Supporting Information

Copper Catalyzed Multicomponent Cascade Reaction for Synthesis of Quinazalinones

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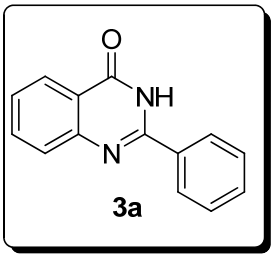
General

All chemicals were of reagent grade quality, purchased commercially from TCI-Chemicals, Sigma-Aldrich, or Spectrochem, and used without further purification. Column chromatography was performed on Merck chromatographic silica gel (100-200 mesh). TLC analyses were performed using Merck silica gel 60 F_{254} precoated aluminium plates. NMR spectra were recorded on Bruker Avance III (500MHz), or Varian Mercury (300 MHz) instruments; chemical shifts, given in ppm, are relative to Me_4Si as the internal standard or to the residual solvent peak. HR-MS data were obtained using a Thermo-Scientific Bruker Daltonik GmbH, Germany Impact II UHR-ToF Mass Spectrometer ESI (Electron Spray Ionization).

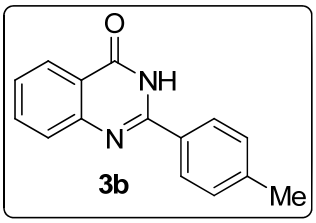
General procedure for the synthesis of Quinazalinone (3):

Oven dried sealed tube with spin bar was charged with 2-bromobenzamide (0.5 mmol), benzyl alcohol (1.0 mmol), sodium azide (1.0 mmol), copper (II) oxide (0.20 mmol), L-proline (0.20 mmol), TEMPO (0.10 mmol), *p*-toluene sulfonic acid (0.20mmol) in 2 mL DMF. Reaction mixture was heated to 110° C for 24 h. Reaction progress was checked using TLC. After completion of reaction it was cooled to room temperature. Crude product was extracted with ethyl acetate (3 x 20 mL). The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated in vaccuo. The crude product was purified by silica gel column chromatography with hexane–ethyl acetate to give quinazalinone (**3**).

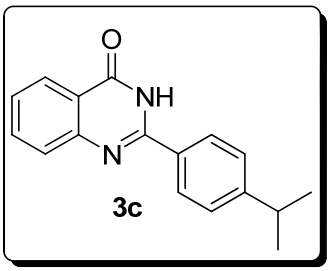
Spectral and Analytical data:



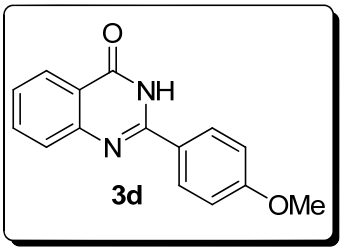
2-Phenylquinazolin-4(3*H*)-one (**3a**)**:** white solid, R_f = 0.5 (ethyl acetate:hexane, 4:6); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.51-7.56 (m, 1H), 7.60-7.63 (m, 3H), 7.81-7.88 (m, 2H), 8.29 (dd, J = 2.75, 6.25 Hz, 2H), 8.36 (dd, J = 1.07, 8.09 Hz, 1H), 11.67 (br.s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 120.9, 126.4, 126.9, 127.9, 128.0, 129.0, 131.6, 132.8, 134.9, 149.5, 151.7, 163.8; HRMS (ESI, m/z) calcd for $C_{14}H_{11}N_2O$ = 223.0871 $[M + H]^+$, found 223.0869.



2-(*p*-Tolyl)quinazolin-4(3*H*)-one (**3b**)**:** white solid, R_f = 0.6 (ethyl acetate:hexane, 4:6); ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.48 (s, 3H), 7.40 (d, J = 7.48 Hz, 2H), 7.52 (t, J = 7.02 Hz, 1H), 7.4 (t, J = 8.27 Hz, 2H), 8.16 (d, J = 7.17 Hz, 2H), 8.35 (d, J = 7.93 Hz, 1H), 11.55 (brs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 21.5, 120.8, 126.3, 126.5, 127.3, 127.9, 129.7, 129.9, 134.8, 142.2, 149.6, 151.8, 163.8; HRMS (ESI, m/z) calcd for $C_{15}H_{13}N_2O$ = 237.1028 $[M + H]^+$, found 237.1024.

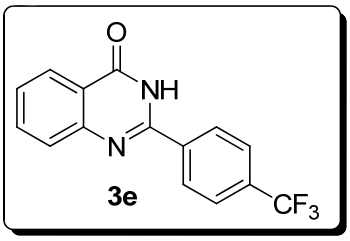


2-(4-Isopropylphenyl)quinazolin-4(3*H*)-one (**3c**)**:** white solid, R_f = 0.6 (ethyl acetate:hexane, 4:6); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.35 (d, J = 7.02 Hz, 6H), 3.05 (sept, J = 7.02 Hz, 1H), 7.46 (d, J = 8.24 Hz, 2H), 7.51-7.55 (m, 1H), 7.80-7.86 (m, 2H), 8.23 (d, J = 8.24 Hz, 2H), 8.35-8.37 (m, 1H), 11.76 (brs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 23.8, 34.2, 120.8, 126.3, 126.5, 127.1, 127.5, 127.9, 130.3, 134.8, 149.6, 151.8, 151.9, 164.0; HRMS (ESI, m/z) calcd for $C_{17}H_{17}N_2O$ = 265.1341 $[M + H]^+$, found 265.1333.



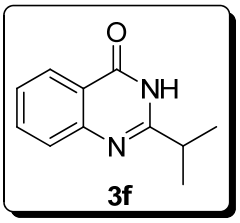
3d

2-(4-Methoxyphenyl)quinazolin-4(3*H*)-one (**3d**)**:** white solid, R_f = 0.3 (ethyl acetate:hexane, 4:6); ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.94 (s, 3H), 7.10 (d, J = 8.55 Hz, 2H), 7.48-7.53 (m, 1H), 7.79-7.83 (m, 2H), 8.22 (d, J = 8.54 Hz, 2H), 8.34 (d, J = 7.93 Hz, 1H), 11.24 (br.s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 55.5, 114.4, 120.6, 125.0, 126.4, 126.5, 127.8, 129.0, 134.8, 149.7, 151.3, 162.5, 163.7.



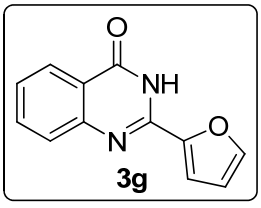
3e

2-(4-(Trifluoromethyl)phenyl)quinazolin-4(3*H*)-one (**3e**)**:** white solid, R_f = 0.3 (ethyl acetate:hexane, 4:6); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.53-7.56 (m, 1H), 7.69-7.77 (m, 3H), 7.80-7.88 (m, 3H), 8.22 (d, J = 7.93 Hz, 1H), 10.88 (br.s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 123.5 (q, $J_{C\text{-}F}$ = 224.34 Hz), 126.9 (q, $J_{C\text{-}F}$ = 4.54 Hz), 127.4, 128.0, 130.6, 130.5, 130.6 (q, $J_{C\text{-}F}$ = 31.79 Hz), 132.2, 135.0, 148.7, 151.3, 162.5; HRMS (ESI, m/z) calcd for $C_{15}H_{10}F_3N_2O$ = 291.0745 $[M + H]^+$, found 291.0736.



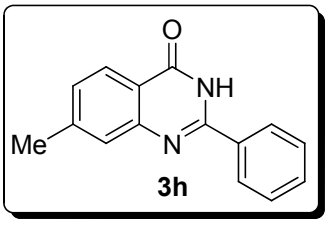
3f

2-Isopropylquinazolin-4(3*H*)-one (**3f**)**:** white solid, R_f = 0.3 (ethyl acetate:hexane, 4:6); ^{1}H NMR (500 MHz, DMSO-D_6): δ 1.27 (d, J = 6.71 Hz, 6H), 2.89 (sept, J = 6.71 Hz, 1H), 7.46 (t, J = 7.63, 1H), 7.62 (d, J = 7.93 Hz, 1H), 7.78 (t, J = 7.93 Hz, 1H), 8.09 (d, J = 7.93 Hz, 1H), 12.14 (br.s, 1H); ^{13}C NMR (125 MHz, DMSO-D_6): δ 20.4, 33.3, 120.9, 125.7, 126.0, 127.0, 134.2, 148.9, 151.3, 161.6, 162.0.



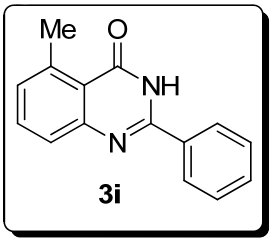
3g

2-(Furan-2-yl)quinazolin-4(3*H*)-one (**3g**)**:** white solid, R_f = 0.3 (ethyl acetate:hexane, 4:6); ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.69 (d, J = 1.53 Hz, 1H), 7.50 (t, J = 7.63, 1H), 7.66-7.70 (m, 2H), 7.78-7.83(m, 2H), 8.34 (d, J = 7.63 Hz, 1H), 11. 47 (brs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 112.8, 114.1, 120.9, 126.4, 126.7, 127.7, 135.0, 143.6, 145.6, 146.3, 149.3, 162.9, 162.0; HRMS (ESI, m/z) calcd for $C_{12}H_9N_2O$ = 213.064 $[M + H]^+$, found 213.0658.



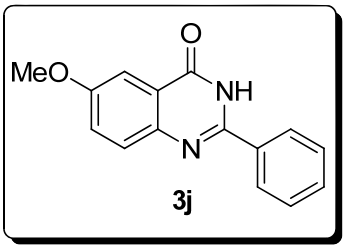
3h

7-Methyl-2-phenylquinazolin-4(3*H*)-one (**3h**)**:** white solid, R_f = 0.3 (ethyl acetate:hexane, 4:6); ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.55 (s, 3H), 7.33 (dd, J = 0.92, 7.02 Hz, 1H), 7.58-7.60 (m, 3H), 7.65 (br.m, 1H), 8.22 (d, J = 7.93 Hz, 1H), 8.25-8.26 (m, 2H), 11.06 (br.s, 1H); ^{13}C NMR (125 MHz, DMSO D_6): δ 21.4, 118.6, 125.7, 127.1, 127.7, 128.0, 128.6, 131.3, 132.8, 145.1, 148.9, 152.3, 162.1.



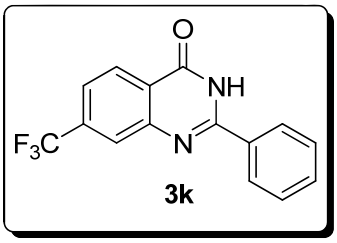
3i

5-Methyl-2-phenylquinazolin-4(3*H*)-one (**3i**)**:** white solid, R_f = 0.3 (ethyl acetate:hexane, 4:6); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.88 (s, 3h), 7.17-7.19 (m, 3H), 7.47-7.50 (m, 2H), 7.56-7.60 (m, 1H), 8.16 (dd, J = 1.59, 5.75 Hz, 2H), 10.93 (br.s, 1H); ^{13}C NMR (125 MHz, DMSO D_6): δ 22.5, 119.3, 125.7, 127.7, 128.6, 128.9, 131.3, 132.5, 133.6, 140.0, 150.3, 152.0, 163.0.



