Electronic Supplementary Material (ESI) for RSC Advances.

Supplementary Information

Discovery of N-Cyclobutylaminoethoxyisoxazole Derivatives as Novel Sigma-1 Receptor Ligands with Neurite Outgrowth Efficacy in Cells

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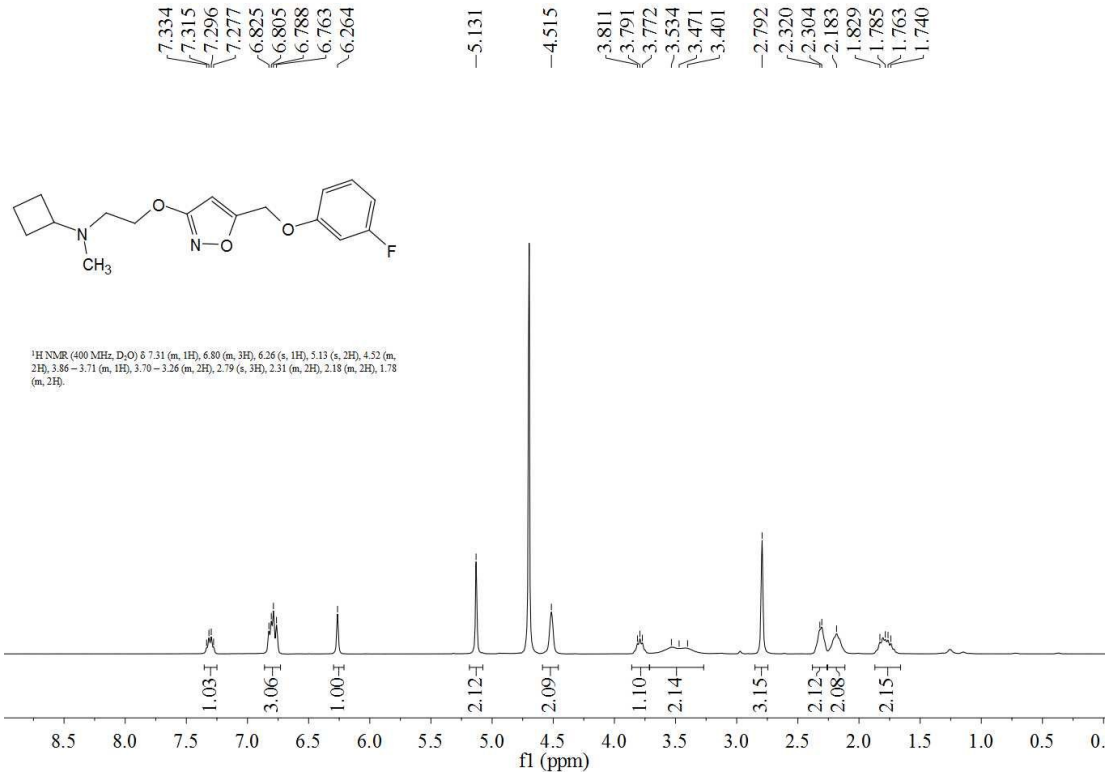
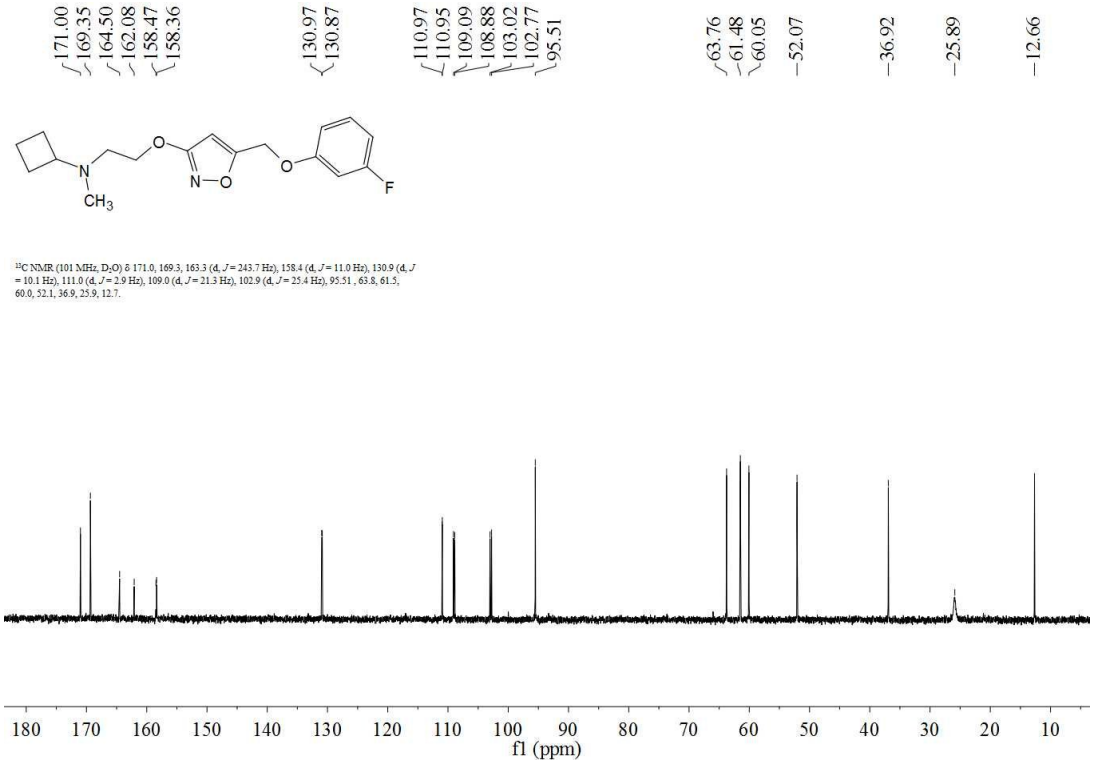
Contents

