

Supporting Information

for

C-5'-Triazolyl-2'-oxa-3'-aza-4'a-carbanucleosides:

Synthesis and biological evaluation

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¹H and ¹³C NMRS7

Experimental section

General: Solvents and reagents are commercial. HRMS were determined with a SQ Quantum XLS Triple Quadrupole GC-MS/MS. NMR spectra (^1H NMR at 300 and 500 MHz, ^{13}C NMR at 75 and 126 MHz) were recorded with Varian instruments and are reported in ppm relative to TMS. Merck silica gel 60-F254 precoated aluminum plates have been used for thin-layer chromatographic separations. Flash chromatography was performed on Merck silica gel (200–400 mesh). Preparative separations were carried out by a MPLC Büchi C-601 by using Merck silica gel 0.040–0.063 mm. Compound **8** was synthesized according to literature procedures.¹¹

Synthesis of ((3*RS*,5*SR*)-5-(3,4-dihydro-5-methyl-2,4-dioxopyrimidin-1(2*H*)-yl)-2-methylisoxazolidin-3-yl)methyl 4-methylbenzensulfonate (**9**).

To a solution of compound **8** (0.386 g, 1.6 mmol) in CH_2Cl_2 (20 mL), Et_3N (0.25 mL, 1.8 mmol) was added. TsCl (0.349 g, 1.8 mmol) was then added slowly at 0°C and the reaction mixture was left under stirring at room temperature for 24 h. After removal of the solvent under vacuum, the residue was purified by MPLC, using $\text{CH}_2\text{Cl}_2/\text{MeOH}$ 99:1, to give **9** in 70% yield (0.443 g).

White solid, m.p. $134\text{--}136^\circ\text{C}$. ^1H NMR (500 MHz, CDCl_3): δ = 1.77 (s, 3H); 1.93–2.04 (m, 1H), 2.32 (s, 3H); 2.63 (s, 3H); 2.82–2.89 (m, 2H); 3.89–4.07 (m, 2H), 5.94–6.02 (m, 1H), 7.23 (d, J = 8.2 Hz, 2H), 7.46 (s, 1H); 7.63 (d, J = 8.2 Hz, 2H), 9.37 (bs, 1H). ^{13}C NMR (126 MHz, CDCl_3): δ = 8.54, 17.48, 36.53, 40.26, 61.81, 63.64, 89.98, 106.58, 123.67, 125.90, 131.73, 138.66, 144.09, 151.95, 160.09. HRMS: calcd for $\text{C}_{17}\text{H}_{21}\text{N}_3\text{O}_6\text{SNa}^+$ 418.1043, found 418.1050.

Synthesis of (3*RS*,5*SR*)-1-(3-(iodomethyl)-2-methylisoxazolidin-5-yl)-5-methylpyrimidine-2,4-(1*H*,3*H*) dione (**10**)

Compound **9** (0.32 g, 0.81 mmol) was added to a solution of NaI (0.600 g, 4 mmol) in acetone (20 mL) and the reaction mixture was refluxed for 72 h. After cooling, acetone was removed under vacuum and chloroform was added to the residue. The resulting organic phase was filtered and evaporated. The residue was purified by MPLC, using $\text{CH}_2\text{Cl}_2/\text{MeOH}$ 99:1, to give the compound **10** in 93% yield (0.260 g).

Pale yellow solid, m.p. $157\text{--}159^\circ\text{C}$. ^1H NMR (300 MHz, CDCl_3): δ = 1.96 (s, 3H), 2.20 (ddd, J = 13.7, 9.3, 4.1 Hz, 1H), 2.51–2.64 (m, 1H), 2.76 (s, 3H), 3.05–3.18 (m, 2H), 3.27 (dd, J = 10.7, 3.3 Hz, 1H), 6.16 (dd, J = 7.8, 4.1 Hz, 1H), 7.77 (s, 1H), 8.54 (bs, 1H). ^{13}C NMR (126 MHz, CDCl_3): δ = 8.44, 25.45, 38.99, 41.18, 63.28, 77.44, 110.20, 132.30, 150.20, 163.4. HRMS: calcd for $\text{C}_{10}\text{H}_{14}\text{N}_3\text{O}_3\text{I}^+$ 373.9972, found 373.9981.

Synthesis of (3*RS*,5*SR*)-1-(3-(azidomethyl)-2-methylisoxazolidin-5-yl)-5-methylpyrimidine-2,4-(1*H*,3*H*)-dione (**11**) and (3*RS*,5*RS*)-1-(3-(azidomethyl)-2-methylisoxazolidin-5-yl)-5-methylpyrimidine-2,4-(1*H*,3*H*)-dione (**12**)

To a solution of compound **10** (0.197 g, 0.56 mmol) in acetonitrile (4 mL) and H_2O (8 mL), NaN_3 (0.04 g, 0.61 mmol) and NH_4Cl (0.06 g, 1.12 mmol) were added. The resulting mixture was stirred at 50°C for 48 h. The solvent was evaporated

under reduced pressure and the residue was washed with CHCl_3 (10 mL). After filtration, the residue was purified by silica gel column chromatography ($\text{CH}_2\text{Cl}_2/\text{MeOH}=99:1$).

The first eluted product was the *cis* derivative **11**. Yield 57%, yellow oil. ^1H NMR (300 MHz, CDCl_3): $\delta = 1.49$ -1.66 (m, 1H); 1.93 (s, 3H), 2.26 (dd, 11.7, 5.1 Hz, 1H), 2.34-2.42 (m, 1H), 2.70 (s, 3H), 3.17 (dd, $J = 11.7$, 4.7 Hz, 1H), 3.85-4.00 (m, 1H), 5.99 (dd, $J = 11.7$, 5.1 Hz, 1H), 7.14 (s, 1H), 8.96 (bs, 1H). ^{13}C NMR (126 MHz, CDCl_3): $\delta = 16.20$, 42.02; 43.40, 51.02, 65.60, 89.00, 111.20, 138.40, 152.60, 164.20. The second eluted product was the *trans* derivative **12**. Yield 28%, yellow oil. ^1H NMR (500MHz, CDCl_3): $\delta = 1.95$ (s, 3H); 2.18 (ddd, $J = 13.2$, 9.2, 3.7 Hz, 1H); 2.83 (s, 3H); 2.91-3.01 (m, 1H); 3.05-3.09 (m, 1H); 4.05 (dd, $J = 11.9$, 5.9 Hz, 1H); 4.31 (dd, $J = 11.9$, 3.8 Hz, 1H); 6.14 (dd, $J = 7.7$, 3.7 Hz, 1H); 7.67 (s, 1H); 8.38 (bs, 1H). ^{13}C NMR (126 MHz, CDCl_3): $\delta = 20.66$; 41.52; 44.38; 62.63; 66.29; 82.45; 110.55; 135.92; 150.23; 163.44.

General procedure for the synthesis of 5'-[1,2,3]-triazolyl-2'-oxa-3'-azanucleosides **13** and **14**.

To a solution of azide **11** or **12** (0.4 mmol) in *tert*-butanol:water (1:1, 20 mL) mixture, NEt_3 (0.4 mmol), the corresponding alkyne **17** (0.4 mmol), $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ (0.1 mmol) and sodium ascorbate (0.2 mmol) were added. The reaction mixture was stirred at room temperature for 5 h. After the completion of reaction, the solvent was evaporated under reduced pressure and the residue was extracted with dichloromethane (20 mL x 3). The organic phase was dried over sodium sulfate, filtered and evaporated under reduced pressure. The residue was purified by MPLC, using CH_2Cl_2 : MeOH 99:1, to give the corresponding triazolyl-2'-oxa-3'-azanucleosides.

1-((3*RS*,5*SR*)-3-((4-(2-hydroxyethyl)-1*H*-1,2,3-triazol-1-yl)methyl)-2-methylisoxazolidin-5-yl)-5-methylpyrimidine-2,4(1*H*,3*H*)-dione (13a**)**. Yield 88%, white solid, m.p. 215-218 °C. ^1H NMR (500 MHz, DMSO): $\delta = 1.78$ (s, 3H), 2.25-2.29 (m, 1H), 2.43-2.47 (m, 1H), 2.64 (s, 3H), 2.71-2.74 (m, 3H), 3.44 (dd, $J = 11.7$, 4.2 Hz, 1H); 3.62 (dt, $J = 6.9$, 5.3 Hz, 2H); 4.69 (t, $J = 5.3$ Hz, 1H); 5.03-5.06 (m, 1H); 5.97 (dd, $J = 11.3$, 2.4 Hz, 1H); 7.71 (s, 1H); 8.01 (s, 1H). ^{13}C NMR (126 MHz, DMSO): $\delta = 16.77$, 34.24, 38.40, 50.62, 59.71, 65.28, 65.59, 84.55, 114.65, 126.32, 141.22, 149.61, 155.30, 168.73. IR (nujol): ν_{max} 3450, 1698. HRMS: calcd for $\text{C}_{14}\text{H}_{20}\text{N}_6\text{O}_4\text{Na}^+$ 359.1438, found 359.1442.

1-((3*RS*,5*SR*)-3-((4-(hydroxymethyl)-1*H*-1,2,3-triazol-1-yl)methyl)-2-methylisoxazolidin-5-yl)-5-methylpyrimidine-2,4(1*H*,3*H*)-dione (13b**)**. Yield 84%, white solid, m.p. 205-210 °C. ^1H NMR (500 MHz, DMSO): $\delta = 1.78$ (s, 3H); 2.24-2.30 (m, 1H), 2.50-2.54 (m, 1H), 2.64 (s, 3H), 2.75 (dd, $J = 11.2$, 9.8 Hz, 1H), 3.41-3.49 (m, 1H), 4.52 (d, $J = 5.5$ Hz, 1H), 5.07-5.13 (m, 1H), 5.21 (t, $J = 5.5$ Hz, 1H), 5.98 (dd, $J = 11.2$, 2.1 Hz, 1H), 7.72 (s, 1H), 8.13 (s, 1H), 9.40 (bs, 1H). ^{13}C NMR (126 MHz, DMSO): $\delta = 12.36$, 33.70, 46.23, 55.33, 60.89, 61.85, 79.85, 110.27, 121.93, 136.59; 148.59, 150.32, 163.78. IR (nujol): ν_{max} 3450, 1696. HRMS: calcd for $\text{C}_{13}\text{H}_{18}\text{N}_6\text{O}_4\text{Na}^+$ 345.1282, found 345.1286.

5-methyl-1-((3*RS*,5*SR*)-2-methyl-3-((4-propyl-1*H*-1,2,3-triazol-1-yl)methyl)isoxazolidin-5-yl)pyrimidine-2,4(1*H*,3*H*)-dione (13c**)**. Yield 80%, white solid, m.p. 132-137 °C. ^1H NMR (500 MHz, CDCl_3): $\delta = 0.96$ (t, $J = 7.4$ Hz, 3H), 1.64-1.72 (m,

2H), 1.94 (s, 3H), 2.22-2.32 (m, 1H), 2.39-2.49 (m, 1H), 2.68 (t, $J = 7.6$ Hz, 2H), 2.76 (s, 3H), 3.05 (dd, $J = 11.7, 11.2$ Hz, 1H), 3.38 (dd, $J = 11.7, 4.0$ Hz, 1H), 4.91-4.97 (m, 1H), 6.15 (dd, $J = 11.0, 2.5$ Hz, 1H), 7.22 (s, 1H); 7.34 (s, 1H), 9.13 (bs, 1H). ^{13}C NMR (126 MHz, CDCl_3): $\delta = 7.74, 8.98, 17.88, 22.83, 30.52, 41.48, 50.55, 56.43, 75.36, 106.95, 115.19, 130.18, 143.49, 145.21, 158.59$. IR (nujol): ν_{max} 1699. HRMS: calcd for $\text{C}_{15}\text{H}_{22}\text{N}_6\text{O}_3\text{Na}^+$ 357.1646, found 357.1642.

5-methyl-1-((3*RS*,5*SR*)-2-methyl-3-((4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl)isoxazolidin-5-yl)-pyrimidine-2,4(1*H*,3*H*)-dione (13d). Yield 78%, white solid, m.p. 268-272 °C. ^1H NMR (300 MHz, CDCl_3): $\delta = 1.96$ (s, 3H), 2.34-2.60 (m, 2H), 2.80 (s, 3H), 3.12-3.16 (m, 1H), 3.39-3.53 (m, 1H), 4.96-5.13 (m, 1H), 6.18 (dd, $J = 10.9, 2.8$ Hz, 1H), 7.20-7.25 (m, 2H), 7.32-7.51 (m, 3H), 7.81 (s, 1H), 7.84 (s, 1H), 8.12 (bs, 1H). ^{13}C NMR (126 MHz, CDCl_3): $\delta = 12.40, 30.70, 46.09, 55.20, 61.27, 80.01, 118.80, 125.58, 128.25, 128.71, 130.25, 134.83, 138.20, 146.32, 150.41, 163.72$. IR (nujol): ν_{max} 1697. HRMS: calcd for $\text{C}_{18}\text{H}_{20}\text{N}_6\text{O}_3\text{Na}^+$ 391.1489, found 391.1493.

1-((3*RS*,5*SR*)-3-((4-(4-methoxyphenyl)-1*H*-1,2,3-triazol-1-yl)methyl)-2-methylisoxazolidin-5-yl)-5-methylpyrimidine-2,4(1*H*,3*H*)-dione (13e). Yield 78%, white solid, m.p. 215-218 °C. ^1H NMR (500 MHz, DMSO): $\delta = 1.51$ (s, 3H), 2.14-2.25 (m, 1H), 2.68 (s, 3H), 2.95-2.99 (m, 1H), 3.12-3.14 (m, 1H), 3.75 (s, 3H), 4.61-4.70 (m, 2H), 6.05 (dd, $J = 8.0, 4.0$ Hz, 1H), 6.97 (d, $J = 8.6$ Hz, 2H), 7.14 (s, 1H), 7.73 (d, $J = 8.6$ Hz, 2H), 8.43 (s, 1H). ^{13}C NMR (126 MHz, DMSO): $\delta = 10.43, 45.50, 50.18, 55.50, 60.30, 65.40, 82.41, 109.67, 114.64, 122.34, 128.50, 132.01, 135.90, 147.70, 152.44, 158.01, 160.65$. IR (nujol): ν_{max} 1697. HRMS: calcd for $\text{C}_{19}\text{H}_{22}\text{N}_6\text{O}_4\text{Na}^+$ 421.1595, found 421.1593.

1-((3*RS*,5*SR*)-3-((4-(4-fluorophenyl)-1*H*-1,2,3-triazol-1-yl)methyl)-2-methylisoxazolidin-5-yl)-5-methylpyrimidine-2,4(1*H*,3*H*)-dione (13f). Yield 85%, white solid, m.p. 269-271 °C. ^1H NMR (500 MHz, CDCl_3): $\delta = 1.97$ (s, 3H), 2.32-2.42 (m, 1H), 2.48-2.57 (m, 1H), 2.80 (s, 3H), 3.12 (dd, $J = 11.3, 9.9$ Hz, 1H), 3.43-3.53 (m, 1H), 4.95-5.09 (m, 1H), 6.17 (dd, $J = 11.2, 2.5$ Hz, 1H), 7.13 (t, $J = 8.7$ Hz, 2H), 7.23 (s, 1H), 7.76 (s, 1H), 7.77-7.85 (m, 2H), 8.00 (bs, 1H). ^{13}C NMR (126 MHz, DMSO): $\delta = 17.09, 38.36, 51.02, 60.25, 65.49, 84.61, 115.03, 121.06$ (d, $J = 21.6$ Hz), 125.45, 132.28, 141.26, 150.49, 155.33, 166.96 (d, $J = 244.4$ Hz), 168.66. IR (nujol): ν_{max} 1685. HRMS: calcd for $\text{C}_{18}\text{H}_{19}\text{N}_6\text{O}_3\text{FNa}^+$ 409.1395, found 409.1399.

1-((3*RS*,5*SR*)-2-methyl-3-((4-(4-pentylphenyl)-1*H*-1,2,3-triazol-1-yl)methyl)isoxazolidin-5-yl)-5-methylpyrimidine-2,4(1*H*,3*H*)-dione (13g). Yield 89%, white solid, m.p. 259-260 °C. ^1H NMR (300 MHz, CDCl_3): $\delta = 0.77$ (t, $J = 6.6$ Hz, 3H), 1.29-1.40 (m, 4H), 1.55-1.71 (m, 2H), 1.95 (s, 3H); 2.27-2.55 (m, 2H), 2.62 (t, $J = 7.4$, 2H), 2.78 (s, 3H), 3.04-3.19 (m, 1H), 3.38-3.51 (m, 1H), 4.95-5.12 (m, 1H), 6.18 (dd, $J = 11.0, 2.6$ Hz, 1H), 7.26 (d, $J = 8.1, 2\text{H}$), 7.28 (s, 1H), 7.72 (d, $J = 8.1$ Hz, 2H), 7.78 (s, 1H), 8.71 (s, 1H). ^{13}C NMR (126 MHz, DMSO): $\delta = 11.88, 13.86, 21.71, 30.54, 31.75, 31.90, 33.37, 46.13, 55.10, 60.57, 79.66, 110.05, 120.07, 121.30, 125.28, 128.74, 136.33, 146.50, 149.01, 168.20$. IR (nujol): ν_{max} 1695. HRMS: calcd for $\text{C}_{23}\text{H}_{30}\text{N}_6\text{O}_3\text{Na}^+$ 461.2272, found 461.2277.

1-((3*RS*,5*RS*)-3-((4-(2-hydroxyethyl)-1*H*-1,2,3-triazol-1-yl)methyl)-2-methylisoxazolidin-5-yl)-5-methylpyrimidine-2,4(1*H*,3*H*)-dione (14a). Yield 79%, white solid. m.p. 202-206 °C; ¹H NMR (500 MHz, CDCl₃): δ = 1.93 (s, 3H); 2.17-2.23 (m, 1H), 2.73 (s, 3H), 2.94 (t, *J* = 5.8 Hz, 2H), 3.01-3.12 (m, 1H), 3.20-3.30 (m, 1H), 3.89-3.99 (m, 2H); 4.44 (dd, *J* = 14.4, 4.9 Hz, 1H), 4.57 (dd, *J* = 14.4, 5.3 Hz, 1H), 6.10 (dd, *J* = 7.6, 3.9 Hz, 1H), 7.32 (s, 1H), 7.45 (s, 1H), 8.03 (bs, 1H). ¹³C NMR (126 MHz, CDCl₃): δ = 14.75, 32.44, 39.41, 51.01, 58.99, 64.38, 65.02, 84.65, 114.01, 125.92, 142.34, 150.40, 157.60, 160.01. IR (nujol): ν_{max} 3450, 1695. HRMS: calcd for C₁₄H₂₀N₆O₄Na⁺ 359.1438, found 359.1443.

1-((3*RS*,5*RS*)-3-((4-(hydroxymethyl)-1*H*-1,2,3-triazol-1-yl)methyl)-2-methylisoxazolidin-5-yl)-5-methylpyrimidine-2,4(1*H*,3*H*)-dione (14b). Yield 81%, white solid. m.p. 198-201 °C, ¹H NMR (500 MHz, CDCl₃): δ = 1.92 (s, 3H), 2.17-2.23 (m, 1H), 2.74 (s, 3H), 3.01-3.12 (m, 1H), 3.19-3.31 (m, 1H), 3.98 (dd, *J* = 7.6, 3.9 Hz, 2H), 4.45 (dd, *J* = 14.5, 4.8 Hz, 1H), 4.60 (dd, *J* = 14.5, 5.2 Hz, 1H), 6.08 (dd, *J* = 7.6, 3.9 Hz, 1H), 7.30 (s, 1H), 7.57 (s, 1H), 8.11 (bs, 1H). ¹³C NMR (126 MHz, CDCl₃): δ = 13.93, 38.52, 41.29, 43.63, 56.71, 66.94, 82.35, 110.09, 120.82, 122.73, 134.93, 157.60, 161.04. IR (nujol): ν_{max} 3496, 1697. HRMS: calcd for C₁₃H₁₈N₆O₄Na⁺ 345.1282, found 345.1287.

5-methyl-1-((3*RS*,5*RS*)-2-methyl-3-((4-propyl-1*H*-1,2,3-triazol-1-yl)methyl)isoxazolidin-5-yl)pyrimidine-2,4(1*H*,3*H*)-dione (14c). Yield 83%, white solid, m.p. 168-170 °C, ¹H NMR (300 MHz, CDCl₃): δ = 0.94 (t, *J* = 7.3 Hz, 3H), 1.66 (sextet, *J* = 7.3, 2H), 1.90 (s, 3H), 2.08-2.22 (m, 1H), 2.60-2.68 (m, 2H), 2.70 (s, 3H), 3.04 (dt, *J* = 14.4, 7.3 Hz, 1H), 3.15-3.29 (m, 1H), 4.42 (dd, *J* = 14.4, 4.8 Hz, 1H), 4.55 (dd, *J* = 14.4, 5.4 Hz, 1H), 6.10 (dd, *J* = 7.6, 4.0 Hz, 1H), 7.31 (s, 1H), 7.32 (s, 1H), 9.02 (bs, 1H). ¹³C NMR (126 MHz, CDCl₃): δ = 12.64, 13.71, 22.63, 27.55, 41.69, 43.87, 49.93, 67.03, 82.34, 110.73, 121.69, 136.26, 148.64, 150.37, 167.73. IR (nujol): ν_{max} 1698. HRMS: calcd for C₁₅H₂₂N₆O₃Na⁺ 357.1646, found 357.1648.