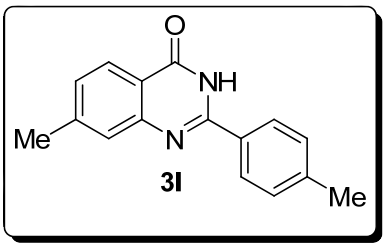
3j

6-Methoxy-2-phenylquinazolin-4(3*H*)-one (**3j**)**:** white solid, R_f = 0.3 (ethyl acetate:hexane, 4:6); ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.97 (s, 3h), 7.28 (s, 1H), 7.43 (dd, J = 2.90, 5.95 Hz, 1H), 7.56-7.60 (m, 3H), 7.71(d, J = 2.75 Hz, 1H), 7.79 (d, J = 8.85 Hz, 1H), 8.10-8.12 (m, 1H), 10. 31 (br.s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 55.8, 105.9, 121.7, 125.2, 126.7, 129.2, 129.7, 131.4, 132.9, 144.0, 149.2, 158.5, 161.2; HRMS (ESI, m/z) calcd for $C_{15}H_{13}N_2O$ = 253.0977 $[M + H]^+$, found 253.0974.



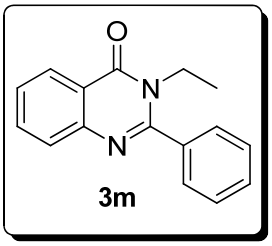
3k

2-Phenyl-7-(trifluoromethyl)quinazolin-4(3*H*)-one (3k): white solid, R_f = 0.4 (ethyl acetate:hexane, 4:6); ^{1}H NMR (500 MHz, DMSO-D_6): δ 7.56-7.65 (m, 3H), 7.82 (dd, J = 1.37, 8.24 Hz, 1H), 8.06 (s, 1H), 8.20-8.22 (m, 2H), 8.35 (d, J = 8.24 Hz, 1H), 12.84 (br.s, 1H).



3l

7-Methyl-2-*p*-tolylquinazolin-4(3*H*)-one(3l): white solid, R_f = 0.5 (ethyl acetate:hexane, 4:6); ^{1}H NMR (500 MHz, DMSO-D_6): δ 2.39 (s, 3H), 2.47 (s, 3H), 7.32-7.36 (m, 3H), 7.54 (s, 1H), 8.03 (d, J = 8.09 Hz, 1H), 8.09 (d, J = 8.09 Hz, 2H), 12.38 (br.s, 1H); ^{13}C NMR (125 MHz, DMSO-D_6): δ 21.0, 21.4, 118.5, 125.7, 127.1, 127.6, 127.9, 129.2, 130.0, 141.4, 145.0, 149.0, 152.2, 162.1.

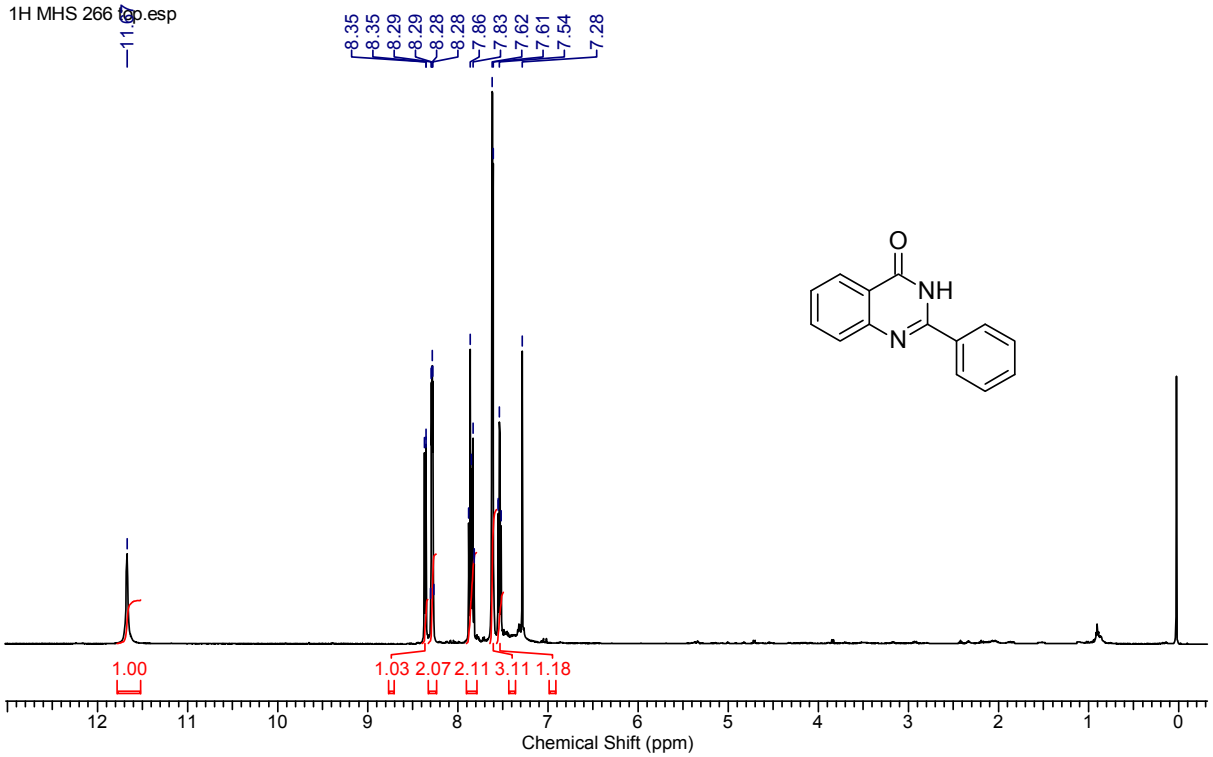


3m

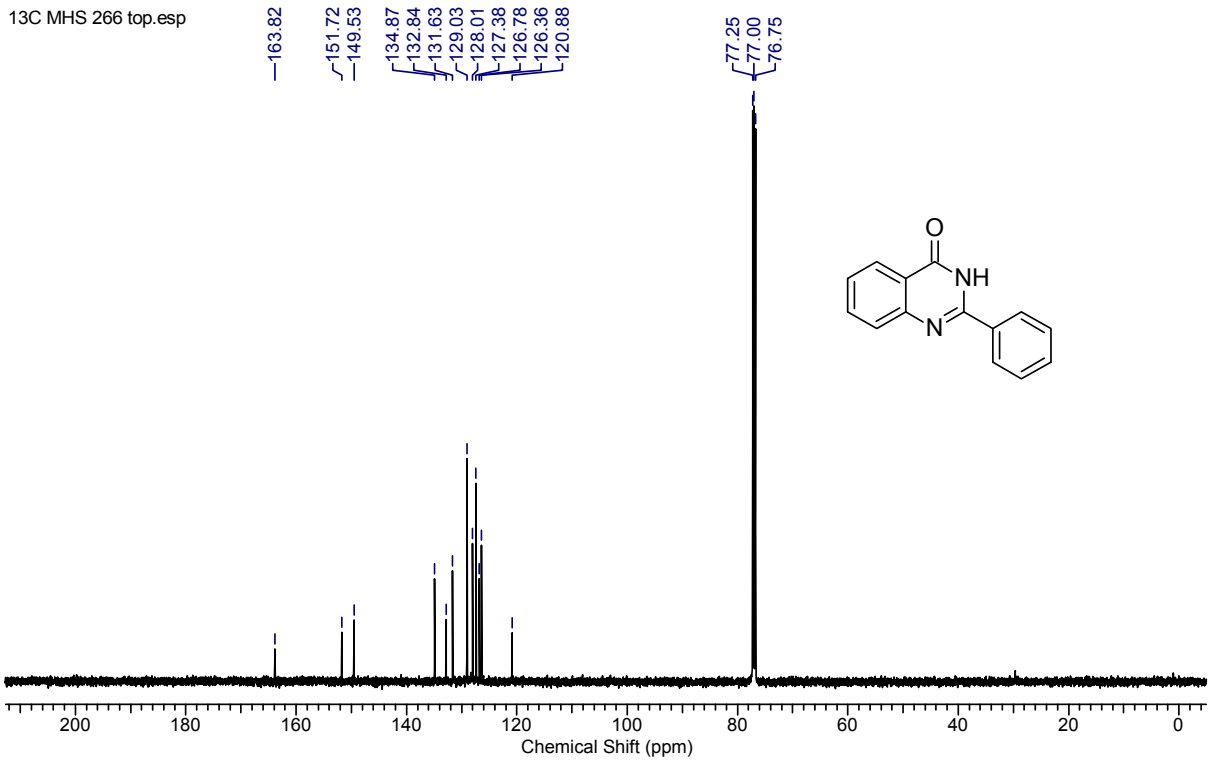
3-Ethyl-2-phenylquinazolin-4(3*H*)-one (3m): white solid, R_f = 0.3 (ethyl acetate:hexane, 4:6); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.24 (t, J = 7.02 Hz, 3H), 4.07 (q, J = 7.02 Hz, 2h), 7.51-7.53 (m, 1H), 7.54-7.58 (m, 5H), 7.75-7.80 (m, 2H), 8.36 (dd, J = 1.22, 6.71 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 14.1, 41.2, 120.9, 126.7, 126.9, 127.4, 127.6, 128.8, 129.8, 134.3, 135.6, 147.2, 156.2, 162.0

Copies of 1H and 13C NMR spectra:

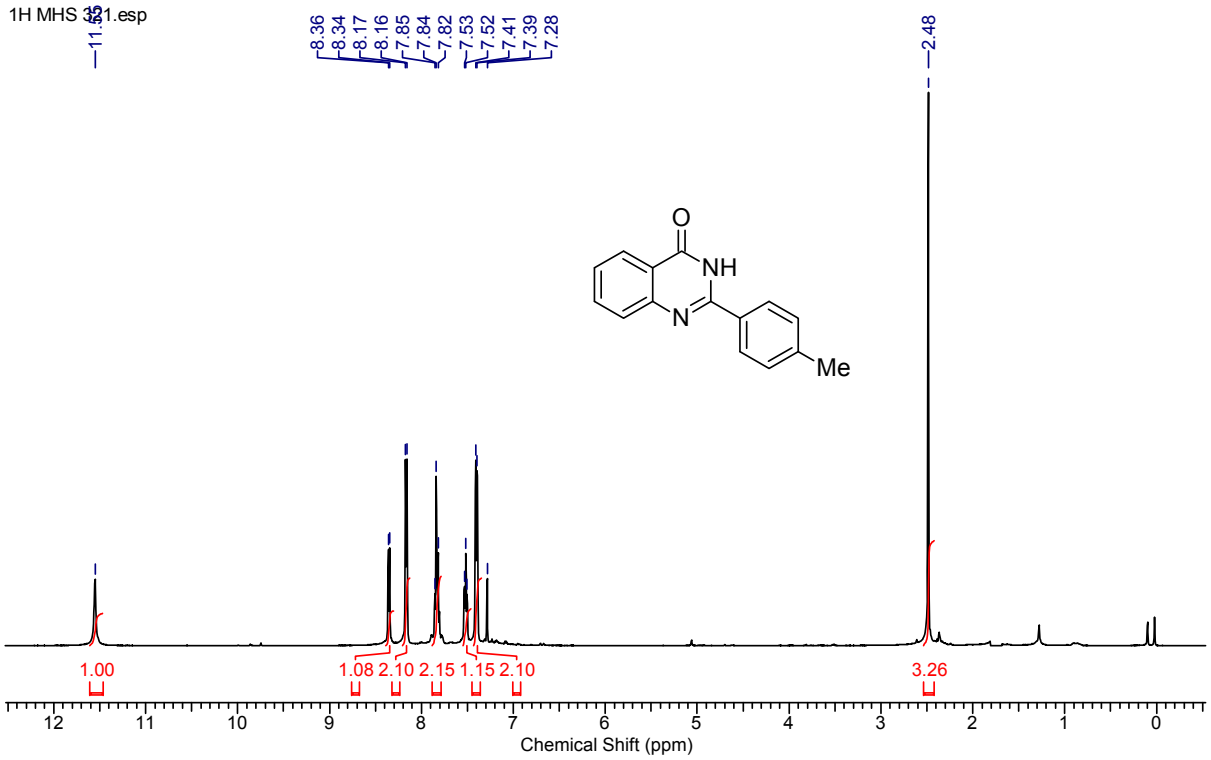
^{1}H NMR spectrum for compound **3a** ($CDCl_3$, 500 MHz)