^{1}H NMR and ^{13}C NMR spectra of compound **17**

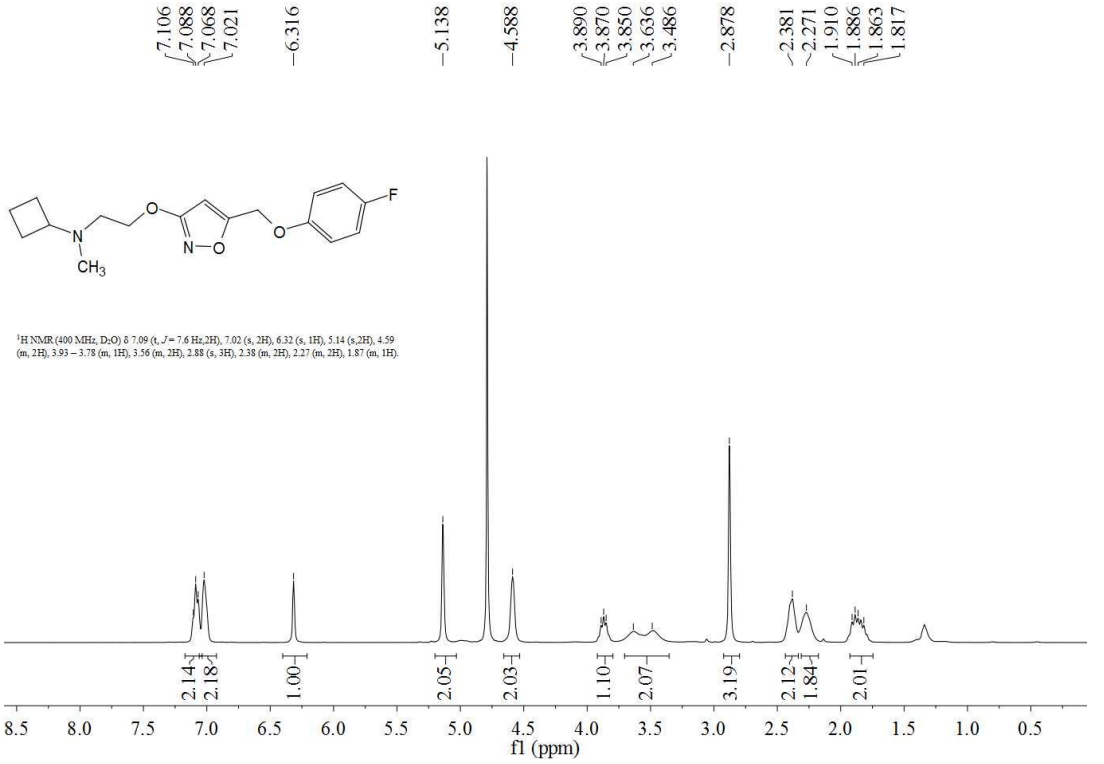


^{1}H NMR (400 MHz, D_2O) δ 7.31 (m, 1H), 6.80 (m, 3H), 6.26 (s, 1H), 5.13 (s, 2H), 4.52 (m, 2H), 3.86 – 3.71 (m, 1H), 3.70 – 3.26 (m, 2H), 2.79 (s, 3H), 2.31 (m, 2H), 2.18 (m, 2H), 1.78 (m, 2H).

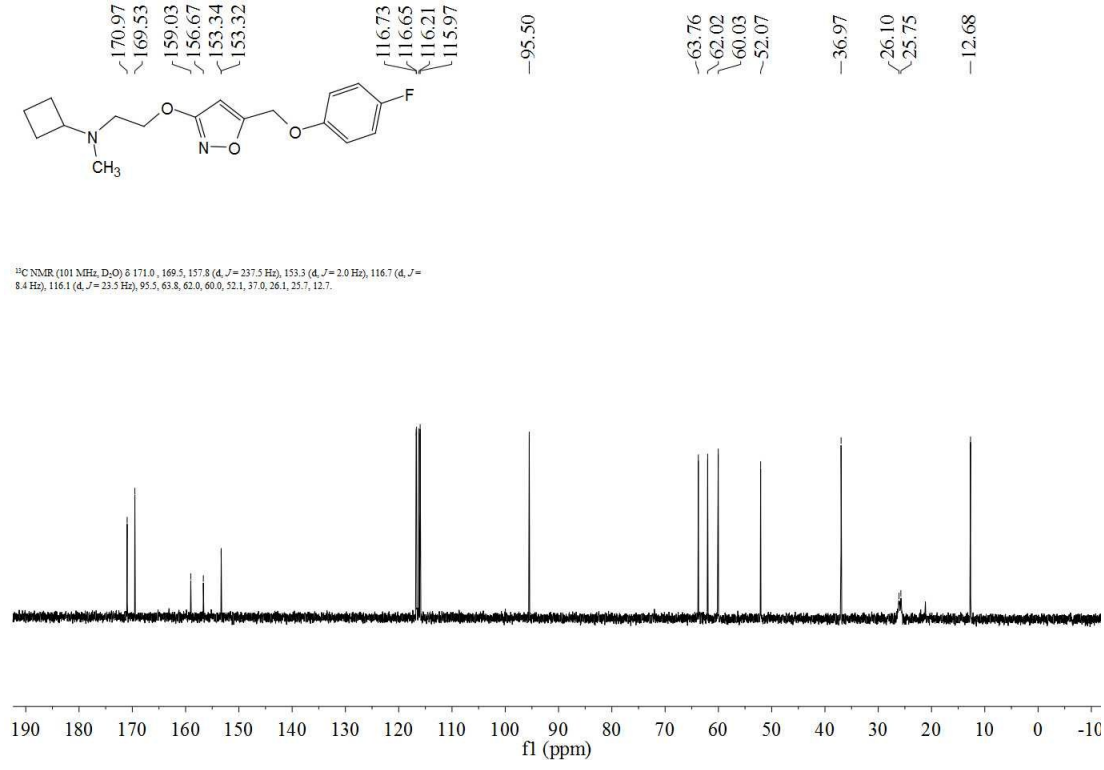


^{13}C NMR (101 MHz, D_2O) δ 171.0, 169.3, 163.3 (d, J = 243.7 Hz), 158.4 (d, J = 11.0 Hz), 130.9 (d, J = 10.1 Hz), 111.0 (d, J = 2.9 Hz), 109.0 (d, J = 21.3 Hz), 102.9 (d, J = 25.4 Hz), 95.51 , 63.8, 61.5, 60.0, 52.1, 36.9, 25.9, 12.7.

^{1}H NMR and ^{13}C NMR spectra of compound **18**

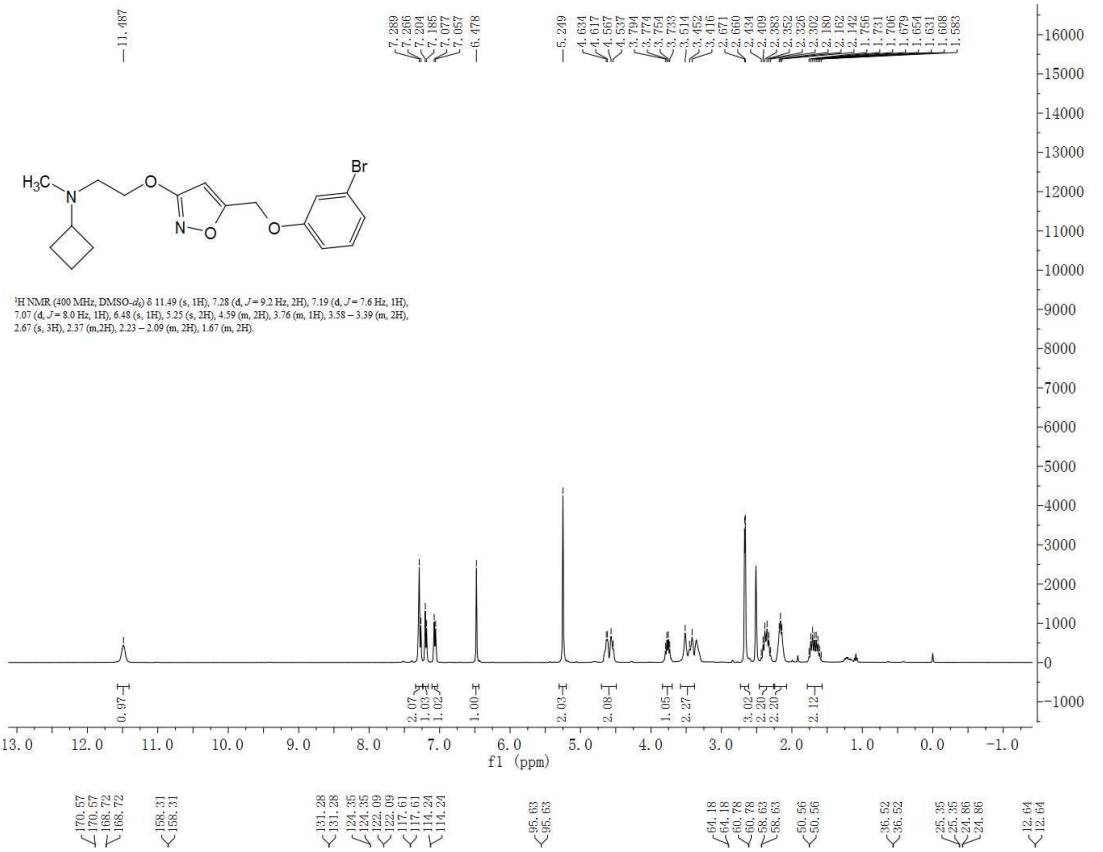


^{1}H NMR (400 MHz, D_2O) δ 7.09 (t, J = 7.6 Hz,2H), 7.02 (s, 2H), 6.32 (s, 1H), 5.14 (s,2H), 4.59 (m, 2H), 3.93 – 3.78 (m, 1H), 3.56 (m, 2H), 2.88 (s, 3H), 2.38 (m, 2H), 2.27 (m, 2H), 1.87 (m, 1H).