5-methyl-1-((3*RS*,5*RS*)-2-methyl-3-((4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl)isoxazolidin-5-yl)pyrimidine-2,4(1*H*,3*H*)-dione (14d). Yield 82%, white solid, m.p. 233-235 °C, ¹H NMR (300 MHz, CDCl₃): δ = 1.72 (s, 3H), 2.17-2.30 (m, 1H), 2.78 (s, 3H), 3.03-3.19 (m, 1H), 3.25-3.33 (m, 1H), 4.45 (dd, *J* = 14.4, 4.3 Hz, 1H), 4.58 (dd, *J* = 14.4, 5.1 Hz, 1H), 6.13 (dd, *J* = 7.7, 4.1 Hz, 1H), 7.21 (s, 1H), 7.33-7.39 (m, 3H), 7.41-7.46 (m, 2H), 7.82 (s, 1H), 7.90 (bs, 1H). ¹³C NMR (126 MHz, CDCl₃): δ = 12.38, 29.67, 41.23, 43.84, 49.67, 66.90, 82.04, 110.52, 111.49, 120.30, 125.65, 128.35, 128.96, 134.89, 151.04, 163.19. IR (nujol): ν_{max} 1699. HRMS: calcd for C₁₈H₂₀N₆O₃Na⁺ 391.1489, found 391.1491.

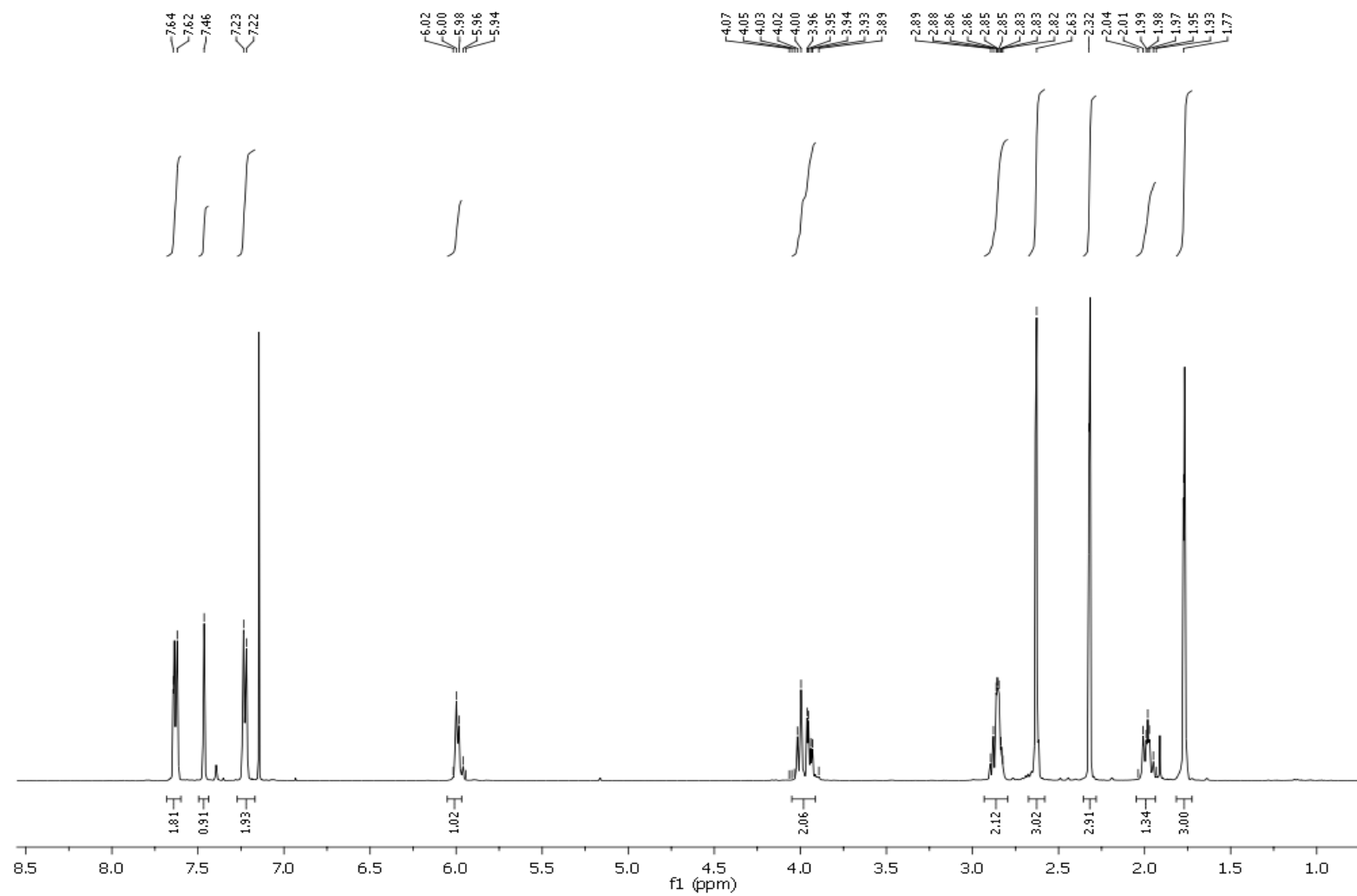
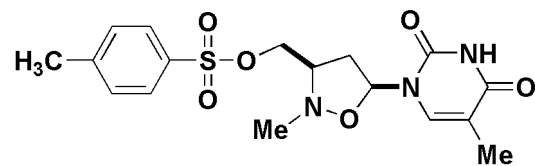
1-((3*RS*,5*RS*)-3-((4-(4-methoxyphenyl)-1*H*-1,2,3-triazol-1-yl)methyl)-2-methylisoxazolidin-5-yl)-5-methylpyrimidine-2,4(1*H*,3*H*)-dione (14e). Yield 82%, white solid, m.p. 202-205 °C, ¹H NMR (300 MHz, CDCl₃): δ = 1.74 (s, 3H), 2.13-2.24 (m, 1H), 2.70 (s, 3H), 3.05-3.15 (m, 1H), 3.25-3.30 (m, 1H), 3.85 (s, 3H), 4.49 (dd, *J* = 13.7, 4.7 Hz, 1H), 4.65 (dd, *J* = 13.7, 4.1 Hz, 1H), 6.11-6.20 (m, 1H), 6.97 (d, *J* = 8.7 Hz, 2H), 7.22 (s, 1H), 7.72-7.76 (m, 3H), 7.90 (bs, 1H). ¹³C NMR (126 MHz, DMSO): δ = 12.57, 43.58,

49.98, 55.49, 59.15, 66.55, 81.38, 110.21, 114.70, 121.97, 126.88, 130.15, 136.98, 146.71, 150.43, 159.45, 163.99. IR (nujol): $\nu_{\max}$ 1696. HRMS: calcd for $C_{19}H_{22}N_6O_4Na^+$ 421.1595, found 421.1598.

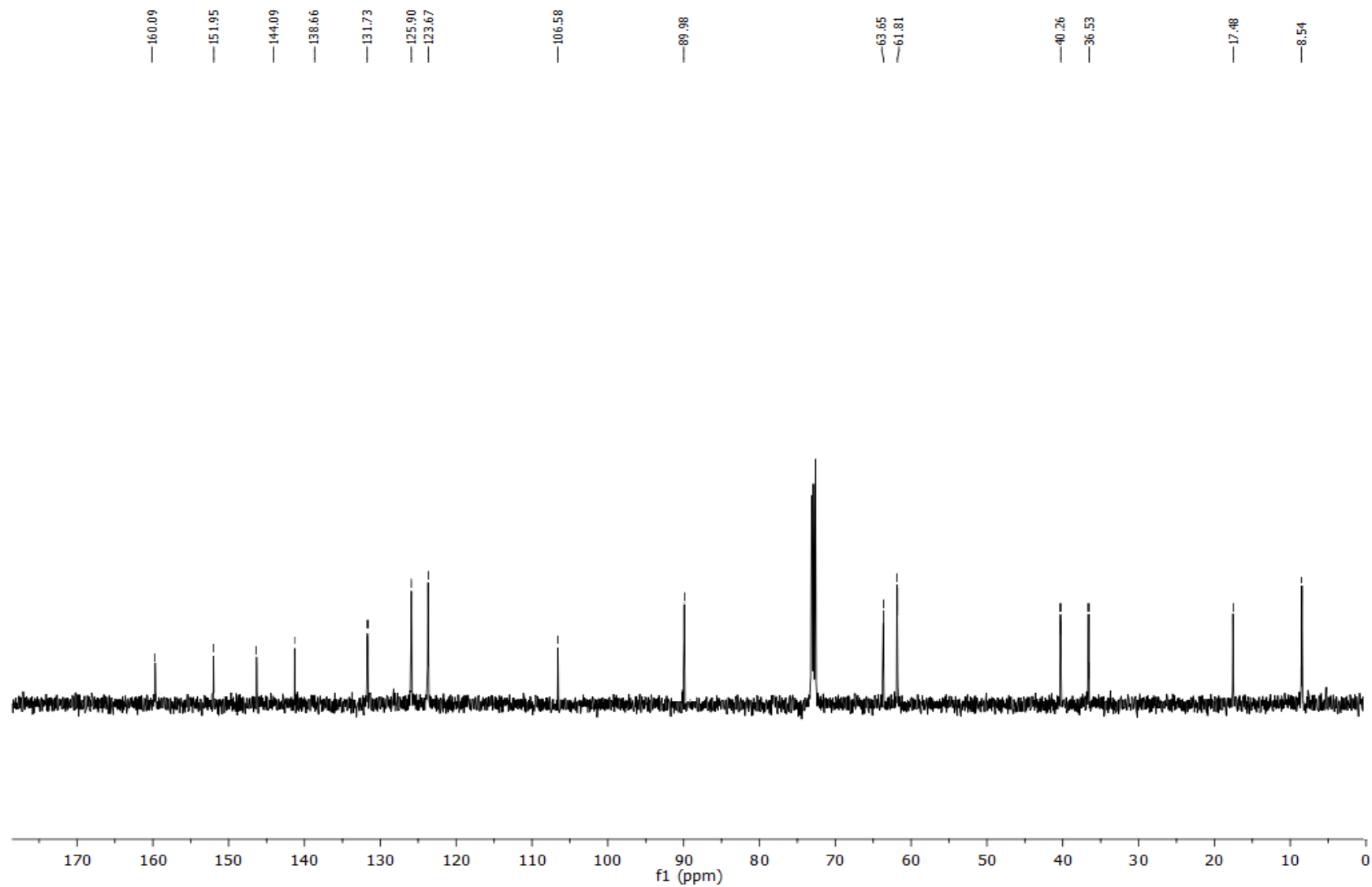
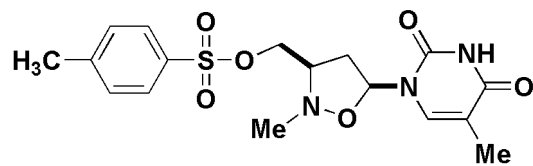
1-((3*RS*,5*RS*)-3-((4-(4-fluorophenyl)-1*H*-1,2,3-triazol-1-yl)methyl)-2-methylisoxazolidin-5-yl)-5-methylpyrimidine-2,4(1*H*,3*H*)-dione (14f). Yield 84%, white solid, m.p. 230-233 °C, 1H NMR (500 MHz, DMSO): δ = 1.50 (s, 3H), 2.11-2.23 (m, 1H), 2.70 (s, 3H), 2.98 (dt, J = 14.0, 8.2 Hz, 1H), 3.11-3.19 (m, 1H), 4.67 (dd, J = 14.6, 4.7 Hz, 1H), 4.72 (dd, J = 14.6, 4.4 Hz, 1H), 6.05 (dd, J = 8.0, 3.9 Hz, 1H), 7.15 (s, 1H), 7.22-7.31 (m, 2H), 7.81-7.91 (m, 2H), 8.55 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 12.39, 33.69, 46.38, 55.61, 60.87, 79.93, 110.28, 116.35 (d, J = 21.7 Hz), 120.77, 127.57, 136.50, 145.81, 150.62, 162.26 (d, J = 243.2 Hz) 163.96. IR (nujol): $\nu_{\max}$ 1690. HRMS: calcd for $C_{18}H_{19}N_6O_3FNa^+$ 409.1395, found 409.1398.

5-methyl-1-((3*RS*,5*RS*)-2-methyl-3-((4-(4-pentylphenyl)-1*H*-1,2,3-triazol-1-yl)methyl)isoxazolidin-5-yl)pyrimidine-2,4(1*H*,3*H*)-dione (14g): Yield 85%, white solid, m.p. 245-248 °C, 1H NMR (300 MHz, $CDCl_3$): δ = 0.98 (t, J = 7.4 Hz, 3H), 1.29-1.37 (m, 2H), 1.61-1.66 (m, 4H), 1.73 (s, 3H), 2.16-2.34 (m, 1H), 2.63 (t, J = 7.4, 2H), 2.76 (s, 3H), 3.09 (dt, J = 14.3, 7.9 Hz, 1H), 3.12-3.31 (m, 1H), 4.52 (dd, J = 14.5, 4.6 Hz, 1H), 4.67 (dd, J = 14.5, 5.0 Hz, 1H), 6.14 (dd, J = 7.7, 4.0 Hz, 1H), 7.23 (d, J = 8.0 Hz, 2H), 7.26 (s, 1H), 7.77 (d, J = 8.0 Hz, 2H), 7.72 (s, 1H), 8.18 (bs, 1H). ^{13}C NMR (126 MHz, DMSO): δ = 7.90, 12.16, 22.60, 30.75, 31.09, 32.45, 34.40, 47.15, 54.43, 62.87, 79.80, 109.65, 120.55, 121.36, 124.99, 127.95, 138.35, 147.67, 150.05, 169.29. IR (nujol): $\nu_{\max}$ 1698. HRMS: calcd for $C_{23}H_{30}N_6O_3Na^+$ 461.2272, found 461.2277.

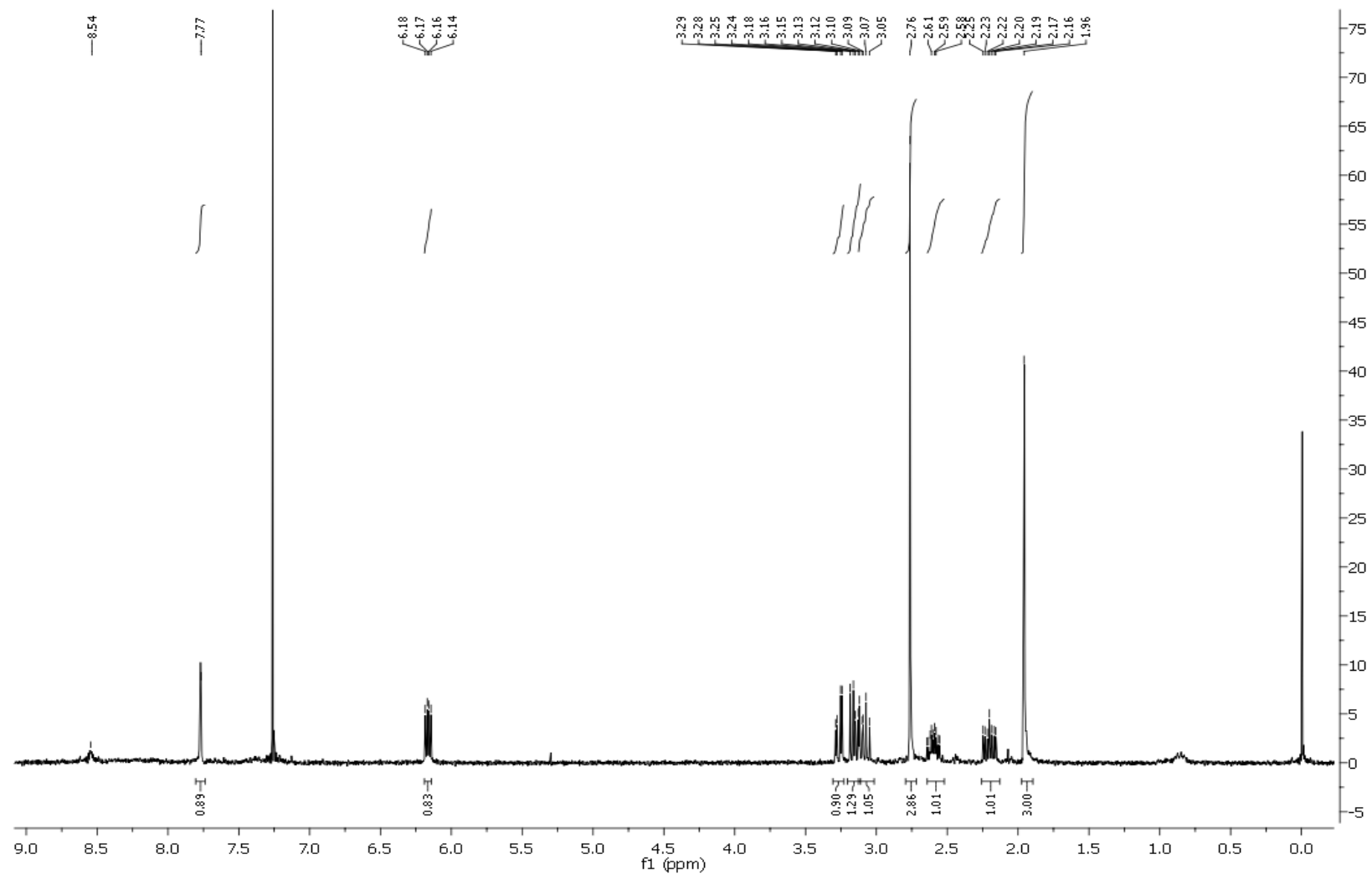
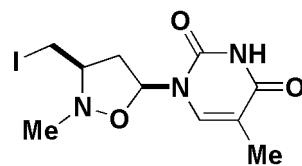
^1H NMR (500 MHz, CDCl_3) of compound **9**



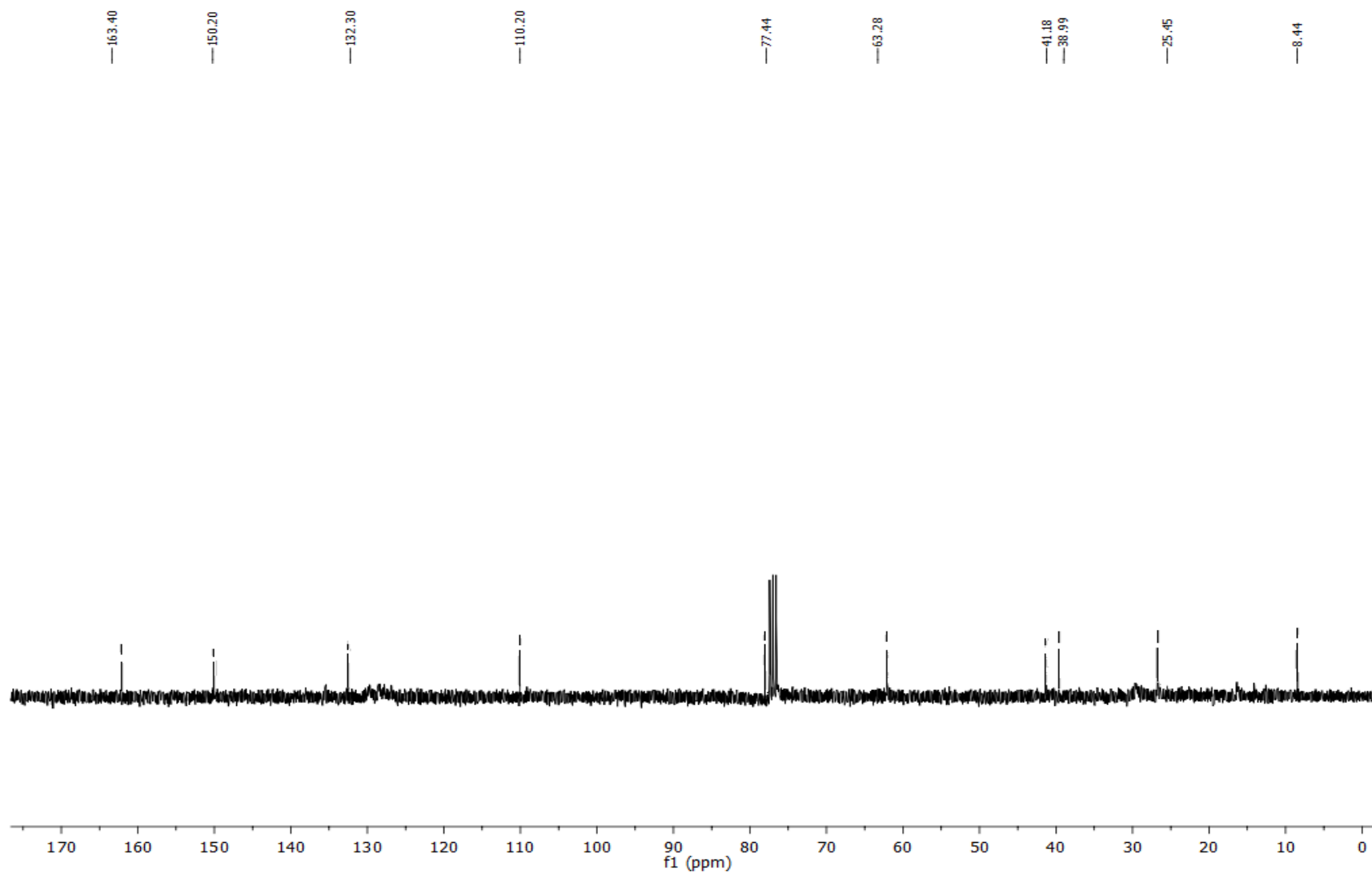
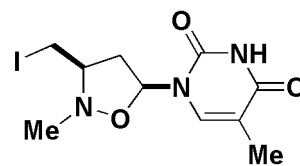
^{13}C NMR (126 MHz, CDCl_3) of compound **9**



