Electronic Supplementary Information

Direct Construction of Benzimidazo[l,2-c]quinazolin-6-ones *via* Transition-Metal-Free Oxidative C-C Bond Cleavage

Ping-Gui Li,[a,b,§] Cheng Yan,[a,§] Shuai Zhu,[a] Shu-Hui Liu,[a] and Liang-Hua Zou[*,a]

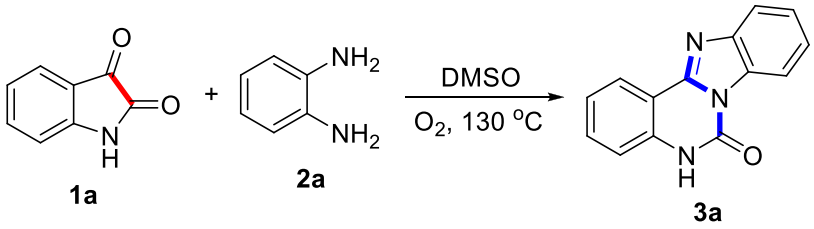
Email: zoulianghua@jiangnan.edu.cn

CONTENTS

1. General Information

All solvents were dried and purified by known procedures and freshly distilled under argon from appropriate drying agents prior to use. Isatins **1h** and **1k** were prepared according to literature[1] and others were commercially available. The products were isolated by column chromatography on silica gel (200-300 mesh) by using petroleum ether (30-60 ℃) and ethyl acetate as eluents. Silica gel for column chromatography was purchased from AnhuiLiangchen Chemical Co, Lt. All yields described herein are isolated yields after column chromatography. Reaction progress and product mixtures were routinely monitored by TLC using TLC SiO_2 sheets, and compounds were visualized under ultraviolet light. ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded on a Bruker AVANCE III 400 spectrometer. The spectra were recorded using DMSO-d_6 as a solvent. ^{1}H NMR chemical shifts are referenced to tetramethylsilane (TMS, 0 ppm). Abbreviations are as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet). High-Resolution Mass Spectra (HRMS) were recorded on Micromass Q-Tof instrument (ESI).

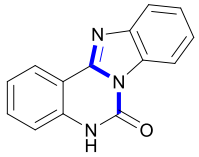
2. General procedure for the Synthesis of Benzo[4,5]imidazo[1,2-c]quinazolin-6(5H)-ones



Take the synthesis of **3a** for example. To a 25 mL sealed tube was added **1a** (0.25 mmol, 36.8 mg), **2a** (0.25 mmol, 27.0 mg) and purged with O_2 for three times. Then DMSO (2 mL) was added and the mixture was stirred at 130 ℃ for 24 h. The reaction was cooled to rt, extracted with *tert*-butyl methyl ether, dried over Na_2SO_4. The solvent was concentrated under reduced pressure. Purification by flash chromatography (petroleum ether/ethyl acetate = 5:1) afforded product **3a** as a light yellow solid (51.6 mg, 88% yield). Product **3a** was obtained as a white solid after recrystallization in methanol.

Procedure for the scaling-up reaction: To a 100 mL pressure flask was added **1a** (6.0 mmol, 882.0 mg), **2a** (6.0 mmol, 648.6 mg) and purged with O_2 for three times. Then DMSO (40 mL) was added and the mixture was stirred at 130 ℃ for 24 h. The reaction was cooled to rt, extracted with *tert*-butyl methyl ether, dried over Na_2SO_4. The solvent was concentrated under reduced pressure. Purification by flash chromatography (petroleum ether/ethyl acetate = 5:1) afforded product **3a** as a light yellow solid (1058.0 mg, 75% yield).

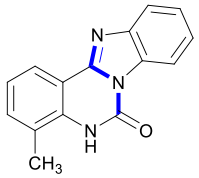
3. Analytical data of the products



Benzimidazo[1,2-c]quinazolin-6(5H)-one (3a)[2]

To a 25 mL sealed tube was added **1a** (0.25 mmol, 36.8 mg), **2a** (0.25 mmol, 27.0 mg) and purged with O_2 for three times. Then DMSO (2 mL) was added and the mixture was stirred at 130 ℃ for 24 h. The reaction was cooled to rt, extracted with *tert*-butyl methyl ether, dried over Na_2SO_4. The solvent was concentrated under reduced pressure. Purification by flash chromatography (petroleum ether/ethyl acetate = 5:1) afforded product **3a** (51.6 mg, 88% yield).

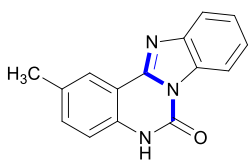
Light yellow solid, m.p.>300 ^oC (lit.>300 ^oC)[2]; ^1H NMR (400 MHz, DMSO-d_6) δ 11.96, 8.36 (d, J = 8.1 Hz, 1H), 8.31 (d, J = 7.8 Hz, 1H), 7.86 (d, J = 7.5 Hz, 1H), 7.67-7.63 (m, 1H), 7.51-7.35 (m, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 148.13, 146.84, 143.98, 137.60, 132.73, 131.09, 125.46, 124.89, 124.11, 123.83, 119.59, 116.36, 115.21, 112.25; ATR-FTIR(cm^{-1}): 3078, 2916, 1718, 1614, 1549, 1479, 1450, 1382, 1342, 1225, 1060, 929, 764; HRMS *m/z* (ESI) calcd for $C_{14}H_{10}N_3O$ $(M+H)^+$ 236.0818, found 236.0818.



4-Methylbenzo[4,5] imidazo[1,2-c]quinazolin-6(5H)-one (3b)

To a 25 mL sealed tube was added **1b** (0.25 mmol, 40.3 mg), **2a** (0.25 mmol, 27.0 mg) and purged with O_2 for three times. Then DMSO (2 mL) was added and the mixture was stirred at 130 ℃ for 24 h. The reaction was cooled to rt, extracted with *tert*-butyl methyl ether, dried over Na_2SO_4. The solvent was concentrated under reduced pressure. Purification by flash chromatography (petroleum ether/ethyl acetate = 5:1) afforded product **3b** (24.9 mg, 40% yield).

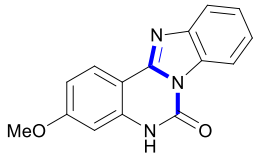
Light yellow solid, m.p.>300 ^oC; ^1H NMR (400 MHz, DMSO-d_6) δ 11.11 (s, 1H), 8.38 (d, J = 7.4 Hz, 1H), 8.21 (d, J = 7.1 Hz, 1H), 7.86 (d, J = 7.6 Hz, 1H), 7.43-7.52 (m, 3H), 7.29 (t, J = 7.6 Hz, 1H), 2.50 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 148.36, 147.11, 144.10, 135.99, 134.05, 131.08, 125.55, 125.18, 124.07, 123.66, 122.77, 119.55, 115.32, 112.35, 18.16; ATR-FTIR(cm^{-1}): 3234, 2919, 1703, 1608, 1554, 1448, 1400, 1345, 1230, 1118, 915, 752, 525; HRMS *m/z* (ESI) calcd for $C_{15}H_{12}N_3O$ $(M+H)^+$ 250.0975, found 250.0976.



2-Methylbenzo[4,5]imidazo[1,2-c]quinazolin-6(5H)-one (3c)

To a 25 mL sealed tube was added **1c** (0.25 mmol, 40.3 mg), **2a** (0.25 mmol, 27.0 mg) and purged with O_2 for three times. Then DMSO (2 mL) was added and the mixture was stirred at 130 ℃ for 24 h. The reaction was cooled to rt, extracted with *tert*-butyl methyl ether, dried over Na_2SO_4. The solvent was concentrated under reduced pressure. Purification by flash chromatography (petroleum ether/ethyl acetate = 5:1) afforded product **3c** (57.3 mg, 92% yield).

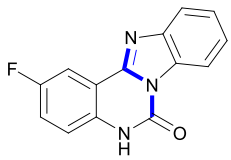
White solid, m.p.>300^{o}C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.87 (s, 1H), 8.35 (d,J = 8.3 Hz, 1H), 8.09 (s, 1H), 7.84 (d, J = 7.9, 1H), 7.48 (td, J = 7.7, 1.3 Hz, 1H), 7.43 (m, 2H), 7.27 (d, J = 8.3 Hz, 1H), 2.41 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 148.11, 146.79, 143.99, 135.40, 133.71, 133.08, 131.09, 125.38, 124.46, 124.00, 119.52, 116.24, 115.18, 112.01, 20.91; ATR-FTIR(cm^{-1}): 3070, 2916, 1726, 1701, 1504, 1449, 1390, 1333, 1201, 822, 757, 743, 540; HRMS *m/z* (ESI) calcd for $C_{15}H_{12}N_3O$ $(M+H)^+$ 250.0975, found 250.0975.



3-Methoxybenzo[4,5]imidazo[1,2-c]quinazolin-6(5H)-one (3d)

To a 25 mL sealed tube was added **1d** (0.25 mmol, 44.3 mg), **2a** (0.25 mmol, 27.0 mg) and purged with O_2 for three times. Then DMSO (2 mL) was added and the mixture was stirred at 130 ℃ for 24 h. The reaction was cooled to rt, extracted with *tert*-butyl methyl ether, dried over Na_2SO_4. The solvent was concentrated under reduced pressure. Purification by flash chromatography (petroleum ether/ethyl acetate = 5:1) afforded product **3d** (59.7 mg, 90% yield).

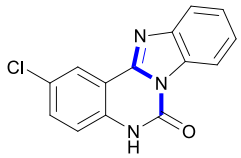
Light yellow solid, m.p.>300^{o}C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.87 (s, 1H), 8.32 (d, J = 7.8 Hz, 1H), 8.21 (d, J = 8.8 Hz, 1H), 7.80 (d, J = 7.9 Hz, 1H), 7.46 (td, J = 7.8, 1.2 Hz, 1H), 7.42-7.38 (m, 1H), 6.98 (dd, J = 8.8, 2.4 Hz, 1H), 6.88 (d, J = 2.4 Hz, 1H), 3.86 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 167.60, 152.99, 151.74, 148.89, 144.14, 135.72, 131.31 (d, J = 14.0 Hz), 130.09, 128.35, 123.95, 119.73 (d, J = 16.2 Hz), 116.67, 110.26, 104.56, 60.81; ATR-FTIR(cm^{-1}): 3060, 2921, 1727, 1623, 1518, 1451, 1375, 1331, 1274, 1228, 1207, 1025, 754, 529;HRMS *m/z* (ESI) calcd for $C_{15}H_{12}N_3O_2$ $(M+H)^+$ 266.0924, found 266.0923.



2-Fluorobenzo[4,5]imidazo[1,2-c]quinazolin-6(5H)-one (3e)

To a 25 mL sealed tube was added **1e** (0.25 mmol, 41.3 mg), **2a** (0.25 mmol, 27.0 mg) and purged with O_2 for three times. Then DMSO (2 mL) was added and the mixture was stirred at 130 ℃ for 24 h. The reaction was cooled to rt, extracted with *tert*-butyl methyl ether, dried over Na_2SO_4. The solvent was concentrated under reduced pressure. Purification by flash chromatography (petroleum ether/ethyl acetate = 5:1) afforded product **3e** (25.3 mg, 40% yield).

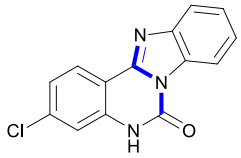
Yellow solid, m.p.>300°C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.03 (s, 1H), 8.37 (d, J = 7.7 Hz, 1H), 8.03 (dd, J = 8.6, 2.8 Hz, 1H), 7.88 (d, J = 7.8 Hz, 1H), 7.56 (td, J = 8.8, 2.9 Hz, 1H), 7.54-7.45 (m, 2H), 7.45-7.41 (m, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 158.28 (d, J = 240.3 Hz), 147.37 (d, J = 3.5 Hz), 146.62, 143.82, 134.35, 131.12, 130.10, 125.04 (d, J = 146.2 Hz), 120.52 (d, J = 24.3 Hz), 119.74, 118.58 (d, J = 8.3 Hz), 115.29, 113.34 (d, J = 9.3 Hz), 110.16 (d, J = 24.7 Hz); ^{19}F NMR (471 MHz, DMSO-d_6) δ -118.69; ATR-FTIR(cm^{-1}): 3061, 2902, 1711, 1615, 1551, 1488, 1448, 1336, 1198, 1143, 755, 602, 538; HRMS *m/z* (ESI) calcd for $C_{14}H_9FN_3O$ $(M+H)^+$254.0724, found 254.0722.



