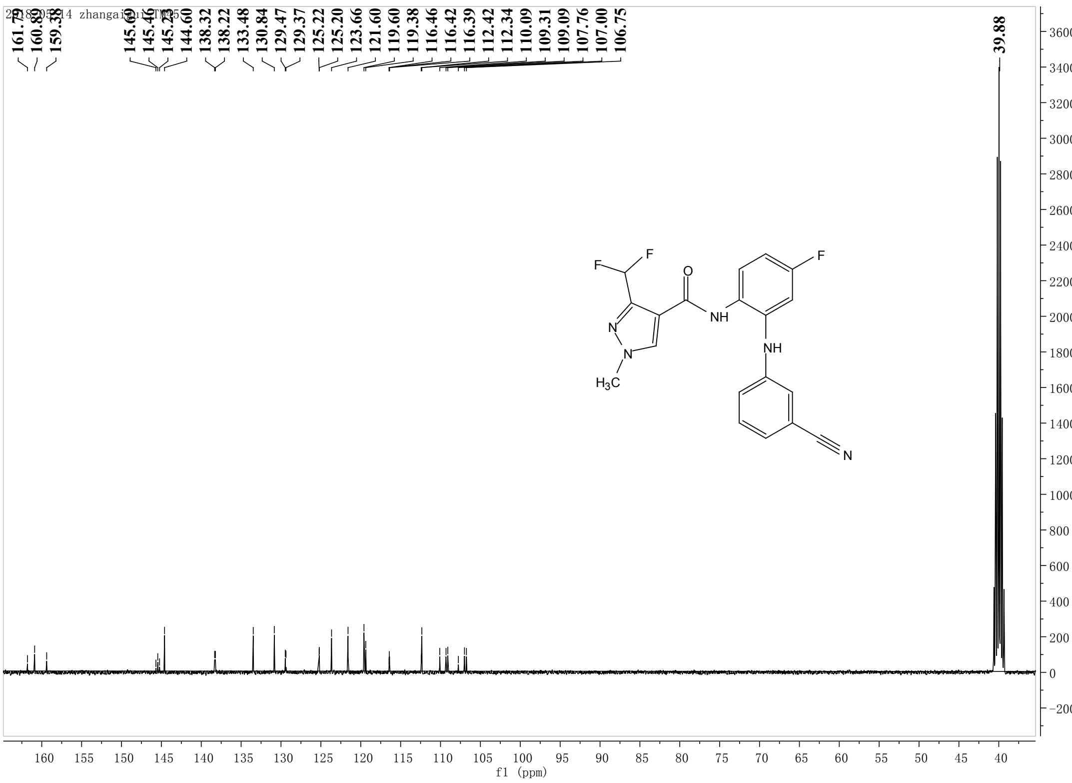
The ^{1}H NMR spectrogram of compound **11**



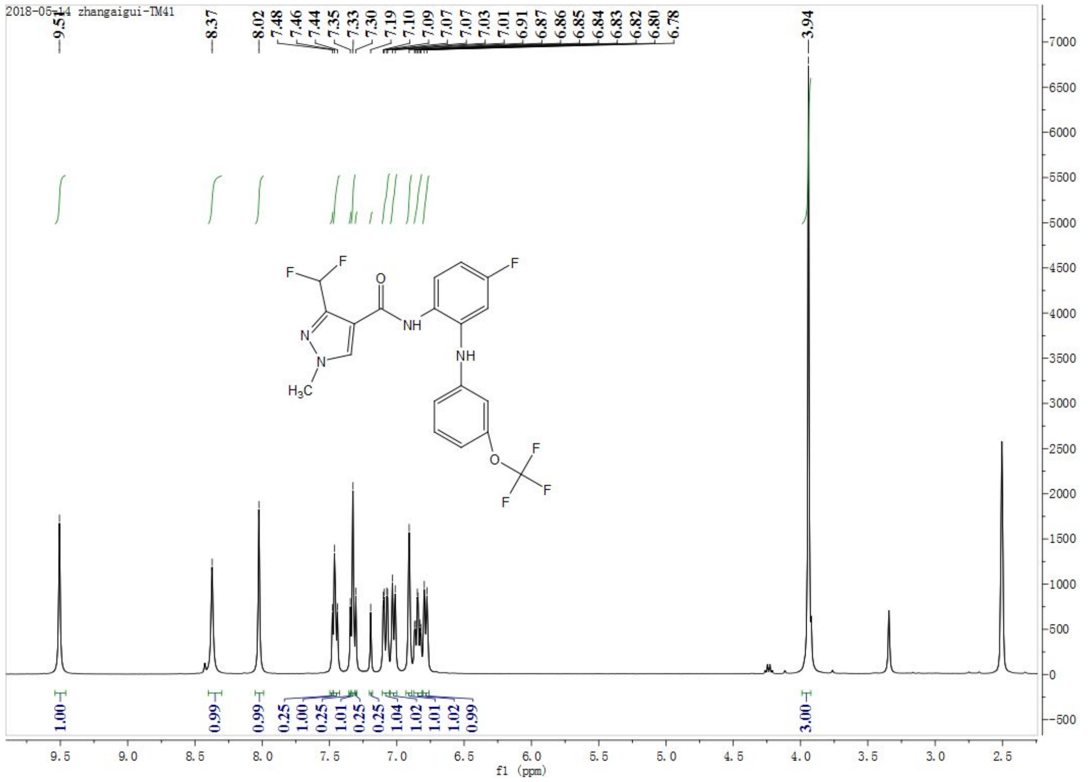
The ^{13}C NMR spectrogram of compound **11**



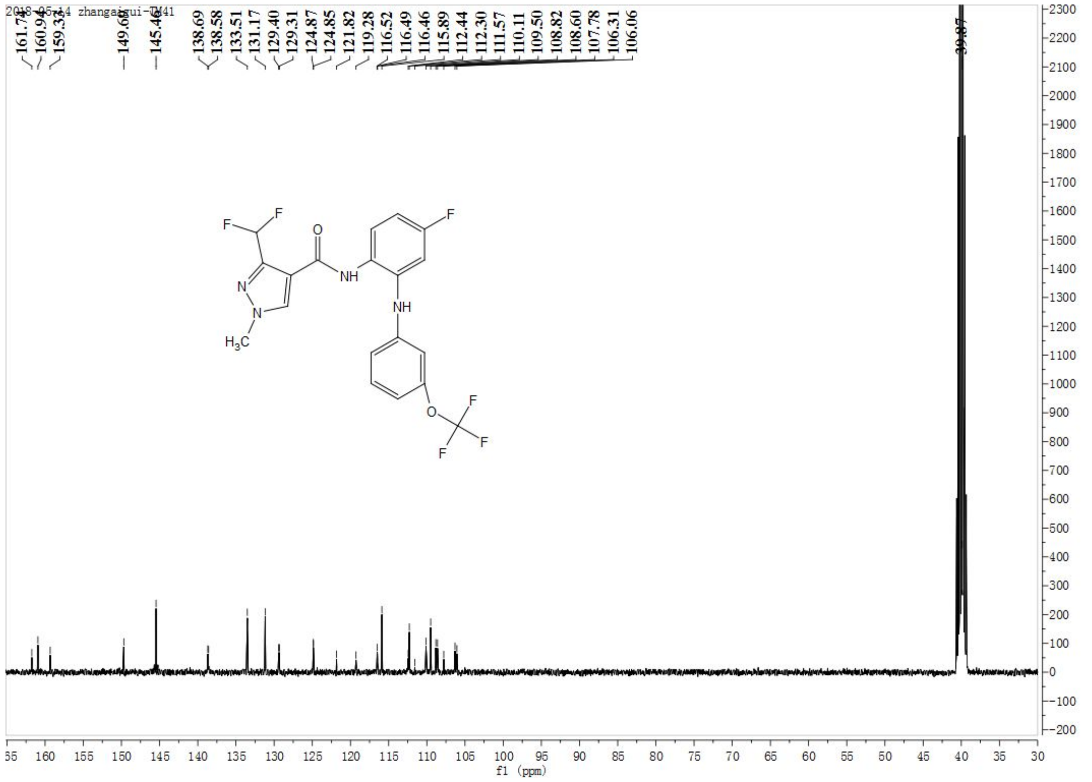
The ^{1}H NMR spectrogram of compound **13**



