Supporting Information

# Fexinidazole Optimization: Enhancing Anti-Leishmanial Profile, Metabolic Stability and hERG Safety

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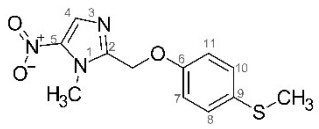
# Content

# 1. Chemical synthesis

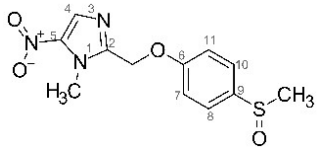
## 1.1 Chemical structures with labeling and their synthetic procedures

1-Methyl-2-{[4-(methylsulfanyl)phenoxy]methyl}-5-nitro-1*H*-imidazole (**5**)[1]



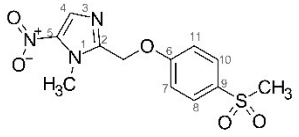
Prepared according to general procedure C. To a solution of 4-(methylthio)phenol (11 mmol, 1.55 g) in DMF (15 mL), $K_2CO_3$ (11 mmol, 1.52 g) was added and the mixture was stirred for 10 min. A solution of intermediate **15** (11 mmol, 1.94 g) in DMF (10 mL) was added slowly while stirring at room temperature. The reaction temperature was raised to 60 °C. The reaction was completed after 3 h. The reaction mixture was cooled and added to an ice-cold water (100 mL). The product was collected by filtration. The product was further purified by recrystallization from methanol. Yield: 59%, light yellow solid; Purity 99.1%; Mp: 107 - 108 °C (solid from methanol); $^1$H NMR (400 MHz, DMSO-$d_6$); δ = 8.07 (s, 1H, C4H), 7.28 (m, $^3J$ = 2.9 Hz, 2H, C8H & C10H), 7.08 (m, $^3J$ = 2.9 Hz, 2H, C7H & C11H), 5.27 (s, 2H, $CH_2$), 3.94 (s, 3H, $N^1CH_3$), 2.43 (s, 3H, $SCH_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 155.8 (C6), 148.0 (C2), 139.7 (C5), 131.6 (C4), 129.9 (C9), 128.8 (C8 & C10), 116.0 (C7 & C11), 62.4 ($\underline{C}H_2$), 33.7 ($N^1\underline{C}H_3$), 16.3 ($S\underline{C}H_3$); IR (cm$^{-1}$): ṽ = 1471 (N-O), 1358 (N-O), 819 (C-H); HRMS ((ESI) *m/z*) calculated for $C_{12}H_{13}N_3O_3S$ [M + H]$^+$: 280.0750, found: 280.0752.

2-[(4-Methanesulfinylphenoxy)methyl]-1-methyl-5-nitro-1*H*-imidazole (**6**)[1]



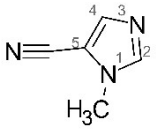
Prepared according to general procedure D. Compound **5** (3 mmol, 840 mg) was dissolved in DCM (10 mL). The solution was cooled in ice-cold water bath. A solution of 3-chloroperoxybenzoic acid (3.3 mmol, 1.04 g) in DCM (20 mL) was added over a period of 30 min. After complete addition, the mixture was stirred for an additional 30 min. The reaction mixture was then washed with 20 mL of aq. $NaHCO_3$ (10%). The product was separated using flash chromatography. The product was further purified by recrystallization from methanol. Yield: 64%, light yellow solid; Purity 99.6%; Mp: 151 - 152 °C (solid from methanol); $^1$H NMR (400 MHz, DMSO-$d_6$); δ = 8.09 (s, 1H, C4H), 7.67 (m, $^3J$ = 2.9 Hz, 2H, C8H & C10H), 7.30 (m, $^3J$ = 2.9 Hz, 2H, C7H & C11H), 5.38 (s, 2H, $CH_2$), 3.96 (s, 3H, $N^1CH_3$), 2.71 (s, 3H, $SO_2CH_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 159.5 (C6), 147.8 (C2), 139.8 (C5), 138.4 (C9), 131.6 (C4), 125.6 (C8 & C10), 115.8 (C7 & C11), 62.3 ($\underline{C}H_2$), 43.3 ($SO_2\underline{C}H_3$), 33.7 ($N^1\underline{C}H_3$); IR (cm$^{-1}$): ṽ = 1468 (N-O), 1290 (C-N), 1141 (S=O); HRMS ((ESI) *m/z*) calculated for $C_{12}H_{13}N_3O_5S$ [M+ H]$^+$: 312.0649, found: 312.0655.

2-[(4-Methanesulfonylphenoxy)methyl]-1-methyl-5-nitro-1*H*-imidazole (**7**)[1]



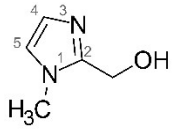
Prepared according to general procedure D. Compound **7** was a second product of the reaction for the synthesis of compound **6**. The product was separated using flash chromatography and was further purified by recrystallization from ethyl acetate. Yield: 36%, off-white solid; Purity 96.8%; Mp: 127 - 128 °C (solid from ethyl acetate); $^{1}$H NMR (400 MHz, DMSO-$d_6$); δ = 8.09 (s, 1H, C4H), 7.90 (m, $^{3}J$ = 3.0 Hz, 2H, C8H & C10H), 7.33 (m, $^{3}J$ = 3.0 Hz, 2H, C7H & C11H), 5.43 (s, 2H, $CH_2$), 3.95 (s, 3H, $N^1CH_3$), 3.17 (s, 3H, $SOCH_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 161.3 (C6), 147.3 (C2), 139.8 (C5), 133.6 (C9), 131.6 (C4), 129.2 (C8 & C10), 115.5 (C7 & C11), 62.4 ($\underline{C}H_2$), 43.9 ($SO\underline{C}H_3$), 33.7 ($N^1\underline{C}H_3$); IR (cm$^{-1}$): ṽ = 1466 (N-O), 1362 (S=O); HRMS ((ESI) *m/z*) calculated for $C_{12}H_{13}N_3O_4S$ [M+ H]$^+$: 296.0700, found: 296.0704.

1-Methyl-1*H*-imidazole-5-carbonitrile (**10**)



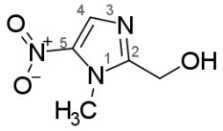
To a solution of 1*H*-imidazole-4-carbonitrile (30 mmol, 2.8 g) in dioxane (40 mL), dimethyl sulfate (45 mmol, 4.3 mL) was added. The mixture was refluxed for 5 h. The reaction mixture was concentrated and water was added. The product was extracted by washing with ethyl acetate (3 x 30 mL). The product was separated using flash chromatography. Yield: 56%, colorless solid; Mp: 143 - 144 °C (solid from ethyl acetate); $^{1}$H NMR (400 MHz, DMSO-$d_6$); δ = 8.00 (s, 1H, C2H), 7.82 (d, *J* = 0.8 Hz, 1H, C4H), 3.78 (s, 3H, $N^1CH_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 142.5 (C2), 139.6 (C4), 111.6 ($\underline{C}N$), 105.0 (C5), 32.6 ($N^1\underline{C}H_3$); IR (cm$^{-1}$) ṽ = 3125 (C-H), 2227 (C-N), 1234 (C-N).

(1-Methyl-1*H*-imidazol-2-yl)methanol (**11**)



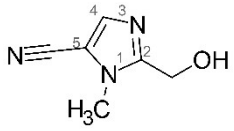
Prepared according to general procedure A. In a pressurized reactor, a mixture of 1-methylimidazole (100 mmol, 8 mL), paraformaldehyde (170 mmol, 5.11 g), and DMSO (25 mL) was heated at 110 °C for 48 h. The DMSO was removed at reduced pressure. Recrystallization from ethanol and washing with acetone yield a pure product. Yield: 68%, light brown solid; Mp: 115 - 116 °C (solid from ethanol); $^{1}$H NMR (400 MHz, DMSO-$d_6$); δ = 7.06 (d, 1H, $^{3}J$ = 1.1 Hz, C4H), 6.75 (d, 1H, $^{3}J$ = 1.2 Hz, C5H), 5.30 (bs, 1H, OH), 4.46 (s, 2H, $CH_2$), 3.64 (s, 3H, $N^1CH_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 147.3 (C2), 126.1 (C4), 122.0 (C5), 55.5 ($\underline{C}H_2$), 32.4 ($N^1\underline{C}H_3$); IR (cm$^{-1}$): ṽ = 1494 (O-H), 1247 (C-N), 1019 (C-O).

(1-Methyl-5-nitro-1*H*-imidazol-2-yl)methanol (**12**)



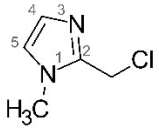
Prepared following general procedure A.[16] In a pressurized reactor, a mixture of 1-methyl-5-nitroimidazole (60 mmol, 7.63 g), paraformaldehyde (102 mmol, 3.1 g), and DMSO (20 mL) was heated at 110 °C for 48 h. The DMSO was removed at reduced pressure. The product was separated using flash chromatography. The product was separated using flash chromatography. Yield: 62%, light brown solid; Mp: 117 - 118 °C (solid from ethanol); $^{1}$H NMR (400 MHz, DMSO-$d_6$); δ = 8.01 (s, 1H, C4H), 5.74 (t, $^{3}J$ = 5.74 Hz, 1H, OH), 4.59 (d, $^{3}J$ = 5.6 Hz, 2H, $CH_2$), 3.92 (s, 3H, $N^1CH_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 152.4 (C2), 139.2 (C5), 131.5 (C4), 56.1 ($\underline{C}H_2$), 33.3 ($N^1\underline{C}H_3$); IR ($cm^{-1}$): $\tilde{\nu}$ = 1469 (C-H), 1037 (C-O).

2-(Hydroxymethyl)-1-methyl-1*H*-imidazole-5-carbonitrile (**13**)



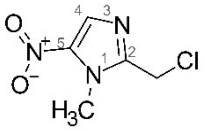

Prepared following general procedure A. In a pressurized reactor, a mixture of compound **10** (12 mmol, 1.4 g), paraformaldehyde (48 mmol, 1.44 g), and DMSO (20 mL) was heated at 125 °C for 48 h. The DMSO was removed at reduced pressure. The product was separated using flash chromatography. Yield: 56%, off-white solid; Mp: 160 - 161 °C (solid from ethanol); $^{1}$H NMR (400 MHz, DMSO-$d_6$); δ = 7.75 (s, 1H, C4H), 5.61 (t, $^{3}J$ = 5.20 Hz, 1H, OH), 4.56 (d, $^{3}J$ = 4.84 Hz, 2H, $CH_2$), 3.75 (s, 3H, $N^1CH_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 152.0 (C2), 137.9 (C4), 111.7 ($\underline{C}N$), 105.8 (C5), 55.5 ($\underline{C}H_2$), 31.9 ($N^1\underline{C}H_3$); IR ($cm^{-1}$): $\tilde{\nu}$ = 3125 (C-H), 2231 (C-N), 1050 (C-O).

2-(Chloromethyl)-1-methyl-1*H*-imidazole (**14**)




Prepared according to general procedure B. A solution of compound **11** (10 mmol, 1.12 g) in DCM (20 mL) was added dropwise to a solution of thionyl chloride (2.65 mL) in DCM (10 mL). After complete addition, the mixture was heated at 40 °C for 30 min. The reaction mixture was evaporated to dryness. Then ethanol (10 mL) was added, and the reaction mixture heated at 40 °C for 10 min and was re-evaporated to dryness to remove the excess thionyl chloride. The residue was recrystallized from DCM: n-hexane (1:1). Yield: 73%, off-white solid; Mp: 172 - 178 °C (solid from DCM: n-hexane (1:1)); $^{1}$H NMR (400 MHz, DMSO-$d_6$); δ = 7.78 (d, 1H, $^{3}J$ = 1.9 Hz, C4H), 7.70 (d, 1H, $^{3}J$ = 1.9 Hz, C5H), 5.19 (s, 2H, $CH_2$), 3.89 (s, 3H; $N^1CH_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 141.5 (C2), 124.8 (C4), 119.3 (C5), 34.3 ($N^1\underline{C}H_3$), 31.7 ($\underline{C}H_2$); IR ($cm^{-1}$): $\tilde{\nu}$ = 1216 (N-H), 850 (C-Cl).

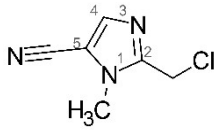
2-(Chloromethyl)-1-methyl-5-nitro-1*H*-imidazole (**15**)




Prepared following general procedure B.[17] A solution of compound **12** (10 mmol, 1.58 g) in DCM (25 mL) was added dropwise to a solution of thionyl chloride (2.7 mL) in DCM (10 mL). After complete addition, the mixture was heated at 40 °C for 30 min. The reaction mixture was

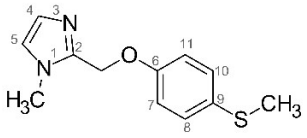
then evaporated to dryness. Then ethanol (10 mL) was added and the reaction mixture was re-evaporated to dryness to remove the excess thionyl chloride. The residue was recrystallized from DCM: n-hexane (1:1). Yield: 75%, off-white solid; Mp: 156 - 158 °C (solid from DCM: n-hexane (1:1)); $^{1}$H NMR (400 MHz, DMSO-$d_6$); δ = 8.08 (s, 1H, C4H), 4.99 (s, 2H, $CH_2$), 3.95 (s, 3H, $N^1CH_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 148.0 (C2), 139.7 (C5), 131.7 (C4), 36.5 ($\underline{C}H_2$), 33.7 ($N^1\underline{C}H_3$); IR ($cm^{-1}$): $\tilde{\nu}$ = 2350 (C-H), 1492 (N-O), 1378 (N-O).

2-(Chloromethyl)-1-methyl-1*H*-imidazole-5-carbonitrile (**16**)



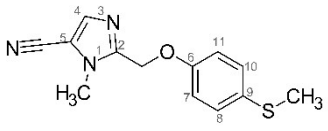
Prepared following general procedure B. A solution of compound **13** (2.2 mmol, 300 mg) in DCM (10 mL) was added dropwise to a solution of thionyl chloride (560 µL) in DCM (2 mL). The mixture was heated at 40 °C for 30 min. The reaction mixture was then evaporated to dryness. Ethanol (5 mL) was added and the reaction mixture was re-evaporated to dryness to remove was the excess thionyl chloride. The product was further purified by recrystallization from ethyl acetate. Yield: 78%, off-white solid; Mp: 139 - 140 °C (solid from ethanol); $^{1}$H NMR (400 MHz, DMSO-$d_6$); δ = 7.87 (s, 1H, C4H), 4.95 (s, $CH_2$), 3.79 (s, 3H, $N^1CH_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 147.7 (C2), 138.2 (C4), 111.3 ($\underline{C}N$), 107.1 (C5), 35.8 ($\underline{C}H_2$), 32.4 ($N^1\underline{C}H_3$); IR ($cm^{-1}$): $\tilde{\nu}$ = 3017 (C-H), 2243 (C-N), 881 (C-Cl).

1-Methyl-2-{[4-(methylsulfanyl)phenoxy]methyl}-1*H*-imidazole (**17**)



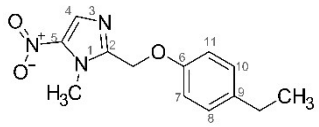
A mixture of compound **14** (6 mmol, 785 mg), $Cs_2CO_3$ (36 mmol, 12 g) and potassium iodide (6 mmol, 1 g) in DMF (30 mL) was set under $N_2$ atmosphere and stirred for 10 min. A solution of 4-(methylthio)phenol (6 mmol, 840 mg) in DMF (5 mL) was added. The reaction mixture was then heated at 80 °C for overnight. The reaction mixture was cooled and DCM (50 mL) was added, followed by filtration. The filtrate was washed with NaOH (5N, 3 x 10 mL) and distilled water. The dried product was recrystallized from ethanol. Yield: 55%, off-white solid; Purity 98.5%; Mp: 68 - 70 °C (solid from ethanol); $^{1}$H NMR (400 MHz, DMSO-$d_6$); δ = 7.27 (m, 2H, *J* = 2.95 Hz, C8H & C10H), 7.18 (d, 1H, $^{3}J$ = 1 Hz, C4H), 7.07 (m, 2H, J = 2.96 Hz, C7H & C11H), 6.87 (d, 1H, $^{3}J$ = 1.1 Hz, C5H), 5.11 (s, 2H, $CH_2$), 3.66 (s, 3H, $N^1CH_3$), 2.42 (s, 3H, $SCH_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 156.3 (C6), 142.9 (C2), 129.2 (C9), 128.9 (C5 & C10), 126.8 (C5), 122.9 (C4), 115.8 (C7 & C11), 62.1 ($\underline{C}H_2$), 32.6 ($N^1\underline{C}H_3$), 16.5 ($S\underline{C}H_3$); IR ($cm^{-1}$): $\tilde{\nu}$ = 1230 (C-N), 812 (C-H); Elemental analysis, calculated C (61.51%), H (6.02%), N (11.96%), O (6.83%), S (13.68%); found C (60.84%), H (5.97%), N (11.69%), S (13.44%).

1-Methyl-2-{[4-(methylsulfanyl)phenoxy]methyl}-1*H*-imidazole-5-carbonitrile (**18**)



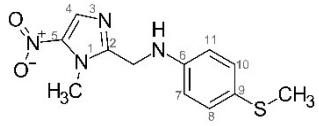
Prepared following general procedure C. To a solution of 4-(methylthio)phenol (1 mmol, 140 mg) in DMF (5 mL), $K_2CO_3$ (1 mmol, 140 mg) added and the mixture was stirred for 10 min. A solution of compound **16** (1 mmol, 156 mg) in DMF (3 mL) was added slowly while stirring at room temperature. The reaction mixture was stirred at 60 °C for 3 h. The reaction mixture was cooled and added to an ice-cold water (100 mL). The product was collected by filtration. The product was further purified by recrystallization from DCM. Yield: 22%, colorless solid; Purity 99.7%; Mp: 116 - 117 °C (solid from DCM); $^1$H NMR (400 MHz, DMSO-$d_6$); δ = 7.84 (s, 1H, C4H), 7.27 (m, $^3J$ = 2.9 Hz, 2H, C8H & C10H), 7.07 (m, $^3J$ = 2.9 Hz, 2H, C7H & C11H), 5.23 (s, 2H, $CH_2$), 3.78 (s, 3H, $N^1CH_3$), 2.42 (s, 3H, $SCH_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 155.9 (C6), 147.8 (C2), 138.3 (C4), 129.8 (C9), 128.8 (C8 & C10), 116.0 (C7 & C11), 111.5 (CN), 106.8 (C5), 61.8 ($CH_2$), 32.3 ($N^1CH_3$), 16.4 ($SCH_3$); IR (cm$^{-1}$): ṽ = 2224 (C≡N), 1231 (C-O); HRMS ((ESI) *m/z*) calculated for $C_{13}H_{13}N_3OS$ [M+ H]$^+$: 260.0852, found: 260.0859.

2-[(4-Ethylphenoxy)methyl]-1-methyl-5-nitro-1*H*-imidazole (**19**)



Prepared following general procedure C. To a solution of 4-ethyl phenol (2.5 mmol, 306 mg) in DMF (5 mL), $K_2CO_3$ (2.5 mmol, 350 mg) was added and the mixture was stirred for around 10 min. A solution of compound **15** (2.5 mmol, 440 mg) in DMF (6 mL) was added slowly. The reaction mixture was stirred for 3 h at 60 °C. The reaction was completed after 3 h. The reaction mixture was cooled and added to an ice-cold water (100 mL). The product was collected by filtration. The product was further purified by recrystallization from methanol. Yield: 33%, very light-yellow solid; Purity 98.7%; Mp: 98 - 99 °C (solid from methanol); $^1$H NMR (400 MHz, DMSO-$d_6$); δ = 8.08 (s, 1H, C4H), 7.16 (m, $^3J$ = 2.8 Hz, 2H, C8H & C10H), 7.01 (m, $^3J$ = 2.9 Hz, 2H, C7H & C11H), 5.24 (s, 2H, $CH_2$), 3.94 (s, 3H, $N^1CH_3$), 2.57 (m, $^3J$ = 7.6 Hz, 2H, $CH_2CH_3$), 2.43 (m, $^3J$ = 7.6 Hz, 3H, $CH_2CH_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 155.6 (C6), 148.1 (C2), 139.7 (C5), 136.9 (C9), 131.5 (C4), 128.8 (C8 & C10), 114.9 (C7 & C11), 62.2 ($CH_2$), 33.6 ($N^1CH_3$), 27.3 ($CH_2CH_3$), 15.9 ($CH_2CH_3$); IR (cm$^{-1}$): ṽ = 1471 (N-O), 1353 (N-O), 1180 (C-O); HRMS ((ESI) *m/z*) calculated for $C_{13}H_{15}N_3O_3$ [M+ H]$^+$: 262.1186, found: 262.1196.

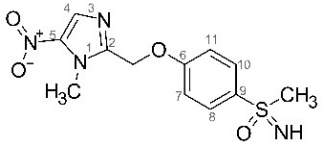
*N*-[(1-Methyl-5-nitro-1*H*-imidazol-2-yl)methyl]-4-(methylsulfanyl)aniline (**20**)



4-(Methylthio)aniline (1.5 mmol, 190 µL) and triethylamine (2 mmol, 280 µL) were added to a solution of compound **15** (1 mmol, 175 mg) in isopropanol (8 mL). The mixture was refluxed for overnight. The product was precipitated with the additional of water. The product was further purified using flash chromatography. Yield: 37%, vermilion solid; Purity 99.1%; Mp: 148 - 149 °C (solid from n-hexane and ethyl acetate); $^1$H NMR (400 MHz, DMSO-$d_6$); δ = 8.04 (s, 1H, C4H), 7.12 (m, $^3J$ = 2.9 Hz, 2H, C8H & C10H), 6.70 (m, $^3J$ = 2.9 Hz, 2H, C7H & C11H), 6.34 (t, $^3J$ = 5.8 Hz, 1H, NH), 4.42 (d, $^3J$ = 5.8 Hz, 2H, $CH_2$), 3.91 (s, 3H, $N^1CH_3$), 2.33 (s, 3H, $SCH_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 151.3 (C2), 146.9 (C6), 139.3 (C5), 131.8 (C4), 130.5 (C8 & C10), 123.2 (C9), 113.4 (C7 & C11), 40.5 ($CH_2$), 33.3 ($N^1CH_3$), 18.1 ($SCH_3$); IR

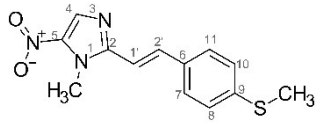
($cm^{-1}$): $\tilde{\nu}$ = 3398 (N-H), 1608 (N-H), 1369 (N-O), 1179 (C-O); HRMS ((ESI) *m/z*) calculated for $C_{12}H_{14}N_4O_2S$ $[M+H]^+$: 279.0910, found: 279.0914.

Imino(methyl){4-[(1-methyl-5-nitro-1*H*-imidazol-2-yl)methoxy]phenyl}-$\lambda^6$-sulfanone (**21**)



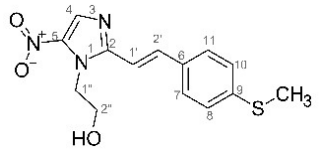
Prepared according to general procedure E. Compound **5** (0.65 mmol, 180 mg) was suspended in methanol (5 mL). Ammonium carbonate (0.95 mmol, 90 mg) and diacetoxyl iodobenzene (1.5 mmol, 445 mg) were added respectively. The mixture was stirred for 10 min at room temperature. The product was isolated using flash chromatography. Yield: 70%, brown solid; Purity 98.7%; Mp: 96 - 97 °C (solid from DCM and methanol); $^1$H NMR (400 MHz, DMSO-$d_6$); δ = 8.10 (s, 1H, C4H), 7.88 (m, $^3J$ = 8.4 Hz, 2H, C8H & C10H), 7.28 (m, $^3J$ = 8.4 Hz, 2H, C7H & C11H), 5.42 (s, 2H, $CH_2$), 4.12 (bs, 1H, SONH), 3.95 (s, 3H, $N^1CH_3$), 3.03 (s, 3H, $SO_2CH_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 160.6 (C6), 147.4 (C2), 139.8 (C5), 136.8 (C9), 131.5 (C4), 129.5 (C8 & C10), 115.1 (C7 & C11), 62.3 ($\underline{C}H_2$), 46.2 (SONH$\underline{C}H_3$), 33.6 ($N^1\underline{C}H_3$); IR ($cm^{-1}$): $\tilde{\nu}$ = 3297 (N-H), 1471 (N-O), 1214 (C-O); HRMS ((ESI) *m/z*) calculated for $C_{12}H_{14}N_4O_4S$ $[M+H]^+$: 311.0809, found: 311.0814.

1-Methyl-2-{2-[4-(methylsulfanyl)phenyl]ethenyl}-5-nitro-1*H*-imidazole (**24**)



Prepared according to general procedure F. To a solution of 1,2-dimethyl-5-nitroimidazole (4 mmol, 565 mg) in ethanol (22 mL), sodium ethoxide (10 mmol, 785 µL) was added. The mixture was stirred vigorously for 10 min. 4-(thiomethyl) benzaldehyde (5.2 mmol, 690 µL) was then added dropwise. The reaction mixture was stirred at 65 °C for overnight. The reaction mixture was cooled and filtered. The precipitate was washed with ethanol and n-hexane to yield a yellow-colored product. Yield: 54%, yellow solid; Mp: 180 - 181 °C (solid from ethanol); $^1$H NMR (400 MHz, DMSO-$d_6$); δ = 8.18 (s, 1H, C4H), 7.75 (m, *J* = 5.1 Hz, 3H, C8H, C10H & C2'H), 7.35 (s, 1H, C1'H), 7.31 (m, *J* = 8.4 Hz, 2H, C7H & C11H), 4.01 (s, 3H, $N^1CH_3$), 2.52 (s, 3H, $SCH_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 150.1 (C2), 140.5 (C6), 139.7 (C5), 137.7 (C2'), 134.4 (C4), 132.1 (C9), 128.4 (C8 & C10), 125.8 (C7 & C11), 112.1 (C1'), 32.9 ($N^1\underline{C}H_3$), 14.4 ($S\underline{C}H_3$); IR ($cm^{-1}$): $\tilde{\nu}$ = 3114 (C-H), 1624 (C=C).

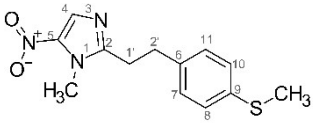
2-{2-[4-(Methylsulfanyl)phenyl]ethenyl}-5-nitro-1*H*-imidazol-1-yl}ethan-1-ol (**25**)



Prepared following general procedure F. To a solution of metronidazole (4.43 mmol, 1.265 g) in ethanol (20 mL), sodium methoxide (11 mmol, 755 mg) was added. The mixture was stirred vigorously for 10 min. 4-(thiomethyl) benzaldehyde (4.9 mmol, 650 µL) was then added dropwise. The reaction mixture was stirred at 65 °C for overnight. The product was isolated

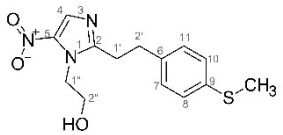
using flash chromatography. Yield: 23%, reddish yellow solid; Mp: 174 - 175 °C (solid from n-hexane and ethyl acetate); $^{1}$H NMR (400 MHz, DMSO-$d_6$); δ = 8.21 (s, 1H, C4H), 7.76 (m, 1H, C2'H), 7.72 (m, $^{3}J$ = 2.5 Hz, 2H, C8H & C10H), 7.35 (m, 1H, C1'H), 7.32 (m, $J$ = 2.7 Hz, 2H, C7H & C11H), 5.01 (t, $^{3}J$ = 5.7 Hz, 1H, OH), 4.63 (t, $^{3}J$ = 5.2 Hz, 2H, C1"$H_2$), 3.73 (m, $^{3}J$ = 5.3 Hz, 2H, C2"$H_2$), 2.52 (s, 3H, $SCH_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 150.8 (C2), 140.2 (C6), 138.6 (C5), 137.1 (C2'), 134.8 (C4), 132.1 (C9), 128.1 (C8 & C10), 125.7 (C7 & C11), 112.9 (C1'), 60.1 (C2"), 47.3 (C1"), 14.3 (S<u>C</u>$H_3$); IR (cm$^{-1}$): ṽ = 3227 (O-H), 1370 (N-O).

1-Methyl-2-{2-[4-(methylsulfanyl)phenyl]ethyl}-5-nitro-1*H*-imidazole (**26**)



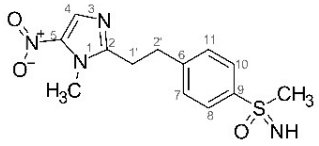
Prepared according to general procedure G. A mixture of compound **24** (0.5 mmol, 140 mg), *p*-toluenesulfonyl hydrazide (2.5 mmol, 470 mg), $K_2CO_3$ (2.5 mmol, 350 mg) in pyridine (10 mL) was refluxed for 13 h. The reaction mixture was cooled and filtered. Ethyl acetate (30 mL) was added to the filtrate, which was then washed with aqueous $CuSO_4$ solution (5%, 3 x 15 mL). The product was isolated using flash chromatography. The product was further purified by recrystallization from methanol. Yield: 36%, off-white solid; Purity 99.6%; Mp: 109 - 110 °C (solid from methanol); $^{1}$H NMR (400 MHz, DMSO-$d_6$); δ = 8.03 (s, 1H, C4H), 7.75 (m, $J$ = 1.8 Hz, 4H, C7H, C8H, C10H & C11H), 3.76 (s, 3H, N$^{1}$$CH_3$), 3.06 (m, $^{3}J$ = 2.3 Hz, 2H, C1'$H_2$), 3.00 (m, $^{3}J$ = 2.8 Hz, 2H, C2'$H_2$), 2.53 (s, 3H, $SCH_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 153.1 (C2), 138.8 (C5), 137.2 (C6), 135.5 (C9), 129.1 (C8 & C10), 126.2 (C7 & C11), 32.8 (N$^{1}$<u>C</u>$H_3$), 31.5 (C2'), 28.4 (C1'), 15.0 (S<u>C</u>$H_3$); IR (cm$^{-1}$): ṽ = 2916 (C-H), 1466 (N-O), 1365 (N-O); HRMS ((ESI) *m/z*) calculated for $C_{13}H_{15}N_3O_2S$ [M+ H]$^{+}$: 278.0958, found: 278.0967.

2-(2-{2-[4-(Methylsulfanyl)phenyl]ethyl}-5-nitro-1*H*-imidazol-1-yl)ethan-1-ol (**27**)



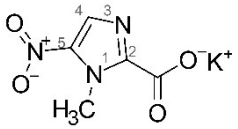
Prepared following general procedure G. A mixture of compound **25** (2.1 mmol, 1.01 g), *p*-toluenesulfonyl hydrazide (10.5 mmol, 2.0 g), $K_2CO_3$ (10.5 mmol, 1.46 g) in pyridine (10 mL) was refluxed for 13 h. The reaction mixture was cooled and filtered. Ethyl acetate (30 mL) was added to the filtrate, which was then washed with aqueous $CuSO_4$ solution (5%, 3 x 15 mL). The product was isolated using flash chromatography. Yield: 24%, dark yellow solid; Purity 96.6%; Mp: 115 - 116 °C (solid from n-hexane and ethyl acetate); $^{1}$H NMR (400 MHz, DMSO-$d_6$); δ = 8.08 (s, 1H, C4H), 7.73 (m, $J$ = 7.4 Hz, 4H, C7H, C8H, C10H & C11H), 5.07 (t, $^{3}J$ = 5.5 Hz, 1H, OH), 4.35 (t, $^{3}J$ = 5.2 Hz, 2H, C1"$H_2$), 3.66 (m, $^{3}J$ = 5.3 Hz, 2H, C2"$H_2$), 3.09 (m, $J$ = 3.87 Hz, 4H, C1'$H_2$ & C2'$H_2$), 2.44 (s, 3H, $SCH_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 154.1 (C2), 138.5 (C6), 137.5 (C5), 135.6 (C9), 133.1 (C4), 129.2 (C8 & C10), 126.4 (C7 & C11), 59.9 (C2"), 47.9 (C1"), 31.7 (C2'), 28.7 (C1'), 15.2 (S<u>C</u>$H_3$); IR (cm$^{-1}$): ṽ = 3237 (O-H), 1450 (N-O), 1372 (N-O), 1266 (C-O); HRMS ((ESI) *m/z*) calculated for $C_{14}H_{17}N_3O_3S$ [M+ H]$^{+}$: 308.1063, found: 308.1077.

Imino(methyl){4-[2-(1-methyl-5-nitro-1*H*-imidazol-2-yl)ethyl]phenyl}-λ$^{6}$-sulfanone (**28**)



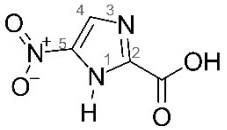
Prepared following general procedure E. Compound **26** (0.65 mmol, 167 mg) was suspended in methanol (10 mL). Ammonium carbonate (0.95 mmol, 90 mg) and diacetoxyl iodobenzene (1.5 mmol, 445 mg) were added respectively. The mixture was stirred for 10 min at room temperature. The product was isolated using flash chromatography. Yield: 74%, off-white solid; Purity 97.8%; Mp: 183 - 184 °C (solid from DCM and methanol); $^{1}$H NMR (400 MHz, DMSO-$d_6$); δ = 8.03 (s, 1H, C4H), 7.84 (m, $^{3}J$ = 2.8 Hz, 2H, C8H & C10H), 7.51 (m, $^{3}J$ = 2.6 Hz, 2H, C7H & C11H), 4.20 (bs, 1H, SONH), 3.80 (s, 3H, N$^{1}$C$H_3$), 3.14 (m, $J$ = 3.3 Hz, 4H, C1'$H_2$ & C2'$H_2$), 3.04 (s, 3H, S$CH_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 152.8 (C2), 145.4 (C6), 142.0 (C9), 138.9 (C5), 132.2 (C4), 129.0 (C7 & C11), 127.3 (C8 & C10), 45.9 (S$\underline{C}H_3$), 32.8 (N$^{1}\underline{C}H_3$), 31.6 (C1'), 27.8 (C2'); IR (cm$^{-1}$): ῦ = 3300 (O-H), 1460 (N-O), 1175 (C-O); HRMS ((ESI) *m/z*) calculated for $C_{13}H_{16}N_4O_3S$ [M+ H]$^{+}$: 309.1016, found: 309.1018.

Potassium;1-methyl-5-nitro-1*H*-imidazole-2-carboxylate (**29**)[2]



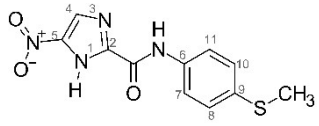
A solution of compound **12** (8 mmol, 1.26 g) in acetone (16 mL) was stirred in ice-cold water for 10 min. Potassium permanganate (11 mmol, 1.74 g) was added in portions. After complete addition, the reaction mixture was stirred at room temperature for 4 h. An additional potassium permanganate (5.5 mmol, 870 mg) was added to the reaction mixture that was replaced at ice-cold water bath. The reaction mixture was stirred at room temperature for an hour. The suspension was filtered using a frit was protected with diatomaceous earth (1 cm). The slurry was washed with water (50 mL). The organic solvent was removed under reduced pressure and a pure product was collected by dehydration using a lyophilizer. Yield: 52%, colorless solid; Mp: 305 - 306 °C (solid from conc. sulfuric acid); $^{1}$H NMR (400 MHz, DMSO-$d_6$); δ = 14.38 (s, 1H, $CO_2$H), 8.48 (s, 1H, C4H), 7.84 (bs, 1H, N$^{1}$H); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 158.9 (C=O), 147.4 (C2), 137.0 (C5), 121.7 (C4); IR (cm$^{-1}$): ῦ = 2907 (O-H), 1690 (C=O), 1518 (N-O).

5-Nitro-1*H*-imidazole-2-carboxylic acid (**31**)[2]



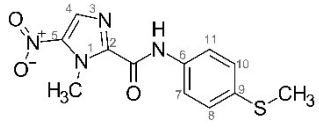
Concentrated sulfuric acid (116 mmol, 7 mL) was added slowly to a round bottom flask charged with 1*H*-imidazole-2-carboxylic acid (10 mmol, 1.12 g). Concentrated nitric acid (65%, 1.5 mL) was then added dropwise. The reaction mixture was stirred to 80 °C for 6 h. The solution was added dropwise to a beaker charged with ice (100 g) which led to the precipitation of the product. Yield: 52%, colorless solid; Mp: 305 - 306 °C (solid from conc. sulfuric acid); $^{1}$H NMR (400 MHz, DMSO-$d_6$); δ = 14.38 (s, 1H, $CO_2$H), 8.48 (s, 1H, C4H), 7.84 (bs, 1H, N$^{1}$H); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 158.9 (C=O), 147.4 (C2), 137.0 (C5), 121.7 (C4); IR (cm$^{-1}$): ῦ = 2907 (O-H), 1690 (C=O), 1518 (N-O).

*N*-[4-(Methylsulfanyl)phenyl]-5-nitro-1*H*-imidazole-2-carboxamide (**32**)



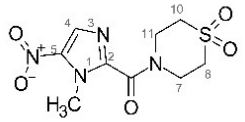
To a solution of compound **31** (5 mmol, 790 mg) in acetonitrile (20 mL), triethylamine (10 mmol, 1.41 mL) and HATU (5 mmol, 2g) were added. The mixture was stirred for 15 min. 4-(Methylthio)aniline (5 mmol, 620 µL)was added and the final mixture was stirred at 40 °C for overnight. Ethyl acetate was added to the reaction mixture, which was then washed with HCl (1N, 30 mL) and brine (30 mL). The product was isolated using flash chromatography. The product was further purified by recrystallization from methanol. Yield: 73%, light yellow solid; Purity 97.8%; Mp: 234 - 235 °C (solid from methanol); $^{1}$H NMR (400 MHz, DMSO-$d_6$); δ = 14.4 (bs, 1H, N$^{1}$H), 10.77 (s, 1H, CONH), 8.54 (s, 1H, C4H), 7.83 (m, $^{3}J$ = 2.9 Hz, 2H, C8H & C10H), 7.30 (m, $^{3}J$ = 2.9 Hz, 2H, C7H & C11H), 2.47 (s, 3H, $SCH_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 155.7 (C=O), 146.8 (C2), 139.6 (C5), 135.3 (C6), 133.3 (C9), 126.6 (C7 & C11), 122.1 (C4), 121.5 (C8 & C10), 15.3 (S<u>C</u>H$_3$); IR (cm$^{-1}$): ṽ = 3347 (N-H), 1665 (C=O), 1525 (N-O), 1360 (N-O); HRMS ((ESI) *m/z*) calculated for $C_{11}H_{10}N_4O_3S$ [M+ H]$^{+}$: 279.0546, found: 279.0535.

1-Methyl-*N*-[4-(methylsulfanyl)phenyl]-5-nitro-1*H*-imidazole-2-carboxamide (**33**)



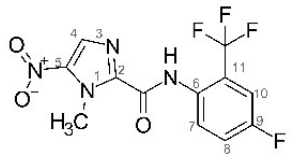
A solution of compound **29** (2.4 mmol, 500 mg) in anhydrous DCM (12 mL) was put in ice-cold water bath and N2 atmosphere, which was followed by the addition oxalyl chloride (3.84 mmol, 330 µL). DMF (2 drops) was then added. The reaction mixture was stirred at room temperature for 2 h. The reaction mixture was evaporated to dryness and toluene was added to co-evaporate the residual oxalyl chloride under reduced pressure. The residue was then suspended in acetonitrile (15 mL). After adding triethylamine (4.8 mmol, 700 µL), the reaction mixture was stirred at room temperature for 15 min. Eventually, 4-(methylthio)aniline (2.4 mmol, 300 µL) was added and the final mixture was stirred at 40 °C for overnight. DCM (50 mL) was added to the mixture, which was then washed with HCl (1N, 20 mL), conc. $NaHCO_3$ (20 mL) and brine (20 mL). The product was isolated using flash chromatography. Yield: 27%, yellow solid; Purity 100%; Mp: 330 - 331 °C (solid from n-hexane and ethyl acetate); $^{1}$H NMR (400 MHz, DMSO-$d_6$); δ = 10.82 (s, 1H, CONH), 8.24 (s, 1H, C4H), 7.80 (m, $^{3}J$ = 2.9 Hz, 2H, C8H & C10H), 7.29 (m, $^{3}J$ = 2.9 Hz, 2H, C7H & C11H), 4.28 (s, 3H, N$^{1}$CH$_3$), 2.47 (s, 3H, $SCH_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 156.2 (C=O), 141.4 (C2), 140.8 (C5), 135.2 (C6), 133.6 (C9), 130.9 (C4), 126.6 (C7 & C11), 121.2 (C8 & C10), 34.8 (N$^{1}$<u>C</u>H$_3$), 15.2 (S<u>C</u>H$_3$); IR (cm$^{-1}$): ṽ = 3337 (N-H), 1688 (C=O), 1536 (N-O), 1369 (N-O), 1275 (C-O); HRMS ((ESI) *m/z*) calculated for $C_{12}H_{12}N_4O_3S$ [M+ H]$^{+}$: 293.0703, found: 293.0698.

4-(1-Methyl-5-nitro-1*H*-imidazole-2-carbonyl)-λ$^{6}$-thiomorpholine-1,1-dione (**34**)



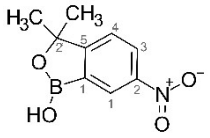
Prepared according to general procedure K. Compound **29** (3 mmol, 633 mg), thiomorpholine 1,1-dioxide (3.3 mmol, 446 mg), HATU (3.6 mmol, 1.4 g) and *N*,*N*-diisopropylethylamine (11.5 mmol, 2 mL) were suspended in DCM (20 mL). The suspension was stirred at room temperature for 2 h. Water was added to the mixture and the product was extracted using DCM (3 x 20 mL). The product was isolated using flash chromatography. Yield: 52%, off-white solid; Purity 97.6%; Mp: 201 - 202 °C (solid from n-hexane and ethyl acetate); $^{1}$H NMR (400 MHz, DMSO-$d_6$); δ = 8.24 (s, 1H, C4H), 4.07 (m, $^{2}J$ = 5.3 Hz, 2H, C7$H_2$), 4.02 (m, $^{2}J$ = 5.3 Hz, 2H, C8$H_2$), 3.96 (s, 3H, N$^{1}$C$H_3$), 3.36 (m, $^{2}J$ = 4.9 Hz, 2H, C10$H_2$), 3.29 (m, $^{2}J$ = 4.6 Hz, 2H, C11$H_2$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 158.1 (C=O), 142.7 (C2), 139.9 (C5), 130.9 (C4), 51.4 (C7), 50.7 (C11), 45.2 (C8), 40.5 (C10), 34.8 (N$^{1}$C$H_3$); IR (cm$^{-1}$): ṽ = 1651 (C=O), 1462 (N-O), 1121 (C-O); HRMS ((ESI) *m/z*) calculated for $C_9H_{12}N_4O_5S$ [M+ H]$^+$: 289.0605, found: 289.0601.

*N*-[4-Fluoro-2-(trifluoromethyl)phenyl]-1-methyl-5-nitro-1*H*-imidazole-2-carboxamide (**35**)



Compound **29** (3 mmol, 650 mg) and 1-methylimidazole (6 mmol, 480 µL) was dissolved in DMF (30 mL), which was followed by the addition of methanesulfonyl chloride (3 mmol, 235 µL) in portions at 0 °C. The mixture was stirred at this condition for 20 min. 2-Amino-5-fluorobenzotrifluride (3 mmol, 390 µL) was then added in portions. The final mixture was stirred at room temperature for 5 h. Ethyl acetate (50 mL) was added and the organic phase was washed with HCl (1N, 20 mL), conc. $NaHCO_3$ (20 mL) and brine (20 mL). The product was isolated by flash chromatography. Yield: 22%, off-white solid; Purity 100%; Mp: 155 - 156 °C (solid from n-hexane and ethyl acetate); $^{1}$H NMR (400 MHz, DMSO-$d_6$); δ = 10.5 (s, 1H, CONH), 8.26 (s, 1H, C4H), 7.78 (m, *J* = 4.0 Hz, 2H, C7H & C10H), 7.67 (m, *J* = 4.0 Hz, 1H, C8H), 4.28 (s, 3H, N$^{1}$C$H_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 161.1 (d, $^{1}J_{C,F}$ = 246.1 Hz, C9F), 157.3 (CO) 141.1 (C2), 140.2 (C5), 131.7 (d, $^{3}J_{C,F}$ = 8 Hz, C7), 130.9 (C4), 130.7 (C11), 126.7 (q, $^{2}J_{C,F}$ = 14 Hz, $CF_3$), 121.3 (C6), 120.4 (d, $^{2}J_{C,F}$ = 22 Hz, C8), 114.3 (q, $^{2,3}J_{C,F}$ = 10 Hz, C10), 34.7 (N$^{1}$C$H_3$); IR (cm$^{-1}$): ṽ = 3361 (N-H), 1697 (C=O), 1545 (N-O), 1273 (C-F); HRMS ((ESI) *m/z*) calculated for $C_{12}H_8F_4N_4O_3$ [M+ H]$^+$: 333.0605, found: 333.0619.

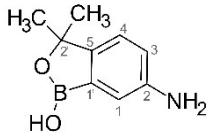
3,3-Dimethyl-6-nitro-1,3-dihydro-2,1-benzoxaborol-1-ol (**36**)[3]



A powdered 1-hydroxy-3,3-dimethyl-2,1-benzooxaborole (6 mmol, 970 mg) added slowly to a round-bottom flask charged with conc. $H_2SO_4$ (12 mL) at -20 °C. This was followed by the slow addition of $HNO_3$ (69%, 2 mL). The reaction mixture was stirred at -15 °C for 10 min. The reaction mixture was then poured to ice-cold water (20 mL) and stirred for 10 min. The precipitate was filtered and washed with n-hexane to yield a pure product. Yield: 72%, off-white solid; Mp: 137 - 138 °C (solid from sulfuric acid); $^{1}$H NMR (400 MHz, DMSO-$d_6$); δ = 8.53 (d, $^{4}J$ = 2.1 Hz, 1H, C1H), 8.34 (dd, $^{3,4}J$ = 3.6 Hz, 1H, C3H), 7.75 (d, $^{3}J$ = 8.4 Hz, 1H, C4H), 1.50 (s, 6H, $(CH_3)_2$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 168.1 (C2), 147.3 (C5), 126.0

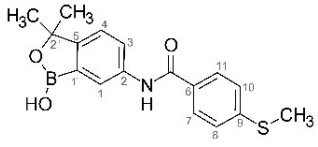
(C3), 125.7 (C1), 122.4 (C4), 83.0 (C2'), 28.6 (s, 2C, ($\underline{C}H_3)_2$); IR ($cm^{-1}$): $\tilde{\nu}$ = 3304 (O-H), 1516 (N-O).

6-Amino-3,3-dimethyl-1,3-dihydro-2,1-benzoxaborol-1-ol (**37**)[3]



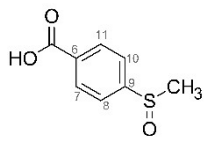
Compound **36** (1 mmol, 207 mg) and Pd/C (10%, 100 mg) was suspended in ethyl acetate (10 mL). The suspension was carefully set under $H_2$ atmosphere and then stirred for overnight. The reaction mixture was filtered using frit protected with 1 cm layer of diatomaceous earth. The filtrate was evaporated to dryness to yield the desired product. Yield: 72%, off-white solid; Mp: 137 - 138 °C (solid from sulfuric acid); $^1$H NMR (400 MHz, DMSO-$d_6$); δ = 8.53 (d, $^4J$ = 2.1 Hz, 1H, C1H), 8.34 (dd, $^{3,4}J$ = 3.6 Hz, 1H, C3H), 7.75 (d, $^3J$ = 8.4 Hz, 1H, C4H), 1.50 (s, 6H, $(CH_3)_2$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 168.1 (C2), 147.3 (C5), 126.0 (C3), 125.7 (C1), 122.4 (C4), 83.0 (C2'), 28.6 (s, 2C, ($\underline{C}H_3)_2$); IR ($cm^{-1}$): $\tilde{\nu}$ = 3304 (O-H), 1516 (N-O).

*N*-(1-Hydroxy-3,3-dimethyl-1,3-dihydro-2,1-benzoxaborol-6-yl)-4-(methylsulfanyl)benzamid e (**38**)



Prepared following general procedure K. To a suspension of compound **37** (1 mmol, 177 mg) and 4-(methylthio)benzoic acid (1 mmol, 170 mg) in anhydrous DCM (15 mL), *N*,*N*-diisopropylethylamine (3 mmol, 530 µL) was added. The suspension was stirred until complete dissolution. HATU (1 mmol, 380 mg) was then added to the reaction solution which was stirred at room temperature for overnight. The reaction solution was washed with HCl (1N, 10 mL), conc. $NaHCO_3$ (10 mL) and brine (10 mL). The product was purified by recrystallization from DCM. Yield: 63%, off-white solid; Purity 100%; Mp: 175 - 176 °C (solid from DCM); $^1$H NMR (400 MHz, DMSO-$d_6$); δ = 10.22 (s, 1H, CONH), 9.06 (s, 1H, OH), 8.07 (d, $^4J$ = 1.8 Hz, 1H, C1H), 7.96 (m, $^3J$ = 2.8 Hz, 2H, C7H & C11H), 7.76 (q, $^{3,4}J$ = 3.4 Hz, 1H, C3H), 7.41 (m, $J$ = 2.4 Hz, 3H, C4H, C8H & C10H), 2.55 (s, 3H, $SCH_3$), 1.46 (s, 6H, $(CH_3)_2$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 164.8 (C=O), 157.5 (C2), 143.0 (C6),138.0 (C5), 130.8 (C9), 128.2 (C7 & C11), 124.9 (C8 & C10), 123.8 (C3), 122.4 (C1), 120.6 (C4), 82.4 (C2'), 29.4 (s, 2C, ($\underline{C}H_3)_2$), 14.1 (S$\underline{C}H_3$); IR ($cm^{-1}$): $\tilde{\nu}$ = 3302 (O-H), 1646 (C=O), 1108 (C-O); HRMS ((ESI) *m/z*) calculated for $C_{17}H_{18}BNO_3S$ $[M+H]^+$: 328.1173, found: 328.1167.