2-Chlorobenzo[4,5]imidazo[1,2-c]quinazolin-6(5H)-one (3f)[2]

To a 25 mL sealed tube was added **1f** (0.25 mmol, 45.4 mg), **2a** (0.25 mmol, 27.0 mg) and purged with O_2 for three times. Then DMSO (2 mL) was added and the mixture was stirred at 130 ℃ for 24 h. The reaction was cooled to rt, extracted with *tert*-butyl methyl ether, dried over Na_2SO_4. The solvent was concentrated under reduced pressure. Purification by flash chromatography (petroleum ether/ethyl acetate = 5:1) afforded product **3f** (55.3 mg, 82% yield).

Light yellow solid, m.p.>300°C (lit.>300°C)[2]; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.07 (s, 1H), 8.35 (d, J = 7.3 Hz, 1H), 8.23 (s, 1H), 7.87 (d, J = 7.4 Hz, 1H), 7.69 (d, J = 8.3 Hz, 1H), 7.53-7.44 (m, 2H), 7.40 (d, J = 8.5 Hz, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 147.04, 146.56, 143.82, 136.58, 132.49, 131.11, 127.67, 125.66, 124.51, 123.73, 119.76, 118.56, 115.28, 113.74; ATR-FTIR(cm^{-1}): 2920, 2850, 1709, 1613, 1553, 1453, 1392, 1330, 1111, 825, 757, 536, 530; HRMS *m/z* (ESI) calcd for $C_{14}H_9ClN_3O$ $(M+H)^+$ 270.0429, found 270.0430.

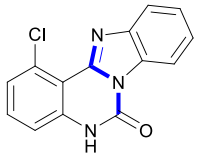


3-Chlorobenzo[4,5]imidazo[1,2-c]quinazolin-6(5H)-one (3g)

To a 25 mL sealed tube was added **1g** (0.25 mmol, 45.4 mg), **2a** (0.25 mmol, 27.0 mg) and purged with O_2 for three times. Then DMSO (2 mL) was added and the mixture was stirred at 130 ℃ for 24 h. The reaction was cooled to rt, extracted with *tert*-butyl methyl ether, dried over Na_2SO_4. The solvent was concentrated under reduced pressure. Purification by flash chromatography (petroleum ether/ethyl acetate = 5:1) afforded product **3g** (61.4 mg, 91% yield).

Light yellow solid, m.p.>300°C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.06 (s, 1H), 8.31 (dd, J = 25.0, 7.3 Hz, 2H), 7.86 (d, J = 7.0 Hz, 1H), 7.48 (dd, J = 13.8, 7.7 Hz, 2H), 7.40 (d, J = 8.2 Hz, 2H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 147.36, 146.66, 143.88, 138.68, 136.77, 131.00, 126.64, 125.58, 124.34, 123.88, 119.66, 115.70, 115.15, 111.28; ATR-FTIR(cm^{-1}): 2857, 1724, 1614, 1587, 1548, 1448, 1369, 1221, 1168, 1086, 752, 693, 546; HRMS *m/z* (ESI) calcd for $C_{14}H_9ClN_3O$ $(M+H)^+$ 270.0429,

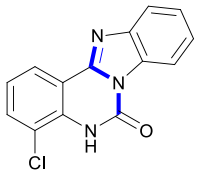
found 270.0427.



1-Chlorobenzo[4,5]imidazo[1,2-c]quinazolin-6(5H)-one(3h)

To a 25 mL sealed tube was added **1h** (0.25 mmol, 45.4 mg), **2a** (0.25 mmol, 27.0 mg) and purged with O_2 for three times. Then DMSO (2 mL) was added and the mixture was stirred at 130 ℃ for 24 h. The reaction was cooled to rt, extracted with *tert*-butyl methyl ether, dried over Na_2SO_4. The solvent was concentrated under reduced pressure. Purification by flash chromatography (petroleum ether/ethyl acetate = 5:1) afforded product **3h** (41.2 mg, 70% yield).

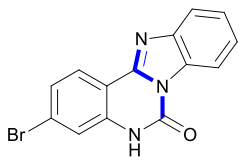
Light yellow solid, m.p.>300^{o}C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.25 (s, 1H), 8.41 (d, J = 7.1 Hz, 1H), 7.93 (d, J = 7.3 Hz, 1H), 7.59 (t, J = 7.9 Hz, 1H), 7.53-7.48 (m, 2H), 7.44 (t, J = 8.3 Hz, 2H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 145.91, 145.48, 143.26, 139.29, 131.80, 131.01, 129.86, 125.47, 125.03, 124.22, 119.55, 114.90, 114.77, 109.87; ATR-FTIR(cm^{-1}): 3602, 2910, 1713, 1605, 1578, 1532, 1447, 1380, 1305, 1228, 1164, 1008, 971, 799, 763, 744, 689, 540; HRMS *m/z* (ESI) calcd for $C_{14}H_9ClN_3O$ $(M+H)^+$ 270.0429, found 270.0431.



4-Chlorobenzo[4,5]imidazo[1,2-c]quinazolin-6(5H)-one (3i)

To a 25 mL sealed tube was added **1i** (0.25 mmol, 45.4 mg), **2a** (0.25 mmol, 27.0 mg) and purged with O_2 for three times. Then DMSO (2 mL) was added and the mixture was stirred at 130 ℃ for 24 h. The reaction was cooled to rt, extracted with *tert*-butyl methyl ether, dried over Na_2SO_4. The solvent was concentrated under reduced pressure. Purification by flash chromatography (petroleum ether/ethyl acetate = 5:1) afforded product **3i** (24.9 mg, 37% yield).

Light yellow solid, m.p.>300 ^{o}C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.41 (s, 1H), 8.38 (d, J = 7.7 Hz, 1H), 8.32 (d, J = 7.7 Hz, 1H), 7.89 (d, J = 7.8 Hz, 1H), 7.80 (d, J= 7.7 Hz, 1H), 7.57-7.45 (m, 2H), 7.38 (t, J = 7.8 Hz, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 147.50, 146.68, 144.02, 134.59, 132.81, 131.13, 125.72, 124.50, 124.48, 123.93, 119.93, 119.77, 115.37, 114.41; ATR-FTIR(cm^{-1}): 3073, 1710, 1609, 1547, 1495, 1444, 1395, 1338, 1225, 1165, 931, 792, 778; HRMS *m/z* (ESI) calcd for $C_{14}H_9ClN_3O$ $(M+H)^+$ 270.0429, found 270.0427.

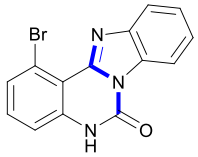


3-Bromobenzo[4,5]imidazo[1,2-c]quinazolin-6(5H)-one(3j)

To a 25 mL sealed tube was added **1j** (0.25 mmol, 56.5 mg), **2a** (0.25 mmol, 27.0 mg)

and purged with O_2 for three times. Then DMSO (2 mL) was added and the mixture was stirred at 130 ℃ for 24 h. The reaction was cooled to rt, extracted with *tert*-butyl methyl ether, dried over Na_2SO_4. The solvent was concentrated under reduced pressure. Purification by flash chromatography (petroleum ether/ethyl acetate = 5:1) afforded product **3j** (48.7 mg, 62% yield).

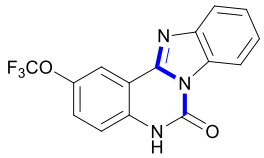
Light yellow solid, m.p.>300 ^oC; ^1H NMR (500 MHz, DMSO-d_6) δ 12.05 (s, 1H), 8.35 (d, J = 7.5 Hz, 1H), 8.24 (d, J = 8.2 Hz, 1H), 7.87 (d, J = 7.9 Hz, 1H), 7.59-7.44 (m, 4H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 147.51, 146.64, 143.89, 138.79, 131.04, 126.73, 125.66, 125.47, 124.42, 123.43, 119.69, 118.69, 115.19, 111.61; ATR-FTIR(cm^{-1}): 2918, 2849, 1724, 1612, 1585, 1546, 1447, 1416, 1366, 1221, 1048, 929, 753, 689, 545; HRMS *m/z* (ESI) calcd for $C_{14}H_9BrN_3O$ $(M+H)^+$ 313.9924, found 313.9925.



1-Bromobenzo[4,5]imidazo[1,2-c]quinazolin-6(5H)-one(3k)

To a 25 mL sealed tube was added **1k** (0.25 mmol, 56.5 mg), **2a** (0.25 mmol, 27.0 mg) and purged with O_2 for three times. Then DMSO (2 mL) was added and the mixture was stirred at 130 ℃ for 24 h. The reaction was cooled to rt, extracted with *tert*-butyl methyl ether, dried over Na_2SO_4. The solvent was concentrated under reduced pressure. Purification by flash chromatography (petroleum ether/ethyl acetate = 5:1) afforded product **3k** (48.7 mg, 62% yield).

Light yellow solid, m.p.>300^oC;^1H NMR (400 MHz, DMSO-d_6) δ 12.11 (s, 1H), 8.41 (d, J = 7.0 Hz, 1H), 7.92 (d, J = 7.0 Hz, 1H), 7.64 (d, J = 7.5 Hz, 1H), 7.57-7.45 (m, 3H), 7.41 (d, J = 8.0 Hz, 1H);^{13}C NMR (101 MHz, DMSO-d_6) δ 146.40, 146.24, 143.44, 139.82, 132.57, 130.55, 129.78, 125.56, 124.76, 120.08, 119.63, 115.93, 115.30, 111.59;ATR-FTIR(cm^{-1}): 3029, 2922, 1710, 1576, 1536, 1445, 1399, 1346, 1303, 1229, 921, 782, 740, 703, 545;HRMS *m/z* (ESI) calcd for $C_{14}H_9BrN_3O$ $(M+H)^+$ 313.9924, found 313.9922.

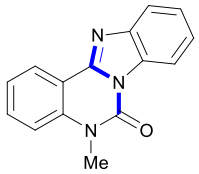


2-(Trifluoromethoxy)benzo[4,5]imidazo[1,2-c]quinazolin-6(5H)-one(3l)

To a 25 mL sealed tube was added **1l** (0.25 mmol, 57.8 mg), **2a** (0.25 mmol, 27.0 mg) and purged with O_2 for three times. Then DMSO (2 mL) was added and the mixture was stirred at 130 ℃ for 24 h. The reaction was cooled to rt, extracted with *tert*-butyl methyl ether, dried over Na_2SO_4. The solvent was concentrated under reduced pressure. Purification by flash chromatography (petroleum ether/ethyl acetate = 5:1) afforded product **3l** (61.4 mg, 77% yield).

Light yellow solid, m.p.>300^oC; ^1H NMR (500 MHz, DMSO-d_6) δ 12.34 (s, 1H), 8.38 (d, J = 7.4 Hz, 1H), 8.17 (d, J = 1.8 Hz, 1H), 7.88 (d, J = 7.4 Hz, 1H), 7.69 (dd, J = 8.9, 2.5 Hz, 1H), 7.61 (d, J = 9.0 Hz, 1H), 7.55-7.44 (m, 2H);^{13}C NMR (101 MHz,

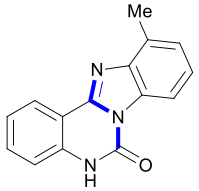
DMSO-d_6) δ 147.02, 146.53, 143.92, 143.91, 143.73, 136.57, 131.03, 125.85, 125.59, 124.48, 119.72, 118.44, 116.58, 115.20, 113.23; ^{19}F NMR (377 MHz, DMSO-d_6) δ -57.25; ATR-FTIR(cm^{-1}): 2918, 1712, 1613, 1556, 1488, 1453, 1392, 1326, 1143, 905, 827, 755, 535; HRMS *m/z* (ESI) calcd for $C_{15}H_9F_3N_3O_2$ $(M+H)^+$ 320.0641, found 320.0642.



5-Methylbenzo[4,5]imidazo[1,2-c]quinazolin-6(5H)-one (3m)[3]

To a 25 mL sealed tube was added **1m** (0.25 mmol, 40.3 mg), **2a** (0.25 mmol, 27.0 mg) and purged with O_2 for three times. Then DMSO (2 mL) was added and the mixture was stirred at 130 ℃ for 24 h. The reaction was cooled to rt, extracted with *tert*-butyl methyl ether, dried over Na_2SO_4. The solvent was concentrated under reduced pressure. Purification by flash chromatography (petroleum ether/ethyl acetate = 5:1) afforded product **3m** (43.6 mg, 70% yield).