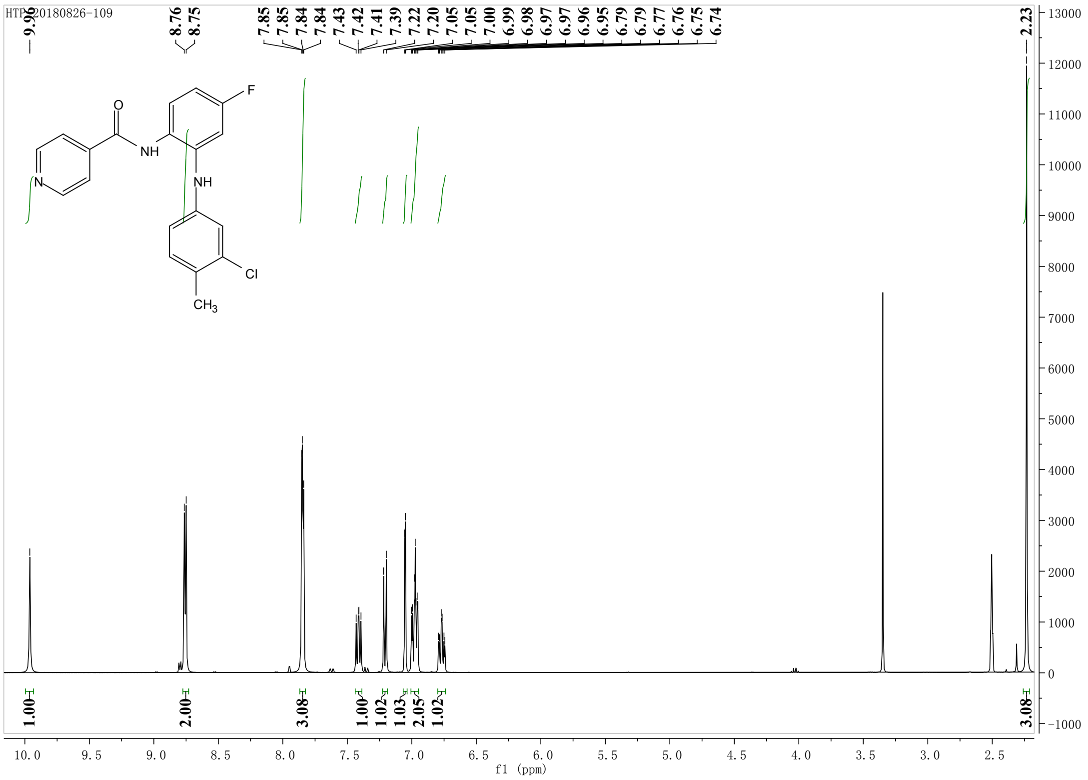
The ^{13}C NMR spectrogram of compound **13**



The ^{1}H NMR spectrogram of compound **14**



The ^{13}C NMR spectrogram of compound **14**



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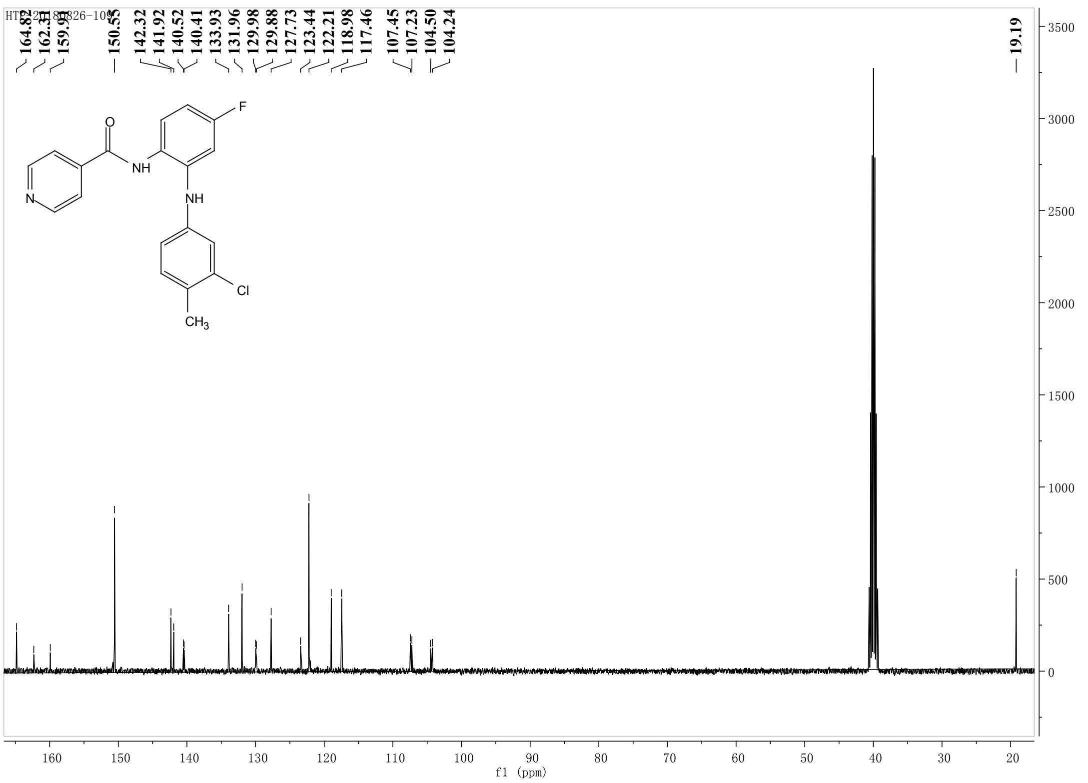
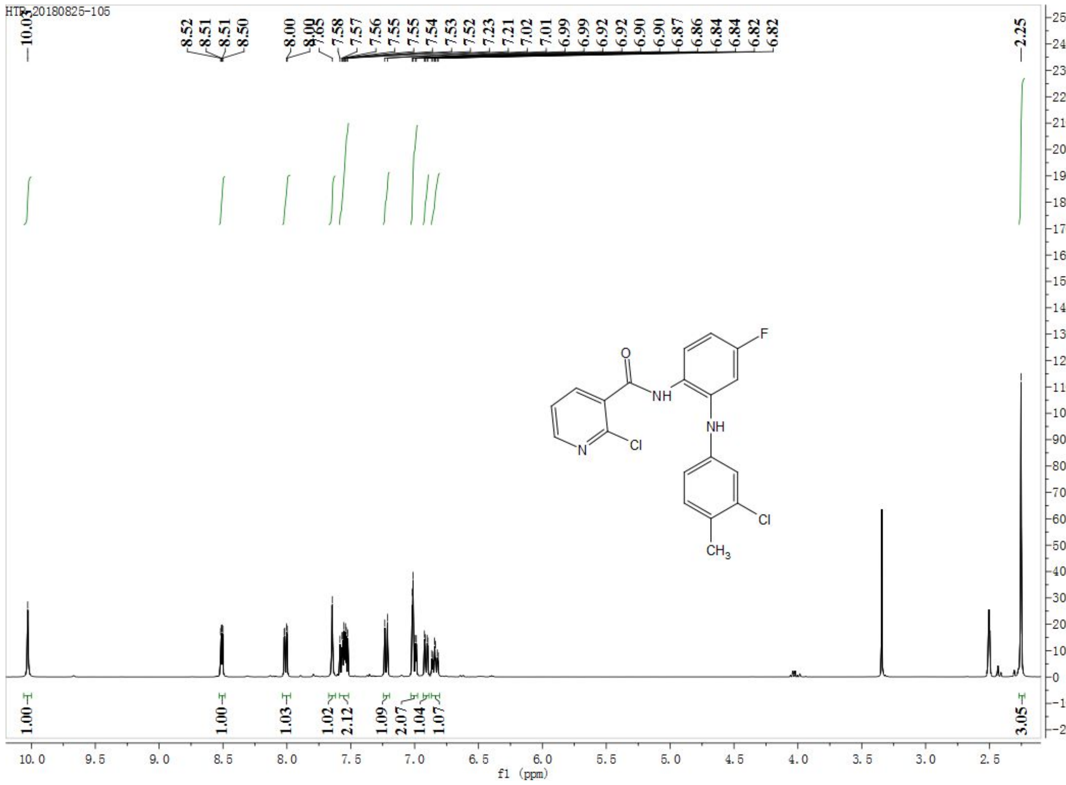
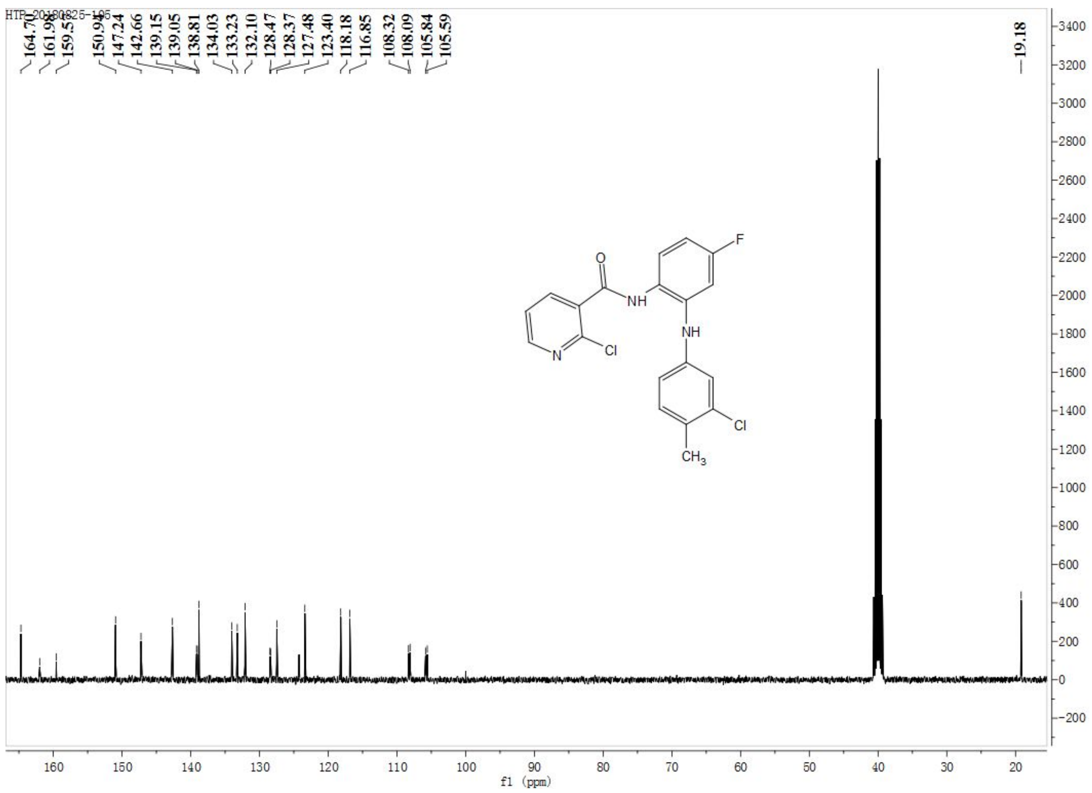


