Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Catalyst-controlled selective mono-/dialkylation of 2-aryl-4-quinazolinones

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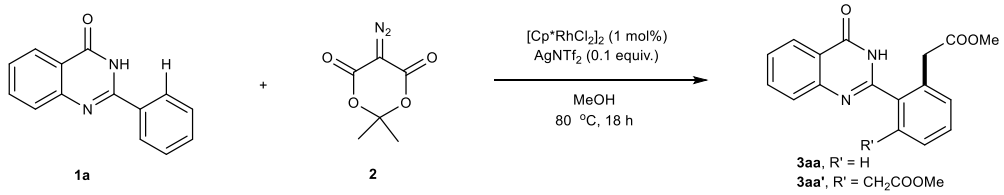
Supporting information

1. General Information

The following starting materials were synthesized according to previously described procedures: 2-aryl-4-quinazolinones **1a-k**, [1]. Other materials were purchased from commercial suppliers and used without further purification. All the reactions were monitored by thin-layer chromatography (TLC) and were visualized using UV light. The product purification was done using silica gel column chromatography. Thin layer chromatography (TLC) characterization was performed with precoated silica gel GF254 (0.2mm), while column chromatography characterization was performed with silica gel (100-200mesh). ^{1}H and ^{13}C NMR spectra were recorded with tetramethylsilane (TMS, δ = 0.00 ppm) as the internal standard. ^{1}H NMR spectra were recorded at 400 MHz (Varian) and ^{13}C NMR spectra were recorded at 100 MHz (Varian). Chemical shifts are reported in ppm downfield from $CDCl_3$ (δ = 7.26 ppm) or DMSO-d_6 (δ = 2.54 ppm) for ^{1}H NMR and chemical shifts for ^{13}C NMR spectra are reported in ppm relative to the central $CDCl_3$ (δ = 77.0 ppm) or DMSO-d_6 (δ = 39.6 ppm). Coupling constants are given in Hz. Melting points were measured with YRT-3 melting point apparatus (Shantou Keyi Instrument & Equipment Co., Ltd., Shantou, China). High resolution mass spectroscopy data of the products were collected on a Waters Micromass GCT or a Bruker Apex IV FTMS instrument.

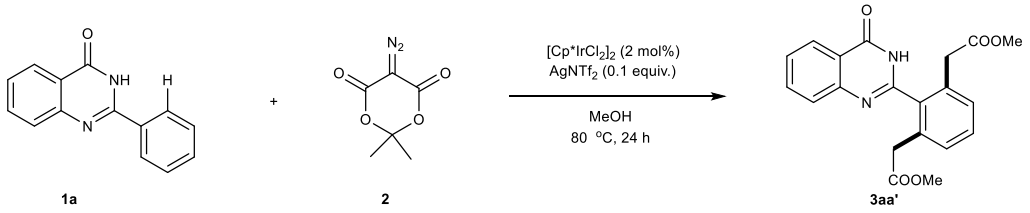
2. General procedure for the Cp*Rh(III)-catalyzed C-H monoalkylation (3aa as an example)



1a 2

A 15mL sealed tube were charged with 2-phenylquinazolin-4(3*H*)-one **1a** (44.4 mg, 0.2 mmol), α-diazotized Meldrum's acid **2** (54.4 mg, 0.32 mmol), $[Cp^*RhCl_2]_2$ (1.2 mg, 1 mol%), $AgNTf_2$ (7.8 mg，0.02 mmol) and MeOH (2 mL). The mixture was stirred at 80 °C for 18 h, then cooled down to ambient temperature. The volatiles were removed under reduced pressure and the analytically pure product **3aa** and **3aa'** were obtained by flash chromatography of silica gel (gradient of Petroleum ether/EtOAc). Both of them are white solids. **3aa** (47.8 mg, 81% yield); **3aa'** (8.1 mg, 11% yield).

3. General procedure for the Cp*Ir(III)-catalyzed C-H dialkylation (3aa' as an example)

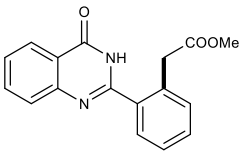


1a 2 3aa'

A 15mL sealed tube were charged with 2-phenylquinazolin-4(3*H*)-one **1a** (44.4 mg, 0.2 mmol), α-diazotized Meldrum's acid **2** (74.9 mg, 0.44 mmol), $[Cp^*IrCl_2]_2$ (3.2 mg, 2 mol%), $AgNTf_2$ (7.8 mg，0.02 mmol) and MeOH (2 mL). The mixture was stirred at 80 °C for 24 h, then cooled down to ambient temperature. The volatiles were removed under reduced pressure and the analytically pure product **3aa'** were obtained by flash chromatography of silica gel (gradient of Petroleum ether/EtOAc). White solids, 65.9 mg, 90% yield.

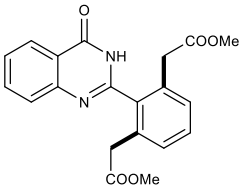
4. Spectroscopic Characterization Data of Products

Methyl 2-(2-(4-oxo-3,4-dihydroquinazolin-2-yl)phenyl)acetate (3aa)



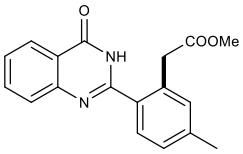
White solid; m.p. 175-176 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ 12.49 (s, 1H), 8.15 (d, *J* = 8.0, 1H), 7.83 (t, *J* = 8.0 Hz, 1H), 7.66 (d, *J* = 8.0 Hz, 1H), 7.59 (d, *J* = 8.0 Hz, 1H),7.54-7.50 (m, 2H), 7.45 (t, *J* = 8.0 Hz, 2H), 3.97 (s, 2H), 3.45 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 168.7, 158.7, 148.7, 144.8, 130.7, 129.8, 129.1, 127.8, 126.9, 125.5, 124.0, 123.7, 123.0, 122.4, 116.82 48.4, 35.5; **HRMS (ESI):** Calcd. for $C_{17}H_{15}N_2O_3$ $[M+H]^+$ 295.1083, found 295.1082.

Dimethyl 2,2'-(2-(4-oxo-3,4-dihydroquinazolin-2-yl)-1,3-phenylene)diacetate (3aa')



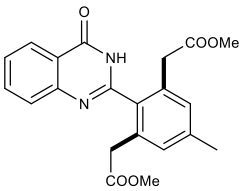
White solid; m.p. 158-162 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ 12.41 (s, 1H), 8.16 (d, *J* = 8.0, 1H), 7.84 (t, *J* = 8.0 Hz, 1H), 7.62 (d, *J* = 8.0 Hz, 1H), 7.56 (t, *J* = 8.0 Hz, 1H), 7.47 (d, *J* = 8.0, 1H), 7.37 (d, *J* = 8.0, 2H), 3.72 (s, 2H), 3.62 (s, 2H), 3.38 (s, 6H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 168.0, 157.3, 147.9, 144.17, 130.8, 130.4, 129.4, 126.6, 126.2, 123.5, 123.4, 122.6, 117.2, 48.5, 35.1; **HRMS (ESI):** Calcd. for $C_{20}H_{19}N_2O_5$ $[M+H]^+$ 367.1294, found 367.1294.

Methyl 2-(2-(4-oxo-3,4-dihydroquinazolin-2-yl)phenyl)acetate (3ba)



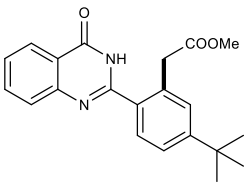
White solid; m.p. 165-166 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ 12.43 (s, 1H), 8.14 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.82 (ddd, *J* = 8.4, 7.2, 1.6 Hz, 1H), 7.58 (dd, *J* = 8.0, 2.8 Hz, 2H), 7.54-7.49 (m, 1H), 7.26 (m, 2H), 3.94 (s, 2H), 3.46 (s, 3H), 2.37 (s, 3H); **^{13}C NMR** (150 MHz, DMSO-d_6) δ 171.8, 162.5, 153.9, 148.7, 140.3, 134.8, 134.2, 133.1, 131.0, 129.9, 128.1, 127.6, 126.9, 126.1, 121.2, 51.8, 39.6, 21.2; **HRMS (ESI):** Calcd. for $C_{18}H_{17}N_2O_3$ $[M+H]^+$ 309.1239, found 309.1240.

Dimethyl 2,2'-(2-(4-oxo-3,4-dihydroquinazolin-2-yl)-1,3-phenylene)diacetate (3ba')



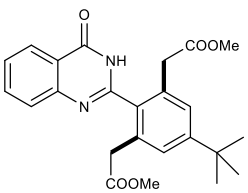
White solid; m.p. 120-122 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ 12.33 (s, 1H), 8.15 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.82 (ddd, *J* = 8.4, 7.2, 1.6 Hz, 1H), 7.61 (d, *J* = 7.6 Hz, 1H), 7.57-7.51 (m, 1H), 7.17 (s, 2H), 3.68 (s, 2H), 3.58 (s, 2H), 3.37 (s, 6H), 2.36 (s, 3H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 171.2, 162.0, 153.0, 149.0, 139.5, 134.8, 133.6, 132.4, 130.7, 127.8, 127.3, 126.2, 121.6, 52.0, 38.9, 21.2; **HRMS (ESI):** Calcd. for $C_{21}H_{21}N_2O_5$ $[M+H]^+$ 381.1450, found381.1451.

Methyl 2-(5-(*tert*-butyl)-2-(4-oxo-3,4-dihydroquinazolin-2-yl)phenyl)acetate (3ca)



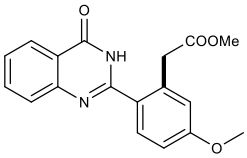
White solid; m.p. 147-148 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ 12.47 (s, 1H), 8.20 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.88 (ddd, *J* = 8.4, 7.2, 1.6Hz, 1H), 7.66 (dd, *J* = 14.0, 8.4 Hz, 2H), 7.61-7.55 (m, 1H), 7.54-7.50 (m, 2H), 4.08 (s, 2H), 3.49 (s, 3H), 1.39 (s, 9H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 170.9, 161.4, 152.9, 152.6, 147.7, 133.8, 133.0, 130.1, 128.6, 128.5, 126.5, 125.9, 125.1, 123.3, 120.2, 50.7, 33.9, 30.3, 28.4; **HRMS (ESI):** Calcd. for $C_{21}H_{23}N_2O_3$ $[M+H]^+$ 351.1709, found 351.1707.

Dimethyl 2,2'-(5-(*tert*-butyl)-2-(4-oxo-3,4-dihydroquinazolin-2-yl)-1,3-phenylene) diacetate (3ca')



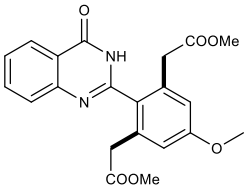
White solid; m.p. 144-146 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.30 (s, 1H), 8.34 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.79 (ddd, *J* = 8.4, 7.2, 1.6 Hz, 1H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.53 (ddd, *J* = 8.2, 7.2, 1.6 Hz, 1H), 7.30 (s, 2H), 3.69 (s, 4H), 3.66 (s, 6H), 1.33 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.3, 160.5, 152.8, 151.1, 147.5, 133.7, 132.0, 130.8, 126.6, 126.4, 126.2, 125.5, 120.2, 51.5, 38.4, 33.8, 30.1; **HRMS (ESI):** Calcd. for $C_{24}H_{27}N_2O_5$ $[M+H]^+$ 423.1920, found 423.1920.

Methyl 2-(5-methoxy-2-(4-oxo-3,4-dihydroquinazolin-2-yl)phenyl)acetate (3da)



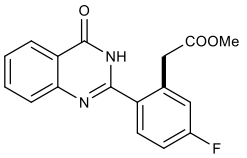
White solid; m.p. 153-155 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ 12.38 (s,1H), 8.13 (dd, *J* = 8.0, 1.2Hz, 1H), 7.81 (ddd, *J* = 8.4, 7.2, 1.6 Hz, 1H), 7.66 (d, *J* = 8.4 Hz, 1H), 7.56 (d, *J* = 7.6 Hz, 1H), 7.52-7.47 (m, 1H), 7.04-6.98 (m, 2H), 3.98 (s, 2H), 3.84 (s, 3H), 3.47 (s, 3H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 171.8, 162.6, 160.9, 153.6, 148.9, 136.5, 134.9, 131.6, 127.5, 126.8, 126.2, 126.1, 121.1, 118.6, 112.4, 55.9, 51.9, 29.5; **HRMS (ESI):** Calcd. for $C_{18}H_{17}N_2O_4$ $[M+H]^+$ 325.1188, found 325.1185.

Dimethyl 2,2'-(5-methoxy-2-(4-oxo-3,4-dihydroquinazolin-2-yl)-1,3-phenylene) diacetate (3da')



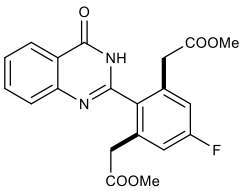
White solid; m.p. 159-160 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ 12.29 (s, 1H), 8.15 (d, *J* = 8.4 Hz, 1H), 7.85-7.78 (m, 1H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.54 (t, *J* = 7.6 Hz, 1H), 6.95 (s, 2H), 3.82 (s, 3H), 3.71 (s, 2H), 3.64 (s, 2H), 3.37 (s, 6H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 171.1, 162.1, 160.0, 152.9, 149.1, 135.4, 134.8, 127.9, 127.8, 127.2, 126.2, 121.5, 115.6, 55.9, 52.0, 39.1; **HRMS (ESI):** Calcd. for $C_{21}H_{21}N_2O_6$ $[M+H]^+$ 397.1400, found 397.1400.

Methyl 2-(5-fluoro-2-(4-oxo-3,4-dihydroquinazolin-2-yl)phenyl)acetate (3ea)



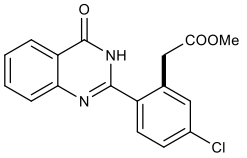
White solid; m.p. 155-156 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ 12.52 (s, 1H), 8.15 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.83 (ddd, *J* = 8.4, 7.2, 1.6 Hz, 1H), 7.73 (dd, *J* = 8.4, 6.0 Hz, 1H), 7.58 (d, *J* = 7.6 Hz, 1H), 7.55-7.51 (m, 1H), 7.37-7.27 (m, 2H), 4.00 (s, 2H), 3.48 (s, 3H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 171.4, 164.2, 162.5, 161.8, 153.1, 148.6, 137.6 (d, *J* = 8.8 Hz), 134.9, 132.4 (d, *J* = 9.1 Hz), 130.4 (d, *J* = 2.9 Hz), 127.6, 127.2, 126.2, 121.3, 119.3 (d, *J* = 22.1 Hz), 114.4 (d, *J* = 21.5 Hz), 52.0; **HRMS (ESI):** Calcd. for $C_{17}H_{14}FN_2O_3$ $[M+H]^+$ 313.0988, found 313.0990.

Dimethyl 2,2'-(5-fluoro-2-(4-oxo-3,4-dihydroquinazolin-2-yl)-1,3-phenylene) diacetate (3ea')



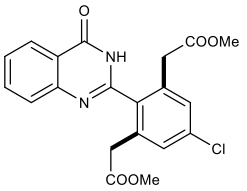
White solid; m.p. 177-178 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ 12.43 (s, 1H), 8.16 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.84 (ddd, *J* = 8.4, 7.2, 1.6 Hz, 1H), 7.62 (d, *J* = 7.6 Hz, 1H), 7.59-7.54 (m, 1H), 7.28 (d, *J* = 9.6 Hz, 2H), 3.75 (s, 2H), 3.65 (s, 2H), 3.40 (s, 6H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 170.7, 162.2 (d, *J* = 245 Hz), 161.0, 152.1, 148.9, 136.6 (d, *J* = 9.1 Hz), 134.9, 131.8 (d, *J* = 3.1 Hz), 127.8, 127.5, 126.2, 121.6, 116.9 (d, *J* = 22.1 Hz), 52.1, 38.7; **HRMS (ESI):** Calcd. for $C_{20}H_{18}FN_2O_5$ $[M+H]^+$ 385.1200, found 385.1201.

Methyl 2-(5-chloro-2-(4-oxo-3,4-dihydroquinazolin-2-yl)phenyl)acetate (3fa)



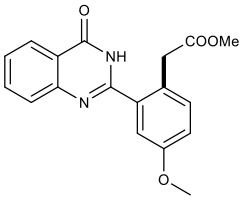
White solid; m.p. 193-194 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ 12.56 (s, 1H), 8.15 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.84 (ddd, *J* = 8.4, 7.2, 1.6 Hz, 1H), 7.70 (d, *J* = 8.4 Hz, 1H), 7.60-7.57 (m, 2H), 7.56-7.51 (m, 2H), 3.99 (s, 2H), 3.48 (s, 3H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 171.4, 162.5, 153.0, 148.6, 136.8, 135.1, 135.0, 132.7, 132.2, 131.8, 127.7, 127.5, 127.3, 126.2, 121.4, 52.0, 39.1; **HRMS (ESI):** Calcd. for $C_{17}H_{14}ClN_2O_3$ $[M+H]^+$ 329.0693, found 329.0693.

Dimethyl 2,2'-(5-chloro-2-(4-oxo-3,4-dihydroquinazolin-2-yl)-1,3-phenylene) diacetate (3fa')



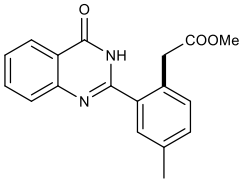
White solid; m.p. 150-152 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ 12.45 (s, 1H), 8.16 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.84 (ddd, *J* = 8.4, 7.2, 1.6 Hz, 1H), 7.62 (d, *J* = 7.6Hz, 1H), 7.60-7.54 (m, 1H), 7.51 (s, 2H), 3.75 (s, 2H), 3.64 (s, 2H), 3.39 (s, 6H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 170.7, 161.9, 151.9, 148.8, 136.1, 134.9, 134.2, 134.0, 129.9, 127.9, 127.6, 126.3, 121.7, 52.2, 38.5; **HRMS (ESI):** Calcd. for $C_{20}H_{18}ClN_2O_5$ $[M+H]^+$ 401.0904, found 401.0905.

Methyl 2-(4-methoxy-2-(4-oxo-3,4-dihydroquinazolin-2-yl)phenyl)acetate (3ga)



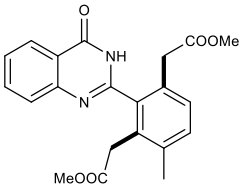
White solid; m.p. 204-208 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ 12.48 (s, 1H), 8.15 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.84 (ddd, *J* = 8.4, 7.2, 1.6 Hz, 1H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.57-7.51 (m, 1H), 7.34 (d, *J* = 8.4 Hz, 1H), 7.25 (d, *J* = 2.8 Hz, 1H), 7.07 (dd, *J* = 8.4, 2.8 Hz, 1H), 3.90 (s, 2H), 3.84 (s, 3H), 3.44 (s, 3H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 172.2, 162.5, 158.4, 153.7, 148.7, 134.9, 134.6, 133.6, 127.7, 127.2, 126.3, 126.2, 121.3, 116.6, 115.1, 55.8, 51.8, 38.7; **HRMS (ESI):** Calcd. for $C_{18}H_{17}N_2O_4$ $[M+H]^+$ 325.1188, found 325.1187.

Methyl 2-(4-methyl-2-(4-oxo-3,4-dihydroquinazolin-2-yl)phenyl)acetate (3ha)



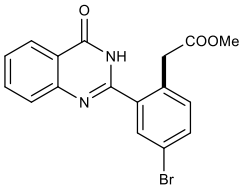
White solid; m.p. 157-158 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ 12.32 (s, 1H), 8.15 (d, *J* = 8.0 Hz, 1H), 7.82 (d, *J* = 4.0 Hz, 1H), 7.68 (d, *J* = 4.0 Hz, 1H), 7.54 (d, *J* = 4.0 Hz, 1H), 7.45 (d, *J* = 4.0 Hz, 1H), 7.10 (d, *J* = 8.0 Hz, 1H), 7.01 (d, *J* = 8.0 Hz, 1H), 3.77 (s, 3H), 3.67 (s, 2H), 2.37 (s, 3H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 172.0, 162.4, 154.0, 148.8, 136.8, 134.9, 133.6, 132.4, 131.3, 131.2, 130.6, 127.7 127.1, 126.2, 121.3, 51.9, 39.0, 21.0; **HRMS (ESI):** Calcd. for $C_{18}H_{17}N_2O_3$ $[M+H]^+$ 309.1239, found 309.1239.