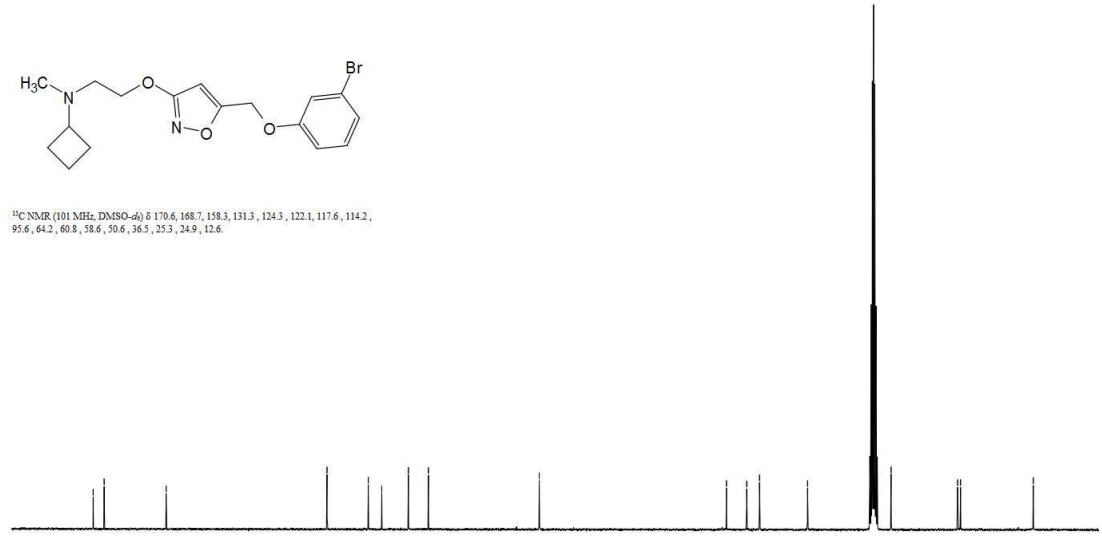


^{13}C NMR (101 MHz, D_2O) δ 171.0 , 169.5, 157.8 (d, J = 237.5 Hz), 153.3 (d, J = 2.0 Hz), 116.7 (d, J = 8.4 Hz), 116.1 (d, J = 23.5 Hz), 95.5, 63.8, 62.0, 60.0, 52.1, 37.0, 26.1, 25.7, 12.7.

^{1}H NMR and ^{13}C NMR spectra of compound **19**

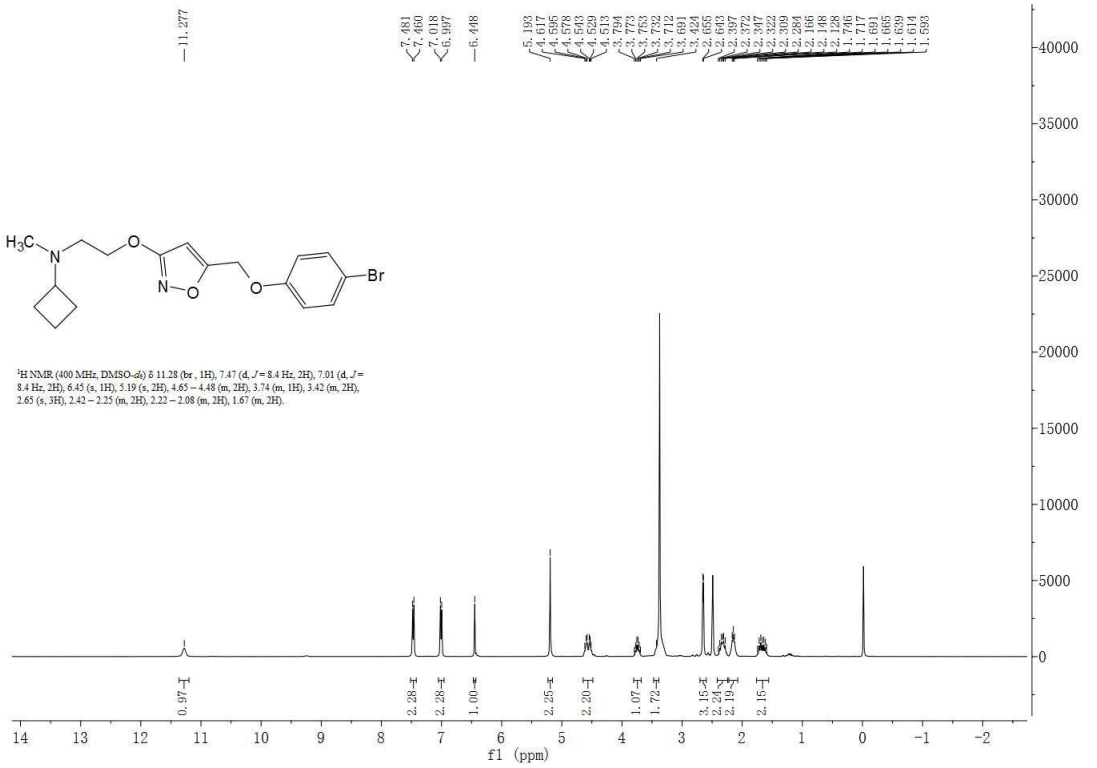


^{1}H NMR (400 MHz, DMSO-d_6) δ 11.49 (s, 1H), 7.28 (d, J = 9.2 Hz, 2H), 7.19 (d, J = 7.6 Hz, 1H), 7.07 (d, J = 8.0 Hz, 1H), 6.48 (s, 1H), 5.25 (s, 2H), 4.59 (m, 2H), 3.76 (m, 1H), 3.58 – 3.39 (m, 2H), 2.67 (s, 3H), 2.37 (m,2H), 2.23 – 2.09 (m, 2H), 1.67 (m, 2H).