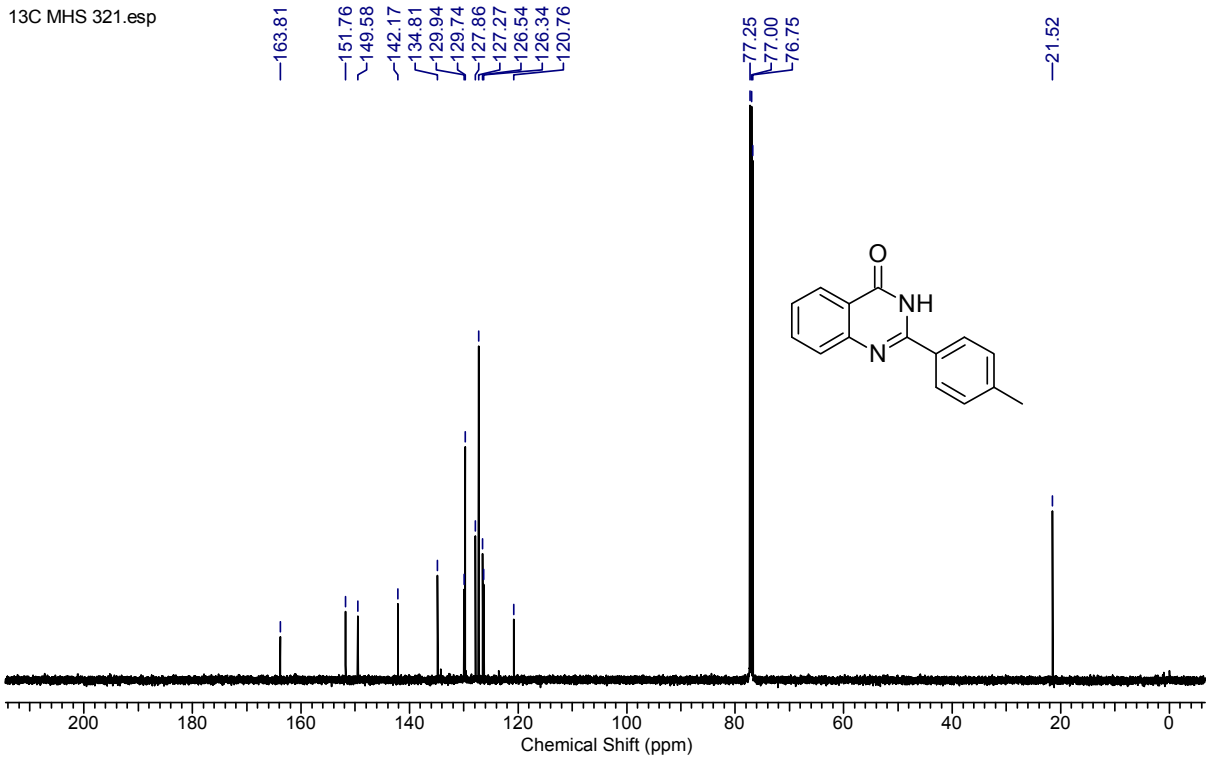
^{13}C NMR spectrum for compound **3a** ($CDCl_3$, 125 MHz)



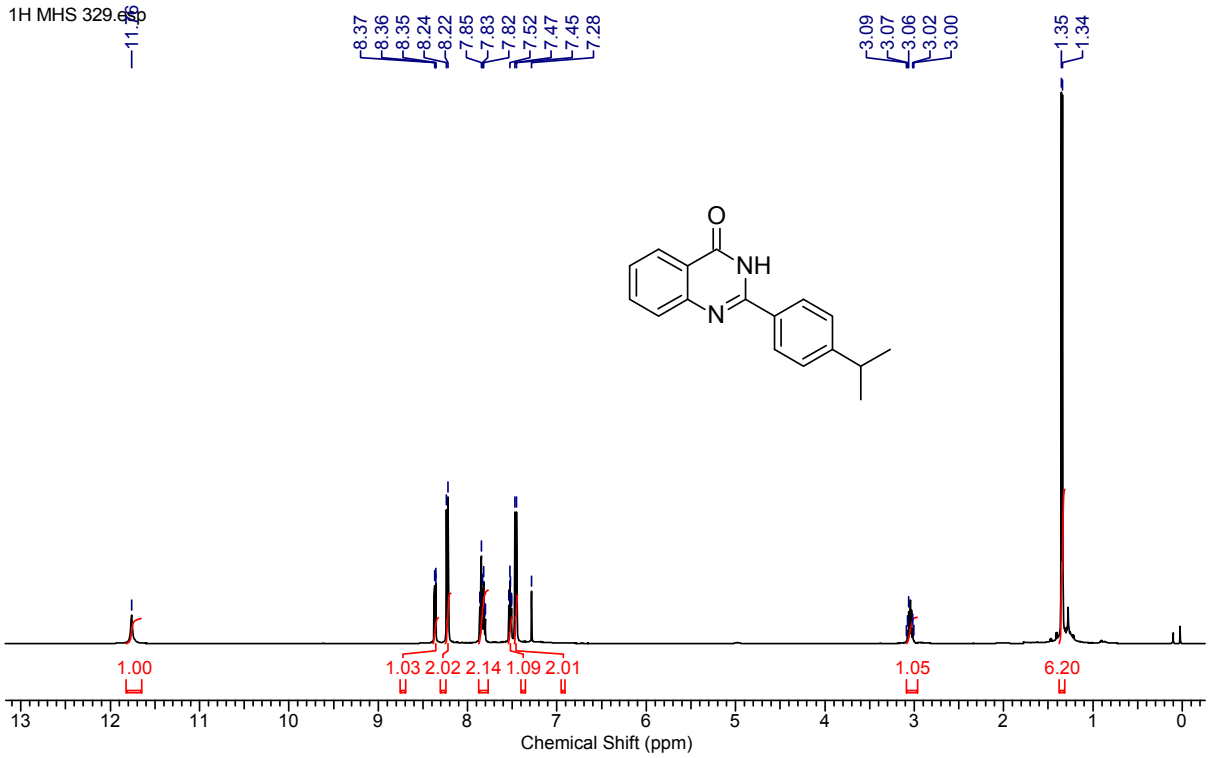
^{1}H NMR spectrum for compound **3b** ($CDCl_3$, 500 MHz)



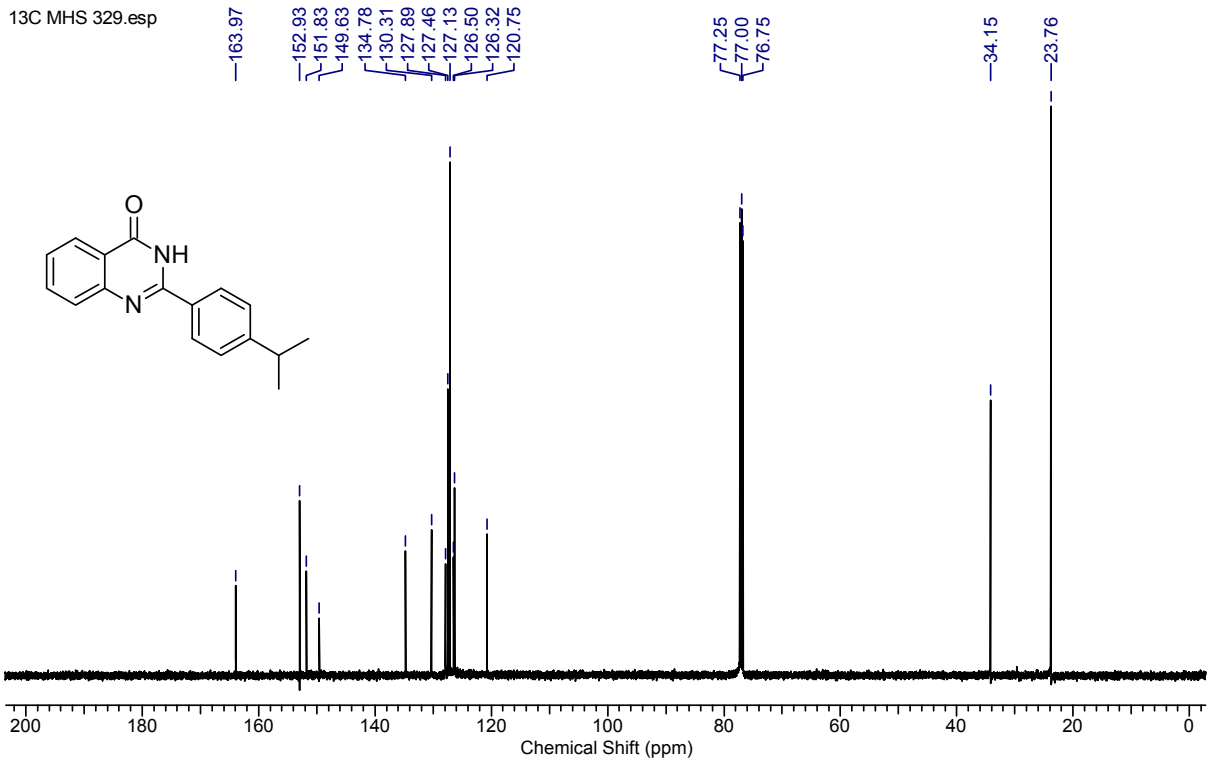
^{13}C NMR spectrum for compound **3b** ($CDCl_3$, 125 MHz)



