-Supporting Information-

TFAA mediated One-Pot Synthesis of *N*-Protected Chiral -Amino Acid-Derived 1,2,4-Oxadiazoles

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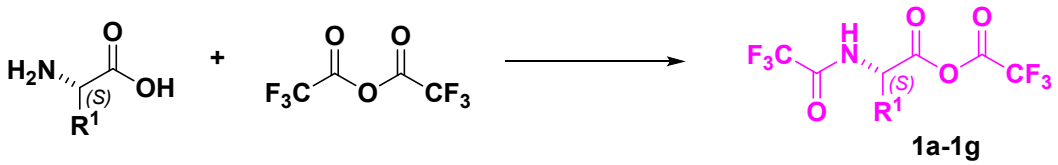
General Remarks

All the reagents were purchased commercially and used without further purification. ^{1}H NMR and ^{13}C NMR were recorded with Bruker 400 MHz. Proton nuclear magnetic resonance spectra (^{1}H NMR) and carbon nuclear magnetic resonance spectra (^{13}C NMR) were recorded at 400 MHz and 100 MHz respectively. The chemical shifts are given in parts per million (ppm) on the delta (δ) scale. The solvent peak was used as a reference value, for ^{1}H NMR: $CDCl_3$ = 7.26 ppm, DMSO-d_6 = 2.50 ppm; for ^{13}C NMR: $CDCl_3$ = 77.16 ppm, DMSO-d_6 = 39.52 ppm with tetramethylsilane as the internal standard. Coupling constants (J) are expressed in hertz (Hz).Multiplicities are reported using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad resonance. All the NMR spectra were recorded at ambient temperature. Analytical thin layer chromatography (TLC) was performed using Silica Gel 60 Å F_{254} pre-coated plates (0.25 mm thickness). Visualization was accomplished by irradiation with a UV lamp and staining with $KMnO_4$. LC-MS mass were recorded with Agilent 6330 Ion Trap Instrument.

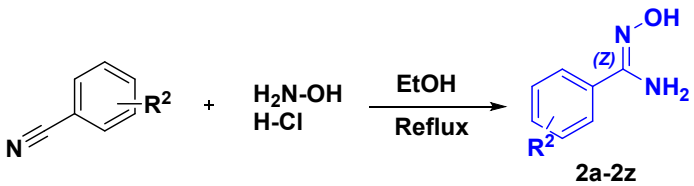
General Procedure for the Preparation of (*S*)-(*S*)-2-(2,2,2-trifluoroacetamido)propanoic 2,2,2-trifluoroacetic anhydride (1):



1a-1g

Trifluoroacetic anhydride (6.0 mmol) was added dropwise into the round bottom flask containing amino acid (1.0 mmol) at 20 °C under N_2 atmosphere and then stirred at room temperature for 10 min. then, the content was allowed to stir for 30 minutes. The reaction mixture was concentrated to remove excess trifluoroacetic anhydride. Dichloromethane (10 V) was added and concentrated. It was repeated in three times and dried under high vacuum. Hexane (10 V) was added to make a slurry and allowed to stir for 10 minutes under nitrogen. (S)-(S)-2-(2,2,2-trifluoroacetamido)propanoic 2,2,2-trifluoroacetic anhydride (**1a-1g**) was filtered as white solid under nitrogen atmosphere.

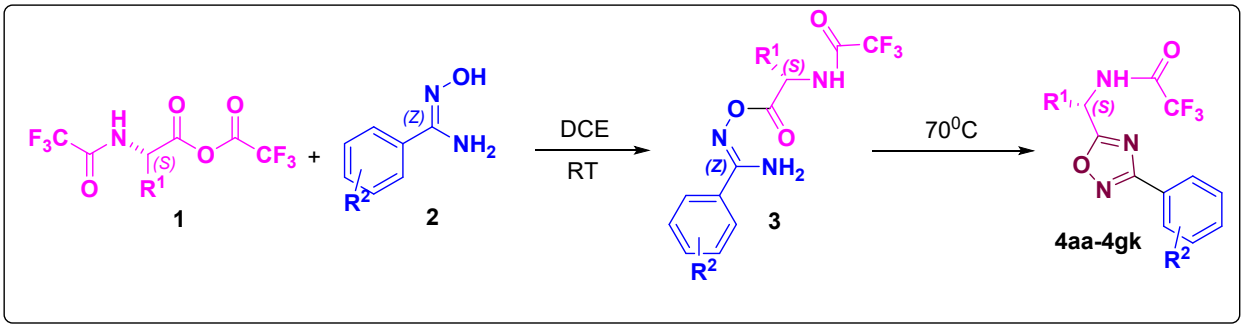
General Procedure for the Preparation of Amidoxime (2):



2a-2z

Sodium bicarbonate (2 equivalents) was added to a stirred suspension of nitrile compound (1 equivalent) and hydroxylamine hydrochloride (2 equivalents) in ethanol (10 ml per gram of nitrile). The reaction mixture was stirred under reflux for 6 hours. After the reaction is completed, the reaction mass was concentrated under pressure. The residue was diluted with cold water. The resulting precipitate was filtered off and washed with cold water to obtain amidoxime **(2)** as a white solid.

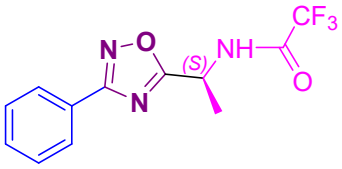
General Procedure for the Preparation of *(S)*-2,2,2-trifluoro-*N*-(1-(3-phenyl-1,2,4-oxadiazol-5-yl)ethyl)acetamide (4):



Amidoxime **2** (1.0 mmol) and compound **1**(2.0 mmol) were taken with 1,2 dichloroethane (10 ml per gram of compound **1**) and stirred at room temperature for 30 minutes and heated to reflux for 60 minutes. The progress of the reaction was monitored by TLC for the absence of aromatic amidoxime **2**. After completion of the reaction, the mixture was cooled to 27 ^{o}C, quenched with cold water. The reaction mixture extracted with Dichloromethane (2 x 10 mL). The combined dichloromethane layer was washed with brine solution. Then the organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude was purified by column chromatography using petroleum ether/ethyl acetate as eluent in silica gel (230-400 mesh) to give 1,2,4 -oxadiazoles **4**.

Characterization Data of *(S)*-2,2,2-trifluoro-*N*-(1-(3-aryl-1,2,4-oxadiazol-5-yl)ethyl)acetamide (4)

***(S)*-2,2,2-trifluoro-*N*-(1-(3-phenyl-1,2,4-oxadiazol-5-yl) ethyl)acetamide (4aa)**



The reaction was carried out according to general procedure, using *(Z)-N'*-hydroxybenzimidamide **2a** (1.0 mmo l), Compound **1a** (2.0 mmol) with 1,2 dichloroethane in reflux condition for 1 h which afforded **4aa** (90%) as white solid. Eluent: petroleum ether/ethyl acetate = 96:04.

mp = 78-80 ^{o}C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.35-10.34 (d, *J*=7.2Hz,1H), 8.03-8.00(m,2H), 7.62-7.56(m,3H), 5.46-5.39(q, *J*=7.2Hz,1H), 1.69-1.67(d, *J*=7.2Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 179.49, 168.17, 156.70 (q, $J_{C\text{-}F}$ = 37 Hz), 131.21, 129.80, 127.49, 126.32, 120.45, 117.59, 114.73, 111.87 ,43.45, 17.82 ppm; MS (ES): m/z calcd for $C_{12}H_{10}F_3N_3O_2$, 285.07; found, 286.12(M^+).

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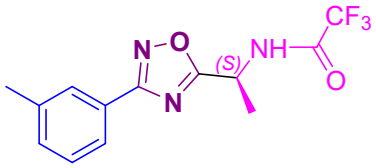
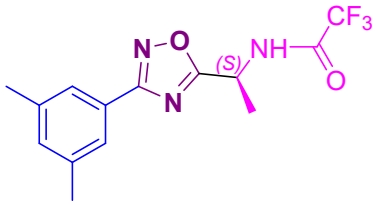
***(S)*-2,2,2-trifluoro-*N*-(1-(3-(m-tolyl)-1,2,4-oxadiazol-5-yl)ethyl)acetamide (4ab)**



The reaction was carried out according to general procedure, using *(Z)-N′*-hydroxy-3-methylbenzimidamide **2b** (1.0 mmol), Compound **1a** (2.0 mmol) with 1,2 dichloroethane in reflux condition for 2 h which afforded **4ab** (80%) as white solid. Eluent: petroleum ether/ethyl acetate = 97:03.

mp = 106-109 °C. ^{1}H NMR (400 MHz, DMSO-d_6): 10.35-10.34 (d, J=7.2Hz,1H), 7.83-7.80(d, J=12Hz, 2H), 7.48-7.40(m,2H), 5.44-5.39(q, J=7.2Hz,1H), 2.40(s,3H), 1.69-1.67(d, J=7.2Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 179.36, 168.22, 156.69 (q, $J_{C\text{-}F}$ = 37 Hz), 139.20, 132.82, 129.67, 127.82, 126.27, 124.66, 120.46, 117.60, 114.73, 111.87, 43.43, 21.29, 17.82 ppm; MS (ES): m/z calcd for $C_{13}H_{12}F_3N_3O_2$, 299.09; found, 300.13(M^+).

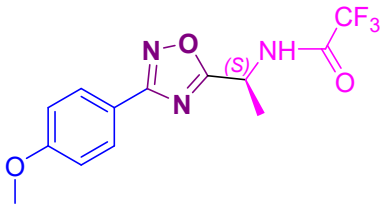
***(S)-N-(*1-(3-(3,5-dimethylphenyl)-1,2,4-oxadiazol-5-yl)ethyl)-2,2,2-trifluoroacetamide (4ac)**



The reaction was carried out according to general procedure, using (Z)-N'-hydroxy-3,5-dimethylbenzimidamide **2c** (1.0 mmol), Compound **1a** (2.0 mmol) with 1,2 dichloroethane in reflux condition for 1 h which afforded **4ac** (79%) as white solid. Eluent: petroleum ether/ethyl acetate = 97:03.

mp = 141-143 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.34 (s,1H), 7.63(s,2H), 7.23(s,1H), 5.43-5.40(m, 1H), 2.36(s,6H), 1.68-1.66(d, J= 8Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 179.25, 168.28, 156.68 (q, $J_{C\text{-}F}$ = 37 Hz), 139.04, 133.56, 126.20, 125.08, 120.46, 117.60, 114.74, 111.87, 43.41, 21.19 ppm; ^{19}F NMR (377 MHz, DMSO-d_6) δ -64.50 (s, 3F). MS (ES): m/z calcd for $C_{14}H_{14}F_3N_3O_2$, 313.10; found, 314.16(M^+).

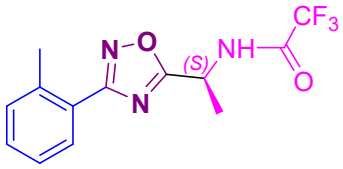
***(S)*-2,2,2-trifluoro-*N*-(1-(3-(4-methoxyphenyl)-1,2,4-oxadiazol-5-yl)ethyl)acetamide (4ad)**



The reaction was carried out according to general procedure, using *(Z)-N′*-hydroxy-4-methoxybenzimidamide **2d** (1.0 mmol), Compound **1a** (2.0 mmol) with 1,2 dichloroethane in reflux condition for 30 min which afforded **4ad** (89%) as white solid. Eluent: petroleum ether/ethyl acetate = 98:02.

mp = 120-123 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01-7.98 (m, 2H), 7.21-7.20(b, 1H), 7.00-6.97(m,2H), 5.49-5.41(m, 1H), 3.87(s,3H), 1.75-1.73(d, J= 7.2Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.27, 168.06, 162.26, 156.50 (q, $J_{C\text{-}F}$ = 38 Hz), 129.18, 119.84, 118.36, 116.98, 114.37, 114.12, 111.26, 55.41, 43.66, 29.71, 19.40 ppm;. MS (ES): m/z calcd for $C_{13}H_{12}F_3N_3O_3$, 315.08; found, 314.14(M^-).

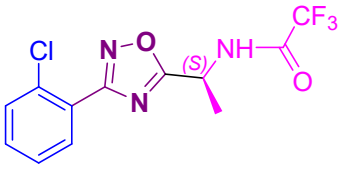
***(S)*-2,2,2-trifluoro-*N*-(1-(3-(o-tolyl)-1,2,4-oxadiazol-5-yl)ethyl)acetamide (4ae)**



The reaction was carried out according to general procedure, using *(Z)*-*N'*-hydroxy-2-methylbenzimidamide **2e** (1.0 mmol), Compound **1a** (2.0 mmol) with 1,2 dichloroethane in reflux condition for 90 min which afforded **4ae** (70%) as white solid. Eluent: petroleum ether/ethyl acetate = 97:03.

mp = 90-92 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.36-10.34 (d, *J*=7.6Hz,1H), 7.93-7.91(m,1H), 7.50-7.47(m,1H), 7.43-7.38(m,2H), 5.47-5.40(m,1H), 2.56(s, 3H), 1.70-1.68(d, *J*=7.6Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 177.37, 168.76, 156.73 (q, $J_{C\text{-}F}$ = 37 Hz), 138.03, 131.95, 131.45, 130.12, 129.84, 126.97, 126.73, 125.68, 120.47, 117.61, 114.75, 111.89, 55.32, 43.41, 21.98, 17.82 ppm;. MS (ES): m/z calcd for $C_{13}H_{12}F_3N_3O_2$, 299.09; found, 300.12(M^+).

***(S)*-*N*-(1-(3-(2-chlorophenyl)-1,2,4-oxadiazol-5-yl)ethyl)-2,2,2-trifluoroacetamide (4af)**



The reaction was carried out according to general procedure, using *(Z)*-2-chloro-*N'*-hydroxybenzimidamide **2f** (1.0 mmol), Compound **1a** (2.0 mmol) with 1,2 dichloroethane in reflux condition for 2 h which afforded **4af** (80%) as white solid. Eluent: petroleum ether/ethyl acetate = 98:03.

mp = 87-89 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.37-10.35 (d, *J*=7.6Hz,1H), 7.92-7.90(d, *J*=8Hz, 1H), 7.70-7.68 (d, *J*=8Hz, 1H), 7.64-7.60(t, *J*=8Hz, 1H), 7.57-7.53(t, *J*=8Hz, 1H), 5.49-5.42(p, *J*=7.2Hz, 1H), 1.69-1.67(d, *J*=7.2Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 178.96, 166.97, 156.72 (q, $J_{C\text{-}F}$ = 37 Hz), 133.16, 132.59, 132.14, 131.85, 131.37, 128.42, 128.19, 125.61, 120.45, 117.59, 114.73, 111.87, 43.44, 17.81 ppm; MS (ES): m/z calcd for $C_{12}H_9ClF_3N_3O_2$, 319.03; found, 320.04(M^+).

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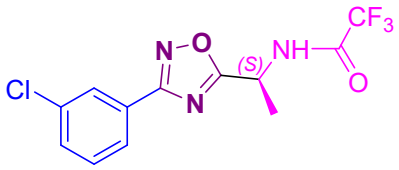
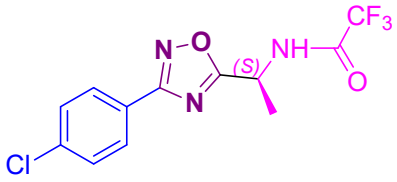
***(S)*-*N*-(1-(3-(3-chlorophenyl)-1,2,4-oxadiazol-5-yl)ethyl)-2,2,2-trifluoroacetamide (4ag)**



The reaction was carried out according to general procedure, using *(Z)*-3-chloro-*N'*-hydroxybenzimidamide **2g** (1.0 mmol), Compound **1a** (2.0 mmol) with 1,2 dichloroethane in reflux condition for 90 min which afforded **4ag** (86%) as white solid. Eluent: petroleum ether/ethyl acetate = 97:03.

mp = 90-92 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.36-10.34 (d, *J*=7.2Hz,1H), 7.99-7.96(m, 2H), 7.71-7.68 (m, 1H), 7.64-7.59(m, 1H), 5.46-5.39(p, *J*=7.2Hz, 1H), 1.68-1.66(d, *J*=7.2Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 179.85, 167.14, 156.71 (q, $J_{C\text{-}F}$ = 37Hz), 134.47, 132.13, 131.92, 128.27, 126.18, 120.44, 117.57, 114.71, 111.85, 43.47, 17.78 ppm; MS (ES): m/z calcd for $C_{12}H_9ClF_3N_3O_2$, 319.03; found, 320.02(M^+).

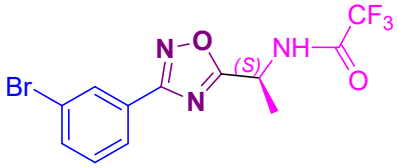
***(S)*-*N*-(1-(3-(4-chlorophenyl)-1,2,4-oxadiazol-5-yl)ethyl)-2,2,2-trifluoroacetamide (4ah)**



The reaction was carried out according to general procedure, using *(Z)*-4-chloro-*N'*-hydroxybenzimidamide **2h** (1.0 mmol), Compound **1a** (2.0 mmol) with 1,2 dichloroethane in reflux condition for 20 min which afforded **4ah** (94%) as white solid. Eluent: petroleum ether/ethyl acetate = 98:02.

mp = 123-124 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.34 (s,1H), 8.03-8.01(d, *J*=8Hz, 2H), 7.67-7.65 (d, *J*=8Hz, 2H), 5.43-5.41(b, 1H), 1.68-1.66(d, *J*= 6.8Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 179.73, 167.39, 156.69 (q, $J_{C\text{-}F}$ = 37 Hz), 136.96, 130.01, 129.30, 125.16, 120.44, 117.58, 114.72, 43.45, 17.78 ppm; m/z calcd for $C_{12}H_9ClF_3N_3O_2$, 319.03; found, 320.05(M^+).

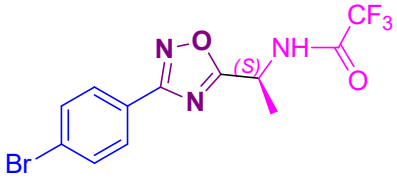
***(S)*-*N*-(1-(3-(3-bromophenyl)-1,2,4-oxadiazol-5-yl)ethyl)-2,2,2-trifluoroacetamide (4ai)**



The reaction was carried out according to general procedure, using *(Z)*-3-bromo-*N'*-hydroxybenzimidamide **2i** (1.0 mmol), Compound **1a** (2.0 mmol) with 1,2 dichloroethane in reflux condition for 100 min which afforded **4ai** (88%) white solid. Eluent: petroleum ether/ethyl acetate = 97:03.

mp = 103-105 °C. ^{1}H NMR (400 MHz, DMSO-d_6): 10.34 (s, 1H), 8.13 (s,1H), 8.04-8.02(d, *J*=7.6Hz, 1H), 7.86-7.84(d, *J*=7.6Hz, 1H), 7.61-7.56(m,1H), 5.45-5.44(b, 1H), 1.70-1.68(d, *J*=8Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 179.84, 167.03, 156.71 (q, $J_{C\text{-}F}$ = 37Hz), 135.02, 132.14, 129.82, 128.47, 126.53, 122.84, 120.44, 117.58, 114.71, 111.85, 43.47, 17.79 ppm; MS (ES): m/z calcd for $C_{12}H_9BrF_3N_3O_2$, 362.98; found, 365.89(M^+).

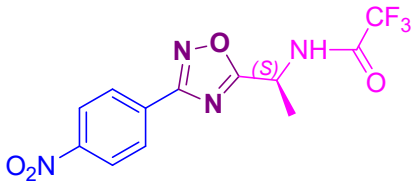
***(S)*-*N*-*(*1-(3-(4-bromophenyl)-1,2,4-oxadiazol-5-yl)ethyl)-2,2,2-trifluoroacetamide (4aj)**



The reaction was carried out according to general procedure, using *(Z)*-4-bromo-*N'*-hydroxybenzimidamide **2j** (1.0 mmol), Compound **1a** (2.0 mmol) with 1,2 dichloroethane in reflux condition for 35 min which afforded **4aj** (96%) as white solid. Eluent: petroleum ether/ethyl acetate = 97:03.

mp = 130-133 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.95-7.92 (m, 2H), 7.65-7.63(m, 2H), 7.14-7.13 (b,1H), 5.51-5.44(p, *J*= 7.2Hz, 1H), 1.76-1.75(d, *J*= 7.2Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 177.85, 167.72, 156.73 (q, $J_{C\text{-}F}$ = 38 Hz), 132.30, 129.00, 126.30, 124.92, 116.95, 114.09, 43.62, 19.38 ppm; MS (ES): m/z calcd for $C_{12}H_9BrF_3N_3O_2$, 362.98; found, 363.86(M^+).

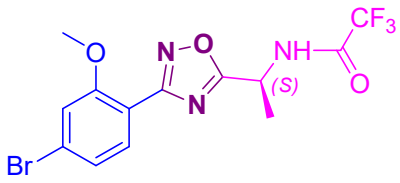
***(S)*-2,2,2-trifluoro-*N*-(1-(3-(4-nitrophenyl)-1,2,4-oxadiazol-5-yl)ethyl)acetamide (4ak)**



The reaction was carried out according to general procedure, using *(Z)-N′*-hydroxy-4-nitrobenzimidamide **2k** (1.0 mmol), Compound **1a** (2.0 mmol) with 1,2 dichloroethane in reflux condition for 40 min which afforded **4ak** (93%) as white solid. Eluent: petroleum ether/ethyl acetate = 97:03.

mp = 144-146 °C. ^{1}H NMR (400 MHz, $CDCl_3$): 8.36-8.33 (m, 2H), 8.26-8.24(m, 2H), 7.16-7.14(b,1H), 5.55-5.48(p, *J*=7.6Hz, 1H), 1.80-1.79(d, *J*= 7.6Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.56, 166.91, 156.83 (q, $J_{C\text{-}F}$ = 38Hz), 149.67, 131.88, 128.55,124.19, 116.93, 114.07, 43.59, 19.23 ppm; m/z calcd for $C_{12}H_9F_3N_4O_4$, 330.06; found, 329.13(M^-).

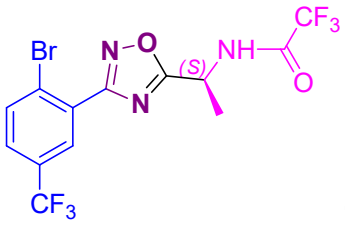
***(S)-N*-(1-(3-(4-bromo-2-methoxyphenyl)-1,2,4-oxadiazol-5-yl)ethyl)-2,2,2-trifluoroacetamide (4al)**



The reaction was carried out according to general procedure, using *(Z)*-4-bromo-*N′*-hydroxy-2-methoxybenzimidamide **2l** (1.0 mmol), Compound **1a** (2.0 mmol) with 1,2 dichloroethane in reflux condition for 35 min which afforded **4al** (92%) as white solid. Eluent: petroleum ether/ethyl acetate = 97:03.

mp = 129-130 °C. ^{1}H NMR (400 MHz, DMSO-*d6)* 10.34-10.32 (d, *J*=7.2Hz,1H), 7.80-7.78(d, *J*=8Hz, 1H), 7.46 (s,1H), 7.35-7.33(d, *J*=8Hz, 1H), 5.42-5.37(b, 1H), 3.92(s,3H), 1.67-1.65(d, *J*=7.2Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 178.16, 165.98, 158.81, 156.68 (q, $J_{C\text{-}F}$ = 37Hz), 132.56, 126.36, 124.14, 120.45, 117.59, 116.24, 114.73, 114.67, 111.87, 56.92, 43.34, 17.86pm; MS (ES): m/z calcd for $C_{13}H_{11}BrF_3N_3O_3$, 392.99; found, 395.90M^+).

***(S)-N*-(1-(3-(2-bromo-5-(trifluoromethyl)phenyl)-1,2,4-oxadiazol-5-yl)ethyl)-2,2,2-trifluoroacetamide (4am)**

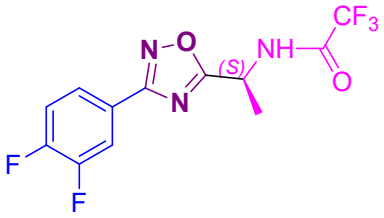


The reaction was carried out according to general procedure, using *(Z)*-2-bromo-*N′*-hydroxy-5-(trifluoromethyl)benzimidamide**2m** (1.0 mmol), Compound **1a** (2.0 mmol) with 1,2 dichloroethane in reflux condition for 40 min which afforded **4am** (82%) as white solid. Eluent: petroleum ether/ethyl acetate = 97:03.

mp = 116-119 °C. ^{1}H NMR (400 MHz, DMSO-d_6): 10.40-10.38 (d, *J*=6.8Hz,1H), 8.15-8.13(d, *J*=8.8Hz, 2H), 7.92-7.91(d, *J*=6.8Hz, 1H), 5.50-5.44(p, *J*=6.8Hz, 1H), 1.70-1.69(d, *J*=6.8Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 179.49, 166.86, 156.77 (q, $J_{C\text{-}F}$ = 37Hz), 136.08, 129.65, 129.43, 129.11, 18.88, 128.76, 128.72, 127.93, 126.49, 125.22, 120.43,

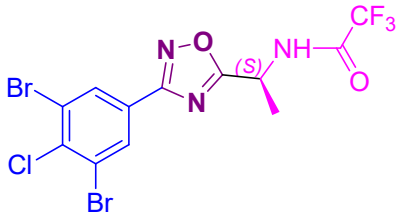
119.81, 117.57, 114.70, 111.85, 43.48, 17.86 ppm; MS (ES): m/z calcd for $C_{13}H_8BrF_6N_3O_2$, 430.97; found, 433.76 (M^+).

***(S)*-*N*-(1-(3-(3,4-difluorophenyl)-1,2,4-oxadiazol-5-yl)ethyl)-2,2,2-trifluoroacetamide (4an)**



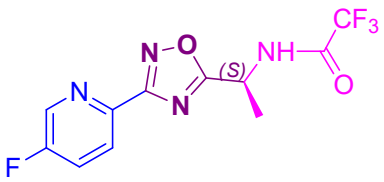
The reaction was carried out according to general procedure, using *(Z)*-3,4-difluoro-*N'*-hydroxybenzimidamide **2n** (1.0 mmol), Compound **1a** (2.0 mmol) with 1,2 dichloroethane in reflux condition for 30 min which afforded **4an** (91%) as white solid. Eluent: petroleum ether/ethyl acetate = 97:03.
mp = 91-93 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.35 (s, 1H), 7.98-7.96(m, 1H), 7.90-7.87(m,1H), 7.70-7.63(m,1H), 5.44-5.41(m,1H), 1.69-1.67(d, *J*=7.2Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 179.90, 166.69, 156.72, (q, $J_{C\text{-}F}$ = 37Hz), 153.35, 153.22, 151.56, 151.43, 150.85, 150.72, 148.97, 125.15, 125.11, 125.07, 125.04, 123.80, 123.77, 123.74, 123.70, 119.24, 117.56, 116.80, 116.61, 114.70, 43.47, 17.74 ppm; ^{19}F NMR (377 MHz, DMSO-d_6) δ -64.50 (s, 3F). MS (ES): m/z calcd for $C_{12}H_8F_5N_3O_2$, 321.05; found, 321.99 (M^+).

***(S)*-*N*-(1-(3-(3,5-dibromo-4-chlorophenyl)-1,2,4-oxadiazol-5-yl)ethyl)-2,2,2-trifluoroacetamide (4ao)**



The reaction was carried out according to general procedure, using *(Z)*-3,5-dibromo-4-chloro-*N'*-hydroxybenzimidamide **2o** (1.0 mmol), Compound **1a** (2.0 mmol) with 1,2 dichloroethane in reflux condition for 90 min which afforded **4ao** (79%) as white solid. Eluent: petroleum ether/ethyl acetate = 97:03. mp = 185-187 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.36 (s, 1H), 8.26 (s, 2H), 5.46-5.41(q, *J*=7.2Hz,1H), 1.69-1.67(d, *J*=7.2Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 180.19, 165.51, 156.72 (q, $J_{C\text{-}F}$ = 36 Hz), 137.29, 131.30, 129.03, 127.40, 124.32, 120.42, 117.56, 114.70, 43.49, 17.79 ppm; ^{19}F NMR (377 MHz, DMSO-d_6) δ -64.50 (s, 3F). MS (ES): m/z calcd for $C_{12}H_7Br_2ClF_3N_3O_2$, 474.85; found, 477.61(M^+).

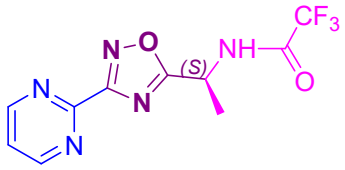
***(S)*-2,2,2-trifluoro-*N*-(1-(3-(5-fluoropyridin-2-yl)-1,2,4-oxadiazol-5-yl)ethyl)acetamide (4ap)**



The reaction was carried out according to general procedure, using *(Z)*-5-fluoro-*N'*-hydroxypicolinimidamide **2p** (1.0 mmol), Compound **1a** (2.0 mmol) with 1,2 dichloroethane in reflux condition for 30 min which afforded **4ap** (88%) as white solid. Eluent: petroleum ether/ethyl acetate = 4:1.

mp = 109-111 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.40-10.38 (d, *J*=7.2Hz,1H), 8.58-8.54(m,1H), 8.50-8.49 (m,1H), 7.63-7.60 (m,1H), 5.51-5.44(p, *J*=7.2Hz, 1H), 1.71-1.69(d, *J*=7.2Hz, 3H) ^{13}C NMR (100 MHz, DMSO-d_6): δ 179.53, 164.09, 164.00, 161.36, 158.93, 156.74 (q, $J_{C\text{-}F}$ = 32 Hz), 150.99, 150.85, 142.24, 142.22, 123.25, 123.21, 120.42, 117.56, 114.70, 111.84, 109.96, 109.62, 43.44, 17.75 ppm; MS (ES): m/z calcd for $C_{11}H_8F_4N_4O_2$, 304.06; found, 305.09 (M^+).

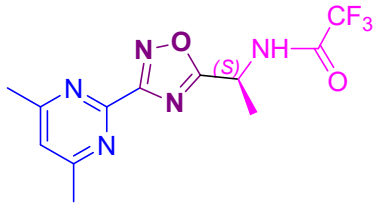
***(S)*-2,2,2-trifluoro-*N*-(1-(3-(pyrimidin-2-yl)-1,2,4-oxadiazol-5-yl)ethyl)acetamide (4aq)**



The reaction was carried out according to general procedure, using (*Z*)-*N'*-hydroxypyrimidine-2-carboximidamide **2q** (1.0 mmol), Compound **1a** (2.0 mmol) with 1,2 dichloroethane in reflux condition for 45 min which afforded **4aq** (83%) as white solid. Eluent: petroleum ether/ethyl acetate = 75:25.

mp = 157-159 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.00-8.98 (d, *J*=4.8Hz, 2H), 7.78-7.60(d, *J*=7.2Hz, 1H), 7.53-7.50(t, *J*=4.8Hz, 1H), 5.64-5.56(p, *J*=7.2Hz, 1H), 1.81-1.79(d, *J*= 7.2Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 179.47, 167.60, 158.08, 156.90 (q, $J_{C\text{-}F}$ = 38 Hz), 155.53, 122.51, 119.77, 116.90, 114.06, 111.20, 43.51, 19.31 ppm; MS (ES): m/z calcd for $C_{10}H_8F_3N_5O_2$, 287.06; found, 288.10 (M^+).

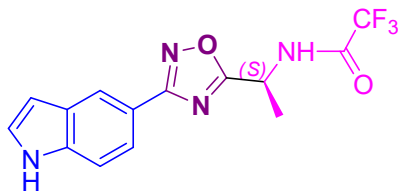
***(S)*-*N*-(1-(3-(4,6-dimethylpyrimidin-2-yl)-1,2,4-oxadiazol-5-yl)ethyl)-2,2,2-trifluoroacetamide (4ar)**



The reaction was carried out according to general procedure, using (*Z*)-*N'*-hydroxy-4,6-dimethylpyrimidine-2-carboximidamide **2r** (1.0 mmol), Compound **1a** (2.0 mmol) with 1,2 dichloroethane in reflux condition for 1 h which afforded **4ar** (79%) as white solid. Eluent: petroleum ether/ethyl acetate = 75:25.

mp = 76-79 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.41-10.39 (d, *J*=7.2Hz,1H), 7.47(s,1H), 5.50-5.43(q, *J*=7.2Hz, 1H), 2.53(s,6H), 1.69-1.68(d, *J*=7.2Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 179.89, 168.08, 168.04, 156.66 (q, $J_{C\text{-}F}$ = 37 Hz), 154.97, 121.87, 121.58, 120.44, 117.58, 114.72, 111.86, 55.36, 43.40, 23.83, 17.93 ppm; MS (ES): m/z calcd for $C_{12}H_{12}F_3N_5O_2$, 315.09; found, 316.12(M^+).

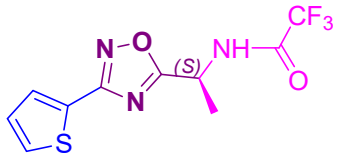
***(S)*-*N*-(1-(3-(1H-indol-5-yl)-1,2,4-oxadiazol-5-yl)ethyl)-2,2,2-trifluoroacetamide (4as)**



The reaction was carried out according to general procedure, using *(Z)*-*N'*-hydroxy-1H-indole-5-carboximidamide **2s** (1.0 mmol), Compound **1a** (2.0 mmol) with 1,2 dichloroethane in reflux condition for 75 min which afforded **4as** (85%) as white solid. Eluent: petroleum ether/ethyl acetate = 50:50.

mp = 159-161 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.48 (s,1H), 10.37-10.36 (d, *J*=7.2Hz, 1H), 8.30-8.29(m,1H), 7.80-7.77(m,1H), 7.59-7.57(m,1H), 7.50-7.48(m,1H), 6.64-6.63(m,1H), 5.47-5.40(q, *J*=7.2Hz, 1H), 1.72-1.70(d, *J*= 7.2Hz, 3H) ^{13}C NMR (100 MHz, DMSO-d_6): δ 178.74, 172.91, 169.31, 156.68 (q, $J_{C\text{-}F}$ = 36 Hz), 138.0, 128.2, 127.46, 120.50, 120.37, 120.19, 117.64, 117.04, 114.77, 112.71, 111.91, 102.70, 48.66, 43.42, 17.90, 16.67ppm; MS (ES): m/z calcd for $C_{14}H_{11}F_3N_4O_2$, 324.08; found, 325.10 (M^+).

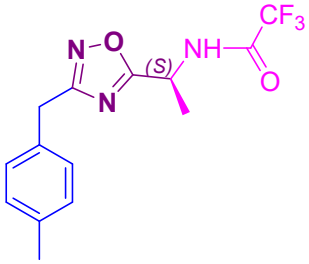
(*S*)-2,2,2-trifluoro-*N*-(1-(3-(thiophen-2-yl)-1,2,4-oxadiazol-5-yl)ethyl)acetamide (4at)



The reaction was carried out according to general procedure, using (*Z*)-*N'*-hydroxythiophene-2-carboximidamide **2t** (1.0 mmol), Compound **1a** (2.0 mmol) with 1,2 dichloroethane in reflux condition for 75 min which afforded **4at** (85%) as white solid. Eluent: petroleum ether/ethyl acetate = 90:10.

mp = 104-106 °C. ^{1}H NMR (400 MHz, DMSO-d_6): 10.37-10.35 (d, *J*=6.8Hz,1H), 7.91-7.89(dd, J=5.2Hz,1.2Hz,1H), 7.84-7.83(dd, J=3.6Hz,1.2Hz,1H), 7.29-7.27(dd, J=5.2Hz,3.6Hz,1H), 5.45-5.38(p, *J*=6.8Hz, 1H), 1.69-1.67(d, *J*=6.8Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 179.40, 164.30, 156.71 (q, $J_{C\text{-}F}$ = 36Hz), 131.39, 131.10, 130.57, 129.25, 129.03, 127.49, 120.43, 117.57, 114.71, 111.85, 55.30, 43.39, 17.76ppm; ^{19}F NMR (377 MHz, DMSO-d_6) δ -64.50 (s, 3F). MS (ES): m/z calcd for $C_{10}H_8F_3N_3O_2S$, 291.03; found, 292.04(M^+).

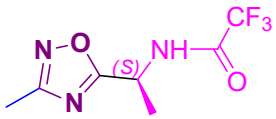
***(S)*-2,2,2-trifluoro-*N*-(1-(3-(4-methylbenzyl)-1,2,4-oxadiazol-5-yl)ethyl)acetamide (4au)**



The reaction was carried out according to general procedure, using (*Z*)-*N'*-hydroxy-2-(p-tolyl)acetimidamide **2u** (1.0 mmol), Compound **1a** (2.0 mmol) with 1,2 dichloroethane in reflux condition for 1h which afforded **4au** (94%) as white solid. Eluent: petroleum ether/ethyl acetate = 97:03.

mp = 81-83 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.20-7.18 (d, *J* = 8.0 Hz, 2H), 7.14-7.12 (d, *J* = 8.0 Hz, 2H), 5.37-5.30 (p, *J* =7.2Hz, 1H), 4.01 (s,2H), 2.32 (s, 3H), 1.64-1.62(d, *J*=7.2Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 177.60, 169.75, 156.71(q, $J_{C\text{-}F}$ = 38 Hz), 137.04, 131.77, 129.49, 129.03, 128.88, 119.79, 116.93, 114.07, 111.22, 43.59, 31.76, 21.06, 19.16 ppm; MS (ES): m/z calcd for $C_{14}H_{14}F_3N_3O_2$, 313.10; found, 314.12(M^+).

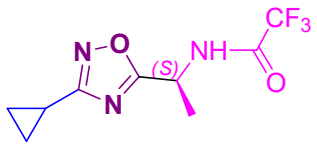
***(S)*-2,2,2-trifluoro-*N*-(1-(3-methyl-1,2,4-oxadiazol-5-yl)ethyl)acetamide (4av)**



The reaction was carried out according to general procedure, using (*Z*)-*N'*-hydroxyacetimidamide **2v** (1.0 mmol), Compound **1a** (2.0 mmol) with 1,2 dichloroethane in reflux condition for 90 min which afforded **4av** (80%) as white solid. Eluent: petroleum ether/ethyl acetate = 97:03.

mp = 60-62 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 (s, 1H), 5.42-5.35 (p, *J* =7.2Hz, 1H), 2.41 (s, 3H), 1.70-1.68(d, *J*=7.2Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 177.38, 167.30, 156.75(q, $J_{C\text{-}F}$ = 38 Hz), 119.79, 116.93, 114.07, 111.21, 43.47, 29.69, 19.17, 11.41 ppm;. MS (ES): m/z calcd for $C_7H_8F_3N_3O_2$, 223.06; found, 224.05(M^+).

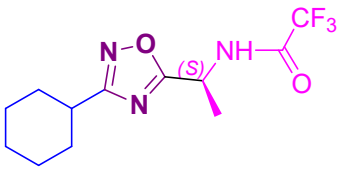
(*S*)-*N*-(1-(3-cyclopropyl-1,2,4-oxadiazol-5-yl)ethyl)-2,2,2-trifluoroacetamide (4aw)



The reaction was carried out according to general procedure, using *(Z)-N'*-hydroxycyclopropanecarboximidamide **2w** (1.0 mmol), Compound **1a** (2.0 mmol) with 1,2 dichloroethane in reflux condition for 90 min which afforded **4aw** (84%) as white solid. Eluent: petroleum ether/ethyl acetate = 97:03.

mp = 60-62 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.15 (s, 1H), 5.37-5.30 (p, *J* =7.2Hz, 1H), 2.12-2.06 (m, 1H), 1.67-1.65(d, *J*=7.2Hz, 3H), 1.11-1.05(m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 177.01, 172.54, 156.66 (q, $J_{C\text{-}F}$ = 38 Hz), 119.78,116.93, 114.07, 111.21, 43.55, 19.27, 7.90, 6.66 ppm; MS (ES): m/z calcd for $C_9H_{10}F_3N_3O_2$, 249.07; found, 250.05(M^+).

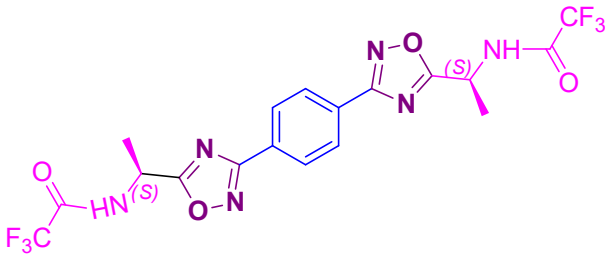
(*S*)-*N*-(1-(3-cyclohexyl-1,2,4-oxadiazol-5-yl)ethyl)-2,2,2-trifluoroacetamide (4ax)



The reaction was carried out according to general procedure, using *(Z)-N'*-hydroxycyclohexanecarboximidamide **2x** (1.0 mmol), Compound **1a** (2.0 mmol) with 1,2 dichloroethane in reflux condition for 45 min which afforded **4ax** (91%) as colorless liquid. Eluent: petroleum ether/ethyl acetate = 95:05.

mp = NA ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.25-10.23 (d, *J*=7.2Hz,1H), 5.34-5.26(p, *J*=7.6Hz, 1H), 2.86-2.76(m, 1H), 1.95-191(m, 2H), 1.77-172(m, 2H), 1.68-164(m, 1H), 1.59-1.57(d, *J*=7.2Hz, 3H), 1.52-146(m, 2H), 1.43-123(m, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 178.44, 174.03, 156.57 (q, $J_{C\text{-}F}$ = 36 Hz), 120.43, 117.57, 114.71, 111.85, 43.27, 35.39, 30.56, 30.53, 25.74, 25.40, 17.87ppm; ^{19}F NMR (377 MHz, DMSO-d_6) δ -64.50 (s, 3F). MS (ES): m/z calcd for C12H16F3N3O2, 291.12; found, 292.14M^+).

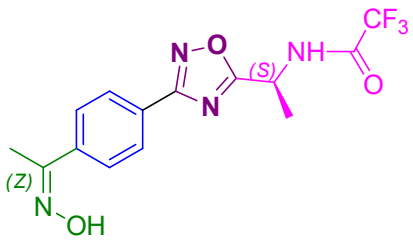
***N*,*N*'-((1*S*,1'*S*)-(1,4-phenylenebis(1,2,4-oxadiazole-3,5-diyl))bis(ethane-1,1-diyl))bis(2,2,2-trifluoroacetamide) (4ay)**



The reaction was carried out according to general procedure, using *(1Z,4Z)-N'1,N'*4-dihydroxyterephthalimidamide **2y** (1.0 mmol), Compound **1a** (2.0 mmol) with 1,2 dichloroethane in reflux condition for 10 h which afforded **4ay** (51%) as white solid. Eluent: petroleum ether/ethyl acetate = 60:40.

mp = 250-252 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.38-10.37 (d, *J*=7.2Hz,2H), 8.23(m, 4H), 5.48-5.41(p, *J*=7.2Hz, 2H), 1.70-1.68(d, *J*=7.2Hz, 6H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 179.86, 167.58, 156.53 (q, $J_{C\text{-}F}$ = 37 Hz), 129.10, 128.49, 117.58, 114.72, 111.86, 43.48, 17.81 ppm; MS (ES): m/z calcd for C18H14F6N6O4, 492.10; found, 493.01(M^+).

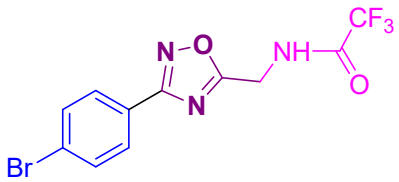
(S,Z)-2,2,2-trifluoro-*N*-(1-(3-(4-(1-(hydroxyimino)ethyl)phenyl)-1,2,4-oxadiazol-5-yl)ethyl)acetamide (4az)



The reaction was carried out according to general procedure, using (*Z*)-*N'*-hydroxy-4-((*Z*)-1-(hydroxyimino)ethyl)benzimidamide **2z** (1.0 mmol), Compound **1a** (2.0 mmol) with 1,2 dichloroethane in reflux condition for 2 h which afforded **4az** (86%) as white solid. Eluent: petroleum ether/ethyl acetate = 97:03.

mp = 175-178 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.48 (s, 1H), 10.36-10.35 (d, *J*=7.2Hz, 1H), 8.04-8.01(d, *J*=8.8Hz, 2H), 7.87-7.85(d, *J*=8.8Hz, 2H), 5.46-5.39(p, J=7.2Hz,1H), 2.20(s,3H), 1.69-1.67(d, *J*=7.2Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 179.52, 167.86, 155.01 (q, $J_{C\text{-}F}$ = 36 Hz), 152.77, 140.38, 127.55, 126.81, 126.19, 120.45, 117.59, 114.73, 111.87, 43.45, 17.82, 11.81ppm; m/z calcd for $C_{14}H_{13}F_3N_4O_3$, 342.09; found, 342.90(M^-).

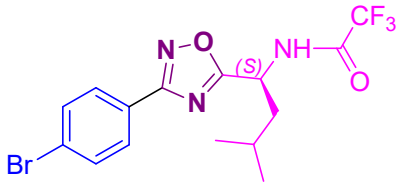
***N*-((3-(4-bromophenyl)-1,2,4-oxadiazol-5-yl)methyl)-2,2,2-trifluoroacetamide (4bj)**



The reaction was carried out according to general procedure, using *(Z)*-4-bromo-*N'*-hydroxybenzimidamide **2j** (1.0 mmol), Compound **1b** (2.0 mmol) with 1,2 dichloroethane in reflux condition for 30 min which afforded **4bj** (80%) as white solid. Eluent: petroleum ether/ethyl acetate = 97:03.

mp = 105 -107 °C. ^{1}H NMR (400 MHz, DMSO-d_6): 10.44 (s, 1H), 7.96-7.93(d, J=8.4Hz, 2H), 7.80-7.78(d, J=8.4Hz, 2H), 4.87(s,2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 176.73, 167.53, 157.43 (q, $J_{C\text{-}F}$ = 37 Hz), 133.17, 132.88, 132.61, 129.65, 129.41, 129.12, 125.81, 125.48, 120.46, 117.60, 114.74, 111.89, 39.33, 36.04 ppm; ^{19}F NMR (377 MHz, DMSO-d_6) δ -64.50 (s, 3F). MS (ES): m/z calcd for $C_{11}H_7BrF_3N_3O_2$, 348.97; found, 347.94(M^-).

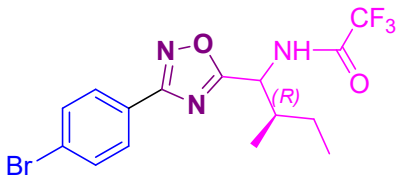
(*S*)-*N*-(1-(3-(4-bromophenyl)-1,2,4-oxadiazol-5-yl)-3-methylbutyl)-2,2,2-trifluoroacetamide (4cj)



The reaction was carried out according to general procedure, using *(Z)*-4-bromo-*N'*-hydroxybenzimidamide **2j** (1.0 mmol), Compound **1c** (2.0 mmol) with 1,2 dichloroethane in reflux condition for 150 min which afforded **4cj** (72%) as white solid. Eluent: petroleum ether/ethyl acetate = 97:03.

mp = 76-79 °C. ^{1}H NMR (400 MHz, DMSO-d_6): 10.33 (s, 1H), 7.96-7.93(d, J=8.4Hz, 2H), 7.81-7.79(d, J=8.4Hz, 2H), 5.35-5.34(b,1H), 2.07-2.00(m,1H), 1.96-1.89(m,1H), 1.71-1.62(m,1H), 0.98-0.93 (m,6H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 179.38, 167.49, 156.87 (q, $J_{C\text{-}F}$ = 37 Hz), 132.93, 129.48, 125.84, 125.48, 120.47, 117.61, 114.74, 45.86, 24.64, 23.07, 21.58 ppm; MS (ES): m/z calcd for $C_{15}H_{15}BrF_3N_3O_2$, 406.20; found, 404.11(M^-).