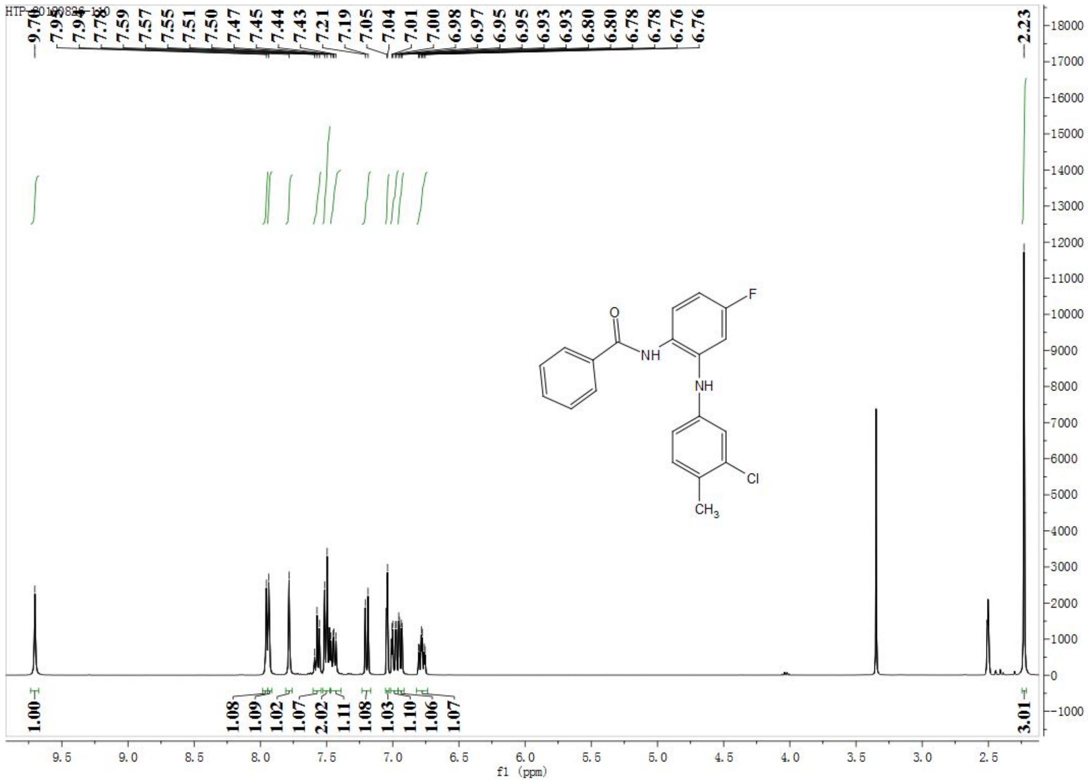
The ^{13}C NMR spectrogram of compound **17**