Dimethyl 2,2'-(4-methyl-2-(4-oxo-3,4-dihydroquinazolin-2-yl)-1,3-phenylene) diacetate (3ha')



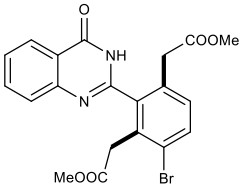
White solid; m.p. 132-134 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ 12.34 (s, 1H), 8.16 (d, *J* = 6.8 Hz, 1H), 7.86-7.79 (m, 1H), 7.64-7.52 (m, 2H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.26 (d, *J* = 8.0 Hz, 1H), 3.52 (m, 2H), 3.44 (s, 2H), 3.37 (d, *J* = 3.2 Hz, 6H), 2.35 (s, 3H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 171.3, 171.0, 162.0, 153.3, 148.9, 137.1, 135.7, 134.9, 132.2, 131.7, 131.0, 129.9, 127.8, 127.4, 126.2, 121.6, 52.1, 52.0, 35.8, 31.2, 20.0; **HRMS (ESI):** Calcd. for $C_{21}H_{21}N_2O_5$ $[M+H]^+$ 381.1450, found 381.1450.

Methyl 2-(4-bromo-2-(4-oxo-3,4-dihydroquinazolin-2-yl)phenyl)acetate (3ia)



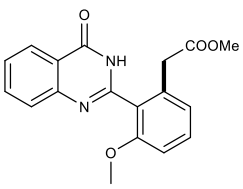
White solid; **^{1}H NMR** (400 MHz, DMSO-d_6) δ 12.42 (s, 1H), 8.15 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.83 (ddd, *J* = 8.4, 7.2, 1.6 Hz, 1H), 7.59 (d, *J* = 7.6 Hz, 1H), 7.55-7.49 (m, 2H), 7.31 (d, *J* = 0.8 Hz, 2H), 3.93 (s, 2H), 2.37 (s, 3H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 172.0, 162.5, 154.1, 148.8, 136.9, 134.9, 133.7, 132.4, 131.3, 131.2, 130.6, 127.7 127.1, 126.2, 121.2, 51.8, 39.1; **HRMS (ESI):** Calcd. for $C_{17}H_{14}BrN_2O_3$ $[M+H]^+$ 373.0188, found 373.0188.

Dimethyl 2,2'-(4-bromo-2-(4-oxo-3,4-dihydroquinazolin-2-yl)-1,3-phenylene) diacetate (3ia')



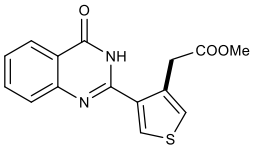
White solid; **^{1}H NMR** (400 MHz, DMSO-d_6) δ 11.47 (s, 1H), 8.07 (d, *J* = 6.8 Hz, 1H), 7.85-7.76 (m, 3H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.37 (d, *J* = 8.0 Hz, 1H), 3.76 (s, 2H), 3.67 (s, 2H), 3.42 (s, 6H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 171.3, 171.0, 162.0, 153.3, 145.0, 137.2, 135.7, 134.9, 132.2, 131.7, 131.0, 129.9, 127.8, 127.4, 126.3, 121.6, 52.1, 52.0, 39.2, 38.8; **HRMS (ESI):** Calcd. for $C_{20}H_{18}BrN_2O_5$ $[M+H]^+$ 445.0399, found 445.0401.

Mthyl 2-(3-methoxy-2-(4-oxo-3,4-dihydroquinazolin-2-yl)phenyl)acetate (3ja)



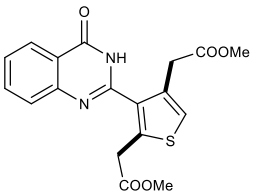
White solid; m.p. 170-171 °C; **^{1}H NMR** (600 MHz, DMSO-d_6) δ 12.32 (s, 1H), 8.15 (d, *J* = 7.6 Hz, 1H), 7.82 (t, *J* = 7.6 Hz, 1H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.54 (t, *J* = 7.6Hz, 1H), 7.45 (t, *J* = 8.0 Hz, 1H), 7.10 (d, *J* = 8.4 Hz, 1H), 7.01 (d, *J* = 7.6 Hz, 1H), 3.77 (s, 3H), 3.67 (s, 2H), 3.42 (s, 3H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 171.2, 162,0, 157.7, 152.0, 149.1, 135.0, 134.8, 131.2, 127.7, 127.2, 126.2, 124.0, 123.5, 121.7, 110.8, 56.2, 52.0, 38.7; **HRMS (ESI):** Calcd. for $C_{18}H_{17}N_2O_4$ $[M+H]^+$ 325.1188, found 325.1188.

Methyl 2-(4-(4-oxo-3,4-dihydroquinazolin-2-yl)thiophen-3-yl)acetate (3ka)



White solid; m.p. 177-178 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ 12.33 (s, 1H), 8.13 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.82 (td, *J* = 8.4, 1.6 Hz, 1H), 7.77 (d, *J* = 8.4 Hz, 1H), 7.58-7.56 (m, 2H), 7.50 (td, *J* = 8.4, 1.6 Hz, 1H), 4.3 (s, 2H), 3.60 (s, 3H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 171.0, 162.5, 149.4, 149.0, 140.4, 135.1, 131.3, 127.9, 127.4, 126.9, 126.3, 124.7, 121.1, 52.3, 35.3; **HRMS (ESI):** Calcd. for $C_{15}H_{13}N_2O_3S$ $[M+H]^+$ 301.0647, found 301.0647.

Dimethyl 2,2'-(3-(4-oxo-3,4-dihydroquinazolin-2-yl)thiophene-2,4-diyl)diacetate (3ka')

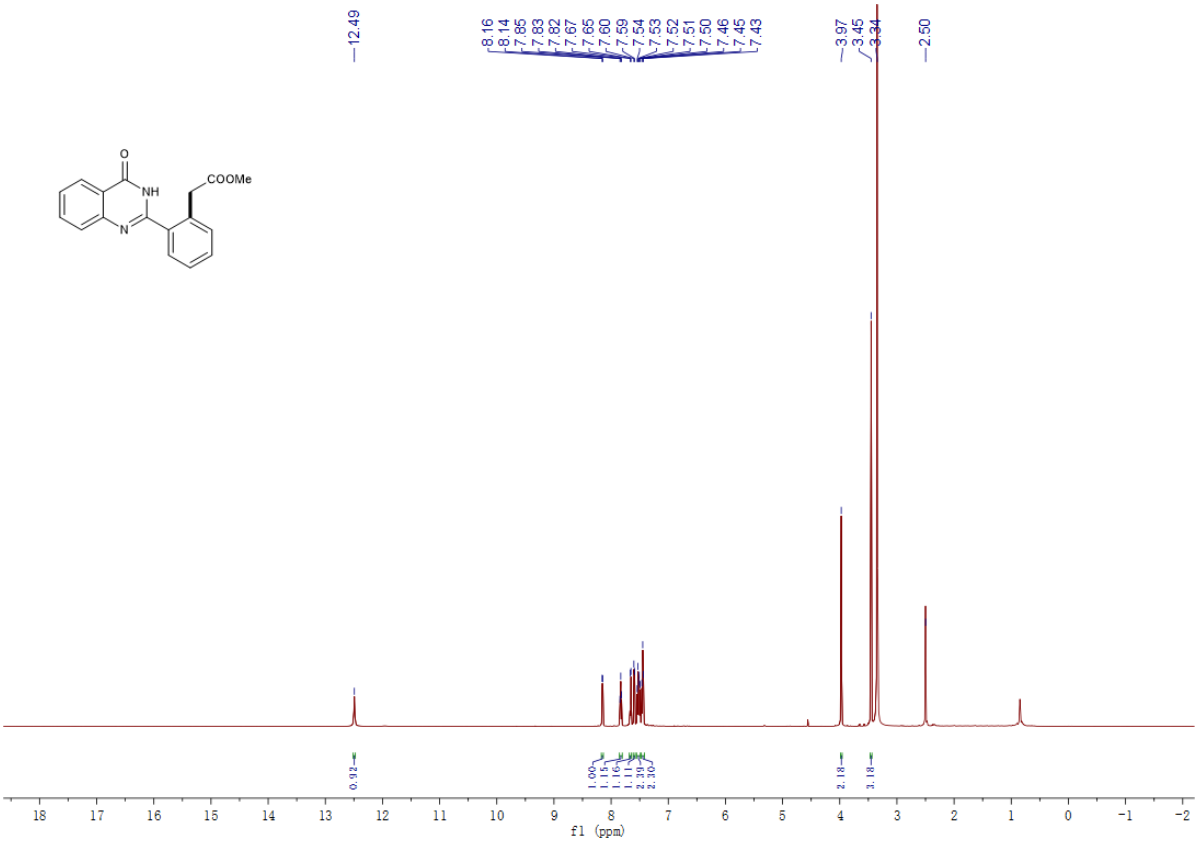


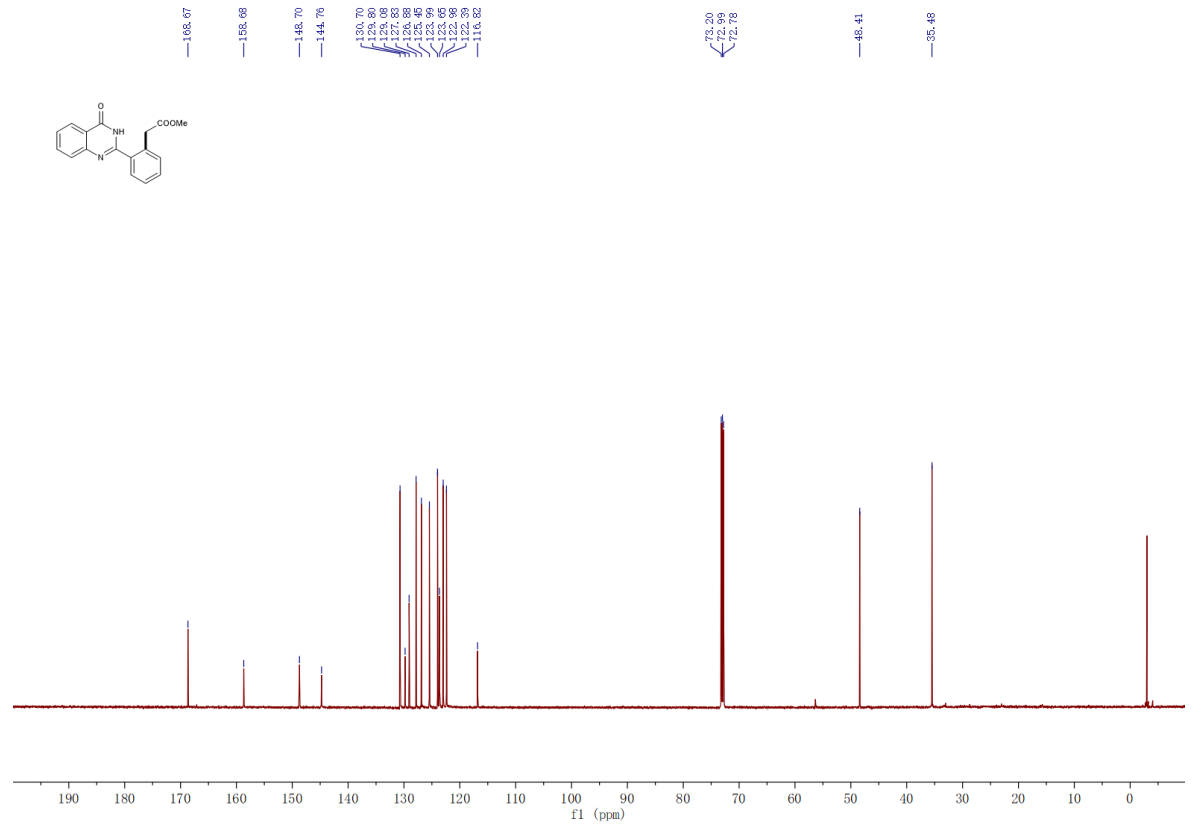
White solid; m.p. 148-149 °C; **^{1}H NMR** (400 MHz, DMSO-d_6) δ 12.31 (s, 1H), 8.13 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.82 (ddd, *J* = 8.4, 7.2, 1.6 Hz, 1H), 7.61 (d, *J* = 7.6 Hz, 1H), 7.55-7.50 (m, 1H), 7.41 (s, 1H), 4.08 (s, 2H), 3.83 (s, 2H), 3.52 (s, 3H), 3.37 (s, 3H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 171.3, 170.6, 162.2, 150.2, 149.1, 137.4, 134.9, 133.9, 133.5, 127.7, 127.1, 126.2, 124.0, 121.4, 52.4, 52.0, 34.9, 34.0; **HRMS (ESI):** Calcd. for $C_{18}H_{17}N_2O_5S$ $[M+H]^+$ 373.0858, found 373.0858.

5. References

[1] D. Qiu, Y. Wang, D. Lu, L. Zhou, Q. Zeng, *Monatsh Chem,* **2015**, *146*, 1343.

