Supplemental Information

for

Chitosan-Supported CuI-Catalyzed Cascade Reaction of 2-Halobenzoic Acids and Amidines for the Synthesis of Quinazolinones

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Contents

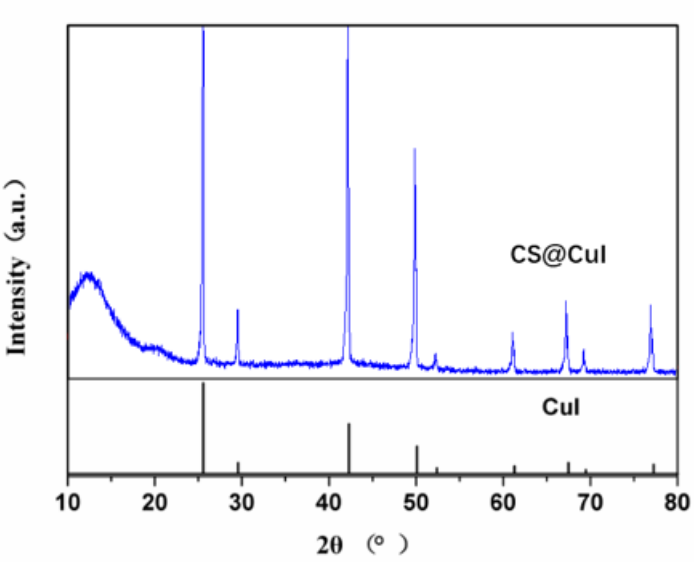
General Information and Materials

Unless otherwise stated, all experiments were carried out open in the air. Reactions were monitored by thin-layer chromatography (TLC). TLC was performed using Huanghai 8±0.2 μm precoated glass plates (0.25 mm) and visualized by UV fluorescence quenching, $KMnO_4$, or phosphomolybdic acid staining. Huanghai silica gel (200 – 300 mess) was used for chromatography. ^1H NMR spectra were recorded at room temperature on a Bruker Advance III 400 MHz spectrometer, and were reported relative to residual $CDCl_3$ (δ 7.26 ppm). ^{13}C NMR spectra were recorded on a Bruker Advance III 400 MHz spectrometer (100 MHz) and were reported relative to $CDCl_3$ (δ 77.16 ppm). Data for ^1H NMR and ^{13}C NMR were reported as chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration) using standard abbreviations for multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, m = multiplet, and brs = broad signal. Unless otherwise noted, all reagents were purchased commercially and used without further purification. Petroleum ether (PE) (60 – 90 ^oC) and ethyl acetate (EA) were used as eluent for silica gel chromatography.

General Procedure for Preparing the Chitosan-Supported on CuI

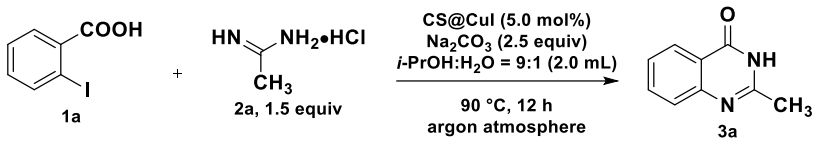
General procedure: Preparation method according to known literature, [1]to a 20 mL flask equipped with a magnetic stirring bar were added CuI (500.2 mg), chitosan (499.8 mg) and H_2O (10.0 mL), the whole system were stirred at room temperature for 3 h. After completion of the reaction, filtered and washed with water (50 mL). Then the filter residue was dried at 50 ^oC to obtain the chitosan-supported on CuI (CS@CuI) and the content of copper in the catalyst was 14.6% by Inductively Coupled Plasma (ICP) atomic emission spectrometry. At the same time, the catalytic material was characterized by XRD, the results show that the CS@CuI diffraction peak corresponds to CuI standard card (JCPDS,

06-0246), indicating that the copper ions on the catalyst are mainly in the form of CuI (Scheme S1).



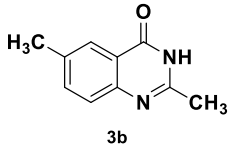
Scheme S1 XRD spectra of CS@CuI

General Procedure for Preparing the Quinazolinones



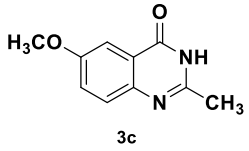
General procedure: Under argon atmosphere, to a 3.0 mL reaction tube equipped with a magnetic stirring bar were added **1a** (124.1 mg, 0.5 mmol), amidines hydrochloride (70.7 mg, 0.75 mmol, 1.5 equiv), CS@CuI (10.0 mg, 5.0 mol%), Na_2CO_3 (132.6 mg, 1.25 mmol) and 2.0 mL of mixed solvents (*i*-PrOH: H_2O = 9:1). The whole reaction was stirred at 90 °C for 12 h. After completion the reaction, it was cooled to room temperature, quenched with H_2O and filtered through celite. The whole aqueous solution was extracted with EA (10 mL × 3), separated and combined the organic phase, then washed with brine, dried over anhydrous Na_2SO_4, filtered and the organic solvents were removed under vacuum and the desired product **3a** (96% yield) was obtained

as a white solid after purification by silica gel chromatography (PE: EA = 5:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.20 (brs, 1H), 8.07 (d, J = 6.3 Hz, 1H), 7.76 (t, J = 7.7 Hz, 1H), 7.56 (d, J = 8.1 Hz, 1H),7.45 (t, J = 7.2 Hz, 1H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.2, 154.7, 149.4, 134.7, 127.0, 126.3, 126.1, 121.1, 21.9. [2]



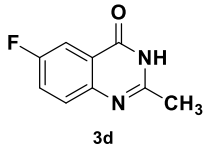
3b

2,6-Dimethylquinazolin-4(3*H*)-one **3b**: ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.10 (brs, 1H), 7.86 (s, 1H), 7.58 (d, J = 8.2 Hz, 1H), 7.47 (d, J = 8.2 Hz, 1H), 2.42 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.7, 153.3, 146.9, 135.5, 135.4, 126.4, 125.0, 120.4, 21.4, 20.7. [3]



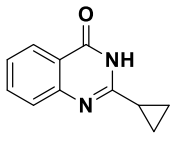
3c

6-Methoxy-2-methylquinazolin-4(3*H*)-one **3c**: ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.18 (brs, 1H), 7.52 (d, J = 8.9 Hz, 1H), 7.45 (d, J = 3.0 Hz, 1H), 7.37 (dd, J = 8.9, 3.0 Hz, 1H), 3.84 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.5, 157.1, 151.8, 143.5, 128.3, 123.7, 121.3, 105.7, 55.5, 21.2. [4]



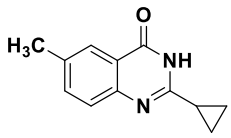
3d

6-Fluoro-2-methylquinazolin-4(3*H*)-one **3d**: ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.38 (brs, 1H), 7.80 – 7.74 (m, 1H), 7.73 – 7.66 (m, 2H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.2 ($J_{C\text{-}F}$ = 3.9 Hz), 159.6 ($J_{C\text{-}F}$ = 242.7 Hz), 153.8 ($J_{C\text{-}F}$ = 2.0 Hz), 145.9 ($J_{C\text{-}F}$ = 1.8 Hz), 129.4 ($J_{C\text{-}F}$ = 8.3 Hz), 122.7 ($J_{C\text{-}F}$ = 23.7 Hz), 121.8 ($J_{C\text{-}F}$ = 2.8 Hz), 110.3 ($J_{C\text{-}F}$ = 23.1 Hz), 21.4. [5]



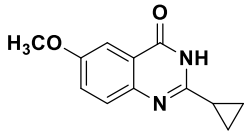
3e

2-Cyclopropylquinazolin-4(3*H*)-one **3e**: 1H NMR (400 MHz, DMSO-d_6) δ 12.46 (brs, 1H), 8.04 (d, J = 6.4 Hz, 1H), 7.72 (t, J = 8.5 Hz, 1H), 7.48 (d, J = 7.7 Hz, 1H), 7.40 (t, J = 8.1 Hz, 1H), 2.01 – 1.89 (m, 1H), 1.13 – 1.07 (m, 2H), 1.06 – 0.98 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.6, 159.0, 149.1, 134.3, 126.5, 125.8, 125.3, 120.6, 13.5, 9.5. [6]



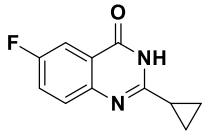
3f

2-Cyclopropyl-6-methylquinazolin-4(3*H*)-one **3f**: ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.35 (brs, 1H), 7.84 (s, 1H), 7.55 (d, *J* = 8.3 Hz, 1H), 7.38 (d, *J* = 8.3 Hz, 1H), 2.40 (s, 3H), 2.00 – 1.87 (m, 1H), 1.10 – 1.05 (m, 2H), 1.04 – 0.97 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.0, 158.5, 147.6, 136.0, 135.3, 126.8, 125.6, 120.8, 21.2, 13.8, 9.8. [7]



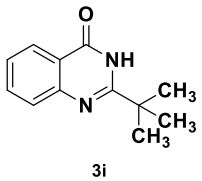
3g

2-Cyclopropyl-6-methoxyquinazolin-4(3*H*)-one **3g**: ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.40 (brs, 1H), 7.44 (s, 1H), 7.43 (d, *J* = 5.2 Hz, 1H), 7.33 (dd, *J* = 9.0, 3.0 Hz, 1H), 3.83 (s, 3H), 1.97 – 1.86 (m, 1H), 1.08 – 1.02 (m, 2H), 1.01 – 0.94 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.9, 157.2, 157.0, 144.1, 128.6, 124.3, 121.7, 106.1, 55.9, 13.7, 9.6. [8]



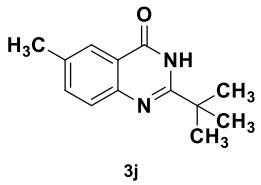
3h

2-Cyclopropyl-6-fluoroquinazolin-4(3*H*)-one **3h**: ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.6 (brs, 1H), 7.71 (dd, *J* = 8.7, 3.0 Hz, 1H), 7.65 – 7.57 (m, 1H), 7.56 – 7.51 (m, 1H), 2.01 – 1.89 (m, 1H), 1.11 – 1.05 (m, 2H), 1.04 – 0.98 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.1, 159.2 ($J_{C\text{-}F}$ = 243.1 Hz), 158.0, 146.0, 129.2 ($J_{C\text{-}F}$ = 8.0 Hz), 122.7 ($J_{C\text{-}F}$ = 23.8 Hz), 121.7 ($J_{C\text{-}F}$ = 8.0 Hz), 110.3 ($J_{C\text{-}F}$ = 22.9 Hz), 13.4, 9.6. [9]



3i

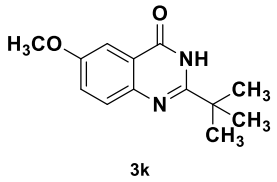
2-(*tert*-Butyl)quinazolin-4(3*H*)-one **3i**: ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.9 (brs, 1H), 8.09 (d, *J* = 7.9 Hz, 1H), 7.78 (t, *J* = 8.5 Hz, 1H), 7.61 (d, *J* = 7.7 Hz, 1H), 7.47 (t, *J* = 8.1 Hz, 1H), 1.35 (s, 9H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 163.1, 162.8, 148.8, 134.8, 127.8, 126.7, 126.1, 121.1, 37.7, 28.3. [7]



3j

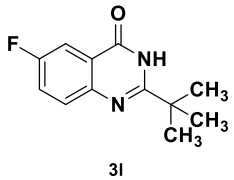
2-(*tert*-Butyl)-6-methylquinazolin-4(3*H*)-one **3j**: ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.83 (brs, 1H), 7.89 (s, 1H), 7.60 (d, *J* = 8.4 Hz, 1H), 7.52 (d, *J* = 8.2 Hz, 1H), 2.43 (s, 3H),

1.34 (s, 9H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.7, 162.2, 146.8, 136.2, 136.0, 127.6, 125.4, 120.8, 37.6, 28.3, 21.2.



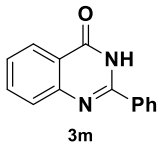
3k

2-(*tert*-Butyl)-6-methoxyquinazolin-4(3*H*)-one **3k**: ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.86 (s, 1H), 7.56 (d, *J* = 8.8 Hz, 1H), 7.48 (d, *J* = 3.0 Hz, 1H), 7.37 (dd, *J* = 8.9, 3.0 Hz, 1H), 3.86 (s, 3H), 1.34 (s, 9H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.6, 160.8, 157.8, 143.2, 129.4, 124.2, 121.8, 106.0, 56.0, 37.5, 28.3.