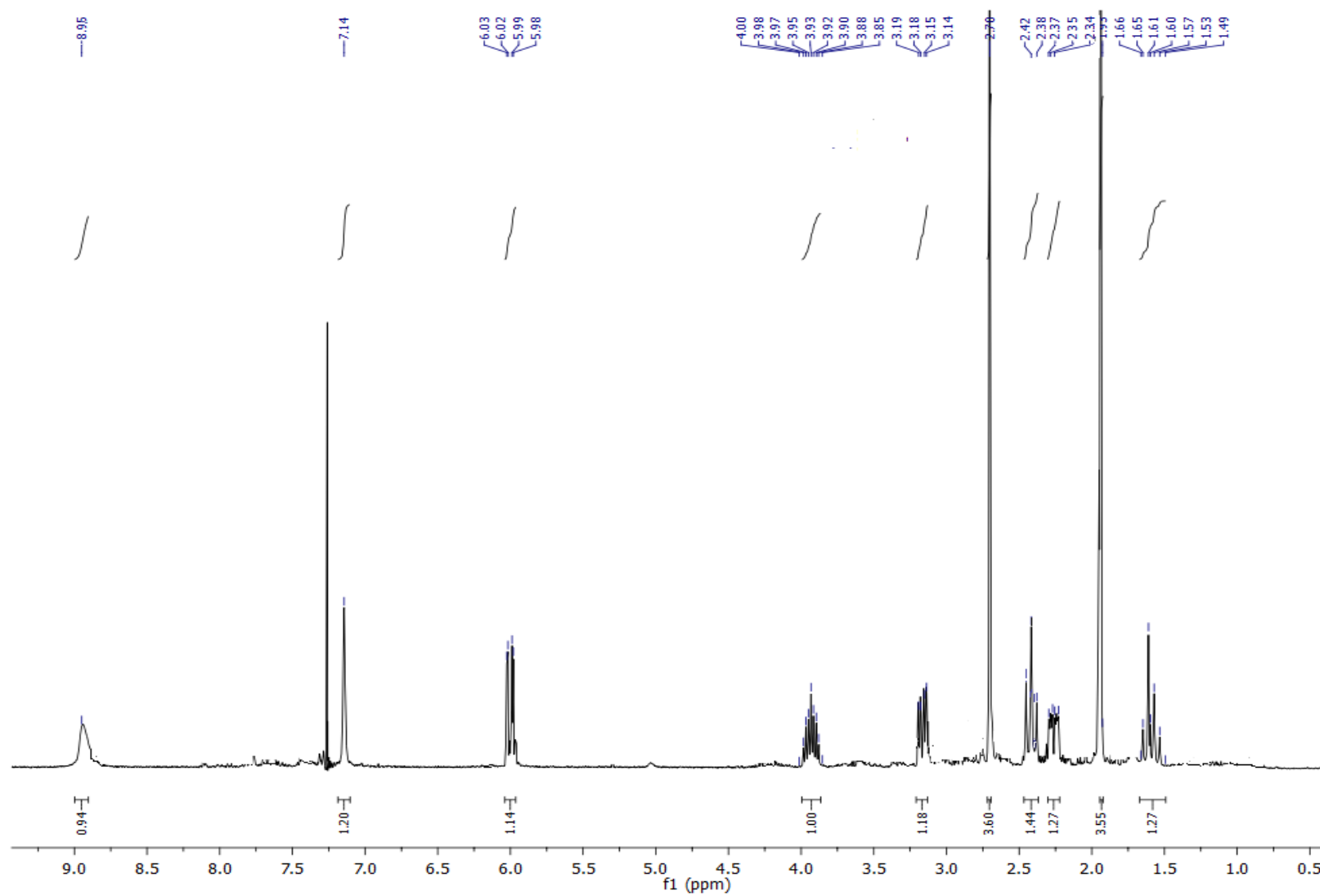
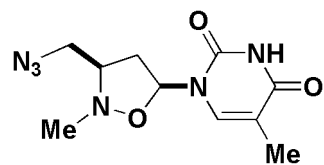
^1H NMR (300 MHz, CDCl_3) of compound **10**



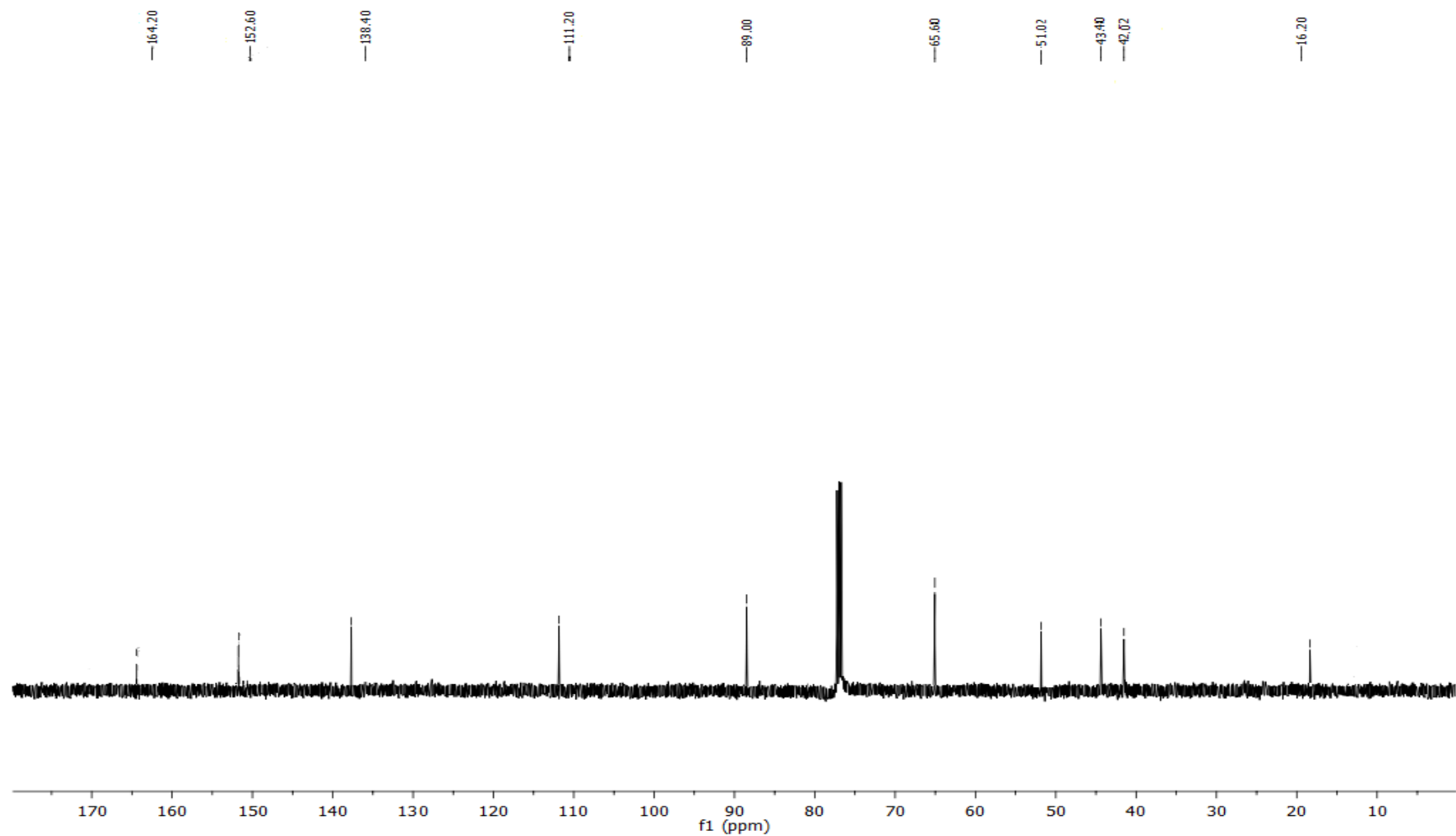
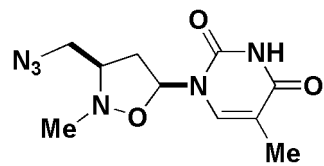
^{13}C NMR (126 MHz, CDCl_3) of compound **10**



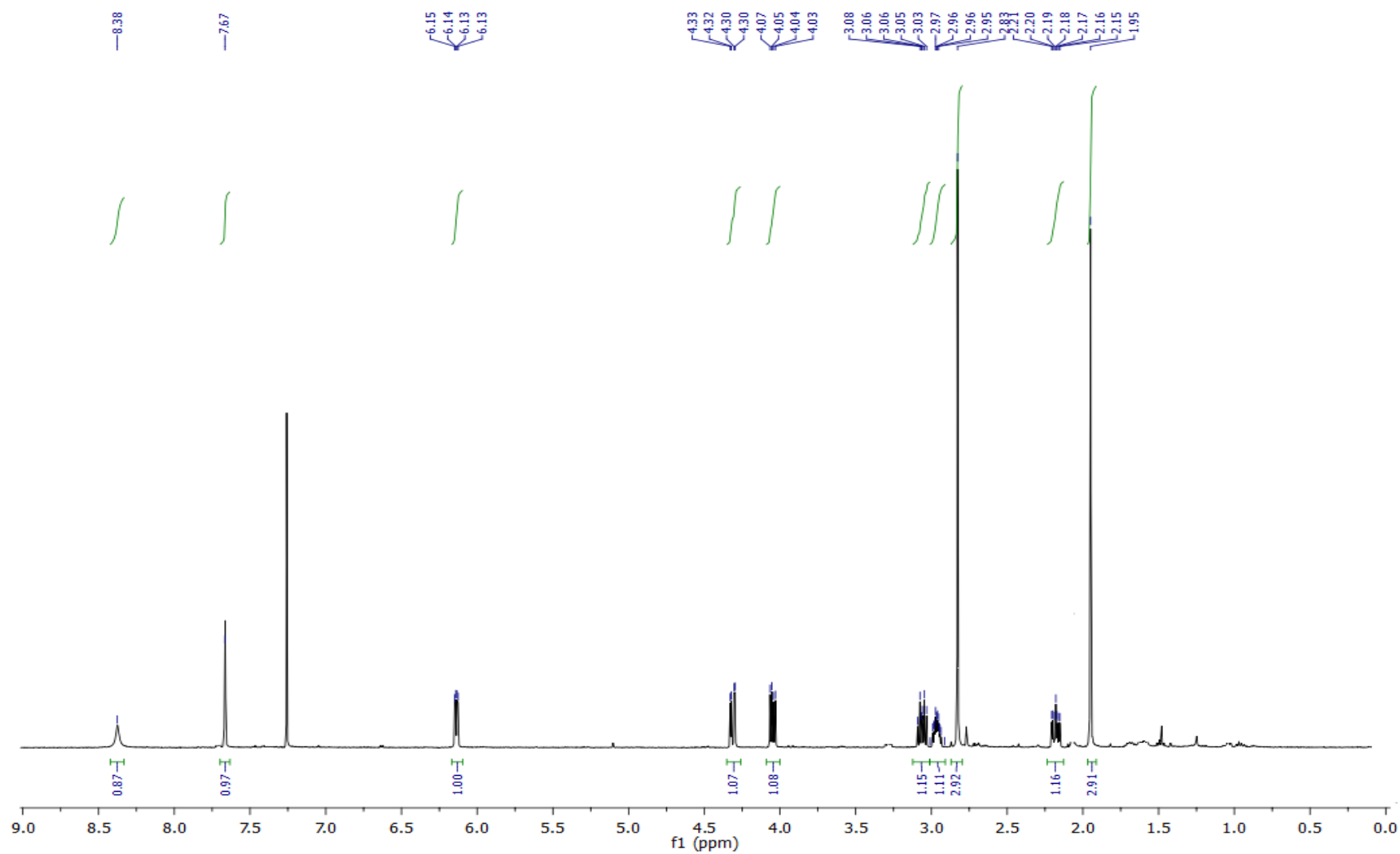
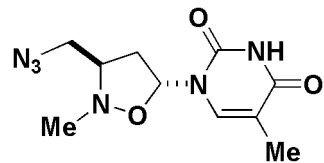
^1H NMR (300 MHz, CDCl_3) of compound **11**



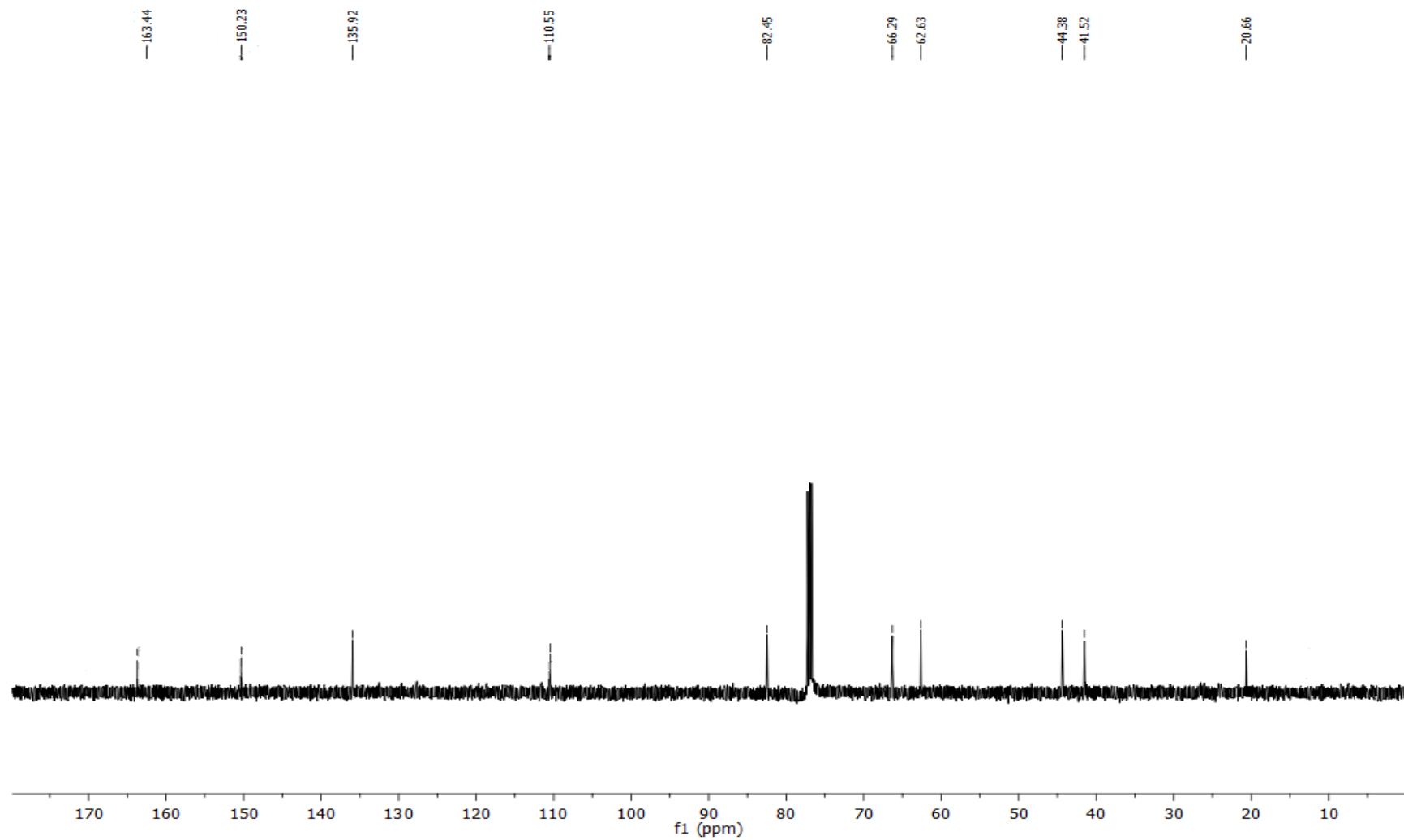
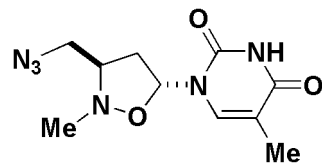
^{13}C NMR (126 MHz, CDCl_3) of compound **11**



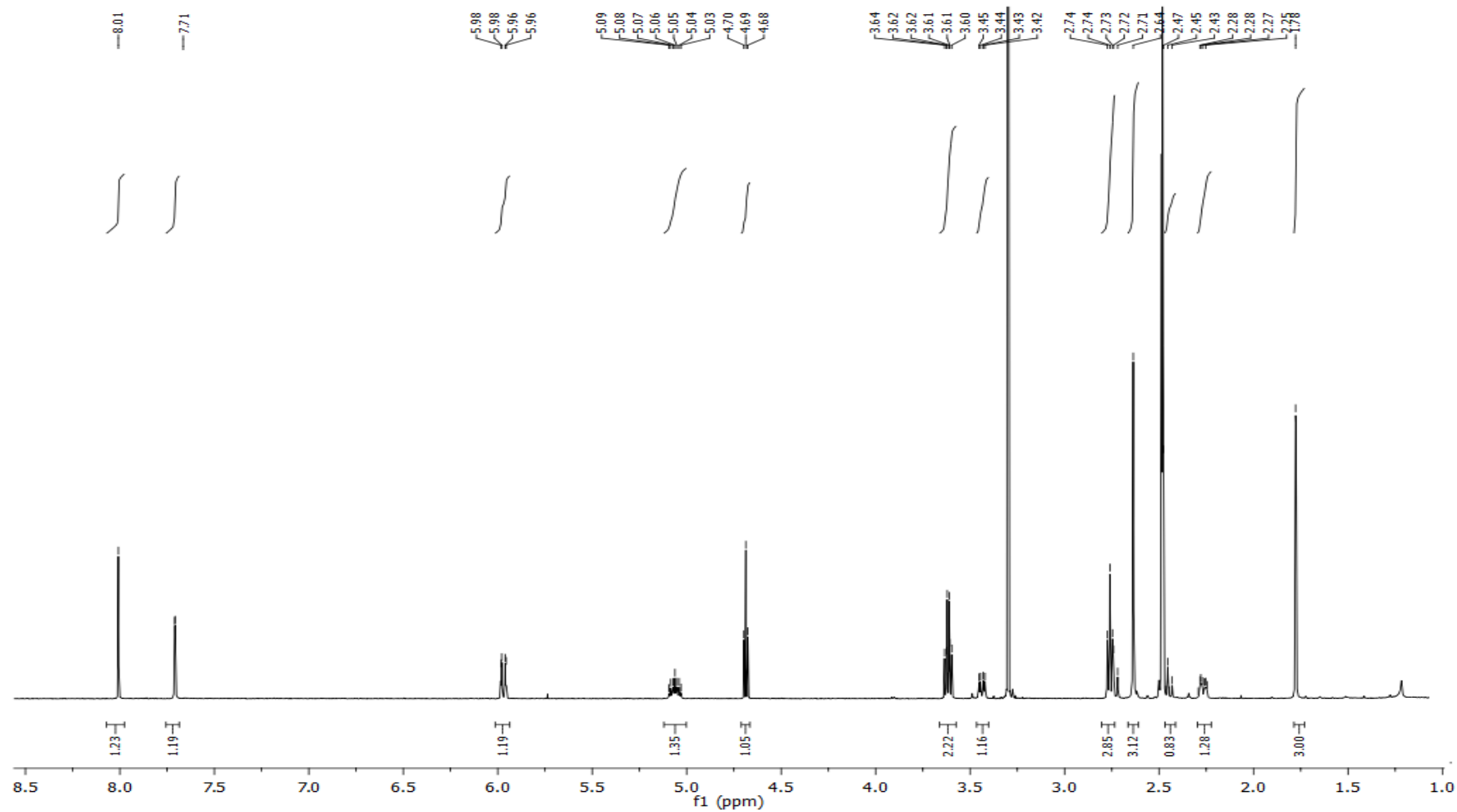
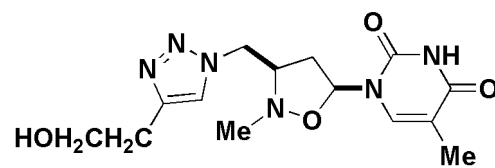
^1H NMR (500 MHz, CDCl_3) of compound **12**