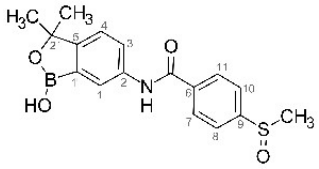
4-Methanesulfinylbenzoic acid (**39**)



Prepared following general procedure D. 4-(Methylthio)benzoic acid (10 mmol, 1.7 g) was dissolved in DCM (25 mL). The solution was cooled in ice-cold water bath. A solution of 3-chloroperoxybenzoic acid (11 mmol, 1.9 g) in DCM (40 mL) was added over a period of 1 h. After complete addition, the mixture was stirred for an additional 30 min. The mixture was left

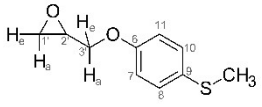
in the refrigerator, which led to the precipitation of nearly all of the excess 3-chloroperoxybenzoic acid. The suspension was filtered. The filtrate was packed for flash chromatography. The product was further purified by recrystallization from methanol. Yield: 49%, colorless solid; Mp: 232 - 233 °C (solid from methanol); $^{1}$H NMR (400 MHz, DMSO-$d_6$); δ = 13.3 (s, 1H, $CO_2H$), 8.13 (m, $^{3}J$ = 2.5 Hz, 2H, C8H & C10H), 7.83 (m, $^{3}J$ = 2.5 Hz, 2H, C7H & C11H), 2.79 (s, 3H, $SOCH_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 166.6 (C=O), 151.3 (C9), 132.7 (C6), 130.0 (C8 & C10), 123.8 (C7 & C11), 43.0 ($SO\underline{C}H_3$); IR (cm$^{-1}$): ṽ = 2763 (O-H), 1699 (C=O), 1260 (C-O), 1002 (S=O).

*N*-(1-Hydroxy-3,3-dimethyl-1,3-dihydro-2,1-benzoxaborol-6-yl)-4-methanesulfinylbenzamide (**40**)



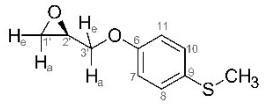
Prepared according to general procedure K. To a suspension of compound **37** (2.5 mmol, 443 mg) and compound **39** (3 mmol, 460 mg) in DCM (20 mL), *N*,*N*-diisopropylethylamine (7.5 mmol, 1.3 mL) was added. The suspension was stirred until complete dissolution. HATU (3 mmol, 950 mg) was then added and the reaction solution was stirred at room temperature for 48 h. DCM (50 mL) was added to the reaction solution, which was then washed with HCl (1N, 10 mL), conc. $NaHCO_3$ (10 mL) and brine (10 mL). The product was isolated using flash chromatography and further purified using recrystallization from ethyl acetate. Yield: 72%, colorless solid; Purity 100%; Mp: 176 - 177 °C (solid from ethyl acetate); $^{1}$H NMR (400 MHz, DMSO-$d_6$); δ = 10.42 (s, 1H, CONH), 9.09 (s, 1H, OH), 8.16 (m, $^{3}J$ = 2.4 Hz, 2H, C7H & C11H), 8.10 (d, $^{4}J$ = 1.8 Hz, 1H, C1H), 7.87 (m, $^{3}J$ = 2.4 Hz, 2H, C8H & C10H), 7.77 (q, $^{3,4}J$ = 3.4 Hz, 1H, C3H), 7.42 (d, $^{3}J$ = 8.2 Hz, 1H, C4H), 2.81 (s, 3H, $SOCH_3$), 1.46 (s, 6H, $(CH_3)_2$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 164.7 (C=O), 157.8 (C2), 149.8 (C6),137.7 (C5), 137.0 (C9), 128.4 (C7 & C11), 123.7 (C3), 123.6 (C8 & C10), 122.4 (C1), 120.7 (C4), 82.4 (C2'), 43.1 ($SO\underline{C}H_3$), 29.3 (s, 2C, $(\underline{C}H_3)_2$); IR (cm$^{-1}$): ṽ = 3246 (O-H), 1640 (C=O), 1024 (S=O); HRMS ((ESI) *m/z*) calculated for $C_{17}H_{18}BNO_4S$ [M+ H]$^{+}$: 344.1122, found: 344.1122.

2-{[4-(Methylsulfanyl)phenoxy]methyl}oxirane (**41**)



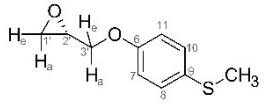
A mixture of 4-(methylthio)phenol (15 mmol, 2.1 g), epibromohydrine (60 mmol, 6 mL) and $K_2CO_3$ (66 mmol, 9.12 g) in butanone (25 mL) was refluxed for 36 h. The product was isolated using flash chromatography. Yield: 80%, off-white solid; Mp: 85 - 86 °C (solid from n-hexane and ethyl acetate); $^{1}$H NMR (400 MHz, DMSO-$d_6$); δ = 7.26 (m, $^{3}J$ = 3.0 Hz, 2H, C8H & C10H), 6.96 (m, $^{3}J$ = 3.0 Hz, 2H, C7H & C11H), 4.32 (m, $^{2,3}J$ = 4.7 Hz, 1H, C3'$H_e$), 3.80 (m, $^{2,3}J$ = 6.0 Hz, 1H, C3'$H_a$), 3.33 (m, 1H, C2'H), 2.85 (m, $^{2,3}J$ = 3.1 Hz, 1H, C1'$H_e$), 2.71 (m, $^{2,3}J$ = 2.6 Hz, 1H, C1'$H_a$), 2.42 (s, 3H, $SCH_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 156.5 (C6), 128.9 (C8 & C10), 128.8 (C9), 115.4 (C7 & C11), 69.1 (C3'), 49.7 (C2'), 43.7 (C1'), 16.4 ($S\underline{C}H_3$); IR (cm$^{-1}$): ṽ = 1490 (C-C), 1234 (C-O), 816 (C-H).

(2*R*)-2-{[4-(Methylsulfanyl)phenoxy]methyl}oxirane (**42**)



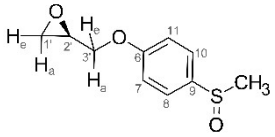
Prepared according to general procedure J. Cesium fluoride (15.5 mmol, 2.36 g) was added to a round bottom flask charged with anhydrous DMF (8 mL). 4-(Methylthio)phenol (5 mmol, 700 mg) was added to the reaction mixture, which was then set under $N_2$ atmosphere. After 1 h of stirring, (*R*)-oxiran-2-ylmethyl 3-nitrobenzenesulfonate (5 mmol, 1.3 g) was added. The reaction mixture was resealed under $N_2$ atmosphere and stirred at room temperature for 36 h. The mixture was added to water and the product was extracted using DCM (3 x 20 mL). The combined organic extract was washed with brine. The compound was isolated using flash chromatography. Yield: 61%, colorless solid; Mp: 93 - 94 °C (solid from n-hexane and ethyl acetate); $^1$H NMR (400 MHz, DMSO-$d_6$); δ = 7.26 (m, $^3J$ = 3.0 Hz, 2H, C8H & C10H), 6.96 (m, $^3J$ = 3.0 Hz, 2H, C7H & C11H), 4.32 (m, $^{2,3}J$ = 4.7 Hz, 1H, C3'$H_e$), 3.83 (m, $^{2,3}J$ = 6.0 Hz, 1H, C3'$H_a$), 3.33 (m, 1H, C2'H), 2.85 (m, $^{2,3}J$ = 3.1 Hz, 1H, C1'$H_e$), 2.73 (m, $^{2,3}J$ = 2.6 Hz, 1H, C1'$H_a$), 2.42 (s, 3H, $SCH_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 156.5 (C6), 128.9 (C8 & C10), 128.8 (C9), 115.4 (C7 & C11), 69.0 (C3'), 49.6 (C2'), 43.7 (C1'), 16.4 ($S\underline{C}H_3$); IR (cm$^{-1}$): $\tilde{\nu}$ = 1492 (C-C), 1236 (C-O), 810 (C-H).

(2*S*)-2-{[4-(Methylsulfanyl)phenoxy]methyl}oxirane (**43**)



Prepared following general procedure J. Cesium fluoride (45 mmol, 7 g) was added to a round bottom flask charged with anhydrous DMF (15 mL). 4-(Methylthio)phenol (15 mmol, 2.1 g) was added to the reaction mixture, which was then set under $N_2$ atmosphere. After 1 h of stirring, (*S*)-oxiran-2-ylmethyl 3-nitrobenzenesulfonate (15 mmol, 3.9 g) was added. The reaction mixture was resealed under $N_2$ atmosphere and stirred at room temperature for 35 h. The mixture was added to water and the product was extracted using DCM (3 x 20 mL). The combined organic extract was washed with brine. The compound was isolated using flash chromatography. Yield: 54%, colorless semi-solid; $^1$H NMR (400 MHz, DMSO-$d_6$); δ = 7.26 (m, $^3J$ = 3.0 Hz, 2H, C8H & C10H), 6.96 (m, $^3J$ = 3.0 Hz, 2H, C7H & C11H), 4.32 (m, $^{2,3}J$ = 4.7 Hz, 1H, C3'$H_e$), 3.83 (m, $^{2,3}J$ = 6.0 Hz, 1H, C3'$H_a$), 3.33 (m, 1H, C2'H), 2.85 (m, $^{2,3}J$ = 3.1 Hz, 1H, C1'$H_e$), 2.71 (m, $^{2,3}J$ = 2.6 Hz, 1H, C1'$H_a$), 2.42 (s, 3H, $SCH_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 156.5 (C6), 128.9 (C8 & C10), 128.8 (C9), 115.4 (C7 & C11), 69.0 (C3'), 49.6 (C2'), 43.7 (C1'), 16.4 ($S\underline{C}H_3$).

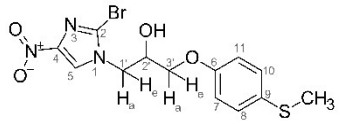
(2*R*)-2-[(4-methanesulfinylphenoxy)methyl]oxirane (**44**)



Prepared following general procedure D. Compound **42** (8 mmol, 1.7 g) was dissolved in DCM (30 mL). The solution was cooled in ice-cold water bath. A solution of 3-chloroperoxybenzoic acid (8.8 mmol, 1.52 g) in DCM (50 mL) was added over a period of 1 h. After complete addition, the mixture was stirred for an additional 1.5 h. The reaction mixture was then washed

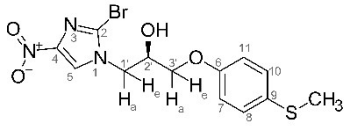
with aq. $NaHCO_3$ (10%, 30 mL). The product was separated using flash chromatography. Yield: 73%, colorless semi-solid; $^1$H NMR (400 MHz, DMSO-$d_6$); δ = 7.64 (m, $^3J$ = 3.0 Hz, 2H, C8H & C10H), 7.17 (m, $^3J$ = 3.0 Hz, 2H, C7H & C11H), 4.43 (m, $^{2,3}J$ = 4.7 Hz, 1H, C3'$H_e$), 3.92 (m, $^{2,3}J$ = 6.0 Hz, 1H, C3'$H_a$), 3.37 (m, 1H, C2'H), 2.87 (m, $^{2,3}J$ = 3.1 Hz, 1H, C1'$H_e$), 2.73 (m, $^{2,3}J$ = 2.5 Hz, 1H, C1'$H_a$), 2.69 (s, 3H, $SOCH_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 160.2 (C6), 137.6 (C9), 125.5 (C8 & C10), 115.3 (C7 & C11), 69.2 (C3'), 49.5 (C2'), 43.7 (C1'), 43.3 ($SO\underline{C}H_3$).

1-(2-Bromo-4-nitro-1*H*-imidazol-1-yl)-3-[4-(methylsulfanyl)phenoxy]propan-2-ol (**45**)



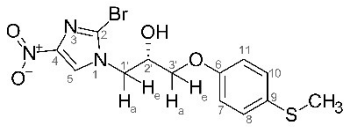
Prepared according to general procedure H. A sealed tube was charged with compound **41** (8 mmol, 644 mg), 2-bromo-4-nitro-1*H*-imidazole (8 mmol, 1.54 g) and *N*,*N*-diisopropylethylamine (40 mmol, 7 mL). The sealed tube was heated at 107 °C for 16 h. The tube was cooled and the residue was dissolved in DCM (50 mL), and the resulting solution was washed with brine. The product was separated using flash chromatography. Yield: 58%, light yellow solid; Purity 100%; Mp: 139 - 140 °C (solid from n-hexane and ethyl acetate); $^1$H NMR (400 MHz, DMSO-$d_6$); δ = 8.52 (s, 1H, C5H), 7.27 (m, $^3J$ = 3.0 Hz, 2H, C8H & C10H), 6.95 (m, $^3J$ = 3.0 Hz, 2H, C7H & C11H), 5.66 (d, $^3J$ = 5.3 Hz, 1H, OH), 4.29 (m, $^{2,3}J$ = 5.4 Hz, 1H, C1'$H_e$), 4.21 (m, $^3J$ = 2.7 Hz, 1H, C2'H), 4.15 (m, $^{2,3}J$ = 7.2 Hz, 1H, C1'$H_a$), 3.99 (m, $^{2,3}J$ = 2.1 Hz, 2H, C3'$H_e$ & C3'$H_a$), 2.42 (s, 3H, $SCH_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 156.5 (C6), 146.1 (C4), 128.9 (C8 & C10), 128.8 (C9), 125.1 (C5), 121.2 (C2), 115.4 (C7 & C11), 69.6 (C3'), 67.2 (C2'), 51.5 (C1'), 16.4 ($S\underline{C}H_3$); IR ($cm^{-1}$): $\tilde{\nu}$ = 3271 (O-H), 1492 (N-O), 1233 (C-O).

(2*R*)-1-(2-Bromo-4-nitro-1*H*-imidazol-1-yl)-3-[4-(methylsulfanyl)phenoxy]propan-2-ol (**46**)



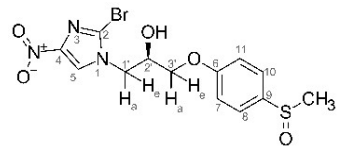
Prepared following general procedure H. A sealed tube was charged with compound **42** (6.11 mmol, 1.2 g), 2-bromo-4-nitro-1*H*-imidazole (6.11 mmol, 1.18 g) and *N*,*N*-diisopropylethylamine (30.6 mmol, 5.35 mL). The sealed tube was heated at 107 °C for 16 h. The tube was cooled and the residue was dissolved in DCM (50 mL), and the resulting solution was washed with brine. The product was separated using flash chromatography. Yield: 69%, colorless semi-solid; $^1$H NMR (400 MHz, DMSO-$d_6$); δ = 8.52 (s, 1H, C5H), 7.27 (m, $^3J$ = 2.9 Hz, 2H, C8H & C10H), 6.95 (m, $^3J$ = 2.9 Hz, 2H, C7H & C11H), 5.66 (d, $^3J$ = 5.3 Hz, 1H, OH), 4.29 (m, 3H, C3'$H_e$, C2'H & C3'$H_a$), 3.97 (m, $^{2,3}J$ = 2.2 Hz, 2H, C1'$H_e$ & C1'$H_a$), 2.42 (s, 3H, $SCH_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 156.5 (C6), 146.1 (C4), 128.9 (C8 & C10), 128.8 (C9), 125.1 (C5), 121.2 (C2), 115.4 (C7 & C11), 69.6 (C3'), 67.2 (C2'), 51.5 (C1'), 16.4 ($S\underline{C}H_3$).

(2*S*)-1-(2-Bromo-4-nitro-1*H*-imidazol-1-yl)-3-[4-(methylsulfanyl)phenoxy]propan-2-ol (**47**)



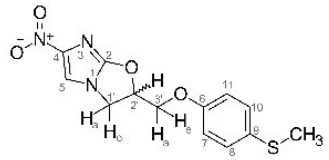
Prepared following general procedure H. A sealed tube was charged with **43** (7.25 mmol, 1.4 g), 2-bromo-4-nitro-1*H*-imidazole (7.25 mmol, 1.39 g) and *N*,*N*-diisopropylethylamine (36.25 mmol, 6.4 mL). The sealed tube was heated at 107 °C for 16 h. The tube was cooled and the residue was dissolved in DCM (50 mL), and the resulting solution was washed with brine. The product was separated using flash chromatography. Yield: 39%, very light-yellow solid; Mp: 165 - 166 °C (solid from n-hexane and ethyl acetate); $^{1}$H NMR (400 MHz, DMSO-$d_6$); δ = 8.52 (s, 1H, C5H), 7.27 (m, $^{3}J$ = 2.9 Hz, 2H, C8H & C10H), 6.95 (m, $^{3}J$ = 3.0 Hz, 2H, C7H & C11H), 5.66 (d, $^{3}J$ = 5.3 Hz, 1H, OH), 4.29 (m, 3H, C3'$H_e$, C2'H & C3'$H_a$), 3.97 (m, $^{2,3}J$ = 2.2 Hz, 2H, C1'$H_e$ & C1'$H_a$), 2.42 (s, 3H, $SCH_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 156.5 (C6), 146.1 (C4), 128.9 (C8 & C10), 128.8 (C9), 125.1 (C5), 121.2 (C2), 115.4 (C7 & C11), 69.6 (C3'), 67.2 (C2'), 51.5 (C1'), 16.4 ($S\underline{C}H_3$); IR (cm$^{-1}$): ṽ = 3272 (O-H), 1233 (C-O), 1103 (C-O).

(2*R*)-1-(2-Bromo-4-nitro-1H-imidazol-1-yl)-3-(4-methanesulfinylphenoxy)propan-2-ol (**48**)



Prepared following general procedure H. A sealed tube was charged with compound **44** (5 mmol, 1.06 g), 2-bromo-4-nitro-1*H*-imidazole (5 mmol, 960 mg) and *N*,*N*-diisopropylethylamine (25 mmol, 4.5 mL). The sealed tube was heated at 107 °C for 16 h. The tube was cooled and the residue was dissolved in DCM (50 mL), and the resulting solution was washed with brine. The product was separated using flash chromatography. Yield: 43%, colorless semi-solid; $^{1}$H NMR (400 MHz, DMSO-$d_6$); δ = 8.54 (s, 1H, C5H), 7.65 (m, $^{3}J$ = 2.9 Hz, 2H, C8H & C10H), 7.16 (m, $^{3}J$ = 3.0 Hz, 2H, C7H & C11H), 5.70 (d, $^{3}J$ = 2.9 Hz, 1H, OH), 4.31 (m, $^{2,3}J$ = 5.6 Hz, 1H, C1'$H_e$), 4.24 (m, $^{3}J$ = 2.8 Hz, 1H, C2'H), 4.17 (m, $^{2,3}J$ = 7.1 Hz, 1H, C1'$H_a$), 4.07 (m, $^{2,3}J$ = 5.0 Hz, 2H, C3'$H_e$ & C3'$H_a$), 2.70 (s, 3H, $SOCH_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 160.2 (C6), 146.1 (C4), 137.6 (C9), 125.5 (C8 & C10), 125.1 (C5), 121.3 (C2), 115.3 (C7 & C11), 69.7 (C3'), 67.1 (C2'), 51.4 (C1'), 43.3 ($SO\underline{C}H_3$).

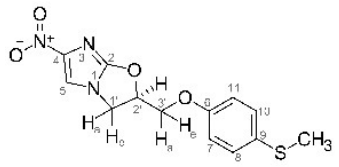
2-{[4-(Methylsulfanyl)phenoxy]methyl}-6-nitro-2*H*,3*H*-imidazo[2,1-b][1,3]oxazole (**49**)



Prepared according to general procedure I. A solution of compound **44** (0.44 mmol, 172 mg) in anhydrous DMF (5 mL) was put in ice-cold water bath. After adding dry NaH 90% (0.7 mmol, 17 mg), the reaction suspension was set under $N_2$ atmosphere and stirred for 70 min. The reaction was quenched by the addition of ice-cold conc. $NaHCO_3$ aqueous solution (15 mL). Brine was added to the reaction mixture and the product was extracted using DCM (3 x 20 mL). Yield: 90%, off-white solid; Purity 98.6%; Mp: 182 - 183 °C (solid from dichloromethane); $^{1}$H NMR (400 MHz, DMSO-$d_6$); δ = 8.17 (s, 1H, C5H), 7.26 (m, $^{3}J$ = 3.1 Hz, 2H, C8H & C10H), 6.95 (m, $^{3}J$ = 3.1 Hz, 2H, C7H & C11H), 5.76 (m, $^{3}J$ = 4.8 Hz, 1H, C2'H), 4.52 (m, $^{2,3}J$ = 6.5

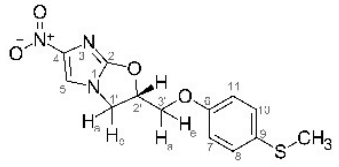
Hz, 1H, C1'$H_e$), 4.42 (m, $^{2,3}J$ = 6.0 Hz, 2H, C3'$H_e$ & C3'$H_a$), 4.23 (m, $^{2,3}J$ = 5.8 Hz, 1H, C1'$H_a$), 2.42 (s, 3H, $SCH_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 156.2 (C2), 156.1 (C6), 145.6 (C4), 129.4 (C9), 128.8 (C8 & C10), 116.0 (C5), 115.6 (C7 & C11), 85.5 (C2'), 68.1 (C3'), 45.1 (C1'), 16.3 (S<u>C</u>$H_3$); IR ($cm^{-1}$): ṽ = 3133 (C-H), 1606 (C=C), 1242 (C-O); HRMS ((ESI) *m/z*) calculated for $C_{13}H_{13}N_3O_4S$ [M+ H]$^+$: 308.0700, found: 308.0687.

(2*R*)-2-{[4-(Methylsulfanyl)phenoxy]methyl}-6-nitro-2*H*,3*H*-imidazo[2,1-b][1,3]oxazole (**50**)



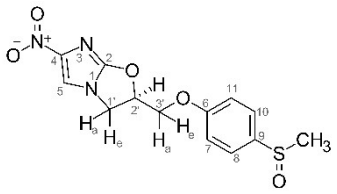
Prepared following general procedure I. A solution of compound **46** (2.65 mmol, 1.03 g) in anhydrous DMF (10 mL) was put in ice-cold water bath. After adding dry NaH 90% (4.11 mmol, 100 mg), the reaction suspension was set under $N_2$ atmosphere and stirred for 70 min. The reaction was quenched by the addition of ice-cold conc. $NaHCO_3$ aqueous solution (20 mL). Brine was added to the reaction mixture and the product was extracted using DCM (3 x 20 mL). Yield: 45%, very light-yellow solid; Purity 98.2%; ee 100%; Mp: 190 - 191 °C (solid from DCM); $^1$H NMR (400 MHz, DMSO-$d_6$); δ = 8.17 (s, 1H, C5H), 7.26 (m, $^3J$ = 3.0 Hz, 2H, C8H & C10H), 6.95 (m, $^3J$ = 3.0 Hz, 2H, C7H & C11H), 5.75 (m, $^3J$ = 2.6 Hz, 1H, C2'H), 4.52 (m, $^{2,3}J$ = 6.6 Hz, 1H, C1'$H_e$), 4.42 (m, $^{2,3}J$ = 6.0 Hz, 2H, C3'$H_e$ & C3'$H_a$), 4.23 (m, $^{2,3}J$ = 5.8 Hz, 1H, C1'$H_a$), 2.42 (s, 3H, $SCH_3$); $^{13}$C NMR (100 MHz, DMSO-d6); δ = 156.2 (C2), 156.1 (C6), 145.6 (C4), 129.4 (C9), 128.8 (C8 & C10), 116.0 (C5), 115.5 (C7 & C11), 85.4 (C2'), 68.1 (C3'), 45.1 (C1'), 16.3 (S<u>C</u>$H_3$); IR ($cm^{-1}$): ṽ = 3132 (C-H), 1607 (C=C), 1494 (N-O), 1243 (C-O); HRMS ((ESI) *m/z*) calculated for $C_{13}H_{13}N_3O_4S$ [M+ H]$^+$: 308.0700, found: 308.0708.

(2*S*)-2-{[4-(Methylsulfanyl)phenoxy]methyl}-6-nitro-2*H*,3*H*-imidazo[2,1-b][1,3]oxazole (**51**)



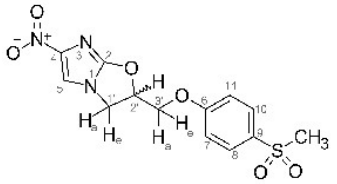
Prepared following general procedure I. A solution of compound **47** (2.51 mmol, 980 mg) in anhydrous DMF (8 mL) was put in ice-cold water bath. After adding dry NaH 90% (3.9 mmol, 98 mg), the reaction suspension was put under $N_2$ atmosphere and stirred for 70 min. The reaction was quenched by the addition of ice-cold conc. $NaHCO_3$ aqueous solution (20 mL). Brine was added to the reaction mixture and the product was extracted using DCM (3 x 20 mL). Yield: 40%, very light-yellow solid; Purity 98.9%; ee 100%; Mp: 192 - 193 °C (solid from DCM); $^1$H NMR (400 MHz, DMSO-$d_6$); δ = 8.17 (s, 1H, C5H), 7.26 (m, $^3J$ = 3.0 Hz, 2H, C8H & C10H), 6.95 (m, $^3J$ = 3.0 Hz, 2H, C7H & C11H), 5.75 (m, $^3J$ = 2.6 Hz, 1H, C2'H), 4.52 (m, $^{2,3}J$ = 6.6 Hz, 1H, C1'$H_e$), 4.42 (m, $^{2,3}J$ = 6.0 Hz, 2H, C3'$H_e$ & C3'$H_a$), 4.23 (m, $^{2,3}J$ = 5.8 Hz, 1H, C1'$H_a$), 2.42 (s, 3H, $SCH_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 156.2 (C2), 156.1 (C6), 145.6 (C4), 129.4 (C9), 128.8 (C8 & C10), 116.0 (C5), 115.5 (C7 & C11), 85.4 (C2'), 68.1 (C3'), 45.1 (C1'), 16.3 (S<u>C</u>$H_3$); IR ($cm^{-1}$): ṽ = 3132 (C-H), 1607 (C=C), 1495 (N-O), 1240 (C-O); HRMS ((ESI) *m/z*) calculated for $C_{13}H_{13}N_3O_4S$ [M+ H]$^+$: 308.0700, found: 308.0714.

(2*S*)-2-[(4-Methanesulfinylphenoxy)methyl]-6-nitro-2*H*,3*H*-imidazo[2,1-b][1,3]oxazole (**52**)



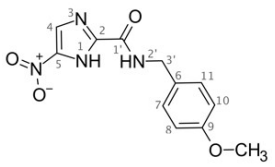
Prepared following general procedure I. A solution of compound **48** (2.13 mmol, 832 mg) in anhydrous DMF (10 mL) was put in ice-cold water bath. After adding dry sodium hydride 90% (3.3 mmol, 80 mg), the reaction suspension was put under nitrogen atmosphere and stirred for 70 min. The reaction was quenched by the addition of ice-cold conc. $NaHCO_3$ aqueous solution (30 mL). Brine was added to the reaction mixture and the product was extracted using DCM (3 x 20 mL). Yield: 52%, light yellow solid; Purity 100%; Mp: 175 - 176 °C (solid from DCM); $^1$H NMR (400 MHz, DMSO-$d_6$); δ = 8.18 (s, 1H, C5H), 7.66 (m, $^3J$ = 3.0 Hz, 2H, C8H & C10H), 7.17 (m, $^3J$ = 3.0 Hz, 2H, C7H & C11H), 5.80 (m, $^3J$ = 2.6 Hz, 1H, C2'H), 4.54 (m, $J$ = 4.8 Hz, 3H, C3'$H_e$, C3'$H_a$ & C1'$H_e$), 4.23 (m, $^{2,3}J$ = 5.8 Hz, 1H, C1'$H_a$), 2.70 (s, 3H, $SOCH_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 159.8 (C6), 156.1 (C2), 145.6 (C4), 138.1 (C9), 125.5 (C8 & C10), 116.0 (C5), 115.4 (C7 & C11), 85.3 (C2'), 68.1 (C3'), 45.1 (C1'), 43.3 ($SO\underline{C}H_3$); IR (cm$^{-1}$): ṽ = 3140 (C-H), 1591 (C=C), 1243 (C-O), 1042 (S=O); HRMS ((ESI) *m/z*) calculated for $C_{13}H_{13}N_3O_5S$ [M+ H]$^+$: 324.0649, found: 324.0659.

2-[(4-Methanesulfonylphenoxy)methyl]-6-nitro-2*H*,3*H*-imidazo[2,1-b][1,3]oxazole (**53**)



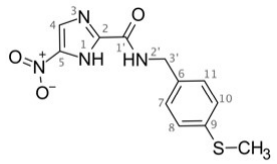
Prepared following general procedure D. Compound **45** (1 mmol, 308 mg) was dissolved in DCM (10 mL). The solution was cooled in ice-cold water bath. A solution of 3-chloroperoxybenzoic acid (2 mmol, 190 mg) in DCM (15 mL) was added very slowly. After complete addition, the mixture was stirred for 6 h. The reaction mixture was then washed with 10 mL of aq. $NaHCO_3$ (10%). The product was separated using flash chromatography. Additional flash chromatography was necessary to improve the purity of the compound. Yield: 15%, colorless solid; Purity 100%; Mp: 230 - 231 °C (solid from DCM and methanol); $^1$H NMR (400 MHz, DMSO-$d_6$); δ = 8.18 (s, 1H, C5H), 7.88 (m, $^3J$ = 3.0 Hz, 2H, C8H & C10H), 7.20 (m, $^3J$ = 3.0 Hz, 2H, C7H & C11H), 5.80 (m, $^3J$ = 2.6 Hz, 1H, C2'H), 4.57 (m, $^{2,3}J$ = 5.2 Hz, 3H, C1'$H_e$, C3'$H_e$ & C3'$H_a$), 4.25 (m, $^{2,3}J$ = 5.8 Hz, 1H, C1'$H_a$), 3.16 (s, 3H, $SCH_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 161.6 (C6), 156.1 (C2), 145.7 (C4), 133.3 (C9), 129.2 (C8 & C10), 116.0 (C5), 115.2 (C7 & C11), 85.1 (C2'), 68.3 (C3'), 45.1 (C1'), 43.9 ($S\underline{C}H_3$); IR (cm$^{-1}$): ṽ = 3140 (C-H), 1595 (C=C), 1291 (S=O); HRMS ((ESI) *m/z*) calculated for $C_{13}H_{13}N_3O_6S$ [M+ H]$^+$: 340.0525, found: 340.0599.

*N*-(4-Methoxybenzyl)-5-nitro-1*H*-imidazole-2-carboxamide (**54**)



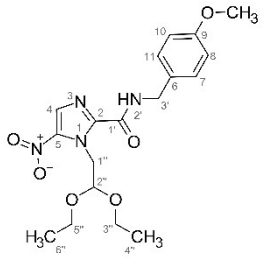
Oxalyl chloride (5.3 mmol, 500 µL) was added to a stirred suspension of intermediate **31** (3 mmol, 471.3 mg) in anhydrous DCM (10 mL). The mixture was cooled to 0 °C, followed by the addition of two drops of DMF. The reaction temperature was raised to room temperature and stirred overnight. A further portion of oxalyl chloride (1.3 mmol, 125 µL) and DMF (2 drops) were added and the reaction mixture was stirred for 1 h. The volatiles were removed under reduced pressure and the residual oxalyl chloride was removed by co-evaporation with toluene. The solid was immediately suspended in DCM (10 mL) and then chilled to 0 °C. Triethylamine (5.9 mmol, 825 µL) was added and the resulting solution was added to a solution of 4-methoxybenzylamine (3 mmol, 392 µL) in DCM (3 mL) at 0 °C. After 15 min, the volatiles were removed in vacuo. The product was further purified by flash column chromatography. Yield: 78%, light yellow solid; Mp: 187 - 188 °C (solid from hexane and ethyl acetate); $^{1}$H NMR (400 MHz, DMSO-$d_6$); δ = 14.27 (bs, 1H, N$^{1}$H), 9.36 (t, $^{3}J$ = 6.3 Hz, 1H, N$^{2'}$H), 8.44 (s, 1H, C4H), 7.27 (m, $^{3}J$ = 2.9 Hz, 2H, C7H & C11H), 6.89 (m, $^{3}J$ = 2.9 Hz, 2H, C9H & C10H), 4.37 (d, $^{3}J$ = 6.3 Hz, 2H, C5$H_2$), 3.72 (s, 3H, $OCH_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 158.2 (C6), 156.9 (C=O), 146.6 (C5), 139.6 (C2), 131.0 (C9), 128.8 (C7 & C11), 121.4 (C4), 113.6 (C8 & C10), 55.0 (C3'), 41.6 ($OCH_3$); IR (cm$^{-1}$): ṽ = 3371 (N-H), 1508 (N-O), 1248 (C-O).

*N*-[4-(methylthio)benzyl]-5-nitro-1*H*-imidazole-2-carboxamide (**55**)



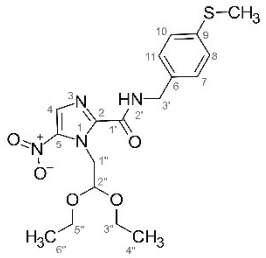
Oxalyl chloride (5.3 mmol, 500 µL) was added to a stirred suspension of compound **31** (3 mmol, 471.3 mg) in anhydrous DCM (10 mL) and then cooled to 0 °C. Two drops of DMF were added to the reaction mixture. The reaction mixture was allowed to warm to room temperature and stirred overnight. A further portion of oxalyl chloride (1.3 mmol, 125 µL,) and DMF (2 drops) were added to the reaction mixture and stirred for 1 h. The volatiles were removed in vacuum and the residual oxalyl chloride was removed by co-evaporation with toluene. The solid was suspended immediately in DCM (10 mL) and the reaction mixture was chilled to 0 °C. Triethylamine (5.9 mmol, 825 µL) was added. The solution was added to a stirred solution of 4-(methylthio)benzylamine (3 mmol, 418 µL) in DCM (3 mL) cooled to 0 °C. After 15 min, the volatiles were removed in vacuo. The product was further purified by flash column chromatography. Yield: 73%, light yellow solid; Mp: 207 - 208 °C (solid from hexane and ethyl acetate); $^{1}$H NMR (400 MHz, DMSO-$d_6$); δ = 14.29 (bs, 1H, N$^{1}$H), 9.44 (t, $^{3}J$ = 6.3 Hz, 1H, N$^{2'}$H), 8.45 (s, 1H, C4H), 7.29 (m, $^{3}J$ = 3.4 Hz, 2H, C7H & C11H), 7.24 (m, $^{3}J$ = 3.5 Hz, 2H, C8H & C10H), 4.40 (d, $^{3}J$ = 6.3 Hz, 2H, C3'$H_2$), 2.45 (s, 3H, $SCH_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 157.1 (C4), 146.7 (C5), 139.5 (C2), 136.4 (C6), 135.7 (C9), 128.1 (C8 & C10), 126.0 (C7 & C11), 121.4 (C4), 41.8 (C3'), 14.9 (S<u>C</u>$H_3$). IR (cm$^{-1}$): ṽ = 3345 (N-H), 1656 (C=O), 1508 (N-O), 828 (C-H).

1-(2,2-Diethoxyethyl)-*N*-[(4-methoxyphenyl)methyl]-5-nitro-1*H*-imidazole-2-carboxamide (**56**)



To a stirred solution of compound **54** (553 mg, 2 mmol) in DMF (10 mL) was added $K_2CO_3$ (6 mmol, 415 mg) and bromoacetaldehyde diethyl acetal (3 mmol, 226 µL). The mixture was heated in a microwave reactor at 180 °C for 15 min. Additional bromoacetaldehyde diethyl acetal (3 mmol, 226 µL) was added and the mixture was heated again in a microwave reactor for another 15 min. The reaction mixture was poured into $H_2O$ and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over $Na_2SO_4$ and filtered. Volatiles were removed in vacuo to give the crude product, which was further purified by flash column chromatography. Yield: 76 %, light yellow oil; $^1$H NMR (400 MHz, DMSO-$d_6$); δ = 9.38 (t, $^3J$ = 6.3 Hz, 1H, N$^{2'}$H), 8.48 (s, 1H, C4H), 7.27 (m, $^3J$ = 2.89 Hz, 2H, C7H & C11H), 6.89 (m, $^3J$ = 2.90 Hz, 2H, C8H & C10H), 4.79 (t, $^3J$ = 5.1 Hz, 1H, C2"H), 4.61 (d, $^3J$ = 5.1 Hz, 2H, C1"$H_2$), 4.35 (d, $^3J$ = 6.3 Hz, 2H, C3'$H_2$), 3.72 (s, 3H, $OCH_3$); 3.61 (dq, $^3J$ = 9.7, 7.0 Hz, 2H, C5"$H_2$), 3.41 (dq, $^3J$ = 9.7, 7.0 Hz, 2H, C3"$H_2$), 1.03 (m, 6H, C4"$H_3$ & C6"$H_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 158.2 (C9), 157.5 (C=O), 144.3 (C2), 137.9 (C5), 130.9 (C6), 128.8 (C7 & C11), 126.1 (C4), 113.5 (C8 & C10), 99.9 (C2"), 62.6 (C3" & C5"), 55.0 ($O\underline{C}H_3$). 50.2 (C1"), 41.6 (C3'), 15.0 (C4" & C6"); IR (cm$^{-1}$): $\tilde{\nu}$ = 1533 (N-O), 1247 (C-O), 832 (C-H).

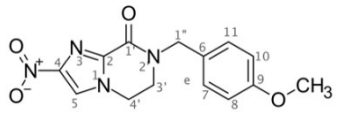
1-(2,2-Diethoxyethyl)-*N*-{[4-(methylsulfanyl)phenyl]methyl}-5-nitro-1*H*-imidazole-2-carbox amide (**57**)



To a stirred solution of compound **55** (585 mg, 2 mmol) in DMF (10 mL) was added $K_2CO_3$ (6 mmol, 415 mg) and bromoacetaldehyde diethyl acetal (3 mmol, 226 µL). The mixture was heated in a microwave reactor at 180 °C for 15 min. Additional bromoacetaldehyde diethyl acetal (3 mmol, 226 µL) was added and the mixture was heated again in a microwave reactor for another 15 min. The reaction mixture was poured into $H_2O$ and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over $Na_2SO_4$ and filtered. Volatiles were removed in vacuo to give the crude product, which was further purified by flash column chromatography. Yield: 75%, light yellow oil; $^1$H NMR (400 MHz, DMSO-$d_6$); δ = 9.44 (t, $^3J$ = 6.3 Hz, 1H, N$^{2'}$H), 8.49 (s, 1H, C4H), 7.29 (m, $^3J$ = 3.40 Hz, 2H, C7H & C11H), 6.89 (m, $^3J$ = 3.53 Hz, 2H, C8H & C10H), 4.79 (t, $^3J$ = 5.1 Hz, 1H, C2"H), 4.60 (d, $^3J$ = 5.1 Hz, 2H, C1"$H_2$), 4.37 (d, $^3J$ = 6.3 Hz, 2H, C3'$H_2$), 3.61 (dq, $^3J$ = 9.7, 7.0 Hz, 2H, C5"$H_2$), 3.40 (dq, $^3J$ = 9.7, 7.0 Hz, 2H, C3"$H_2$), 2.45 (s, 3H, $SCH_3$), 1.03 (m, 6H, C4"$H_3$ & C6"$H_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$); δ = 157.6 (C=O), 144.3 (C2), 137.8 (C5), 136.4 (C9), 135.7 (C6), 128.1 (C8 &

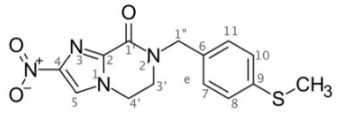
C10), 126.2 (C4), 126.0 (C7 & C11), 99.9 (C2"), 62.6 (C3" & C5"), 50.2 (C1"), 41.7 (C3'), 14.93 (C4" & C6"), 14.86 (O<u>C</u>H$_3$). IR (cm$^{-1}$): ṽ = 2920 (C-H), 1534 (N-O).

7-[(4-Methoxyphenyl)methyl]-2-nitro-5*H*,6*H*,7*H*,8*H*-imidazo[1,2-a]pyrazin-8-one (**58**)



To a stirred suspension of compound **56** (0.4 mmol, 157 mg) in $H_2O$ (11 mL) was added 1 mL of conc. HCl. The reaction was refluxed for 4.5 h. After that, the solvent was removed in vacuo and the crude product was purified by recrystallization from methanol. Yield: 57%, light yellow solid; Purity 95.3%; Mp: 276 - 277 °C (solid from methanol); $^1$H NMR (400 MHz, DMSO-d$_6$) δ = 8.80 (s, 1H, C4H), 7.60 (d, $^3J$ = 5.9 Hz, 1H, C4'H), 7.42 (d, $^3J$ = 5.9 Hz, 1H, C3'H), 7.33 (m, $^3J$ = 2.9 Hz, 2H, C7H & C11H), 6.91 (m, $^3J$ = 2.2 Hz, 2H, C8H & C10H), 5.05 (s, 2H, C1"H$_2$), 3.73 (s, 3H, OCH$_3$); $^{13}$C NMR (100 MHz, DMSO-d$_6$); δ = 158.9 (C9), 152.6 (C=O), 147.9 (C5), 135.0 (C2), 129.4 (C7 & C11), 128.4 (C6), 123.3 (C4'), 116.5 (C4), 114.0 (C8 & C10), 107.2 (C4"), 55.0 (O<u>C</u>H$_3$), 49.6 (C1"); IR (cm$^{-1}$): ṽ = 3096 (C-H), 1537 (N-O); HRMS ((ESI) *m/z*) calculated for $C_{14}H_{13}N_4O_4$ [M+ H]$^+$: 301.0931, found: 301.0929.

7-{[4-(Methylsulfanyl)phenyl]methyl}-2-nitro-5*H*,6*H*,7*H*,8*H*-imidazo[1,2-a]pyrazin-8-one (**59**)



To a stirred suspension of compound **57** (0.4 mmol, 164 mg) in $H_2O$ (11 mL) was added 1 mL of conc. HCl. The reaction was refluxed for 4.5 h. After that, the solvent was removed in vacuo and the crude product was purified by recrystallization from methanol. Yield: 49%, light yellow solid; Purity 95.6%; Mp: 264 - 265 °C (solid from methanol); $^1$H NMR (400 MHz, DMSO); δ = 8.81 (s, 1H, C4H), 7.60 (d, $^3J$ = 5.9 Hz, 1H, C4'H), 7.42 (d, $^3J$ = 5.9 Hz, 1H, C3'H), 7.33 (m, $^3J$ = 2.6 Hz, 2H, C7H & C11H), 7.26 (m, $^3J$ = 2.7 Hz, 2H, C8H & C10H), 5.08 (s, 2H, C1"H$_2$), 2.45 (s, 3H, SCH$_3$). $^{13}$C NMR (100 MHz, DMSO-d$_6$); δ = 152.7 (C=O), 147.9 (C4), 137.7 (C9), 135.0 (C2), 133.0 (C6), 128.5 (C7 & C11), 126.0 (C8 & C10), 123.3 (C3'), 116.5 (C2), 107.3 (C4'), 49.7 (C1"), 14.6 (S<u>C</u>H$_3$). IR (cm$^{-1}$): ṽ = 3076 (C-H), 1671 (C=O), 1538 (N-O); HRMS ((ESI) *m/z*) calculated for $C_{14}H_{13}N_4O_3S$ [M+ H]$^+$: 317.0703, found: 317.0718.

## 1.2 Determination of purity of compounds

### 1.2.1 HPLC analysis conditions

The purity of the synthesized analogs was determined using Merck-Hitachi D-7000 HPLC, which was equipped with HPLC pump (L-7100), autosampler (L-7200), DAD detector (L-7450) and column oven (L-7350). Chromatograms were collected and analyzed with the D-7000 HPLC system manager (D-7000 HSM). The following conditions were used;

- Mobile phase A: $KH_2PO_4$ phosphate buffer (50 mM, pH = 3); mobile phase B: acetonitrile
- Gradient elution: 0-5 min, 80% mobile phase A; 5-15 min, 80→10% mobile phase A; 15-25 min, 10% mobile phase A; 25-30 min, 10→80% mobile phase A; 30-50 min, 80% mobile phase A.

- Flow rate: 1 mL/min
- Column: ProntoSIL 120-5-C18H 125x4.0mm; column temperature: 30 °C
- Detection: λ = 254 and 280 nm

For compound **38**, the LC-MS data is given. Moreover, HPLC traces of compound **58** and **59** were determined under different condition from the other. The HPLC analysis was done using a Shimadzu HPLC equipped with LC-20AD pump, SIL-20AC HT autosampler and SPD-M20A PDA detector. The condition used were as follows;

- Mobile phase A: water; mobile phase B: methanol
- Gradient elution: 0-18 min, 50→5% mobile phase A; 18-20 min, 5% mobile phase A.
- Flow rate: 1 mL/min
- Column: Phenomenex Luna® 5 µm C18(2) 100 Å, 250 x 4.6 mm

## 1.3 Determination of enantiomeric purity

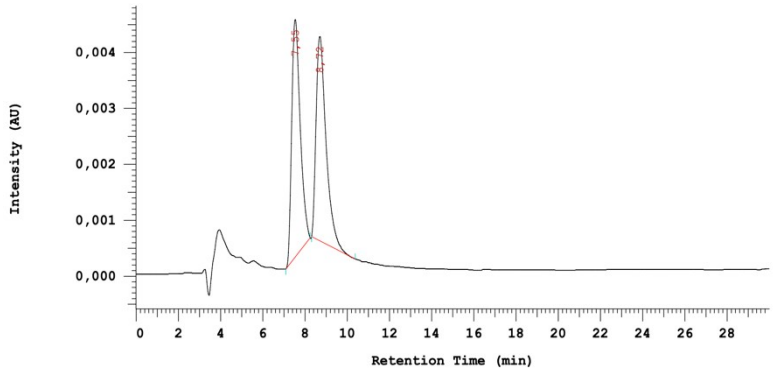
### 1.3.1 Chiral HPLC method

The Merck-Hitachi D-7000 HPLC equipped with D-7000 HSM interface module, L-7400 detector, HPLC pump, and column oven was used for confirmation of chiral purity.

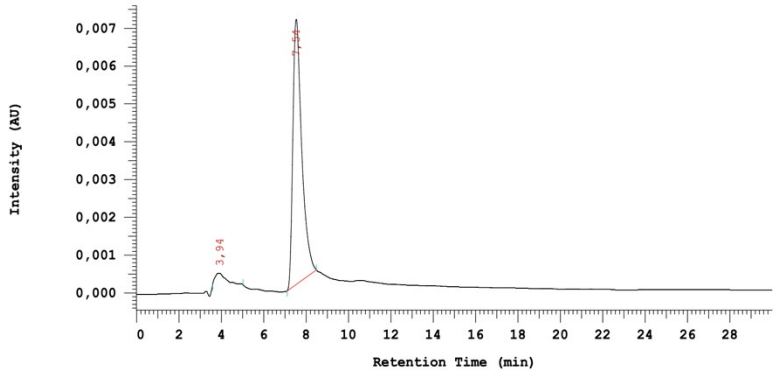
- Isocratic elution: 80% isopropanol and 20% n-hexane, 30 min
- Flow rate: 1 mL/min
- Column: Chiralcel OD-H 1 125x4.0mm; Column temperature: 35 °C
- Detection wave length, λ = 298 nm

#### 1.3.1.1 Chromatogram for analogue *rac*-49

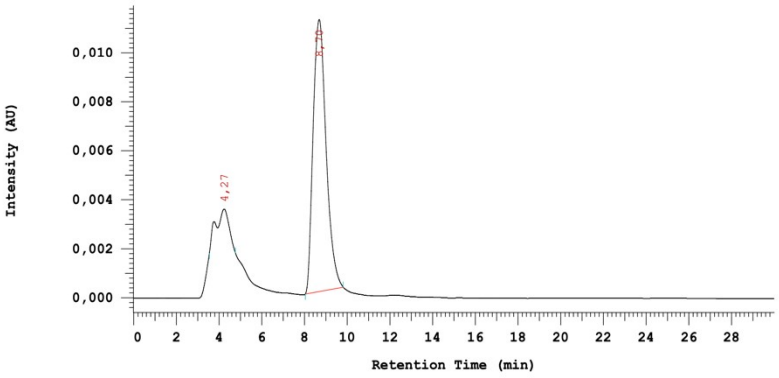
The chromatogram of compound **49** revealed two almost identical peaks at 7.55 and 8.72 min. Separate analysis of compound **50** and compound **51** displayed only a single peak, which indicate the enantiomeric purity of each analogues. Furthermore, the retention time from the analysis of compound **50** and compound **51**, 7.54 and 8.70 min respectively, are almost identical to the retention times of the two peaks identified from the analysis of compound **49**. Those result confirms that compound **49** is a racemate of enantiomers **50** and **51**.



### 1.3.1.2 Chromatogram for enantiomer 50




### 1.3.1.3. Chromatogram for enantiomer 51




# 2. Anti-promastigote and anti-amastigote activity profiles

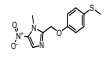
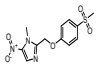
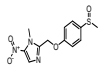
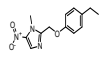
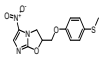
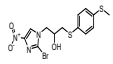
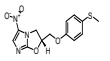
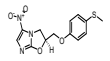
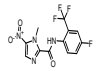
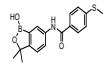
## 2.1 Anti-promastigote and anti-amastigote activity profiles

Statistical significance of analogues was compared with the control miltefosine (*P < 0.05, **P < 0.01, ***P < 0.001).

