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Copper catalyzed alkyne–azide cycloaddition with 3-propargyl-γ-butyrolactones

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General remarks. ^{1}H and ^{13}C NMR spectra were recorded on Varian Mercury-300 MHz in DMSO-CCl_4 mixture (1:3) or on Bruker AVANCE 400 MHz spectrometer in $CDCl_3$ or DMSO-d_6. Chemical shifts (δ) in ppm are reported as quoted relative to the residual signals of chloroform-*d* (7.25 for ^{1}H NMR and 77.0 for ^{13}C NMR) or DMSO-d_6 (2.49 for ^{1}H NMR and 39.5 for ^{13}C NMR) as internal references. The coupling constants (*J*) are given in Hertz. IR spectra were recorded on Thermo Nicolet IR 200 or Nicolet Avatar 330 FT. ESI-MS spectra were measured with Orbitrap Elite instrument. The silica gel used for column chromatography was 230-400 Mesh. TLC analysis was performed on "Silufol UV-254" plates. All reagents were of reagent grade and were used as such or distilled prior to use. Melting points were determined on "Boetius" micro-heating stage and "SMP10".

Synthesis of 1,2,3-triazoles 7-18 (general procedure). A 3 ml vial with a screw cup was charged with the corresponding azide (1.1 mmol), DMSO (2 ml), DIPEA (0.142 g, 1.1 mmol), CuI (0.019 g, 0.1 mmol) the corresponding 3-propargyl-γ-butyrolactone (1 mmol) and heated (65 °C) for 5 h. The mixture was poured into 0.1 M HCl (30 ml) and extracted with CH_2Cl_2 (3×10 ml). The combined extracts were dried over Na_2SO_4, the volatiles were evaporated and the residue was purified by column chromatography on silica gel using mixture of CH_2Cl_2 and MeOH (30:1) as the eluent.

Ethyl 2-{4-[(5-methyl-2-oxotetrahydrofuran-3-yl)methyl]-1*H*-1,2,3-triazol-1-yl}acetate, mixture of diastereomers (7). White powder, yield 261 mg (98%); m.p. 87 °C; IR (cm^{-1}), υ: 1742, 1762 (C=O). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 1.30 (t, *J* = 7.2 Hz, 3H, $\underline{CH_3}CH_2O$), 1.34 (d, *J* = 6.4 Hz, 0.9H, $\underline{CH_3}CH$, minor), 1.35 (d, *J* = 6.2 Hz, 2.1H, $\underline{CH_3}CH$, major), 1.64-1.73 (m, 0.7H, major), 2.04-2.11 (m, 0.3H, minor), 2.29-2.36 (m, 0.3H, minor), 2.50–2.56 (m, 0.7H, major), 2.99-3.16 (m, 2H, CH_2Het), 3.19-3.28 (m, 1H, CHC=O), 4.26 (q, *J* = 7.2 Hz, 2H, $CH_3\underline{CH_2}O$), 4.45-4.55 (m, 1H, $CH_3\underline{CH}$), 5.13 (s, 2H, NCH_2), 7.56 (s, 1H, Het). ^{13}C NMR (101 MHz, $CDCl_3$), δ: 13.6 (CH_3), 20.3 (major), 20.7 (minor), 25.2 (major), 25.7 (minor), 33.5 (minor), 35.7 (major), 38.9 (minor), 41.2 (major), 50.4 (CH_2N), 61.9 (CH_2O), 74.7 (O$\underline{C}$HMe, minor), 75.0 (O$\underline{C}$HMe, major), 123.2 (C=$\underline{C}$H-N), 144.2 ($\underline{C}$=CH-N), 165.9 (C=O), 177.7 (C=O, major), 178.0 (C=O, minor). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{12}H_{18}N_3O_4^+$ 268.1292; Found 268.1269.

Ethyl 2-{4-[(5,5-dimethyl-2-oxotetrahydrofuran-3-yl)methyl]-1*H*-1,2,3-triazol-1-yl}acetate (8). Pale brownish viscous oil, yield 278 mg (99%); IR (cm^{-1}), υ: 1751, (C=O). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 1.30 (t, *J* = 7.2 Hz, 3H, $\underline{CH_3}CH_2O$), 1.37 (s, 3H, CH_3), 1.38 (s, 3H, CH_3), 1.89-1.95 (m, 1H), 2.27-2.33 (m, 1H), 3.00-3.06 (m, 1H, CHC=O), 3.18-3.27 (m, 2H, CH_2Het), 4.26 (q, *J* = 7.2 Hz, 2H, $CH_3\underline{CH_2}O$), 5.13 (s, 2H, NCH_2), 7.55 (s, 1H, Het). ^{13}C NMR (101 MHz, $CDCl_3$), δ: 13.6, 25.5, 26.6, 28.4, 39.9, 40.6, 50.4 (CH_2N), 62.0 (CH_2O), 82.3 ($\underline{C}Me_2$), 123.2

(C=CH-N), 144.3 (C=CH-N), 165.8 (C=O), 177.3 (C=O). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{13}H_{20}N_3O_4^+$ 282.1449; Found 282.1457.

3-[(1-Benzyl-1*H*-1,2,3-triazol-4-yl)methyl]-5-methyldihydrofuran-2(3*H*)-one, mixture of diastereomers (9). White powder, yield 231 mg (85%); m.p. 85-86 °C; IR (cm^{-1}), υ: 1753 (C=O). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 1.28 (d, *J* = 6.1 Hz, 2.1H, CH_3CH, major), 1.29 (d, *J* = 6.4 Hz, 0.9H, CH_3CH, minor), 1.57–1.66 (m, 0.7H, major), 1.99-2.05 (m, 0.3H, minor), 2.23-2.30 (m, 0.3H, minor), 2.44-2.51 (m, 0.7H, major), 2.88-3.19 (m, 3H, CHCH_2Het), 4.39-4.50 (m, 1H), 5.43 (d, *J* = 14.9 Hz, 1H, CH_2Ph), 5.48 (d, *J* = 14.9 Hz, 1H, CH_2Ph), 7.18-7.25 (m, 2H, Ph), 7.28-7.39 (m, 4H, Ph, Het). ^{13}C NMR (101 MHz, $CDCl_3$), δ: 20.3 (major), 20.7 (minor), 25.3 (major), 25.8 (minor), 33.6 (minor), 35.8 (major), 38.9 (minor), 41.3 (major), 53.7 (CH_2Ph), 74.7 (OCHMe, minor), 75.00 (OCHMe, major), 121.8 (C_{arom}), 127.5 (C_{arom}), 128.3 (C_{arom}), 128.7 (C_{arom}), 134.3 (C_{arom}), 144.4 (C=CH-N), 177.7 (C=O). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{18}N_3O_2^+$ 272.1394; Found 272.1376.

3-[(1-Benzyl-1*H*-1,2,3-triazol-4-yl)methyl]-5,5-dimethyldihydrofuran-2(3*H*)-one (10). White powder, yield 270 mg (95%); m.p. 103-105 °C; IR (cm^{-1}), υ: 1759 (C=O). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 1.32 (s, 3H, CH_3), 1.33 (s, 3H, CH_3), 1.84-1.90 (m, 1H, CH_2 in cycle), 2.24-2.29 (m, 1H), 2.92-2.98 (m, 1H, CHCH_2Het), 3.13-3.22 (m, 2H, CHCH_2Het), 5.45 (d, *J* = 14.9 Hz, 1H, CH_2Ph), 5.50 (d, *J* = 14.9 Hz, 1H, CH_2Ph), 7.20-7.24 (m, 2H, Ph), 7.31-7.37 (m, 4H, Ph, Het). ^{13}C NMR (101 MHz, $CDCl_3$), δ: 25.6, 26.6, 28.3, 39.9, 40.5, 53.7 (CH_2Ph), 82.2 (CMe_2), 121.8 (C_{arom}), 127.5 (C_{arom}), 128.3 (C_{arom}), 128.7 (C_{arom}), 134.3 (C_{arom}), 144.4 (C=CH-N), 177.3 (C=O). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{20}N_3O_2^+$ 286.1551; Found 286.1548.

3-{[1-(4-Methoxyphenyl)-1*H*-1,2,3-triazol-4-yl]methyl}-5-methyldihydrofuran-2(3*H*)-one, mixture of diastereomers (11). White powder, yield 250 mg (87%); m.p. 89-90 °C; IR (cm^{-1}), υ: 1754 (C=O). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 1.31 (d, *J* = 6.1 Hz, 0.9H, CH_3CH, minor), 1.32 (d, *J* = 6.0 Hz, 2.1H, CH_3CH, major), 1.65-1.74 (m, 0.7H, major), 2.04-2.12 (m, 0.3H, minor), 2.29-2.37 (m, 0.3H, minor), 2.50-2.57 (m, 0.7H, major), 2.97-3.15 (m, 2H), 3.19-3.28 (m, 1H), 3.81 (s, 3H, OMe), 4.42-4.58 (m, 1H, CHO), 6.96 (d, *J* = 8.8 Hz, 2H, Ar), 7.57 (d, *J* = 8.8 Hz, 2H, Ar), 7.79 (s, 1H, Het). ^{13}C NMR (101 MHz, $CDCl_3$), δ: 20.3 (major), 20.7 (minor), 25.3 (major), 25.7 (minor), 33.5 (minor), 35.9 (major), 38.9 (minor), 41.3 (major), 55.2 (OCH_3), 74.8 (OCHMe, minor), 75.1 (OCHMe, major), 114.3 (C_{arom}), 120.2 (C_{arom}), 121.6 (C_{arom}), 130.0 (C_{arom}), 144.6 (C=CH-N), 159.3 (=C-OMe), 177.7 (C=O). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{18}N_3O_3^+$ 288.1343; Found 288.1333.

3-{[1-(4-Methoxyphenyl)-1*H*-1,2,3-triazol-4-yl]methyl}-5,5-dimethyldihydrofuran-2(3*H*)-one (12). White powder, yield 300 mg (99%); m.p. 125-128 °C; IR (cm^{-1}), υ: 1759 (C=O). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 1.36 (s, 6H, 2Me), 1.93-1.99 (m, 1H), 2.29-2.35 (m, 1H), 2.98-3.08

(m, 1H, CHCO), 3.19-3.31 (m, 2H, CH_2Het), 3.83 (s, 3H, OMe), 6.98 (d, *J* = 9.0, 2H, Ar), 7.59 (d, *J* = 9.0, 2H, Ar), 7.79 (s, 1H, Het). ^{13}C NMR (101 MHz, $CDCl_3$), δ: 25.6, 26.6, 28.4, 40.0, 40.6, 55.2 (OCH_3), 82.3 (O<u>C</u>Me_2), 114.3 (C_{arom}), 120.1 (C_{arom}), 121.6 (C_{arom}), 130.1 (C=<u>C</u>H-N), 144.4 (<u>C</u>=CH-N), 159.3 (=<u>C</u>-OMe), 177.3 (C=O). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{20}N_3O_3^+$ 302.1499; Found 302.1471.

5-**Methyl-3-{[1-(4-nitrophenyl)-1*H*-1,2,3-triazol-4-yl]methyl}dihydrofuran-2(3*H*)-one, mixture of diastereomers (13)**. Brick red powder, yield 296 mg (98%); m.p. 144-146 °C; IR (cm^{-1}), υ: 1756 (C=O). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 1.36 (d, *J* = 6.1 Hz, 3H, Me), 1.70-1.79 (m, 0.7H, major), 2.21-2.17 (m, 0.3H, minor), 2.33-2.40 (m, 0.3H, minor), 2.55-2.61 (m, 0.7H, major), 3.06-3.20 (m, 2H), 3.21-3.33 (m, 1H), 4.47-4.56 (m, 0.7H, CHO, major), 4.56-4.64 (m, 0.3H, CHO, minor), 7.97 (d, *J* = 9.0 Hz, 2H, Ar), 8.05 (s, 1H, Het), 8.39 (d, *J* = 9.0 Hz, 2H, Ar). ^{13}C NMR (101 MHz, $CDCl_3$), δ: 20.3 (major), 20.7 (minor), 25.1 (major), 25.5 (minor), 33.6 (minor), 35.8 (major), 38.6 (minor), 41.2 (major), 74.8 (O<u>C</u>HMe, minor), 75.2 (O<u>C</u>HMe, major), 119.9 (<u>C</u>H_{arom}), 120.1 (<u>C</u>H_{arom}), 125.1 (C=<u>C</u>H-N), 140.7 (C_{arom}), 145.5 (<u>C</u>=CH-N), 146.7 (C–NO_2), 177.6 (C=O). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{15}N_4O_4^+$ 303.1088; Found 303.1099.

5,5-Dimethyl-3-{[(1-(4-nitrophenyl)-1*H*-1,2,3-triazol-4-yl]methyl}dihydrofuran-2(3*H*)-one (14). Brick red powder, yield 284 mg (90%); m.p. 194-195 °C (EtOH); IR (cm^{-1}), υ: 1757 (C=O). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 1.39 (s, 3H, CH_3), 1.40 (s, 3H, CH_3), 1.95-2.01 (m, 1H), 2.33-2.39 (m, 1H), 3.07-3.15 (m, 1H, <u>CH</u>CH_2Het), 3.24-3.32 (m, 2H, CH<u>CH_2</u>Het), 7.97 (d, *J* = 9.1 Hz, 2H, Ar), 8.03 (s, 1H, Het), 8.40 (d, *J* = 9.1 Hz, 2H, Ar). ^{13}C NMR (101 MHz, $CDCl_3$), δ: 25.3, 26.5, 28.4, 40.0, 40.4, 82.4 (O<u>C</u>Me_2), 119.9 (<u>C</u>H_{arom}), 120.1 (<u>C</u>H_{arom}), 125.1 (C=<u>C</u>H-N), 140.7 (C_{arom}), 145.5 (<u>C</u>=CH-N), 146.7 (C–NO_2), 177.2 (C=O). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{17}N_4O_4^+$ 317.1244; Found 317.1237.

3,3-Dimethyl-8-({4-[(5-methyl-2-oxotetrahydrofuran-3-yl)methyl]-1*H*-1,2,3-triazol-1-yl}methyl)-2,7-dioxaspiro[4.4]nonane-1,6-dione (15). Slightly brown powder, yield 324 mg (86%); m.p. 115-117 °C; R_F(CH_2Cl_2:MeOH 30:1)=0.28. ^{1}H NMR (400 MHz, $CDCl_3$), δ: 1.20-1.28 (m, 3H, Me), 1.34 (s, 2.1H, CH_3, major), 1.37 (s, 0.9H, CH_3, minor), 1.44 (s, 2.1H, CH_3, major), 1.48 (s, 0.9H, CH_3, minor), 1.49-1.61 (m, 0.6H), 1.94 (dd, *J* = 13.8, 5.2 Hz, 1H), 2.04-2.18 (m, 1.4H), 2.23-2.32 (m, 0.2H), 2.33-2.46 (m, 0.7H), 2.50-2.63 (m, 1.7H), 2.76-3.16 (m, 3.6H), 4.35-4.59 (m, 1.8H), 4.63-4.72 (m, 1.2H), 4.87-4.96 (m, 0.3H), 5.08-5.18 (m, 0.7H), 7.53-7.54 (m, 1H, Het). ^{13}C NMR (101 MHz, $CDCl_3$), δ: 20.5 (major), 20.9 (minor), 25.4, 25.5, 25.6, 25.8, 25.9, 28.2 (minor), 28.3 (major), 28.7 (major), 28.9(minor), 33.8, 33.9, 36.0, 36.1, 36.2, 36.9, 37.0, 38.8, 38.9, 40.6, 41.0, 41.1, 41.2, 43.8, 45.3, 51.6, 51.8, 52.6, 52.7, 53.0, 53.7, 74.82, 74.84, 74.9, 75.1, 75.2, 75.7, 75.8, 76.2, 76.3, 123.3; 144.4 (<u>C</u>=CH-N, minor), 144.6 (<u>C</u>=CH-N, major); 172.7, 172.8,

173.5, 173.6, 177.7, 177.8, 178.0, 178.1 (C=O). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{24}N_3O_6^+$ 378.1660; Found 378.1666.