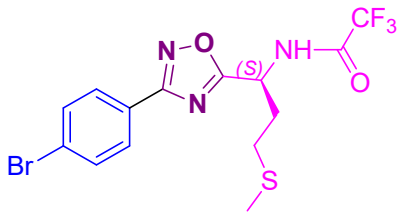
***N*-((2*R*)-1-(3-(4-bromophenyl)-1,2,4-oxadiazol-5-yl)-2-methylbutyl)-2,2,2-trifluoroacetamide (4dj)**



The reaction was carried out according to general procedure, using *(Z)*-4-bromo-*N'*-hydroxybenzimidamide **2j** (1.0 mmol), Compound **1d** (2.0 mmol) with 1,2 dichloroethane in reflux condition for 2 h which afforded **4dj** (76%) as white solid. Eluent: petroleum ether/ethyl acetate = 97:03.

mp = 76-79 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95-7.93(d, J=8.4Hz, 2H), 7.65-7.63(d, J=8.4Hz, 2H), 7.05-7.03(d, J=8.4Hz, 1H), 5.41-5.37(q, J=6Hz, 1H), 2.21-2.12 (m, 1H), 1.60-1.50(m,1H), 1.35-1.26(m, 1H), 1.01-0.96 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.84, 167.55, 156.89 (q, $J_{C\text{-}F}$ = 38 Hz), 132.28, 129.03, 126.26, 124.97, 119.91, 117.05, 114.19, 51.70, 38.96, 25.16, 14.91, 11.21 ppm; MS (ES): m/z calcd for $C_{15}H_{15}BrF_3N_3O_2$, 406.20; found, 404.07(M^-).

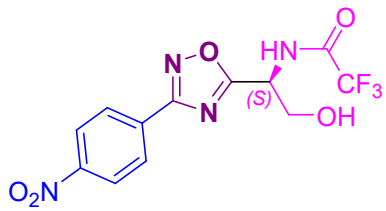
(*S*)-*N*-(1-(3-(4-bromophenyl)-1,2,4-oxadiazol-5-yl)-3-(methylthio)propyl)-2,2,2-trifluoroacetamide (4ej)



The reaction was carried out according to general procedure, using *(Z)*-4-bromo-*N'*-hydroxybenzimidamide **2j** (1.0 mmol), Compound **1e** (2.0 mmol) with 1,2 dichloroethane in reflux condition for 5 h which afforded **4ej** (68%) as white solid. Eluent: petroleum ether/ethyl acetate = 97:03.

mp = 95-97 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.36 (s, 1H), 7.96-7.94(d, *J*=8.8Hz, 2H), 7.81-7.89(d, *J*=8.8Hz, 2H), 5.48-5.44(dd, J=5.2Hz,3.2Hz,1H), 2.69-2.56(m,2H), 2.41-2.28(m,2H), 2.09(s.3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 178.8, 167.51, 157.20 (q, $J_{C\text{-}F}$ = 37 Hz), 132.92, 129.48, 125.86, 125.46, 117.55, 114.69, 46.48, 30.98, 30.19, 29.55, 14.94 ppm; MS (ES): m/z calcd for $C_{14}H_{13}BrF_3N_3O_2S$, 422.99; found, 422.04(M^-).

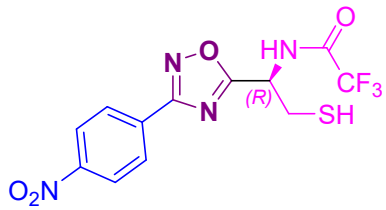
(S)-2,2,2-trifluoro-N-(2-hydroxy-1-(3-(4-nitrophenyl)-1,2,4-oxadiazol-5-yl)ethyl)acetamide (4fk)



The reaction was carried out according to general procedure, using *(Z)-N'*-hydroxy-4-nitrobenzimidamide **2k** (1.0 mmol), Compound **1f** (2.0 mmol) with 1,2 dichloroethane in reflux condition for 120 min which afforded **4fk** (70%) as white solid. Eluent: petroleum ether/ethyl acetate = 6:4.

mp = 104-106 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.39-10.37 (d, *J*=7.2Hz, 1H), 8.42-8.40 (d, *J*=9.2Hz, 2H), 8.27-8.25 (d, *J*=9.2Hz, 2H), 5.55 (br s,1H), 5.36-5.31(q, *J*=7.2Hz, 1H), 4.06-4.02(m,1H), 3.99-3.94(m,1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 178.09, 166.94, 157.41 (q, $J_{C\text{-}F}$ = 37 Hz), 149.76, 132.00, 128.99, 125.01, 117.52, 60.91, 50.24, ppm; MS (ES): m/z calcd for $C_{12}H_9F_3N_4O_5$, 346.22; found, 345.04(M^-).

(R)-2,2,2-trifluoro-N-(2-mercapto-1-(3-(4-nitrophenyl)-1,2,4-oxadiazol-5-yl)ethyl)acetamide (4gk)



The reaction was carried out according to general procedure, using *(Z)-N'*-hydroxy-4-nitrobenzimidamide **2k** (1.0 mmol), Compound **1g** (2.0 mmol) with 1,2 dichloroethane in reflux condition for 3 h which afforded **4ej** (64%) as white solid. Eluent: petroleum ether/ethyl acetate = 8:2.

mp = 128-130 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.43-10.41 (d, *J*=8Hz, 1H), 8.43-8.40 (d, *J*=8.8Hz, 2H), 8.28-8.26 (d, *J*=8.8Hz, 2H), 5.45-5.44 (d, *J*=6Hz, 1H), 3.35-3.28 (m,1H), 3.17-3.13(m,1H), 2.93-2.89(m,1H) ; ^{13}C NMR (100

MHz, DMSO-d_6): δ 178.28, 166.95, 157.22 (q, $J_{C\text{-}F}$ = 37 Hz), 149.79, 131.94, 128.98, 125.01, 120.42, 117.56, 114.70, 111.84, 50.19, 25.76, ppm; MS (ES): m/z calcd for $C_{12}H_9F_3N_4O_4S$, 362.28; found, 360.98(M^-).

