Pd/C as an Efficient Heterogeneous Catalyst for Carbonylative Four-Component Synthesis of 4(*3H*)-Quinazolinones

Kishore Natte, Helfried Neumann, and Xiao-Feng Wu*

Leibniz-Institut für Katalyse an der Universität Rostock, Albert-Einstein-Straße 29a, 18059 Rostock (Germany)
E-mail: xiao-feng.wu@catalysis.de

General Methods

NMR spectra were recorded on Bruker Avance 300 and Bruker ARX 400 spectrometers. Chemical shifts (ppm) are given relative to solvent: references for $CDCl_3$ were 7.26 ppm (1H NMR) and 77.00 ppm (13C NMR). Multiplets were assigned as s (singlet), d (doublet), t (triplet), dd (doublet of doublet), m (multiplet) and br. s (broad singlet). All measurements were carried out at room temperature unless otherwise stated. Electron impact (EI) mass spectra were recorded on AMD 402 mass spectrometer (70 eV). High resolution mass spectra (HRMS) were recorded on Agilent 6210. The data are given as mass units per charge (m/z). Gas chromatography analysis was performed on an Agilent HP-5890 instrument with a FID detector and HP-5 capillary column (polydimethylsiloxane with 5% phenyl groups, 30 m, 0.32 mm i.d., 0.25 μm film thickness) using argon as carrier gas.

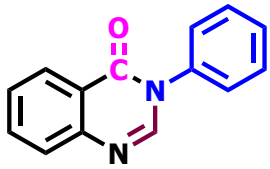
General Procedure for the Synthesis of Quinazolinone:

A 12 mL vial was charged with 10% Pd/C (1 mol%; 10 mg), 2-iodoaniline (1 mmol) and a stirring bar. Then, aniline (1.1 mmol), trimethyl orthoformate (2 mmol), DiPEA (3 mmol), and toluene (3 mL) were injected by syringe under argon. The vial (or several vials) was placed in an alloy plate, which was transferred into a 300 mL autoclave of the 4560 series from Parr Instruments® under argon atmosphere. After flushing the autoclave three times with CO, a pressure of 10 bar CO was adjusted at ambient temperature. Then, the reaction was performed for 20 h at 110 °C. After the reaction finished, the autoclave was cooled down to room temperature and the pressure was released carefully. The solution was filtered through whatmann filter paper and washed the reaction mixture with acetone (2-3 ml). After evaporation of the organic solvent the residue was adsorbed on silica gel and the crude product was purified by column chromatography using n-heptane/ethyl acetate (70:30) as eluent.

Procedure for Catalyst Recycling

The catalyst obtained after filtration was thoroughly washed with distilled water (3-5 mL) and then with methanol, acetone and ethyl acetate (3-5 mL) to remove any traces of organic material if present. The resulting catalyst was dried in an oven at 80 °C for 6 h and was then used for the next cycle.

Characterization of Products



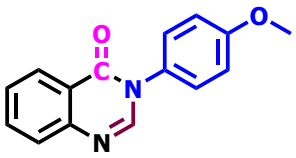
3-Phenylquinazolin-4(3*H*)-one

^{1}H NMR (300 MHz, Chloroform-d): δ 8.38 (ddd, J = 8.0, 1.5, 0.7 Hz, 1H), 8.13 (s, 1H), 7.89 – 7.73 (m, 2H), 7.60 – 7.48 (m, 4H), 7.46 – 7.38 (m, 2H).

^{13}C NMR (75 MHz, CDCl3) δ = 160.63, 147.76, 145.98, 137.38, 134.47, 129.53, 129.00, 127.54, 127.47, 127.06, 126.90, 122.32.

GC-MS (EI, 70eV): m/z(%) = 222 (M+, 100), 193 (10) , 119(10), 77 (15).

HRMS (ESI): calcd. for $[C_{14}H_{10}N_2O + H]^+$: 223.08659; found: 223.0866.

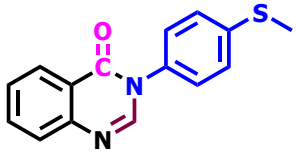


3-(4-Methoxyphenyl)quinazolin-4(3*H*)-one

^{1}H NMR (300 MHz, Chloroform-d): δ 8.36 (ddd, J = 8.0, 1.5, 0.7 Hz, 1H), 8.11 (s, 1H), 7.84 – 7.71 (m, 2H), 7.54 (ddd, J = 8.2, 6.5, 1.9 Hz, 1H), 7.36 – 7.28 (m, 2H), 7.08 – 6.99 (m, 2H), 3.86 (s, 3H).

^{13}C NMR (75 MHz, CDCl3): 161.60, 160.46, 148.46, 146.97, 135.04, 130.70, 128.70, 128.68, 128.66, 128.11, 128.09, 127.69, 122.91, 115.38, 77.16, 56.15.

HRMS (ESI): calcd. for $[C_{15}H_{12}N_2O_2 + H]$: 253. 07567; found: 253.07597.



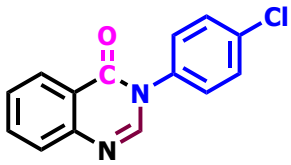
3-(4-(Methylthio)phenyl)quinazolin-4(3*H*)-one

^{1}H NMR (400 MHz, Chloroform-d) δ 8.38 – 8.28 (m, 1H), 8.10 (s, 1H), 7.85 – 7.70 (m, 2H), 7.53 (ddd, J = 8.2, 6.7, 1.6 Hz, 1H), 7.38 – 7.27 (m, 2H), 7.10 – 6.96 (m, 2H), 3.86 (s, 3H).

δ C (101 MHz, CDCl3) 161.09, 159.95, 147.96, 146.46, 134.54, 130.20, 128.94, 128.17, 127.61, 127.59, 127.18, 122.40, 119.74, 114.87, 114.34, 55.64.

GC-MS (EI, 70eV): m/z(%)=268 (M+, 100), 235 (40), 222 (10), 119(10), 76 (5).

HRMS (ESI): calcd. for $[C_{15}H_{12}N_2OS + H]^+$: 269:07331; found: 269:07341.



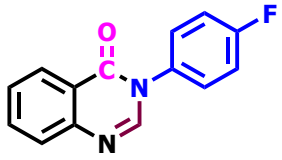
3-(4-Chlorophenyl)quinazolin-4(3*H*)-one

^{1}H NMR (300 MHz, DMSO-d_6) δ = 8.40 (s, 1H), 8.20 (d, J=8.0, 1H), 7.96-7.91 (m, 1H), 7.83-7.80 (m, 2H), 7.67-7.60 (m, 4H).

^{13}C NMR (75 MHz, DMSO-d_6) δ = 160.73, 148.53, 147.68, 139.69, 135.63, 134.09, 131.64, 129.68, 128.34, 128.21, 127.31, 124.2, 122.68.

GC-MS (EI, 70eV): m/z(%)=256 (M+, 9+7), 255 (100), 111 (23), 76 (15).

HRMS (ESI): calcd. for [$C_{14}H_9ClN_2O$]: 256.03779; found: 256.03914.



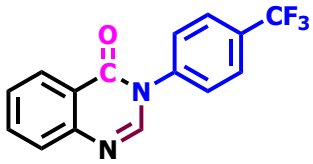
3-(4-Fluorophenyl)quinazolin-4(3*H*)-one

^{1}H NMR (300 MHz, Chloroform-d) δ 8.26 (ddd, J = 8.0, 1.5, 0.7 Hz, 1H), 8.01 (s, 1H), 7.79 – 7.61 (m, 2H), 7.47 (ddd, J = 8.2, 6.7, 1.7 Hz, 1H), 7.38 – 7.28 (m, 2H), 7.22 – 7.09 (m, 2H).

^{13}C NMR (75 MHz, Chloroform-d) δ = 162,65 (d, *J* = 249.71 Hz), 160.84, 147.86, 145.88, 134.75, 133.42 (d, *J* = 3.26 Hz), 129.02, 128.90, 127.75 (d, *J* = 10.17 Hz), 127.18, 122.28, 116.70 (d, *J* = 23.12 Hz).

GC-MS (EI, 70eV): m/z(%) = m/z(%) = 240(M^+, 100), 212 (20), 192 (5), 137(15), 77 (35).

HRMS (ESI): calcd. for [$C_{14}H_9FN_2O$ + H]$^+$: 241:07717; found: 241:07726.



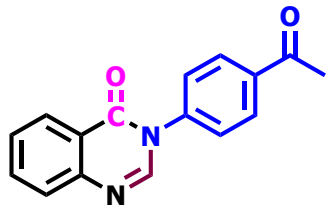
3-(4-(Trifluoromethyl)phenyl)quinazolin-4(3*H*)-one

^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.35 (ddd, *J* = 8.0, 1.5, 0.6 Hz, 1H), 8.10 (s, 1H), 7.87 – 7.72 (m, 4H), 7.64 – 7.51 (m, 3H).

^{13}C NMR (75 MHz, CDCl3) δ = 160.37, 147.61, 145.07, 140.36, 134.85, 131.19 (q, J=33.0), 127.91, 127.66, 127.47, 127.14, 126.77 (q, J=3.8), 123.50 (q, J=270.8), 122.07.

GC-MS (EI, 70eV): m/z(%)=290(M+, 100), 262 (10), 145 (30), 119 (20), 92 (10).

HRMS (ESI): calcd. for [$C_{15}H_9F_3N_2O$ + H]$^+$: 291.07397; found: 291.07416.



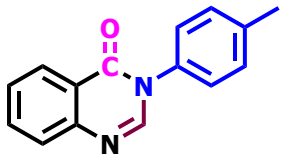
3-(4-Acetylphenyl)quinazolin-4(3*H*)-one

^{1}H NMR (300 MHz, CDCl3) δ = 8.33 (d, J=8.8, 1H), 8.11 (s, 1H), 8.09-7.97 (m, 2H), 7.84-7.49 (m, 5H), 2.62 (s, 3H).

^{13}C NMR (75 MHz, CDCl3) δ = 196.53, 160.51, 147.78, 145.42, 138.42, 137.81, 134.73, 131.47, 129.87, 128.79, 127.78, 127.60, 127.04, 126.68, 122.08, 26.63.

GC-MS (EI, 70eV): m/z(%)=264(M+, 100), 249 (80), 221 (30), 192 (10).

HRMS (ESI): calcd. for $[C_{16}H_{12}N_2O_2 + H]^+$: 265.09715; found: 265.09744.



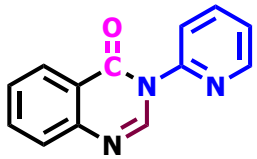
3-(*p*-Tolyl)quinazolin-4(3*H*)-one

^{1}H NMR (300 MHz, CDCl3) δ = 8.36 (d, *J*=7.9, 1H), 8.11 (s, 1H), 7.89-7.67 (m, 2H), 7.50-7.60 (m, 1H), 7.43-7.28 (m, 4H), 2.43 (s, 3H).

^{13}C NMR (75 MHz, CDCl3) δ = 159.81, 146.78, 145.24, 138.18, 133.83, 133.46, 129.18, 126.53, 126.46, 126.11, 125.67, 121.32, 20.21.

GC-MS (EI, 70eV): m/z(%)=236 (M+, 100), 221 (5), 207 (10), 119(10), 91 (10).

HRMS (ESI): calcd. for $[C_{15}H_{12}N_2O + H]^+$: 237.10224; found: 237.10228.



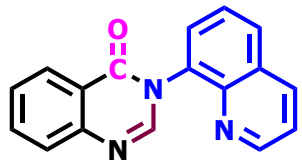
3-(Pyridin-2-yl)quinazolin-4(3*H*)-one

^{1}H NMR (300 MHz, CDCl3) δ = 8.89-8.55 (m, 2H), 8.49-8.32 (m, 1H), 8.00-7.30 (m, 6H).

^{13}C NMR (75 MHz, CDCl3) δ = 160.32, 149.54, 149.11, 147.50, 144.81, 137.98, 134.71, 127.57, 127.54, 127.11, 123.56, 121.96, 121.43.

GC-MS (EI, 70eV): m/z(%)=223(M+, 100), 195 (70), 169 (25), 78 (30).

HRMS (ESI): calcd. for $[C_{13}H_9N_3O + H]^+$: 224.08184; found: 224.08197.



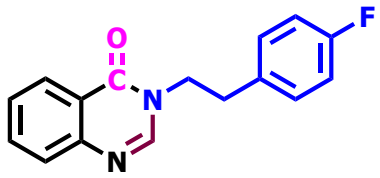
3-(Quinolin-8-yl)quinazolin-4(3*H*)-one

^{1}H NMR (300 MHz, CDCl3) δ = 8.82-8.70 (m, 4H), 8.21- 8.12 (m, 2H), 7.55-7.44 (m, 5H).

^{13}C NMR (75 MHz, CDCl3) δ = 159.20, 148.96, 148.37, 138.22, 136.38, 136.05, 133.50, 127.91, 127.26, 126.55, 122.51, 122.47, 122.19, 121.71, 117.54, 110.96.

GC-MS (EI, 70eV): m/z(%)=273(M+, 100), 244 (80), 155 (5), 102 (5).

HRMS (ESI): calcd. for $[C_{17}H_{11}N_3O + H]^+$: 274.09749; found: 274.09767.



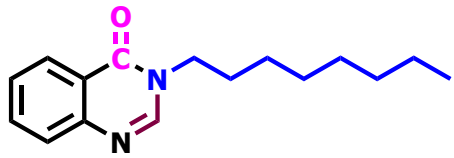
3-(4-Fluorophenethyl)quinazolin-4(3*H*)-one

^{1}H NMR (300 MHz, DMSO-d_6) δ 7.35 – 7.29 (m, 2H), 6.98 (ddd, J = 8.1, 7.1, 1.6 Hz, 1H), 6.80 (ddd, J = 8.2, 1.2, 0.6 Hz, 1H), 6.71 (ddd, J = 8.2, 7.1, 1.2 Hz, 1H), 6.43 – 6.36 (m, 2H), 6.31 – 6.23 (m, 2H), 3.40 – 3.30 (m, 2H), 2.17 (t, J = 7.3 Hz, 2H).

^{13}C NMR (75 MHz, DMSO-d_6) δ= 160.99 (d, J = 242.0 Hz), 147.77, 134.23, 134.03 (d, J = 3.2 Hz), 130.65 (d, J = 7.8 Hz), 128.57, 127.12, 126.97, 125.97, 121.44, 117.51, 115.22 (d, J = 21.2 Hz), 47.24, 33.36.

GC-MS (EI, 70 eV): m/z (%) [M+] 268 (9), 130 (23), 129 (20), 122 (100), 109 (43), 77 (24).

HRMS (ESI): calcd. for $[C_{16}H_{13}FN_2O+H]^+$: 269.0298; found: 269.0299.



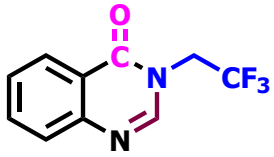
3-Octylquinazolin-4(3*H*)-one

^{1}H NMR (300 MHz, CDCl3) δ = 8.42-8.16 (m, 1H), 8.03 (d, J=14.8, 1H), 7.83-7.44 (m, 3H), 4.02 (t, J=7.35, 2H), 1.82 (quint, J=7.12, J=14.81, 2H), 1.21-1.45 (m, 10H), 0.89 (t, J=6.93, 3H).

^{13}C NMR (75 MHz, CDCl3) δ = 161.01, 151.32, 147.97, 146.35, 134.20, 132.63, 127.79, 127.41, 127.27, 126.82, 125.90, 124.89, 122.17, 49.28, 34.52, 31.20.

GC-MS (EI, 70eV): m/z(%)=258(M+, 40), 241 (15), 229 (15), 215 (20), 201 (15), 187 (25), 173 (30), 160 (80), 146 (100), 130 (20), 118 (15), 77(5).

HRMS (ESI): calcd. for $[C_{16}H_{22}N_2O + H]^+$: 259.18049; found: 259.18072.



3-(2,2,2-Trifluoroethyl)quinazolin-4(3*H*)-one

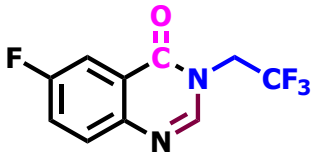
^{1}H NMR (300 MHz, DMSO-d_6) δ 7.57 (d, *J* = 0.9 Hz, 1H), 7.37 – 7.30 (m, 1H), 7.05 (ddd, *J* = 8.5, 7.2, 1.6 Hz, 1H), 6.92 – 6.82 (m, 1H), 6.77 (ddd, *J* = 8.2, 7.2, 1.2 Hz, 1H), 4.13 (q, *J* = 9.2 Hz, 2H).

^{19}F NMR (282 MHz, DMSO-d_6) δ -69.27 (t, J = 9.3 Hz).

^{13}C NMR (75 MHz, CDCl3) δ = 159.76, 147.36, 147.33, 135.08, 127.76, 127.42, 126.35, 123.91 (q, *J* = 279.2 Hz), 121.08, 44.84 (q, *J* = 34.13 Hz).

GC-MS (EI, 70 eV): m/z (%) [M+] 228 (100), 208 (29), 159 (12), 110 (10), 77 (24), 69 (26).

HRMS (ESI): calcd. for $[C_{10}H7F_3N_2O+ H]^+$: 228.0847, found: 228.0948



6-Fluoro-3-(2,2,2-trifluoroethyl)quinazolin-4(3*H*)-one

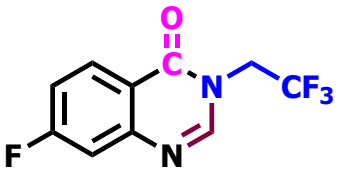
^{1}H NMR (400 MHz, Chloroform-d) δ 8.26 (dd, J = 8.9, 6.0 Hz, 1H), 7.98 (s, 1H), 7.31 (dd, J = 9.4, 2.5 Hz, 1H), 7.23 – 7.14 (m, 1H), 4.60 (q, J = 8.5 Hz, 2H).

^{19}F NMR (282 MHz, Chloroform-d) δ -70.48 (t, J = 9.2 Hz), -103.62 (S).

^{13}C NMR (75 MHz, CDCl3) δ = 166,79 (d, *J* = 256.65 Hz), 159.68, 149.86 (d, *J* = 12.90 Hz), 146.51, 129.99 (d, *J* = 10.15 Hz), 123.16 (q, *J* = 279.10 Hz), 118.37 (d, *J* = 1.88 Hz), 116.77 (d, *J* = 22.96 Hz), 113.46 (d, *J* = 21.77 Hz), 45.46 (q, *J* = 35.78 Hz).

GC-MS (EI, 70eV): m/z(%)=246 (M+, 100), 226 (10), 177 (03), 147 (40), 110 (03).

HRMS (ESI): calcd. for $[C_{10}H_6F_4N_2O+ H]^+$: 247.1426, found: 247.1536



7-Fluoro-3-(2,2,2-trifluoroethyl)quinazolin-4(3*H*)-one

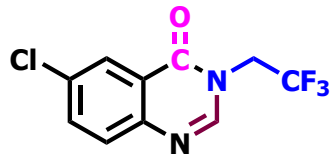
^{1}H NMR (300 MHz, Chloroform-d) δ 8.26 (ddd, J = 8.9, 6.0, 0.4 Hz, 1H), 7.98 (s, 1H), 7.31 (dd, J = 9.3, 2.5 Hz, 1H), 7.25 – 7.13 (m, 1H), 4.60 (q, J = 8.5 Hz, 2H).

^{19}F NMR (282 MHz, Chloroform-d) δ -70.49 (S), -103.84 (S).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 166,78 (d, *J* = 256.55 Hz), 159.68, 149.86 (d, *J* = 13.42 Hz), 146.51, 129.99 (d, *J* = 10.32 Hz), 123.15 (q, *J* = 280.90 Hz), 118.36 (d, *J* = 2.21 Hz), 116.76 (d, *J* = 23.61 Hz), 113.46 (d, *J* = 22.04 Hz), 45.46 (q, *J* = 35.62 Hz).

GC-MS (EI, 70eV): m/z(%)=246 (M+, 100), 226 (10), 177 (03), 147 (40), 110 (03).

HRMS (ESI): calcd. for $[C_{10}H_6F_4N_2O+ H]^+$: 247.1436, found: 247.1546



6-Chloro-3-(2,2,2-trifluoroethyl)quinazolin-4(3*H*)-one

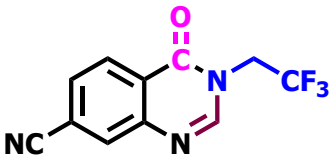
^{1}H NMR (400 MHz, Chloroform-d) δ 8.28 (d, J = 8.45 Hz, 1H), 8.08 (s, 1H), 7.77 (d, J = 2.07 Hz, 1H), 7.50-7.57 (m, 1H), 4.71 (q, J = 8.46 Hz, 2H).

^{19}F NMR (282 MHz, Chloroform-d) δ -70.43 (t, J = 8.39 Hz).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 159.82, 148.57, 146.46, 128.66, 128.61, 127.49, 123.16 (q, *J* = 280.08 Hz), 120.11, 45.53 (q, *J* = 35.71 Hz).