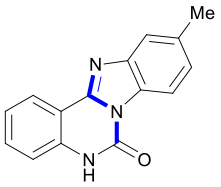
White solid, m.p.>300 ^{o}C (lit.>300 ^{o}C)[3]; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.43 (dd, J = 7.8, 1.5 Hz, 1H), 8.39 (dd, J = 7.1, 1.0 Hz, 1H), 7.87 (dd, J = 7.2, 1.1 Hz, 1H), 7.81-7.75 (m, 1H), 7.65 (d, J = 8.4 Hz, 1H), 7.54-7.43 (m, 3H), 3.73 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 146.73, 146.60, 143.44, 138.10, 132.56, 130.92, 125.13, 124.68, 123.71, 123.55, 119.11, 115.58, 114.88, 112.69, 30.41; ATR-FTIR(cm^{-1}): 3391, 2919, 2848, 1684, 1609, 1554, 1478, 1446, 1426, 1385, 1359, 1246, 750; HRMS *m/z* (ESI) calcd for $C_{15}H_{12}N_3O$ $(M+H)^+$ 250.0975, found 250.0973.



11-Methylbenzo[4,5]imidazo[1,2-c]quinazolin-6(5H)-one (3n)

To a 25 mL sealed tube was added **1a** (0.25 mmol, 36.8 mg), **2b** (0.25 mmol, 30.6 mg) and purged with O_2 for three times. Then DMSO (2 mL) was added and the mixture was stirred at 130 ℃ for 24 h. The reaction was cooled to rt, extracted with *tert*-butyl methyl ether, dried over Na_2SO_4. The solvent was concentrated under reduced pressure. Purification by flash chromatography (petroleum ether/ethyl acetate = 5:1) afforded product **3n** (44.9 mg, 72% yield).

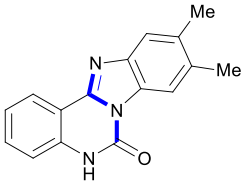
Light yellow solid, m.p.>300 ^{o}C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.94 (s, 1H), 8.33 (dd, J = 7.8, 0.8 Hz, 1H), 8.18 (d, J = 7.6 Hz, 1H), 7.68-7.62 (m, 1H), 7.43-7.27 (m, 4H), 2.67 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 147.35, 146.91, 143.16, 137.49, 132.55, 130.69, 129.14, 125.70, 124.89, 124.04, 123.80, 116.31, 112.67, 112.38, 17.06; ATR-FTIR(cm^{-1}): 3051, 2921, 1711, 1607, 1552, 1401, 1320, 1286, 1235, 776, 753, 682, 546; HRMS *m/z* (ESI) calcd for $C_{15}H_{12}N_3O$ $(M+H)^+$ 250.0975, found 250.0973.



10-Methylbenzo[4,5]imidazo[1,2-c]quinazolin-6(5H)-one (3o)

To a 25 mL sealed tube was added **1a** (0.25 mmol, 36.8 mg), **2c** (0.25 mmol, 30.6 mg) and purged with O_2 for three times. Then DMSO (2 mL) was added and the mixture was stirred at 130 ℃ for 24 h. The reaction was cooled to rt, extracted with *tert*-butyl methyl ether, dried over Na_2SO_4. The solvent was concentrated under reduced pressure. Purification by flash chromatography (petroleum ether/ethyl acetate = 5:1) afforded product **3o** (41.8 mg, 67% yield).

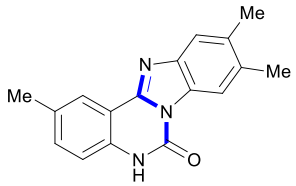
Light yellow solid, m.p.>300 ^oC; ^1H NMR (500 MHz, DMSO-d_6) δ 11.94 (s, 1H), 8.30 (t, J = 7.3 Hz, 1H), 8.24-8.17 (m, 1H), 7.76-7.61 (m, 2H), 7.43-7.24 (m, 3H), 2.50 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 148.11, 146.79, 144.31, 137.54, 134.90, 132.58, 129.10, 125.46, 124.84, 123.82, 119.38, 116.32, 114.69, 112.28, 21.80; ATR-FTIR(cm^{-1}): 3049, 2917, 2849, 1712, 1550, 1478, 1383, 1340, 1232, 807, 750, 666, 622, 598, 545; HRMS *m/z* (ESI) calcd for $C_{15}H_{12}N_3O$ $(M+H)^+$ 250.0975, found 250.0976.



9,10-Dimethylbenzo[4,5]imidazo[1,2-c]quinazolin-6(5H)-one(3p)[2]

To a 25 mL sealed tube was added **1a** (0.25 mmol, 36.8 mg), **2d** (0.25 mmol, 34.1 mg) and purged with O_2 for three times. Then DMSO (2 mL) was added and the mixture was stirred at 130 ℃ for 24 h. The reaction was cooled to rt, extracted with *tert*-butyl methyl ether, dried over Na_2SO_4. The solvent was concentrated under reduced pressure. Purification by flash chromatography (petroleum ether/ethyl acetate = 5:1) afforded product **3p** (26.3 mg, 40% yield).

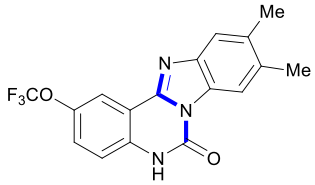
Light yellow solid, m.p.>300 ^oC (lit.>300 ^oC)[2]; ^1H NMR (400 MHz, DMSO-d_6) δ 11.90 (s, 1H), 8.27 (dd, J = 7.9, 1.1 Hz, 1H), 8.12 (s, 1H), 7.67-7.58 (m, 2H), 7.42-7.30 (m, 2H), 2.40 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 147.29, 146.82, 142.49, 137.34, 134.11, 132.97, 132.36, 129.40, 124.67, 123.77, 119.60, 116.28, 115.20, 112.39, 20.63, 20.56; ATR-FTIR(cm^{-1}): 3066, 2913, 1717, 1625, 1596, 1551, 1439, 1380, 1343, 1230, 1159, 1021, 994, 854, 742, 666, 605; HRMS *m/z* (ESI) calcd for $C_{16}H_{14}N_3O$ $(M+H)^+$ 264.1131, found 264.1131.



2,9,10-Trimethylbenzo[4,5]imidazo[1,2-c]quinazolin-6(5H)-one (3q)

To a 25 mL sealed tube was added **1c** (0.25 mmol, 40.3 mg), **2d** (0.25 mmol, 34.1 mg) and purged with O_2 for three times. Then DMSO (2 mL) was added and the mixture was stirred at 130 ℃ for 24 h. The reaction was cooled to rt, extracted with *tert*-butyl methyl ether, dried over Na_2SO_4. The solvent was concentrated under reduced pressure. Purification by flash chromatography (petroleum ether/ethyl acetate = 5:1) afforded product **3q** (22.9 mg, 33% yield).

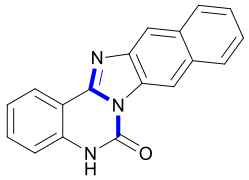
Yellow solid, m.p.>300 ^oC; ^1H NMR (400 MHz, DMSO-d_6) δ 11.81 (s, 1H), 8.09 (d, J = 17.9 Hz, 2H), 7.59 (s, 1H), 7.43 (d, J = 7.6 Hz, 1H), 7.26 (d, J = 7.8 Hz, 1H), 2.41 (s, 3H), 2.39 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 147.30, 146.80, 142.53, 135.17, 134.04, 133.37, 133.01, 132.86, 129.43, 124.31, 119.56, 116.20, 115.20, 112.21, 20.93, 20.63, 20.54; ATR-FTIR(cm^{-1}): 3104, 2918, 1727, 1699, 1597, 1554, 1459, 1388, 1332, 1205, 816, 739, 630, 597, 555, 541; HRMS *m/z* (ESI) calcd for $C_{17}H_{16}N_3O(M+H)^+$278.1287, found 278.1293.



9,10-Dimethyl-2-(trifluoromethoxy)benzo[4,5]imidazo[1,2-c]quinazolin-6(5H)-one (3r)

To a 25 mL sealed tube was added **1l** (0.25 mmol, 57.8 mg), **2d** (0.25 mmol, 34.1 mg) and purged with O_2 for three times. Then DMSO (2 mL) was added and the mixture was stirred at 130 ℃ for 24 h. The reaction was cooled to rt, extracted with *tert*-butyl methyl ether, dried over Na_2SO_4. The solvent was concentrated under reduced pressure. Purification by flash chromatography (petroleum ether/ethyl acetate = 5:1) afforded product **3r** (48.5 mg, 70% yield).

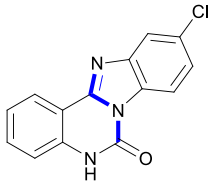
Yellow solid, m.p.>300 ^oC; ^1H NMR (400 MHz, DMSO-d_6) δ 12.04 (s, 1H), 8.07 (s, 2H), 7.6-7.58 (m, 2H), 7.44 (s, 1H), 2.36 (s, 6H); ^{13}C NMR (101 MHz, CF_3COOD) δ 143.09, 141.87, 139.79, 137.58, 136.31, 131.35, 126.53, 124.48, 122.02, 115.10, 112.15, 112.05, 109.17, 101.88, 100.00, 14.94, 14.86; ^{19}F NMR (376 MHz, DMSO-d_6) δ -57.21; ATR-FTIR(cm^{-1}): 2922, 1710, 1554, 1489, 1386, 1328, 1209, 1169, 864, 817, 749, 662, 606, 556; HRMS *m/z* (ESI) calcd for $C_{17}H_{13}F_3N_3O_2$ $(M+H)^+$ 348.0954, found 348.0960. (**Note**: The^{13}C NMR spectra of **3r** was recorded using CF_3COOD as solvent since it is difficult to be dissolved in DMSO-d_6.)



Naphtho[2',3':4,5]imidazo[1,2-c]quinazolin-6(5H)-one (3s)

To a 25 mL sealed tube was added **1a** (0.25 mmol, 36.8 mg), **2e** (0.25 mmol, 39.6 mg) and purged with O_2 for three times. Then DMSO (2 mL) was added and the mixture was stirred at 130 ℃ for 24 h. The reaction was cooled to rt, extracted with *tert*-butyl methyl ether, dried over Na_2SO_4. The solvent was concentrated under reduced pressure. Purification by flash chromatography (petroleum ether/ethyl acetate = 5:1) afforded product **3s** (21.4 mg, 30% yield).

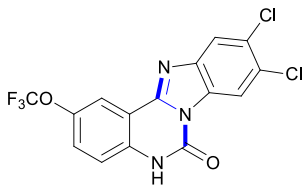
Light yellow solid, m.p.>300 ^oC; ^1H NMR (400 MHz, DMSO-d_6) δ 11.98 (s, 1H), 8.87 (s, 1H), 8.37 (s, 2H), 8.15 (d, J = 19.6 Hz, 2H), 7.71 (s, 1H), 7.47 (d, J = 49.7 Hz, 4H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 151.26, 147.03, 143.63, 138.52, 133.62, 131.65, 131.28, 130.73, 128.74, 128.49, 125.53, 125.30, 125.23, 123.87, 116.41, 116.18, 112.10, 112.04; ATR-FTIR(cm^{-1}): 2918, 2849, 1714, 1625, 1597, 1552, 1479, 1439, 1387, 1350, 1327, 1227, 1183, 1157, 922, 866, 743, 726, 662, 602; HRMS *m/z* (ESI) calcd for $C_{18}H_{12}N_3O(M+H)^+$ 286.0975, found 286.0980.



10-Chlorobenzo[4,5]imidazo[1,2-c]quinazolin-6(5H)-one (3t)

To a 25 mL sealed tube was added **1a** (0.25 mmol, 36.8 mg), **2f** (0.25 mmol, 35.7 mg) and purged with O_2 for three times. Then DMSO (2 mL) was added and the mixture was stirred at 130 ℃ for 24 h. The reaction was cooled to rt, extracted with *tert*-butyl methyl ether, dried over Na_2SO_4. The solvent was concentrated under reduced pressure. Purification by flash chromatography (petroleum ether/ethyl acetate = 5:1) afforded product **3t** (47.9 mg, 71% yield).

Light yellow solid, m.p.>300 ^oC; ^1H NMR (500 MHz, DMSO-d_6) δ 12.07 (s, 1H), 8.31 (dt, J = 7.6, 5.8 Hz, 2H), 7.97-7.84 (m, 1H), 7.68 (t, J = 6.2 Hz, 1H), 7.55-7.46 (m, 1H), 7.45-7.35 (m, 2H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 146.61, 137.90, 133.07, 129.72, 129.70, 128.13, 125.70, 125.03, 124.21, 120.88, 119.10, 116.46, 114.83, 111.93; ATR-FTIR(cm^{-1}): 3077, 2924, 1714, 1546, 1479, 1437, 1342, 1231, 1099, 865, 810, 747, 578; HRMS *m/z* (ESI) calcd for $C_{14}H_9ClN_3O(M+H)^+$ 270.0429, found 270.0427.