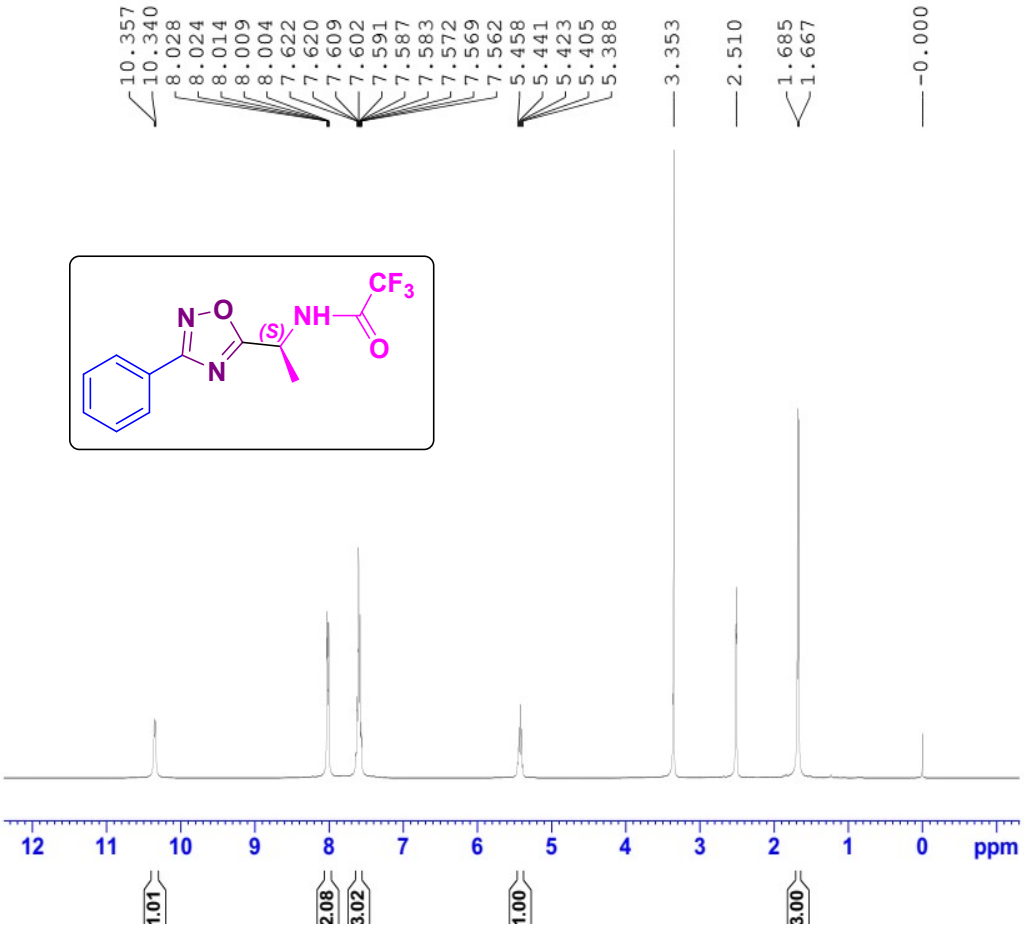


Fig. 1. ^{1}H NMR spectrum (DMSO-d_6, 400 MHz) of compound **4aa**

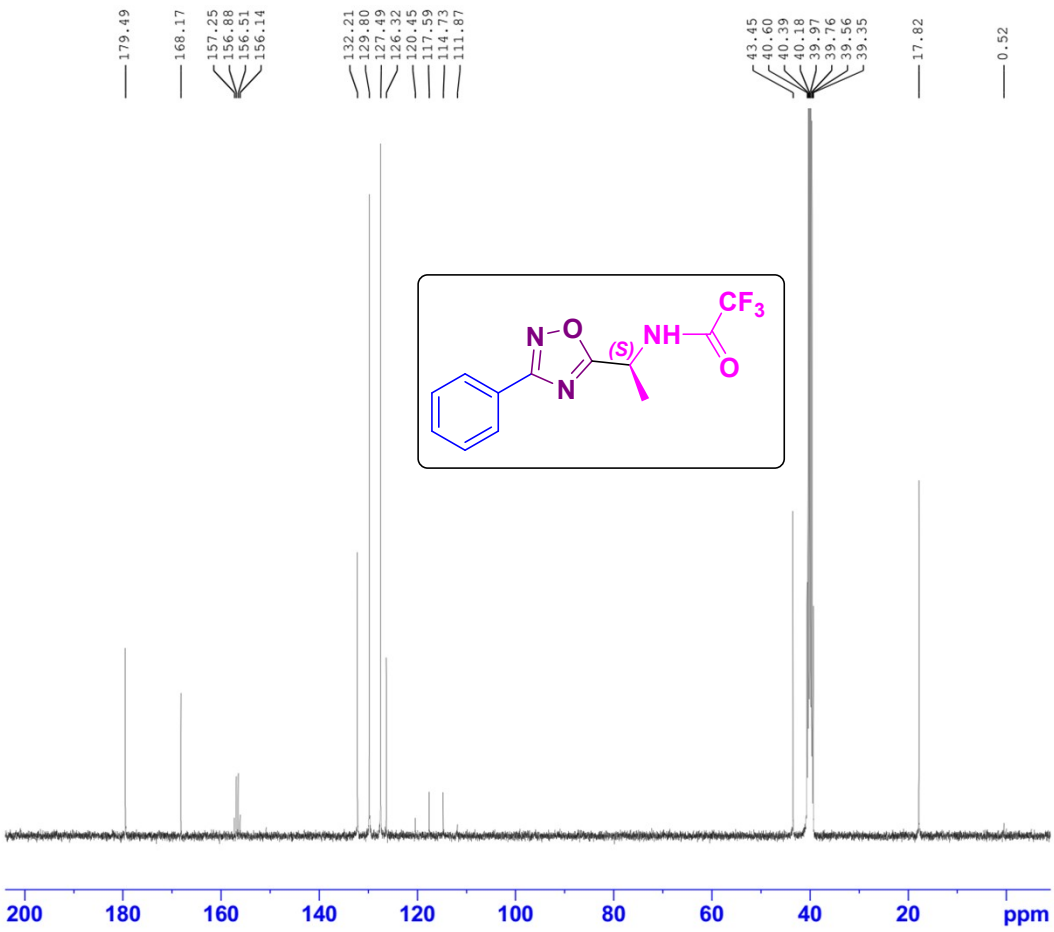


Fig. 2. ^{13}C NMR spectrum (DMSO-d_6, 100 MHz) of compound **4aa**

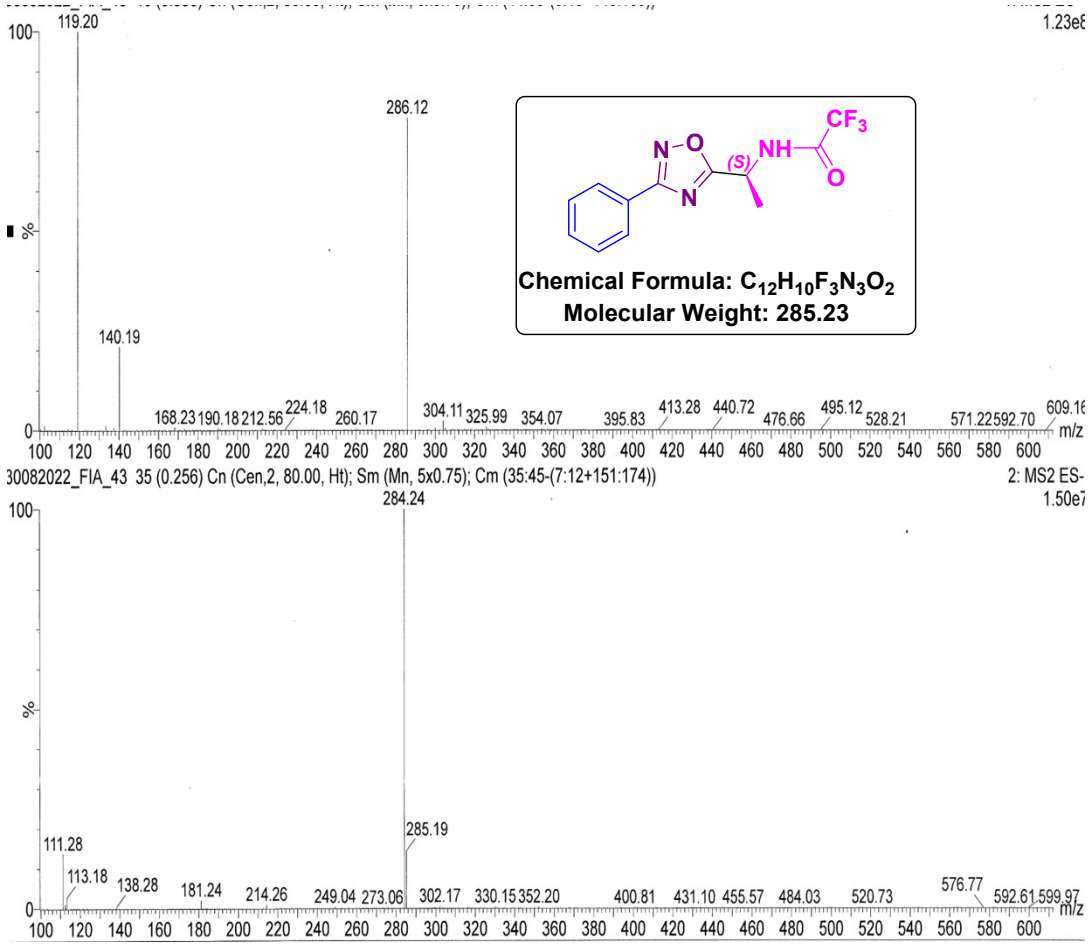


Fig. 3. Mass spectrum of compound **4aa**

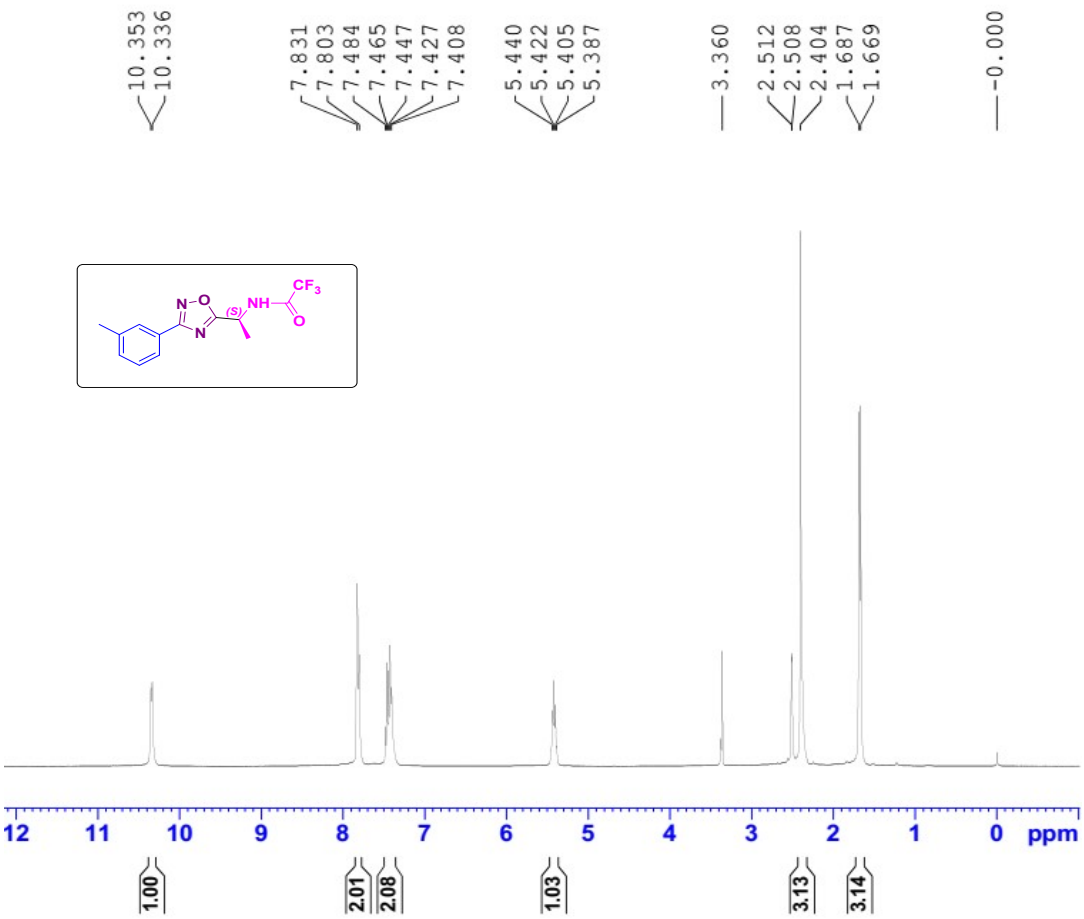


Fig. 4. ^{1}H NMR spectrum (DMSO-d_6, 400 MHz) of compound **4ab**

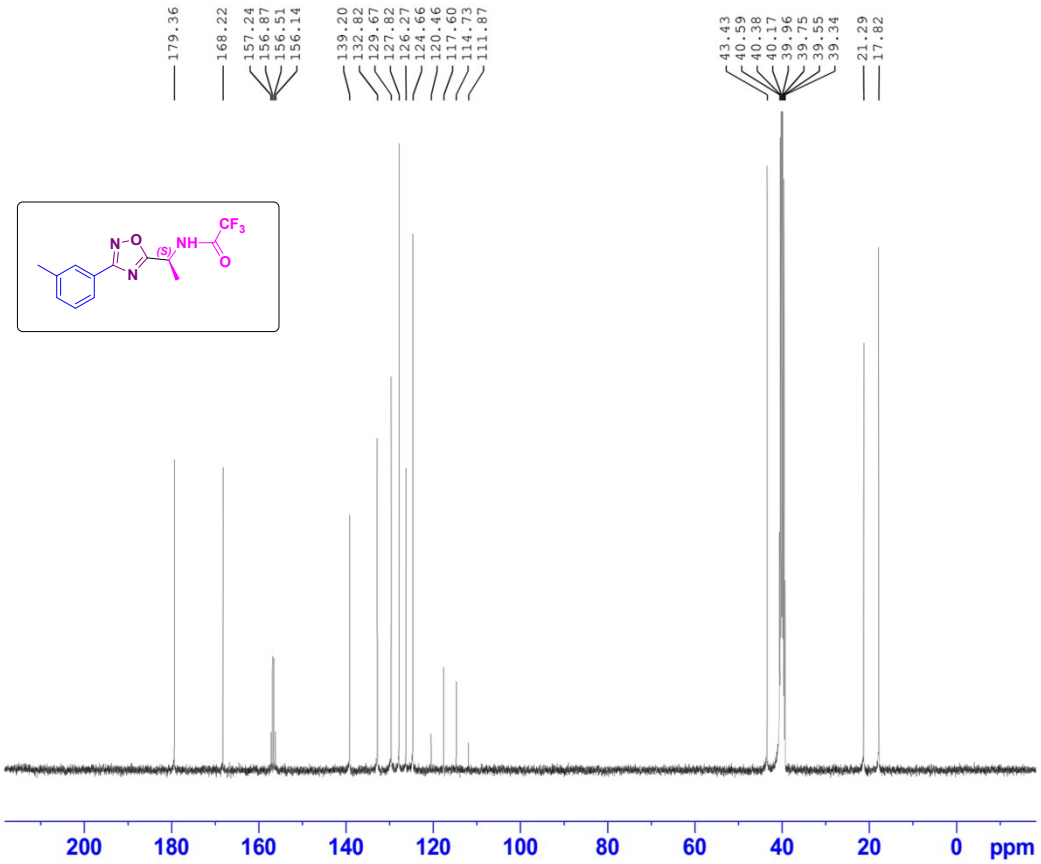


Fig. 5. ^{13}C NMR spectrum (DMSO-d_6, 100 MHz) of compound **4ab**

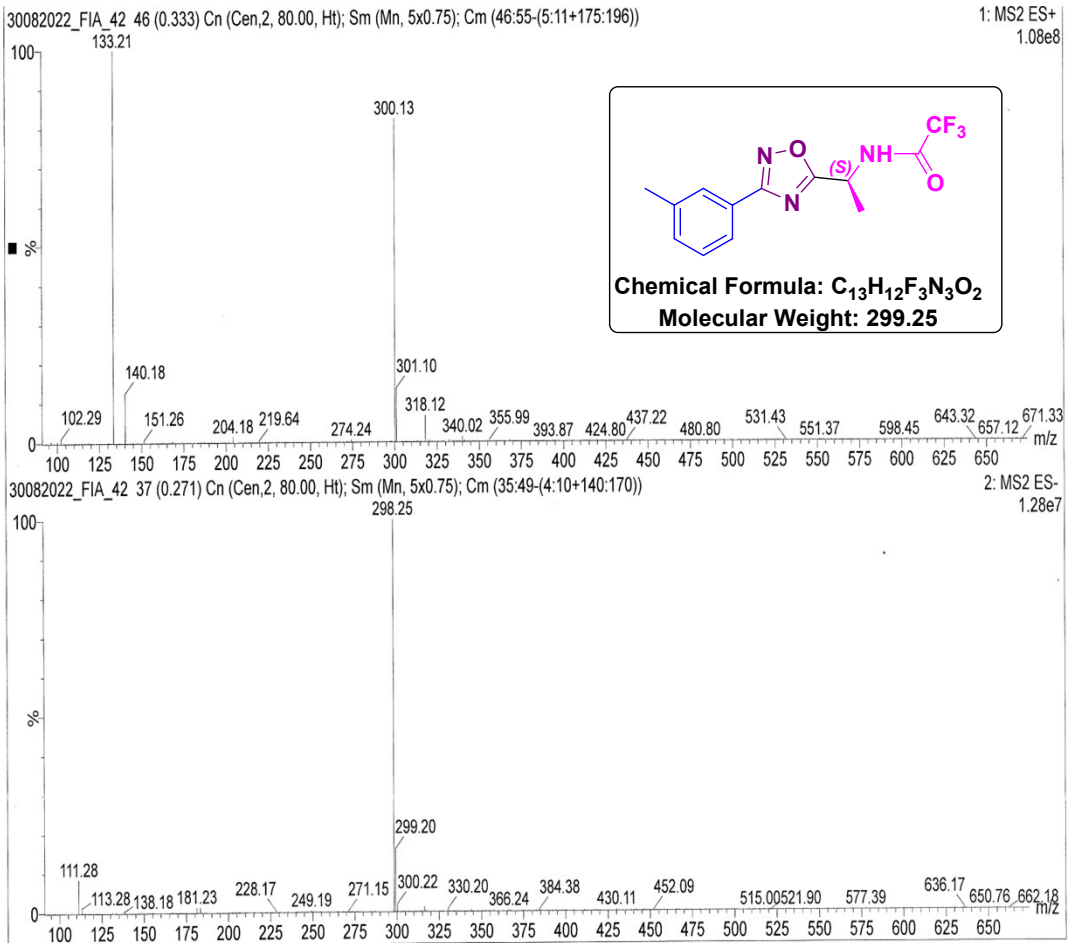


Fig. 6. Mass spectrum of compound **4ab**

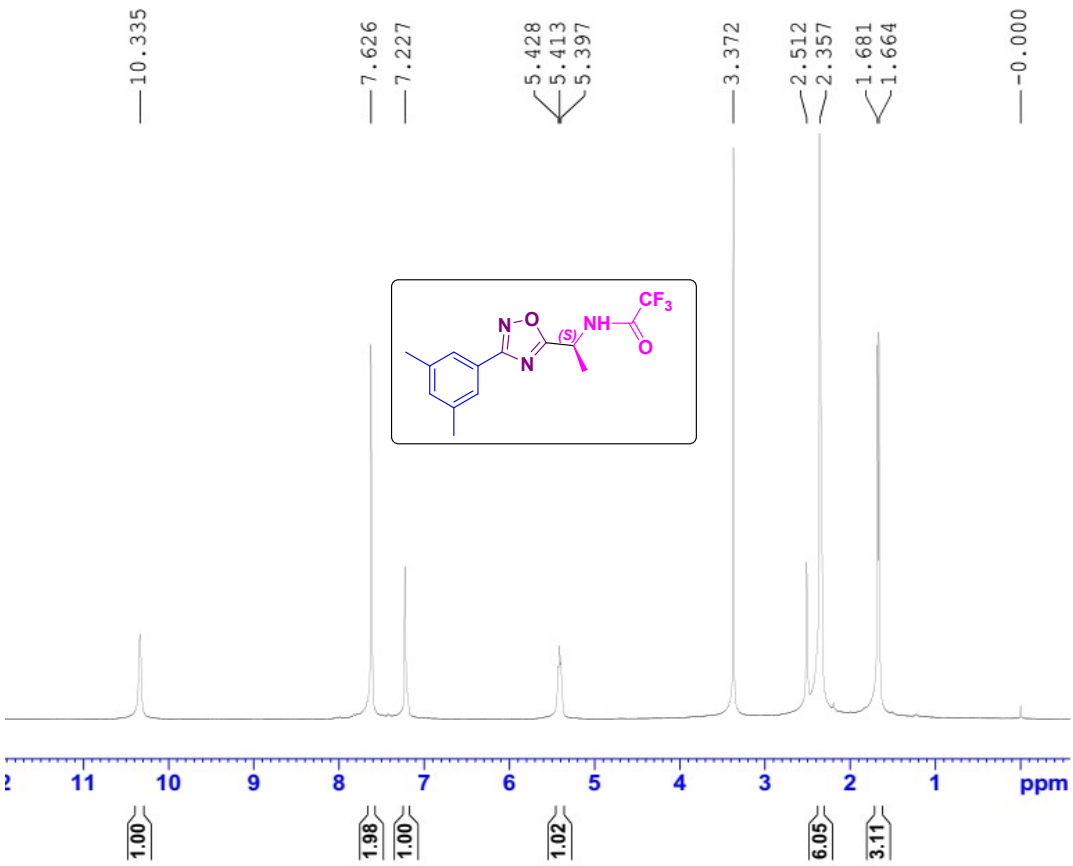


Fig. 7. ^{1}H NMR spectrum (DMSO-d_6, 400 MHz) of compound **4ac**

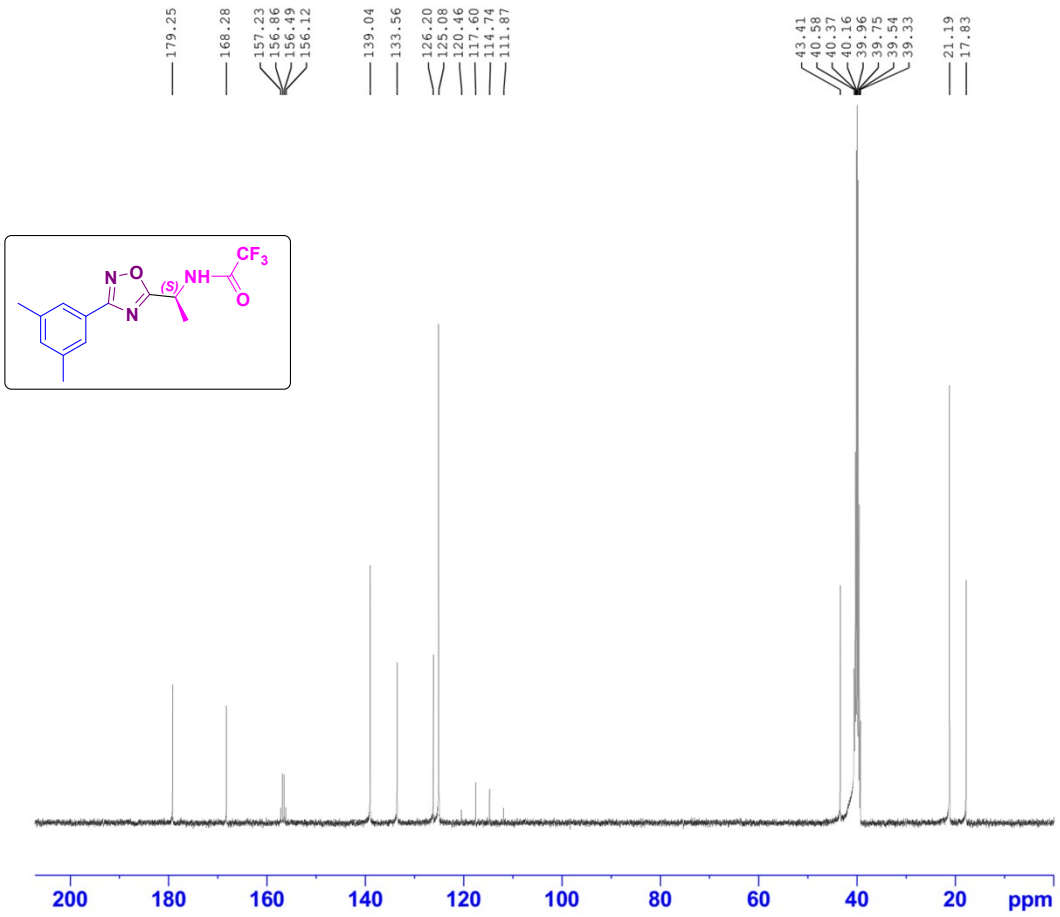


Fig. 8. ^{13}C NMR spectrum (DMSO-d_6, 100 MHz) of compound **4ac**

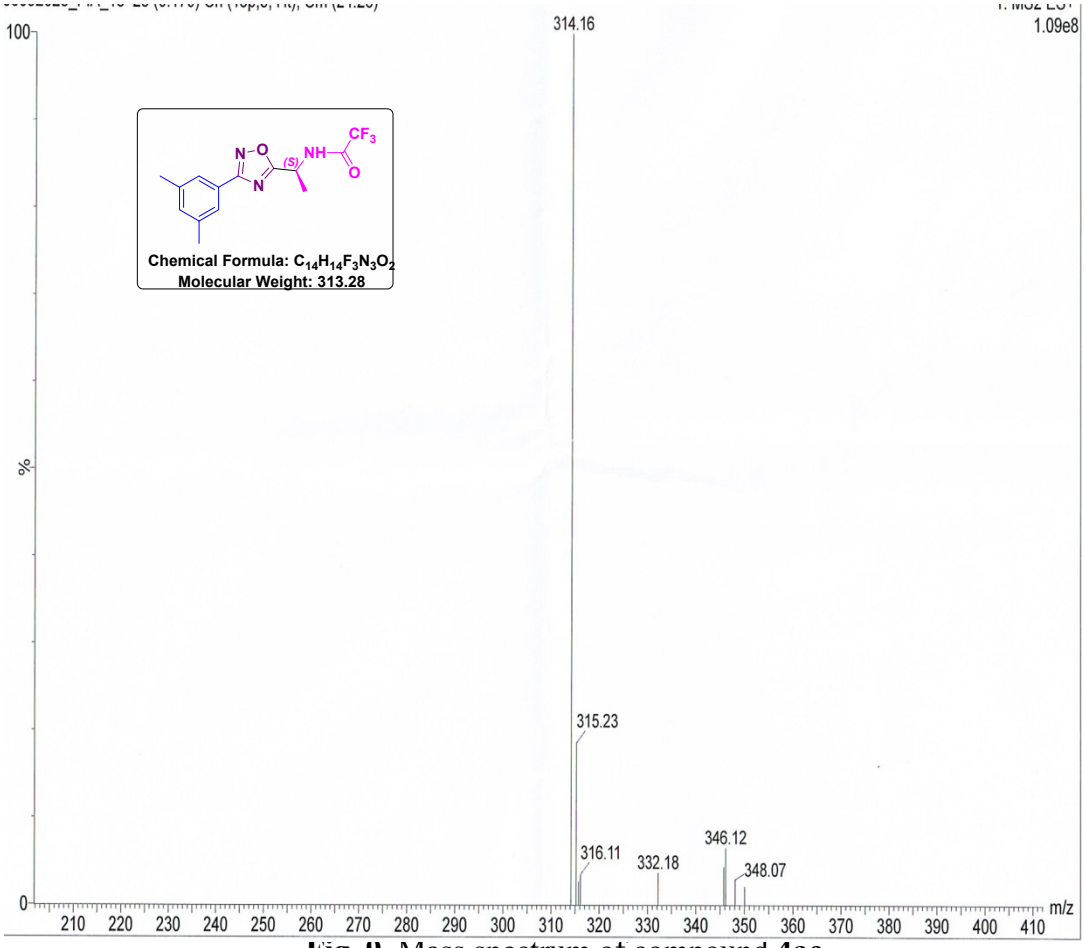


Fig. 9. Mass spectrum of compound **4ac**

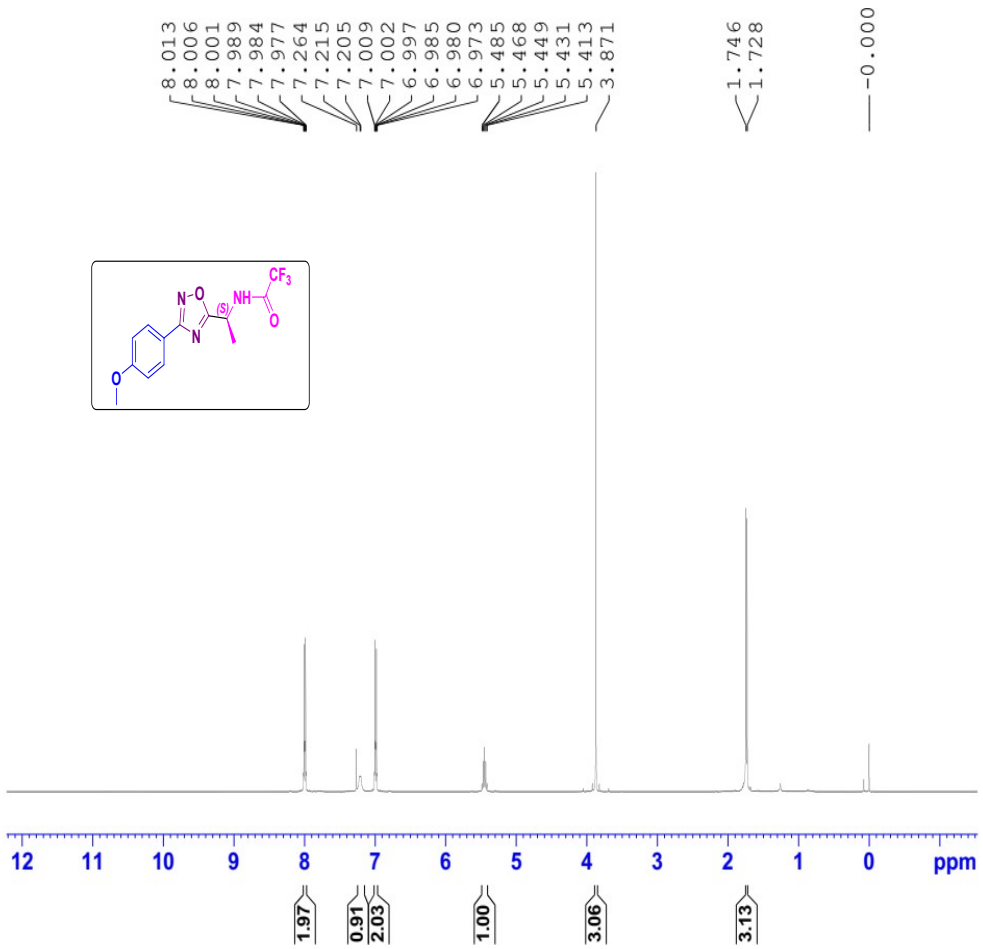


Fig. 10. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of compound **4ad**

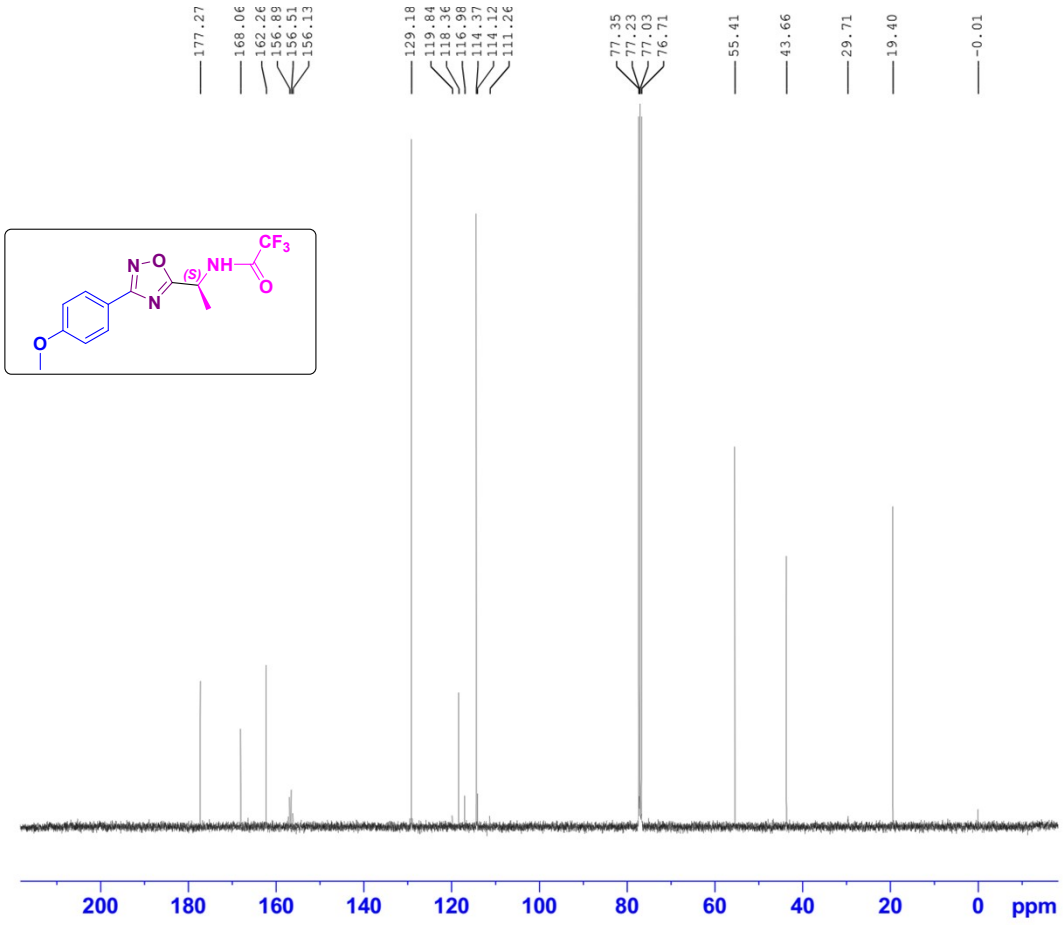


Fig.11. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of compound **4ad**

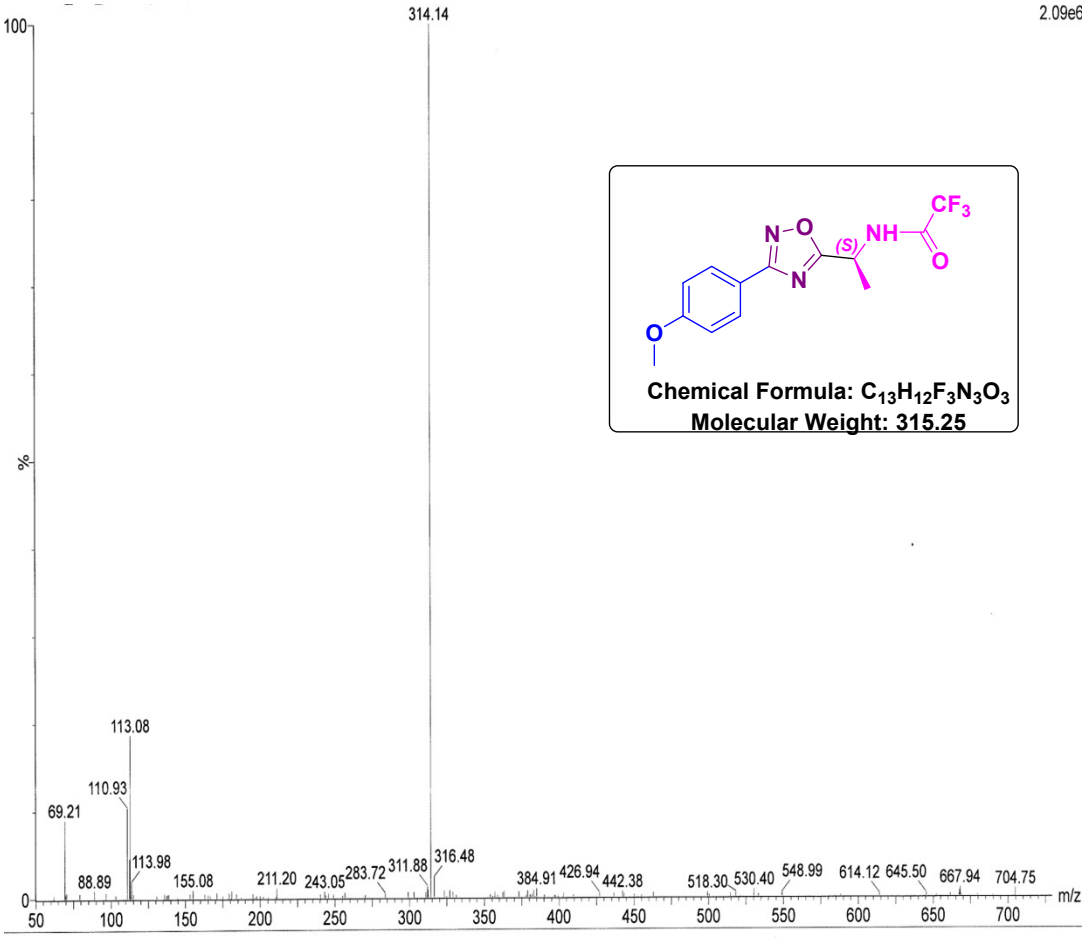


Fig. 12. Mass spectrum of compound **4ad**

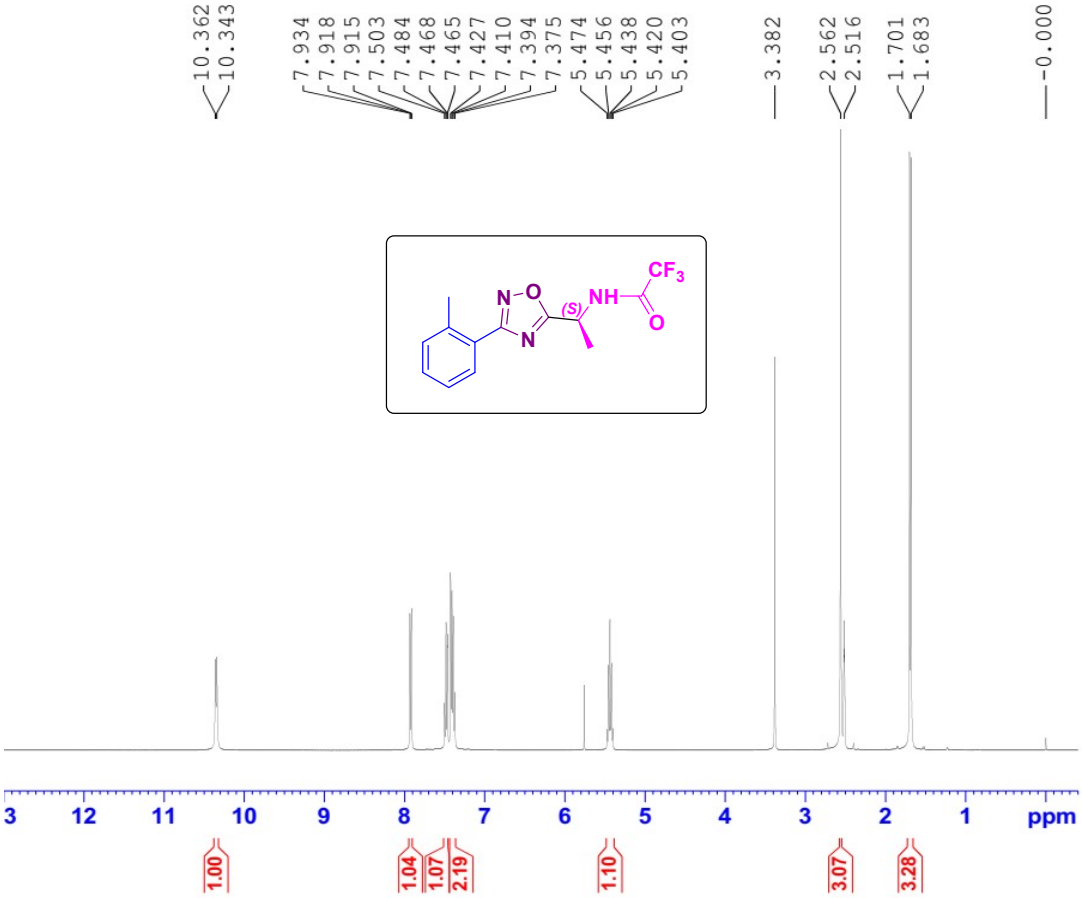


Fig. 13. ^{1}H NMR spectrum (DMSO-d_6, 400 MHz) of compound **4ae**

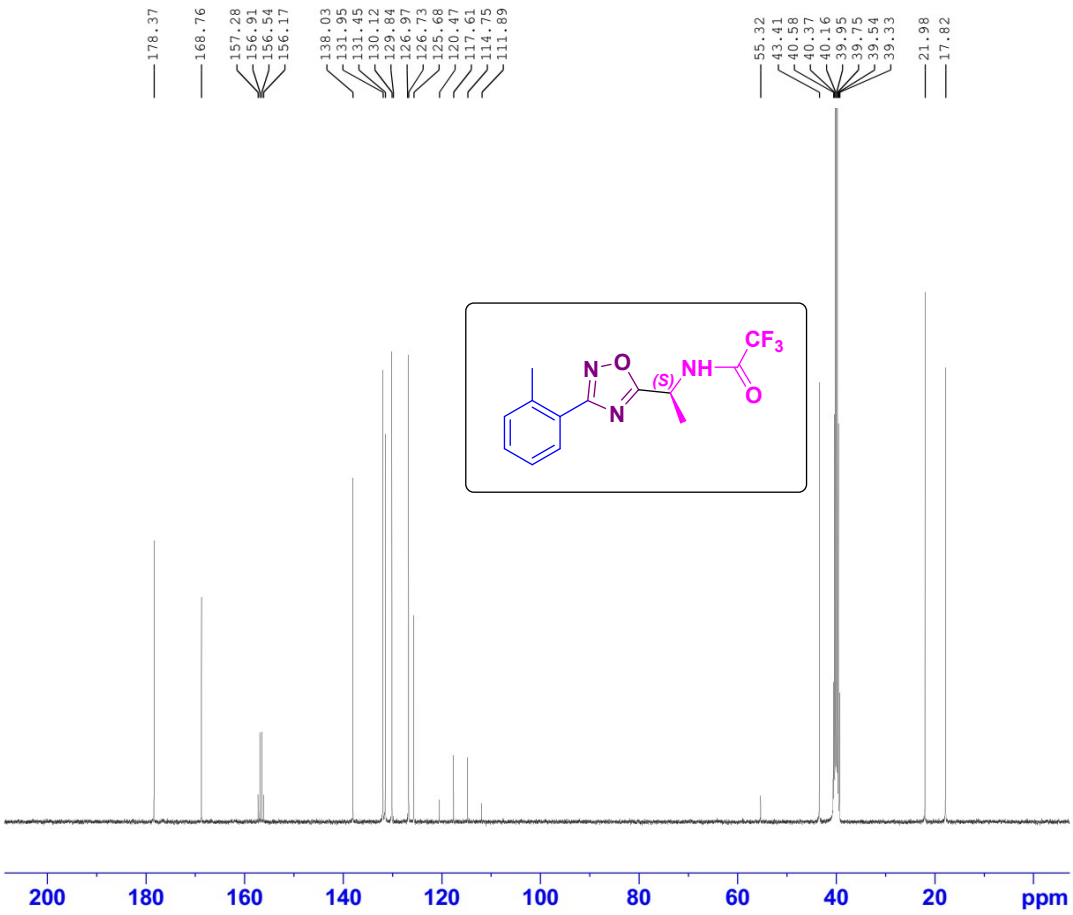


Fig. 14. ^{13}C NMR spectrum (DMSO-d_6, 100 MHz) of compound **4ae**

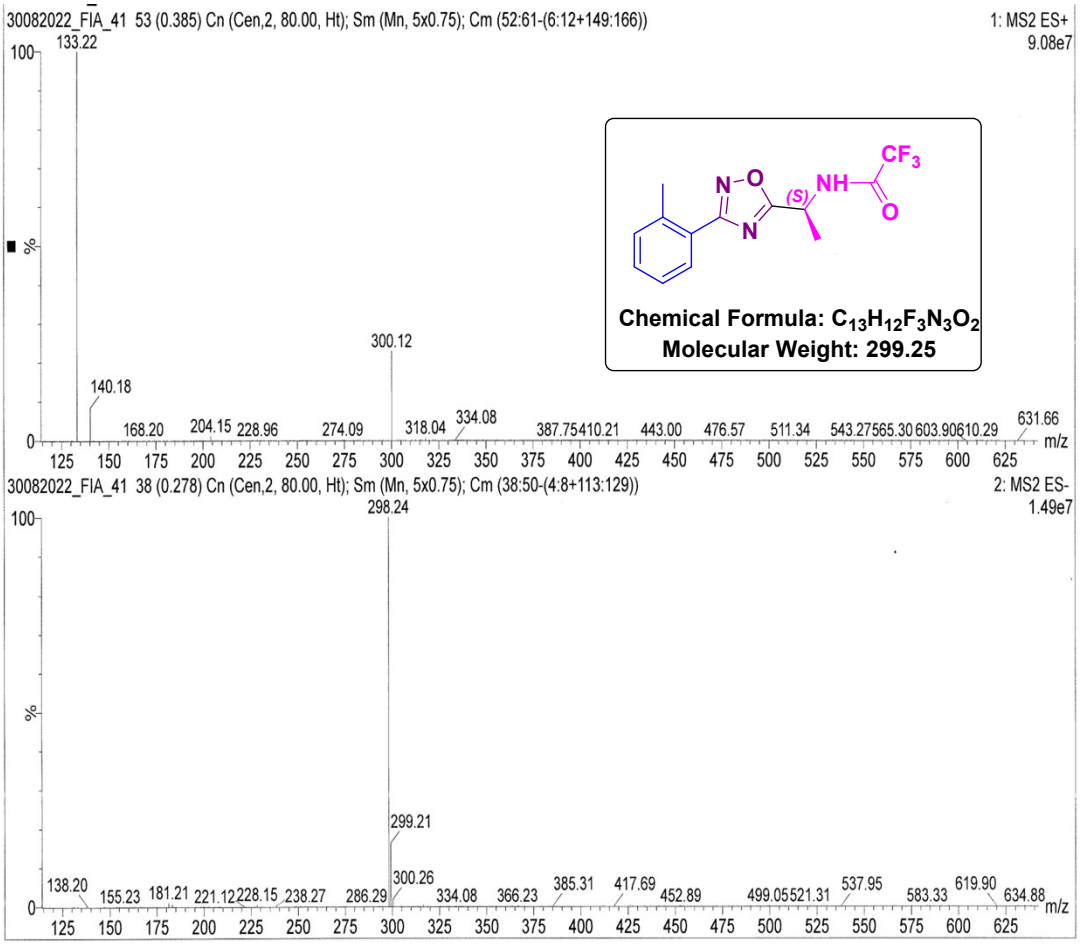


Fig. 15. Mass spectrum of compound **4ae**

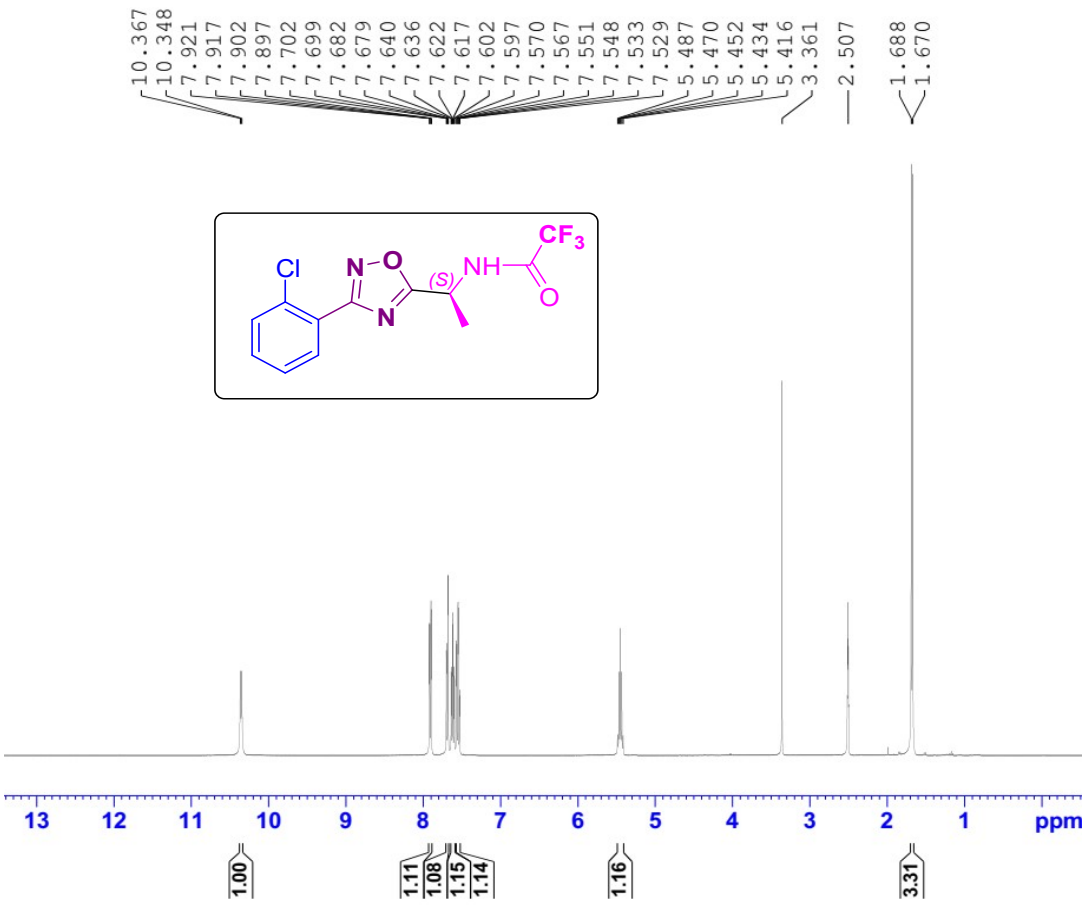


Fig. 16. ^{1}H NMR spectrum (DMSO-d_6, 400 MHz) of compound **4af**

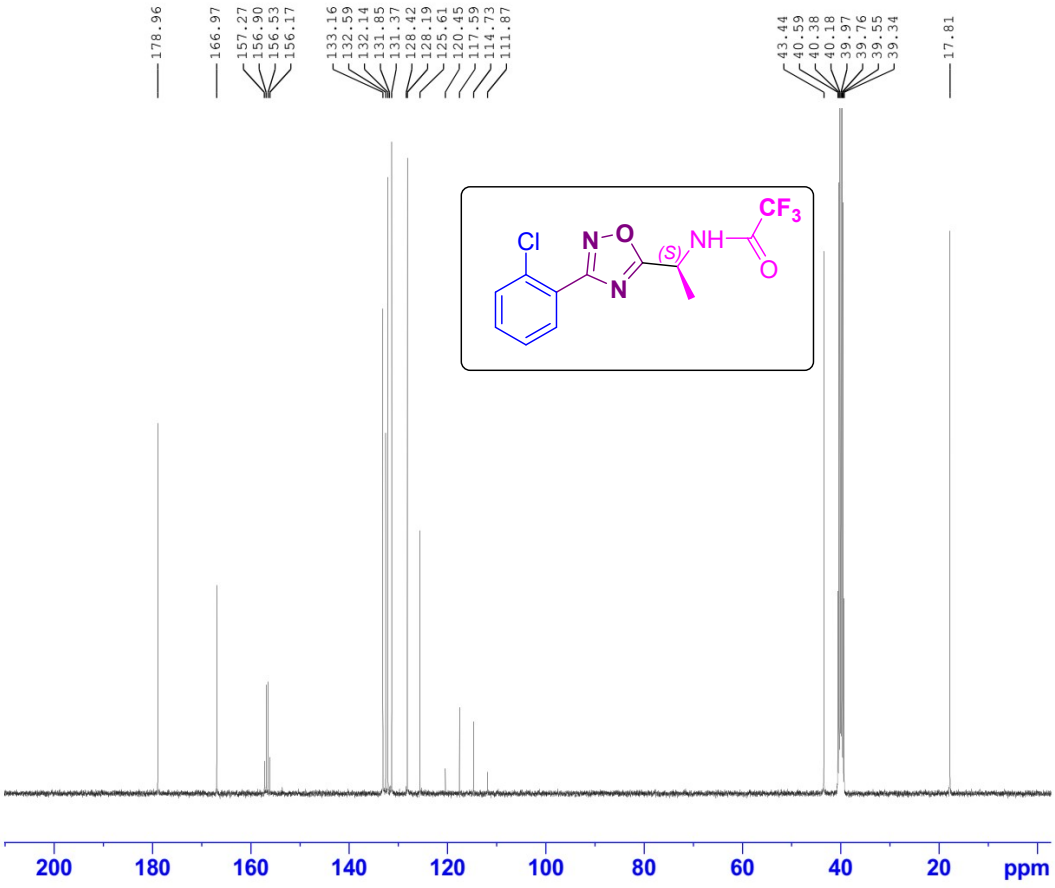


Fig. 17. ^{13}C NMR spectrum (DMSO-d_6, 100 MHz) of compound **4af**

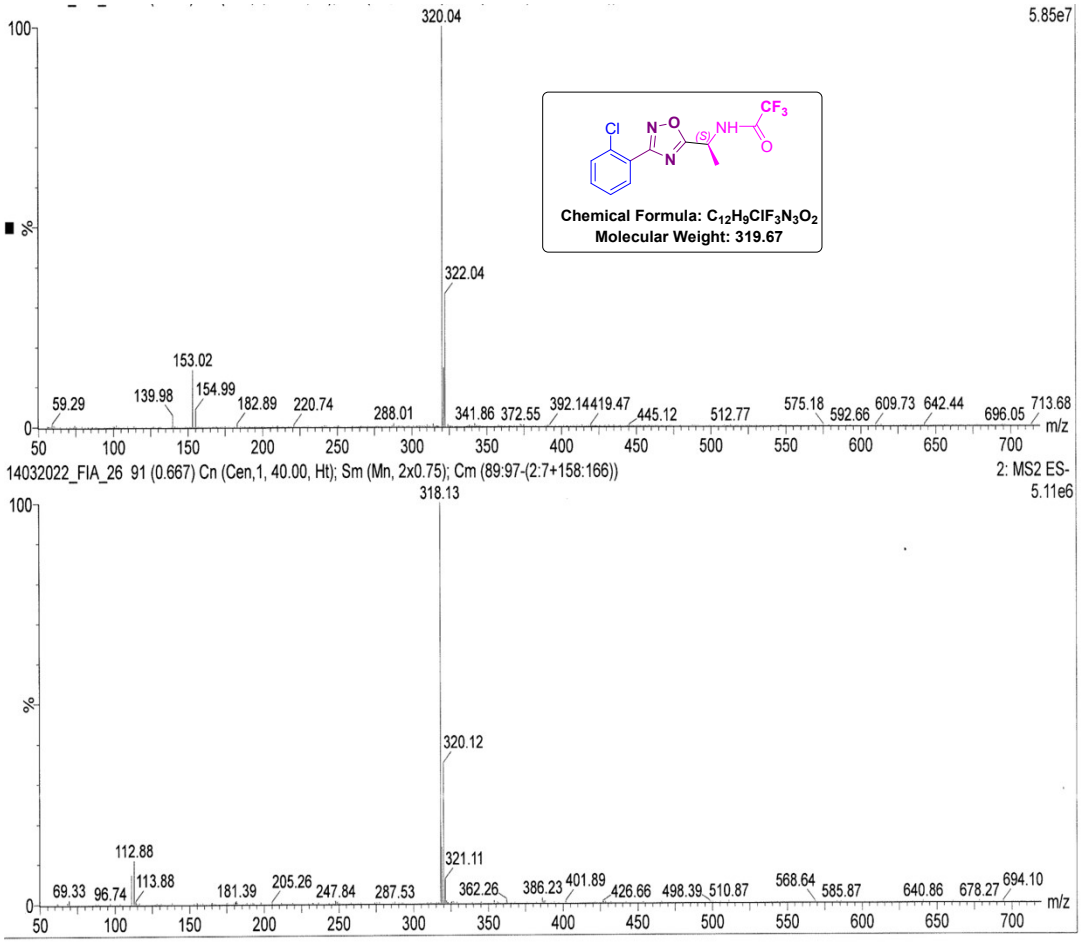