GC-MS (EI, 70eV): m/z(%)=262(M^+, 100), 242 (20), 193 (05), 163 (20), 83 (07).

HRMS (ESI): calcd. for $[C_{10}H_6ClF_3N_2O]$: 262.0634; found: 262.0641.



4-Oxo-3-(2,2,2-trifluoroethyl)-3,4-dihydroquinazoline-7-carbonitrile

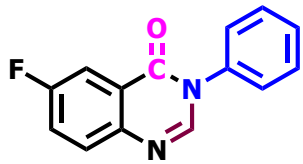
^{1}H NMR (400 MHz, Chloroform-d) δ 8.64 (dd, J = 2.0, 0.6 Hz, 0H), 8.13 (d, J = 1.1 Hz, 0H), 7.99 (dd, J = 8.5, 2.0 Hz, 0H), 7.83 (dd, J = 8.5, 0.6 Hz, 0H), 4.69 (q, J = 8.4 Hz, 1H).

^{19}F NMR (282 MHz, Chloroform-d) δ -70.37(S).

^{13}C NMR (75 MHz, CDCl3) δ = 158.98, 150.15, 147.80, 137.02, 132.48, 129.29, 123.15 (q, *J* = 280.90 Hz), 122.25, 117.55, 11.75, 45.46 (q, *J* = 35.62 Hz).

GC-MS (EI, 70eV): m/z(%)=253(M+, 100), 233 (20), 184 (10), 154 (20), 83 (05).

HRMS (ESI): calcd. for $[C_{11}H_6F_3N_3O+H]^+$: 254.18235; found: 254.18336.



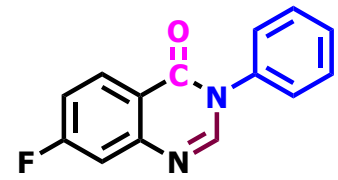
6-Fluoro-3-phenylquinazolin-4(3*H*)-one

^{1}H NMR (400 MHz, Chloroform-d) δ 8.44 (dd, J = 8.9, 6.1 Hz, 1H), 8.19 (s, 1H), 7.65 – 7.53 (m, 3H), 7.50 – 7.44 (m, 3H), 7.35 – 7.28 (m, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 166,61 (d, *J* = 257.68 Hz), 160.09, 150.15 (d, *J* = 12.79 Hz), 147.33, 137.26, 130.02 (d, *J* = 10.19 Hz), 129.75, 129.31, 127.00, 119.14 (d, *J* = 1.81 Hz), 116.41 (d, *J* = 23.83 Hz), 113.12 (d, *J* = 21.87 Hz).

GC-MS (EI, 70eV): m/z(%)=240(M+, 100), 212 (20), 192 (5), 137(15), 77 (35).

HRMS (ESI): calcd. for $[C_{14}H_9FN_2O + H]^+$: 241:07817; found: 241:07819.



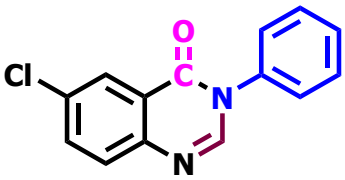
7-Fluoro-3-phenylquinazolin-4(3*H*)-one

^{1}H NMR (300 MHz, Chloroform-d) δ 8.43 (dd, J = 8.9, 6.1 Hz, 1H), 8.19 (s, 1H), 7.68 – 7.51 (m, 3H), 7.49 – 7.45 (m, 3H), 7.38 – 7.23 (m, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ = δ = 166,61 (d, *J* = 256.10 Hz), 160.09, 150.12 (d, *J* = 12.65 Hz), 147.33, 137.25, 130.02 (d, *J* = 10.67 Hz), 129.75, 129.31, 127.00, 119.13 (d, *J* = 1.59 Hz), 116.43 (d, *J* = 23.85 Hz), 113.12 (d, *J* = 21.86 Hz).

GC-MS (EI, 70eV): m/z(%)=240(M+, 100), 212 (20), 192 (5), 137(15), 77 (35).

HRMS (ESI): calcd. for $[C_{14}H_9FN_2O + H]^+$: 241:07717; found: 241:07726.



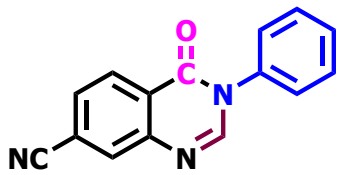
6-Chloro-3-phenylquinazolin-4(3*H*)-one

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.28 (d, J=2.1, 1H), 8.10 (s, 1H), 7.74-7.68 (m, 2H), 7.57- 7.47 (m, 3H), 7.40 (d, J=6.9, 2H).

^{13}C NMR (100 MHz, CDCl3) δ = 159.61, 146.26, 146.17, 137.09, 134.86, 133.41, 129.62, 129.19, 129.15, 126.81, 126.38, 123.33.

GC-MS (EI, 70eV): m/z(%)=256(M+, 100), 228 (10), 192 (5), 153(10), 77 (25).

HRMS (ESI): calcd. for $[C_{14}H_9ClN_2O + H]^+$: 257.04762; found: 257.04772.

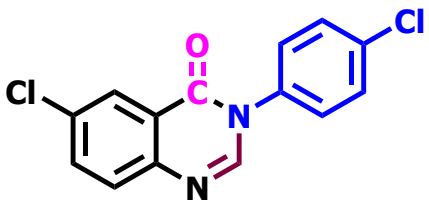


4-Oxo-3-phenyl-3,4-dihydroquinazoline-7-carbonitrile

^{1}H NMR (400 MHz, Chloroform-d) δ 8.68 (dt, J = 2.0, 0.6 Hz, 1H), 8.23 (s, 1H), 8.05 – 7.89 (m, 1H), 7.86 (d, J = 8.5 Hz, 1H), 7.63 – 7.49 (m, 3H), 7.47 – 7.37 (m, 2H).

δ C (101 MHz, $CDCl_3$) 159.33, 150.52, 148.61, 136.75, 136.55, 132.59, 129.92, 129.68, 129.04, 126.81, 122.99, 117.83, 111.27.

HRMS (ESI): calcd. for $[C_{15}H_9N_3O + H]^+$: 248.07532; found: 248.07631

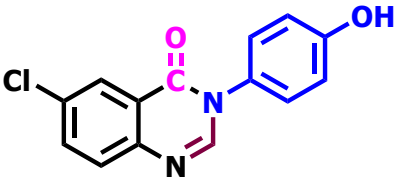


6-Chloro-3-(4-chlorophenyl)quinazolin-4(3*H*)-one

^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.26 (dd, *J* = 8.6, 0.5 Hz, 1H), 8.08 (s, 1H), 7.75 (d, *J* = 2.0 Hz, 1H), 7.58 – 7.44 (m, 3H), 7.43 – 7.31 (m, 2H).

δ C (75 MHz, CDCl3) 160.03, 148.78, 146.76, 141.06, 135.58, 135.41, 129.97, 128.67, 128.47, 128.28, 127.32, 120.70.

HRMS (ESI): calcd. for $[C_{14}H_8Cl_2N_2O+ H]^+$: 291.0053; found: 291.0054.

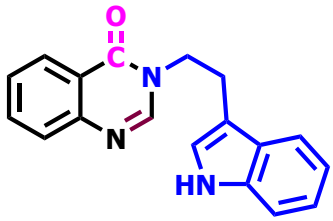


6-Chloro-3-(4-hydroxyphenyl)quinazolin-4(3*H*)-one

^{1}H NMR (300 MHz, DMSO-d6) δ 9.88 (s, 1H), 8.33 (s, 1H), 8.16 (dd, J = 8.6, 0.4 Hz, 1H), 7.78 (d, J = 2.0 Hz, 1H), 7.61 (dd, J = 8.6, 2.1 Hz, 1H), 7.36 – 7.24 (m, 2H), 6.96 – 6.84 (m, 2H).

δ C (75 MHz, DMSO) 159.65, 157.71, 149.02, 148.84, 139.02, 128.48, 128.45, 127.48, 126.37, 122.61, 120.76, 115.55.

HRMS (ESI): calcd. For $[C_{14}H_9ClN_2O_2+ H]^+$: 272.0427; found: 272.0428



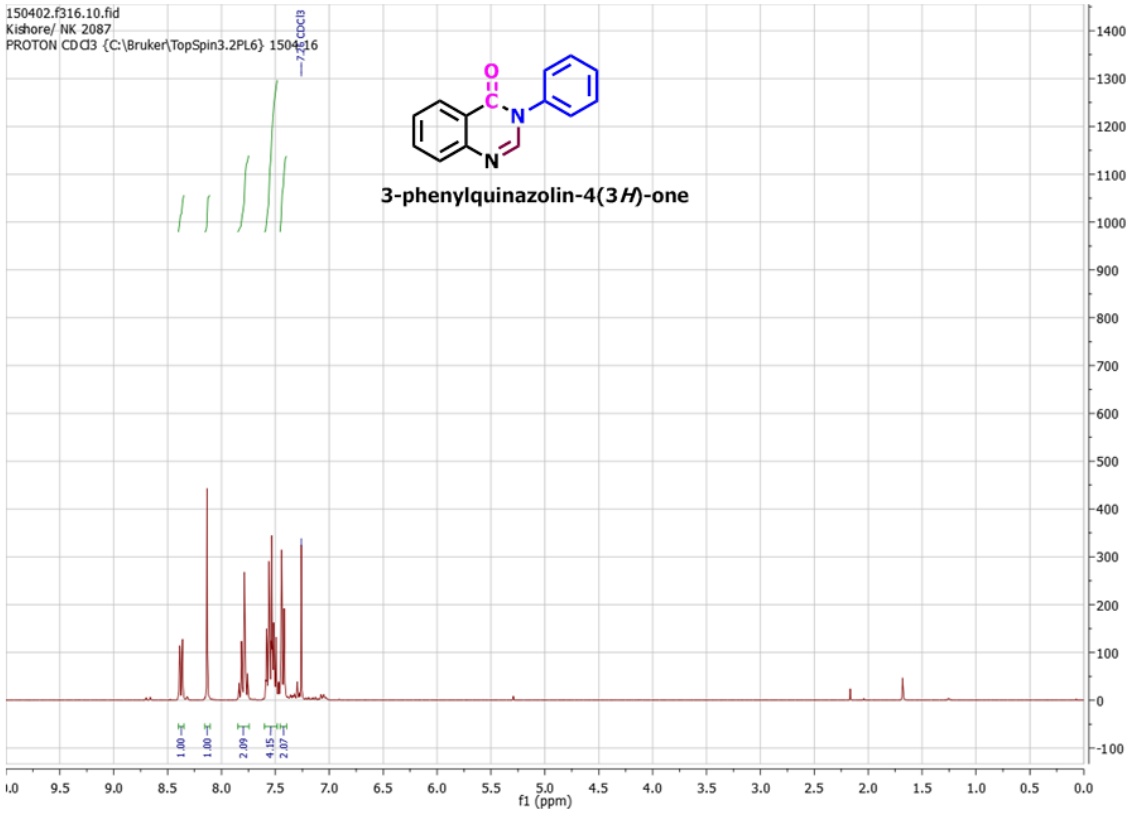
3-(2-(1*H*-Indol-3-yl)ethyl)quinazolin-4(3*H*)-one

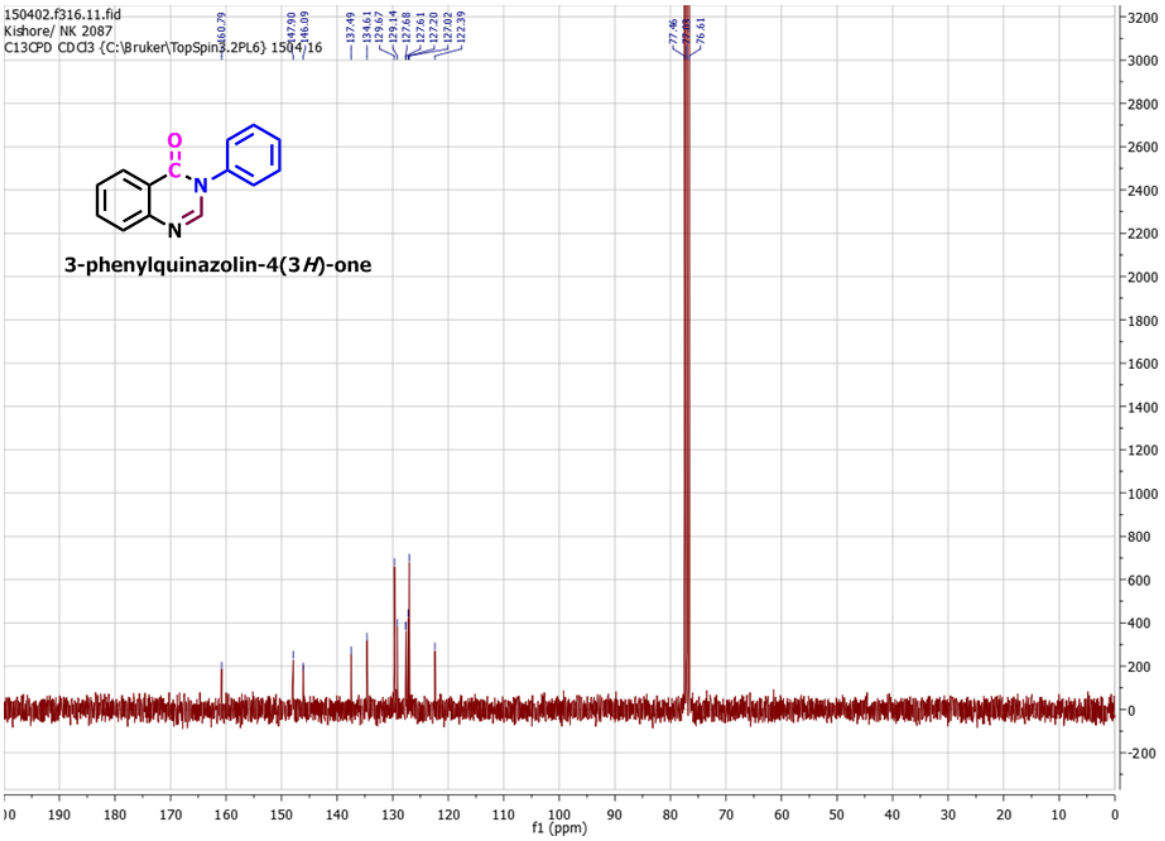
^{1}H NMR (300 MHz, CDCl3) δ = 8.35 (d, J=9.4, 2H), 7.71 (t, J=8.4, 1H), 7.66 (d, J=7.9, 2H), 7.47 (d, J=6.1, 2H), 7.32 (d, J=8.1, 1H), 7.21 (d, J=7.8, 1H), 7.12 (t, J=6.9, 1H), 6.82 (d, J=2.2, 1H), 4.28 (t, J=6.7, 2H), 3.25 (t, J=6.7, 2H).

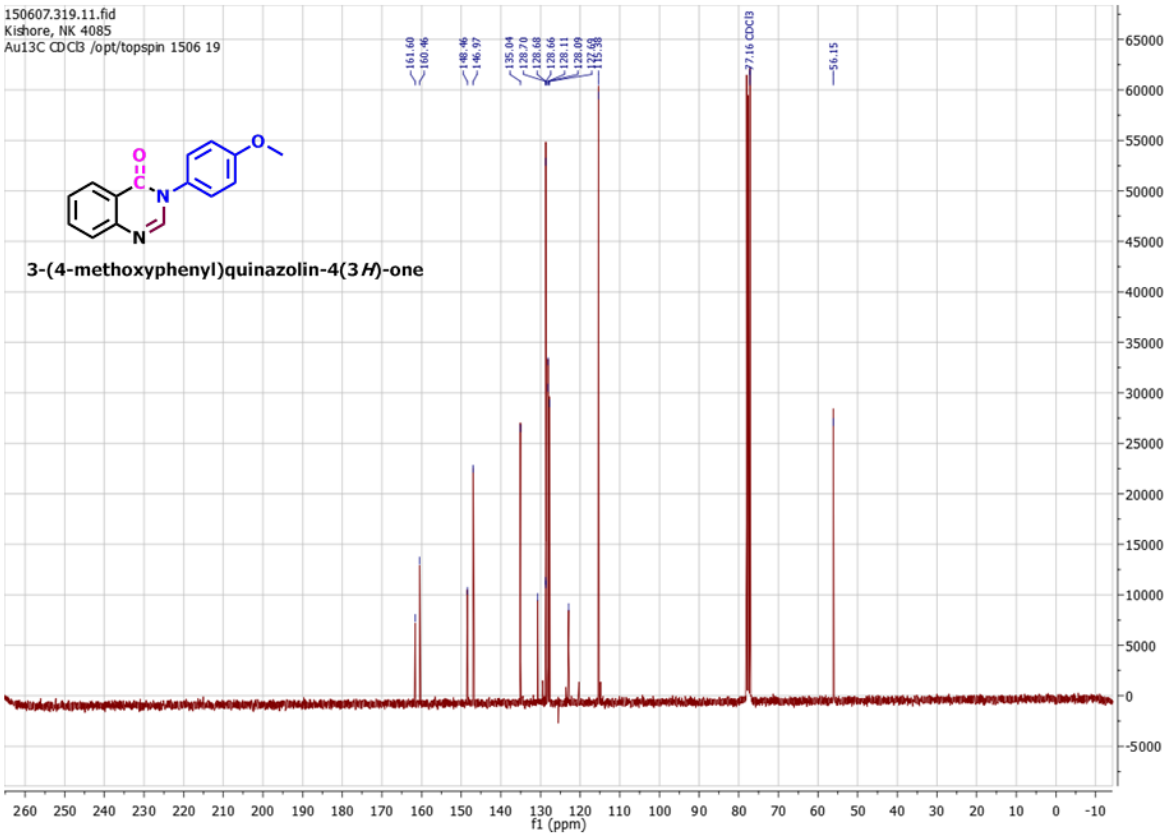
^{13}C NMR (75 MHz, CDCl3) δ = 161.01, 147.99, 146.67, 136.42, 134.14, 127.21, 127.11, 126.75, 126.59, 122.78, 122.26, 123.01, 119.64, 118.28, 111.49, 111.10, 47.52, 24.87.

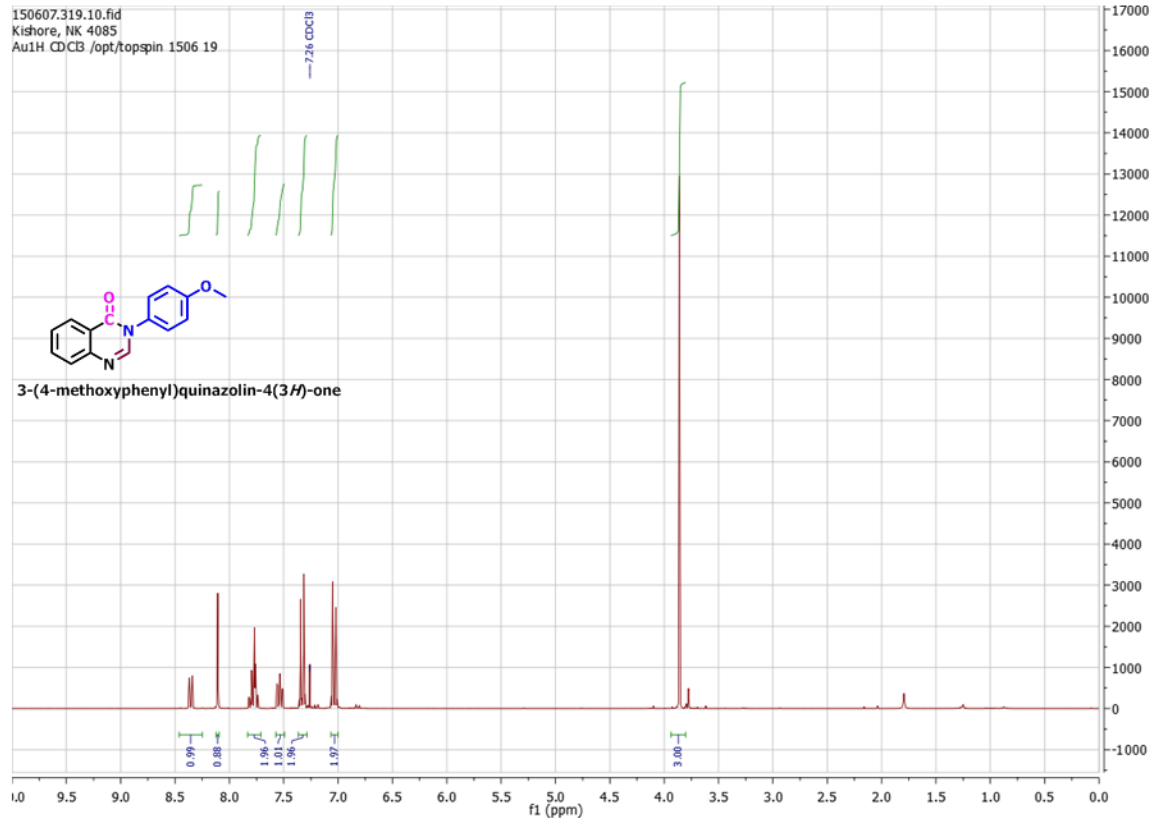
GC-MS (EI, 70eV): m/z(%)=289(M+, 5), 143 (100), 130 (20), 77 (5).