6. ^{1}H NMR and ^{13}C NMR Spectra of Products

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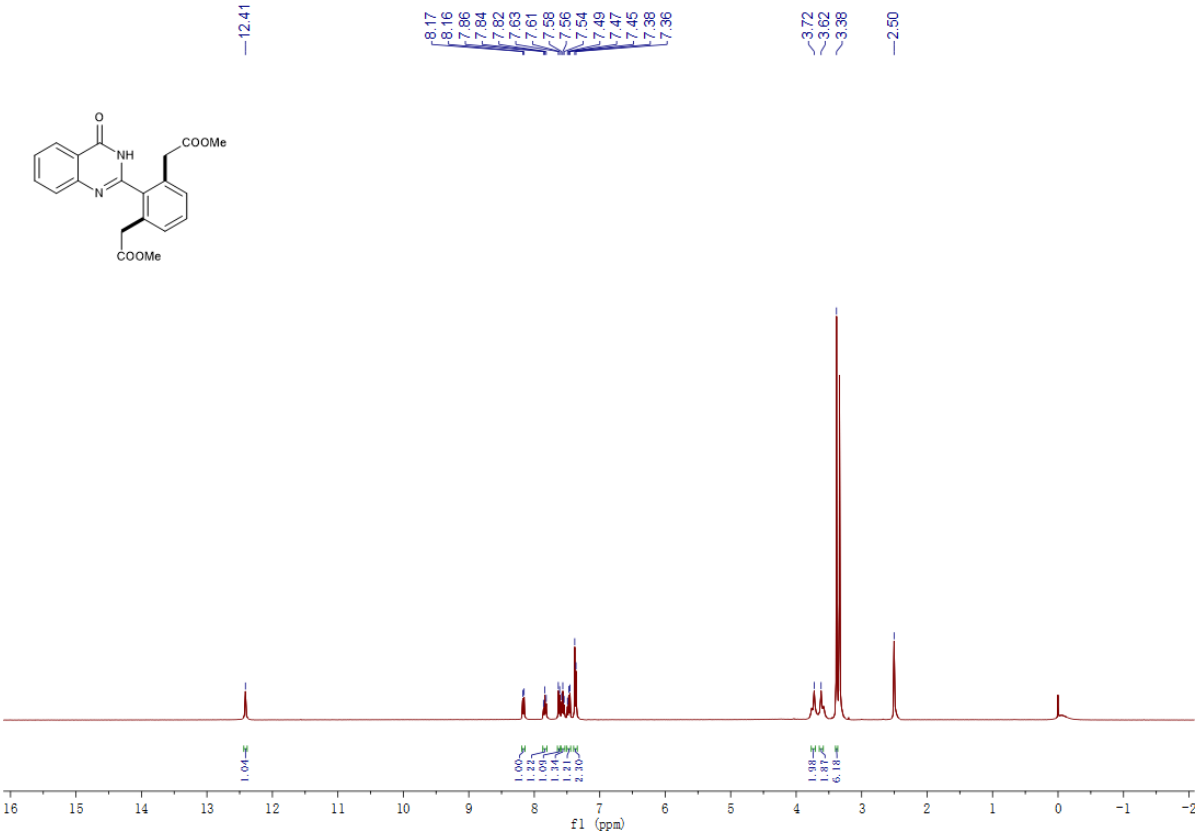
158.68
148.70
144.76
130.70
129.80
129.08
127.88
126.45
125.45
123.99
123.65
122.98
122.39
116.82
73.20
72.99
72.78
48.41
35.48
O
NH
N
COOMe
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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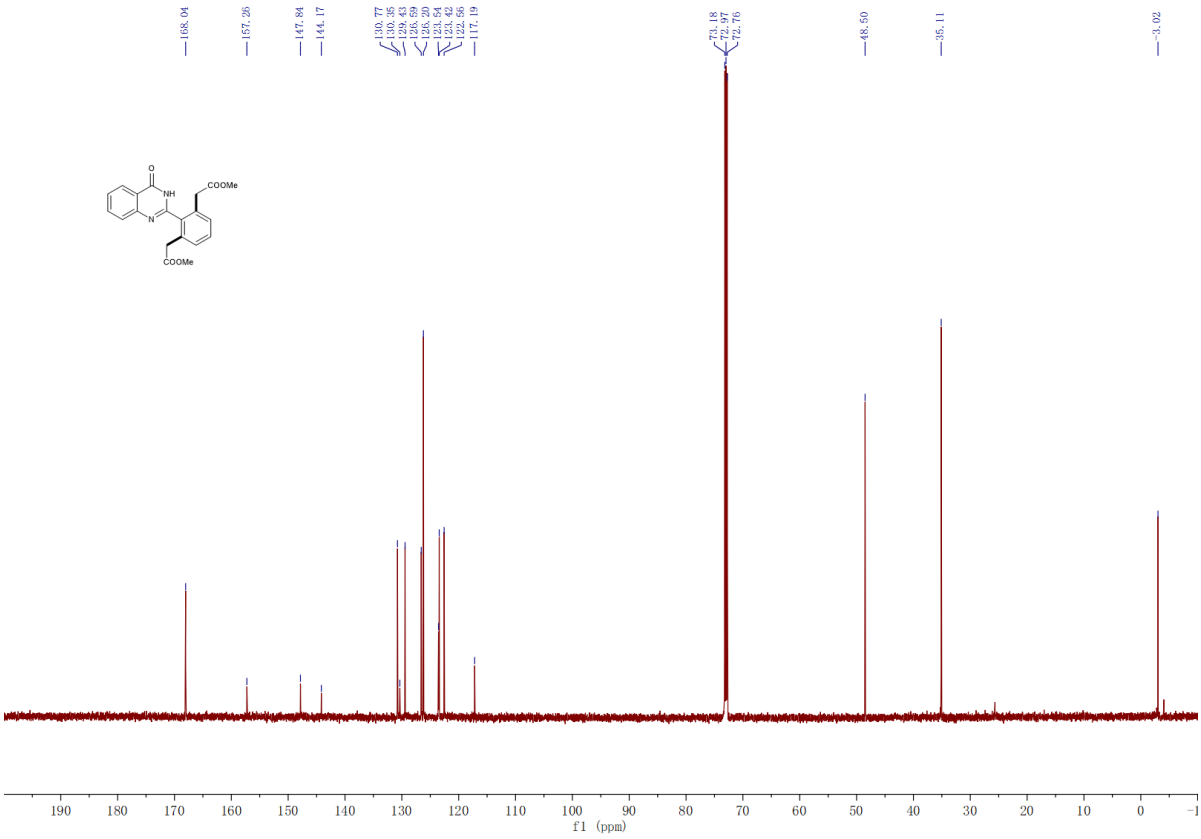
8.17
8.16
7.86
7.84
7.82
7.63
7.61
7.58
7.56
7.54
7.49
7.47
7.45
7.38
7.36
3.72
3.62
3.38
2.50
O
NH
N
COOMe
COOMe
1.04
1.00
1.22
1.09
1.34
1.21
2.30
1.98
1.87
6.18
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2
f1 (ppm)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157.26
147.84
144.17
130.77
130.35
129.43
126.59
126.20
123.54
123.42
122.56
117.19
73.18
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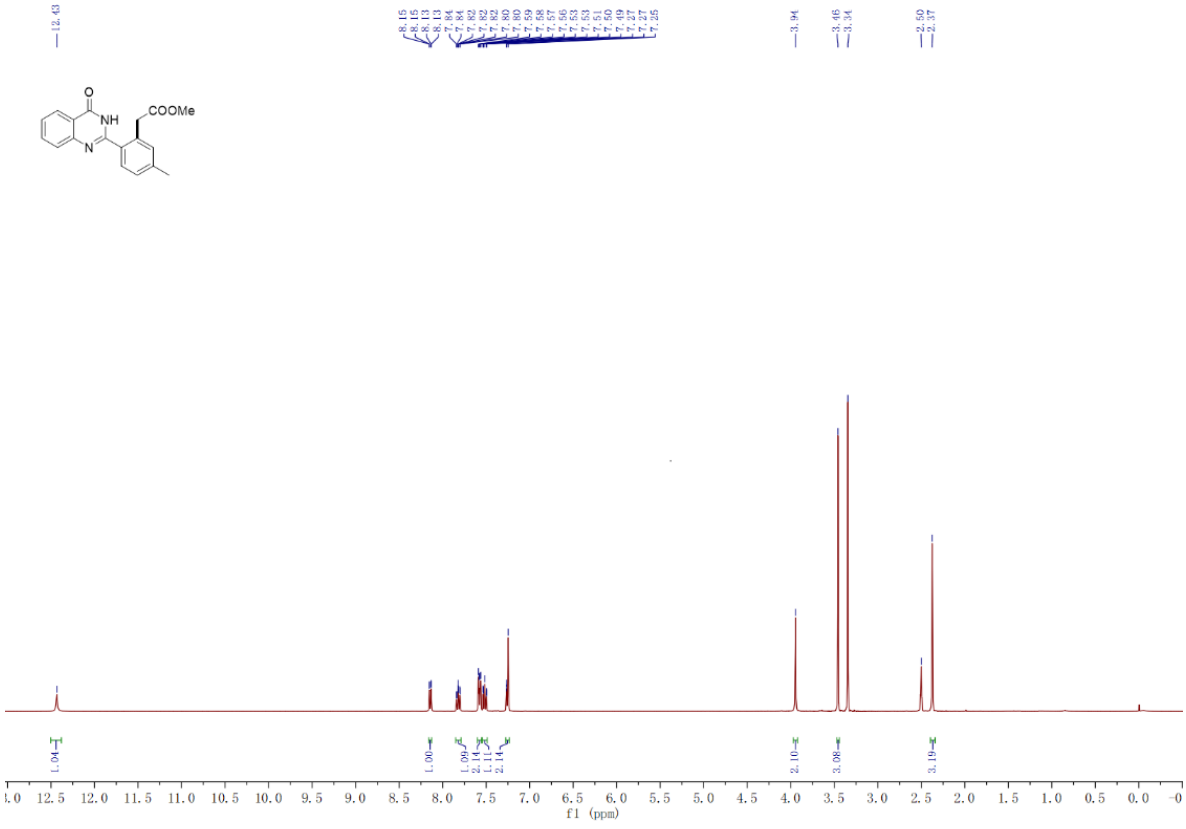
72.76
48.50
35.11
-3.02
COOMe
COOMe
NH
N
O
f1 (ppm)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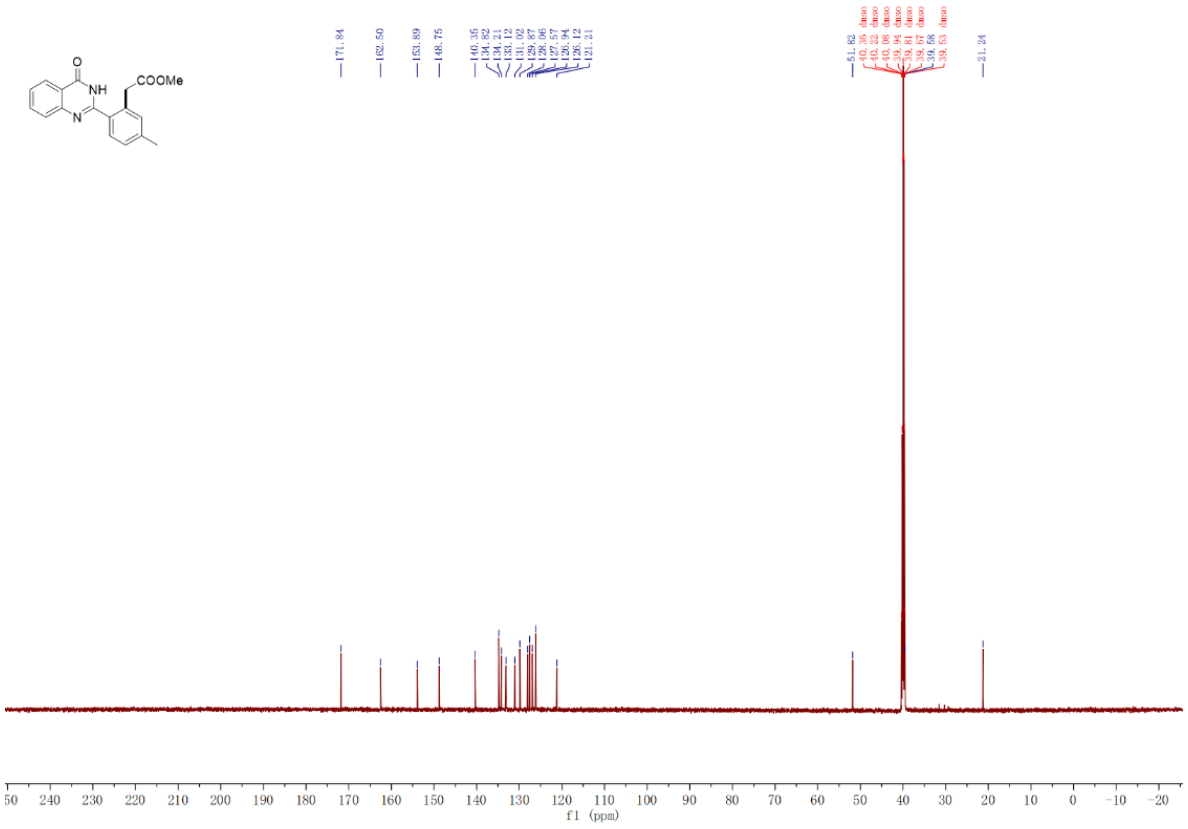
7.58
7.58
7.57
7.57
7.56
7.56
7.53
7.53
7.51
7.51
7.50
7.50
7.49
7.49
7.27
7.27
7.25
3.94
3.46
3.34
2.50
2.37
1.04
1.00
1.09
2.14
2.11
2.14
2.10
3.08
3.19
COOMe
NH
N
O
f1 (ppm)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NH
N
COOMe
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162.50
153.89
148.75
140.35
134.52
134.21
133.12
131.02
129.87
129.06
127.57
126.94
126.12