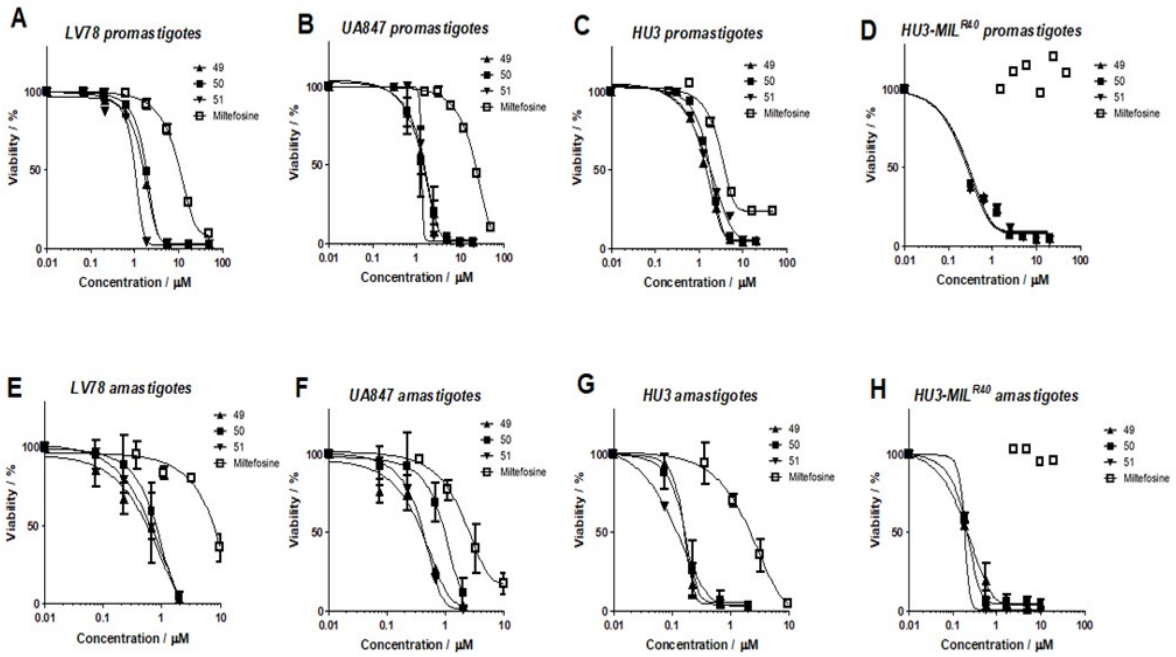
Table 1: anti-promastigote activity profile

| No. | Cpds | Structure | Mean $IC_{50}$ (μM) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Anti-promastigote activity | | | | | | | | | | Cytotoxicity | |
| | | | *L. amazonensis* | | *L. braziliensis* | | *L. major* | | *L. donovani* | | MIL-resistant | | Mouse fibroblast | Mouse macrophage |
| | | | LV78 | P-value | UA847 | P-value | FV1 | P-value | HU3 | P-value | Ld HU3-MILR40 | p-value | L929 | RAW264.7 |
| 17 | Asu-05 |  | >20 | | >20 | | >20 | | >20 | | >20 | | >100 | >91.1 |
| 5 | Asu-08 |  | 7.0 ± 2.6 | 0.0108* | 3.9 ± 0.9 | 0.0131* | 1.9 ± 1.6 | 0.0125* | 3.3 ± 0.7 | | 5.5 ± 1.8 | < 0.0001*** | >100 | >100 |
| 7 | Asu-09 |  | 9.4 ± 2.5 | 0.0206* | 5.9 ± 2.1 | 0.0263* | 1.7 ± 0.9 | 0.0075** | 3.8 ± 0.8 | | 5.6 ± 1.6 | < 0.0001*** | >100 | >100 |
| 6 | Asu-10 |  | 7.8 ± 1.8 | 0.0112* | 4.3 ± 1.1 | 0.0147* | 1.4 ± 0.6 | 0.0051** | 3.4 ± 1.0 | | 4.3 ± 1.0 | < 0.0001*** | >100 | >100 |
| 19 | Asu-17 |  | 4.5 ± 1.2 | 0.0139* | 3.9 ± 0.8 | 0.0128* | 1.4 ± 0.4 | 0.0433* | 5.0 ± 2.0 | | 5.3 ± 1.5 | < 0.0001*** | 71.8 ± 0.0 | >68.5 |
| 21 | Asu-21 |  | 14.6 ± 7.7 | | 9.6 ± 1.7 | | 2.7 ± 0.6 | | 12.2 ± 4.3 | | 12.3 ± 2.2 | < 0.0001*** | >100 | >100 |
| 18 | Asu-25 |  | >20 | | >20 | | >20 | | >20 | | >20 | | >100 | >99.8 |
| 26 | Asu-28 |  | 27.2 ± 17.8 | | 17.5 ± 2.2 | | 9.1 ± 1.5 | | 12.5 ± 5.4 | | 7.1 ± 1.2 | < 0.0001*** | >100 | >91.7 |
| 20 | Asu-29 |  | >20 | | >20 | | 9.5 ± 2.4 | | >20 | | 11.9 ± 2.1 | < 0.0001*** | >100 | >100 |
| 28 | Asu-39 |  | >20 | | >20 | | 11.8 ± 1.3 | | >20 | | >20 | < 0.0001*** | >100 | >100 |
| 27 | Asu-40 |  | >20 | | >20 | | >20 | | >20 | | >20 | | >100 | >100 |
| 32 | Asu-53 |  | >20 | | >20 | | >20 | | >20 | | >13.9 | | 84.7 ± 12.5 | >68.7 |
| 49 | Asu-55 |  | 1.8 ± 0.2 | 0.0081** | 1.5 ± 0.6 | 0.0068** | 3.4 ± 1.1 | | 1.0 ± 0.4 | 0.0353* | 0.4 ± 0.2 | < 0.0001*** | >100 | >100 |
| 53 | Asu-57 |  | >20 | | >20 | | >20 | | >20 | | 4.5 ± 0.4 | 0.0002*** | >100 | >100 |
| ??? | Asu-62 | | 6.4 ± 0.8 | 0.0198* | 6.6 ± 1.6 | 0.0303* | 2.6 ± 0.3 | | 5.5 ± 0.7 | | 6.1 ± 1.5 | < 0.0001*** | 52.3 ± 26.3 | 32.1 ± 1.9 |
| 50 | Asu-65 |  | 1.9 ± 0.1 | 0.0084** | 1.4 ± 0.8 | 0.0068** | 5.7 ± 1.0 | | 1.1 ± 0.6 | 0.0375* | 0.4 ± 0.3 | < 0.0001*** | >100 | >95.3 |
| 51 | Asu-67 |  | 1.2 ± 0.3 | 0.0073** | 1.4 ± 0.2 | 0.0066** | 3.1 ± 0.8 | | 1.1 ± 0.6 | 0.0375* | 0.5 ± 0.4 | < 0.0001*** | >92.2 | >68.5 |
| 33 | Asu-68 |  | >20 | | >20 | | 6.5 ± 3.4 | | >20 | | >20 | | >100 | >100 |
| 34 | Asu-71 | | 13.3 ± 3.2 | | 12.2 ± 1.2 | | 3.4 ± 0.3 | | 7.5 ± 2.6 | | 13.7 ± 4.8 | 0.0002*** | >100 | >100 |
| 35 | Asu-75 | | 4.5 ± 2.2 | 0.0155* | 2.3 ± 1.0 | 0.0086** | 1.2 ± 0.3 | 0.0372* | 8.1 ± 1.4 | | 12.2 ± 4.7 | 0.0007*** | >100 | >100 |
| 38 | Asu-80 | | 3.6 ± 1.5 | 0.0120* | 4.4 ± 0.4 | 0.0145* | 3.9 ± 0.5 | | 11.9 ± 5.9 | | 15.4 ± 2.2 | 0.0008*** | >100 | 73.6 ± 1.7 |
| 52 | Asu-82 | | >20 | | >20 | | >20 | | 10.2 ± 2.7 | | 7.1 ± 5.3 | 0.0004*** | >100 | >100 |
| 40 | Asu-86 | | >20 | | >20 | | >20 | | >16.8 | | >20 | | >100 | >100 |
| 58 | VN-240 | | >20 | | >20 | | 6.9 ± 0.7 | | >12.4 | | >18.5 | | >100 | >100 |
| 59 | VN-242 | | >20 | | >20 | | 8.9 ± 5.4 | | >16.6 | | >20 | | >57.5 | 48.1 ± 13.8 |
| 4 | MIL | | 22.0 ± 7.2 | | 17.8 ± 6.2 | | 7.0 ± 3.8 | | 6.9 ± 3.3 | | >40 | | 81.5 ± 20.0 | 9.9 ± 2.9 |

Table 2: anti-amastigote activity profile

| | Amastigotes | | | | | | | | Mouse cell lines |
|---|---|---|---|---|---|---|---|---|---|
| Compound | *L. amazonensis* *LV78* | *P-value* | *L. brazilinensis* *UA847* | *P -value* | *L. donovani* *HU3* | *P-value* | *MIL-resistant* *HU3* | *P-value* | *Peritoneal elicited macrophage (PEM)* |
| Asu-08  | >10 | | >10 | | >10 | | >10 | | >81.7 |
| Asu-09  | >10 | | >10 | | >10 | | >10 | | >100 |
| Asu-10  | >10 | | >10 | | >10 | | >10 | | >100 |
| Asu-17  | >10 | | >10 | | >10 | | >10 | | >100 |
| Asu-55  | 0.7 ± 0.3 | 0.0001*** | 0.7 ± 0.6 | | 0.3 ± 0.3 | 0.0002*** | 0.4 ± 0.2 | < 0.0001*** | >100 |
| Asu-62  | >10 | | >10 | | >10 | | >10 | | >50 |
| Asu-65  | 0.7 ± 0.4 | 0.0001*** | 1.0 ± 0.8 | | 0.4 ± 0.3 | 0.0003*** | 0.6 ± 0.0 | < 0.0001*** | >85.7 |
| Asu-67  | 0.6 ± 0.1 | 0.0008*** | 0.5 ± 0.3 | | 0.4 ± 0.4 | 0.0016** | 0.4 ± 0.3 | < 0.0001*** | >87.9 |
| Asu-75  | >10 | | >10 | | >10 | | >10 | | >100 |
| Asu-80  | >10 | | >10 | | >10 | | >10 | | >100 |
| Miltefosine | 9.6 ± 1.7 | | 3.2 ± 2.4 | | 2.7 ± 0.2 | | >20 | | >40 |

## 2.2 Dose-response curves of selected compounds




## 3. MTT cell viability assay

The percent of viability of TAMH and HEP-G2 cells at the respective concentration of the test compound after 24 h and 48 h of incubations are given in Table below;

| Compound | Concertation (µM) | TAMH (%, 24 h) | | TAMH (48 h) | | HEP-G2 (24 h) | | HEP-G2 (48 h) | |
|---|---|---|---|---|---|---|---|---|---|
| | | Mean | SD | Mean | SD | Mean | SD | Mean | SD |
| **5** | 62.5 | 93.0 | 9.8 | 100 | 13.1 | 90.2 | 16.0 | 95.4 | 5.4 |
| **6** | 125 | 101.0 | 4.4 | 92.0 | 24 | 87.7 | 12.1 | 83.1 | 21.2 |
| **7** | 125 | 99.0 | 4.6 | 95.5 | 6.3 | 105.1 | 17.1 | 82.5 | 21.2 |
| **17** | 125 | 82.4 | 9.9 | 94.1 | 1.5 | 92.4 | 22.9 | 88.1 | 5.9 |
| **18** | 62.5 | 97.2 | 11.4 | 98.8 | 14.2 | 86.2 | 11.4 | 93.7 | 22.1 |
| **19** | 31.25 | 74.9 | 3.7 | 87.2 | 9.1 | 73.4 | 8.1 | 89.2 | 7.8 |
| **20** | 15.625 | 87.2 | 10.4 | 95.1 | 12.8 | 87.1 | 28.5 | 79.5 | 12.4 |
| **21** | 125 | 84.8 | 6.0 | 94.8 | 10.3 | 79.1 | 15.4 | 75.4 | 3.5 |
| **26** | 31.25 | 86.5 | 9.7 | 97.7 | 11.5 | 84.3 | 14.6 | 63.1 | 9.9 |
| **27** | 125 | 78.8 | 9.4 | 81.4 | 13.3 | 50.1 | 6.8 | 50.7 | 8.7 |
| **28** | 125 | 65.8 | 7.3 | 73.2 | 10.3 | 71.3 | 0.9 | 51.3 | 4.2 |
| **32** | 15.625 | 56.2 | 11.8 | 56.3 | 0.4 | 48.8 | 13.2 | 69.4 | 27.0 |
| **33** | 7.8125 | 92.7 | 7.5 | 97.1 | 17.5 | 93.0 | 16.4 | 91.0 | 5.21 |
| **34** | 15.625 | 80.8 | 9.7 | 85.5 | 5.6 | 67.4 | 29.8 | 67.9 | 6.0 |
| **35** | 15.625 | 80.2 | 7.9 | 82.5 | 6.7 | 74.1 | 17.9 | 61.7 | 1.7 |
| **38** | 15.625 | 65.9 | 6.7 | 83.9 | 14.3 | 52.8 | 17.3 | 54.0 | 9.7 |
| **40** | 125 | 60.9 | 8.9 | 81.7 | 12.8 | 44.2 | 8.0 | 54.2 | 7.6 |
| **49** | 7.8125 | 78.2 | 9.8 | 95.5 | 7.3 | 56.4 | 5.6 | 78.5 | 10.4 |
| **50** | 7.8125 | 87.8 | 5.2 | 94.2 | 5.5 | 60.5 | 8.1 | 78.2 | 10.3 |
| **51** | 7.8125 | 83.9 | 6.4 | 90.8 | 5.3 | 56.0 | 9.1 | 82.1 | 2.3 |
| **52** | 125 | 58.9 | 2.6 | 72.3 | 10.3 | 40.8 | 5.3 | 55.0 | 8.5 |
| **53** | 125 | 80.4 | 1.9 | 75.0 | 5.5 | 53.5 | 3.4 | 66.7 | 20.3 |
| **58** | 7.8125 | 69.5 | 8.8 | 72.4 | 5.9 | 46.5 | 8.3 | 51.9 | 9.5 |
| **59** | 7.8125 | 73.3 | 9.1 | 67.9 | 10 | 60.1 | 12.6 | 76.6 | 11.9 |

# 4. Microsomes and S9 incubation assays

## 4.1 Materials

- $KH_2PO_4$ phosphate buffer (50 mM pH = 7.4)
- $MgCl_2.6H_20$ (10 mM)
- EDTA disodium dihydrate (5 mM)
- $NADP^+$ (0.3 mM)
- G-6-P (5.3 mM)
- G-6-P-DH (Sigma Aldrich 3.5 IU/mL). The purchased concentration (250 IU) was diluted with 100 µL aqueous solution of $(NH_4)_2SO_4$ (3.2 M, pH 7.0).
- Sprague Dalle rat liver microsomes, Thermo Fischer (Art-Nr RTMCPL), 20 mg/mL
- Sprague Dalle rat S9 fraction, Thermo Fischer (Art-Nr RTS9PL), 20 mg/mL
- Human microsomes, Thermo Fischer (HMCCPL), 20 mg/mL
- Test compounds (2 mM stock solution in acetonitrile)
- Methimazole (100 mM stock solution in methanol)
- GSH (2 mM stock solution in the phosphate buffer above that was prepared just before use).

## 4.2 Procedure for microsomes incubation

Pre-incubation solution (4.5 mL) was prepared by the addition of G-6-P-DH solution (5 µL) to a solution of $NADP^+$ (1.0 mg) and G-6-P (6.8 mg) in 4.5 mL of $KH_2PO_4$ phosphate buffer (50 mM pH = 7.4) containing $MgCl_2.6H_20$ (10 mM) and EDTA disodium dihydrate (5 mM). An incubation suspension (5 mL) was prepared by homogenizing the mixture of rat or human liver microsomes (0.5 mL) with the pre-incubation solution. The suspension was divided into four aliquots (1.1 mL) in a 2 mL Eppendorf vials, which was then warmed at 37 °C for 10 min using water bath. A test compound (11 µL) was added to each vial, which was then vortexed and returned to the water bath. At 0, 16 min and 32 min, 350 µL of incubation suspension was removed immediately after vortexing the test compound and added to a 1.5 mL Eppendorf vial containing 350 µL of ice-cold acetonitrile. The vials were kept in an ice-cold box for 15-30 min to allow precipitate of proteins. Eventually, the vials were centrifuge at 14,000g at 0 °C for 10 min and store in in a freezer. Before HPLC analysis, the centrifugation was repeated and clear supernatant was transferred to HPLC vials.

## 4.3 Procedure for S9 incubation

The same procedure used for microsomes incubation was applied. However, the S9 fraction (1 mL) was used instead of microsomes (0.5 mL) and accordingly, slight amount adjustment of each material was necessary. Moreover, for the S9 incubation assay in the presence of GSH, 3 µL of GSH was added to aliquots immediately following the addition of test compounds.

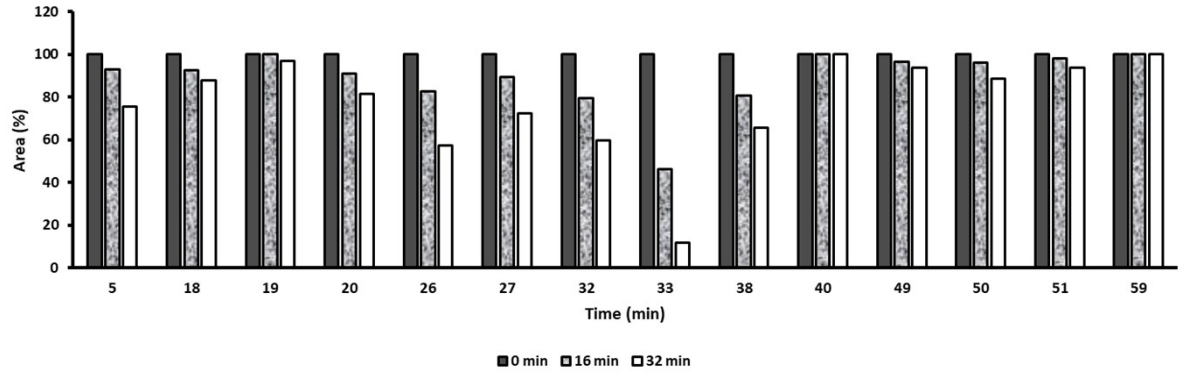
## 4.4 HPLC analysis

The same HPLC instrument used for purity analysis was employed for the analysis of the filtrate of microsomes and S9 incubations. The conditions used were as follows;

- Mobile phase A: $KH_2PO_4$ phosphate buffer (20 mM pH = 3); mobile phase B: acetonitrile
- Gradient elution: 0-5 min, 80% mobile phase A; 5-15 min, 80→30% mobile phase A; 15-25 min, 30% mobile phase A; 25-30 min, 30→80% mobile phase A; 30-45 min, 80% mobile phase A.
- Flow rate: 1 mL/min

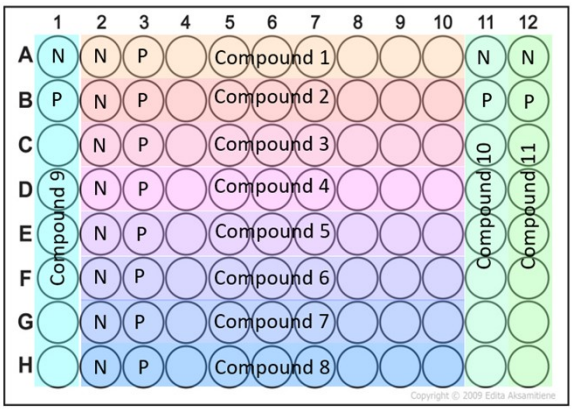
- Column: ProntoSIL 120-5-C18H 125x4.0mm; column temperature: 30 °C
- Detection wave lengths, λ = 254 and 280 nm

### 4.5 S9 incubation without GSH




## 5. hERG activity evaluations

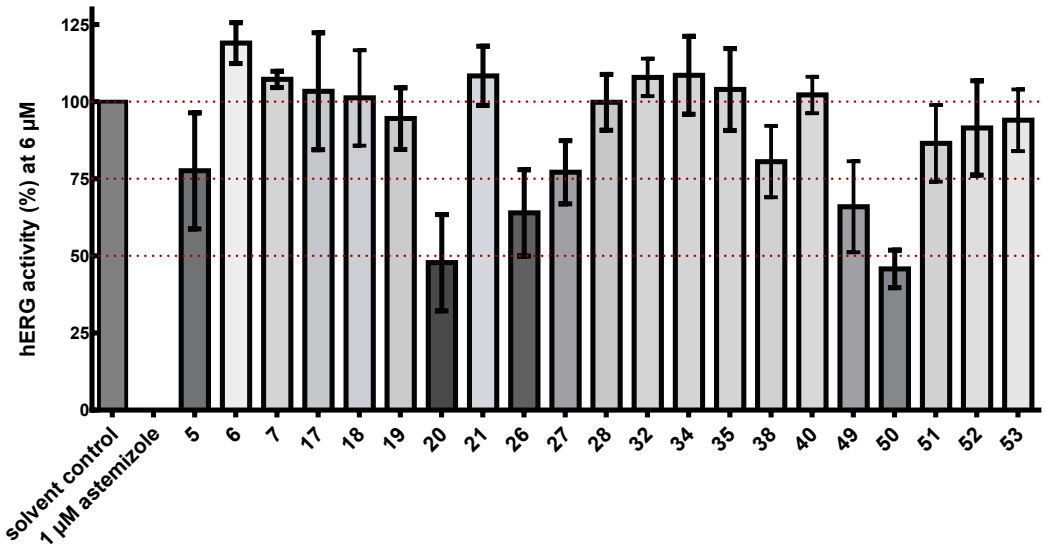
### 5.1 Plate Loading Schedule




N: Negative control, 0.5% DMSO; maximal activity of hERG channels

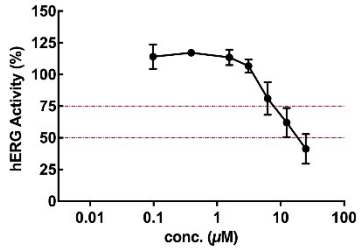
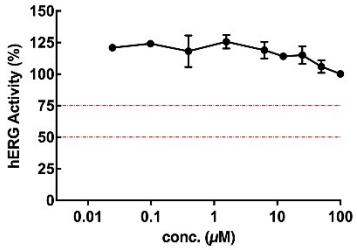
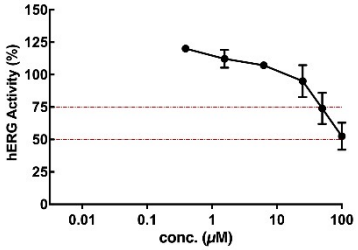
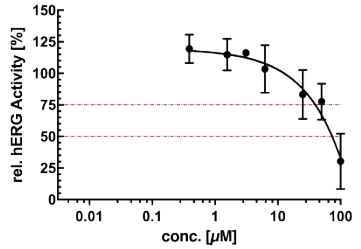
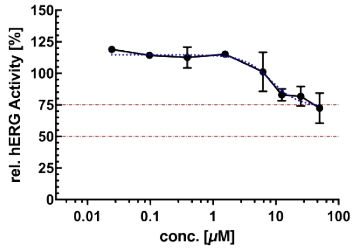
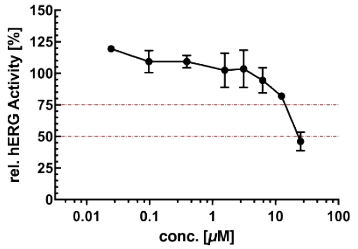
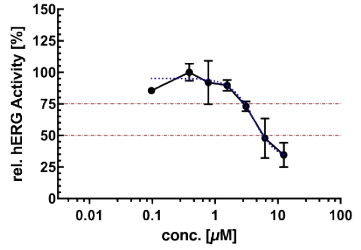
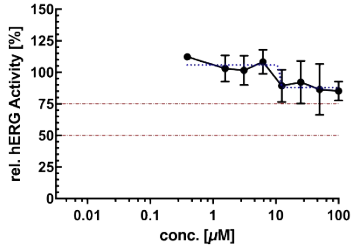
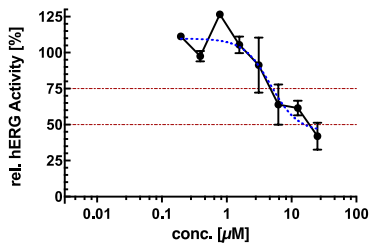
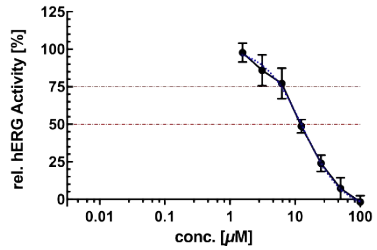
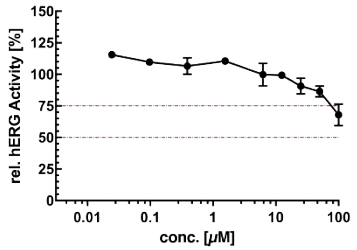
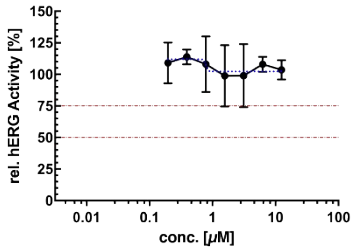
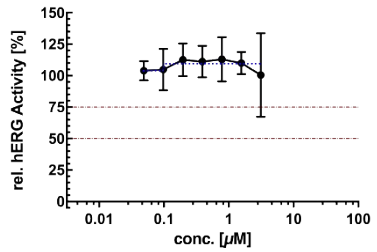
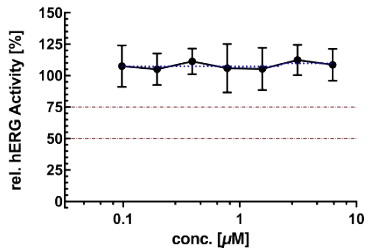
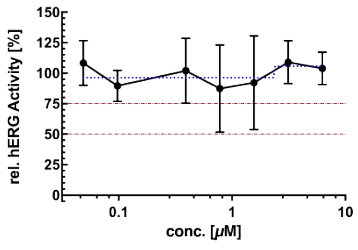
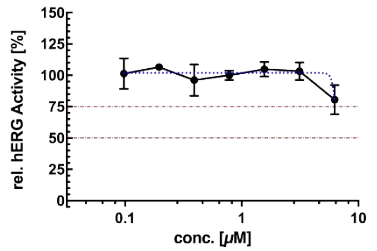
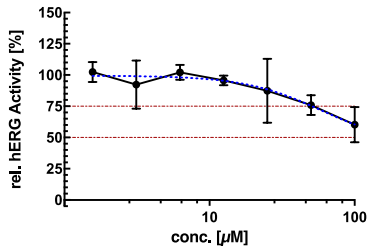
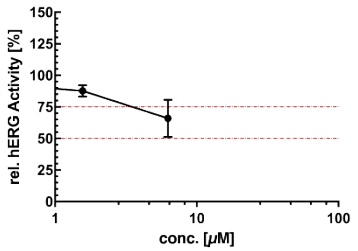
P: Positive control, 1 µM astemizole; maximal Inhibition of hERG channels

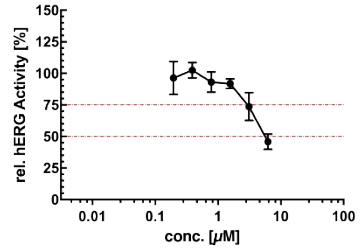
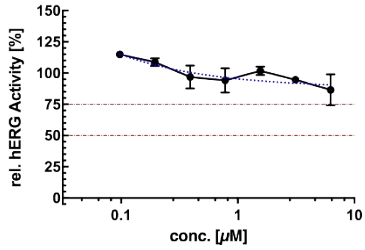
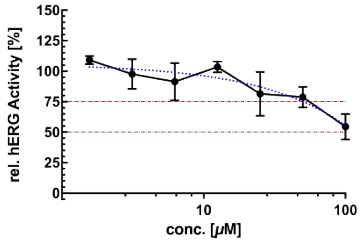
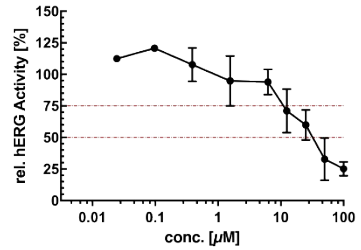
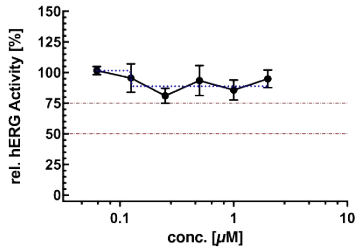
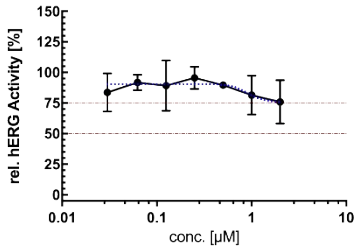
## 5.2 The hERG activity with solvent control and astemizole




## 5.3 The $IC_{50}$ and $IC_{25}$ of the synthesized analogues

The dose-response curve and the concentrations reducing the half of the maximum hERG current or $IC_{50}$ values are given in the table below. The $IC_{50}$ values of some analogues cannot be determined. In such instance, the $IC_{25}$ value is provided.

| **5**: $IC_{50}$ = 10.7 µM | **6**: $IC_{25}$ > 100 µM | **7**: $IC_{25}$ = 42.2 µM |
|---|---|---|
|  |  |  |
| **17**: $IC_{50}$ = 60.7 µM | **18**: $IC_{50}$ = 27.1 µM | **19**: $IC_{250}$ = 24.1 µM |
|  |  |  |
| **20**: $IC_{50}$ = 7.03 µM | **21**: $IC_{25}$ > 100 µM | **26**: $IC_{50}$ = 19.2 µM |
|  |  |  |
| **27**: $IC_{50}$ = 12.9 µM | **28**: $IC_{25}$ = 49.4 µM | **32**: $IC_{25}$ > 12.5 µM |
|  |  |  |
| **33**: $IC_{25}$ > 3.125 µM | **34**: $IC_{25}$ > 6.25 µM | **35**: $IC_{25}$ > 6.25 µM |
|  |  |  |
| **38**: $IC_{25}$ > 6.25 µM | **40**: $IC_{25}$ = 25.7 µM | **49**: $IC_{25}$ = 2.9 µM |
|  |  |  |

| **50**: $IC_{50}$ = 4.9 µM | **51**: $IC_{50}$ > 6.25 µM | **52**: $IC_{25}$ = 30.1 µM |
|---|---|---|
|  |  |  |
| **53**: $IC_{50}$ = 25.9 µM | **58**: $IC_{25}$ > 2 µM | **59**: $IC_{25}$ > 2 µM |
|  |  |  |



## 6. References

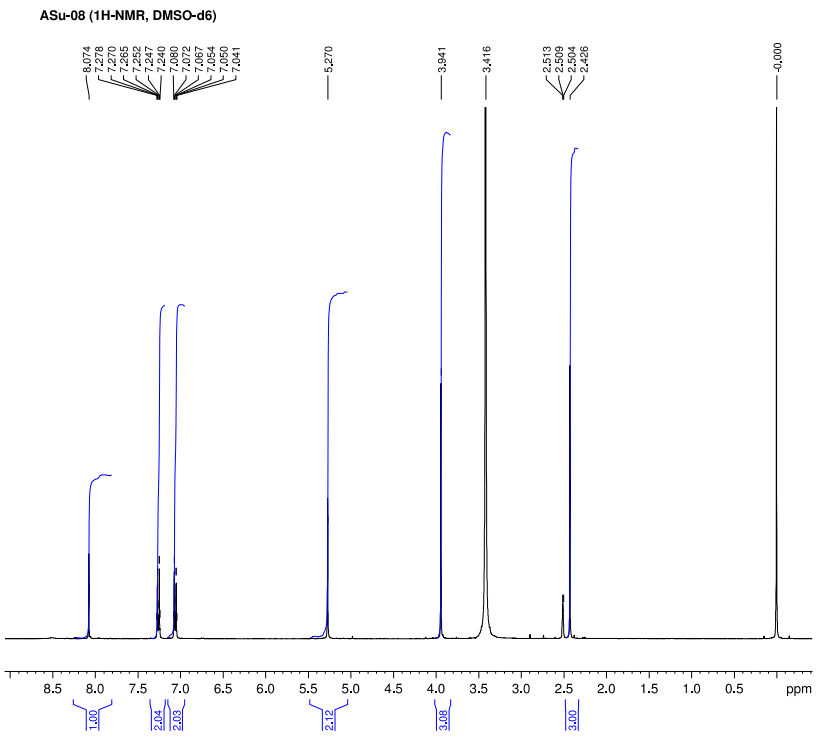
1 US4042705A, 1976.

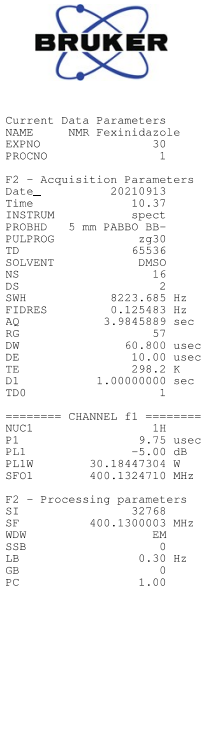
2 A. M. Jarrad, C. W. Ang, A. Debnath, H. J. Hahn, K. Woods, L. Tan, M. L. Sykes, A. J. Jones, R. Pelingon, M. S. Butler, V. M. Avery, N. P. West, T. Karoli, M. A. T. Blaskovich and M. A. Cooper, *J. Med. Chem.*, 2018, **61**, 11349–11371.

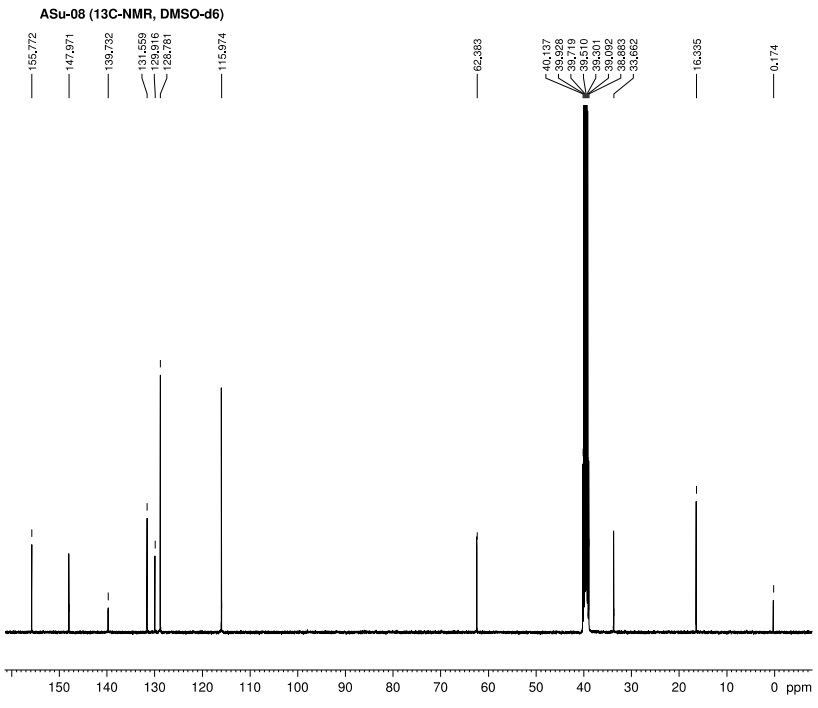
3 WO 2020/051575 A1, 2020.

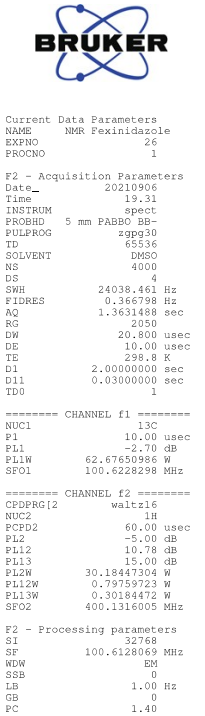
# 7. $^{1}$H NMR and $^{13}$C NMR Spectra

1-Methyl-2-{[4-(methylsulfanyl)phenoxy]methyl}-5-nitro-1*H*-imidazole (**5**)

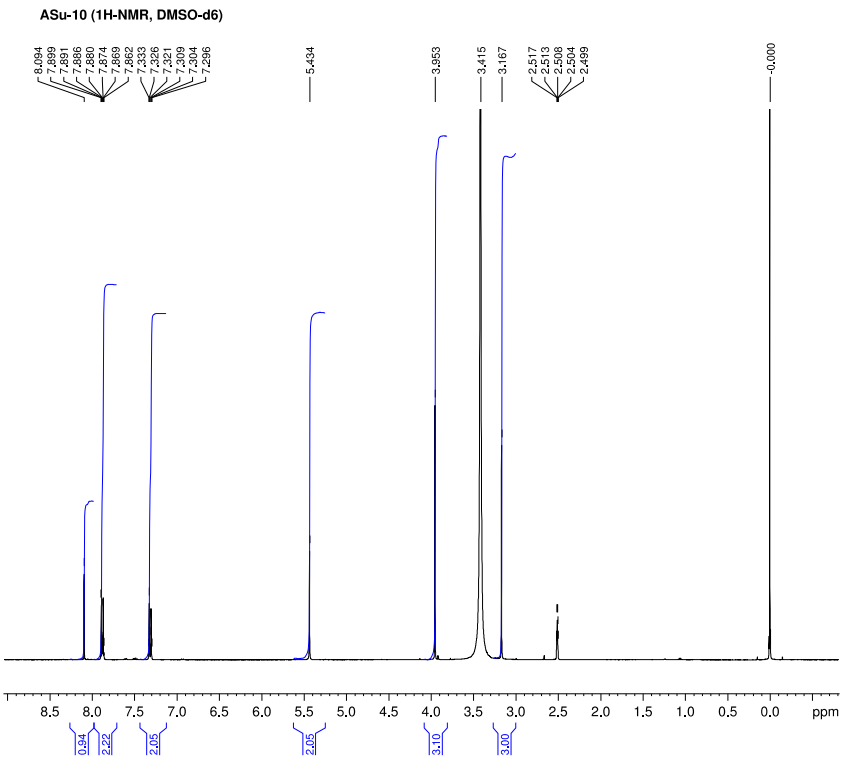


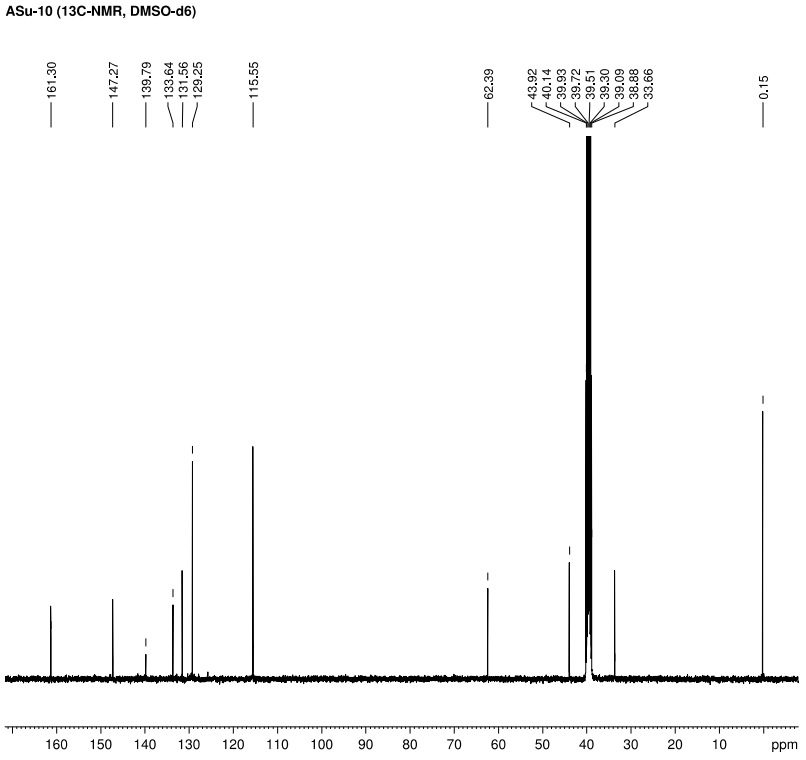



2-[(4-Methanesulfinylphenoxy)methyl]-1-methyl-5-nitro-1*H*-imidazole (**6**)

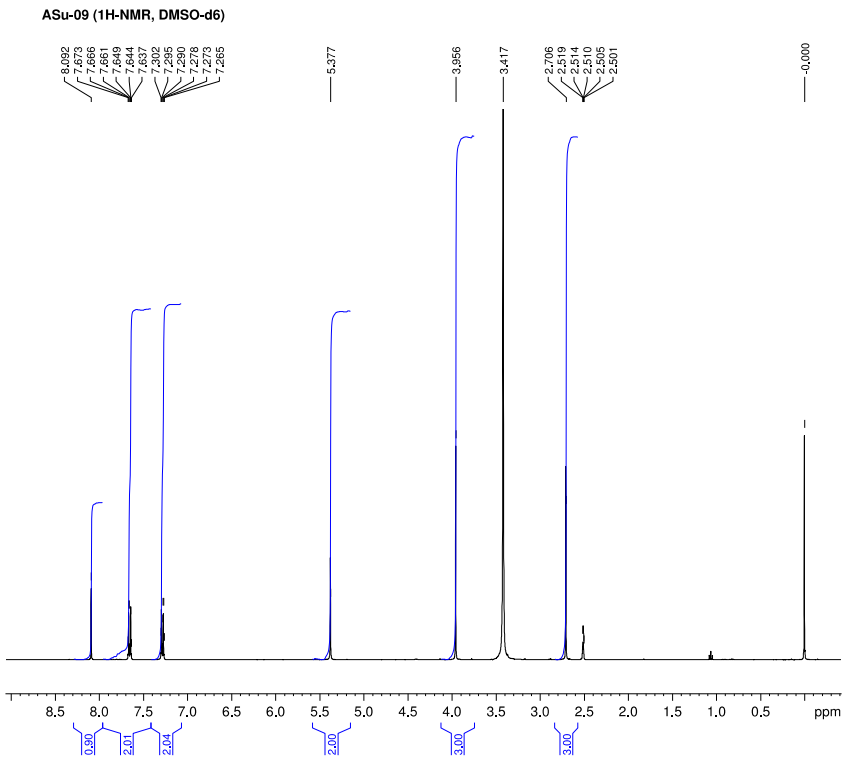



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                   33
PROCNO                   1

F2 - Acquisition Parameters
Date_              20210921
Time                 10.49
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG              zg30
TD                  65536
SOLVENT              DMSO
NS                     16
DS                      2
SWH              8223.685 Hz
FIDRES           0.125483 Hz
AQ               3.9845889 sec
RG                   71.8
DW                 60.800 usec
DE                 10.00 usec
TE                 298.1 K
D1              1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                   9.75 usec
PL1                 -5.00 dB
PL1W         30.18447304 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                  32768
SF             400.1300003 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.00
```

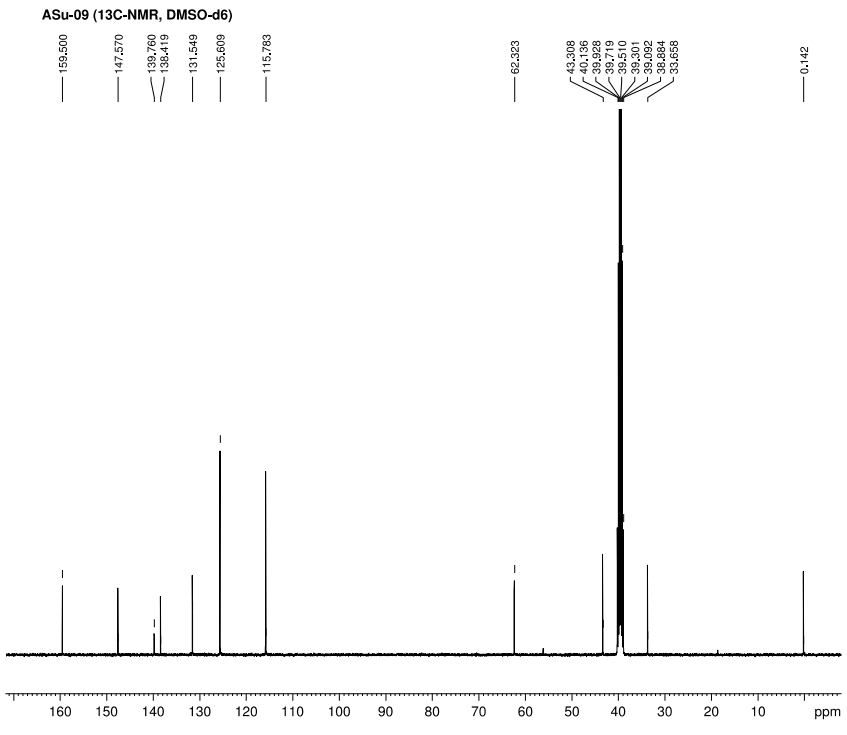



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                   35
PROCNO                   1

F2 - Acquisition Parameters
Date_              20210922
Time                  0.26
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG            zgpg30
TD                  65536
SOLVENT              DMSO
NS                   3000
DS                      4
SWH             24038.461 Hz
FIDRES           0.366798 Hz
AQ               1.3631488 sec
RG                   2050
DW                 20.800 usec
DE                 10.00 usec
TE                 298.6 K
D1              2.00000000 sec
D11             0.03000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                  13C
P1                 10.00 usec
PL1                -2.70 dB
PL1W         62.67650986 W
SFO1        100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                   1H
PCPD2              60.00 usec
PL2                -5.00 dB
PL12               10.78 dB
PL13               15.00 dB
PL2W         30.18447304 W
PL12W         0.79759723 W
PL13W         0.30184472 W
SFO2        400.1316005 MHz

F2 - Processing parameters
SI                  32768
SF             100.6128106 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   1.40
```

2-[(4-Methanesulfonylphenoxy)methyl]-1-methyl-5-nitro-1*H*-imidazole (**7**)

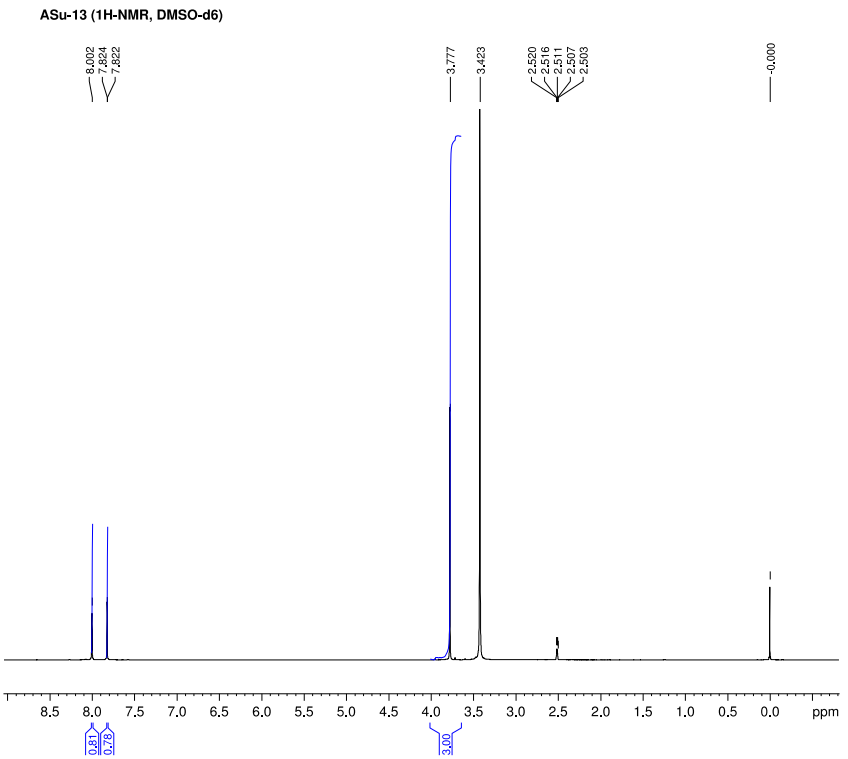



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                   34
PROCNO                   1

F2 - Acquisition Parameters
Date_               20210921
Time                   11.16
INSTRUM                spect
PROBHD   5 mm PABBO BB-
PULPROG                zg30
TD                    65536
SOLVENT                DMSO
NS                       16
DS                        2
SWH                8223.685 Hz
FIDRES            0.125483 Hz
AQ                 3.9845889 sec
RG                       57
DW                   60.800 usec
DE                   10.00 usec
TE                   298.3 K
D1                1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      1H
P1                     9.75 usec
PL1                   -5.00 dB
PL1W            30.18447304 W
SFO1           400.1324710 MHz

F2 - Processing parameters
SI                    32768
SF               400.1299996 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.00
```

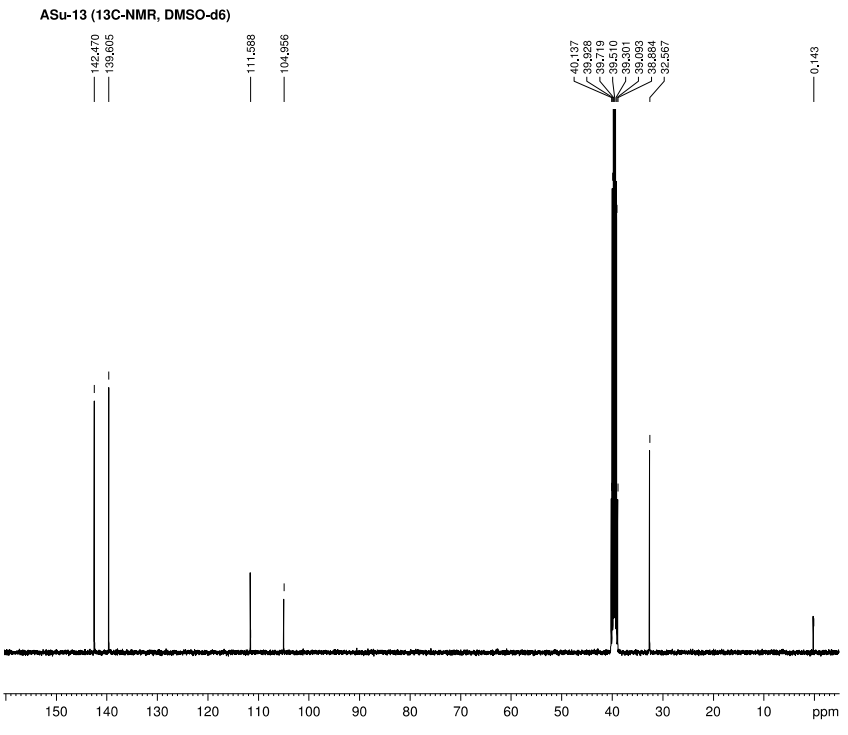



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                   40
PROCNO                   1

F2 - Acquisition Parameters
Date_               20210922
Time                    5.14
INSTRUM                spect
PROBHD   5 mm PABBO BB-
PULPROG             zgpg30
TD                    65536
SOLVENT                DMSO
NS                     3000
DS                        4
SWH               24038.461 Hz
FIDRES            0.366798 Hz
AQ                 1.3631488 sec
RG                     2050
DW                   20.800 usec
DE                   10.00 usec
TE                   298.7 K
D1                2.00000000 sec
D11               0.03000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     13C
P1                   10.00 usec
PL1                   -2.70 dB
PL1W            62.67650986 W
SFO1           100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2            waltz16
NUC2                      1H
PCPD2                60.00 usec
PL2                   -5.00 dB
PL12                  10.78 dB
PL13                  15.00 dB
PL2W            30.18447304 W
PL12W            0.79759723 W
PL13W            0.30184472 W
SFO2           400.1316005 MHz

F2 - Processing parameters
SI                    32768
SF               100.6128104 MHz
WDW                      EM
SSB                       0
LB                     1.00 Hz
GB                        0
PC                     1.40
```