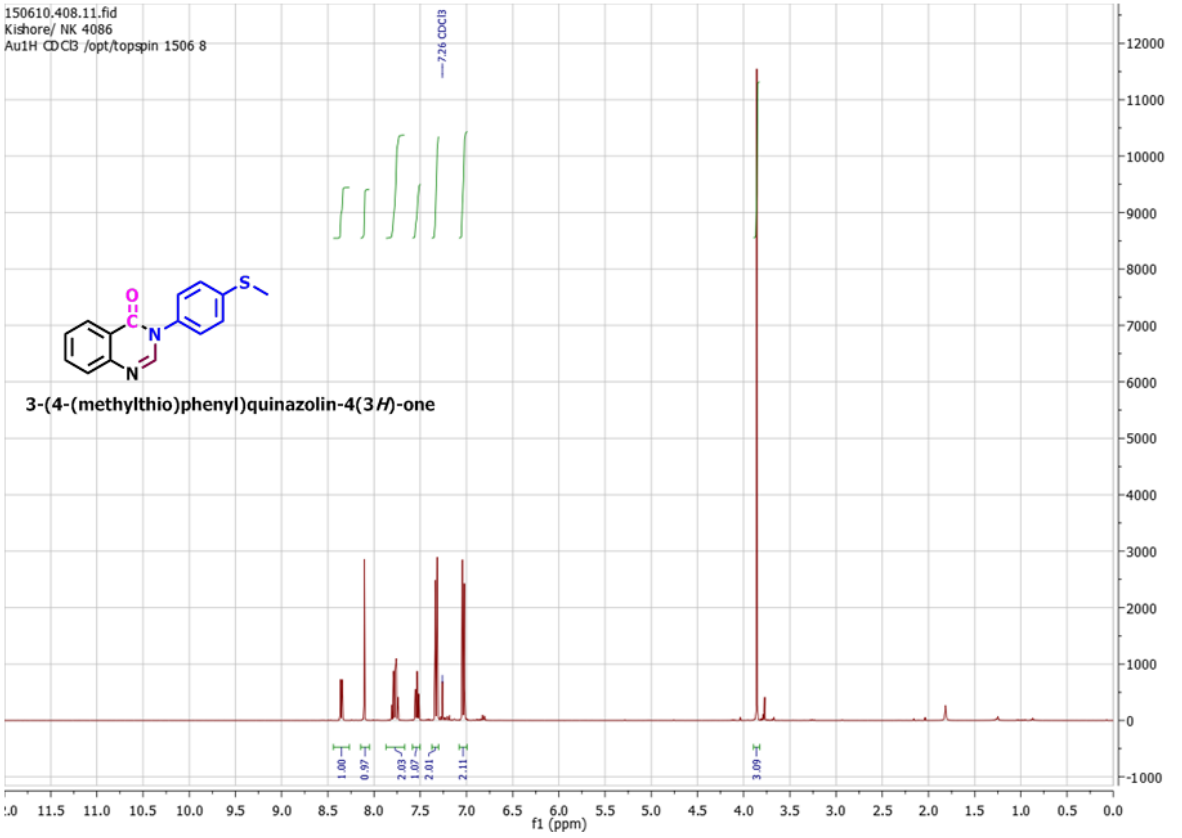
HRMS (ESI): calcd. for $[C_{18}H_{15}N_3O + H]^+$: 290.12879; found: 290.12895.

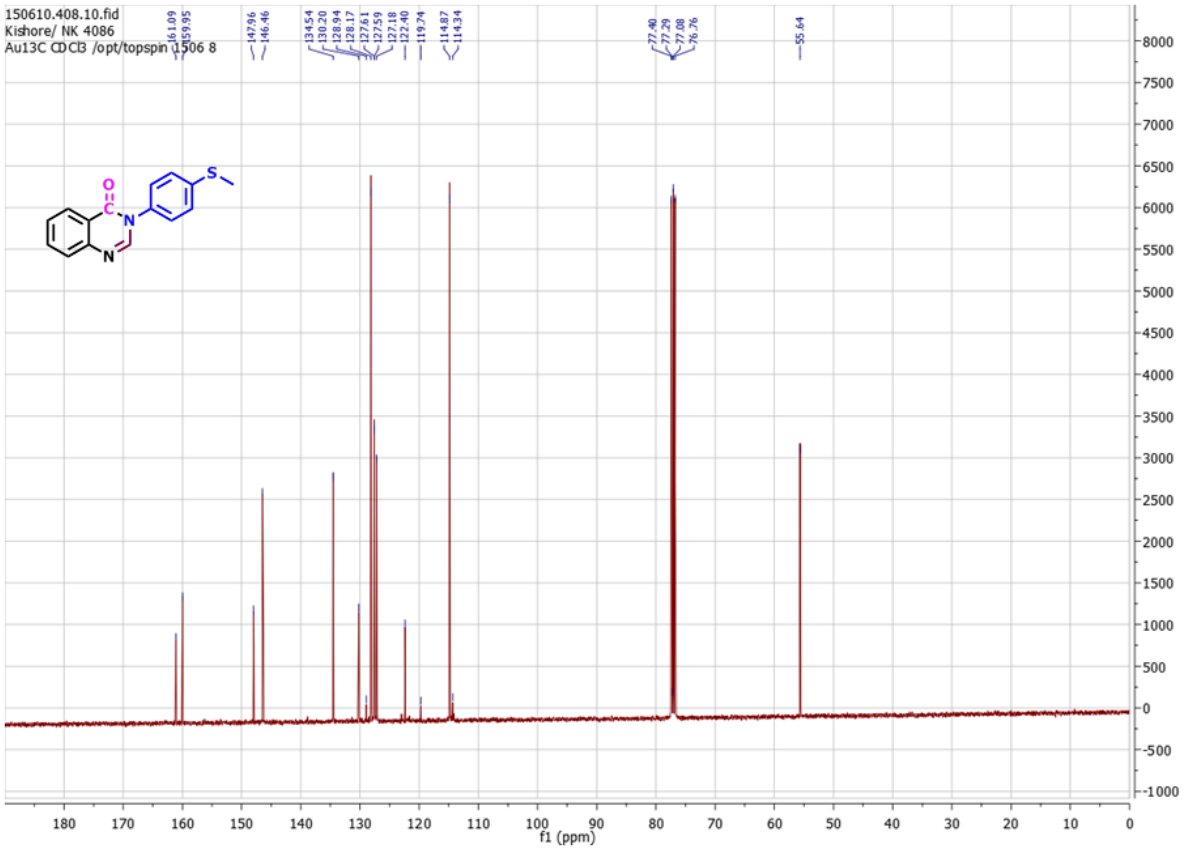

150402.f316.10.fid
Kishore/ NK 2087
PROTON CDCl3 {C:\Bruker\TopSpin3.2PL6} 1504-16
7.26 CDCl3
3-phenylquinazolin-4(3H)-one
1.00
1.00
2.09
4.15
2.07
f1 (ppm)

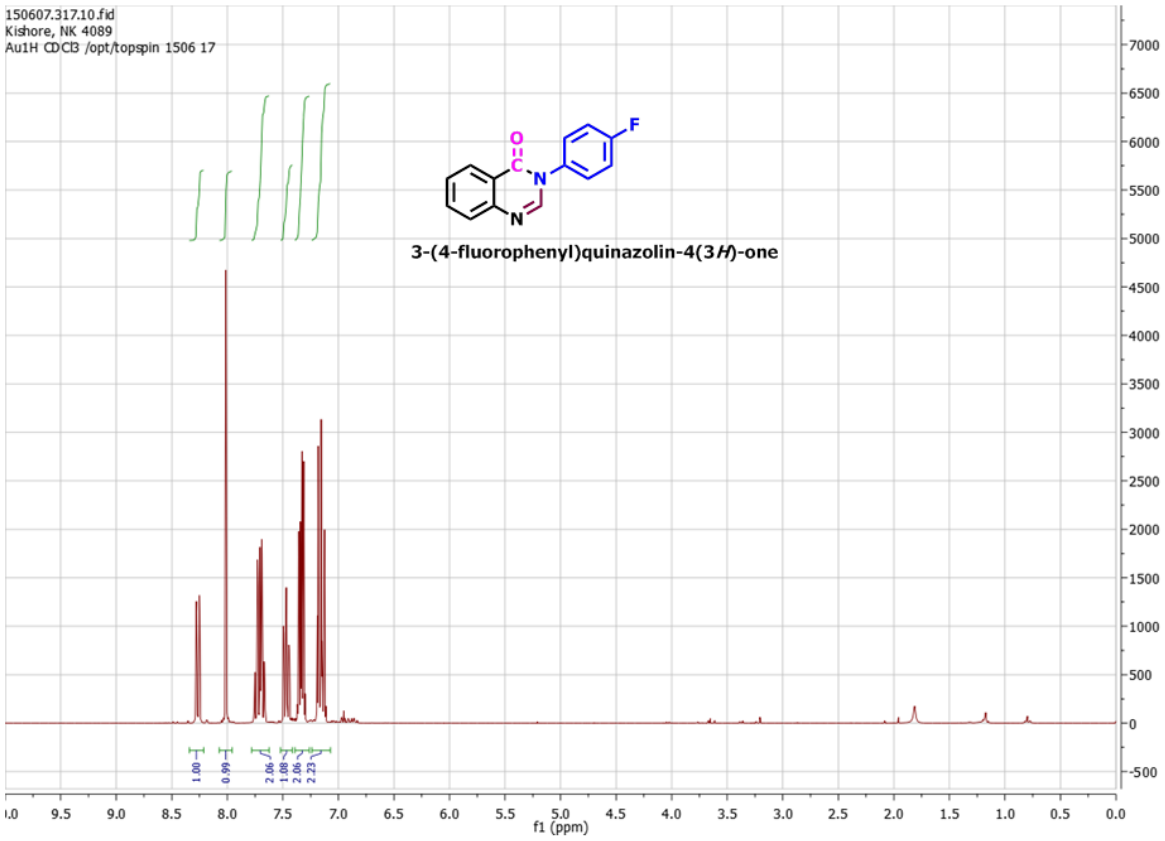

150402.f316.11.fid
Kishore/ NK 2087
C13CPD CDCl3 {C:\Bruker\TopSpin3.2PL6} 1504-16
160.79
147.90
146.09
137.49
134.61
129.67
129.14
127.68
127.61
127.20
127.02
122.39
77.46
77.04
76.61
3-phenylquinazolin-4(3H)-one
f1 (ppm)

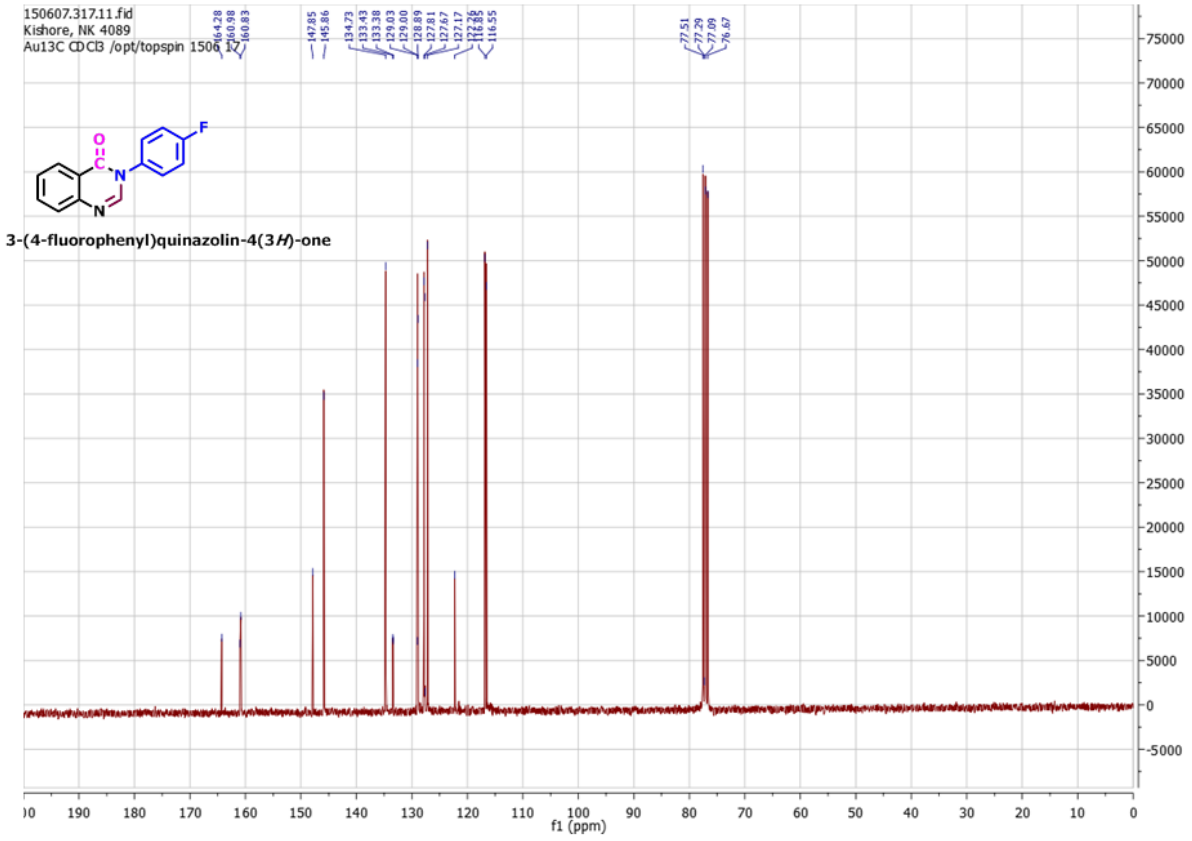

150607.319.11.fid
Kishore, NK 4085
Au13C CDCl3 /opt/topspin 1506 19
161.60
160.46
148.46
146.97
135.04
128.70
128.68
128.66
128.11
128.09
127.60
115.58
77.16 CDCl3
56.15
3-(4-methoxyphenyl)quinazolin-4(3H)-one
f1 (ppm)

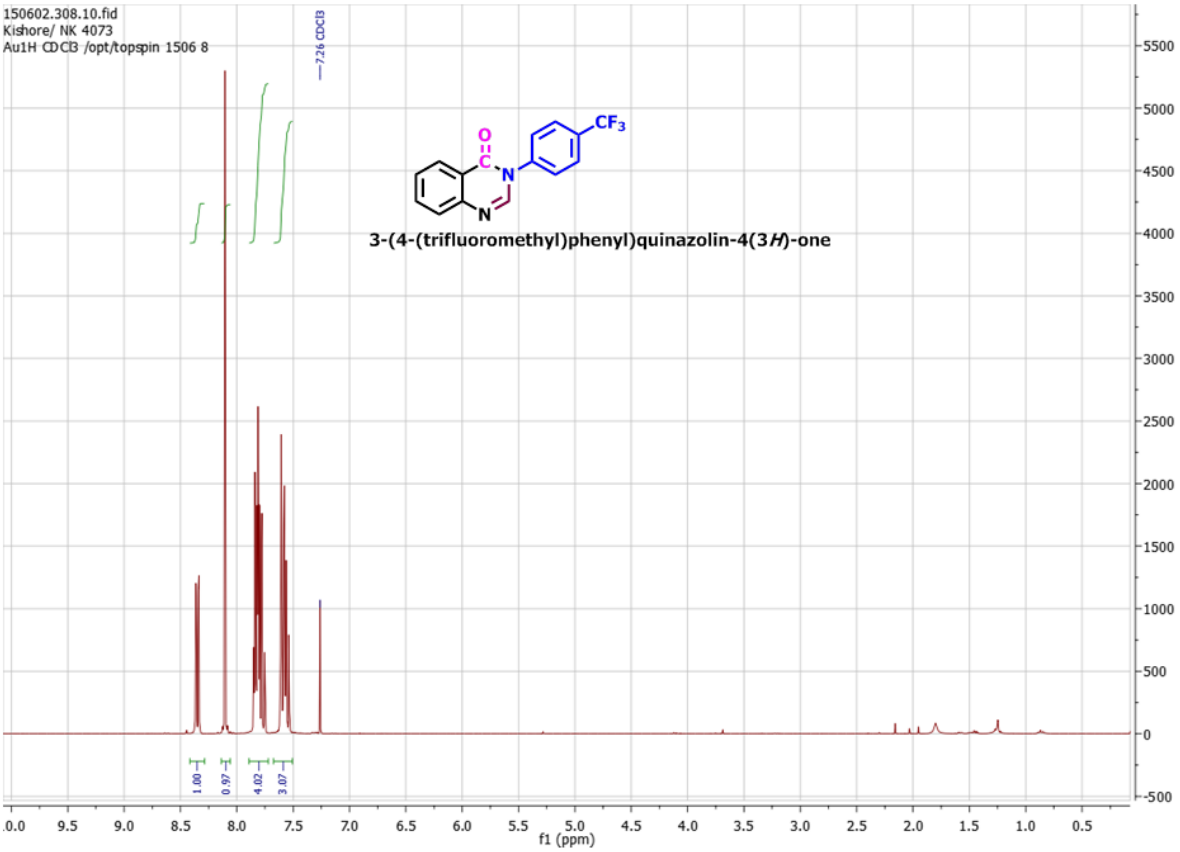

150607.319.10.fid
Kishore, NK 4085
Au1H CDCl3 /opt/topspin 1506 19
7.26 CDCl3
0.99
0.88
1.96
1.01
1.96
1.97
3.00
3-(4-methoxyphenyl)quinazolin-4(3H)-one
f1 (ppm)

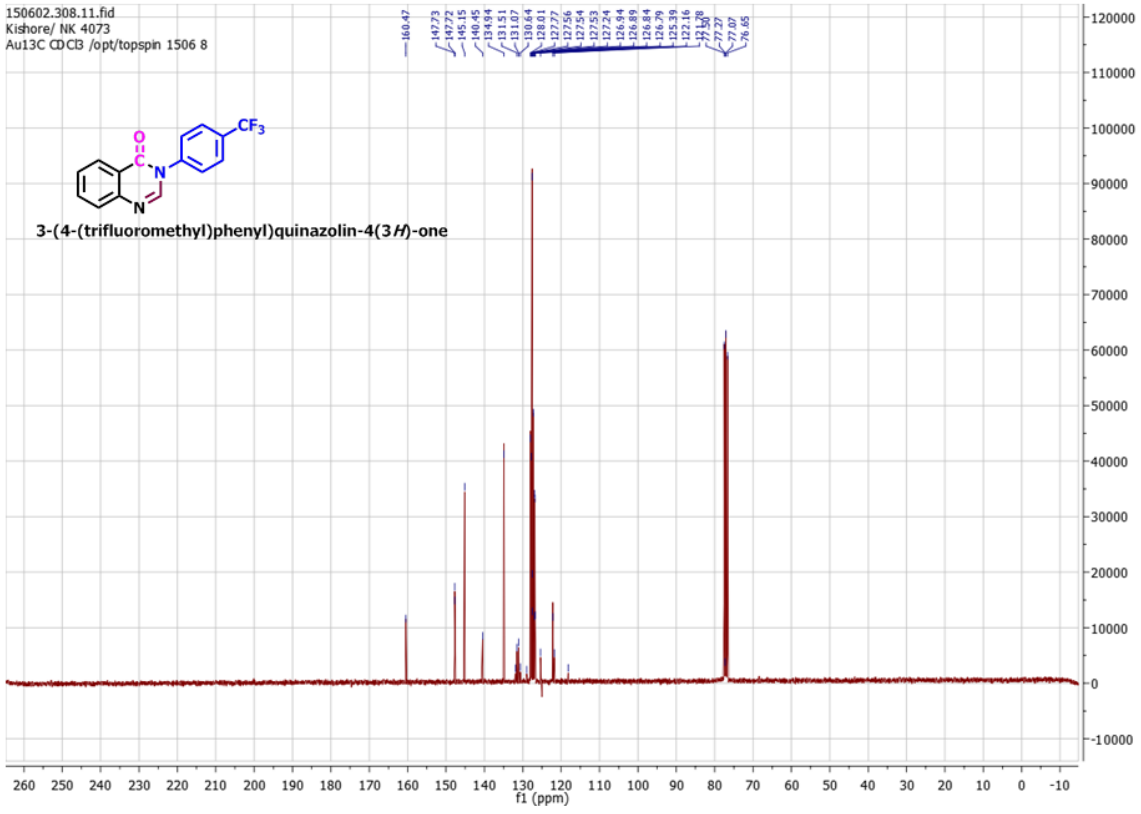

150610.408.11.fid
Kishore/ NK 4086
Au1H CDCl3 /opt/topspin 1506 8
7.26 CDCl3
3-(4-(methylthio)phenyl)quinazolin-4(3H)-one
1.00
0.97
2.03
1.07
2.01
2.11
3.09
f1 (ppm)