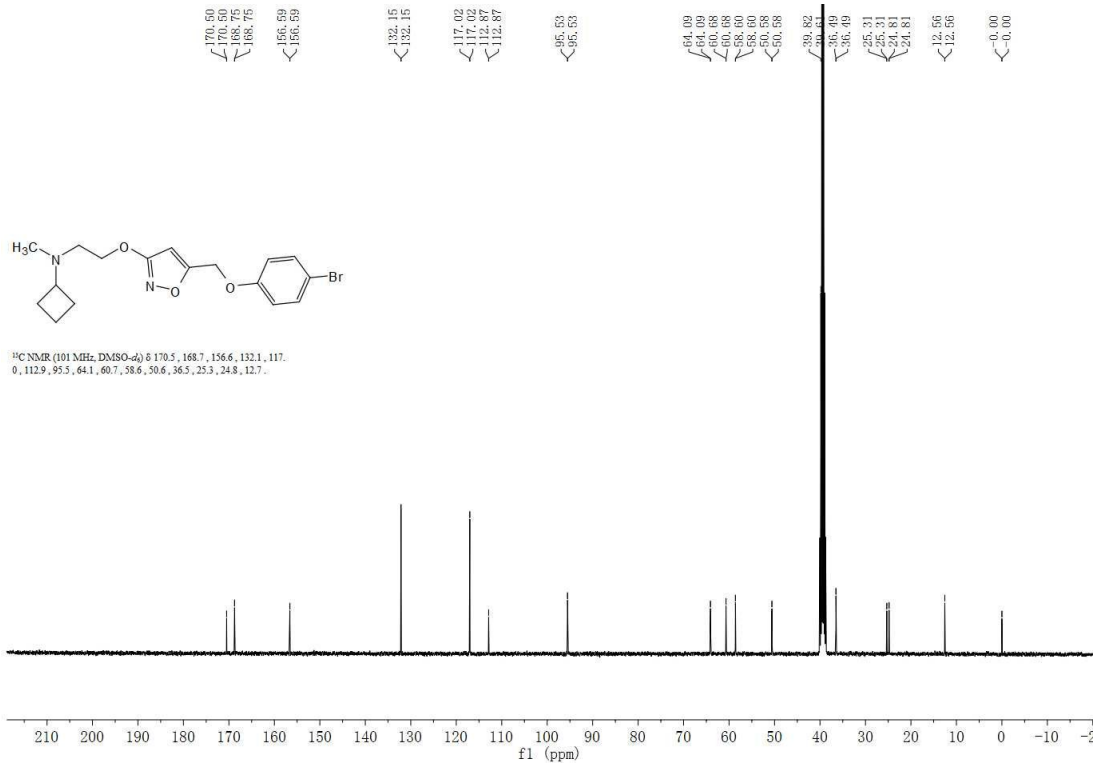


^{13}C NMR (101 MHz, DMSO-d_6) δ 170.6, 168.7, 158.3, 131.3 , 124.3 , 122.1, 117.6 , 114.2 , 95.6 , 64.2 , 60.8 , 58.6 , 50.6 , 36.5 , 25.3 , 24.9 , 12.6.

^{1}H NMR and ^{13}C NMR spectra of compound **20**

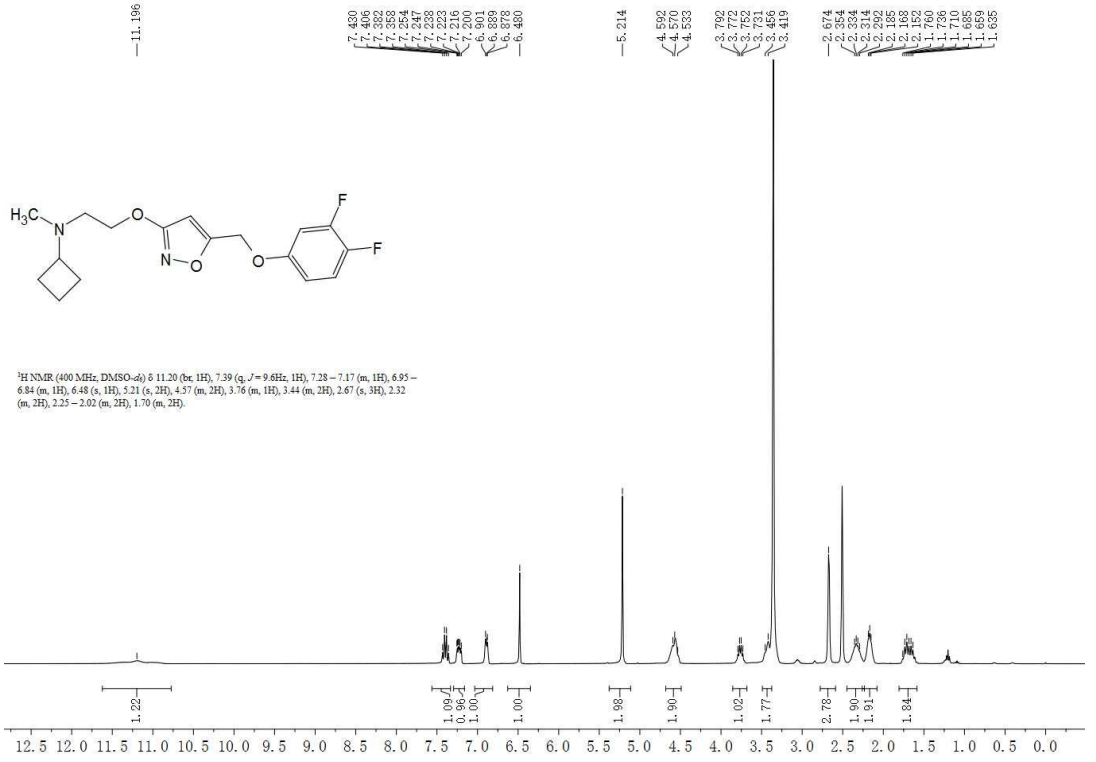


^{1}H NMR (400 MHz, DMSO-d_6) δ 11.28 (br , 1H), 7.47 (d, J = 8.4 Hz, 2H), 7.01 (d, J = 8.4 Hz, 2H), 6.45 (s, 1H), 5.19 (s, 2H), 4.65 – 4.48 (m, 2H), 3.74 (m, 1H), 3.42 (m, 2H), 2.65 (s, 3H), 2.42 – 2.25 (m, 2H), 2.22 – 2.08 (m, 2H), 1.67 (m, 2H).

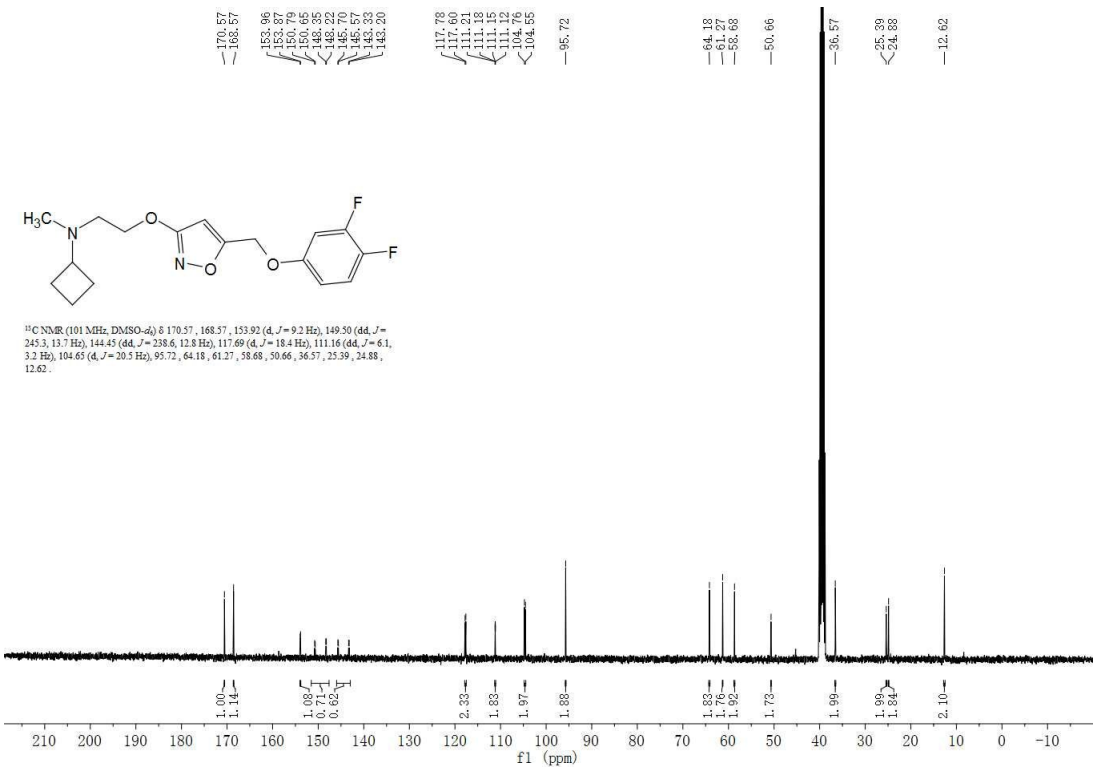


^{13}C NMR (101 MHz, DMSO-d_6) δ 170.5 , 168.7 , 156.6 , 132.1 , 117.0 , 112.9 , 95.5 , 64.1 , 60.7 , 58.6 , 50.6 , 36.5 , 25.3 , 24.8 , 12.7 .