Fig. 18. Mass spectrum of compound **4af**

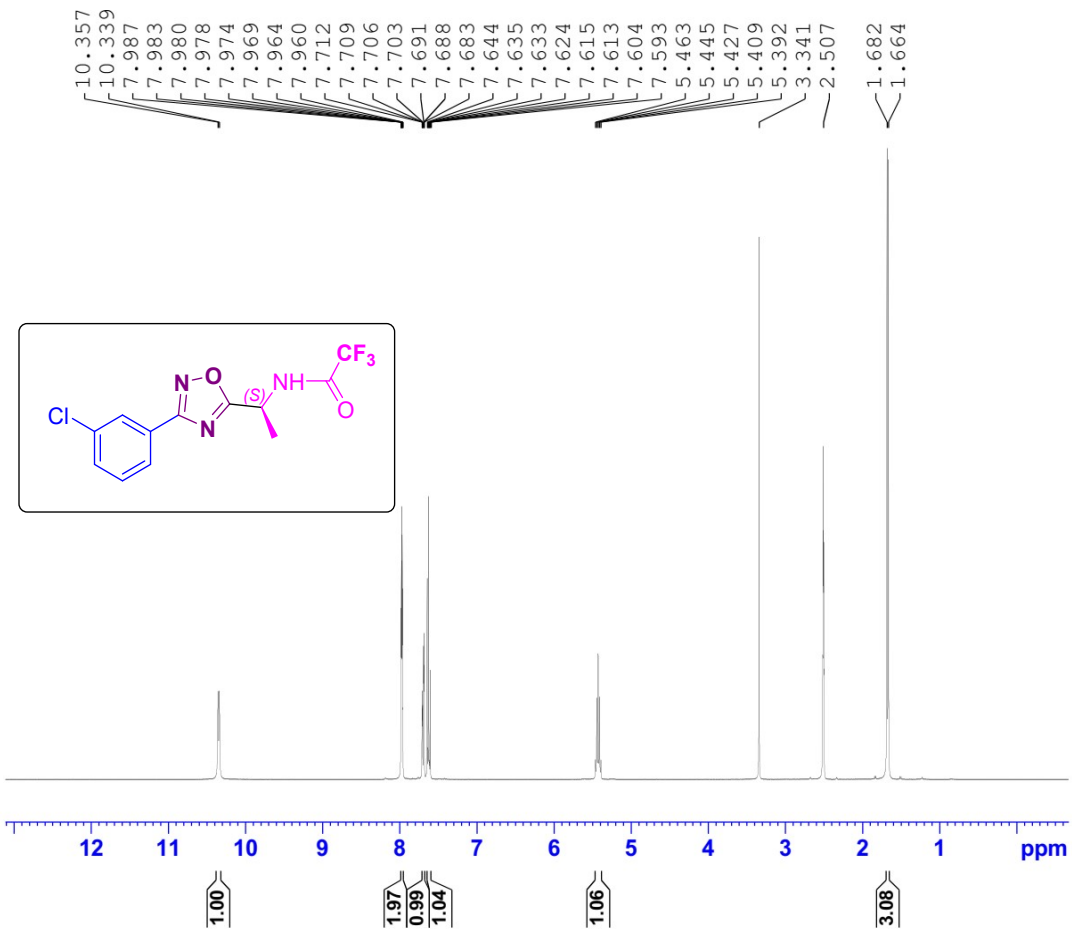


Fig.19. ^{1}H NMR spectrum (DMSO-d_6, 400 MHz) of compound **4ag**

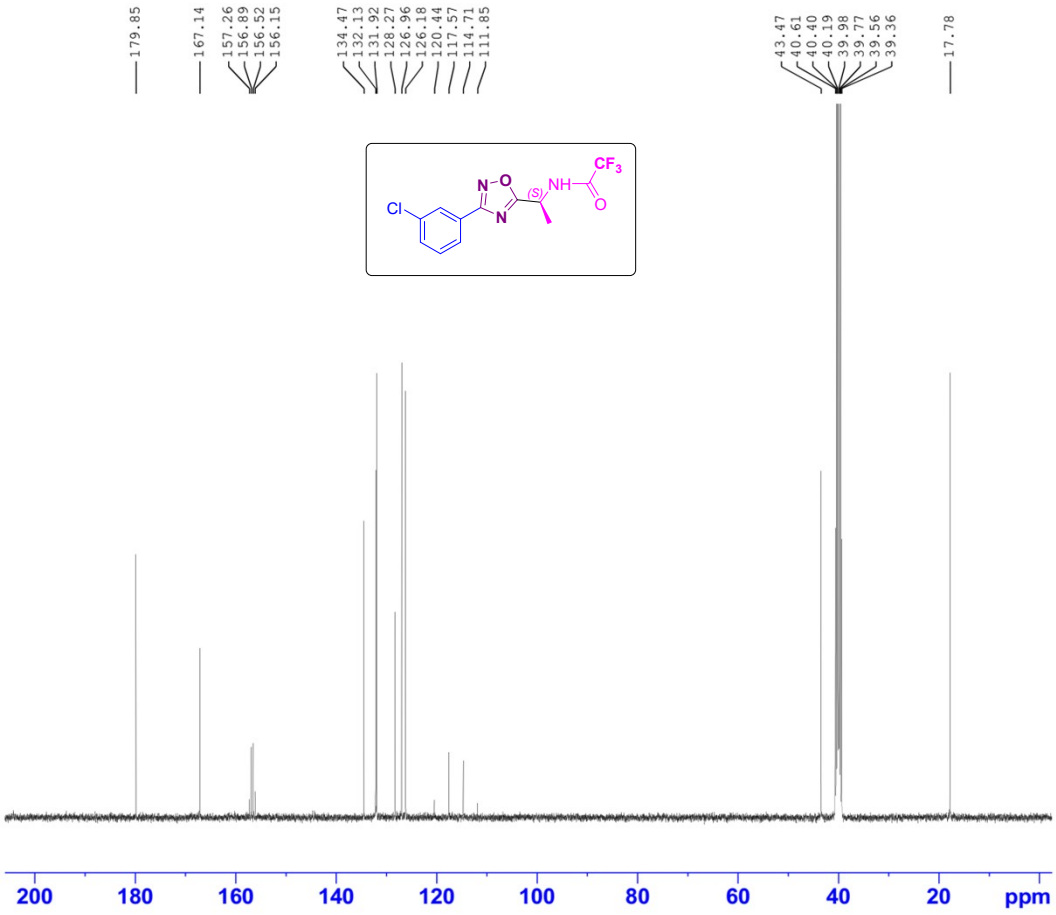


Fig. 20. ^{13}C NMR spectrum (DMSO-d_6, 100 MHz) of compound **4ag**

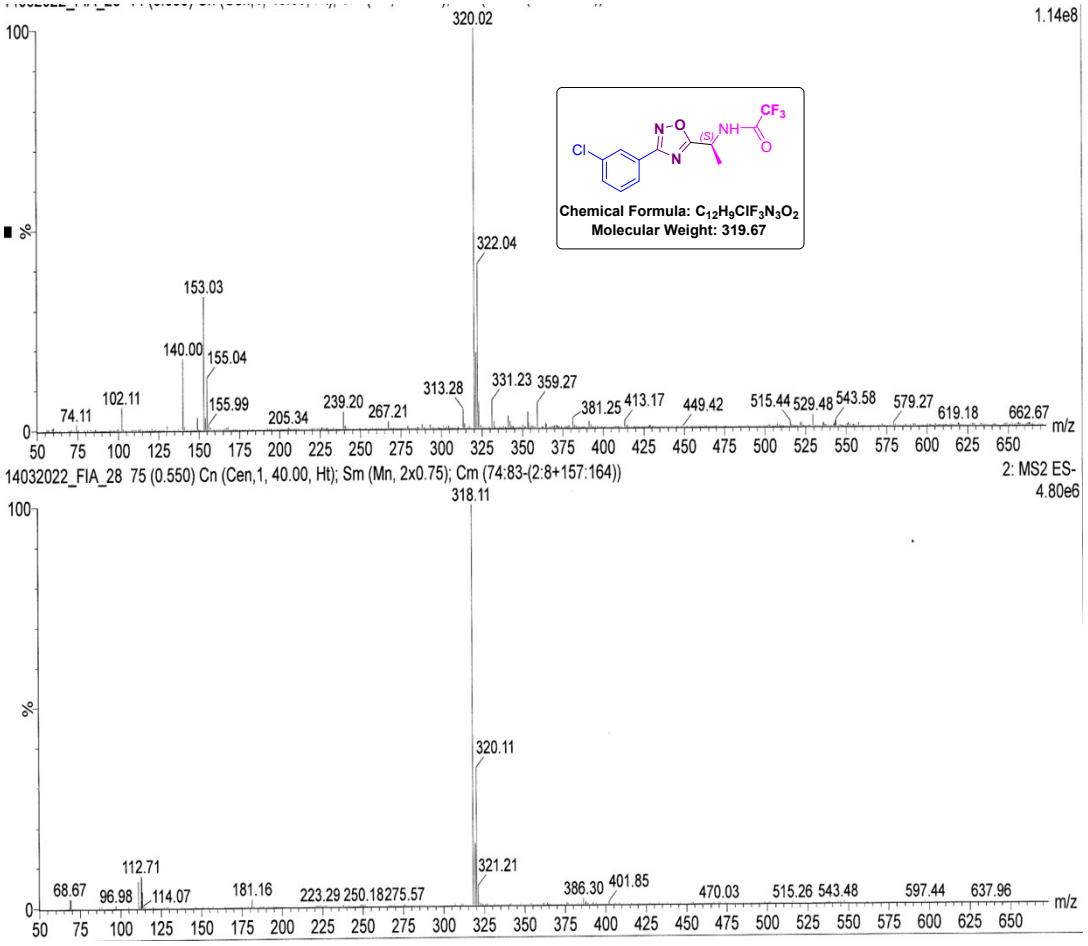


Fig. 21. Mass spectrum of compound **4ag**

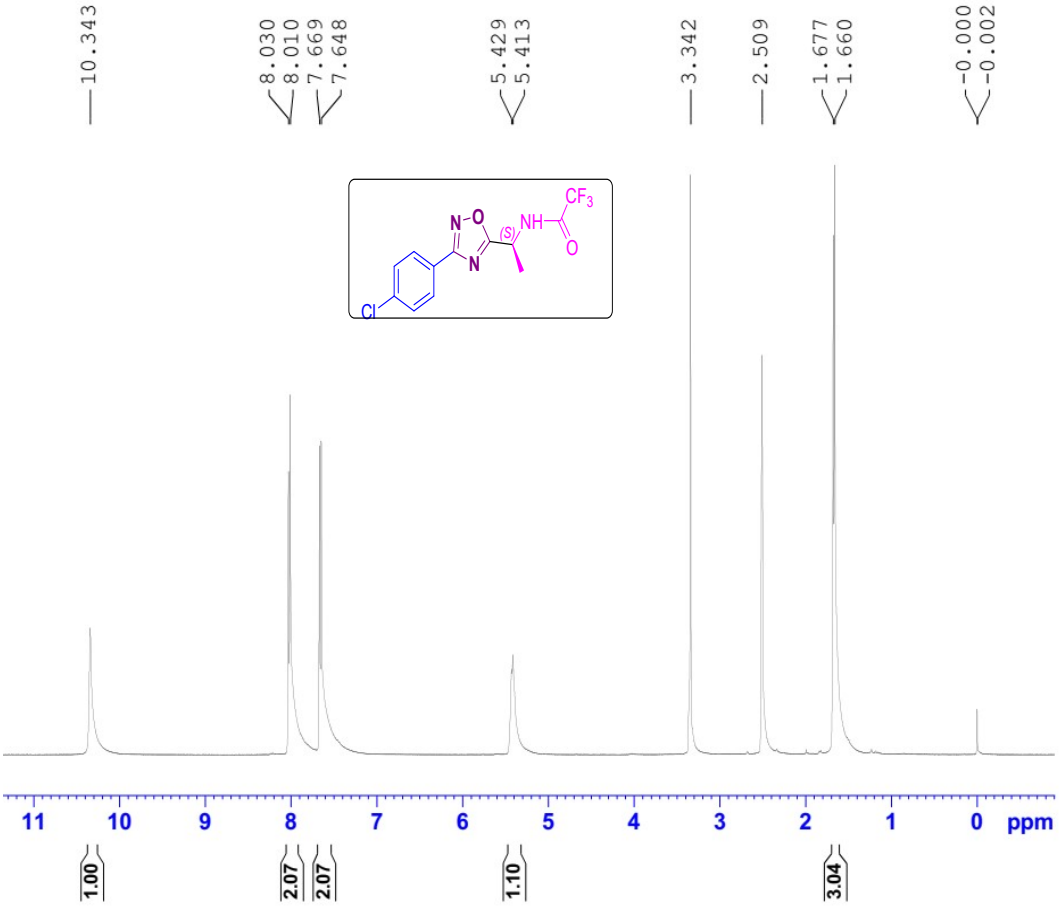


Fig. 22. ^{1}H NMR spectrum (DMSO-d_6, 400 MHz) of compound **4ah**

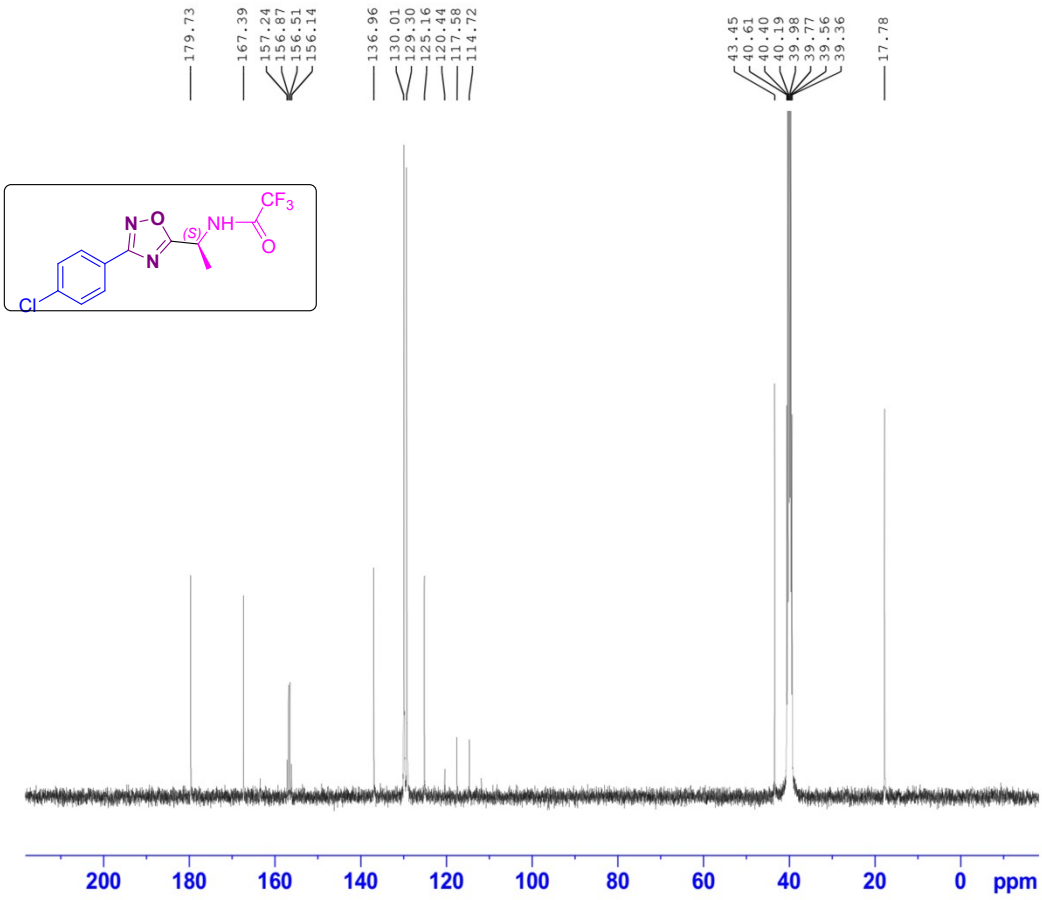


Fig. 23. ^{13}C NMR spectrum (DMSO-d_6, 100 MHz) of compound **4ah**

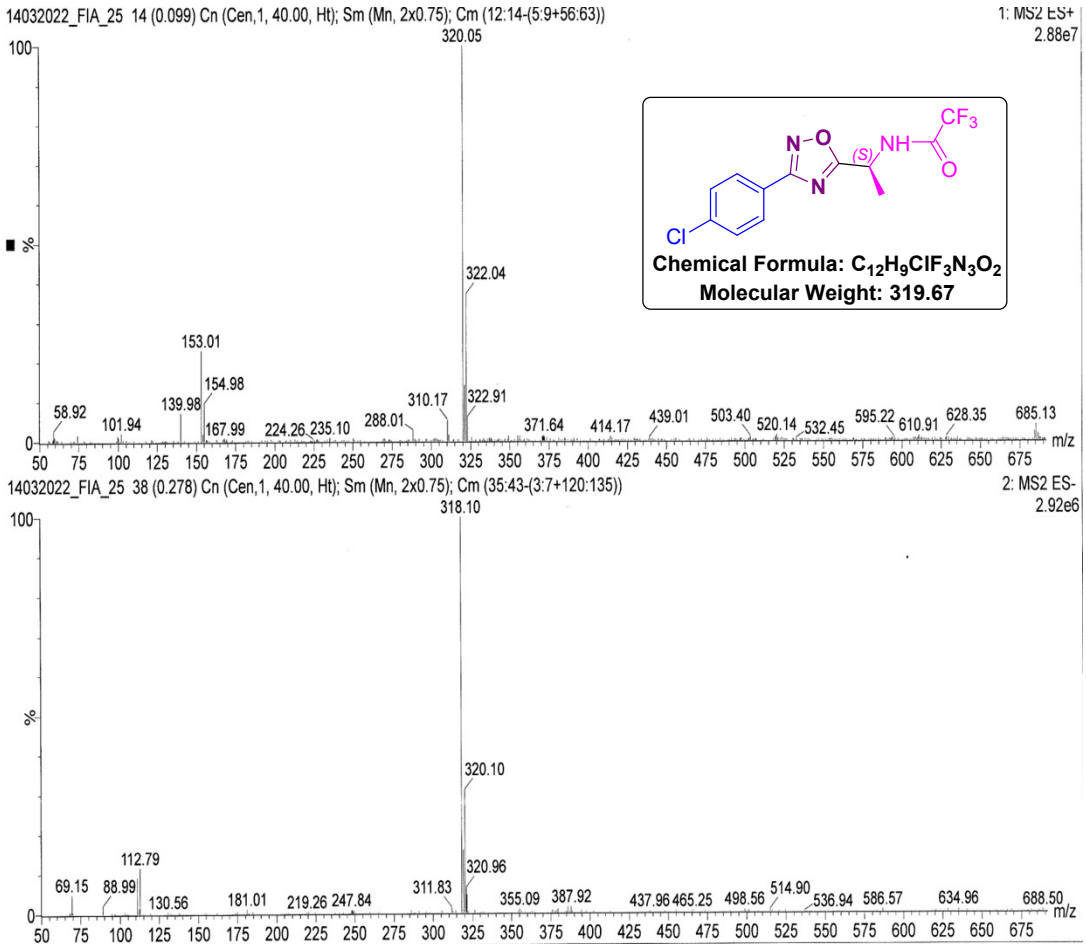


Fig. 24. Mass spectrum of compound **4ah**

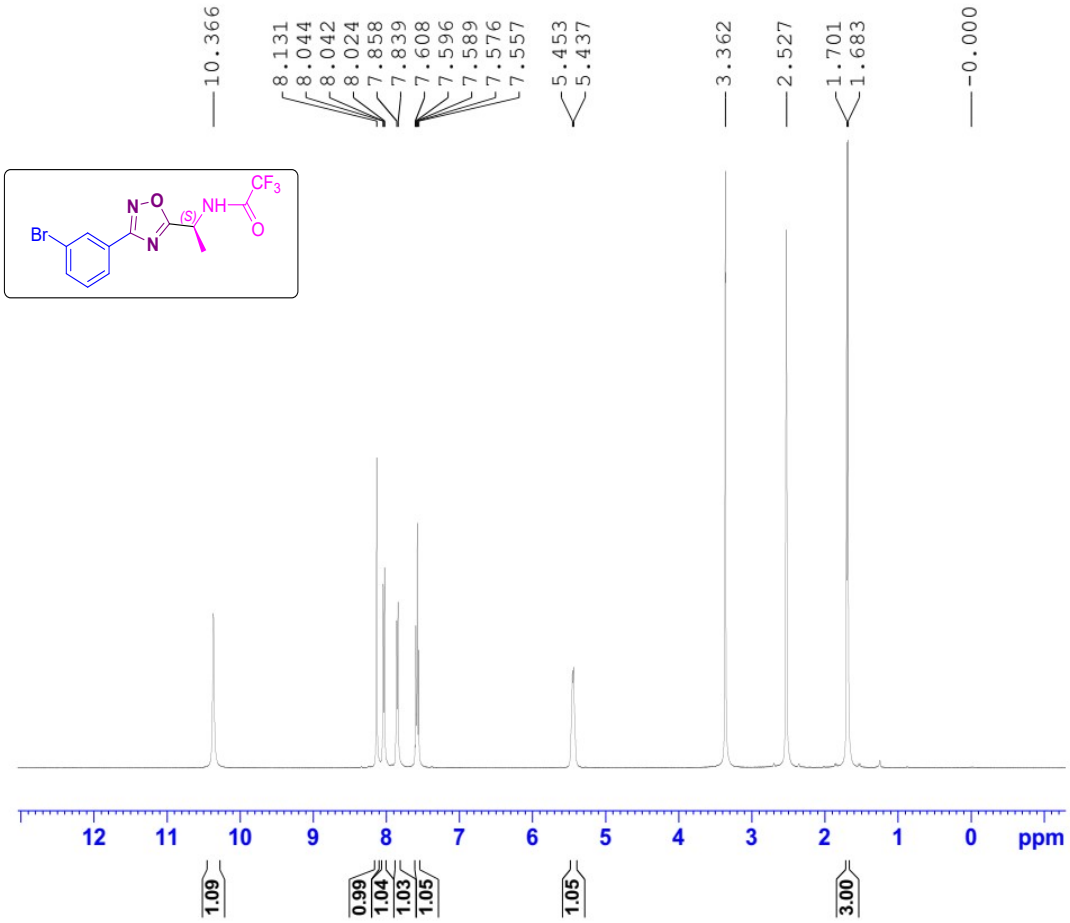


Fig. 25. ^{1}H NMR spectrum (DMSO-d_6, 400 MHz) of compound **4ai**

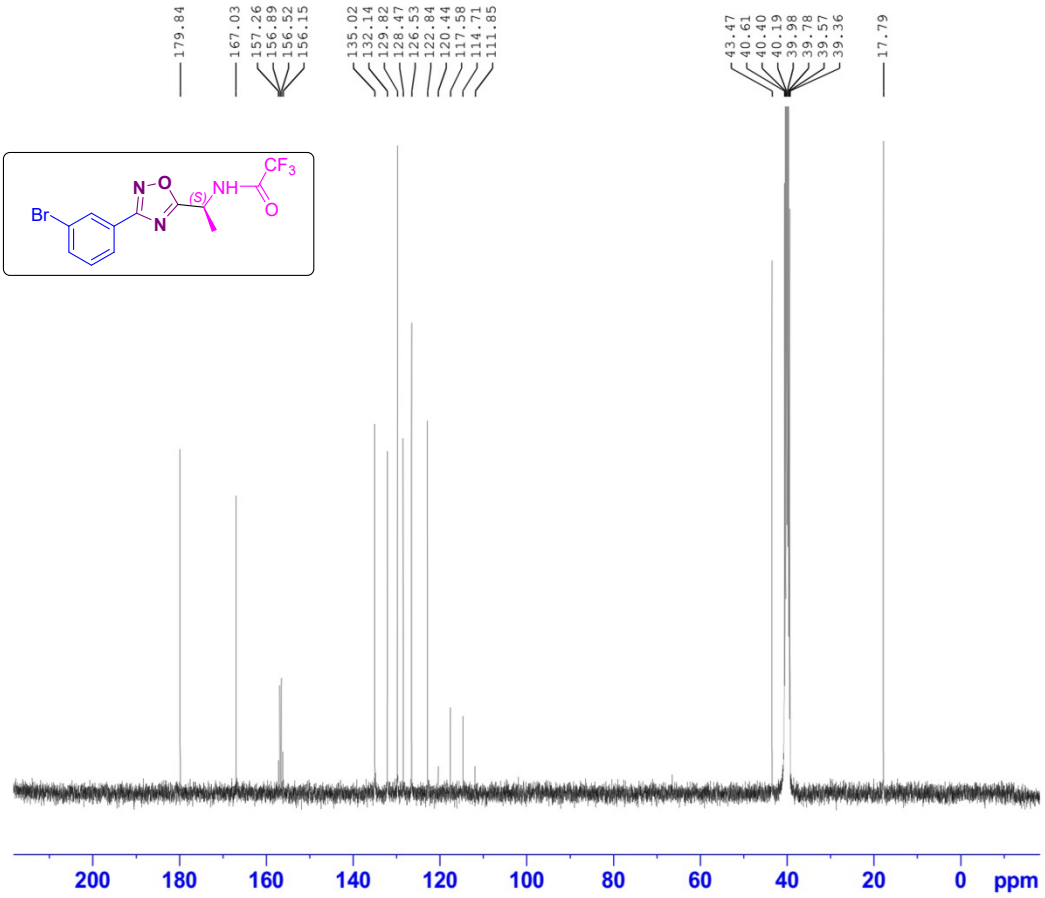


Fig. 26. ^{13}C NMR spectrum (DMSO-d_6, 100 MHz) of compound **4ai**

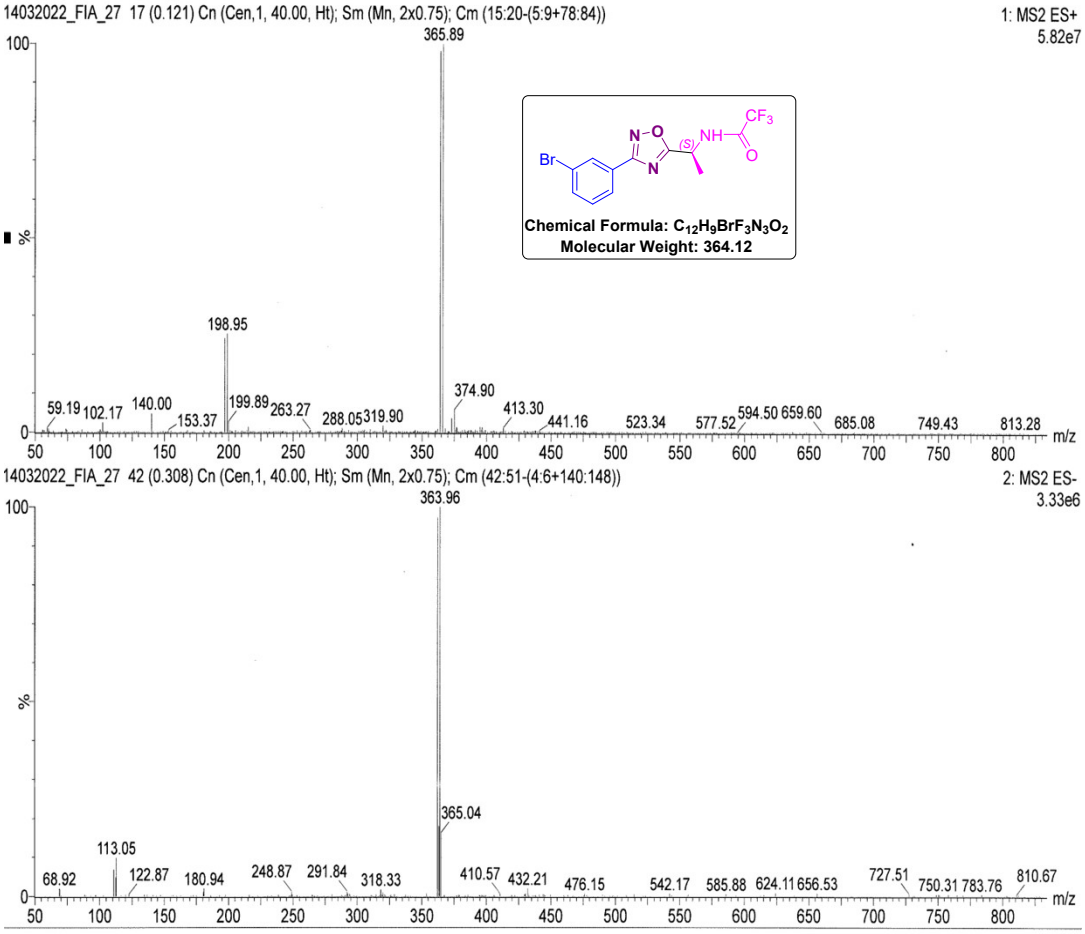


Fig. 27. Mass spectrum of compound **4ai**

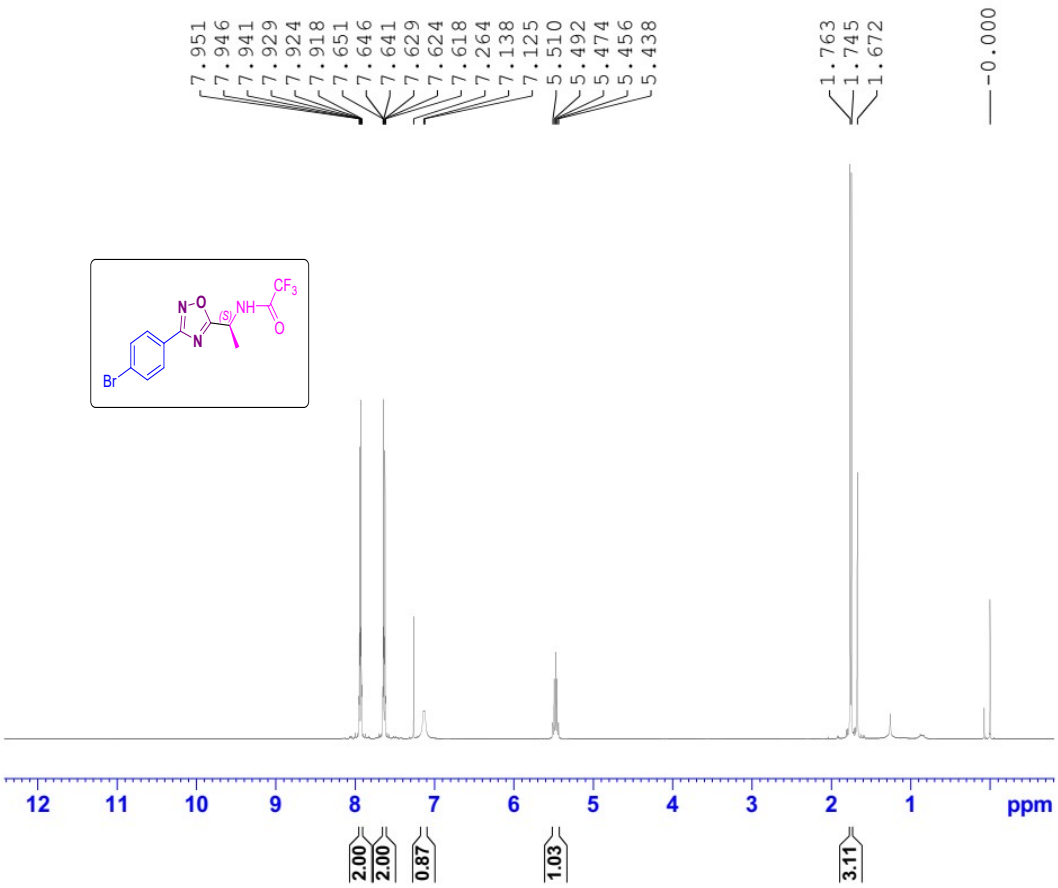


Fig. 28. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of compound **4aj**

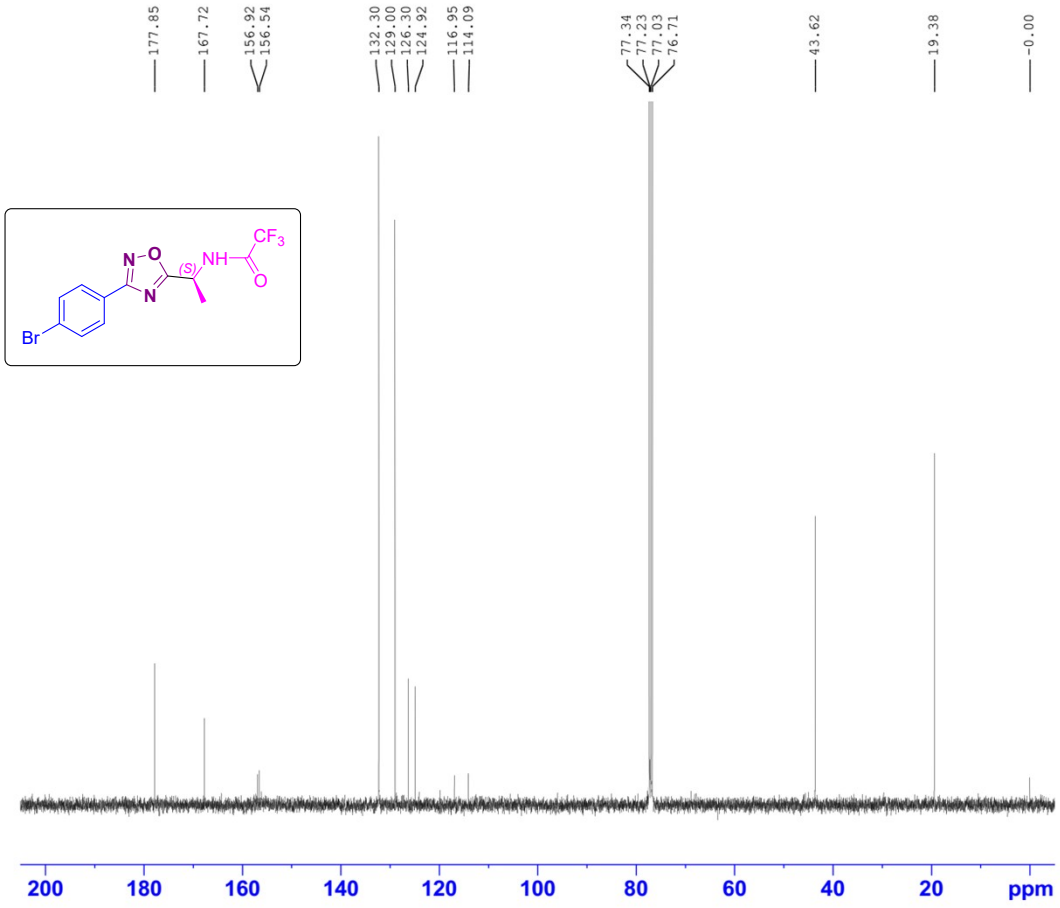


Fig.29. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of compound **4aj**

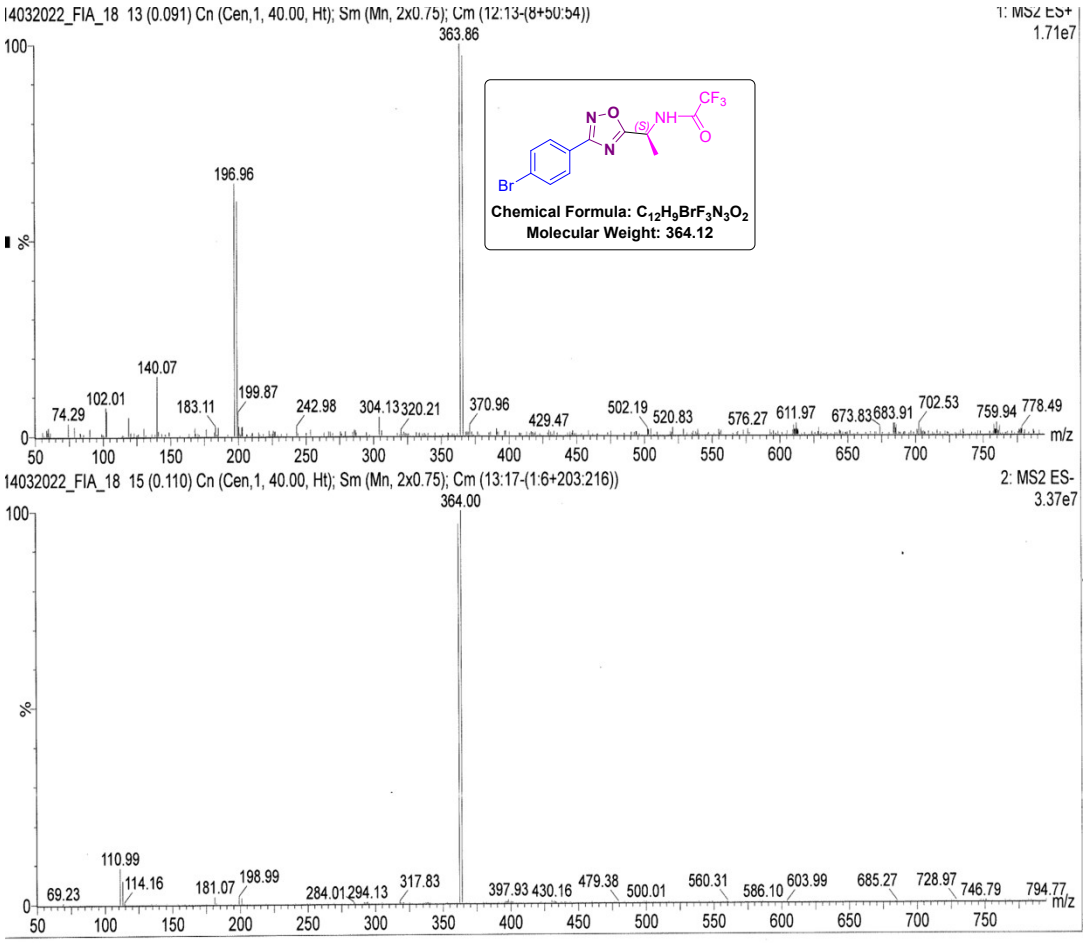


Fig. 30. Mass spectrum of compound **4aj**

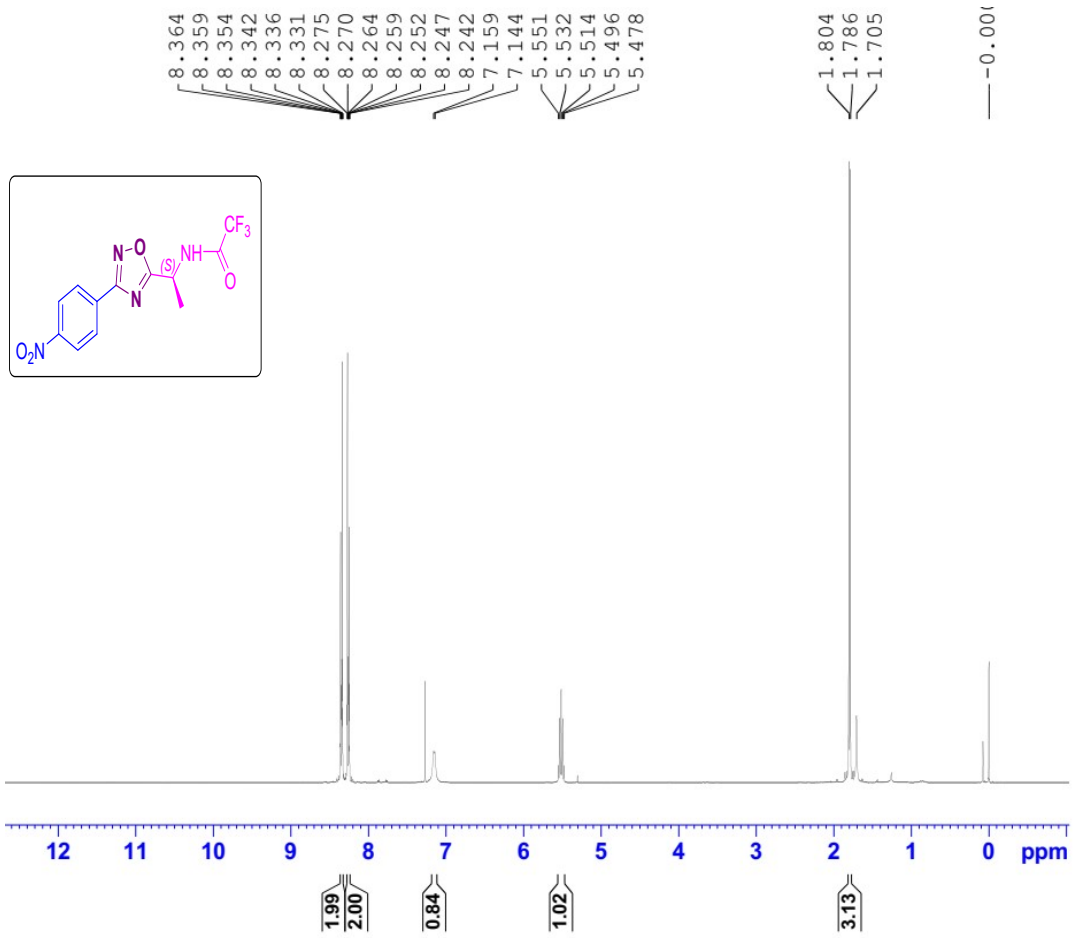


Fig. 31. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of compound **4ak**

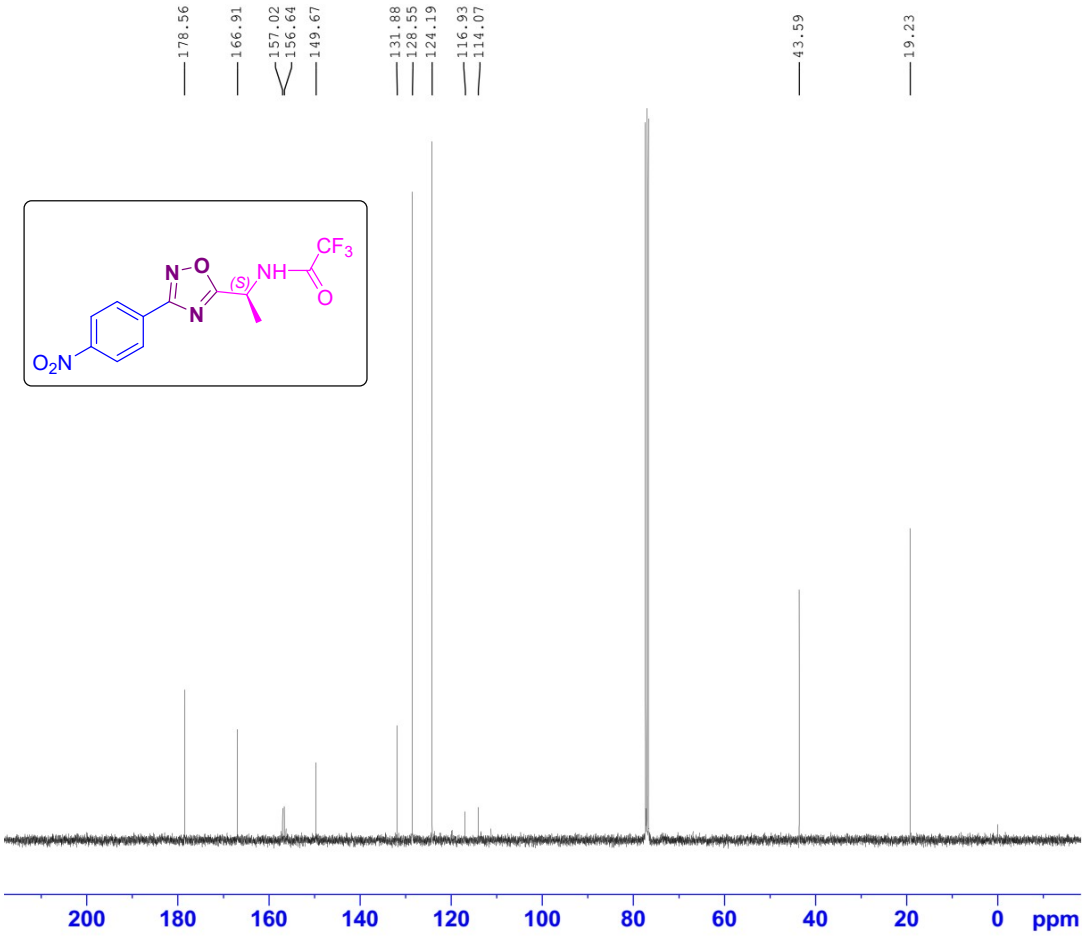


Fig.32. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of compound **4ak**

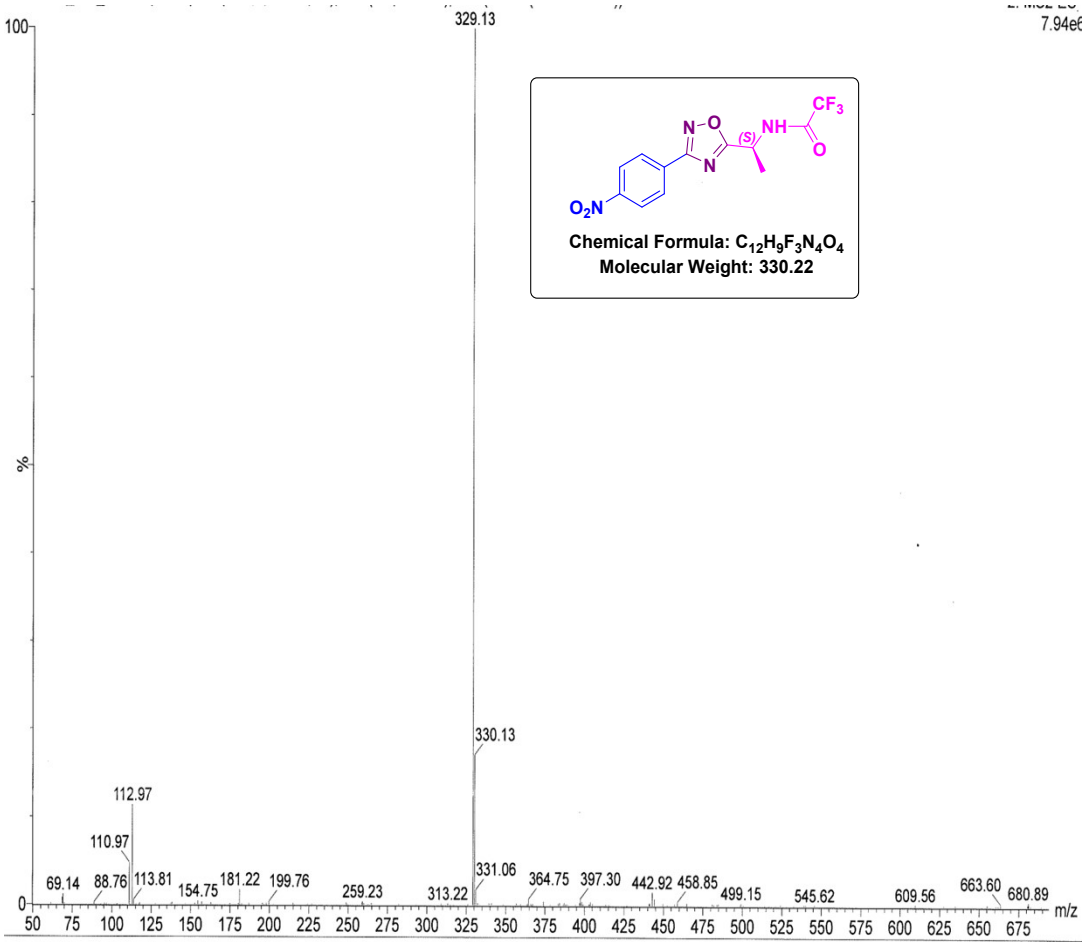


Fig. 33. Mass spectrum of compound **4ak**

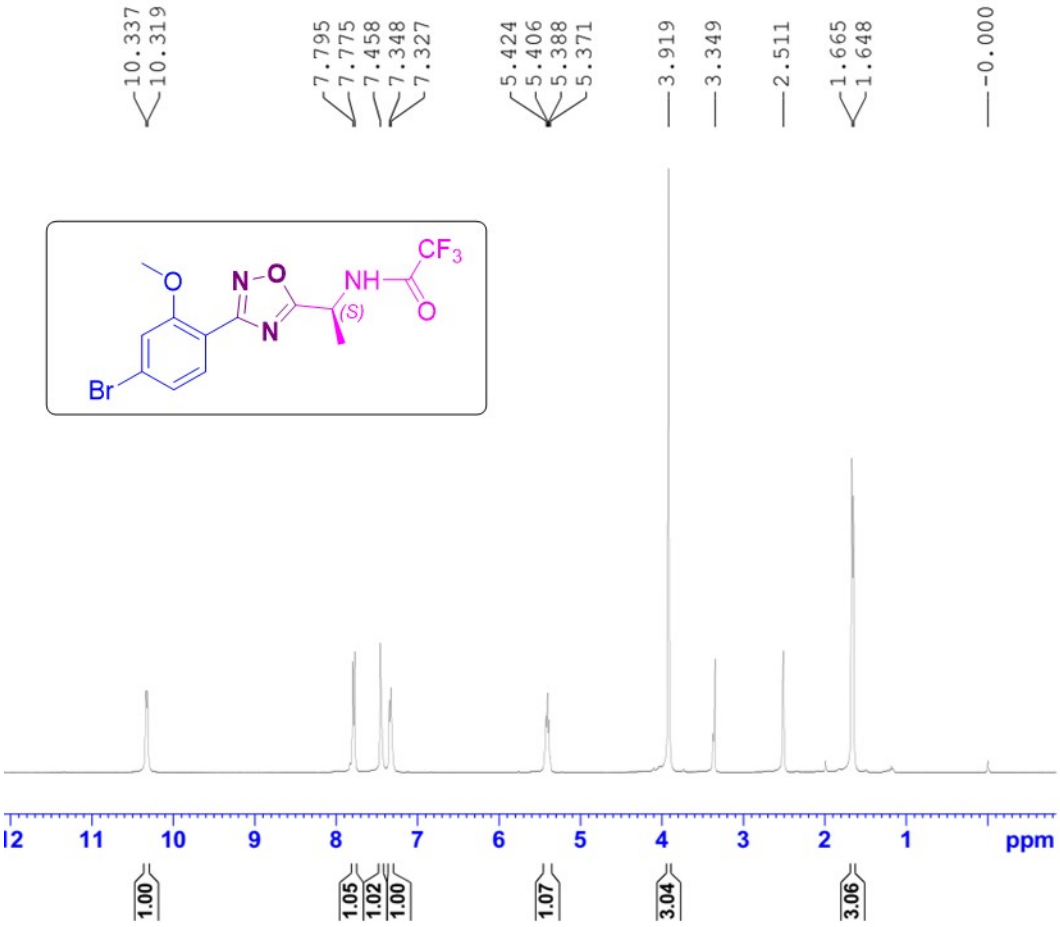


Fig. 34. [1]H NMR spectrum (DMSO-d_6, 400 MHz) of compound **4al**

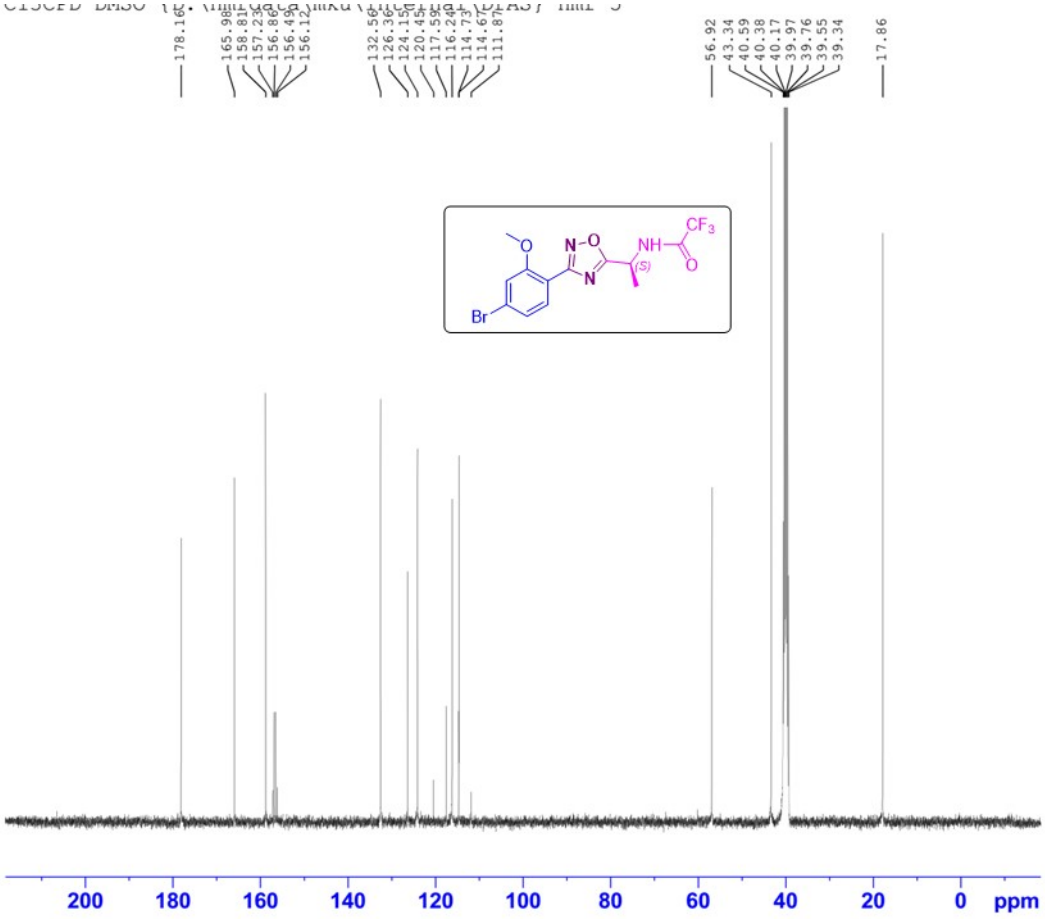


Fig. 35. ^{13}C NMR spectrum (DMSO-d_6, 100 MHz) of compound **4al**