The [1]H NMR spectrogram of compound **18**



The [13]C NMR spectrogram of compound **18**



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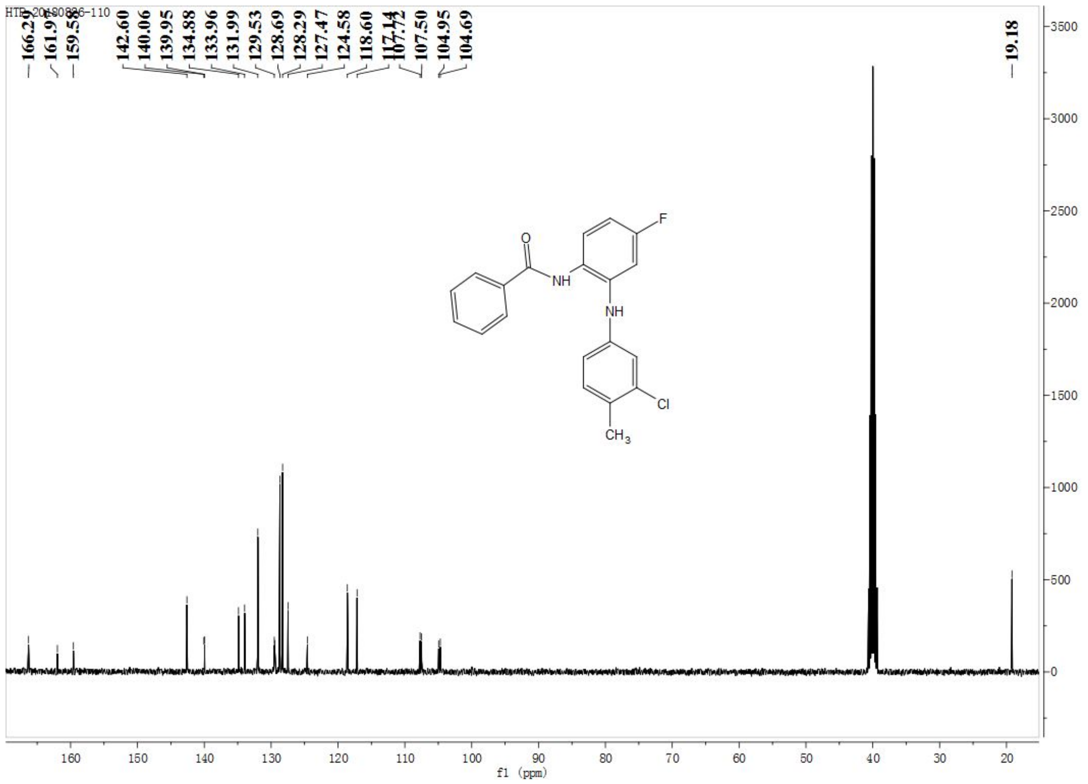
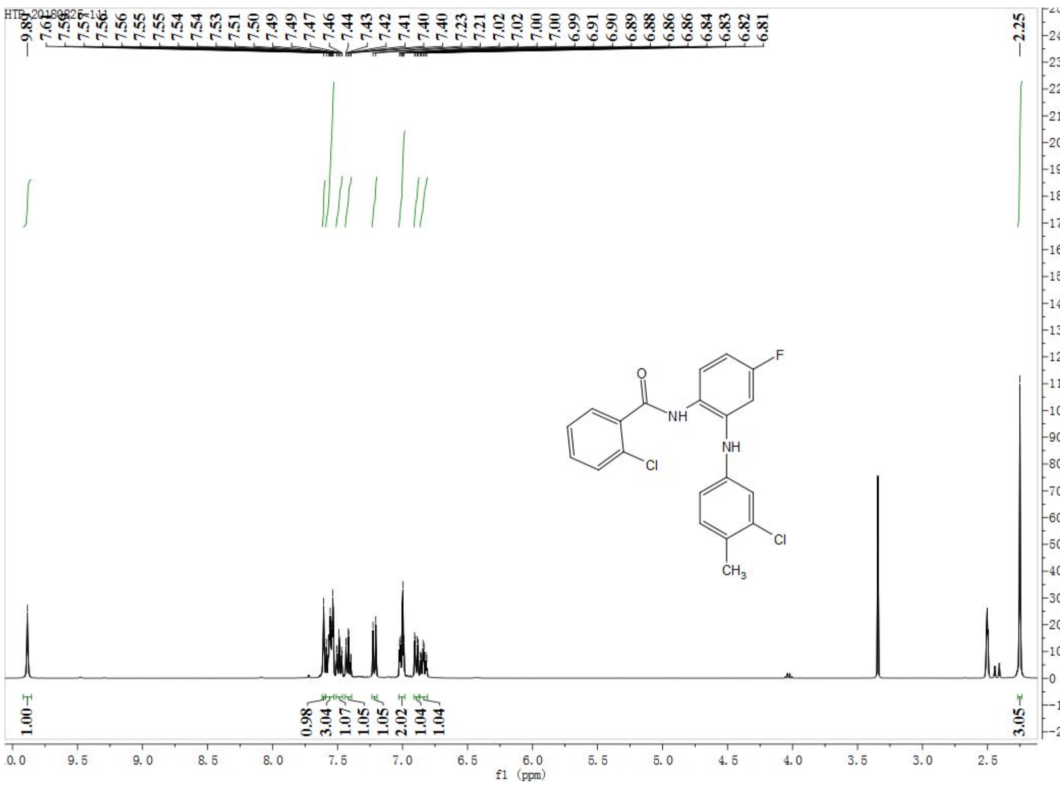
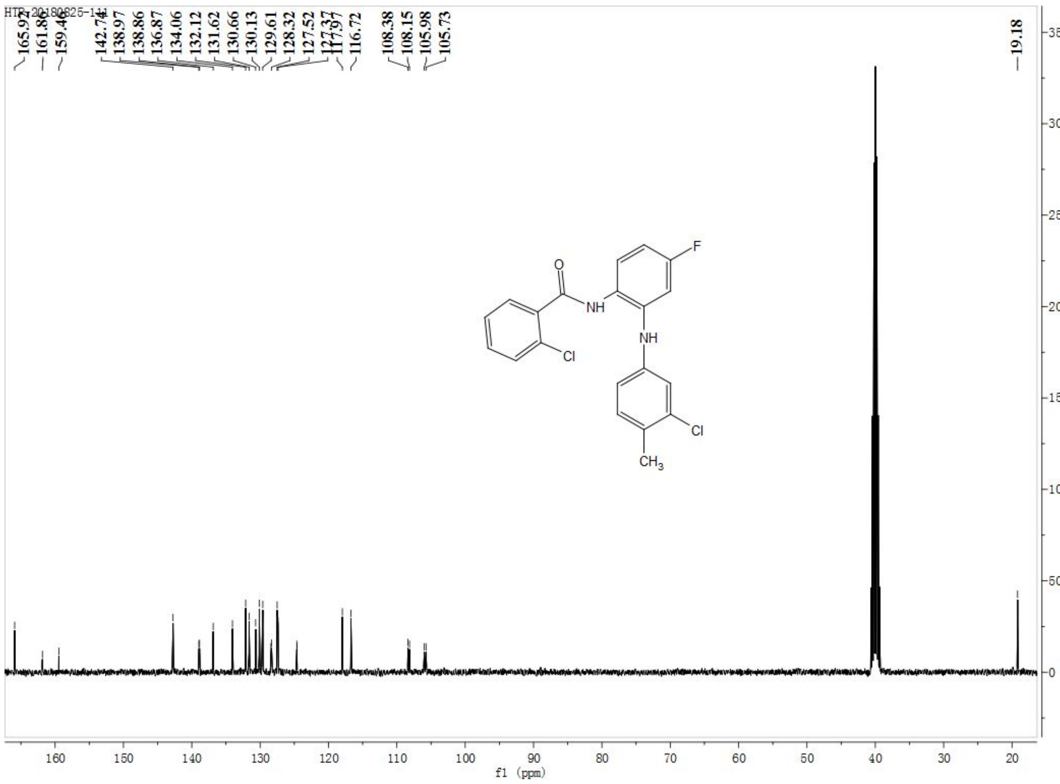


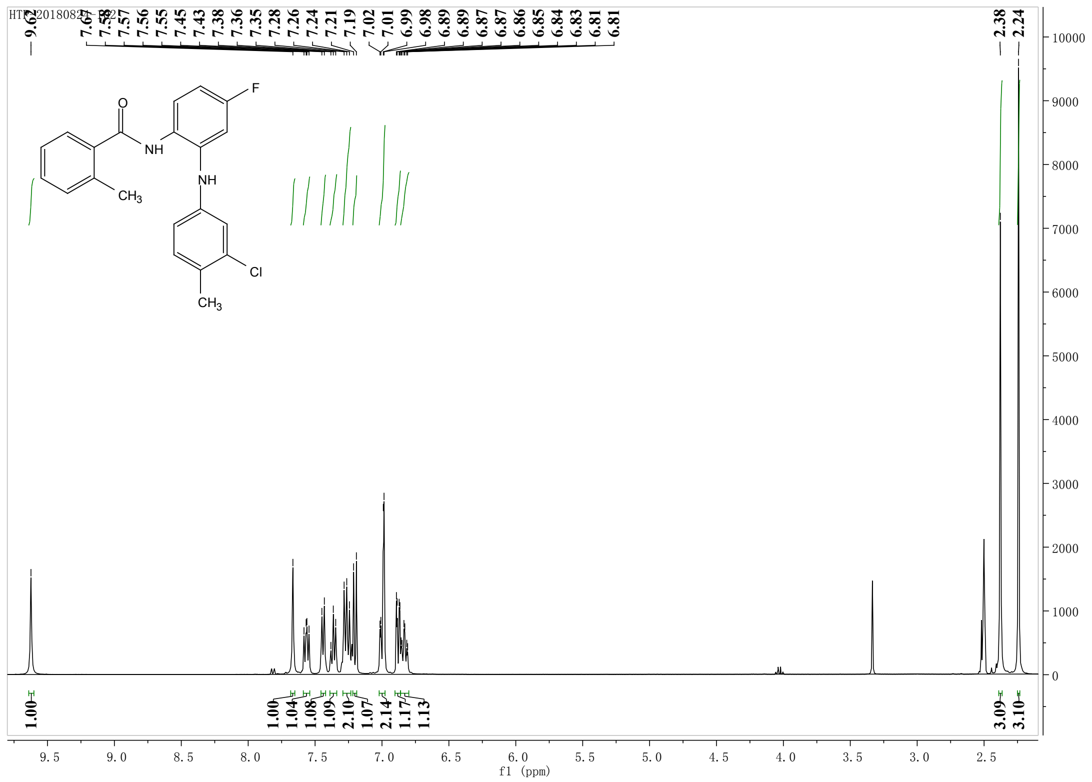
The [13]C NMR spectrogram of compound **19**