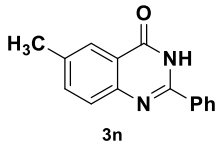
3l

2-(*tert*-Butyl)-6-fluoroquinazolin-4(3*H*)-one **3l**: ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.09 (brs, 1H), 7.80 (dd, *J* = 8.5, 2.8 Hz, 1H), 7.76 – 7.66 (m, 2H), 1.39 (s, 9H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.6 ($J_{C\text{-}F}$ = 2.2 Hz), 162.2 ($J_{C\text{-}F}$ = 3.6 Hz), 160.2 ($J_{C\text{-}F}$ = 243.1 Hz), 145.6 ($J_{C\text{-}F}$ = 1.8 Hz), 130.6 ($J_{C\text{-}F}$ = 8.3 Hz), 123.2 ($J_{C\text{-}F}$ = 23.9 Hz), 122.3 ($J_{C\text{-}F}$ = 4.8 Hz), 110.7 ($J_{C\text{-}F}$ = 23.0 Hz), 37.7, 28.2.



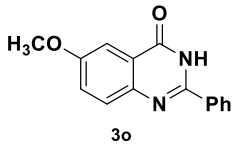
3m

2-Phenylquinazolin-4(3*H*)-one **3m**: ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.43 (brs, 1H), 8.27 – 8.09 (m, 3H), 7.85 (t, *J* = 7.6 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.65 – 7.46 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.3, 152.4, 148.7, 134.6, 132.7, 131.4, 128.6, 127.8, 127.4, 126.6, 125.9, 121.0. [10]



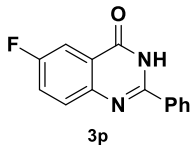
3n

6-Methyl-2-phenylquinazolin-4(3*H*)-one **3n**: ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.45 (brs, 1H), 8.22 – 8.11 (m, 2H), 7.95 (s, 1H), 7.68 – 7.62 (m, 2H), 7.61 – 7.49 (m, 3H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.2, 151.5, 146.7, 136.3, 135.9, 132.8, 131.2, 128.6, 127.6, 127.4, 125.3, 120.7, 20.9. [3]



3o

6-Methoxy-2-phenylquinazolin-4(3*H*)-one **3o**: ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.50 (brs, 1H), 8.22 – 8.11 (m, 2H), 7.70 (d, J = 8.9 Hz, 1H), 7.61 – 7.49 (m, 4H), 7.44 (dd, J = 8.9, 3.0 Hz, 1H), 3.89 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.1, 157.7, 150.2, 143.2, 132.8, 131.1, 129.2, 128.6, 127.5, 124.1, 121.8, 105.9, 55.7. [11]



3p

6-Fluoro-2-phenylquinazolin-4(3*H*)-one **3p**: ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.67 (brs, 1H), 8.16 (d, J = 6.7 Hz, 2H), 7.88 – 7.78 (m, 2H), 7.76 – 7.68 (m, 1H), 7.63 – 7.51 (m, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.8, 160.0 ($J_{C\text{-}F}$ = 244.0 Hz), 151.9, 145.6, 132.6, 131.4, 130.3 ($J_{C\text{-}F}$ = 7.9 Hz), 128.6, 127.8, 123.1 ($J_{C\text{-}F}$ = 23.9 Hz), 122.2 ($J_{C\text{-}F}$ = 8.5 Hz), 110.5 ($J_{C\text{-}F}$ = 23.1 Hz). [5]

References

[1] Baig, R. B. N.; Varma, R. S. *Green Chem*. **2013**, *15*, 1839.

[2] Mondal, P. P.; Pal, A.; Prakash, A. K.; Sahoo, B. *Chem. Commun*. **2022**, *58*, 13202.

[3] Wang, X.; Lerchen, A.; Glorius, F. *Org. Lett*. **2016**, *18*, 2090.

[4] Pitta, E.; Balabon, O.; Rogacki, M. K.; Gómez, J.; Cunningham, F.; Joosens, J.; Augustyns, K.; Van der Veken, P.; Bates, R. *Eur. J. Med. Chem*. **2017**, *125*, 890.

[5] Xu, Y.; Xie, Q.; Li, W.; Sun, H.; Wang, Y.; Shao, L. *Tetrahedron* **2015**, *71*, 4853.

[6] Jia, F.-C.; Zhou, Z.-W.; Xu, C.; Wu, Y.-D.; Wu, A.-X. *Org. Lett*. **2016**, *18*, 2942.

[7] Li, Z.; Dong, J.; Chen, X.; Li, Q.; Zhou, Y.; Yin, S.-F. *J. Org. Chem*. **2015**, *80*, 9392.

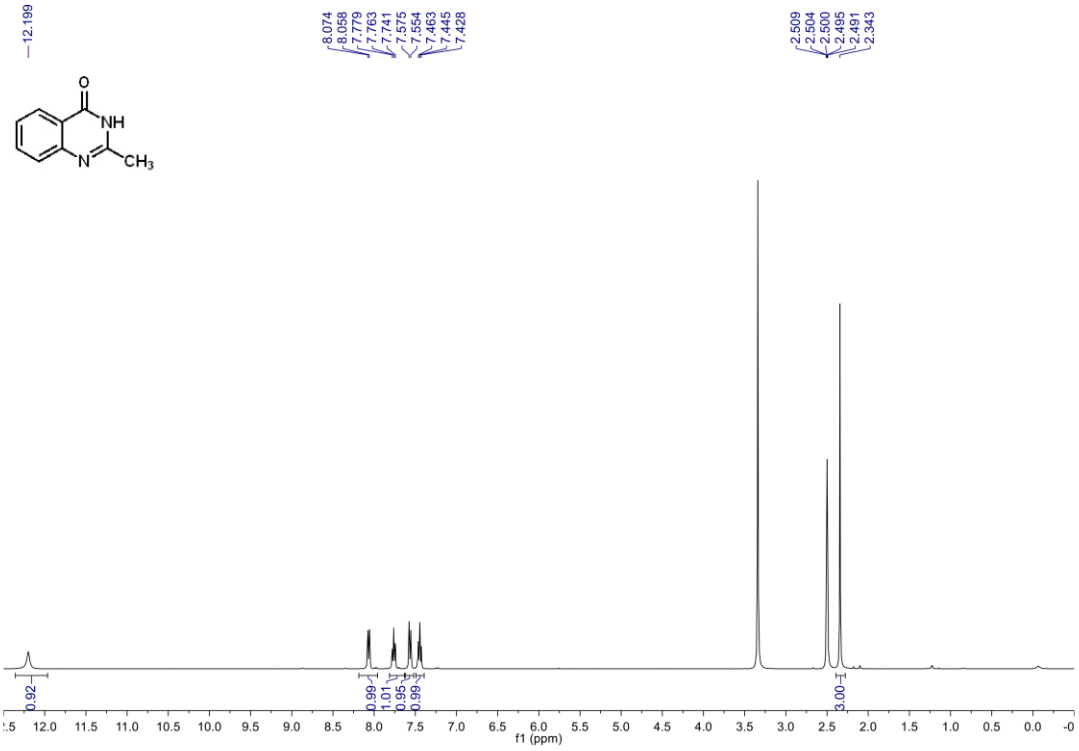
[8] Peddibhotla, S.; Hedrick, M. P.; Hershberger, P.; Maloney, P.R.; Li, Y.; Milewski, M.; Gosalia, P.; Gray, W.; Mehta, A.; Sugarman,E.; Hood, B.; Suyama, E.; Nguyen, K.; Heynen-Genel, S.; Vasile, S.;Salaniwal, S.; Stonich, D.; Su, Y.; Mangravita-Novo, A.; Vicchiarelli,M.; Roth, G. P.; Smith, L. H.; Chung, T. D.; Hanson, G. R.; Thomas,J. B.; Caron, M. G.; Barak, L. S.; Pinkerton, A. B. *ACS Med. Chem. Lett*. **2013**, *4*, 846.

[9] Yu, L.; Wang, M.; Li, P.; Wang, L. *Appl. Organomet. Chem*. **2012**, *26*, 576.

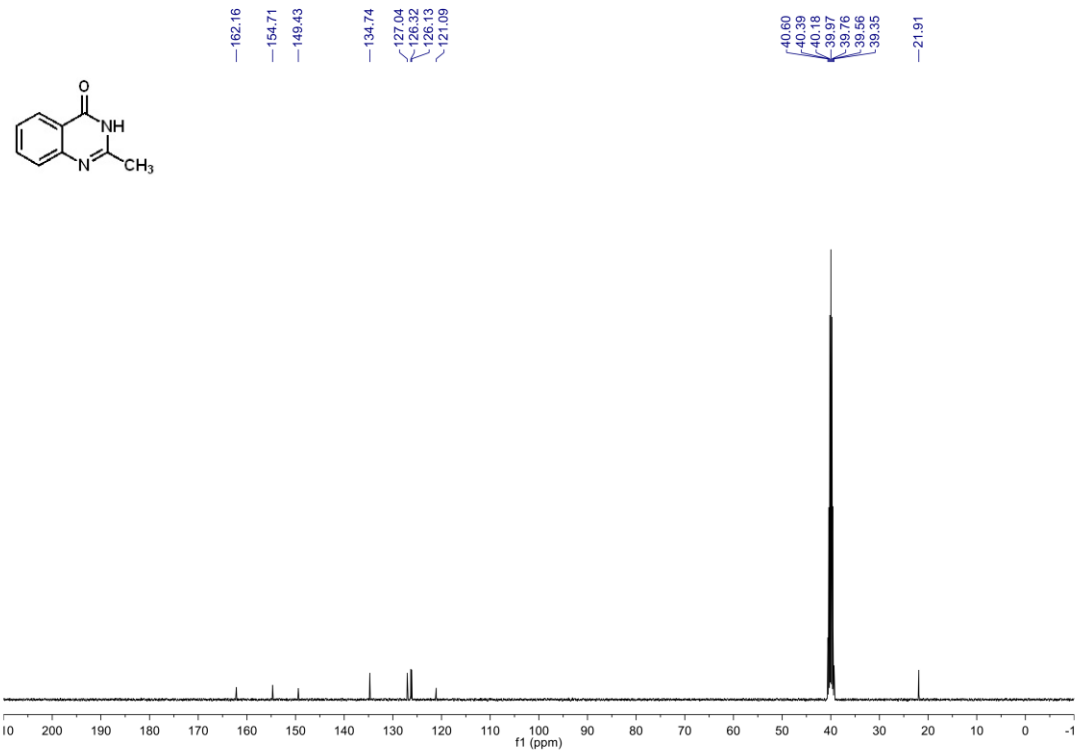
[10] Lv, X.; Abrams, R.; Martin, R. *Angew. Chem., Int. Ed*. **2023**, *62*, No. e202217386.

[11] Xu, G.; Wang, L.; Li, M.; Tao, M.; Zhang, W. *Green Chem*. **2017**, *19*, 5818.

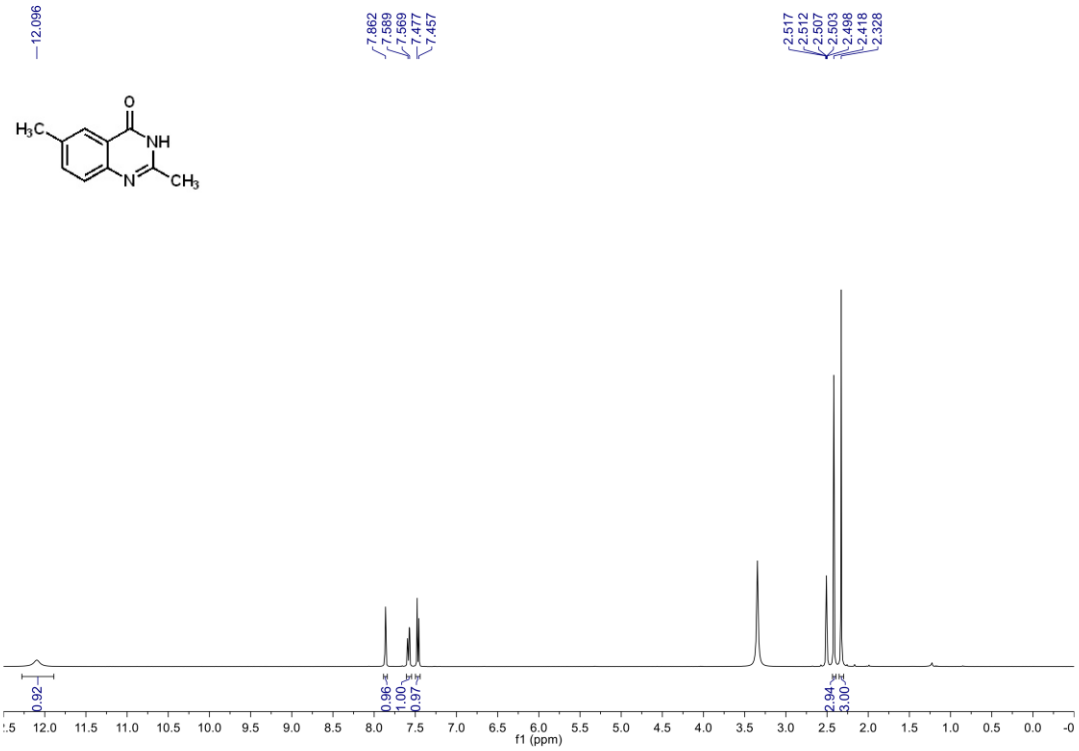
^{1}H NMR spectrum and ^{13}C NMR spectrum