8-({4-[(5,5-Dimethyl-2-oxotetrahydrofuran-3-yl)methyl]-1*H*-1,2,3-triazol-1-yl}methyl)-3,3-dimethyl-2,7-dioxaspiro[4.4]nonane-1,6-dione (16). Slightly brown powder, yield 322 mg (82%); m.p. 66-68 °C; $R_F(CH_2Cl_2$:MeOH 30:1)=0.26. ^{1}H NMR (400 MHz, $CDCl_3$), δ: 1.26 (s, 3H, Me), 1.29 (s, 3H, Me), 1.35 (s, 2.1H, CH_3, major), 1.38 (s, 0.9H, CH_3, minor), 1.44 (s, 2.1H, CH_3, major), 1.48 (s, 0.9H, CH_3, minor), 1.74-1.84 (m, 1H), 1.94 (dd, *J* = 13.8, 4.3 Hz, 0.7H), 2.04–2.29 (m, 2.3H), 2.48-2.63 (m, 1.5H), 2.77-2.88 (m, 1.5H), 3.05–3.18 (m, 2H), 4.49–4.58 (m, 0.8H), 4.64–4.72 (m, 1.2H), 4.87–4.96 (m, 0.3H), 5.09–5.18 (m, 0.7H), 7.53-7.54 (m, 1H, Het). ^{13}C NMR (101 MHz, $CDCl_3$), δ: 25.7, 25.8, 26.7, 28.2, 28.3, 28.5, 28.8, 28.9, 36.9, 36.95, 37.03, 40.2, 40.26, 40.34, 40.4, 43.79, 43.81, 45.3, 45.5, 51.7, 51.8, 52.69, 52.73, 53.0, 53.66, 53.68, 75.7, 75.8, 76.18, 76.24, 82.4, 82.5, 84.2, 84.4, 123.3, 144.4 (C=CH-N, minor), 144.6 (C=CH-N, major); 172.7, 172.8, 173.5, 173.6, 177.3, 177.4, (C=O). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{26}N_3O_6^+$ 392.1816; Found 392.1826.

***N*^{2}-Benzyl-*N*^{1}-(1-benzyl-2-{4-[(5-methyl-2-oxotetrahydrofuran-3-yl)methyl]-1*H*-1,2,3-triazol-1-yl}ethyl)-*N*^{2}-(trifluoroacetyl)glycinamide (17)**. Slightly brown powder, yield 484 mg (87%); m.p. 73-75 °C; $R_F(CH_2Cl_2$:MeOH 30:1)=0.26. ^{1}H NMR (400 MHz, $CDCl_3$), δ: 1.28–1.32 (m, 3H, Me), 1.56-1.66 (m, 0.7H), 1.96-2.06 (m, 0.3H), 2.14-2.25 (m, 0.5H), 2.33 (br s, 0.3H), 2.38-2.54 (m, 0.7H), 2.72-3.20 (m, 5.5H), 3.61–3.89 (m, 2H), 4.36–4.70 (m, 6H), 6.67-6.69 (m, 0.6H, Ph), 6.93-7.00 (m, 0.4H, Ph), 7.08-7.34 (m, 10H, Ph, Het, NHCO), 7.46-7.58 (m, 1H, Ph). ^{19}F NMR (376 MHz, $CDCl_3$), δ: -69.17…-69.20 (m, 1.96 F, CF_3), -69.97…-69.99 (m, 1.04 F, CF_3). ^{13}C NMR (101 MHz, $CDCl_3$), δ: 20.5, 21.0, 25.4, 25.5, 25.9, 26.1, 33.9, 34.0, 35.9, 36.0, 36.2, 36.3, 37.4, 37.5, 37.6, 39.1, 39.2, 41.40, 41.43, 41.48, 41.53, 48.2, 48.3, 48.5, 50.6, 50.7, 50.9, 51.0, 51.1, 51.2, 51.4, 51.6, 51.9, 52.1, 75.15, 75.21, 75.3, 75.4, 75.46, 75.52, 75.6, 116.2 (q, *J*=288.2 Hz, CF_3), 116.3 (q, *J*=287.5 Hz, CF_3), 123.3, 123.6, 123.7, 126.9, 127.0, 127.6, 128.1, 128.3, 128.6, 128.8, 128.9, 128.96, 129.04, 133.79, 133.81, 134.46, 136.37, 136.42, 143.9-144.6 (m, C=CH-N), 157.0-157.7 (m, C(O)CF_3); 166.40, 166.45, 166.49, 166.54, 178.1, 178.2, 178.4, 178.6 (C=O). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{28}H_{31}F_3N_5O_4^+$ 558.2323; Found 558.2333.

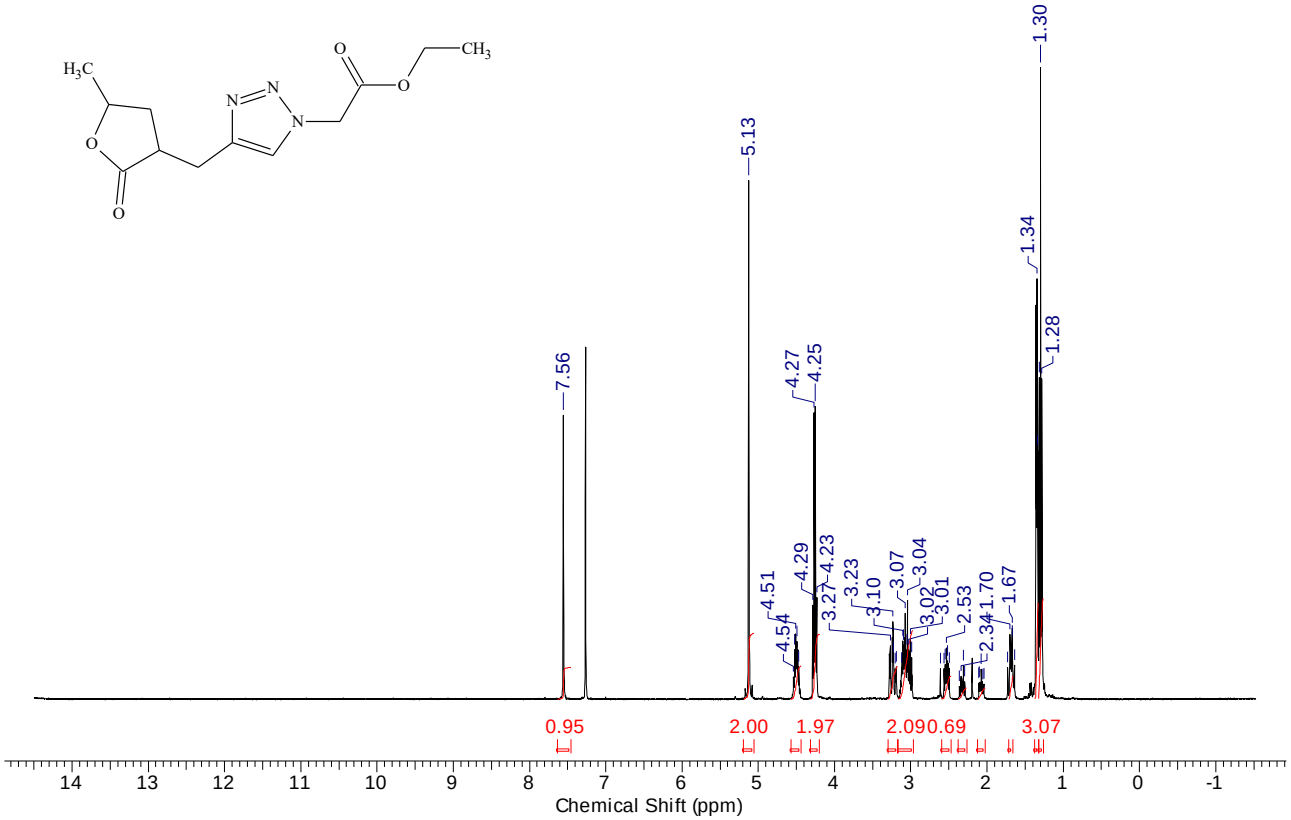
***N*^{2}-Benzyl-*N*^{1}-(1-benzyl-2-{4-[(5,5-dimethyl-2-oxotetrahydrofuran-3-yl)methyl]-1*H*-1,2,3-triazol-1-yl}ethyl)-*N*^{2}-(trifluoroacetyl)glycinamide (18)**. Slightly brown powder, yield 528 mg (93%); m.p. 127-129 °C; $R_F(CH_2Cl_2$:MeOH 30:1)=0.45. ^{1}H NMR (400 MHz, $CDCl_3$), δ: 1.31–1.36 (m, 6H, Me), 1.81-1.91 (m, 1H), 2.21-2.38 (m, 1.3H), 2.52–3.23 (m, 5.7H), 3.64–3.87 (m, 2H), 4.36–4.69 (m, 5H), 6.68-6.73 (m, 0.6H, Ph), 6.99-7.03 (m, 0.4H, Ph), 7.08-7.34 (m, 10H, Ph, Het, NHCO), 7.46-7.56 (m, 1H, Ph). ^{19}F NMR (376 MHz, $CDCl_3$), δ: -69.14 (m, 1.90 F, CF_3), -69.94…-69.97 (m, 1.10 F, CF_3). ^{13}C NMR (101 MHz, $CDCl_3$), δ: 25.7, 25.8, 25.96, 26.02, 26.8, 26.9, 27.5,

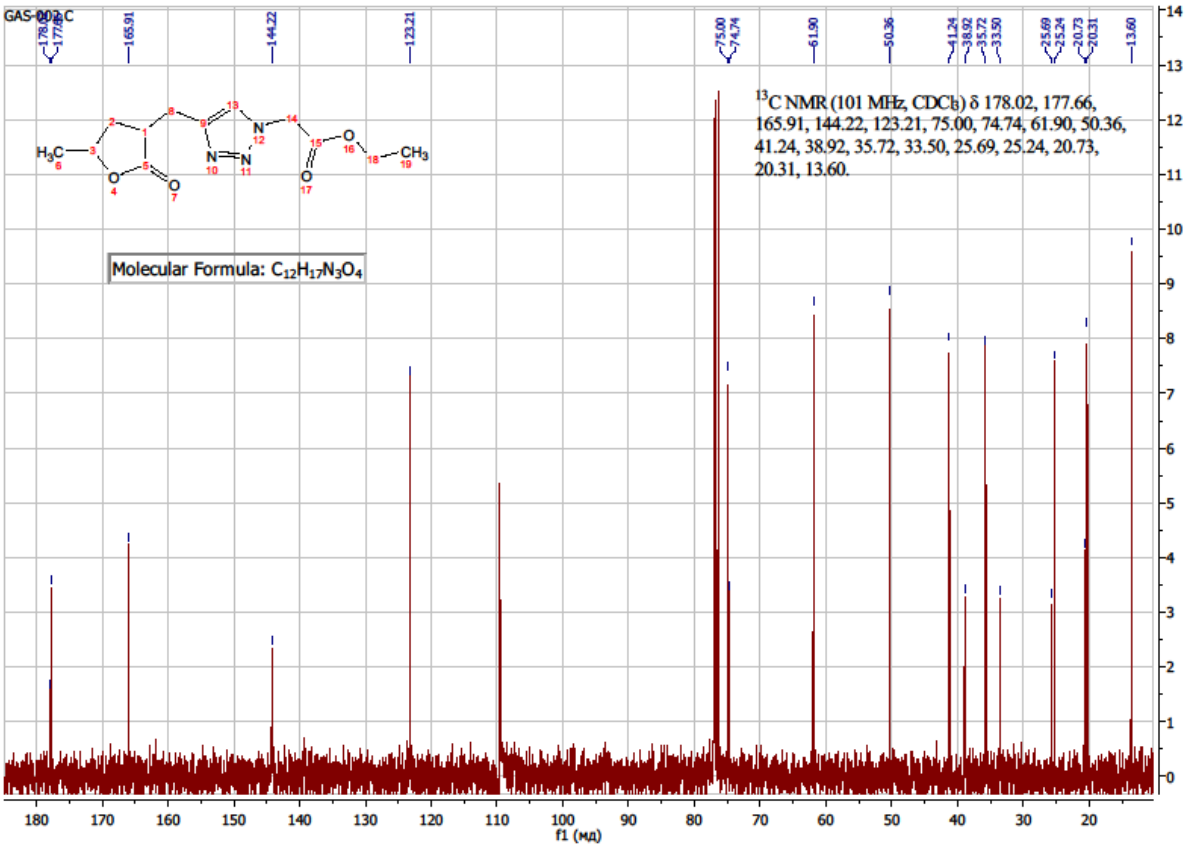
28.47, 28.53, 28.6, 29.2, 34.4, 36.2, 37.3, 37.6, 39.7, 40.0, 40.1, 40.2, 40.3, 40.4, 40.5, 40.6, 40.67, 40.70, 48.3, 48.5, 50.6, 50.7, 50.8, 51.07, 51.09, 51.3, 51.4, 51.9, 52.0, 82.67, 82.69, 82.75, 82.78, 82.80, 82.9, 116.2 (q, *J*=288.8 Hz, CF_3), 116.3 (q, *J*=287.7 Hz, CF_3), 123.2-123.4 (m), 123.6-123.7 (m), 126.8, 126.9, 127.6, 128.1, 128.29, 128.31, 128.6, 128.75, 128.84, 128.9, 129.0, 133.79, 133.81, 134.46, 134.47, 136.38, 136.40, 136.43, 144.0-144.2 (m, C=CH-N), 157.0-157.7 (m, C(O)CF_3); 166.37, 166.42, 166.48, 166.50, 176.3, 177.6, 177.8, 177.9 (C=O). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{29}H_{32}F_3N_5O_4^+$ 572.2479; Found 572.2487.

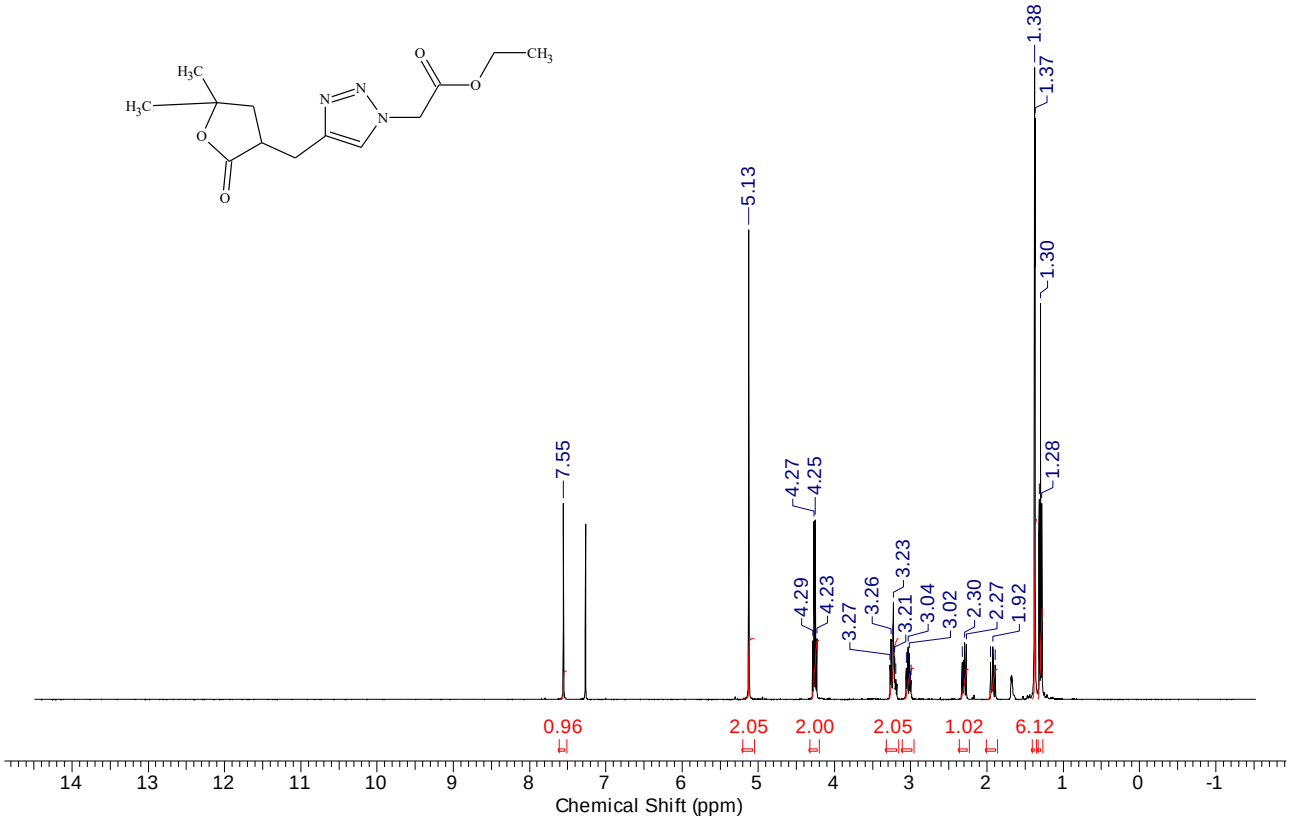
Diynes 19 and **20 (general procedure)**. A mixture of the corresponding 3-(prop-2-ynyl)dihydrofuran-2(3*H*)-one **5** or **6** (0.01 mol), triethylamine (0.03 mol) in the abs. acetonitrile (3 mL) stirred for 15 min at room temperature and then CuI (0.02 mmol) were added. The mixture was stirred for 1 h at room temperature in contact with air and then for 5 h under reflux. The mixture was cooled, diluted with water (20 ml) and extracted with Et_2O (3×10 ml). The combined extracts were dried over $MgSO_4$, the volatiles were evaporated The resulting crystals were washed with water and recrystallized.