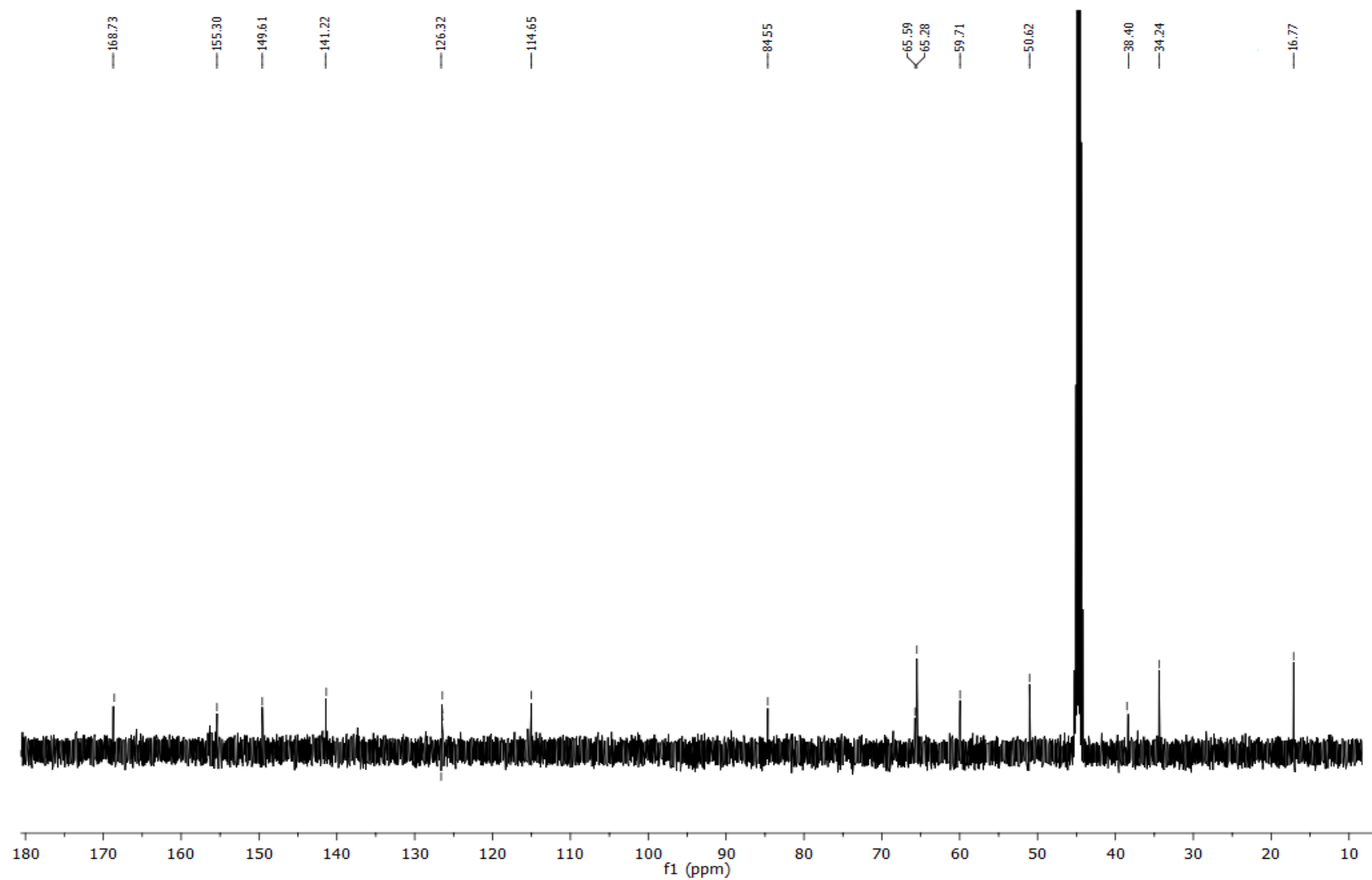
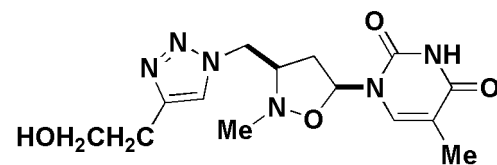
^{13}C NMR (126 MHz, CDCl_3) of compound **12**



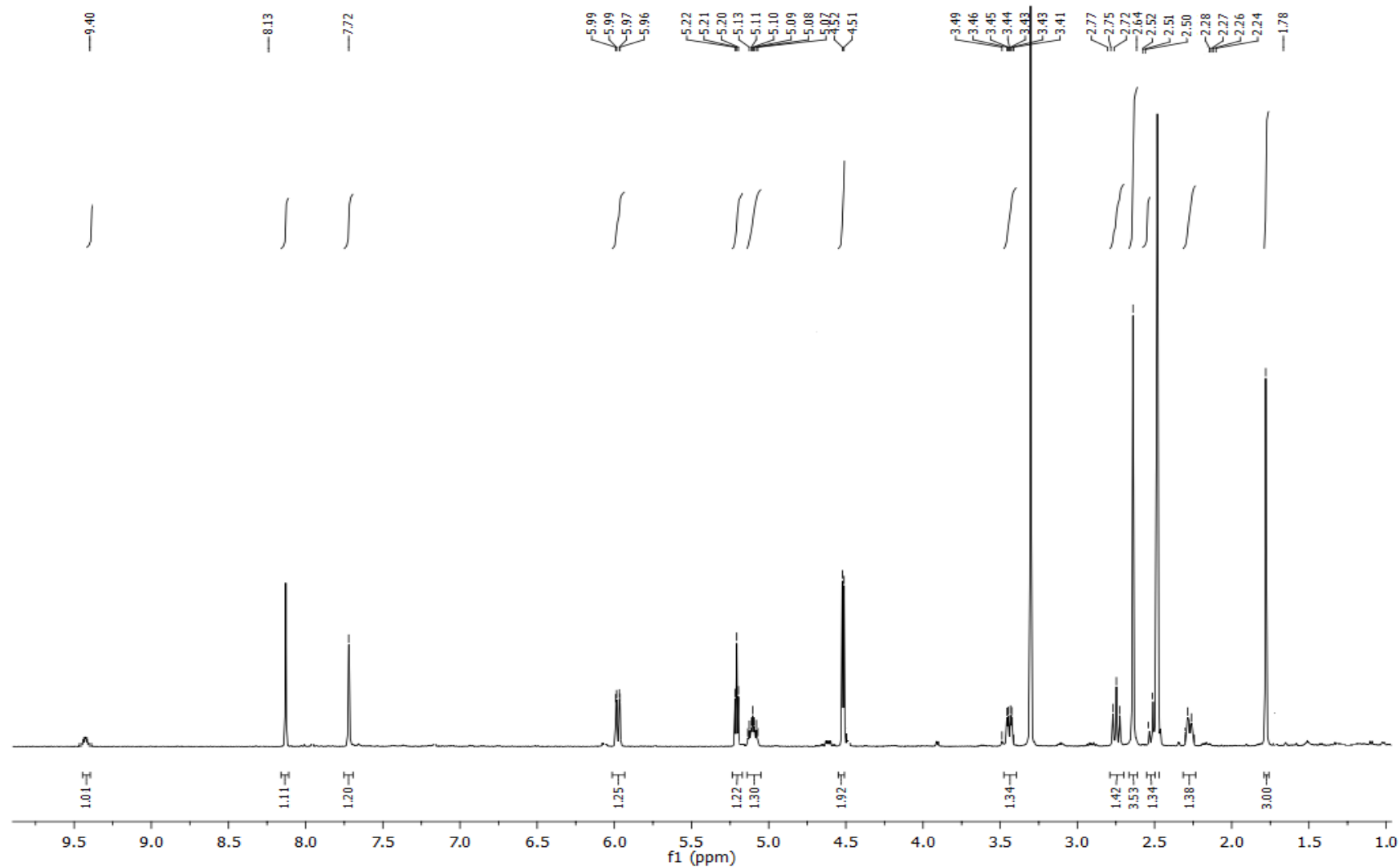
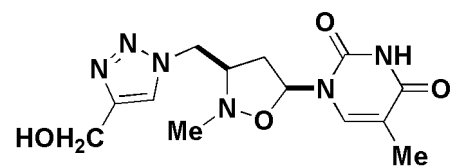
¹H NMR (500 MHz, DMSO) of compound **13a**



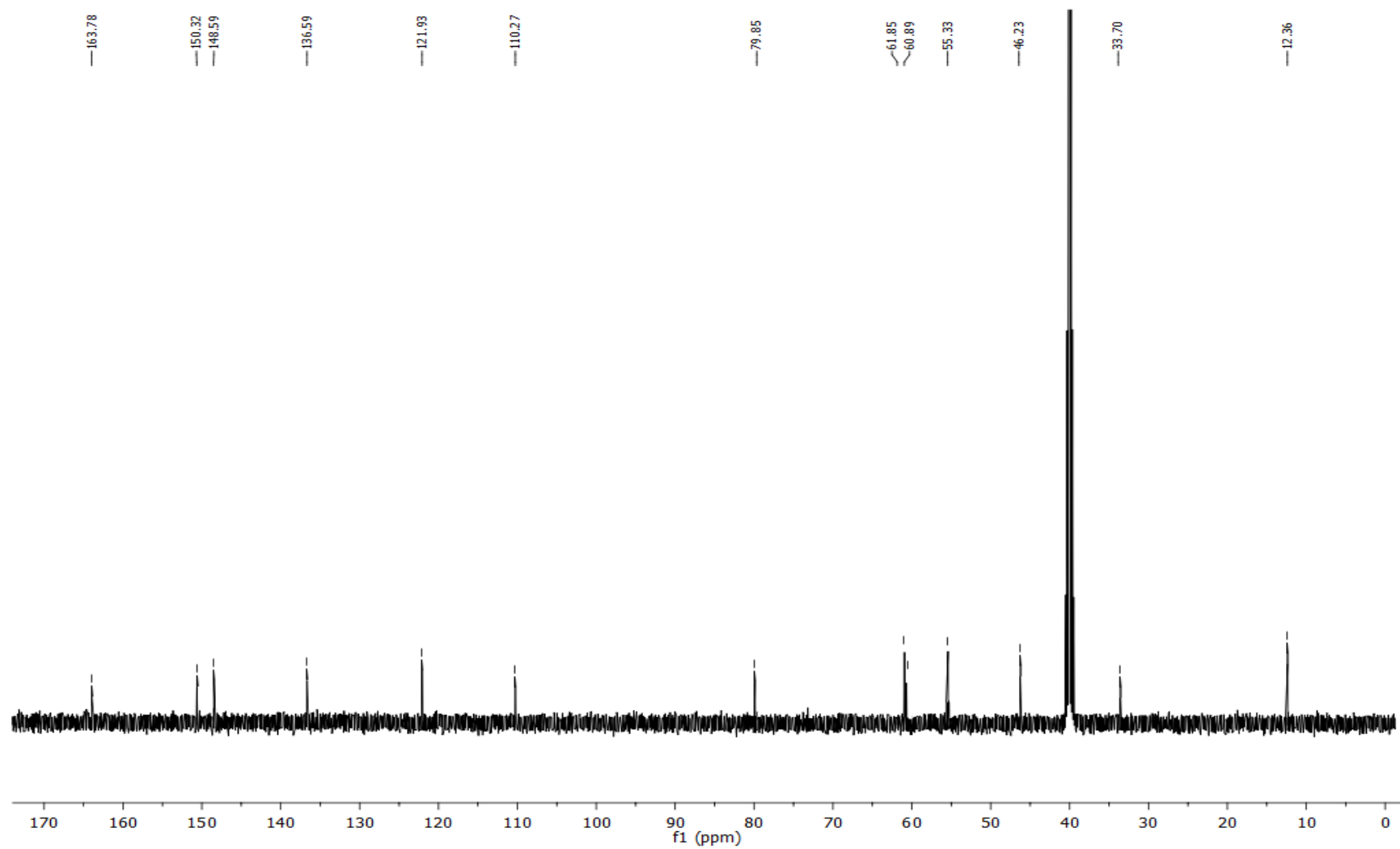
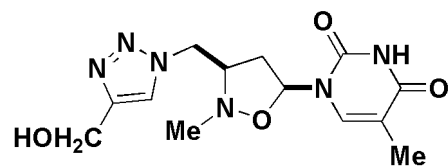
^{13}C NMR (126 MHz, DMSO) of compound **13a**



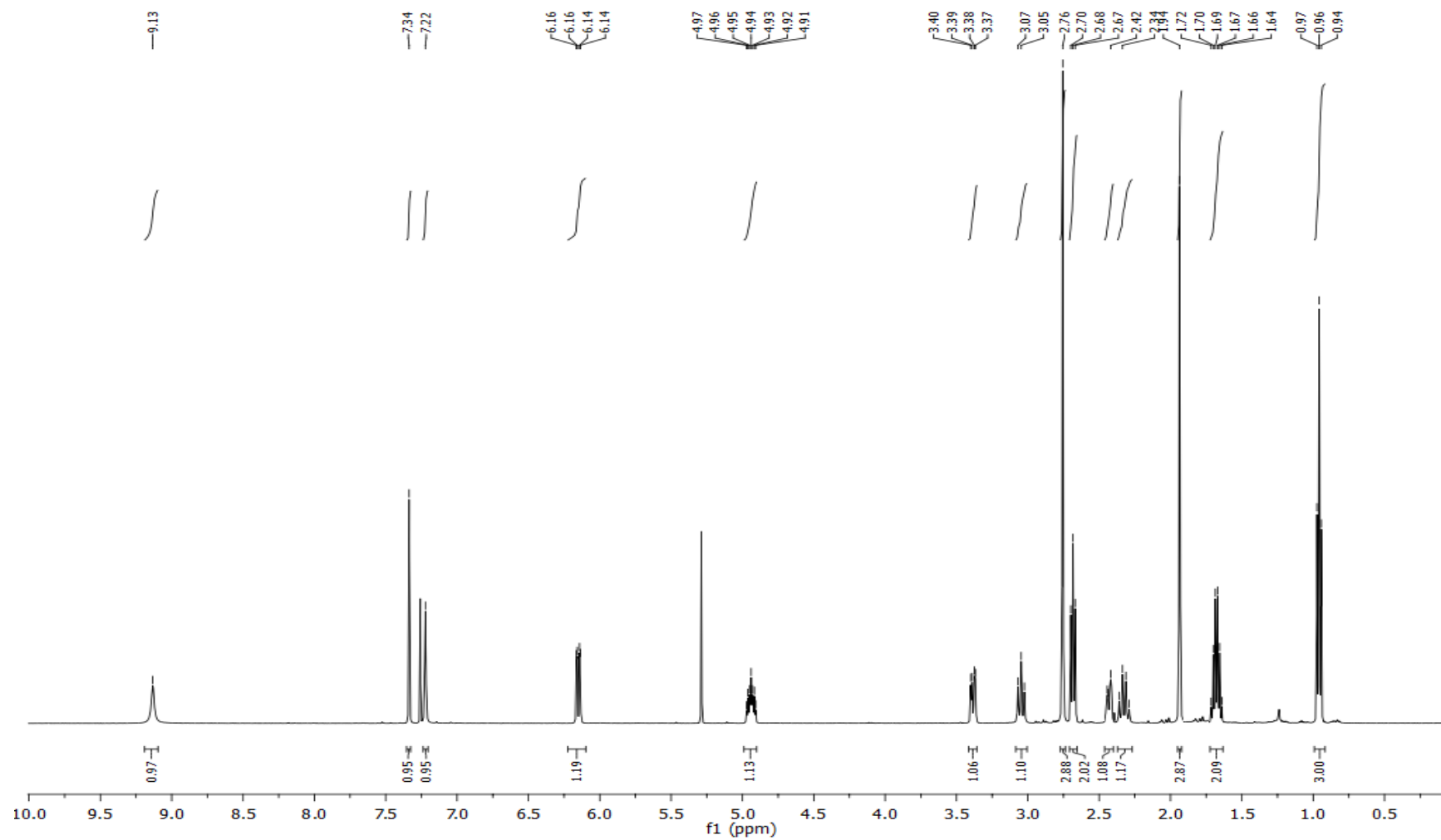
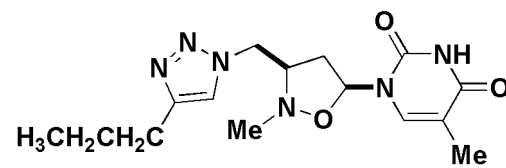
^1H NMR (500 MHz, DMSO) of compound **13b**



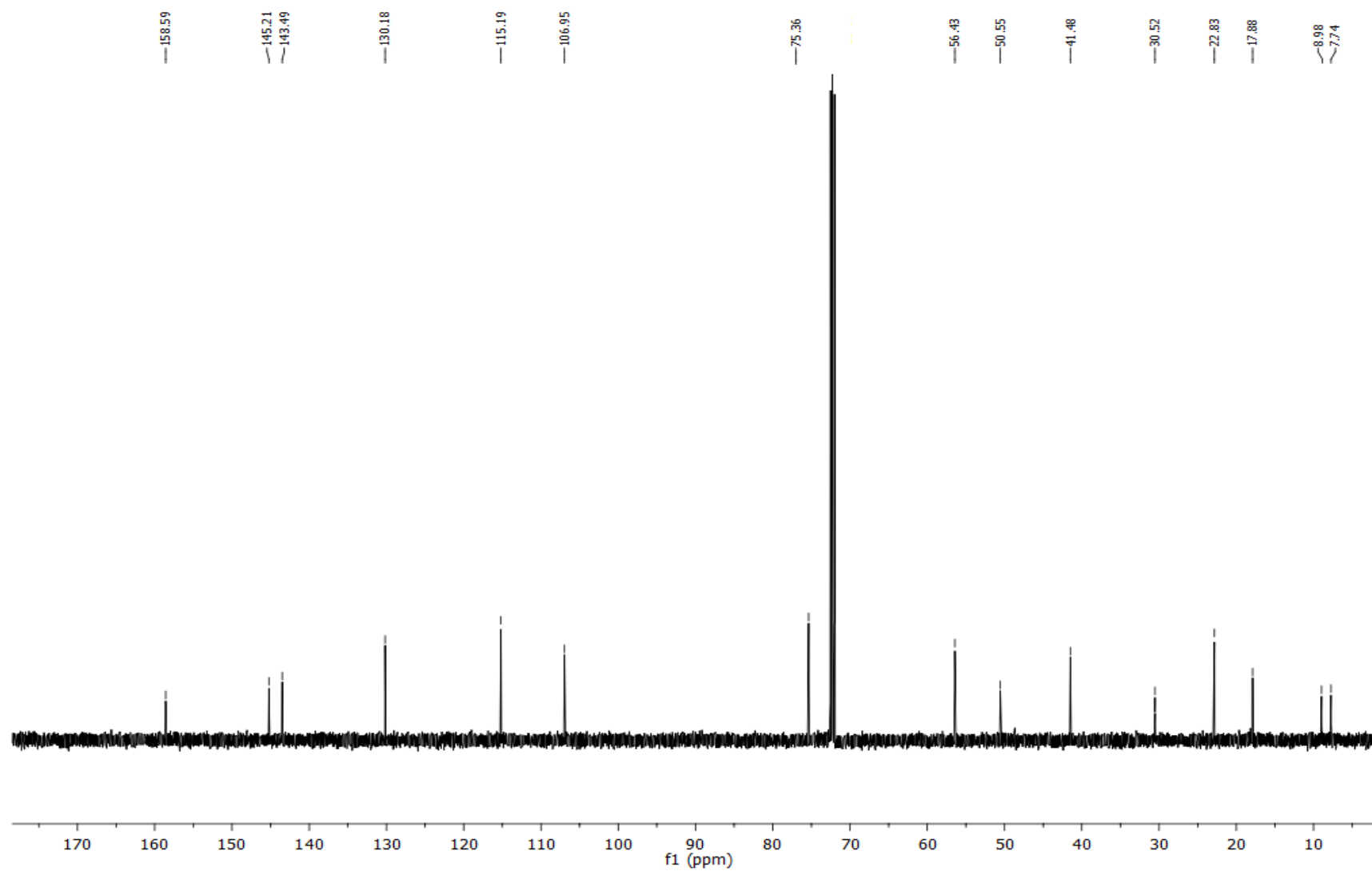
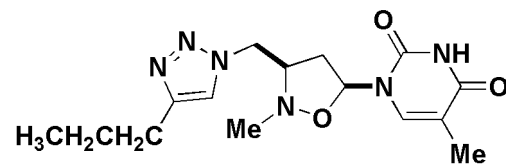
^{13}C NMR (126 MHz, DMSO) of compound **13b**