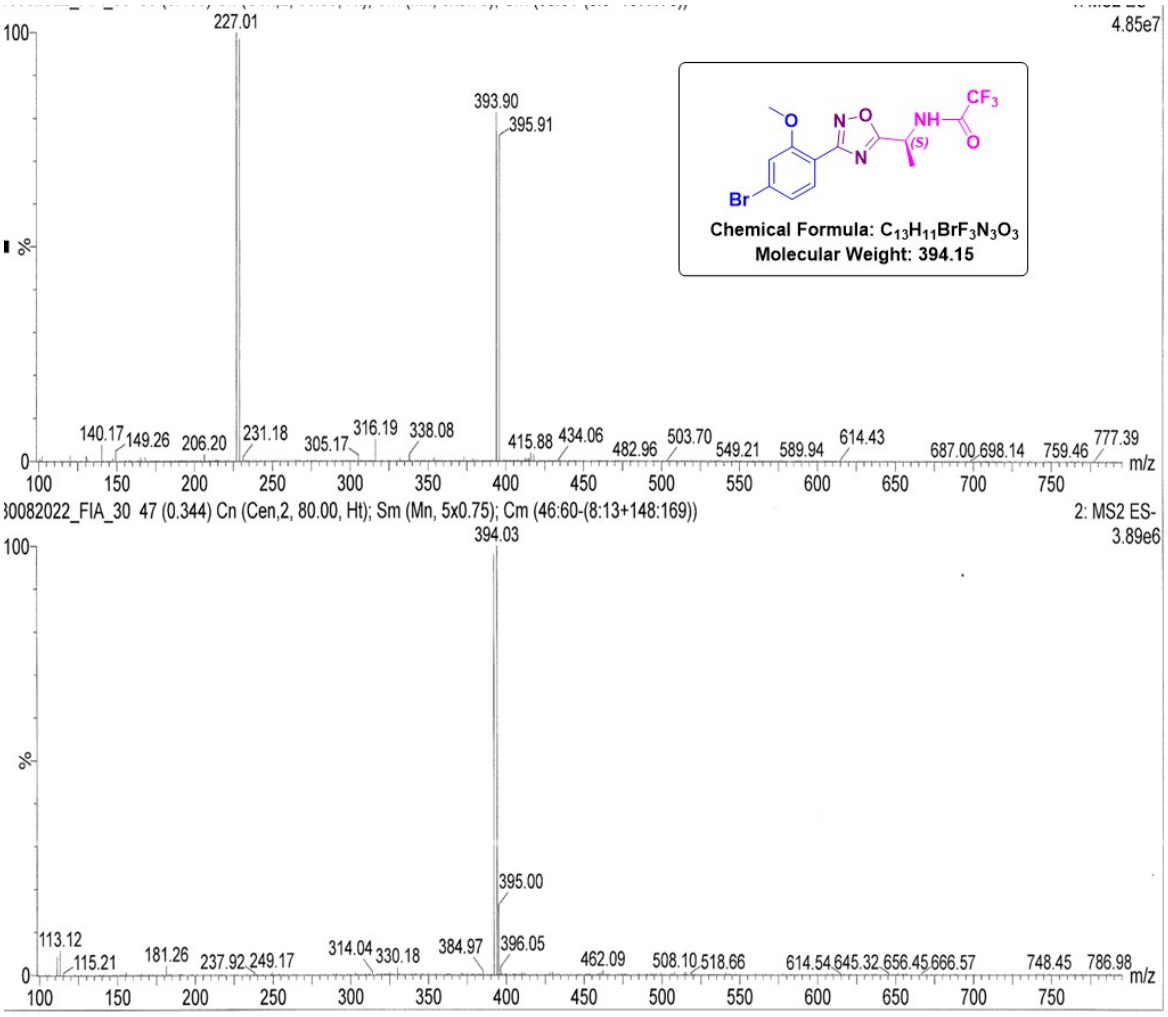


Fig. 36. Mass spectrum of compound **4al**

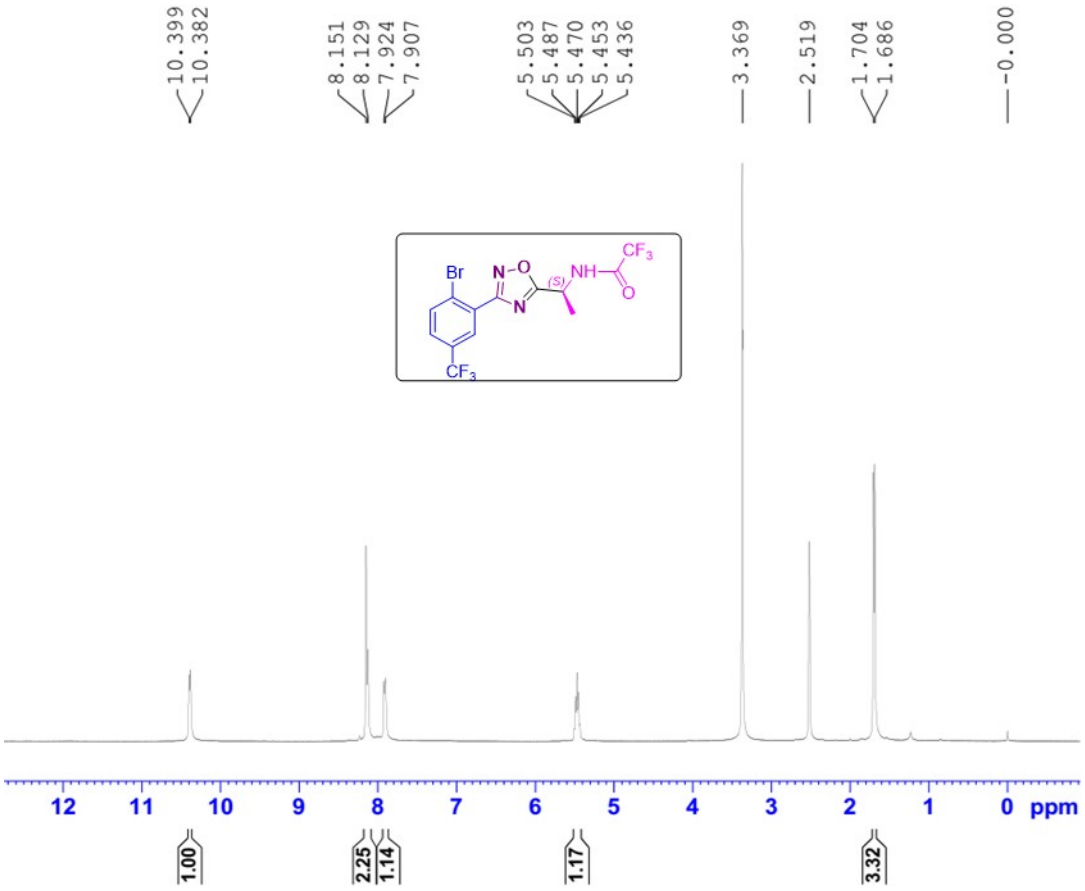


Fig. 37. ^{1}H NMR spectrum (DMSO-d_6, 400 MHz) of compound **4am**

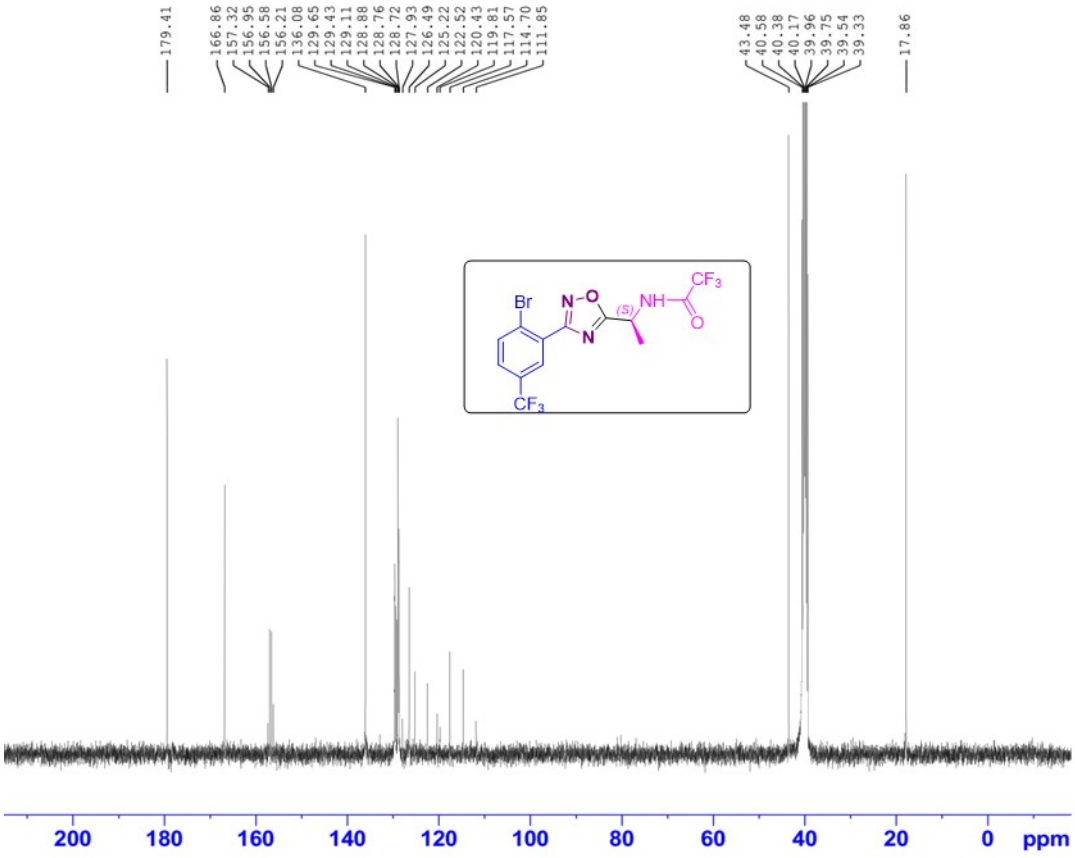


Fig. 38. ^{13}C NMR spectrum (DMSO-d_6, 100 MHz) of compound **4am**

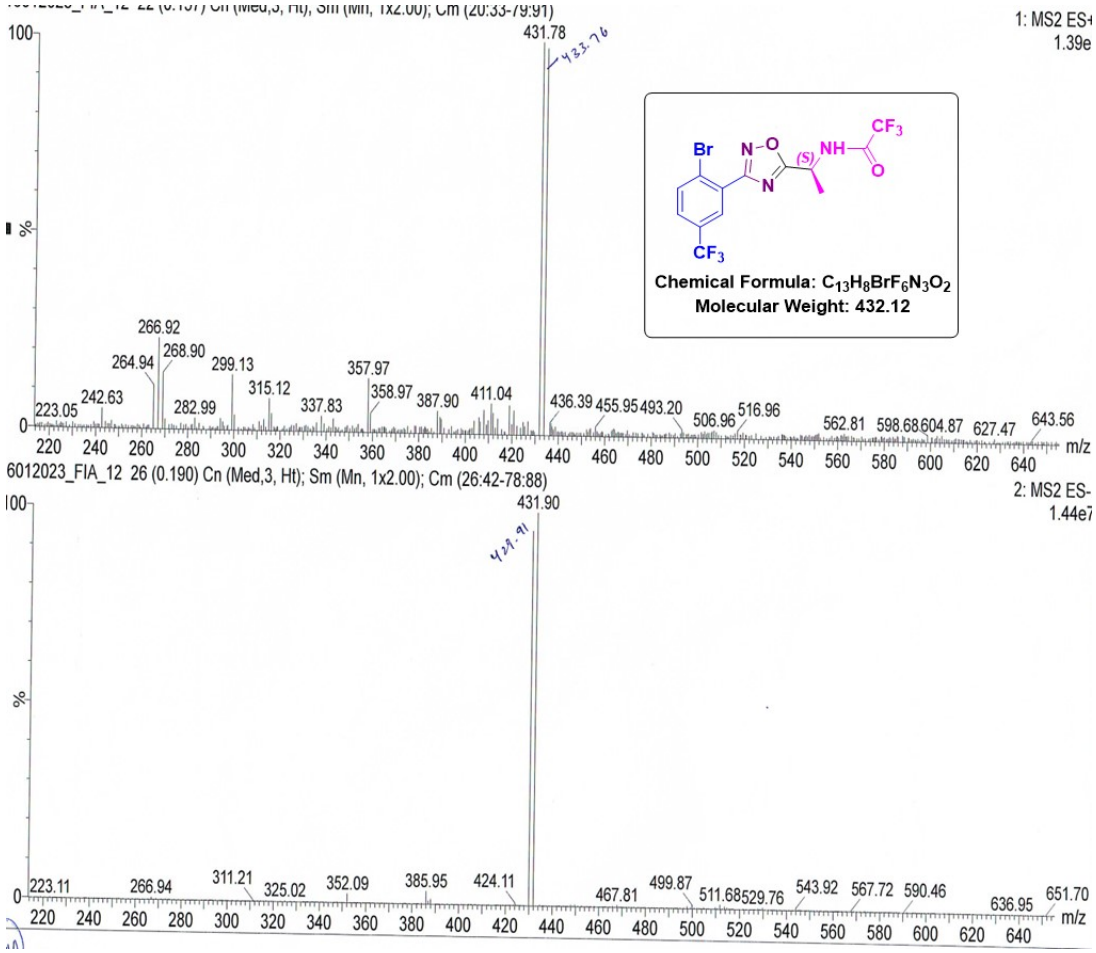


Fig. 39. Mass spectrum of compound **4am**

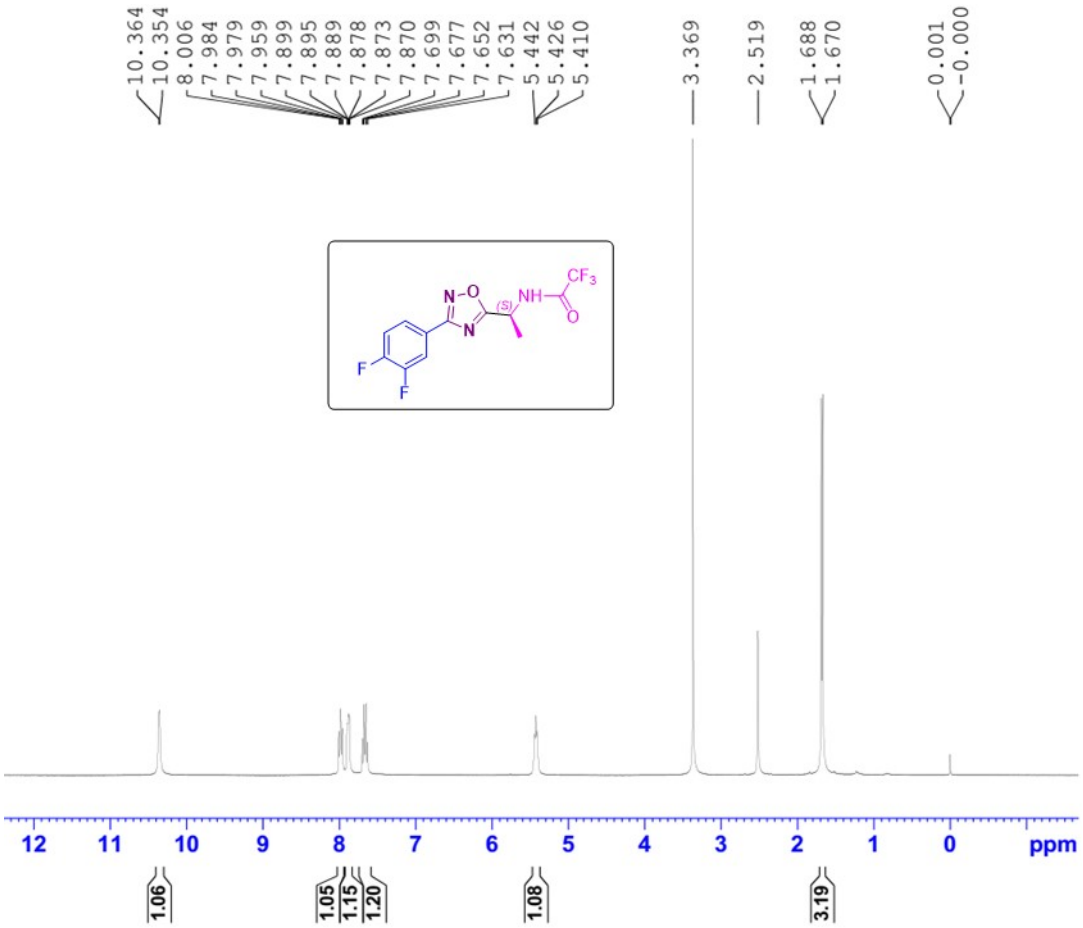


Fig. 40. [1]H NMR spectrum (DMSO-d_6, 400 MHz) of compound **4an**

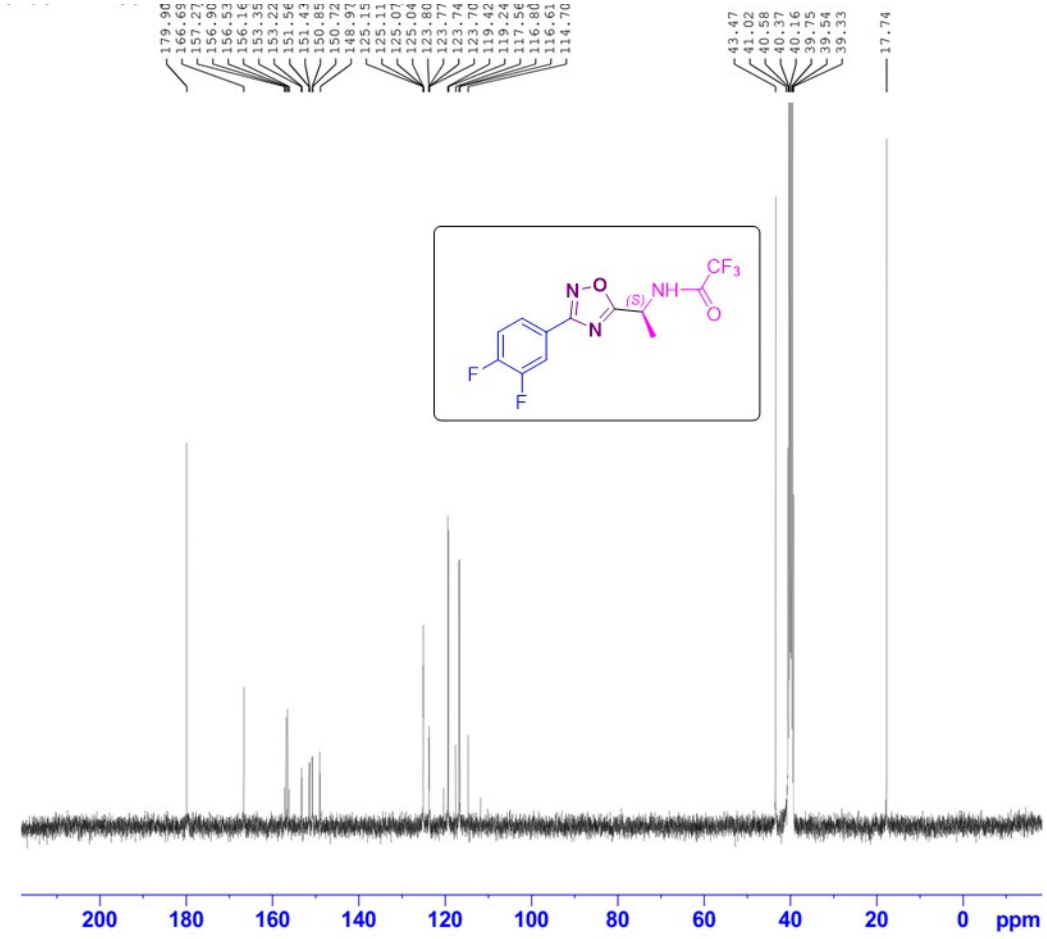


Fig. 41. ^{13}C NMR spectrum (DMSO-d_6, 100 MHz) of compound **4an**

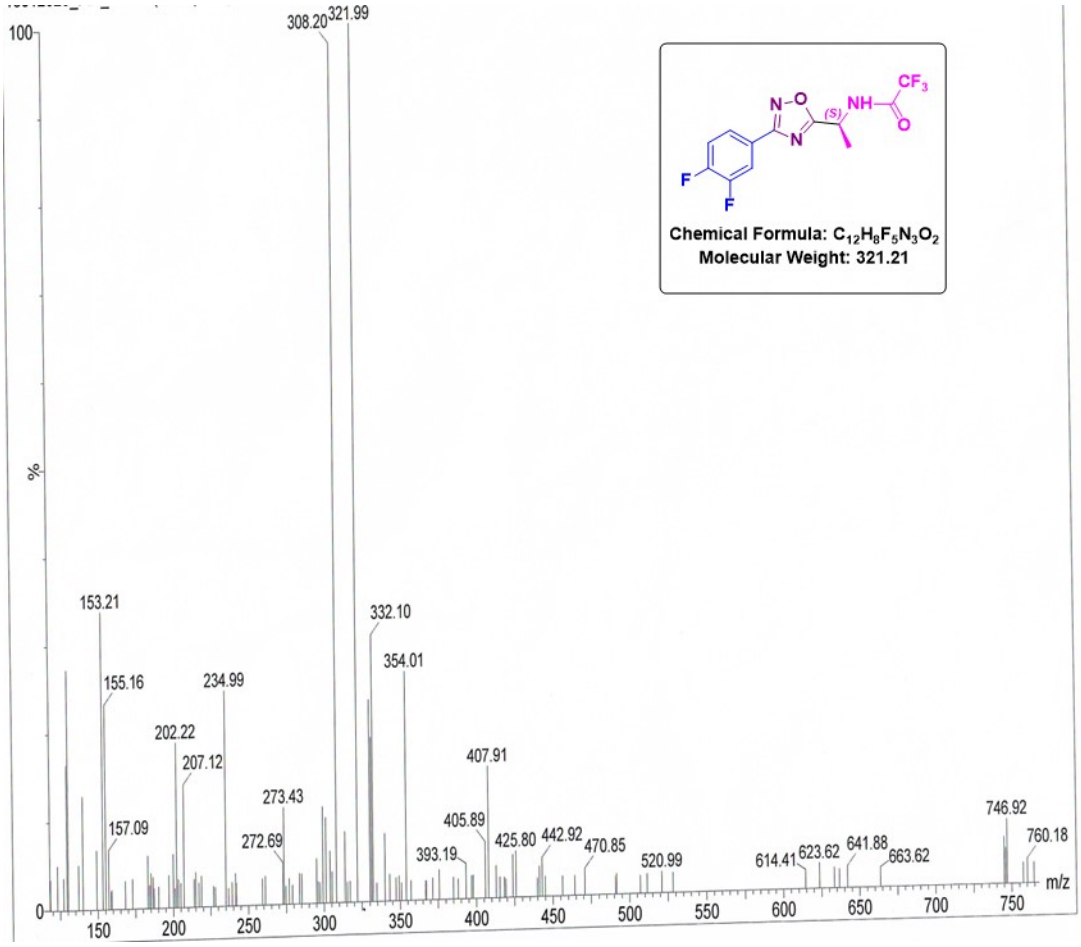


Fig. 42. Mass spectrum of compound **4an**

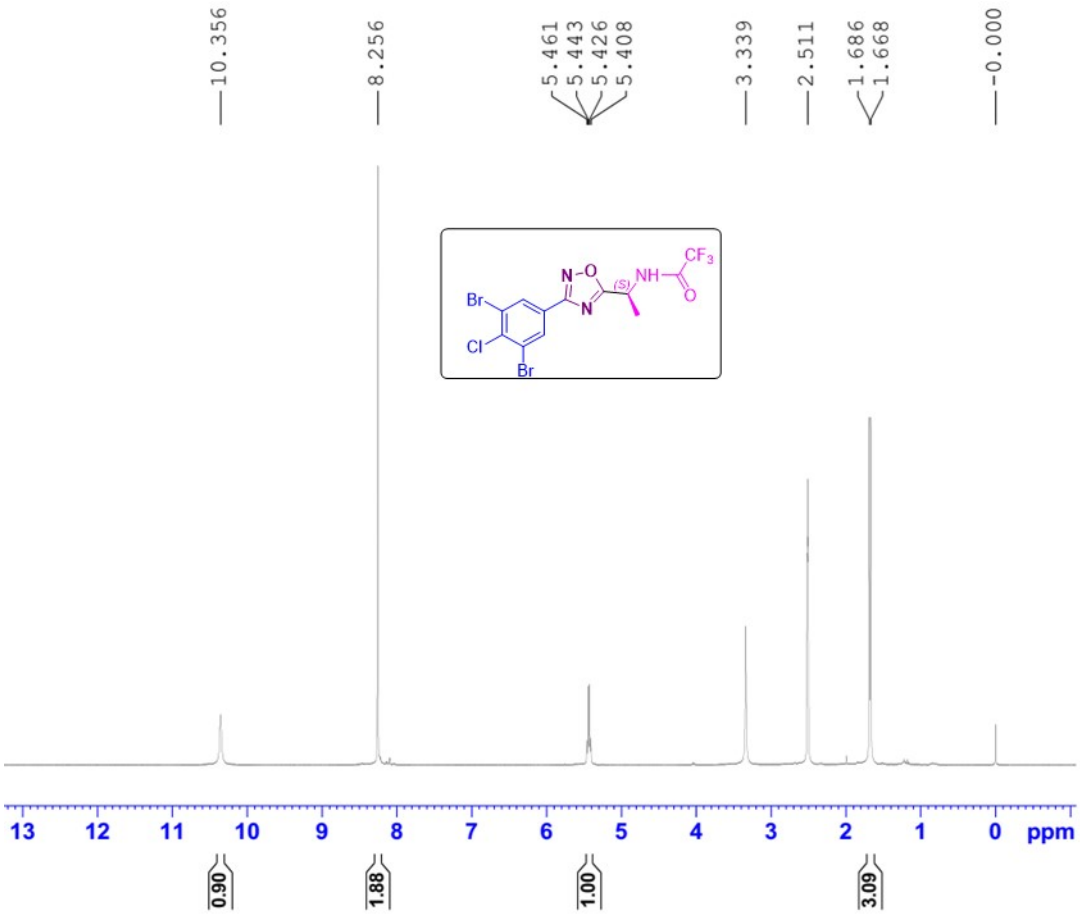


Fig. 43. ^{1}H NMR spectrum (DMSO-d_6, 400 MHz) of compound **4ae**

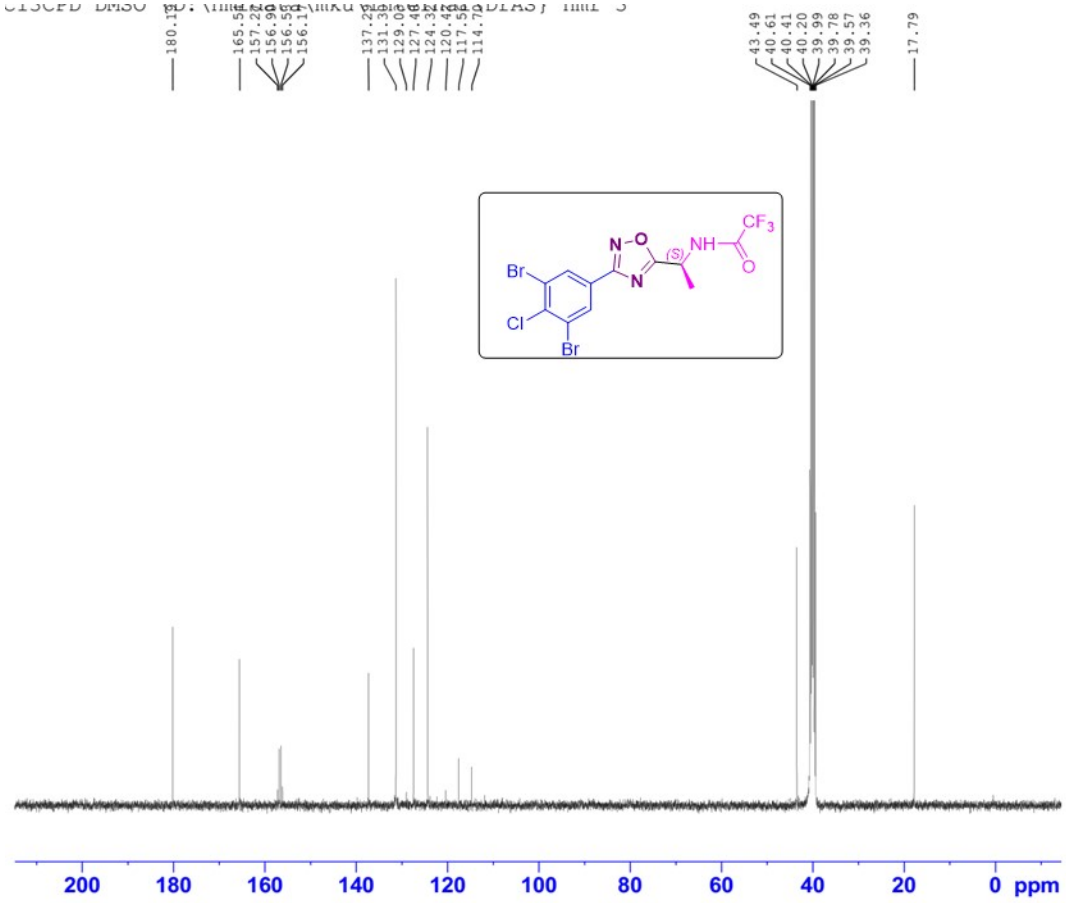


Fig. 44. ^{13}C NMR spectrum (DMSO-d_6, 100 MHz) of compound **4ae**

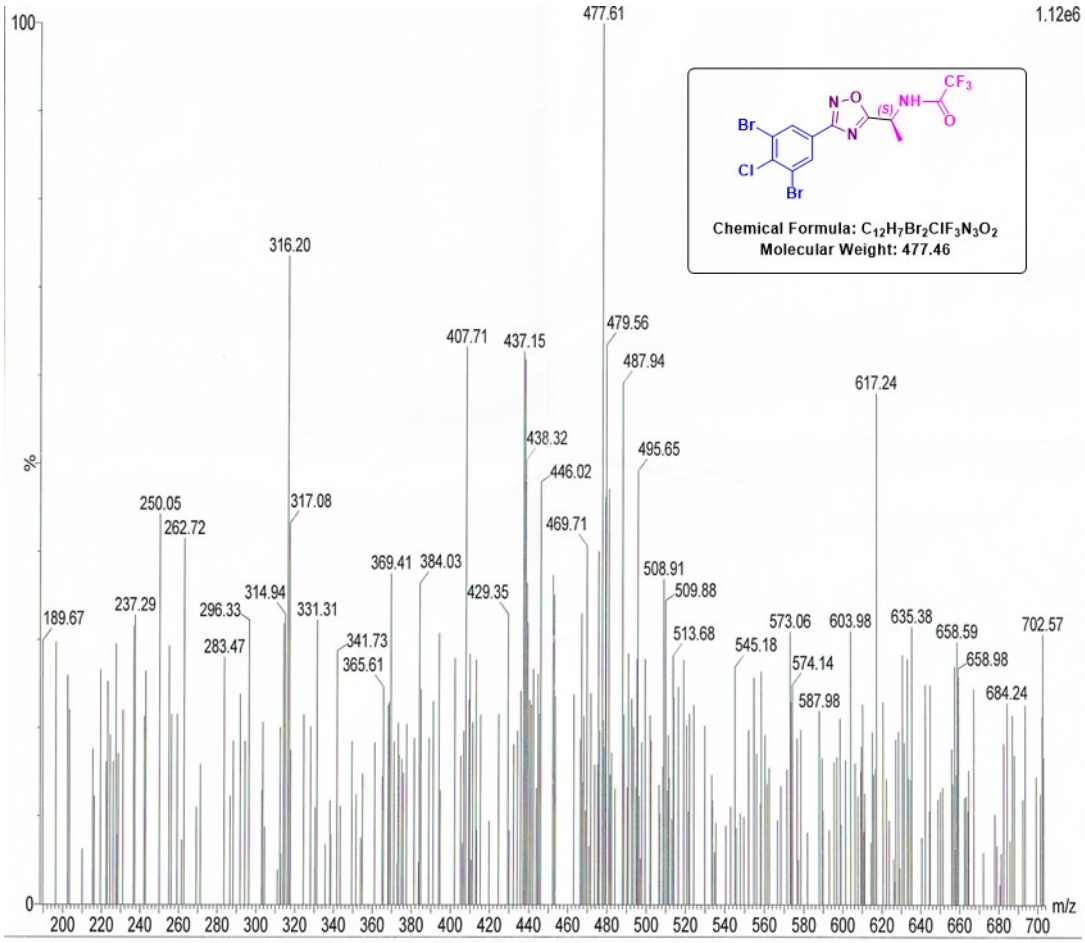


Fig. 45. Mass spectrum of compound **4ao**

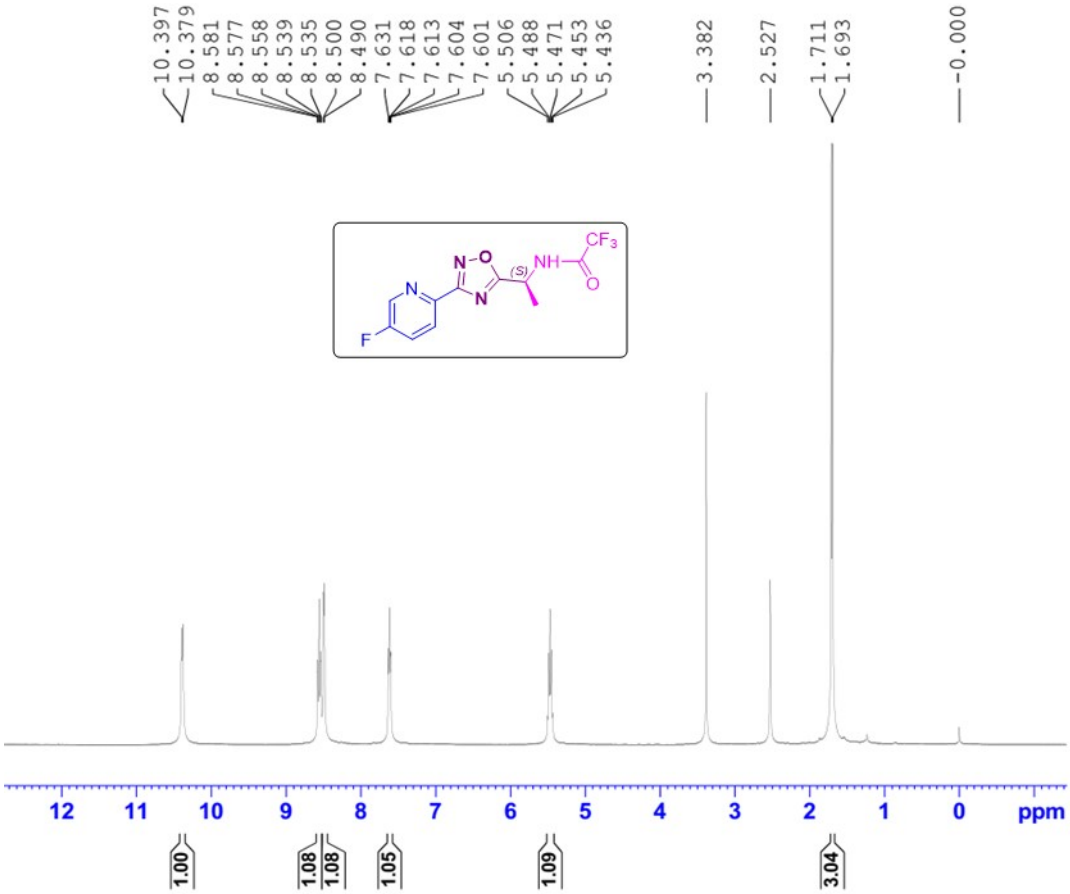


Fig. 46. ^{1}H NMR spectrum (DMSO-d_6, 400 MHz) of compound **4ap**

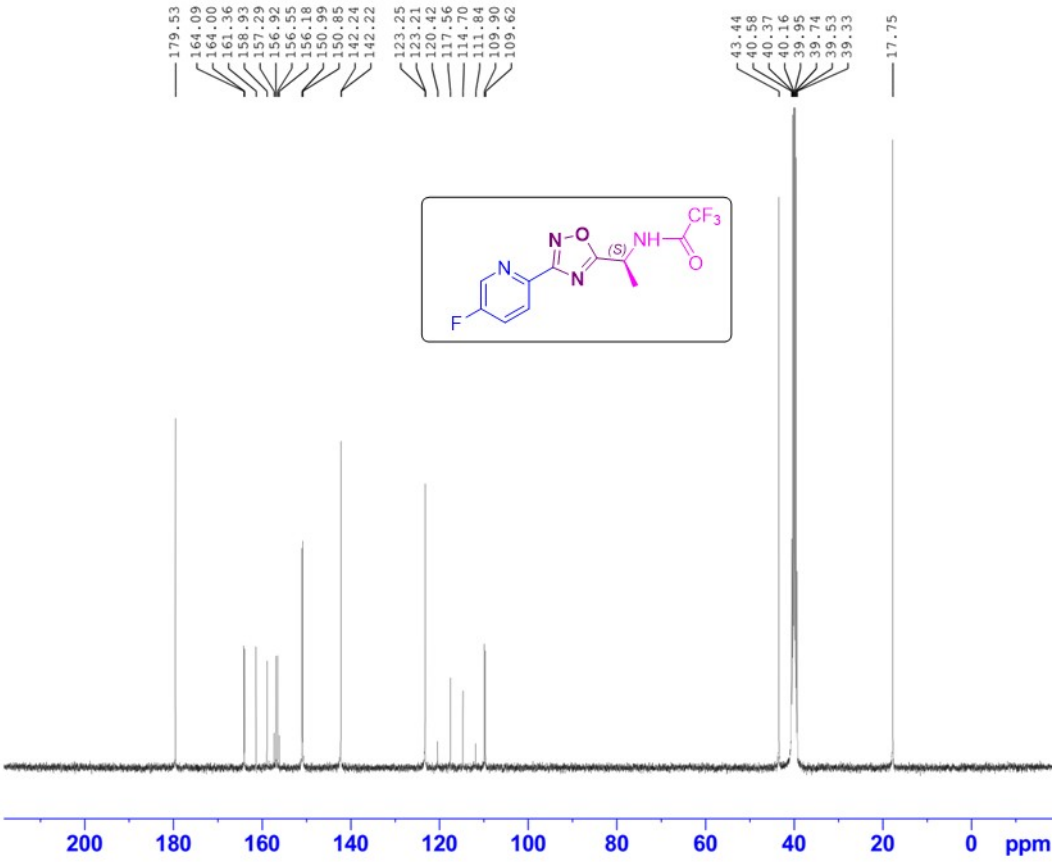


Fig. 47. ^{13}C NMR spectrum (DMSO-d_6, 100 MHz) of compound **4ap**

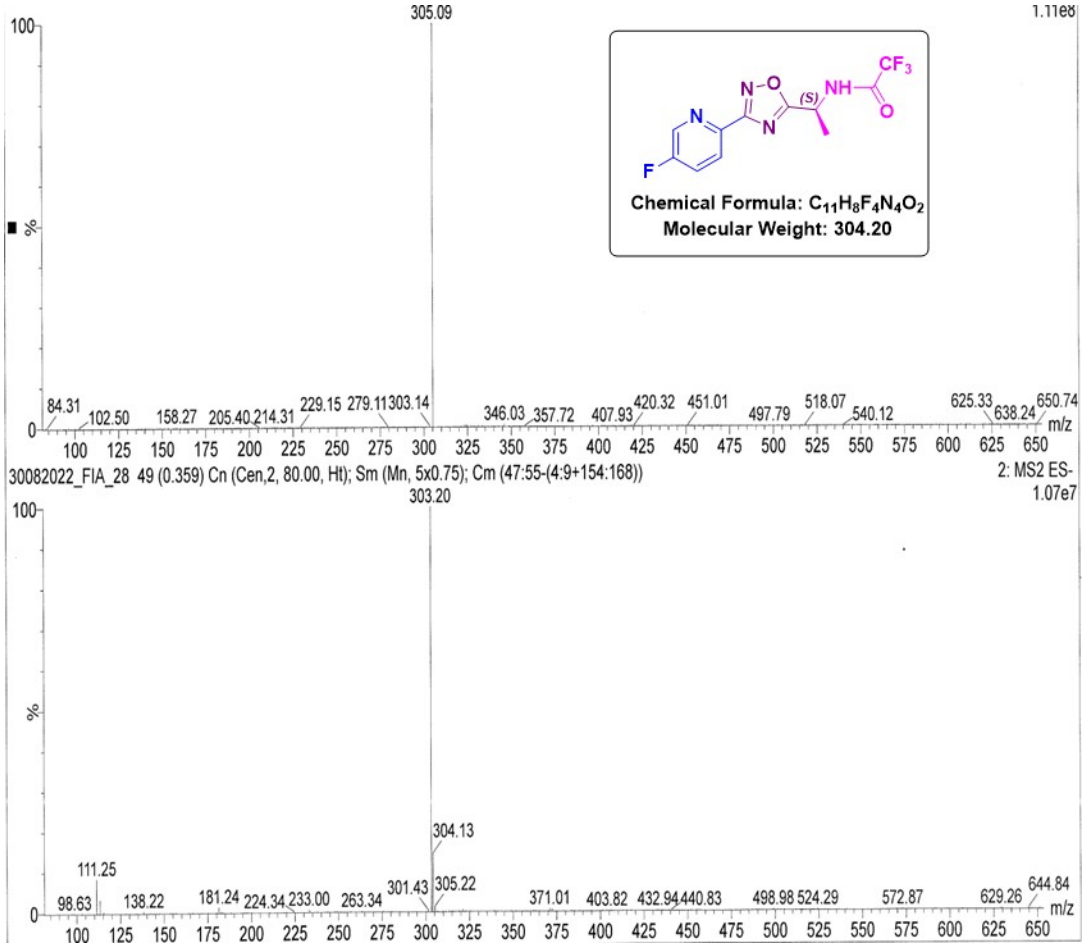


Fig. 48. Mass spectrum of compound **4ap**

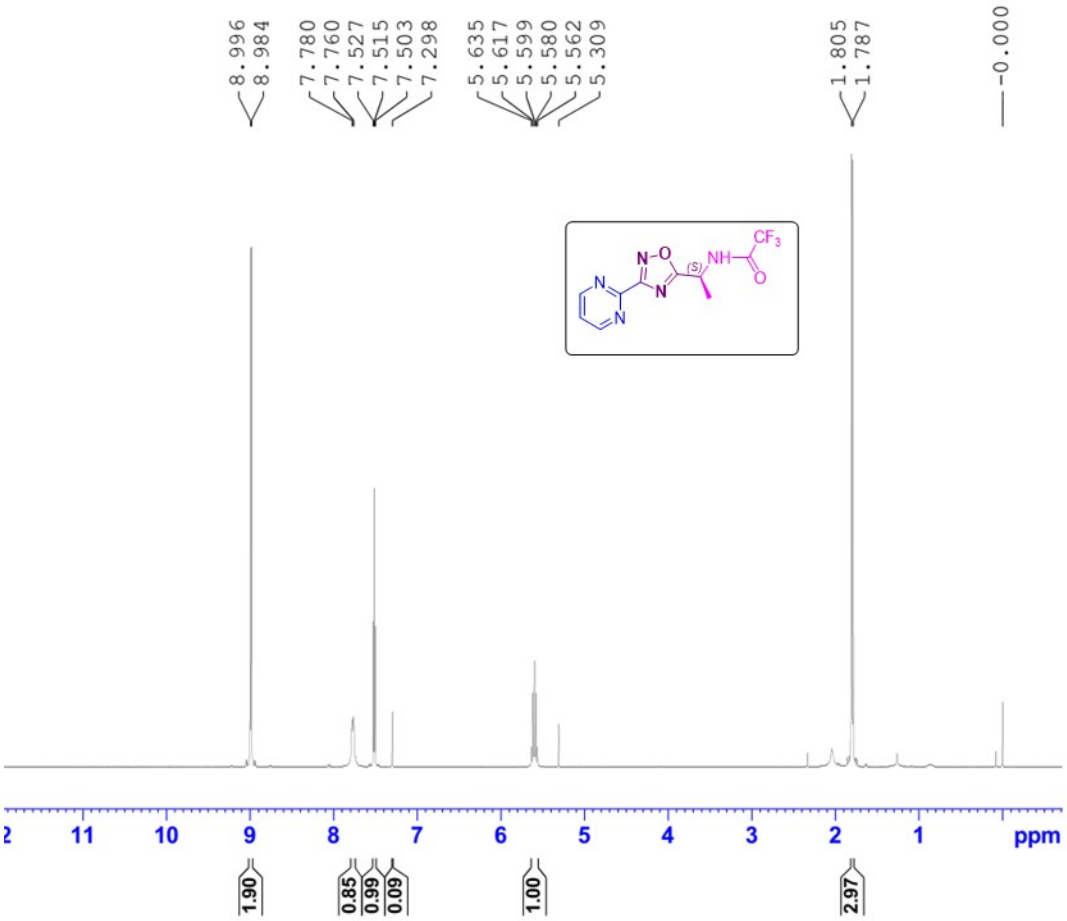


Fig. 49. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of compound **4aq**

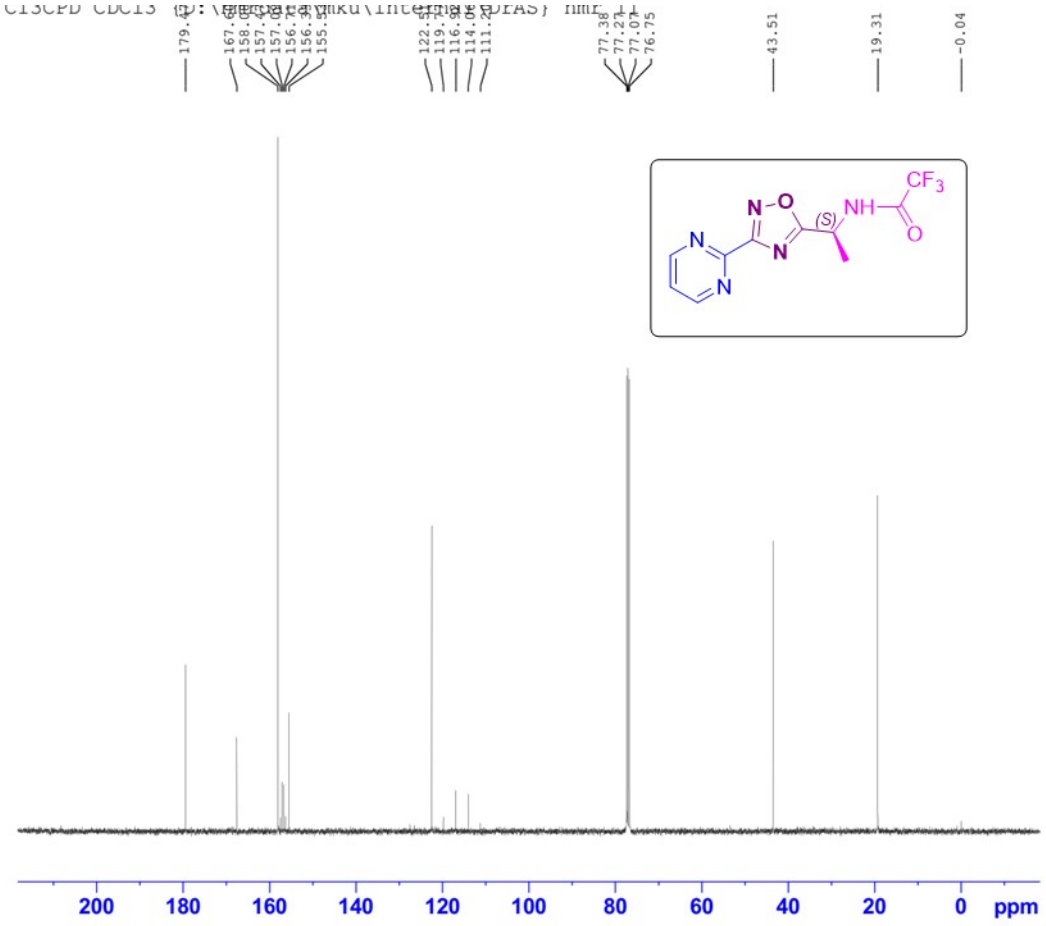


Fig. 50. ^{13}C NMR spectrum ($CDCl_3$, 400 MHz) of compound **4aq**

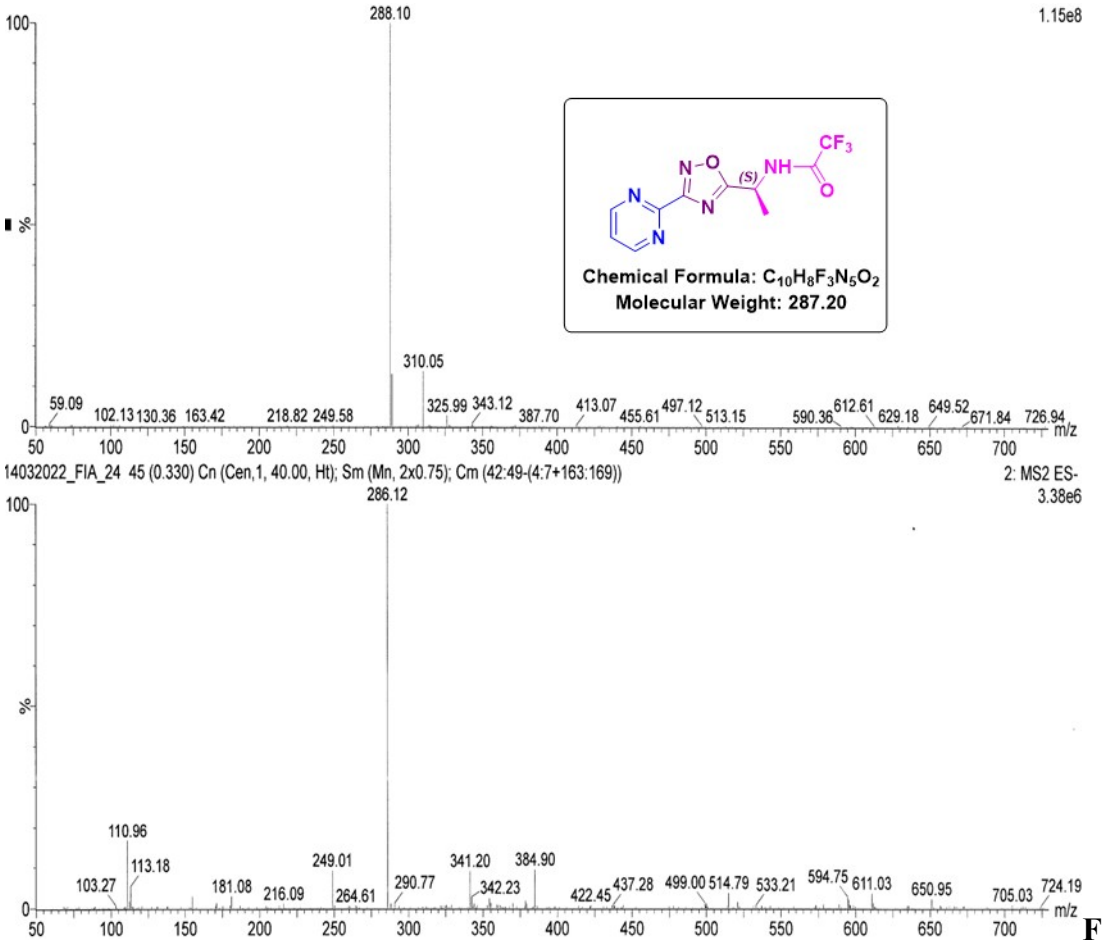


Fig. 51. Mass spectrum of compound **4aq**

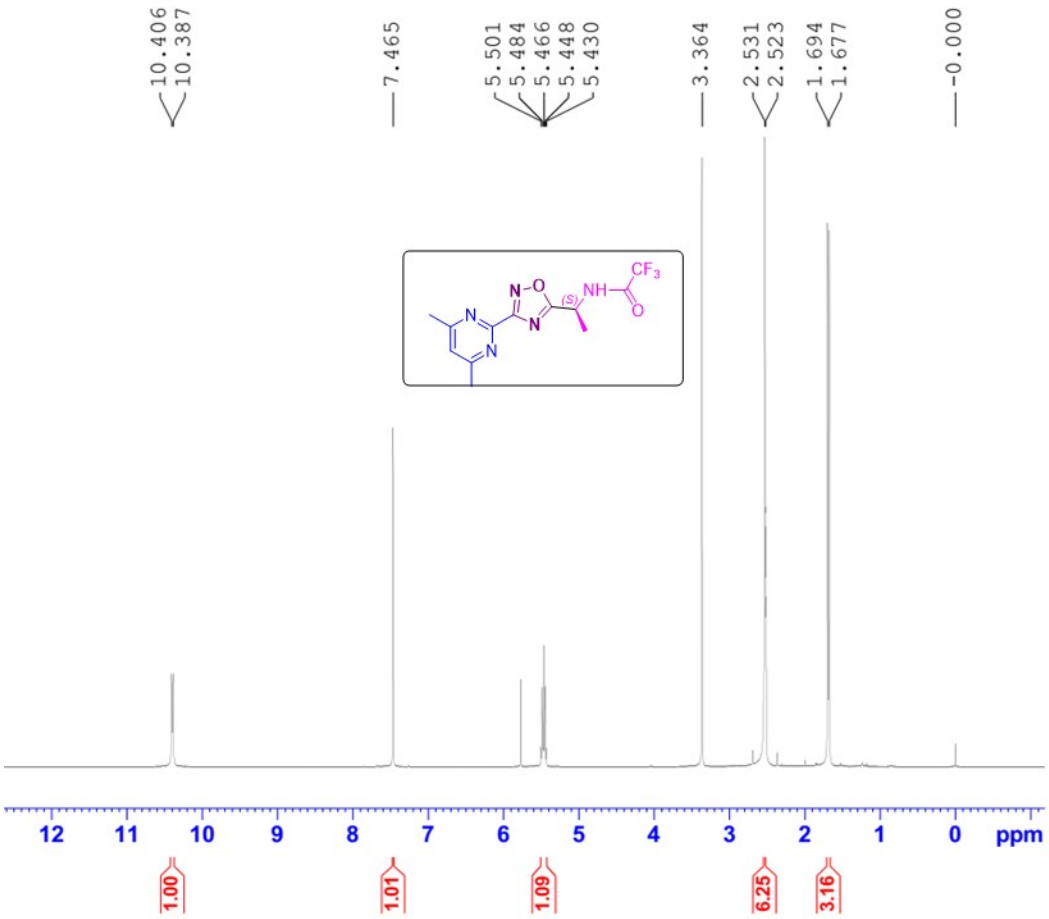


Fig. 52. ^{1}H NMR spectrum (DMSO-d_6, 400 MHz) of compound **4ar**

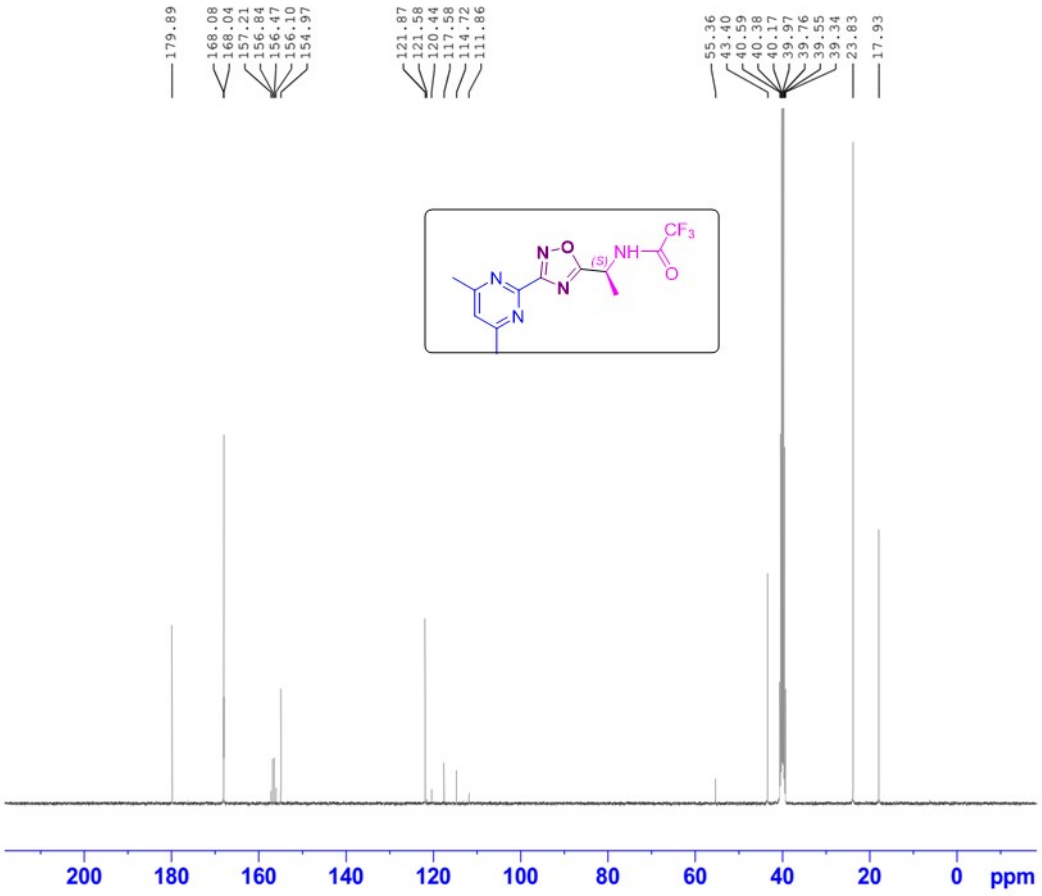
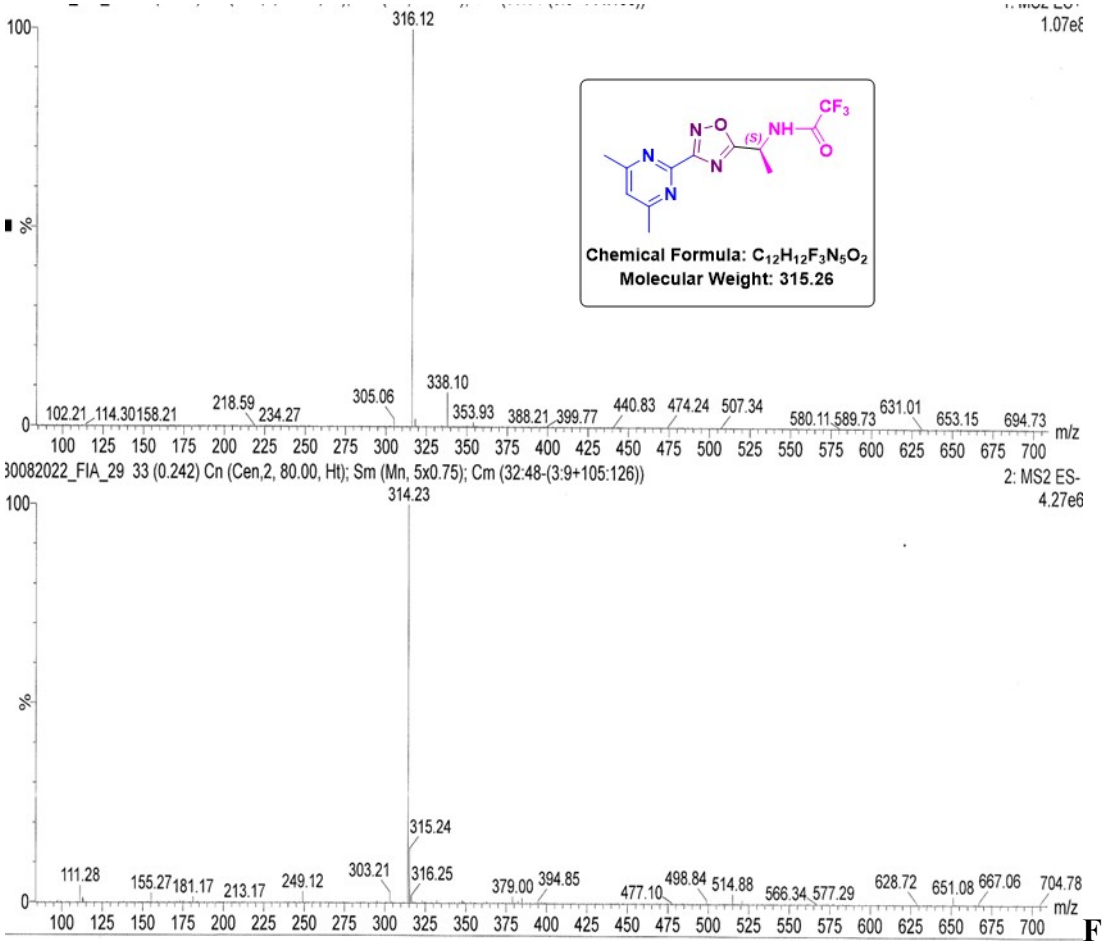