^{1}H NMR and ^{13}C NMR spectra of compound **21**



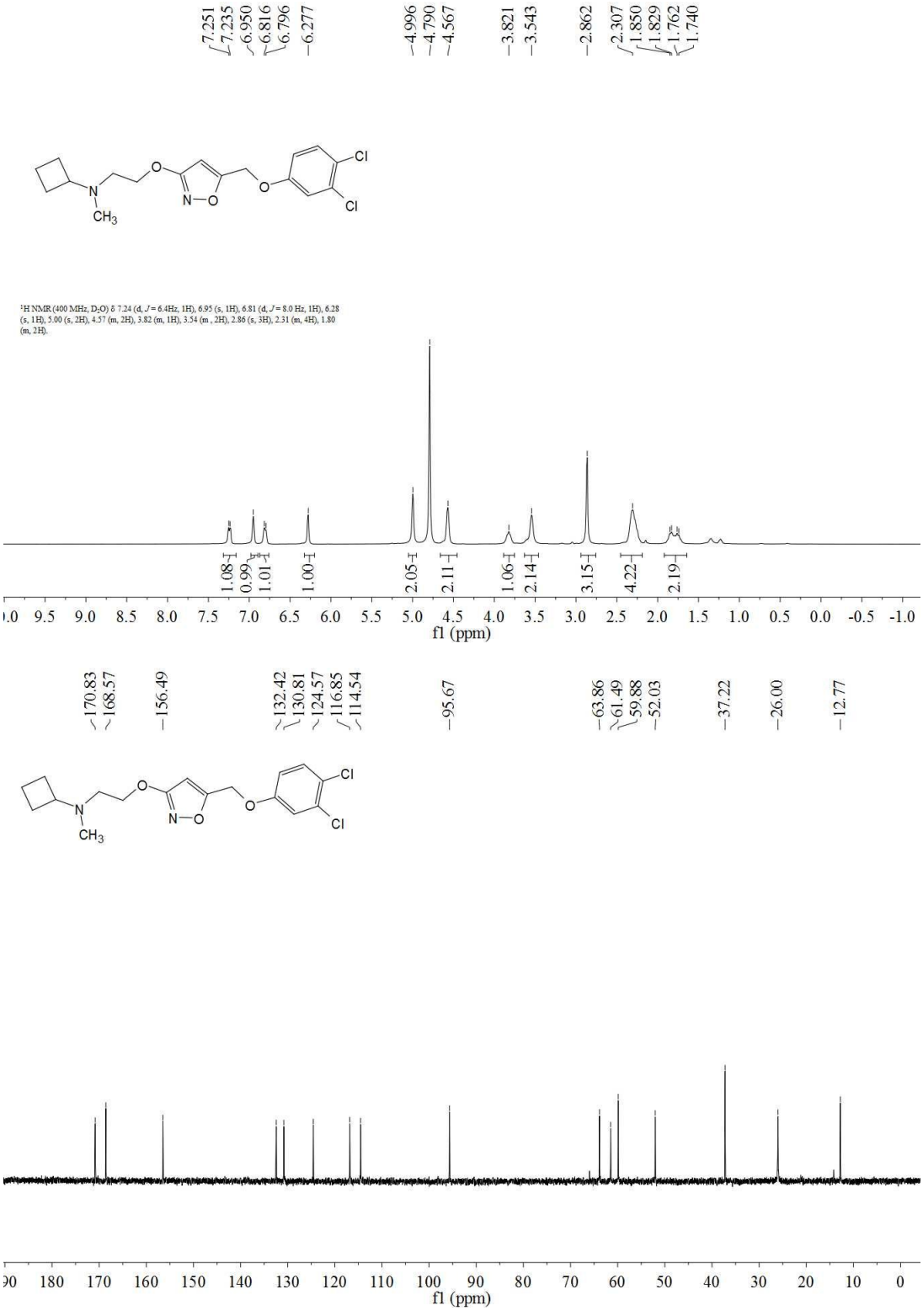
^{1}H NMR (400 MHz, DMSO-d_6) δ 11.20 (br, 1H), 7.39 (q, J = 9.6Hz, 1H), 7.28 – 7.17 (m, 1H), 6.95 – 6.84 (m, 1H), 6.48 (s, 1H), 5.21 (s, 2H), 4.57 (m, 2H), 3.76 (m, 1H), 3.44 (m, 2H), 2.67 (s, 3H), 2.32 (m, 2H), 2.25 – 2.02 (m, 2H), 1.70 (m, 2H).



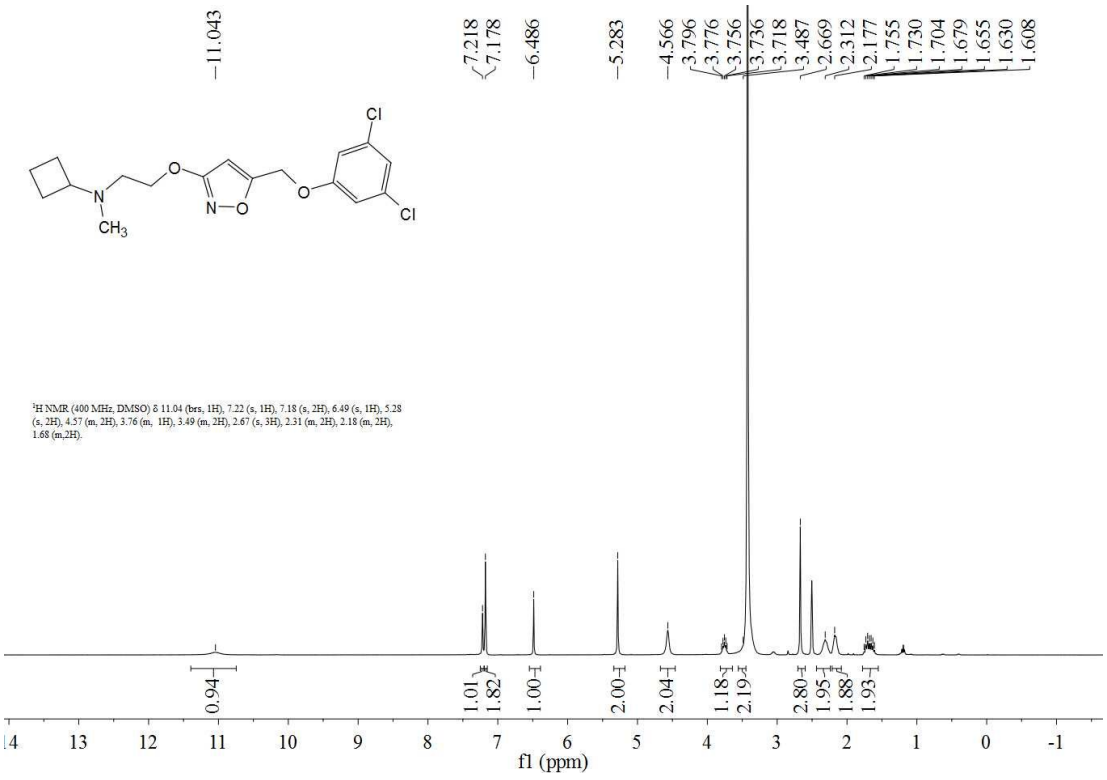
^{13}C NMR (101 MHz, DMSO-d_6) δ 170.57 , 168.57 , 153.92 (d, J = 9.2 Hz), 149.50 (dd, J = 245.3, 13.7 Hz), 144.45 (dd, J = 238.6, 12.8 Hz), 117.69 (d, J = 18.4 Hz), 111.16 (dd, J = 6.1, 3.2 Hz), 104.65 (d, J = 20.5 Hz), 95.72 , 64.18 , 61.27 , 58.68 , 50.66 , 36.57 , 25.39 , 24.88 , 12.62 .