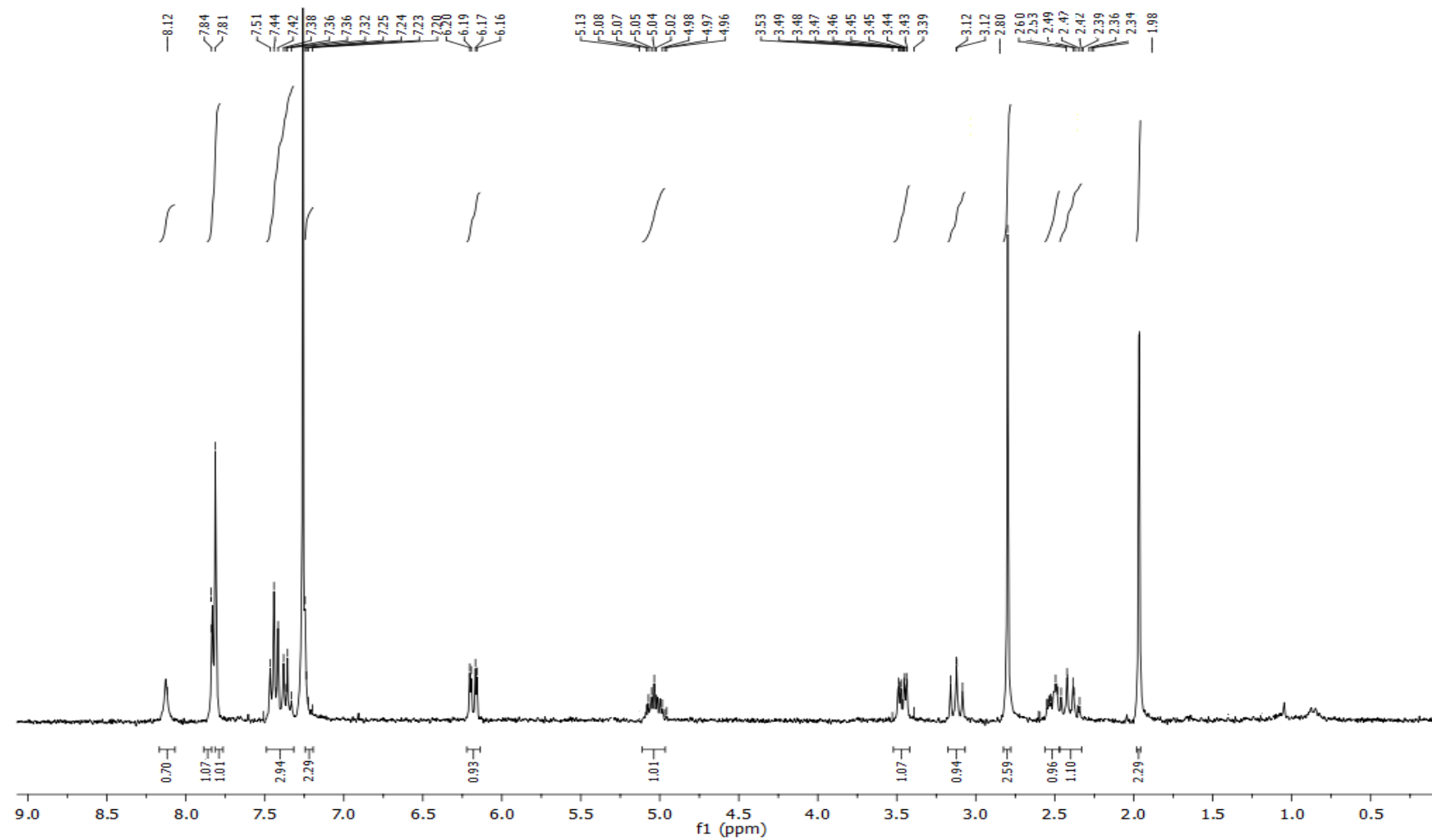
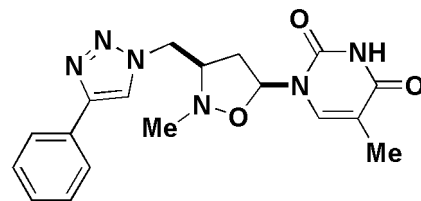
¹H NMR (500 MHz, CDCl₃) of compound **13c**



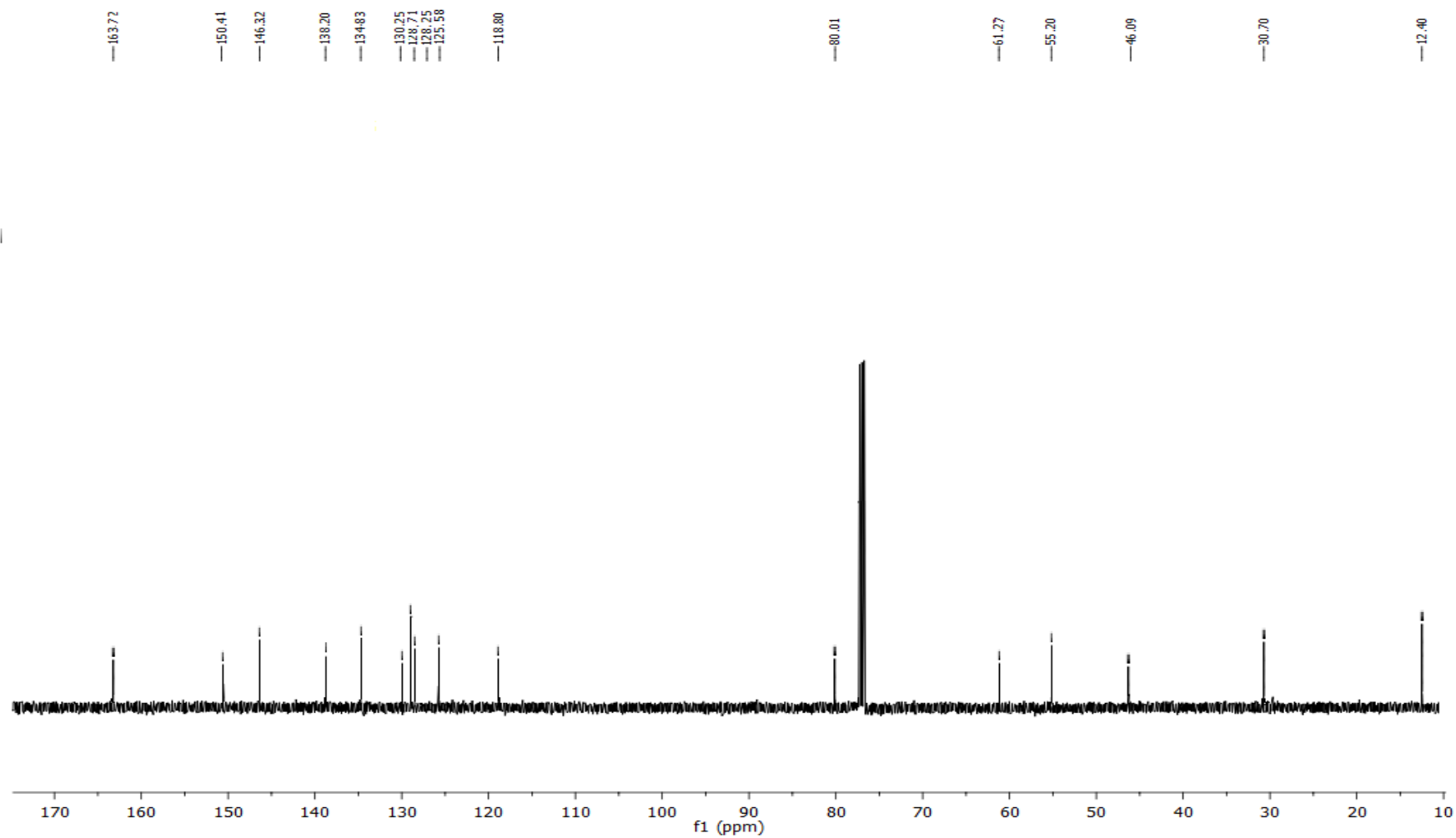
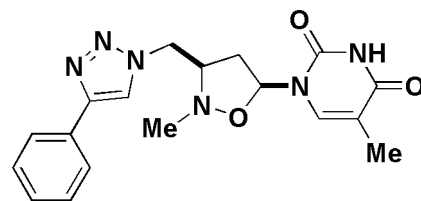
^{13}C NMR (126 MHz, CDCl_3) of compound **13c**



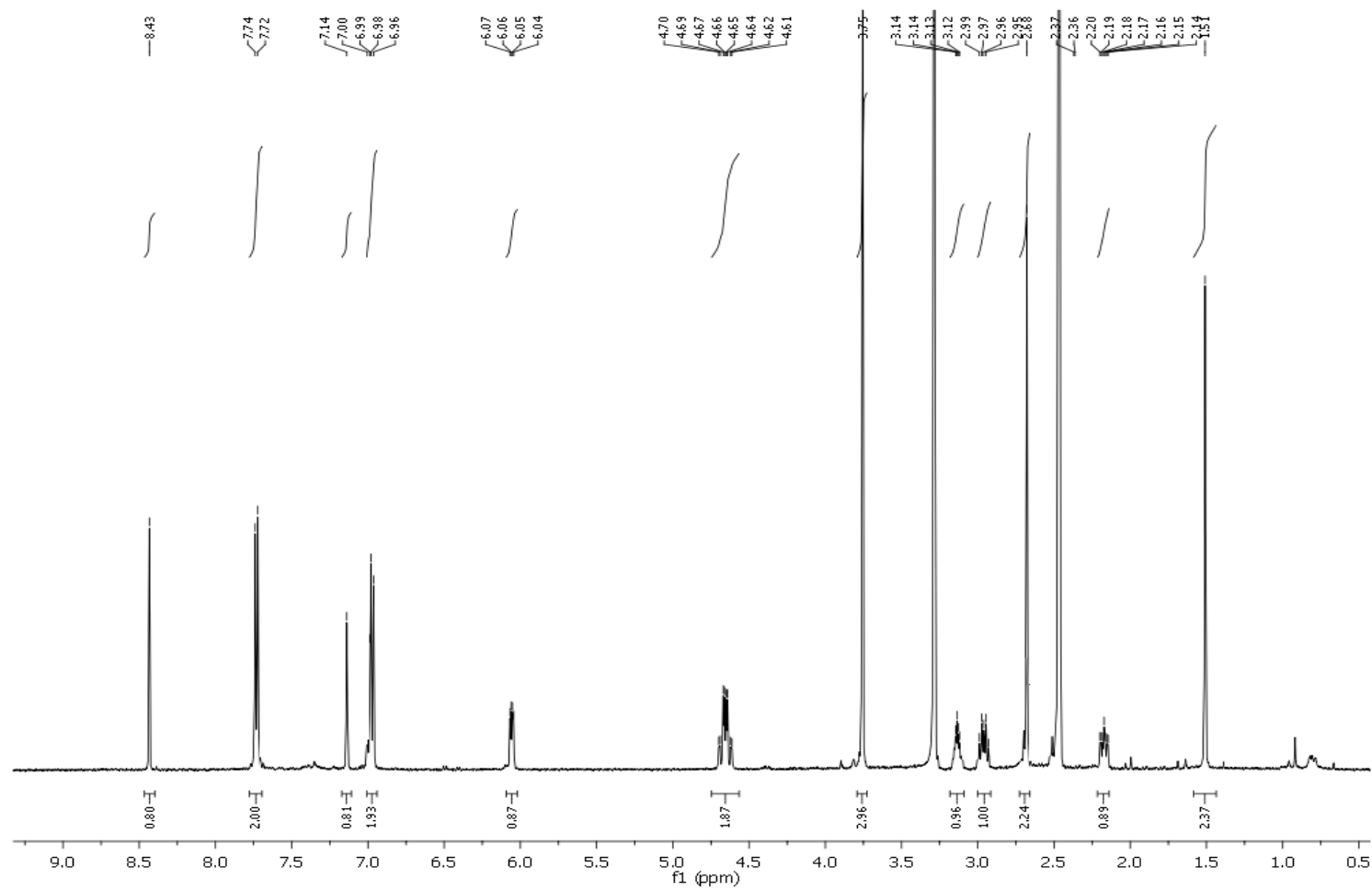
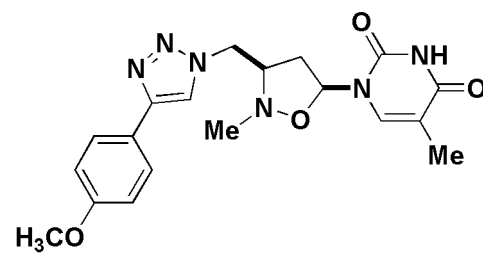
^1H NMR (300 MHz, CDCl_3) of compound **13d**



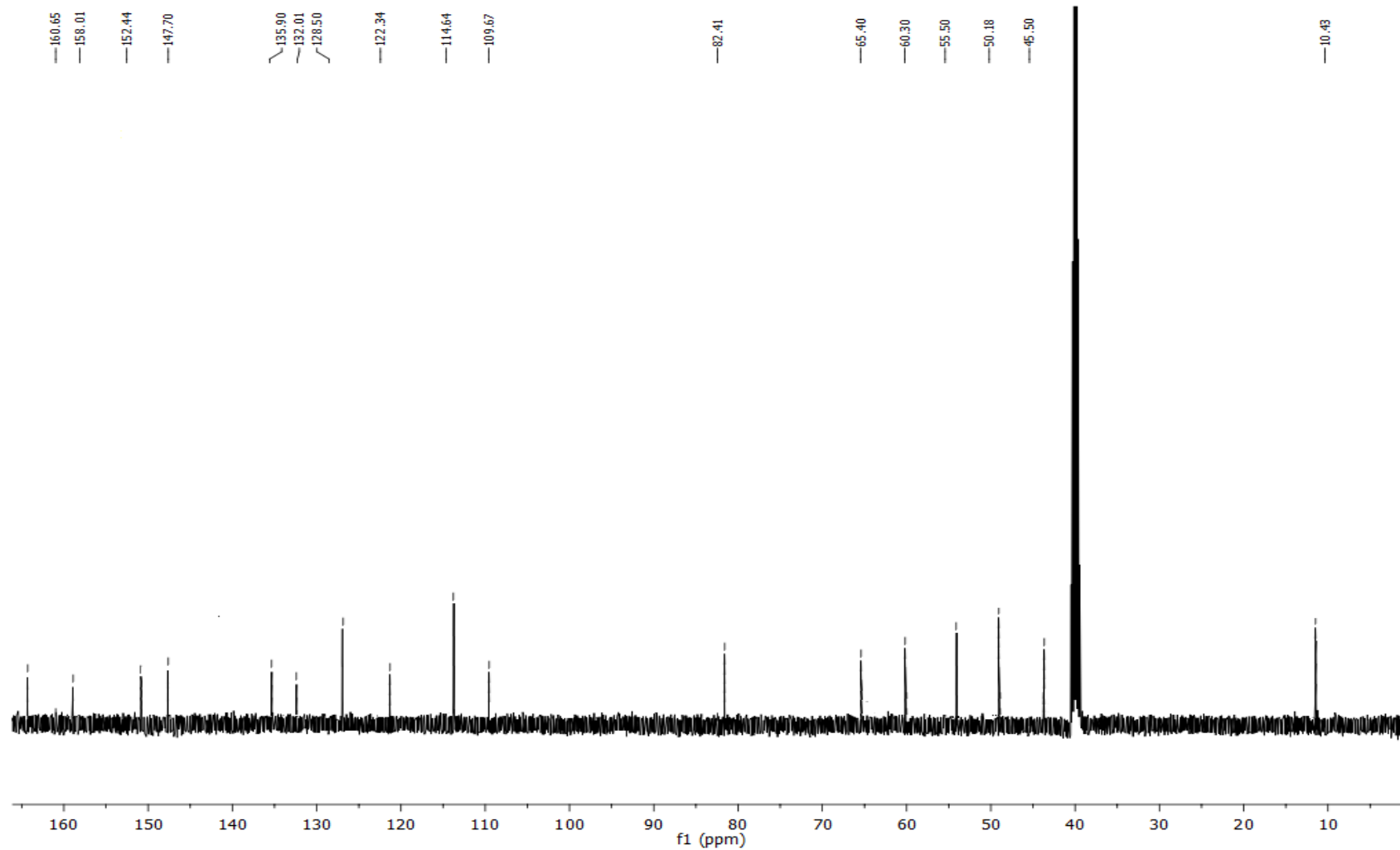
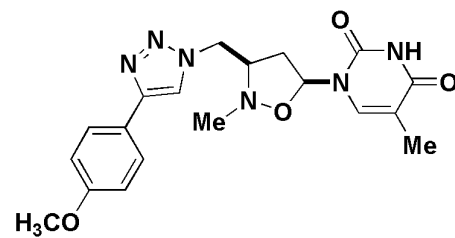
^{13}C NMR (126 MHz, CDCl_3) of compound **13d**



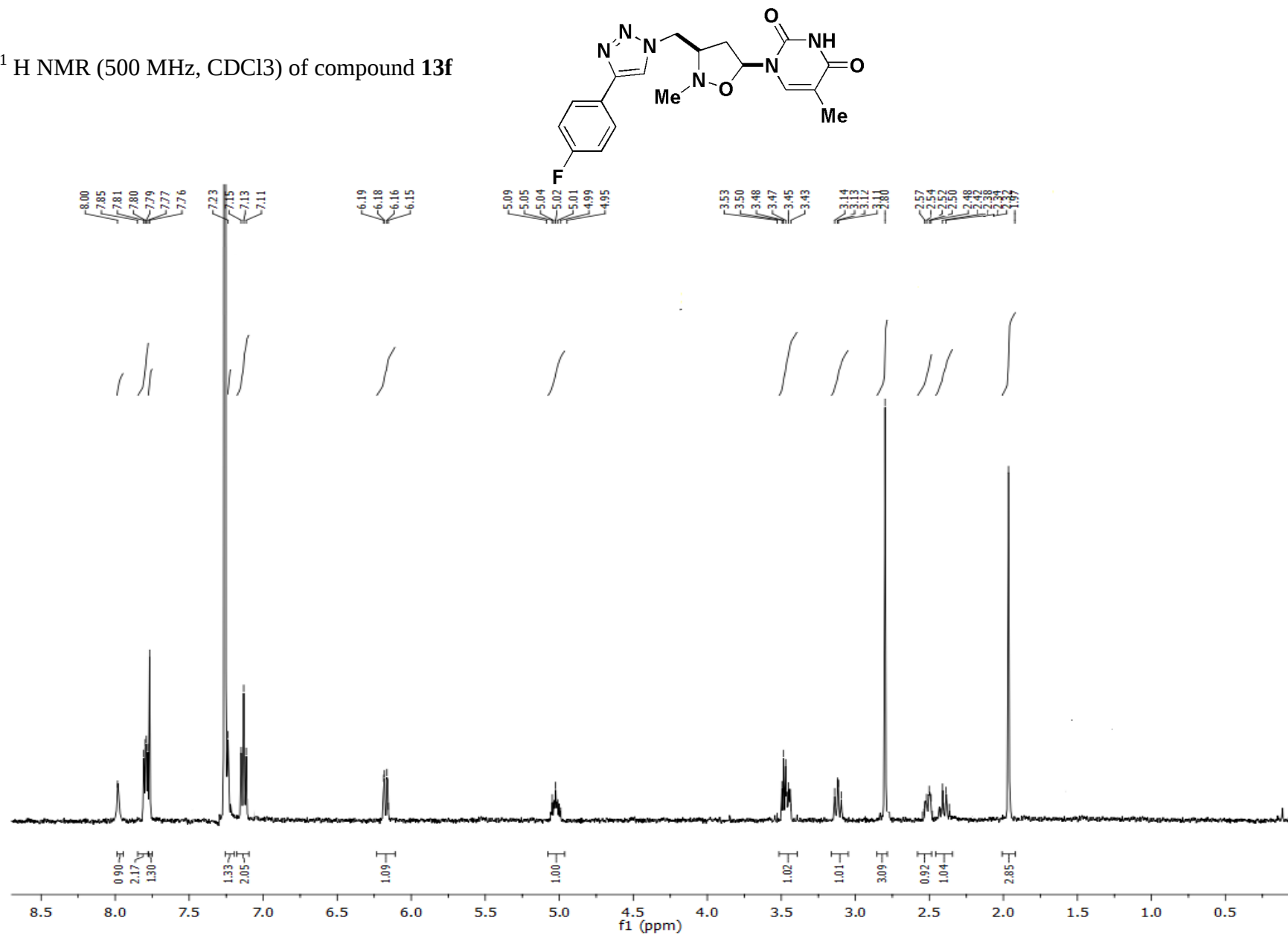
^1H NMR (500 MHz, DMSO) of compound **13e**