Fig. 53. ^{13}C NMR spctrum (DMSO-d_6, 100 MHz) of compound **4ar**



ig. 54. Mass spectrum of compound **4ar**

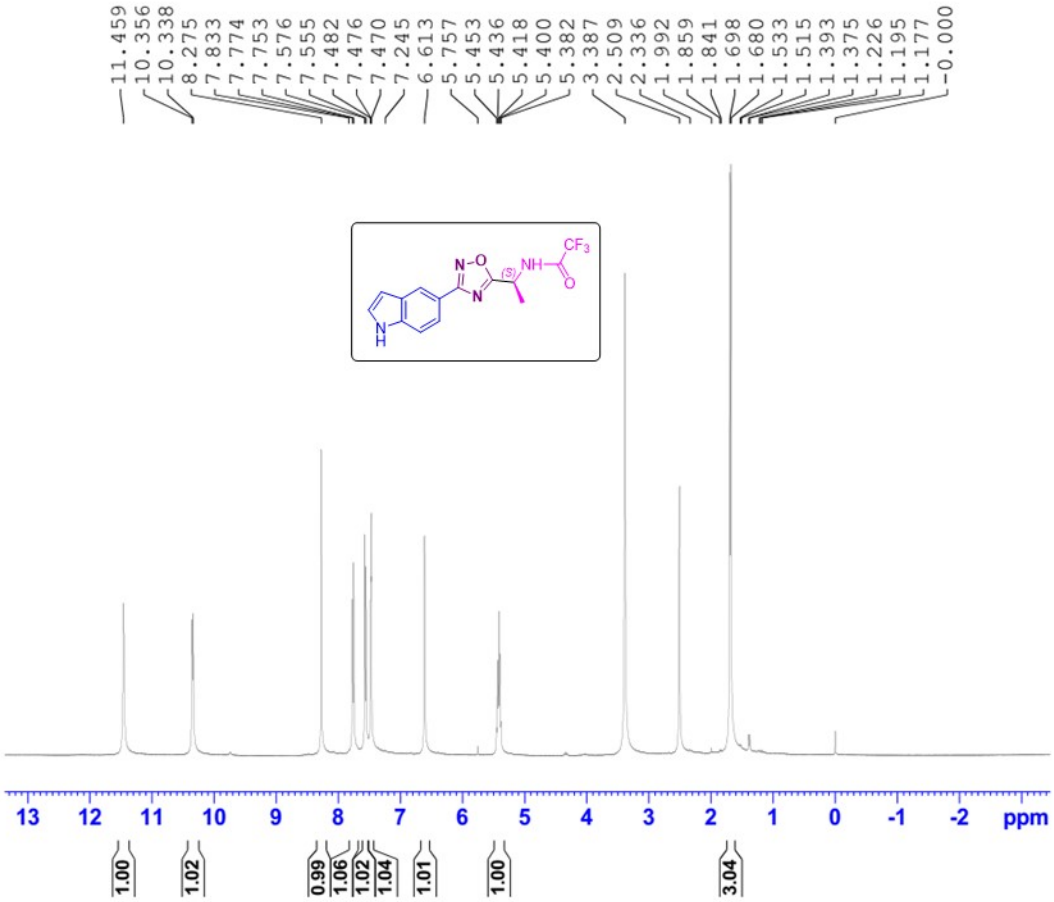


Fig. 55. ^{1}H NMR spectrum (DMSO-d_6, 400 MHz) of compound **4as**

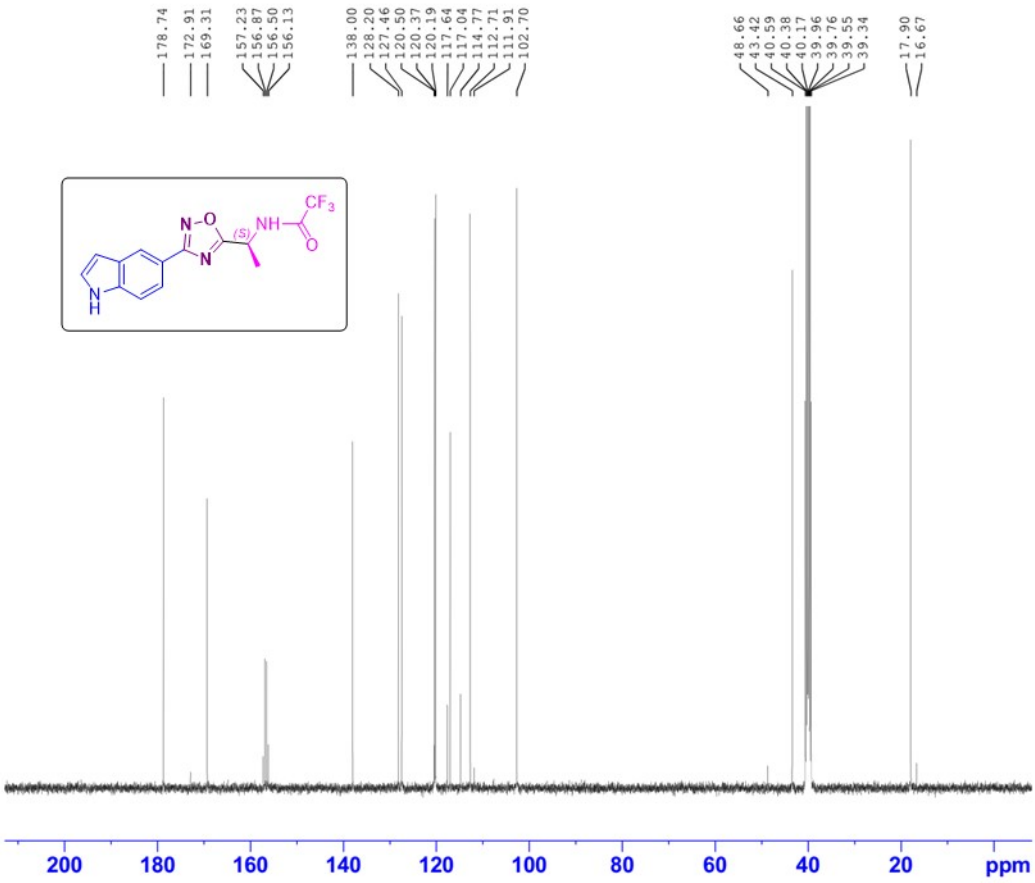


Fig. 56. ^{13}C NMR spectrum (DMSO-d_6, 100 MHz) of compound **4as**

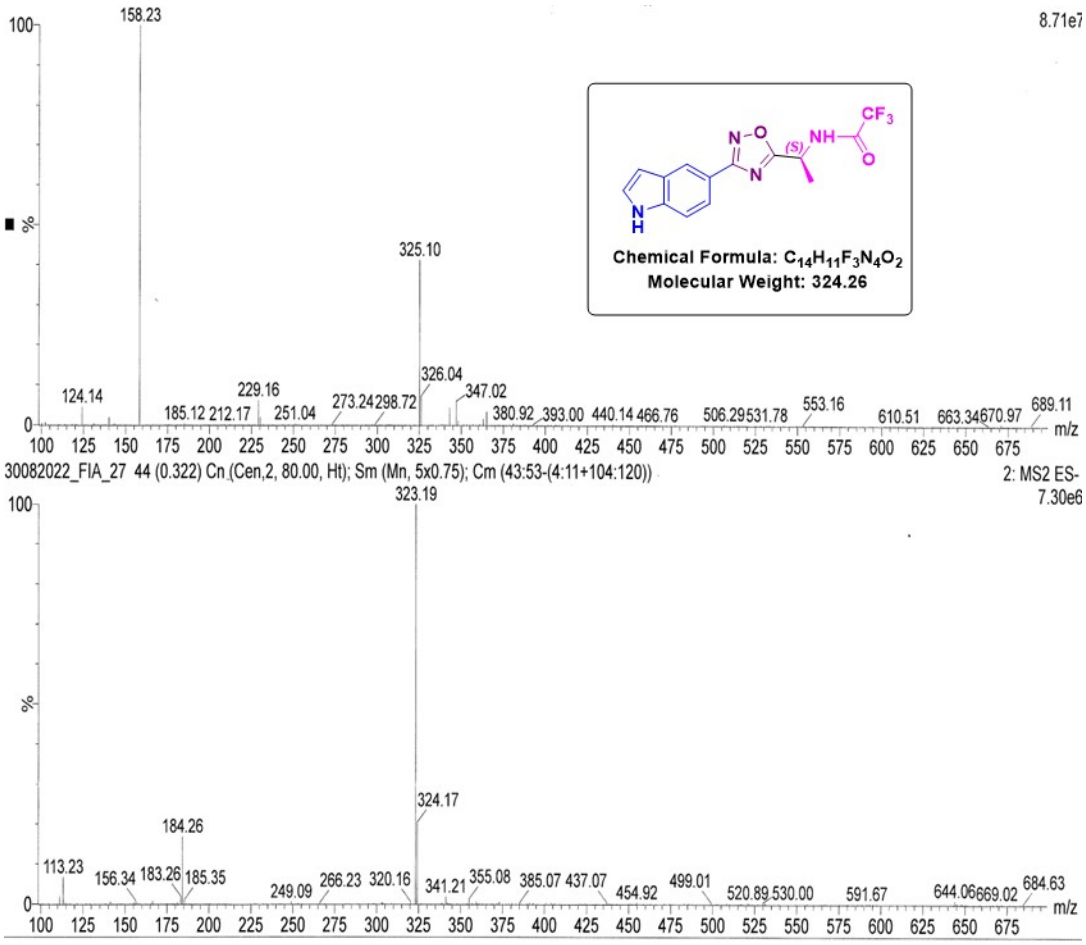


Fig. 57. Mass spectrum of compound **4as**

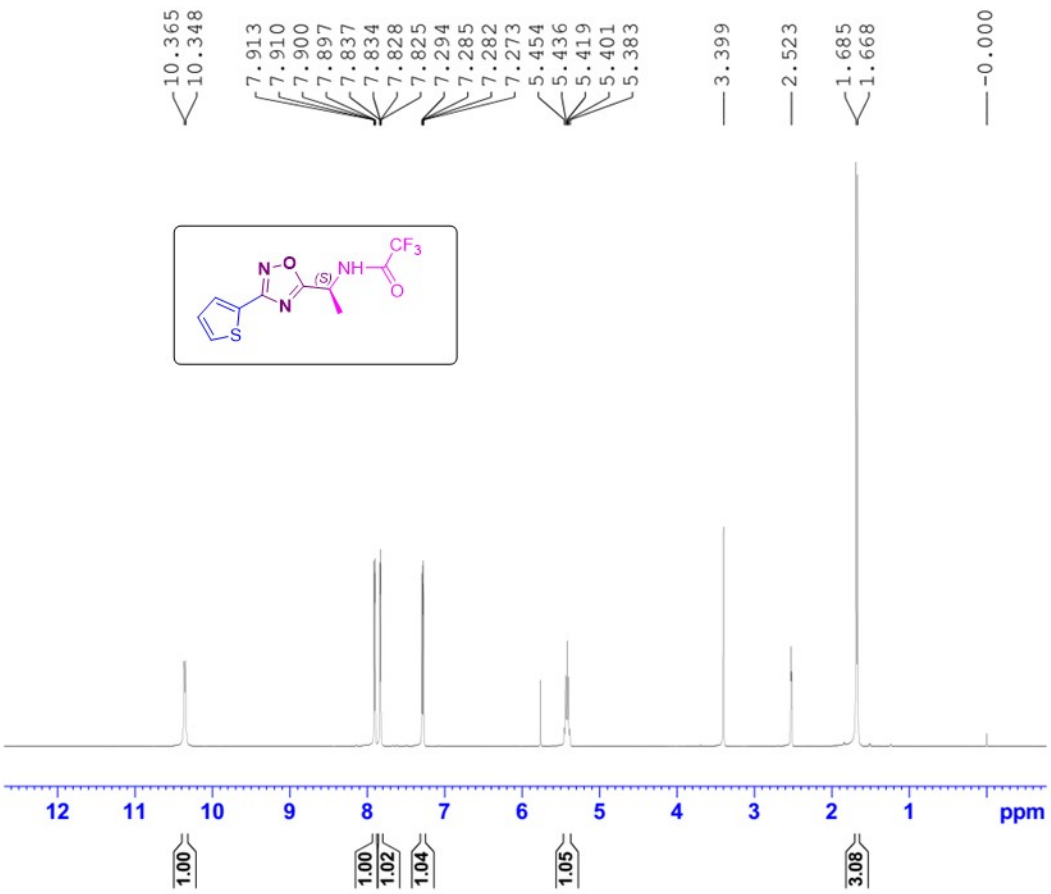


Fig. 58. ^{1}H NMR spectrum (DMSO-d_6, 400 MHz) of compound **4at**

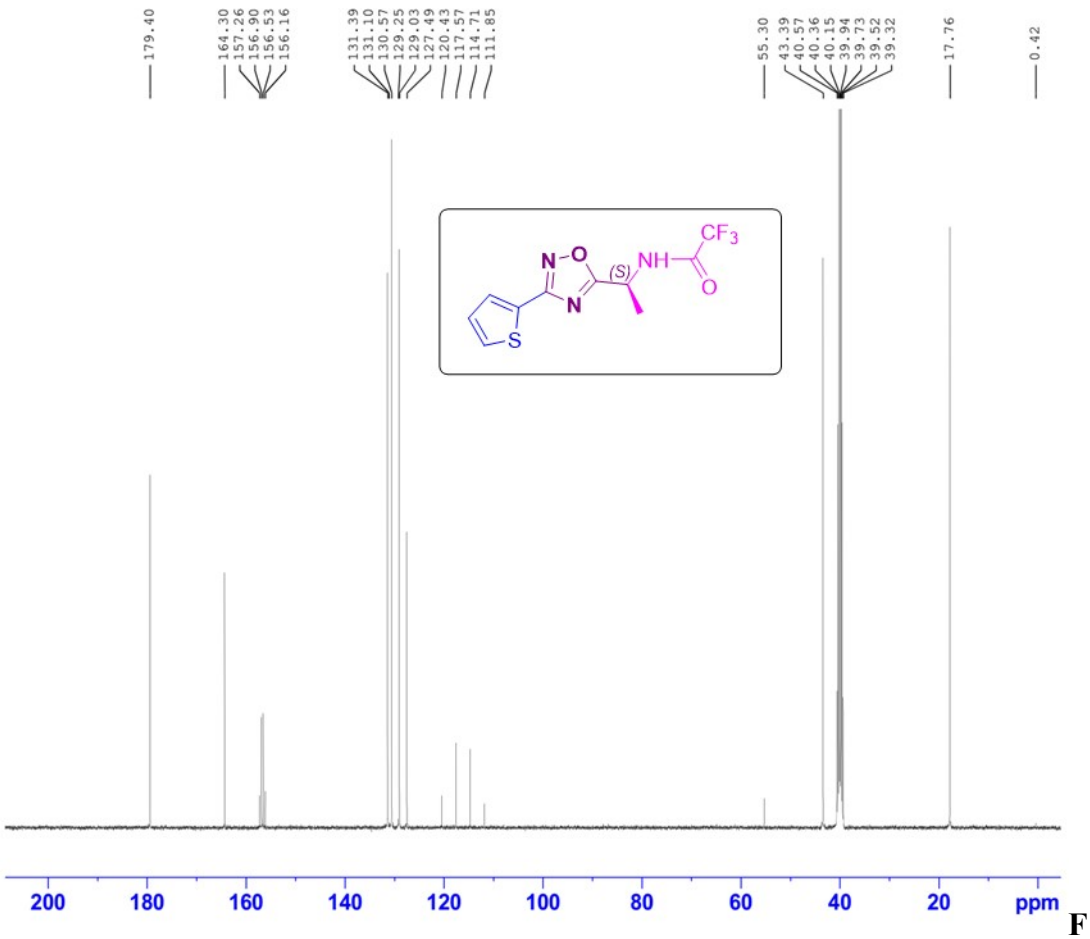


Fig. 59. ^{13}C NMR spectrum (DMSO-d_6, 100 MHz) of compound **4at**

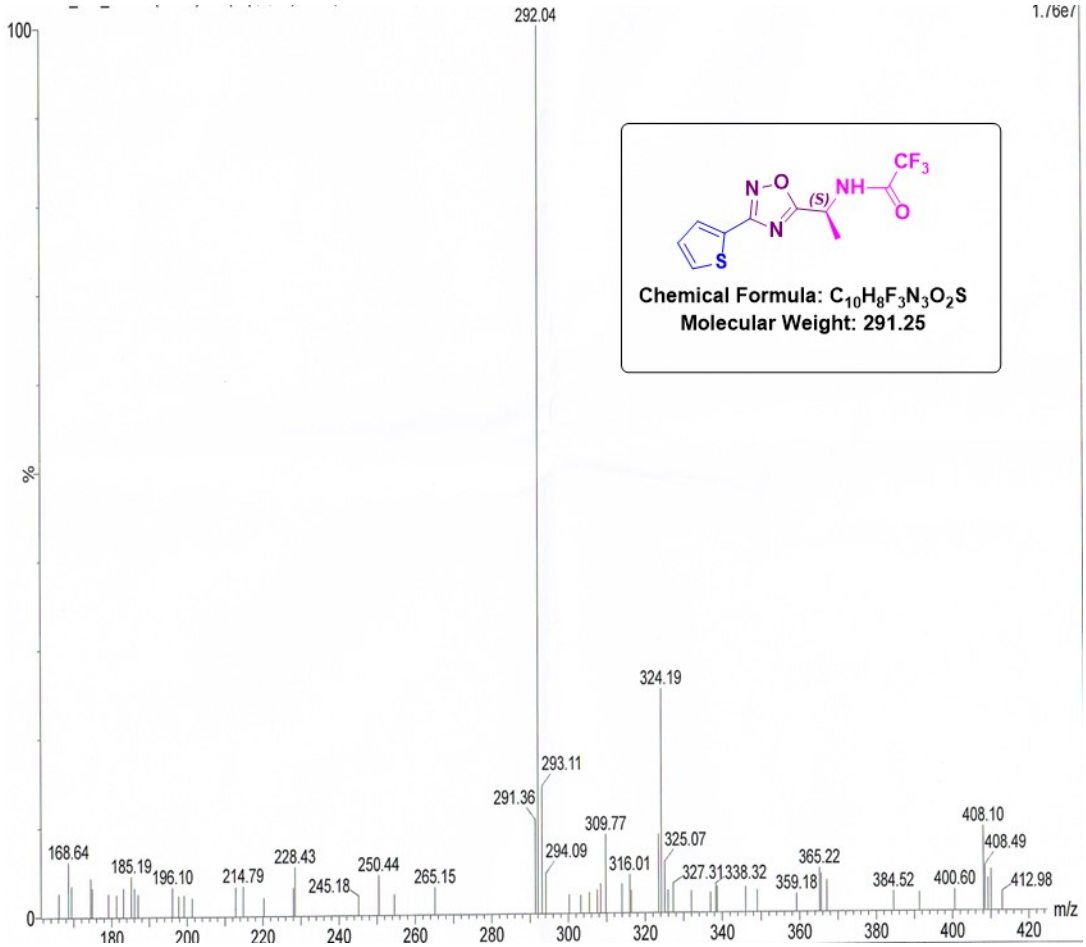


Fig. 60. Mass spectrum of compound **4at**

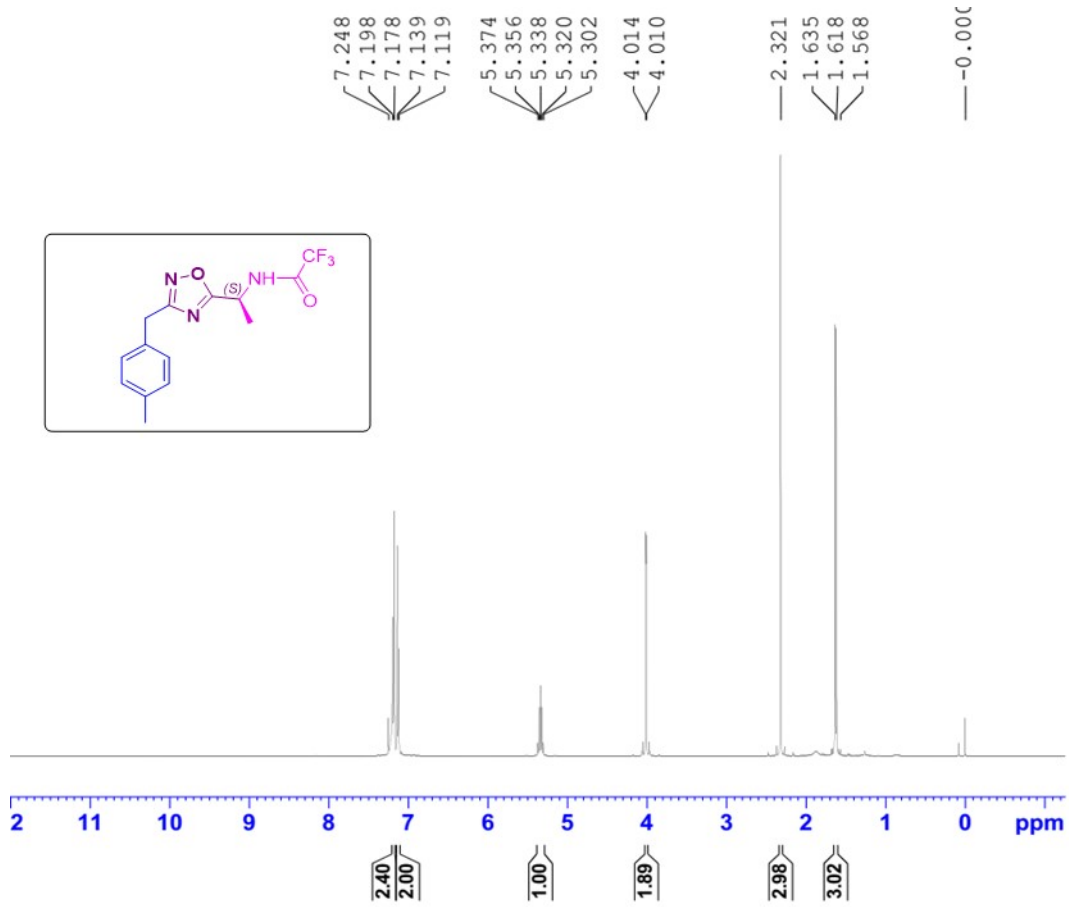


Fig. 61. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of compound **4au**

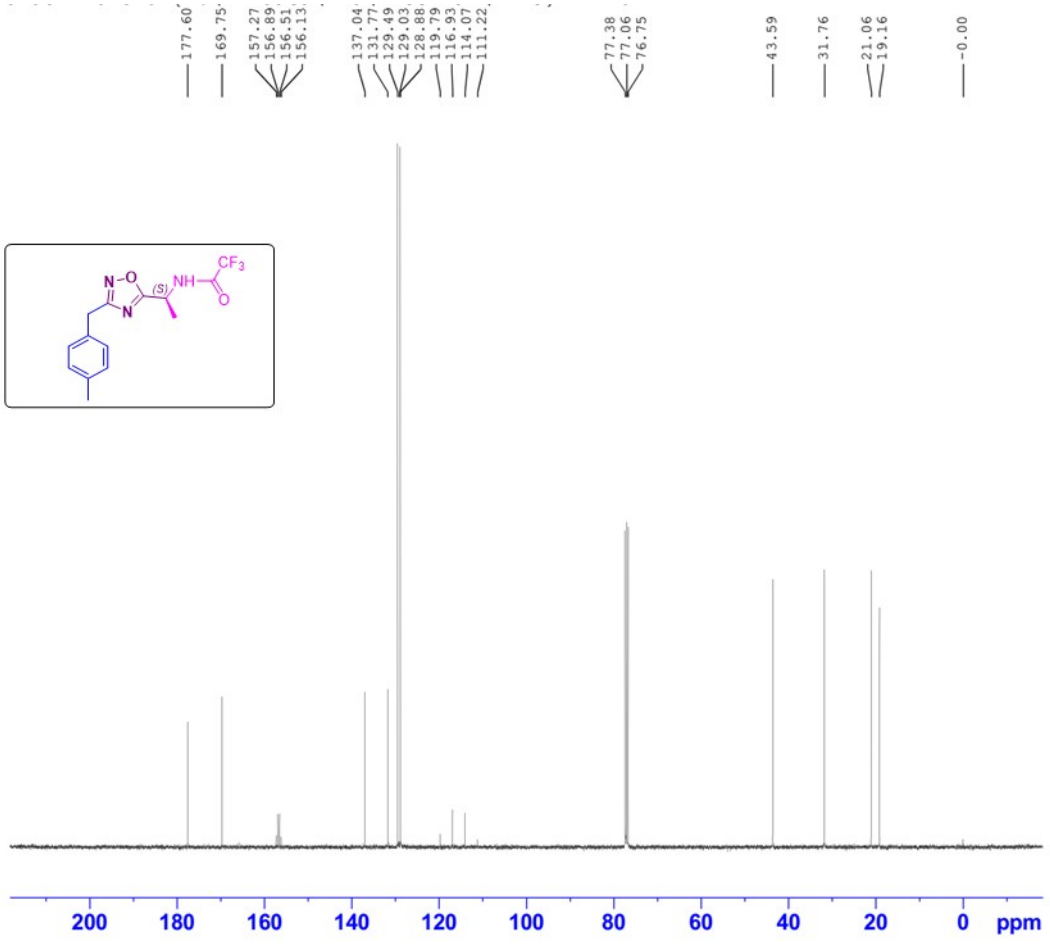


Fig.62. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of compound **4au**

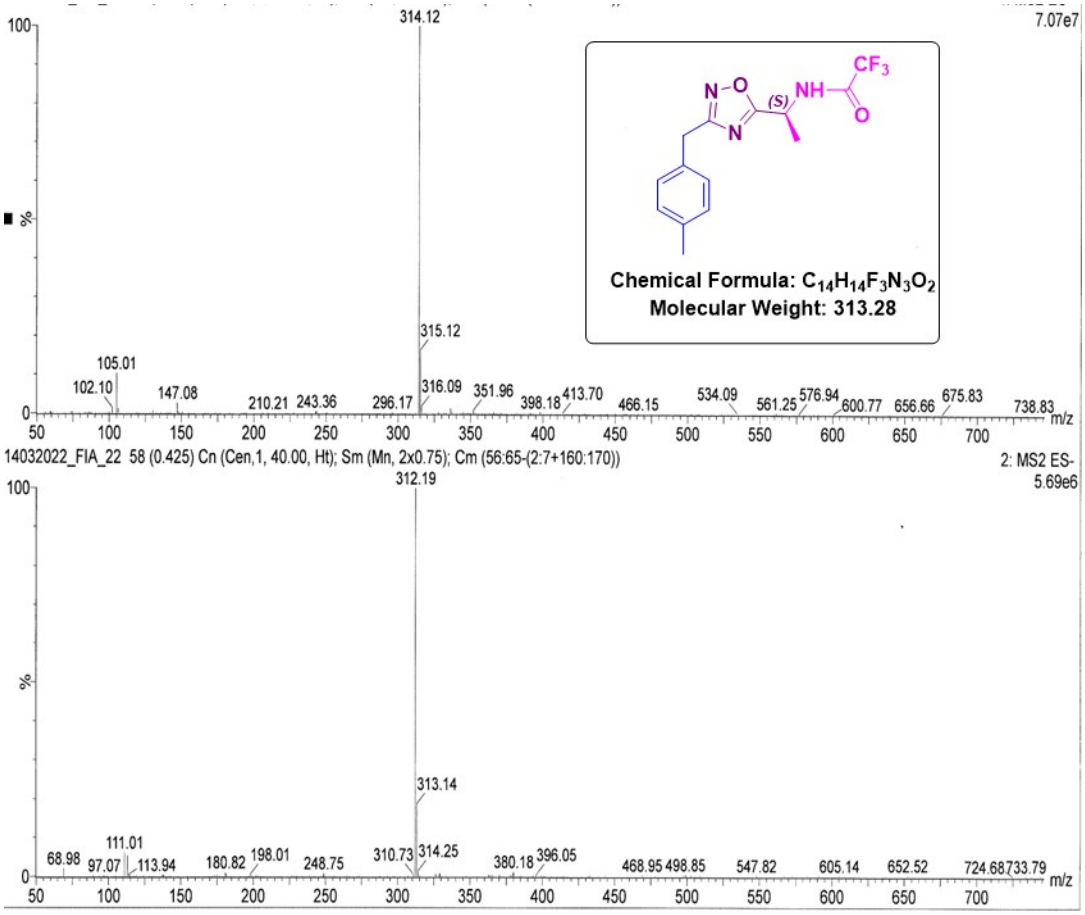


Fig. 63. Mass spectrum of compound **4au**

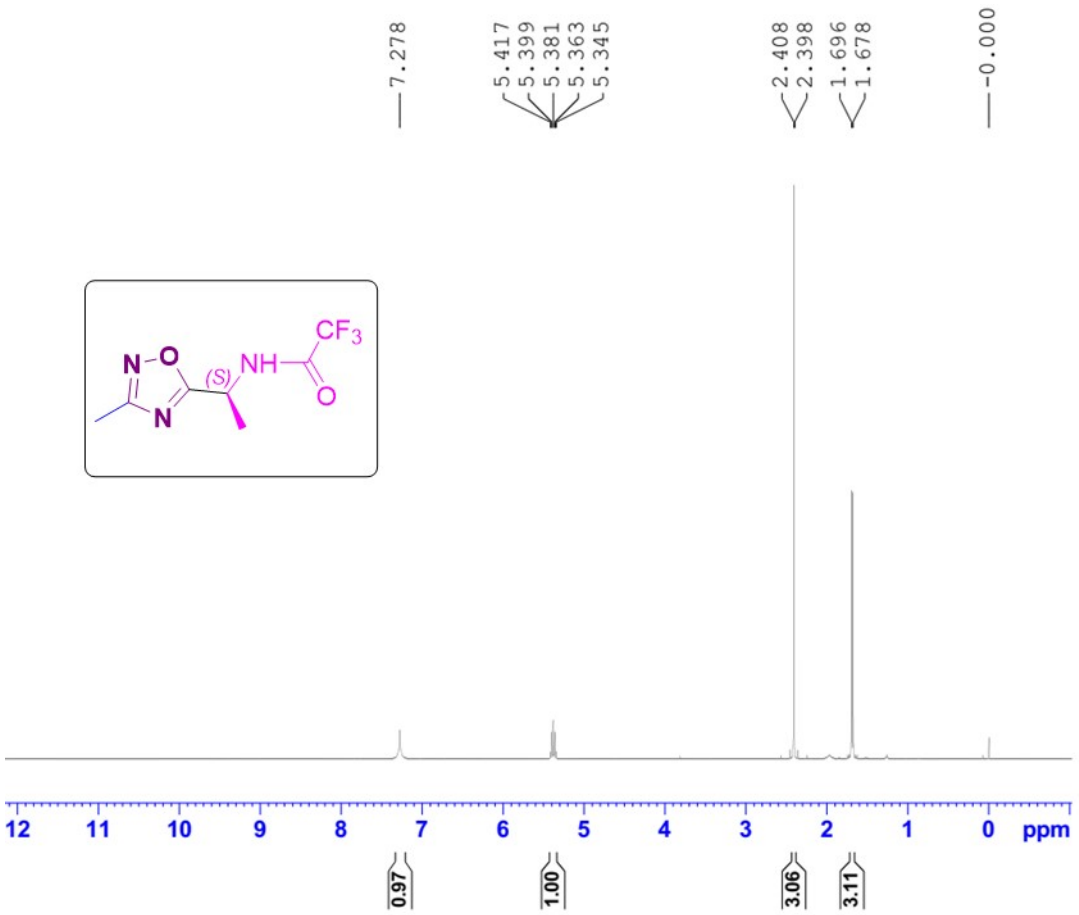


Fig. 64. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of compound **4av**

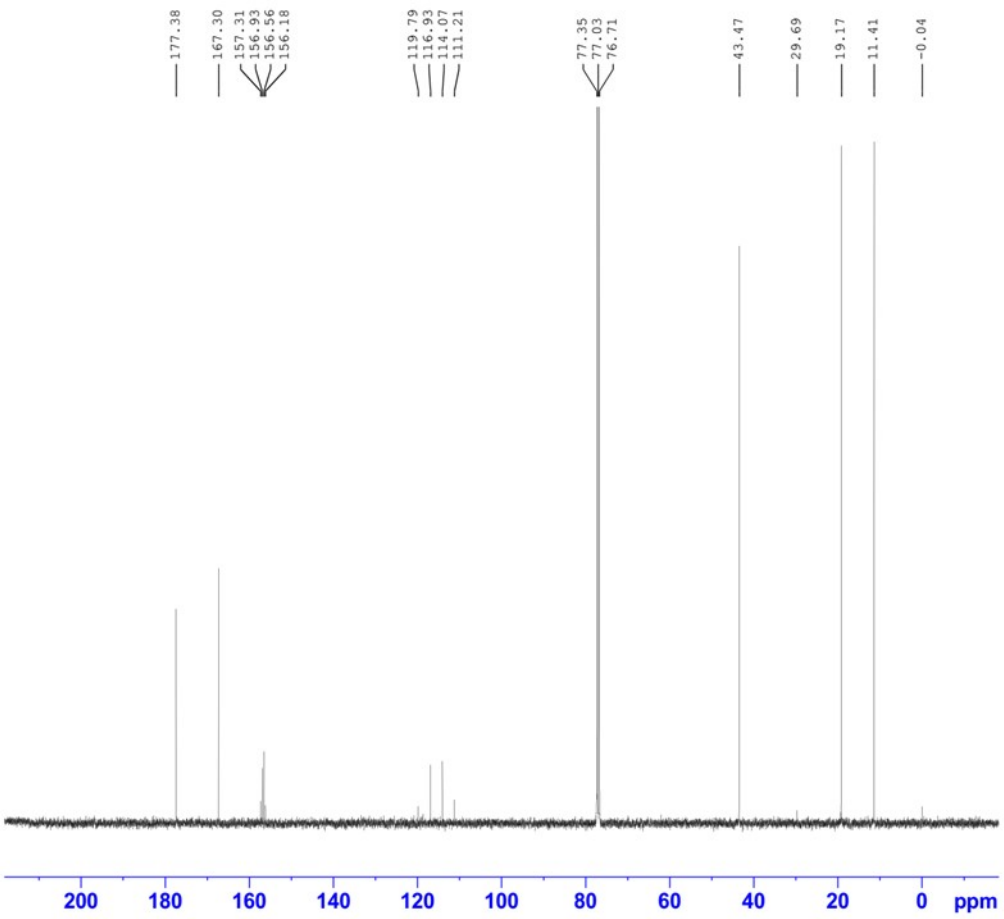


Fig.65. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of compound **4av**

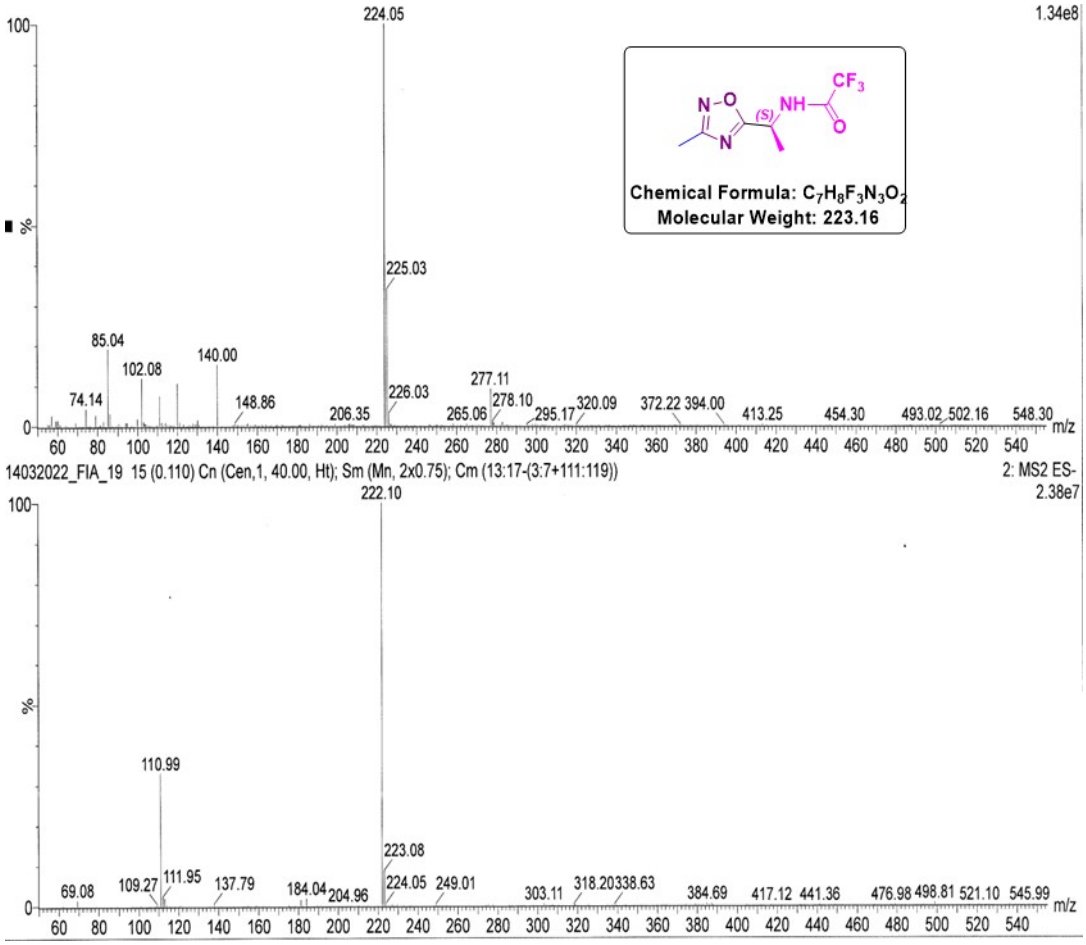
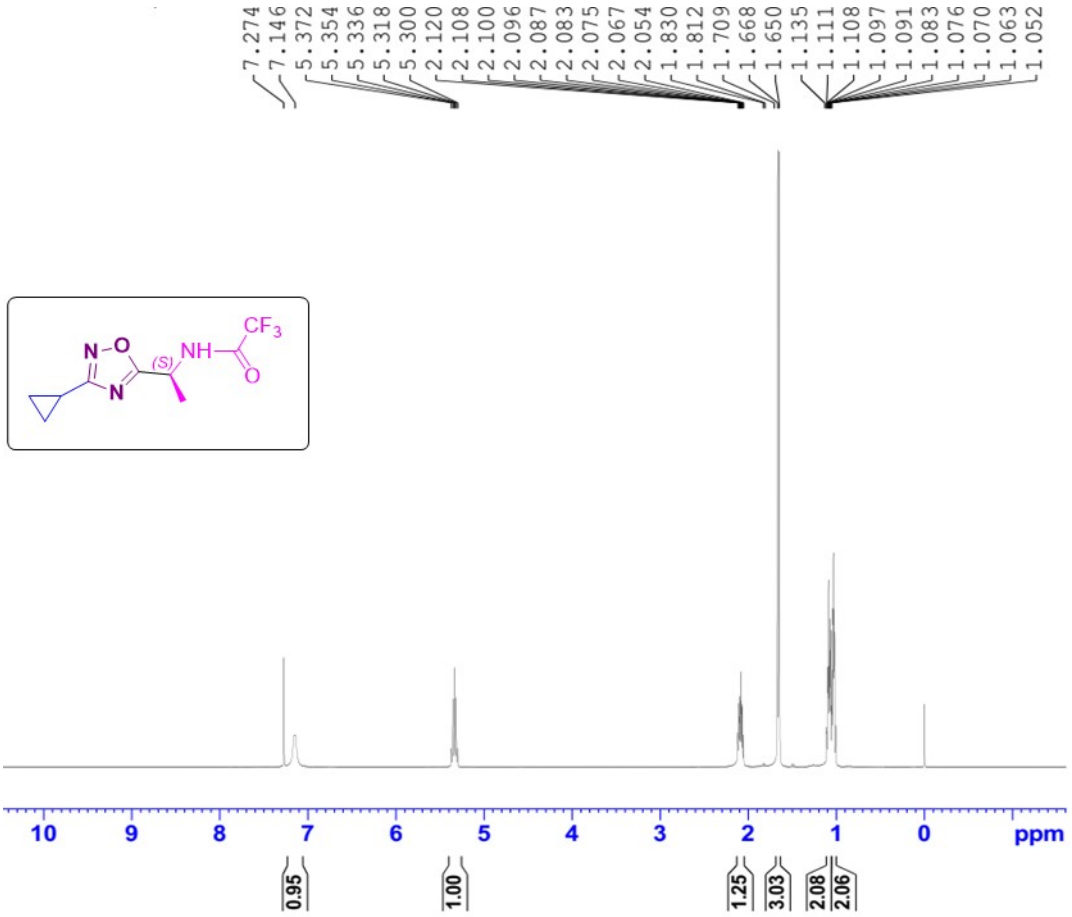


Fig. 66. Mass spectrum of compound **4av**



F

ig.67. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of compound **4aw**

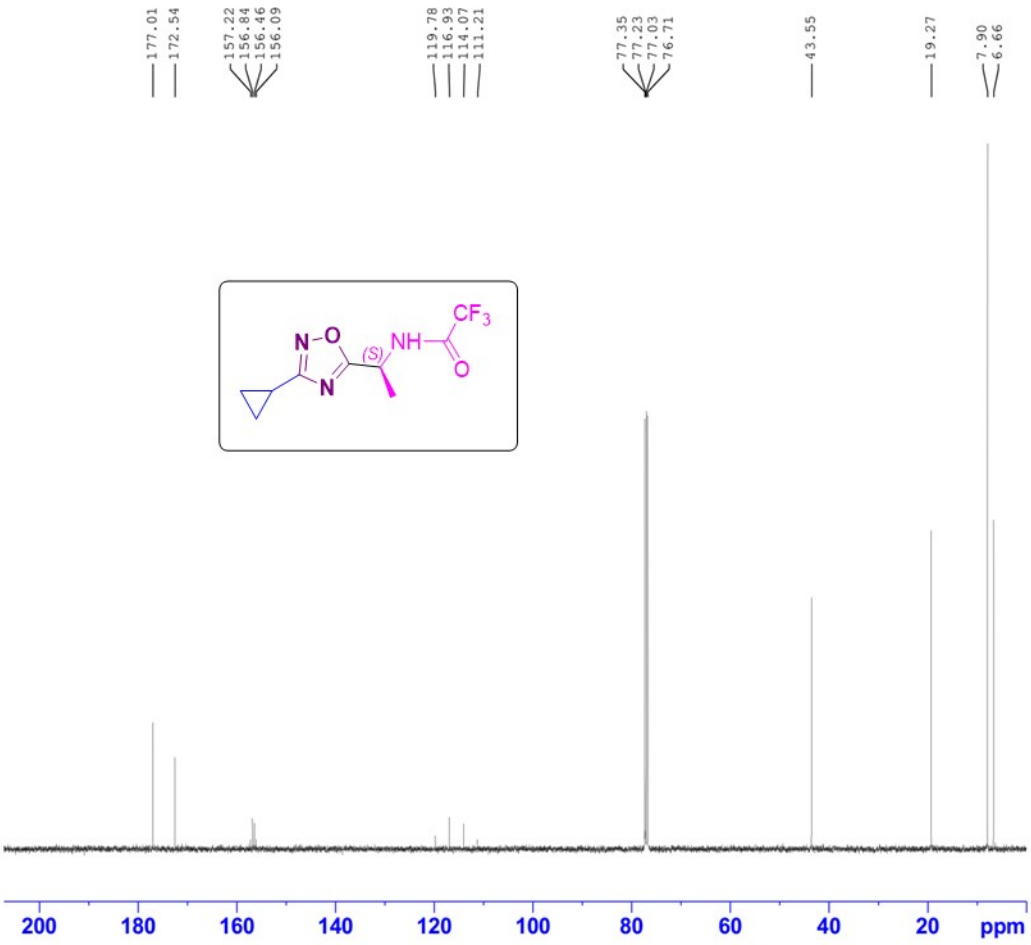


Fig.68. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of compound **4aw**

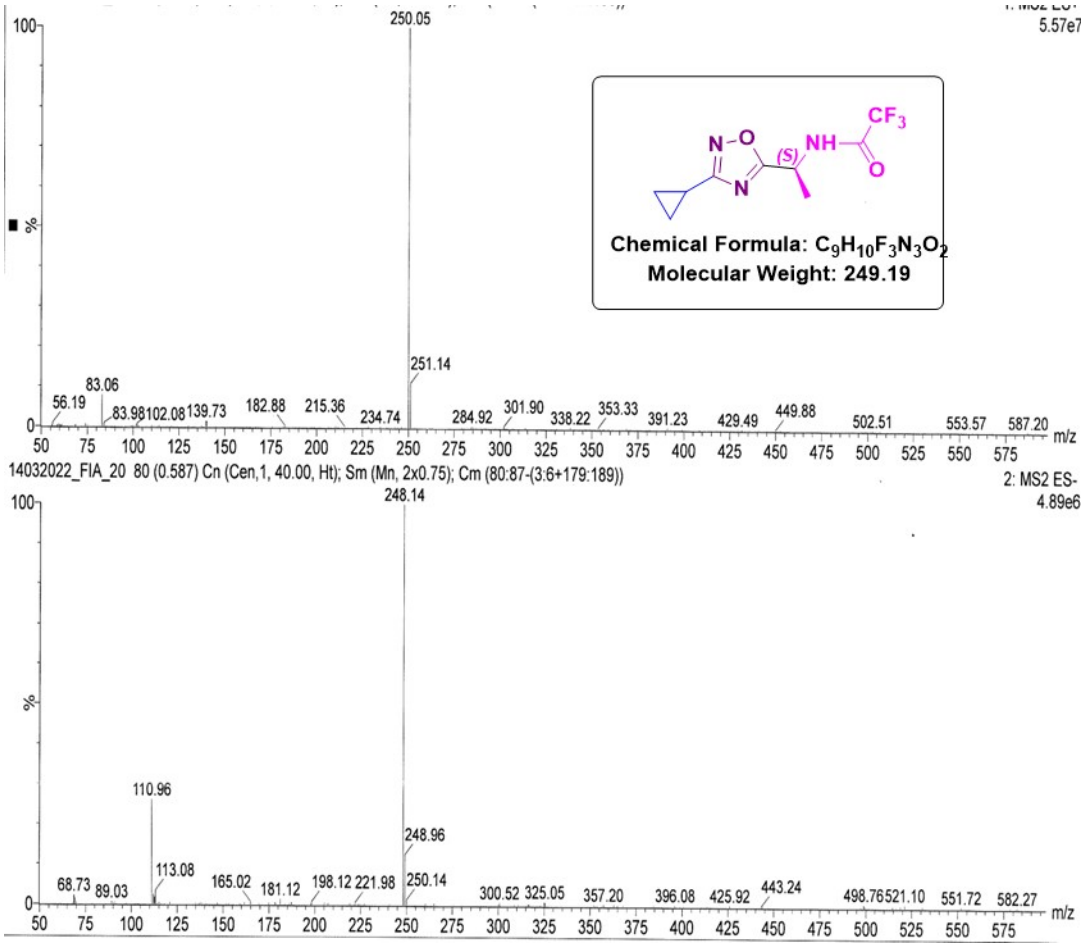
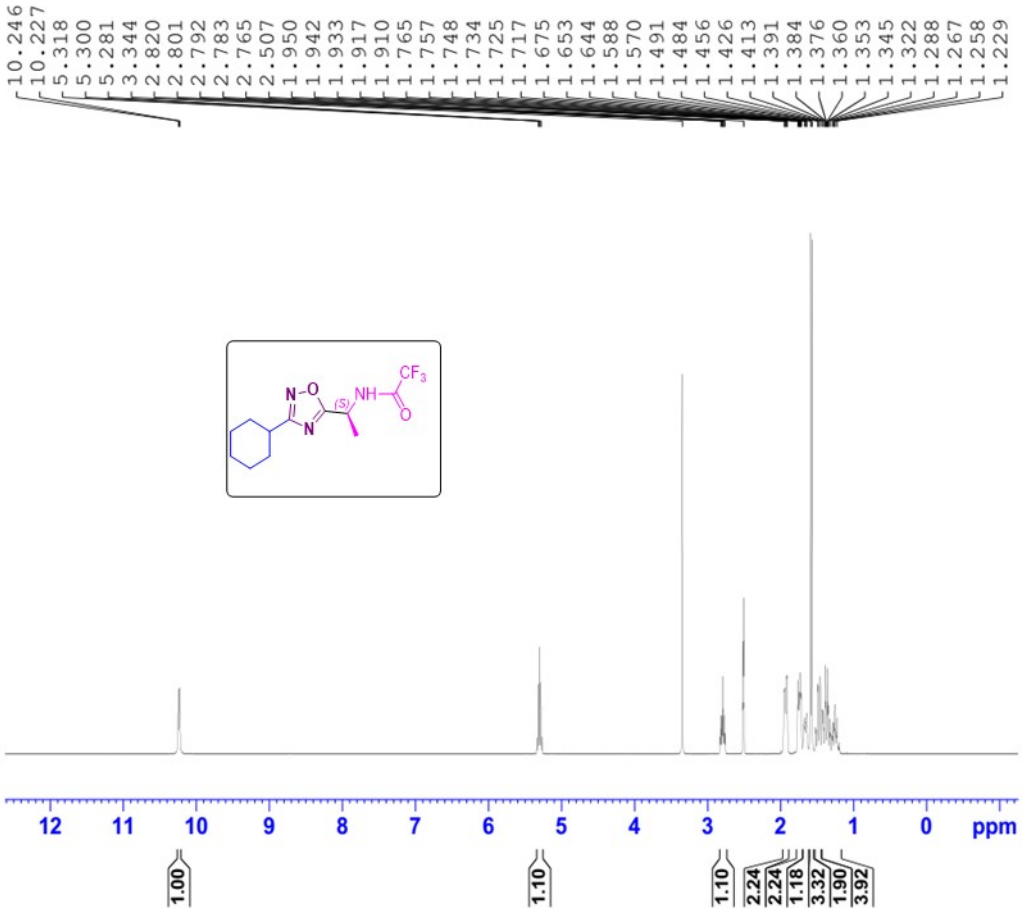