^{1}H NMR and ^{13}C NMR spectra of compound **22**

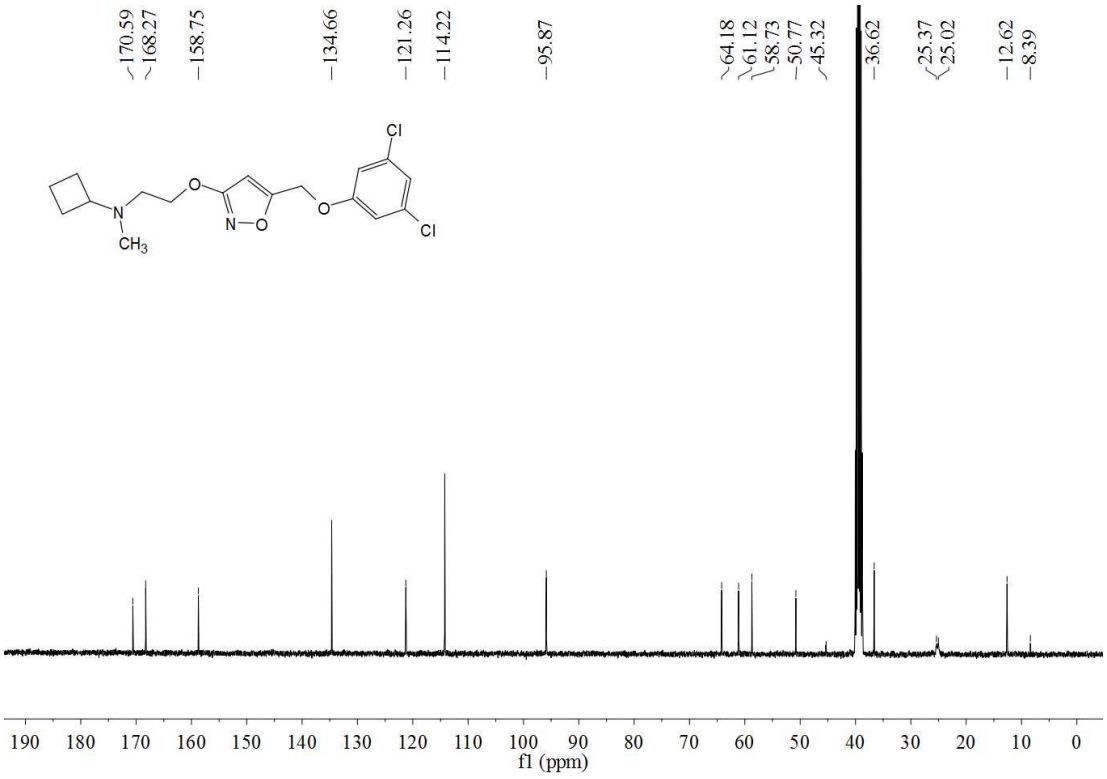
^{1}H NMR and ^{13}C NMR spectra of compound **23**



^{1}H NMR and ^{13}C NMR spectra of compound **24**

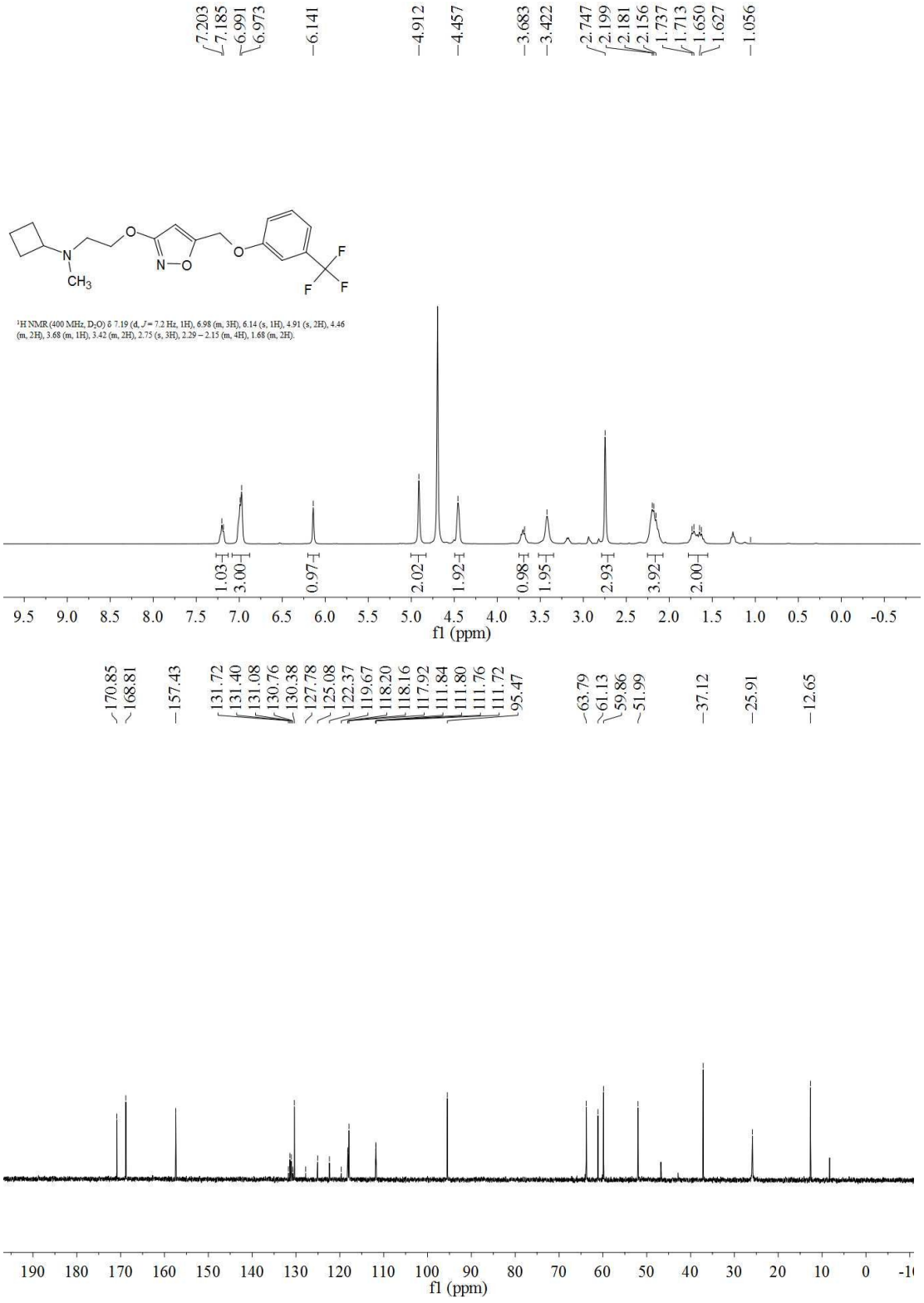


^{1}H NMR (400 MHz, DMSO) δ 11.04 (brs, 1H), 7.22 (s, 1H), 7.18 (s, 2H), 6.49 (s, 1H), 5.28 (s, 2H), 4.57 (m, 2H), 3.76 (m, 1H), 3.49 (m, 2H), 2.67 (s, 3H), 2.31 (m, 2H), 2.18 (m, 2H), 1.68 (m,2H).