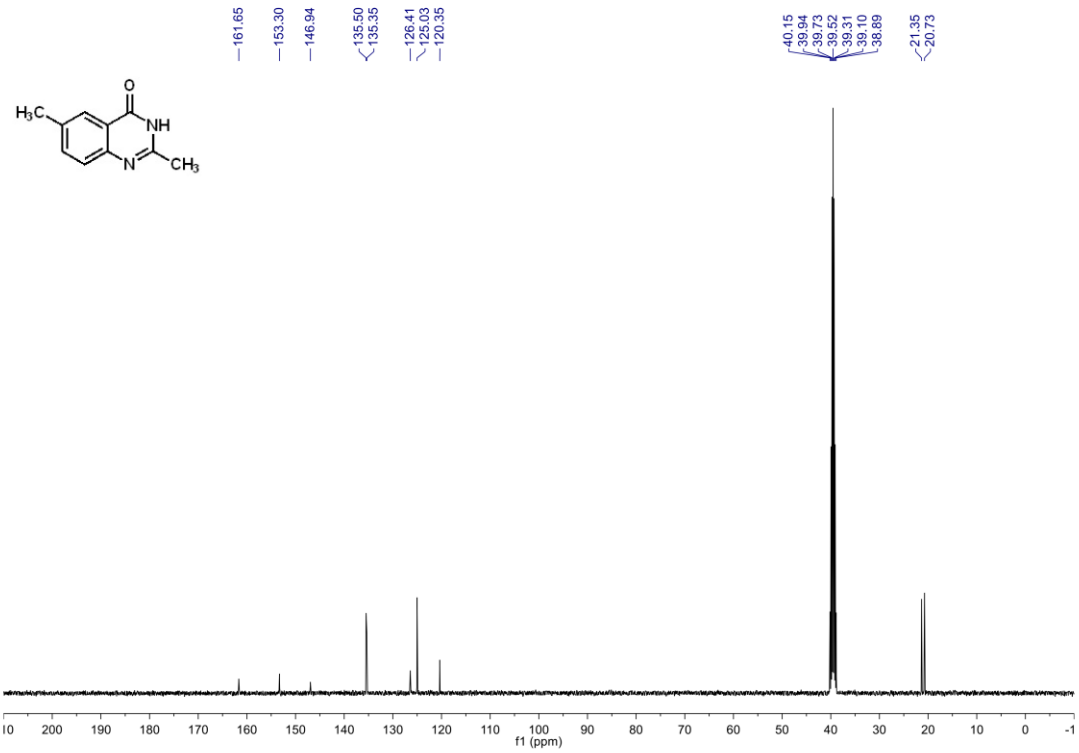
^{1}H NMR (400 MHz, DMSO-d_6) of compound **3a.**



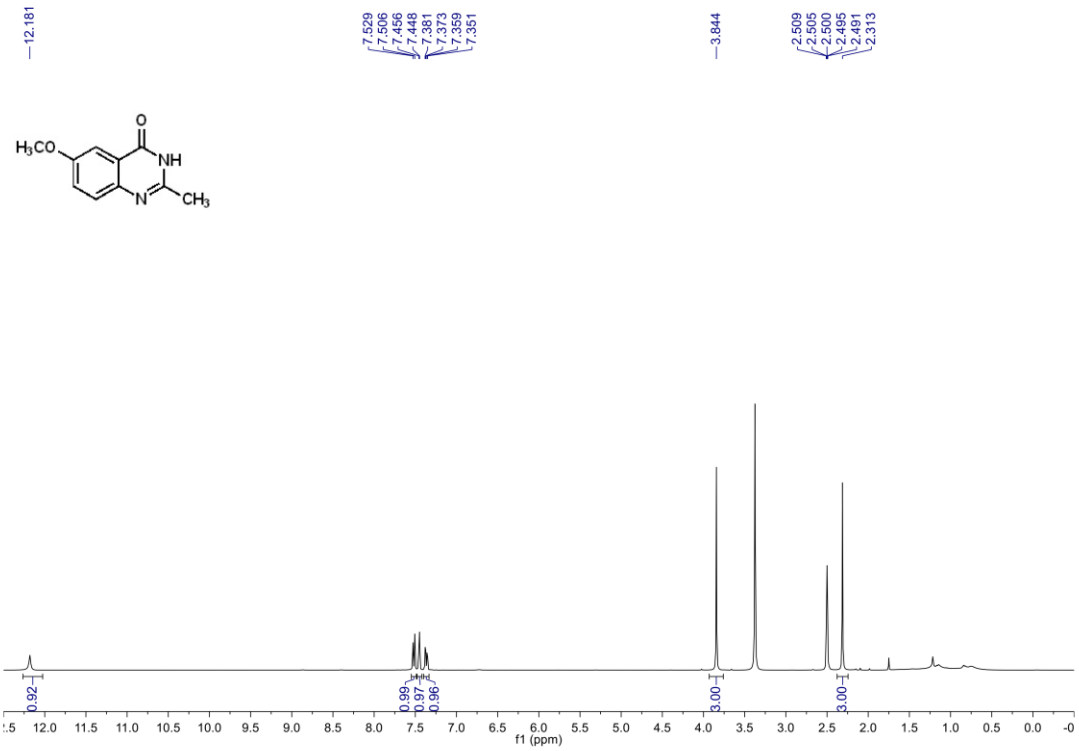
^{13}C NMR (100 MHz, DMSO-d_6) of compound **3a.**



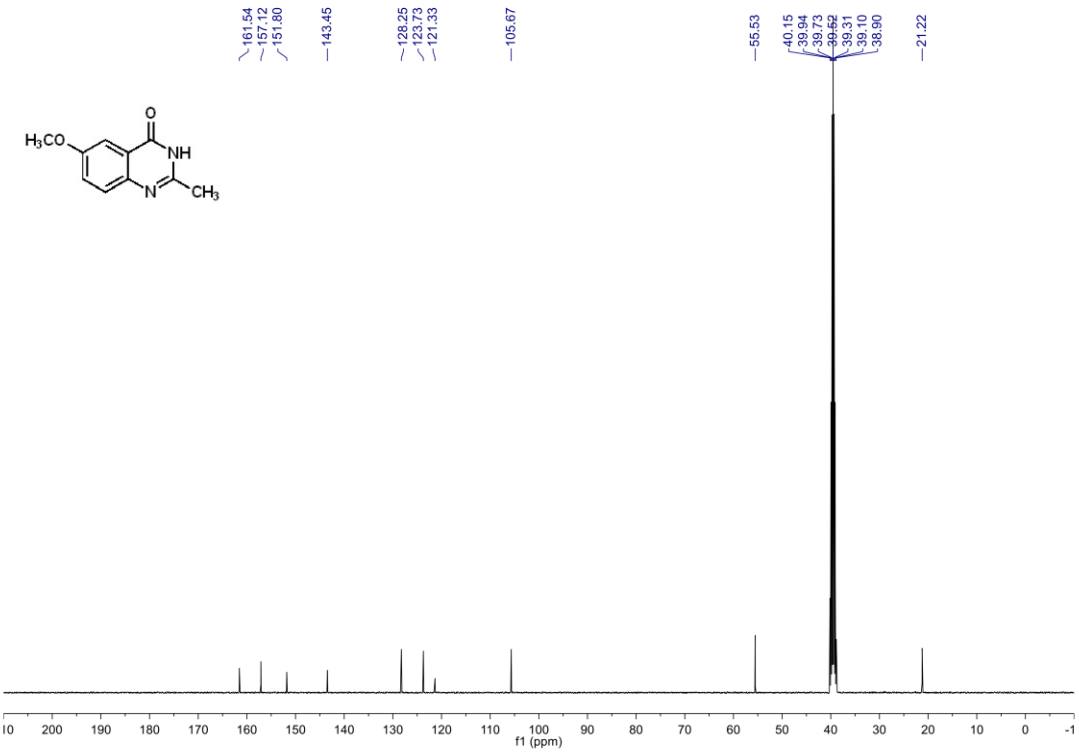
^{1}H NMR (400 MHz, DMSO-d_6) of compound **3b.**



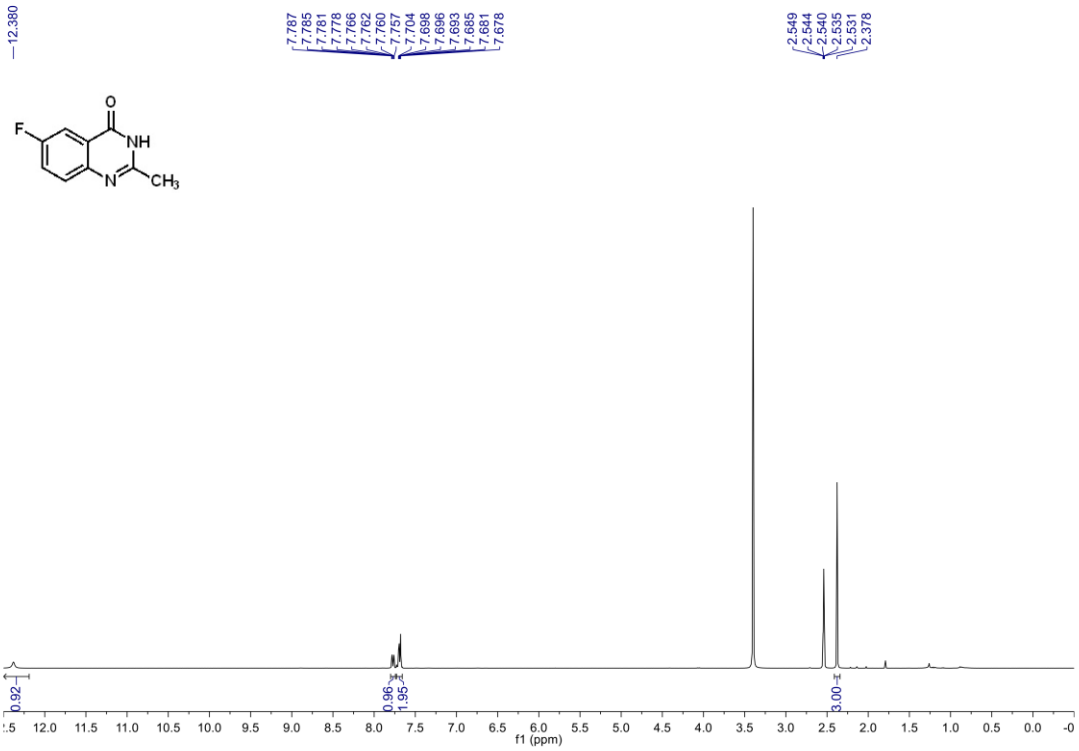
^{13}C NMR (100 MHz, DMSO-d_6) of compound **3b.**



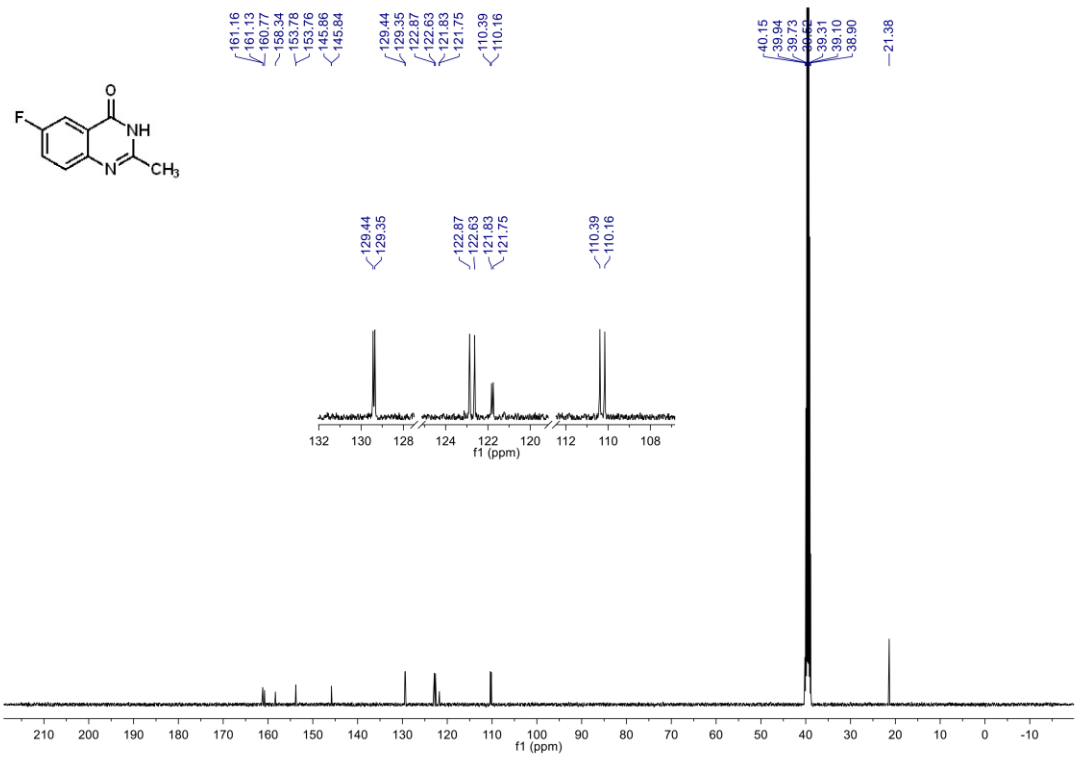
^{1}H NMR (400 MHz, DMSO-d_6) of compound **3c.**