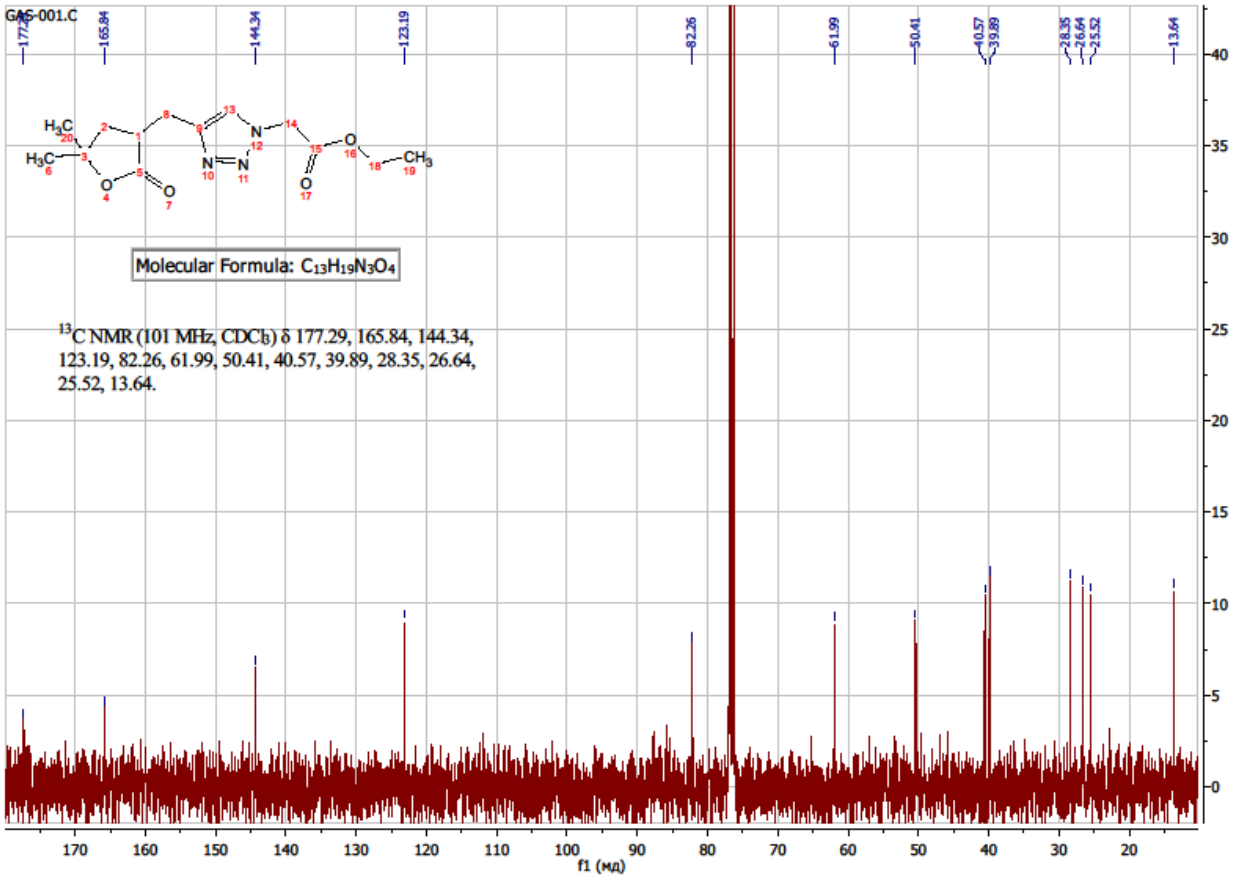
3,3'-(Hexa-2,4-diyne-1,6-diyl)bis(5-metyldihydrofuran-2(3*H*)-one) (19). Light yellow amorphous substance, yield 0.92g (67%). ^{1}H NMR (300 MHz, DMSO-d_6), δ: 1.26-1.56 (m, 6H, $2CH_3$), 1.64-1.85 (m, 1H, CH), 2.01-2.18 (m, 1H, CH), 2.24-2.43 (m, 2H, CH_2), 2.43-2.66 (m, 4H, $2CH_2$), 2.20-3.02 (m, 2H, CH_2), 4.41-4.60 (m, 1H, CH), 4.63-4.80 (m, 1H, CH). ^{13}C NMR (75 MHz, DMSO-d_6), δ: 18.9 19.5, 20.4, 20.8, 33.4, 35.3, 37.9, 40.2, 69.8, 69.9, 70.2, 74.8, 74.9, 176.6(C=O), 177.0(C=O). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{19}O_4^+$ 275.1278; Found 275.1289.

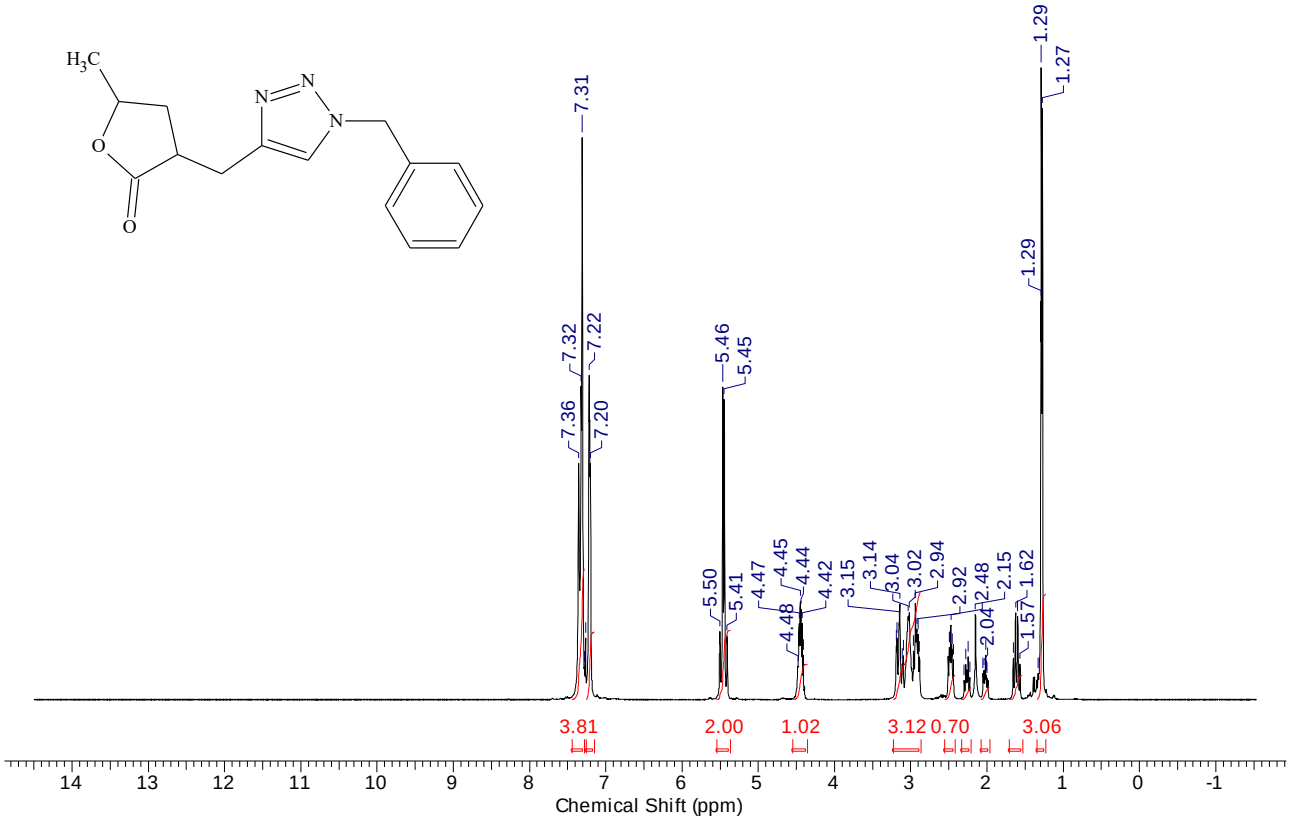
3,3'-(Hexa-2,4-diyne-1,6-diyl)bis(5,5-dimetyldihydrofuran-2(3*H*)-one) (20). White powder, yield 1.06 g (70%); m.p. 141-142 °C (EtOH: H_2O - 5 : 6). IR (cm^{-1}), υ: 1183 C-O-C; 1763 C=O; 2219 C≡C. ^{1}H NMR (300 MHz, DMSO-d_6), δ: 1.39 (s, 6H, $2CH_3$), 1.47 (s, 6H, $2CH_3$), 1.86-1.98 (m, 1H, CH), 1.95-2.05 (m, 1H, CH), 2.24-2.39 (m, 2H, CH_2), 2.46-2.76 (m, 4H, $2CH_2$), 2.95-3.15 (m, 2H, CH_2). ^{13}C NMR (75 MHz, DMSO-d_6), δ: 18.8, 19.6, 26.6, 26.7, 28.3, 28.4, 38.9, 38.9, 39.0, 39.3, 66.4, 71.2, 74.2, 80.2, 81.1, 81.3, 174.8 (C=O). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{23}O_4^+$ 303.1591; Found 303.1581.

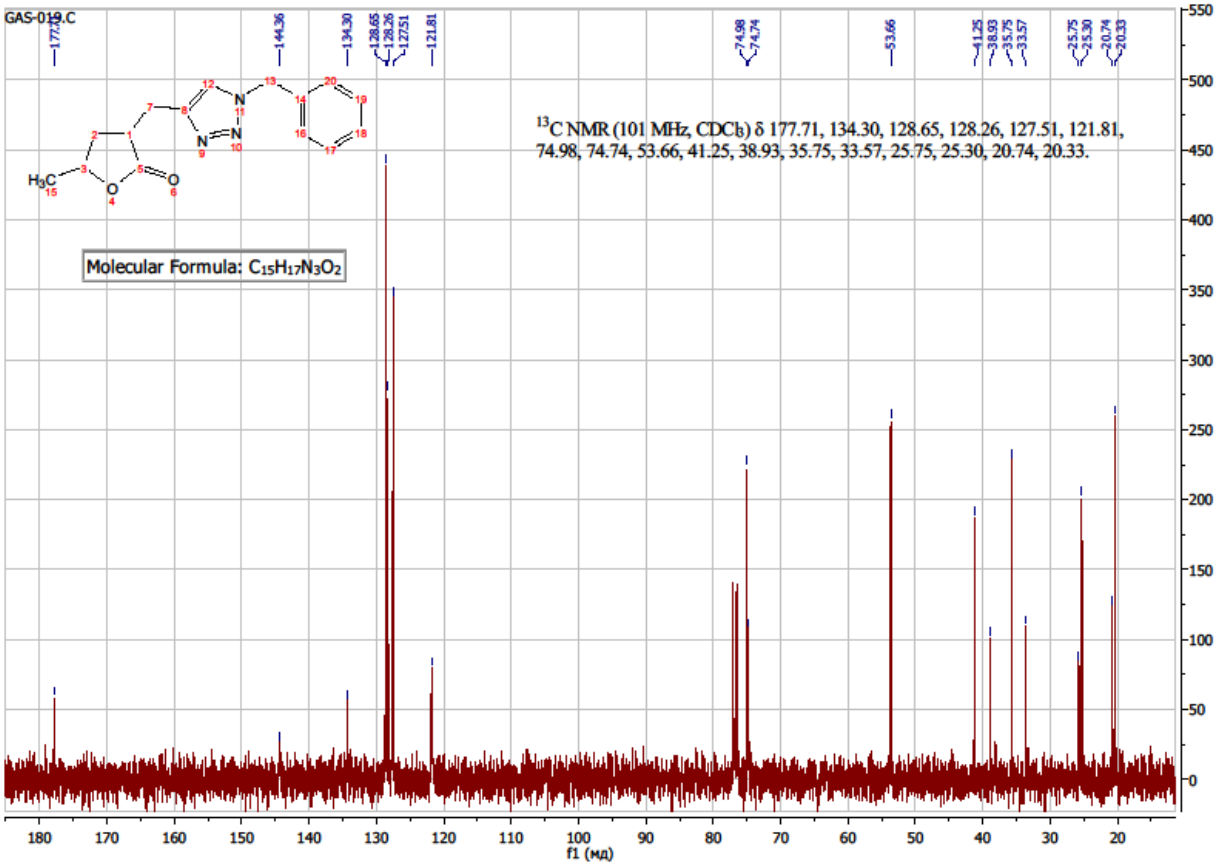

7.56
5.13
4.27
4.25
4.51
4.54
4.29
4.23
3.27
3.23
3.10
3.07
3.04
3.02
3.01
2.53
2.34
1.70
1.67
1.34
1.30
1.28
0.95
2.00
1.97
2.09
0.69
3.07
Chemical Shift (ppm)

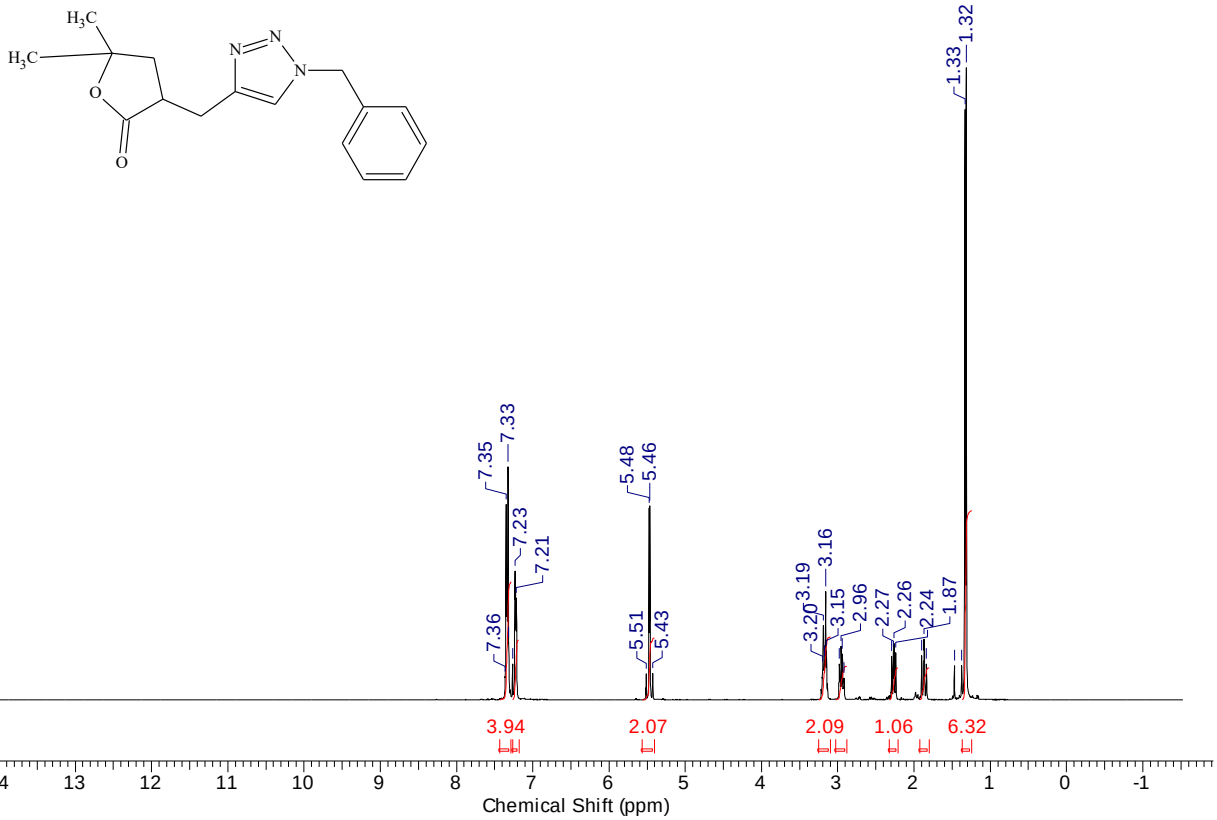

Molecular Formula: C12H17N3O4
13C NMR (101 MHz, CDCl3) δ 178.02, 177.66, 165.91, 144.22, 123.21, 75.00, 74.74, 61.90, 50.36, 41.24, 38.92, 35.72, 33.50, 25.69, 25.24, 20.73, 20.31, 13.60.
f1 (мд)