9,10-Dichloro-2-(trifluoromethoxy)benzo[4,5]imidazo[1,2-c]quinazolin-6(5H)-one

(3u)

To a 25 mL sealed tube was added **1a** (0.25 mmol, 36.8 mg), **2g** (0.25 mmol, 44.3 mg) and purged with O_2 for three times. Then DMSO (2 mL) was added and the mixture was stirred at 130 ℃ for 24 h. The reaction was cooled to rt, extracted with *tert*-butyl methyl ether, dried over Na_2SO_4. The solvent was concentrated under reduced pressure. Purification by flash chromatography (petroleum ether/ethyl acetate = 5:1) afforded product **3a** (65.0 mg, 67% yield).

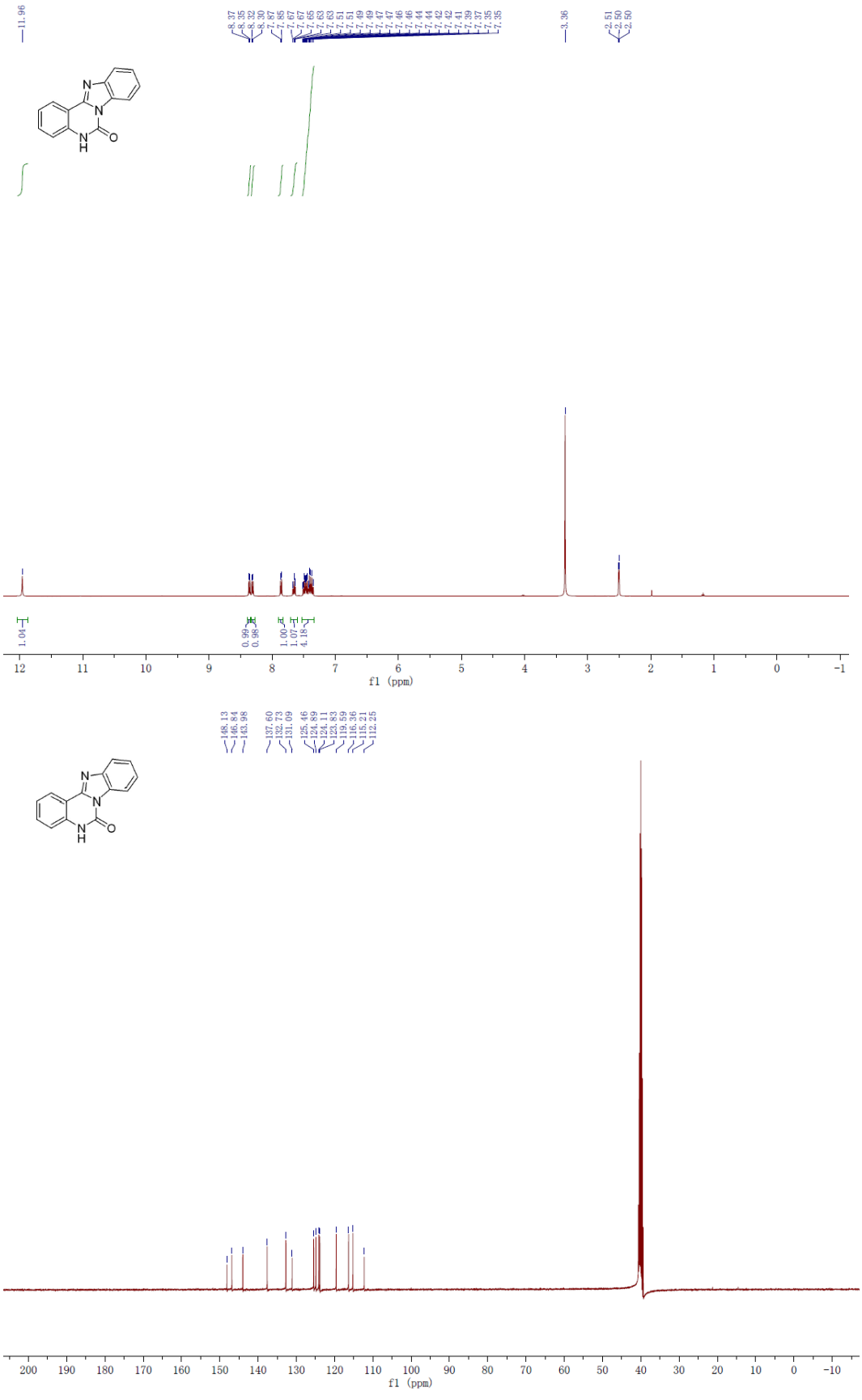
Yellow solid, m.p.>300^oC; ^1H NMR (400 MHz, DMSO-d_6) δ 12.29 (s, 1H), 8.36-8.08 (m, 3H), 7.70-7.46 (m, 2H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 148.59, 145.68, 143.97, 142.91, 136.50, 129.85, 128.15, 126.57, 126.33, 120.58, 119.27, 118.57, 116.34, 115.78, 112.28; ^{19}F NMR (376 MHz, DMSO-d_6) δ -57.25; ATR-FTIR(cm^{-1}): 3087, 2917, 1714, 1548, 1384, 1322, 1181, 866, 833, 810, 779, 750, 658, 583; HRMS *m/z* (ESI) calcd for $C_{15}H_7Cl_2F_3N_3O_2$ $(M+H)^+$ 387.9861, found 387.9867.

4. Reference

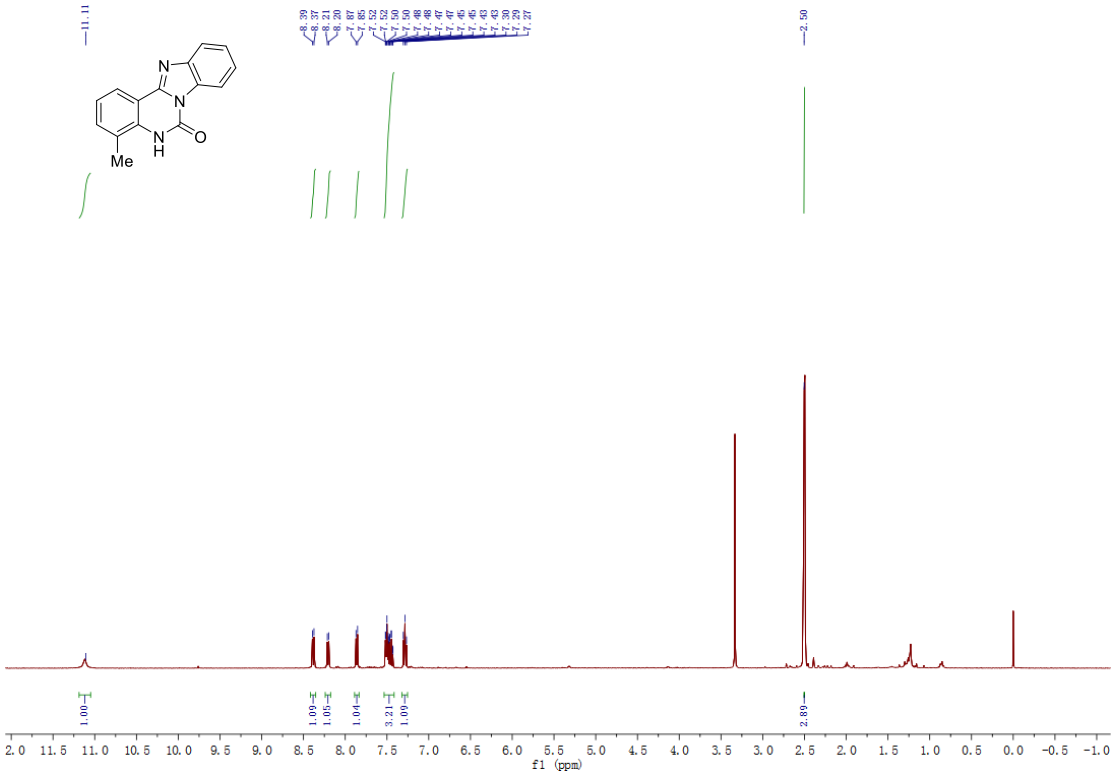
1. P. N. Tosso,Y. Kong, L. Scher, R. Cummins, J. Schneider, S. Rahim, K. T. Holman, J. Toretsky, K. Wang, A. Ueren and M. L. Brown, *J. Med. Chem.* **2014**, *57*, 10290−10303
2. X. Zhao and D.-Q. Shi, *J. Heterocyclic. Chem.* **2010**, *47*, 524–527.
3. H.-B. Zhao, Z.-W. Hou, Z.-J. Liu, Z.-F. Zhou, J. Song, H.-C. Xu, *Angew. Chem. Int. Ed.* **2017**, *56*, 587–590.

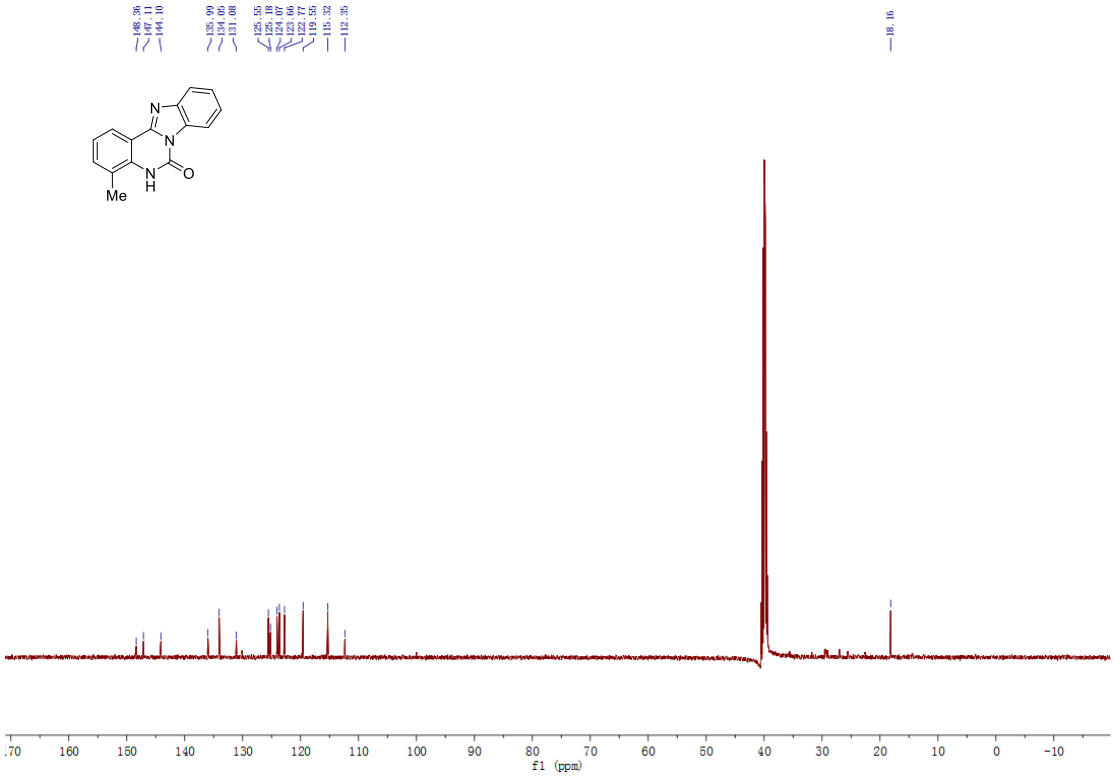
5. NMR spectra

Benzimidazo[1,2-c]quinazolin-6(5H)-one (3a)