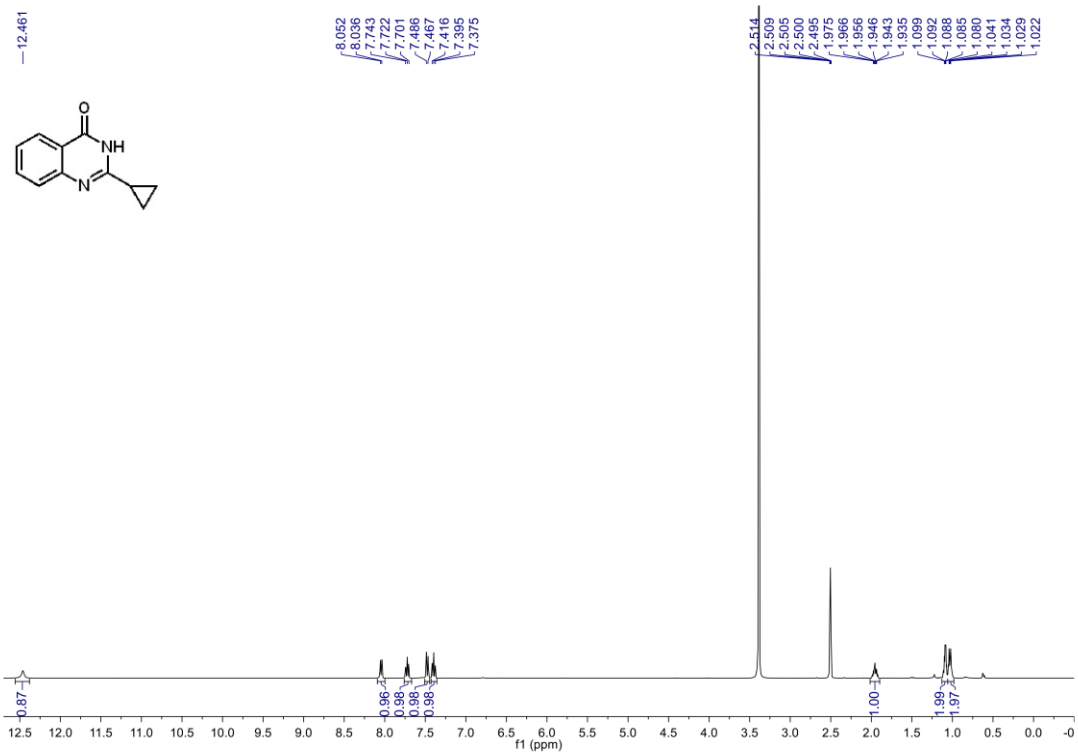
^{13}C NMR (100 MHz, DMSO-d_6) of compound **3c.**



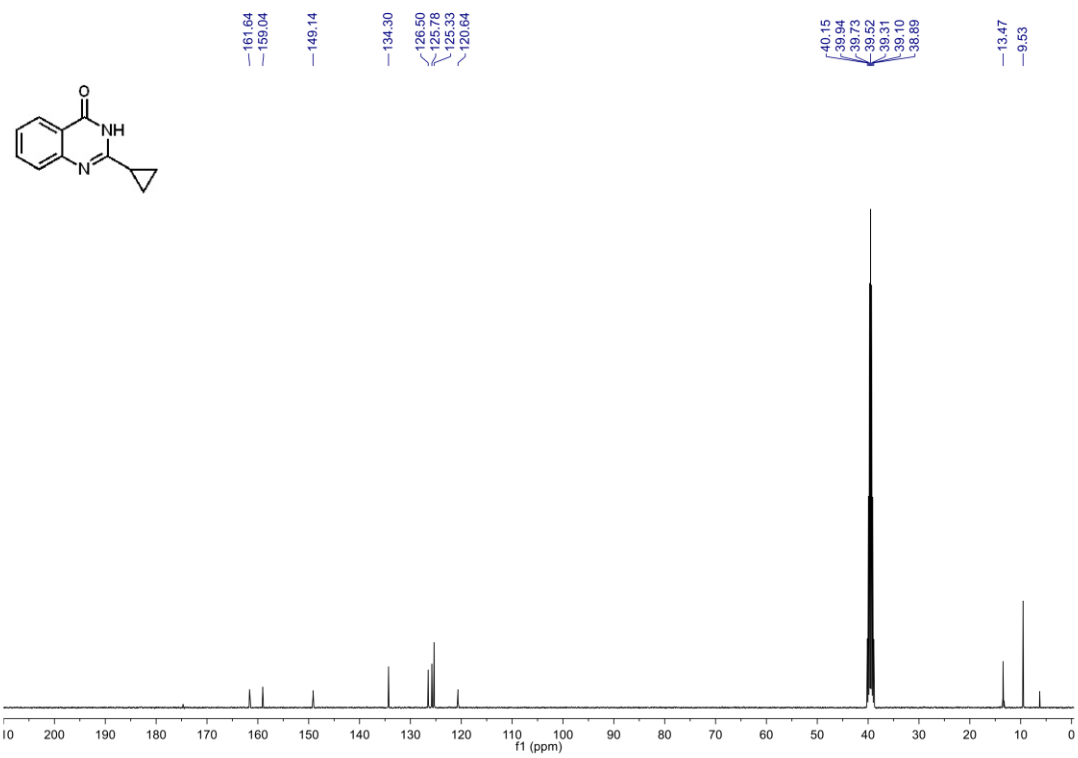
^{1}H NMR (400 MHz, DMSO-d_6) of compound **3d.**



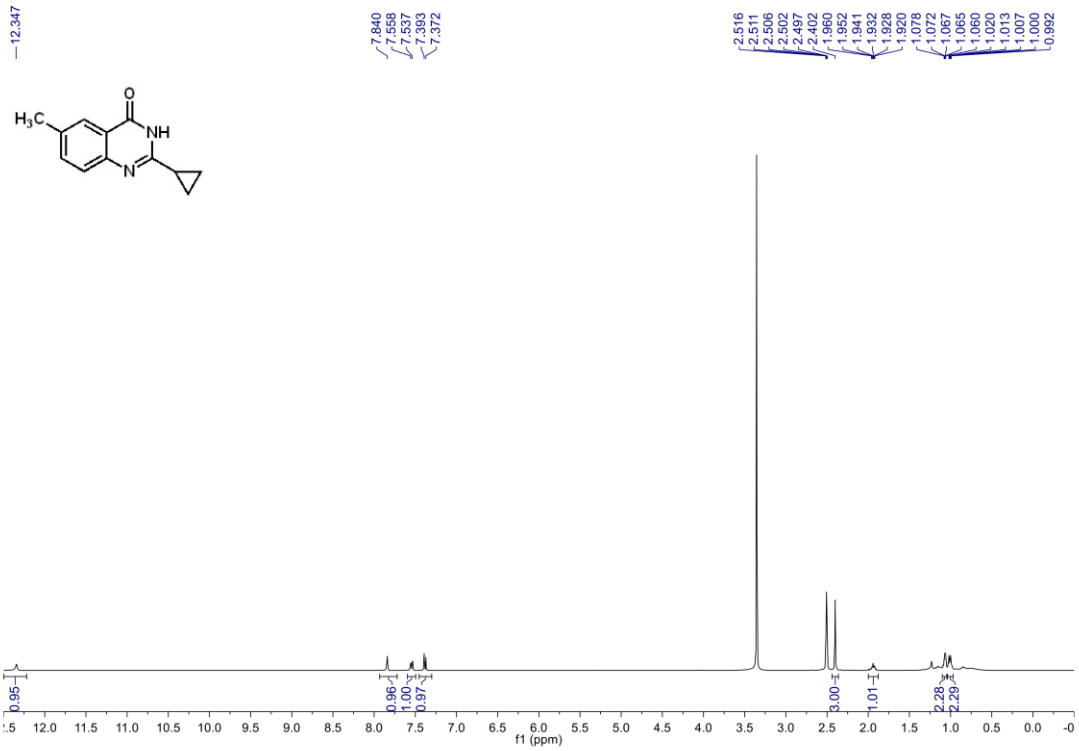
^{13}C NMR (100 MHz, DMSO-d_6) of compound **3d.**



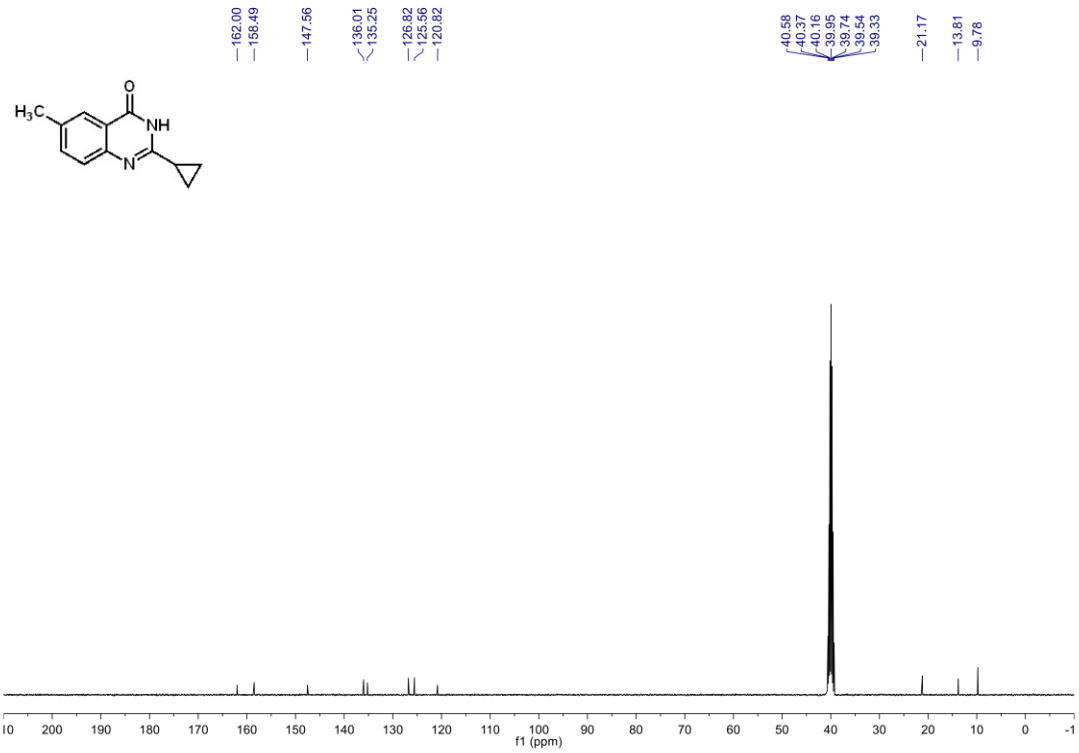
^{1}H NMR (400 MHz, DMSO-d_6) of compound **3e.**



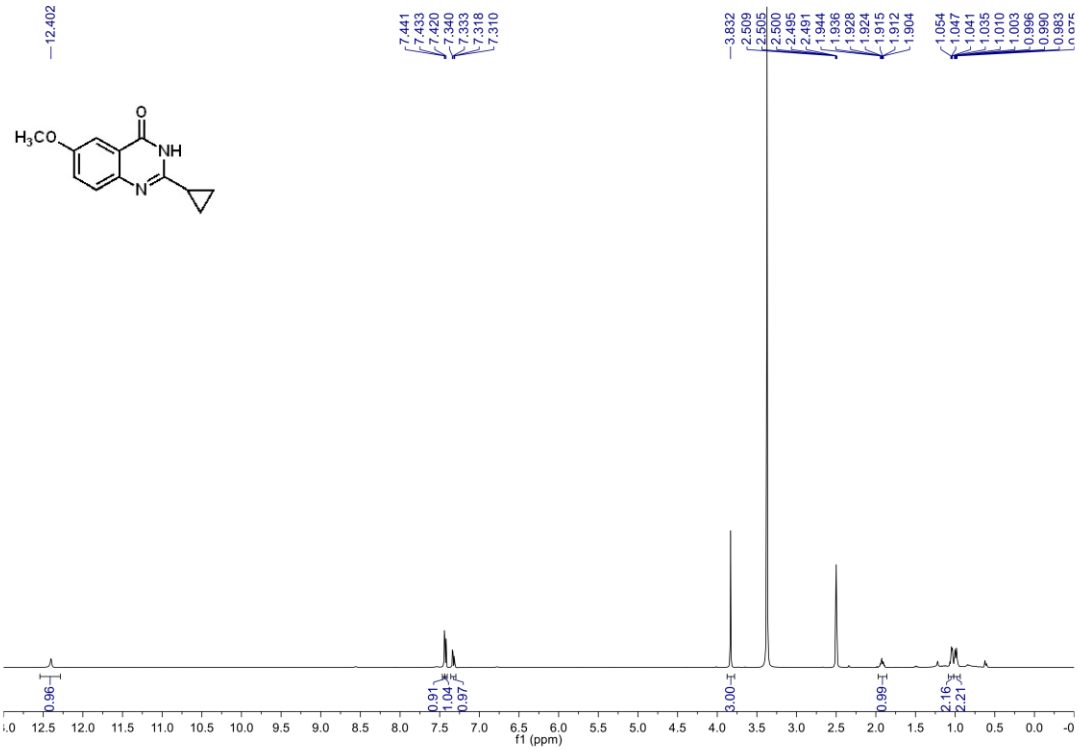
^{13}C NMR (100 MHz, DMSO-d_6) of compound **3e.**