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40.22
40.08
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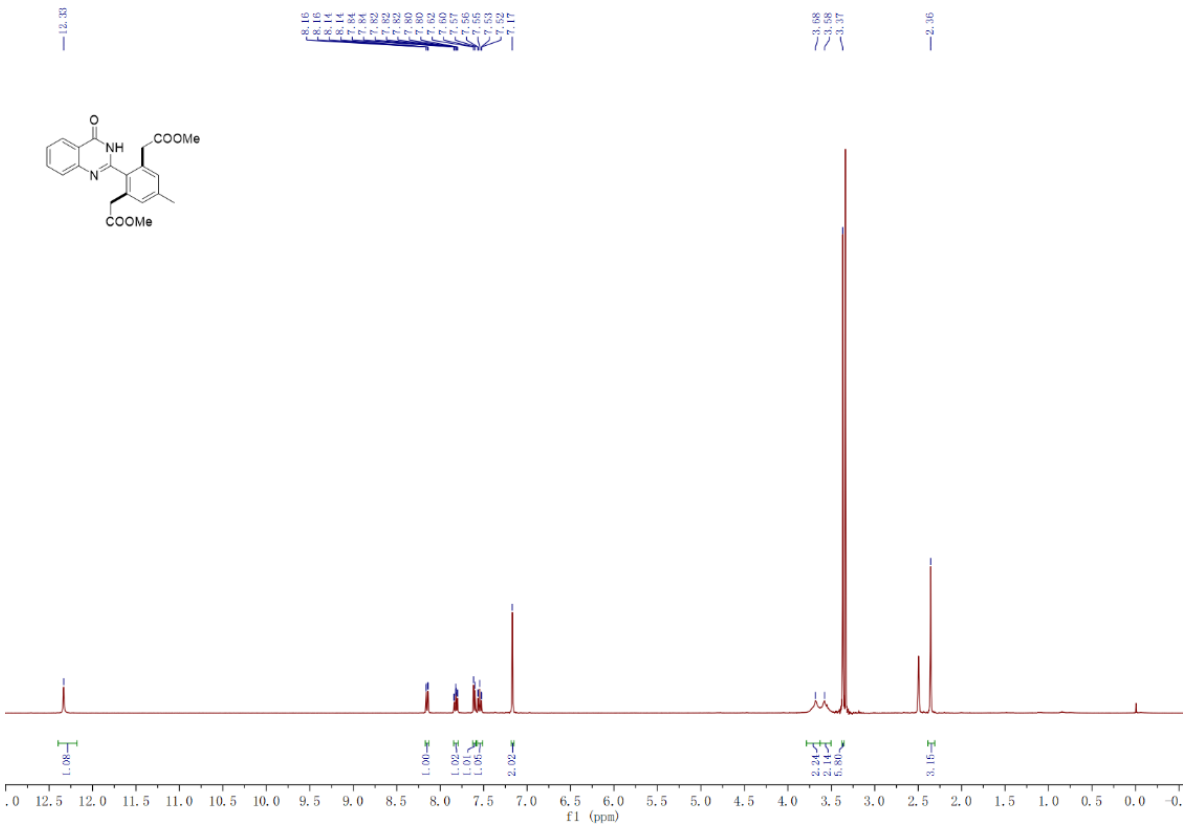
39.81
39.67
39.53
21.24
f1 (ppm)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7.82
7.82
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7.60
7.57
7.56
7.55
7.53
7.52
7.17
3.68
3.58
3.37
2.36
O
NH
N
COOMe
COOMe
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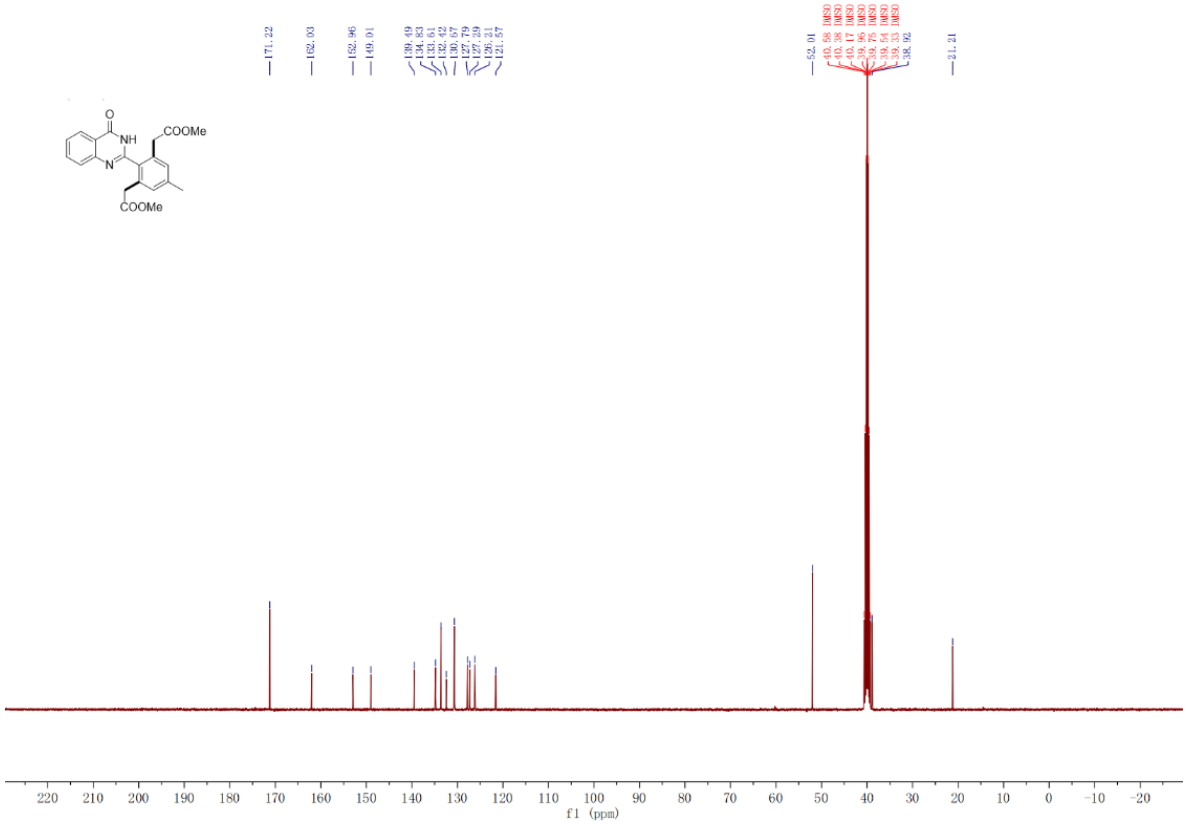
1.02
1.01
1.05
2.02
2.24
2.14
6.80
3.16
f1 (ppm)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132.61
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126.21
121.57
52.01
40.58
40.38
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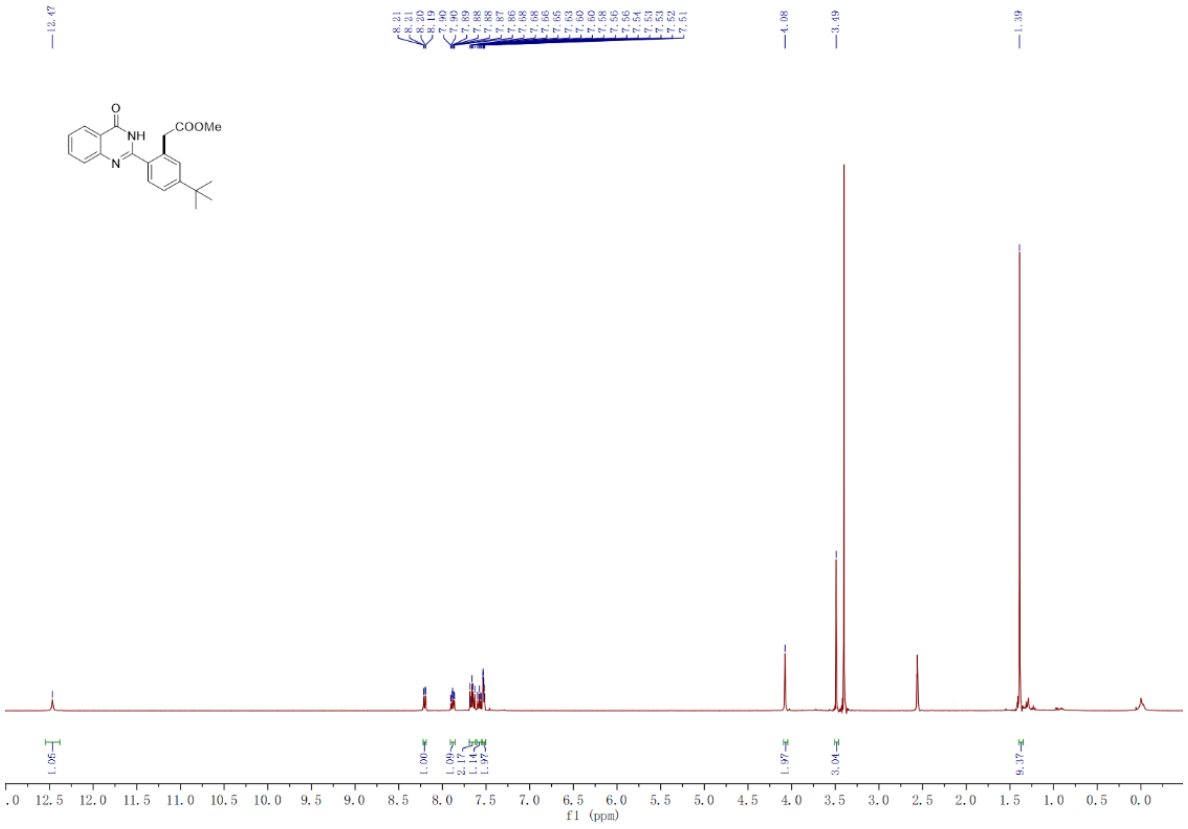
39.54
39.33
38.92
21.21
COOMe
COOMe
NH
N
O
f1 (ppm)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7.65
7.53
7.52
7.60
7.58
7.56
7.55
7.54
7.53
7.52
7.51
4.08
3.49
1.39
1.06
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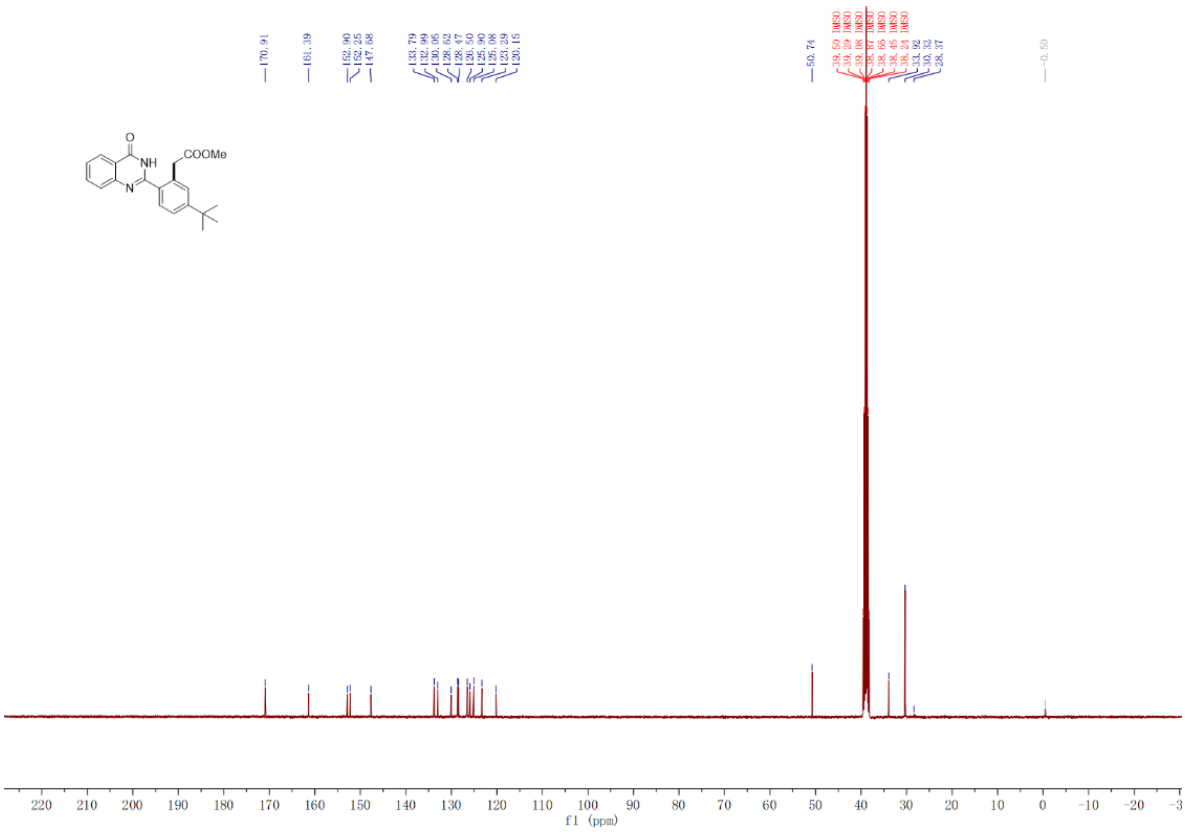
1.97
3.04
9.37
COOMe
NH
N
O
f1 (ppm)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N
COOMe
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128.62
128.47
126.56
125.90
125.08
123.29
120.15
60.74
39.59
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38.87
38.66
38.45
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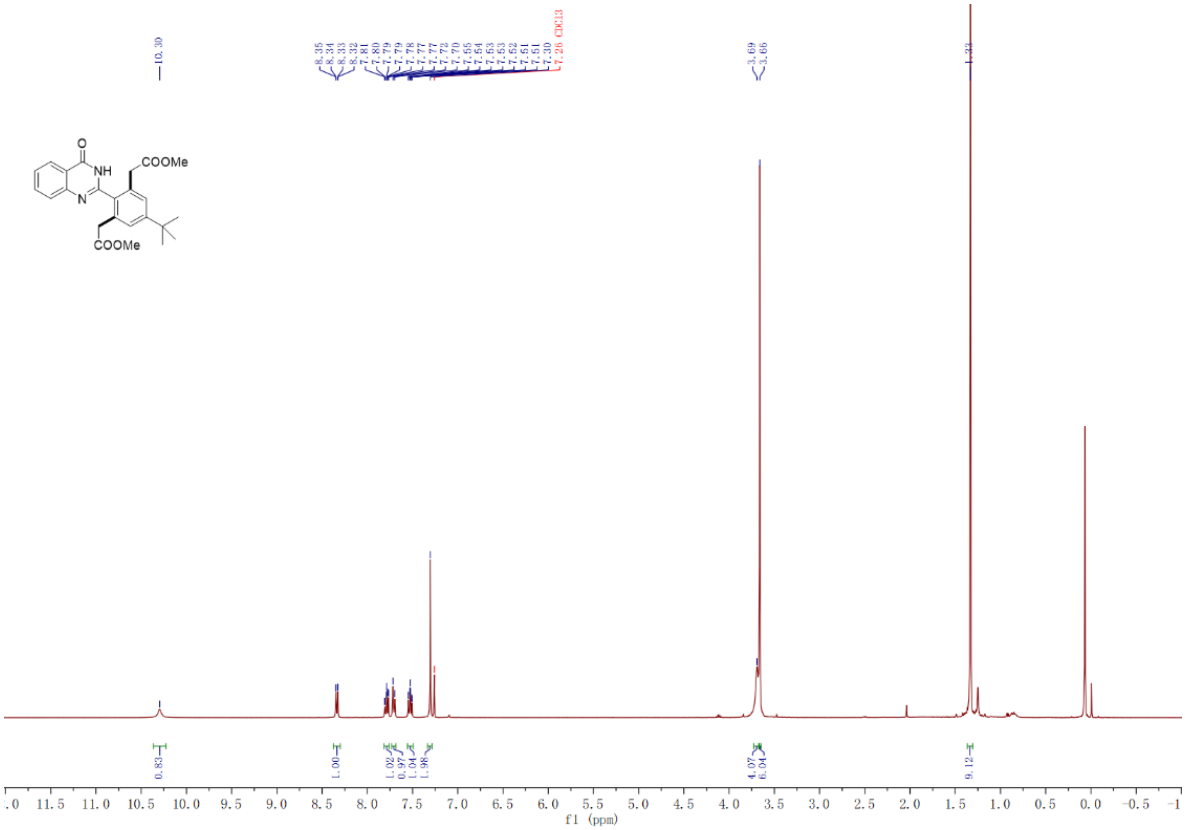
30.32
28.37
0.59
f1 (ppm)