The ^{1}H NMR spectrogram of compound **20**



The ^{13}C NMR spectrogram of compound **20**



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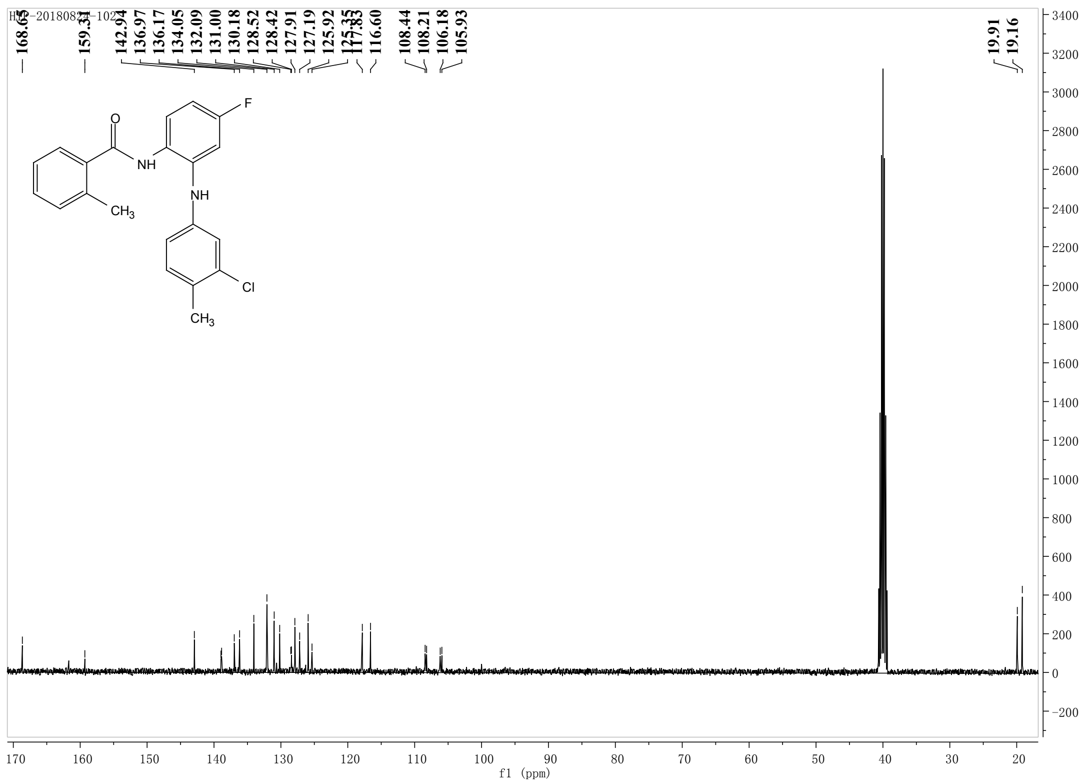

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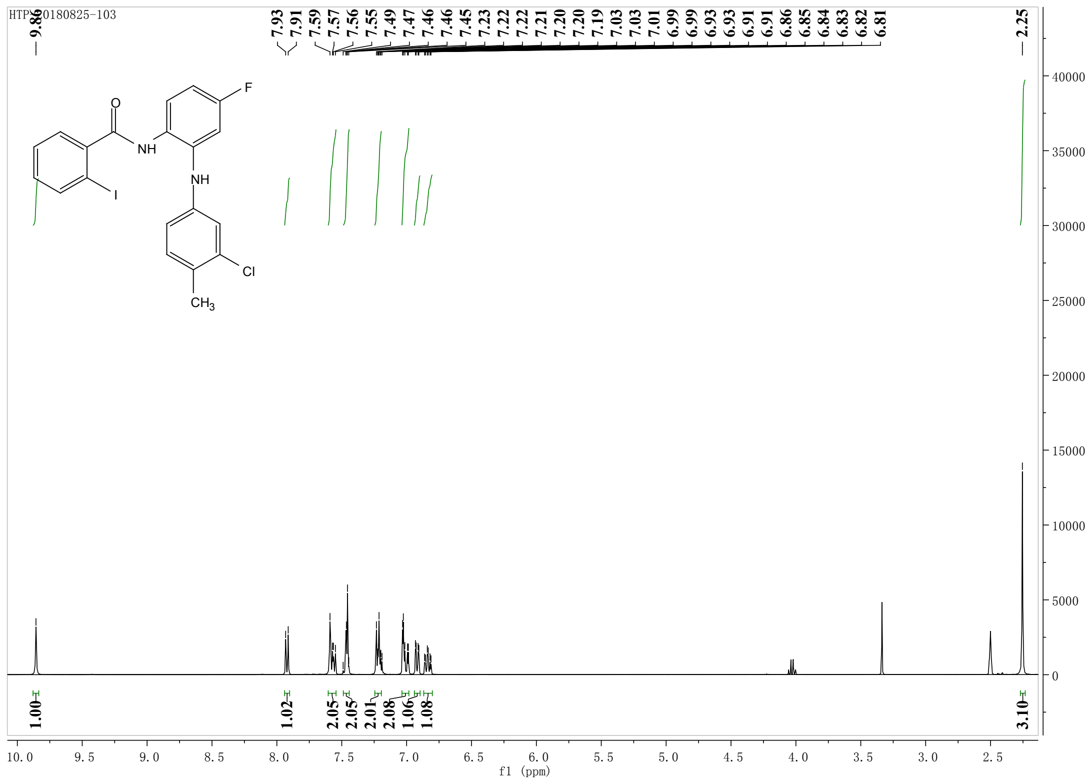

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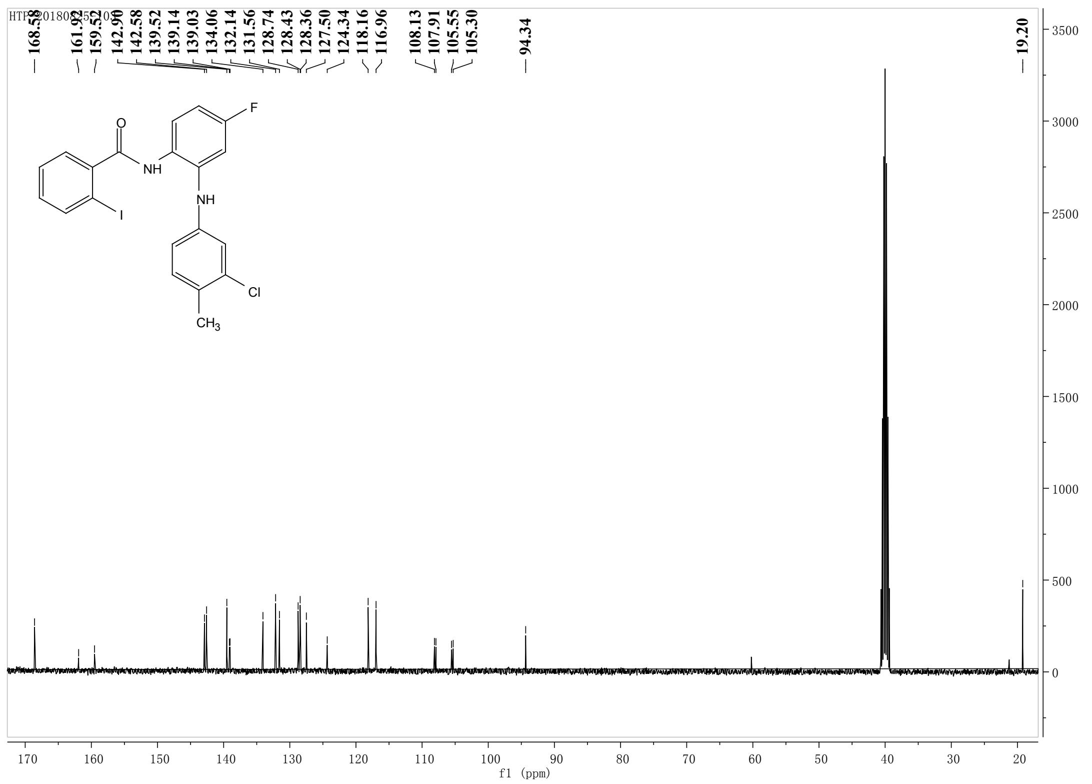