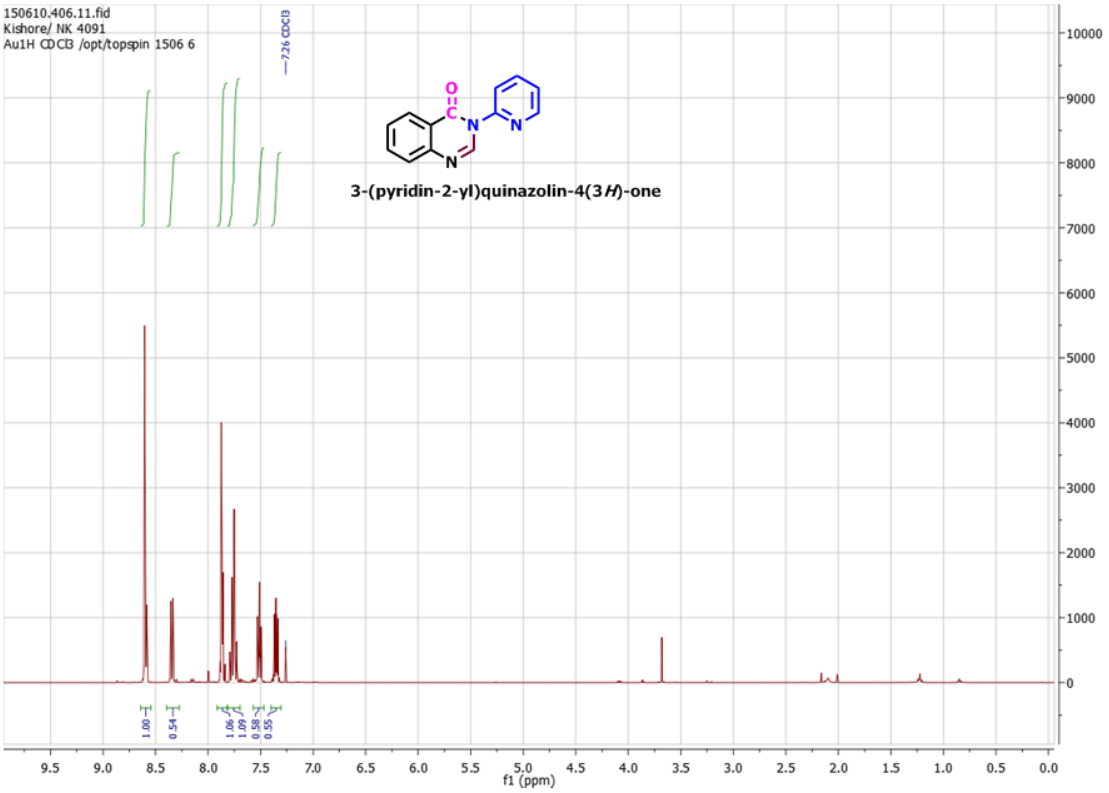

150610.408.10.fid
Kishore/ NK 4086
Au13C CDCl3 /opt/topspin 1506 8
161.09
159.95
147.96
146.46
134.54
130.20
128.94
128.17
127.61
127.59
127.18
122.40
119.74
114.87
114.34
77.40
77.29
77.08
76.76
55.64
f1 (ppm)

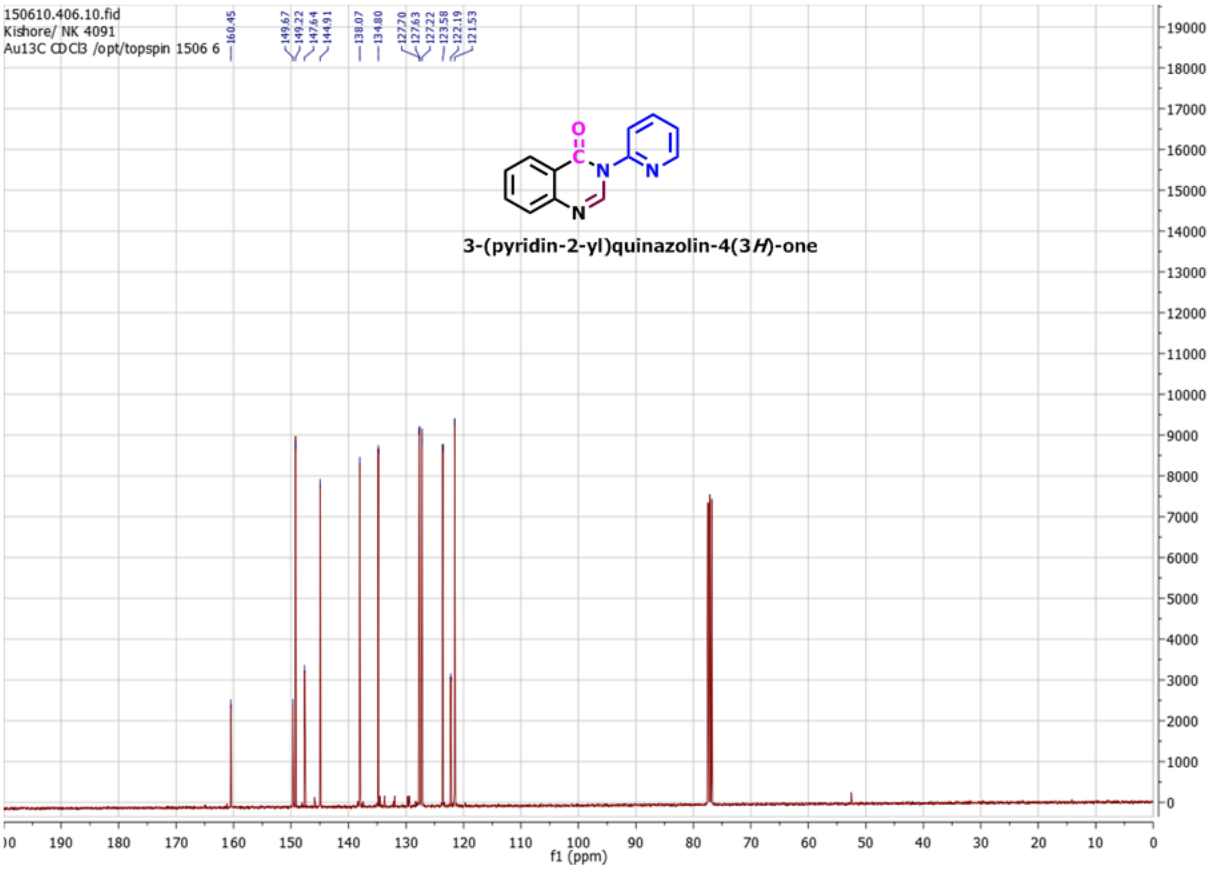

150607.317.10.fid
Kishore, NK 4089
Au1H CDCl3 /opt/topspin 1506 17
3-(4-fluorophenyl)quinazolin-4(3H)-one
f1 (ppm)

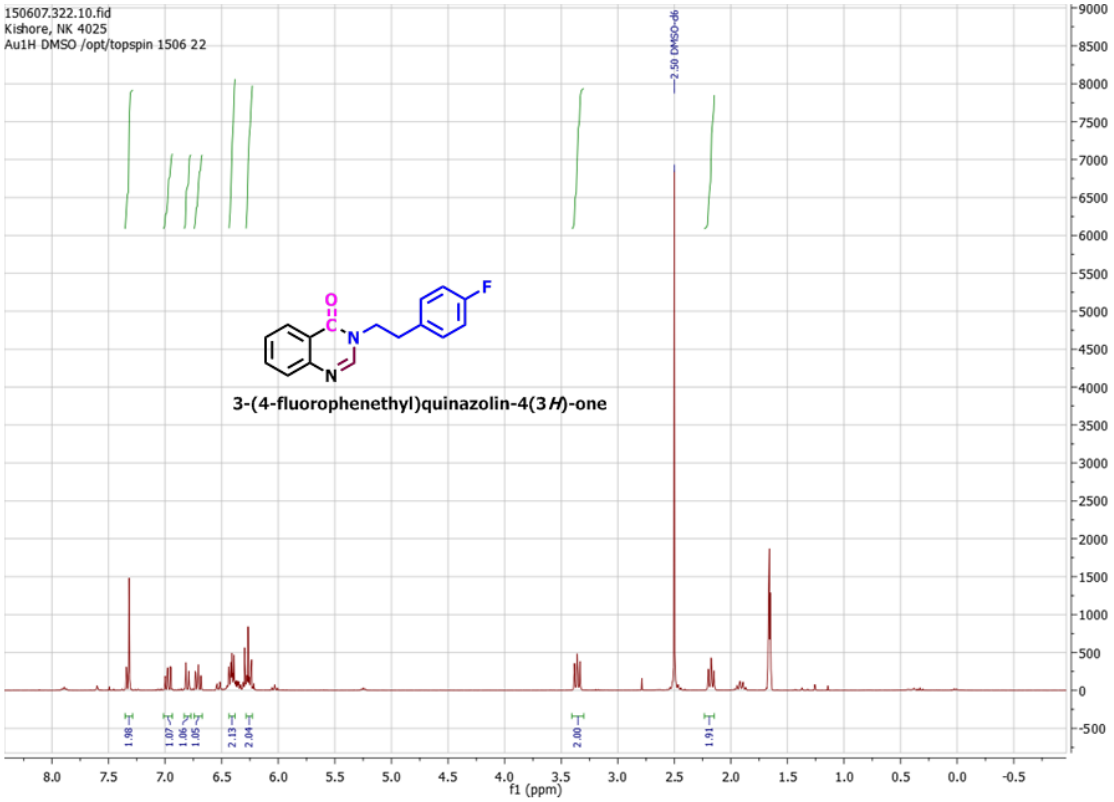

150607.317.11.fid
Kishore, NK 4089
Au13C CDCl3 /opt/topspin 1506 17
3-(4-fluorophenyl)quinazolin-4(3H)-one
f1 (ppm)

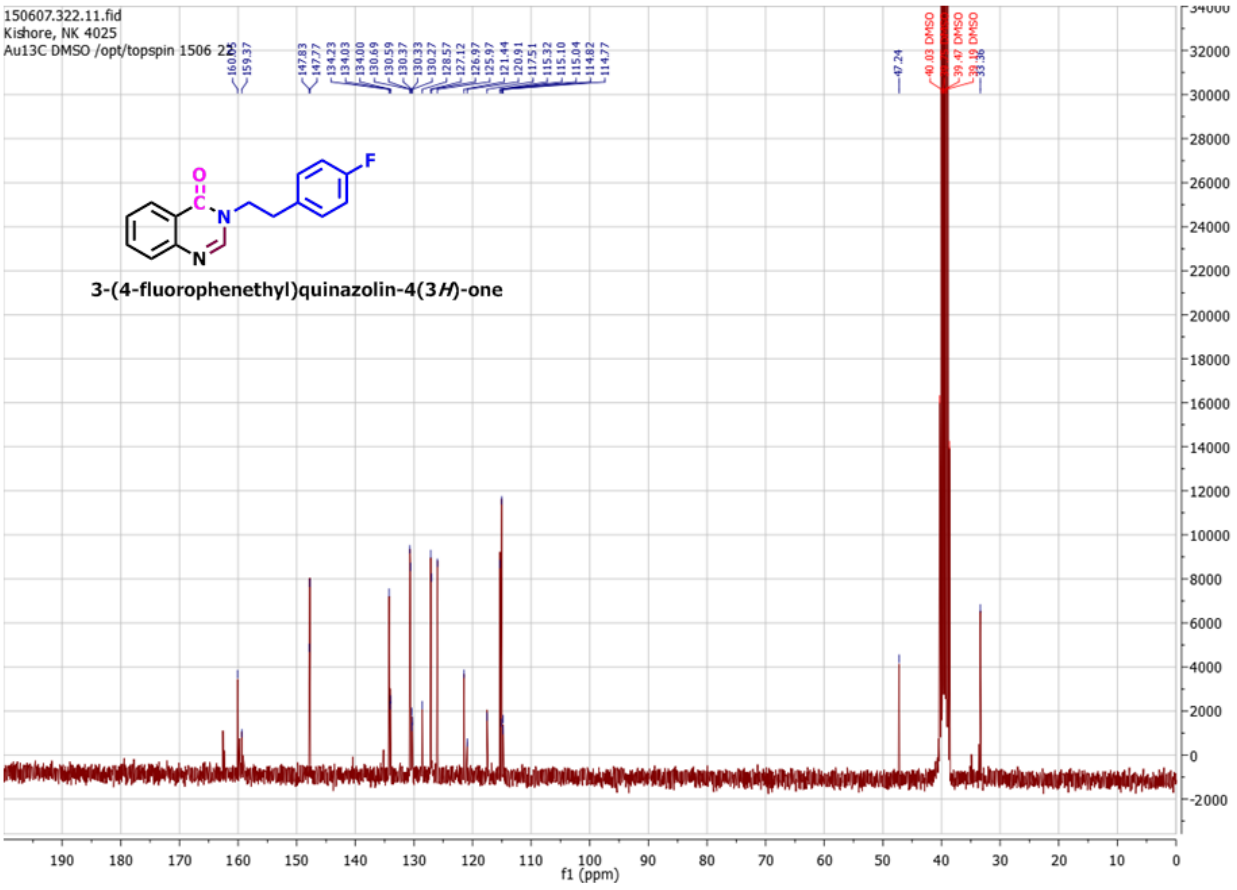

150602.308.10.fid
Kishore/ NK 4073
Au1H CDCl3 /opt/topspin 1506 8
7.26 CDCl3
3-(4-(trifluoromethyl)phenyl)quinazolin-4(3H)-one
1.00
0.97
4.02
3.07
f1 (ppm)

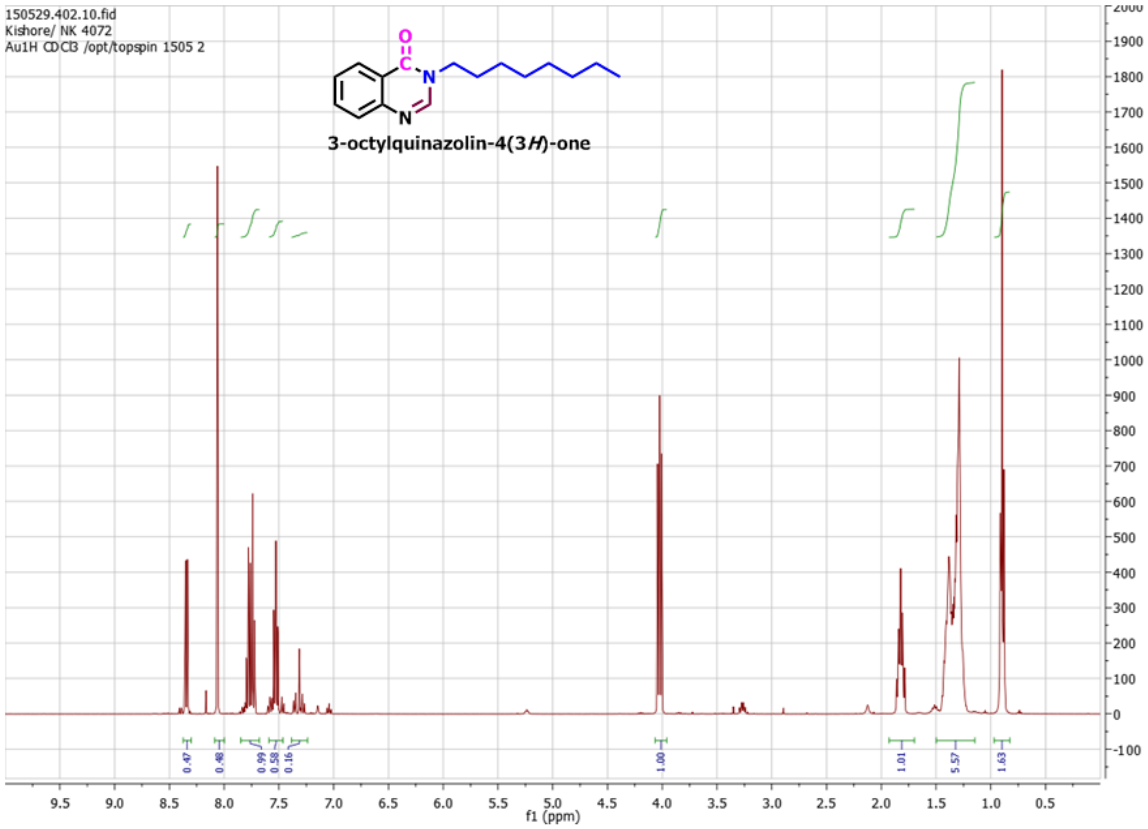

150602.308.11.fid
Kishore/ NK 4073
Au13C CDCl3 /opt/topspin 1506 8
160.47
147.73
147.72
145.15
140.45
134.94
131.51
131.07
130.64
128.01
127.77
127.56
127.54
127.53
127.24
126.94
126.89
126.84
126.79
125.39
122.16
77.27
77.07
76.85
3-(4-(trifluoromethyl)phenyl)quinazolin-4(3H)-one
f1 (ppm)

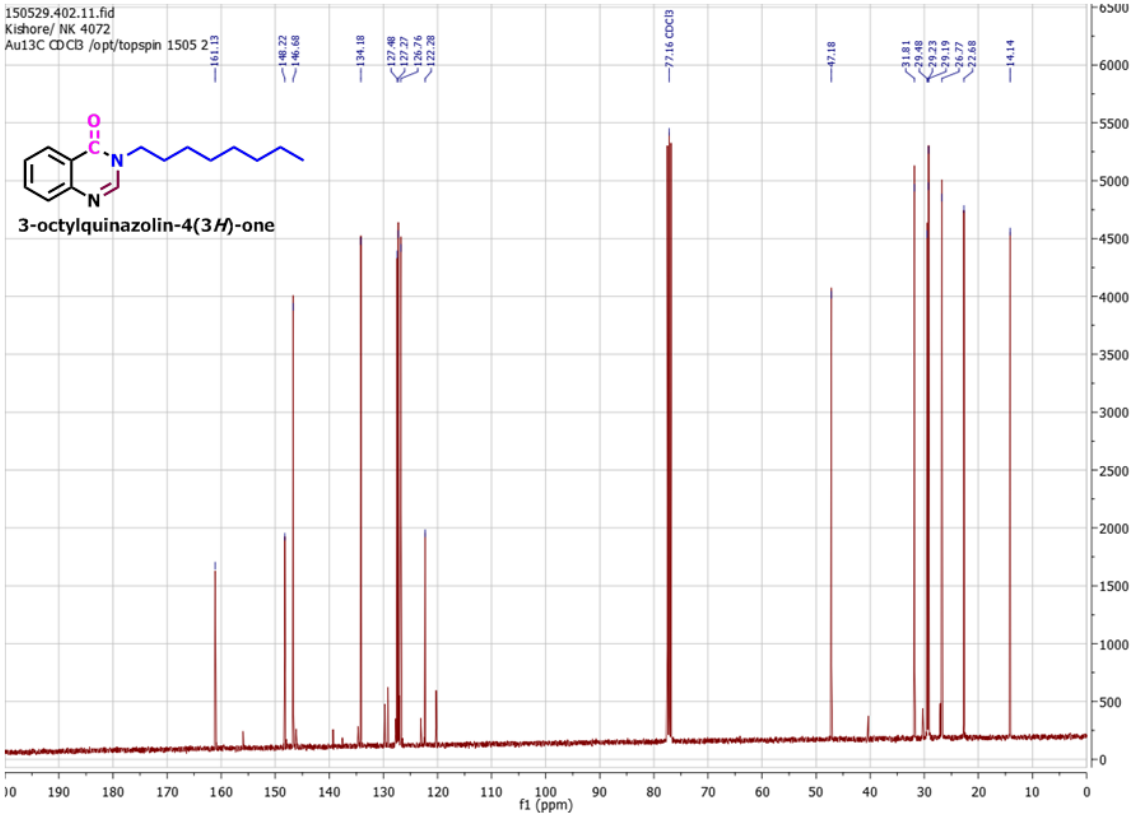

150610.406.11.fid
Kishore/ NK 4091
Au1H CDCl3 /opt/topspin 1506 6
7.26 CDCl3
3-(pyridin-2-yl)quinazolin-4(3H)-one
f1 (ppm)