O
NH
N
COOMe
COOMe
10.39
8.35
8.34
8.33
8.32
7.81
7.80
7.79
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7.78
7.77
7.77
7.72
7.70
7.55
7.54
7.53
7.53
7.52
7.51
7.51
7.30
7.26 CDCl3
3.69
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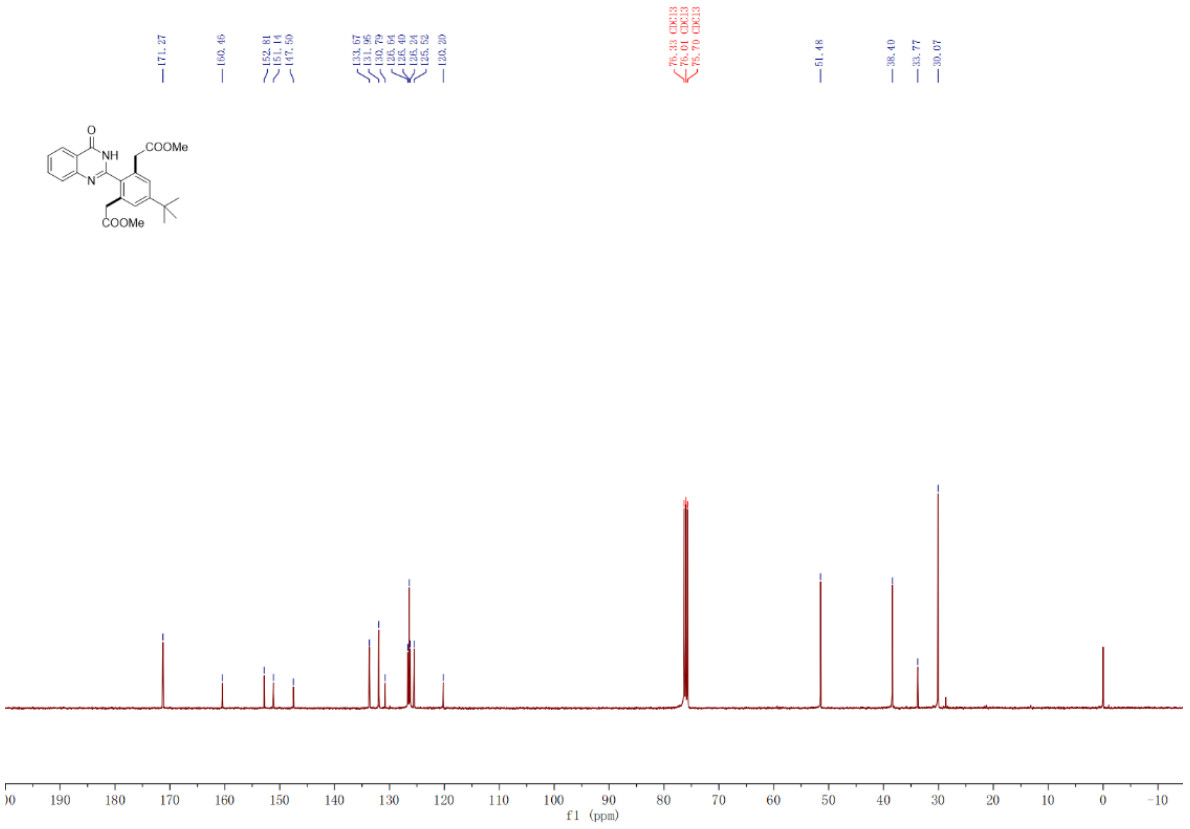
9.12
f1 (ppm)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77.33 CDCl3
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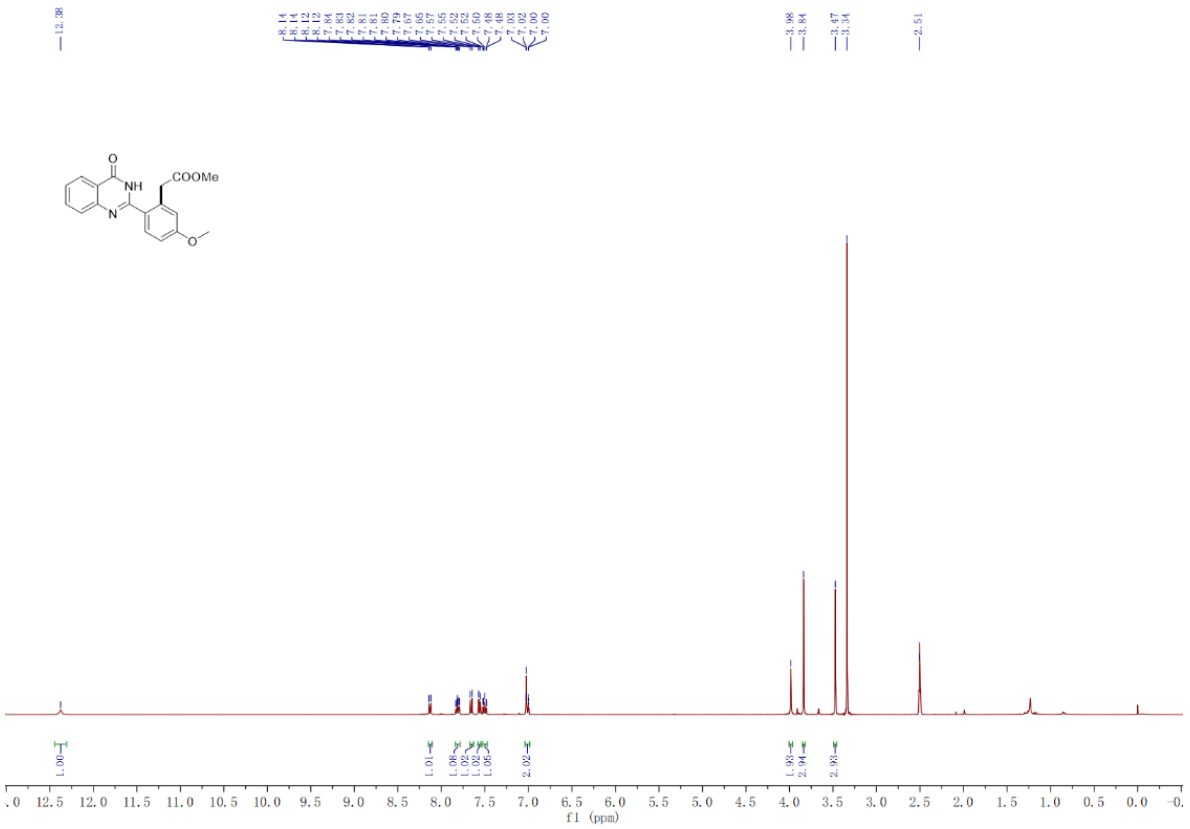
COOMe
f1 (ppm)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7.50
7.48
7.48
7.03
7.02
7.00
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3.47
3.34
2.51
O
NH
N
COOMe
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1.08
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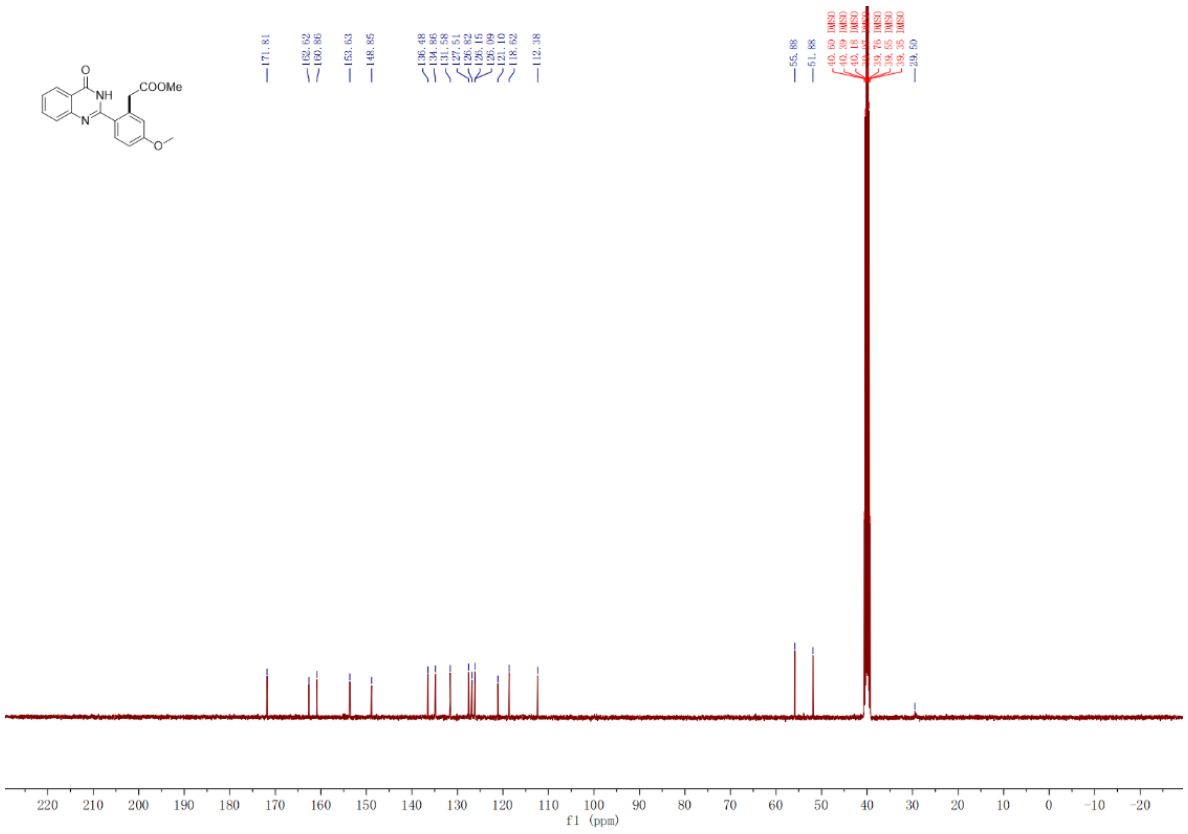
2.93
f1 (ppm)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121.10
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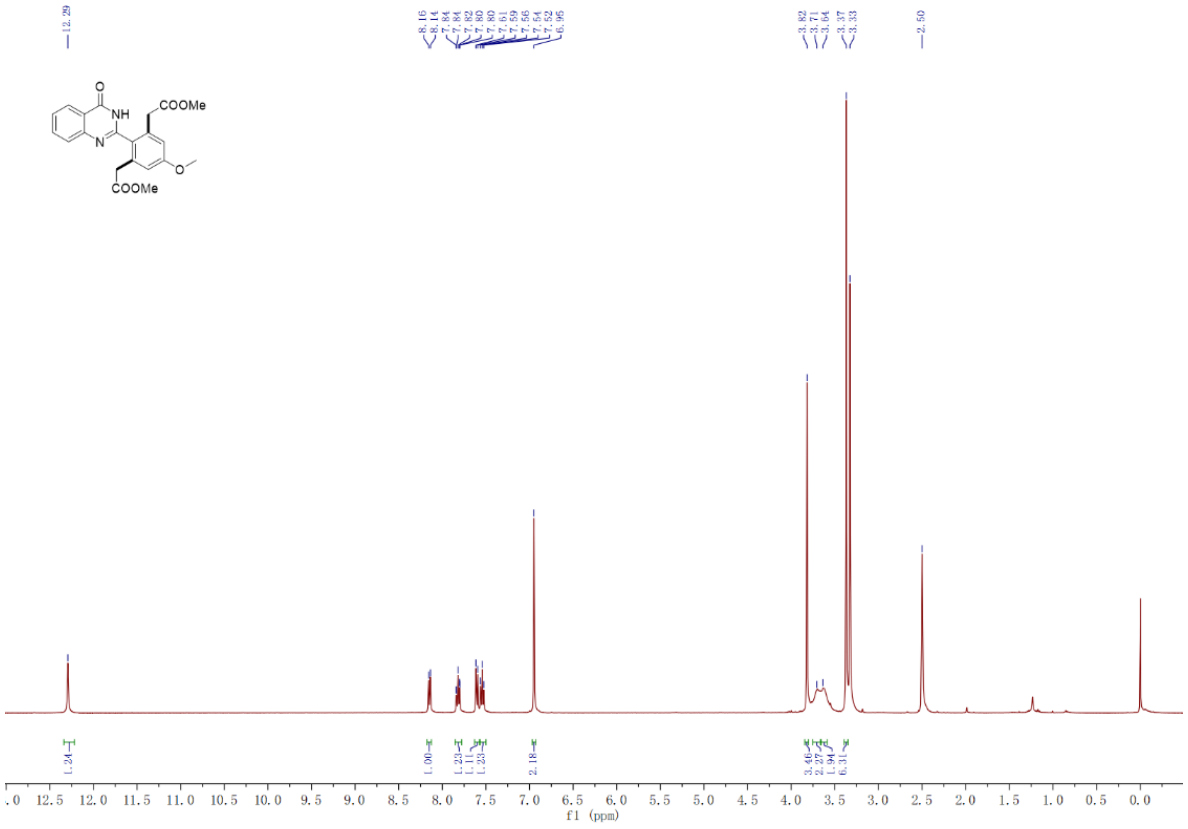
39.35
29.59
f1 (ppm)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COOMe
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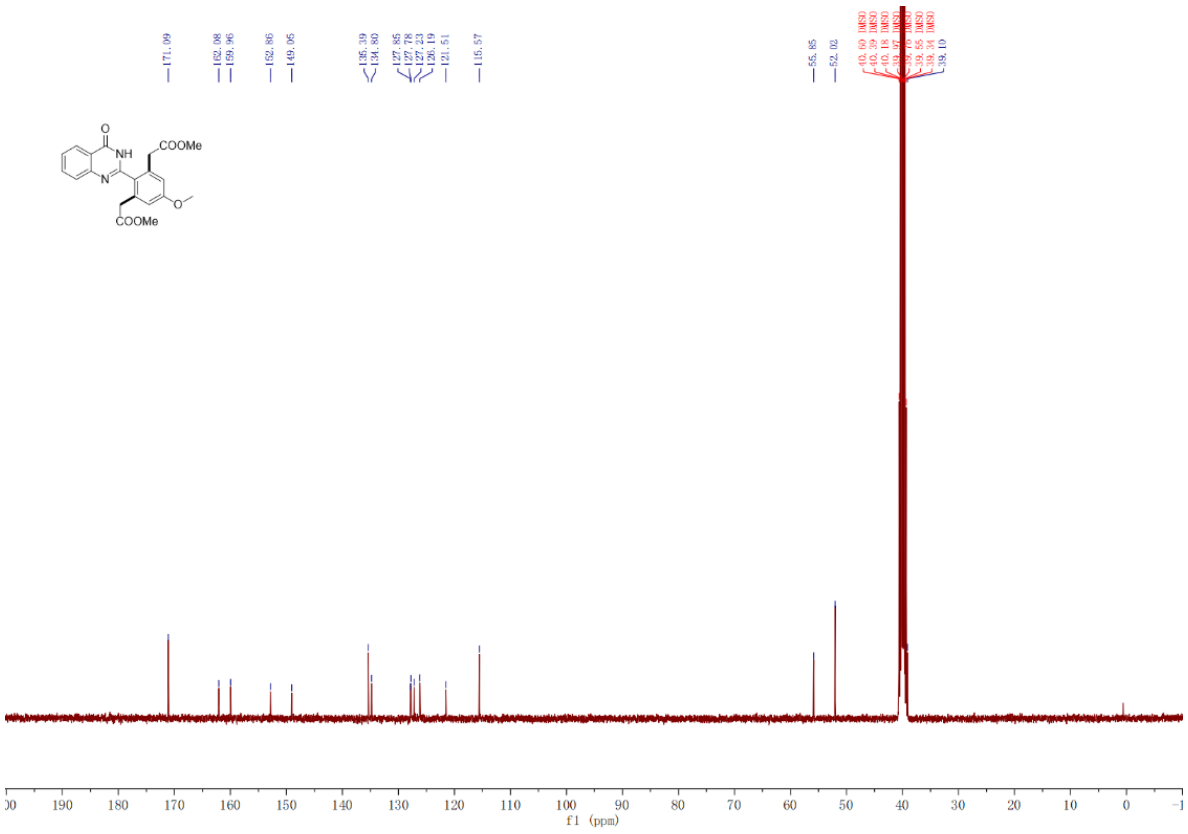
6.31
f1 (ppm)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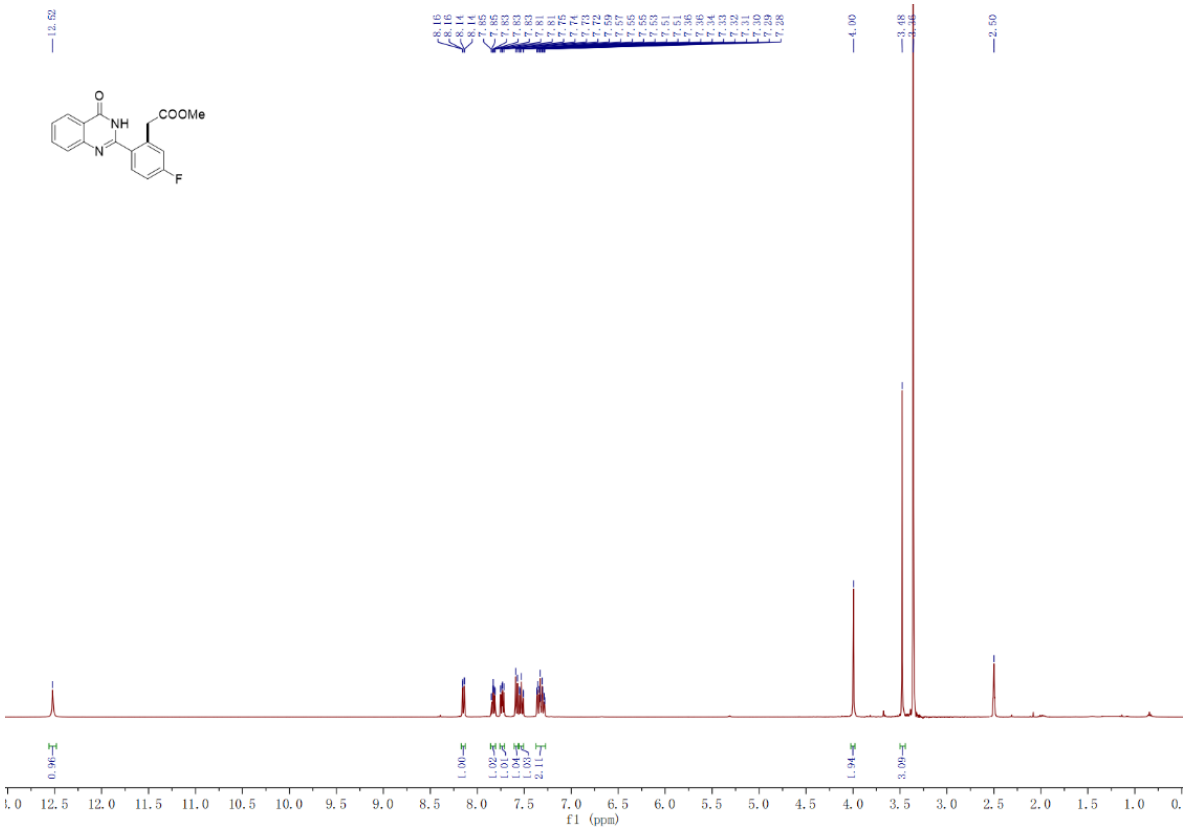
COOMe
COOMe
NH
N
O
f1 (ppm)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7.36
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7.32
7.31
7.30
7.29
7.28
4.00
3.48
3.46
2.50
0.96
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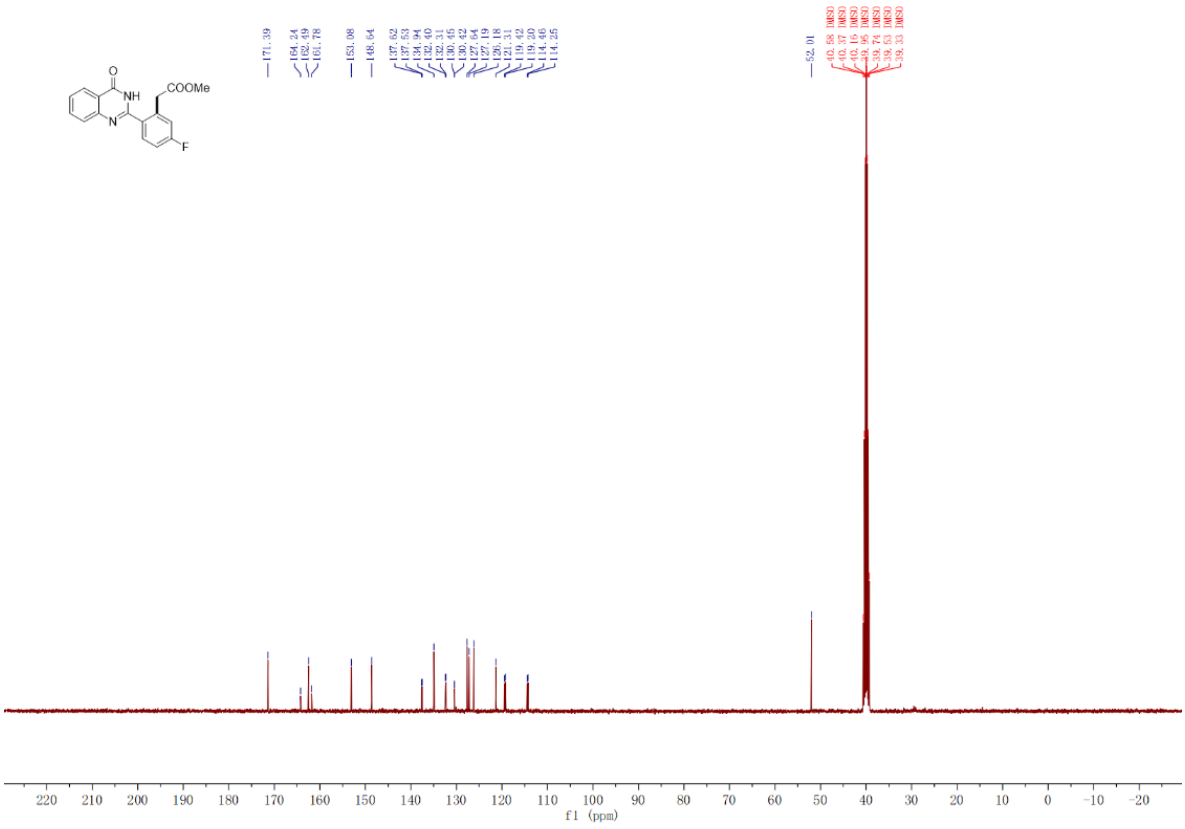
2.11
1.94
3.09
COOMe
NH
N
F
f1 (ppm)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NH
N
COOMe
F
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132.60
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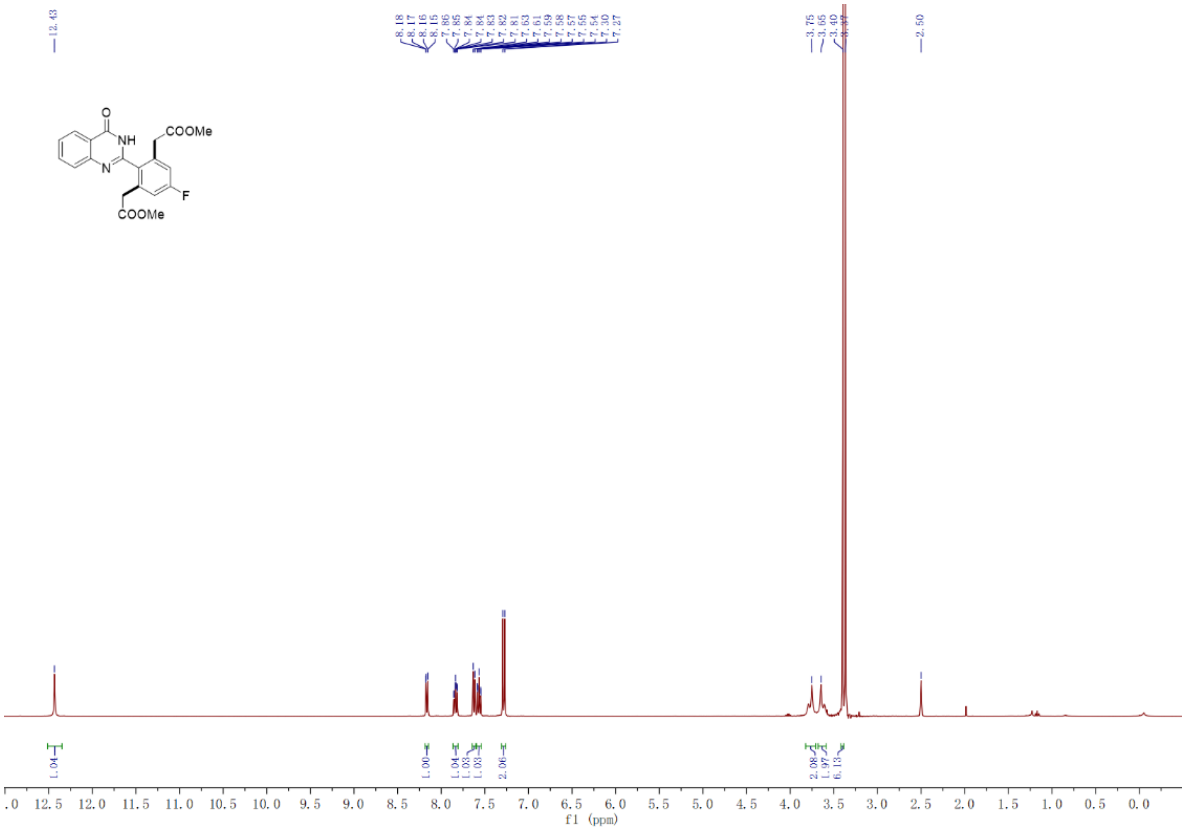
130.45
130.42
127.64
127.19
126.18
121.31
119.42
119.20
114.46
114.25
52.01
40.58 DMSO
40.37 DMSO
40.15 DMSO
39.95 DMSO
39.74 DMSO
39.53 DMSO
39.33 DMSO
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)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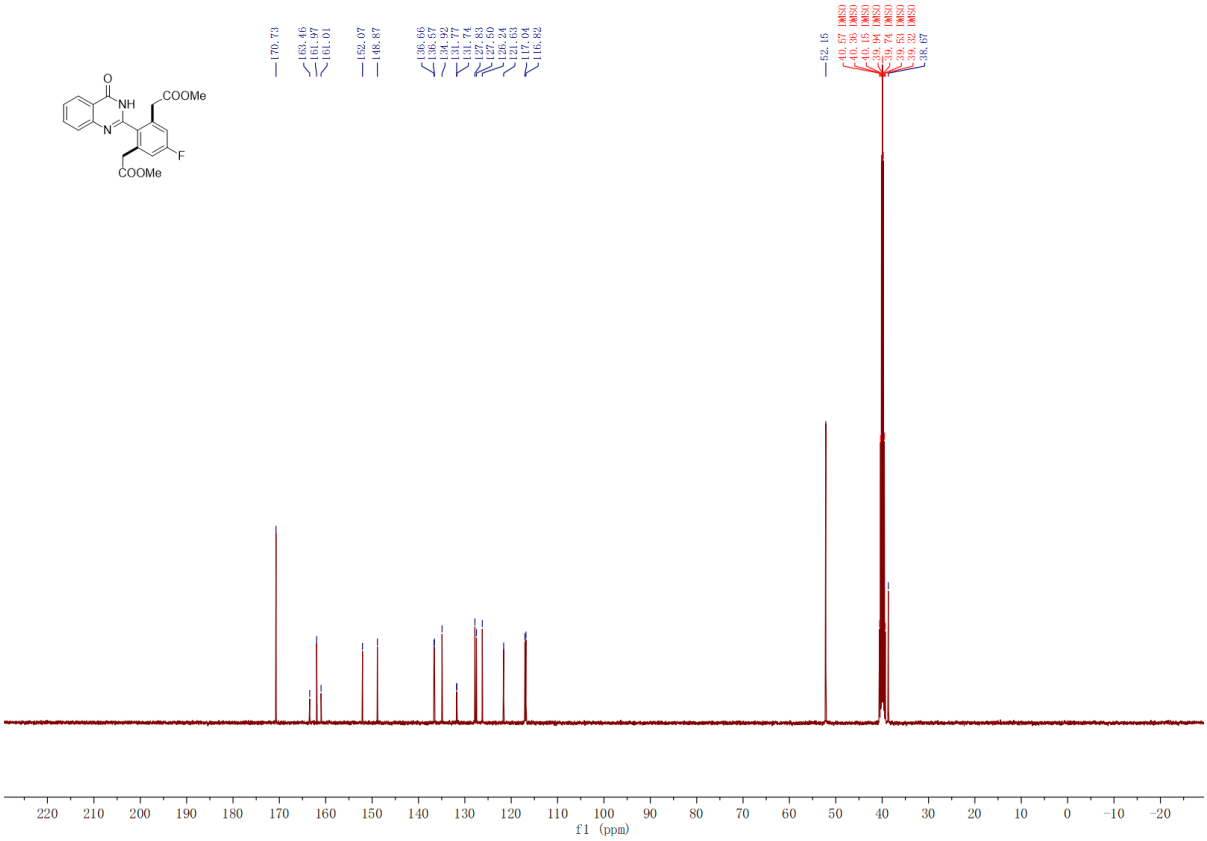
7.84
7.83
7.82
7.81
7.63
7.61
7.59
7.58
7.57
7.56
7.54
7.30
7.27
3.75
3.66
3.60
3.32
2.50
O
NH
N
COOMe
F
COOMe
1.04
1.00
1.04
1.03
1.03
2.06
2.08
1.97
6.13
.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