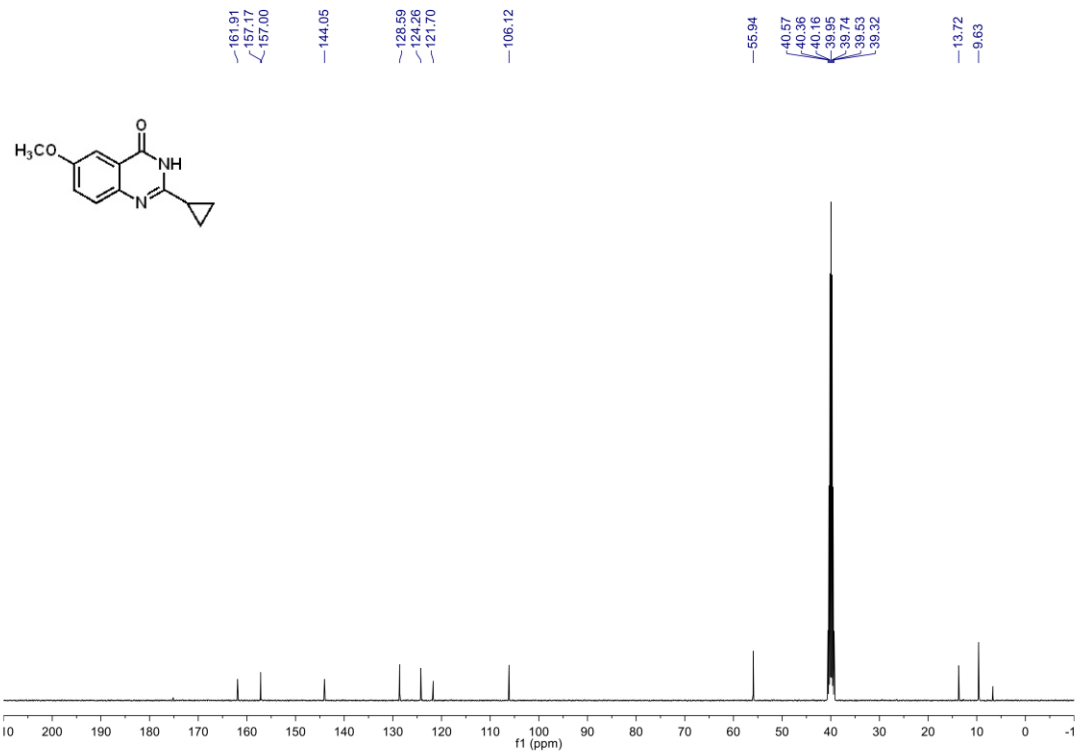
^{1}H NMR (400 MHz, DMSO-d_6) of compound **3f.**



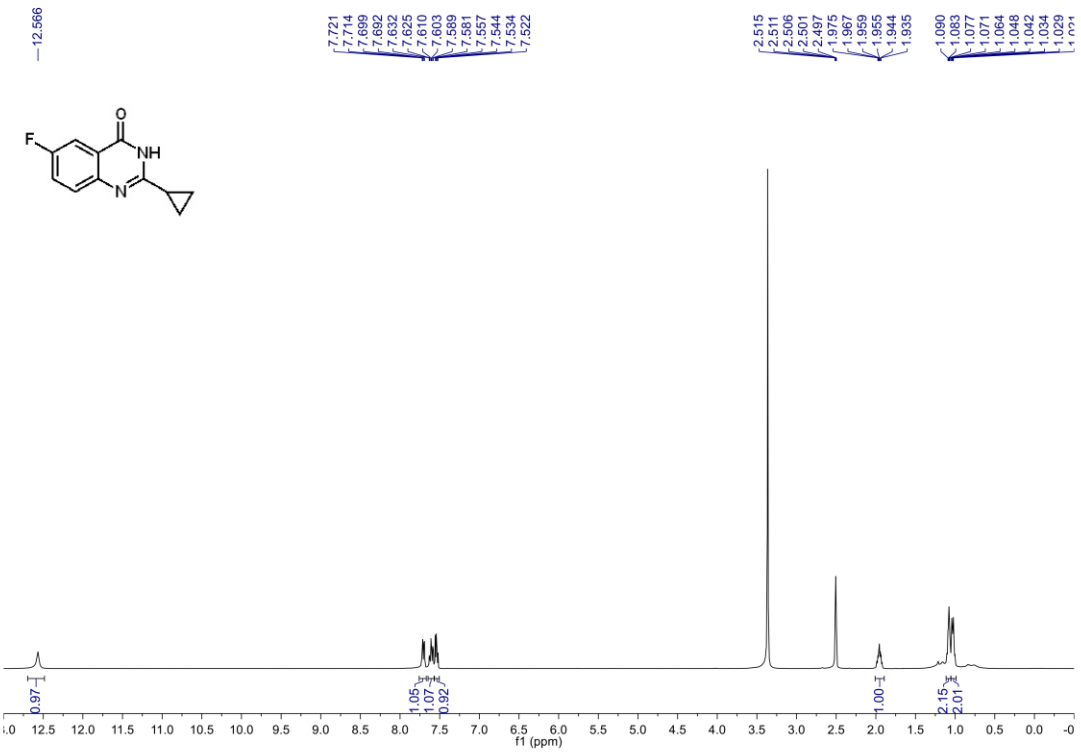
^{13}C NMR (100 MHz, DMSO-d_6) of compound **3f.**



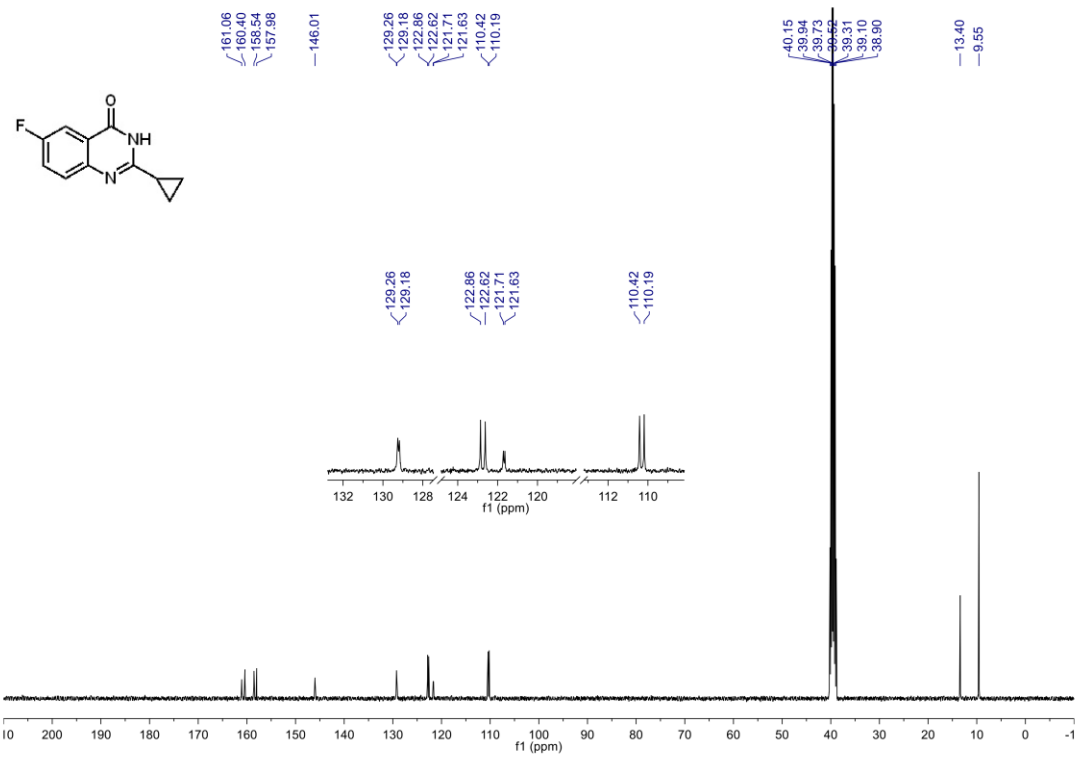
^{1}H NMR (400 MHz, DMSO-d_6) of compound **3g.**



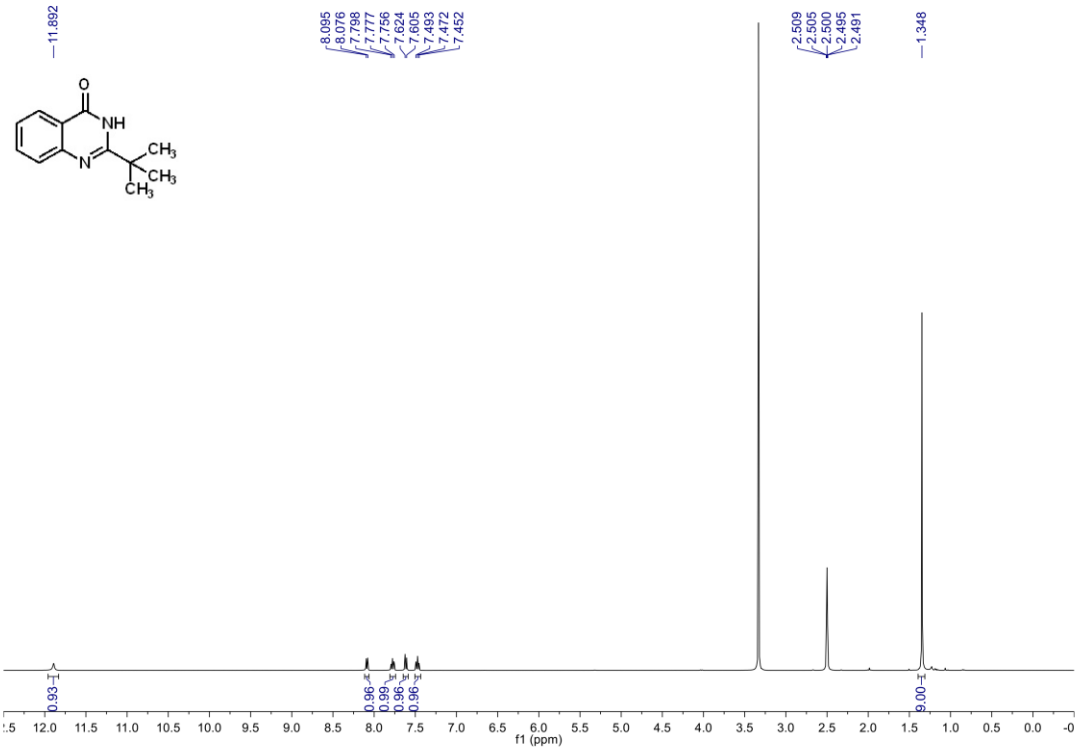
^{13}C NMR (100 MHz, DMSO-d_6) of compound **3g.**



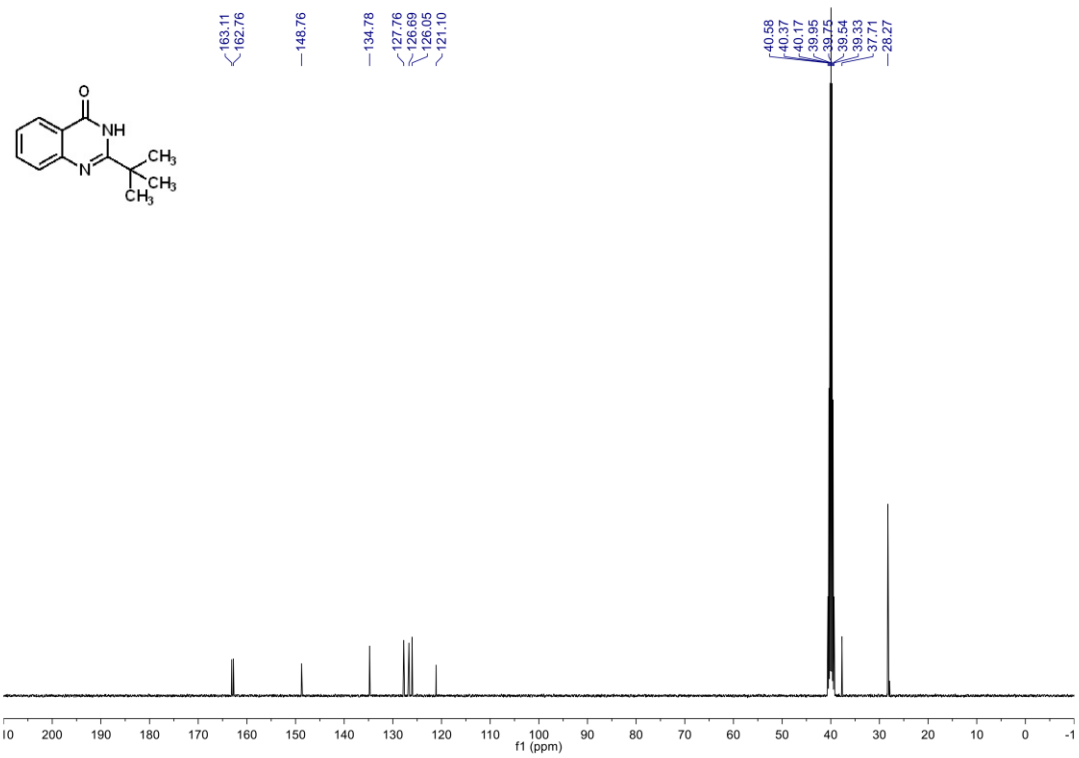
^{1}H NMR (400 MHz, DMSO-d_6) of compound **3h.**