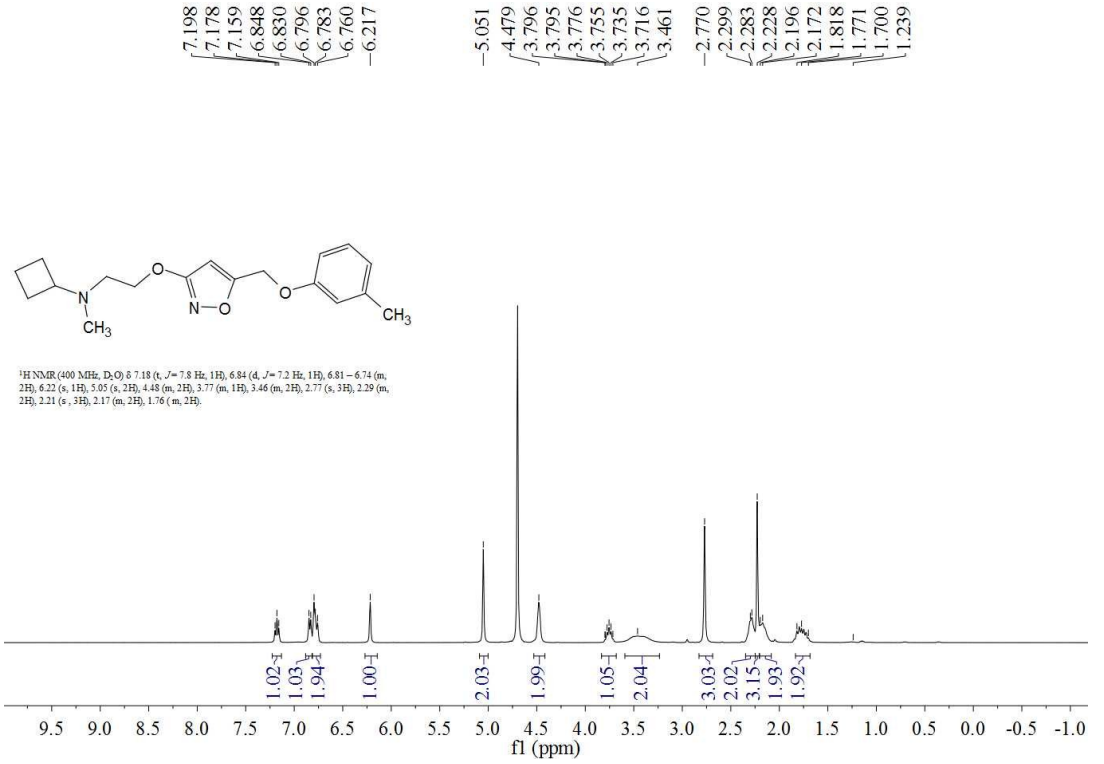


^{1}H NMR and ^{13}C NMR spectra of compound **25**

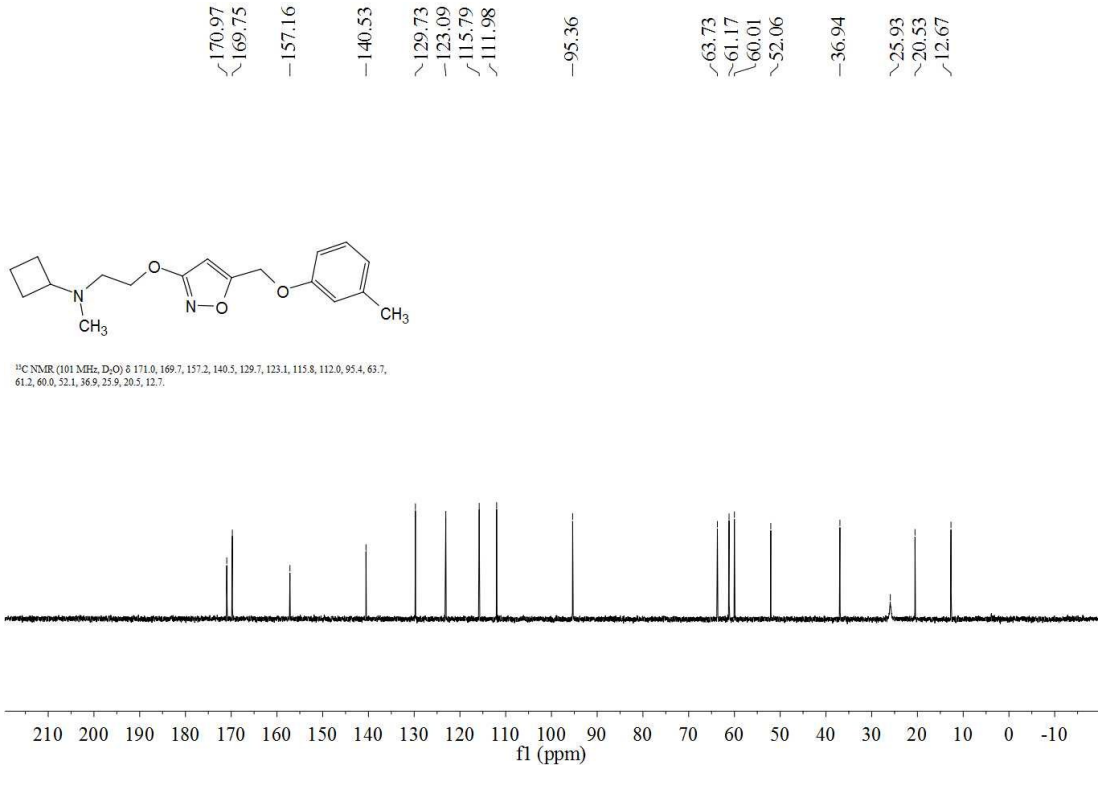
^{1}H NMR and ^{13}C NMR spectra of compound **26**



^{1}H NMR and ^{13}C NMR spectra of compound **27**

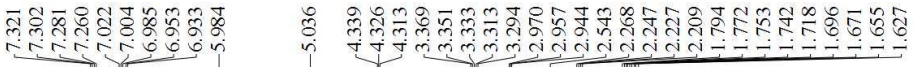


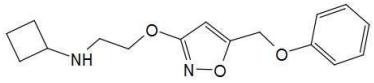
^{1}H NMR (400 MHz, D_2O) δ 7.18 (t, J = 7.8 Hz, 1H), 6.84 (d, J = 7.2 Hz, 1H), 6.81 – 6.74 (m, 2H), 6.22 (s, 1H), 5.05 (s, 2H), 4.48 (m, 2H), 3.77 (m, 1H), 3.46 (m, 2H), 2.77 (s, 3H), 2.29 (m, 2H), 2.21 (s , 3H), 2.17 (m, 2H), 1.76 (m, 2H).



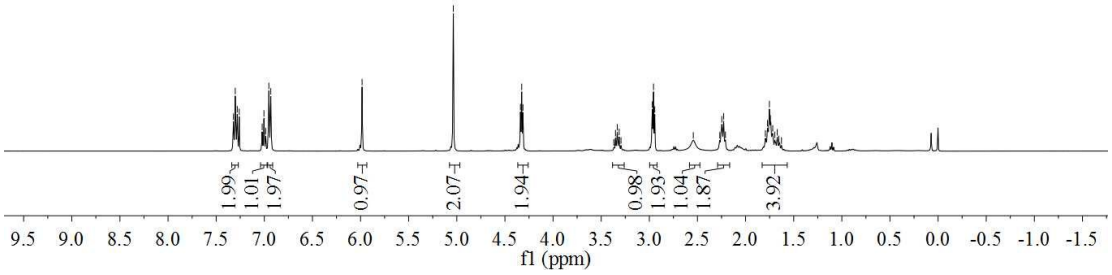
^{13}C NMR (101 MHz, D_2O) δ 171.0, 169.7, 157.2, 140.5, 129.7, 123.1, 115.8, 112.0, 95.4, 63.7, 61.2, 60.0, 52.1, 36.9, 25.9, 20.5, 12.7.