O
NH
N
COOMe
F
COOMe
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161.01
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148.87
136.66
136.57
134.92
131.77
131.74
127.83
127.50
126.24
121.63
117.04
116.82
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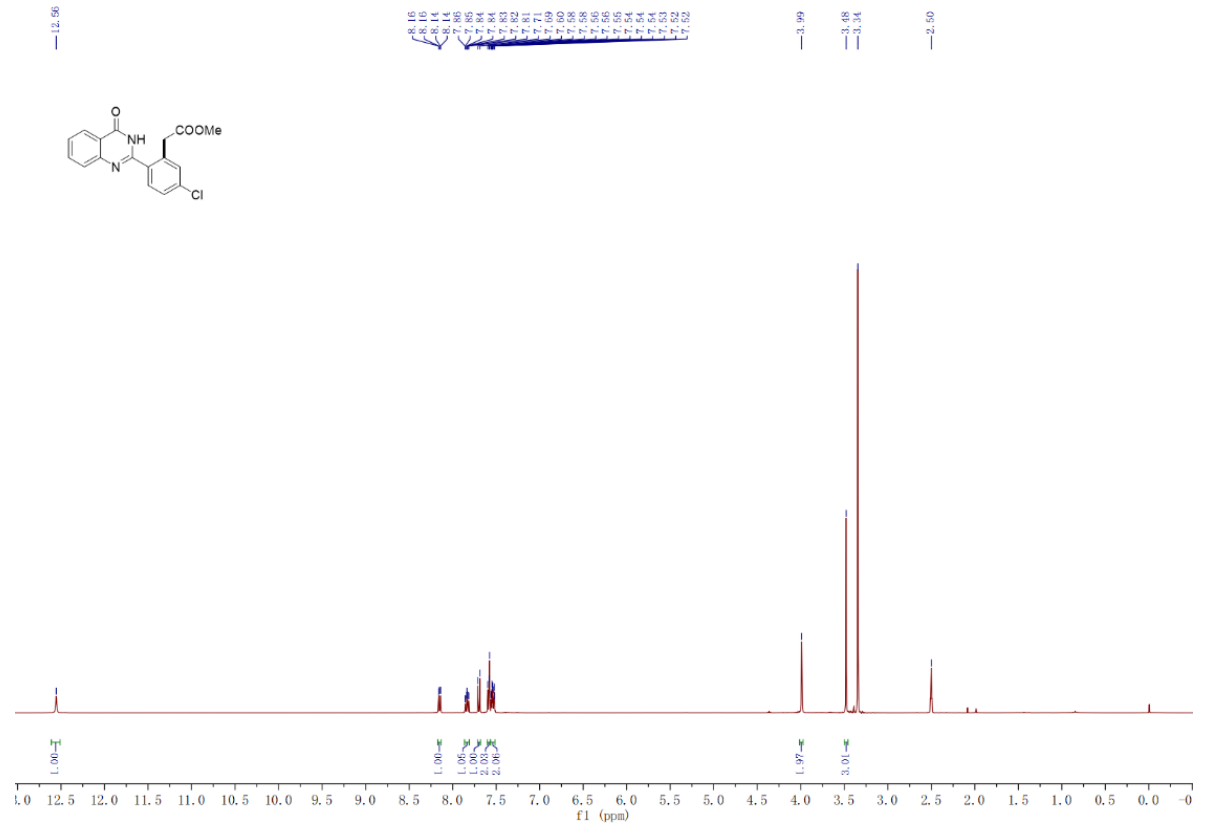
40.36
40.15
39.94
39.74
39.53
39.32
38.67
f1 (ppm)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7.84
7.83
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7.71
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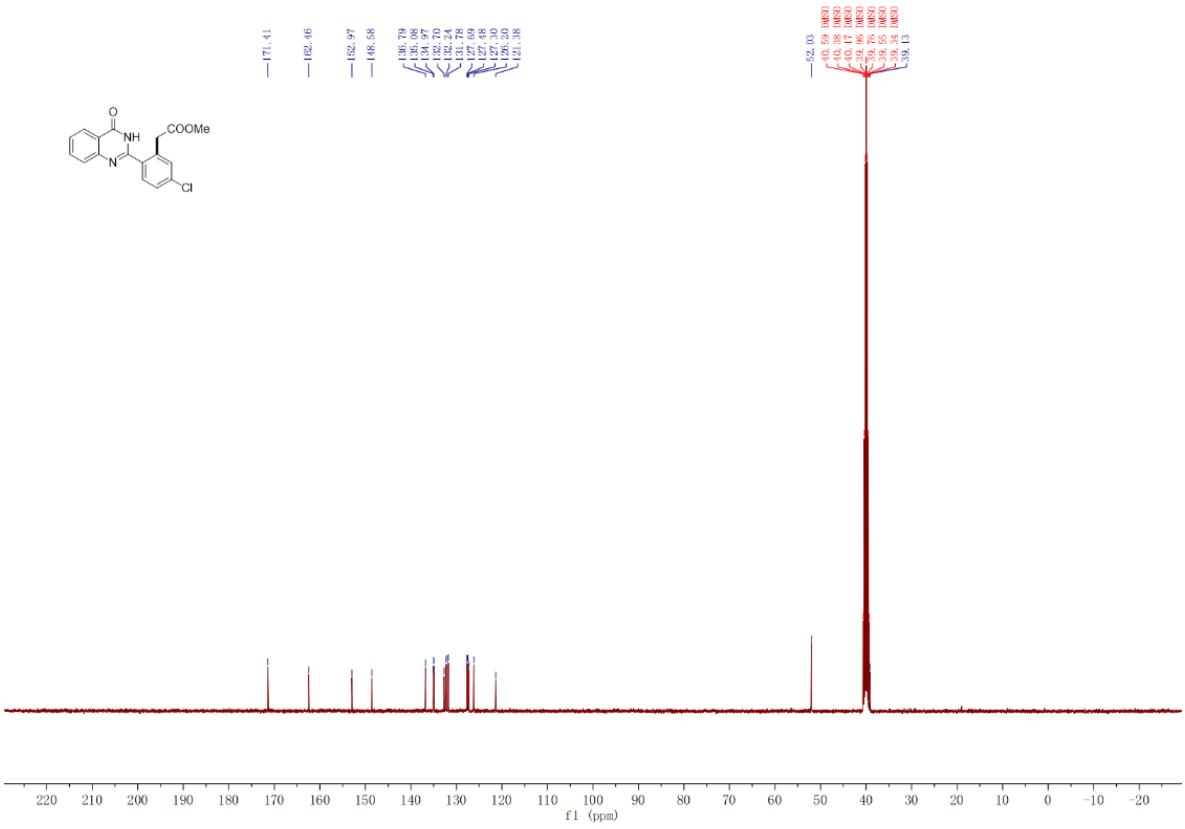
7.60
7.58
7.58
7.56
7.56
7.55
7.54
7.54
7.53
7.53
7.52
7.52
3.99
3.48
3.34
2.50
O
NH
N
COOMe
Cl
1.00
1.00
1.05
1.00
2.03
2.06
1.97
3.01
f1 (ppm)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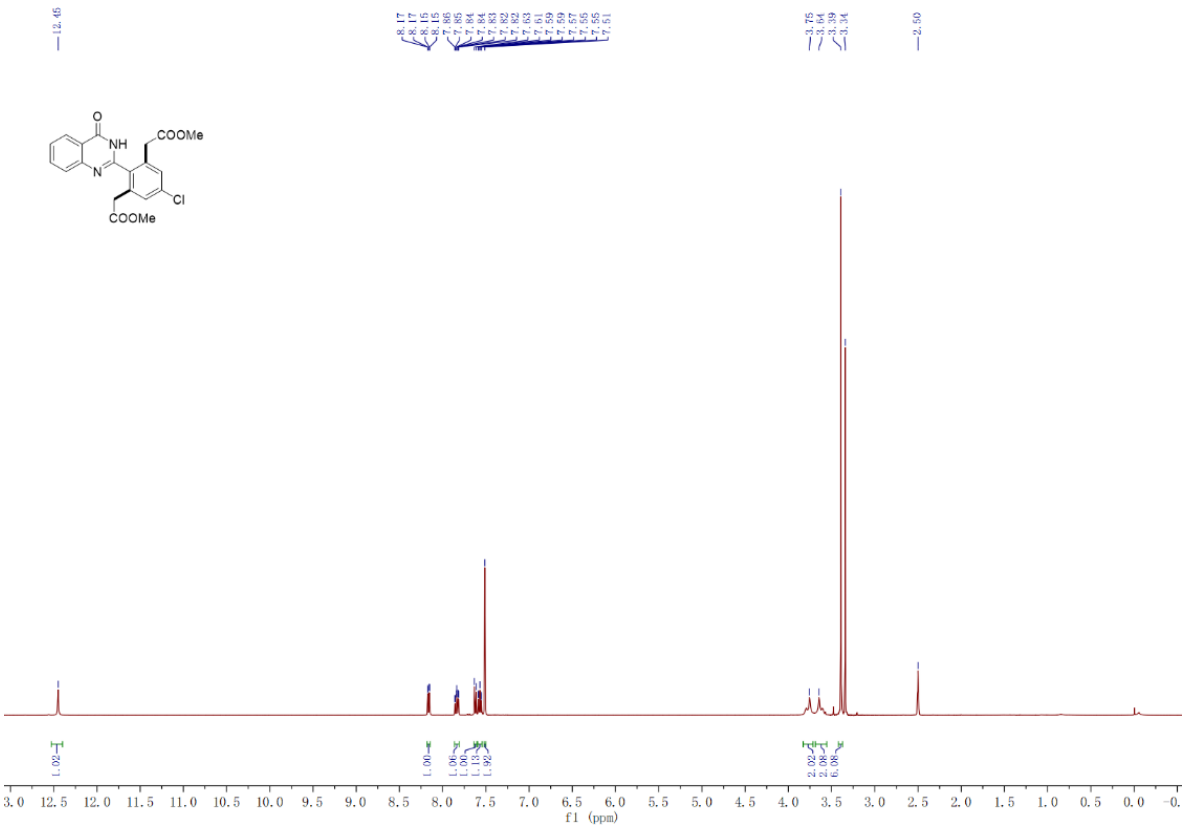
135.08
134.97
132.70
132.24
131.78
127.68
127.48
127.30
126.20
121.38
52.03
40.59
40.38
40.17
39.96
39.76
39.55
39.34
39.13
O
NH
N
COOMe
Cl
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)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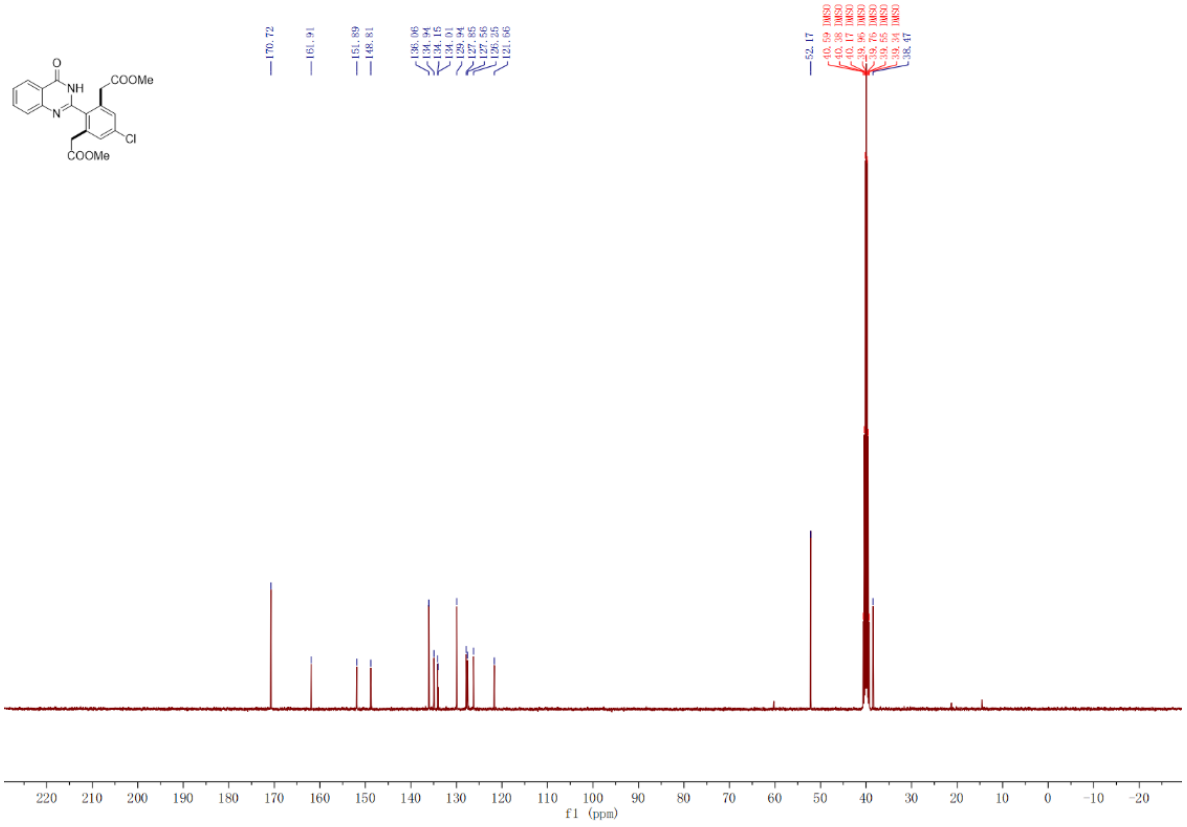
7.83
7.82
7.63
7.61
7.59
7.57
7.55
7.51
3.75
3.64
3.39
3.34
2.50
O
NH
N
COOMe
Cl
COOMe
1.02
1.00
1.06
1.20
1.13
1.92
2.02
2.08
6.00
3.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.
f1 (ppm)