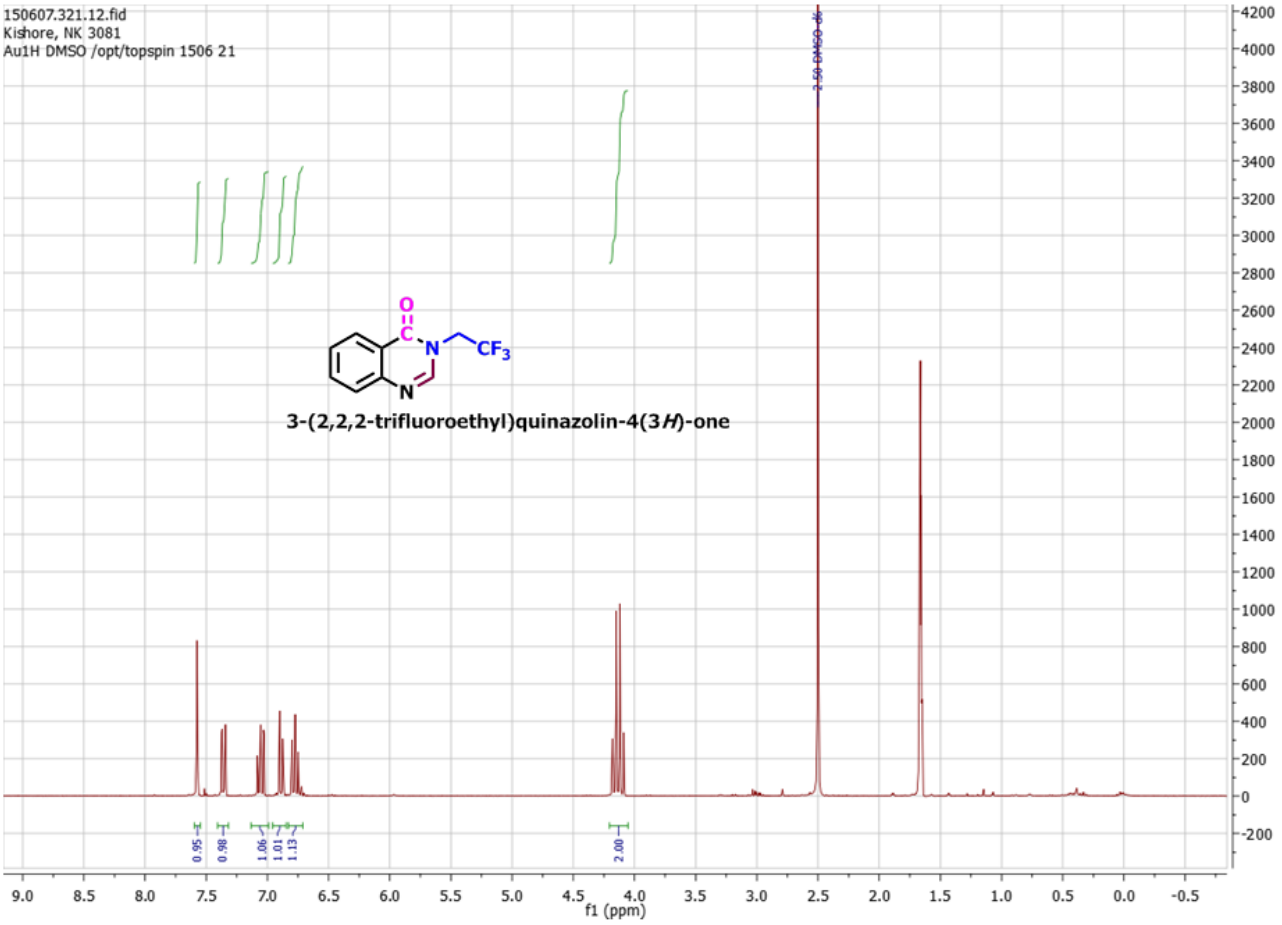

150610.406.10.fid
Kishore/ NK 4091
Au13C CDCl3 /opt/topspin 1506 6
160.45
149.67
149.22
147.64
144.91
138.07
134.80
127.70
127.63
127.22
123.58
122.19
121.53
3-(pyridin-2-yl)quinazolin-4(3H)-one
f1 (ppm)

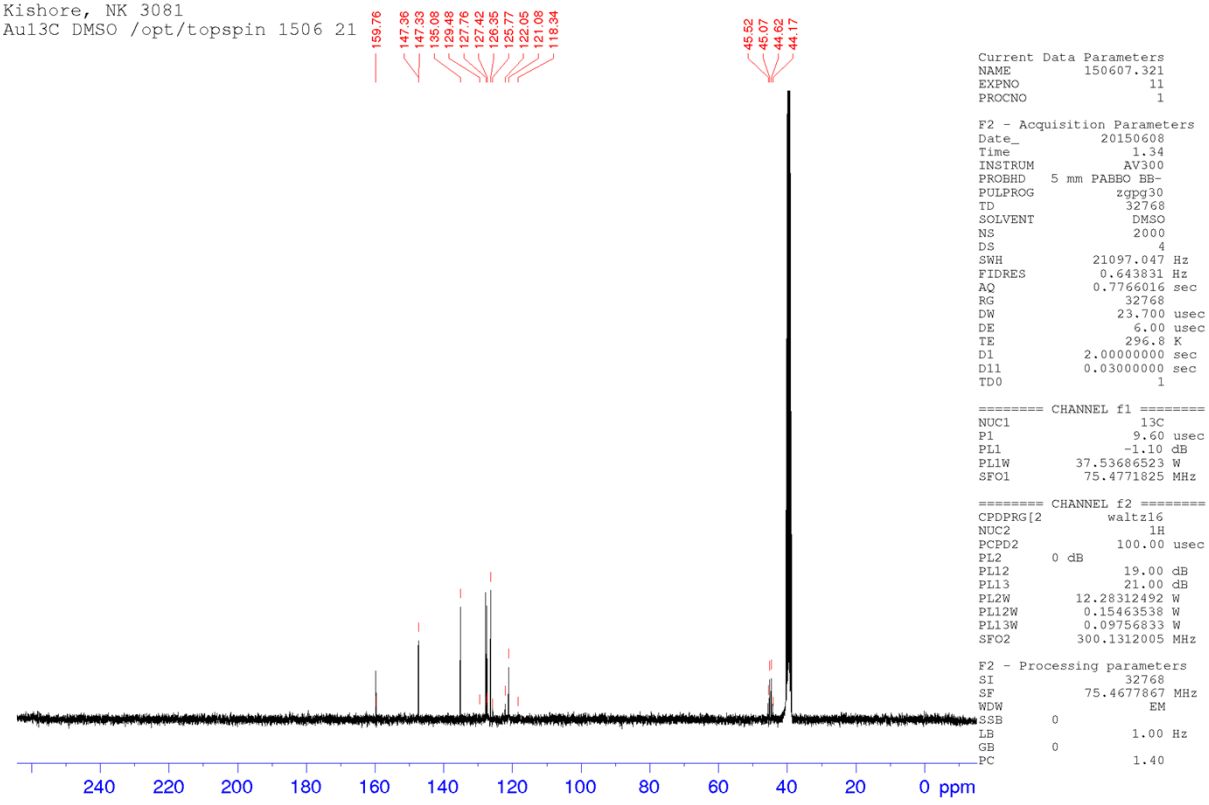

150607.322.10.fid
Kishore, NK 4025
Au1H DMSO /opt/topspin 1506 22
2.50 DMSO-d6
3-(4-fluorophenethyl)quinazolin-4(3H)-one
f1 (ppm)


150607.322.11.fid
Kishore, NK 4025
Au13C DMSO /opt/topspin 1506 22
40.03 DMSO
39.47 DMSO
38.90 DMSO
3-(4-fluorophenethyl)quinazolin-4(3H)-one
f1 (ppm)

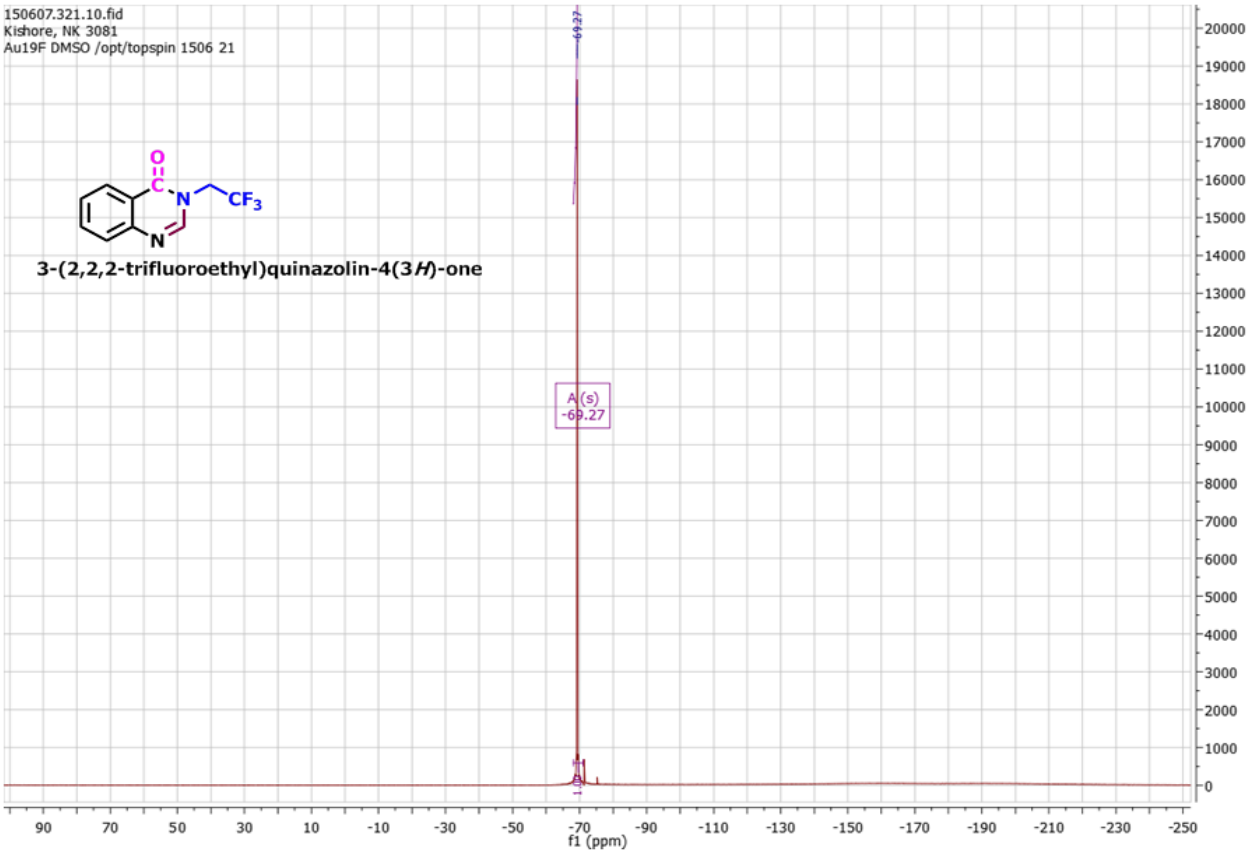

150529.402.10.fid
Kishore/ NK 4072
Au1H CDCl3 /opt/topspin 1505 2
3-octylquinazolin-4(3H)-one
f1 (ppm)

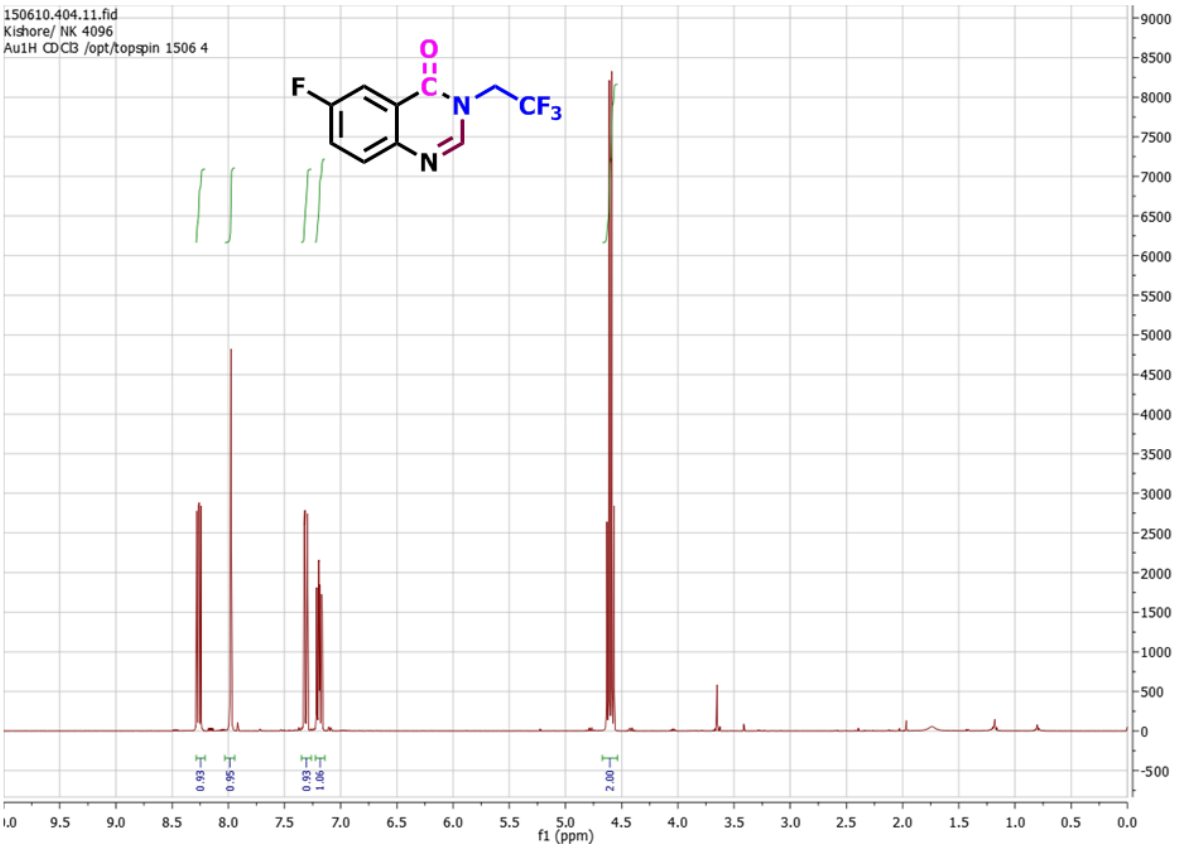

150529.402.11.fid
Kishore/ NK 4072
Au13C CDCl3 /opt/topspin 1505 2
161.13
148.22
146.68
134.18
127.48
127.27
126.76
122.28
77.16 CDCl3
47.18
31.81
29.48
29.23
29.19
26.77
22.68
14.14
3-octylquinazolin-4(3H)-one
f1 (ppm)



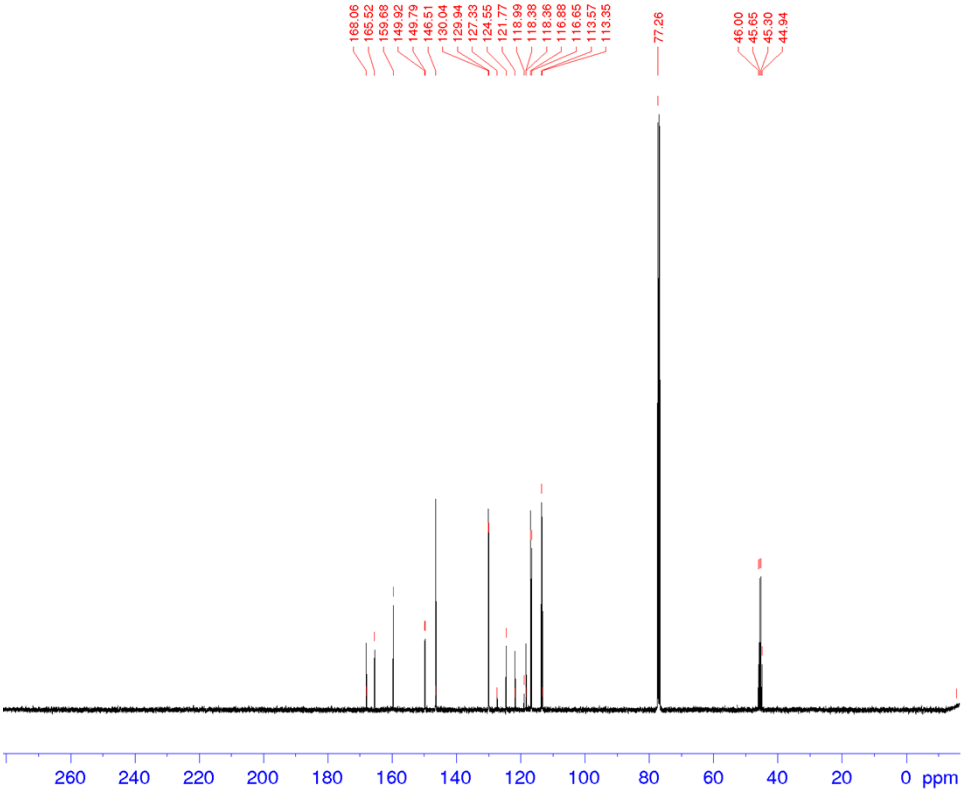



```
Current Data Parameters
NAME                  150607.321
EXPNO                         11
PROCNO                         1

F2 - Acquisition Parameters
Date_                  20150608
Time                       1.34
INSTRUM                   AV300
PROBHD    5 mm PABBO BB-
PULPROG                 zgpg30
TD                       32768
SOLVENT                   DMSO
NS                        2000
DS                           4
SWH                  21097.047 Hz
FIDRES                0.643831 Hz
AQ                    0.7766016 sec
RG                       32768
DW                      23.700 usec
DE                       6.00 usec
TE                      296.8 K
D1                   2.00000000 sec
D11                  0.03000000 sec
TD0                            1

======== CHANNEL f1 ========
NUC1                        13C
P1                         9.60 usec
PL1                       -1.10 dB
PL1W                37.53686523 W
SFO1                 75.4771825 MHz

======== CHANNEL f2 ========
CPDPRG[2                waltz16
NUC2                        1H
PCPD2                    100.00 usec
PL2             0 dB
PL12                      19.00 dB
PL13                      21.00 dB
PL2W                12.28312492 W
PL12W                0.15463538 W
PL13W                0.09756833 W
SFO2                300.1312005 MHz

F2 - Processing parameters
SI                           32768
SF                  75.4677867 MHz
WDW                             EM
SSB             0
LB                        1.00 Hz
GB              0
PC                        1.40
```

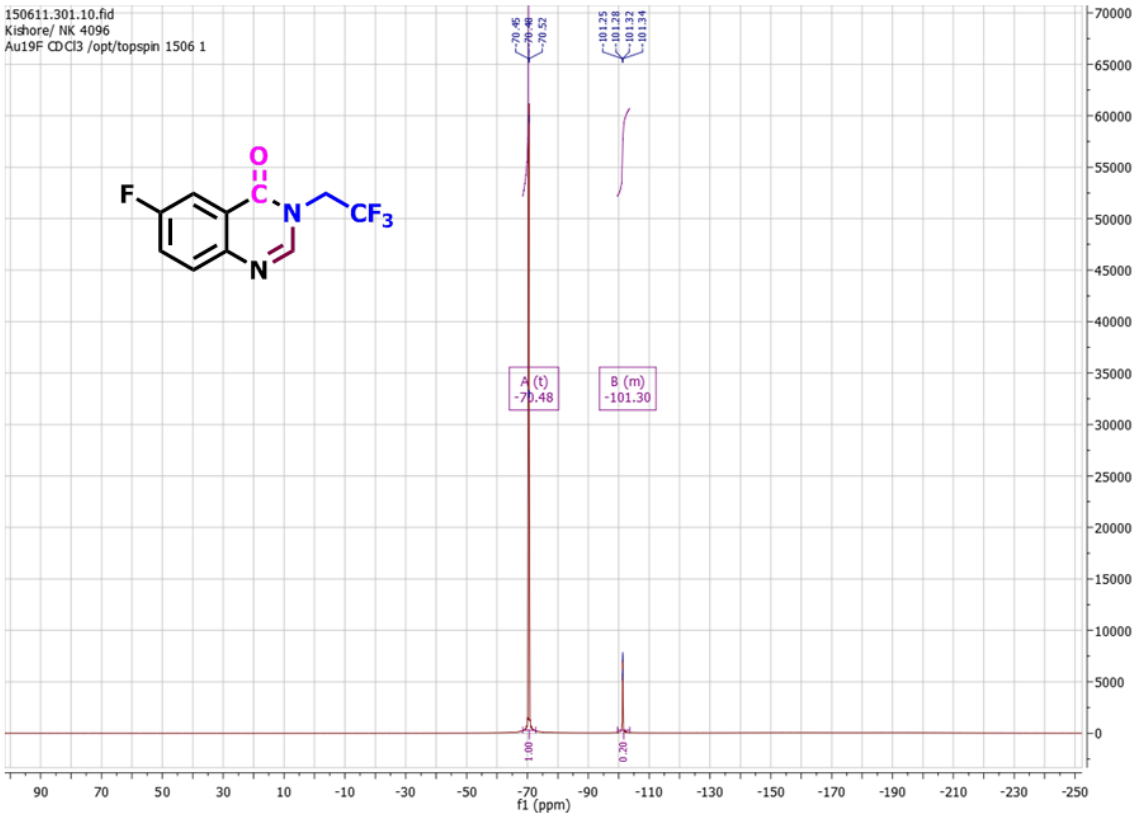

150607.321.10.fid
Kishore, NK 3081
Au19F DMSO /opt/topspin 1506 21
3-(2,2,2-trifluoroethyl)quinazolin-4(3H)-one
A (s)
-69.27
f1 (ppm)