1-Methyl-1*H*-imidazole-5-carbonitrile (**10**)




```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                   61
PROCNO                   1

F2 - Acquisition Parameters
Date_               20211007
Time                   11.20
INSTRUM                spect
PROBHD   5 mm PABBO BB-
PULPROG                zg30
TD                    65536
SOLVENT                DMSO
NS                       16
DS                        2
SWH                8223.685 Hz
FIDRES            0.125483 Hz
AQ                3.9845889 sec
RG                       64
DW                  60.800 usec
DE                  10.00 usec
TE                  298.1 K
D1              1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                     1H
P1                    9.75 usec
PL1                  -5.00 dB
PL1W          30.18447304 W
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                    32768
SF            400.1299990 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    1.00
```




```
Current Data Parameters
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EXPNO                   62
PROCNO                   1

F2 - Acquisition Parameters
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Time                   0.55
INSTRUM                spect
PROBHD   5 mm PABBO BB-
PULPROG             zgpg30
TD                    65536
SOLVENT                DMSO
NS                     1024
DS                        4
SWH               24038.461 Hz
FIDRES            0.366798 Hz
AQ                1.3631488 sec
RG                     2050
DW                  20.800 usec
DE                  10.00 usec
TE                  298.6 K
D1              2.00000000 sec
D11             0.03000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    13C
P1                  10.00 usec
PL1                 -2.70 dB
PL1W          62.67650986 W
SFO1         100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2           waltz16
NUC2                     1H
PCPD2               60.00 usec
PL2                 -5.00 dB
PL12                10.78 dB
PL13                15.00 dB
PL2W          30.18447304 W
PL12W          0.79759723 W
PL13W          0.30184472 W
SFO2         400.1316005 MHz

F2 - Processing parameters
SI                    32768
SF           100.6128095 MHz
WDW                     EM
SSB                      0
LB                    1.00 Hz
GB                       0
PC                    1.40
```
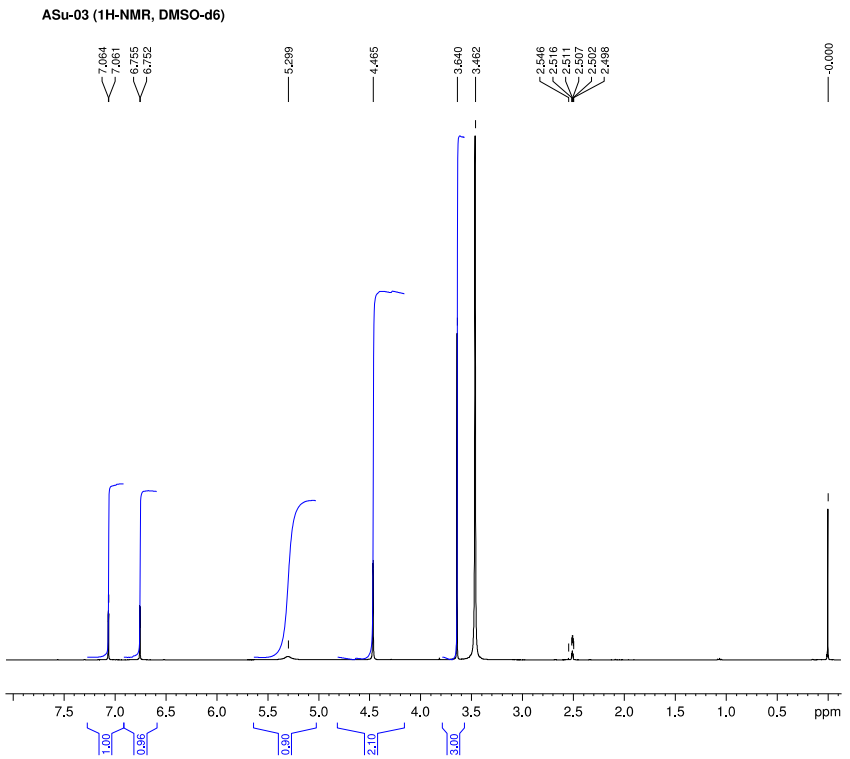
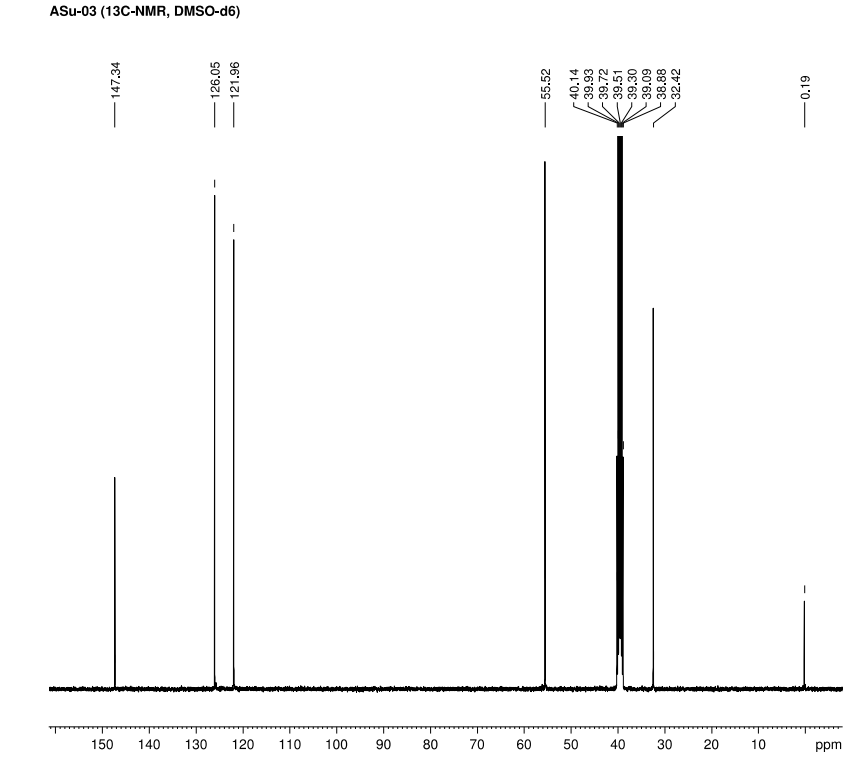

(1-Methyl-1*H*-imidazol-2-yl)methanol (**11**)

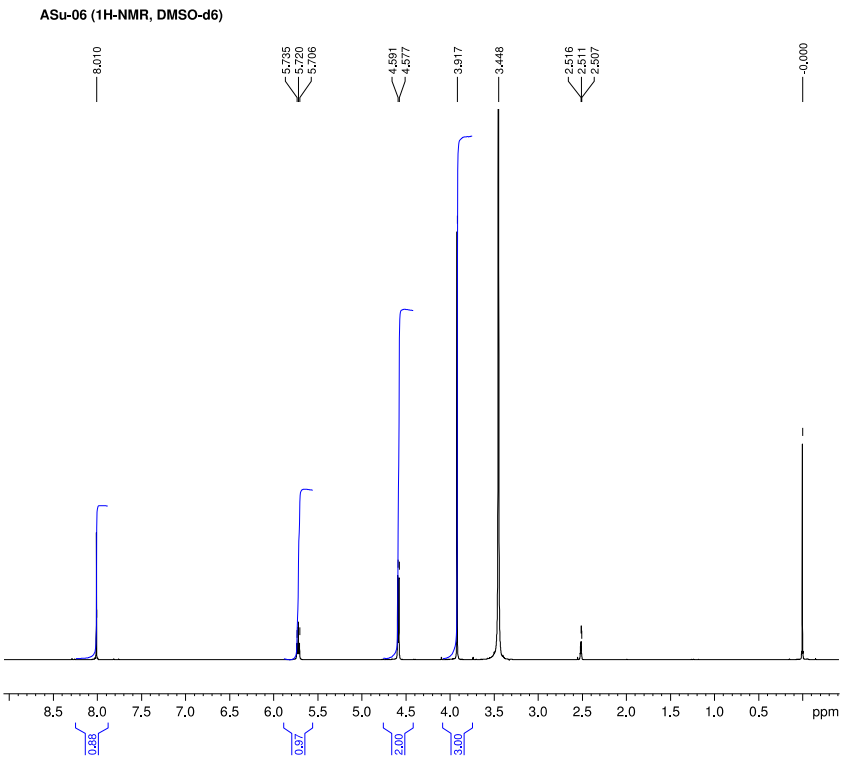



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                    3
PROCNO                   1

F2 - Acquisition Parameters
Date_              20210809
Time                 15.51
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG              zg30
TD                  65536
SOLVENT              DMSO
NS                     16
DS                      2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ              3.9845889 sec
RG                   45.2
DW                60.800 usec
DE                10.00 usec
TE                298.2 K
D1             1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                   9.75 usec
PL1                 -5.00 dB
PL1W         30.18447304 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                   32768
SF           400.1300009 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.00
```

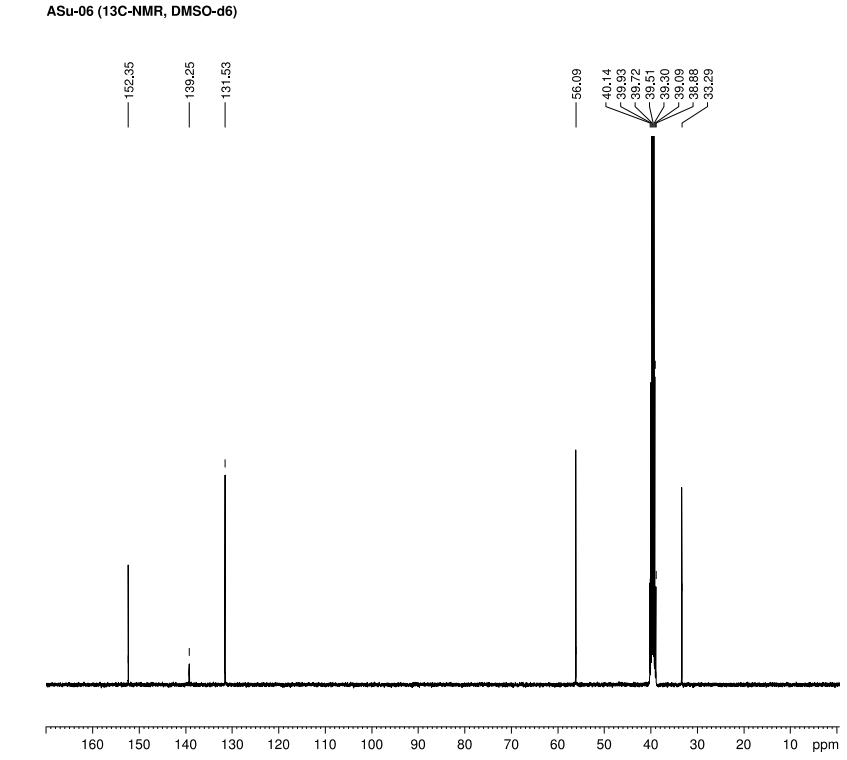



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                    4
PROCNO                   1

F2 - Acquisition Parameters
Date_              20210811
Time                  4.19
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG            zgpg30
TD                  65536
SOLVENT              DMSO
NS                   3000
DS                      4
SWH            24038.461 Hz
FIDRES          0.366798 Hz
AQ              1.3631488 sec
RG                   2050
DW                20.800 usec
DE                10.00 usec
TE                298.6 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                  13C
P1                  10.00 usec
PL1                 -2.70 dB
PL1W         62.67650986 W
SFO1        100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                   1H
PCPD2                60.00 usec
PL2                  -5.00 dB
PL12                 10.78 dB
PL13                 15.00 dB
PL2W         30.18447304 W
PL12W         0.79759723 W
PL13W         0.30184472 W
SFO2        400.1316005 MHz

F2 - Processing parameters
SI                   32768
SF           100.6128064 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   1.40
```

(1-Methyl-5-nitro-1*H*-imidazol-2-yl)methanol (**12**)

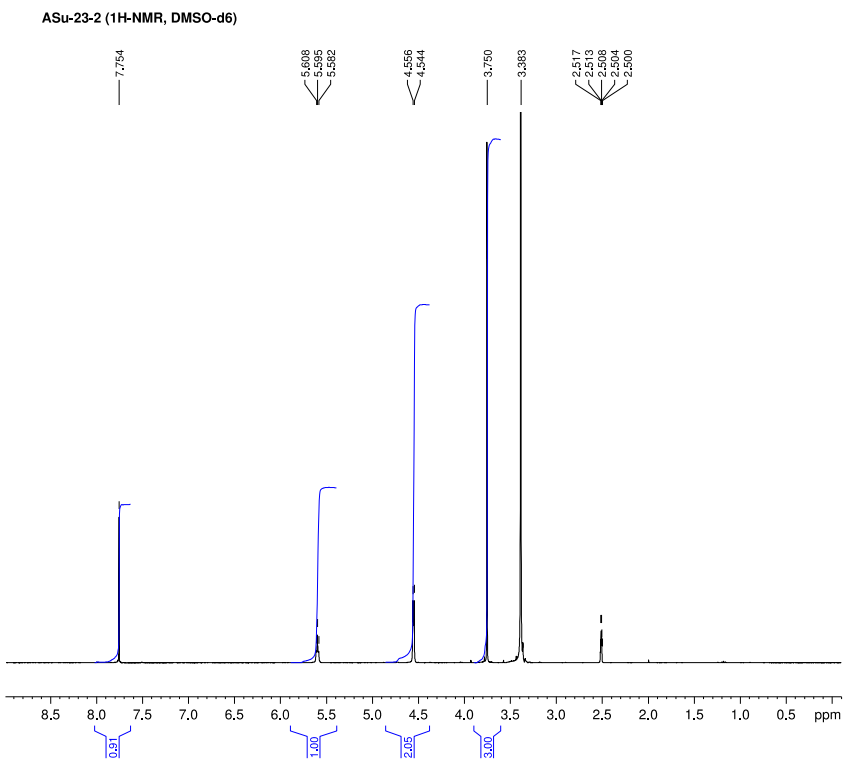



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                   13
PROCNO                   1

F2 - Acquisition Parameters
Date_              20210825
Time                 11.17
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG              zg30
TD                  65536
SOLVENT              DMSO
NS                     16
DS                      2
SWH              8223.685 Hz
FIDRES           0.125483 Hz
AQ               3.9845889 sec
RG                   50.8
DW                 60.800 usec
DE                 10.00 usec
TE                 298.3 K
D1              1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                  9.75 usec
PL1                -5.00 dB
PL1W         30.18447304 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                  32768
SF             400.1299990 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.00
```



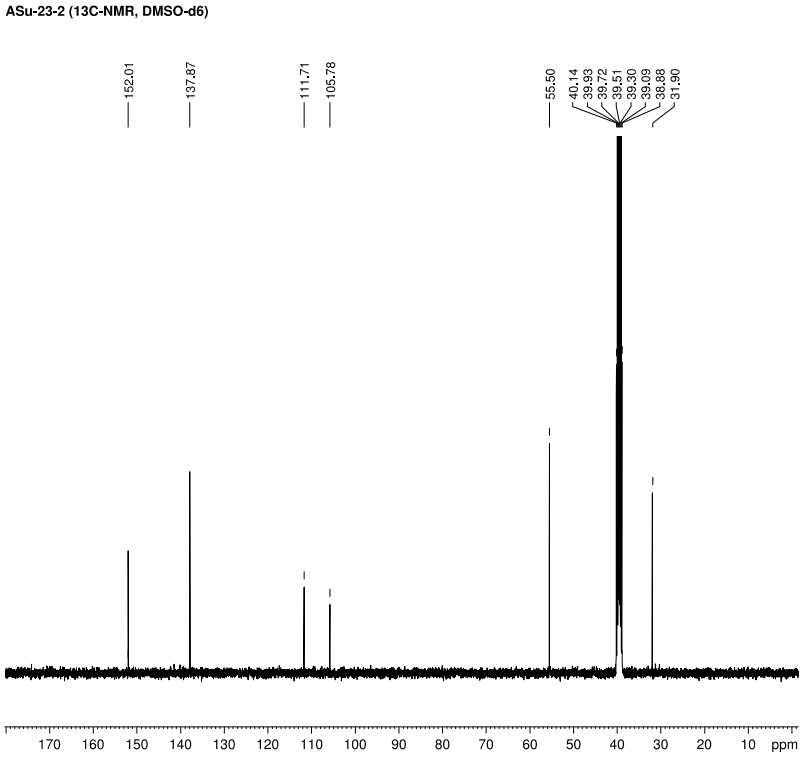

```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                  457
PROCNO                   1

F2 - Acquisition Parameters
Date_              20230802
Time                 17.37
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG            zgpg30
TD                  65536
SOLVENT              DMSO
NS                    1024
DS                       4
SWH             24038.461 Hz
FIDRES           0.366798 Hz
AQ               1.3631488 sec
RG                    2050
DW                 20.800 usec
DE                 10.00 usec
TE                 298.7 K
D1              2.00000000 sec
D11             0.03000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                  13C
P1                 10.00 usec
PL1                -2.70 dB
PL1W         62.67650986 W
SFO1        100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                   1H
PCPD2              60.00 usec
PL2                -5.00 dB
PL12               10.78 dB
PL13               15.00 dB
PL2W         30.18447304 W
PL12W         0.79759723 W
PL13W         0.30184472 W
SFO2        400.1316005 MHz

F2 - Processing parameters
SI                  32768
SF             100.6128169 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   1.40
```

2-(Hydroxymethyl)-1-methyl-1*H*-imidazole-5-carbonitrile (**13**)




BRUKER

```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                  124
PROCNO                   1

F2 - Acquisition Parameters
Date_               20220104
Time                  10.48
INSTRUM               spect
PROBHD   5 mm PABBO BB-
PULPROG                zg30
TD                    65536
SOLVENT                DMSO
NS                       16
DS                        2
SWH                8223.685 Hz
FIDRES            0.125483 Hz
AQ                 3.9845889 sec
RG                      71.8
DW                    60.800 usec
DE                    10.00 usec
TE                    296.0 K
D1                 1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      1H
P1                      9.75 usec
PL1                    -5.00 dB
PL1W             30.18447304 W
SFO1            400.1324710 MHz

F2 - Processing parameters
SI                        32768
SF                400.1300000 MHz
WDW                        EM
SSB                         0
LB                       0.30 Hz
GB                          0
PC                       1.00
```

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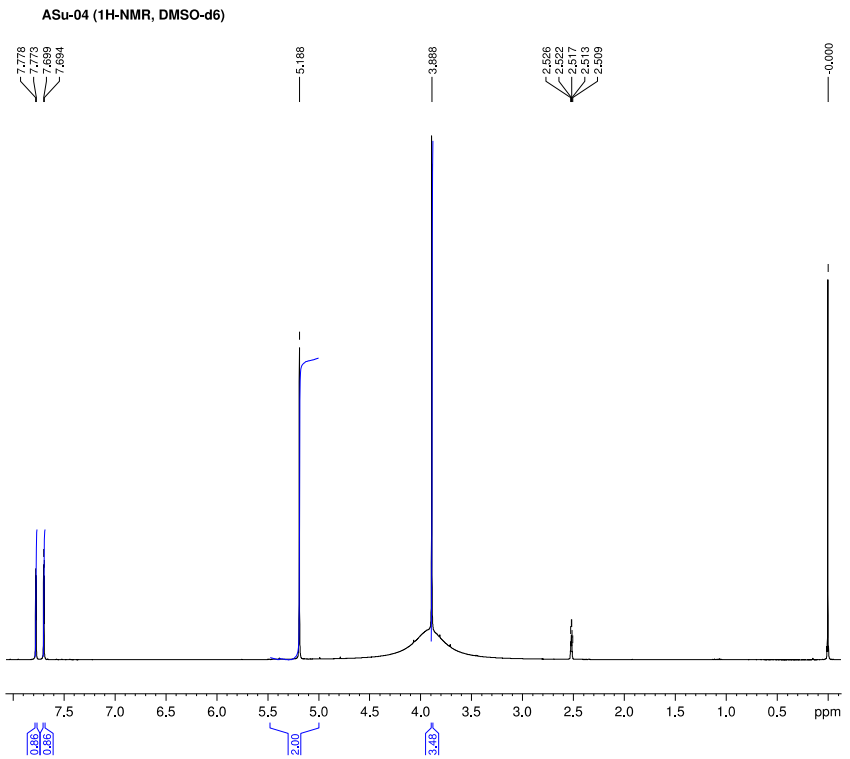
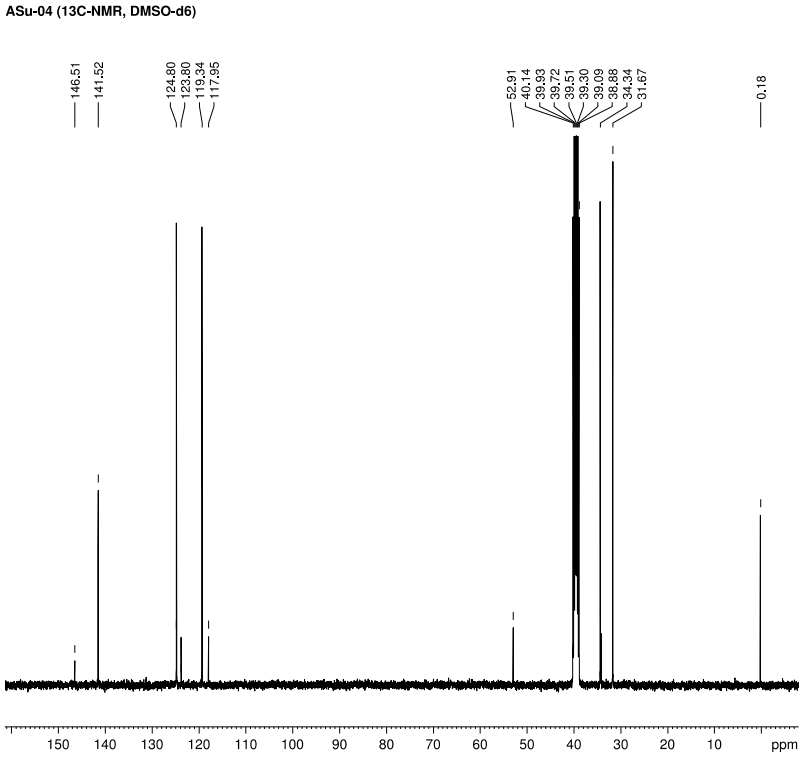
```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                  126
PROCNO                   1

F2 - Acquisition Parameters
Date_               20220104
Time                  16.48
INSTRUM               spect
PROBHD   5 mm PABBO BB-
PULPROG             zgpg30
TD                    65536
SOLVENT                DMSO
NS                      1024
DS                         4
SWH               24038.461 Hz
FIDRES            0.366798 Hz
AQ                 1.3631488 sec
RG                      2050
DW                    20.800 usec
DE                    10.00 usec
TE                    297.7 K
D1                 2.00000000 sec
D11                0.03000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     13C
P1                    10.00 usec
PL1                    -2.70 dB
PL1W             62.67650986 W
SFO1            100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2            waltz16
NUC2                      1H
PCPD2                 60.00 usec
PL2                    -5.00 dB
PL12                   10.78 dB
PL13                   15.00 dB
PL2W             30.18447304 W
PL12W             0.79759723 W
PL13W             0.30184472 W
SFO2            400.1316005 MHz

F2 - Processing parameters
SI                        32768
SF                100.6128132 MHz
WDW                        EM
SSB                         0
LB                    1.00 Hz
GB                          0
PC                       1.40
```

2-(Chloromethyl)-1-methyl-1*H*-imidazole (**14**)

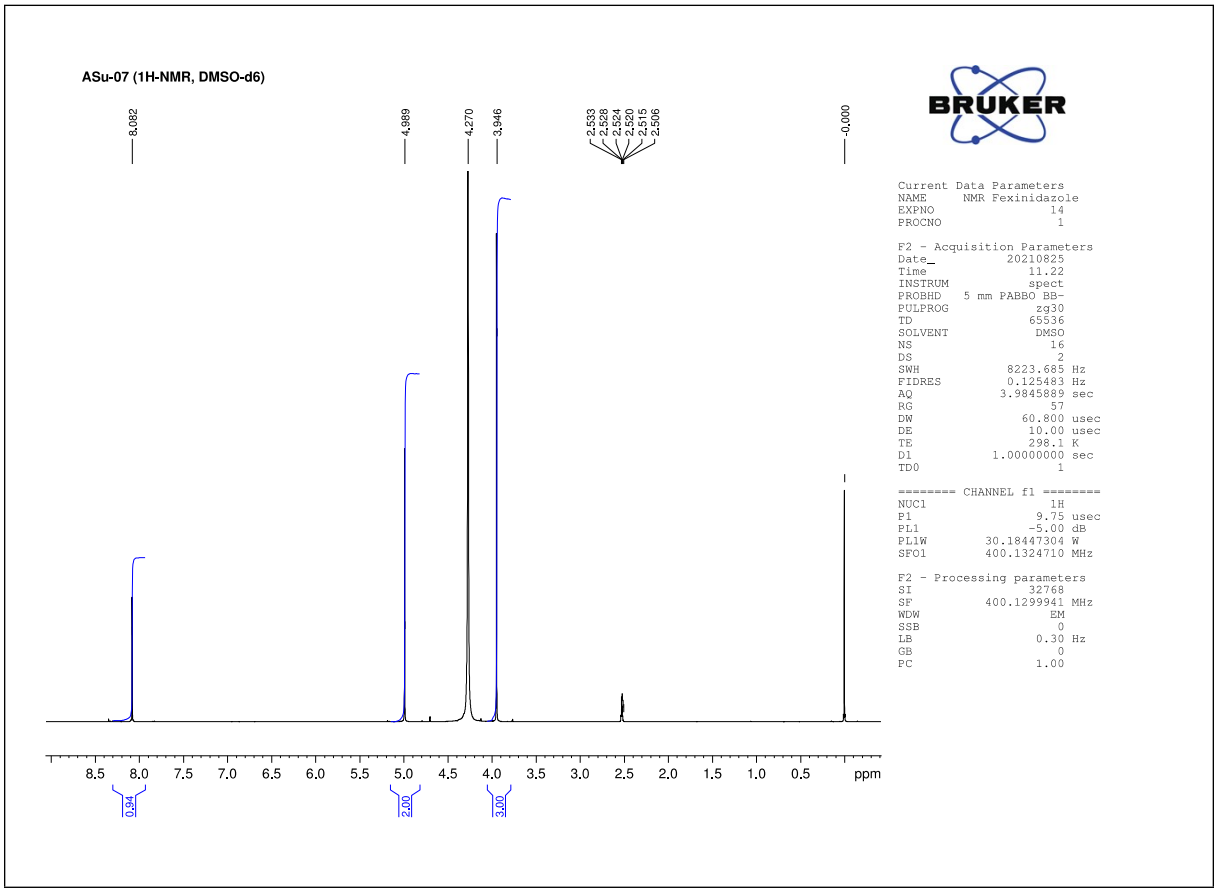


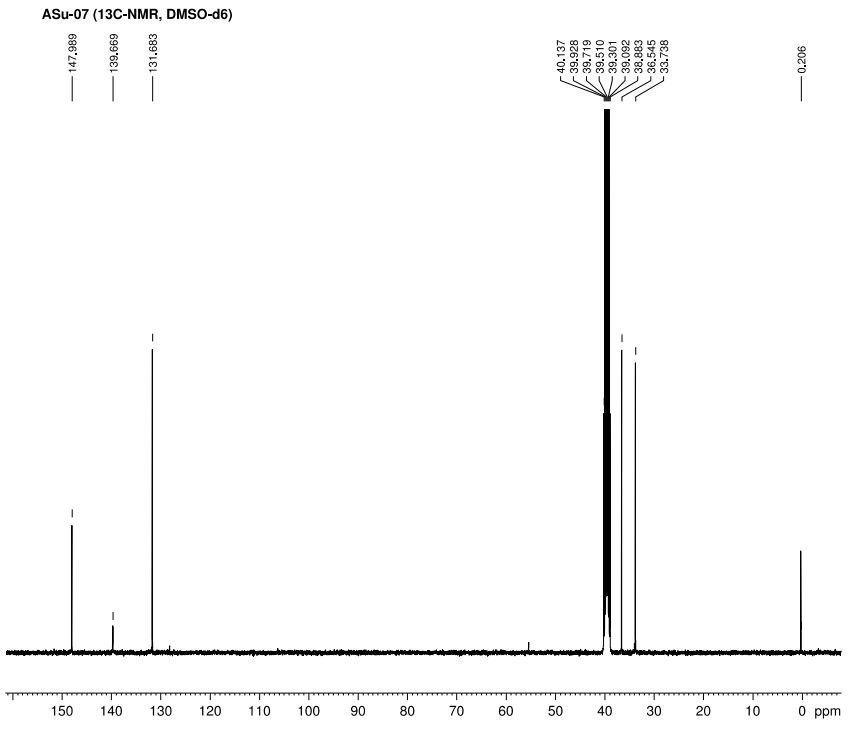

```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                    7
PROCNO                   1

F2 - Acquisition Parameters
Date_              20210811
Time                 15.35
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG              zg30
TD                  65536
SOLVENT              DMSO
NS                     16
DS                      2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ              3.9845889 sec
RG                   50.8
DW                60.800 usec
DE                10.00 usec
TE                298.2 K
D1             1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                   9.75 usec
PL1                 -5.00 dB
PL1W         30.18447304 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                   32768
SF          400.1299967 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    1.00
```




```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                    8
PROCNO                   1

F2 - Acquisition Parameters
Date_              20210813
Time                  2.51
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG           zgpg30
TD                  65536
SOLVENT              DMSO
NS                    3000
DS                       4
SWH            24038.461 Hz
FIDRES          0.366798 Hz
AQ              1.3631488 sec
RG                    2050
DW                20.800 usec
DE                10.00 usec
TE                298.7 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                  13C
P1                 10.00 usec
PL1                 -2.70 dB
PL1W         62.67650986 W
SFO1        100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                   1H
PCPD2              60.00 usec
PL2                 -5.00 dB
PL12                10.78 dB
PL13                15.00 dB
PL2W         30.18447304 W
PL12W         0.79759723 W
PL13W         0.30184472 W
SFO2        400.1316005 MHz

F2 - Processing parameters
SI                   32768
SF          100.6128077 MHz
WDW                     EM
SSB                      0
LB                    1.00 Hz
GB                       0
PC                    1.40
```

2-(Chloromethyl)-1-methyl-5-nitro-1*H*-imidazole (**15**)



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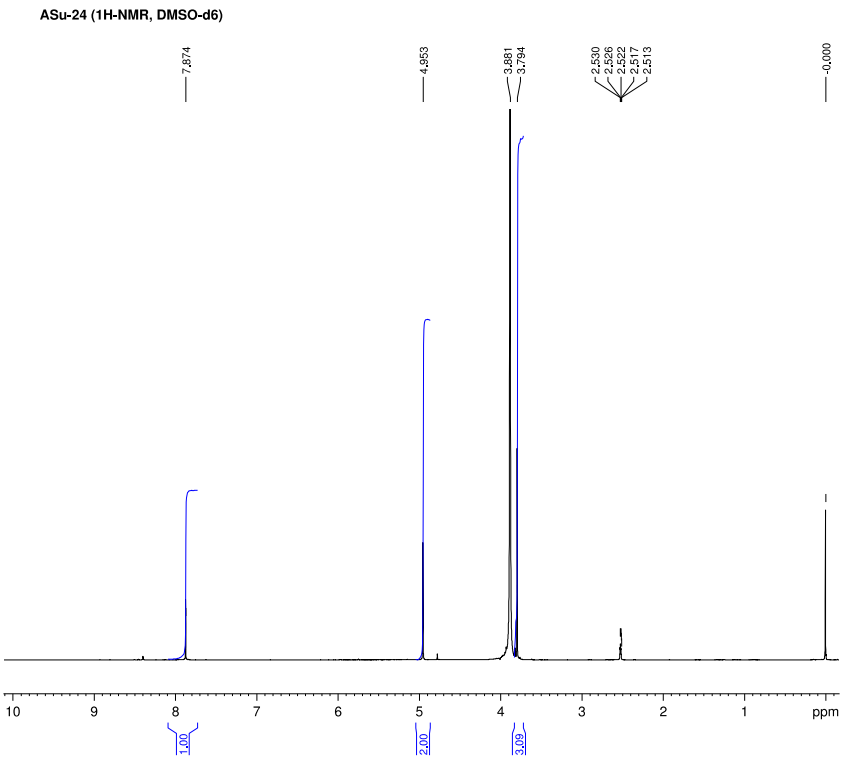
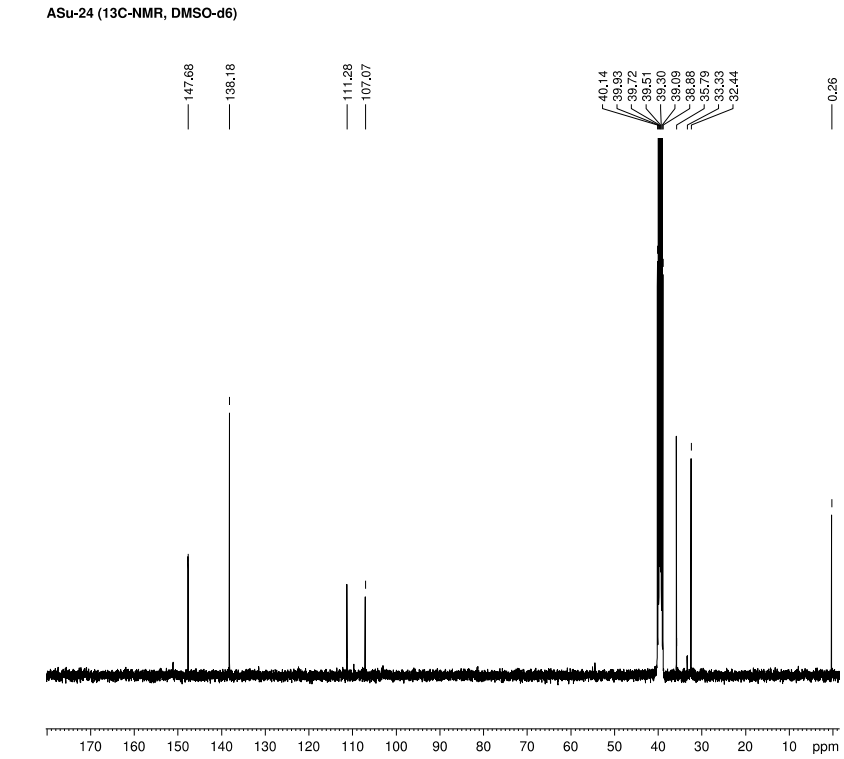
```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                   15
PROCNO                   1

F2 - Acquisition Parameters
Date_           20210825
Time                19.54
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG             zgpg30
TD                  65536
SOLVENT               DMSO
NS                    3000
DS                       4
SWH             24038.461 Hz
FIDRES          0.366798 Hz
AQ              1.3631488 sec
RG                   2050
DW                 20.800 usec
DE                 10.00 usec
TE                 298.6 K
D1              2.00000000 sec
D11             0.03000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                   13C
P1                   10.00 usec
PL1                  -2.70 dB
PL1W          62.67650986 W
SFO1          100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2             waltz16
NUC2                    1H
PCPD2                60.00 usec
PL2                  -5.00 dB
PL12                 10.78 dB
PL13                 15.00 dB
PL2W          30.18447304 W
PL12W          0.79759723 W
PL13W          0.30184472 W
SFO2          400.1316005 MHz

F2 - Processing parameters
SI                   32768
SF            100.6128025 MHz
WDW                     EM
SSB                      0
LB                    1.00 Hz
GB                       0
PC                    1.40
```

2-(Chloromethyl)-1-methyl-1*H*-imidazole-5-carbonitrile (**16**)

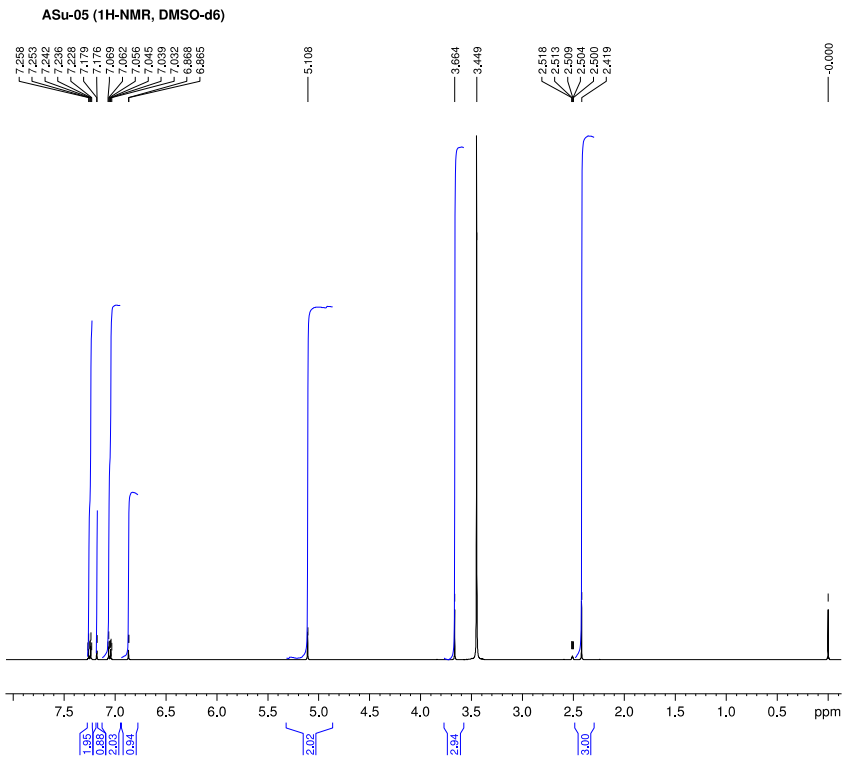



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                  138
PROCNO                   1

F2 - Acquisition Parameters
Date_               20220112
Time                   18.56
INSTRUM                spect
PROBHD   5 mm PABBO BB-
PULPROG                zg30
TD                    65536
SOLVENT                DMSO
NS                       16
DS                        2
SWH                8223.685 Hz
FIDRES             0.125483 Hz
AQ                 3.9845889 sec
RG                      40.3
DW                    60.800 usec
DE                    10.00 usec
TE                    295.4 K
D1                1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                     1H
P1                     9.75 usec
PL1                   -5.00 dB
PL1W            30.18447304 W
SFO1           400.1324710 MHz

F2 - Processing parameters
SI                       32768
SF                400.1299947 MHz
WDW                         EM
SSB                          0
LB                        0.30 Hz
GB                           0
PC                        1.00
```

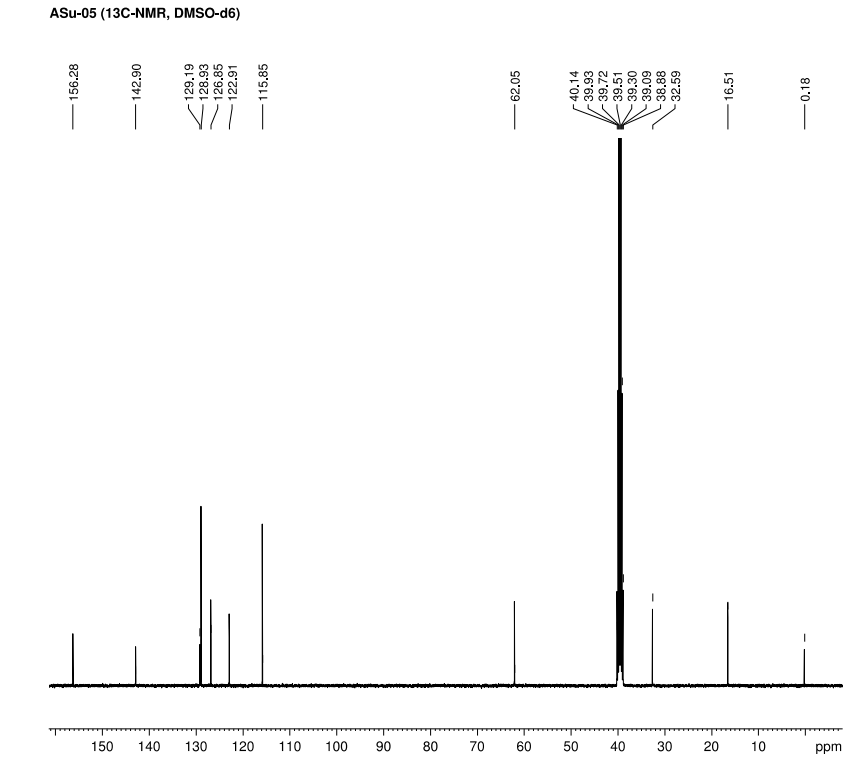



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                  139
PROCNO                   1

F2 - Acquisition Parameters
Date_               20220112
Time                   19.57
INSTRUM                spect
PROBHD   5 mm PABBO BB-
PULPROG             zgpg30
TD                    65536
SOLVENT                DMSO
NS                     1024
DS                        4
SWH               24038.461 Hz
FIDRES             0.366798 Hz
AQ                 1.3631488 sec
RG                      2050
DW                    20.800 usec
DE                    10.00 usec
TE                    296.8 K
D1                2.00000000 sec
D11               0.03000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    13C
P1                    10.00 usec
PL1                   -2.70 dB
PL1W            62.67650986 W
SFO1           100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2            waltz16
NUC2                     1H
PCPD2                 60.00 usec
PL2                   -5.00 dB
PL12                  10.78 dB
PL13                  15.00 dB
PL2W            30.18447304 W
PL12W            0.79759723 W
PL13W            0.30184472 W
SFO2           400.1316005 MHz

F2 - Processing parameters
SI                       32768
SF                100.6127986 MHz
WDW                         EM
SSB                          0
LB                        1.00 Hz
GB                           0
PC                        1.40
```

1-Methyl-2-{[4-(methylsulfanyl)phenoxy]methyl}-1*H*-imidazole (**17**)

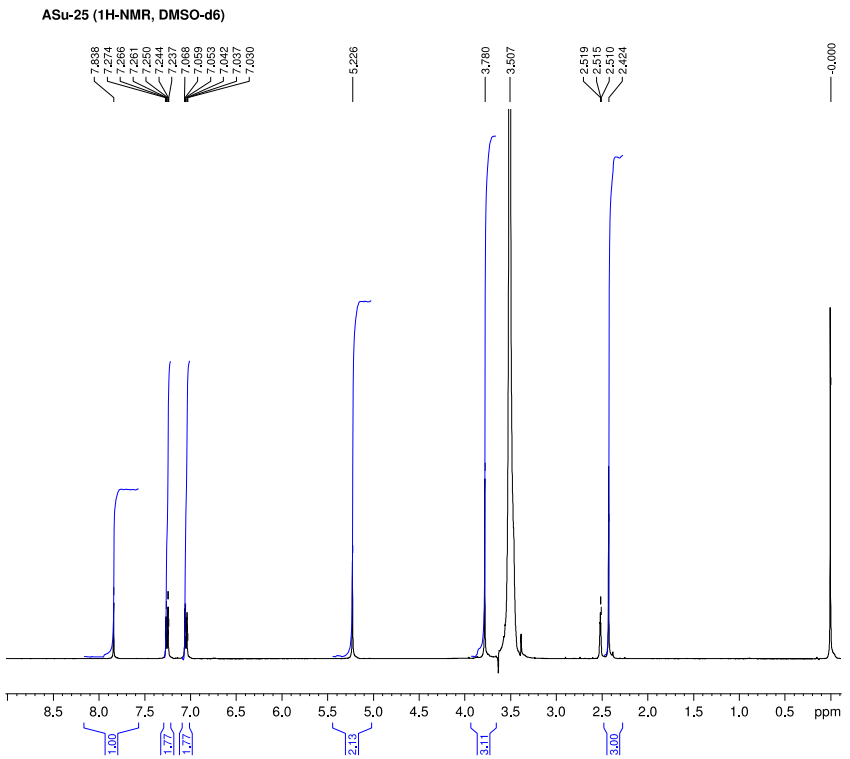



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                   18
PROCNO                   1

F2 - Acquisition Parameters
Date_               20210827
Time                  10.04
INSTRUM               spect
PROBHD    5 mm PABBO BB-
PULPROG                zg30
TD                    65536
SOLVENT                DMSO
NS                       16
DS                        2
SWH                8223.685 Hz
FIDRES            0.125483 Hz
AQ                3.9845889 sec
RG                     50.8
DW                   60.800 usec
DE                   10.00 usec
TE                   298.2 K
D1              1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     1H
P1                    9.75 usec
PL1                  -5.00 dB
PL1W          30.18447304 W
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                    32768
SF             400.1300000 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.00
```

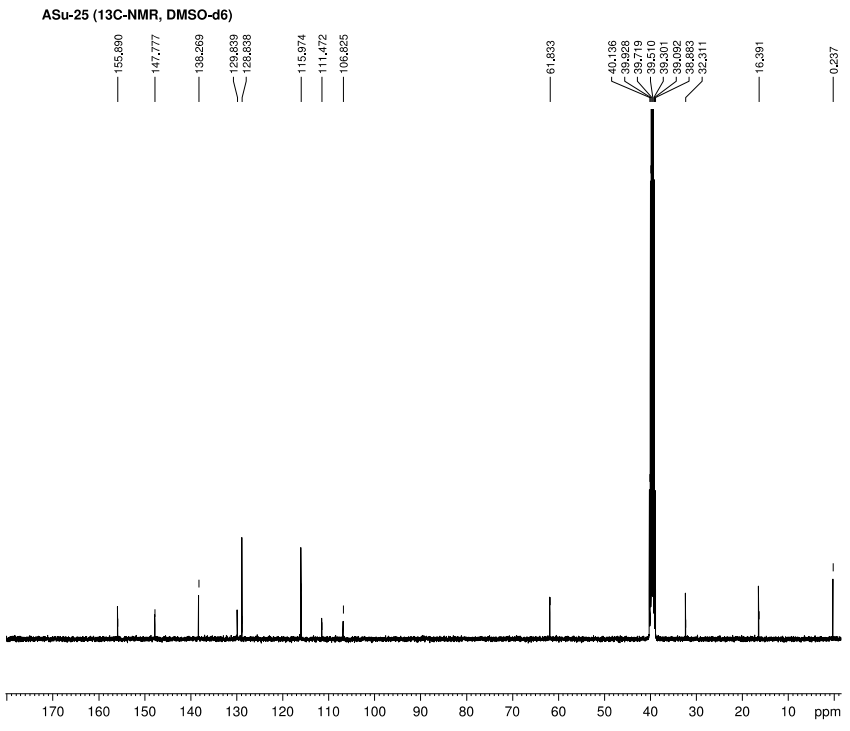



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                   19
PROCNO                   1

F2 - Acquisition Parameters
Date_               20210831
Time                  11.24
INSTRUM               spect
PROBHD    5 mm PABBO BB-
PULPROG             zgpg30
TD                    65536
SOLVENT                DMSO
NS                      1024
DS                         4
SWH               24038.461 Hz
FIDRES            0.366798 Hz
AQ                1.3631488 sec
RG                      2050
DW                   20.800 usec
DE                   10.00 usec
TE                   298.7 K
D1              2.00000000 sec
D11             0.03000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                    13C
P1                   10.00 usec
PL1                  -2.70 dB
PL1W          62.67650986 W
SFO1         100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                     1H
PCPD2                60.00 usec
PL2                  -5.00 dB
PL12                 10.78 dB
PL13                 15.00 dB
PL2W          30.18447304 W
PL12W          0.79759723 W
PL13W          0.30184472 W
SFO2         400.1316005 MHz