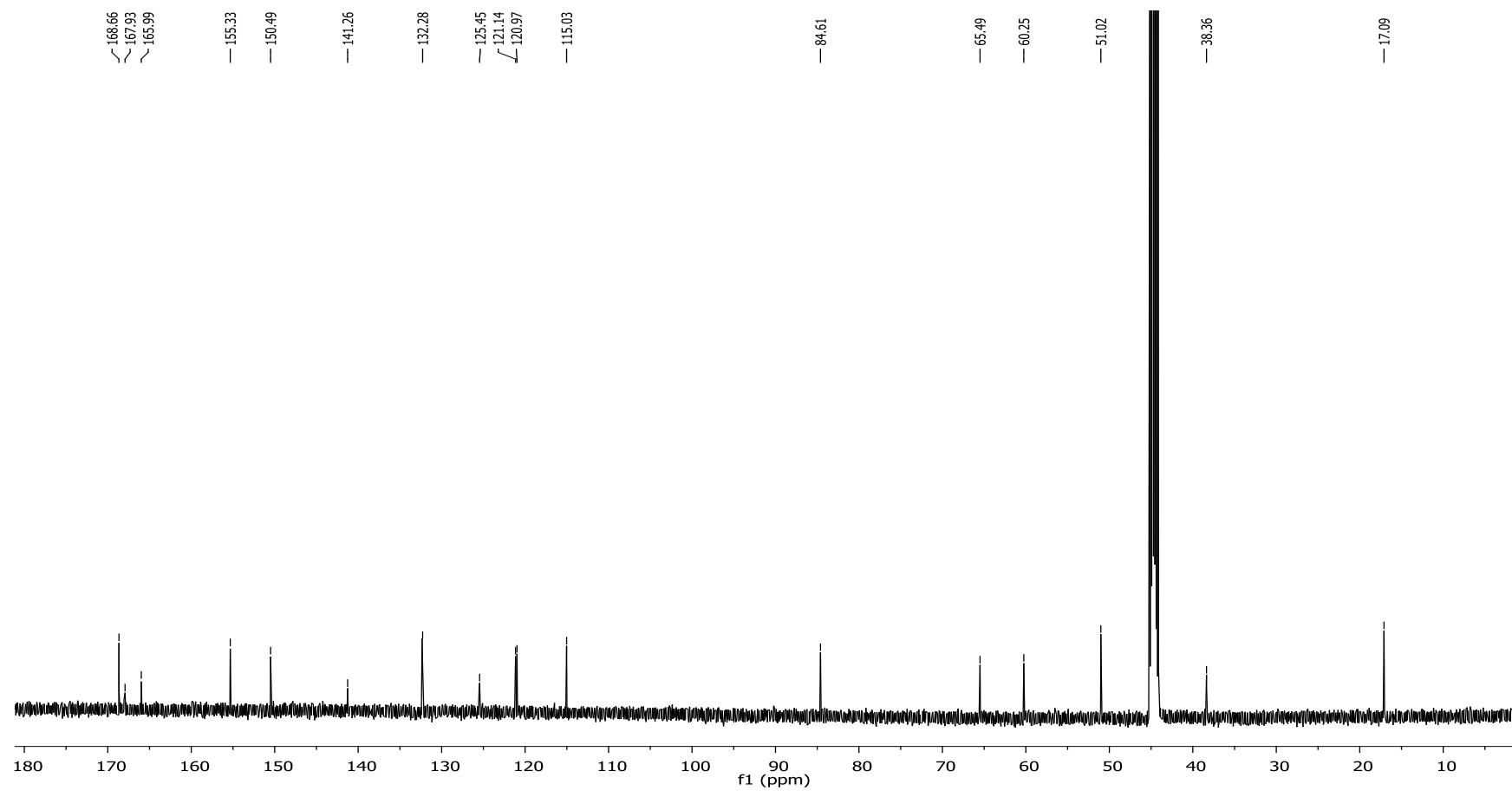
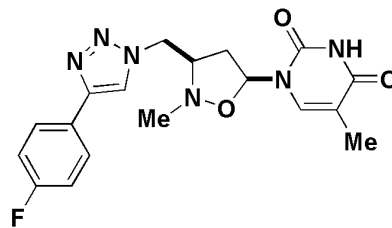
^{13}C NMR (126 MHz, DMSO) of compound **13e**



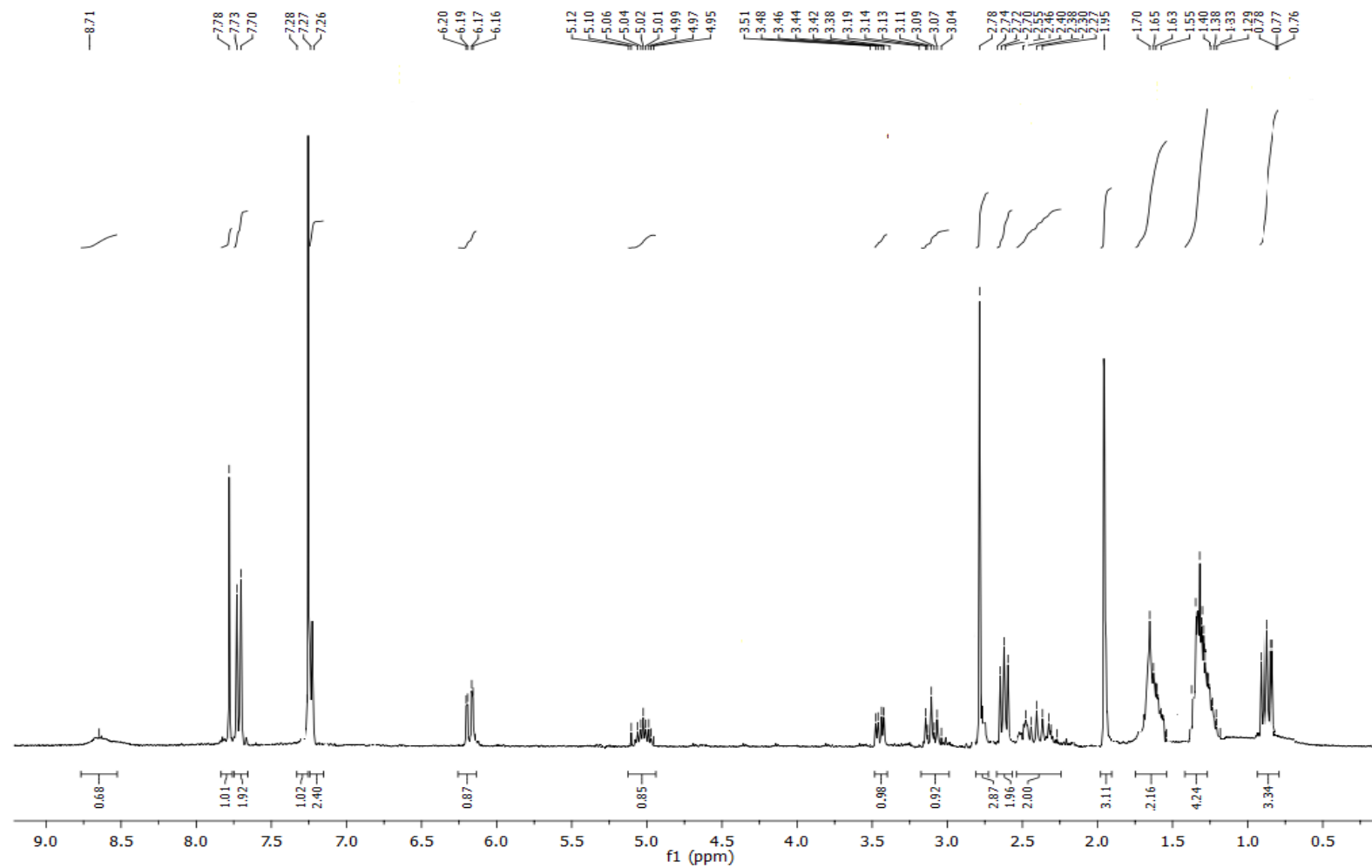
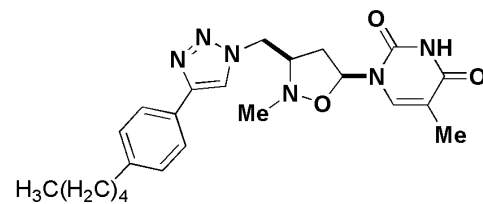
¹H NMR (500 MHz, CDCl₃) of compound **13f**



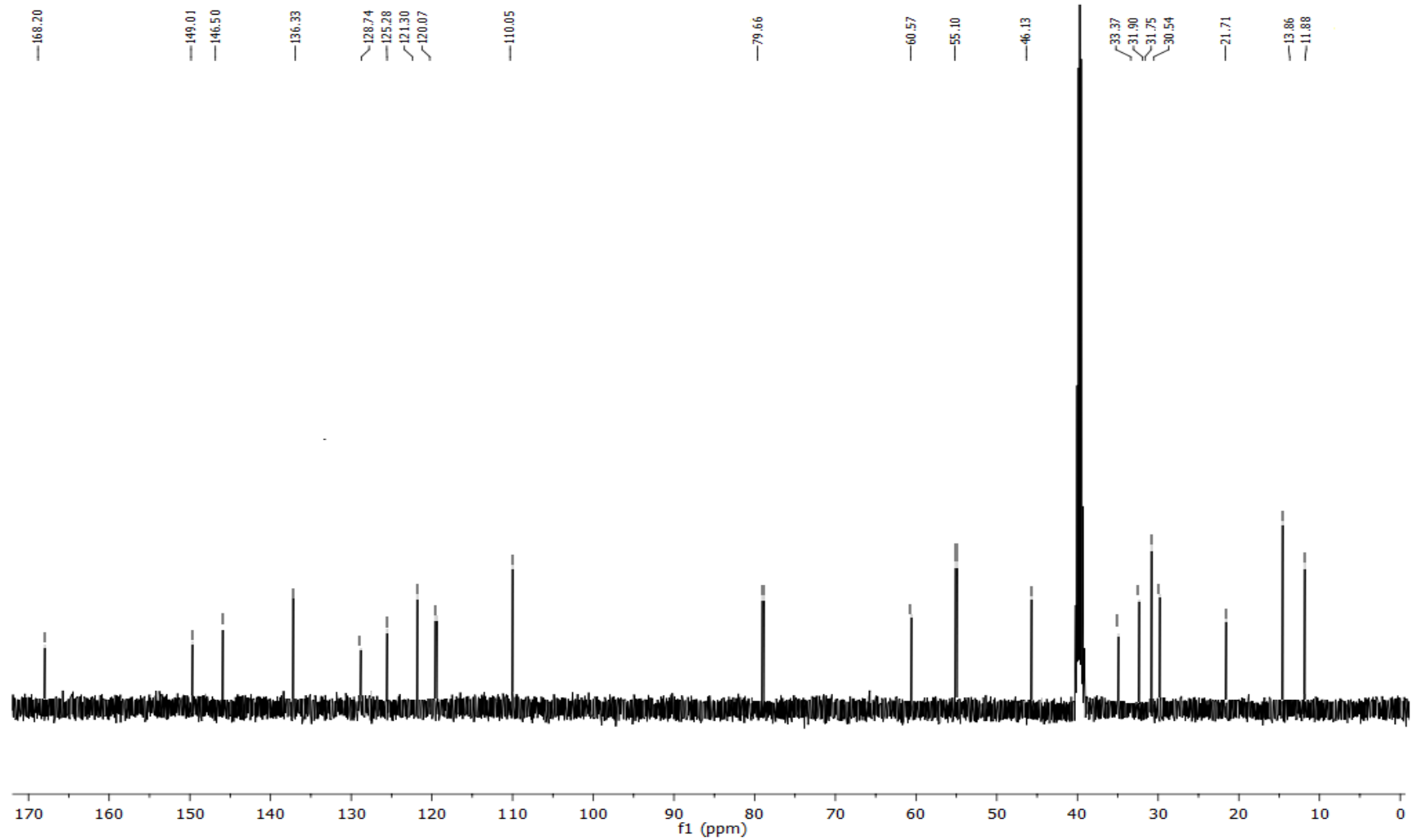
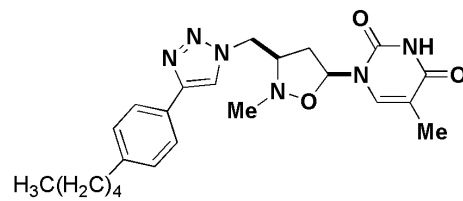
^{13}C NMR (126 MHz, DMSO) of compound **13f**



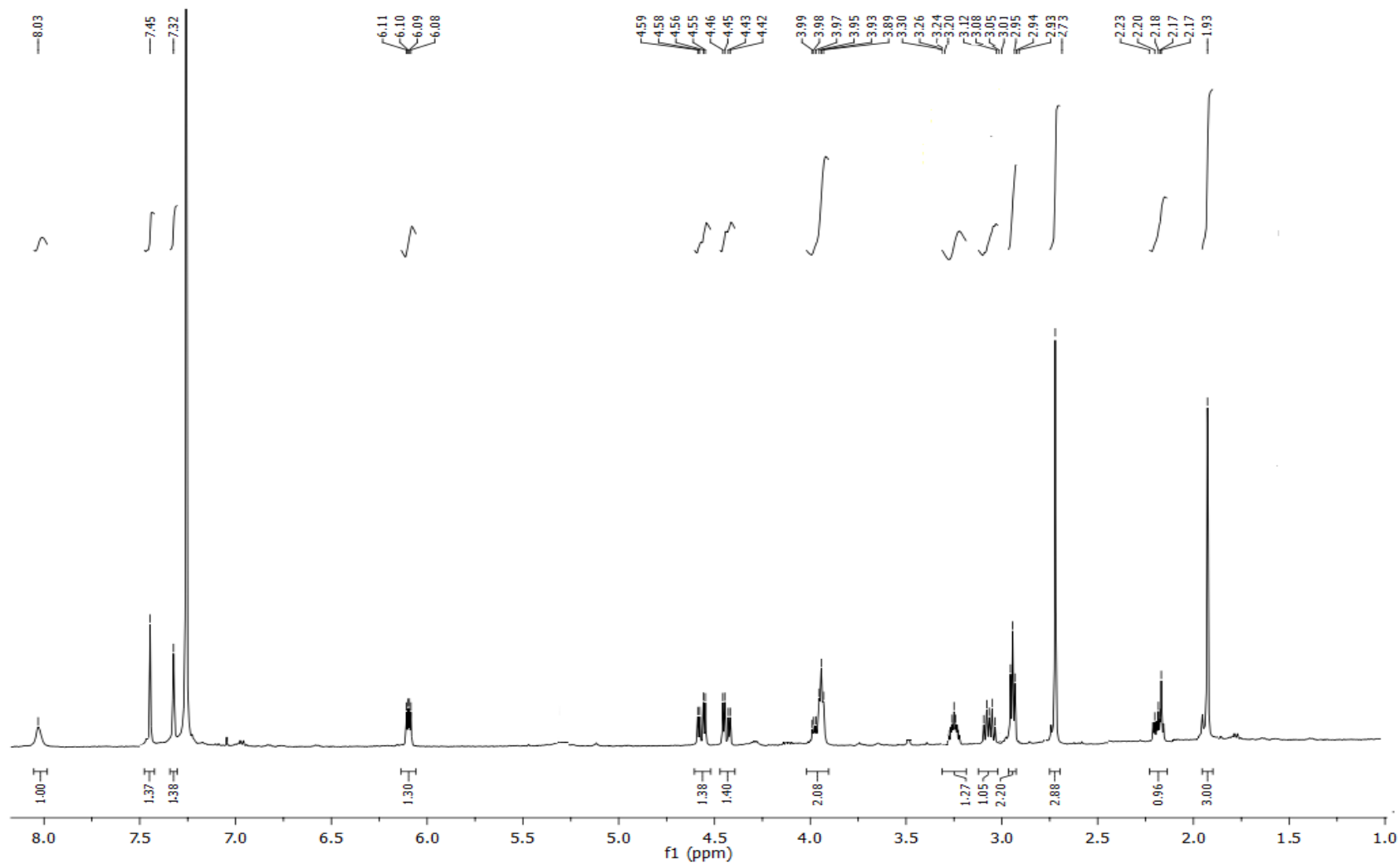
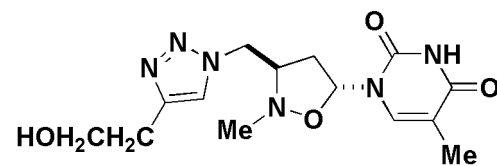
^1H NMR (300 MHz, CDCl_3) of compound **13g**



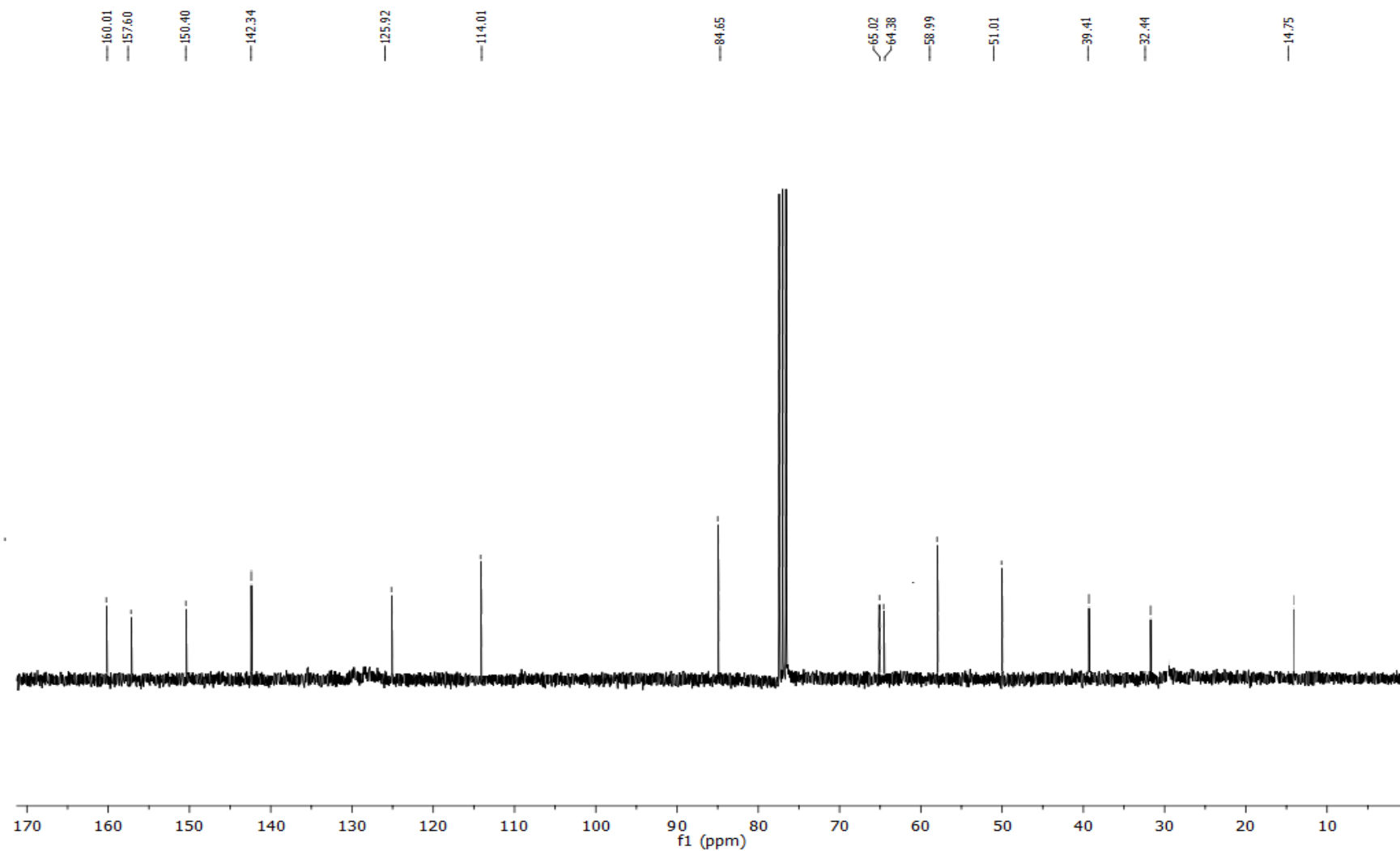
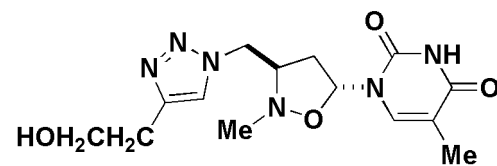
¹³C NMR (126 MHz, DMSO) of compound **13g**



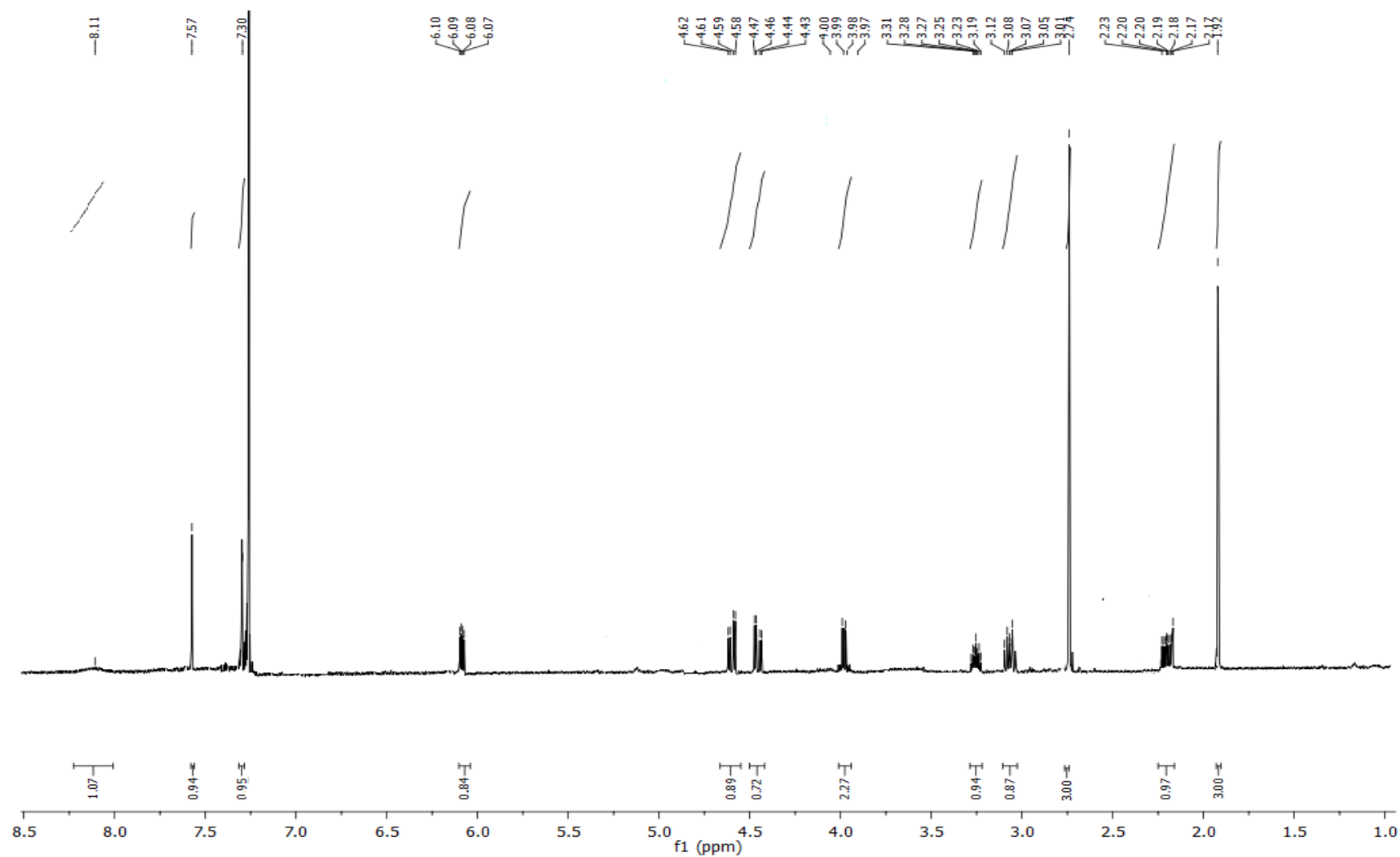
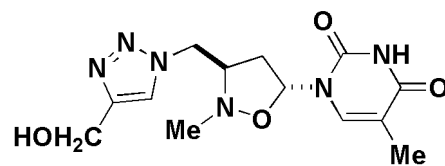
^1H NMR (500 MHz, CDCl_3) of compound **14a**