150610.404.11.fid
Kishore/ NK 4096
Au1H CDCl3 /opt/topspin 1506 4
0.93
0.95
0.93
1.06
2.00
f1 (ppm)

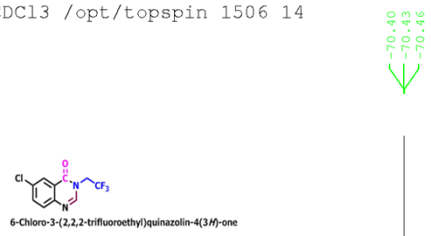
Kishore/ NK 4096
Au13C CDCl3 /opt/topspin 1506 4



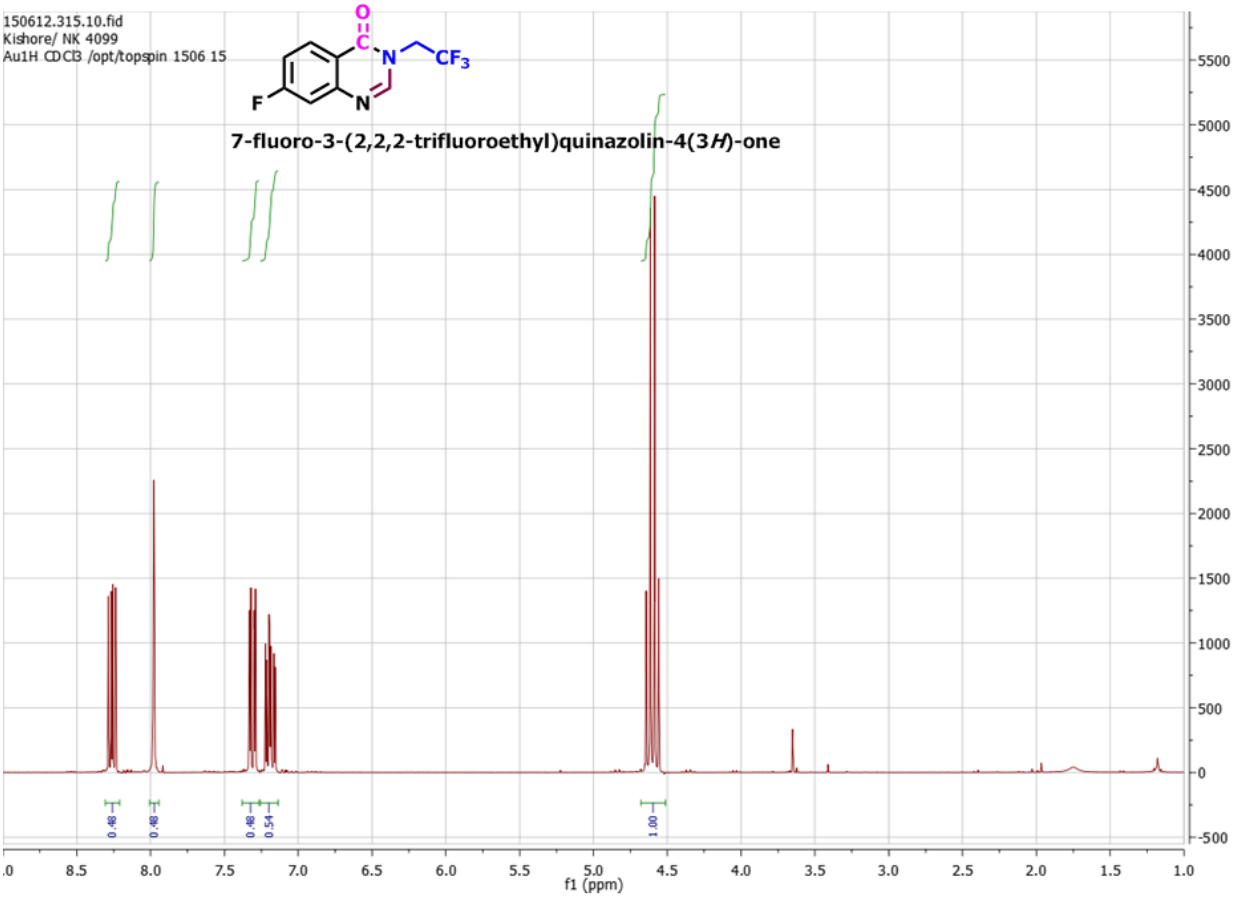

```
Current Data Parameters
NAME                  150610.404
EXPNO                         10
PROCNO                         1

F2 - Acquisition Parameters
Date_                  20150610
Time                      19.42
INSTRUM                   AV400
PROBHD    5 mm PABBO BB-
PULPROG                 zgpg30
TD                       65536
SOLVENT                  CDCl3
NS                        2000
DS                           4
SWH                  29940.119 Hz
FIDRES                0.456850 Hz
AQ                    1.0944512 sec
RG                         3251
DW                       16.700 usec
DE                        6.50 usec
TE                       297.0 K
D1                    1.70000005 sec
D11                   0.03000000 sec
TD0                            1

======== CHANNEL f1 ========
NUC1                         13C
P1                         10.00 usec
PL1                        -0.50 dB
PL1W                37.20265579 W
SFO1               100.6260690 MHz

======== CHANNEL f2 ========
CPDPRG[2                waltz16
NUC2                         1H
PCPD2                    100.00 usec
PL2                       -2.00 dB
PL12                      17.00 dB
PL13                      19.00 dB
PL2W                15.44655800 W
PL12W                0.19446065 W
PL13W                0.12269637 W
SFO2               400.1318000 MHz

F2 - Processing parameters
SI                         32768
SF                 100.6127690 MHz
WDW                           EM
SSB                0
LB                         1.00 Hz
GB                 0
PC                         1.00
```

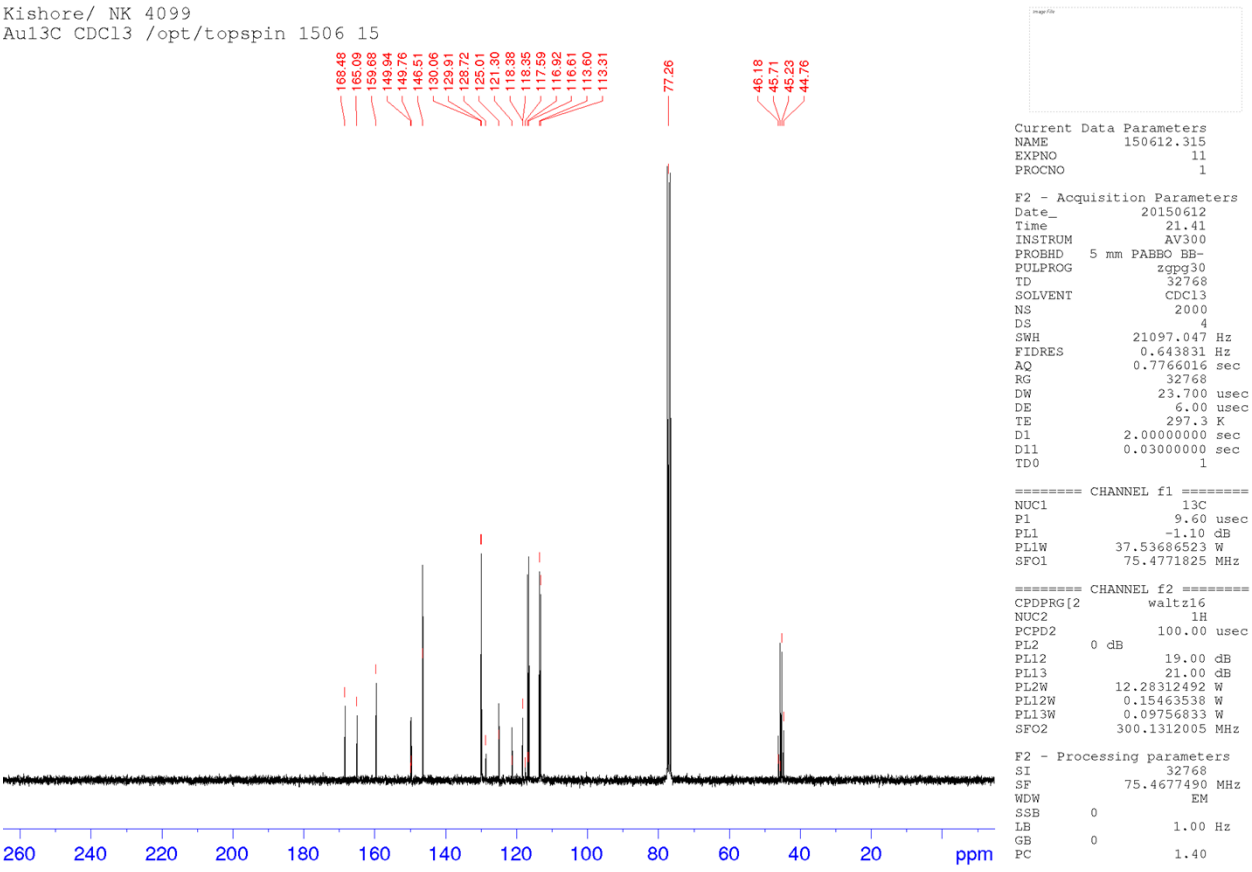


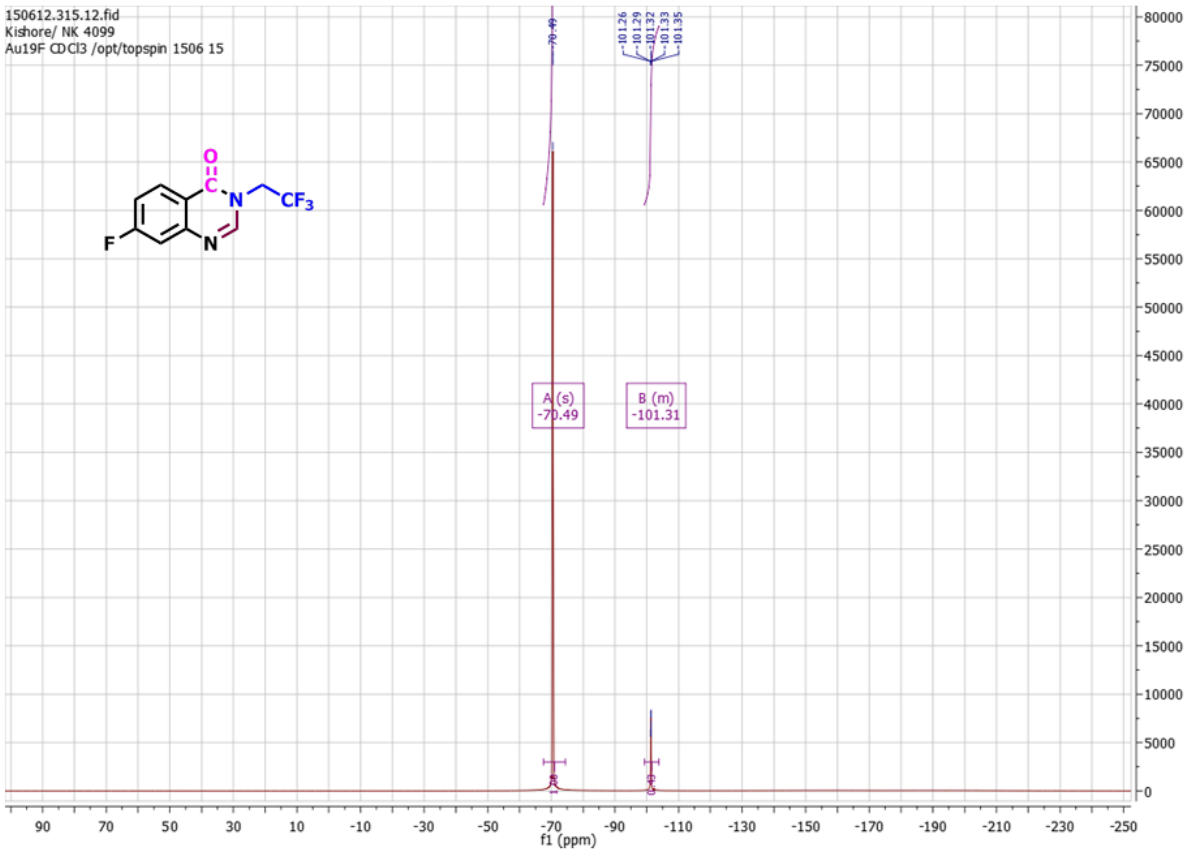
Kishore/ NK 4098-1
Au19F CDCl3 /opt/topspin 1506 14

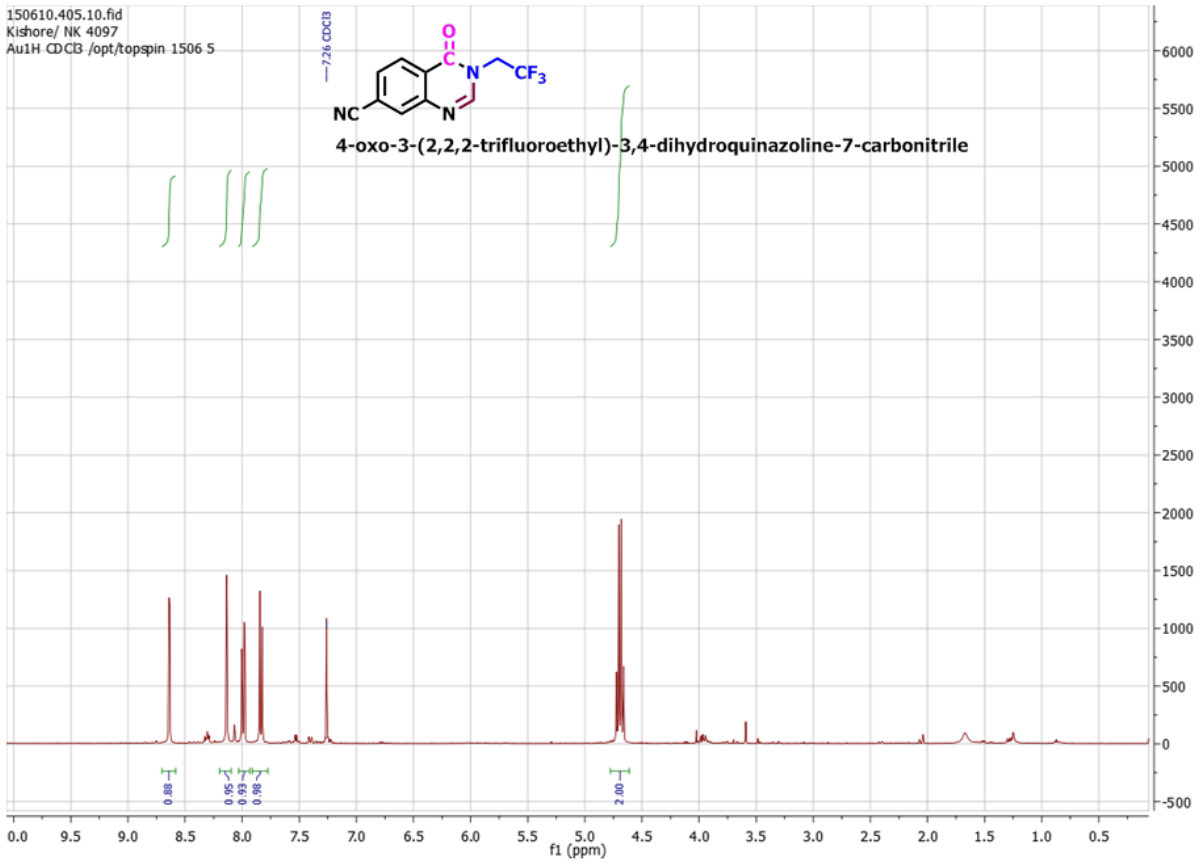



```
Current Data Parameters
NAME          150612.314
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20150612
Time              16.44
INSTRUM           AV300
PROBHD   5 mm PABBO BB-
PULPROG         zgflqn
TD                65536
SOLVENT           CDCl3
NS                  128
DS                    4
SWH          100000.000 Hz
FIDRES         1.525879 Hz
AQ             0.3276800 sec
RG                1625.5
DW                5.000 usec
DE               10.00 usec
TE               296.8 K
D1            2.00000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                 19F
P1                11.00 usec
PL1               -3.00 dB
PL1W        19.39594650 W
SFO1        282.3830019 MHz

F2 - Processing parameters
SI                65536
SF          282.4042500 MHz
WDW                  EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.00
```

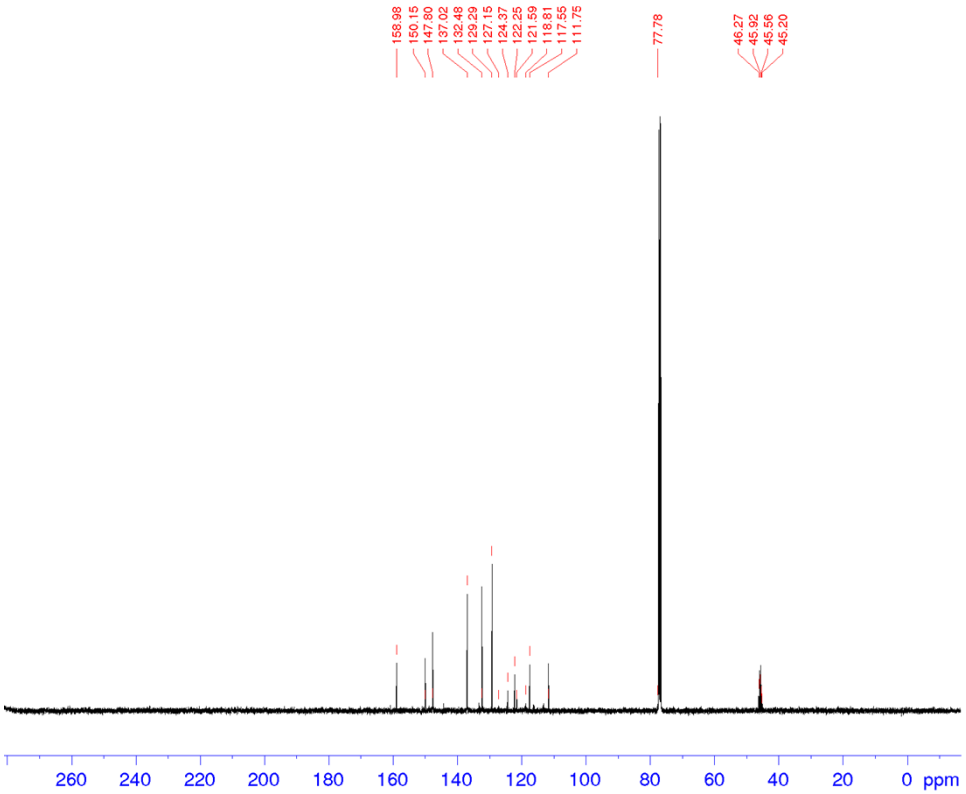



Kishore/ NK 4099
Au13C CDCl3 /opt/topspin 1506 15
168.48
165.09
159.68
149.94
149.76
146.51
130.06
129.91
128.72
125.01
121.30
118.38
118.35
117.59
116.92
116.61
113.60
113.31
77.26
46.18
45.71
45.23
44.76
260
240
220
200
180
160
140
120
100
80
60
40
20
ppm
Current Data Parameters
NAME 150612.315
EXPNO 11
PROCNO 1
F2 - Acquisition Parameters
Date_ 20150612
Time 21.41
INSTRUM AV300
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 32768
SOLVENT CDCl3
NS 2000
DS 4
SWH 21097.047 Hz
FIDRES 0.643831 Hz
AQ 0.7766016 sec
RG 32768
DW 23.700 usec
DE 6.00 usec
TE 297.3 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.60 usec
PL1 -1.10 dB
PL1W 37.53686523 W
SFO1 75.4771825 MHz
======== CHANNEL f2 ========
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 0 dB
PL12 19.00 dB
PL13 21.00 dB
PL2W 12.28312492 W
PL12W 0.15463538 W
PL13W 0.09756833 W
SFO2 300.1312005 MHz
F2 - Processing parameters
SI 32768
SF 75.4677490 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