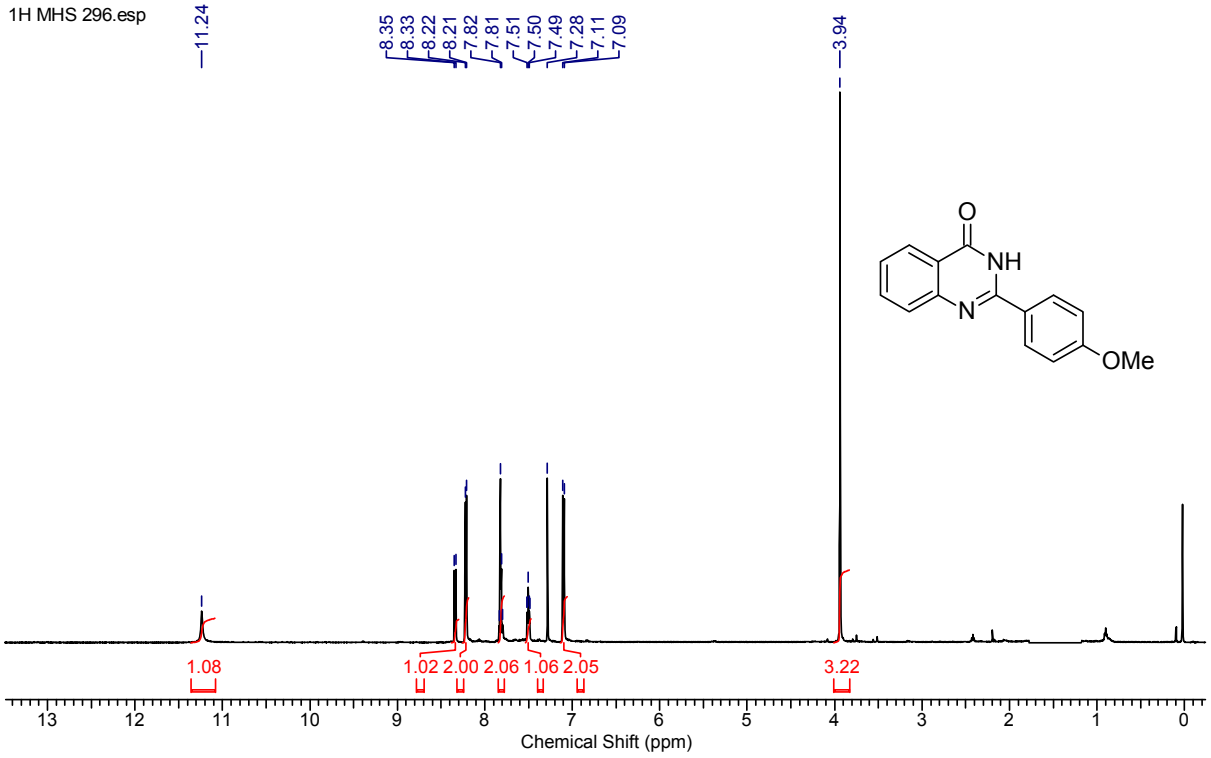
^{1}H NMR spectrum for compound **3c** ($CDCl_3$, 500 MHz)



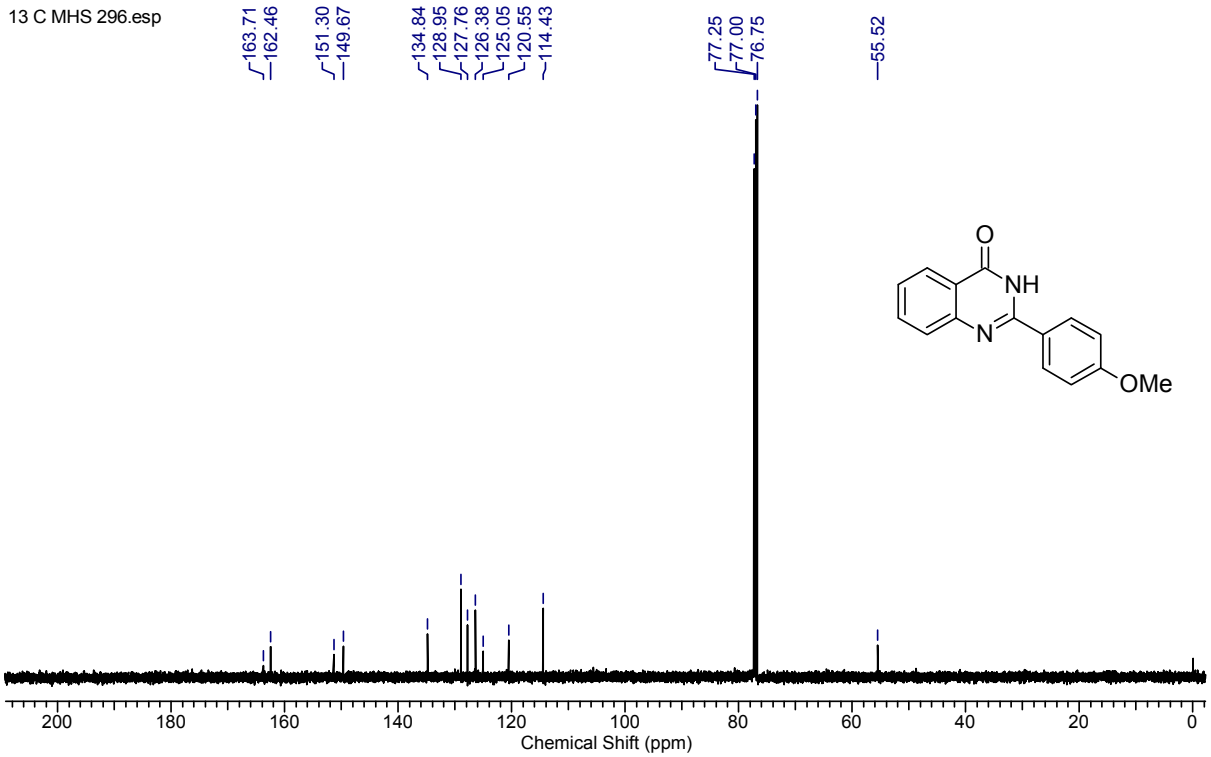
^{13}C NMR spectrum for compound **3c** ($CDCl_3$, 125 MHz)



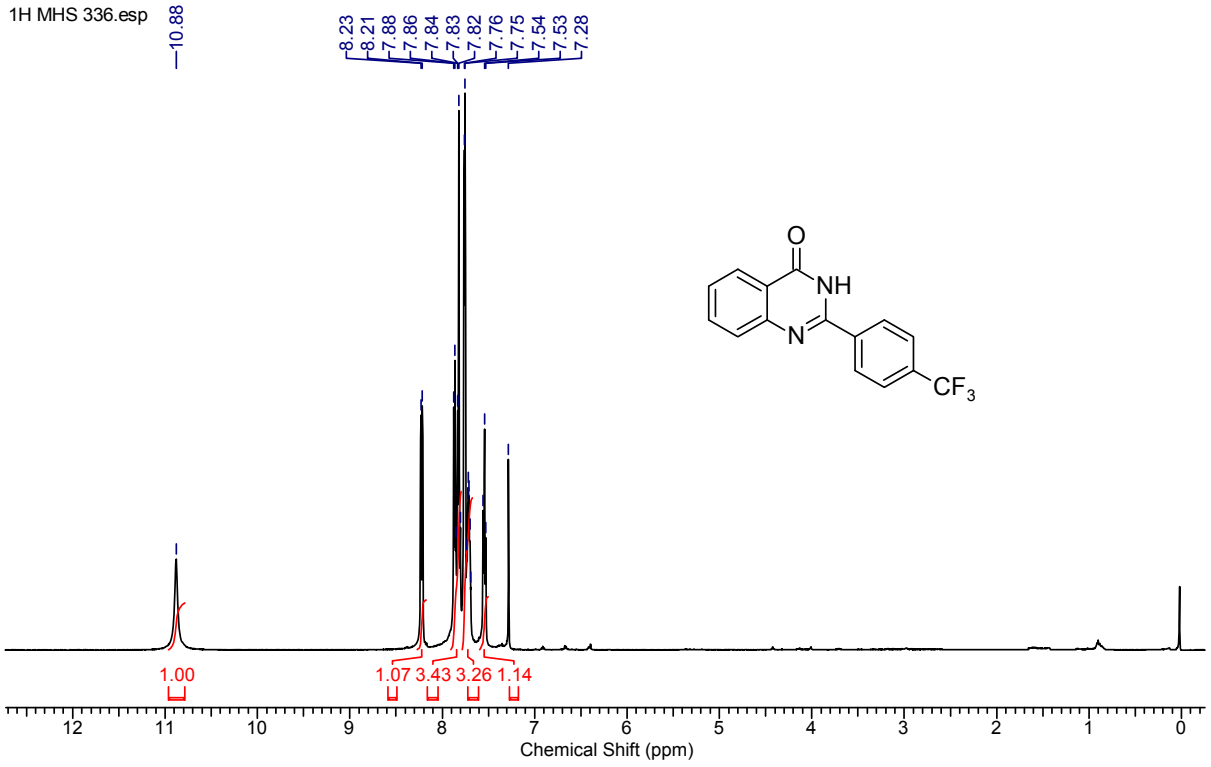
^{1}H NMR spectrum for compound **3d** ($CDCl_3$, 500 MHz)



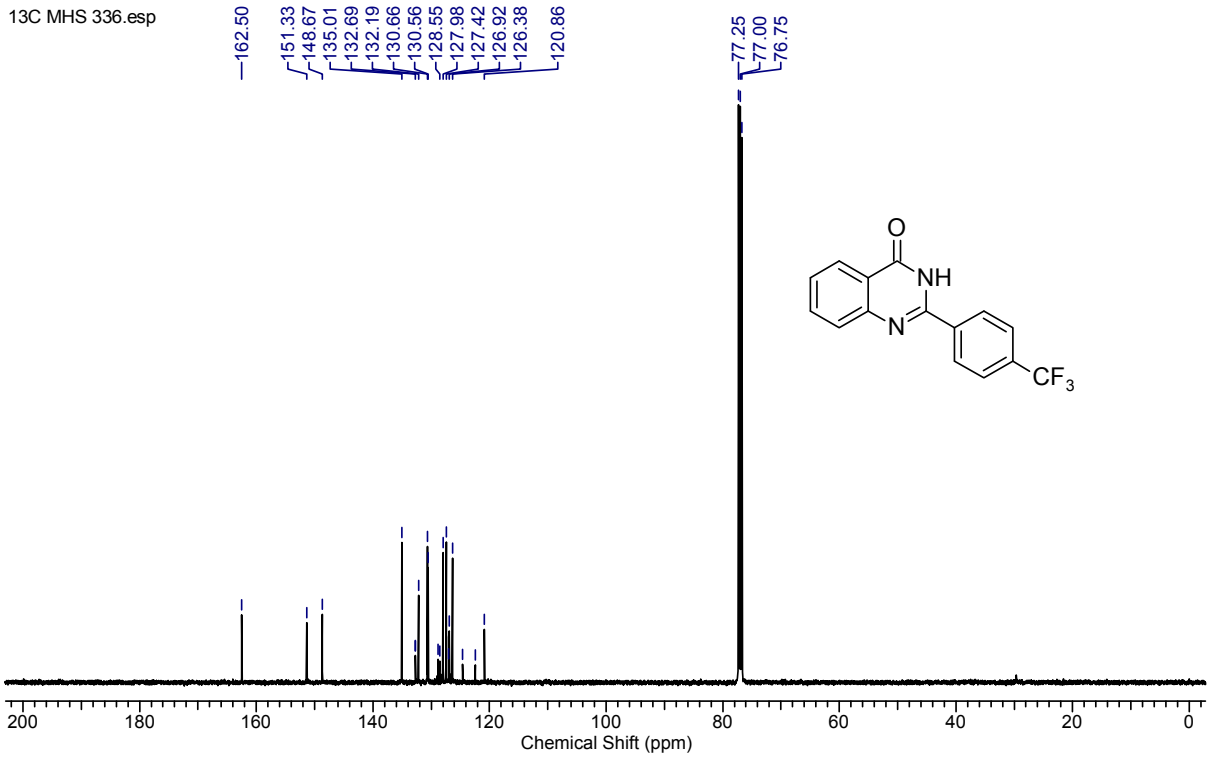
^{13}C NMR spectrum for compound **3d** ($CDCl_3$, 125 MHz)