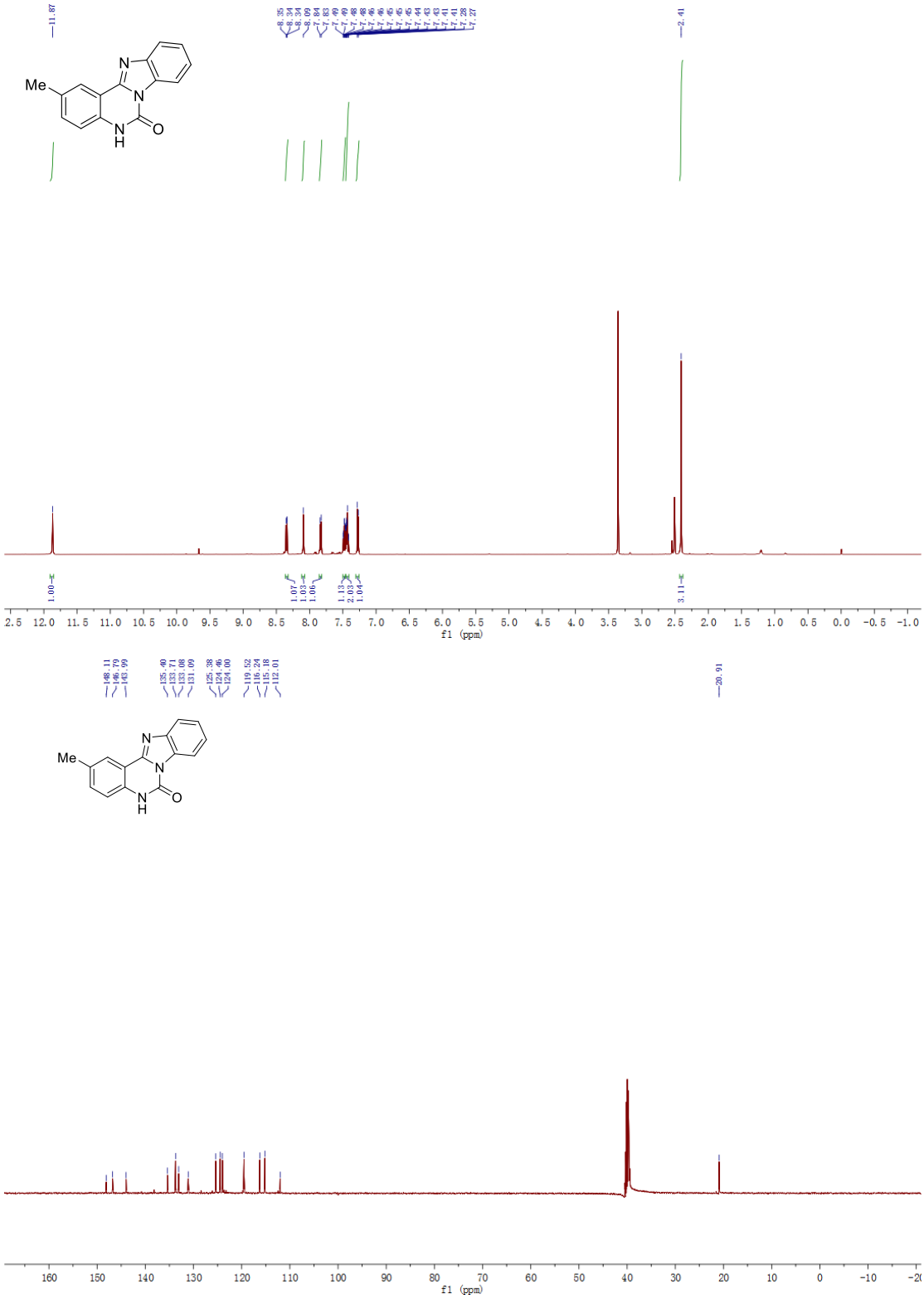


4-Methylbenzo[4,5] imidazo[1,2-c]quinazolin-6(5H)-one (3b)

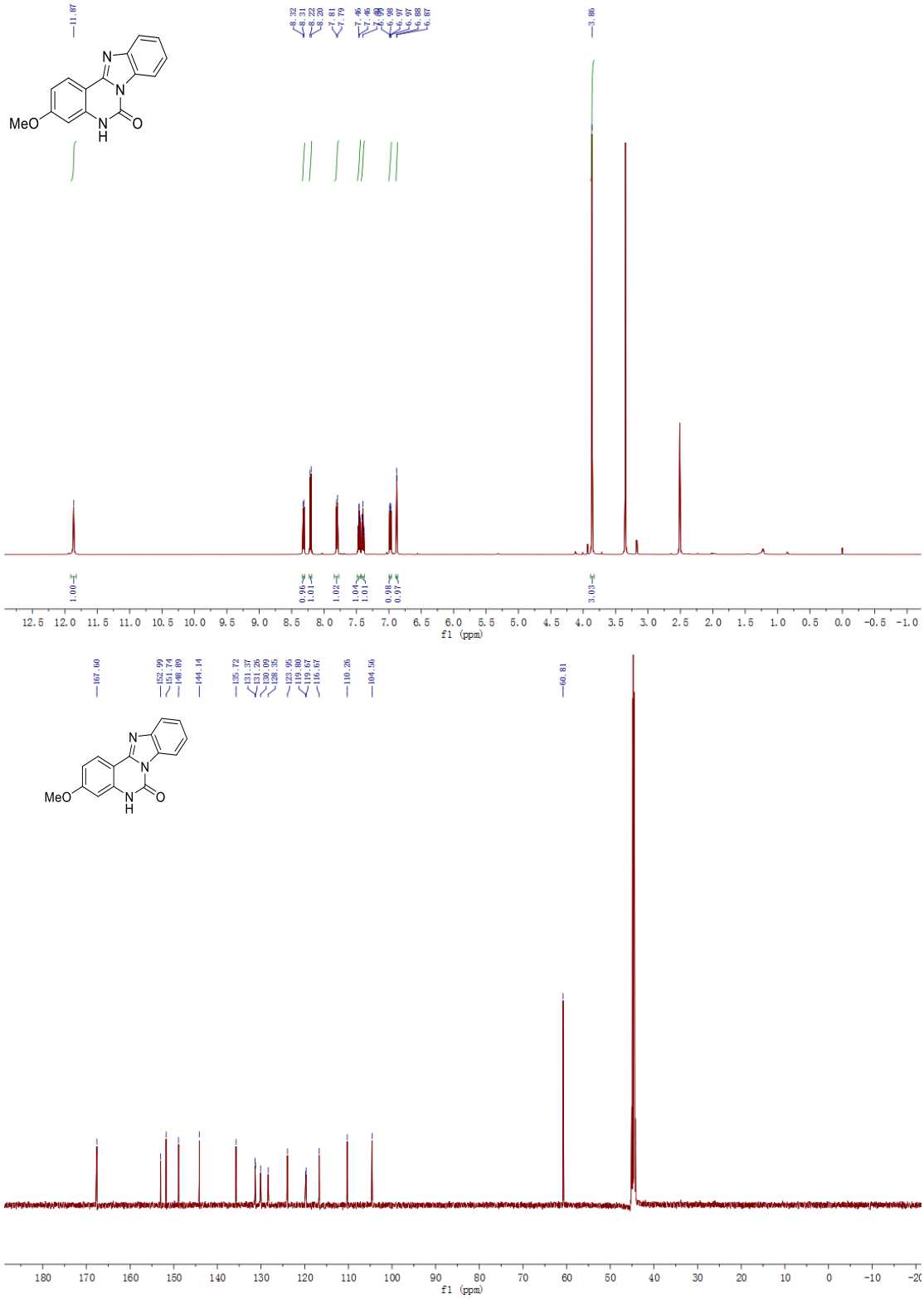




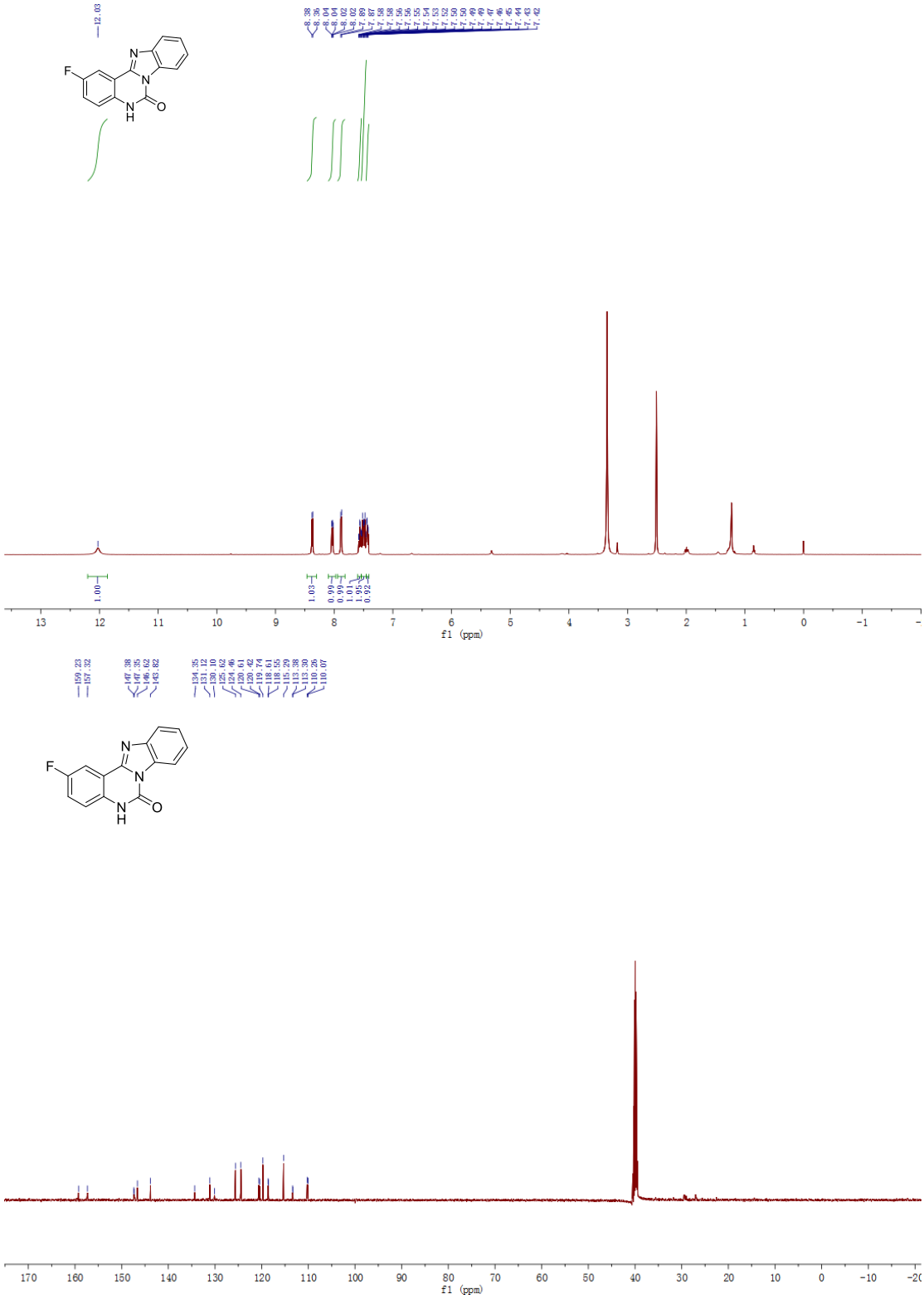
2-Methylbenzo[4,5]imidazo[1,2-c]quinazolin-6(5H)-one (3c)

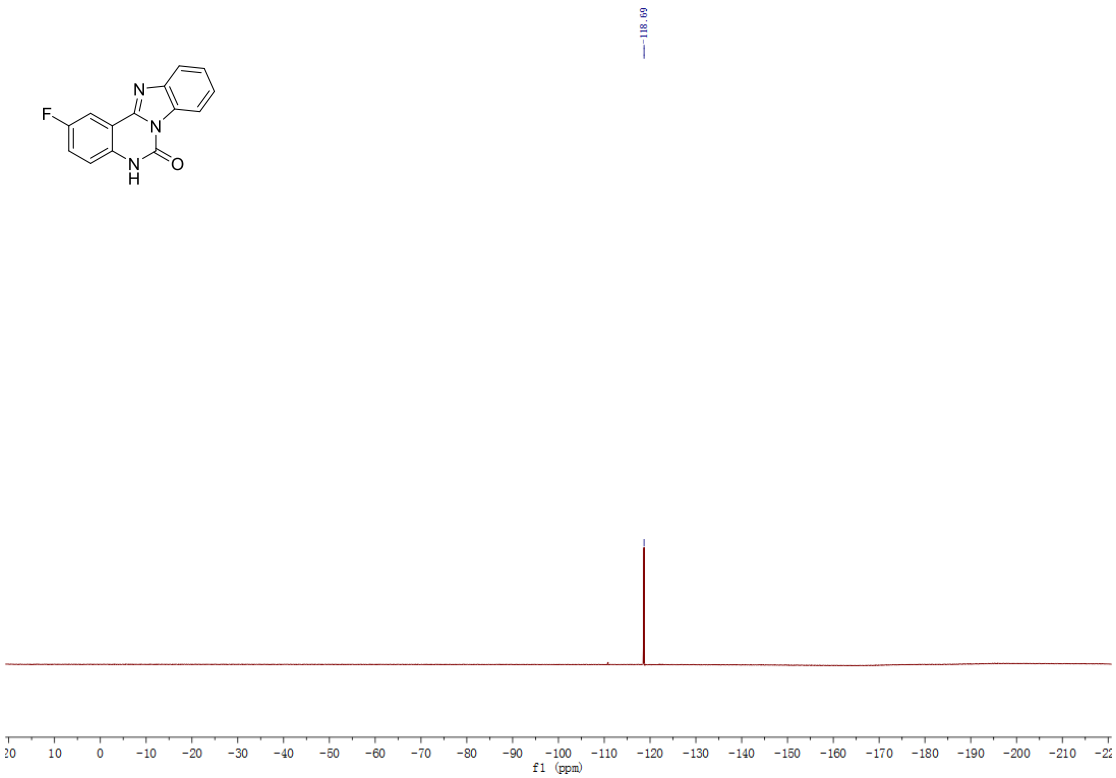


3-Methoxybenzo[4,5]imidazo[1,2-c]quinazolin-6(5H)-one (3d)