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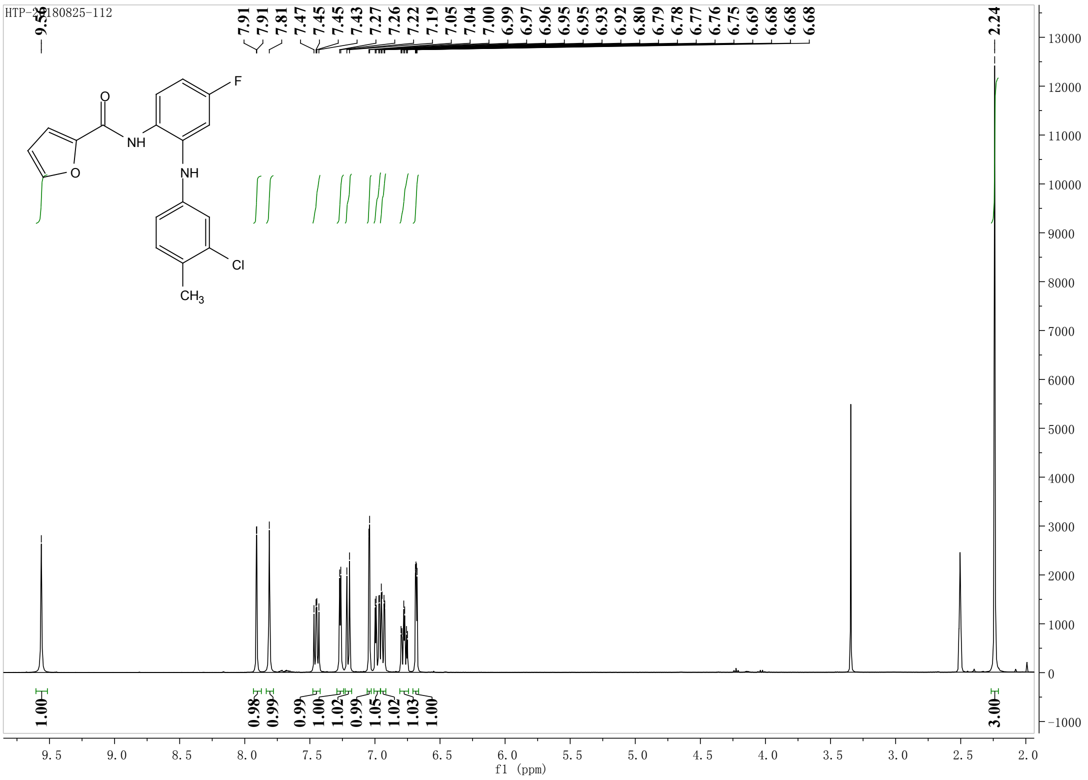
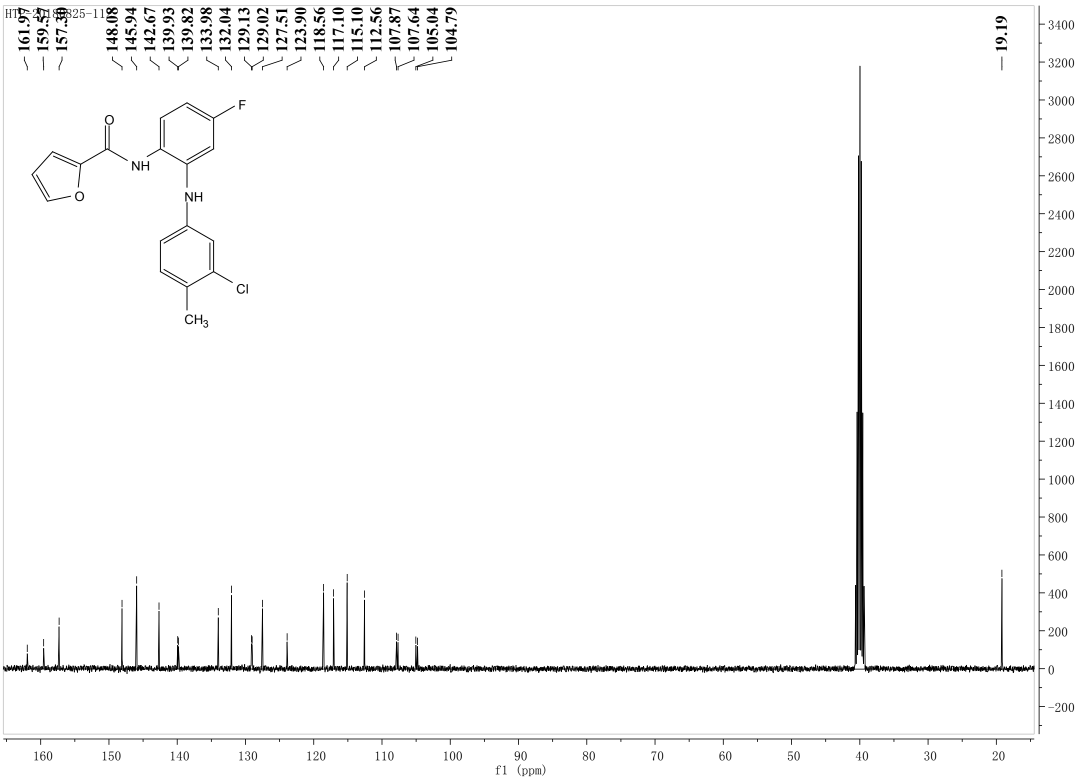
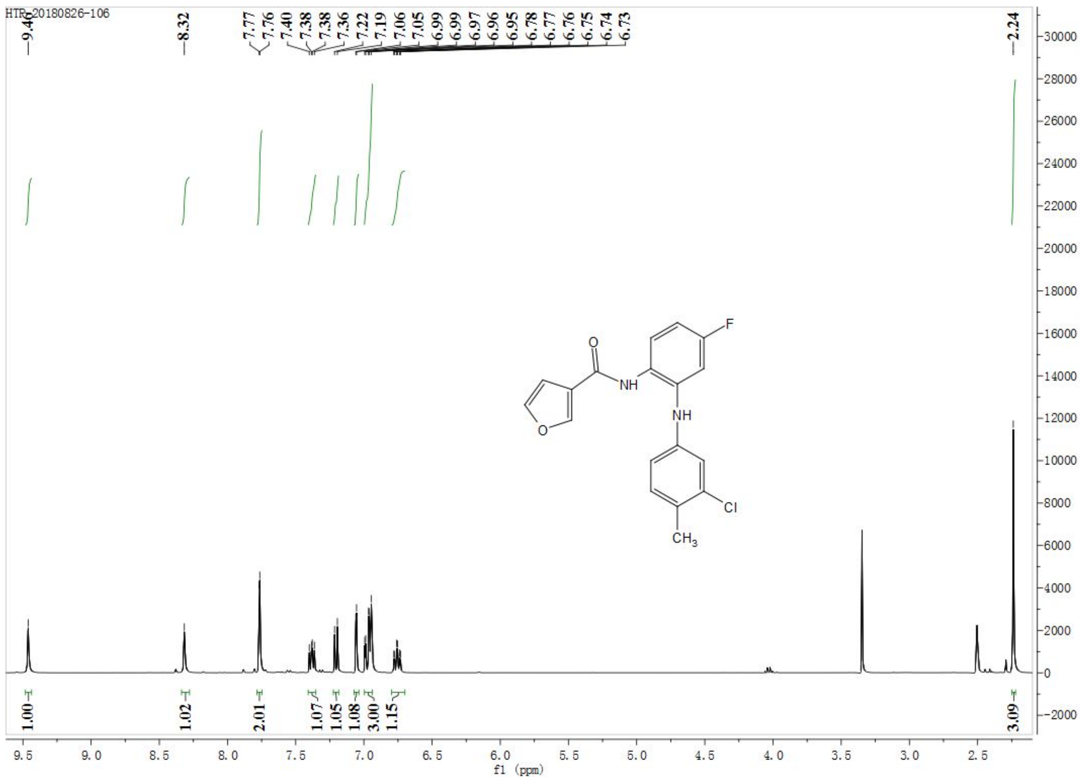


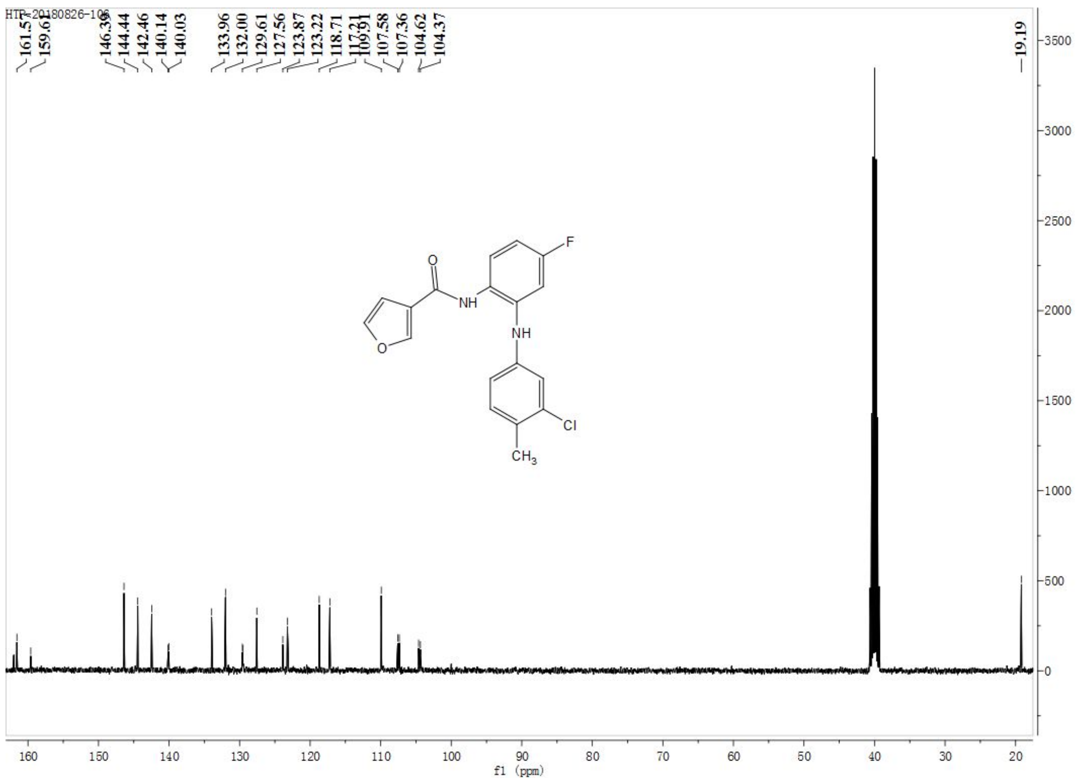
The ^{1}H NMR spectrogram of compound **24**