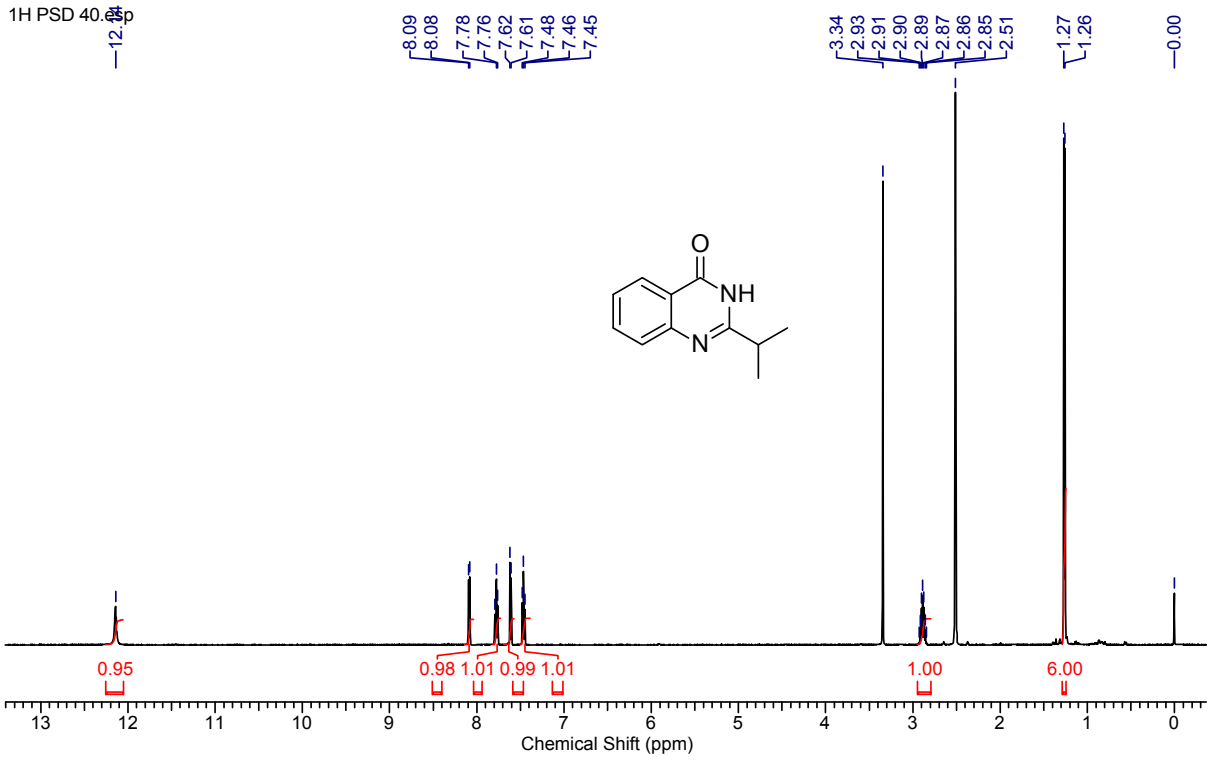
^{1}H NMR spectrum for compound **3e** ($CDCl_3$, 500 MHz)



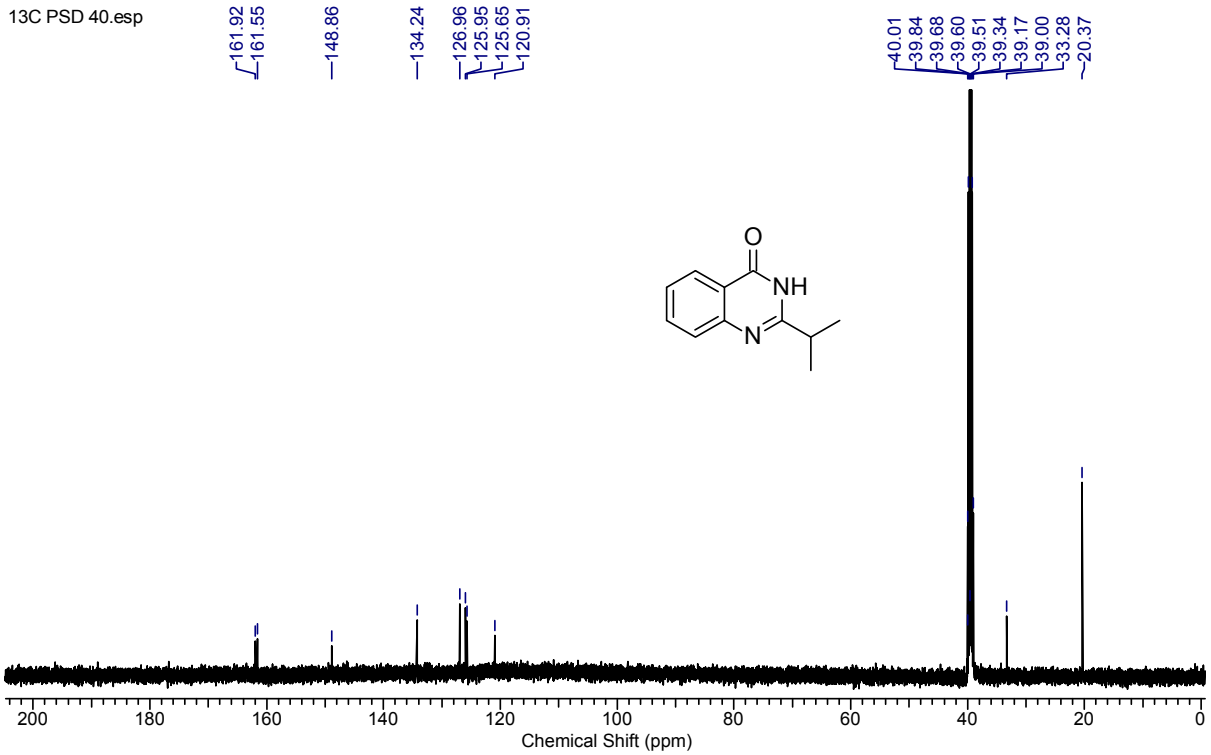
^{13}C NMR spectrum for compound **3e** ($CDCl_3$, 125 MHz)



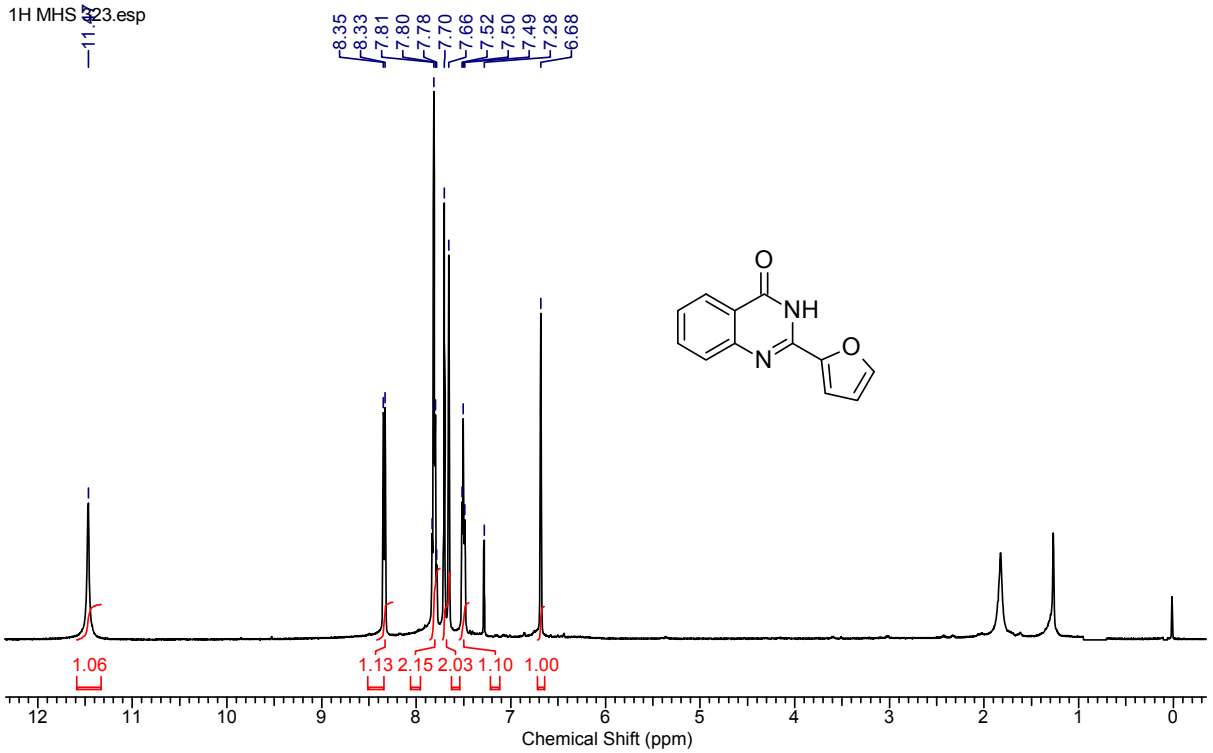
^{1}H NMR spectrum for compound **3f** (DMSO-D_6, 500 MHz)