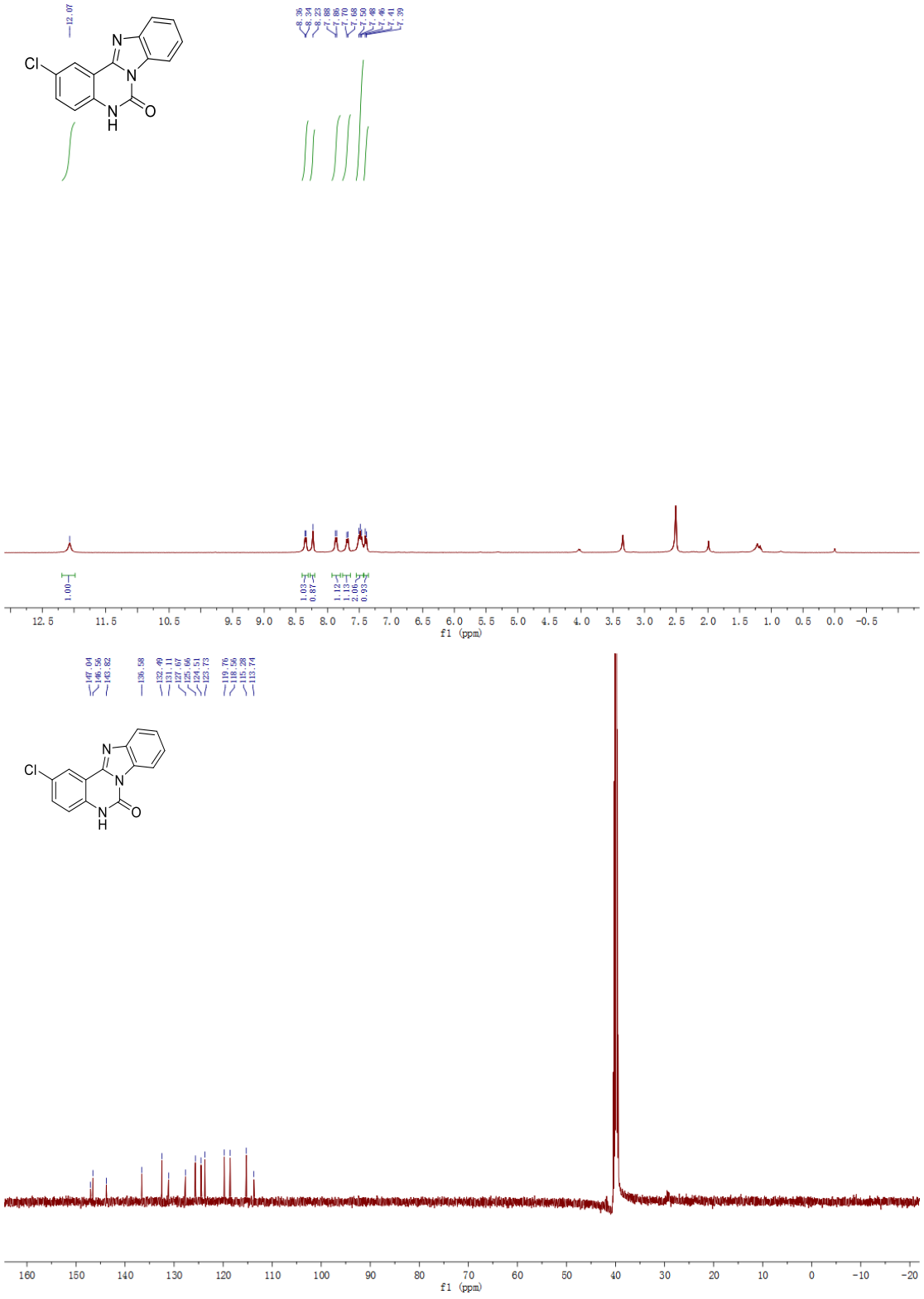


2-Fluorobenzo[4,5]imidazo[1,2-c]quinazolin-6(5H)-one(3e)

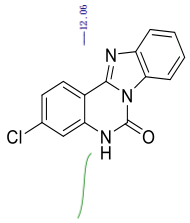


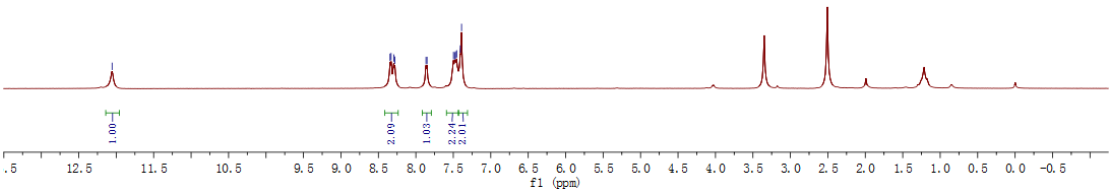

F
N
N
N
H
O
-118.69
f1 (ppm)

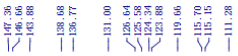
2-Chlorobenzo[4,5]imidazo[1,2-c]quinazolin-6(5H)-one (3f)

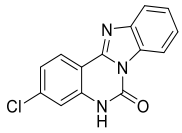


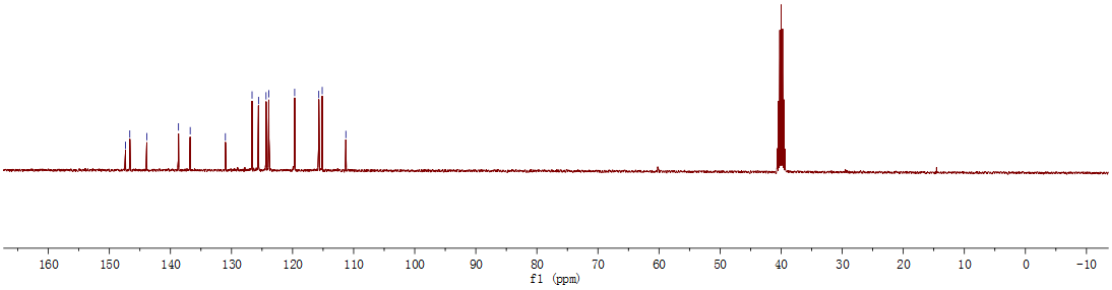
3-Chlorobenzo[4,5]imidazo[1,2-c]quinazolin-6(5H)-one (3g)