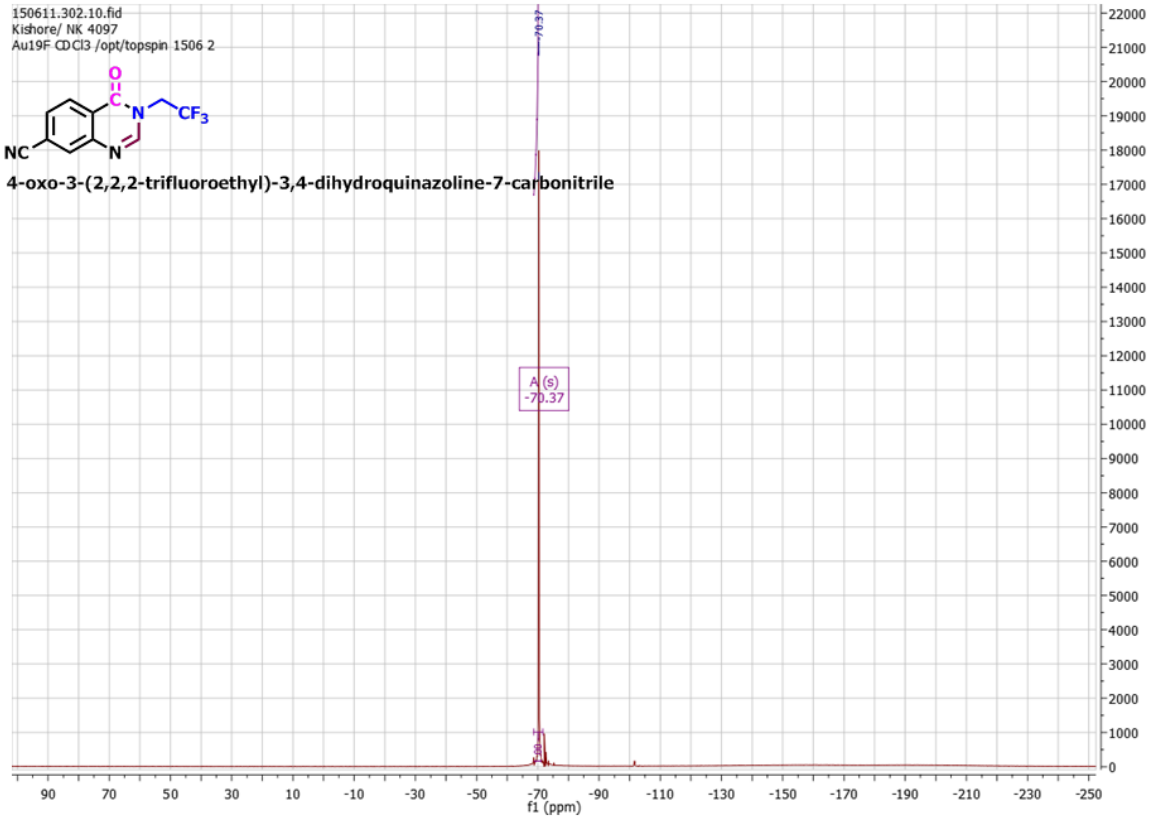

150612.315.12.fid
Kishore/ NK 4099
Au19F CDCl3 /opt/topspin 1506 15
-70.49
-101.26
-101.29
-101.32
-101.33
-101.35
O
C
N
CF3
F
N
A (s)
-70.49
B (m)
-101.31
80000
75000
70000
65000
60000
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
90
70
50
30
10
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
-230
-250
f1 (ppm)

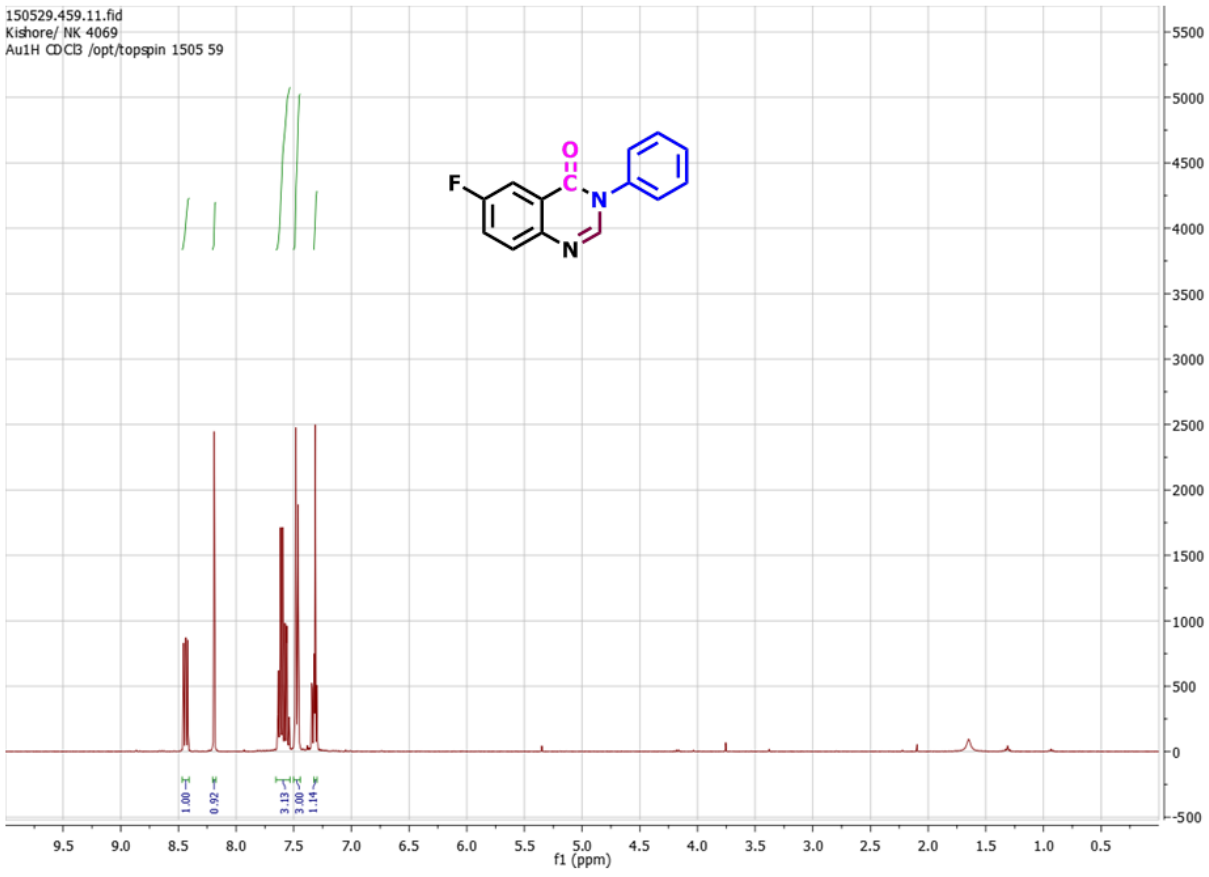


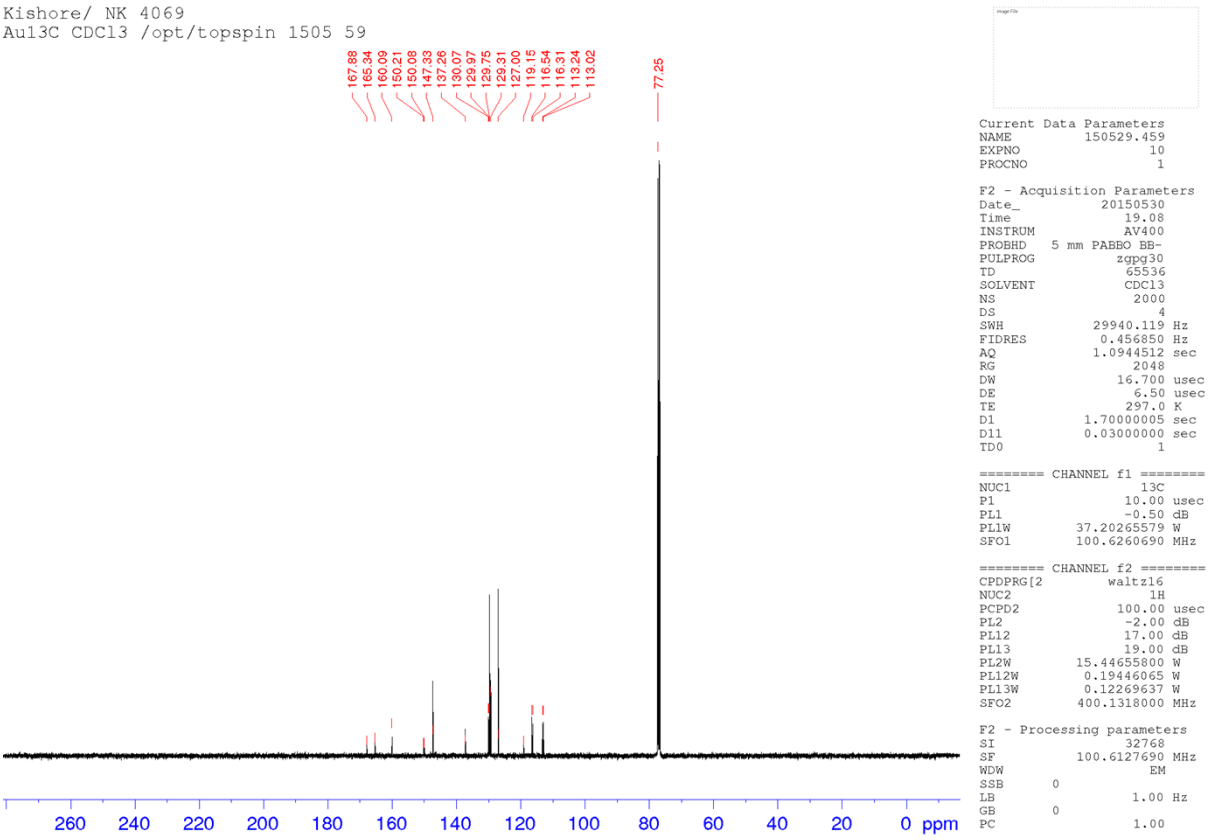
Kishore/ NK 4097
Au13C CDCl3 /opt/topspin 1506 5

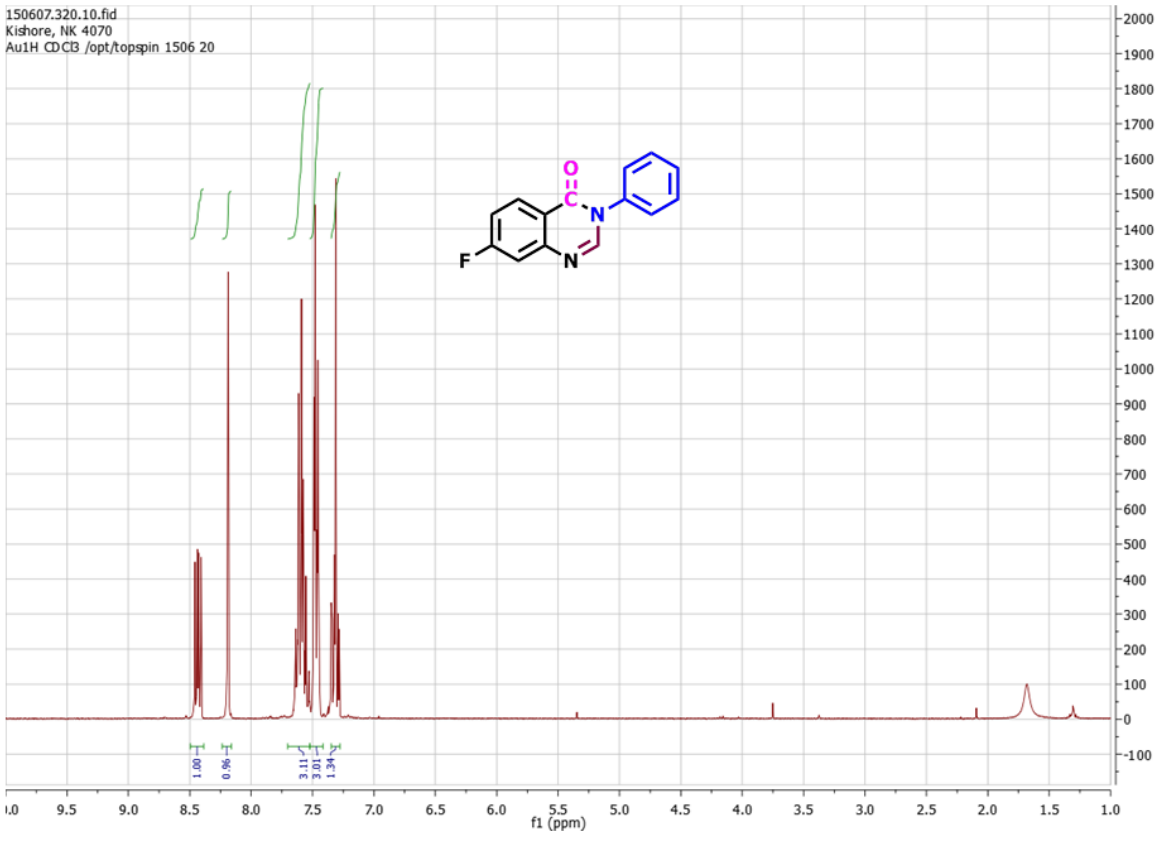


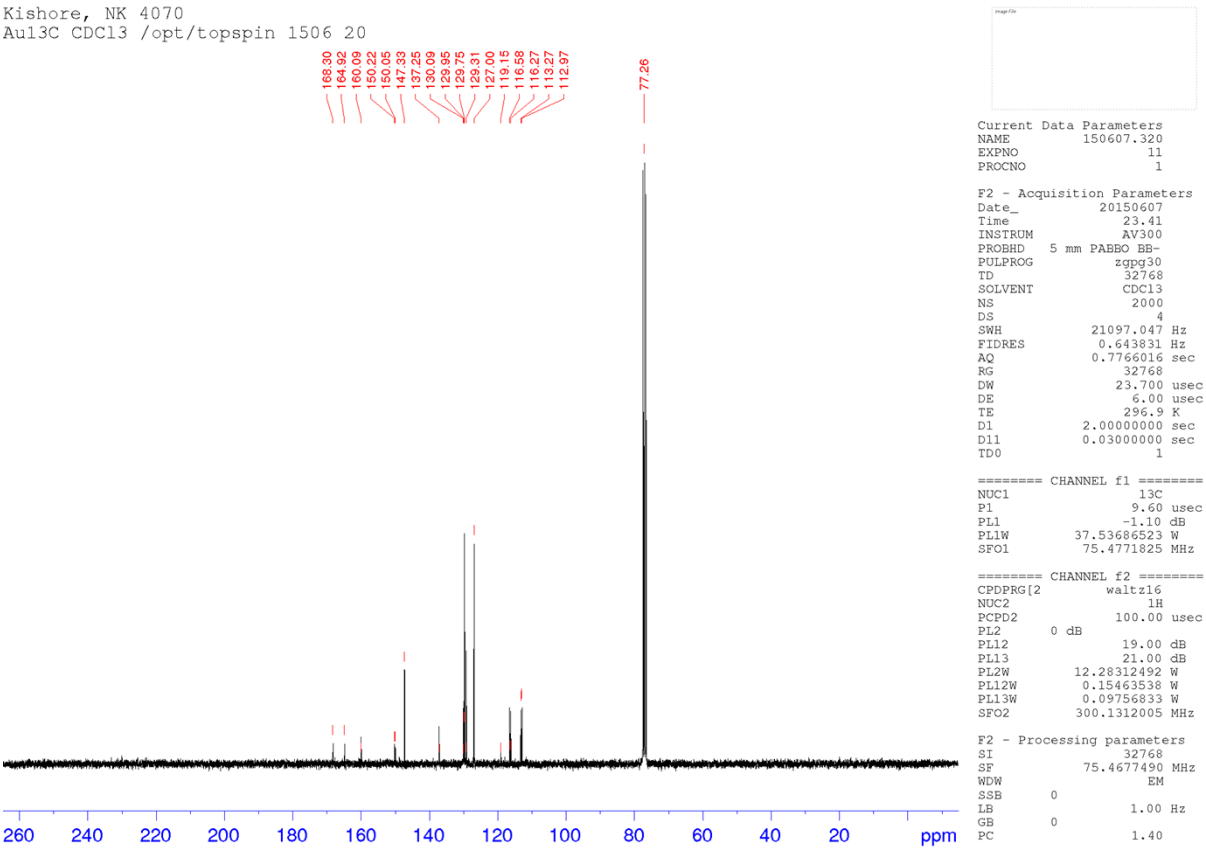

```
Current Data Parameters
NAME                 150610.405
EXPNO                        11
PROCNO                        1

F2 - Acquisition Parameters
Date_                 20150610
Time                     21.32
INSTRUM                  AV400
PROBHD     5 mm PABBO BB-
PULPROG                zgpg30
TD                      65536
SOLVENT                 CDCl3
NS                       2000
DS                          4
SWH                 29940.119 Hz
FIDRES                0.456850 Hz
AQ                    1.0944512 sec
RG                       2896.3
DW                       16.700 usec
DE                        6.50 usec
TE                       297.0 K
D1                    1.70000005 sec
D11                   0.03000000 sec
TD0                           1

======== CHANNEL f1 ========
NUC1                        13C
P1                        10.00 usec
PL1                       -0.50 dB
PL1W                37.20265579 W
SFO1                100.6260690 MHz

======== CHANNEL f2 ========
CPDPRG[2                waltz16
NUC2                        1H
PCPD2                    100.00 usec
PL2                       -2.00 dB
PL12                      17.00 dB
PL13                      19.00 dB
PL2W                15.44655800 W
PL12W                0.19446065 W
PL13W                0.12269637 W
SFO2                400.1318000 MHz

F2 - Processing parameters
SI                        32768
SF                  100.6127690 MHz
WDW                          EM
SSB                 0
LB                        1.00 Hz
GB                  0
PC                        1.00
```

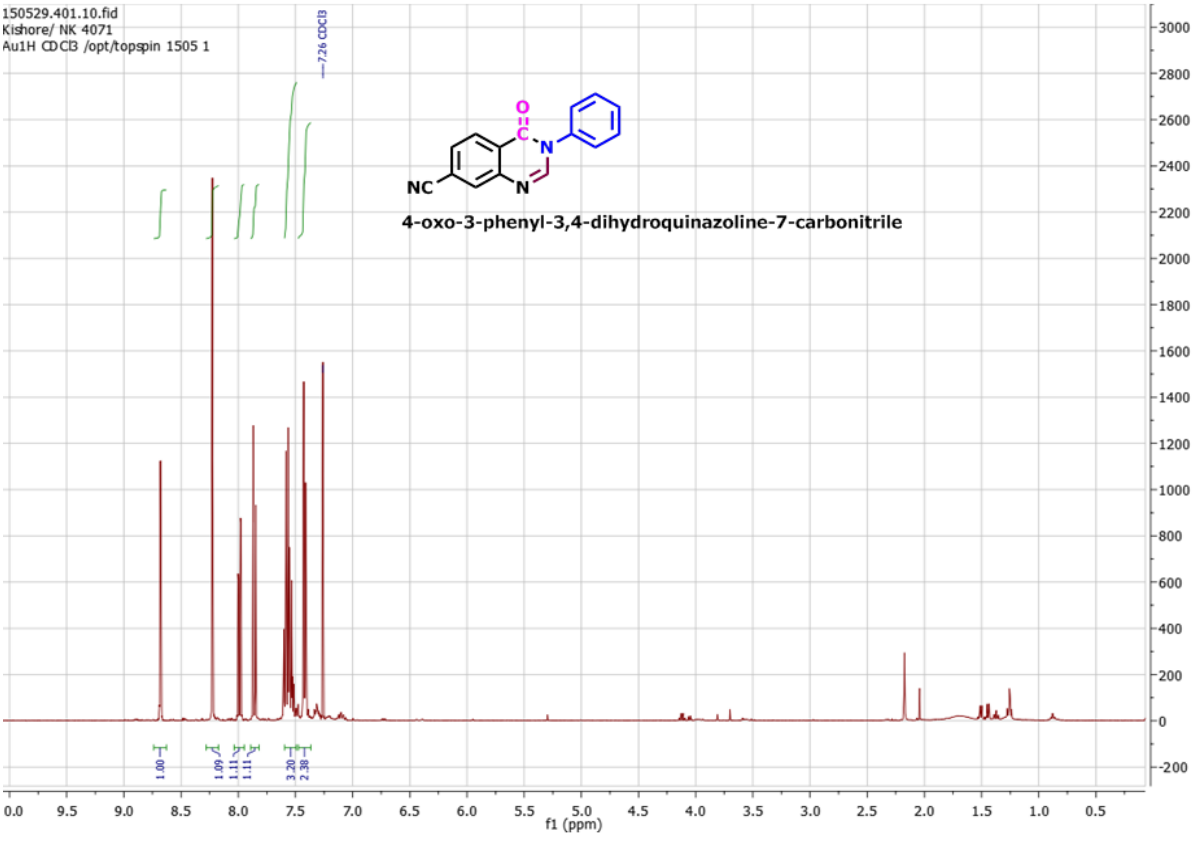

150611.302.10.fid
Kishore/ NK 4097
Au19F CDCl3 /opt/topspin 1506 2
4-oxo-3-(2,2,2-trifluoroethyl)-3,4-dihydroquinazoline-7-carbonitrile
A (s)
-70.37
f1 (ppm)