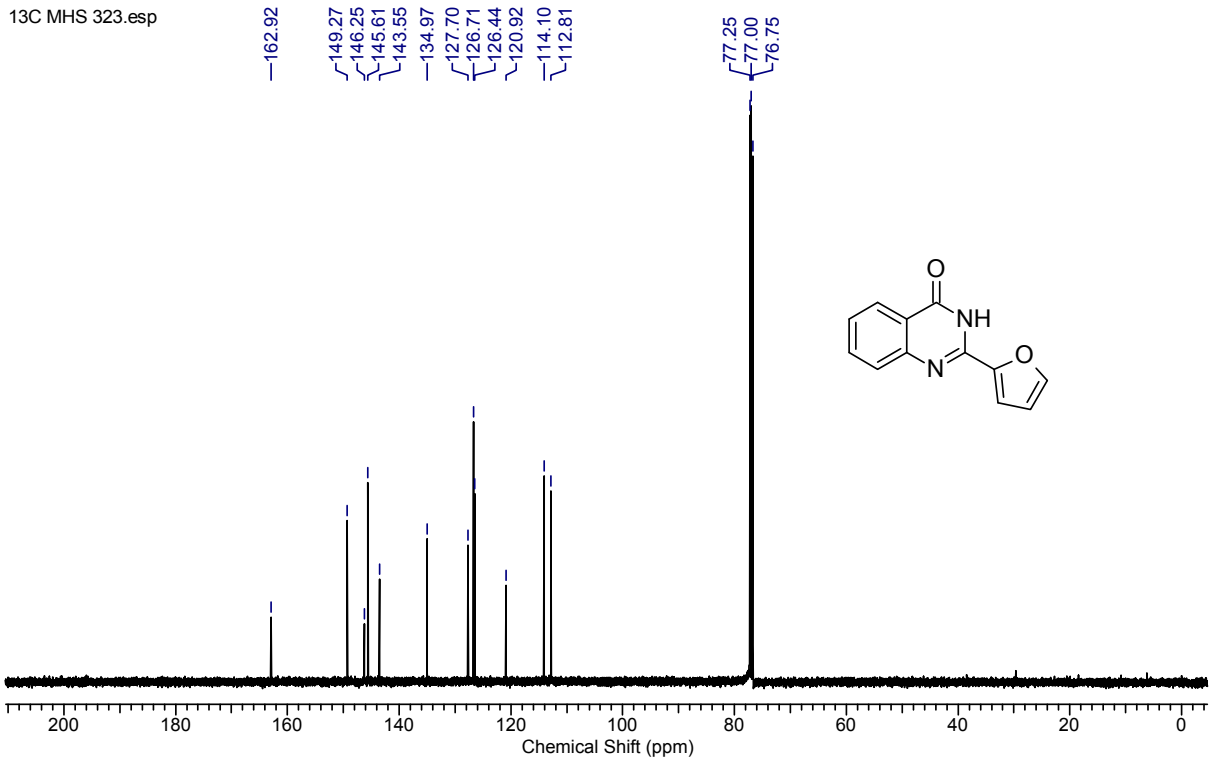
^{13}C NMR spectrum for compound **3f** (DMSO-D_6, 125 MHz)



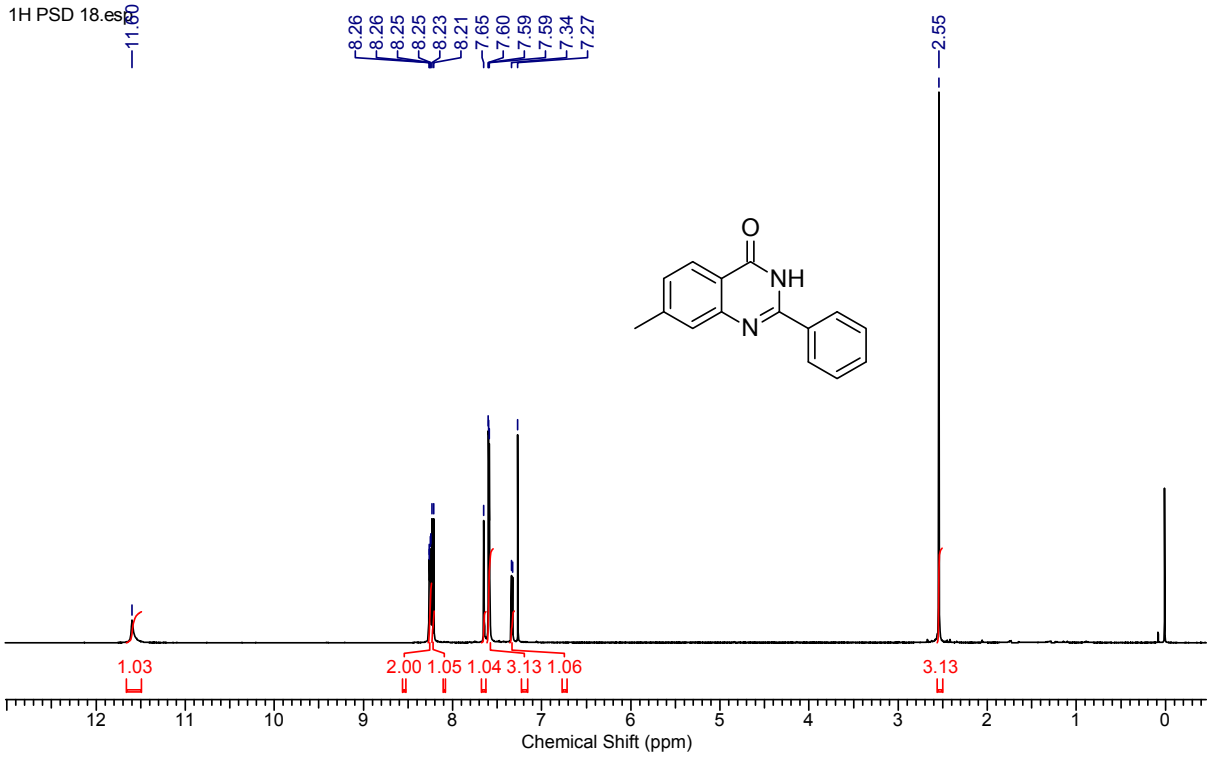
^{1}H NMR spectrum for compound **3g** ($CDCl_3$, 500 MHz)



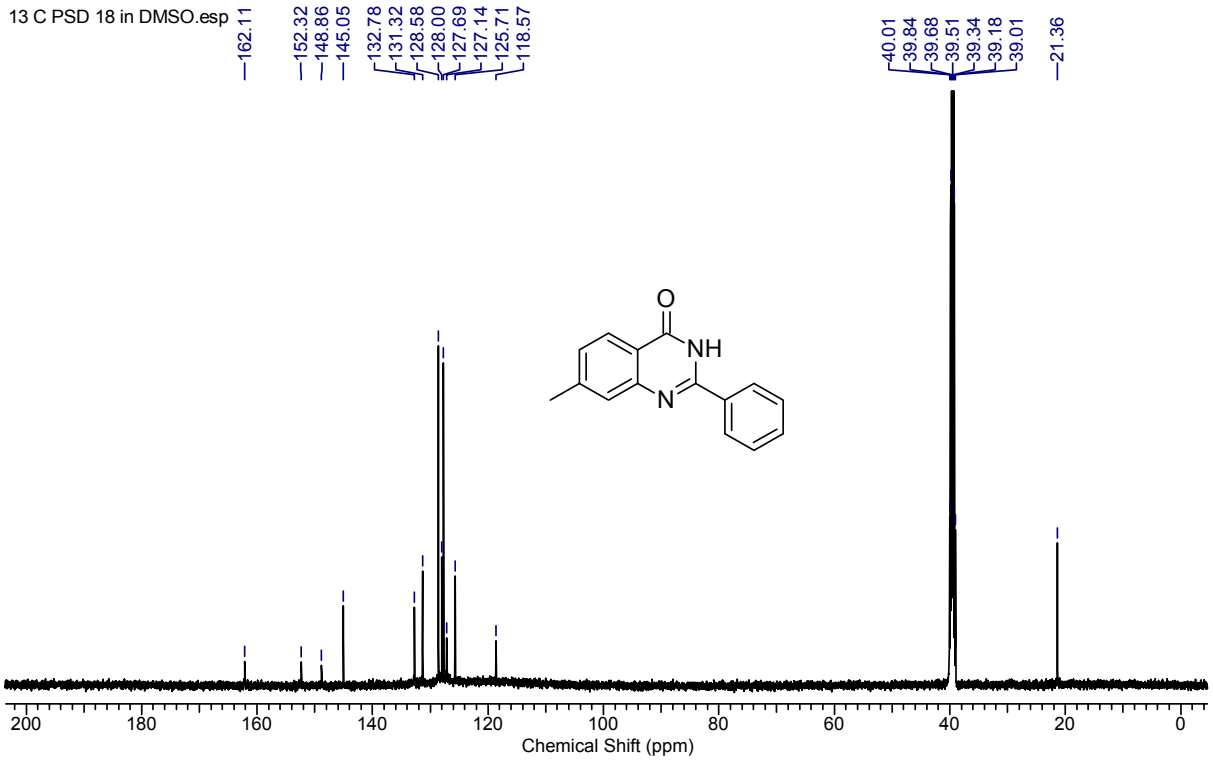
^{13}C NMR spectrum for compound **3g** ($CDCl_3$, 125 MHz)



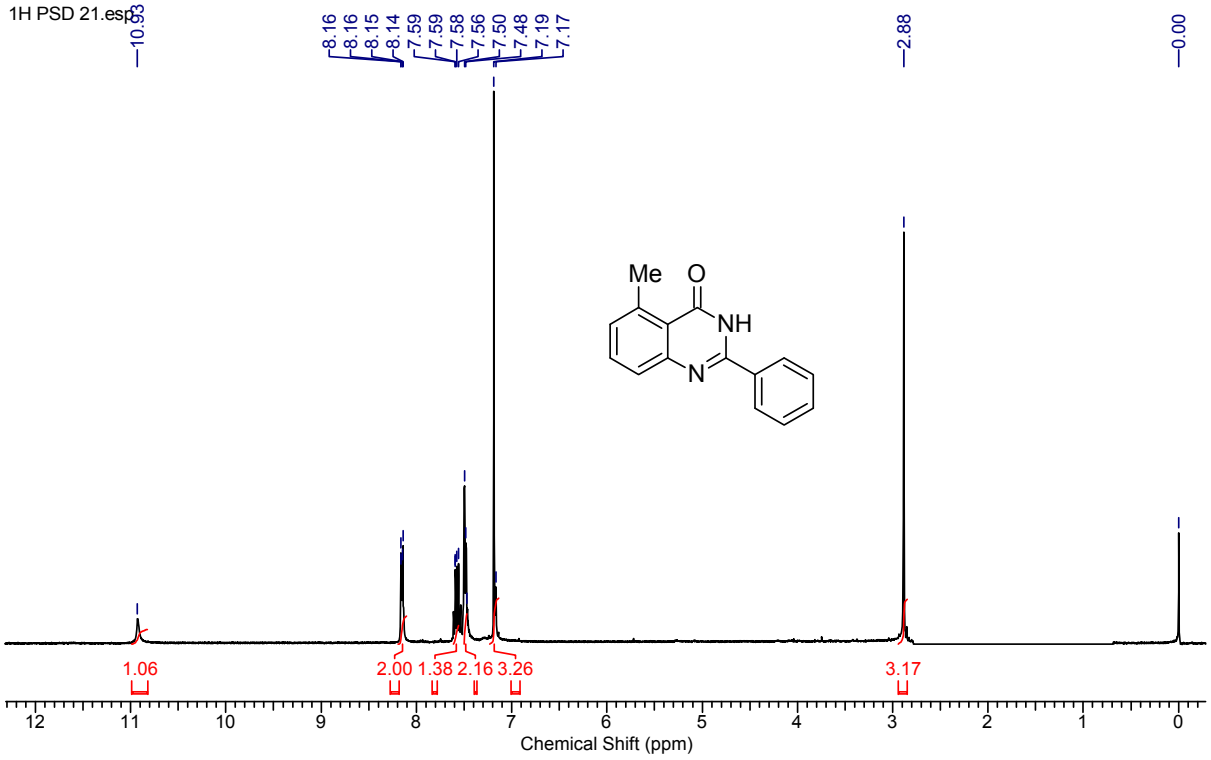
^{1}H NMR spectrum for compound **3h** ($CDCl_3$, 500 MHz)