F2 - Processing parameters
SI                    32768
SF             100.6128076 MHz
WDW                      EM
SSB                       0
LB                     1.00 Hz
GB                        0
PC                     1.40
```

1-Methyl-2-{[4-(methylsulfanyl)phenoxy]methyl}-1*H*-imidazole-5-carbonitrile (**18**)

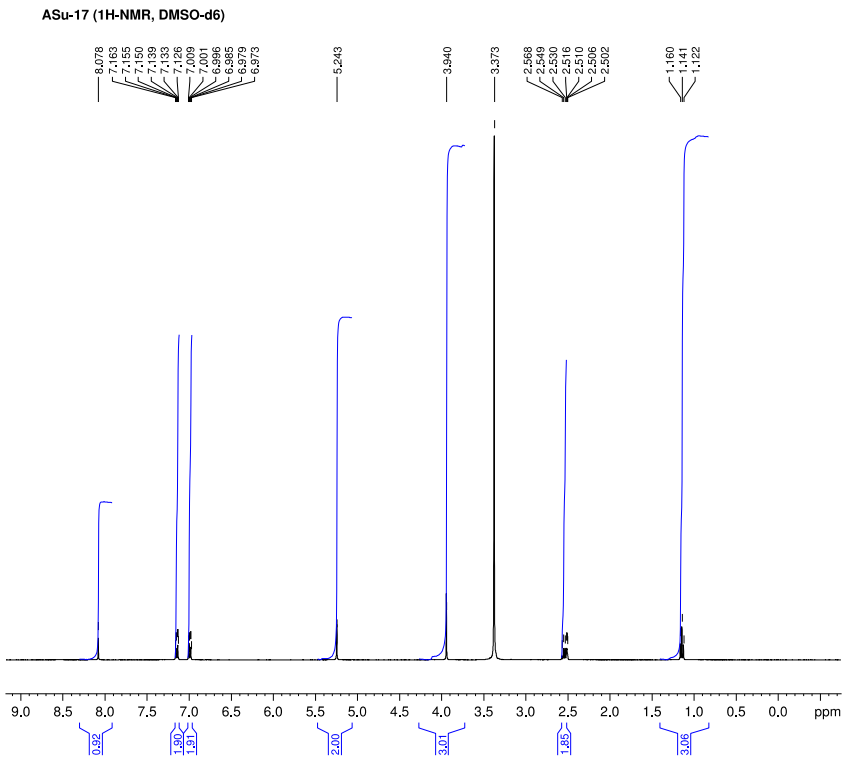



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                  137
PROCNO                   1

F2 - Acquisition Parameters
Date_               20220112
Time                   14.04
INSTRUM                spect
PROBHD    5 mm PABBO BB-
PULPROG                zg30
TD                    65536
SOLVENT                DMSO
NS                       16
DS                        2
SWH                8223.685 Hz
FIDRES            0.125483 Hz
AQ                 3.9845889 sec
RG                      45.2
DW                    60.800 usec
DE                    10.00 usec
TE                    295.6 K
D1                1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      1H
P1                      9.75 usec
PL1                    -5.00 dB
PL1W            30.18447304 W
SFO1           400.1324710 MHz

F2 - Processing parameters
SI                        32768
SF                400.1299976 MHz
WDW                        EM
SSB                         0
LB                       0.30 Hz
GB                          0
PC                       1.00
```

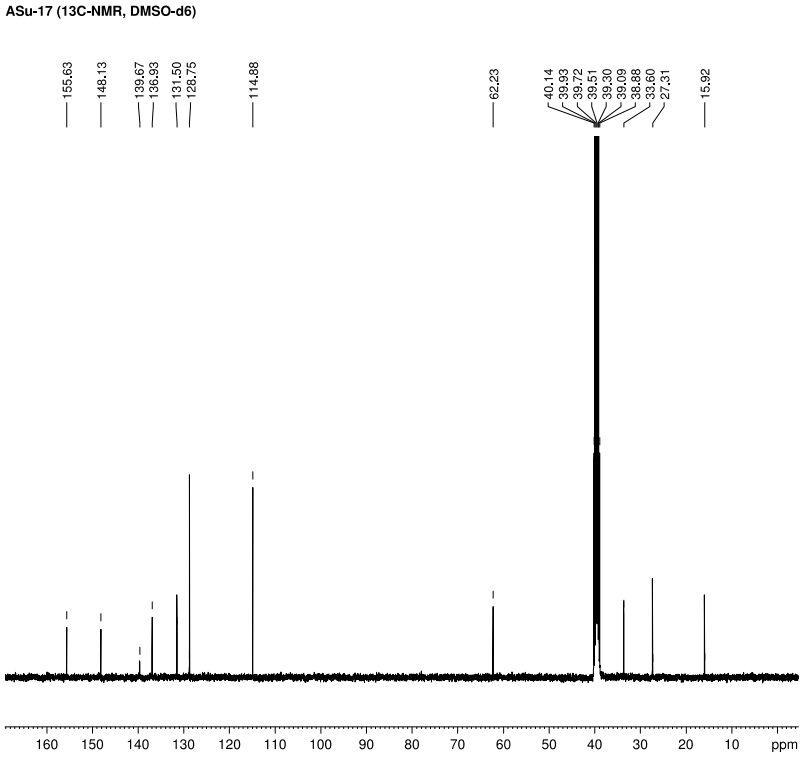



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                  141
PROCNO                   1

F2 - Acquisition Parameters
Date_               20220112
Time                   23.24
INSTRUM                spect
PROBHD    5 mm PABBO BB-
PULPROG             zgpg30
TD                    65536
SOLVENT                DMSO
NS                     1024
DS                        4
SWH               24038.461 Hz
FIDRES            0.366798 Hz
AQ                 1.3631488 sec
RG                      2050
DW                    20.800 usec
DE                    10.00 usec
TE                    296.8 K
D1                2.00000000 sec
D11               0.03000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     13C
P1                    10.00 usec
PL1                   -2.70 dB
PL1W           62.67650986 W
SFO1          100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2           waltz16
NUC2                      1H
PCPD2                 60.00 usec
PL2                   -5.00 dB
PL12                  10.78 dB
PL13                  15.00 dB
PL2W           30.18447304 W
PL12W           0.79759723 W
PL13W           0.30184472 W
SFO2          400.1316005 MHz

F2 - Processing parameters
SI                        32768
SF                100.6128009 MHz
WDW                        EM
SSB                         0
LB                       1.00 Hz
GB                          0
PC                       1.40
```

2-[(4-Ethylphenoxy)methyl]-1-methyl-5-nitro-1*H*-imidazole (**19**)

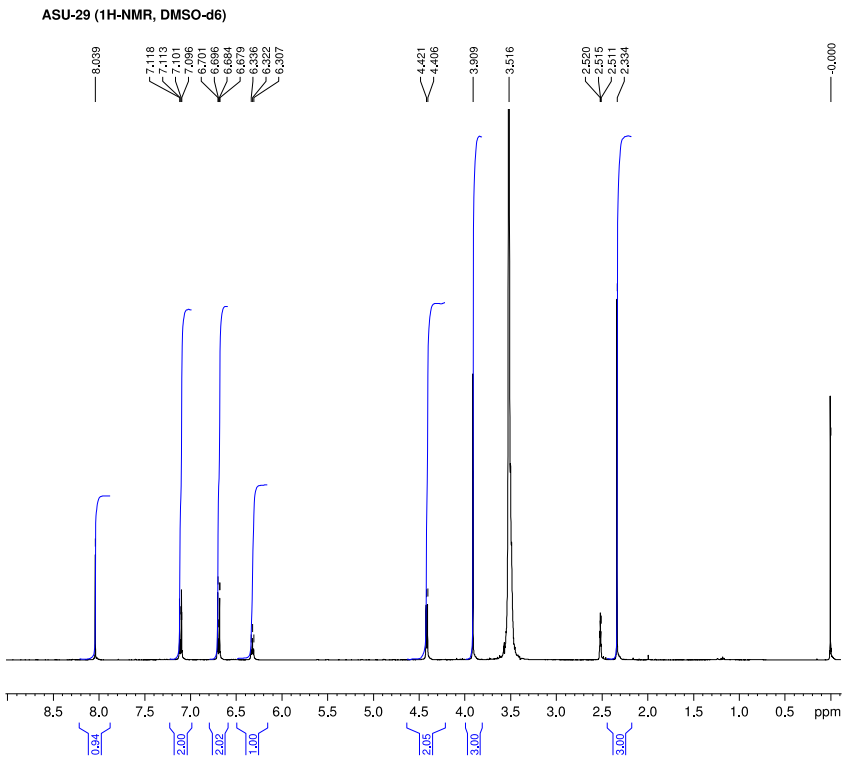



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                   84
PROCNO                   1

F2 - Acquisition Parameters
Date_              20211122
Time                 13.29
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG              zg30
TD                  65536
SOLVENT              DMSO
NS                     16
DS                      2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ              3.9845889 sec
RG                   80.6
DW                60.800 usec
DE                10.00 usec
TE                296.5 K
D1             1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                  9.75 usec
PL1                -5.00 dB
PL1W         30.18447304 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                  32768
SF            400.1300000 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.00
```

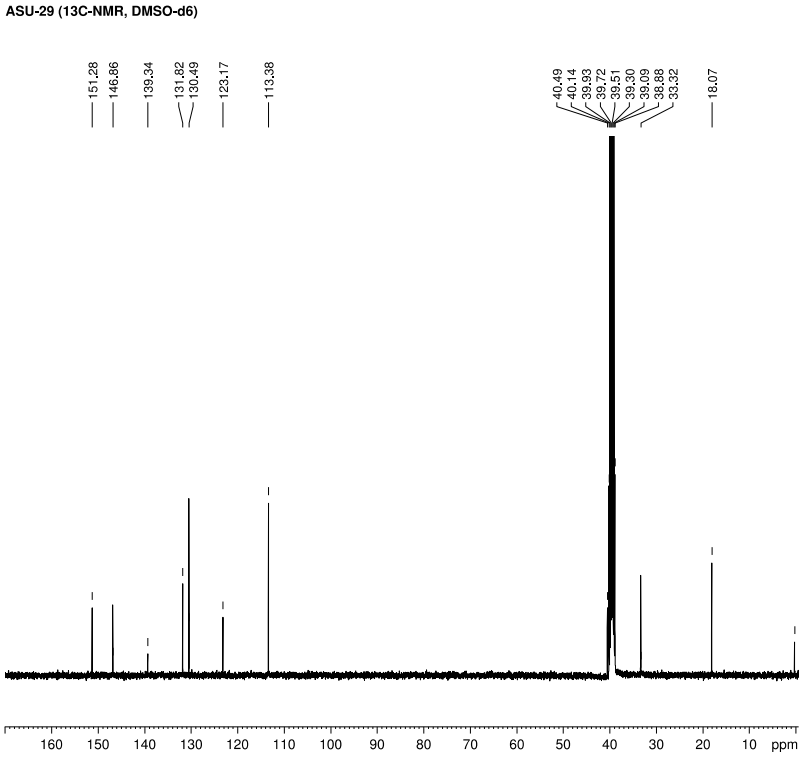



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                   93
PROCNO                   1

F2 - Acquisition Parameters
Date_              20211123
Time                  4.45
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG            zgpg30
TD                  65536
SOLVENT              DMSO
NS                    1024
DS                       4
SWH            24038.461 Hz
FIDRES          0.366798 Hz
AQ              1.3631488 sec
RG                    2050
DW                20.800 usec
DE                10.00 usec
TE                297.7 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                   13C
P1                  10.00 usec
PL1                 -2.70 dB
PL1W         62.67650986 W
SFO1        100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                   1H
PCPD2               60.00 usec
PL2                 -5.00 dB
PL12                10.78 dB
PL13                15.00 dB
PL2W         30.18447304 W
PL12W         0.79759723 W
PL13W         0.30184472 W
SFO2        400.1316005 MHz

F2 - Processing parameters
SI                  32768
SF            100.6128141 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   1.40
```

*N*-[(1-Methyl-5-nitro-1*H*-imidazol-2-yl)methyl]-4-(methylsulfanyl)aniline (**20**)

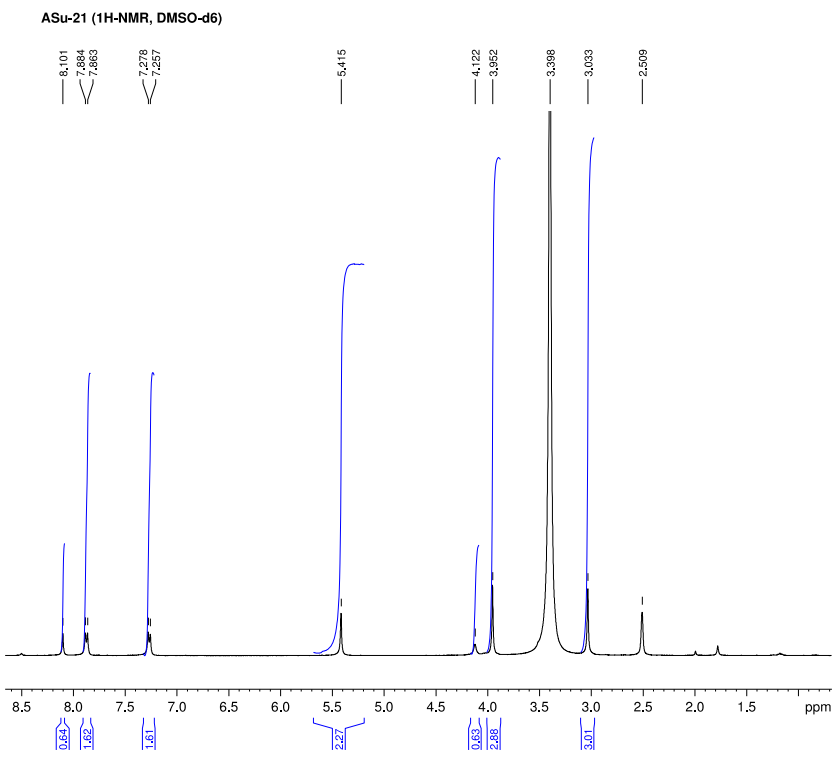



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                  159
PROCNO                   1

F2 - Acquisition Parameters
Date_               20220217
Time                    9.55
INSTRUM                spect
PROBHD    5 mm PABBO BB-
PULPROG                zg30
TD                    65536
SOLVENT                DMSO
NS                       16
DS                        2
SWH                8223.685 Hz
FIDRES            0.125483 Hz
AQ                 3.9845889 sec
RG                      40.3
DW                   60.800 usec
DE                   10.00 usec
TE                   295.9 K
D1                1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                     1H
P1                    9.75 usec
PL1                  -5.00 dB
PL1W           30.18447304 W
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                       32768
SF                400.1299974 MHz
WDW                         EM
SSB                          0
LB                        0.30 Hz
GB                           0
PC                        1.00
```

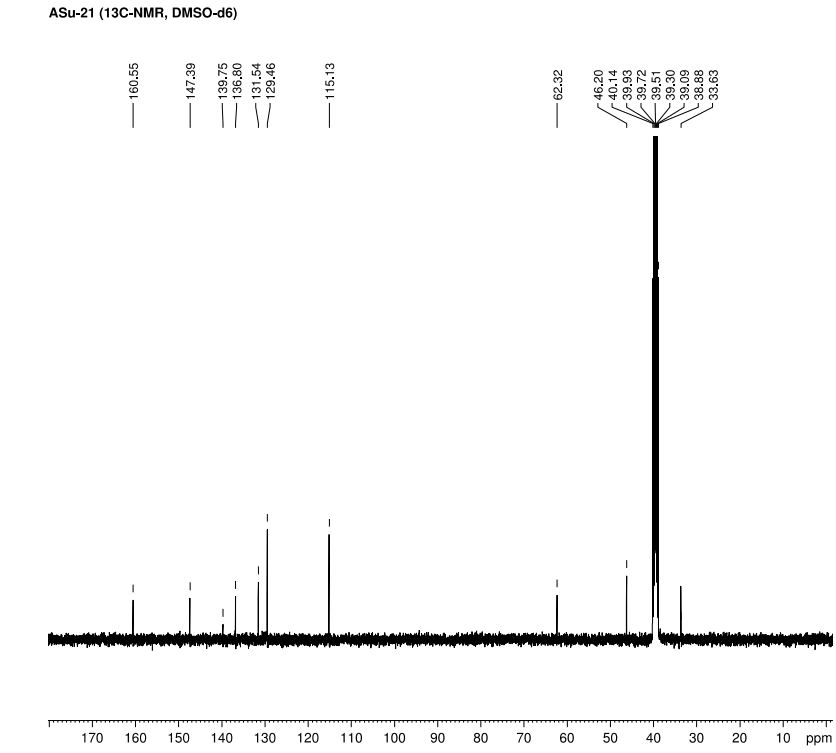



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                  160
PROCNO                   1

F2 - Acquisition Parameters
Date_               20220218
Time                    9.35
INSTRUM                spect
PROBHD    5 mm PABBO BB-
PULPROG             zgpg30
TD                    65536
SOLVENT                DMSO
NS                     1024
DS                        4
SWH               24038.461 Hz
FIDRES            0.366798 Hz
AQ                 1.3631488 sec
RG                      2050
DW                   20.800 usec
DE                   10.00 usec
TE                   297.6 K
D1                2.00000000 sec
D11               0.03000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    13C
P1                   10.00 usec
PL1                  -2.70 dB
PL1W           62.67650986 W
SFO1          100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2            waltz16
NUC2                     1H
PCPD2                60.00 usec
PL2                  -5.00 dB
PL12                 10.78 dB
PL13                 15.00 dB
PL2W           30.18447304 W
PL12W           0.79759723 W
PL13W           0.30184472 W
SFO2          400.1316005 MHz

F2 - Processing parameters
SI                       32768
SF                100.6128004 MHz
WDW                         EM
SSB                          0
LB                        1.00 Hz
GB                           0
PC                        1.40
```

Imino(methyl){4-[(1-methyl-5-nitro-1*H*-imidazol-2-yl)methoxy]phenyl}-λ$^6$-sulfanone (**21**)

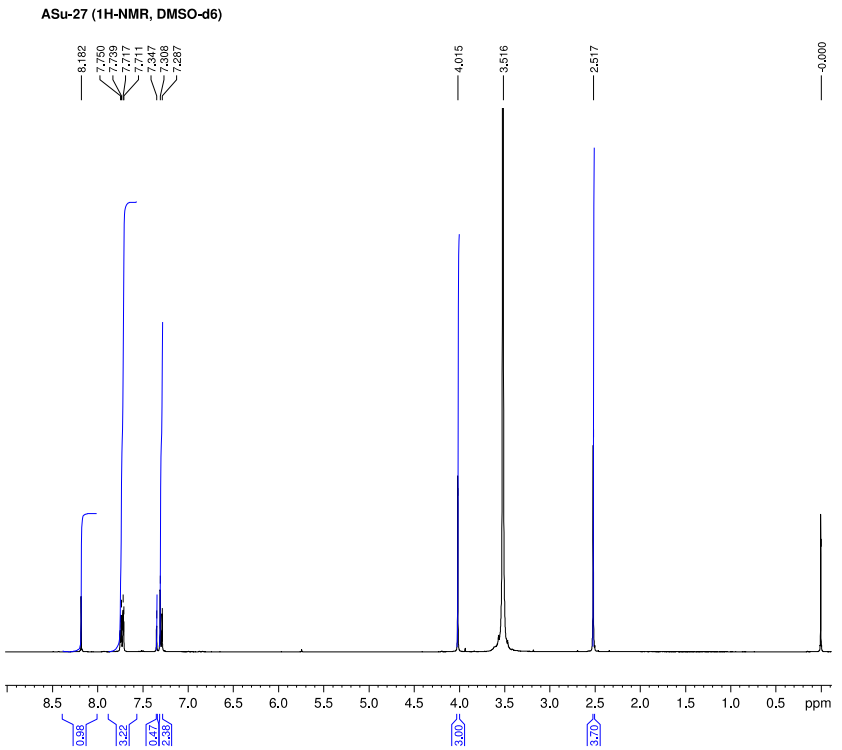



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                  110
PROCNO                   1

F2 - Acquisition Parameters
Date_           20211213
Time              10.09
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG           zg30
TD               65536
SOLVENT           DMSO
NS                  16
DS                   2
SWH           8223.685 Hz
FIDRES        0.125483 Hz
AQ            3.9845889 sec
RG                90.5
DW              60.800 usec
DE              10.00 usec
TE              295.4 K
D1           1.00000000 sec
TD0                  1

======== CHANNEL f1 ========
NUC1                1H
P1                9.75 usec
PL1              -5.00 dB
PL1W       30.18447304 W
SFO1       400.1324710 MHz

F2 - Processing parameters
SI               32768
SF          400.1300000 MHz
WDW                 EM
SSB                  0
LB                0.30 Hz
GB                   0
PC                1.00
```

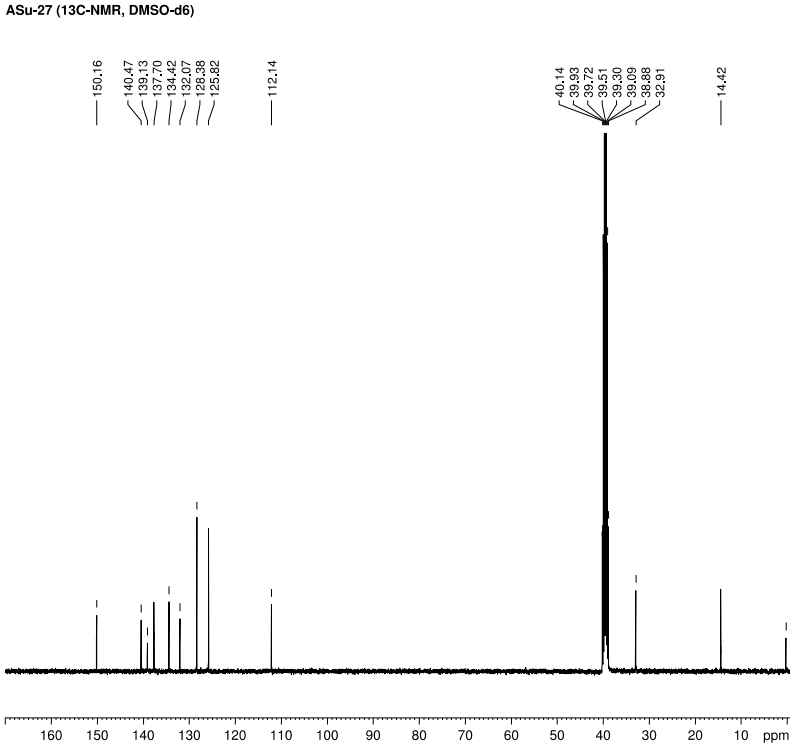



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                  114
PROCNO                   1

F2 - Acquisition Parameters
Date_           20211215
Time              16.53
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG         zgpg30
TD               65536
SOLVENT           DMSO
NS                1024
DS                   4
SWH          24038.461 Hz
FIDRES        0.366798 Hz
AQ            1.3631488 sec
RG                2050
DW              20.800 usec
DE              10.00 usec
TE              297.8 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                  1

======== CHANNEL f1 ========
NUC1               13C
P1               10.00 usec
PL1              -2.70 dB
PL1W       62.67650986 W
SFO1       100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2        waltz16
NUC2                1H
PCPD2            60.00 usec
PL2              -5.00 dB
PL12             10.78 dB
PL13             15.00 dB
PL2W       30.18447304 W
PL12W       0.79759723 W
PL13W       0.30184472 W
SFO2       400.1316005 MHz

F2 - Processing parameters
SI               32768
SF          100.6128138 MHz
WDW                 EM
SSB                  0
LB                1.00 Hz
GB                   0
PC                1.40
```

1-Methyl-2-{2-[4-(methylsulfanyl)phenyl]ethenyl}-5-nitro-1*H*-imidazole (**24**)

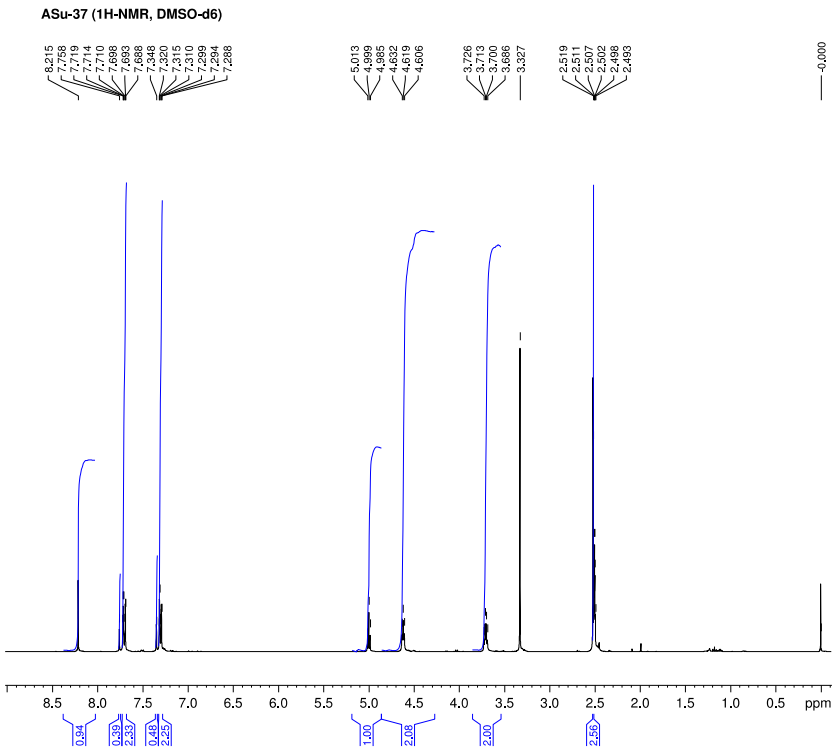



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                  153
PROCNO                   1

F2 - Acquisition Parameters
Date_              20220203
Time                 14.17
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG              zg30
TD                  65536
SOLVENT              DMSO
NS                      16
DS                       2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ              3.9845889 sec
RG                    40.3
DW                60.800 usec
DE                10.00 usec
TE                295.7 K
D1             1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    1H
P1                   9.75 usec
PL1                 -5.00 dB
PL1W         30.18447304 W
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                   32768
SF           400.1299965 MHz
WDW                     EM
SSB                      0
LB                  0.30 Hz
GB                       0
PC                    1.00
```

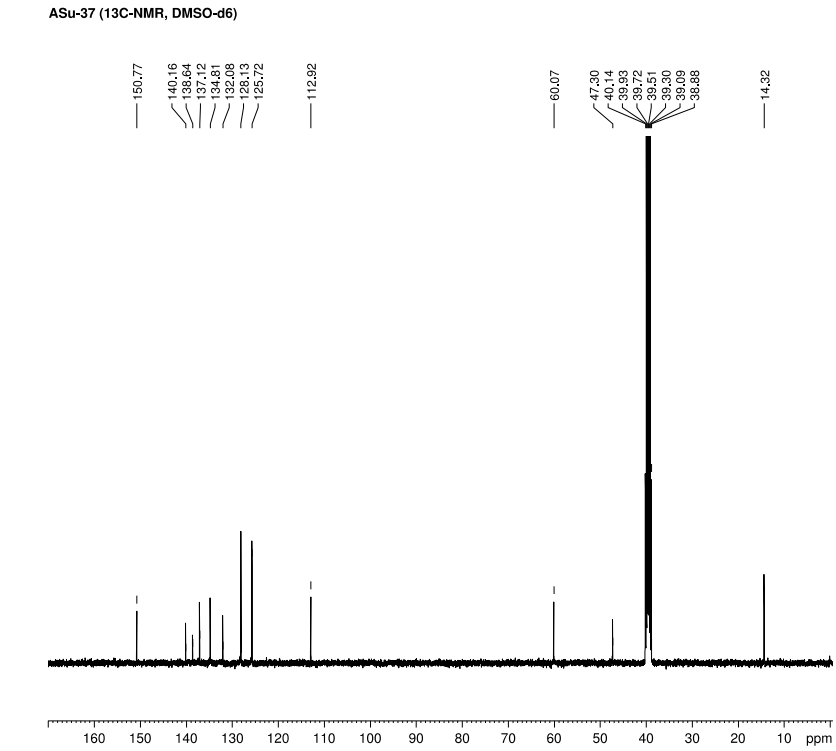



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                  154
PROCNO                   1

F2 - Acquisition Parameters
Date_              20220203
Time                 17.11
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG            zgpg30
TD                  65536
SOLVENT              DMSO
NS                    1024
DS                       4
SWH            24038.461 Hz
FIDRES          0.366798 Hz
AQ              1.3631488 sec
RG                    2050
DW                20.800 usec
DE                10.00 usec
TE                296.7 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                   13C
P1                  10.00 usec
PL1                 -2.70 dB
PL1W         62.67650986 W
SFO1         100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                    1H
PCPD2                60.00 usec
PL2                 -5.00 dB
PL12                10.78 dB
PL13                15.00 dB
PL2W         30.18447304 W
PL12W         0.79759723 W
PL13W         0.30184472 W
SFO2         400.1316005 MHz

F2 - Processing parameters
SI                   32768
SF           100.6128005 MHz
WDW                     EM
SSB                      0
LB                   1.00 Hz
GB                       0
PC                    1.40
```

2-{2-[4-(Methylsulfanyl)phenyl]ethenyl}-5-nitro-1*H*-imidazol-1-yl}ethan-1-ol (**25**)

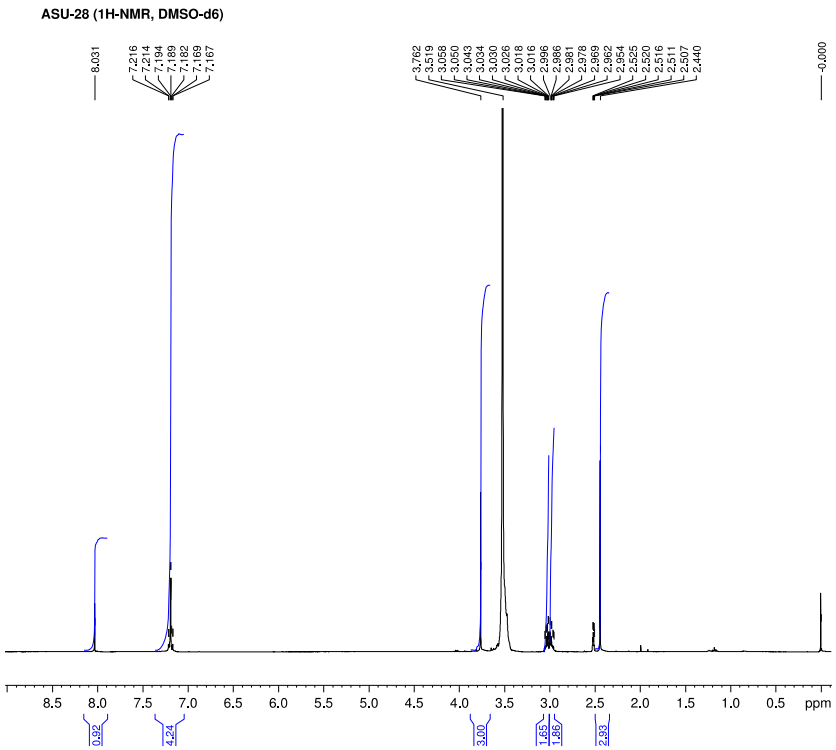



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                  262
PROCNO                   1

F2 - Acquisition Parameters
Date_              20220720
Time                 15.16
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG              zg30
TD                  65536
SOLVENT              DMSO
NS                     24
DS                      2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ              3.9845889 sec
RG                    114
DW                60.800 usec
DE                10.00 usec
TE                297.9 K
D1             1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                  9.75 usec
PL1                -5.00 dB
PL1W         30.18447304 W
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                  32768
SF           400.1300027 MHz
WDW                    EM
SSB                     0
LB                 0.30 Hz
GB                      0
PC                   1.00
```

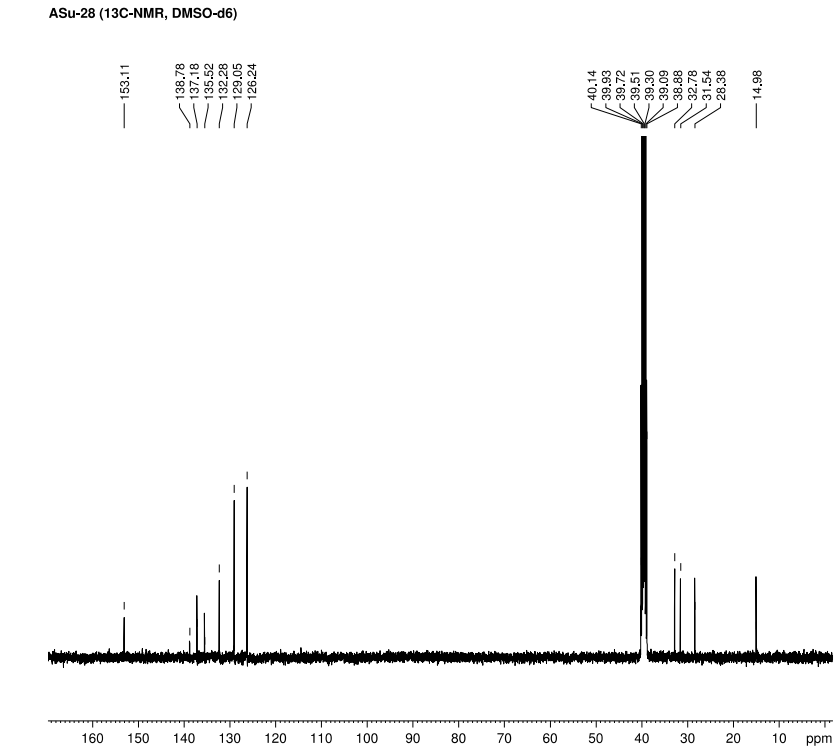



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                  264
PROCNO                   1

F2 - Acquisition Parameters
Date_              20220721
Time                 19.52
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG            zgpg30
TD                  65536
SOLVENT              DMSO
NS                   1024
DS                      4
SWH            24038.461 Hz
FIDRES          0.366798 Hz
AQ              1.3631488 sec
RG                   2050
DW                20.800 usec
DE                10.00 usec
TE                299.1 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                  13C
P1                 10.00 usec
PL1                -2.70 dB
PL1W         62.67650986 W
SFO1         100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                   1H
PCPD2              60.00 usec
PL2                -5.00 dB
PL12               10.78 dB
PL13               15.00 dB
PL2W         30.18447304 W
PL12W         0.79759723 W
PL13W         0.30184472 W
SFO2         400.1316005 MHz

F2 - Processing parameters
SI                  32768
SF           100.6128191 MHz
WDW                    EM
SSB                     0
LB                 1.00 Hz
GB                      0
PC                   1.40
```

1-Methyl-2-{2-[4-(methylsulfanyl)phenyl]ethyl}-5-nitro-1*H*-imidazole (**26**)

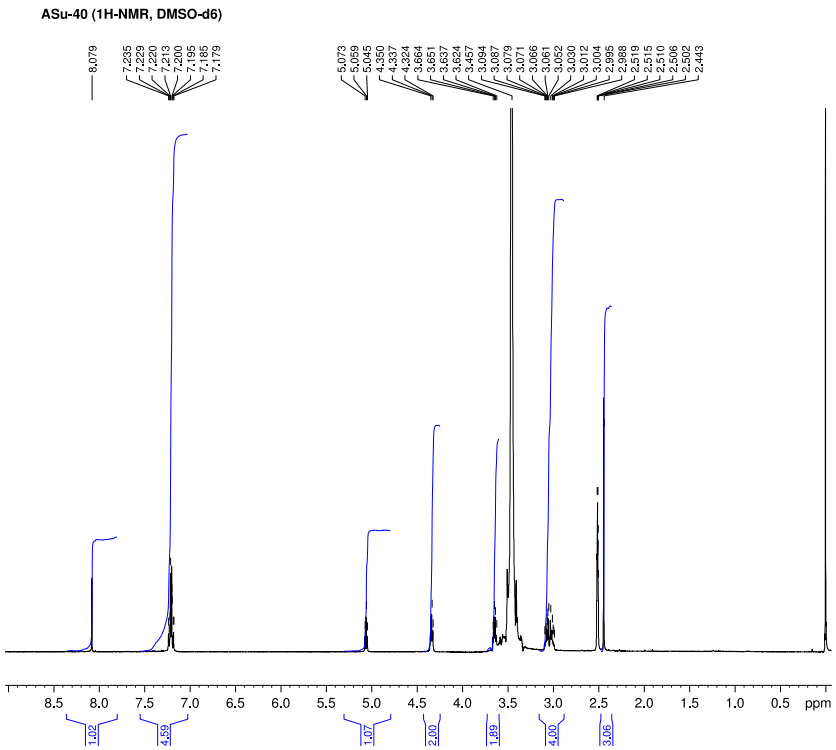



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                  165
PROCNO                   1

F2 - Acquisition Parameters
Date_              20220228
Time                 15.48
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG              zg30
TD                  65536
SOLVENT              DMSO
NS                      16
DS                       2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ              3.9845889 sec
RG                    40.3
DW                60.800 usec
DE                10.00 usec
TE                295.9 K
D1             1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    1H
P1                   9.75 usec
PL1                 -5.00 dB
PL1W         30.18447304 W
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                   32768
SF           400.1299971 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    1.00
```

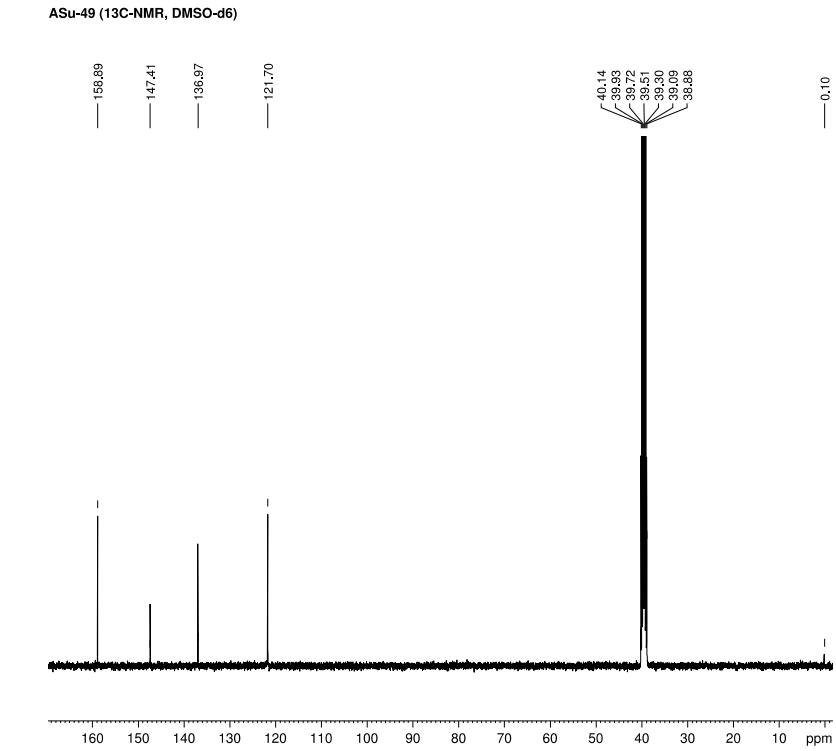



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                  454
PROCNO                   1

F2 - Acquisition Parameters
Date_              20230615
Time                 17.14
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG            zgpg30
TD                  65536
SOLVENT              DMSO
NS                    1024
DS                       4
SWH            24038.461 Hz
FIDRES          0.366798 Hz
AQ              1.3631488 sec
RG                    2050
DW                20.800 usec
DE                10.00 usec
TE                299.0 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                   13C
P1                  10.00 usec
PL1                 -2.70 dB
PL1W         62.67650986 W
SFO1         100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                    1H
PCPD2                60.00 usec
PL2                 -5.00 dB
PL12                10.78 dB
PL13                15.00 dB
PL2W         30.18447304 W
PL12W         0.79759723 W
PL13W         0.30184472 W
SFO2         400.1316005 MHz

F2 - Processing parameters
SI                   32768
SF           100.6128194 MHz
WDW                     EM
SSB                      0
LB                    1.00 Hz
GB                       0
PC                    1.40
```

2-(2-{2-[4-(Methylsulfanyl)phenyl]ethyl}-5-nitro-1*H*-imidazol-1-yl)ethan-1-ol (**27**)

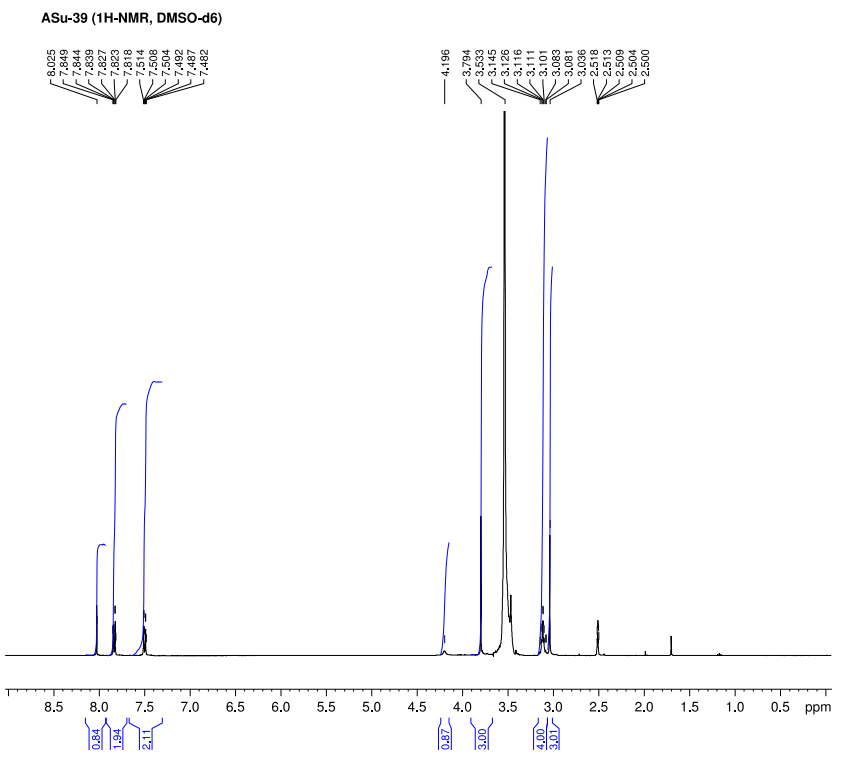



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                  234
PROCNO                   1

F2 - Acquisition Parameters
Date_           20220629
Time              10.20
INSTRUM           spect
PROBHD  5 mm PABBO BB-
PULPROG           zg30
TD               65536
SOLVENT           DMSO
NS                  16
DS                   2
SWH           8223.685 Hz
FIDRES        0.125483 Hz
AQ            3.9845889 sec
RG                  64
DW              60.800 usec
DE              10.00 usec
TE              296.9 K
D1          1.00000000 sec
TD0                  1

======== CHANNEL f1 ========
NUC1                 1H
P1                9.75 usec
PL1              -5.00 dB
PL1W       30.18447304 W
SFO1       400.1324710 MHz

F2 - Processing parameters
SI               32768
SF          400.1299996 MHz
WDW                 EM
SSB                  0
LB                0.30 Hz
GB                   0
PC                1.00
```

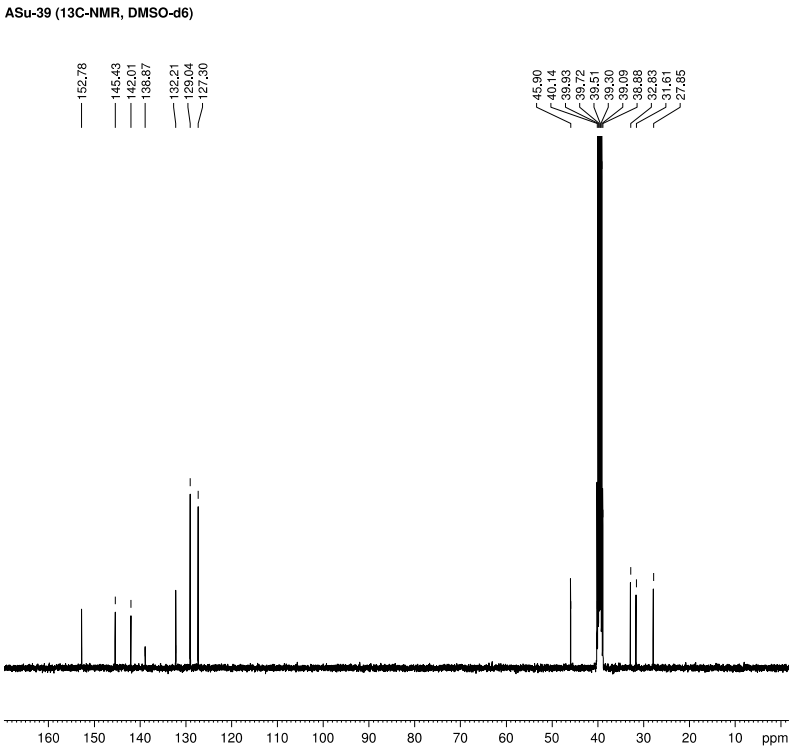



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                  279
PROCNO                   1

F2 - Acquisition Parameters
Date_           20220823
Time              17.06
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG         zgpg30
TD               65536
SOLVENT           DMSO
NS                1024
DS                   4
SWH          24038.461 Hz
FIDRES        0.366798 Hz
AQ            1.3631488 sec
RG                2050
DW              20.800 usec
DE              10.00 usec
TE              298.9 K
D1          2.00000000 sec
D11         0.03000000 sec
TD0                  1

======== CHANNEL f1 ========
NUC1                13C
P1               10.00 usec
PL1              -2.70 dB
PL1W       62.67650986 W
SFO1       100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2        waltz16
NUC2                1H
PCPD2            60.00 usec
PL2              -5.00 dB
PL12             10.78 dB
PL13             15.00 dB
PL2W       30.18447304 W
PL12W       0.79759723 W
PL13W       0.30184472 W
SFO2       400.1316005 MHz

F2 - Processing parameters
SI               32768
SF          100.6128148 MHz
WDW                 EM
SSB                  0
LB                1.00 Hz
GB                   0
PC                1.40
```

Imino(methyl){4-[2-(1-methyl-5-nitro-1*H*-imidazol-2-yl)ethyl]phenyl}-$\lambda^6$-sulfanone (**28**)

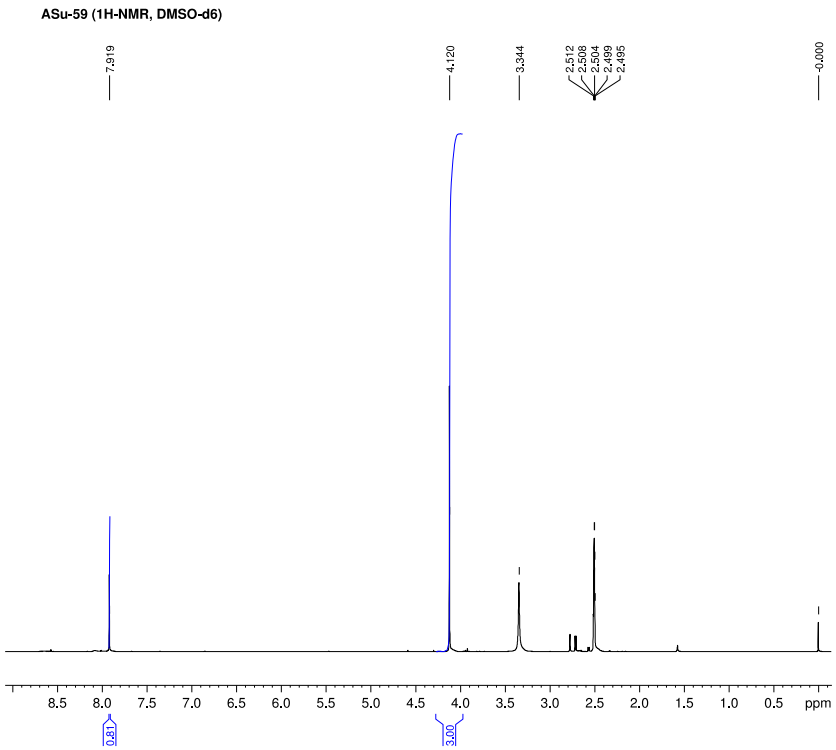



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                  184
PROCNO                   1

F2 - Acquisition Parameters
Date_           20220329
Time              15.50
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG           zg30
TD               65536
SOLVENT           DMSO
NS                  16
DS                   2
SWH           8223.685 Hz
FIDRES        0.125483 Hz
AQ            3.9845889 sec
RG                  36
DW              60.800 usec
DE              10.00 usec
TE              296.4 K
D1           1.00000000 sec
TD0                  1

======== CHANNEL f1 ========
NUC1                1H
P1                9.75 usec
PL1              -5.00 dB
PL1W       30.18447304 W
SFO1       400.1324710 MHz

F2 - Processing parameters
SI               32768
SF          400.1300000 MHz
WDW                 EM
SSB                  0
LB                0.30 Hz
GB                   0
PC                1.00
```

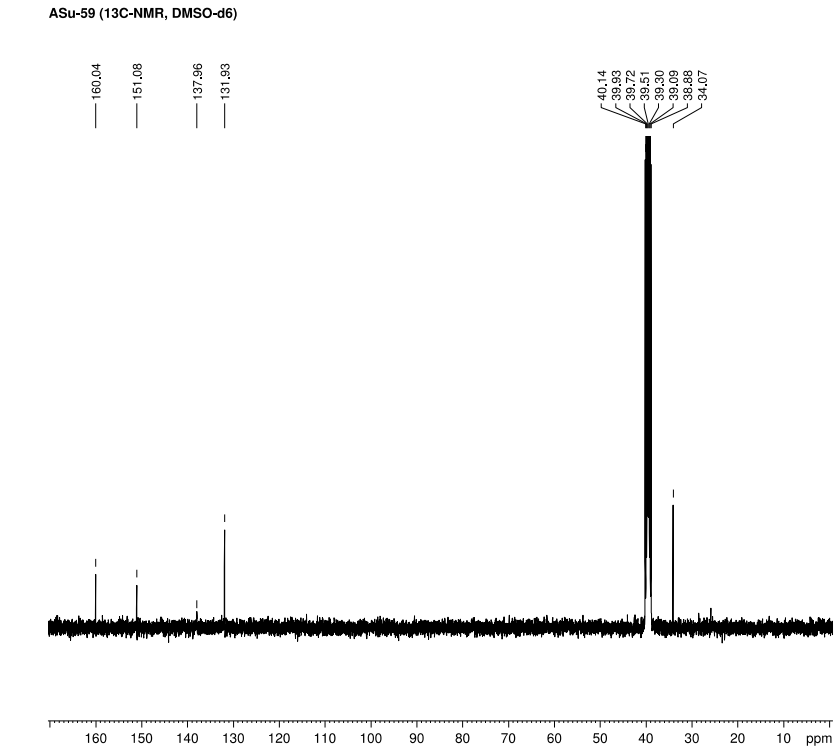



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                  461
PROCNO                   1

F2 - Acquisition Parameters
Date_           20230802
Time              20.24
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG         zgpg30
TD               65536
SOLVENT           DMSO
NS                1024
DS                   4
SWH          24038.461 Hz
FIDRES        0.366798 Hz
AQ            1.3631488 sec
RG                2050
DW              20.800 usec
DE              10.00 usec
TE              298.6 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                  1

======== CHANNEL f1 ========
NUC1                13C
P1               10.00 usec
PL1              -2.70 dB
PL1W       62.67650986 W
SFO1      100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2        waltz16
NUC2                1H
PCPD2            60.00 usec
PL2              -5.00 dB
PL12             10.78 dB
PL13             15.00 dB
PL2W       30.18447304 W
PL12W       0.79759723 W
PL13W       0.30184472 W
SFO2      400.1316005 MHz