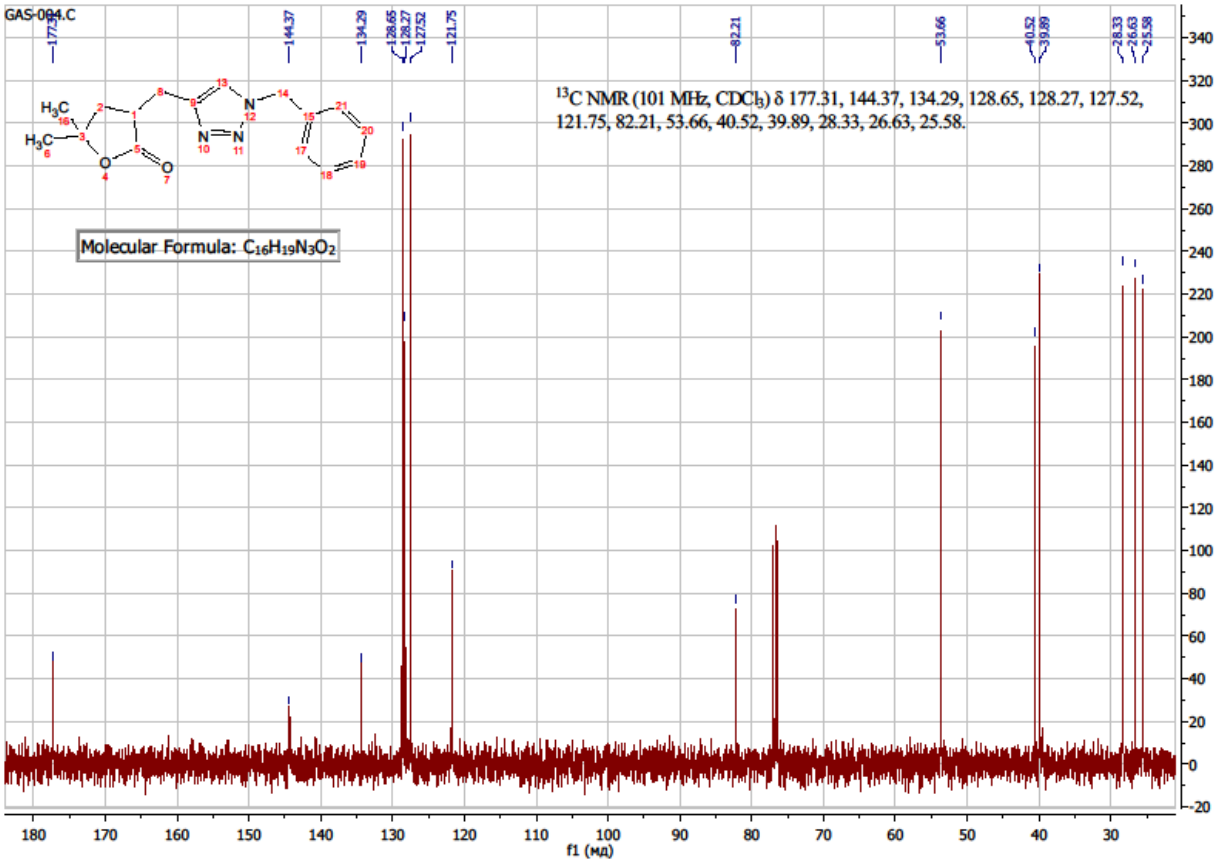

1.38
1.37
5.13
1.30
7.55
4.27
4.25
1.28
4.29
4.23
3.27
3.26
3.23
3.21
3.04
3.02
2.30
2.27
1.92
0.96
2.05
2.00
2.05
1.02
6.12
Chemical Shift (ppm)

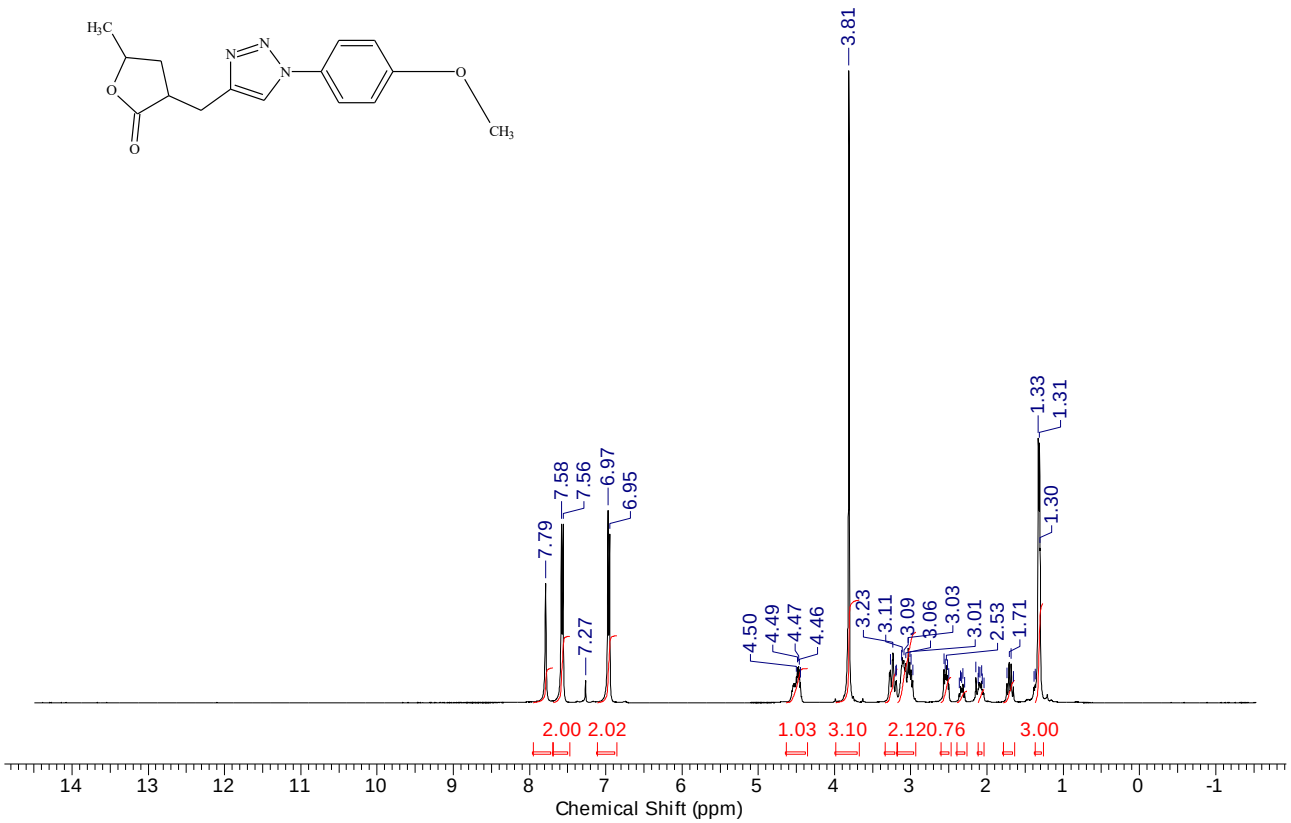

GAS-001.C
Molecular Formula: C13H19N3O4
13C NMR (101 MHz, CDCl3) δ 177.29, 165.84, 144.34, 123.19, 82.26, 61.99, 50.41, 40.57, 39.89, 28.35, 26.64, 25.52, 13.64.
f1 (мд)


7.31
7.32
7.22
7.36
7.20
5.46
5.45
5.50
5.41
4.47
4.45
4.44
4.48
4.42
3.15
3.14
3.04
3.02
2.94
2.92
2.48
2.15
2.04
1.62
1.57
1.29
1.27
3.81
2.00
1.02
3.12
0.70
3.06
Chemical Shift (ppm)


GAS-019.C
^{13}C NMR (101 MHz, CDCl$_3$) δ 177.71, 134.30, 128.65, 128.26, 127.51, 121.81, 74.98, 74.74, 53.66, 41.25, 38.93, 35.75, 33.57, 25.75, 25.30, 20.74, 20.33.
Molecular Formula: C15H17N3O2
f1 (ppm)


Chemical Shift (ppm)
7.35
7.33
7.36
7.23
7.21
5.48
5.46
5.51
5.43
3.19
3.16
3.20
3.15
2.96
2.27
2.26
2.24
1.87
1.33
1.32
3.94
2.07
2.09
1.06
6.32


GAS-094.C
Molecular Formula: C16H19N3O2
13C NMR (101 MHz, CDCl3) δ 177.31, 144.37, 134.29, 128.65, 128.27, 127.52, 121.75, 82.21, 53.66, 40.52, 39.89, 28.33, 26.63, 25.58.
f1 (мд)


3.81
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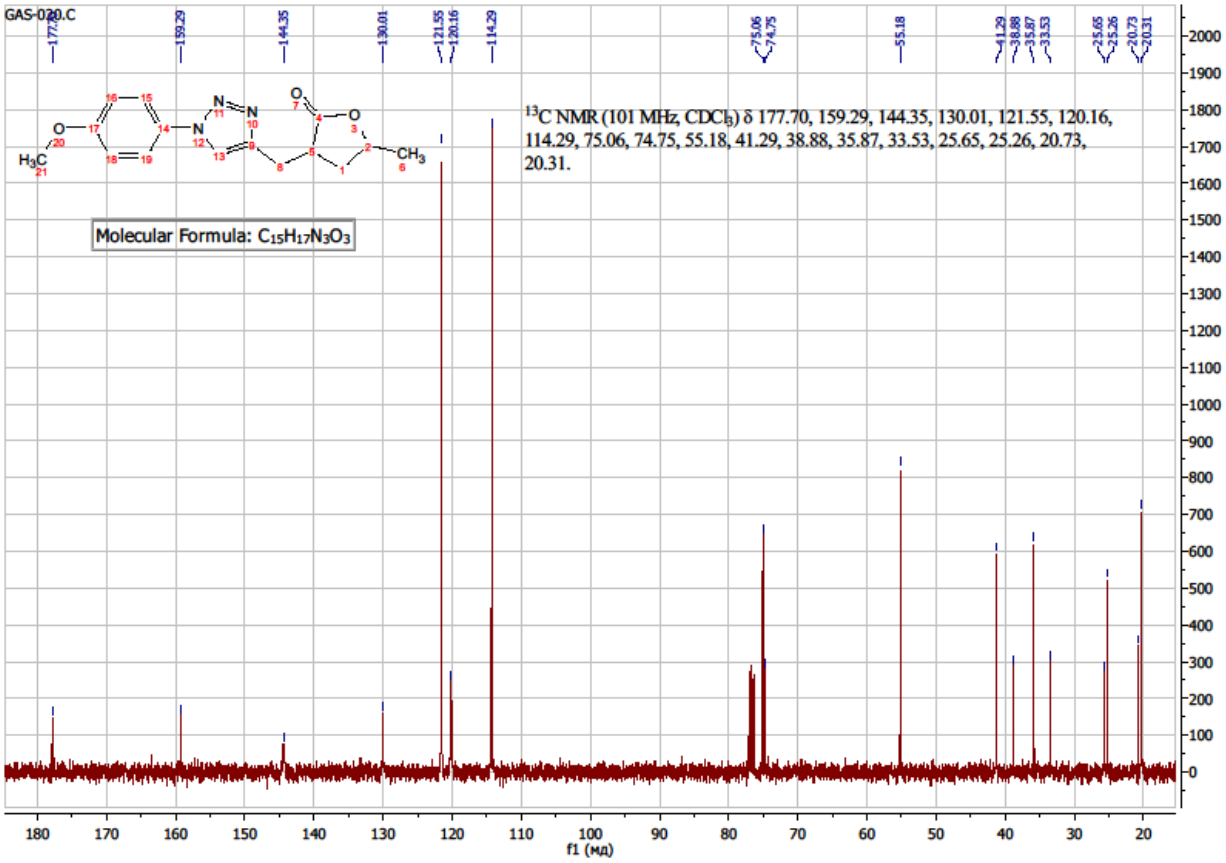
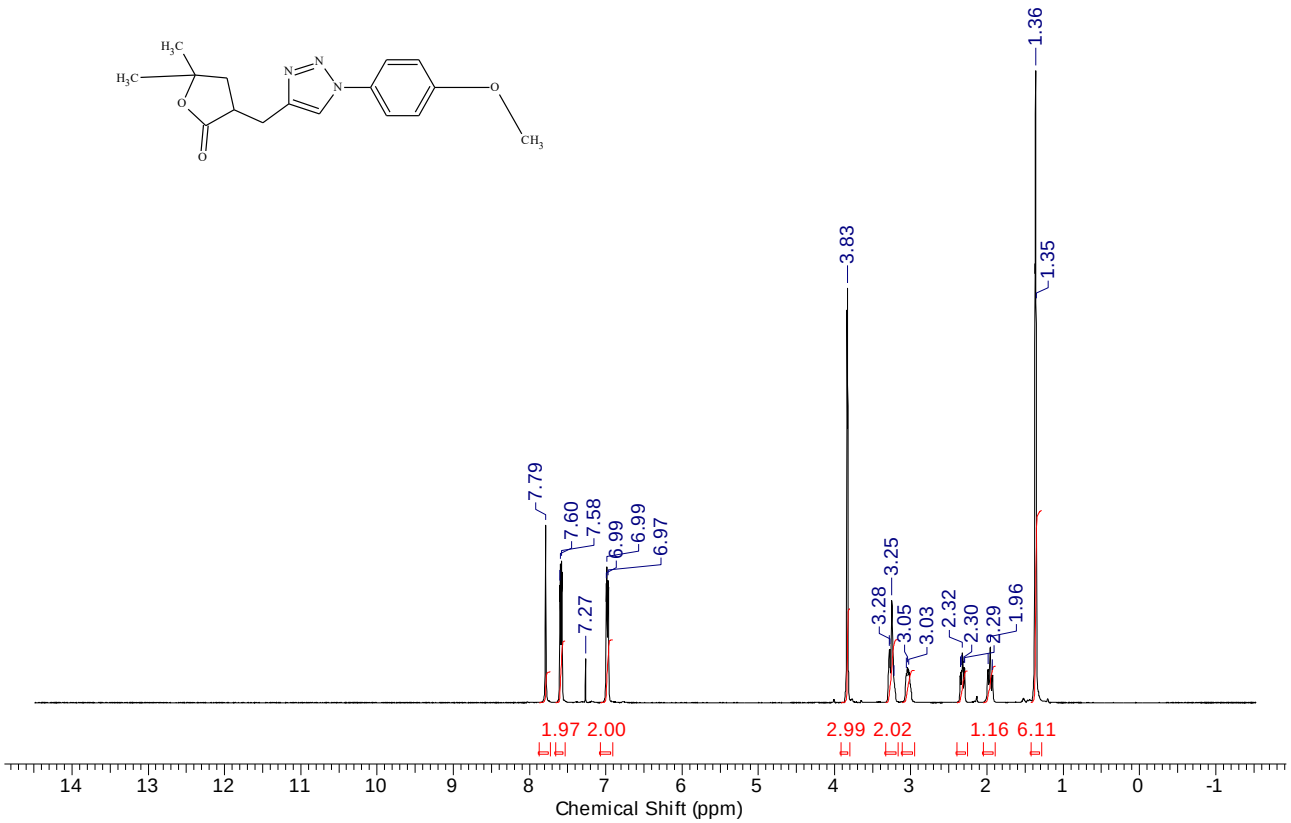
1.31
1.30
7.79
7.58
7.56
6.97
6.95
7.27
4.50
4.49
4.47
4.46
3.23
3.11
3.09
3.06
3.03
3.01
2.53
1.71
2.00 2.02
1.03 3.10
2.120.76
3.00
Chemical Shift (ppm)


GAS-020.C
Molecular Formula: C15H17N3O3
13C NMR (101 MHz, CDCl3) δ 177.70, 159.29, 144.35, 130.01, 121.55, 120.16, 114.29, 75.06, 74.75, 55.18, 41.29, 38.88, 35.87, 33.53, 25.65, 25.26, 20.73, 20.31.
f1 (мд)