Fig. 69. Mass spectrum of compound **4aw**



Fi. 70. ^{1}H NMR spectrum (DMSO-d_6, 400 MHz) of compound **4ax**

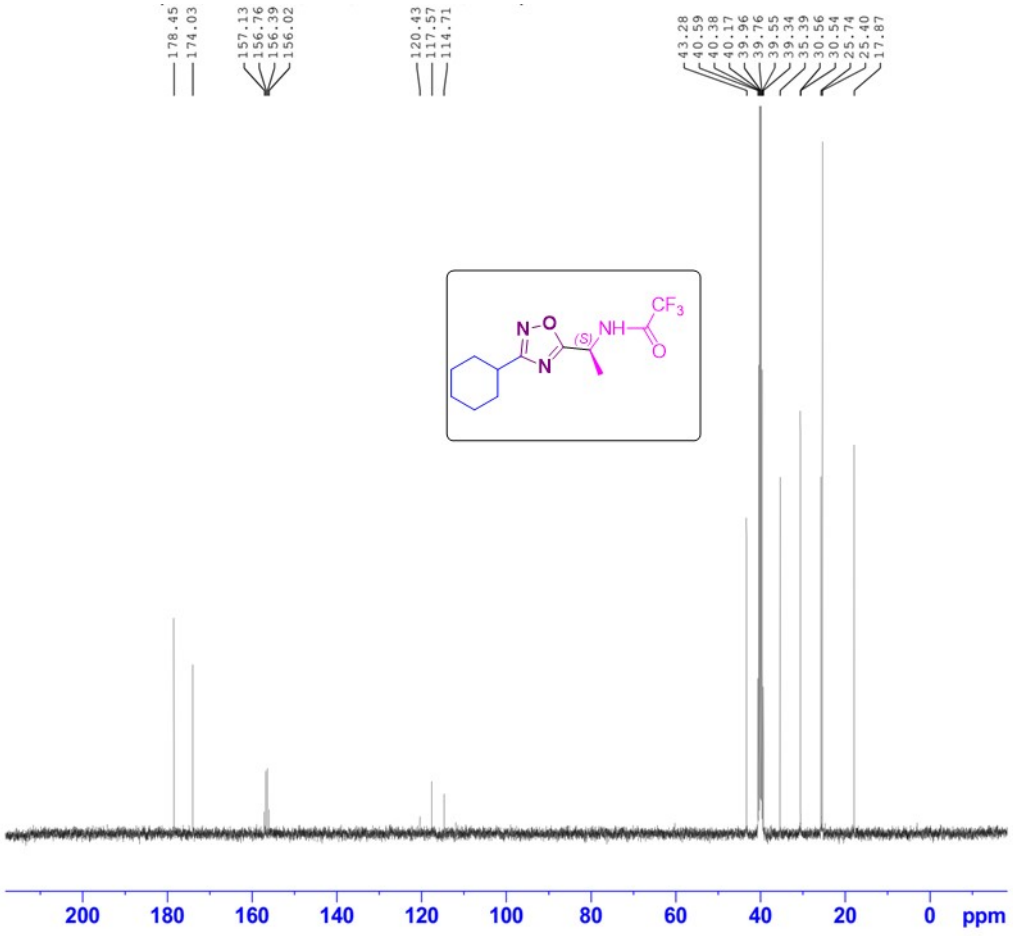


Fig. 71. ^{13}C NMR spectrum (DMSO-d_6, 100 MHz) of compound **4ax**

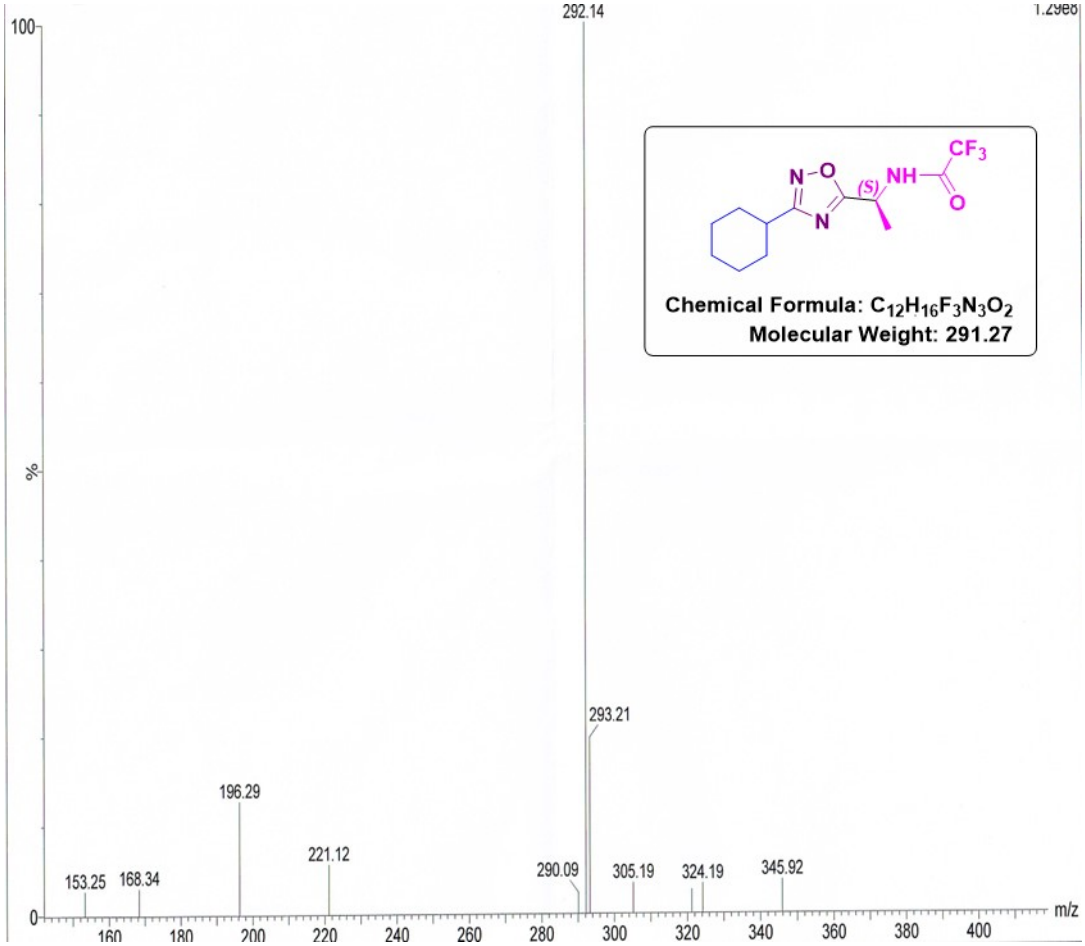


Fig. 72. Mass spectrum of compound **4ax**

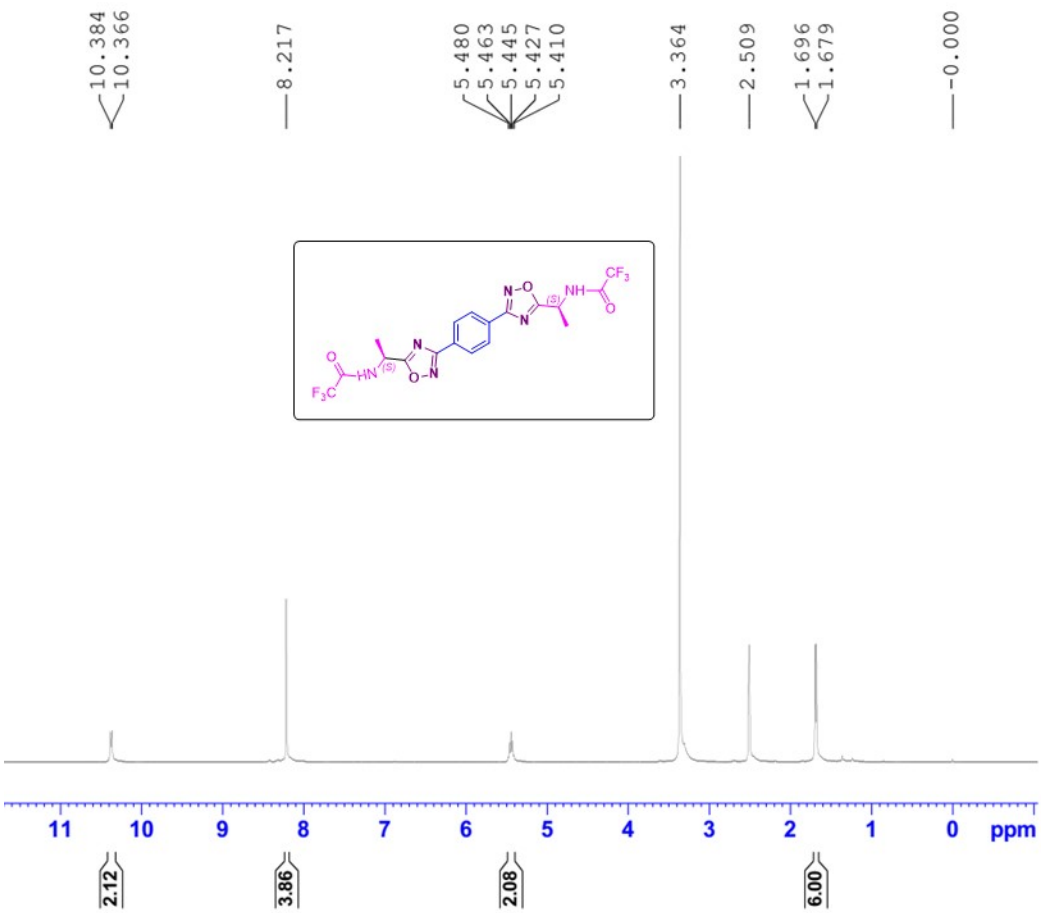


Fig. 73. ^{1}H NMR spectrum (DMSO-d_6, 400 MHz) of compound **4ay**

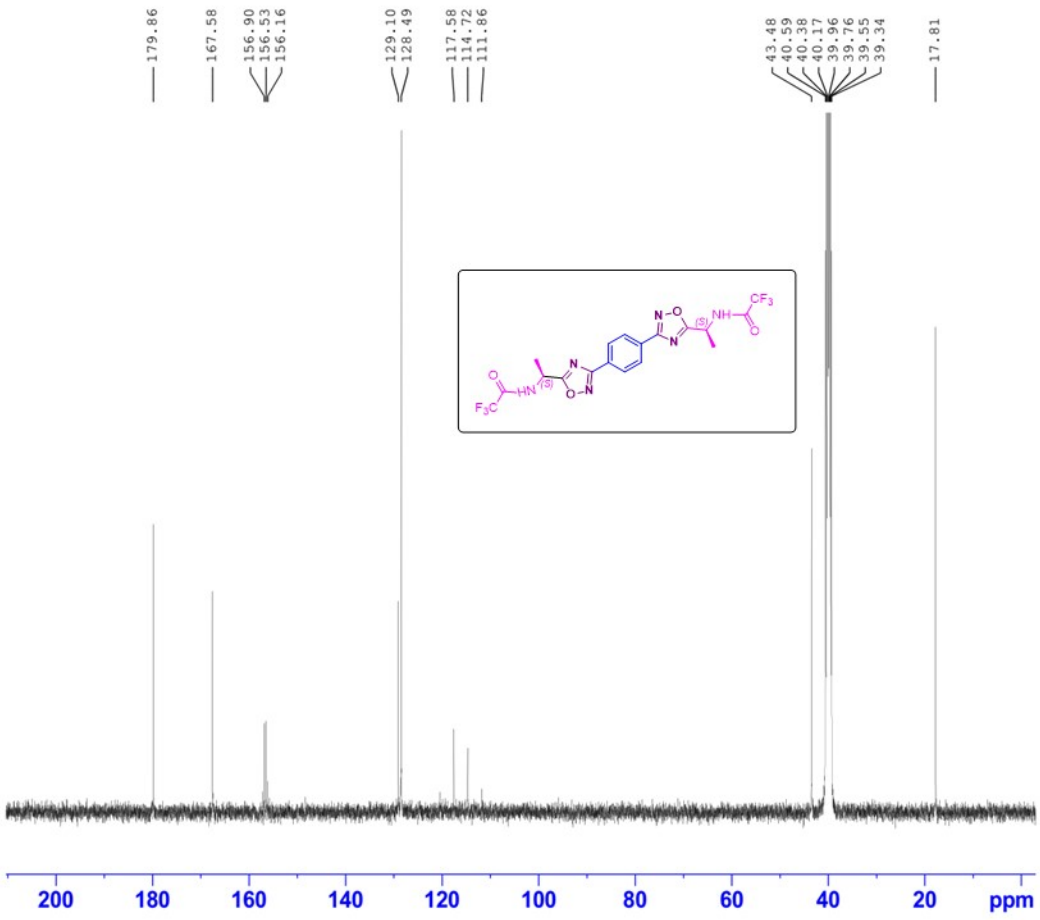


Fig. 74. ^{13}C NMR spectrum (DMSO-d_6, 100 MHz) of compound **4ay**

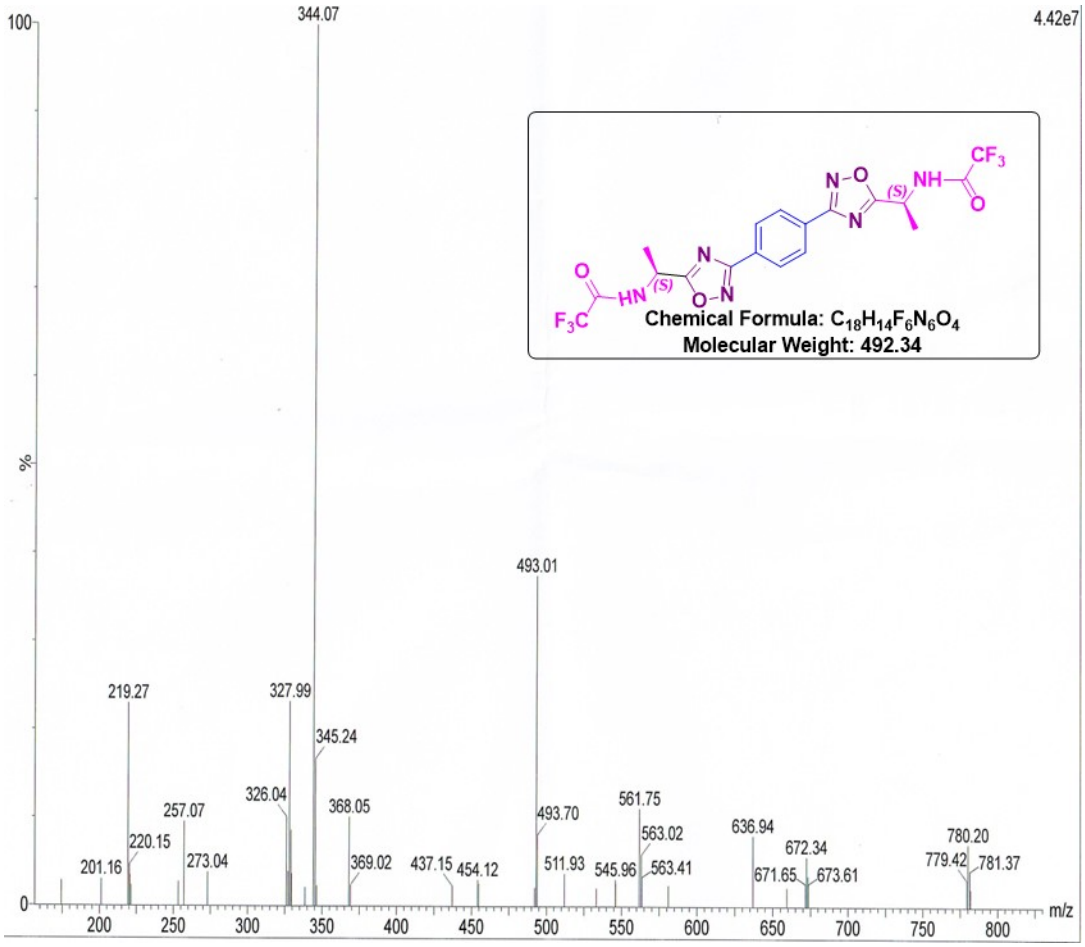


Fig. 75. Mass spectrum of compound **4ay**

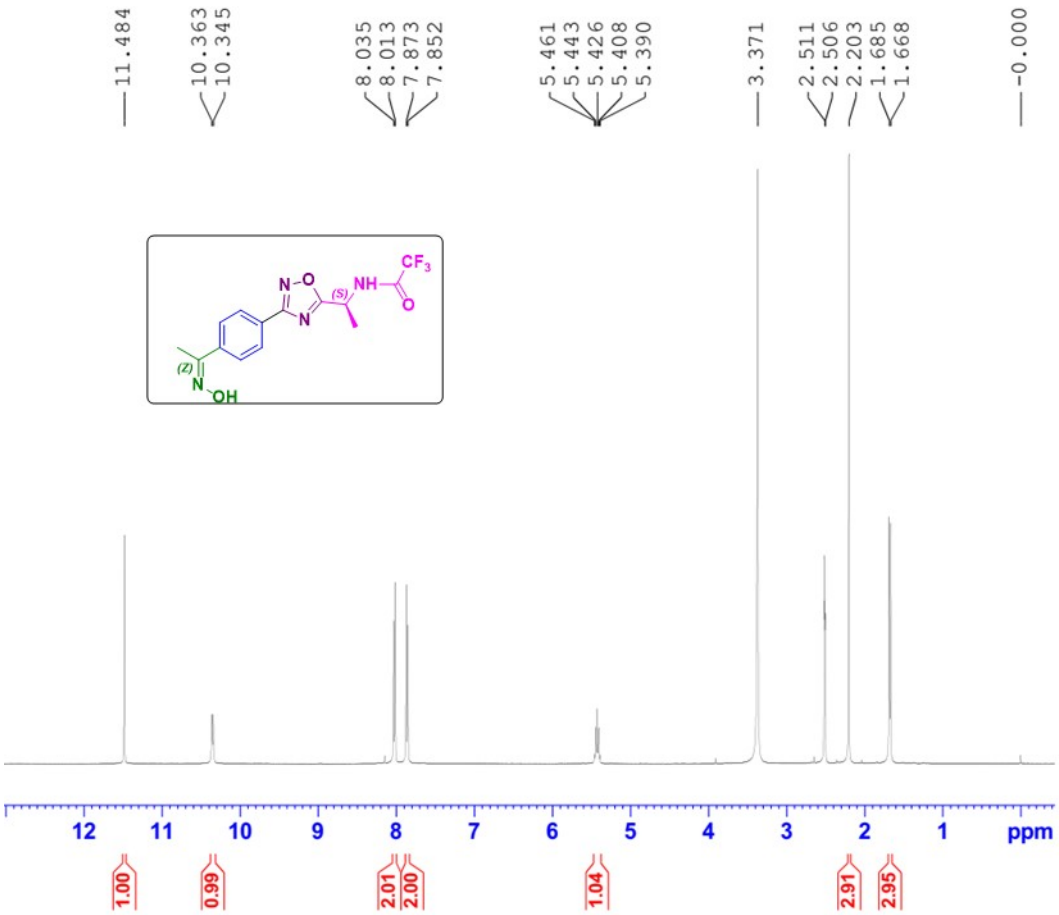


Fig. 76. ^{1}H NMR spectrum (DMSO-d_6, 400 MHz) of compound **4az**

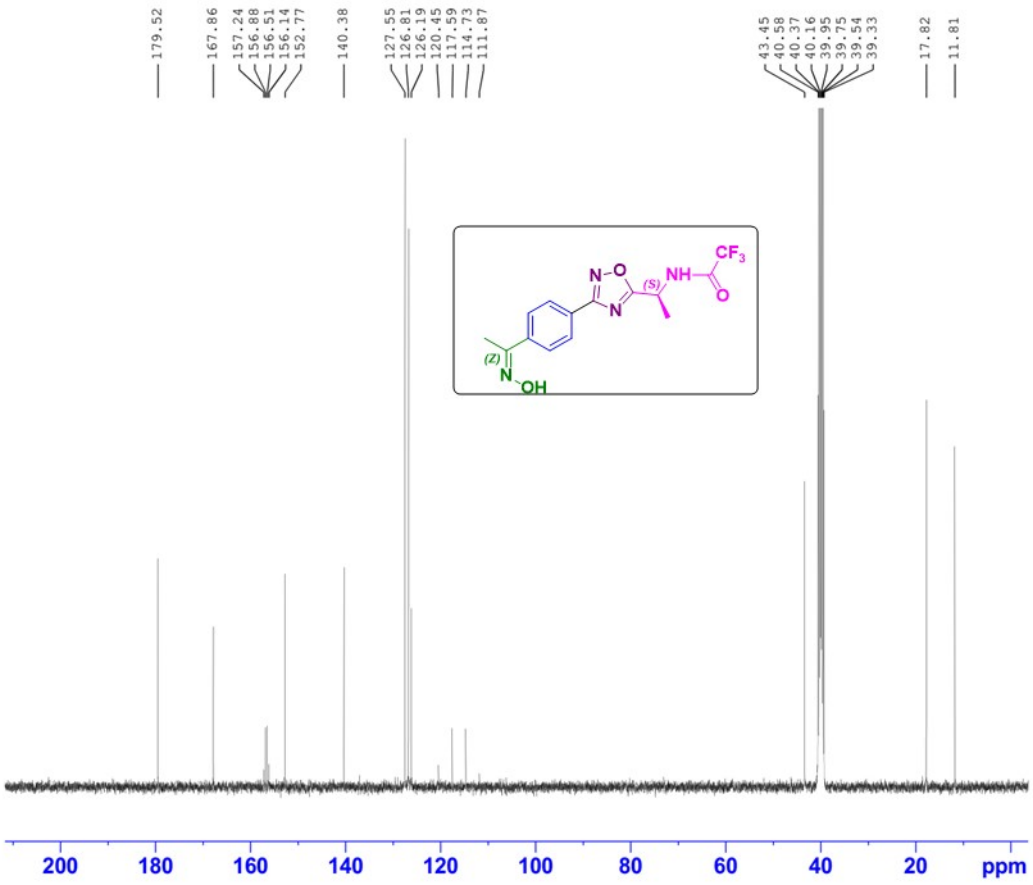


Fig. 77. ^{13}C NMR spectrum (DMSO-d_6, 100 MHz) of compound **4az**

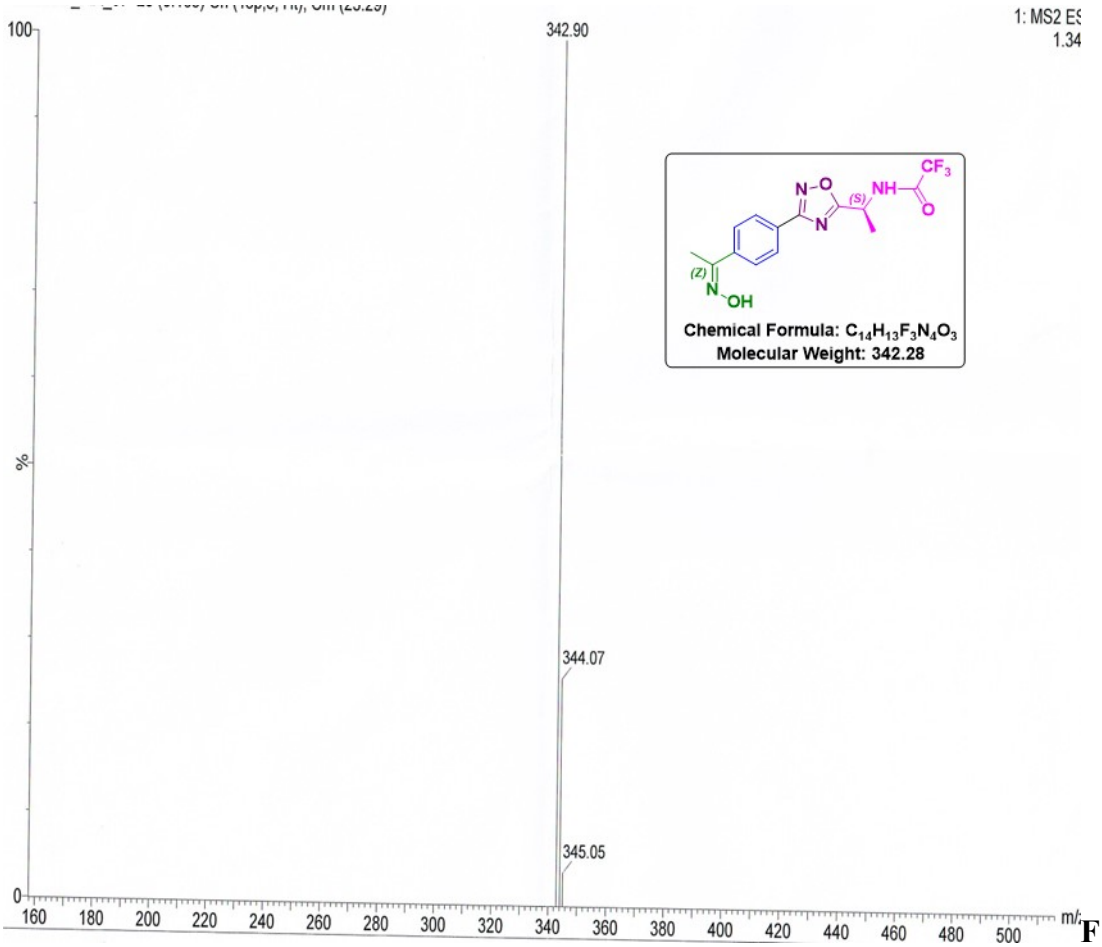


Fig. 78. Mass spectrum of compound **4az**

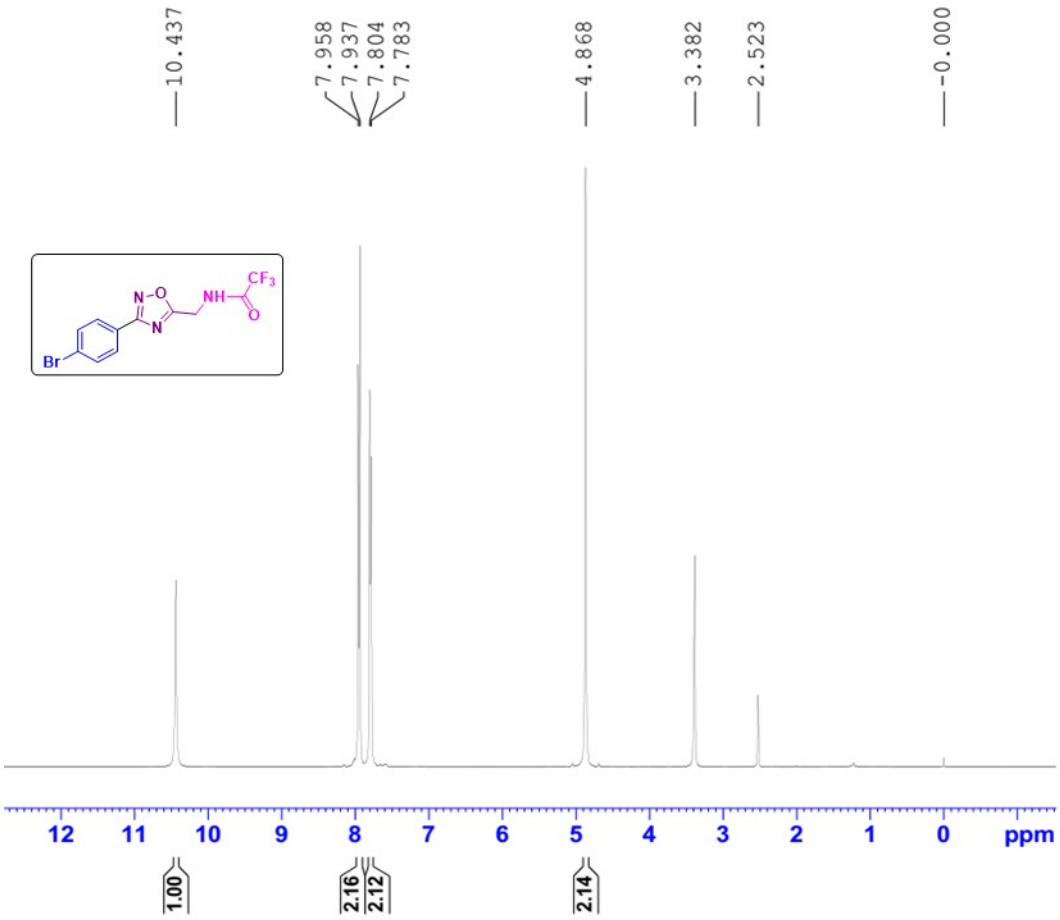


Fig. 79. ^{1}H NMR spectrum (DMSO-d_6, 400 MHz) of compound **4bj**

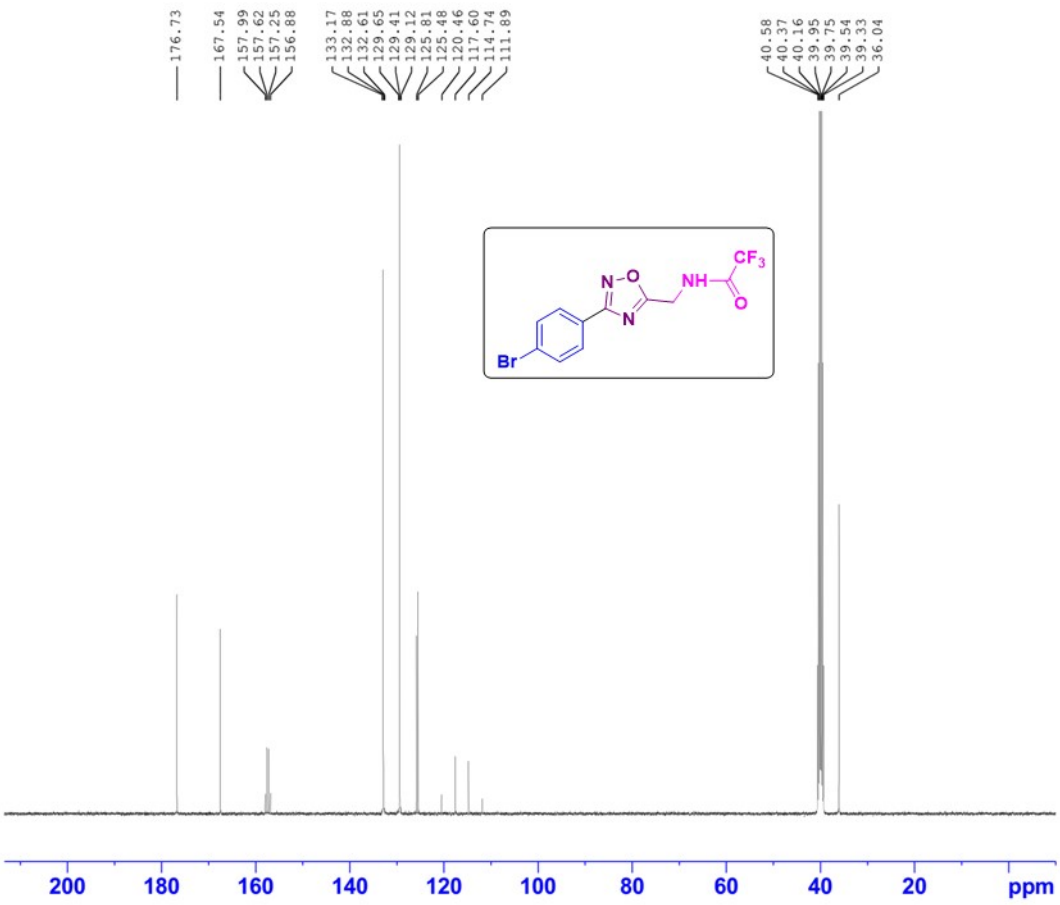


Fig. 80. ^{13}C NMR spectrum (DMSO-d_6, 100 MHz) of compound **4bj**

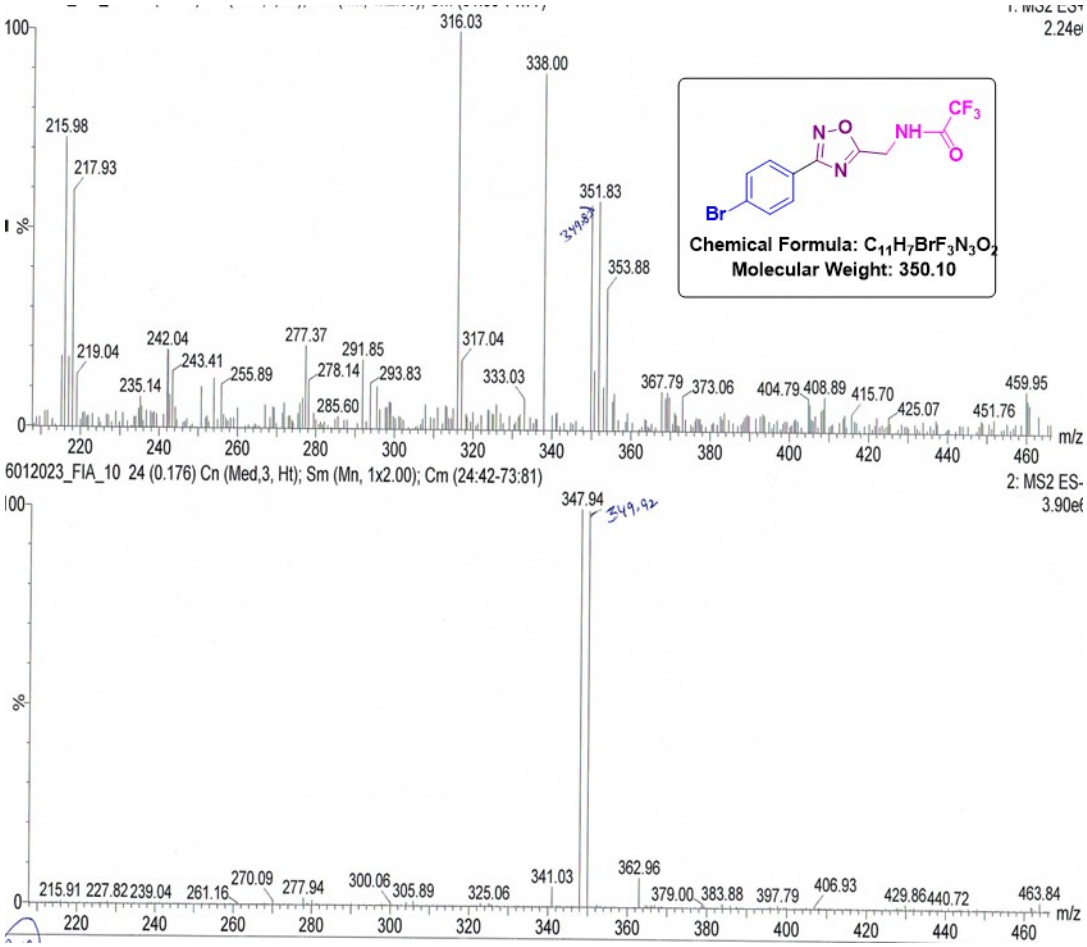


Fig. 81. Mass spectrum of compound **4bj**

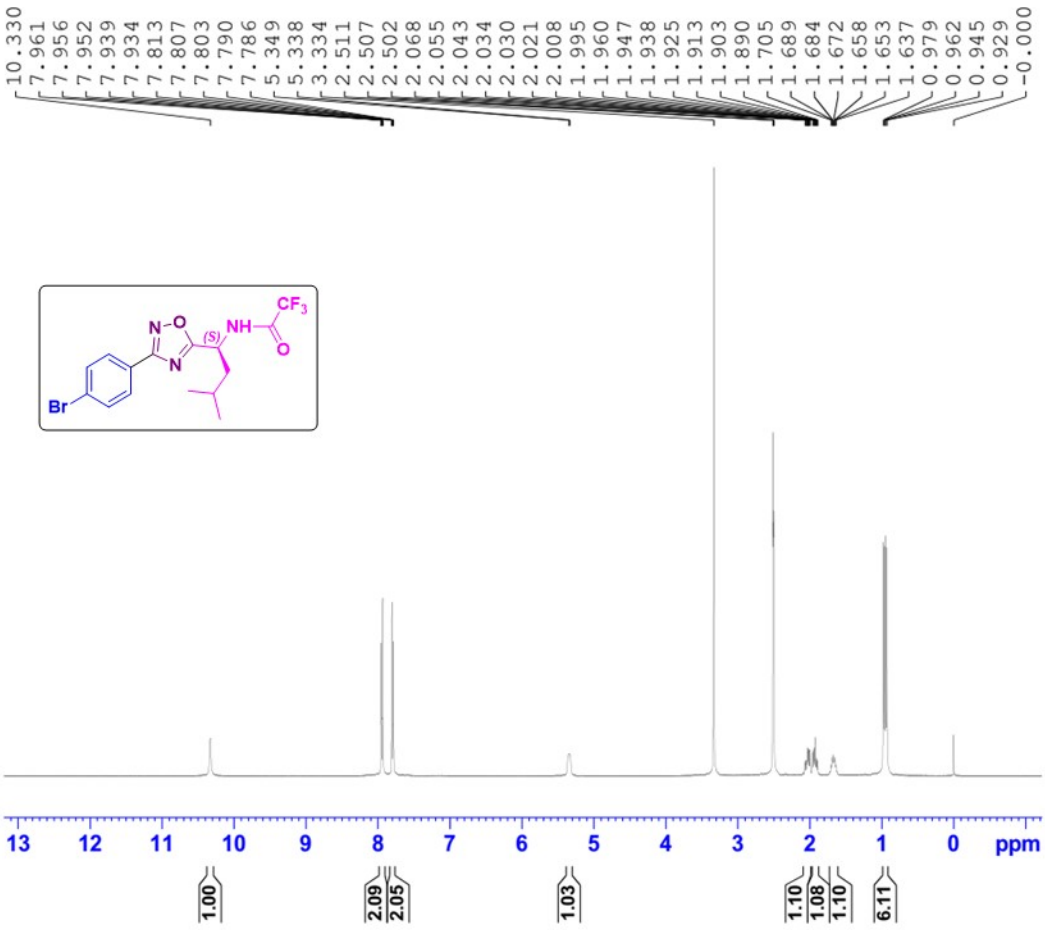


Fig. 82. ^{1}H NMR spectrum (DMSO-d_6, 400 MHz) of compound **4cj**

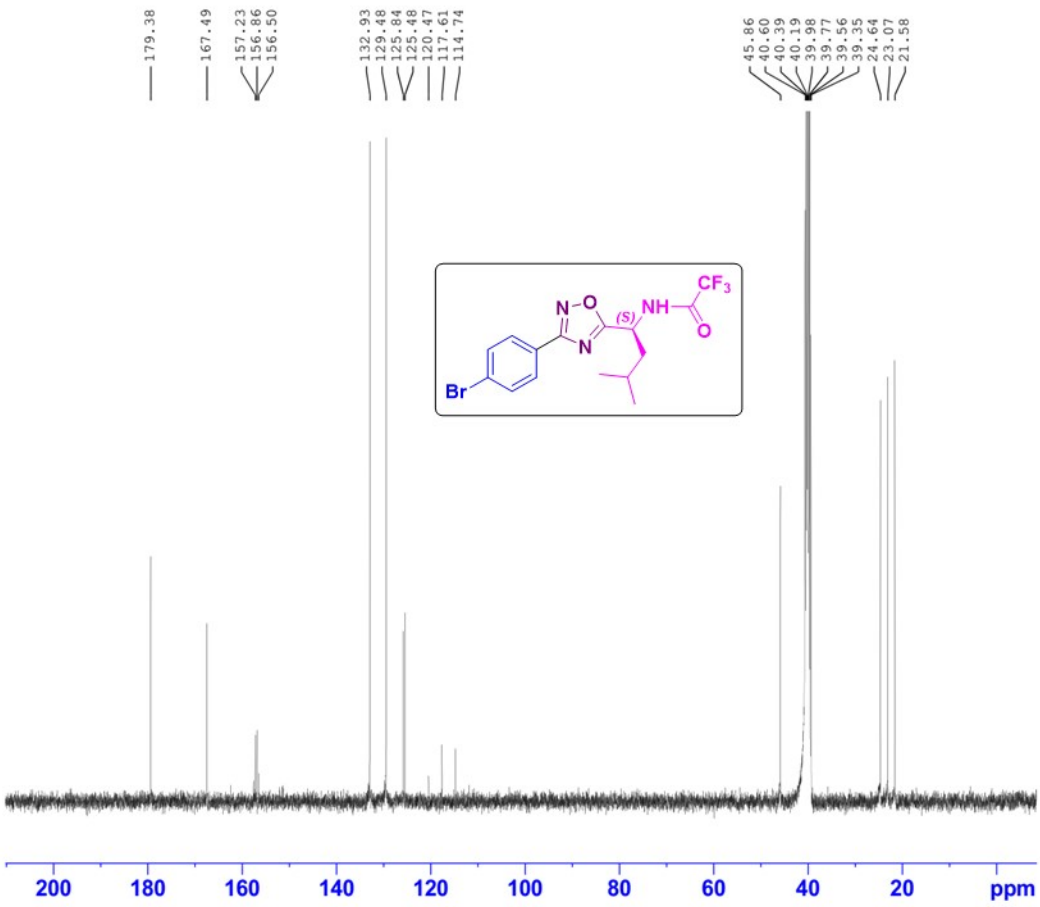


Fig. 83. ^{13}C NMR spectrum (DMSO-d_6, 100 MHz) of compound **4cj**

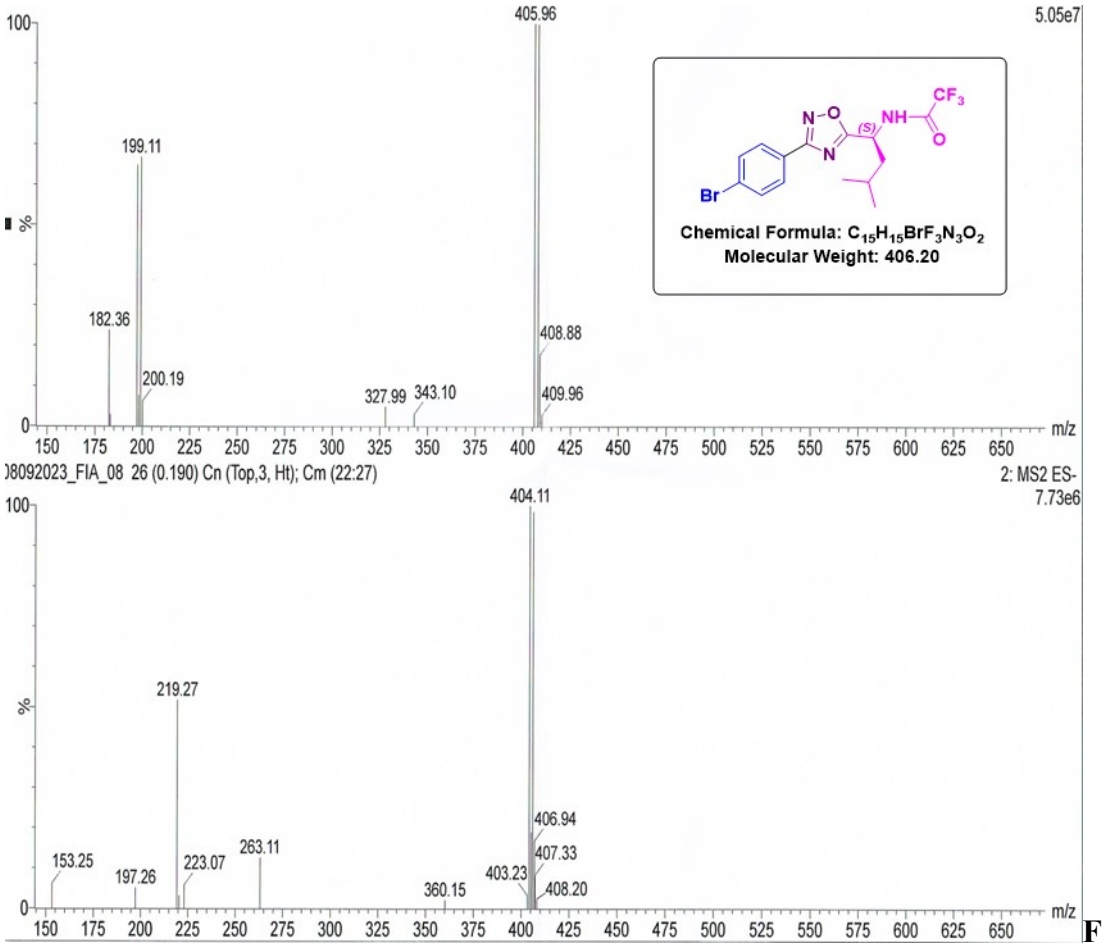


Fig. 84. Mass spectrum of compound **4cj**

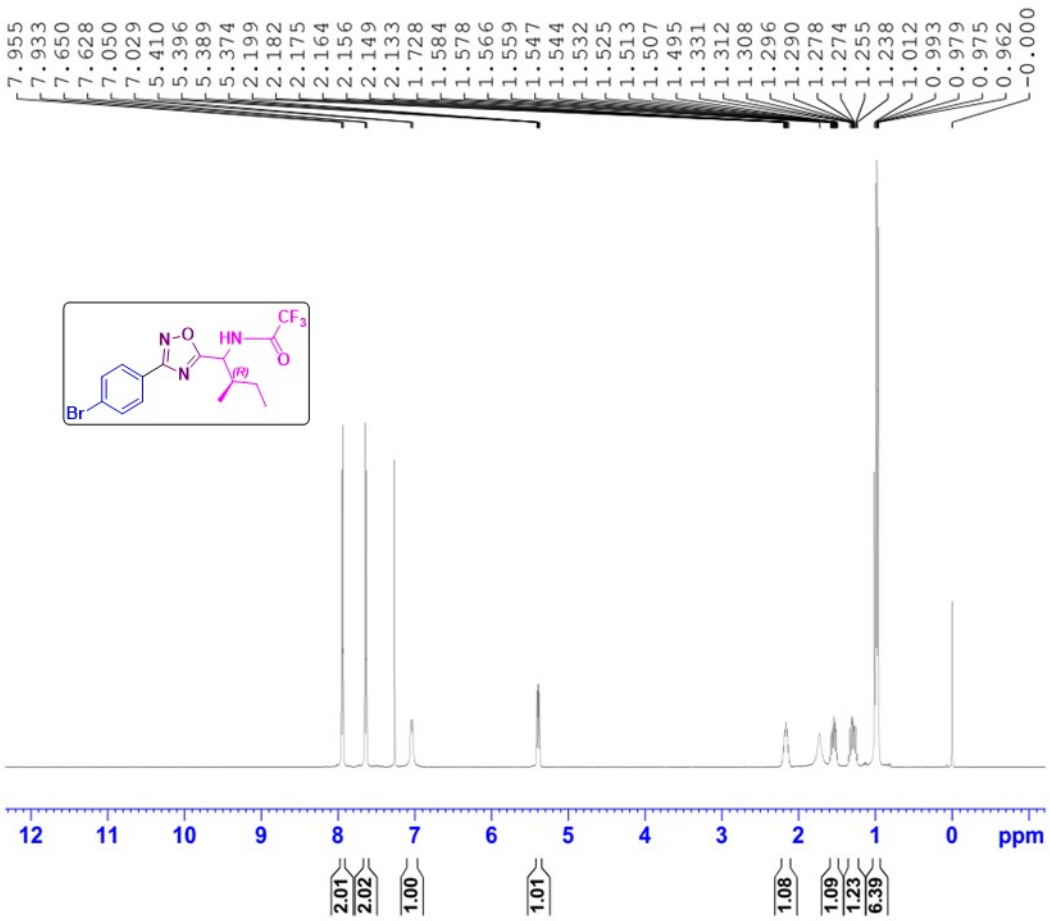


Fig. 85. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of compound **4dj**

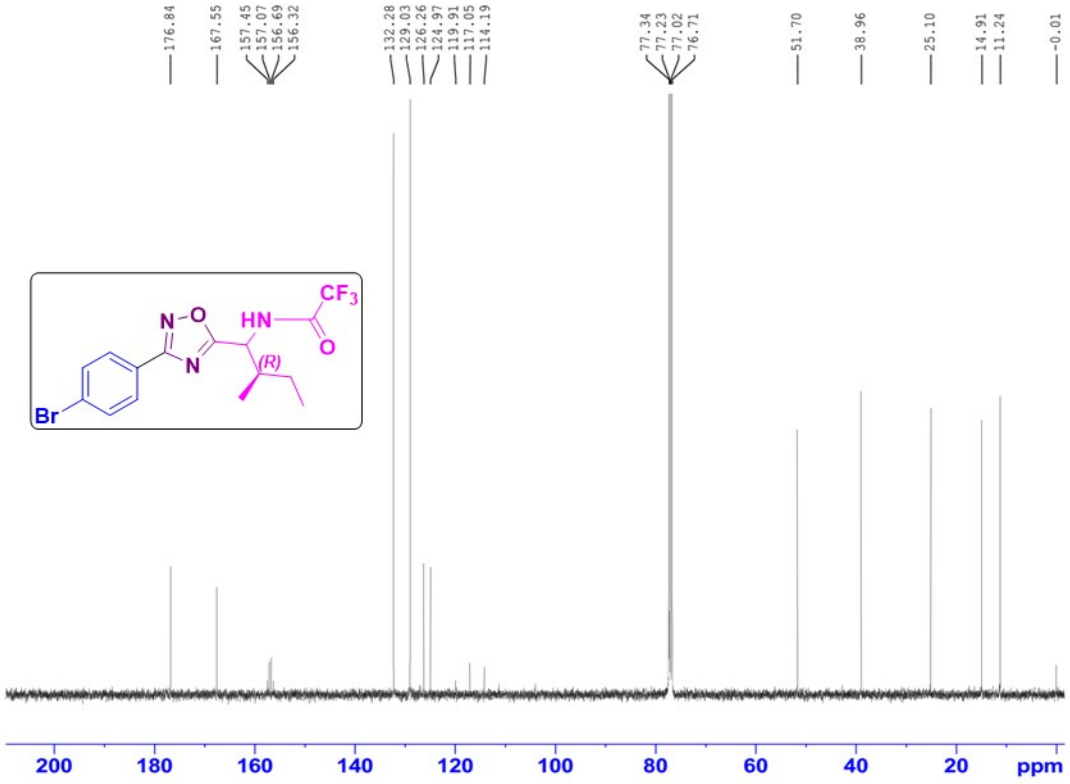


Fig. 86. ^{13}C NMR spectrum (DMSO-d_6, 100 MHz) of compound **4dj**

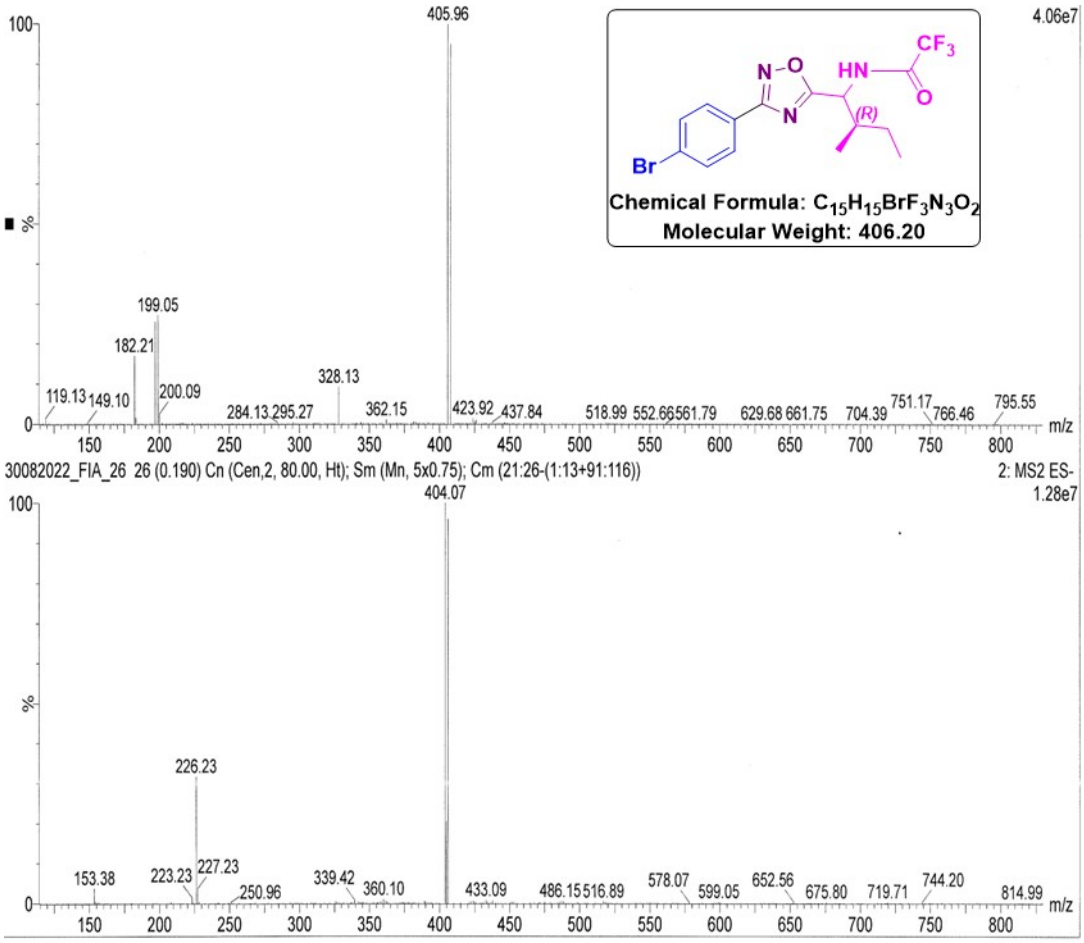


Fig. 87. Mass spectrum of compound **4dj**

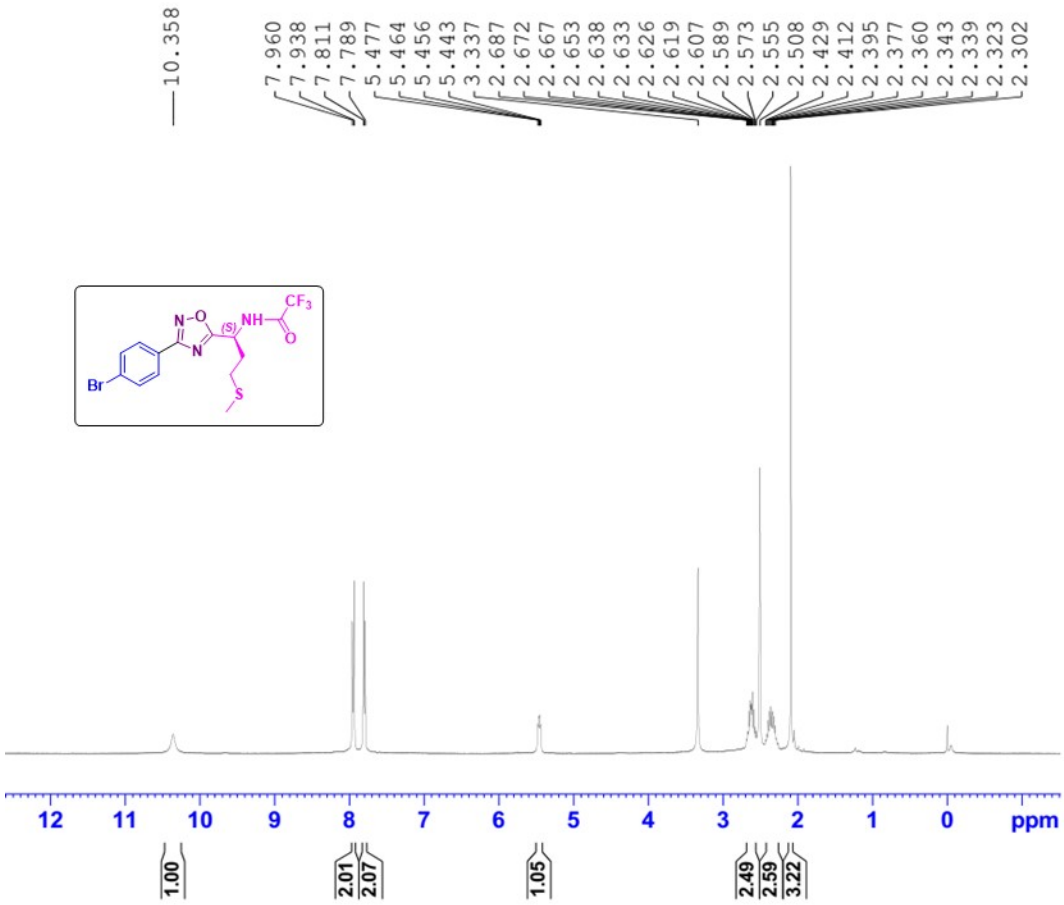


Fig. 88. ^{1}H NMR spectrum (DMSO-d_6, 400 MHz) of compound **4ej**

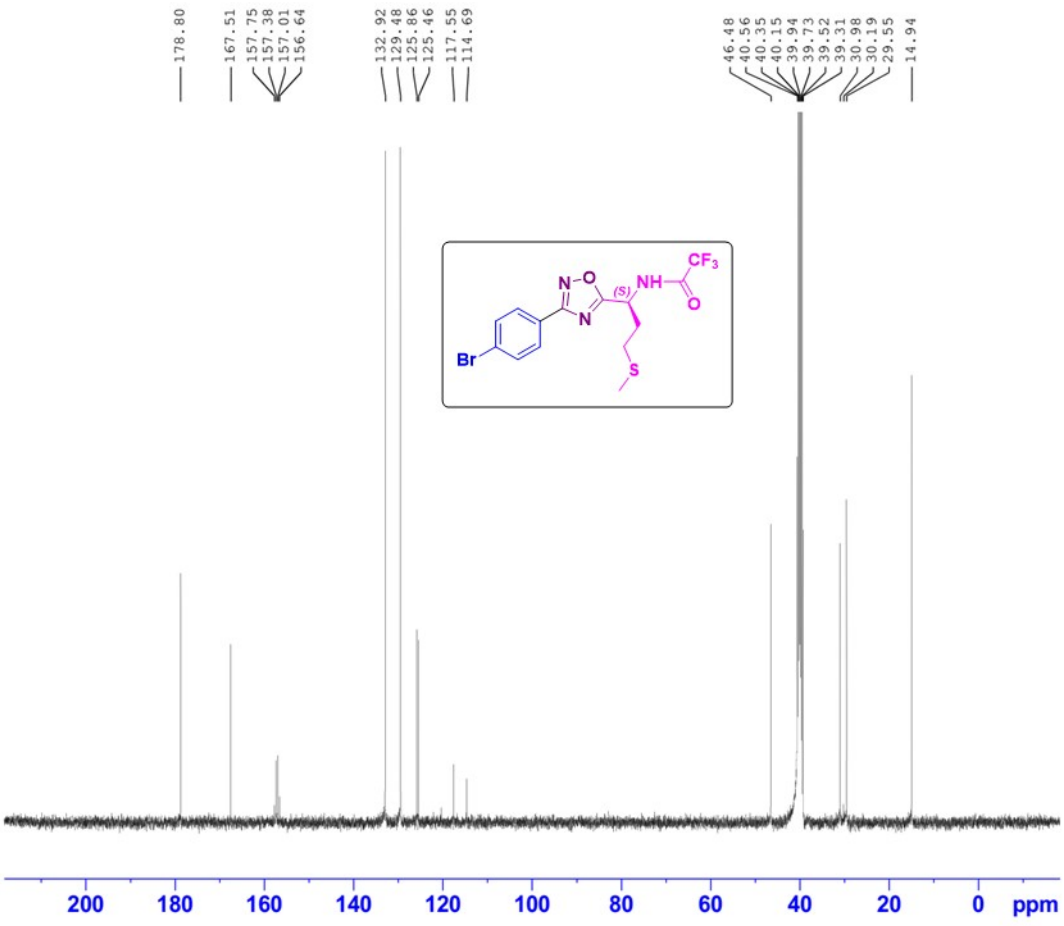


Fig. 89. ^{13}C NMR spectrum (DMSO-d_6, 100 MHz) of compound **4ej**

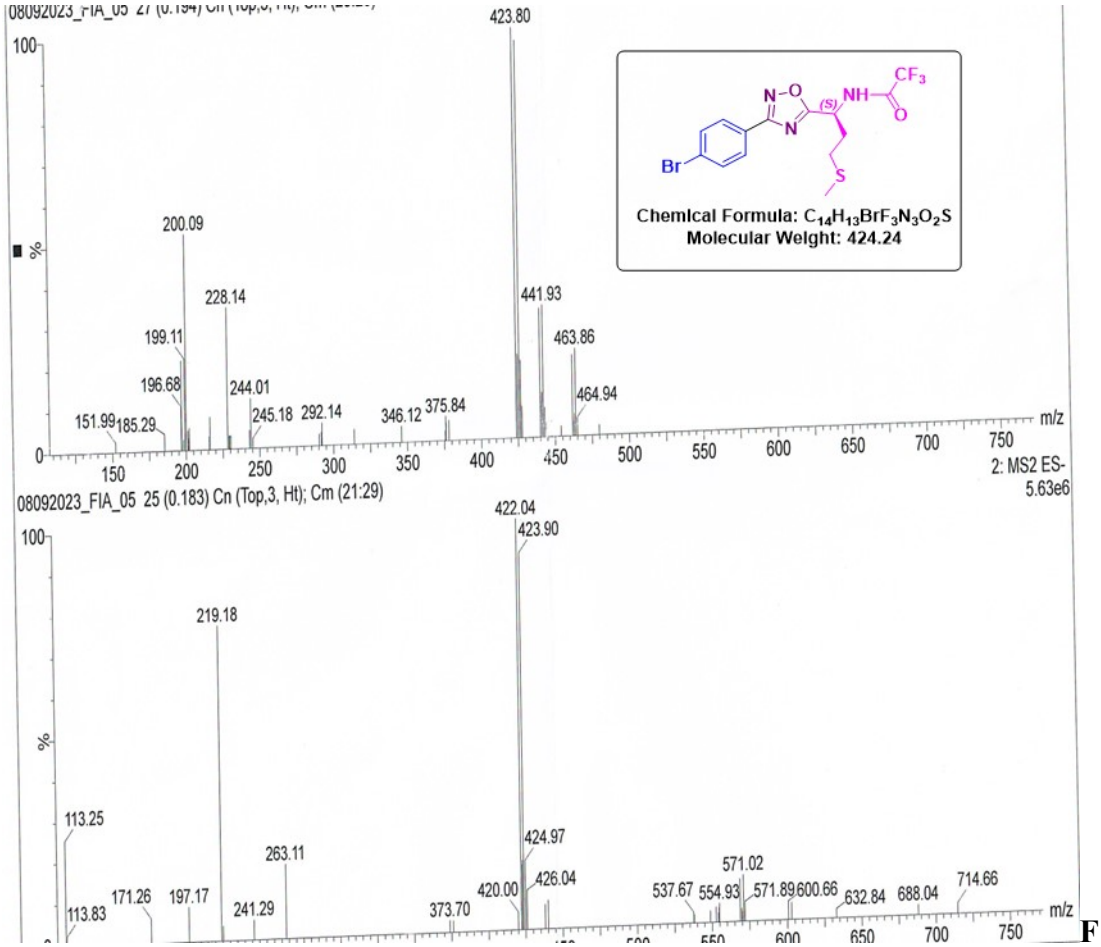


Fig. 90. Mass spectrum of compound **4ej**

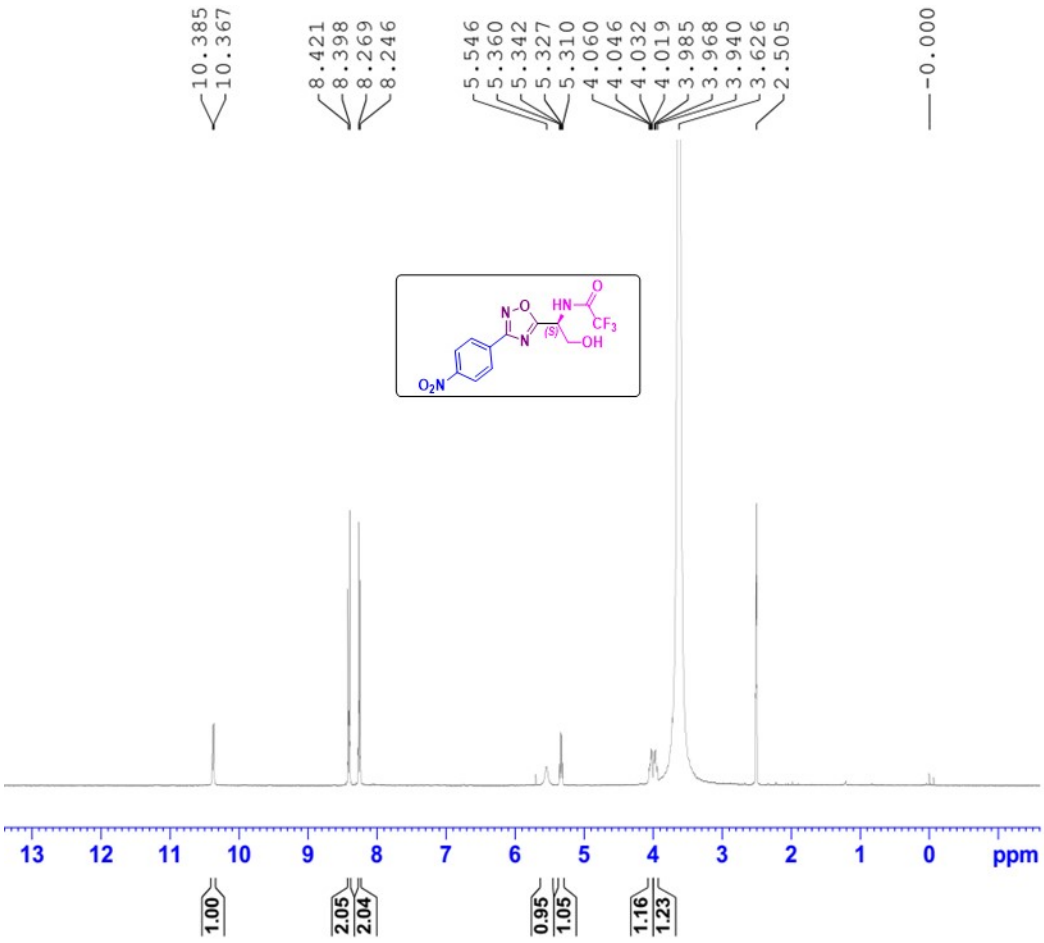


Fig.91 . ^{1}H NMR spectrum (DMSO-d_6, 400 MHz) of compound **4fk**

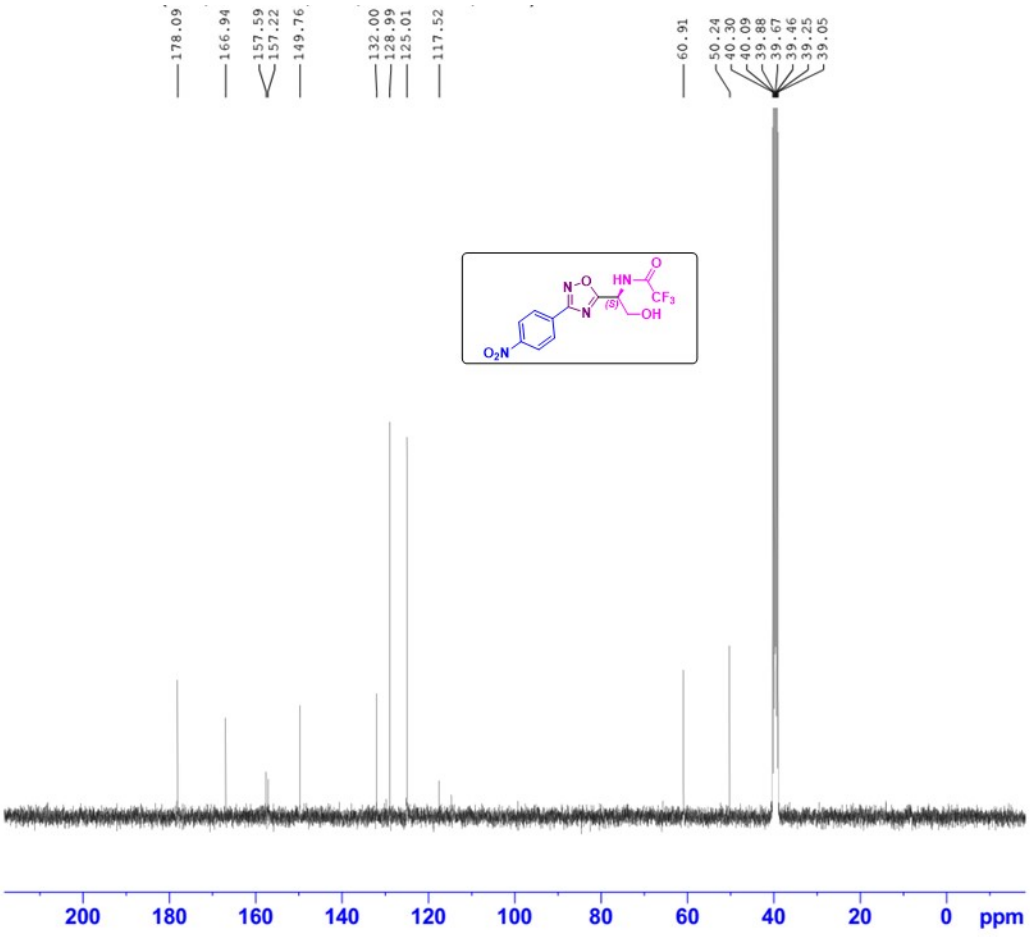


Fig. 92. ^{13}C NMR spectrum (DMSO-d_6, 100 MHz) of compound **4fk**

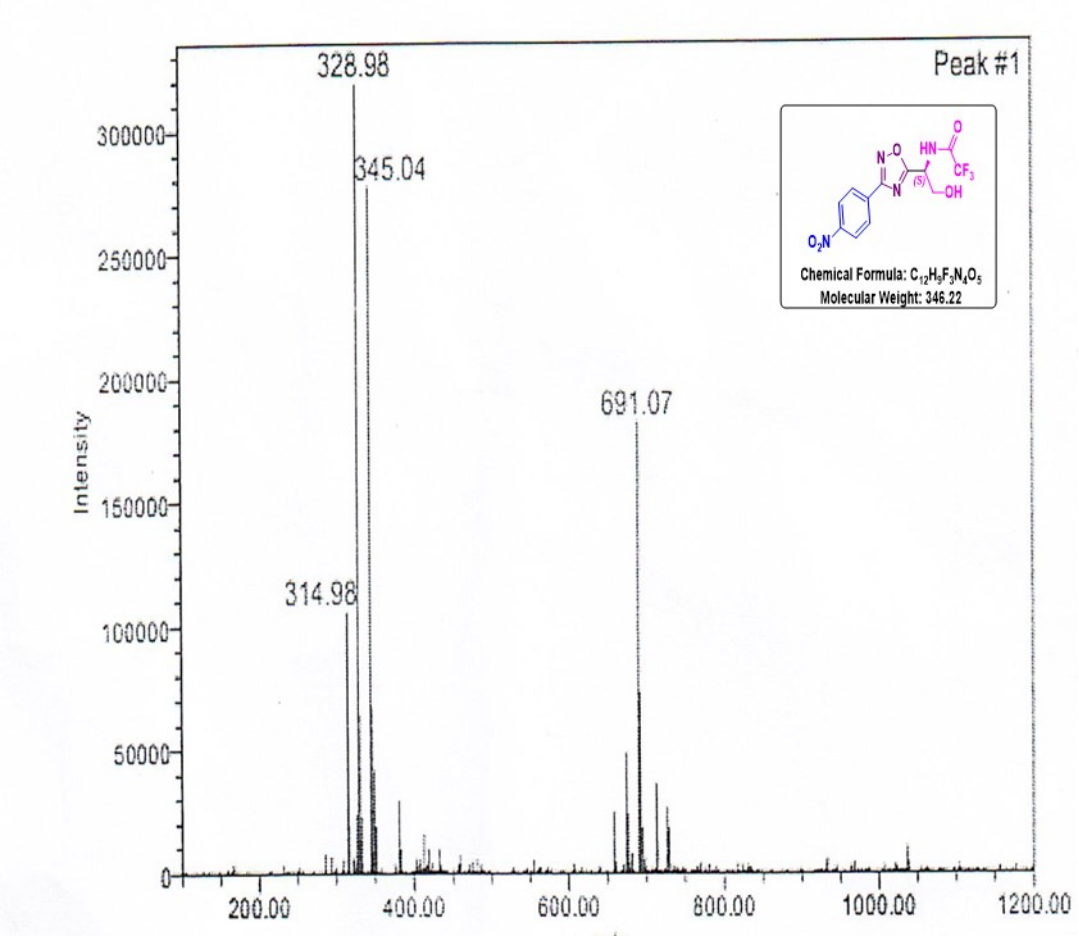


Fig. 93. Mass spectrum of compound **4fk**

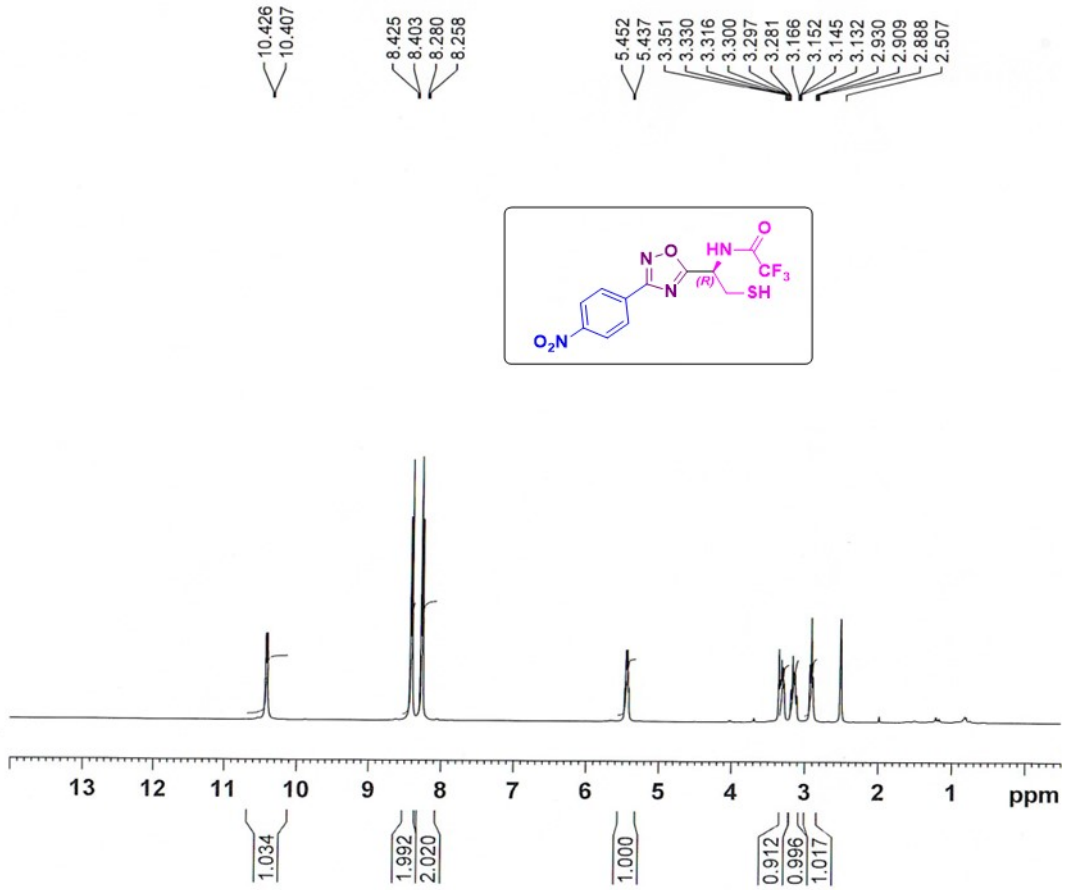


Fig.94 . ^{1}H NMR spectrum (DMSO-d_6, 400 MHz) of compound **4gk**

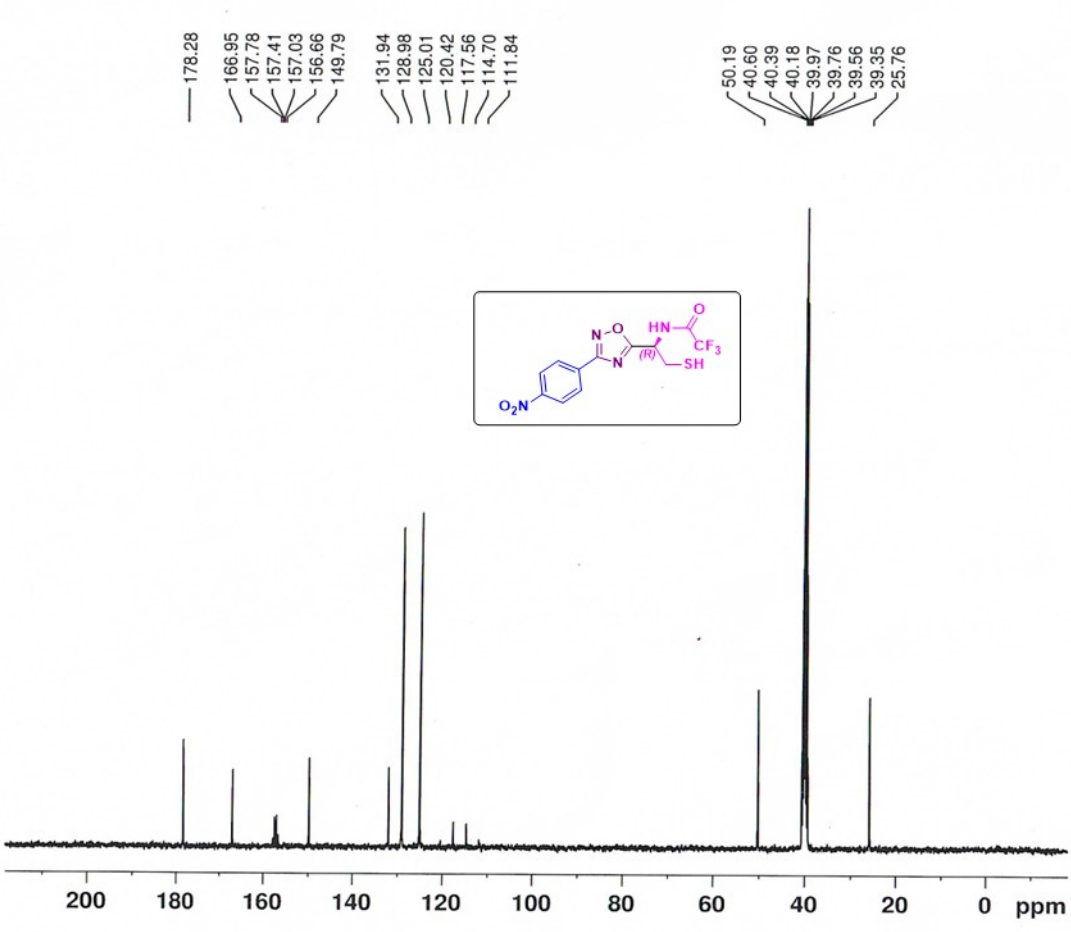


Fig. 95. ^{13}C NMR spectrum (DMSO-d_6, 100 MHz) of compound **4gk**

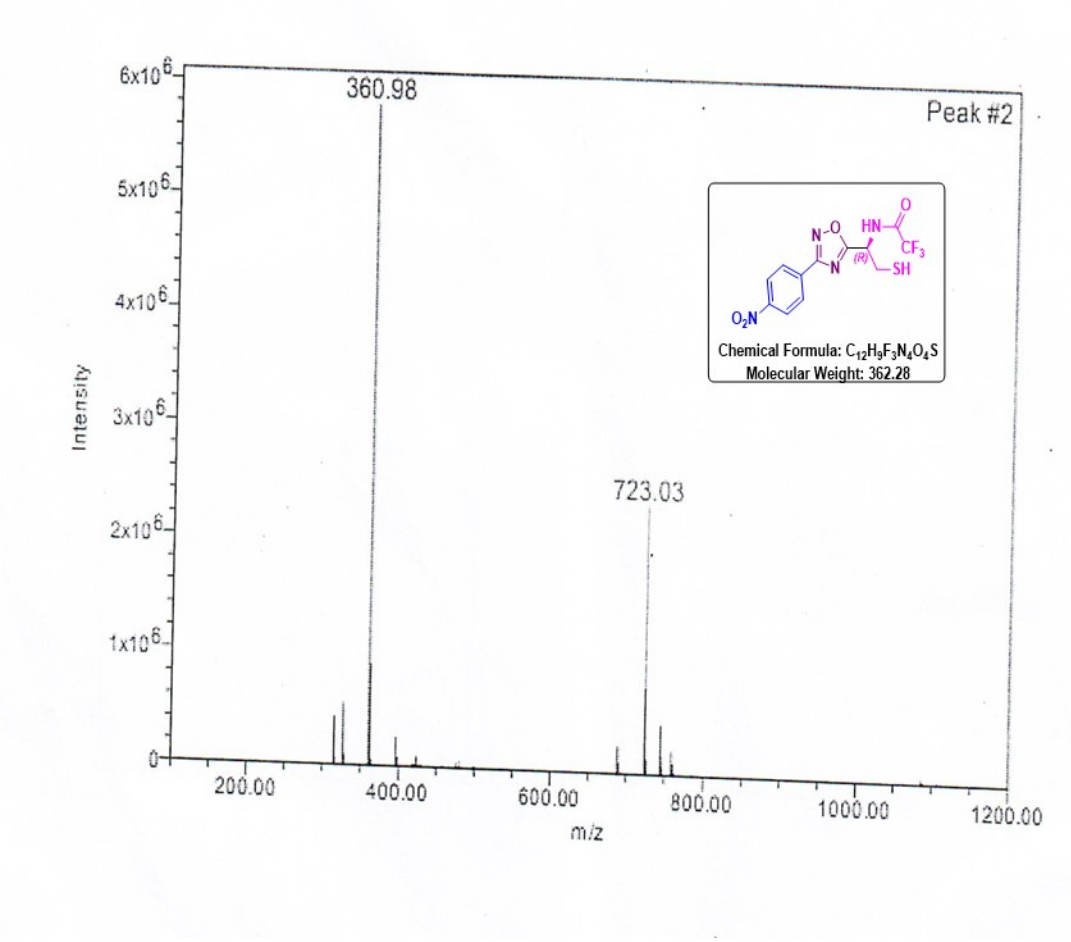
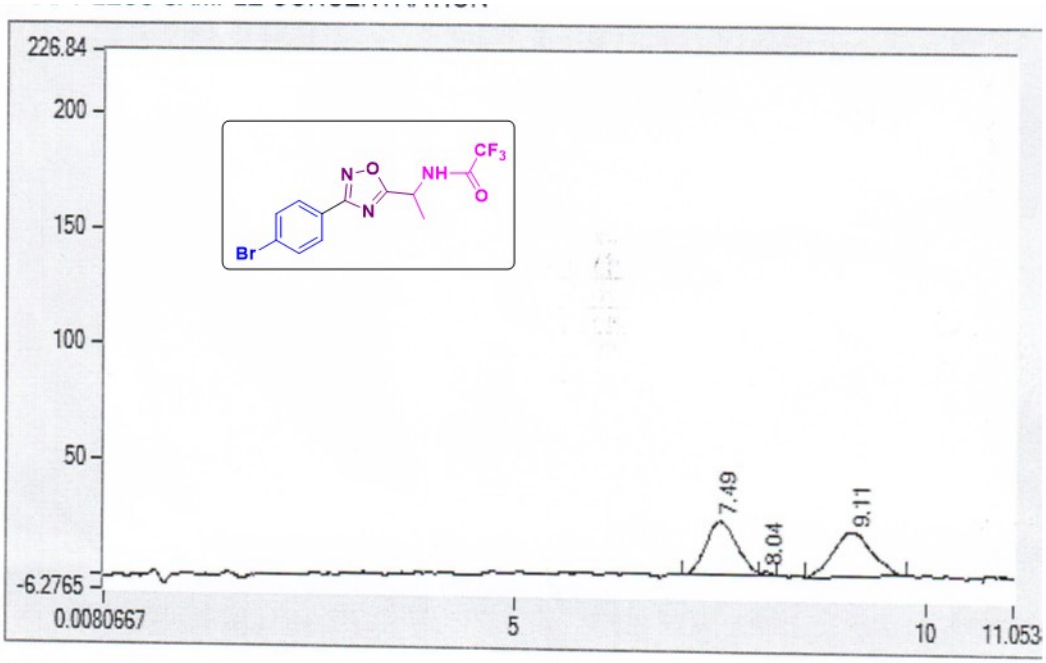


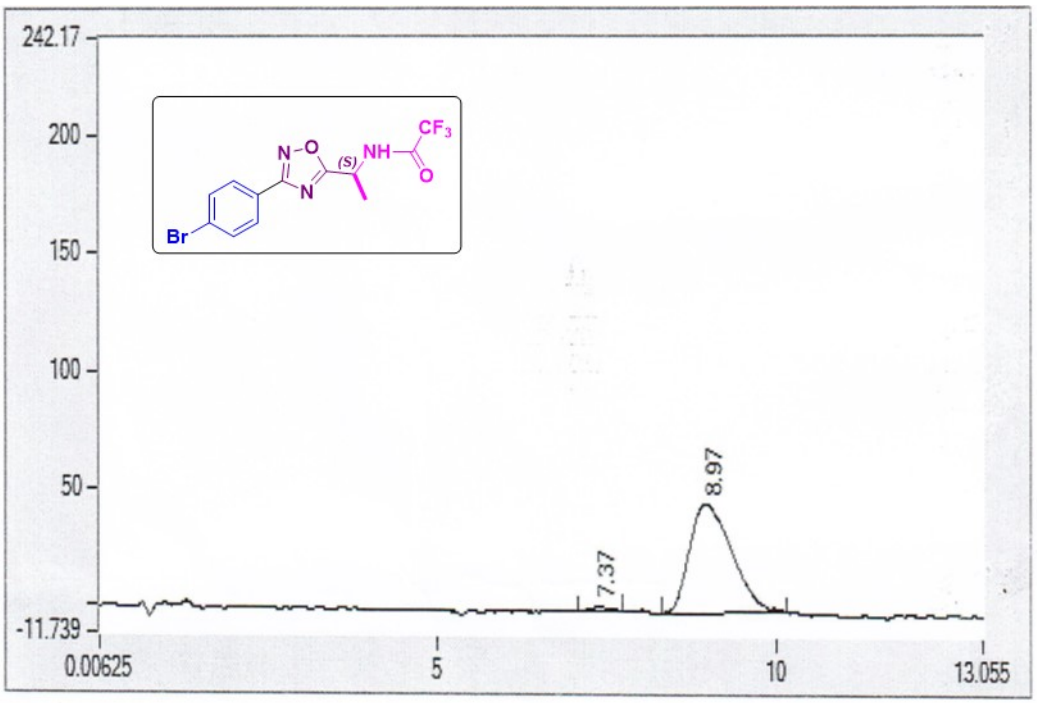
Fig. 96. Mass spectrum of compound **4gk**



Results UV1

Sr.No.	Beginning	RT	Area	Area %
1	7.019	7.49	600.199	51.985
2	7.957	8.04	12.888	1.116
3	8.529	9.11	541.481	46.899

Fig. 97. Chiral HPLC of racemic compound **4aj**



Results UV1

Sr.No.	Beginning	RT	Area	Area %
1	7.055	7.37	20.667	1.034
2	8.294	8.97	1977.649	98.966

Fig. 98. Chiral HPLC of compound **4aj**

Table S1. Crystal data and structure refinement for **4an**.

Identification code	**4an**	
Empirical formula	$C_{12} H_8 F_5 N_3 O_2$	
Formula weight	321.21	
Temperature	297(2) K	
Wavelength	1.54178 Å	
Crystal system	Triclinic	
Space group	P -1	
Unit cell dimensions	a = 5.2116(2) Å	α= 97.903(2)°.
	b = 7.7885(3) Å	β= 98.647(2)°.
	c = 16.4336(7) Å	γ = 97.738(2)°.
Volume	644.93(4) $Å^3$	
Z	2	
Density (calculated)	1.654 Mg/m^3	
Absorption coefficient	1.458 mm^{-1}	
F(000)	324	
Crystal size	0.290 x 0.134 x 0.103 mm^3	
Theta range for data collection	2.756 to 70.211°.	
Index ranges	-6<=h<=6, -9<=k<=9, -20<=l<=20	
Reflections collected	20587	
Independent reflections	2434 [R(int) = 0.0382]	

Completeness to theta = 67.679°	99.1 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.8404 and 0.7143
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2434 / 0 / 204
Goodness-of-fit on F^2	1.081
Final R indices [I>2sigma(I)]	R1 = 0.0731, wR2 = 0.2152
R indices (all data)	R1 = 0.0833, wR2 = 0.2304
Extinction coefficient	n/a
Largest diff. peak and hole	0.895 and -0.470 e.$Å^{-3}$

Table S2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **4an**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	3804(6)	6886(4)	5720(2)	57(1)
C(2)	5076(8)	7418(5)	6538(2)	64(1)
C(3)	7462(7)	8457(5)	6724(2)	63(1)
C(4)	8703(7)	9002(5)	6110(2)	69(1)
C(5)	7485(7)	8494(5)	5295(2)	62(1)
C(6)	5027(6)	7454(4)	5090(2)	49(1)
C(7)	3751(5)	6975(4)	4214(2)	49(1)
C(8)	3108(5)	6795(4)	2919(2)	48(1)
C(9)	3115(5)	6907(4)	2011(2)	47(1)
C(10)	5541(6)	8072(5)	1886(2)	60(1)
C(11)	498(6)	4218(4)	1200(2)	52(1)
C(12)	553(7)	2486(5)	639(2)	65(1)
N(1)	4877(5)	7496(3)	3561(1)	49(1)
N(2)	1447(6)	6037(4)	3989(2)	66(1)
N(3)	2855(5)	5150(3)	1532(2)	50(1)
O(1)	983(4)	5895(3)	3114(1)	66(1)

O(2)	-1597(4)	4646(3)	1288(2)	69(1)
F(1)	8614(5)	8942(4)	7531(1)	89(1)
F(2)	3964(6)	6940(4)	7164(2)	101(1)
F(3)	-175(9)	2606(4)	-134(2)	135(1)
F(4)	-1121(6)	1200(3)	806(2)	107(1)
F(5)	2815(6)	1930(4)	742(2)	120(1)

Table S3. Bond lengths [Å] and angles [°] for **4an**.

C(1)-C(2)	1.387(5)
C(1)-C(6)	1.387(4)
C(1)-H(1)	0.9300
C(2)-F(2)	1.325(4)
C(2)-C(3)	1.357(5)
C(3)-F(1)	1.351(4)
C(3)-C(4)	1.362(5)
C(4)-C(5)	1.373(5)
C(4)-H(4)	0.9300
C(5)-C(6)	1.388(4)
C(5)-H(5)	0.9300
C(6)-C(7)	1.467(4)
C(7)-N(2)	1.292(4)
C(7)-N(1)	1.380(4)
C(8)-N(1)	1.294(4)
C(8)-O(1)	1.334(3)
C(8)-C(9)	1.507(4)
C(9)-N(3)	1.460(4)
C(9)-C(10)	1.511(4)

C(9)-H(10)	0.9800
C(10)-H(10A)	0.9600
C(10)-H(10B)	0.9600
C(10)-H(10C)	0.9600
C(11)-O(2)	1.207(4)
C(11)-N(3)	1.335(4)
C(11)-C(12)	1.532(5)
C(12)-F(3)	1.290(4)
C(12)-F(5)	1.305(4)
C(12)-F(4)	1.324(4)
N(2)-O(1)	1.409(3)
N(3)-H(3A)	0.81(4)

C(2)-C(1)-C(6)	118.3(3)
C(2)-C(1)-H(1)	120.9
C(6)-C(1)-H(1)	120.9
F(2)-C(2)-C(3)	118.1(3)
F(2)-C(2)-C(1)	120.6(4)
C(3)-C(2)-C(1)	121.3(3)
F(1)-C(3)-C(2)	119.0(3)
F(1)-C(3)-C(4)	120.0(3)

C(2)-C(3)-C(4)	121.0(3)
C(3)-C(4)-C(5)	118.8(4)
C(3)-C(4)-H(4)	120.6
C(5)-C(4)-H(4)	120.6
C(4)-C(5)-C(6)	121.3(3)
C(4)-C(5)-H(5)	119.4
C(6)-C(5)-H(5)	119.4
C(1)-C(6)-C(5)	119.3(3)