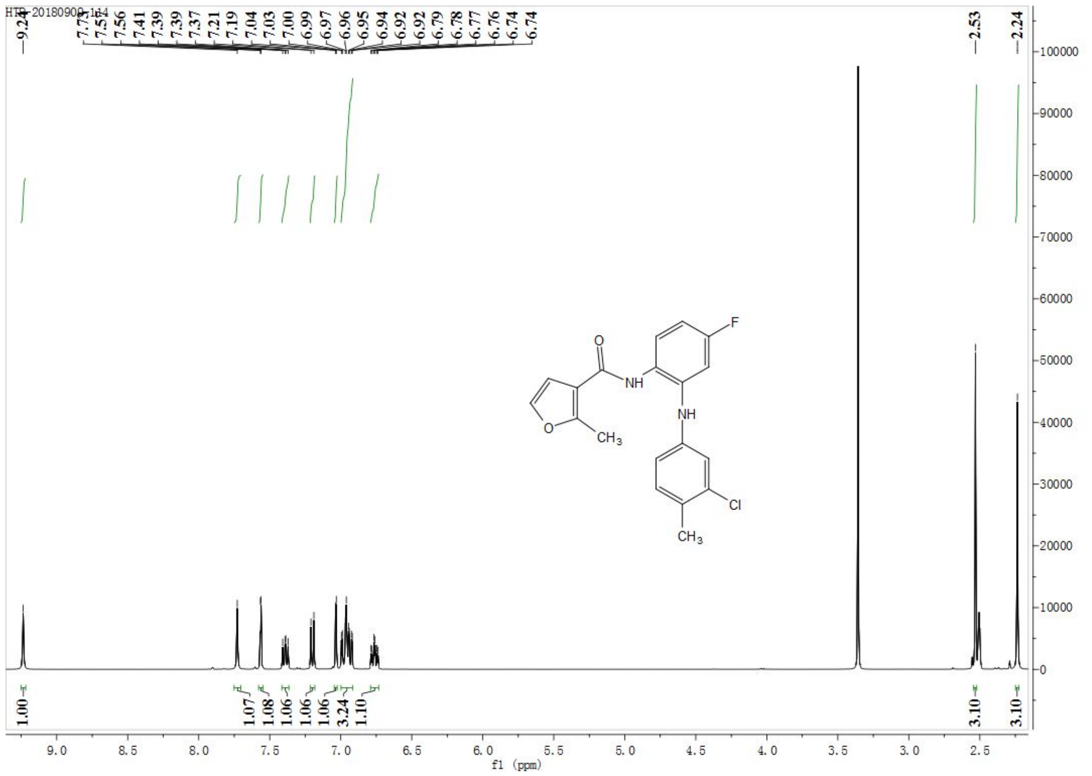
The ^{13}C NMR spectrogram of compound **24**



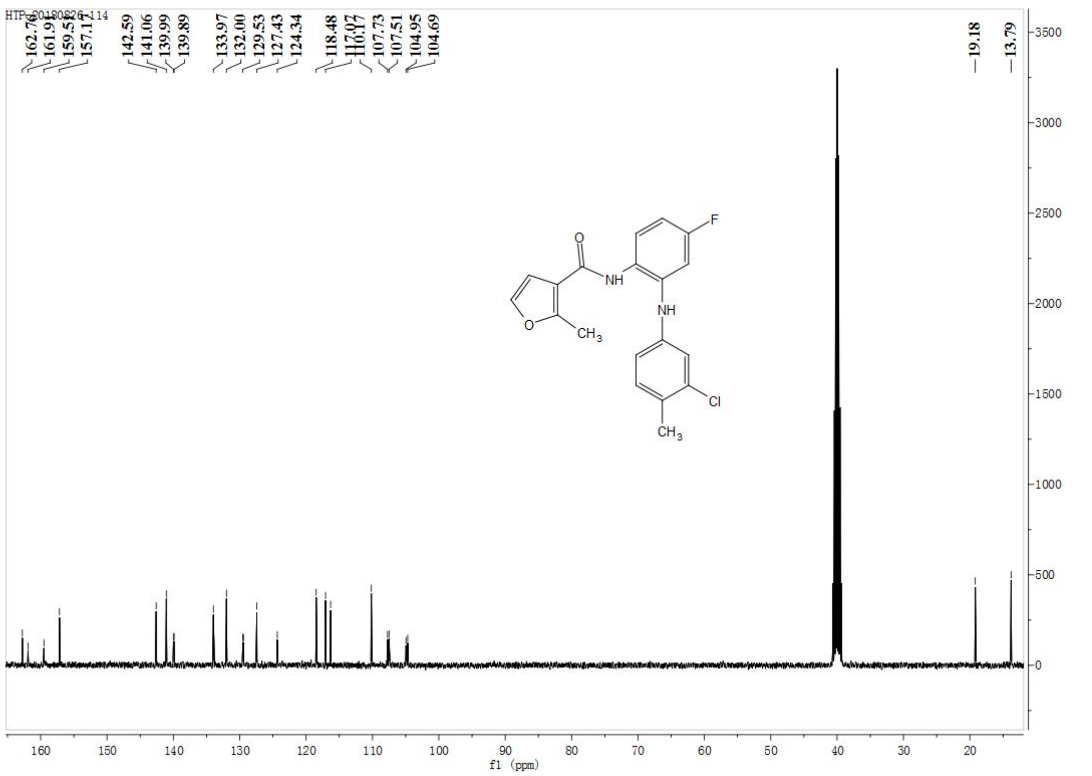
The ^{1}H NMR spectrogram of compound **25**



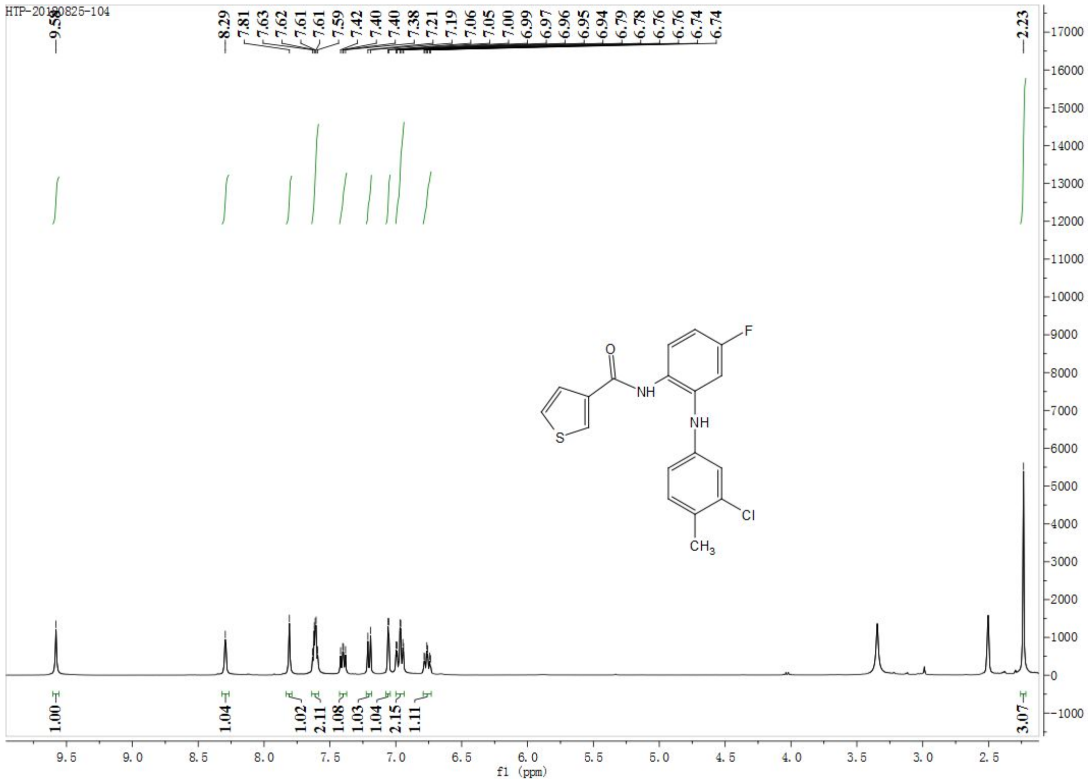
The ^{13}C NMR spectrogram of compound **25**