COOMe
NH
N
Cl
COOMe
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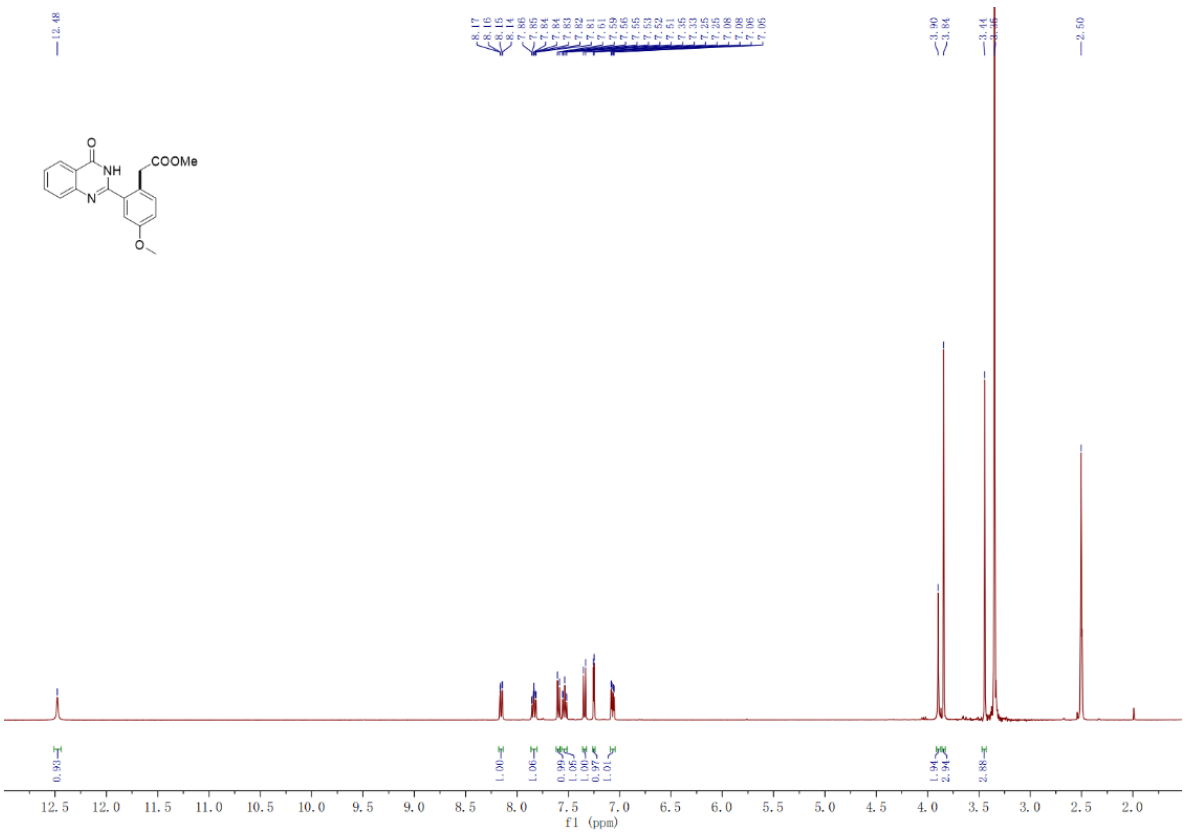
161.91
151.89
148.81
126.06
134.94
134.15
134.01
129.94
127.85
127.55
126.25
121.66
52.17
40.59
40.38
40.17
39.96
39.76
39.55
39.34
38.47
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)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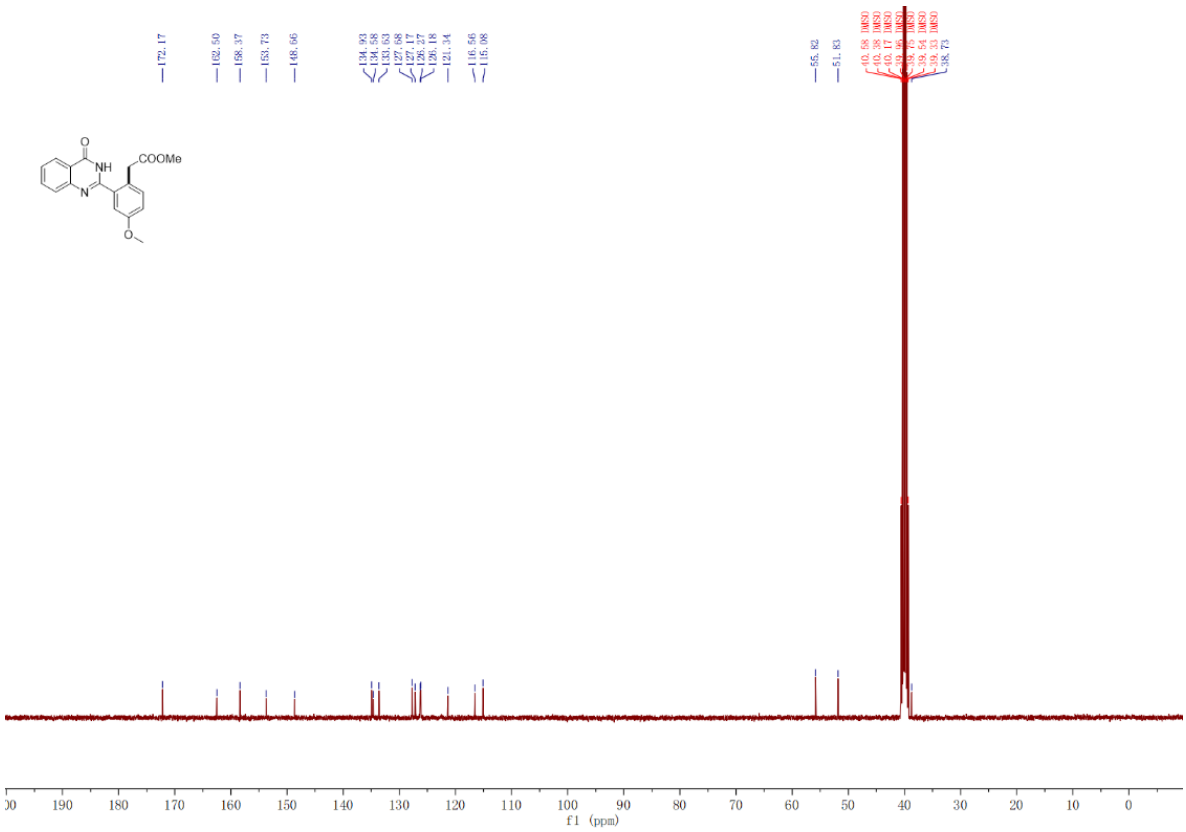
7.84
7.83
7.82
7.81
7.61
7.59
7.56
7.55
7.53
7.52
7.51
7.35
7.33
7.25
7.08
7.06
7.05
3.90
3.84
3.44
3.36
2.50
COOMe
NH
N
O
0.93
1.00
1.06
0.99
1.00
0.97
1.01
1.94
2.94
2.88
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0
f1 (ppm)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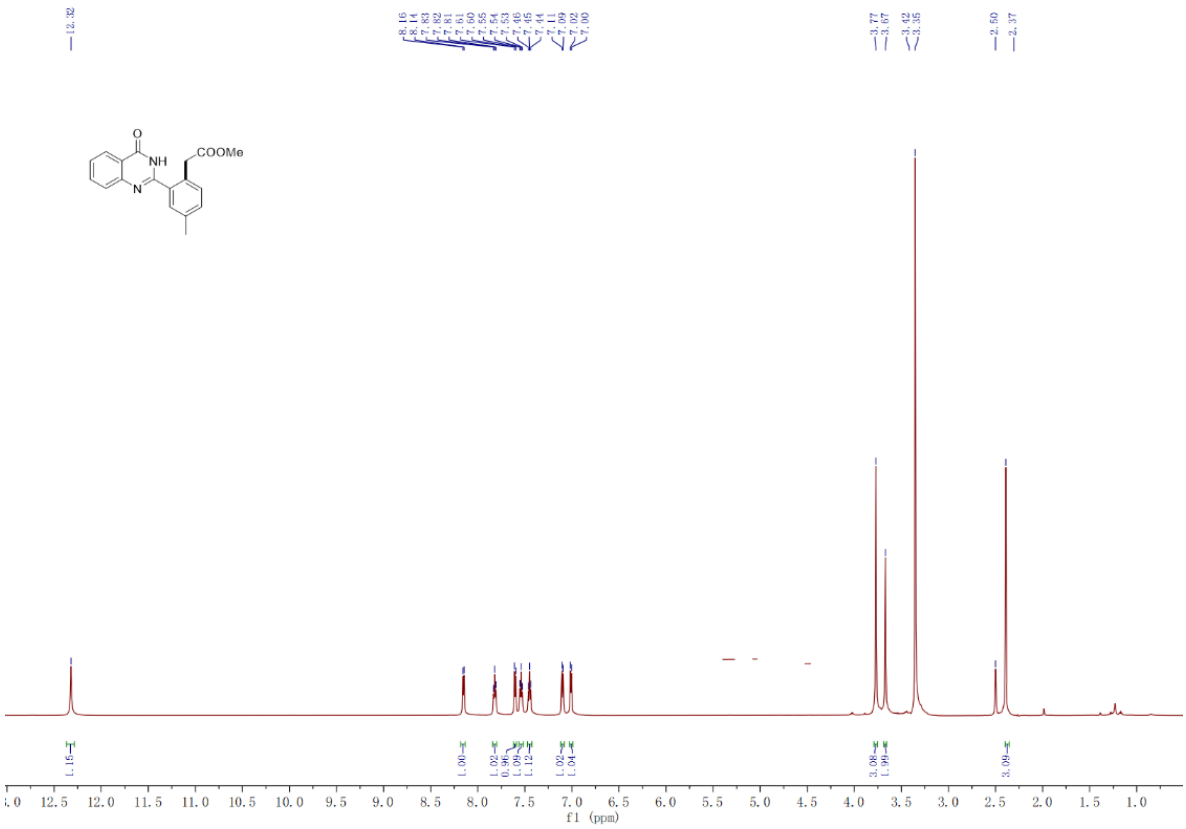
134.58
133.53
127.68
127.17
126.27
126.18
121.34
116.56
115.08
55.82
51.83
40.58
40.38
40.17
39.96
39.75
39.54
39.33
38.73
O
NH
N
COOMe
O
f1 (ppm)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7.82
7.81
7.61
7.60
7.55
7.54
7.53
7.46
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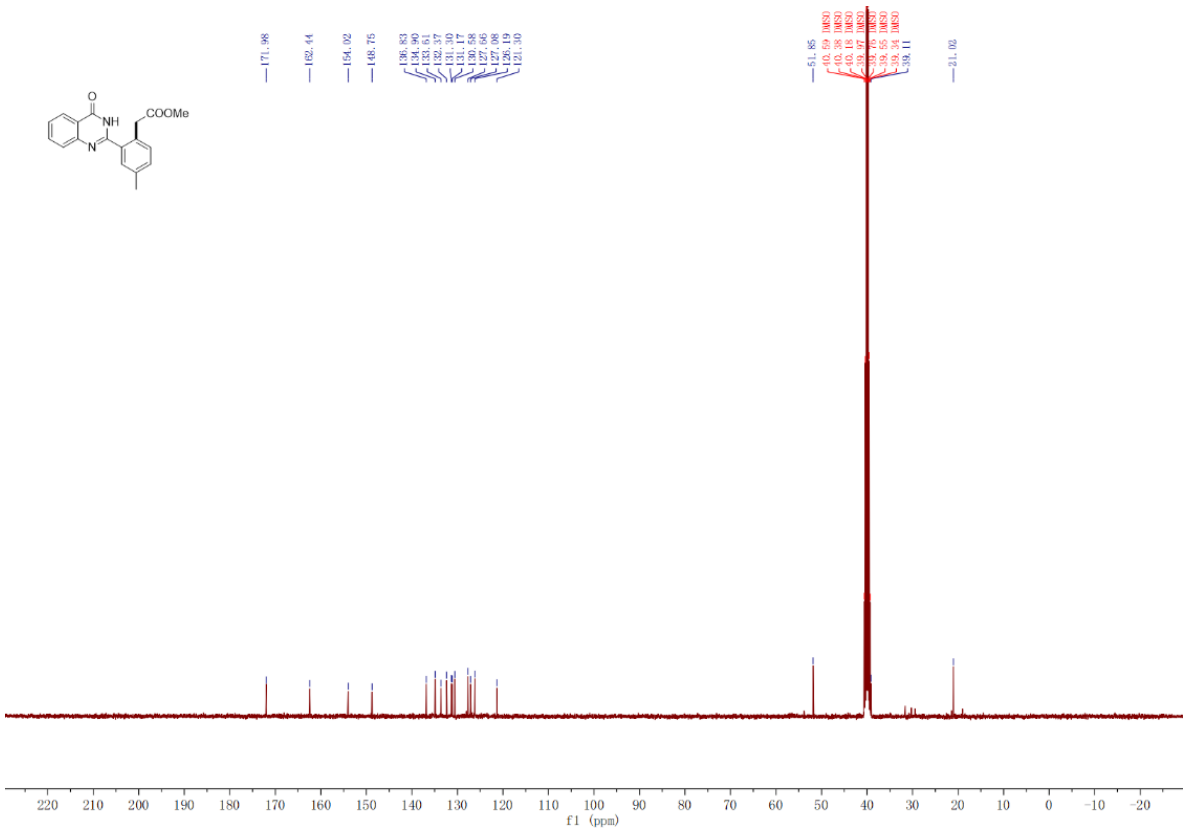
7.44
7.11
7.09
7.02
7.00
3.77
3.67
3.42
3.35
2.50
2.37
O
NH
N
COOMe
1.16
1.00
1.02
0.96
1.09
1.12
1.02
1.04
3.08
1.99
3.09
f1 (ppm)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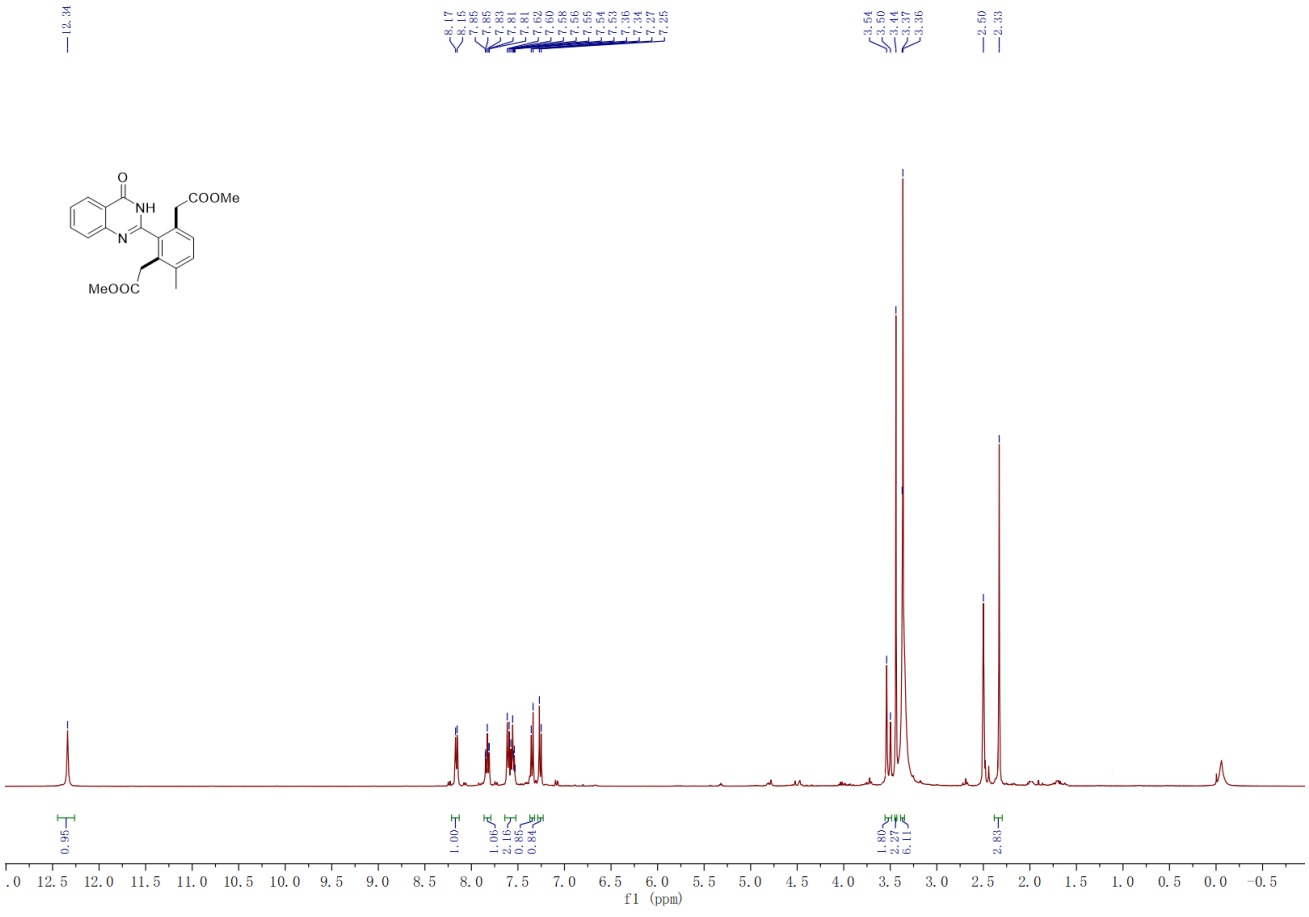
133.61
132.37
131.30
131.17
130.58
127.66
127.08
126.19
121.30
51.85
40.69
40.38
40.07
39.97
39.76
39.55
39.34
39.11
21.02
O
NH
N
COOMe
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)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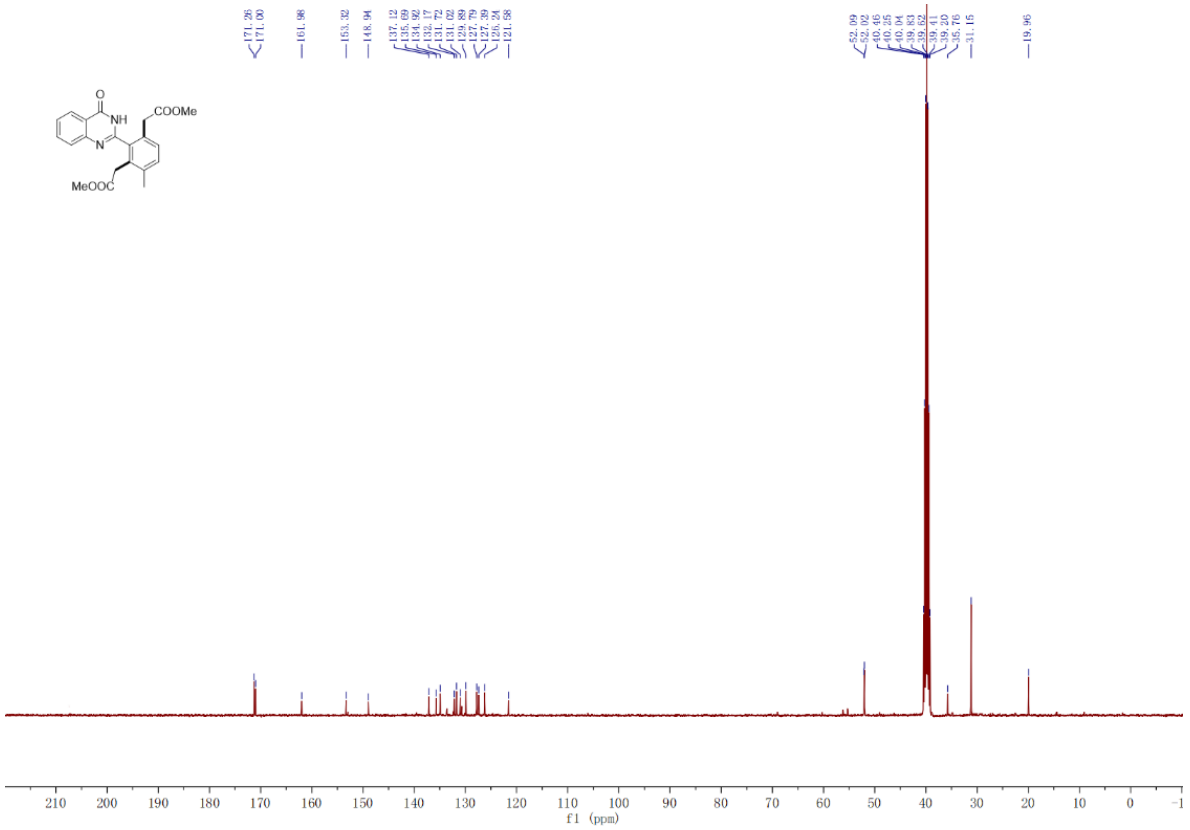
7.85
7.85
7.83
7.81
7.81
7.62
7.60
7.58
7.56
7.55
7.54
7.53
7.36
7.34
7.27
7.25
3.54
3.50
3.44
3.37
3.36
2.50
2.33
O
NH
N
COOMe
MeOOC
0.95
1.00
1.06
2.16
0.85
0.84
1.80
2.27
6.11
2.83
.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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171.00
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153.32
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137.12
135.69
134.92
133.17
131.72
131.02
129.89
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52.09
52.02
49.65
40.25
40.04
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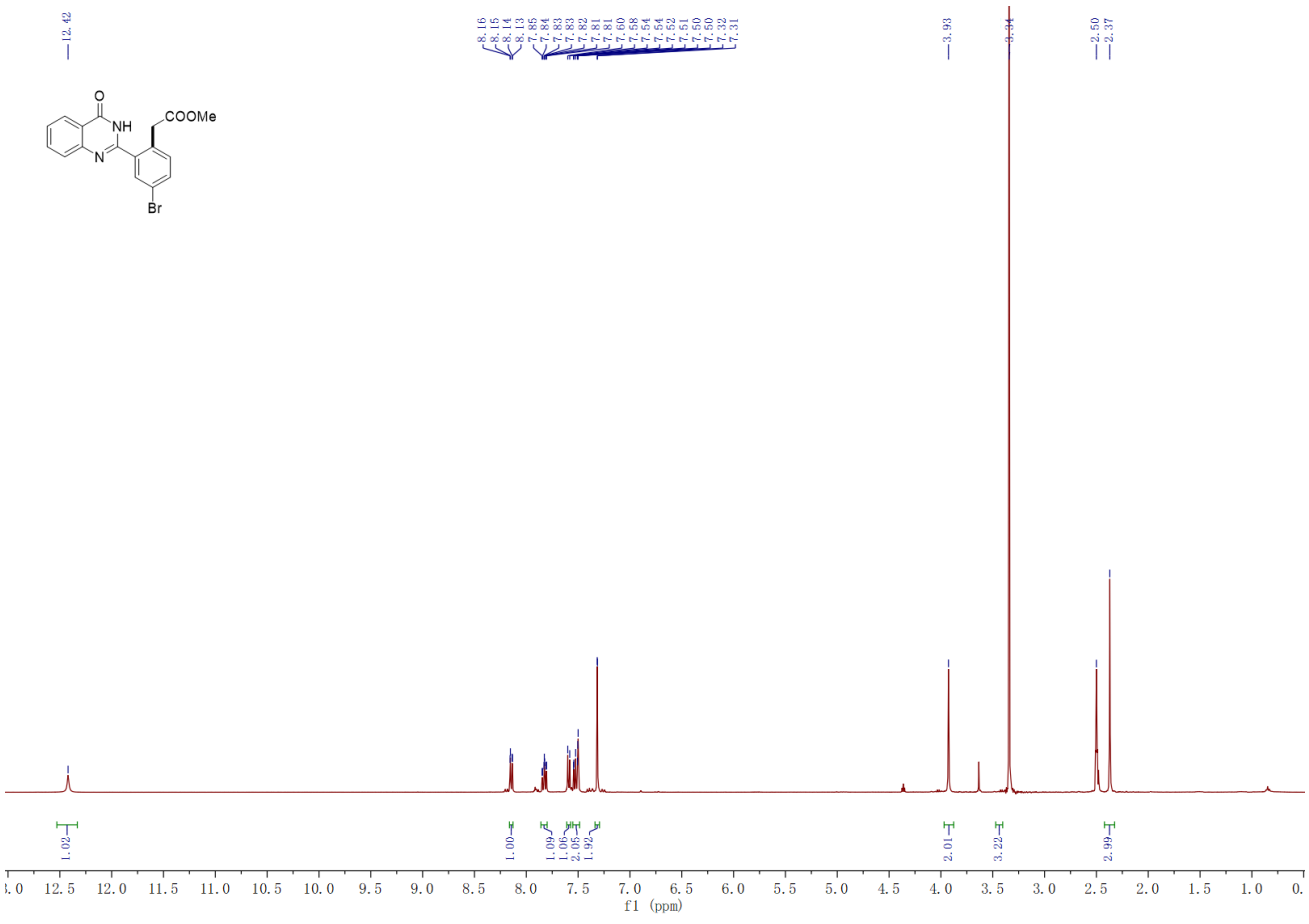
39.20
35.76
31.15
19.96
O
NH
N
COOMe
MeOOC
f1 (ppm)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7.83
7.82
7.81
7.60
7.58
7.54
7.53
7.51
7.50
7.32
7.31
3.93
3.94
2.50
2.37
O
NH
N
COOMe
Br
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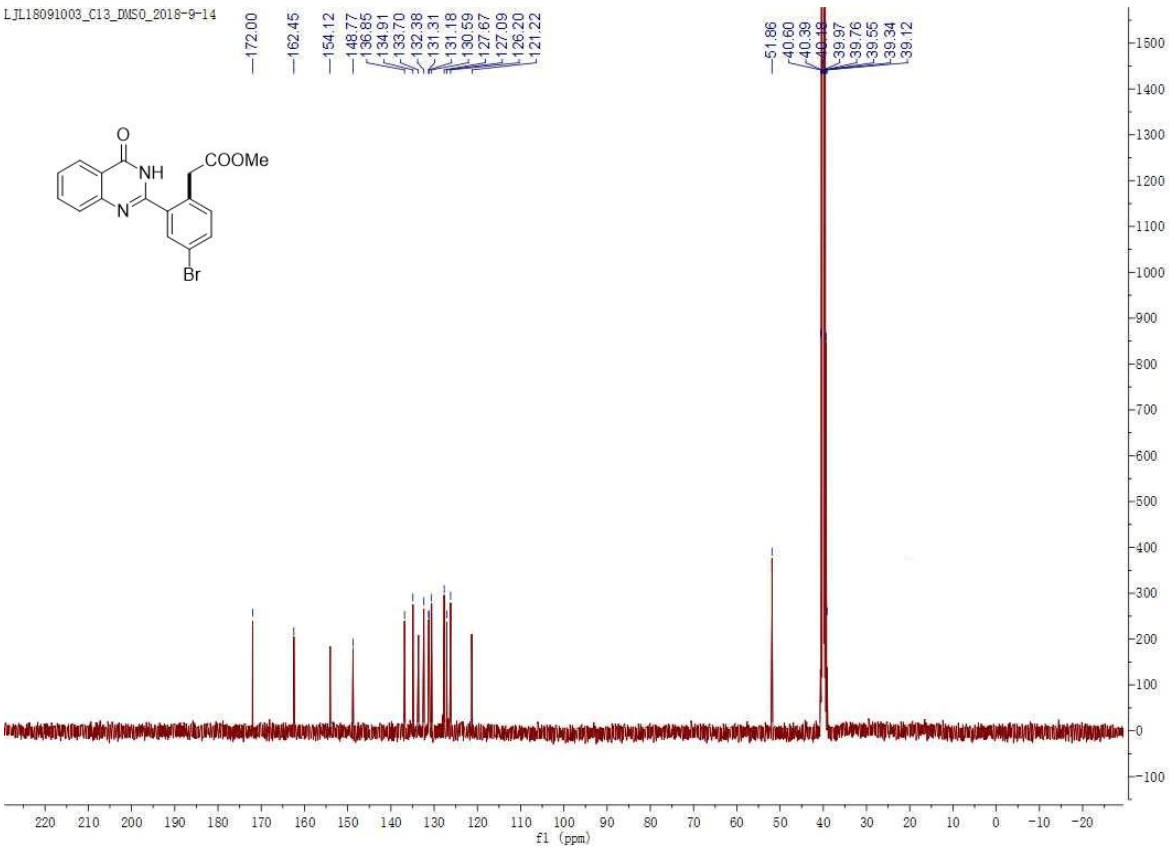
1.00
1.09
1.05
2.05
1.92
2.01
3.22
2.99
f1 (ppm)