^{1}H NMR and ^{13}C NMR spectra of compound **28**

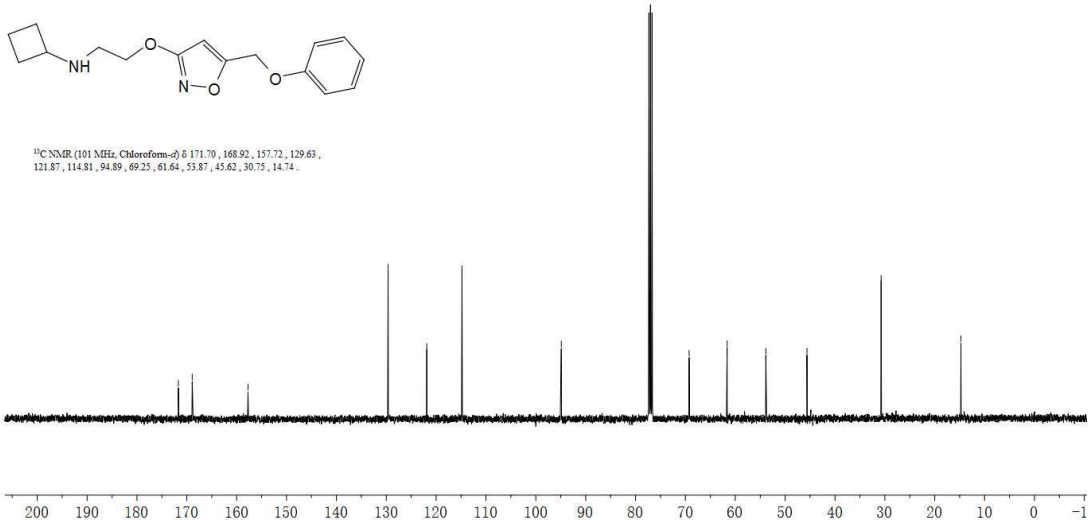




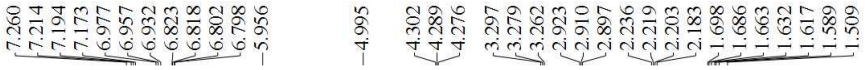
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (t, *J* = 8.0 Hz, 2H), 7.00 (t, *J* = 7.4 Hz, 1H), 6.94 (d, *J* = 8.0 Hz, 2H), 5.98 (s, 1H), 5.04 (s, 2H), 4.33 (t, *J* = 5.2 Hz, 2H), 3.44 – 3.26 (m, 1H), 2.96 (t, *J* = 5.2 Hz, 2H), 2.54 (br, 1H), 2.32 – 2.16 (m, 2H), 1.88 – 1.51 (m, 4H).

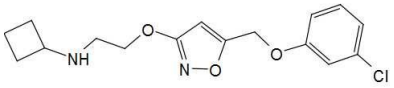


^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.70 , 168.92 , 157.72 , 129.63 , 121.87 , 114.81 , 94.89 , 69.25 , 61.64 , 53.87 , 45.62 , 30.75 , 14.74 .

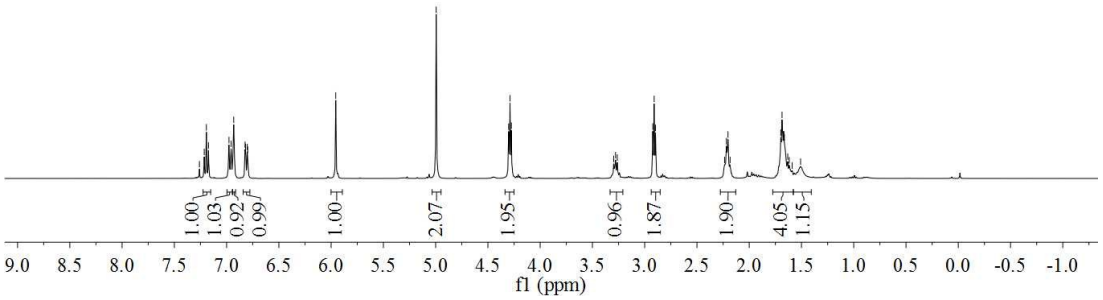


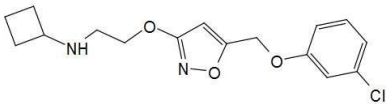
^{1}H NMR and ^{13}C NMR spectra of compound **29**



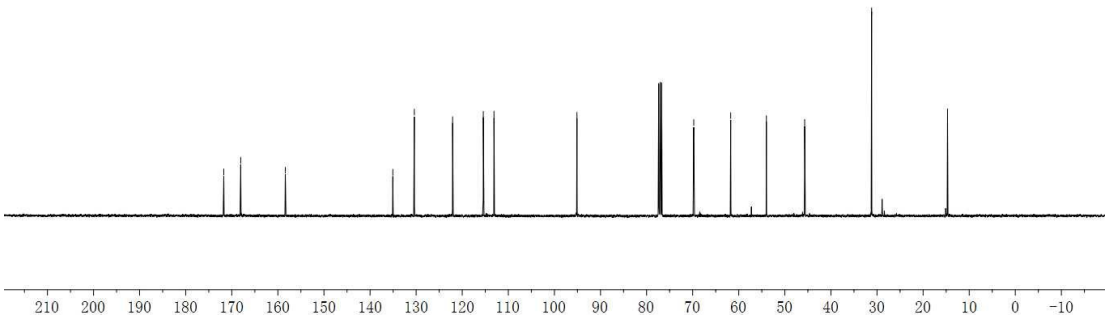


^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (t, J = 8.2Hz, 1H), 6.97 (d, J = 8.0 Hz, 1H), 6.93 (s, 1H), 6.81 (dd, J = 8.2, 1.8 Hz, 1H), 5.96 (s, 1H), 4.99 (s, 2H), 4.29 (t, J = 4.0 Hz, 2H), 3.34 – 3.21 (m, 1H), 2.91 (t, J = 4.0 Hz, 2H), 2.26 – 2.12 (m, 2H), 1.75 – 1.57 (m, 4H), 1.51 (m, 1H).

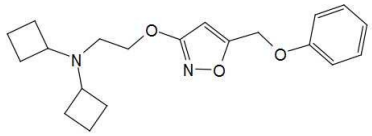




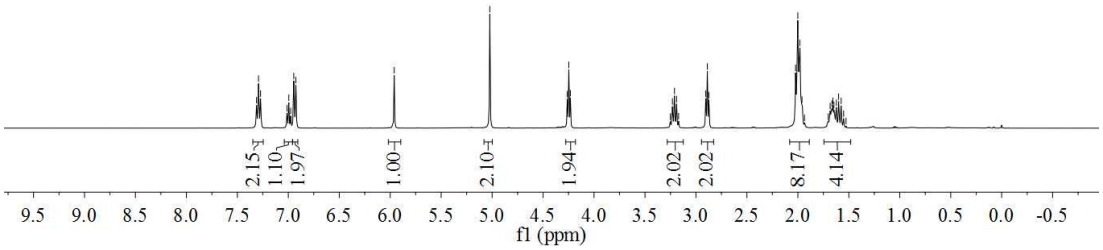
^{13}C NMR (101 MHz, Chloroform-d) δ 171.74 , 168.06 , 158.39 , 135.06 , 130.39 , 122.09 , 115.43 , 113.11 , 95.11 , 69.77 , 61.75 , 54.01 , 45.70 , 31.18 , 14.70 .

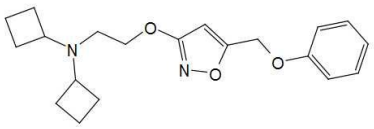


^{1}H NMR and ^{13}C NMR spectra of compound **30**



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (t, J = 8.0 Hz, 2H), 6.99 (t, J = 7.4 Hz, 1H), 6.94 (d, J =8.0 Hz, 2H), 5.96 (s, 1H), 5.02 (s, 2H), 4.25 (t, J = 6.2 Hz, 2H), 3.28 – 3.14 (m, 2H), 2.89 (t, J = 6.2 Hz, 2H), 2.11 – 1.85 (m, 8H), 1.72 – 1.50 (m, 4H).





^{13}C NMR (101 MHz, Chloroform-d) δ 171.61 , 168.85 , 157.73 , 129.61 , 121.84 , 114.80 , 94.95 , 67.78 , 61.64 , 57.36 , 46.24 , 28.76 , 15.09 .