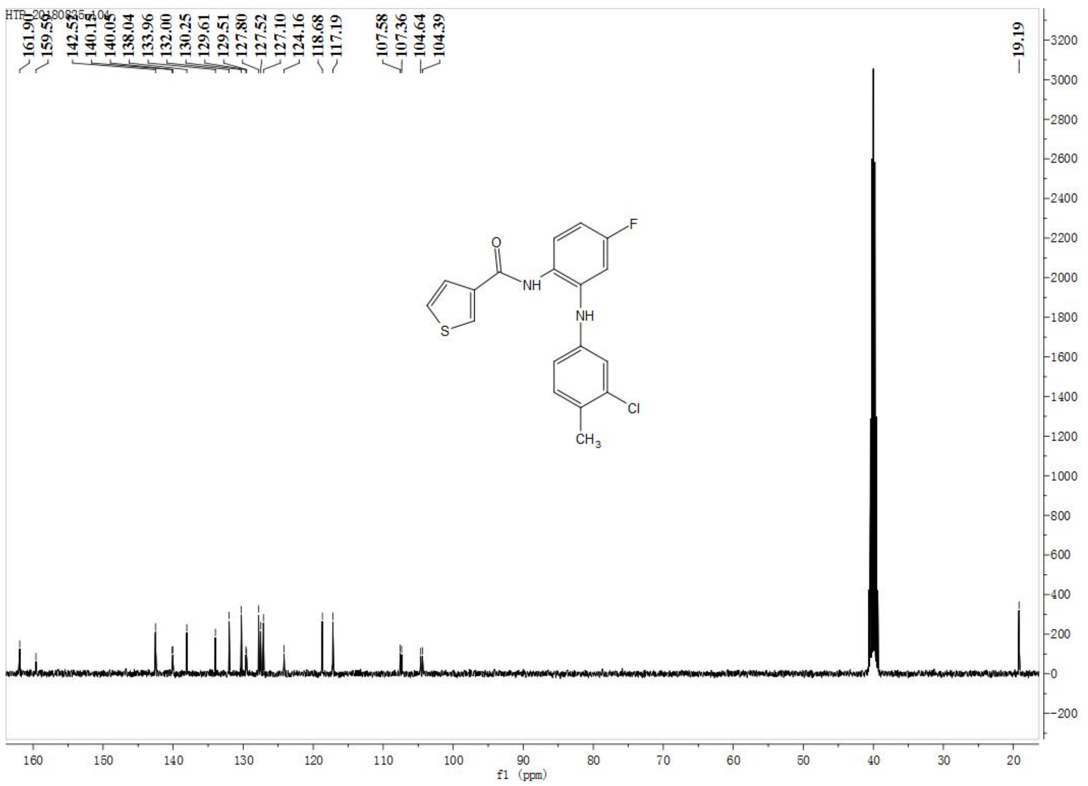
The ^{1}H NMR spectrogram of compound **26**



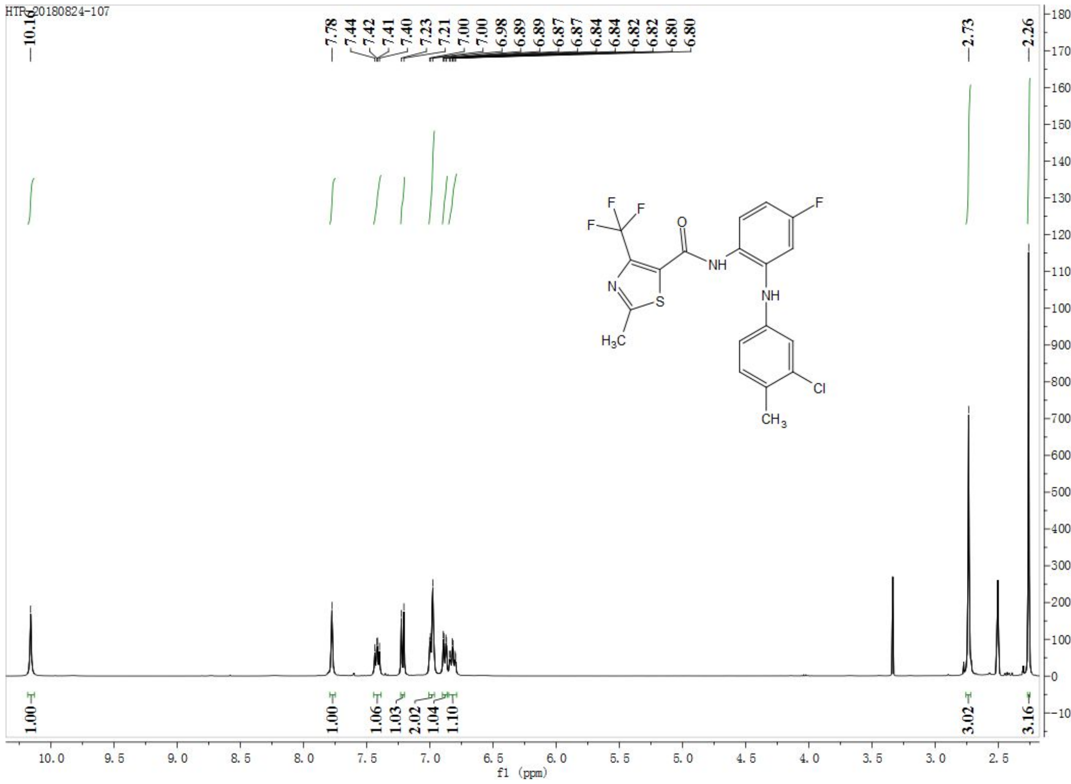
The ^{13}C NMR spectrogram of compound **26**



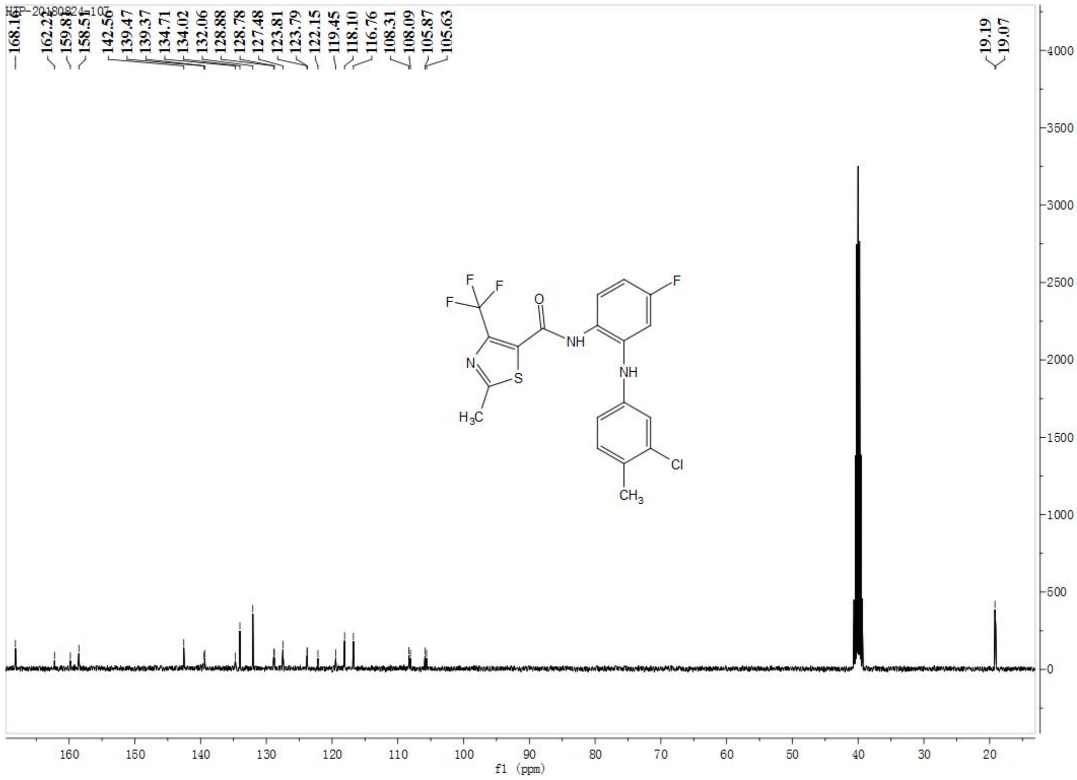
The [1]H NMR spectrogram of compound **28**



The [13]C NMR spectrogram of compound **28**



The ^{1}H NMR spectrogram of compound **29**



The ^{13}C NMR spectrogram of compound **29**