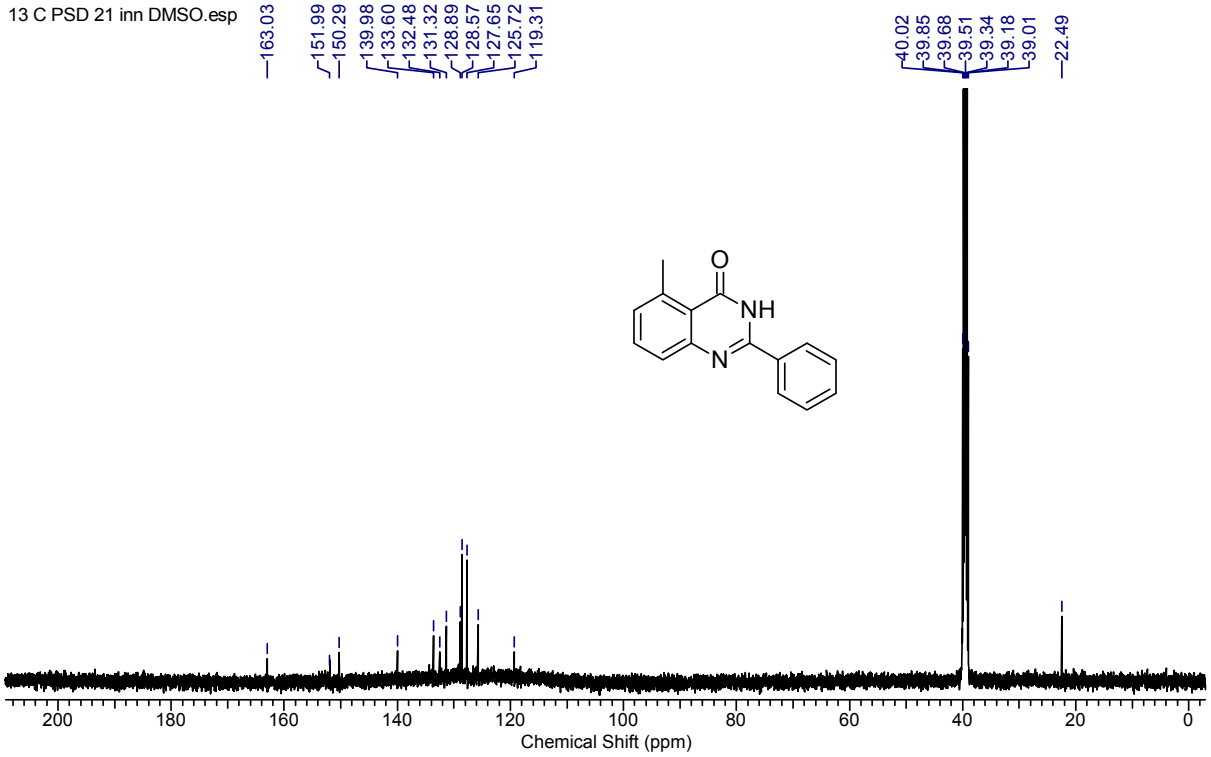
^{13}C NMR spectrum for compound **3h** (DMSO-D_6, 125 MHz)



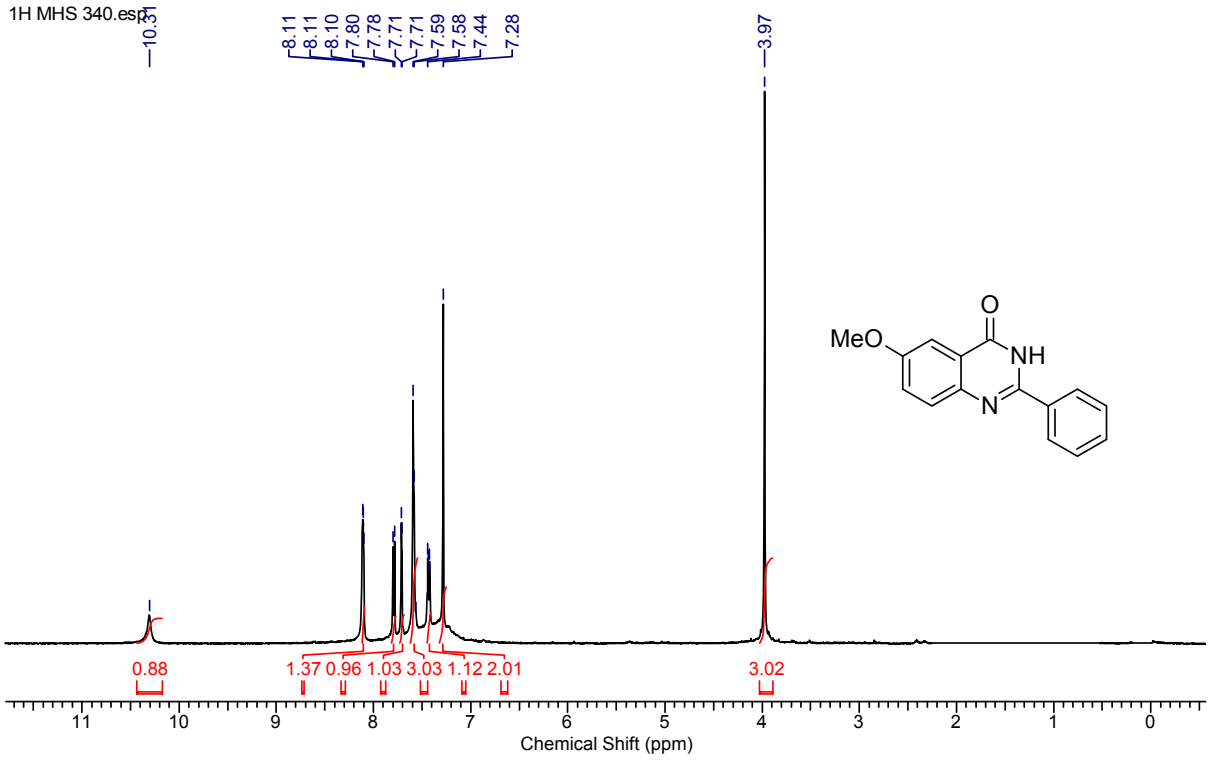
[1]H NMR spectrum for compound **3i** ($CDCl_3$, 400 MHz)



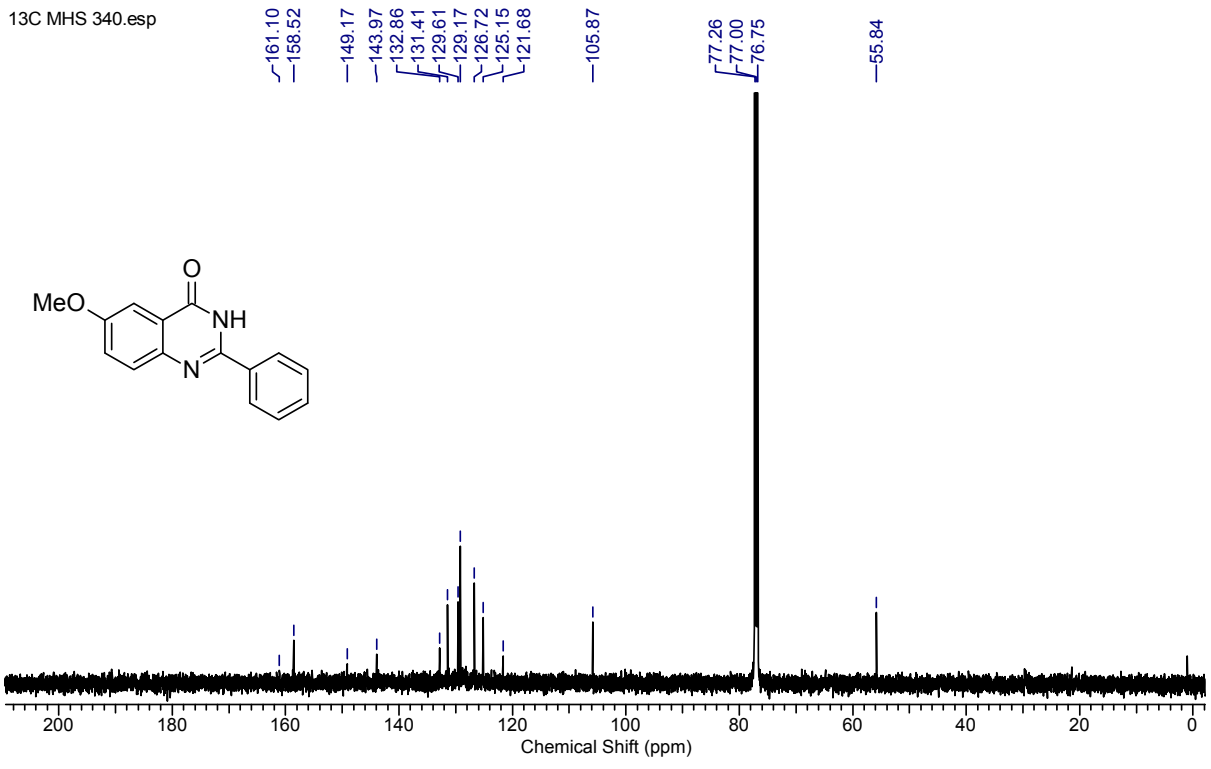
[13]C NMR spectrum for compound **3i** (DMSO-D_6, 125 MHz)