1.36
1.35
3.83
7.79
7.60
7.58
6.99
6.99
6.97
7.27
3.28
3.25
3.05
3.03
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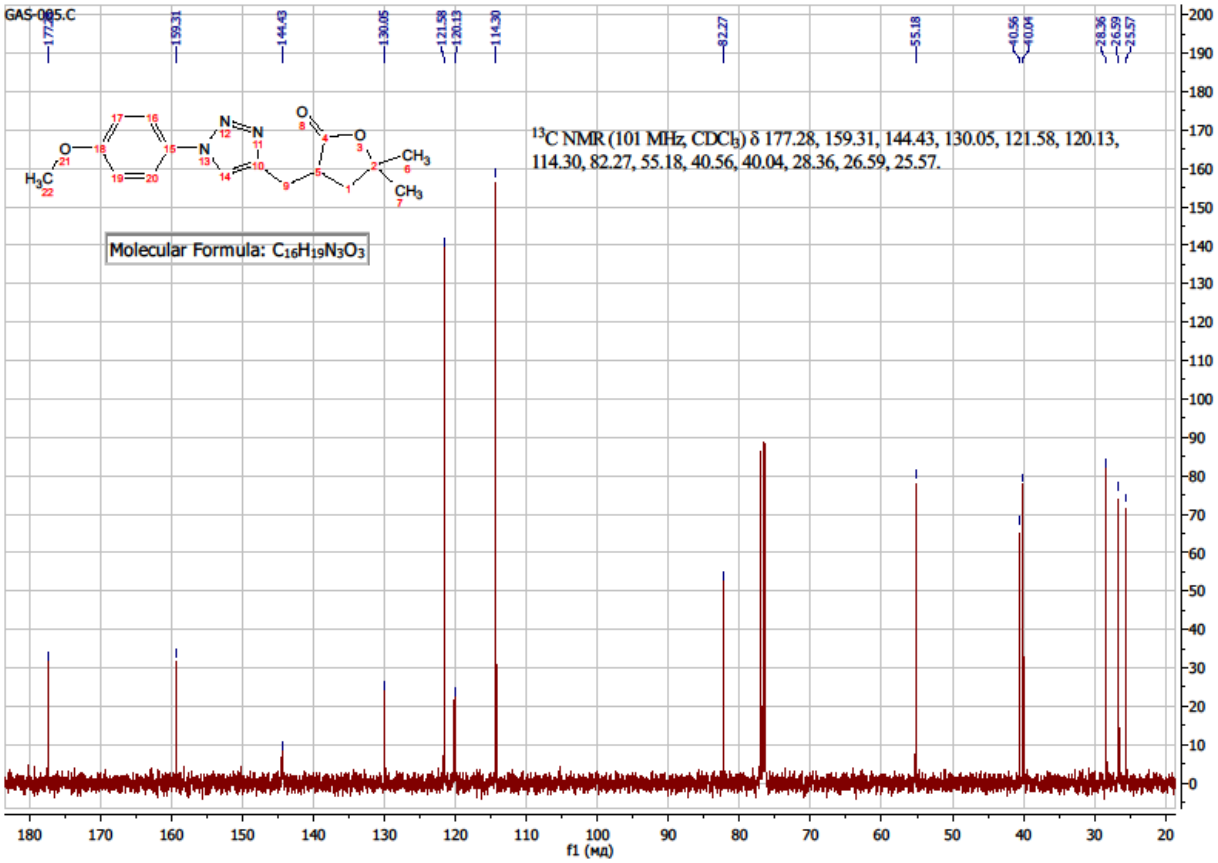
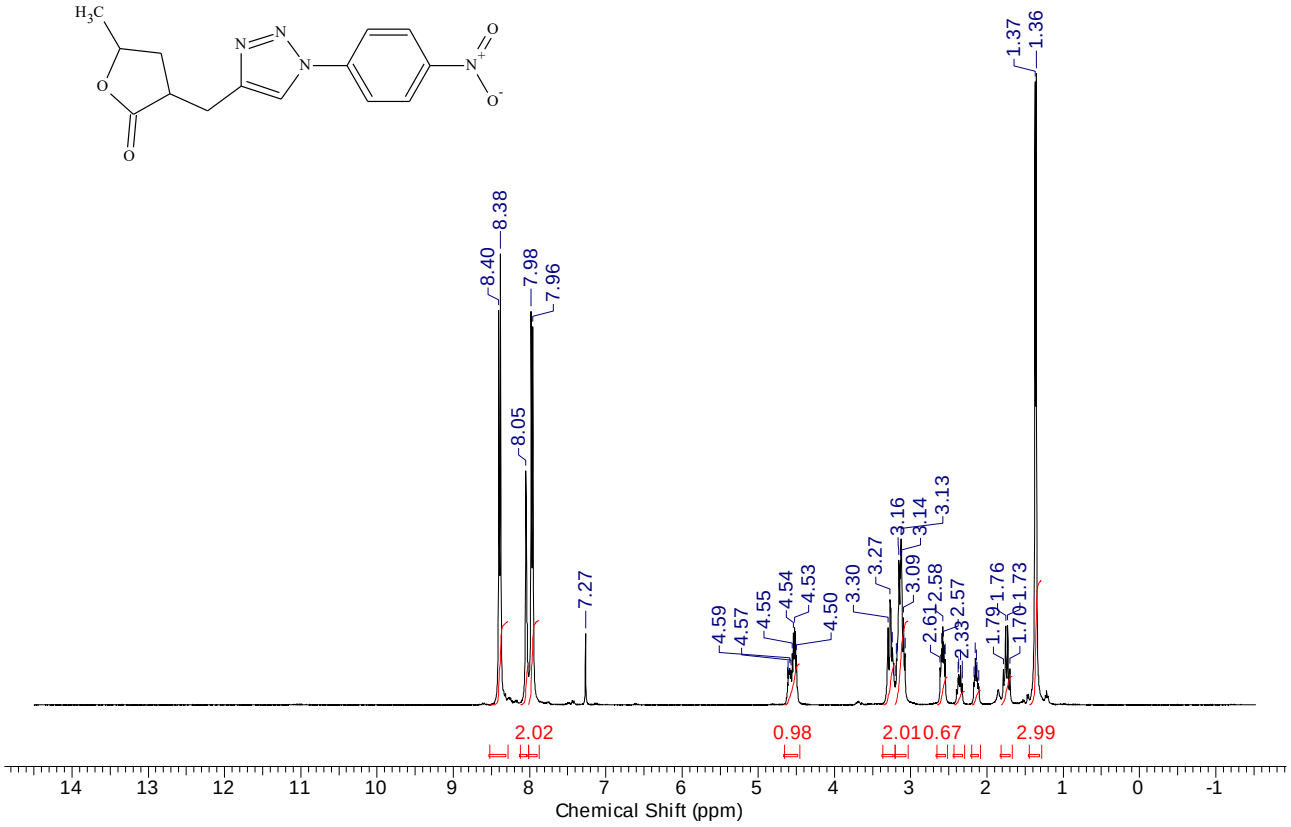
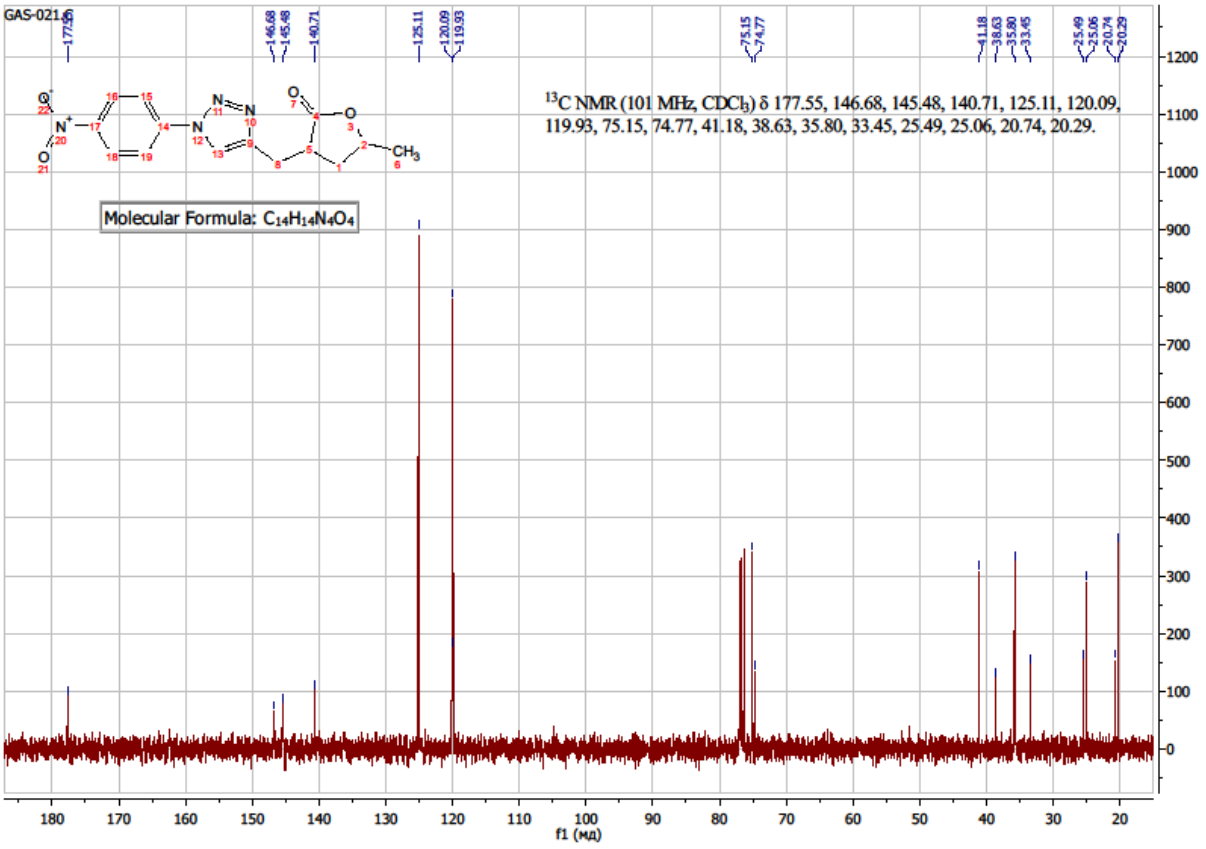
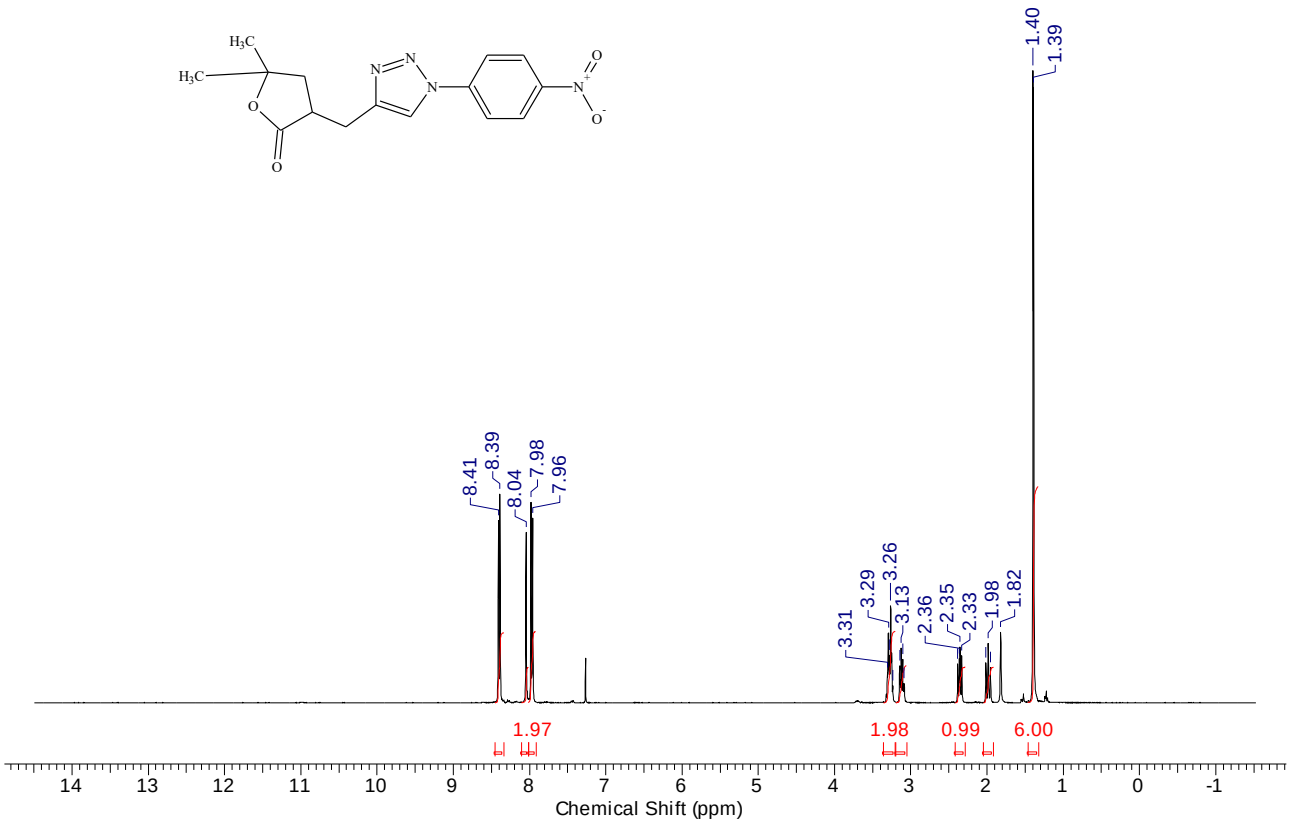
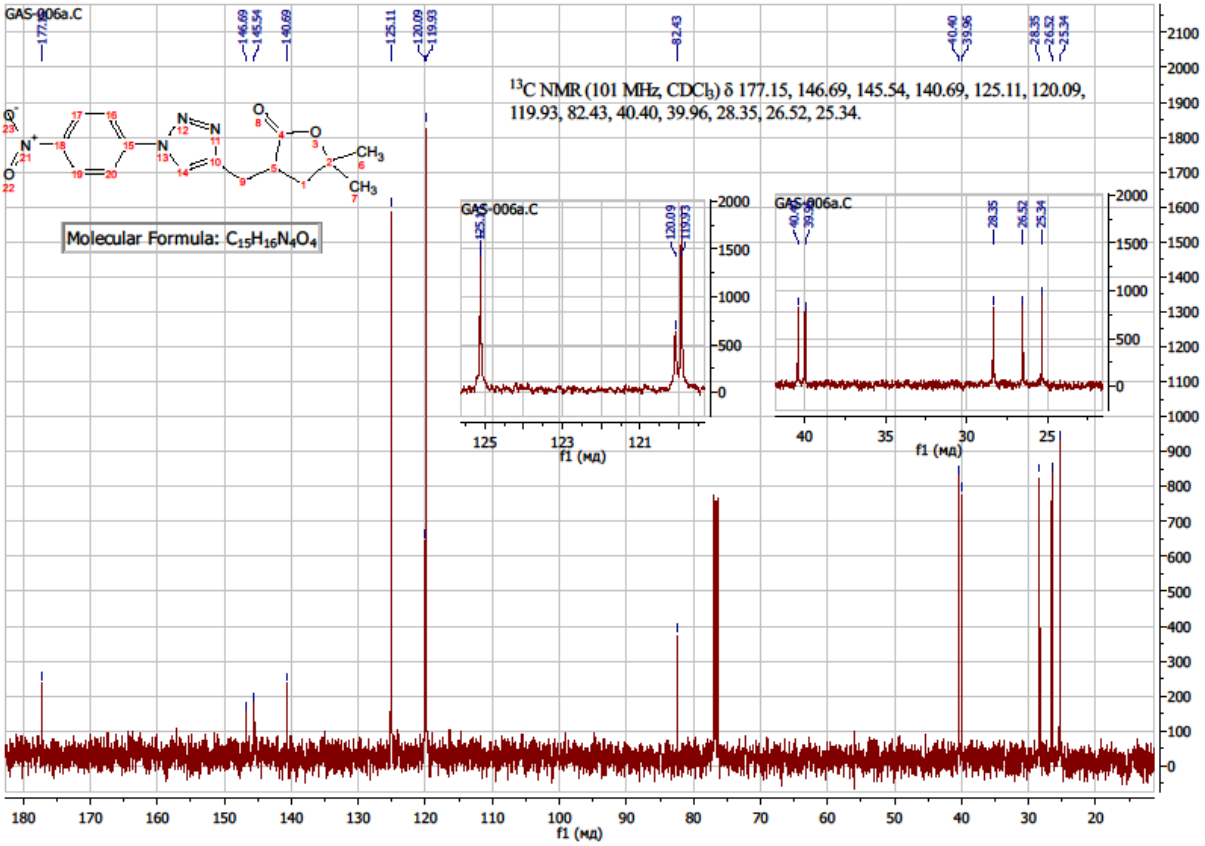
2.30
2.29
1.96
1.97 2.00
2.99 2.02
1.16 6.11
Chemical Shift (ppm)


GAS-005.C
^{13}C NMR (101 MHz, CDCl$_3$) δ 177.28, 159.31, 144.43, 130.05, 121.58, 120.13, 114.30, 82.27, 55.18, 40.56, 40.04, 28.36, 26.59, 25.57.
Molecular Formula: C$_{16}$H$_{19}$N$_3$O$_3$
f1 (ppm)