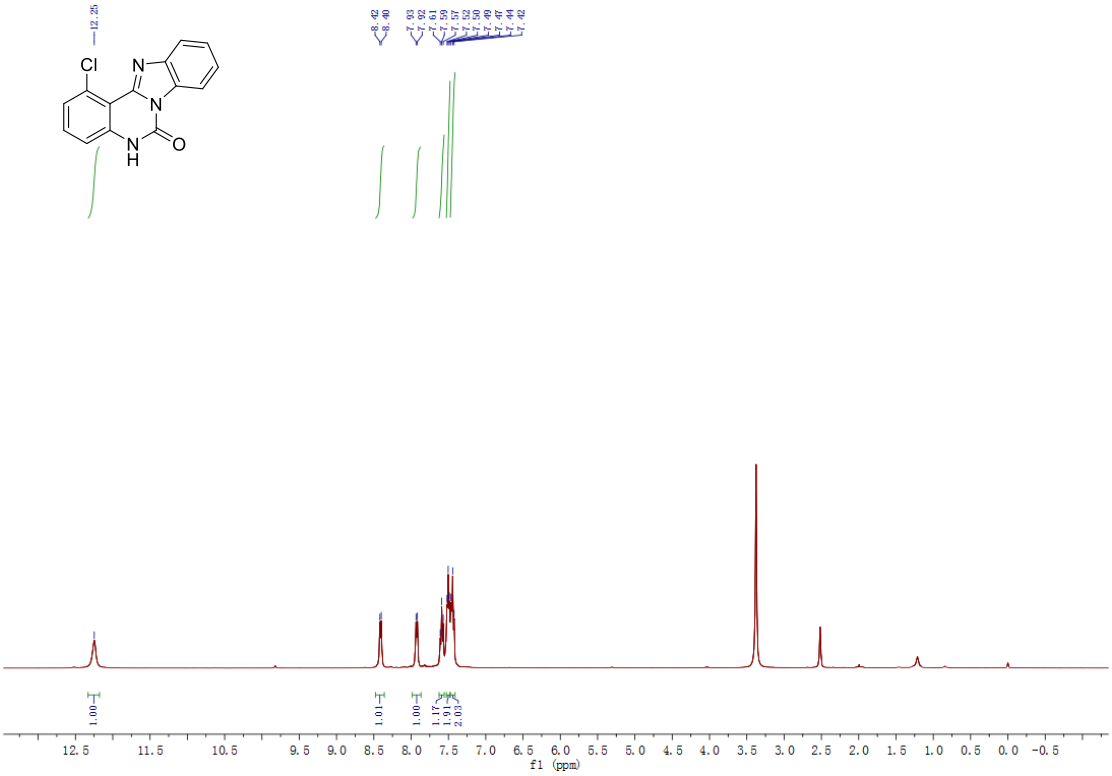


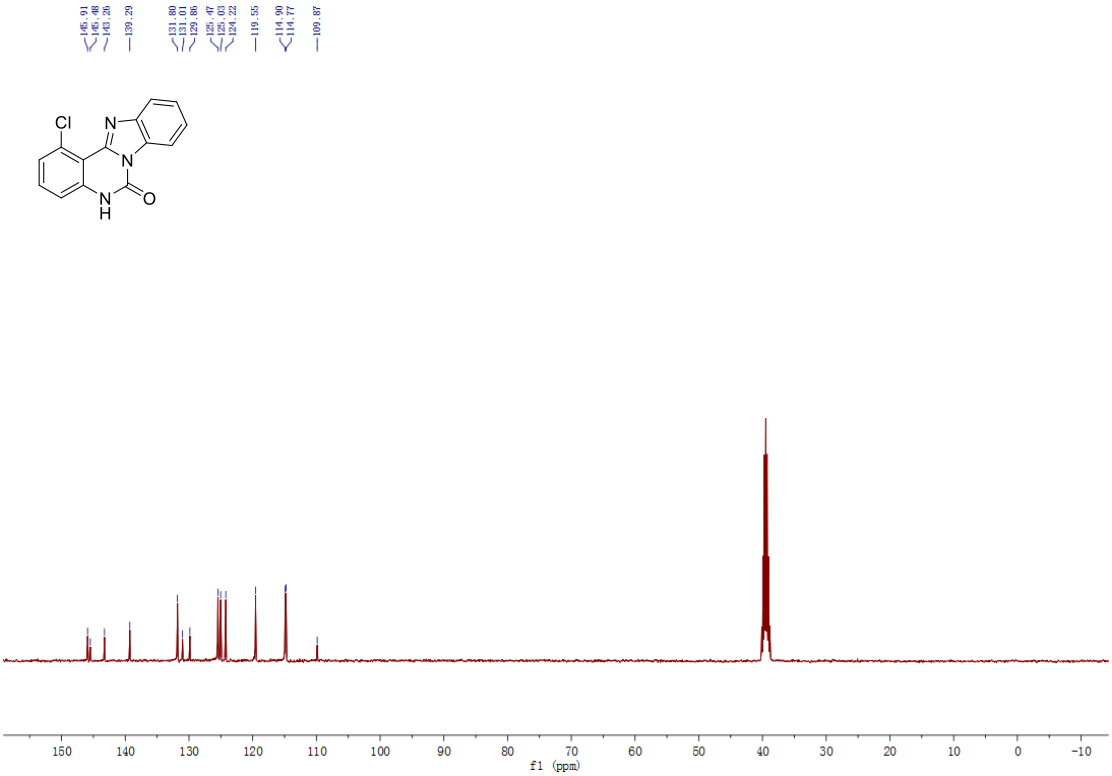




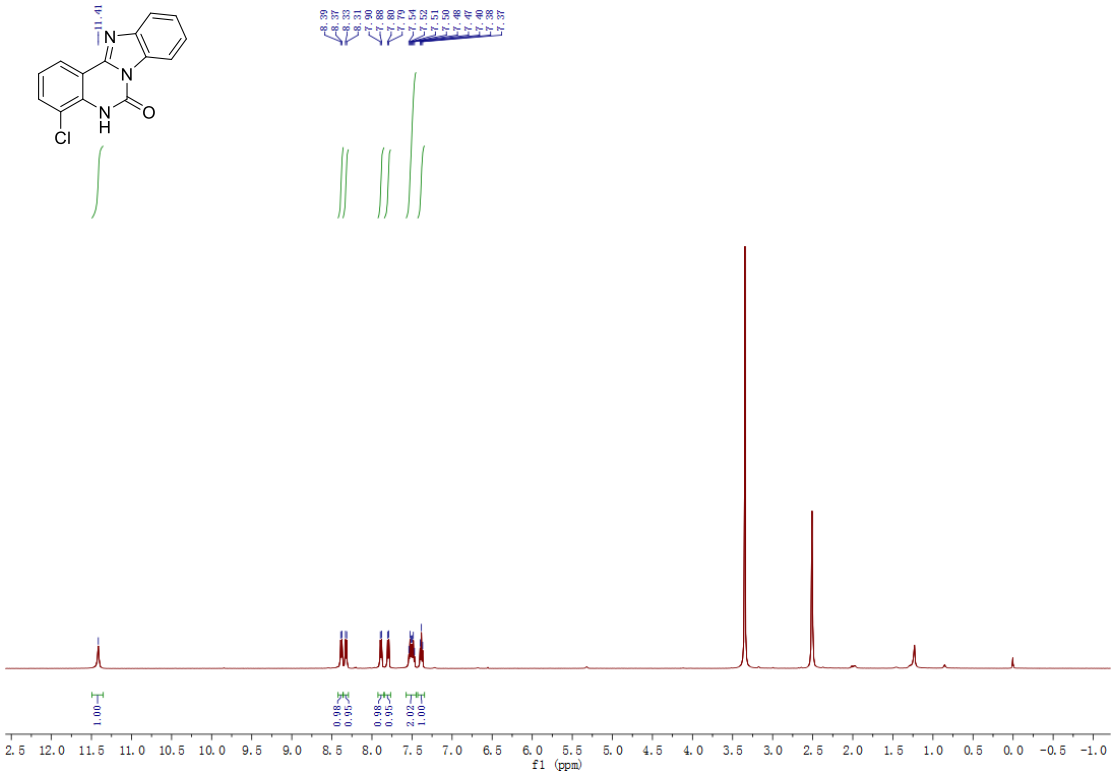


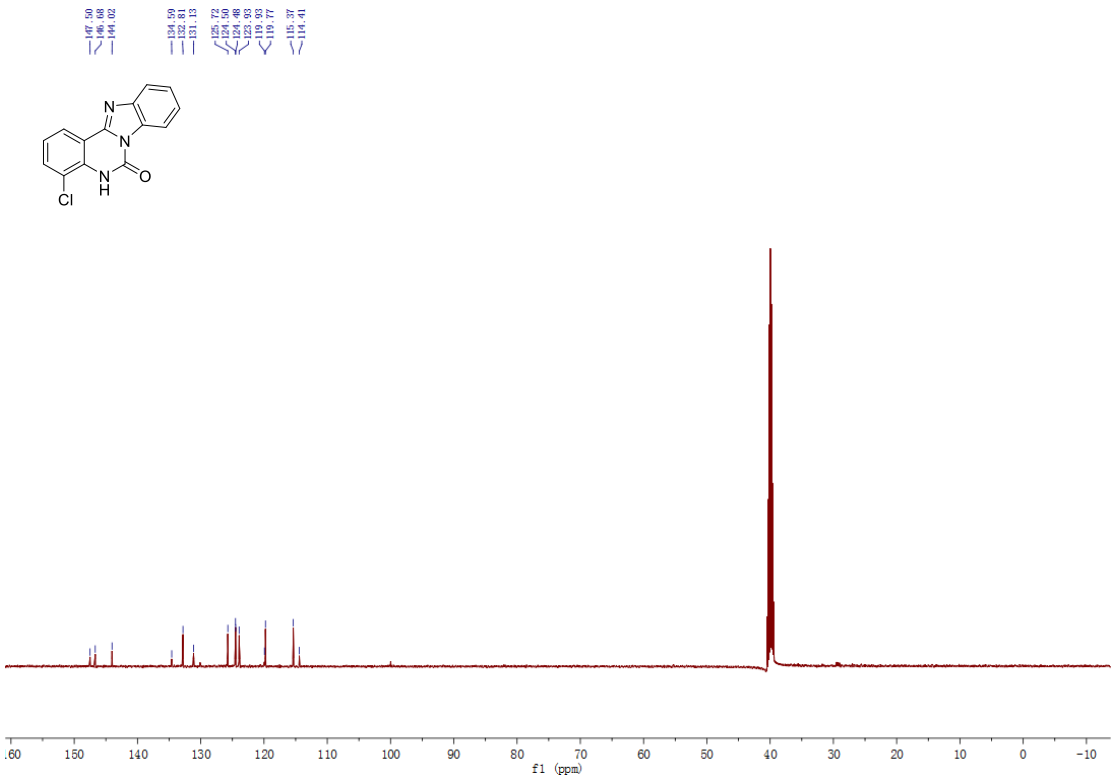
1-Chlorobenzo[4,5]imidazo[1,2-c]quinazolin-6(5H)-one (3h)



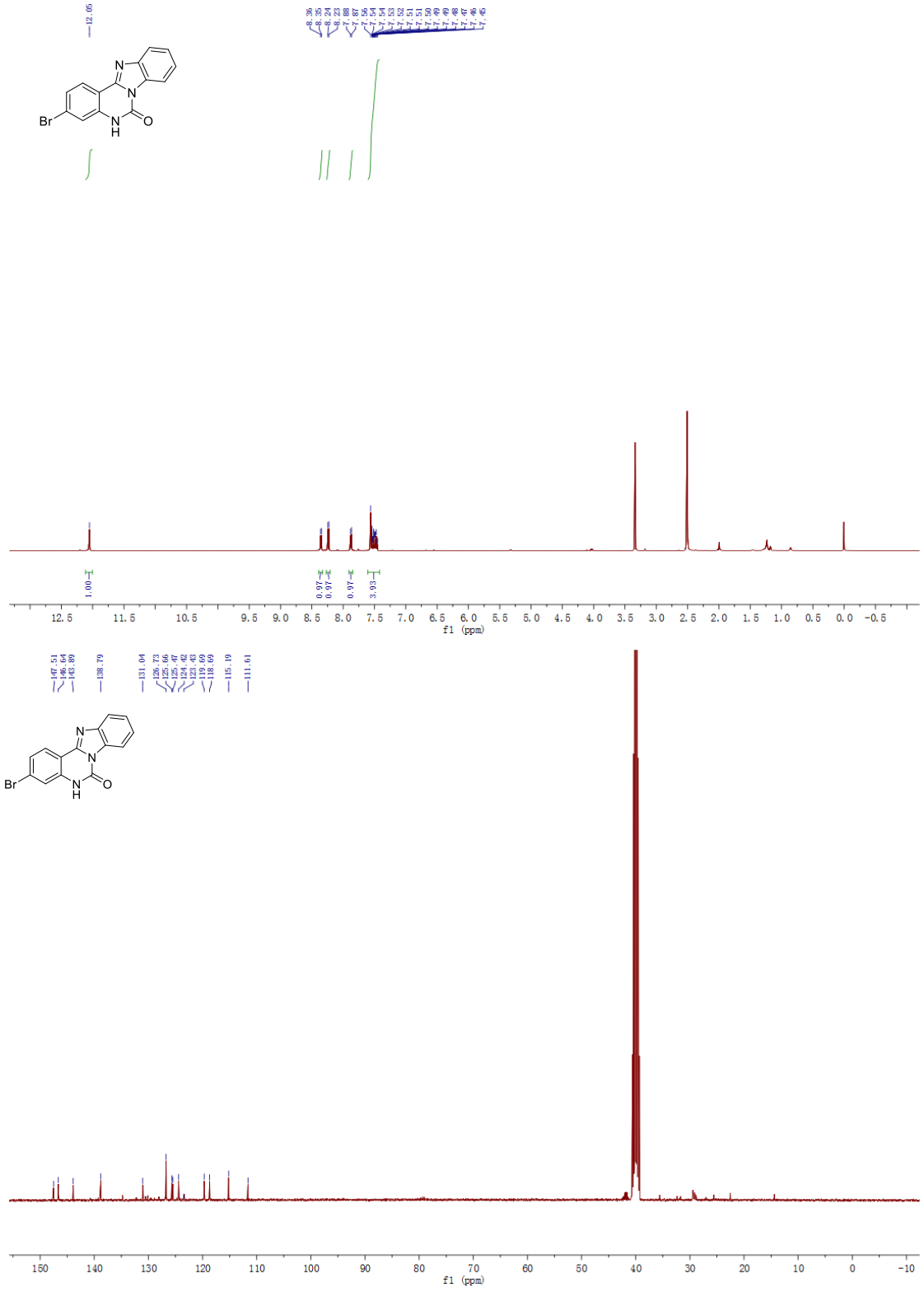


4-Chlorobenzo[4,5]imidazo[1,2-c]quinazolin-6(5H)-one (3i)