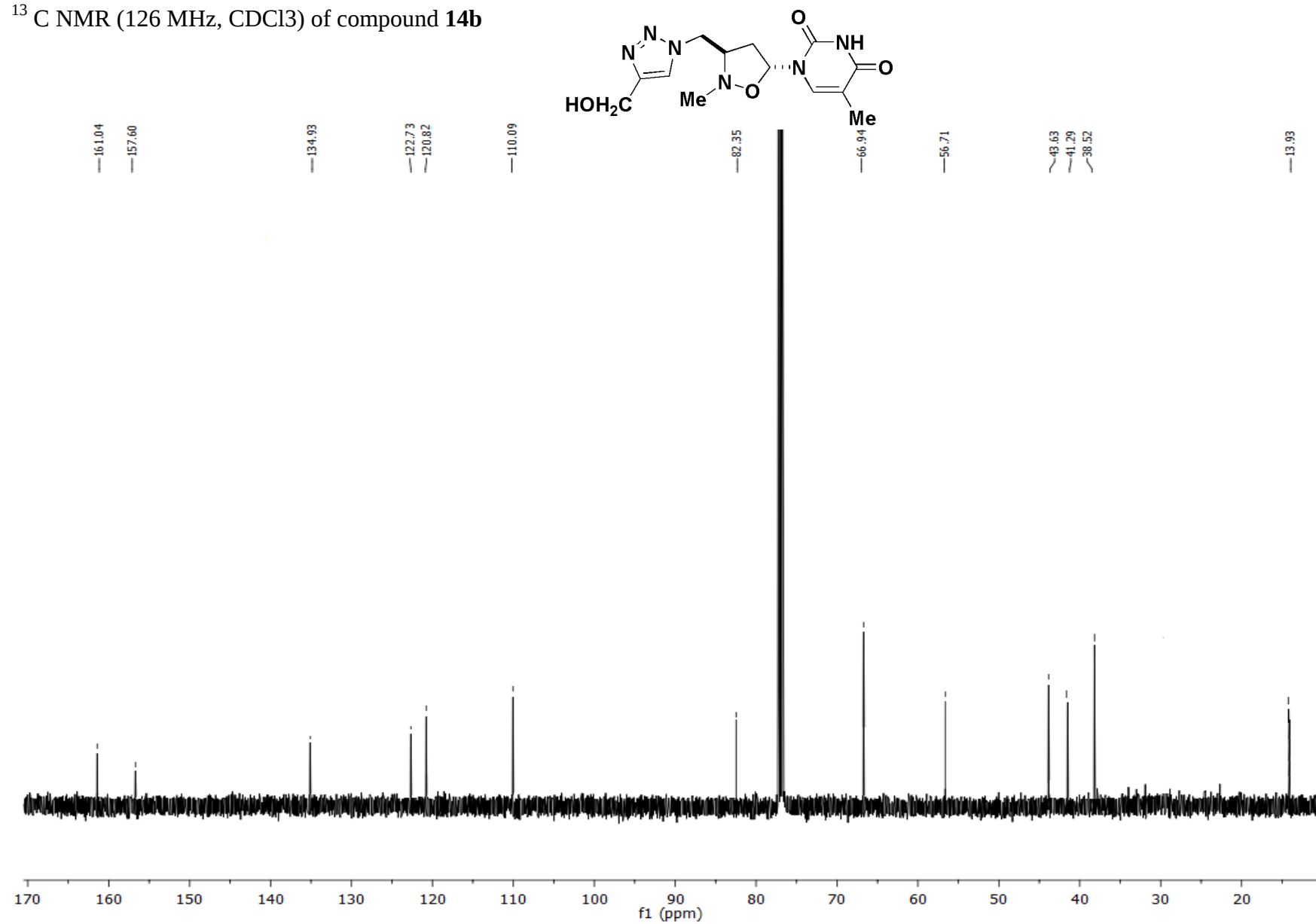
^{13}C NMR (126 MHz, CDCl_3) of compound **14a**



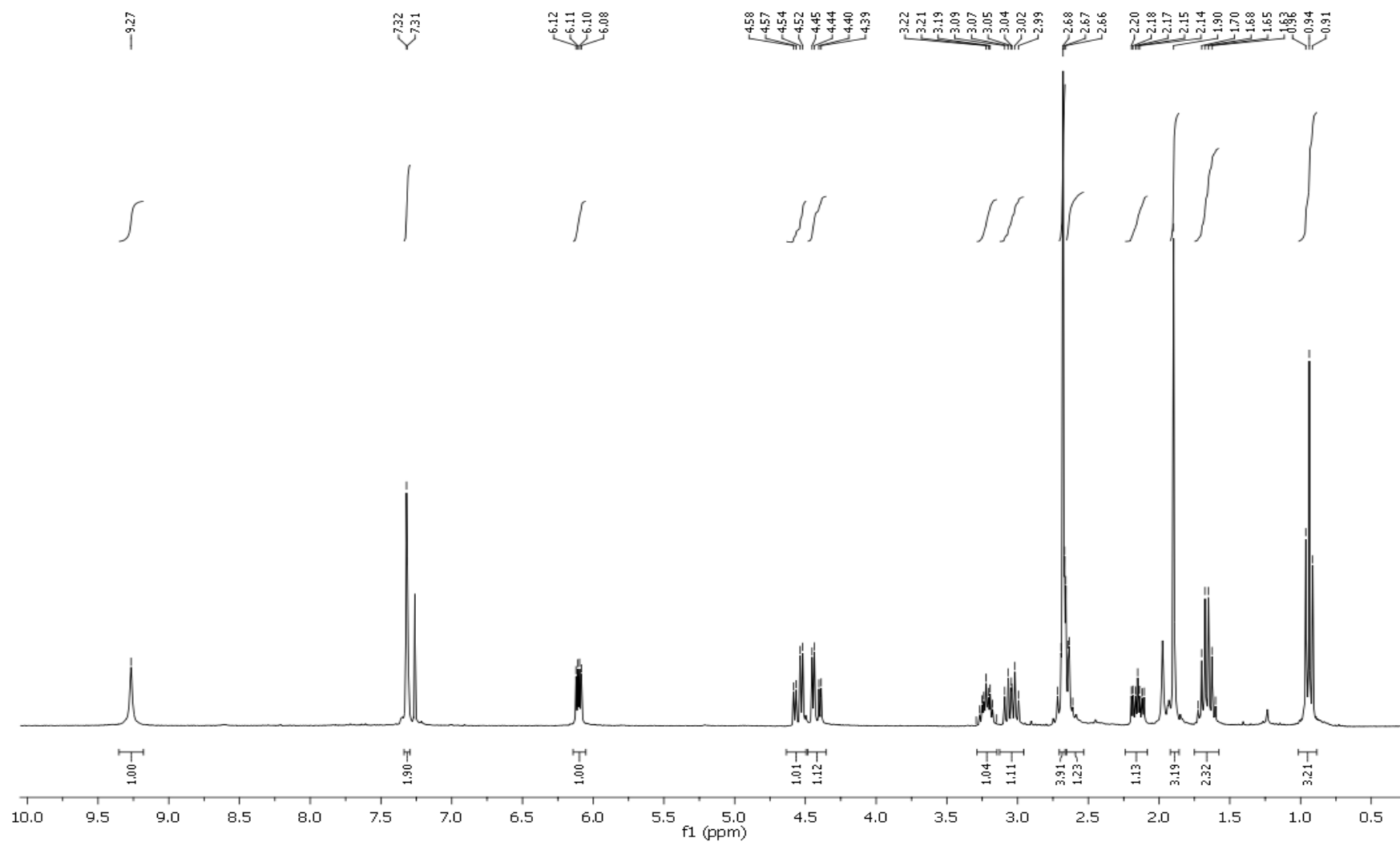
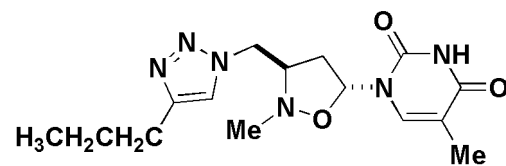
¹H NMR (500 MHz, CDCl₃) of compound **14b**



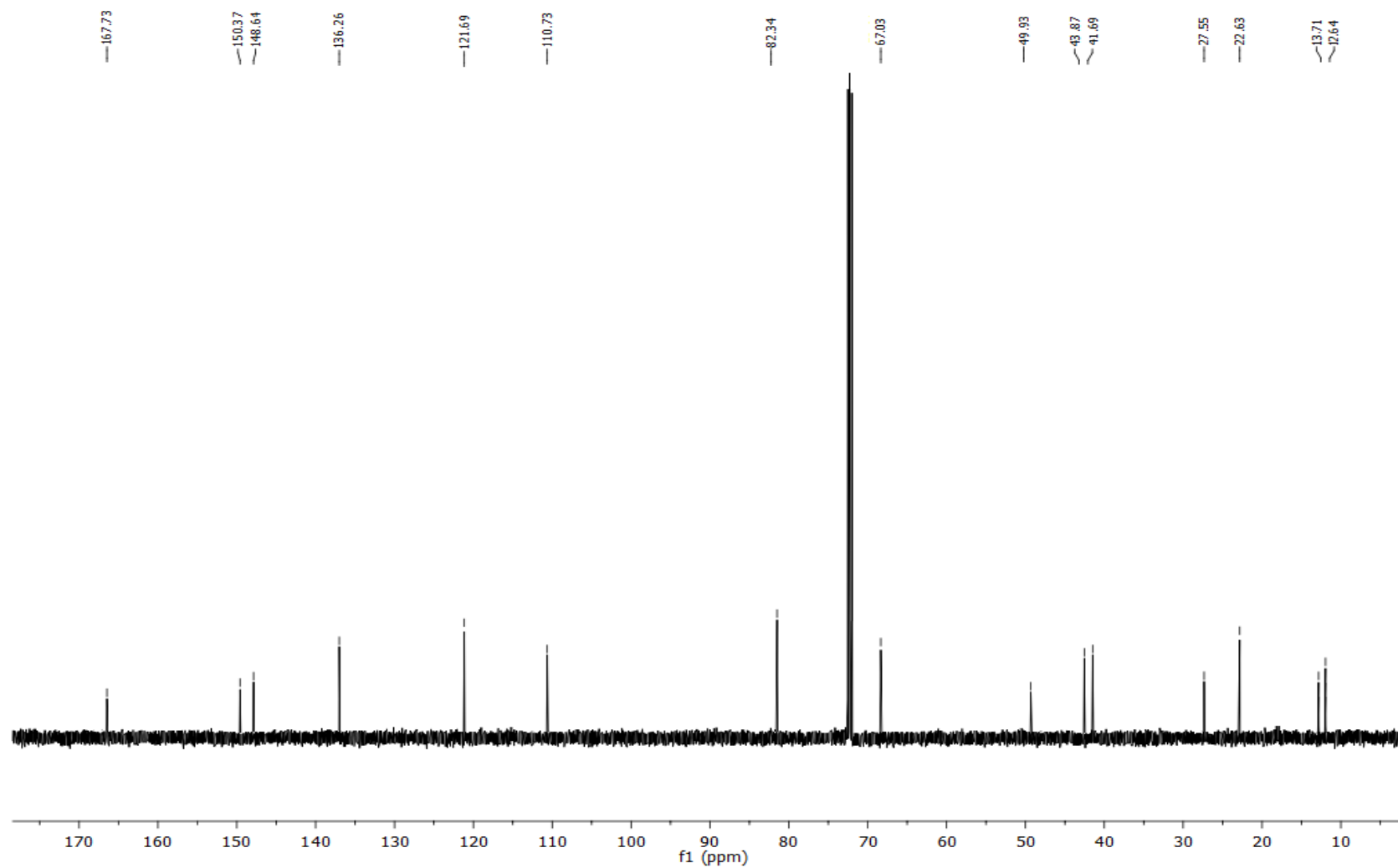
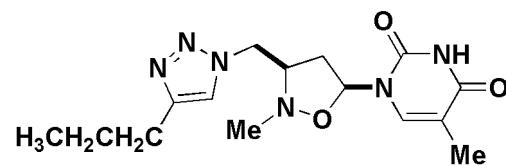
^{13}C NMR (126 MHz, CDCl_3) of compound **14b**



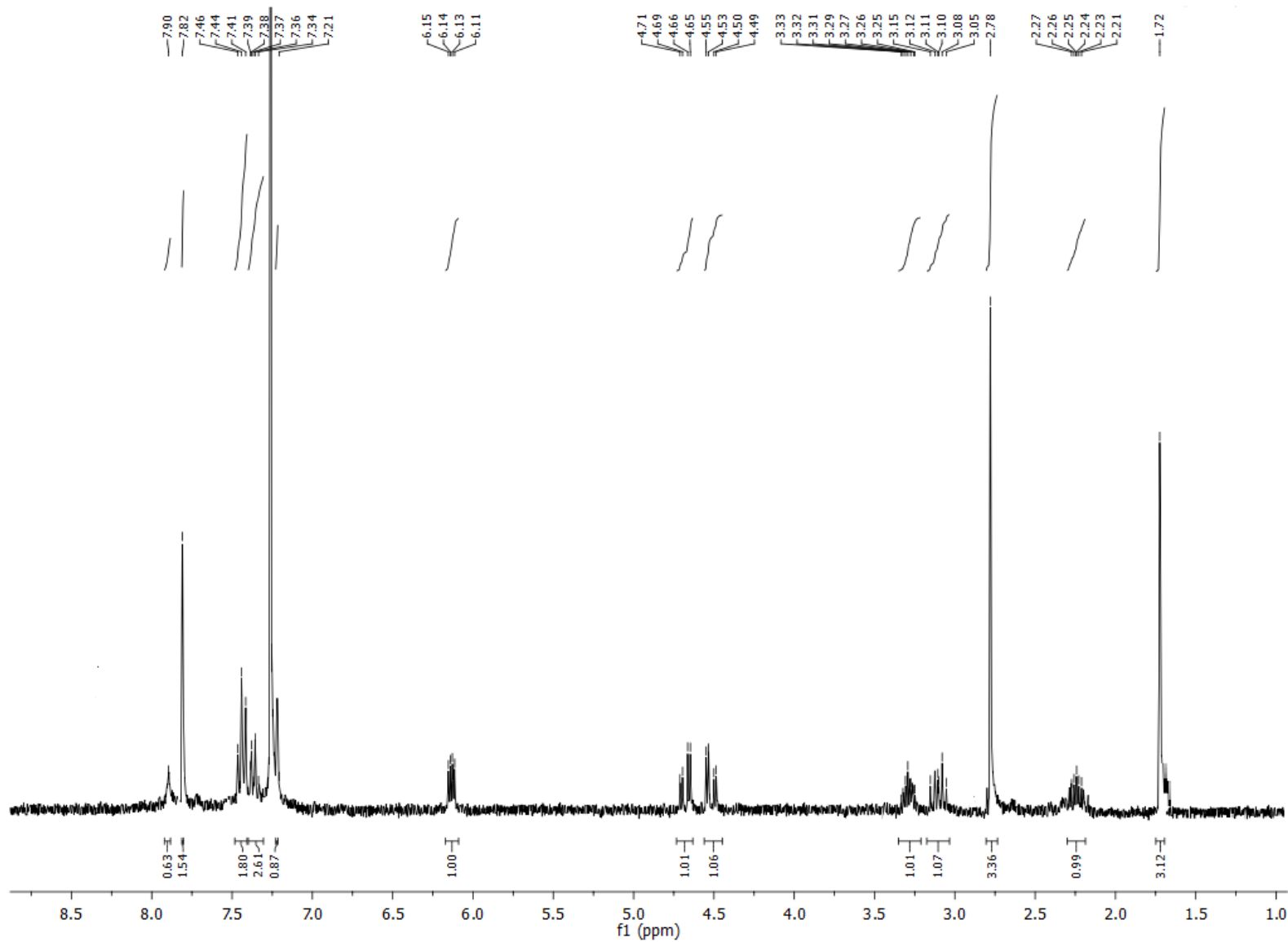
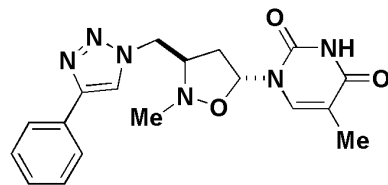
¹H NMR (300 MHz, CDCl₃) of compound **14c**



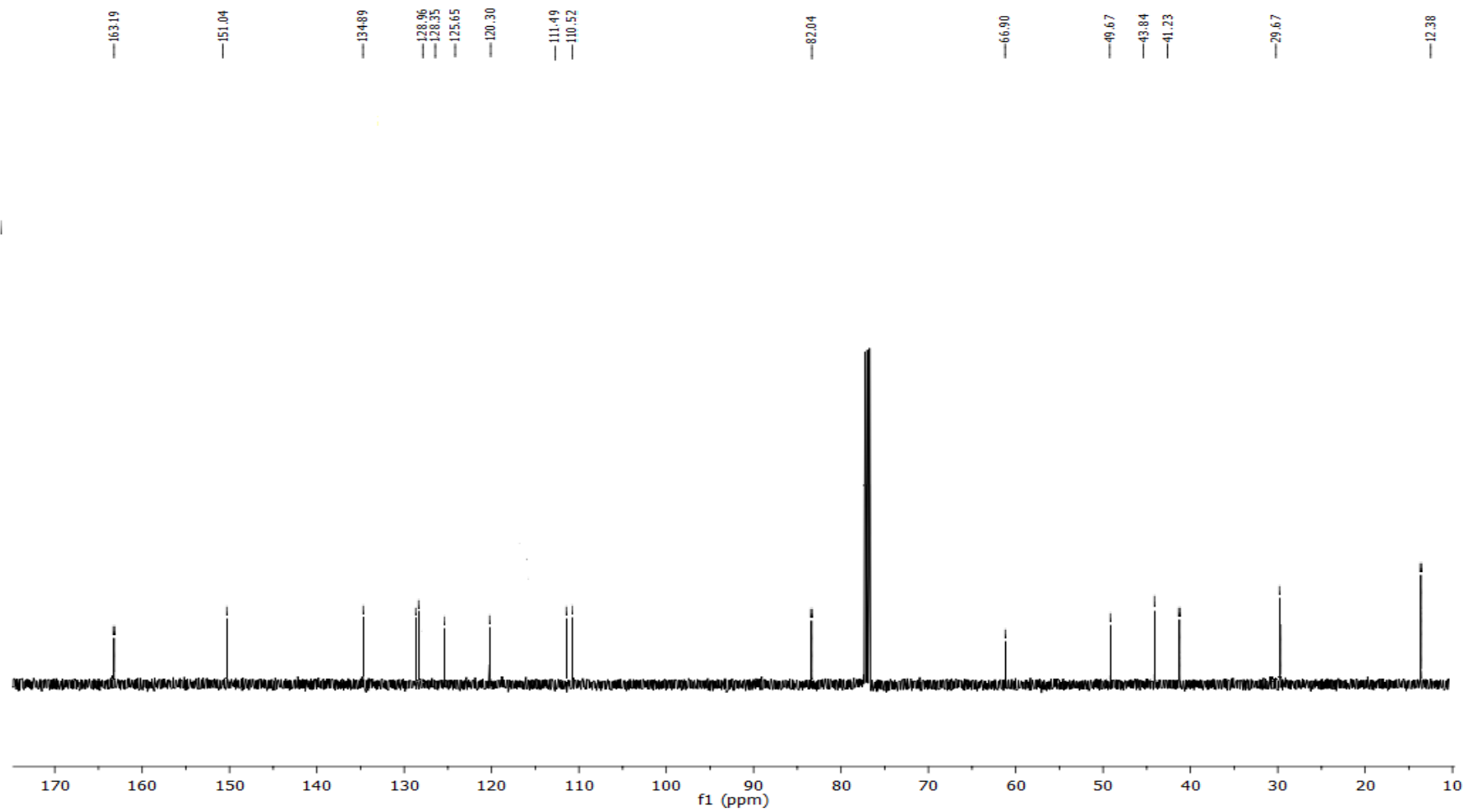
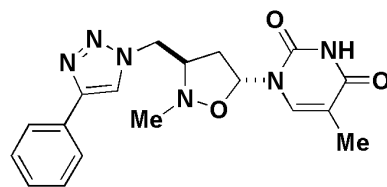
^{13}C NMR (126 MHz, CDCl_3) of compound **14c**