C(1)-C(6)-C(7)	120.9(3)
C(5)-C(6)-C(7)	119.8(3)
N(2)-C(7)-N(1)	114.2(3)
N(2)-C(7)-C(6)	122.4(3)
N(1)-C(7)-C(6)	123.4(3)
N(1)-C(8)-O(1)	113.5(3)
N(1)-C(8)-C(9)	129.1(3)
O(1)-C(8)-C(9)	117.4(2)
N(3)-C(9)-C(8)	110.0(2)
N(3)-C(9)-C(10)	111.2(2)
C(8)-C(9)-C(10)	111.8(2)
N(3)-C(9)-H(10)	107.9
C(8)-C(9)-H(10)	107.9

C(10)-C(9)-H(10) 107.9

C(9)-C(10)-H(10A)109.5

C(9)-C(10)-H(10B)109.5

H(10A)-C(10)-H(10B)

C(9)-C(10)-H(10C)109.5

H(10A)-C(10)-H(10C)

H(10B)-C(10)-H(10C)

O(2)-C(11)-N(3) 125.9(3)

O(2)-C(11)-C(12) 119.1(3)

N(3)-C(11)-C(12) 115.1(3)

F(3)-C(12)-F(5) 110.3(4)

F(3)-C(12)-F(4) 106.4(3)

F(5)-C(12)-F(4) 104.3(3)

F(3)-C(12)-C(11) 110.6(3)

F(5)-C(12)-C(11) 114.1(3)

F(4)-C(12)-C(11) 110.8(3)

C(8)-N(1)-C(7) 102.4(2)

C(7)-N(2)-O(1) 103.9(2)

C(11)-N(3)-C(9) 121.3(2)

C(11)-N(3)-H(3A)118(3)

C(9)-N(3)-H(3A) 120(3)

C(8)-O(1)-N(2) 105.9(2)

Symmetry transformations used to generate equivalent atoms:

Table S4. Anisotropic displacement parameters ($Å^2 x\ 10^3$)for **4an**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2 a^{*2} U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	60(2)	57(2)	54(2)	6(1)	9(1)	8(1)
C(2)	82(2)	69(2)	46(2)	13(1)	15(2)	23(2)
C(3)	70(2)	65(2)	49(2)	-2(1)	-1(1)	19(2)
C(4)	65(2)	79(2)	58(2)	2(2)	2(2)	7(2)
C(5)	59(2)	69(2)	51(2)	3(1)	6(1)	1(2)
C(6)	54(2)	48(2)	45(2)	4(1)	7(1)	14(1)
C(7)	48(2)	49(2)	48(2)	3(1)	10(1)	10(1)
C(8)	41(1)	51(2)	49(2)	0(1)	9(1)	5(1)
C(9)	41(1)	52(2)	46(1)	1(1)	6(1)	7(1)
C(10)	55(2)	63(2)	59(2)	4(1)	15(1)	-2(1)
C(11)	49(2)	56(2)	46(2)	4(1)	2(1)	2(1)
C(12)	67(2)	65(2)	52(2)	-4(1)	1(1)	-1(2)
N(1)	45(1)	54(1)	45(1)	1(1)	6(1)	3(1)
N(2)	57(2)	87(2)	49(1)	8(1)	9(1)	-8(1)
N(3)	39(1)	56(1)	50(1)	-3(1)	6(1)	7(1)
O(1)	50(1)	92(2)	47(1)	4(1)	7(1)	-16(1)

O(2)	41(1)	76(2)	84(2)	-2(1)	6(1)	2(1)
F(1)	99(2)	113(2)	45(1)	0(1)	-6(1)	14(1)
F(2)	110(2)	124(2)	63(1)	20(1)	21(1)	-14(2)
F(3)	247(4)	99(2)	47(1)	-1(1)	-1(2)	28(2)
F(4)	124(2)	68(2)	113(2)	-3(1)	21(2)	-19(1)
F(5)	89(2)	96(2)	150(3)	-54(2)	1(2)	24(2)

Table S5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for **4an**

	x	y	z	U(eq)
H(1)	2174	6169	5598	69
H(4)	10345	9706	6241	83
H(5)	8323	8853	4872	74
H(10)	1579	7425	1805	57
H(10A)	7081	7644	2124	90
H(10B)	5559	9250	2155	90
H(10C)	5523	8063	1301	90
H(3A)	4150(80)	4750(50)	1430(20)	66(11)

Table S6. Torsion angles [°] for **4an.**

C(6)-C(1)-C(2)-F(2)	178.6(3)
C(6)-C(1)-C(2)-C(3)	-0.4(5)
F(2)-C(2)-C(3)-F(1)	0.8(5)
C(1)-C(2)-C(3)-F(1)	179.8(3)
F(2)-C(2)-C(3)-C(4)	-179.6(3)
C(1)-C(2)-C(3)-C(4)	-0.6(5)
F(1)-C(3)-C(4)-C(5)	-179.8(3)
C(2)-C(3)-C(4)-C(5)	0.6(6)
C(3)-C(4)-C(5)-C(6)	0.4(6)
C(2)-C(1)-C(6)-C(5)	1.3(5)
C(2)-C(1)-C(6)-C(7)	-178.4(3)
C(4)-C(5)-C(6)-C(1)	-1.4(5)
C(4)-C(5)-C(6)-C(7)	178.3(3)
C(1)-C(6)-C(7)-N(2)	0.9(5)
C(5)-C(6)-C(7)-N(2)	-178.8(3)
C(1)-C(6)-C(7)-N(1)	-179.8(3)
C(5)-C(6)-C(7)-N(1)	0.5(4)
N(1)-C(8)-C(9)-N(3)	121.8(3)
O(1)-C(8)-C(9)-N(3)	-60.2(3)

N(1)-C(8)-C(9)-C(10)	-2.3(4)
O(1)-C(8)-C(9)-C(10)	175.8(3)
O(2)-C(11)-C(12)-F(3)	71.0(4)
N(3)-C(11)-C(12)-F(3)	-107.1(4)
O(2)-C(11)-C(12)-F(5)	-163.9(3)
N(3)-C(11)-C(12)-F(5)	17.9(4)
O(2)-C(11)-C(12)-F(4)	-46.6(4)
N(3)-C(11)-C(12)-F(4)	135.2(3)
O(1)-C(8)-N(1)-C(7)	0.3(3)
C(9)-C(8)-N(1)-C(7)	178.5(3)
N(2)-C(7)-N(1)-C(8)	-0.6(3)
C(6)-C(7)-N(1)-C(8)	-179.9(3)
N(1)-C(7)-N(2)-O(1)	0.6(4)
C(6)-C(7)-N(2)-O(1)	180.0(3)
O(2)-C(11)-N(3)-C(9)	-4.3(5)
C(12)-C(11)-N(3)-C(9)	173.7(3)
C(8)-C(9)-N(3)-C(11)	89.6(3)
C(10)-C(9)-N(3)-C(11)	-146.0(3)
N(1)-C(8)-O(1)-N(2)	0.0(4)
C(9)-C(8)-O(1)-N(2)	-178.3(3)
C(7)-N(2)-O(1)-C(8)	-0.4(3)

Symmetry transformations used to generate equivalent atoms:

Table S7. Hydrogen bonds for sp302f-c [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(1)-H(1)...N(2)#1	0.93	2.61	3.452(4)	151.0
N(3)-H(3A)...O(2)#2	0.81(4)	2.28(4)	3.048(3)	160(4)

Symmetry transformations used to generate equivalent atoms:

#1 -x,-y+1,-z+1 #2 x+1,y,z

General procedure for antibacterial studies:

The *in vitro* antibacterial activities of the newer chiral *N*-protected-amino acid-derived 1,2,4-oxadiazoles (**4aa-4ej**) was performed against human pathogenic bacterial strains *viz.,* three gram positive bacteria, *Bacillus cereus* (ATCC 11778), *Staphylococcus aureus* (ATCC 25923) and *Enterococcus faecalis* (ATCC 19433) and three gram negative bacteria, *Klebsiella pneumonia* (ATCC 4352), *Escherichia coli* (ATCC 25922) and *Pseudomonas aeruginosa* (ATCC 15692). The novel *N*-protected-amino acid-derived 1,2,4-oxadiazoles (**4aa-4ej**) were prepared as stock solution of 1000 µg/mL concentration in DMSO solvent. The agar well diffusion method was used to determine the antibacterial activity of the synthesized compounds (**4aa-4ej**).[1] The media Muller-Hinton agar (Hi media) was used for the bactericidal study and the nutrient agar plates (13 x 13 cm petridish) were swabbed with cultured bacteria and the agar plates were incubated at 37°C for 24 h in aerobic conditions. A total of 4 mm diameter wells were punched into the agar and filled with 50 µL (From 1000 µg/mL) of synthesized compounds (**4aa-4ej**). The standard drug Gentamycin and Tetracycline was used as a positive control and the bare DMSO solvent was used as negative control.

Minimum Inhibitory Concentration (MIC)

The antibacterial efficacy of newly synthesized chiral *N*-protected-amino acid-derived 1,2,4-oxadiazole compound (**4al**) was studied by using broth dilution method and the MIC was determined in Muller Hinton broth using serial dilution method in various concentrations like 100, 50, 25, 12.5, 6.25, 3.13, 1.56, 0.78, 0.39 and 0.19 µg/mL in sterile 96 well plates. According to the McFarland turbidity standards, 50 µL of 106 colony forming unit (cfu/mL) of standard microorganism suspensions were inoculated on

to 96 well micro plates and incubated at 37 °C between 18 and 24 h. At the end of the incubation period, the plates were screened for the presence or absence of growth. The lowest level of concentration that inhibited the visible growth of bacteria was taken as the minimum inhibitory concentration (MIC). The sample of **4al** was evaluated for three times (triplicate) against each microorganism.

References:

1. D. Natarajan, S. J. Britto, K. Srinivasan, N. Nagamurugan, C. Mohanasundari, G. Perumal, *J. Ethnopharmacol*., 2005, **102**, 123–126.