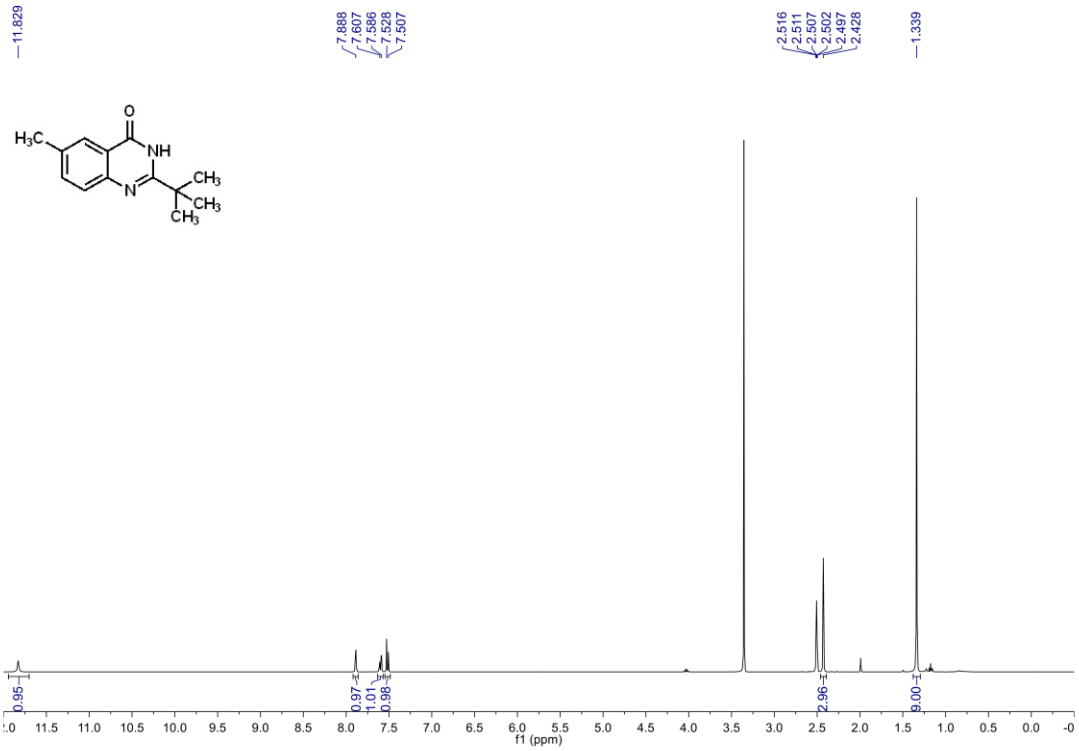
^{13}C NMR (100 MHz, DMSO-d_6) of compound **3h.**



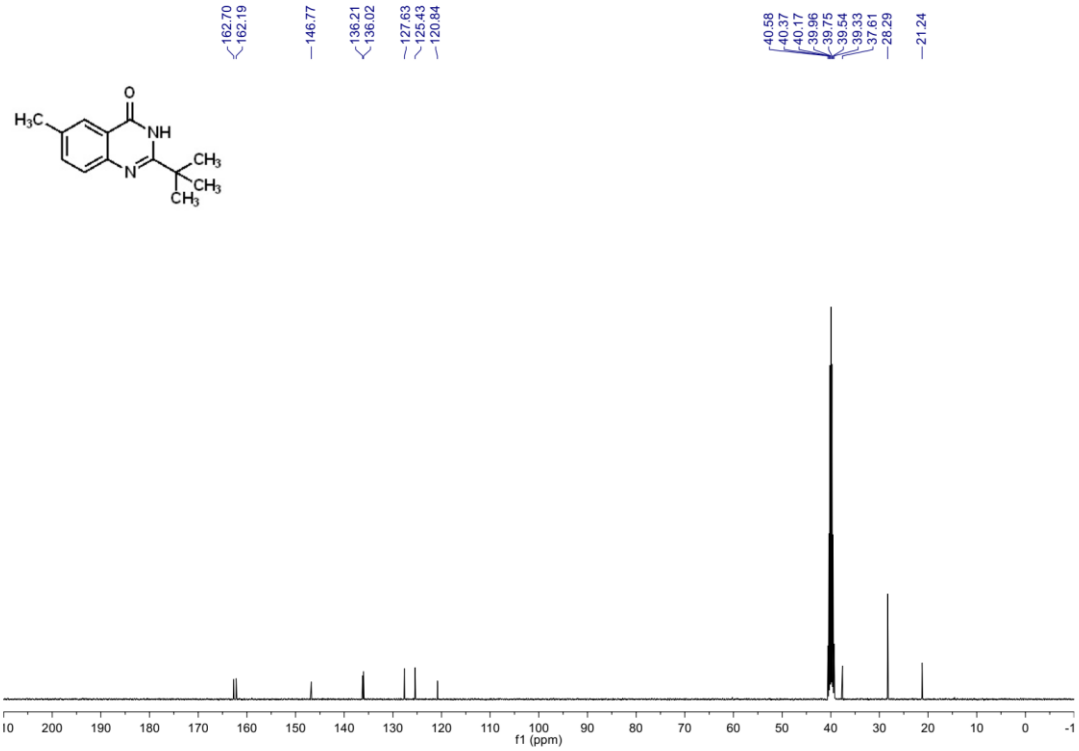
^{1}H NMR (400 MHz, DMSO-d_6) of compound **3i.**



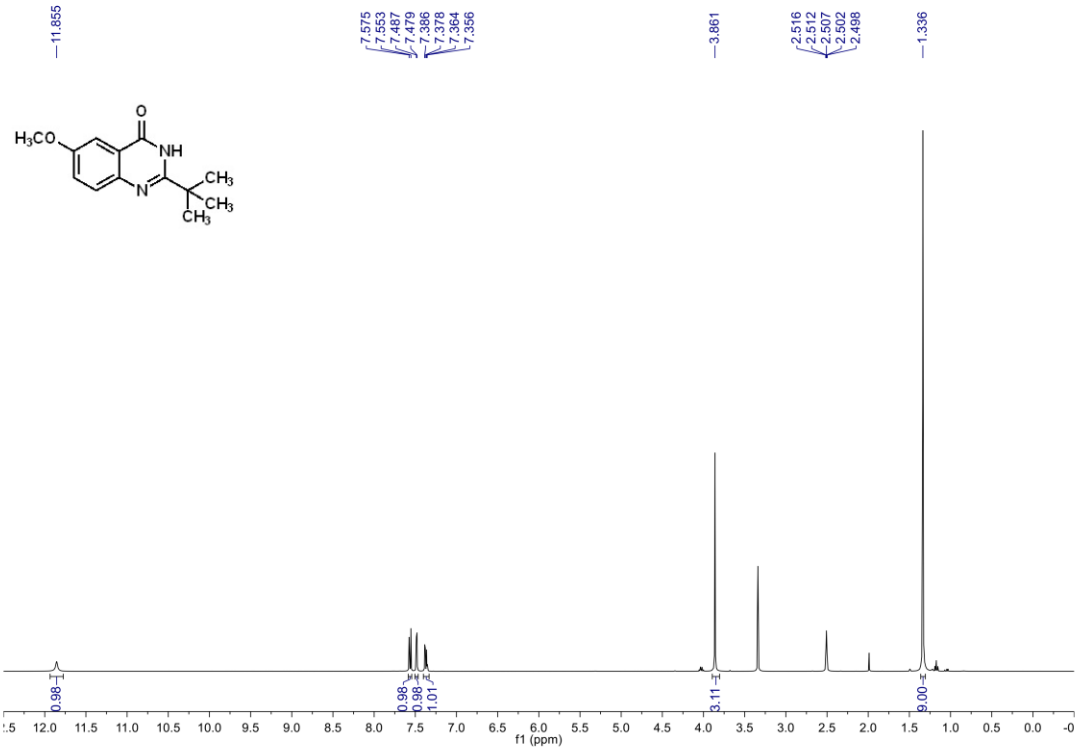
^{13}C NMR (100 MHz, DMSO-d_6) of compound **3i.**



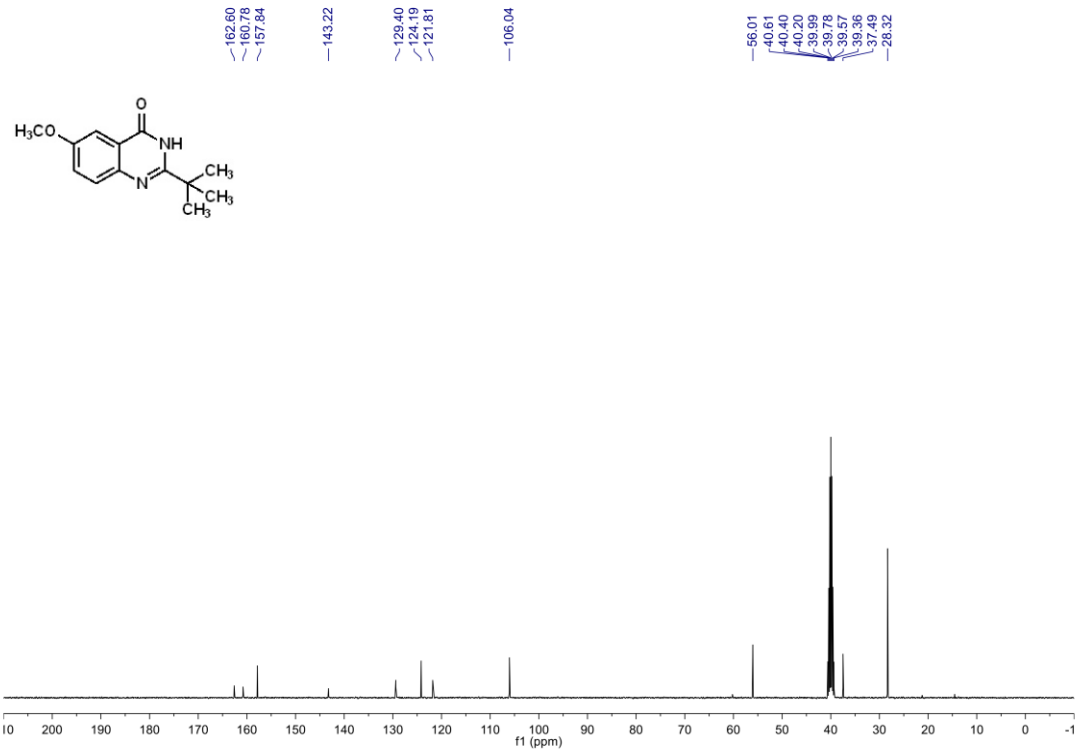
^{1}H NMR (400 MHz, DMSO-d_6) of compound **3j.**