F2 - Processing parameters
SI               32768
SF          100.6128185 MHz
WDW                 EM
SSB                  0
LB                1.00 Hz
GB                   0
PC                1.40
```

Potassium;1-methyl-5-nitro-1*H*-imidazole-2-carboxylate (**29**)

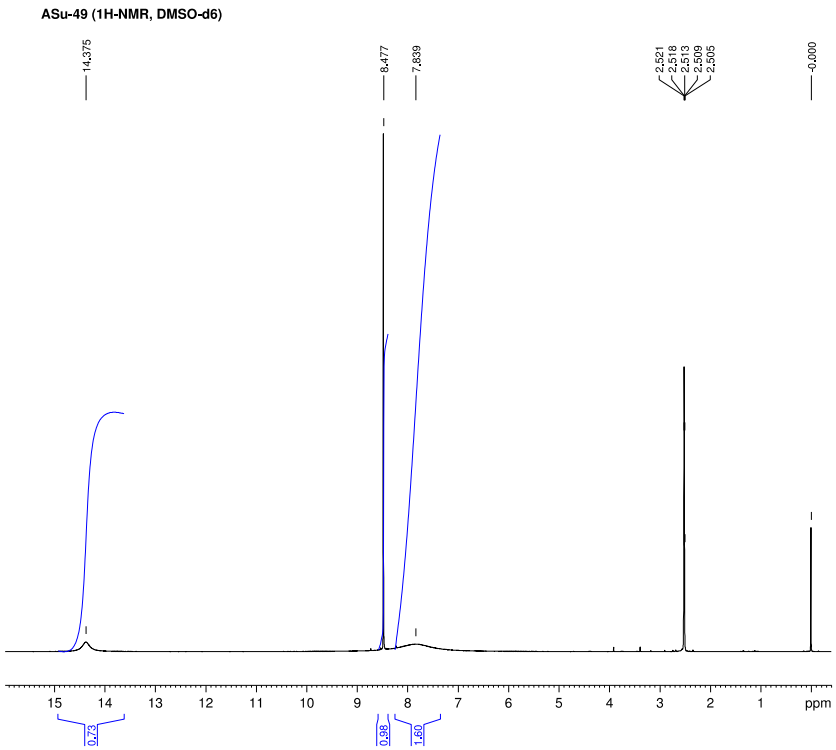



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                  347
PROCNO                   1

F2 - Acquisition Parameters
Date_              20221024
Time                 13.41
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG              zg30
TD                  65536
SOLVENT              DMSO
NS                      16
DS                       2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ              3.9845889 sec
RG                     128
DW                60.800 usec
DE                10.00 usec
TE                298.1 K
D1             1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    1H
P1                   9.75 usec
PL1                 -5.00 dB
PL1W         30.18447304 W
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                   32768
SF           400.1300022 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    1.00
```

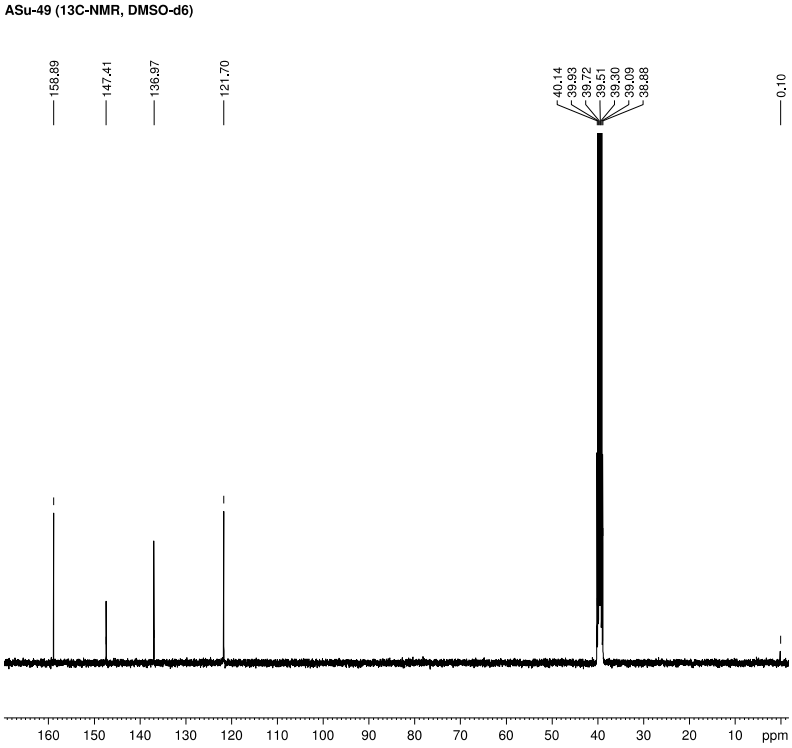



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                  348
PROCNO                   1

F2 - Acquisition Parameters
Date_              20221024
Time                 17.08
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG            zgpg30
TD                  65536
SOLVENT              DMSO
NS                    1024
DS                       4
SWH            24038.461 Hz
FIDRES          0.366798 Hz
AQ              1.3631488 sec
RG                    2050
DW                20.800 usec
DE                10.00 usec
TE                298.6 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                   13C
P1                  10.00 usec
PL1                 -2.70 dB
PL1W         62.67650986 W
SFO1         100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                    1H
PCPD2                60.00 usec
PL2                 -5.00 dB
PL12                10.78 dB
PL13                15.00 dB
PL2W         30.18447304 W
PL12W         0.79759723 W
PL13W         0.30184472 W
SFO2         400.1316005 MHz

F2 - Processing parameters
SI                   32768
SF           100.6128182 MHz
WDW                     EM
SSB                      0
LB                    1.00 Hz
GB                       0
PC                    1.40
```

5-Nitro-1*H*-imidazole-2-carboxylic acid (**31**)

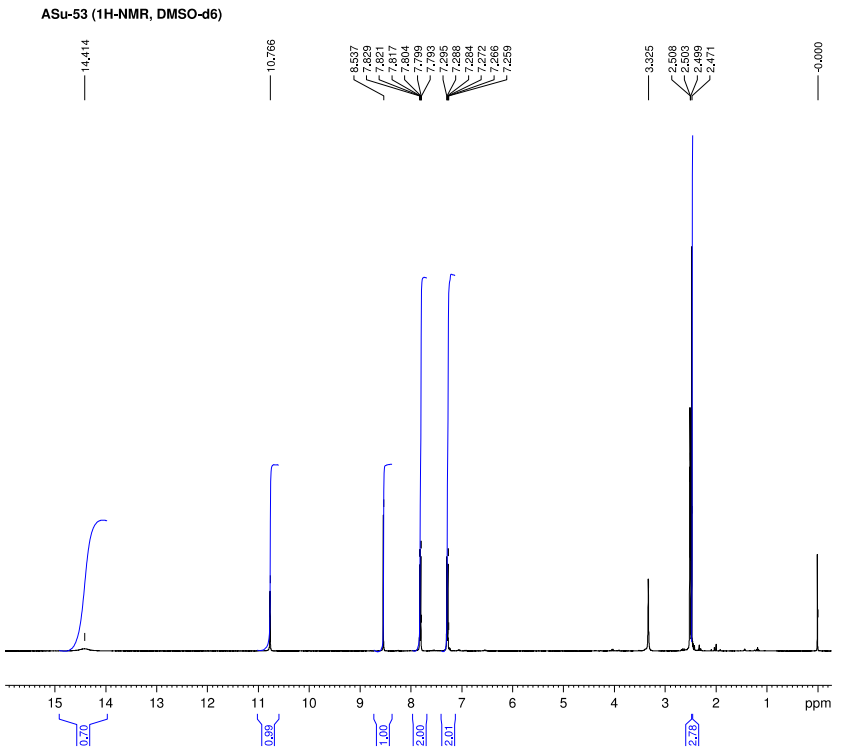



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                 277
PROCNO                  1

F2 - Acquisition Parameters
Date_           20220823
Time              10.28
INSTRUM           spect
PROBHD  5 mm PABBO BB-
PULPROG           zg30
TD                65536
SOLVENT            DMSO
NS                   16
DS                    2
SWH            8223.685 Hz
FIDRES        0.125483 Hz
AQ            3.9845889 sec
RG                  114
DW               60.800 usec
DE               10.00 usec
TE                298.2 K
D1           1.00000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                 1H
P1                9.75 usec
PL1               -5.00 dB
PL1W       30.18447304 W
SFO1      400.1324710 MHz

F2 - Processing parameters
SI                32768
SF          400.1299985 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 1.00
```

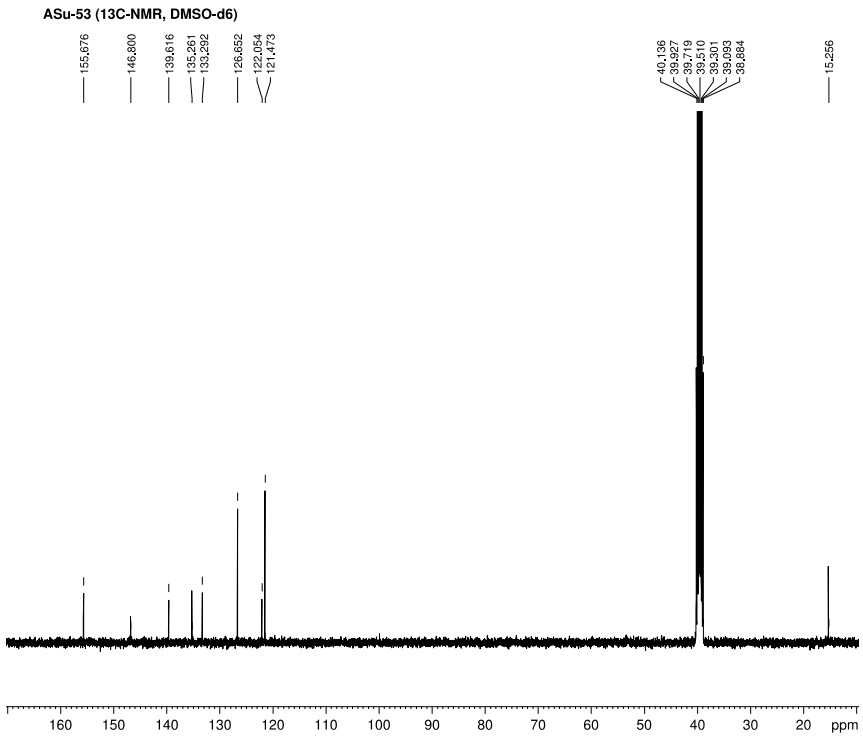



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                 279
PROCNO                  1

F2 - Acquisition Parameters
Date_           20220823
Time              17.06
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG          zgpg30
TD                65536
SOLVENT            DMSO
NS                 1024
DS                    4
SWH           24038.461 Hz
FIDRES        0.366798 Hz
AQ            1.3631488 sec
RG                 2050
DW               20.800 usec
DE               10.00 usec
TE                298.9 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                13C
P1               10.00 usec
PL1               -2.70 dB
PL1W       62.67650986 W
SFO1      100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2         waltz16
NUC2                 1H
PCPD2             60.00 usec
PL2               -5.00 dB
PL12              10.78 dB
PL13              15.00 dB
PL2W       30.18447304 W
PL12W       0.79759723 W
PL13W       0.30184472 W
SFO2      400.1316005 MHz

F2 - Processing parameters
SI                32768
SF          100.6128148 MHz
WDW                  EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 1.40
```

*N*-[4-(Methylsulfanyl)phenyl]-5-nitro-1*H*-imidazole-2-carboxamide (**32**)

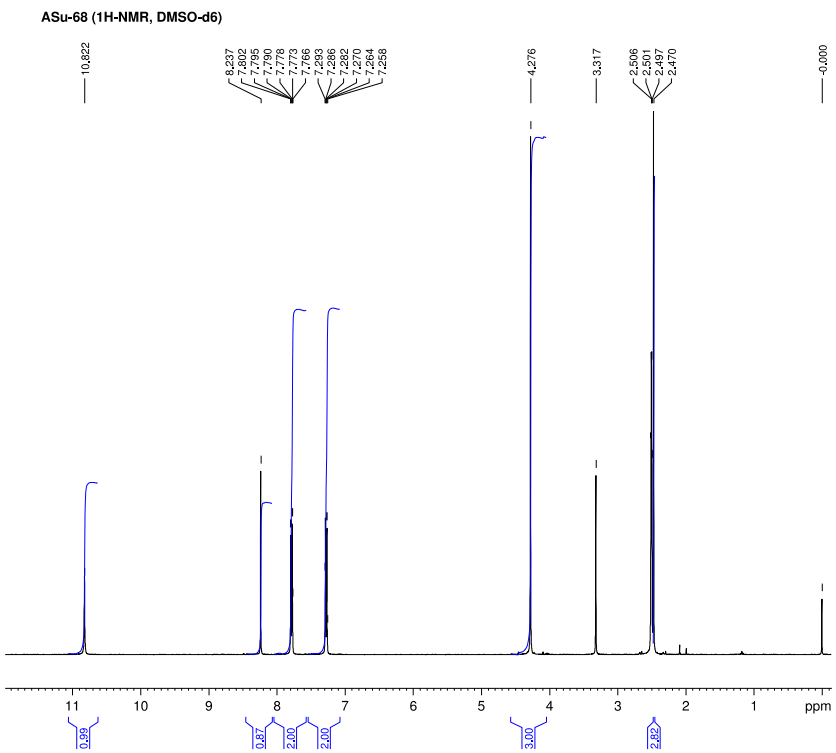


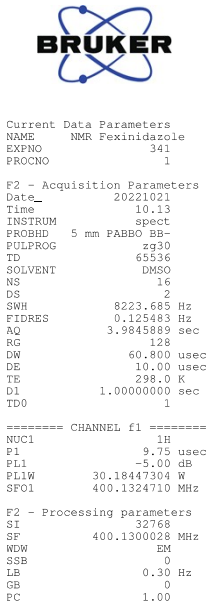

```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                286
PROCNO                 1

F2 - Acquisition Parameters
Date_           20220829
Time              10.23
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG           zg30
TD               65536
SOLVENT           DMSO
NS                   16
DS                    2
SWH           8223.685 Hz
FIDRES        0.125483 Hz
AQ            3.9845889 sec
RG                  203
DW             60.800 usec
DE             10.00 usec
TE                298.1 K
D1           1.00000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                 1H
P1                9.75 usec
PL1              -5.00 dB
PL1W       30.18447304 W
SFO1      400.1324710 MHz

F2 - Processing parameters
SI                32768
SF          400.1300024 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 1.00
```

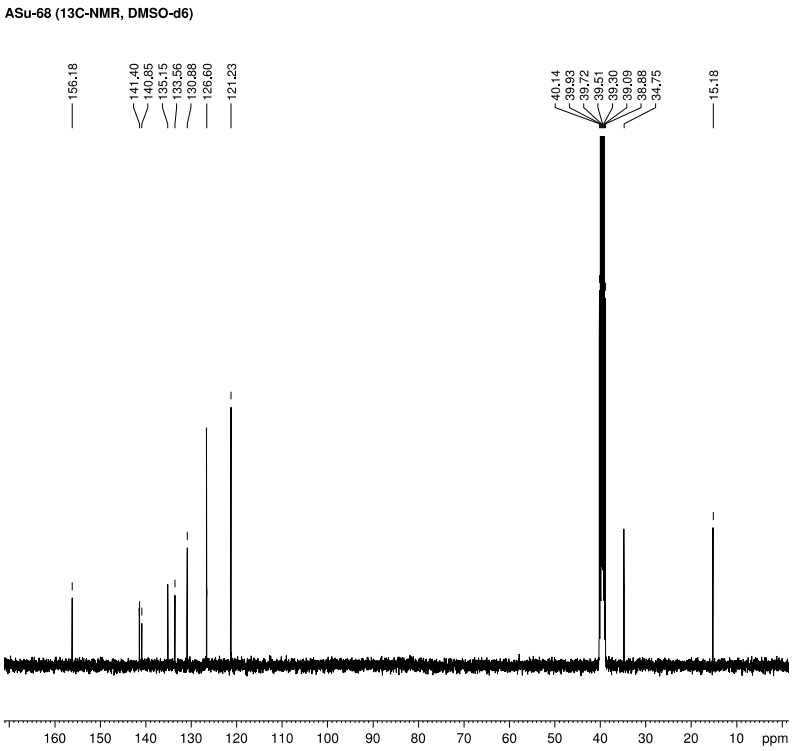


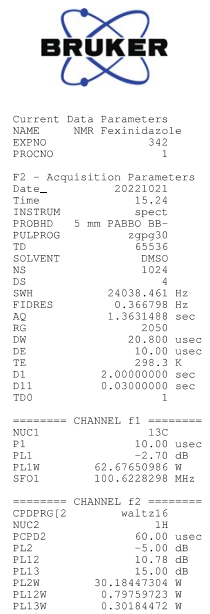

```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                287
PROCNO                 1

F2 - Acquisition Parameters
Date_           20220829
Time              23.11
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG         zgpg30
TD               65536
SOLVENT           DMSO
NS                 1024
DS                    4
SWH          24038.461 Hz
FIDRES        0.366798 Hz
AQ            1.3631488 sec
RG                 2050
DW             20.800 usec
DE              10.00 usec
TE                298.8 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                13C
P1               10.00 usec
PL1              -2.70 dB
PL1W       62.67650986 W
SFO1      100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2         waltz16
NUC2                 1H
PCPD2             60.00 usec
PL2               -5.00 dB
PL12              10.78 dB
PL13              15.00 dB
PL2W       30.18447304 W
PL12W       0.79759723 W
PL13W       0.30184472 W
SFO2      400.1316005 MHz

F2 - Processing parameters
SI                32768
SF          100.6128188 MHz
WDW                  EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 1.40
```

1-Methyl-*N*-[4-(methylsulfanyl)phenyl]-5-nitro-1*H*-imidazole-2-carboxamide (**33**)

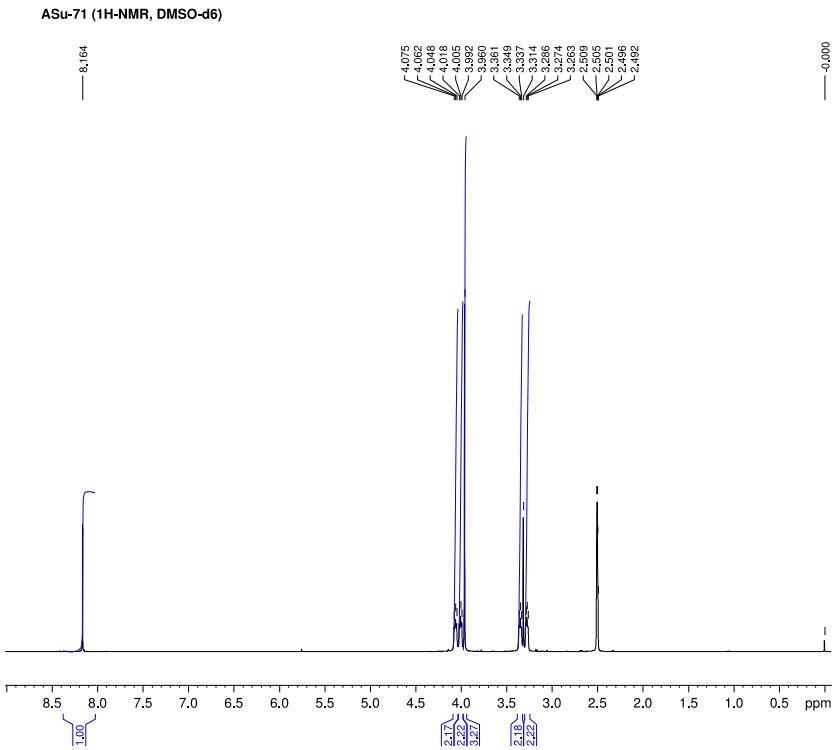


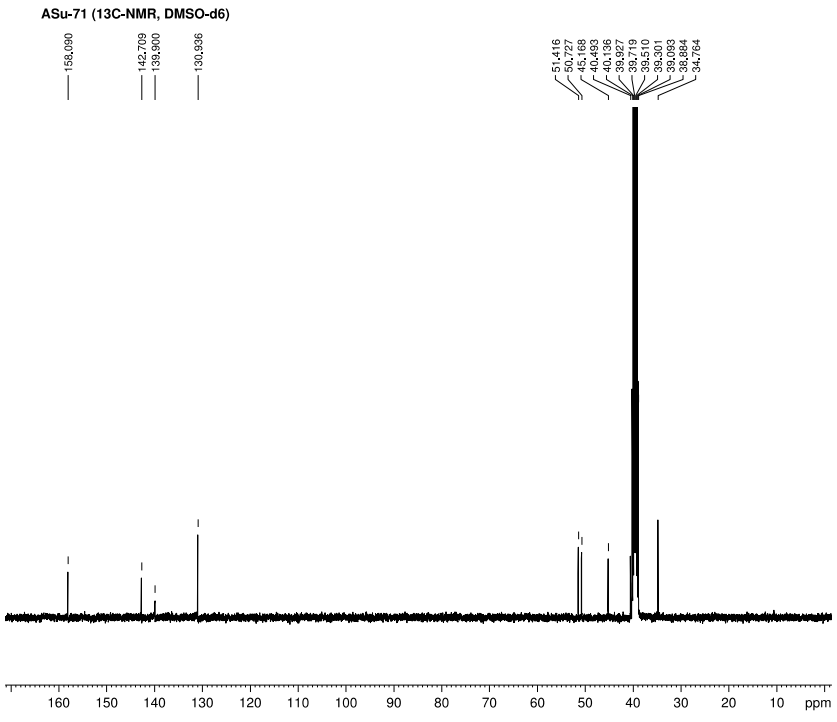



4-(1-Methyl-5-nitro-1*H*-imidazole-2-carbonyl)-λ$^{1}$6-thiomorpholine-1,1-dione (**34**)

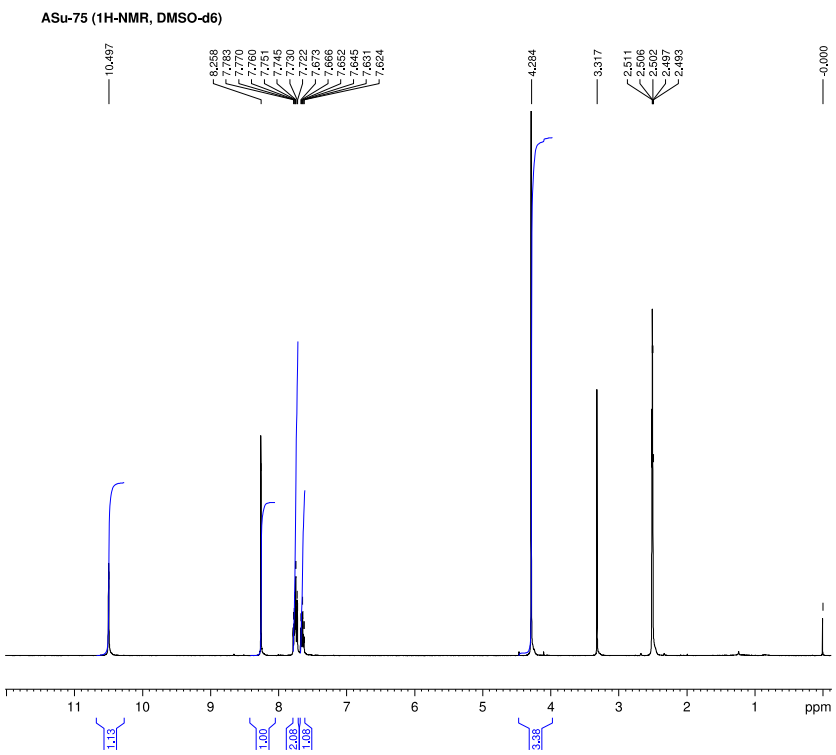



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                  385
PROCNO                   1

F2 - Acquisition Parameters
Date_              20230320
Time                 10.57
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG              zg30
TD                  65536
SOLVENT              DMSO
NS                     16
DS                      2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ              3.9845889 sec
RG                    181
DW                60.800 usec
DE                10.00 usec
TE                298.2 K
D1             1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                  9.75 usec
PL1                -5.00 dB
PL1W         30.18447304 W
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                  32768
SF           400.1300032 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.00
```




```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                  392
PROCNO                   1

F2 - Acquisition Parameters
Date_              20230321
Time                 16.33
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG            zgpg30
TD                  65536
SOLVENT              DMSO
NS                   1024
DS                      4
SWH            24038.461 Hz
FIDRES          0.366798 Hz
AQ              1.3631488 sec
RG                   2050
DW                20.800 usec
DE                10.00 usec
TE                298.2 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                  13C
P1                 10.00 usec
PL1                -2.70 dB
PL1W         62.67650986 W
SFO1        100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                   1H
PCPD2              60.00 usec
PL2                -5.00 dB
PL12               10.78 dB
PL13               15.00 dB
PL2W         30.18447304 W
PL12W         0.79759723 W
PL13W         0.30184472 W
SFO2        400.1316005 MHz

F2 - Processing parameters
SI                  32768
SF           100.6128189 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   1.40
```

*N*-[4-Fluoro-2-(trifluoromethyl)phenyl]-1-methyl-5-nitro-1*H*-imidazole-2-carboxamide (**35**)

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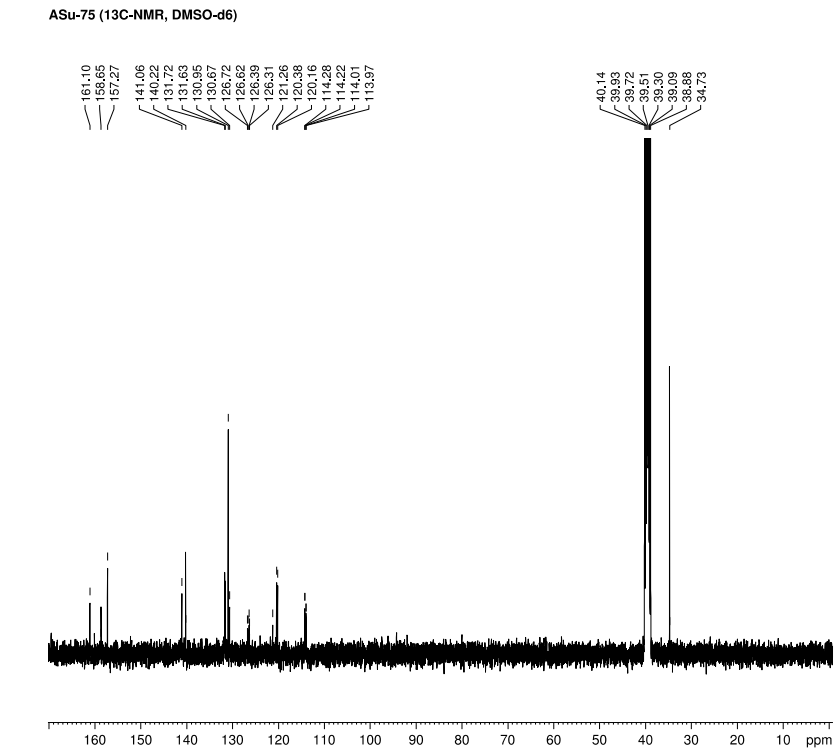
```
Current Data Parameters
NAME       NMR Fexinidazole
EXPNO                   381
PROCNO                    1

F2 - Acquisition Parameters
Date_           20230315
Time              10.02
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG           zg30
TD               65536
SOLVENT           DMSO
NS                  16
DS                   2
SWH           8223.685 Hz
FIDRES        0.125483 Hz
AQ            3.9845889 sec
RG                 203
DW              60.800 usec
DE              10.00 usec
TE              298.3 K
D1          1.00000000 sec
TD0                  1

======== CHANNEL f1 ========
NUC1                1H
P1               9.75 usec
PL1             -5.00 dB
PL1W       30.18447304 W
SFO1      400.1324710 MHz

F2 - Processing parameters
SI               32768
SF          400.1300027 MHz
WDW                 EM
SSB                  0
LB              0.30 Hz
GB                   0
PC              1.00
```

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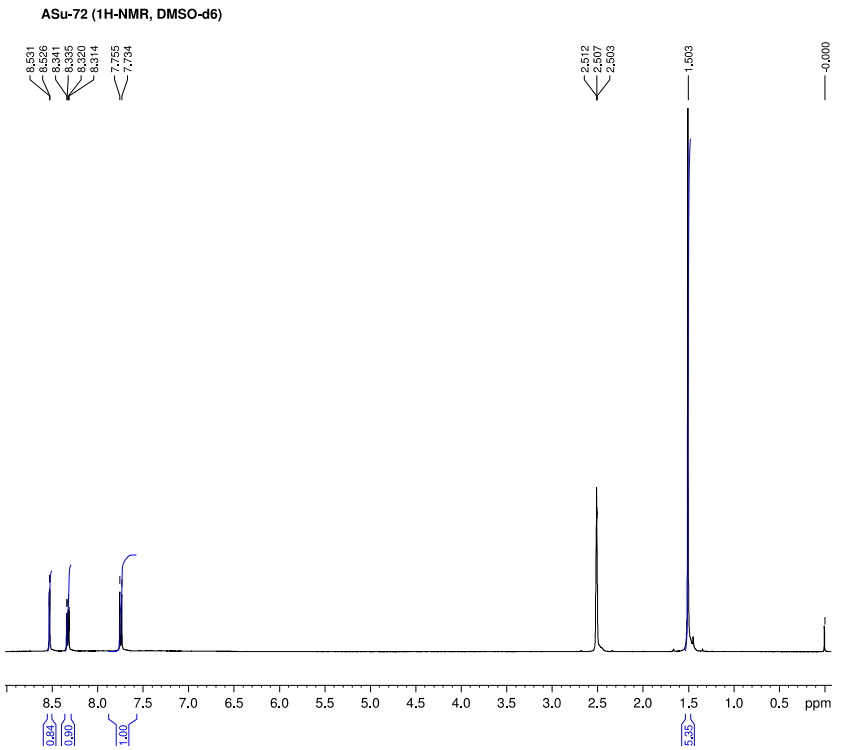
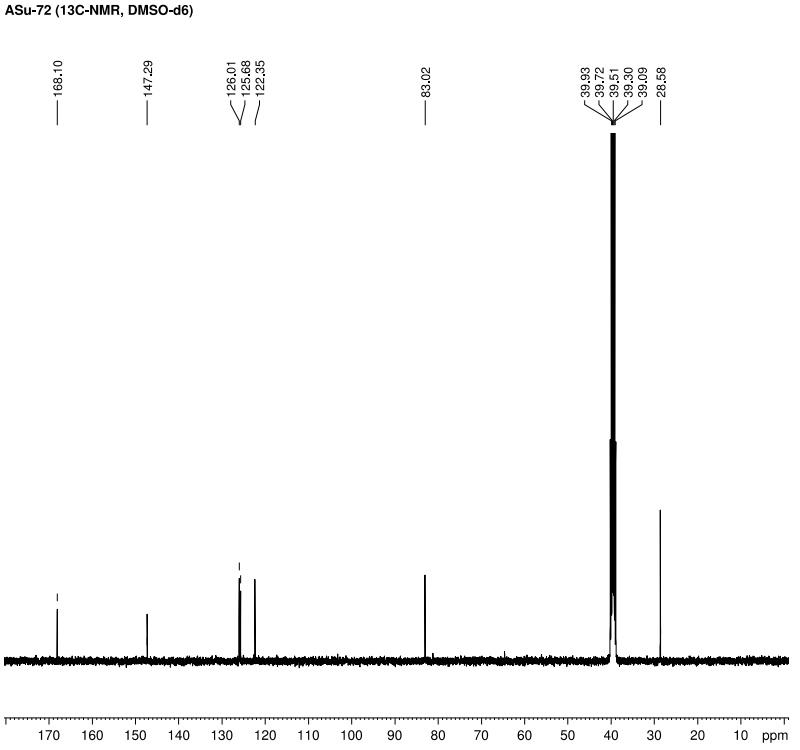
```
Current Data Parameters
NAME       NMR Fexinidazole
EXPNO                   386
PROCNO                    1

F2 - Acquisition Parameters
Date_           20230320
Time              16.56
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG         zgpg30
TD               65536
SOLVENT           DMSO
NS                1024
DS                   4
SWH          24038.461 Hz
FIDRES        0.366798 Hz
AQ            1.3631488 sec
RG                2050
DW              20.800 usec
DE              10.00 usec
TE              298.2 K
D1          2.00000000 sec
D11         0.03000000 sec
TD0                  1

======== CHANNEL f1 ========
NUC1               13C
P1              10.00 usec
PL1             -2.70 dB
PL1W       62.67650986 W
SFO1      100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2        waltz16
NUC2                1H
PCPD2           60.00 usec
PL2             -5.00 dB
PL12            10.78 dB
PL13            15.00 dB
PL2W       30.18447304 W
PL12W       0.79759723 W
PL13W       0.30184472 W
SFO2      400.1316005 MHz

F2 - Processing parameters
SI               32768
SF          100.6128184 MHz
WDW                 EM
SSB                  0
LB              1.00 Hz
GB                   0
PC              1.40
```

3,3-Dimethyl-6-nitro-1,3-dihydro-2,1-benzoxaborol-1-ol (**36**)

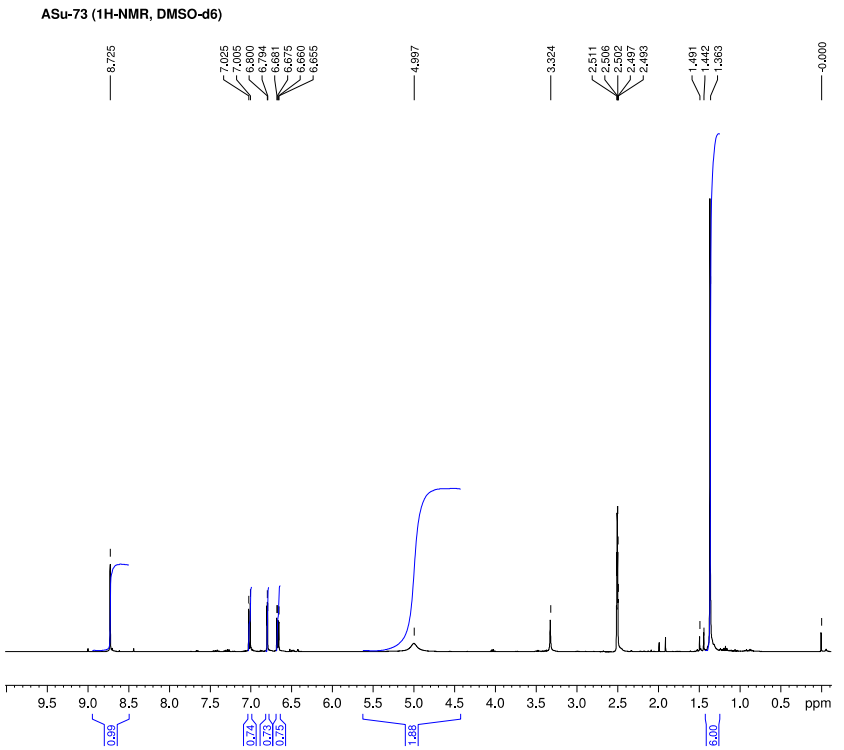



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                 360
PROCNO                  1

F2 - Acquisition Parameters
Date_           20230221
Time              11.05
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG           zg30
TD               65536
SOLVENT           DMSO
NS                   16
DS                    2
SWH            8223.685 Hz
FIDRES        0.125483 Hz
AQ            3.9845889 sec
RG                  181
DW               60.800 usec
DE               10.00 usec
TE               298.0 K
D1            1.00000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                 1H
P1                9.75 usec
PL1              -5.00 dB
PL1W        30.18447304 W
SFO1       400.1324710 MHz

F2 - Processing parameters
SI                32768
SF           400.1300005 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 1.00
```

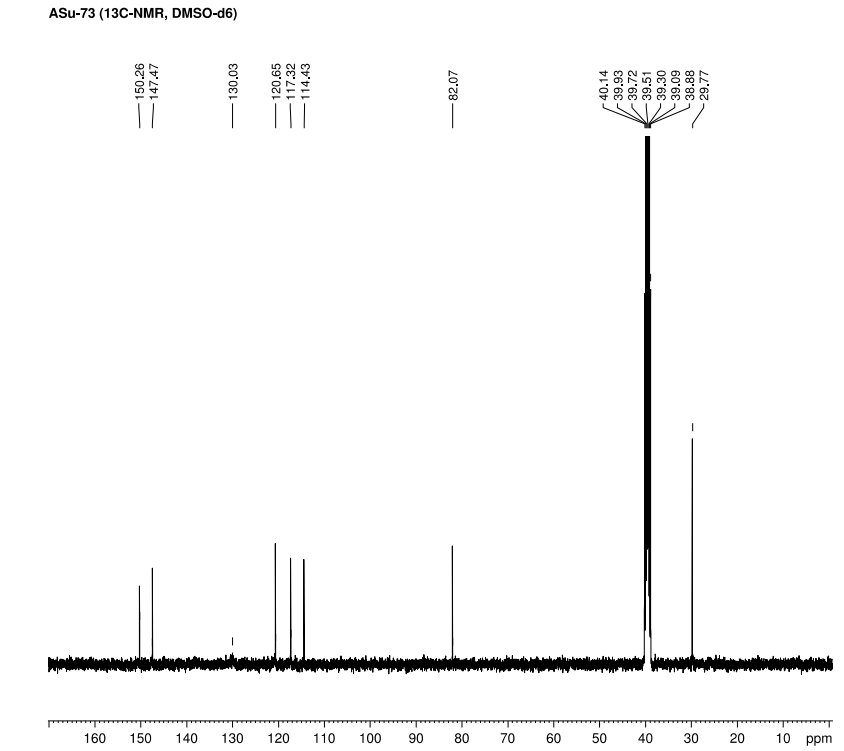



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                 365
PROCNO                  1

F2 - Acquisition Parameters
Date_           20230222
Time              15.57
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG         zgpg30
TD               65536
SOLVENT           DMSO
NS                 1024
DS                    4
SWH           24038.461 Hz
FIDRES        0.366798 Hz
AQ            1.3631488 sec
RG                 2050
DW               20.800 usec
DE               10.00 usec
TE               298.3 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                13C
P1               10.00 usec
PL1              -2.70 dB
PL1W        62.67650986 W
SFO1       100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2        waltz16
NUC2                1H
PCPD2            60.00 usec
PL2              -5.00 dB
PL12             10.78 dB
PL13             15.00 dB
PL2W        30.18447304 W
PL12W        0.79759723 W
PL13W        0.30184472 W
SFO2       400.1316005 MHz

F2 - Processing parameters
SI                32768
SF           100.6128181 MHz
WDW                  EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 1.40
```

6-Amino-3,3-dimethyl-1,3-dihydro-2,1-benzoxaborol-1-ol (**37**)

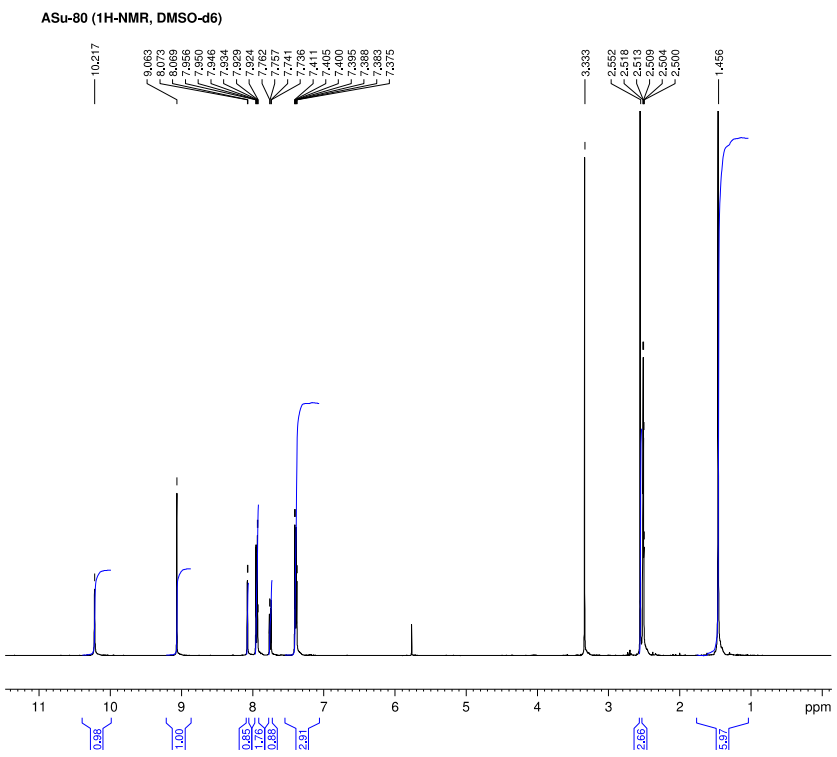



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                 366
PROCNO                  1

F2 - Acquisition Parameters
Date_           20230301
Time              13.38
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG           zg30
TD               65536
SOLVENT           DMSO
NS                   16
DS                    2
SWH           8223.685 Hz
FIDRES        0.125483 Hz
AQ            3.9845889 sec
RG                  101
DW             60.800 usec
DE             10.00 usec
TE               297.9 K
D1          1.00000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                 1H
P1                9.75 usec
PL1              -5.00 dB
PL1W       30.18447304 W
SFO1       400.1324710 MHz

F2 - Processing parameters
SI                32768
SF          400.1300026 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 1.00
```




```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                 367
PROCNO                  1

F2 - Acquisition Parameters
Date_           20230301
Time              17.03
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG         zgpg30
TD               65536
SOLVENT           DMSO
NS                 1024
DS                    4
SWH          24038.461 Hz
FIDRES        0.366798 Hz
AQ            1.3631488 sec
RG                 2050
DW             20.800 usec
DE             10.00 usec
TE               298.2 K
D1          2.00000000 sec
D11         0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                13C
P1               10.00 usec
PL1              -2.70 dB
PL1W       62.67650986 W
SFO1       100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2        waltz16
NUC2                1H
PCPD2            60.00 usec
PL2              -5.00 dB
PL12             10.78 dB
PL13             15.00 dB
PL2W       30.18447304 W
PL12W       0.79759723 W
PL13W       0.30184472 W
SFO2       400.1316005 MHz

F2 - Processing parameters
SI                32768
SF          100.6128188 MHz
WDW                  EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 1.40
```

*N*-(1-hydroxy-3,3-dimethyl-1,3-dihydro-2,1-benzoxaborol-6-yl)-4-(methylsulfanyl)benzamide (**38**)

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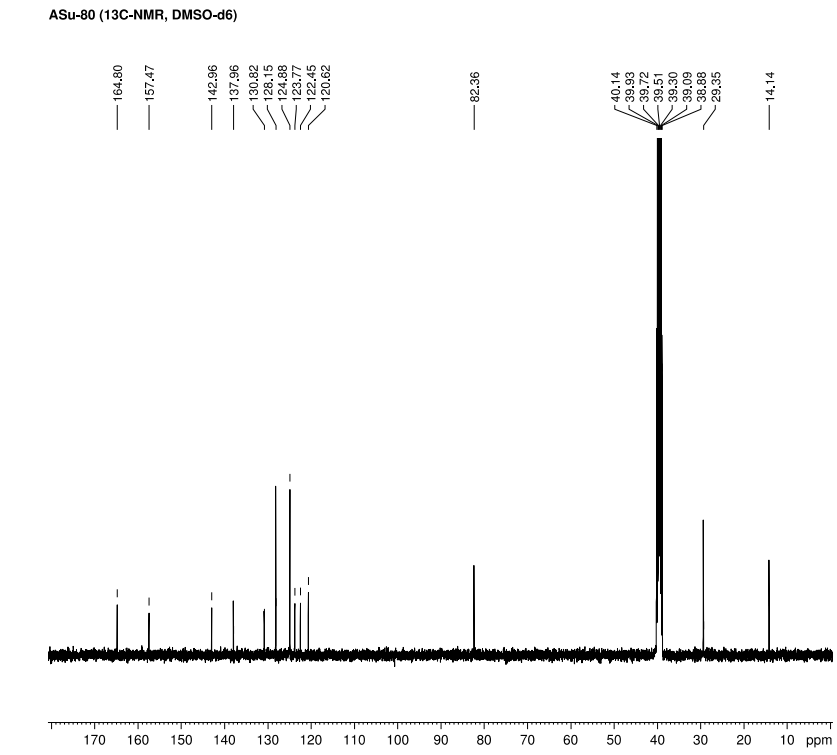
```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                419
PROCNO                 1

F2 - Acquisition Parameters
Date_           20230508
Time              10.33
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG           zg30
TD               65536
SOLVENT           DMSO
NS                  16
DS                   2
SWH           8223.685 Hz
FIDRES        0.125483 Hz
AQ            3.9845889 sec
RG                 101
DW              60.800 usec
DE              10.00 usec
TE              298.1 K
D1           1.00000000 sec
TD0                  1

======== CHANNEL f1 ========
NUC1                1H
P1               9.75 usec
PL1             -5.00 dB
PL1W       30.18447304 W
SFO1       400.1324710 MHz

F2 - Processing parameters
SI               32768
SF          400.1300000 MHz
WDW                 EM
SSB                  0
LB                0.30 Hz
GB                   0
PC                1.00
```

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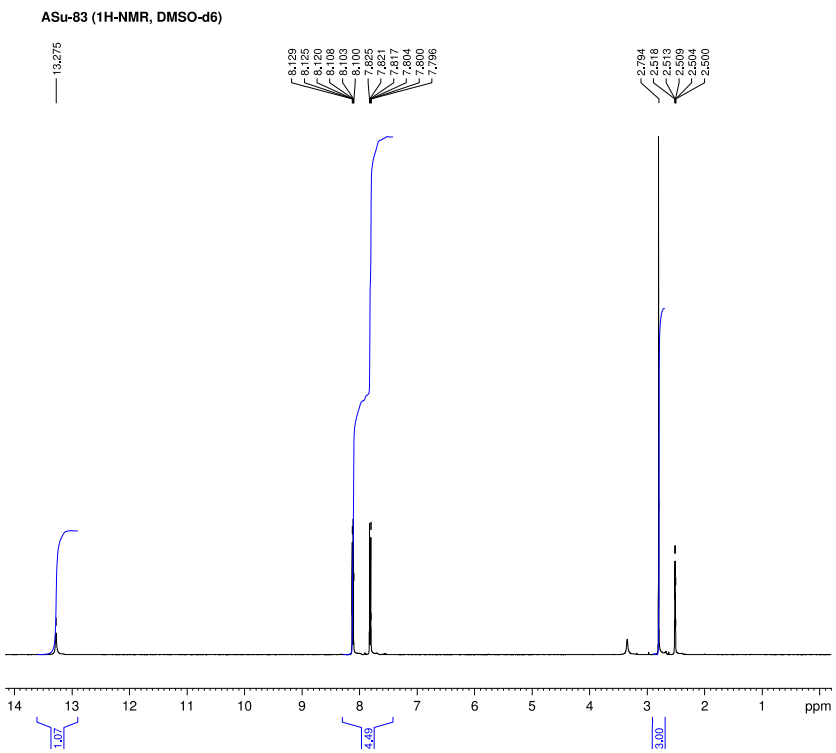
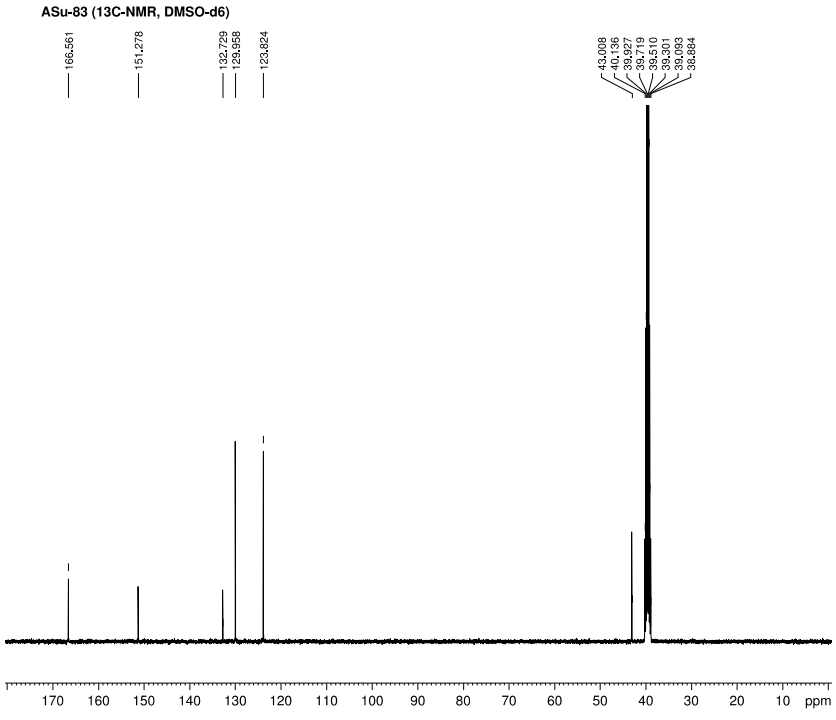
```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                421
PROCNO                 1

F2 - Acquisition Parameters
Date_           20230508
Time              16.42
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG         zgpg30
TD               65536
SOLVENT           DMSO
NS                1024
DS                   4
SWH          24038.461 Hz
FIDRES        0.366798 Hz
AQ            1.3631488 sec
RG                2050
DW              20.800 usec
DE              10.00 usec
TE              298.5 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                  1

======== CHANNEL f1 ========
NUC1                13C
P1              10.00 usec
PL1             -2.70 dB
PL1W       62.67650986 W
SFO1       100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2        waltz16
NUC2                1H
PCPD2           60.00 usec
PL2             -5.00 dB
PL12            10.78 dB
PL13            15.00 dB
PL2W       30.18447304 W
PL12W       0.79759723 W
PL13W       0.30184472 W
SFO2       400.1316005 MHz