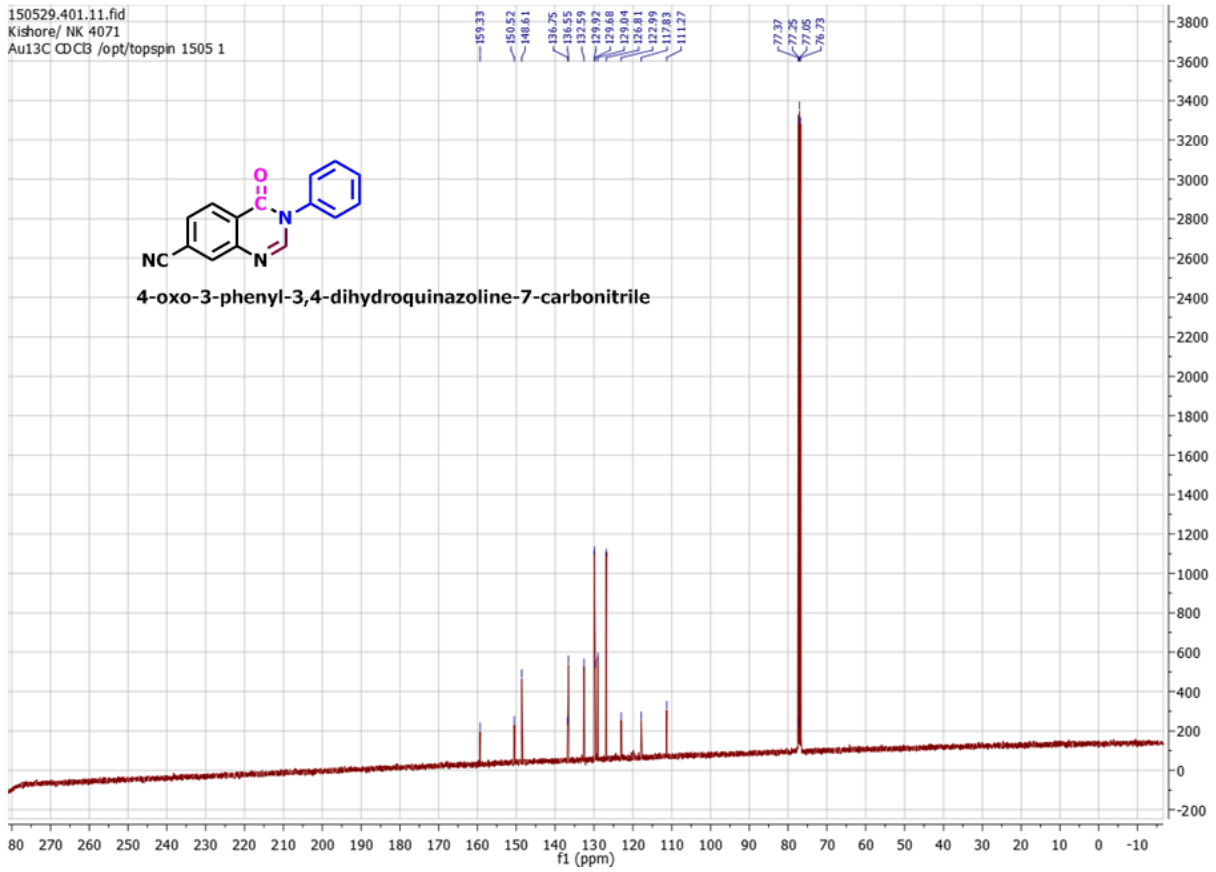

150529.459.11.fid
Kishore/ NK 4069
Au1H CDCl3 /opt/topspin 1505 59
1.00
0.92
3.13
3.00
1.14
f1 (ppm)

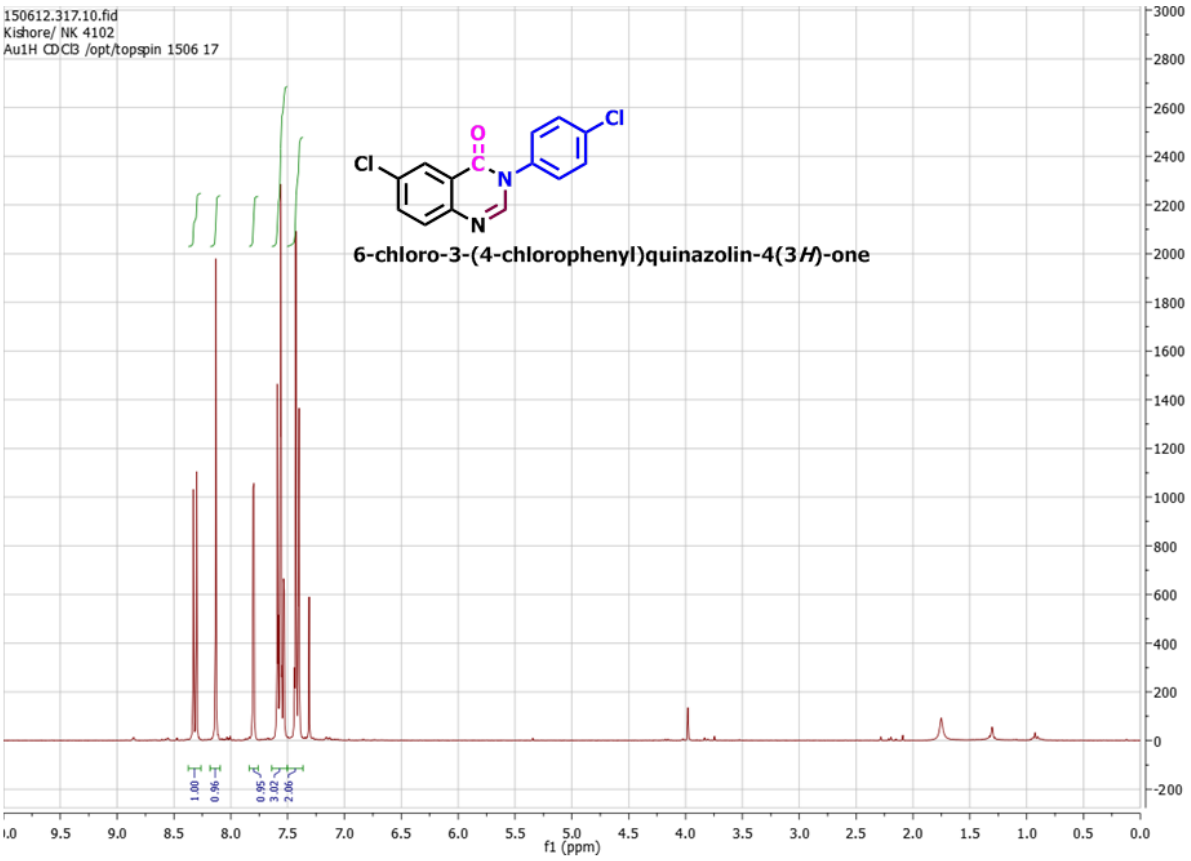

Kishore/ NK 4069
Au13C CDCl3 /opt/topspin 1505 59
167.88
165.34
160.09
150.21
150.08
147.33
137.26
130.07
129.97
129.75
129.31
127.00
119.15
116.54
116.31
113.24
113.02
77.25
260 240 220 200 180 160 140 120 100 80 60 40 20 0 ppm
Current Data Parameters
NAME 150529.459
EXPNO 10
PROCNO 1
F2 - Acquisition Parameters
Date_ 20150530
Time 19.08
INSTRUM AV400
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 2000
DS 4
SWH 29940.119 Hz
FIDRES 0.456850 Hz
AQ 1.0944512 sec
RG 2048
DW 16.700 usec
DE 6.50 usec
TE 297.0 K
D1 1.70000005 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 10.00 usec
PL1 -0.50 dB
PL1W 37.20265579 W
SFO1 100.6260690 MHz
======== CHANNEL f2 ========
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 -2.00 dB
PL12 17.00 dB
PL13 19.00 dB
PL2W 15.44655800 W
PL12W 0.19446065 W
PL13W 0.12269637 W
SFO2 400.1318000 MHz
F2 - Processing parameters
SI 32768
SF 100.6127690 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.00

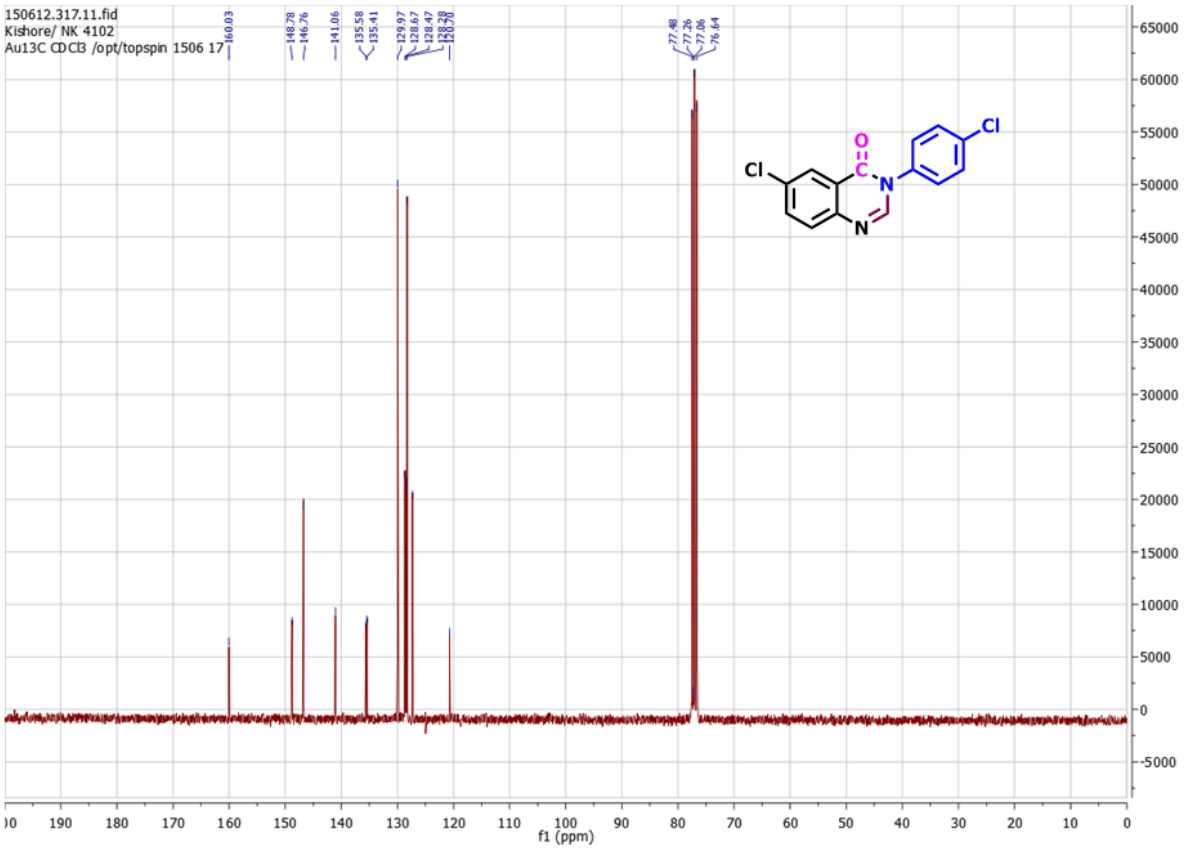

150607.320.10.fid
Kishore, NK 4070
Au1H CDCl3 /opt/topspin 1506 20
O
C
N
F
N
1.00
0.96
3.11
3.01
1.34
f1 (ppm)

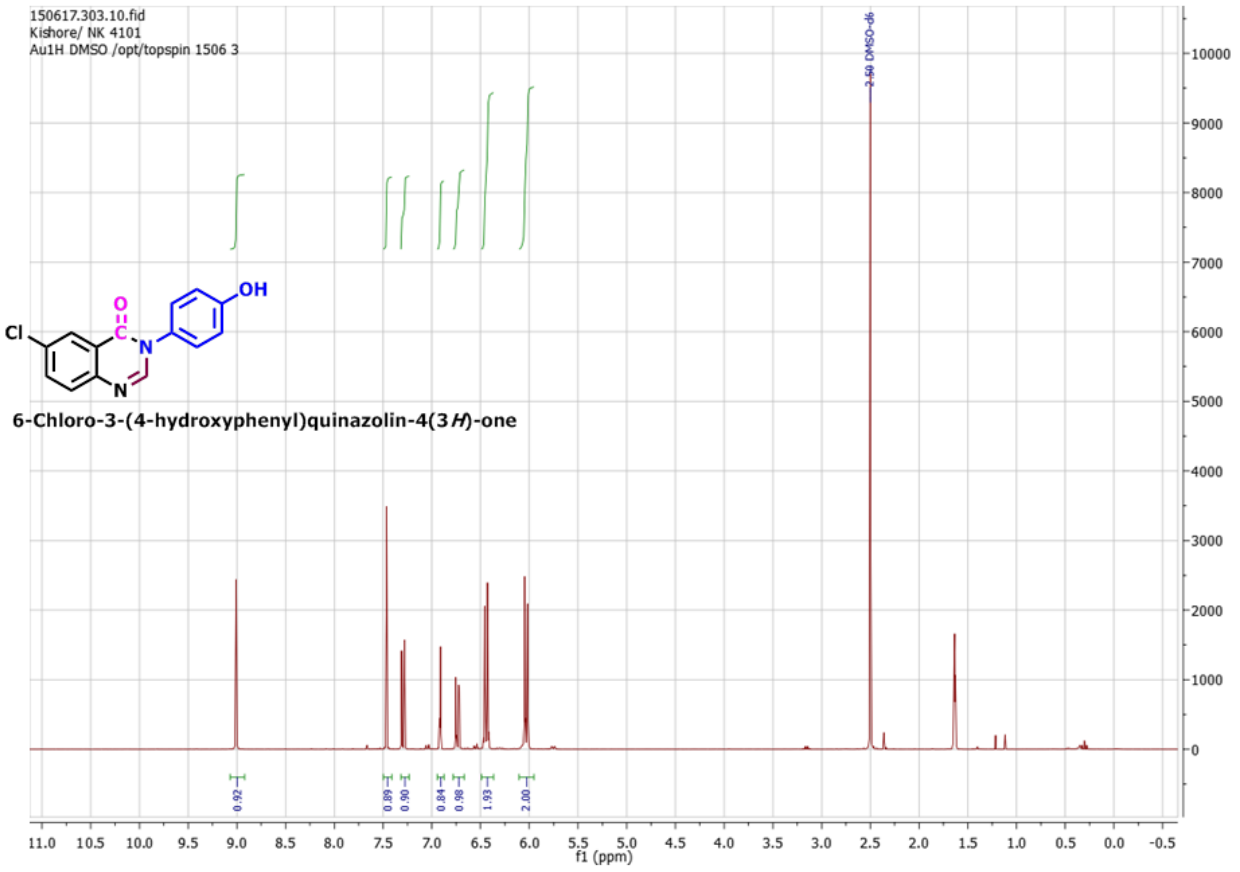

Kishore, NK 4070
Au13C CDCl3 /opt/topspin 1506 20
168.30
164.92
160.09
150.22
150.05
147.33
137.25
130.09
129.95
129.75
129.31
127.00
119.15
116.58
116.27
113.27
112.97
77.26
260
240
220
200
180
160
140
120
100
80
60
40
20
ppm
Current Data Parameters
NAME 150607.320
EXPNO 11
PROCNO 1
F2 - Acquisition Parameters
Date_ 20150607
Time 23.41
INSTRUM AV300
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 32768
SOLVENT CDCl3
NS 2000
DS 4
SWH 21097.047 Hz
FIDRES 0.643831 Hz
AQ 0.7766016 sec
RG 32768
DW 23.700 usec
DE 6.00 usec
TE 296.9 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.60 usec
PL1 -1.10 dB
PL1W 37.53686523 W
SFO1 75.4771825 MHz
======== CHANNEL f2 ========
CPDPRG[2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 0 dB
PL12 19.00 dB
PL13 21.00 dB
PL2W 12.28312492 W
PL12W 0.15463538 W
PL13W 0.09756833 W
SFO2 300.1312005 MHz
F2 - Processing parameters
SI 32768
SF 75.4677490 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

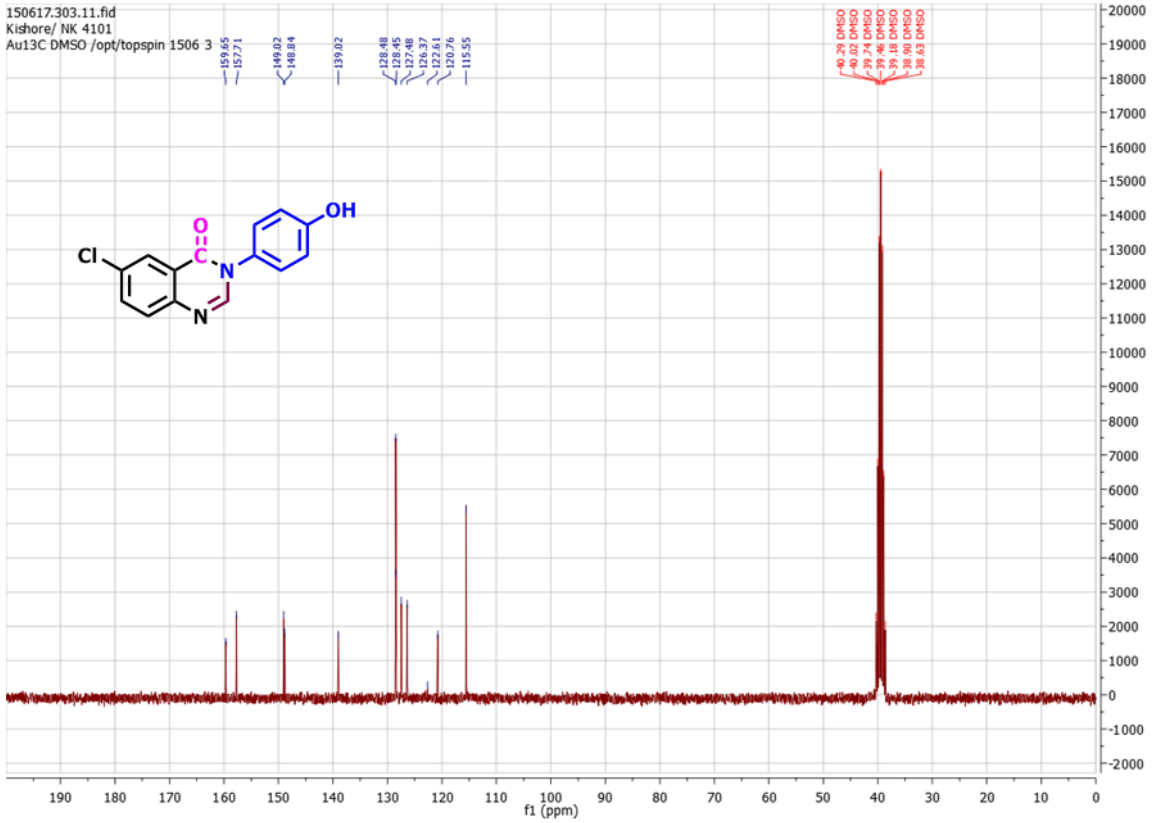

150529.401.10.fid
Kishore/ NK 4071
Au1H CDCl3 /opt/topspin 1505 1
7.26 CDCl3
O
C
N
NC
N
4-oxo-3-phenyl-3,4-dihydroquinazoline-7-carbonitrile
1.00
1.09
1.11
1.11
3.20
2.38
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200


150529.401.11.fid
Kishore/ NK 4071
Au13C CDCl3 /opt/topspin 1505 1
159.33
150.52
148.61
136.75
136.55
132.59
129.92
129.68
129.04
126.81
122.99
117.83
111.27
77.37
77.25
77.05
76.73
O
C
N
NC
N
4-oxo-3-phenyl-3,4-dihydroquinazoline-7-carbonitrile
f1 (ppm)


150612.317.10.fid
Kishore/ NK 4102
Au1H CDCl3 /opt/topspin 1506 17
Cl
O
C
N
N
Cl
6-chloro-3-(4-chlorophenyl)quinazolin-4(3H)-one
1.00
0.96
0.95
3.02
2.06
f1 (ppm)


150612.317.11.fid
Kishore/ NK 4102
Au13C CDCl3 /opt/topspin 1506 17
160.03
148.78
146.76
141.06
135.58
135.41
129.97
128.67
128.47
128.28
120.70
77.48
77.26
77.06
76.64
Cl
O
C
N
N
Cl
65000
60000
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
-5000
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


150617.303.10.fid
Kishore/ NK 4101
Au1H DMSO /opt/topspin 1506 3
2.50 DMSO-d6
Cl
O
C
N
N
OH
6-Chloro-3-(4-hydroxyphenyl)quinazolin-4(3H)-one
0.92
0.89
0.90
0.84
0.98
1.93
2.00
f1 (ppm)


150617.303.11.fid
Kishore/ NK 4101
Au13C DMSO /opt/topspin 1506 3
159.65
157.71
149.02
148.84
139.02
128.48
128.45
127.48
126.37
122.61
120.76
115.55
40.29 DMSO
40.02 DMSO
39.74 DMSO
39.46 DMSO
39.18 DMSO
38.90 DMSO
38.63 DMSO
Cl
O
C
N
N
OH
f1 (ppm)