8.40
8.38
8.05
7.98
7.96
7.27
4.59
4.57
4.55
4.54
4.53
4.50
3.30
3.27
3.16
3.14
3.13
3.09
2.61
2.58
2.57
2.33
1.79
1.76
1.73
1.70
1.37
1.36
2.02
0.98
2.01
0.67
2.99
Chemical Shift (ppm)

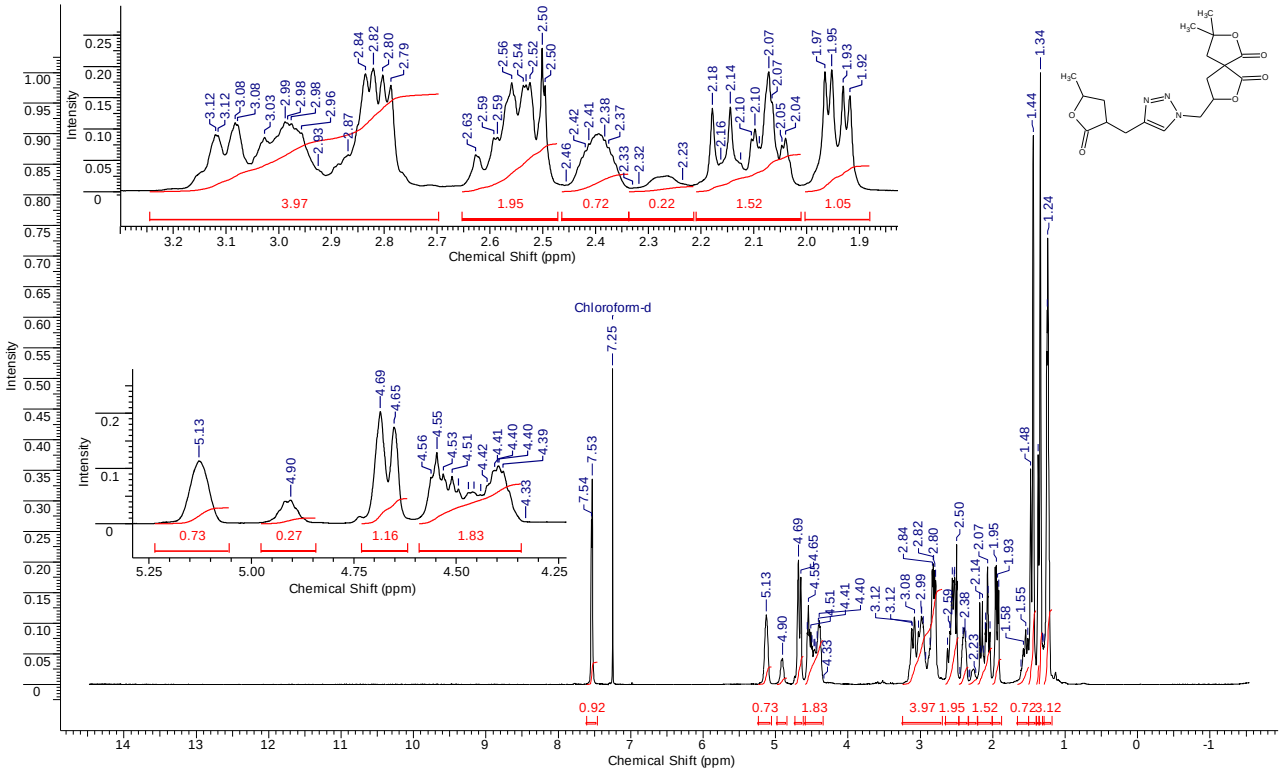

GAS-0216
Molecular Formula: C14H14N4O4
13C NMR (101 MHz, CDCl3) δ 177.55, 146.68, 145.48, 140.71, 125.11, 120.09, 119.93, 75.15, 74.77, 41.18, 38.63, 35.80, 33.45, 25.49, 25.06, 20.74, 20.29.
f1 (мд)


1.40
1.39
8.41
8.39
8.04
7.98
7.96
3.31
3.29
3.26
3.13
2.36
2.35
2.33
1.98
1.82
1.97
1.98
0.99
6.00
Chemical Shift (ppm)


GAS-006a.C
^{13}C NMR (101 MHz, CDCl$_3$) δ 177.15, 146.69, 145.54, 140.69, 125.11, 120.09, 119.93, 82.43, 40.40, 39.96, 28.35, 26.52, 25.34.
Molecular Formula: C15H16N4O4
f1 (мд)

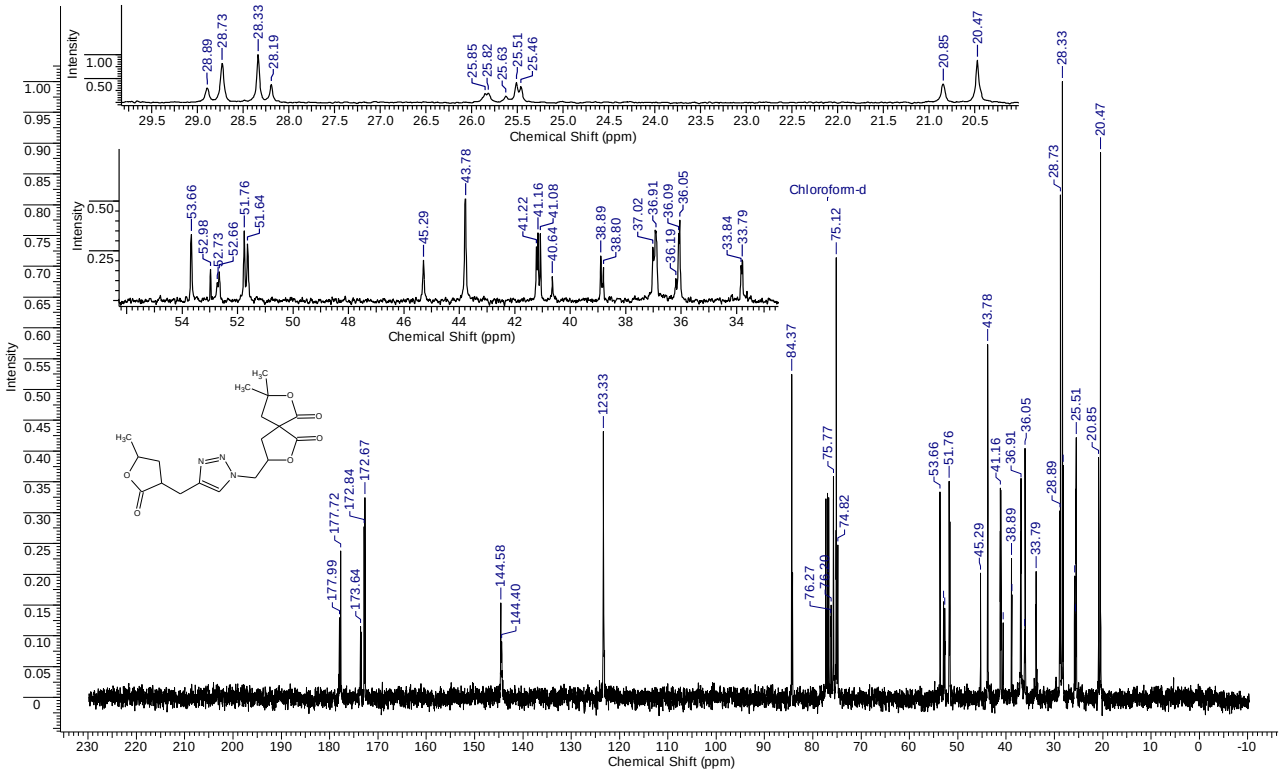
20 Apr 2017

Acquisition Time (sec)	2.5559	**Comment**	Imported from UXNMR.			**Date**	01 Apr 2017 13:30:16
File Name	D:\BN\output\2017\04.апрель\BM-1005.H_001001r			**Frequency (MHz)**	400.13	**Nucleus**	1H
Original Points Count	16384	**Points Count**	65536	**Pulse Sequence**	zg30	**Solvent**	DMSO-D6
Number of Transients	4	**Sweep Width (Hz)**	6410.26	**Temperature (degree C)**	27.000		



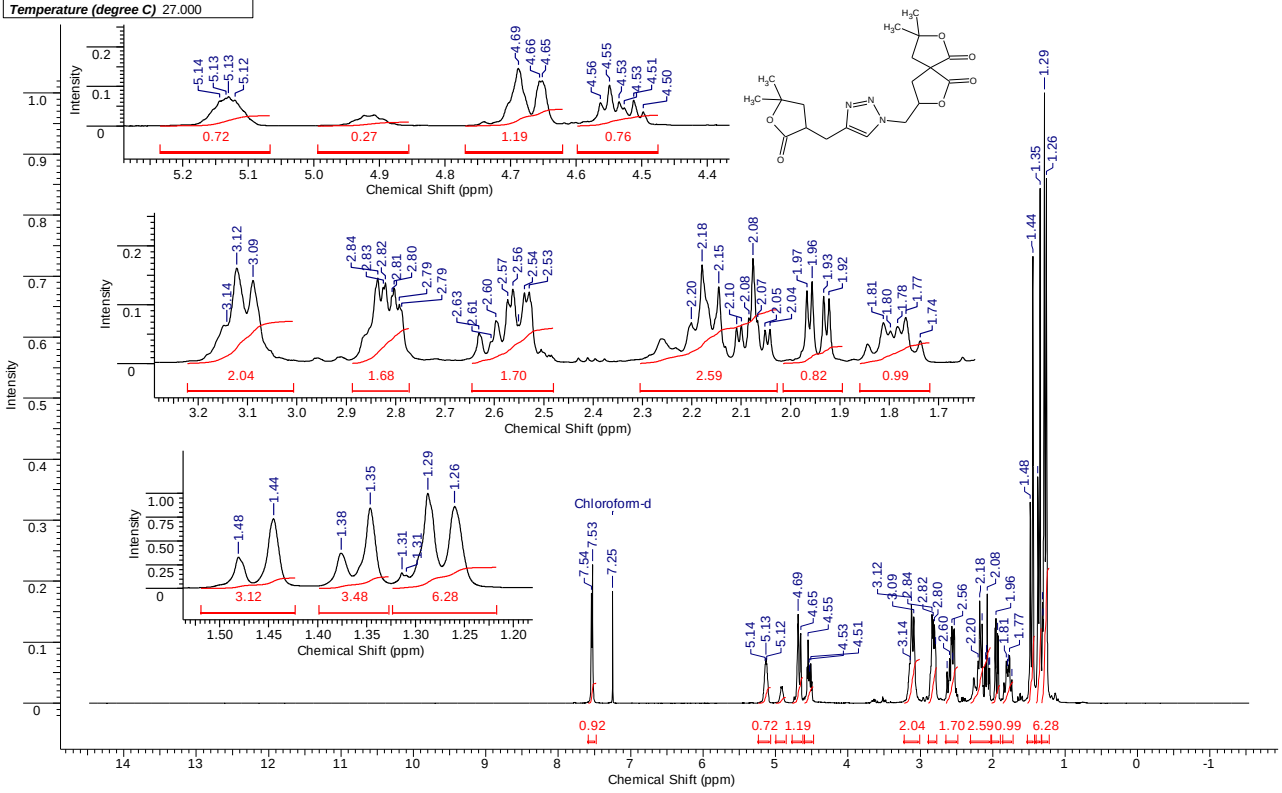
20 Apr 2017

Acquisition Time (sec)	0.4999	**Comment**	Imported from UXNMR.			**Date**	01 Apr 2017 13:34:30
File Name	D:\BN\output\2017\04.апрель\BM-1005.C_002001r			**Frequency (MHz)**	100.61	**Nucleus**	13C
Number of Transients	128	**Original Points Count**	12076	**Points Count**	65536	**Pulse Sequence**	zgpg30
Solvent	CHLOROFORM-D			**Sweep Width (Hz)**	24154.59	**Temperature (degree C)**	27.000



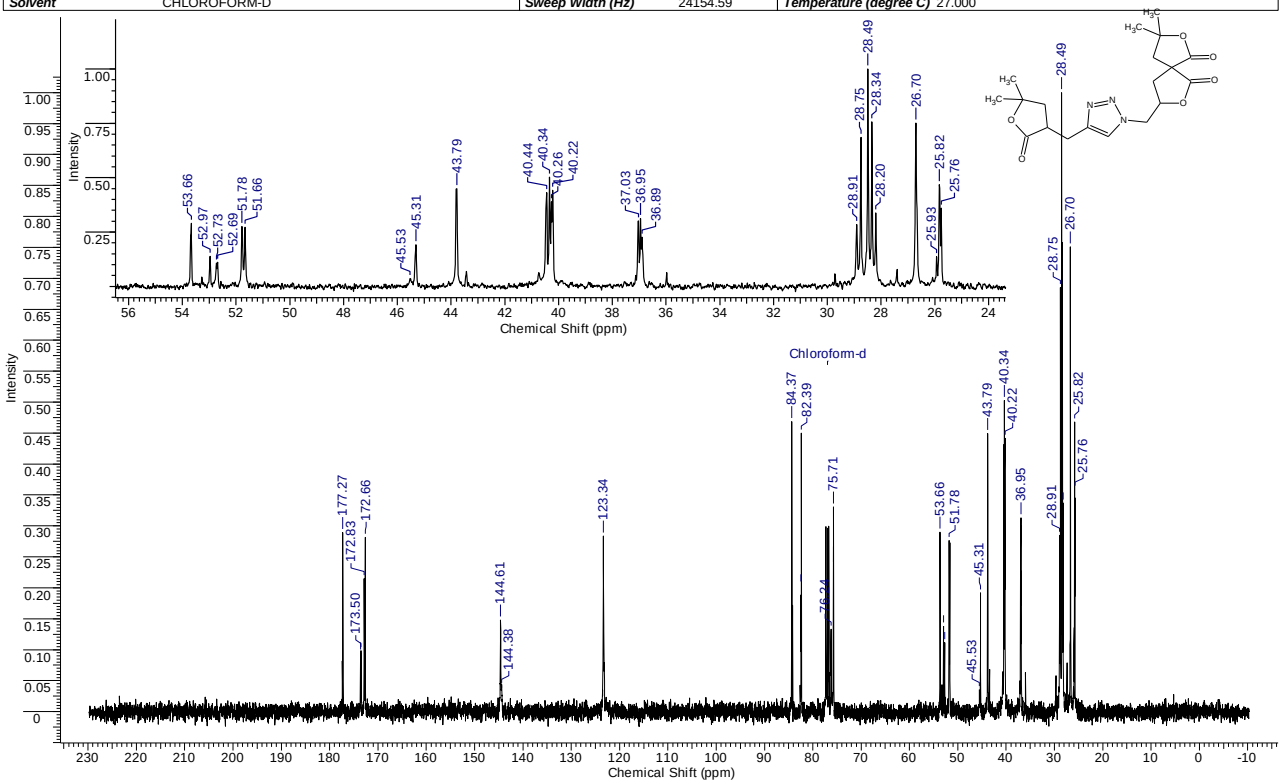
20 Apr 2017

Acquisition Time (sec)	2.5559	***Comment***	Imported from UXNMR.			***Date***	04 Apr 2017 14:23:58
File Name	D:\BN\output\2017\04.апрель\BM-1006.H_001001r			***Frequency (MHz)***	400.13	***Nucleus***	1H
Number of Transients	4	***Original Points Count***	16384	***Points Count***	65536	***Pulse Sequence***	zg30
Solvent	DMSO-D6	***Sweep Width (Hz)***	6410.26	***Temperature (degree C)***	27.000		