F2 - Processing parameters
SI               32768
SF          100.6128190 MHz
WDW                 EM
SSB                  0
LB                1.00 Hz
GB                   0
PC                1.40
```

# 4-Methanesulfinylbenzoic acid (**39**)

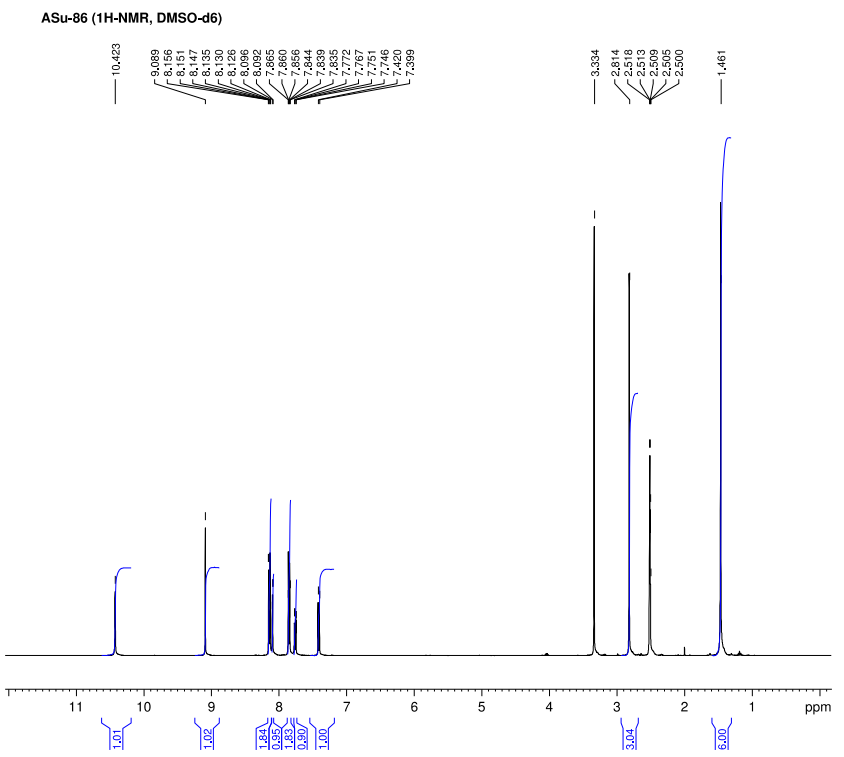


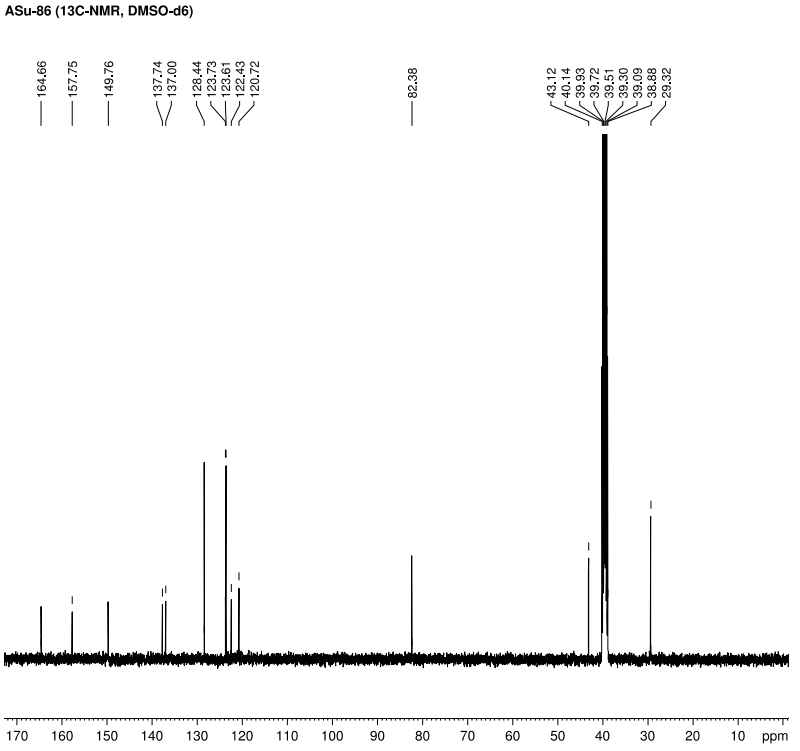

```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                  430
PROCNO                   1

F2 - Acquisition Parameters
Date_              20230510
Time                 10.32
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG              zg30
TD                  65536
SOLVENT              DMSO
NS                     16
DS                      2
SWH              8223.685 Hz
FIDRES           0.125483 Hz
AQ               3.9845889 sec
RG                    101
DW                60.800 usec
DE                10.00 usec
TE                298.1 K
D1             1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                  9.75 usec
PL1                -5.00 dB
PL1W         30.18447304 W
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                  32768
SF           400.1300000 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.00
```




```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                  431
PROCNO                   1

F2 - Acquisition Parameters
Date_              20230511
Time                 20.07
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG            zgpg30
TD                  65536
SOLVENT              DMSO
NS                   1024
DS                      4
SWH              24038.461 Hz
FIDRES           0.366798 Hz
AQ               1.3631488 sec
RG                   2050
DW                20.800 usec
DE                10.00 usec
TE                298.9 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                  13C
P1                 10.00 usec
PL1                -2.70 dB
PL1W         62.67650986 W
SFO1         100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                   1H
PCPD2              60.00 usec
PL2                -5.00 dB
PL12               10.78 dB
PL13               15.00 dB
PL2W         30.18447304 W
PL12W         0.79759723 W
PL13W         0.30184472 W
SFO2         400.1316005 MHz

F2 - Processing parameters
SI                  32768
SF           100.6128183 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   1.40
```

*N*-(1-hydroxy-3,3-dimethyl-1,3-dihydro-2,1-benzoxaborol-6-yl)-4-methanesulfinylbenzamide (**40**)

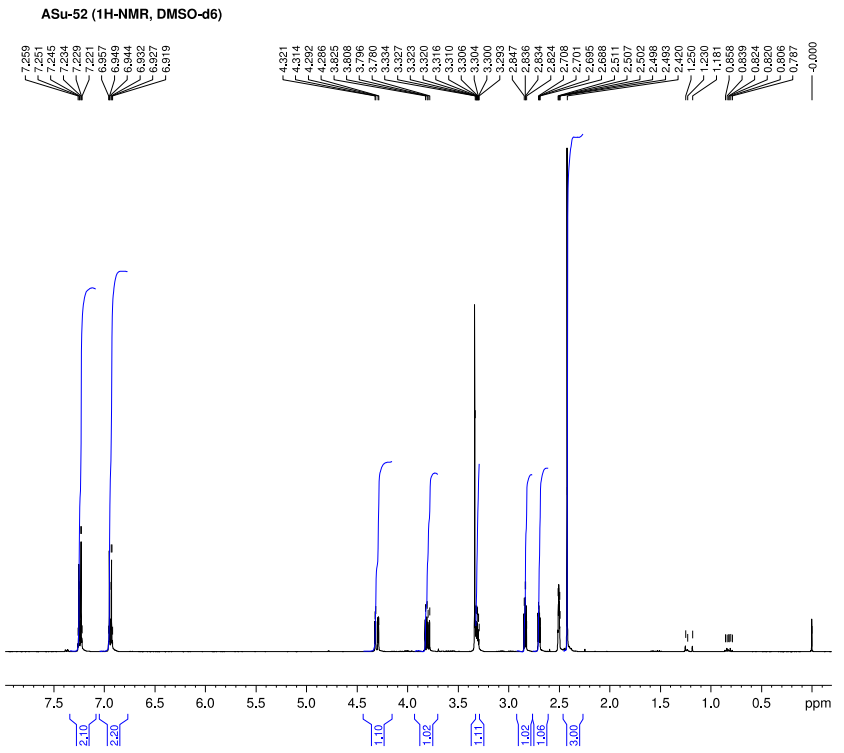


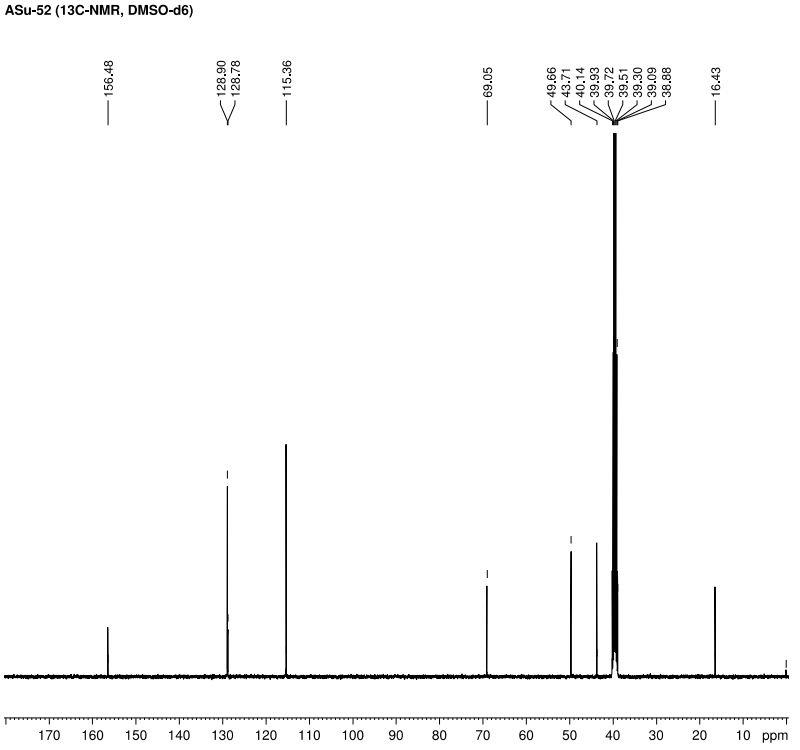

```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                  445
PROCNO                   1

F2 - Acquisition Parameters
Date_           20230607
Time              10.49
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG           zg30
TD               65536
SOLVENT           DMSO
NS                  16
DS                   2
SWH           8223.685 Hz
FIDRES        0.125483 Hz
AQ            3.9845889 sec
RG                 161
DW              60.800 usec
DE              10.00 usec
TE              298.2 K
D1           1.00000000 sec
TD0                  1

======== CHANNEL f1 ========
NUC1                1H
P1               9.75 usec
PL1              -5.00 dB
PL1W       30.18447304 W
SFO1       400.1324710 MHz

F2 - Processing parameters
SI               32768
SF          400.1300000 MHz
WDW                 EM
SSB                  0
LB                0.30 Hz
GB                   0
PC                1.00
```

```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                  446
PROCNO                   1

F2 - Acquisition Parameters
Date_           20230607
Time              19.25
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG         zgpg30
TD               65536
SOLVENT           DMSO
NS                1024
DS                   4
SWH          24038.461 Hz
FIDRES        0.366798 Hz
AQ            1.3631488 sec
RG                2050
DW              20.800 usec
DE              10.00 usec
TE              299.3 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                  1

======== CHANNEL f1 ========
NUC1                13C
P1              10.00 usec
PL1              -2.70 dB
PL1W       62.67650986 W
SFO1       100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2        waltz16
NUC2                1H
PCPD2            60.00 usec
PL2              -5.00 dB
PL12             10.78 dB
PL13             15.00 dB
PL2W       30.18447304 W
PL12W       0.79759723 W
PL13W       0.30184472 W
SFO2       400.1316005 MHz

F2 - Processing parameters
SI               32768
SF          100.6128194 MHz
WDW                 EM
SSB                  0
LB                1.00 Hz
GB                   0
PC                1.40
```

2-{[4-(Methylsulfanyl)phenoxy]methyl}oxirane (**41**)

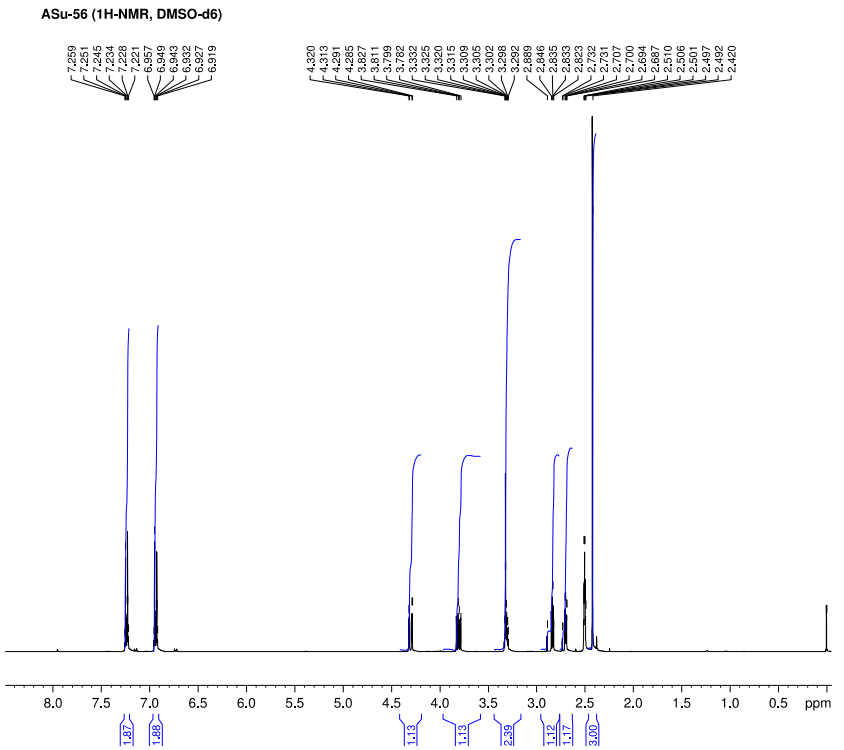


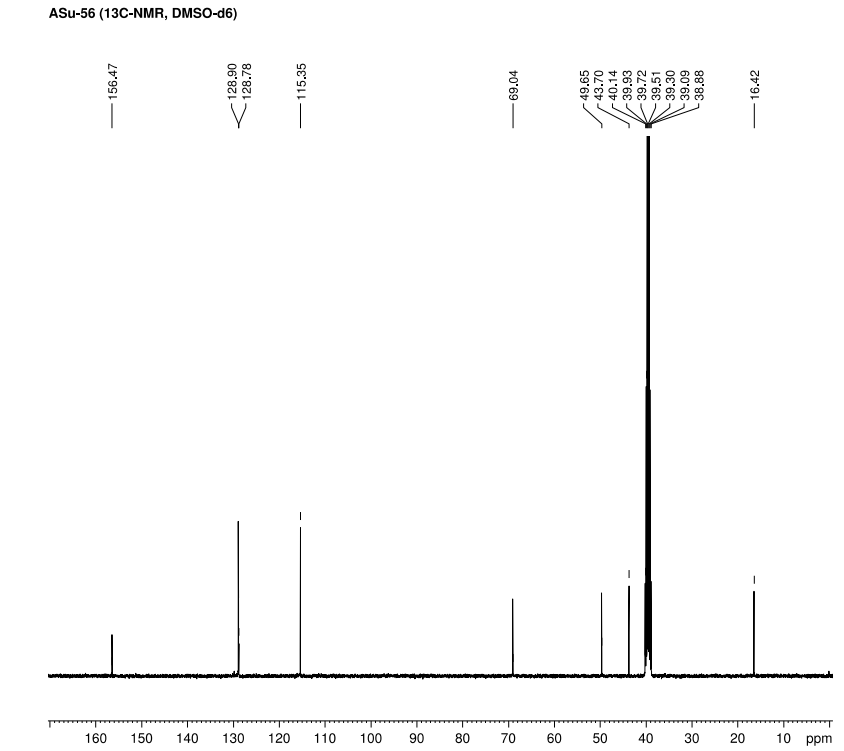

```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                  256
PROCNO                   1

F2 - Acquisition Parameters
Date_              20220719
Time                 10.23
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG              zg30
TD                  65536
SOLVENT              DMSO
NS                     16
DS                      2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ              3.9845889 sec
RG                   90.5
DW                60.800 usec
DE                10.00 usec
TE                296.9 K
D1            1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                  9.75 usec
PL1                -5.00 dB
PL1W         30.18447304 W
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                  32768
SF           400.1300029 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.00
```



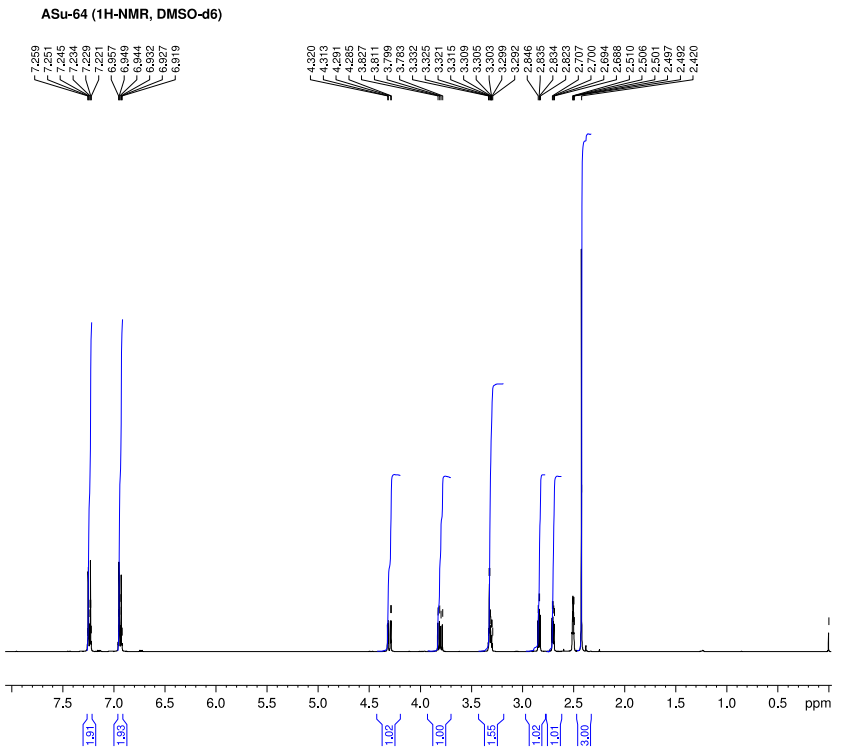

```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                  257
PROCNO                   1

F2 - Acquisition Parameters
Date_              20220719
Time                 16.32
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG            zgpg30
TD                  65536
SOLVENT              DMSO
NS                   1024
DS                      4
SWH            24038.461 Hz
FIDRES          0.366798 Hz
AQ              1.3631488 sec
RG                   2050
DW                20.800 usec
DE                10.00 usec
TE                298.7 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                  13C
P1                 10.00 usec
PL1                -2.70 dB
PL1W         62.67650986 W
SFO1         100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                   1H
PCPD2              60.00 usec
PL2                -5.00 dB
PL12               10.78 dB
PL13               15.00 dB
PL2W         30.18447304 W
PL12W         0.79759723 W
PL13W         0.30184472 W
SFO2         400.1316005 MHz

F2 - Processing parameters
SI                  32768
SF           100.6128186 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   1.40
```

(2*R*)-2-{[4-(Methylsulfanyl)phenoxy]methyl}oxirane (**42**)

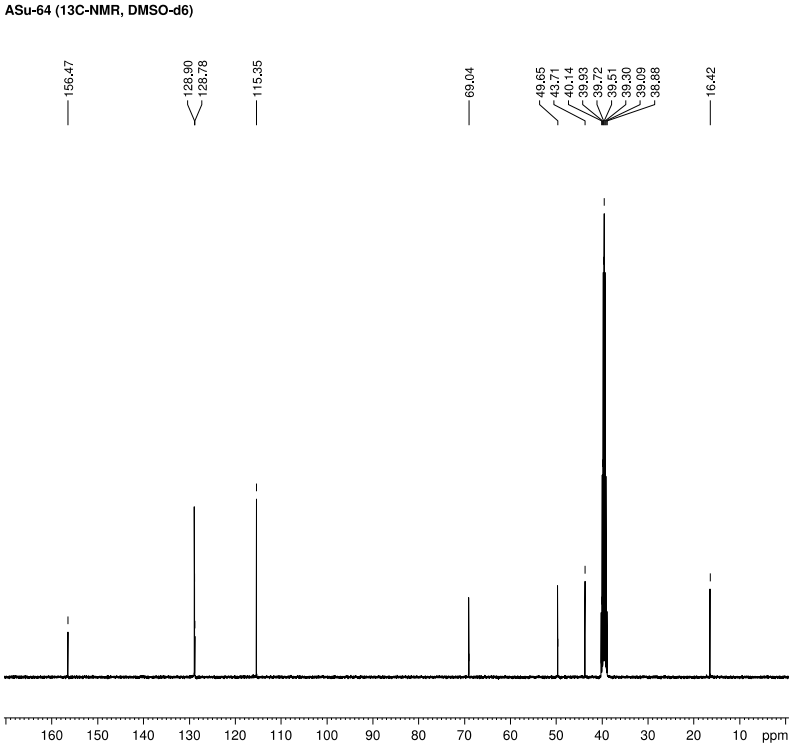


(2*S*)-2-{[4-(Methylsulfanyl)phenoxy]methyl}oxirane (**43**)

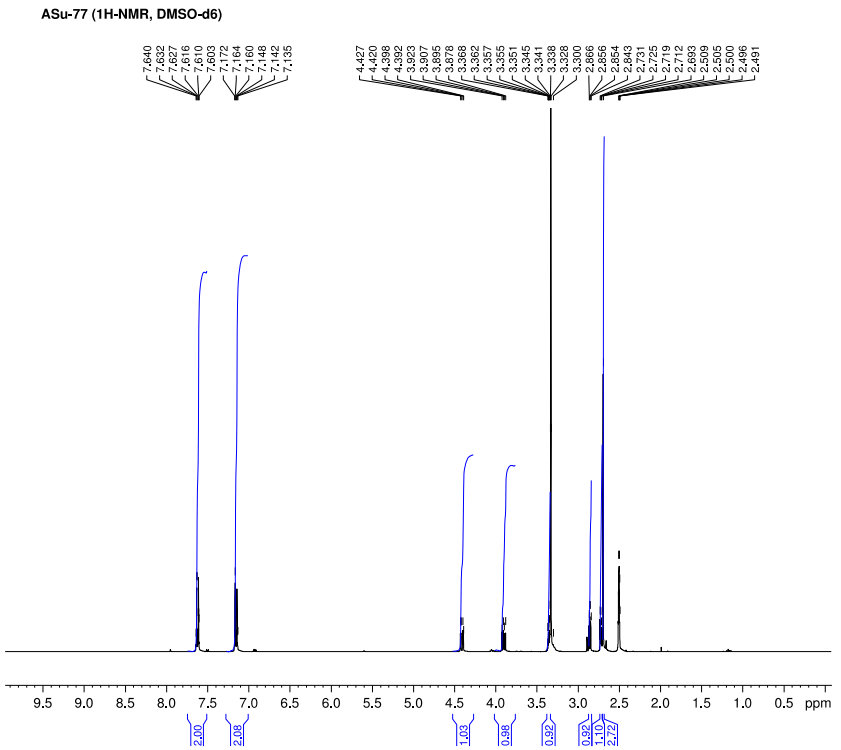



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                  320
PROCNO                   1

F2 - Acquisition Parameters
Date_           20220928
Time               10.10
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG            zg30
TD                65536
SOLVENT            DMSO
NS                   16
DS                    2
SWH           8223.685 Hz
FIDRES        0.125483 Hz
AQ            3.9845889 sec
RG                  101
DW             60.800 usec
DE             10.00 usec
TE                298.1 K
D1           1.00000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                  1H
P1              9.75 usec
PL1             -5.00 dB
PL1W       30.18447304 W
SFO1      400.1324710 MHz

F2 - Processing parameters
SI                32768
SF          400.1300030 MHz
WDW                  EM
SSB                   0
LB             0.30 Hz
GB                    0
PC                 1.00
```




```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                  321
PROCNO                   1

F2 - Acquisition Parameters
Date_           20220928
Time               19.36
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG          zgpg30
TD                65536
SOLVENT            DMSO
NS                 1024
DS                    4
SWH          24038.461 Hz
FIDRES        0.366798 Hz
AQ            1.3631488 sec
RG                 2050
DW             20.800 usec
DE             10.00 usec
TE                298.6 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                 13C
P1             10.00 usec
PL1             -2.70 dB
PL1W       62.67650986 W
SFO1      100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2        waltz16
NUC2                  1H
PCPD2          60.00 usec
PL2             -5.00 dB
PL12            10.78 dB
PL13            15.00 dB
PL2W       30.18447304 W
PL12W       0.79759723 W
PL13W       0.30184472 W
SFO2      400.1316005 MHz

F2 - Processing parameters
SI                32768
SF          100.6128193 MHz
WDW                  EM
SSB                   0
LB             1.00 Hz
GB                    0
PC                 1.40
```

(2*R*)-2-[(4-Methanesulfinylphenoxy)methyl]oxirane (**44**)

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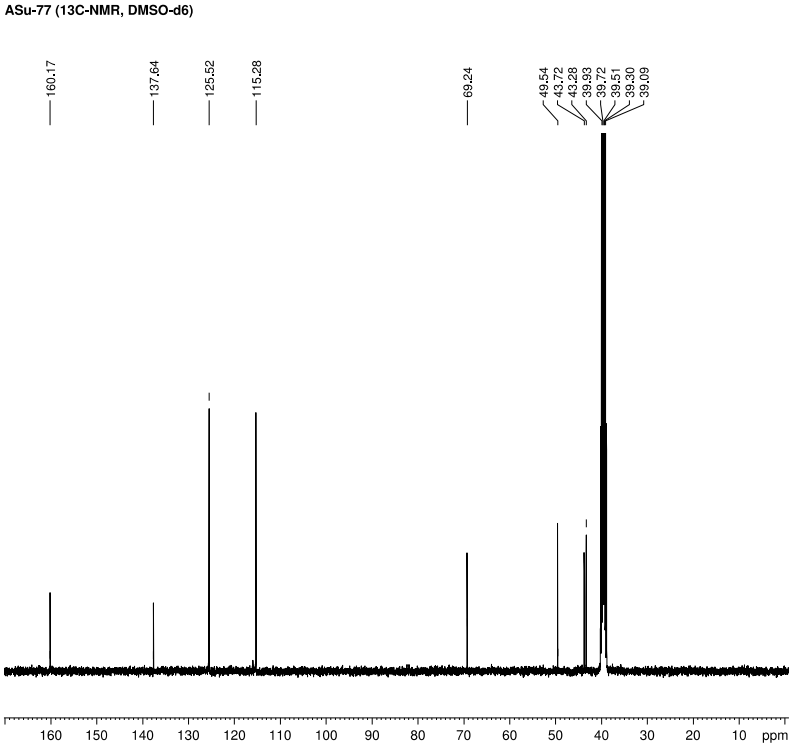
```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                 409
PROCNO                  1

F2 - Acquisition Parameters
Date_           20230426
Time              10.19
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG           zg30
TD               65536
SOLVENT           DMSO
NS                   16
DS                    2
SWH            8223.685 Hz
FIDRES        0.125483 Hz
AQ            3.9845889 sec
RG                 90.5
DW               60.800 usec
DE               10.00 usec
TE               298.0 K
D1            1.00000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                 1H
P1                9.75 usec
PL1              -5.00 dB
PL1W        30.18447304 W
SFO1       400.1324710 MHz

F2 - Processing parameters
SI                32768
SF           400.1300033 MHz
WDW                  EM
SSB                   0
LB                0.30 Hz
GB                    0
PC                1.00
```

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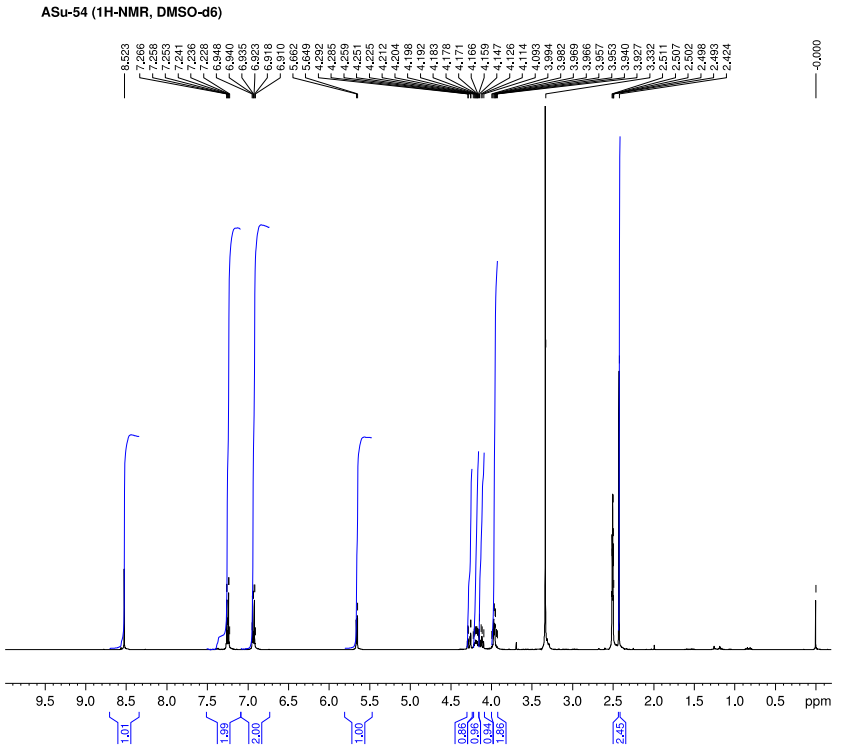
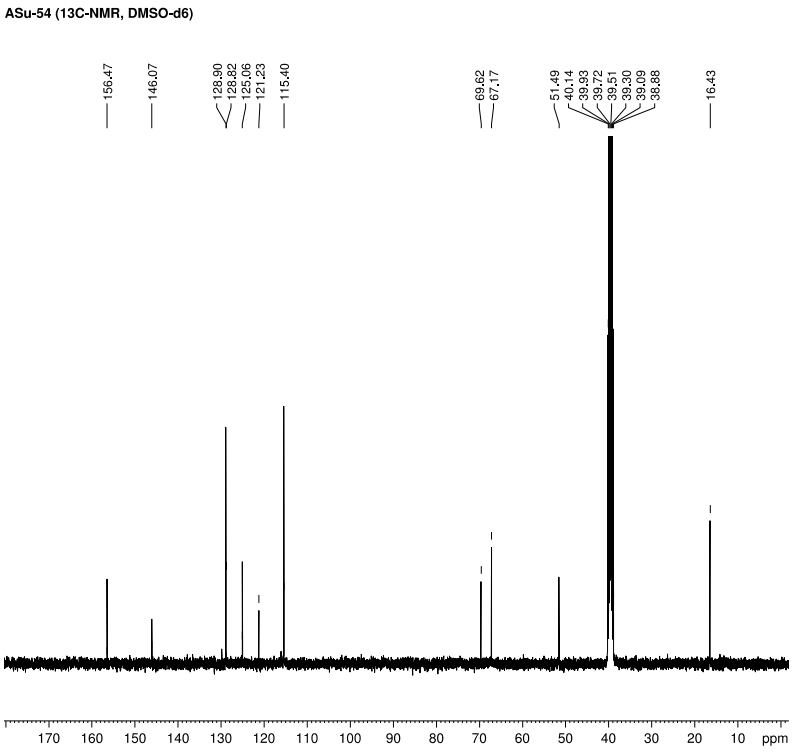
```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                 410
PROCNO                  1

F2 - Acquisition Parameters
Date_           20230426
Time              13.49
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG         zgpg30
TD               65536
SOLVENT           DMSO
NS                 1024
DS                    4
SWH           24038.461 Hz
FIDRES        0.366798 Hz
AQ            1.3631488 sec
RG                 2050
DW               20.800 usec
DE               10.00 usec
TE               298.2 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                13C
P1               10.00 usec
PL1              -2.70 dB
PL1W        62.67650986 W
SFO1       100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2        waltz16
NUC2                1H
PCPD2            60.00 usec
PL2              -5.00 dB
PL12             10.78 dB
PL13             15.00 dB
PL2W        30.18447304 W
PL12W        0.79759723 W
PL13W        0.30184472 W
SFO2       400.1316005 MHz

F2 - Processing parameters
SI                32768
SF           100.6128180 MHz
WDW                  EM
SSB                   0
LB                1.00 Hz
GB                    0
PC                1.40
```

1-(2-Bromo-4-nitro-1*H*-imidazol-1-yl)-3-[4-(methylsulfanyl)phenoxy]propan-2-ol (**45**)

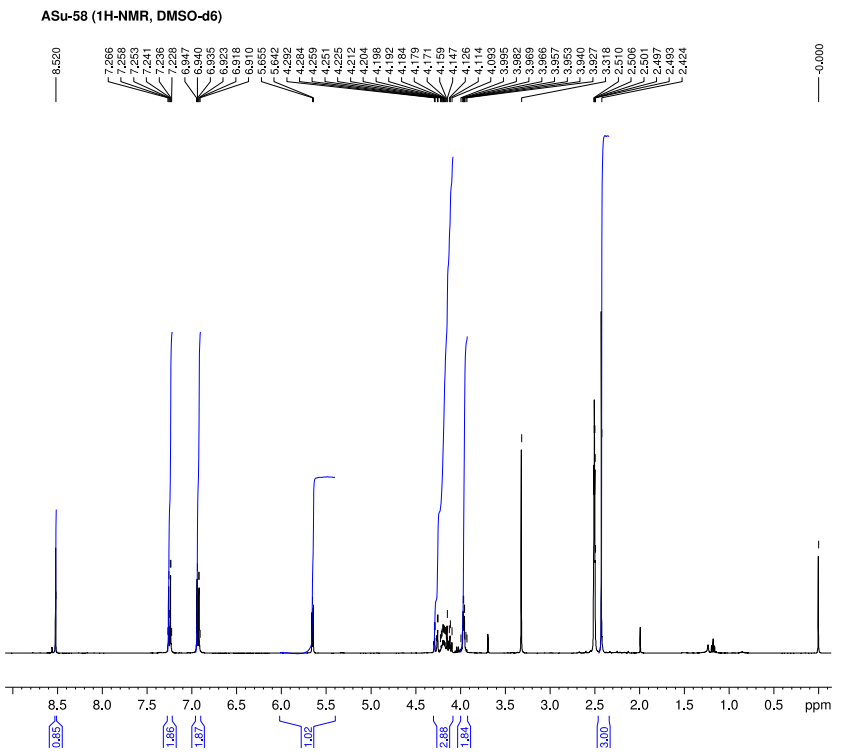



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                 267
PROCNO                  1

F2 - Acquisition Parameters
Date_           20220722
Time              11.46
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG           zg30
TD               65536
SOLVENT           DMSO
NS                  17
DS                   2
SWH           8223.685 Hz
FIDRES        0.125483 Hz
AQ            3.9845889 sec
RG                 128
DW              60.800 usec
DE              10.00 usec
TE              296.8 K
D1          1.00000000 sec
TD0                  1

======== CHANNEL f1 ========
NUC1                1H
P1               9.75 usec
PL1             -5.00 dB
PL1W       30.18447304 W
SFO1       400.1324710 MHz

F2 - Processing parameters
SI               32768
SF          400.1300027 MHz
WDW                 EM
SSB                  0
LB              0.30 Hz
GB                   0
PC              1.00
```




```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                 465
PROCNO                  1

F2 - Acquisition Parameters
Date_           20230802
Time              23.11
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG         zgpg30
TD               65536
SOLVENT           DMSO
NS                1024
DS                   4
SWH          24038.461 Hz
FIDRES        0.366798 Hz
AQ            1.3631488 sec
RG                2050
DW              20.800 usec
DE              10.00 usec
TE              298.7 K
D1          2.00000000 sec
D11         0.03000000 sec
TD0                  1

======== CHANNEL f1 ========
NUC1                13C
P1              10.00 usec
PL1             -2.70 dB
PL1W       62.67650986 W
SFO1      100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2         waltz16
NUC2                1H
PCPD2           60.00 usec
PL2             -5.00 dB
PL12            10.78 dB
PL13            15.00 dB
PL2W       30.18447304 W
PL12W       0.79759723 W
PL13W       0.30184472 W
SFO2      400.1316005 MHz

F2 - Processing parameters
SI               32768
SF          100.6128187 MHz
WDW                 EM
SSB                  0
LB              1.00 Hz
GB                   0
PC              1.40
```

(2*R*)-1-(2-Bromo-4-nitro-1*H*-imidazol-1-yl)-3-[4-(methylsulfanyl)phenoxy]propan-2-ol (**46**)

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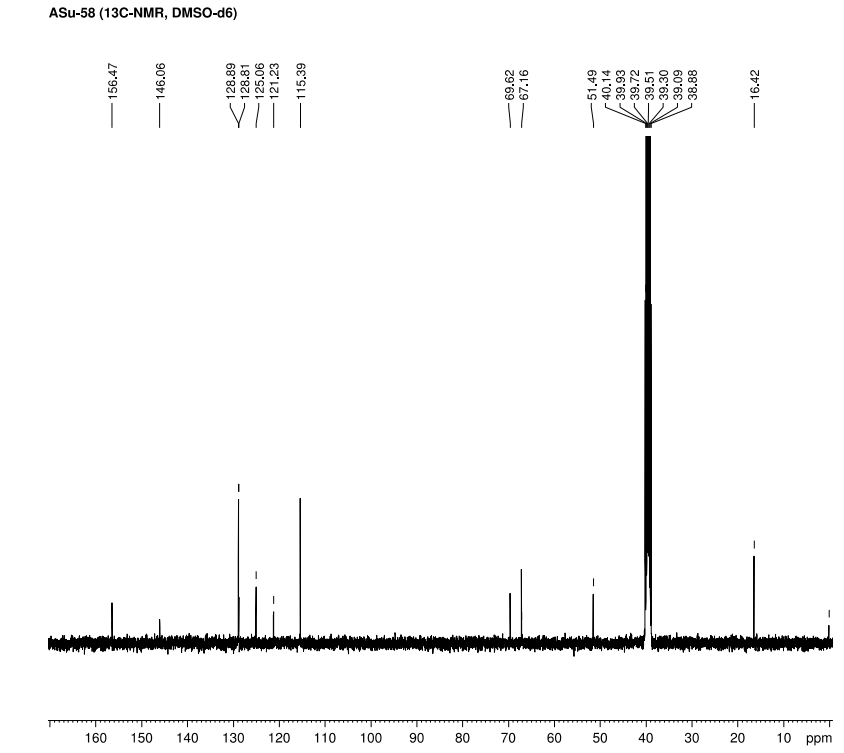
```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                  315
PROCNO                   1

F2 - Acquisition Parameters
Date_              20220927
Time                 11.25
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG              zg30
TD                  65536
SOLVENT               DMSO
NS                      16
DS                       2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ              3.9845889 sec
RG                     203
DW                60.800 usec
DE                10.00 usec
TE                298.3 K
D1             1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    1H
P1                   9.75 usec
PL1                 -5.00 dB
PL1W         30.18447304 W
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                   32768
SF           400.1300030 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    1.00
```

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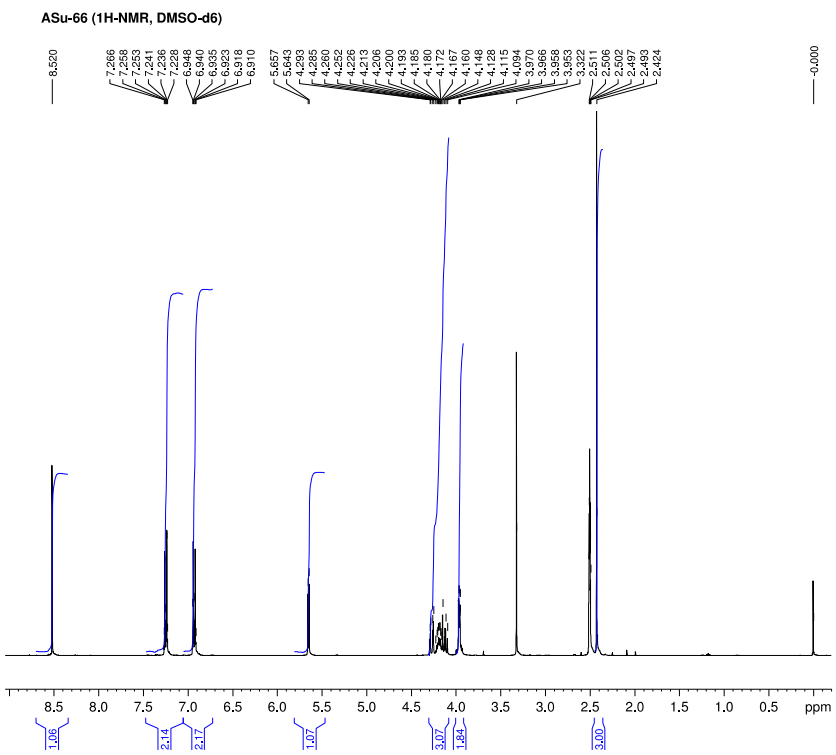
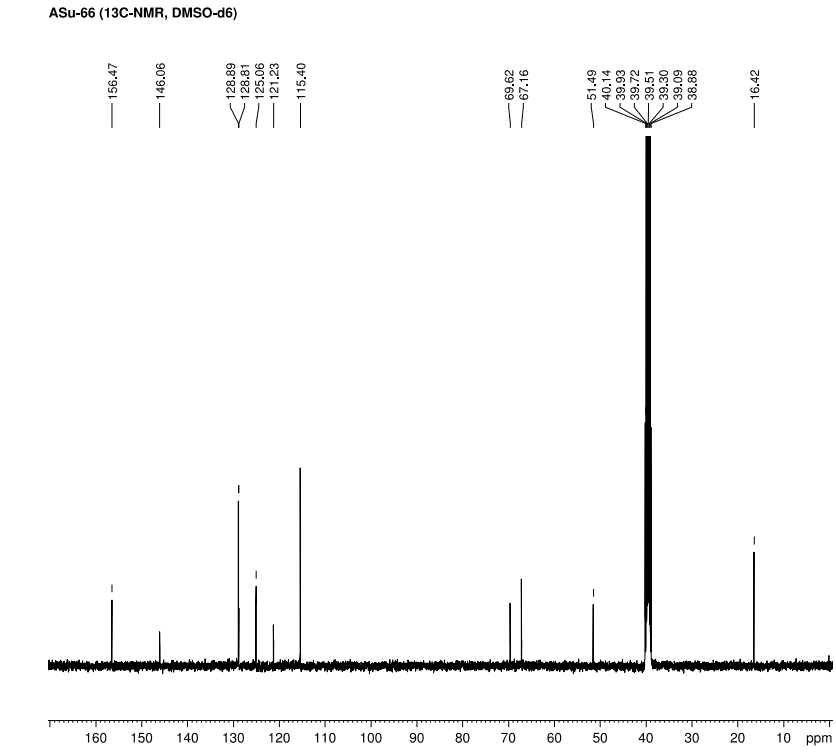
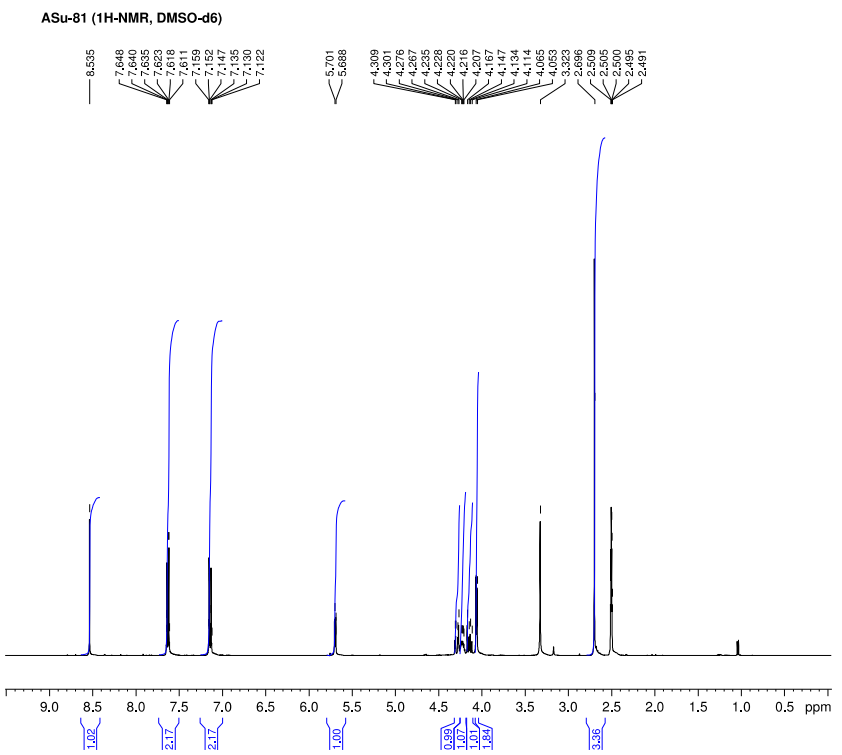
```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                  317
PROCNO                   1

F2 - Acquisition Parameters
Date_              20220927
Time                 22.40
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG           zgpg30
TD                  65536
SOLVENT               DMSO
NS                    1024
DS                       4
SWH            24038.461 Hz
FIDRES          0.366798 Hz
AQ              1.3631488 sec
RG                    2050
DW                20.800 usec
DE                10.00 usec
TE                298.6 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                   13C
P1                  10.00 usec
PL1                 -2.70 dB
PL1W         62.67650986 W
SFO1         100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                    1H
PCPD2               60.00 usec
PL2                 -5.00 dB
PL12                10.78 dB
PL13                15.00 dB
PL2W         30.18447304 W
PL12W         0.79759723 W
PL13W         0.30184472 W
SFO2         400.1316005 MHz

F2 - Processing parameters
SI                   32768
SF           100.6128194 MHz
WDW                     EM
SSB                      0
LB                    1.00 Hz
GB                       0
PC                    1.40
```

(2*S*)-1-(2-Bromo-4-nitro-1*H*-imidazol-1-yl)-3-[4-(methylsulfanyl)phenoxy]propan-2-ol (**47**)

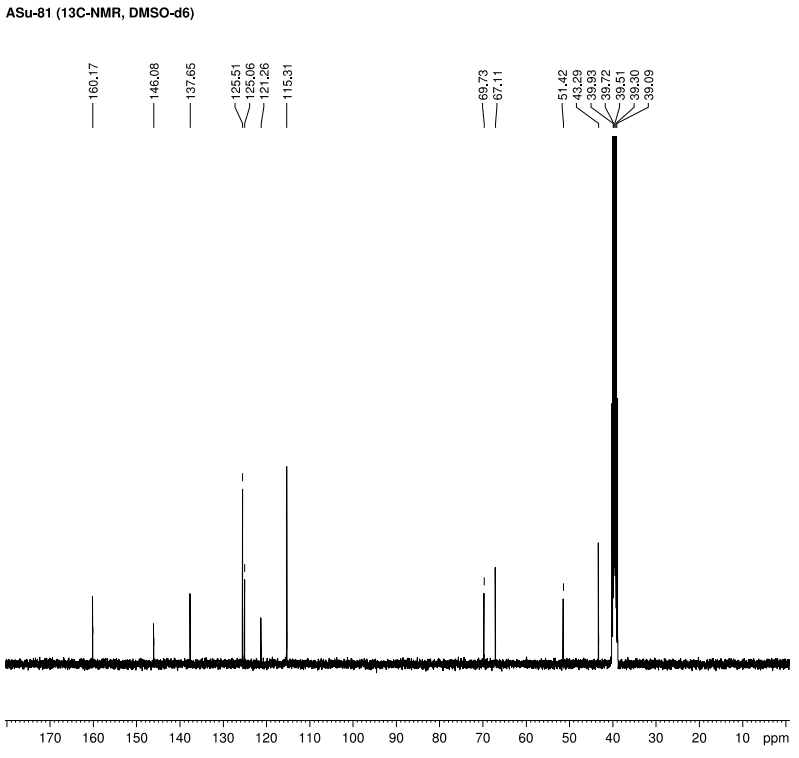


(2*R*)-1-(2-Bromo-4-nitro-1H-imidazol-1-yl)-3-(4-methanesulfinylphenoxy)propan-2-ol (**48**)

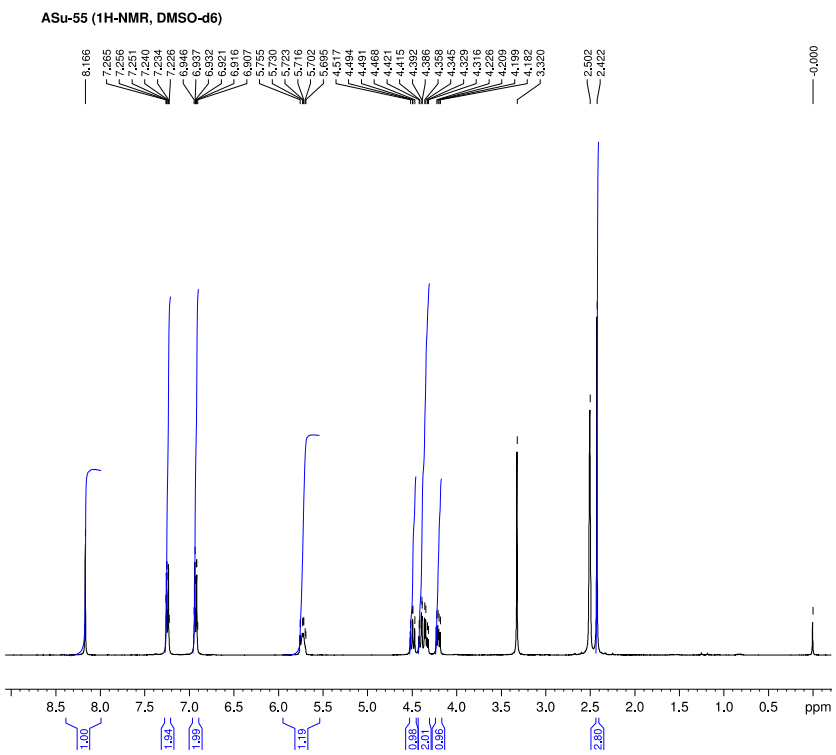



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                  414
PROCNO                   1

F2 - Acquisition Parameters
Date_           20230503
Time              15.03
INSTRUM           spect
PROBHD    5 mm PABBO BB-
PULPROG            zg30
TD                65536
SOLVENT            DMSO
NS                   16
DS                    2
SWH            8223.685 Hz
FIDRES        0.125483 Hz
AQ            3.9845889 sec
RG                  101
DW               60.800 usec
DE               10.00 usec
TE               298.1 K
D1            1.00000000 sec
TD0                  1

======== CHANNEL f1 ========
NUC1                1H
P1                9.75 usec
PL1              -5.00 dB
PL1W        30.18447304 W
SFO1       400.1324710 MHz

F2 - Processing parameters
SI                32768
SF          400.1300034 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 1.00
```