LJL18091003_C13_DMSO_2018-9-14
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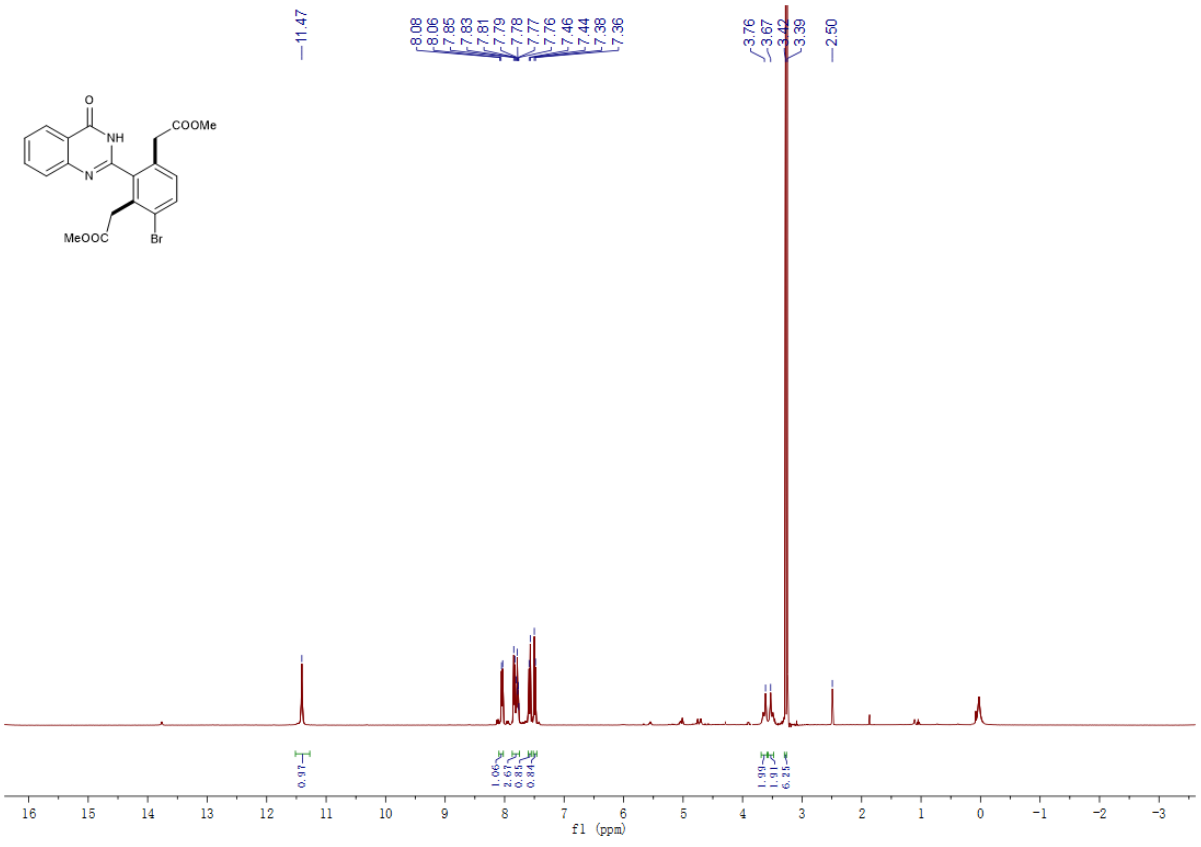
154.12
148.77
136.85
134.91
133.70
132.38
131.31
131.18
130.59
127.67
127.09
126.20
121.22
51.86
40.60
40.39
40.18
39.97
39.76
39.55
39.34
39.12
O
NH
N
COOMe
Br
f1 (ppm)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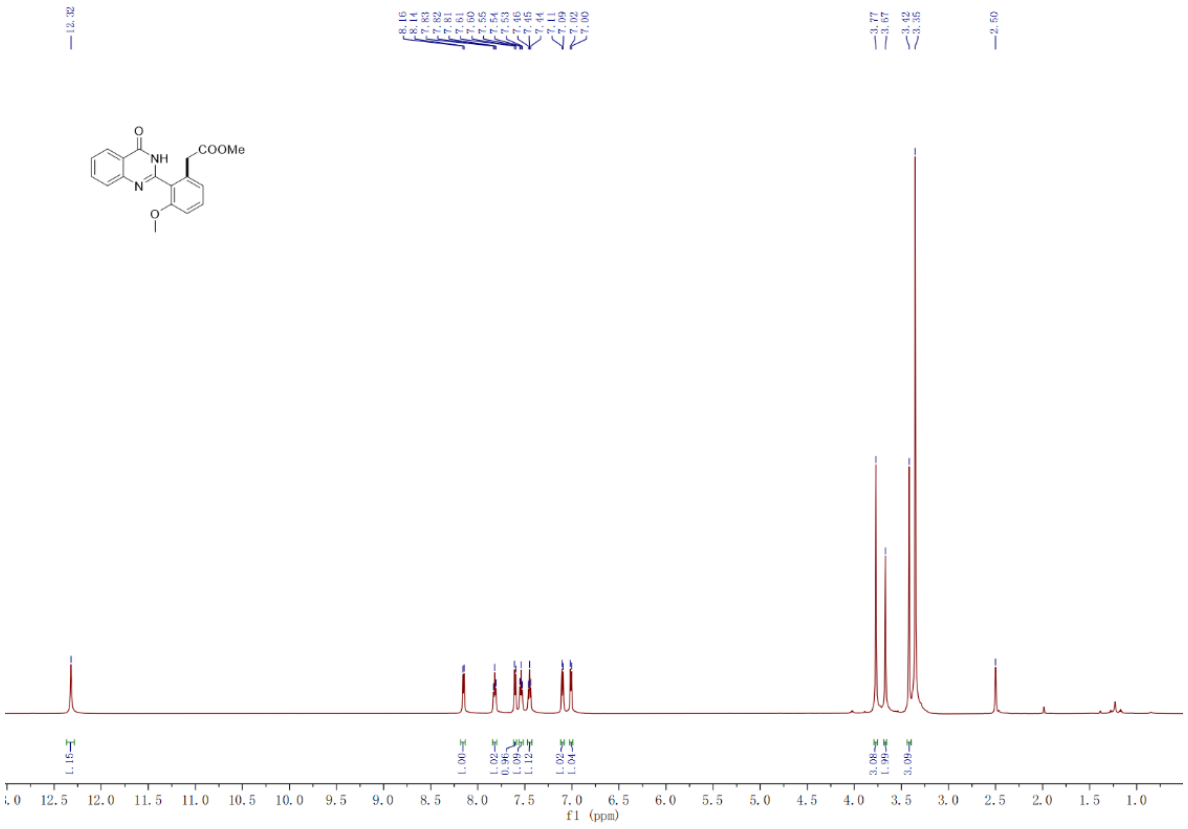
7.81
7.79
7.78
7.77
7.76
7.46
7.44
7.38
7.36
3.76
3.67
3.42
3.39
2.50
O
NH
N
COOMe
MeOOC
Br
0.97
1.00
2.67
0.81
0.84
1.99
1.91
6.25
f1 (ppm)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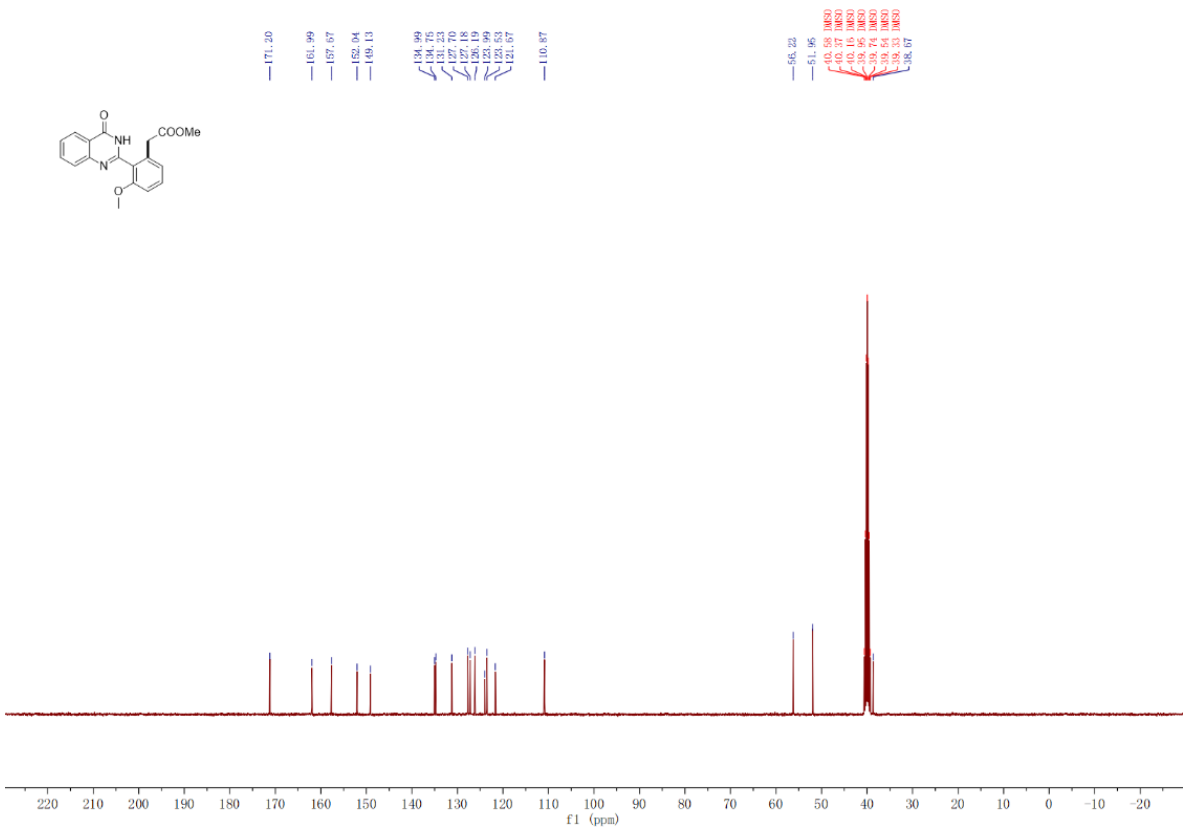
7.60
7.55
7.54
7.53
7.46
7.45
7.44
7.11
7.09
7.02
7.00
3.77
3.67
3.42
3.35
2.69
COOMe
NH
N
O
1.15
1.00
1.02
0.96
1.09
1.12
1.02
1.04
3.08
1.99
3.09
f1 (ppm)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126.19
123.99
123.55
121.67
110.87
56.22
51.95
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39.95
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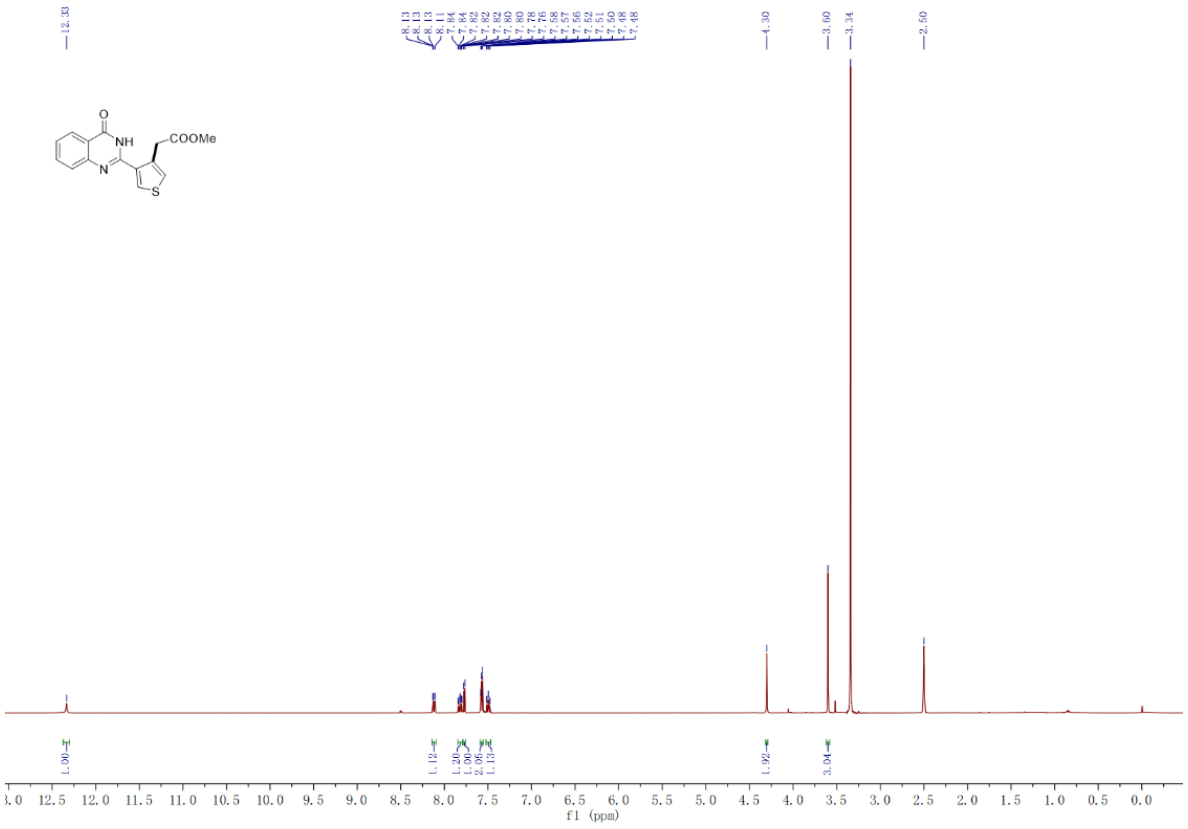
39.54
39.33
38.67
COOMe
NH
N
O
f1 (ppm)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8.13
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7.82
7.82
7.80
7.80
7.78
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7.58
7.57
7.56
7.52
7.51
7.50
7.48
7.48
4.30
3.60
3.34
2.50
O
NH
N
S
COOMe
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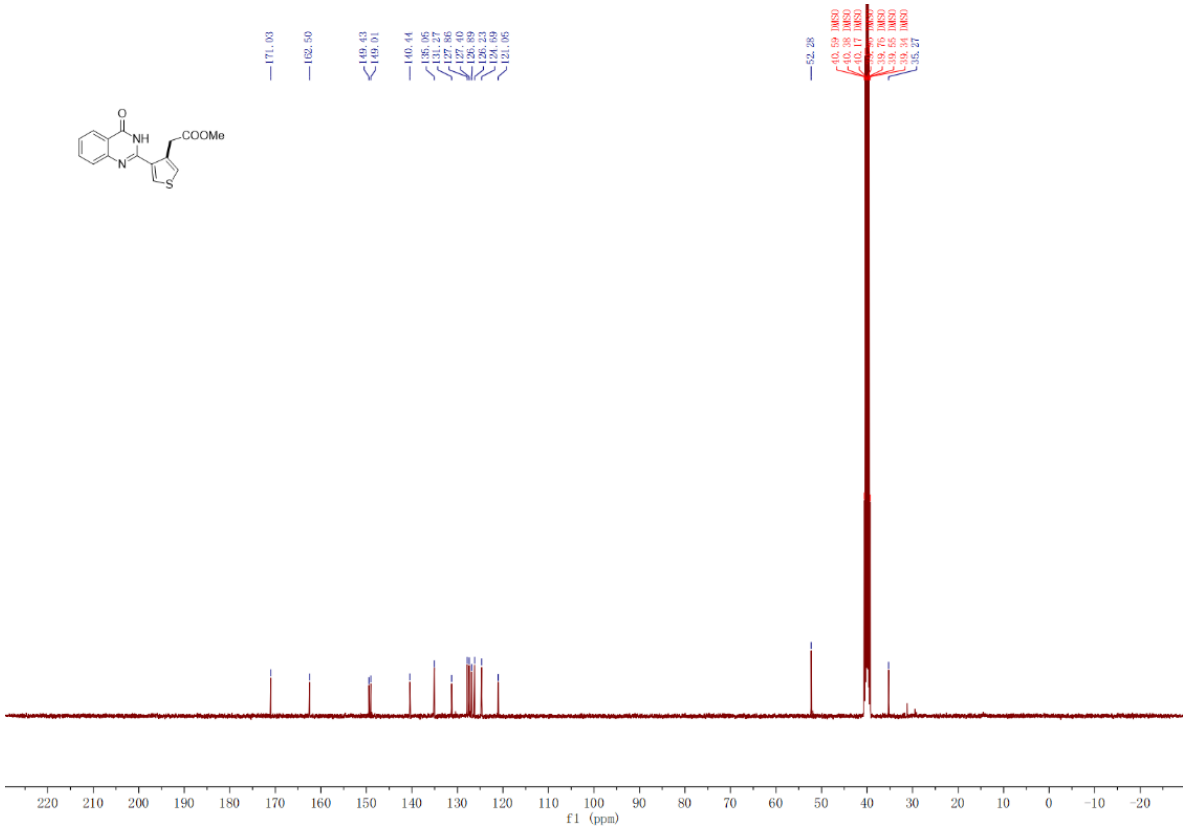
1.12
1.20
1.00
2.05
1.13
1.92
3.04
f1 (ppm)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126.89
126.23
124.69
121.95
52.28
40.59
40.38
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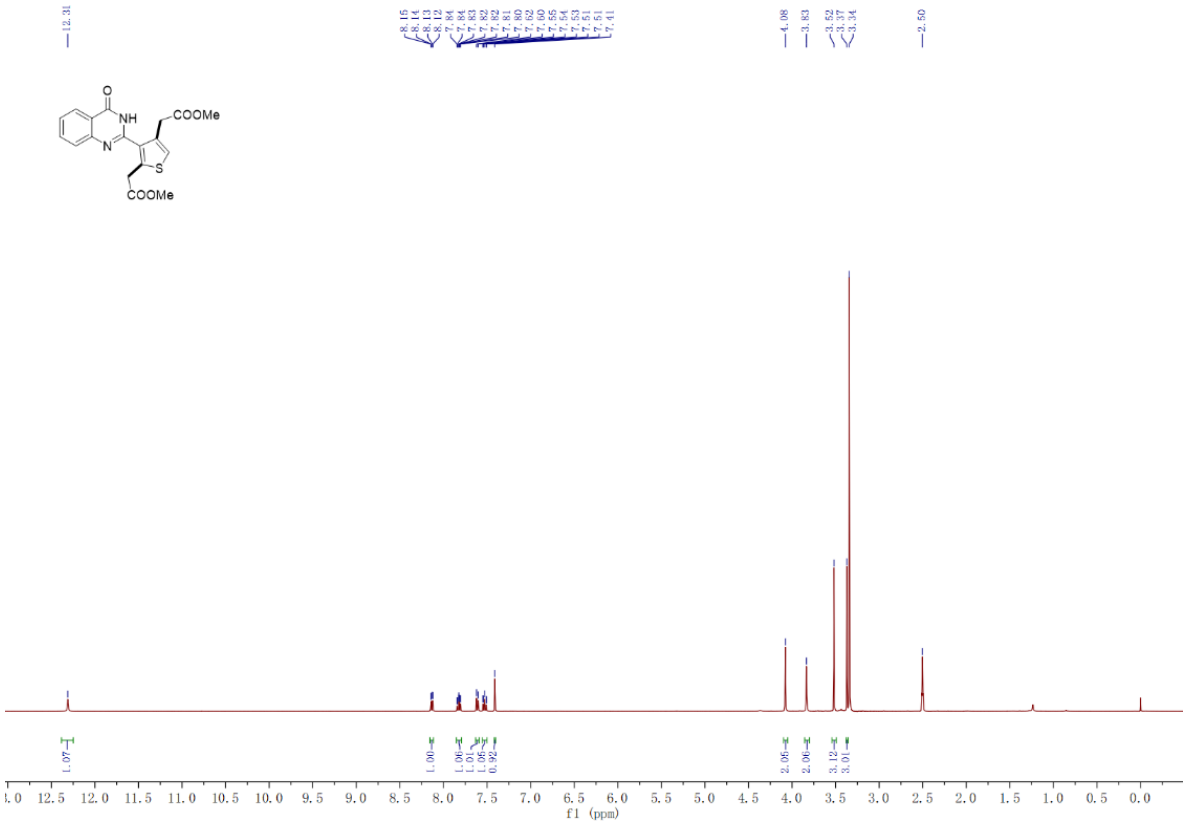
39.96
39.75
39.55
39.34
35.27
O
NH
N
S
COOMe
f1 (ppm)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7.82
7.82
7.81
7.80
7.02
7.02
7.00
7.55
7.54
7.53
7.51
7.51
7.41
4.08
3.83
3.52
3.37
3.34
2.50
O
NH
N
S
COOMe
COOMe
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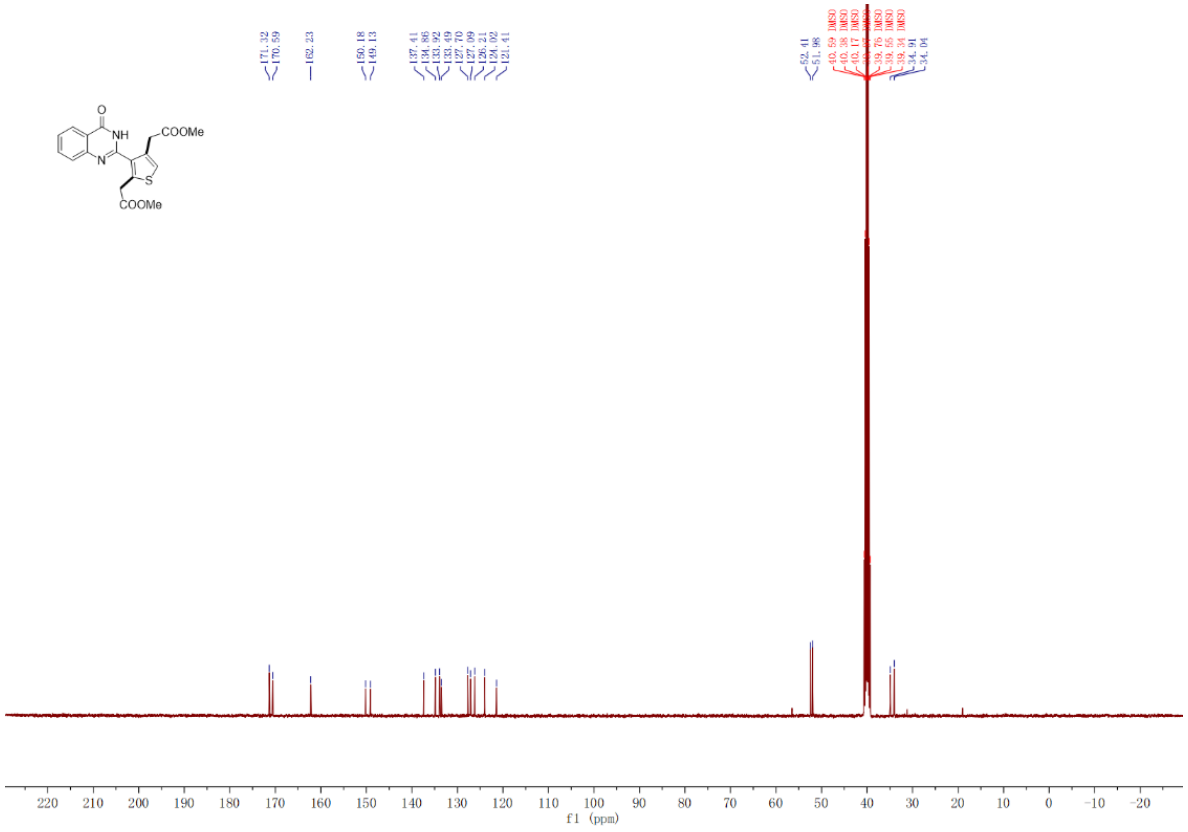
1.06
1.02
1.06
0.92
2.06
2.00
3.12
3.01
f1 (ppm)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137.41
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133.49
127.70
127.09
126.21
124.02
121.41
52.41
51.98
40.59
40.38
40.17
39.95
39.74
39.53
39.32
39.11
38.90
34.91
34.04
O
NH
N
S
COOMe
COOMe
f1 (ppm)