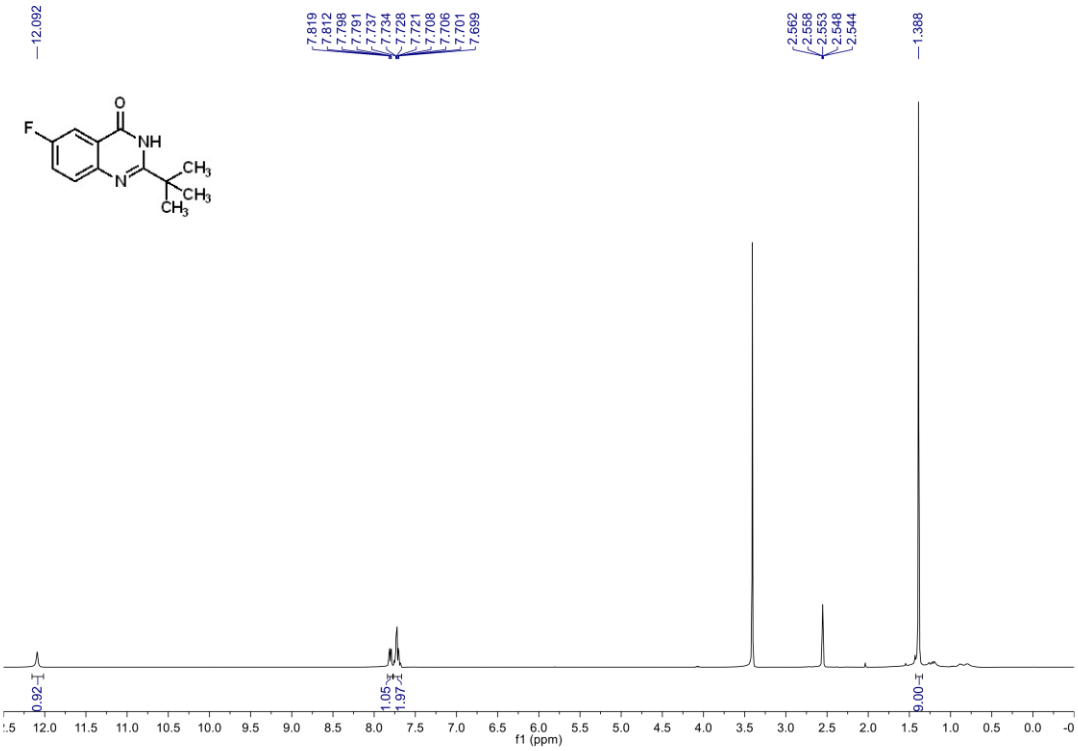
^{13}C NMR (100 MHz, DMSO-d_6) of compound **3j.**



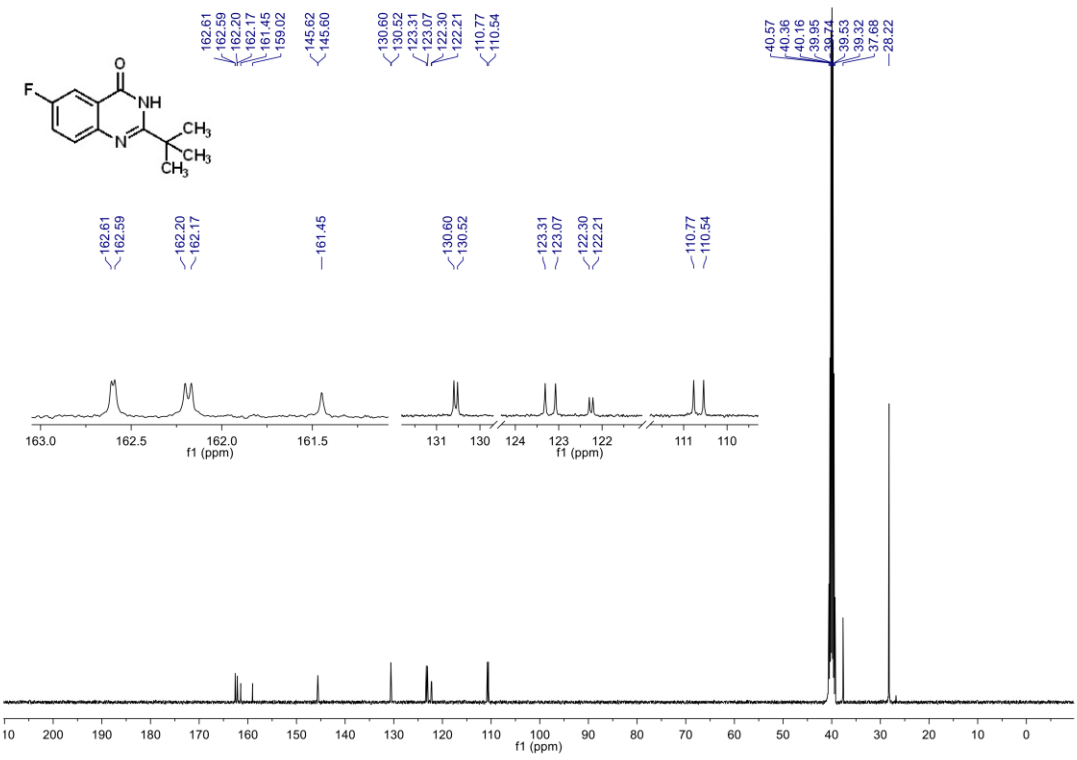
^{1}H NMR (400 MHz, DMSO-d_6) of compound **3k.**



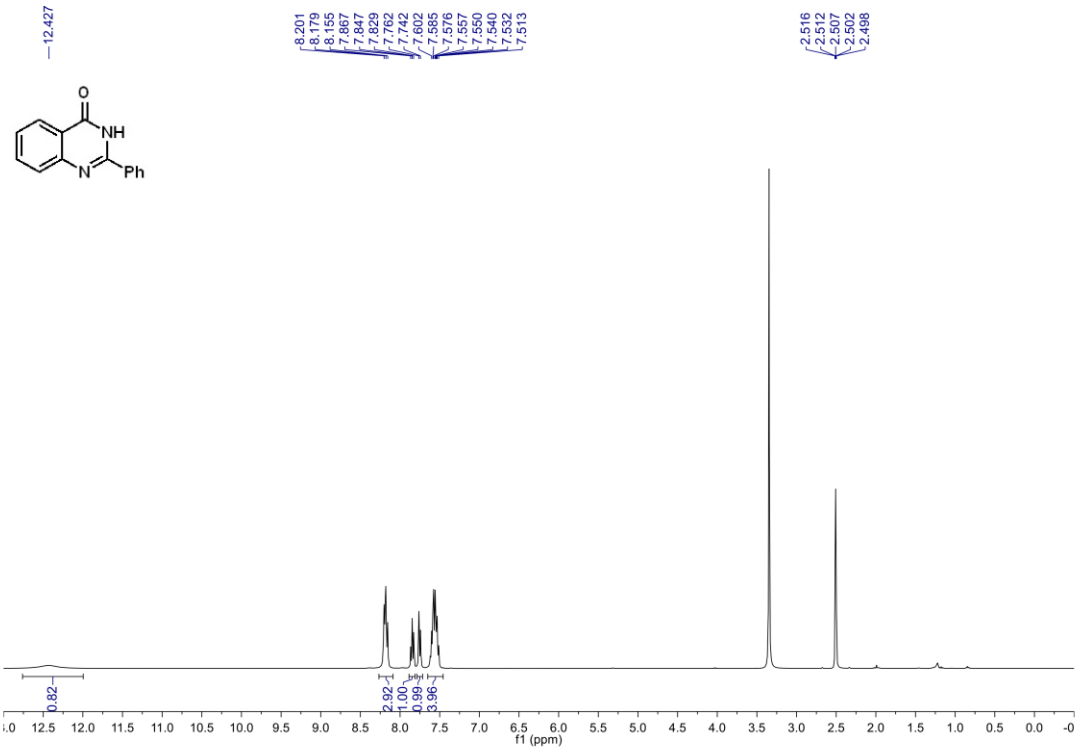
^{13}C NMR (100 MHz, DMSO-d_6) of compound **3k.**



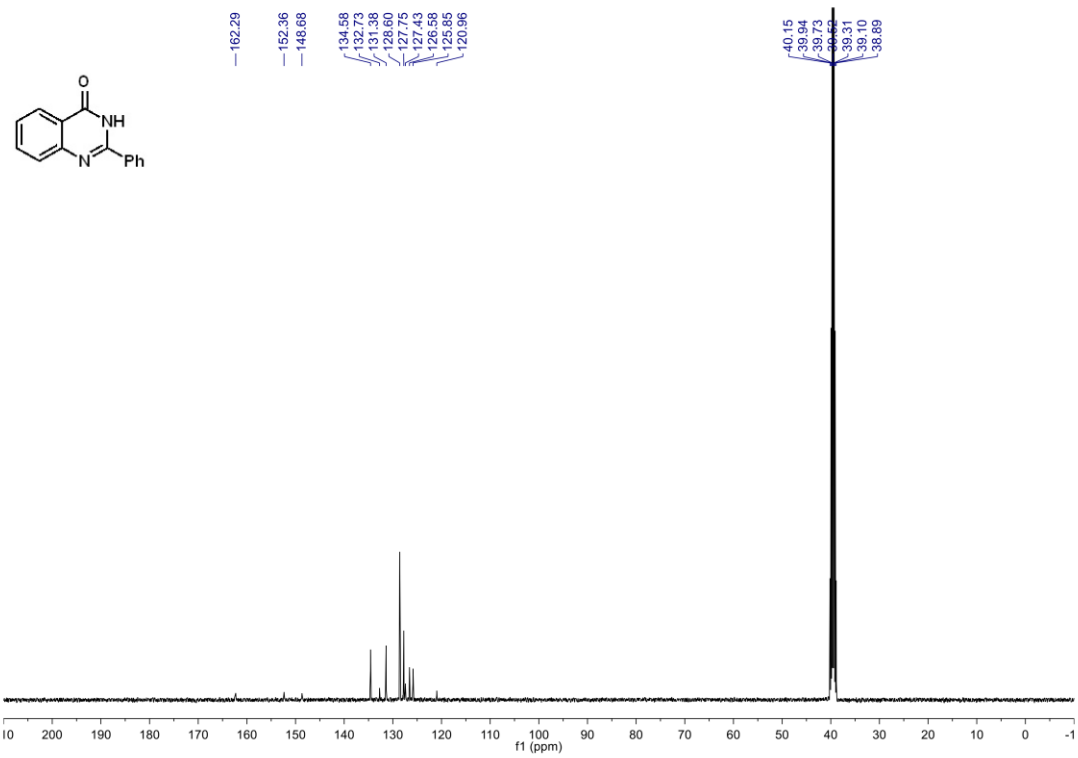
^{1}H NMR (400 MHz, DMSO-d_6) of compound **3l.**



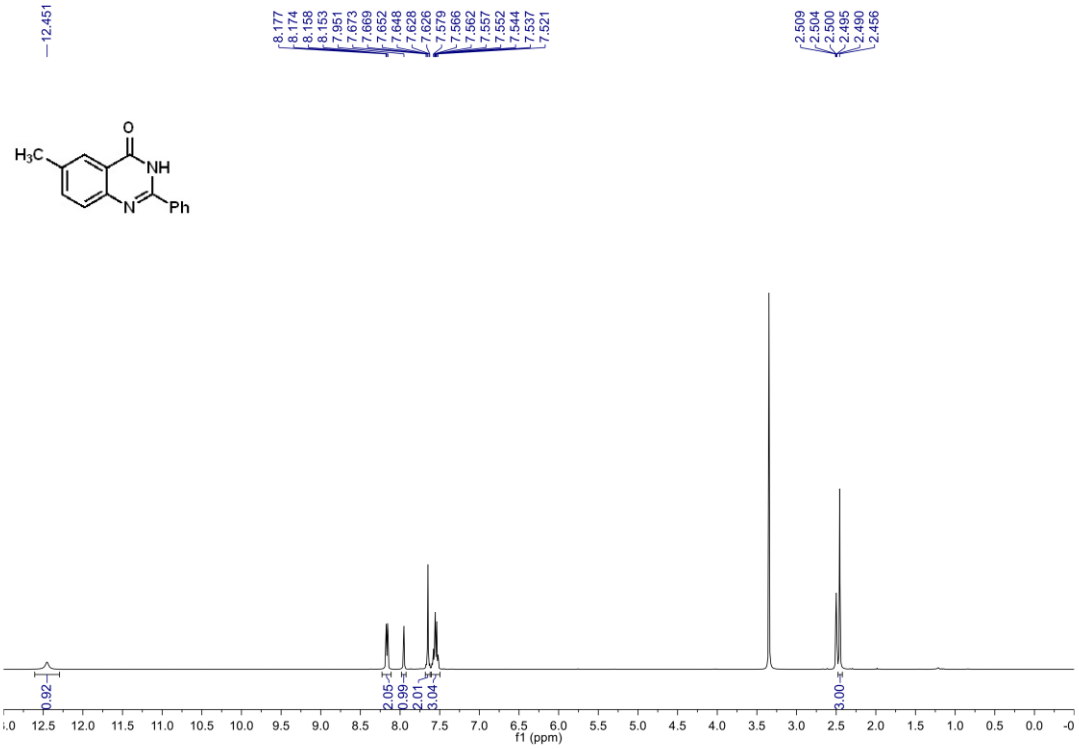
^{13}C NMR (100 MHz, DMSO-d_6) of compound **3l.**