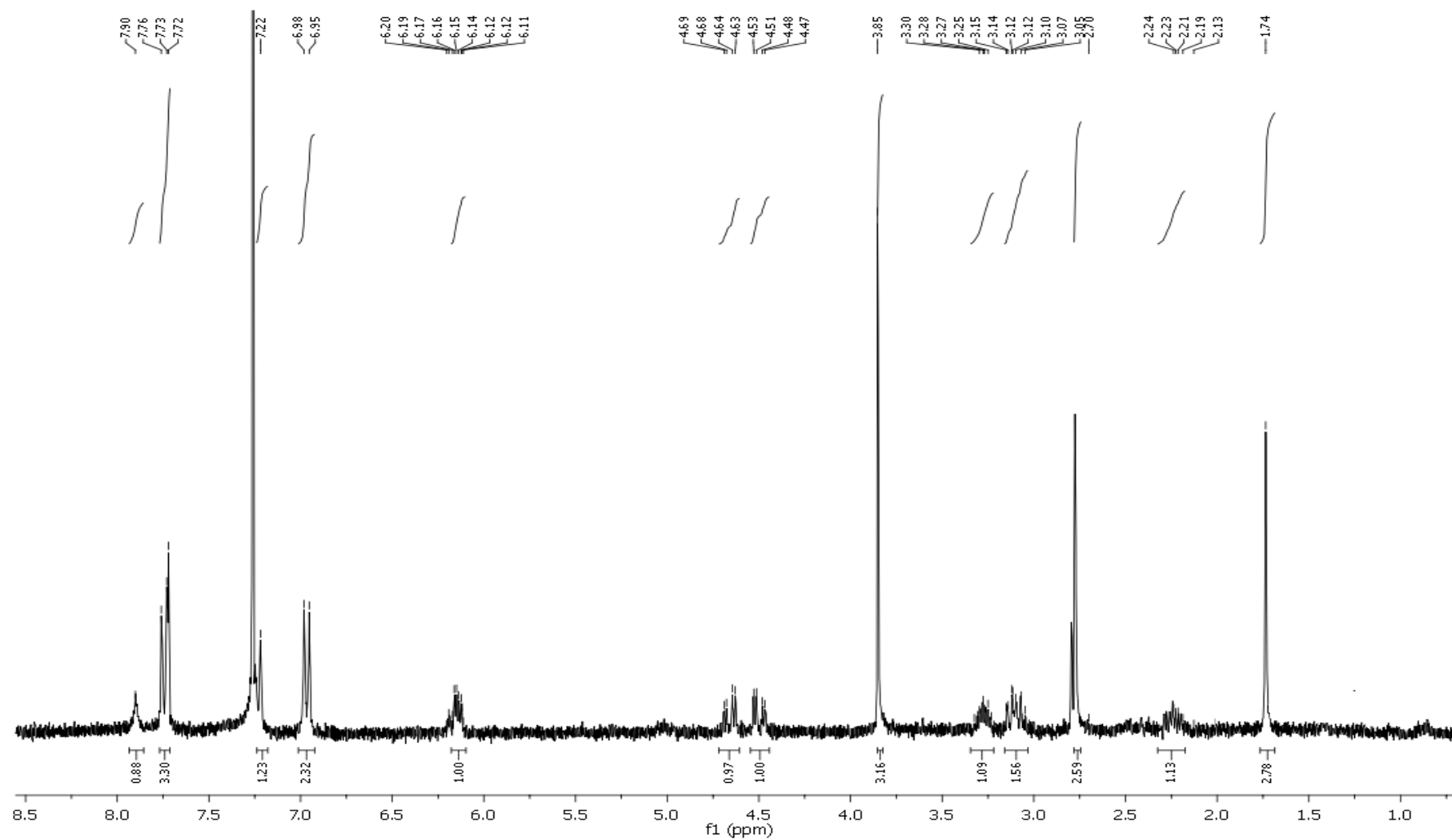
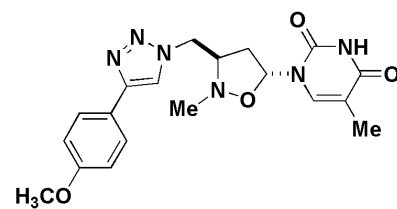
^1H NMR (300 MHz, CDCl_3) of compound **14d**



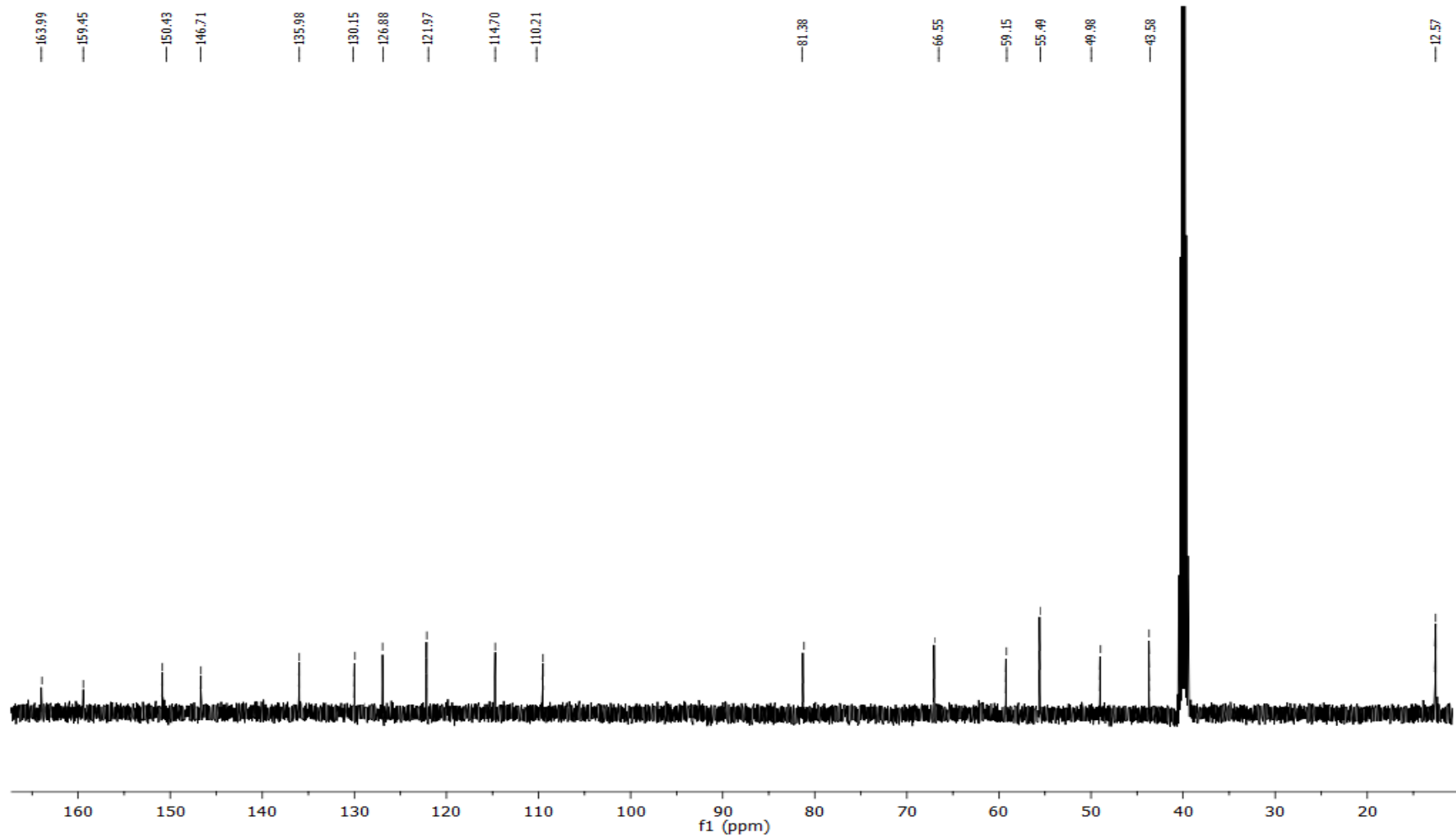
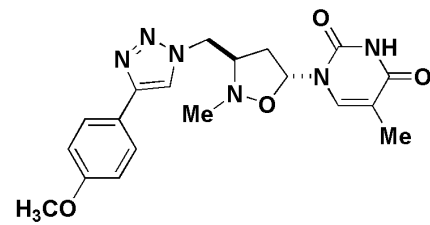
^{13}C NMR (126 MHz, CDCl_3) of compound **14d**



^1H NMR (300 MHz, CDCl_3) of compound **14e**



^{13}C NMR (126 MHz, DMSO) of compound **14e**

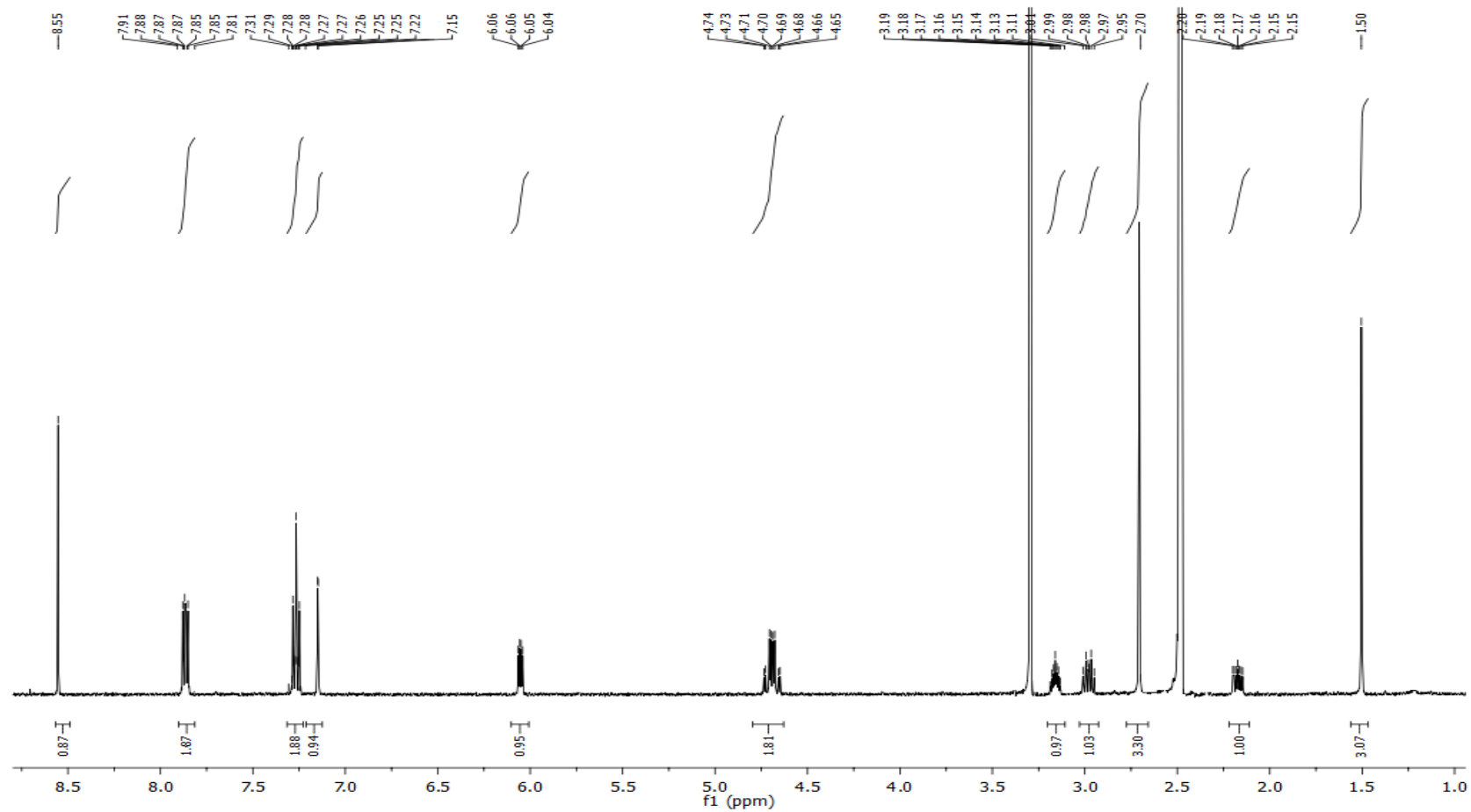
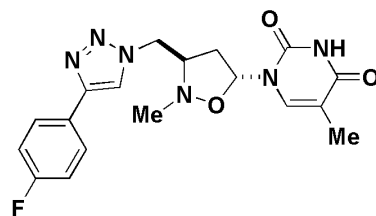


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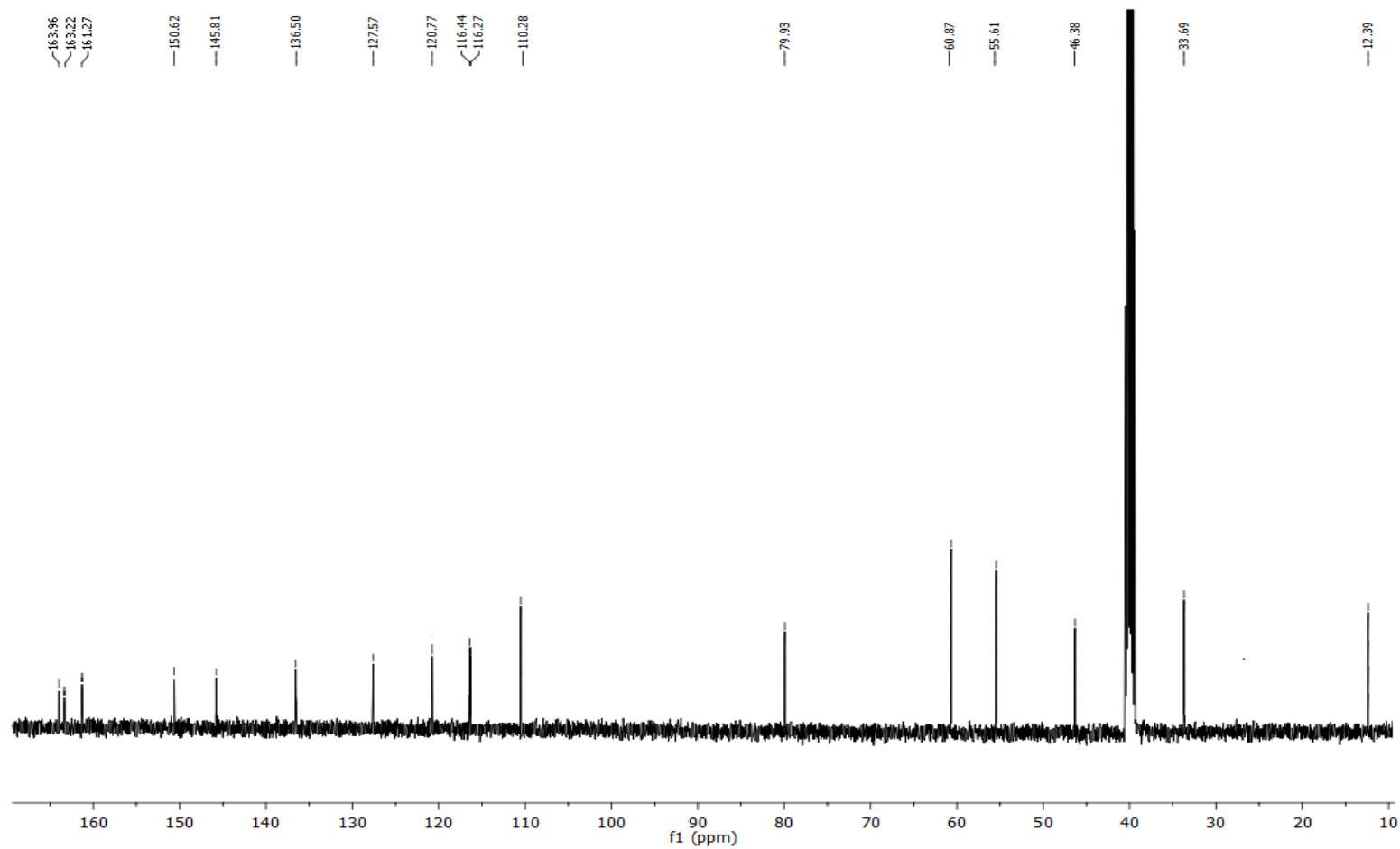
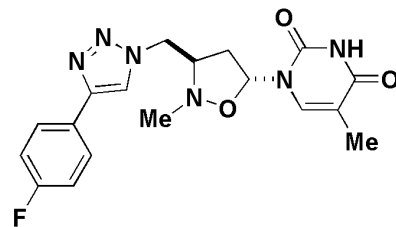
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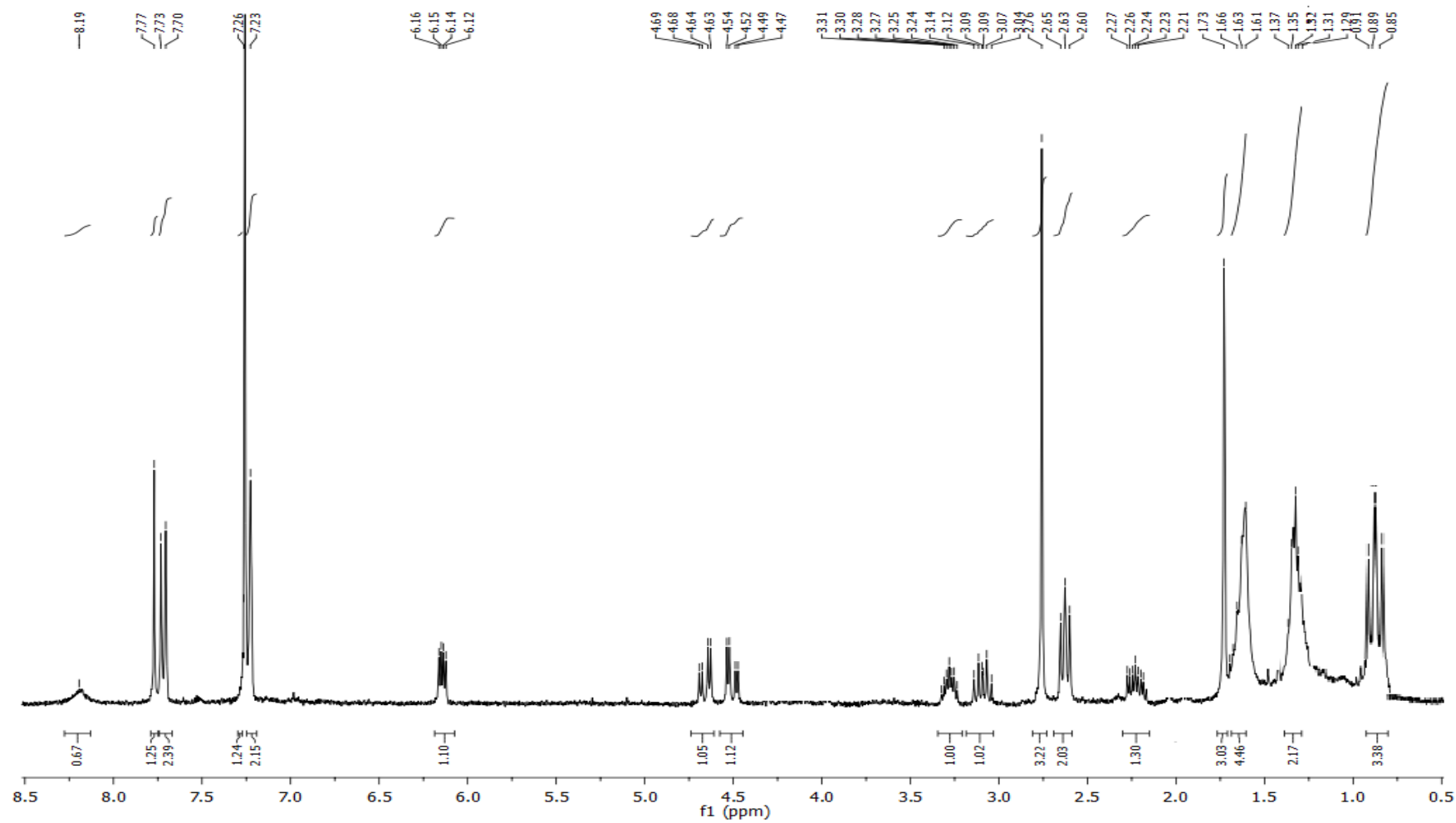
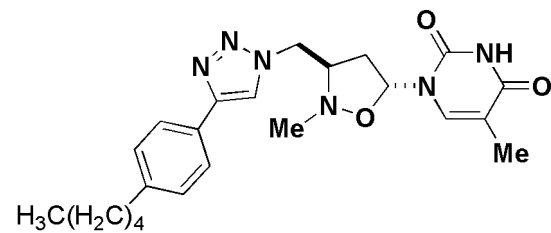
NMR (500 MHz, DMSO) of compound **14f**



^{13}C NMR (126 MHz, CDCl_3) of compound **14f**



^1H NMR (300 MHz, CDCl_3) of compound **14g**



NMR (126 MHz, DMSO) of compound **14g**