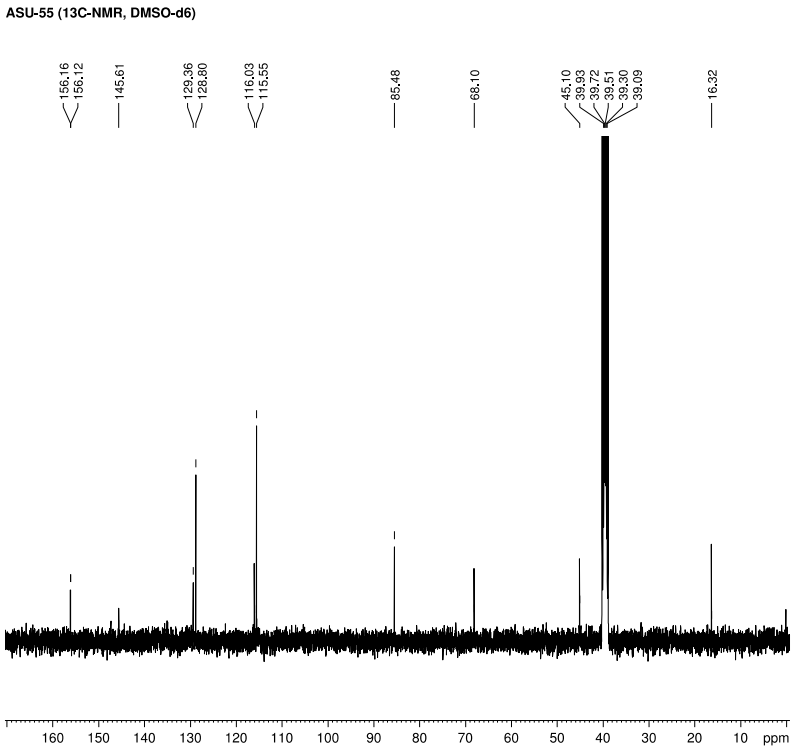



```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                  416
PROCNO                   1

F2 - Acquisition Parameters
Date_           20230504
Time              10.48
INSTRUM           spect
PROBHD    5 mm PABBO BB-
PULPROG          zgpg30
TD                65536
SOLVENT            DMSO
NS                 1024
DS                    4
SWH           24038.461 Hz
FIDRES        0.366798 Hz
AQ            1.3631488 sec
RG                 2050
DW               20.800 usec
DE               10.00 usec
TE               298.2 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                  1

======== CHANNEL f1 ========
NUC1                13C
P1               10.00 usec
PL1              -2.70 dB
PL1W        62.67650986 W
SFO1       100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2         waltz16
NUC2                1H
PCPD2            60.00 usec
PL2              -5.00 dB
PL12             10.78 dB
PL13             15.00 dB
PL2W        30.18447304 W
PL12W        0.79759723 W
PL13W        0.30184472 W
SFO2       400.1316005 MHz

F2 - Processing parameters
SI                32768
SF          100.6128187 MHz
WDW                  EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 1.40
```

2-{[4-(Methylsulfanyl)phenoxy]methyl}-6-nitro-2*H*,3*H*-imidazo[2,1-b][1,3]oxazole (**49**)

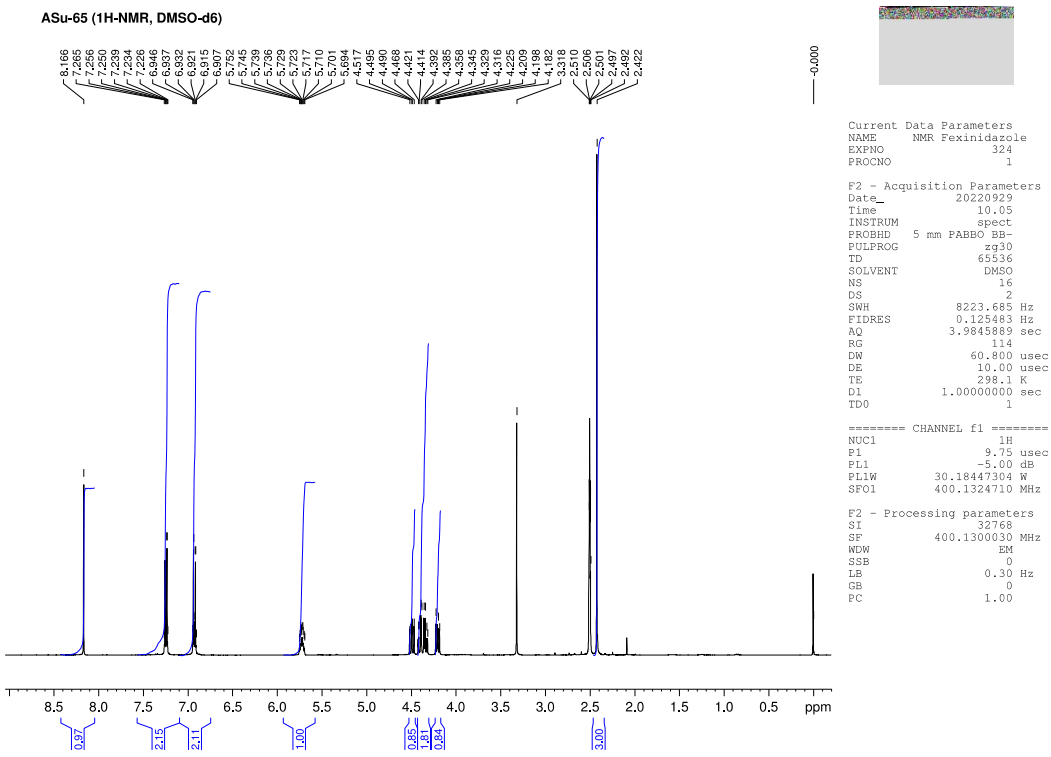


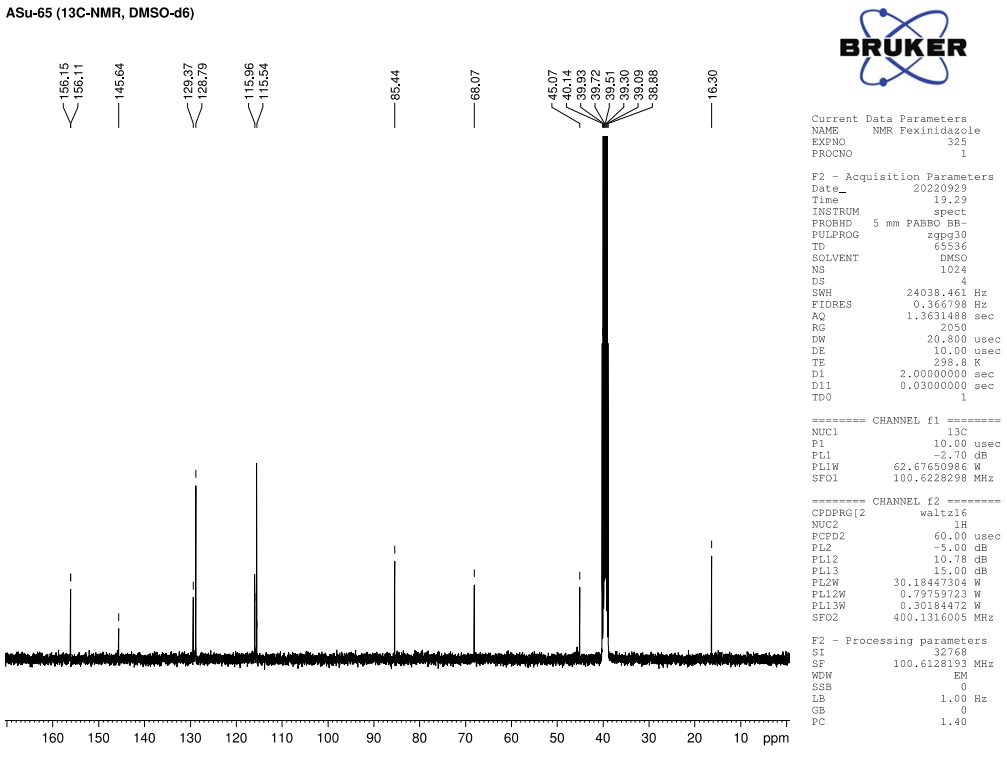

```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                 351
PROCNO                  1

F2 - Acquisition Parameters
Date_           20221025
Time              11.21
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG           zg30
TD               65536
SOLVENT           DMSO
NS                  16
DS                   2
SWH           8223.685 Hz
FIDRES        0.125483 Hz
AQ            3.9845889 sec
RG                 114
DW              60.800 usec
DE              10.00 usec
TE              298.1 K
D1           1.00000000 sec
TD0                  1

======== CHANNEL f1 ========
NUC1                1H
P1               9.75 usec
PL1             -5.00 dB
PL1W       30.18447304 W
SFO1      400.1324710 MHz

F2 - Processing parameters
SI               32768
SF        400.1300029 MHz
WDW                 EM
SSB                  0
LB                0.30 Hz
GB                   0
PC                1.00
```



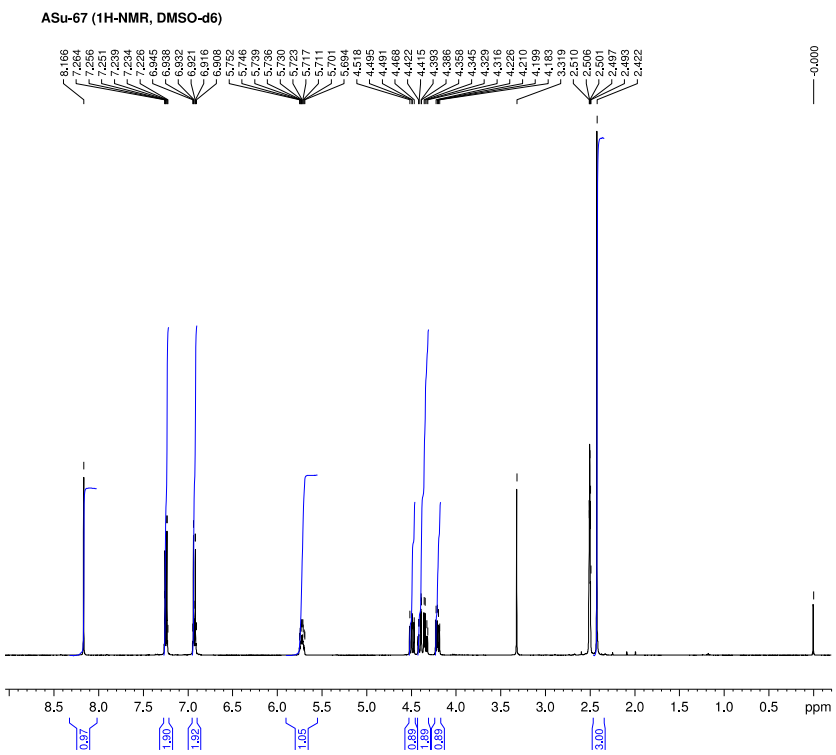

```
Current Data Parameters
NAME      NMR Fexinidazole
EXPNO                 270
PROCNO                  1

F2 - Acquisition Parameters
Date_           20220729
Time              10.54
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG         zgpg30
TD               65536
SOLVENT           DMSO
NS                1024
DS                   4
SWH          24038.461 Hz
FIDRES        0.366798 Hz
AQ            1.3631488 sec
RG                2050
DW              20.800 usec
DE              10.00 usec
TE              298.1 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                  1

======== CHANNEL f1 ========
NUC1                13C
P1              10.00 usec
PL1             -2.70 dB
PL1W       62.67650986 W
SFO1      100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2        waltz16
NUC2                1H
PCPD2           60.00 usec
PL2             -5.00 dB
PL12            10.78 dB
PL13            15.00 dB
PL2W       30.18447304 W
PL12W       0.79759723 W
PL13W       0.30184472 W
SFO2      400.1316005 MHz

F2 - Processing parameters
SI               32768
SF        100.6128180 MHz
WDW                 EM
SSB                  0
LB                1.00 Hz
GB                   0
PC                1.40
```

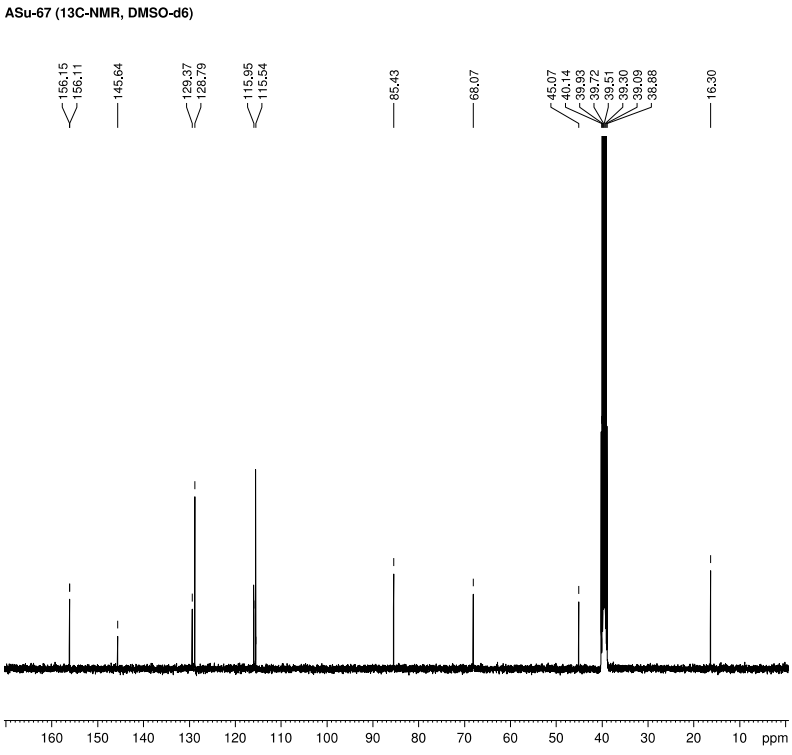
(2*R*)-2-{[4-(Methylsulfanyl)phenoxy]methyl}-6-nitro-2*H*,3*H*-imidazo[2,1-b][1,3]oxazole (**50**)



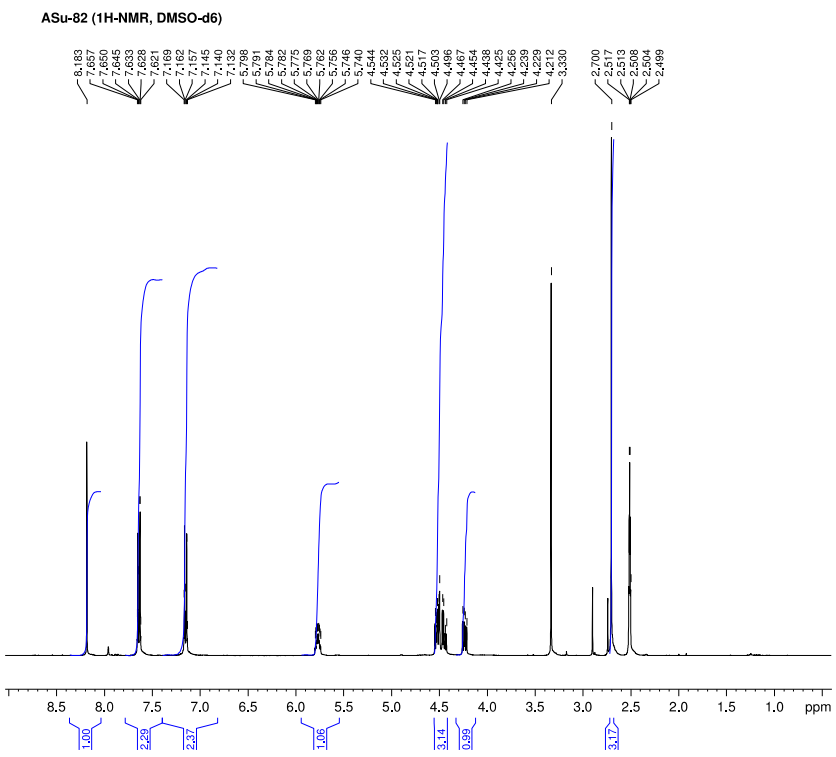



(2*S*)-2-{[4-(Methylsulfanyl)phenoxy]methyl}-6-nitro-2*H*,3*H*-imidazo[2,1-b][1,3]oxazole (**51**)

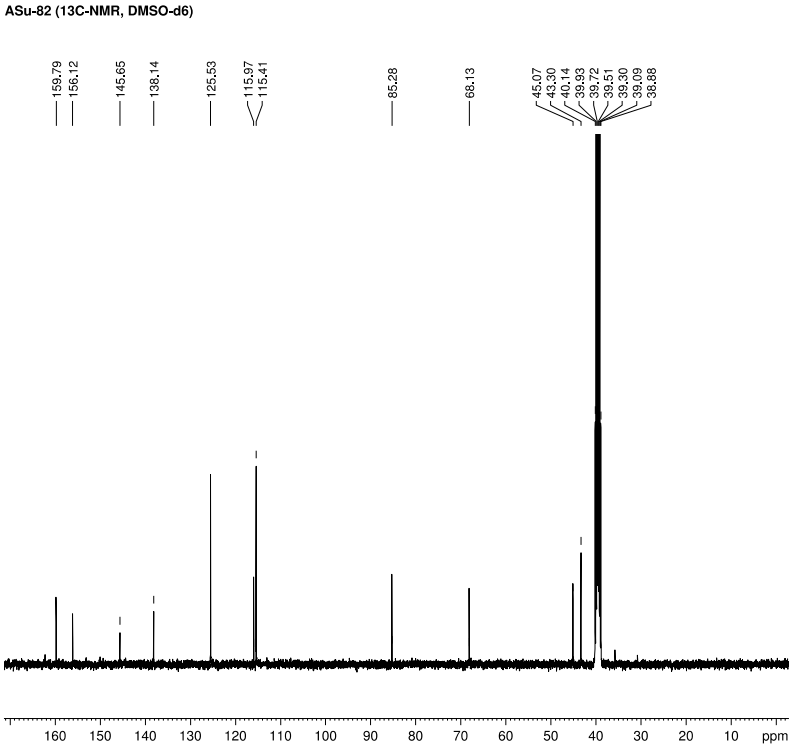


(2*S*)-2-[(4-Methanesulfinylphenoxy)methyl]-6-nitro-2*H*,3*H*-imidazo[2,1-b][1,3]oxazole (**52**)

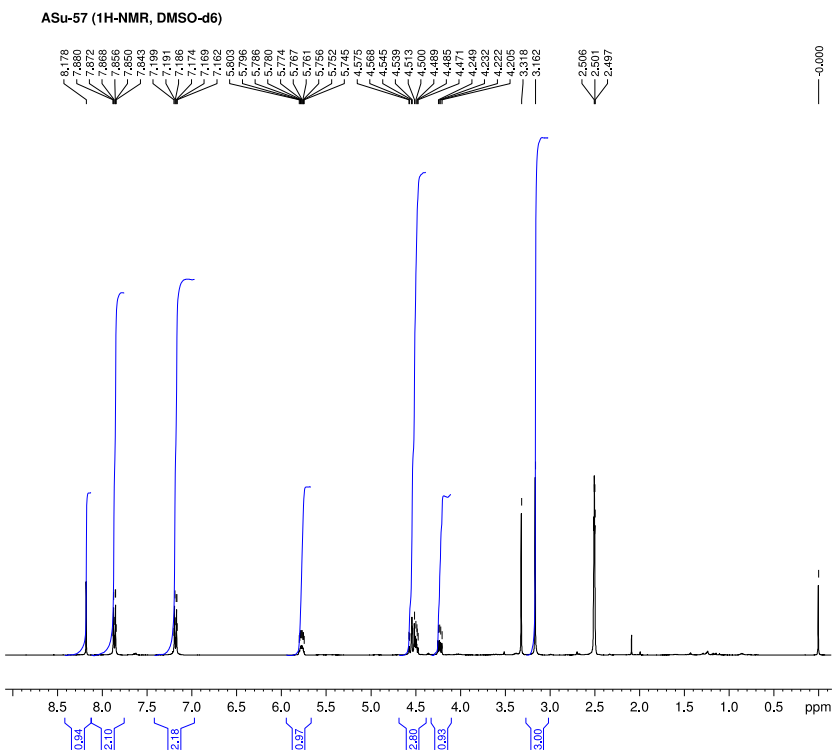


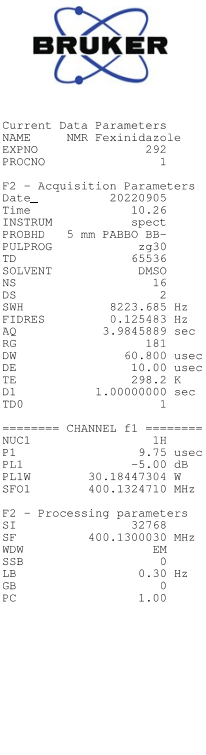

```
Current Data Parameters
NAME       NMR Fexinidazole
EXPNO                   420
PROCNO                    1

F2 - Acquisition Parameters
Date_           20230508
Time              10.37
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG           zg30
TD               65536
SOLVENT           DMSO
NS                  16
DS                   2
SWH           8223.685 Hz
FIDRES        0.125483 Hz
AQ            3.9845889 sec
RG                 101
DW              60.800 usec
DE              10.00 usec
TE              298.1 K
D1          1.00000000 sec
TD0                  1

======== CHANNEL f1 ========
NUC1                1H
P1                9.75 usec
PL1              -5.00 dB
PL1W       30.18447304 W
SFO1       400.1324710 MHz

F2 - Processing parameters
SI               32768
SF          400.1300000 MHz
WDW                 EM
SSB                  0
LB                0.30 Hz
GB                   0
PC                1.00
```

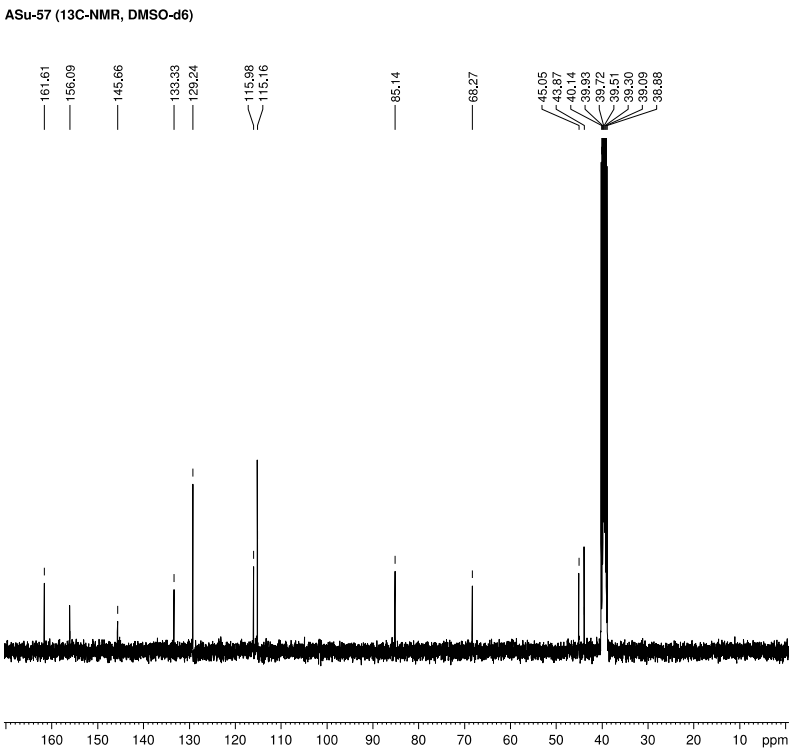


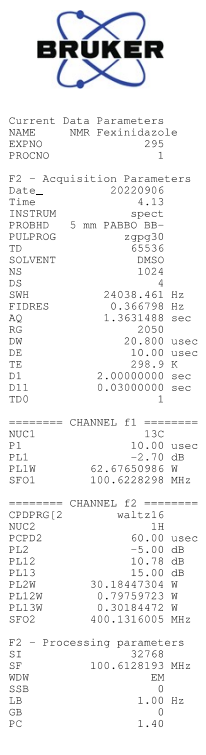

```
Current Data Parameters
NAME       NMR Fexinidazole
EXPNO                   425
PROCNO                    1

F2 - Acquisition Parameters
Date_           20230508
Time              18.37
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG         zgpg30
TD               65536
SOLVENT           DMSO
NS                1024
DS                   4
SWH          24038.461 Hz
FIDRES        0.366798 Hz
AQ            1.3631488 sec
RG                2050
DW              20.800 usec
DE              10.00 usec
TE              298.8 K
D1          2.00000000 sec
D11         0.03000000 sec
TD0                  1

======== CHANNEL f1 ========
NUC1               13C
P1              10.00 usec
PL1             -2.70 dB
PL1W       62.67650986 W
SFO1      100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2        waltz16
NUC2                1H
PCPD2            60.00 usec
PL2             -5.00 dB
PL12             10.78 dB
PL13             15.00 dB
PL2W       30.18447304 W
PL12W       0.79759723 W
PL13W       0.30184472 W
SFO2      400.1316005 MHz

F2 - Processing parameters
SI               32768
SF          100.6128193 MHz
WDW                 EM
SSB                  0
LB                1.00 Hz
GB                   0
PC                1.40
```

2-[(4-Methanesulfonylphenoxy)methyl]-6-nitro-2*H*,3*H*-imidazo[2,1-b][1,3]oxazole (**53**)

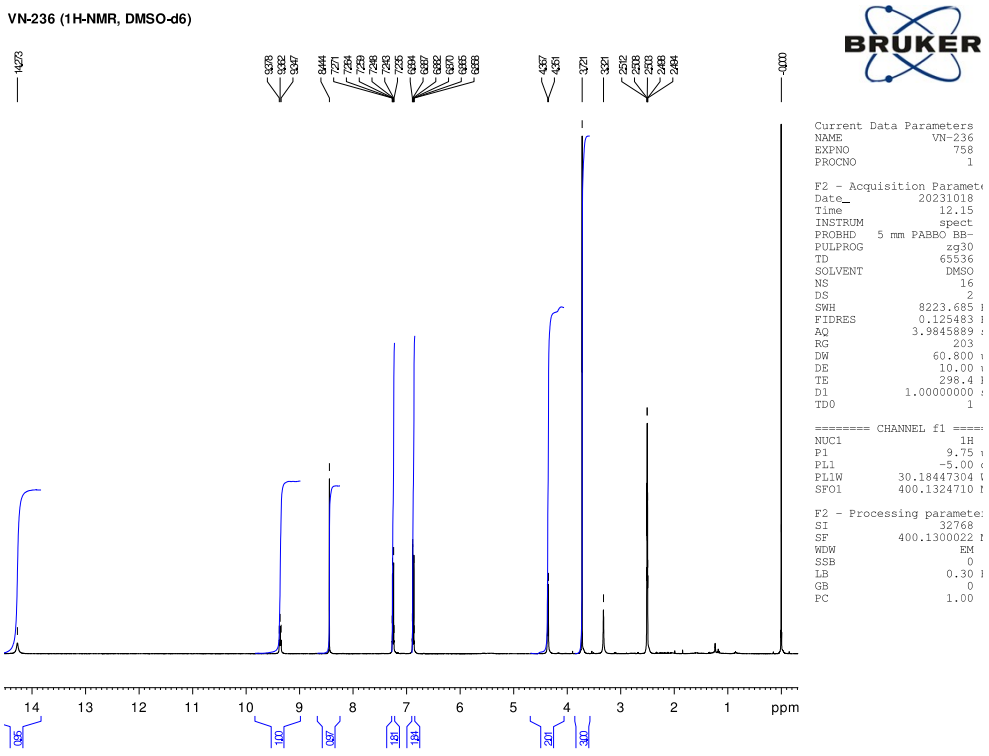


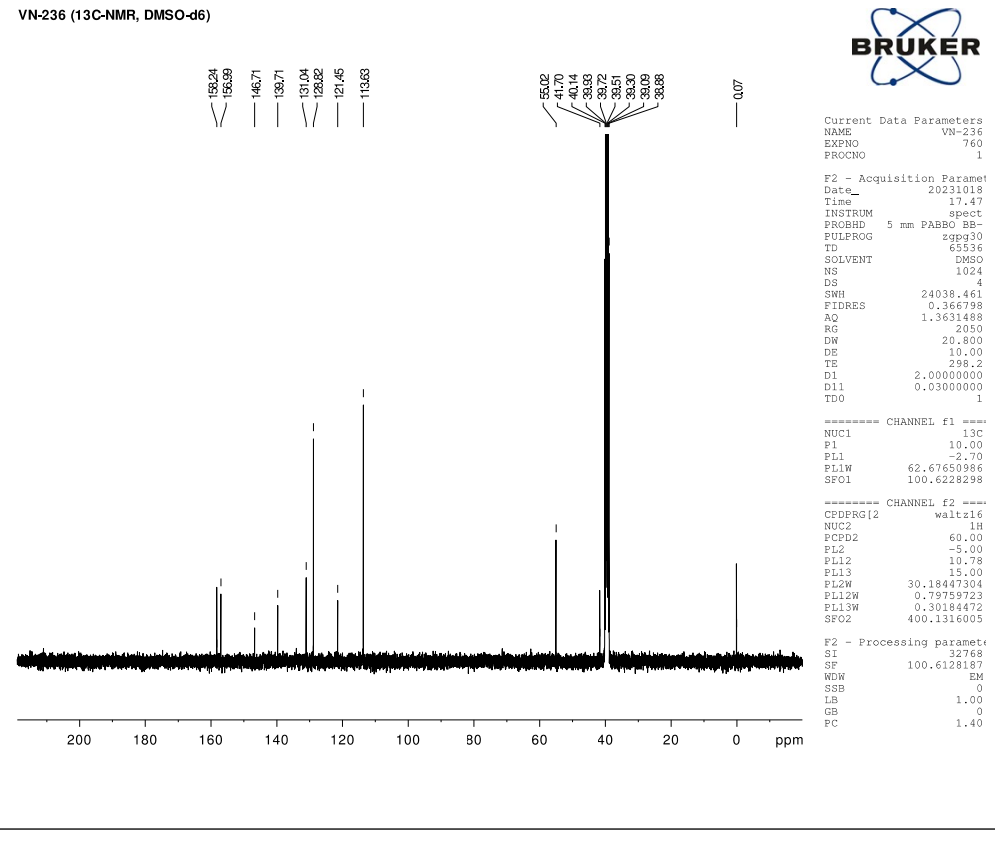



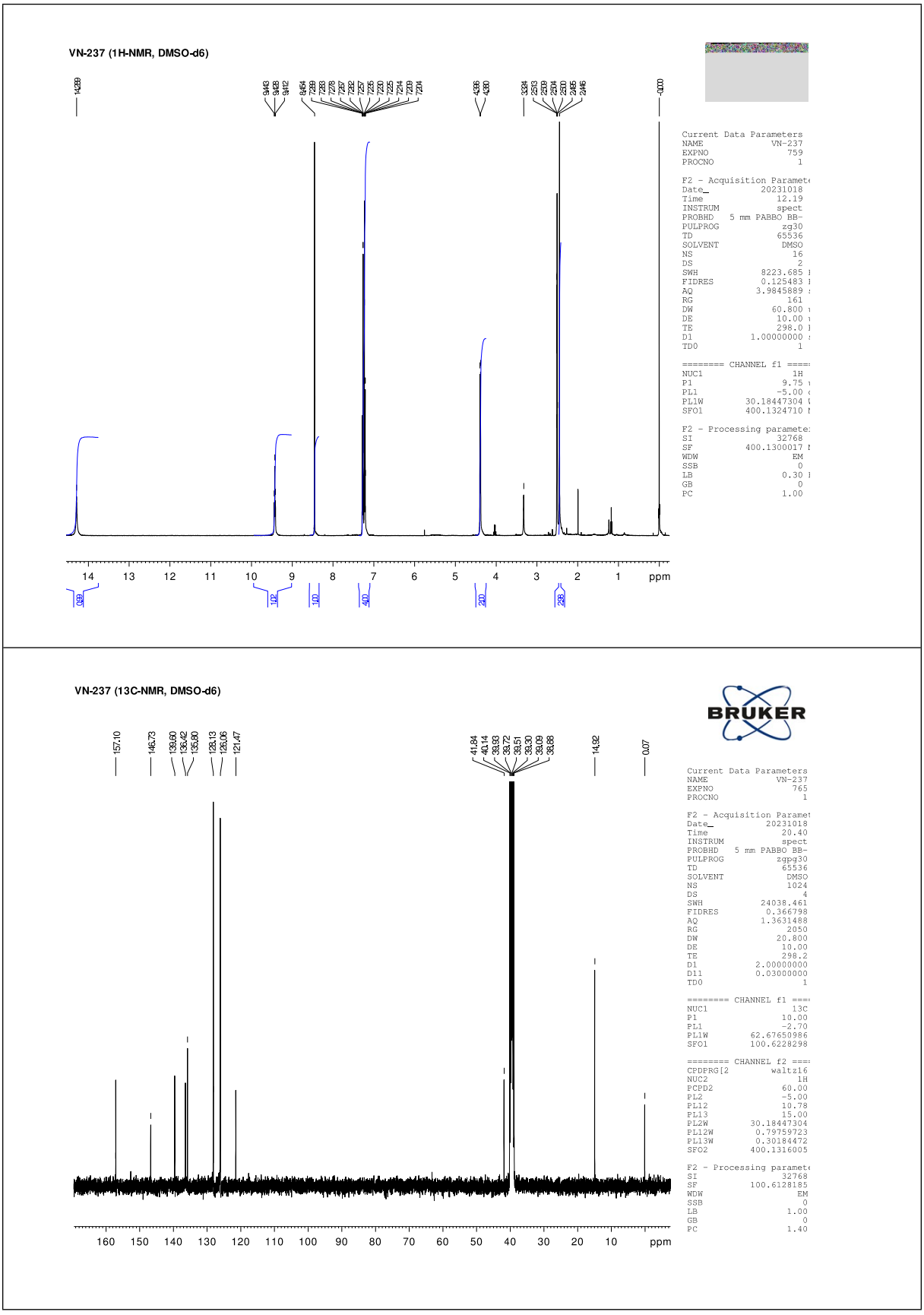



*N*-(4-Methoxybenzyl)-5-nitro-1*H*-imidazole-2-carboxamide (**54**)

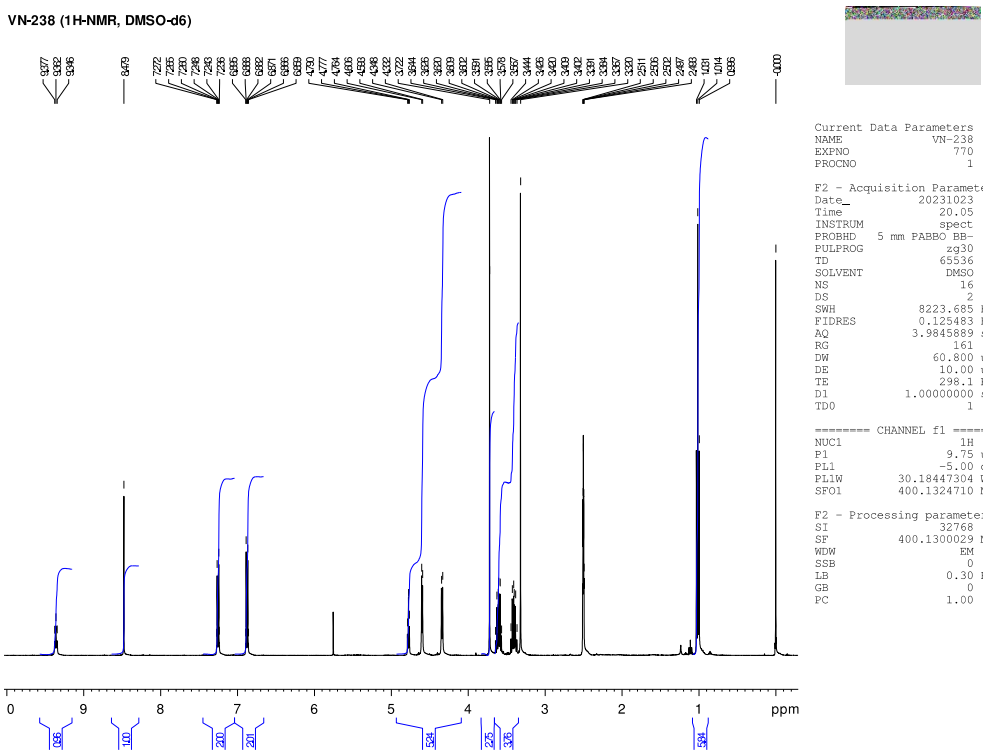


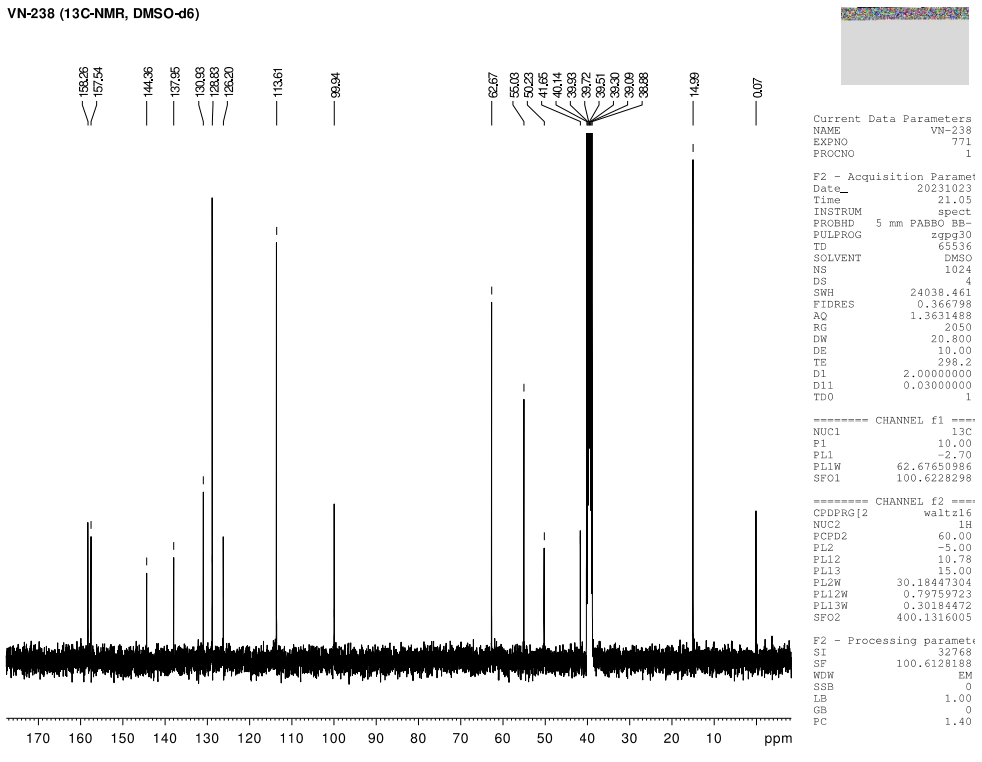



*N*-[4-(Methylthio)benzyl]-5-nitro-1*H*-imidazole-2-carboxamide (**55**)

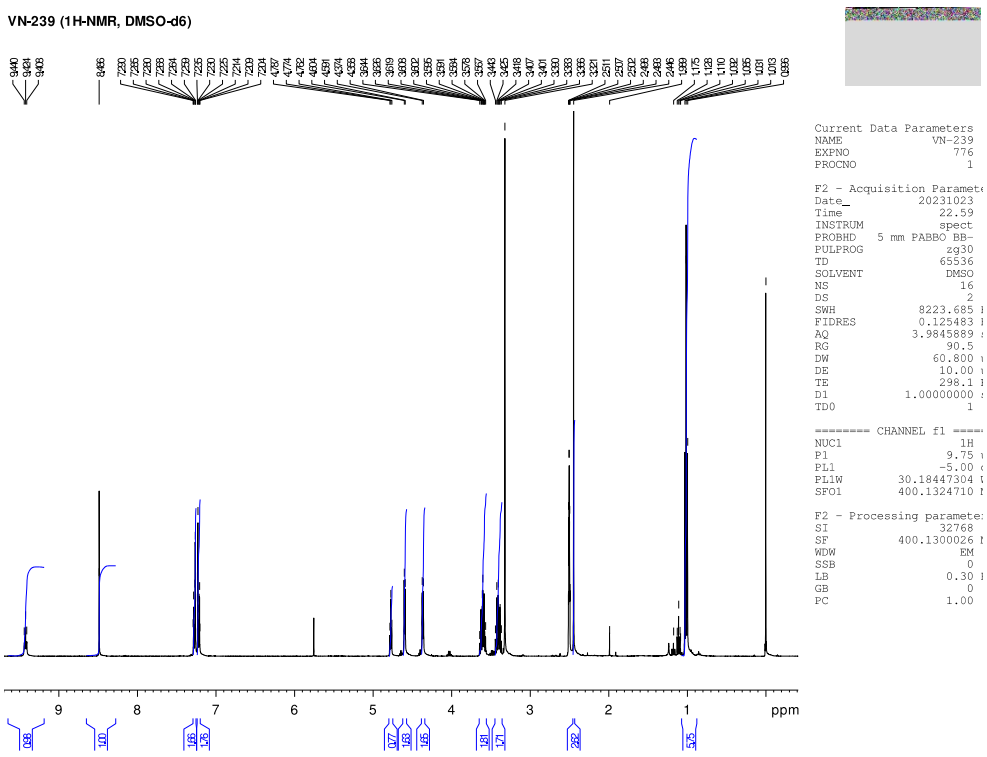


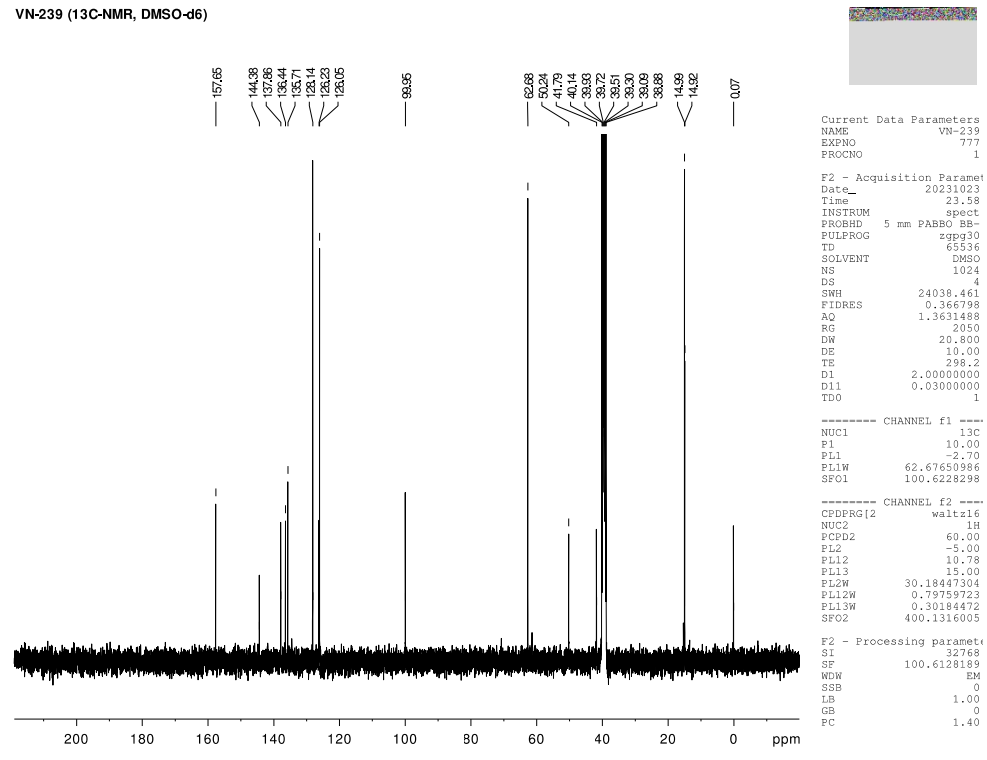
1-(2,2-Diethoxypropyl)-*N*-[(4-methoxyphenyl)methyl]-5-nitro-1*H*-imidazole-2-carbox amide (**56**)



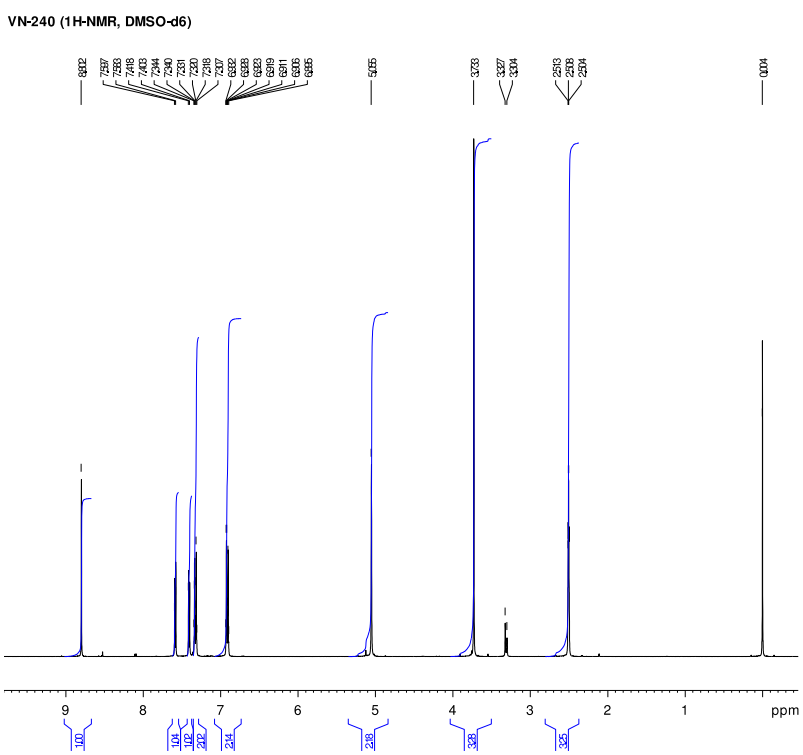



1-(2,2-Diethoxypropyl)-N-{[4-(methylsulfanyl)phenyl]methyl}-5-nitro-1*H*-imidazole-2-carboxamide (**57**)



7-[(4-Methoxyphenyl)methyl]-2-nitro-5*H*,6*H*,7*H*,8*H*-imidazo[1,2-a]pyrazin-8-one (**58**)



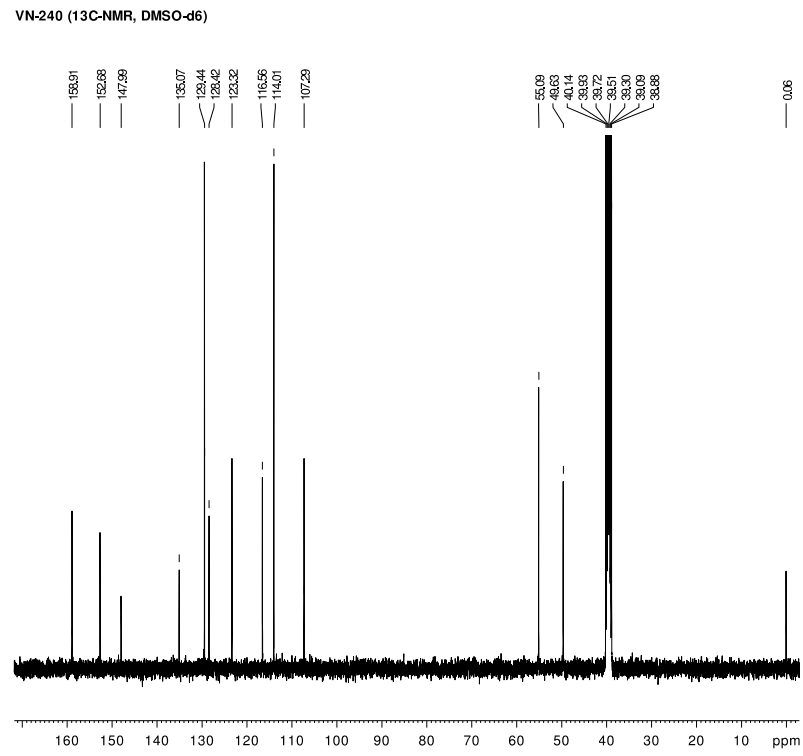


Current Data Parameters
NAME VN-240
EXPNO 539
PROCNO 1

F2 - Acquisition Paramete
Date_ 20221122
Time 15.59
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 16
DS 2
SWH 8223.685
FIDRES 0.125483
AQ 3.9845889
RG 114
DW 60.800
DE 10.00
TE 298.2
D1 1.00000000
TD0 1

======== CHANNEL f1 ====
NUC1 1H
P1 9.75
PL1 -5.00
PL1W 30.18447304
SFO1 400.1324710

F2 - Processing paramete
SI 32768
SF 400.1300015
WDW EM
SSB 0
LB 0.30
GB 0
PC 1.00



Current Data Parameters
NAME VN-240
EXPNO 540
PROCNO 1

F2 - Acquisition Paramet
Date_ 20221124
Time 18.47
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 1024
DS 4
SWH 24038.461
FIDRES 0.366798
AQ 1.3631488
RG 2050
DW 20.800
DE 10.00
TE 298.1
D1 2.00000000
D11 0.03000000
TD0 1

======== CHANNEL f1 ====
NUC1 13C
P1 10.00
PL1 -2.70
PL1W 62.67650986
SFO1 100.6228298

======== CHANNEL f2 ====
CPDPRG[2 waltz16
NUC2 1H
PCPD2 60.00
PL2 -5.00
PL12 10.78
PL13 15.00
PL2W 30.18447304
PL12W 0.79759723
PL13W 0.30184472
SFO2 400.1316005

F2 - Processing paramete
SI 32768
SF 100.6128191
WDW EM
SSB 0
LB 1.00
GB 0
PC 1.40

7-{[4-(Methylsulfanyl)phenyl]methyl}-2-nitro-5*H*,6*H*,7*H*,8*H*-imidazo[1,2-a]pyrazin-8-one (**59**)