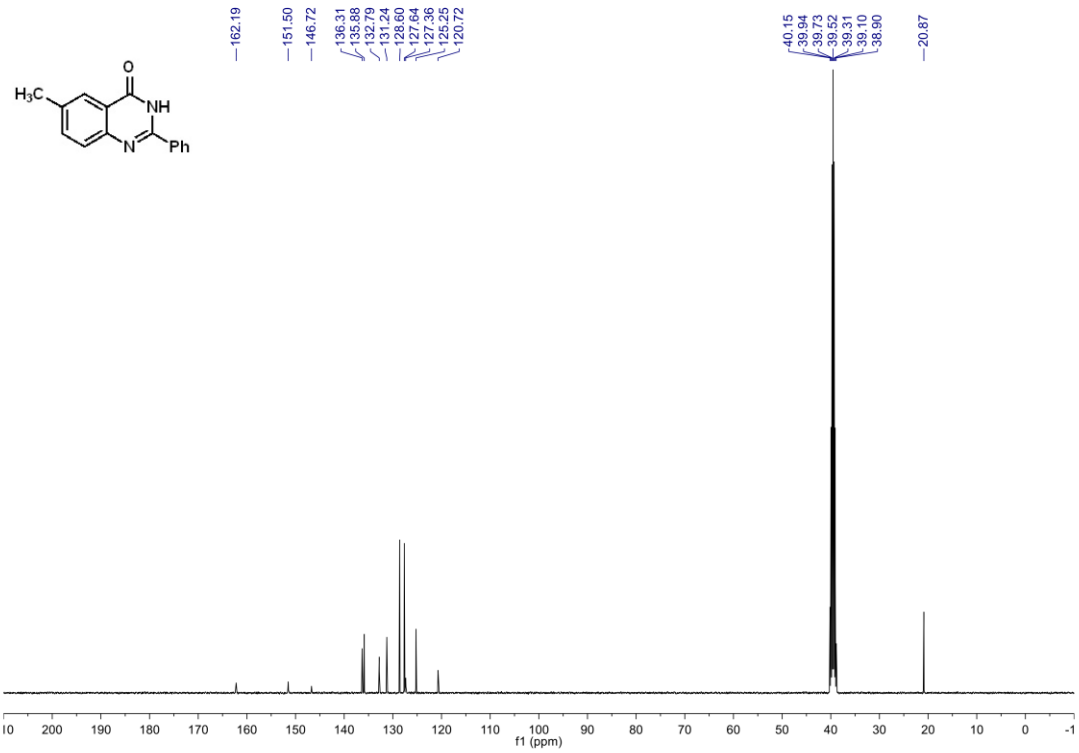
^{1}H NMR (400 MHz, DMSO-d_6) of compound **3m.**



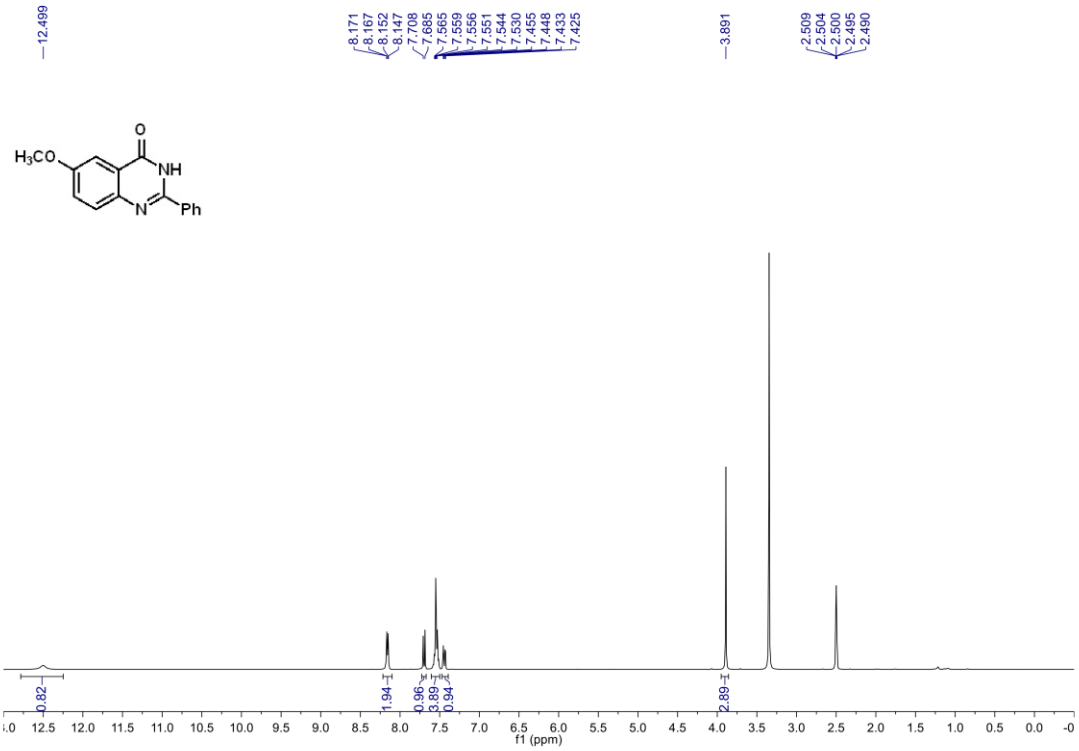
^{13}C NMR (100 MHz, DMSO-d_6) of compound **3m.**



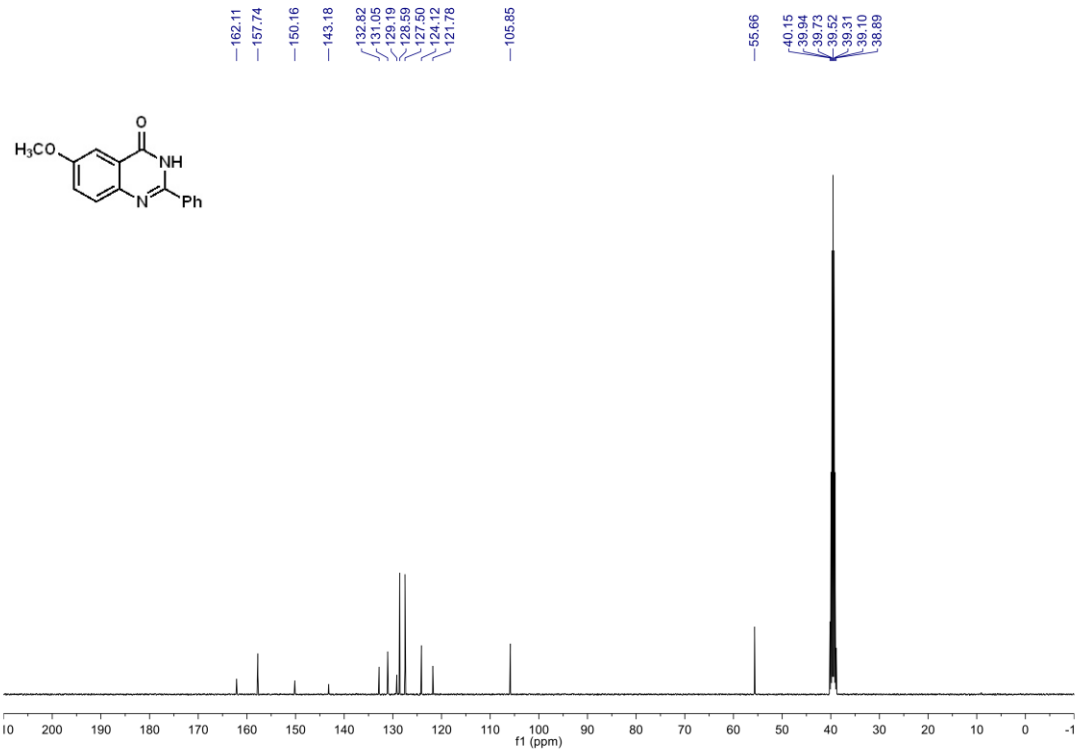
^{1}H NMR (400 MHz, DMSO-d_6) of compound **3n.**



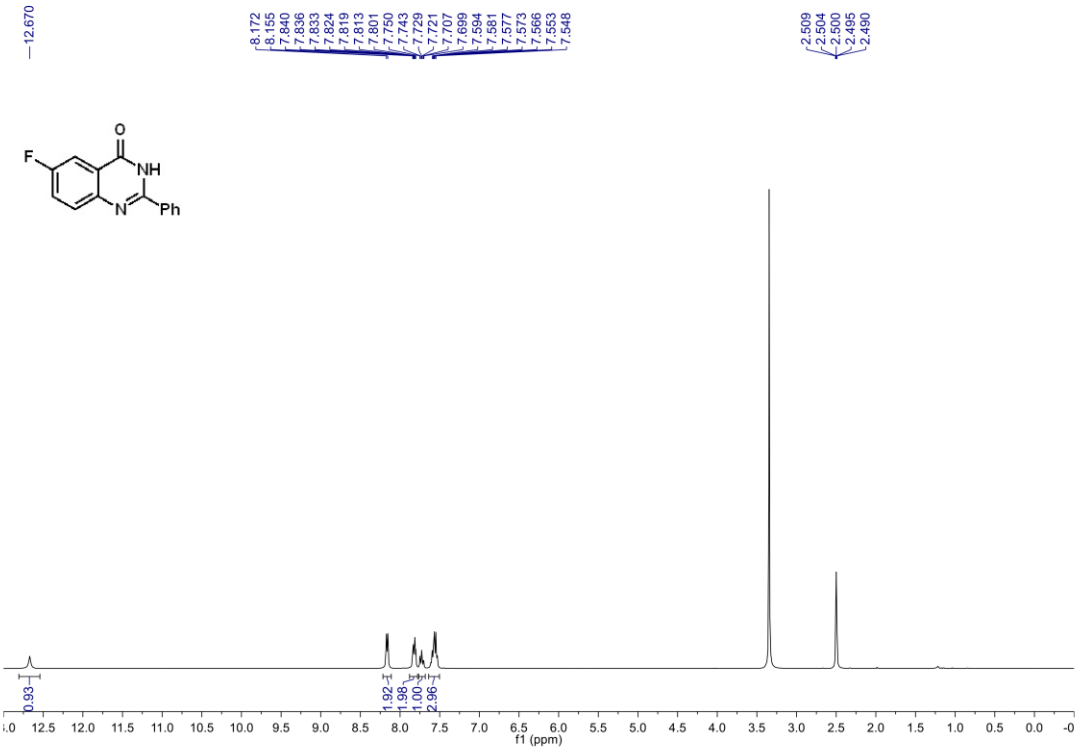
^{13}C NMR (100 MHz, DMSO-d_6) of compound **3n.**



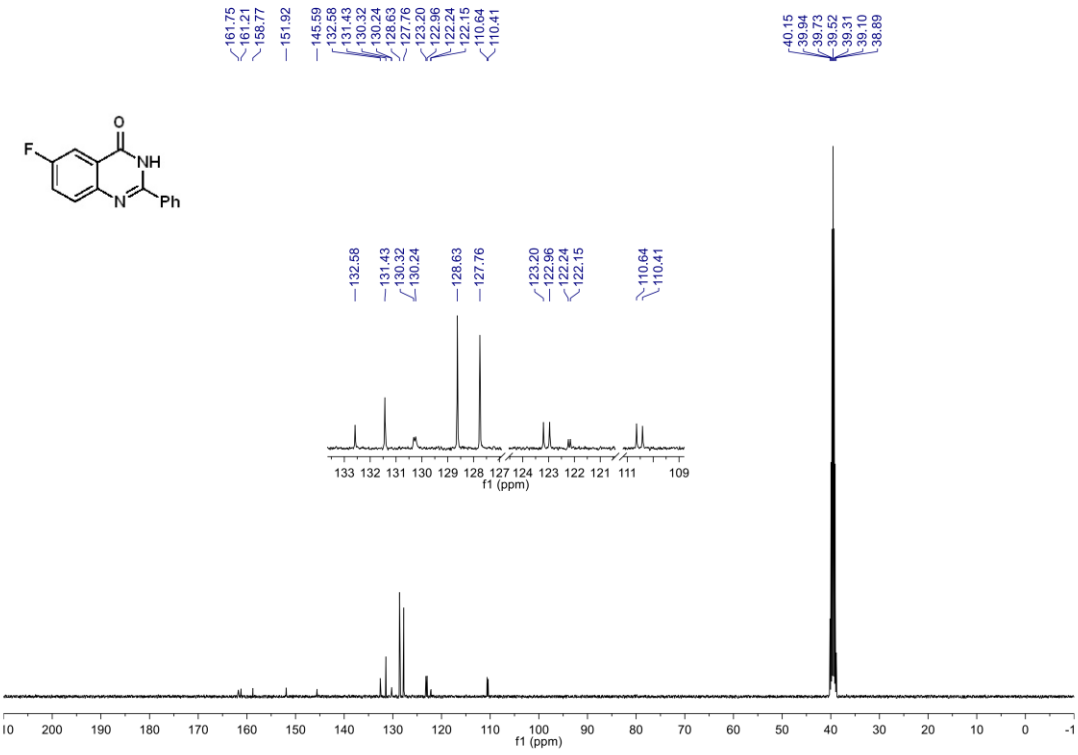
^{1}H NMR (400 MHz, DMSO-d_6) of compound **3o.**



^{13}C NMR (100 MHz, DMSO-d_6) of compound **3o.**



^{1}H NMR (400 MHz, DMSO-d_6) of compound **3p.**



^{13}C NMR (100 MHz, DMSO-d_6) of compound **3p.**