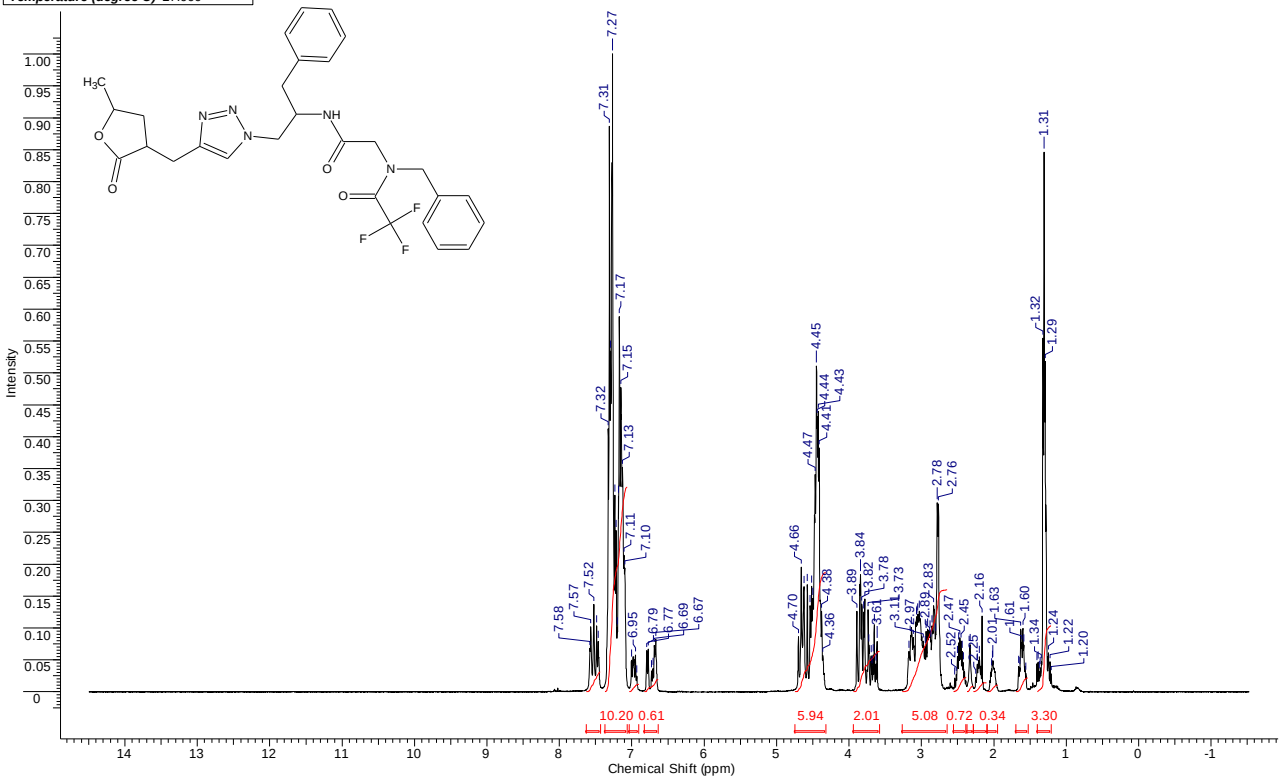
21 Apr 2017

Acquisition Time (sec)	0.4999	***Comment***	Imported from UXNMR.			***Date***	04 Apr 2017 14:28:08
File Name	D:\BN\output\2017\04.апрель\BM-1006.C_002001r			***Frequency (MHz)***	100.61	***Nucleus***	13C
Number of Transients	128	***Original Points Count***	12076	***Points Count***	65536	***Pulse Sequence***	zgpg30
Solvent	CHLOROFORM-D			***Sweep Width (Hz)***	24154.59	***Temperature (degree C)***	27.000



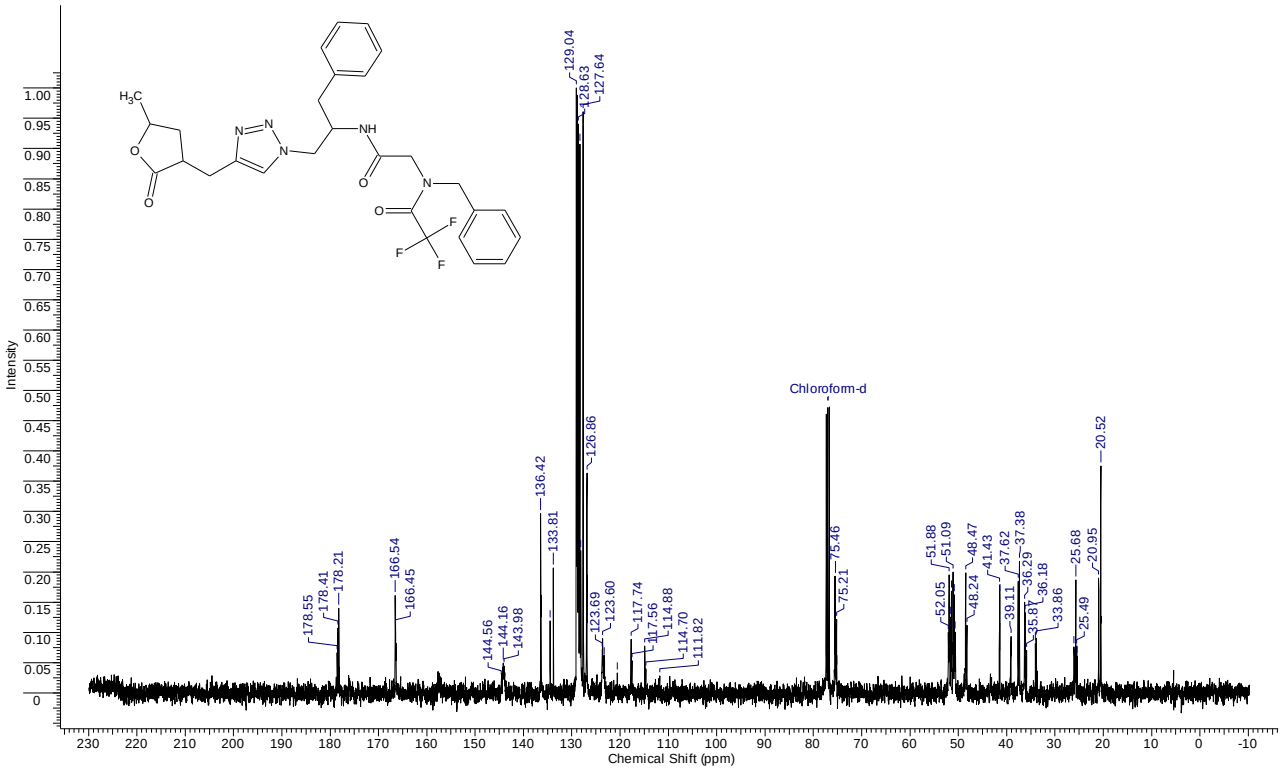
21 Apr 2017

Acquisition Time (sec)	2.5559	**Comment**	Imported from UXNMR.	**Date**	01 Apr 2017 13:36:04		
File Name	D:\BN\output\2017\04.апрель\BM-1008.H_001001r	**Frequency (MHz)**	400.13	**Nucleus**	1H	**Number of Transients**	4
Original Points Count	16384	**Points Count**	65536	**Pulse Sequence**	zg30	**Solvent**	DMSO-D6	**Sweep Width (Hz)**	6410.26
Temperature (degree C)	27.000						



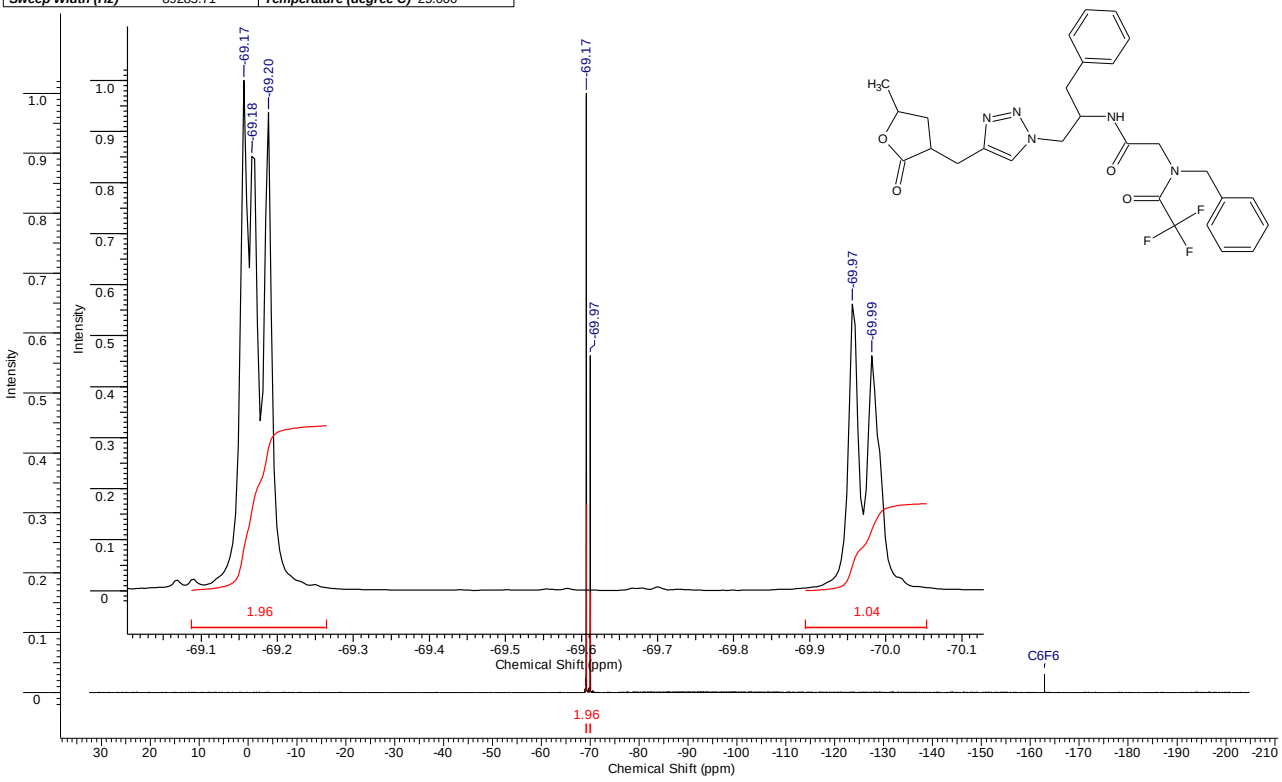
21 Apr 2017

Acquisition Time (sec)	0.4999	**Comment**	Imported from UXNMR.	**Date**	01 Apr 2017 13:41:22		
File Name	D:\BN\output\2017\04.апрель\BM-1008.C_002001r	**Frequency (MHz)**	100.61	**Nucleus**	13C		
Number of Transients	165	**Original Points Count**	12076	**Points Count**	65536	**Pulse Sequence**	zgpg30
Solvent	CHLOROFORM-D			**Sweep Width (Hz)**	24154.59	**Temperature (degree C)**	27.000



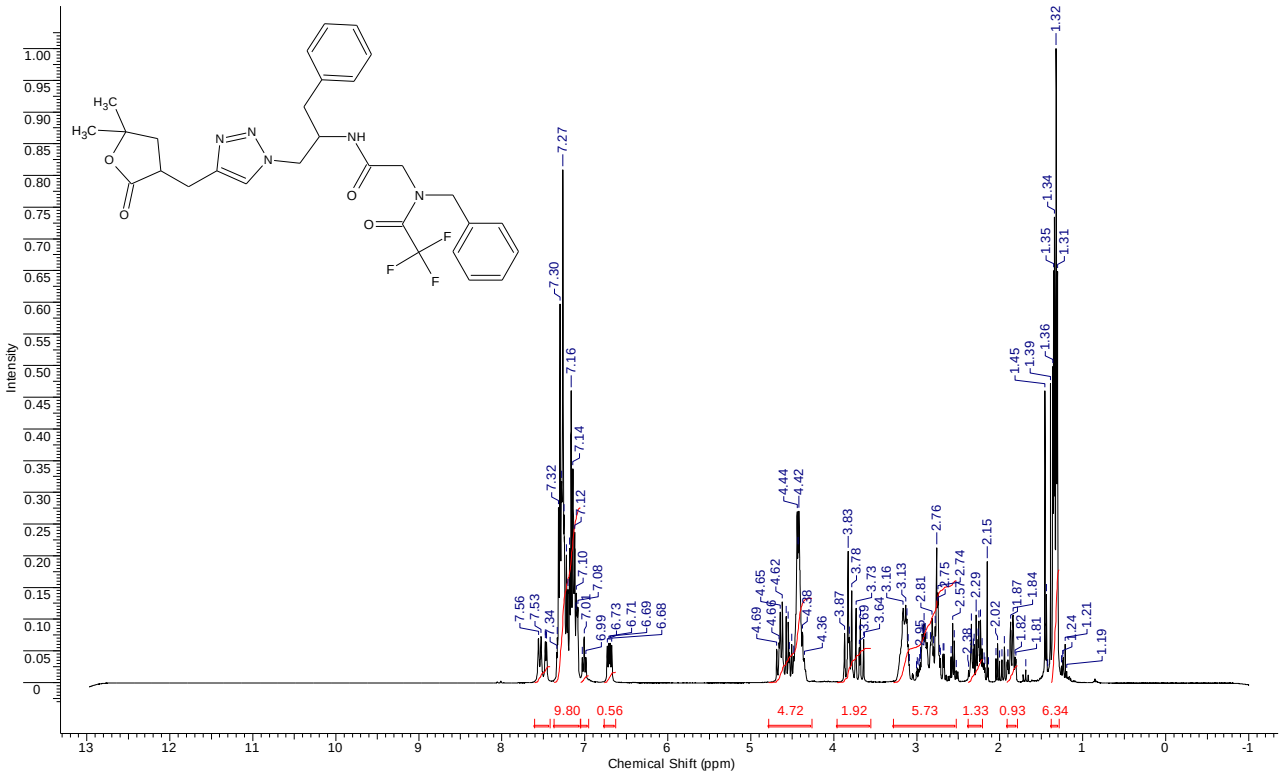
21 Apr 2017

Acquisition Time (sec)	0.7340	**Date**	Apr 3 2017	**File Name**	D:\BN\output\F19\2017.04.03\BM-1008_20170403_01\FLUORINE_01
Frequency (MHz)	376.31	**Nucleus**	19F	**Number of Transients**	10
Points Count	65536	**Pulse Sequence**	s2pul	**Solvent**	CHLOROFORM-D
Sweep Width (Hz)	89285.71	**Temperature (degree C)**	25.000		



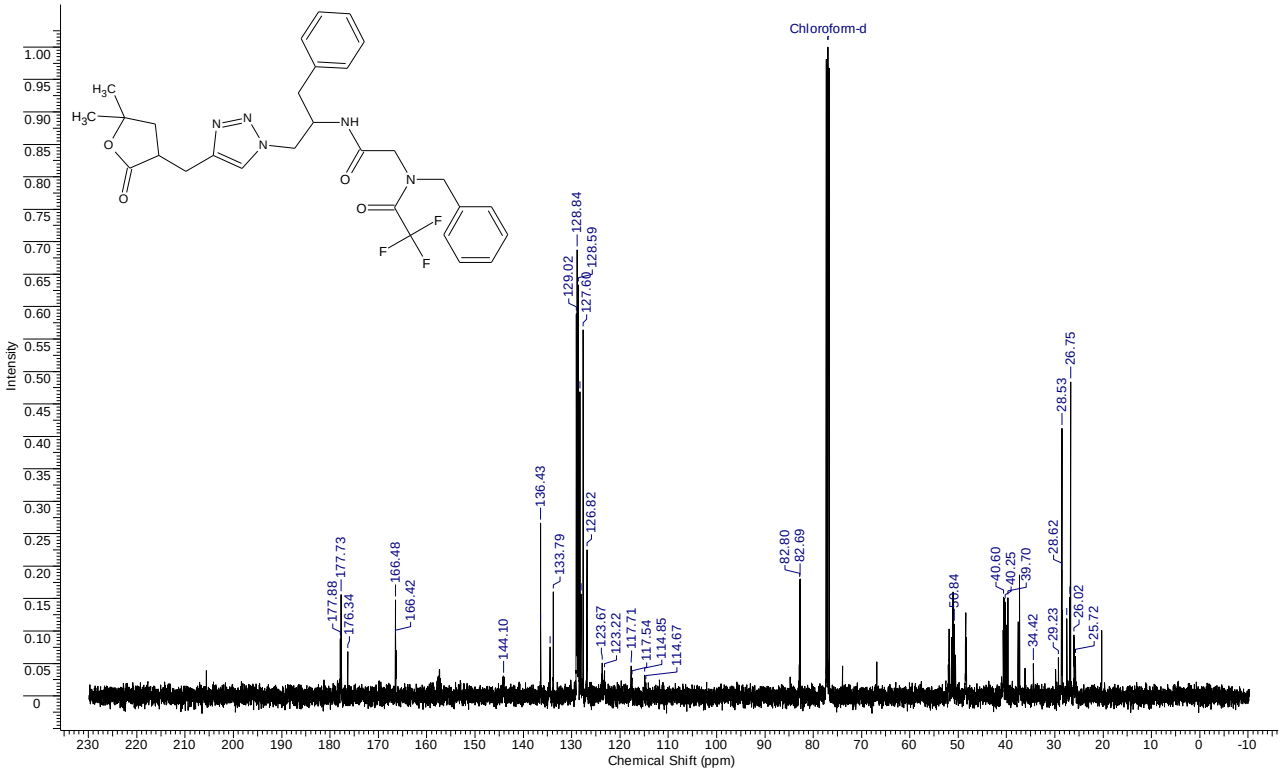
21 Apr 2017

Acquisition Time (sec)	2.9295	**Comment**	Imported from UXNMR.			**Date**	01 Apr 2017 19:25:48
File Name	D:\BN\output\2017\04.апрель\BM-1009\BM-1009_001001r			**Frequency (MHz)**	400.13	**Nucleus**	1H
Number of Transients	8	**Original Points Count**	16384	**Points Count**	65536	**Pulse Sequence**	zg30
Solvent	CHLOROFORM-D			**Sweep Width (Hz)**	5592.84	**Temperature (degree C)**	27.000