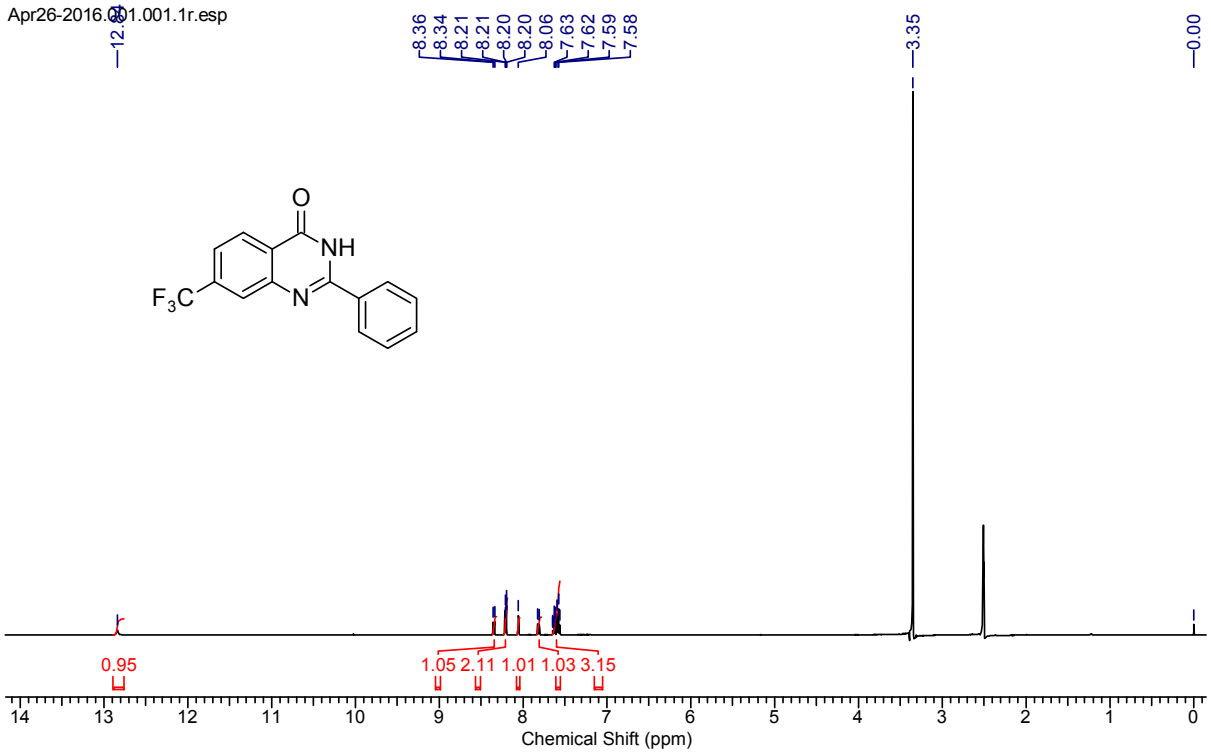
^{1}H NMR spectrum for compound **3j** ($CDCl_3$, 500 MHz)



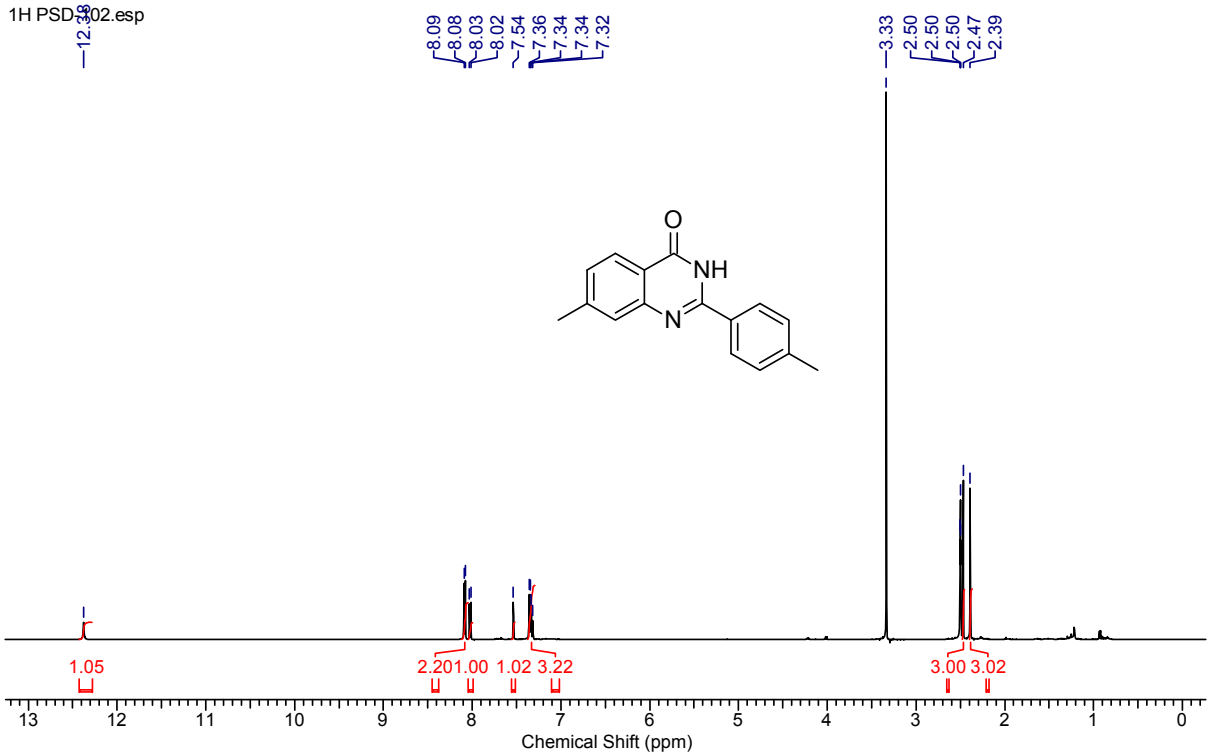
^{13}C NMR spectrum for compound **3j** ($CDCl_3$, 125 MHz)



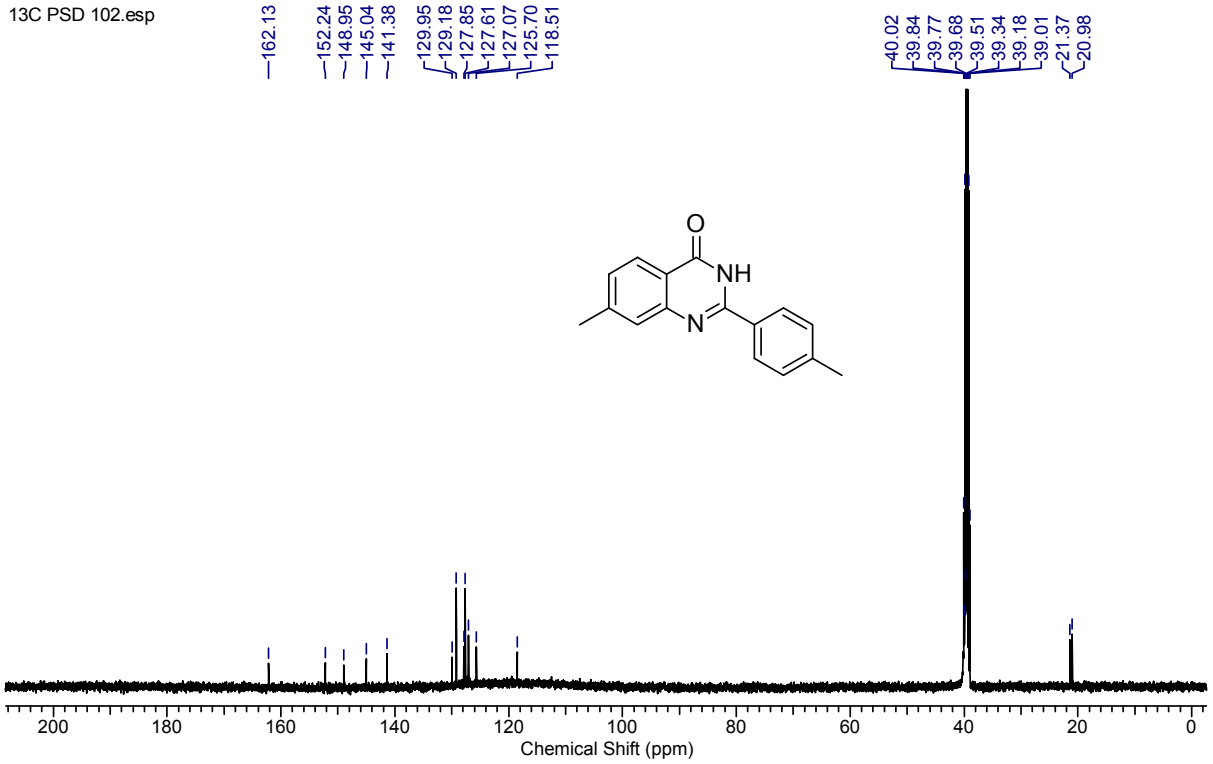
^{1}H NMR spectrum for compound **3k** (DMSO-D_6, 500 MHz)



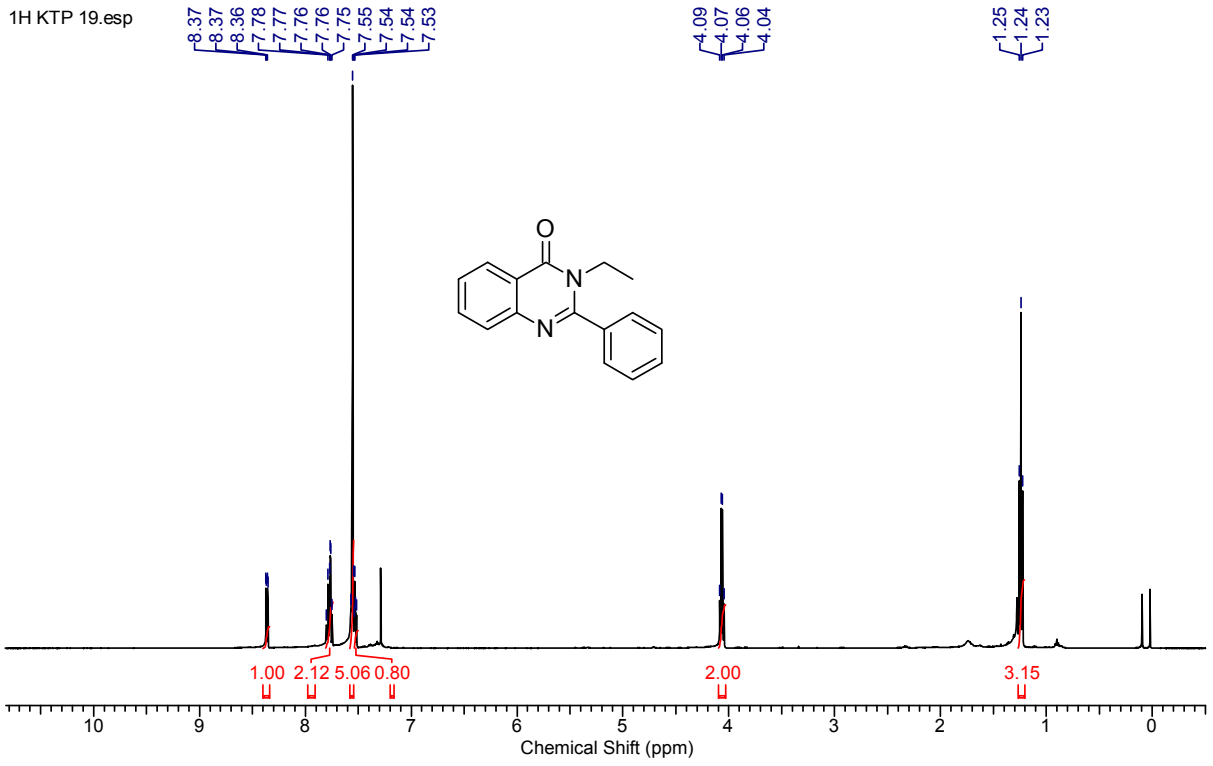
^{1}H NMR spectrum for compound **3l** (DMSO D_6, 500 MHz)



^{13}C NMR spectrum for compound **3l** (DMSO D_6, 125 MHz)



^{1}H NMR spectrum for compound **3m** ($CDCl_3$, 500 MHz)



^{13}C NMR spectrum for compound **3m** ($CDCl_3$, 125 MHz)