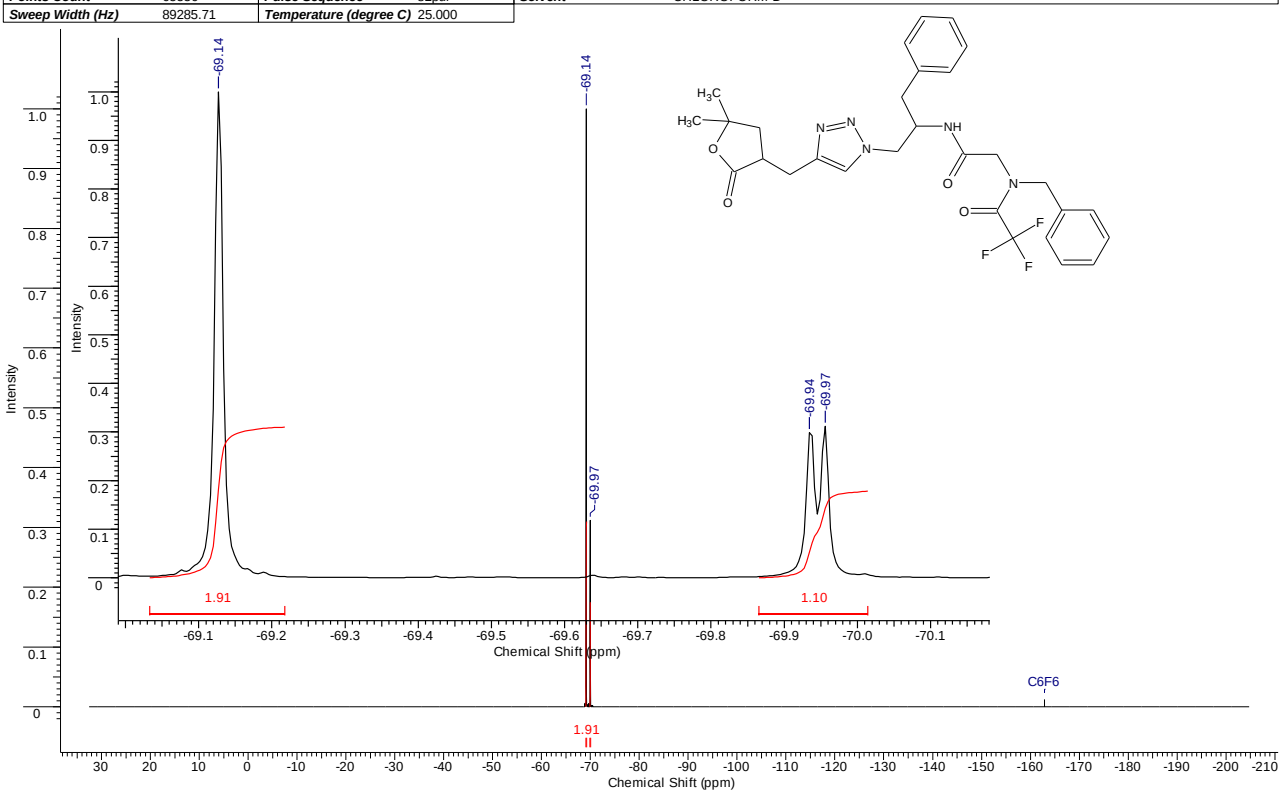
21 Apr 2017

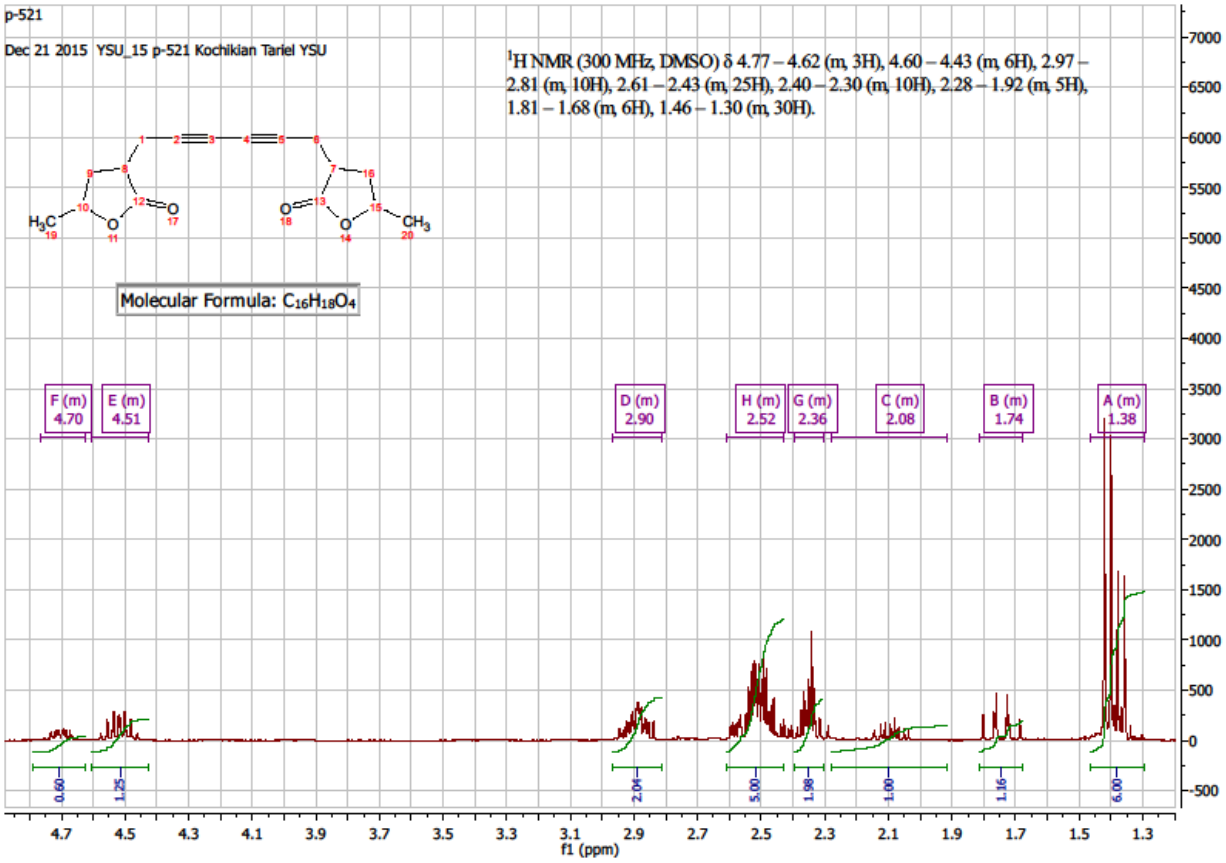
Acquisition Time (sec)	0.6783	**Comment**	Imported from UXNMR.	**Date**	01 Apr 2017 19:32:48
File Name	D:\BN\output\2017\04.апрель\BM-1009\BM-1009_002001r	**Frequency (MHz)**	100.61	**Nucleus**	13C
Number of Transients	128	**Original Points Count**	16384	**Points Count**	131072	**Pulse Sequence**	zgpg30
Solvent	CHLOROFORM-D			**Sweep Width (Hz)**	24154.59	**Temperature (degree C)**	27.000

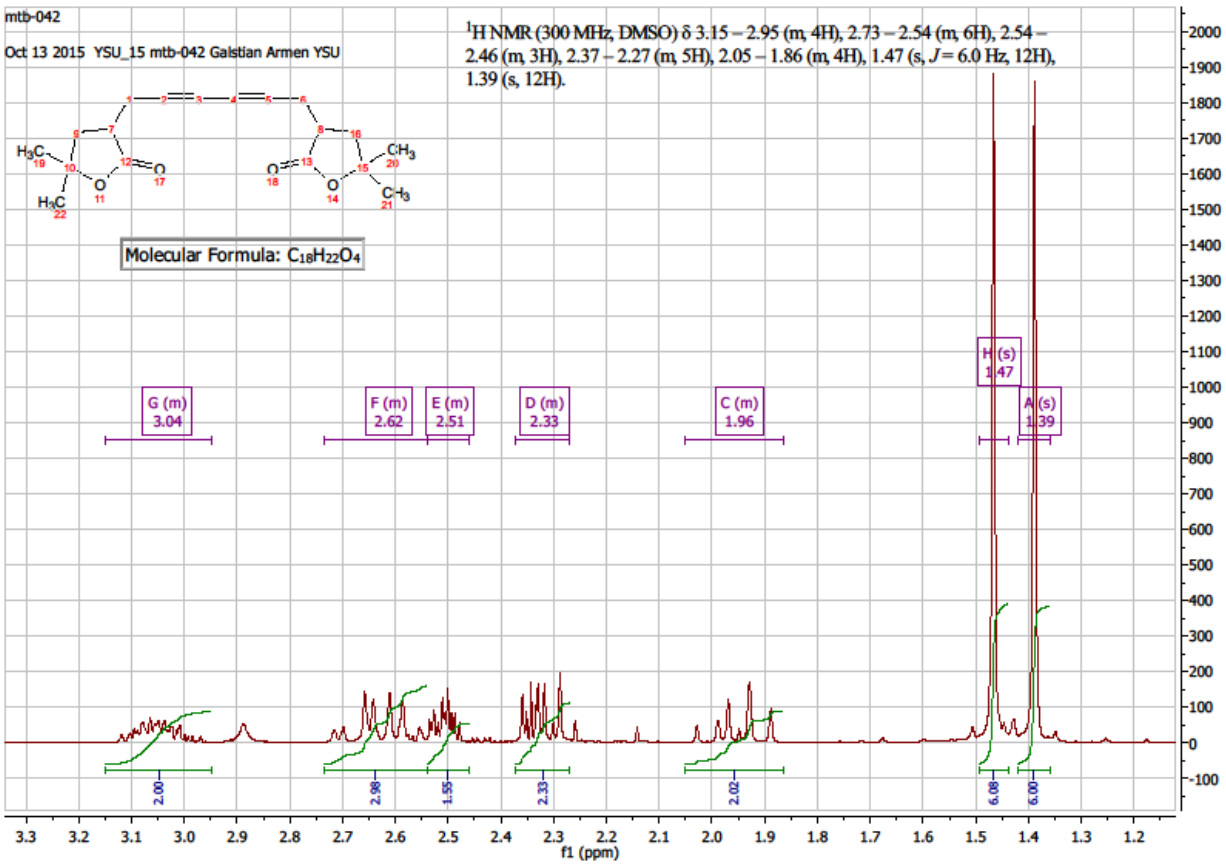


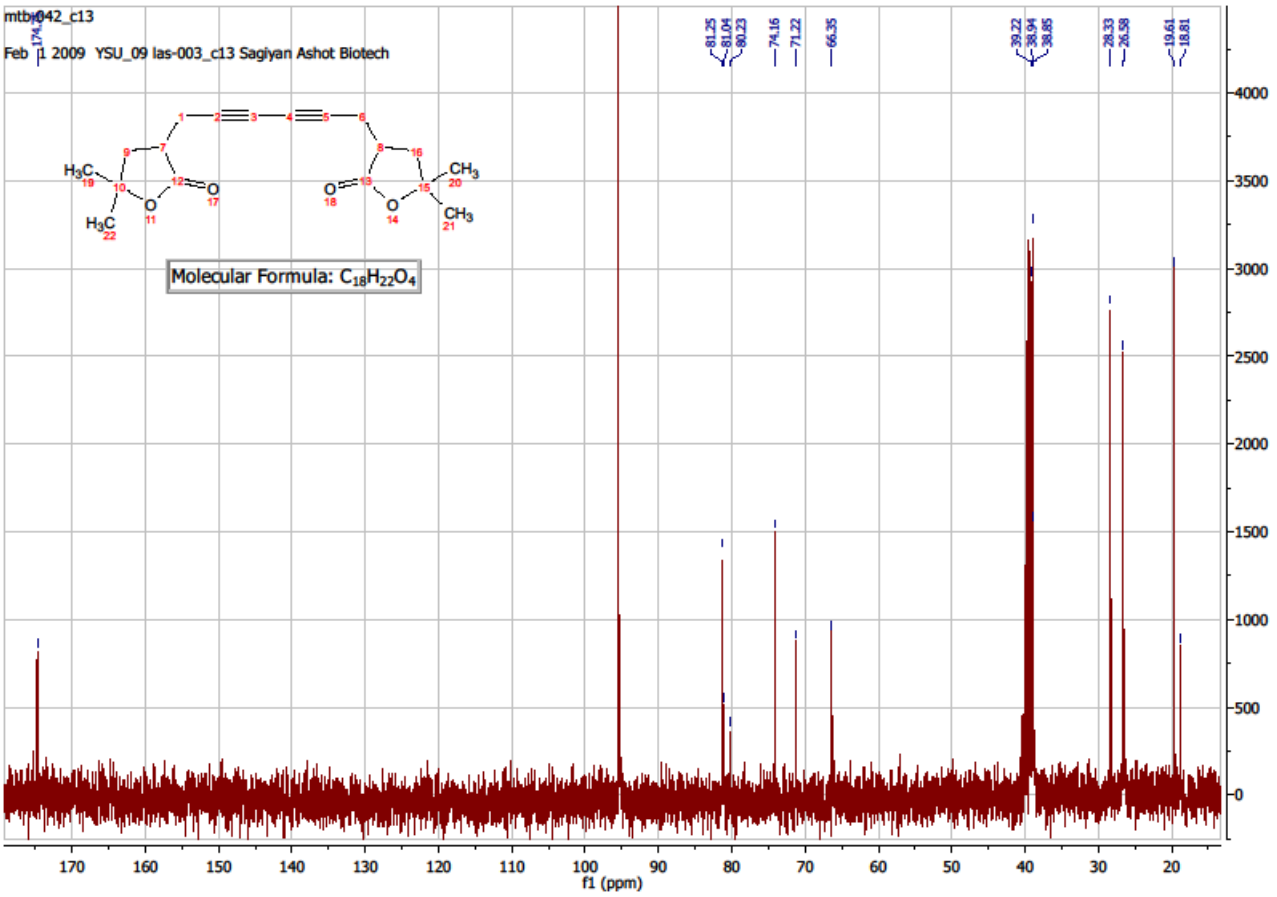
21 Apr 2017

Acquisition Time (sec)	0.7340	**Date**	Apr 3 2017	**File Name**	D:\BN\output\F19\2017.04.03\BM-1009_20170403_01\FLUORINE_01	
Frequency (MHz)	376.31	**Nucleus**	19F	**Number of Transients**	10	**Original Points Count**	65536
Points Count	65536	**Pulse Sequence**	s2pul	**Solvent**	CHLOROFORM-D	
Sweep Width (Hz)	89285.71	**Temperature (degree C)**	25.000			




p-521
Dec 21 2015 YSU_15 p-521 Kochikian Tariel YSU
^{1}H NMR (300 MHz, DMSO) δ 4.77 – 4.62 (m, 3H), 4.60 – 4.43 (m, 6H), 2.97 – 2.81 (m, 10H), 2.61 – 2.43 (m, 25H), 2.40 – 2.30 (m, 10H), 2.28 – 1.92 (m, 5H), 1.81 – 1.68 (m, 6H), 1.46 – 1.30 (m, 30H).
Molecular Formula: C16H18O4
F (m) 4.70
E (m) 4.51
D (m) 2.90
H (m) 2.52
G (m) 2.36
C (m) 2.08
B (m) 1.74
A (m) 1.38
0.60
1.25
2.04
5.00
1.88
1.00
1.16
6.00
f1 (ppm)


mtb-042
Oct 13 2015 YSU_15 mtb-042 Galstian Armen YSU
^{1}H NMR (300 MHz, DMSO) δ 3.15 – 2.95 (m, 4H), 2.73 – 2.54 (m, 6H), 2.54 – 2.46 (m, 3H), 2.37 – 2.27 (m, 5H), 2.05 – 1.86 (m, 4H), 1.47 (s, J = 6.0 Hz, 12H), 1.39 (s, 12H).
Molecular Formula: C18H22O4
G (m) 3.04
F (m) 2.62
E (m) 2.51
D (m) 2.33
C (m) 1.96
H (s) 1.47
A (s) 1.39
2.00
2.98
1.55
2.33
2.02
6.08
6.00
f1 (ppm)


mtbx042_c13
Feb 1 2009 YSU_09 las-003_c13 Sagiyan Ashot Biotech
Molecular Formula: C18H22O4
81.25
81.04
80.23
74.16
71.22
66.35
39.22
38.94
38.85
28.33
26.58
19.61
18.81
f1 (ppm)