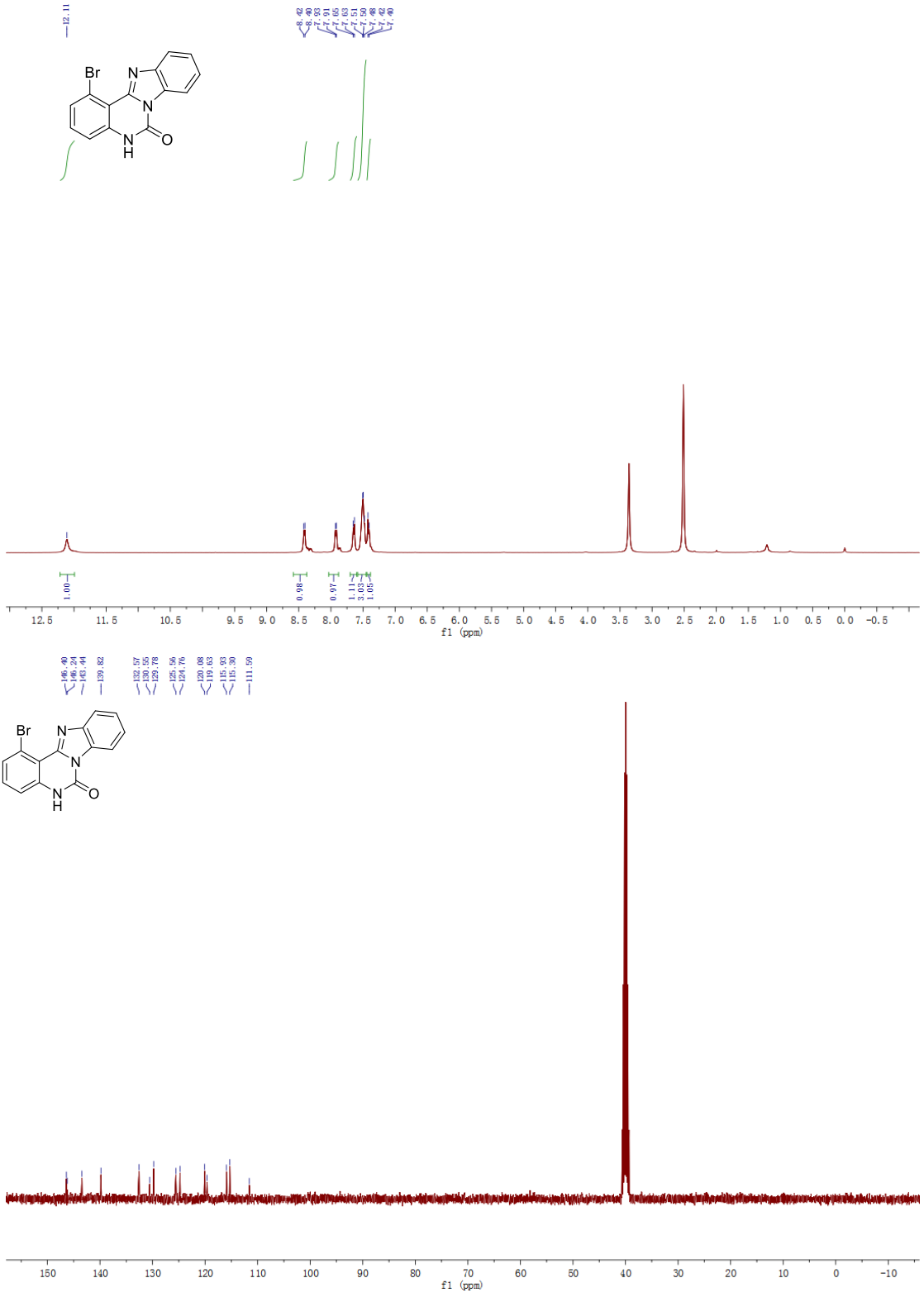




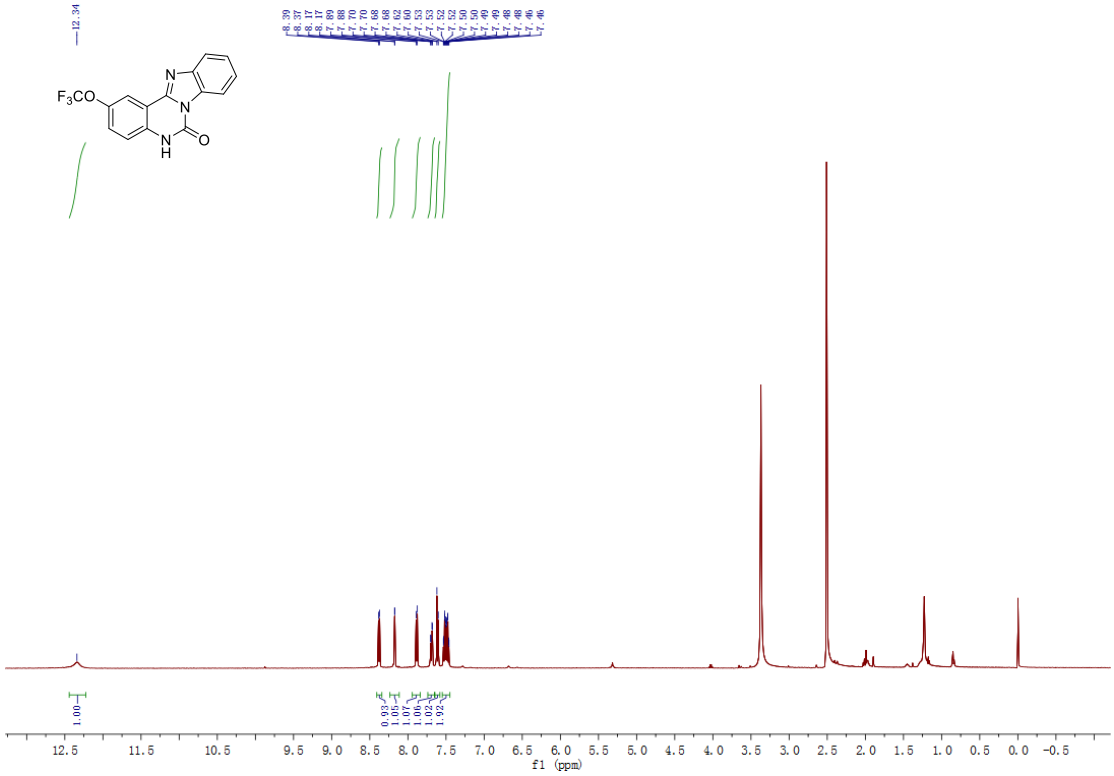
3-Bromobenzo[4,5]imidazo[1,2-c]quinazolin-6(5H)-one (3j)

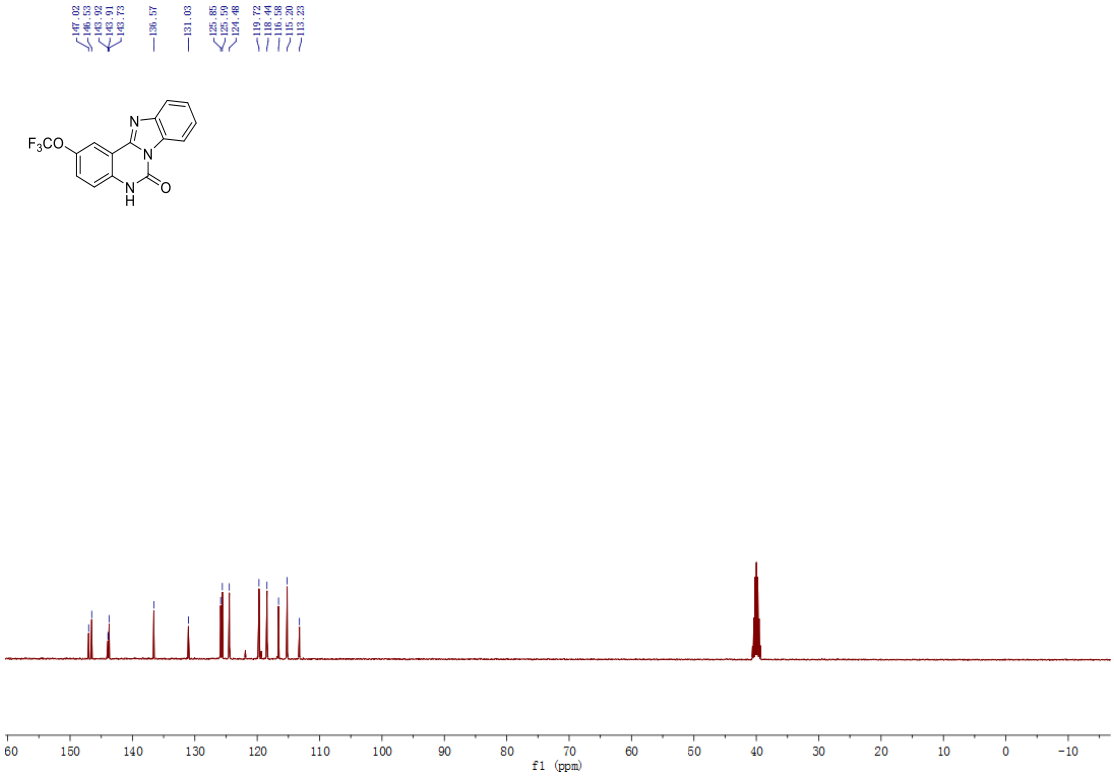


1-Bromobenzo[4,5]imidazo[1,2-c]quinazolin-6(5H)-one (3k)



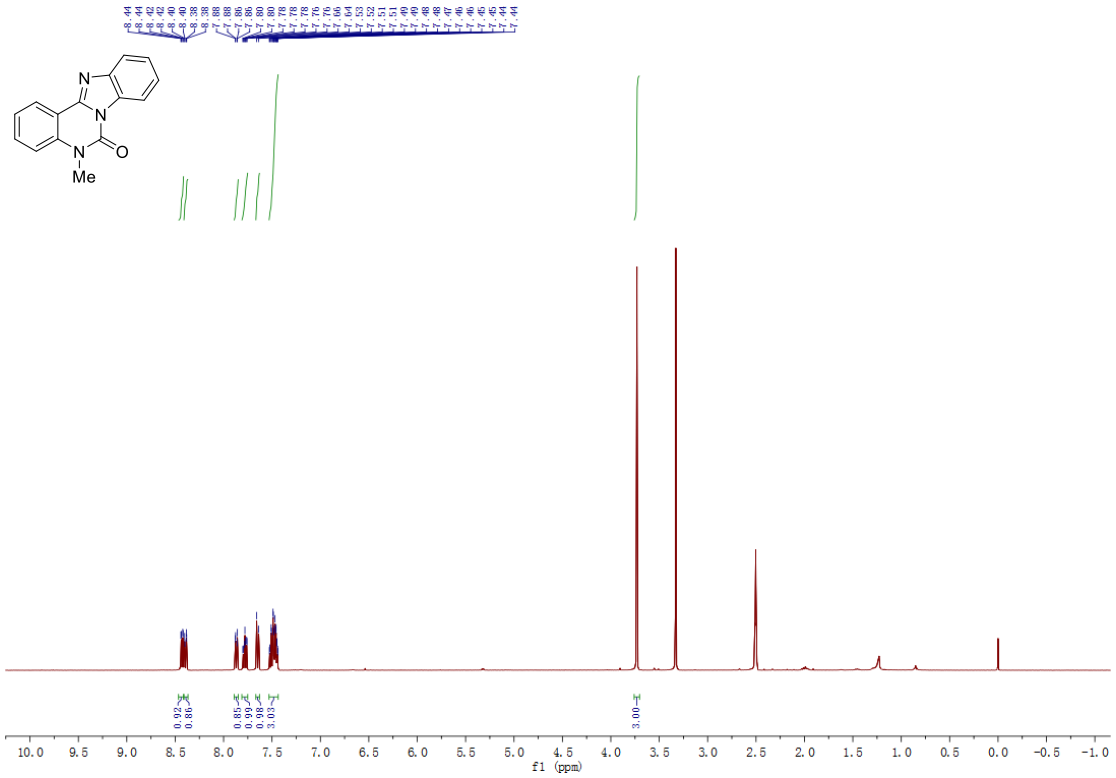
2-(Trifluoromethoxy)benzo[4,5]imidazo[1,2-c]quinazolin-6(5H)-one (3l)

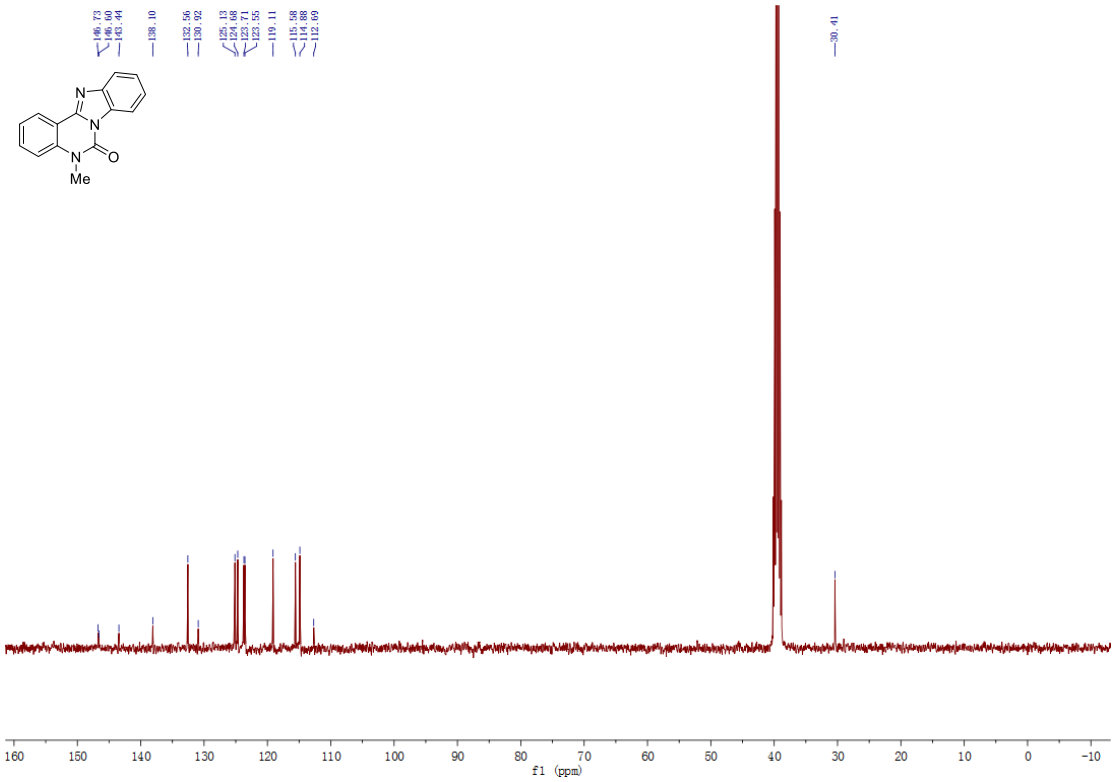




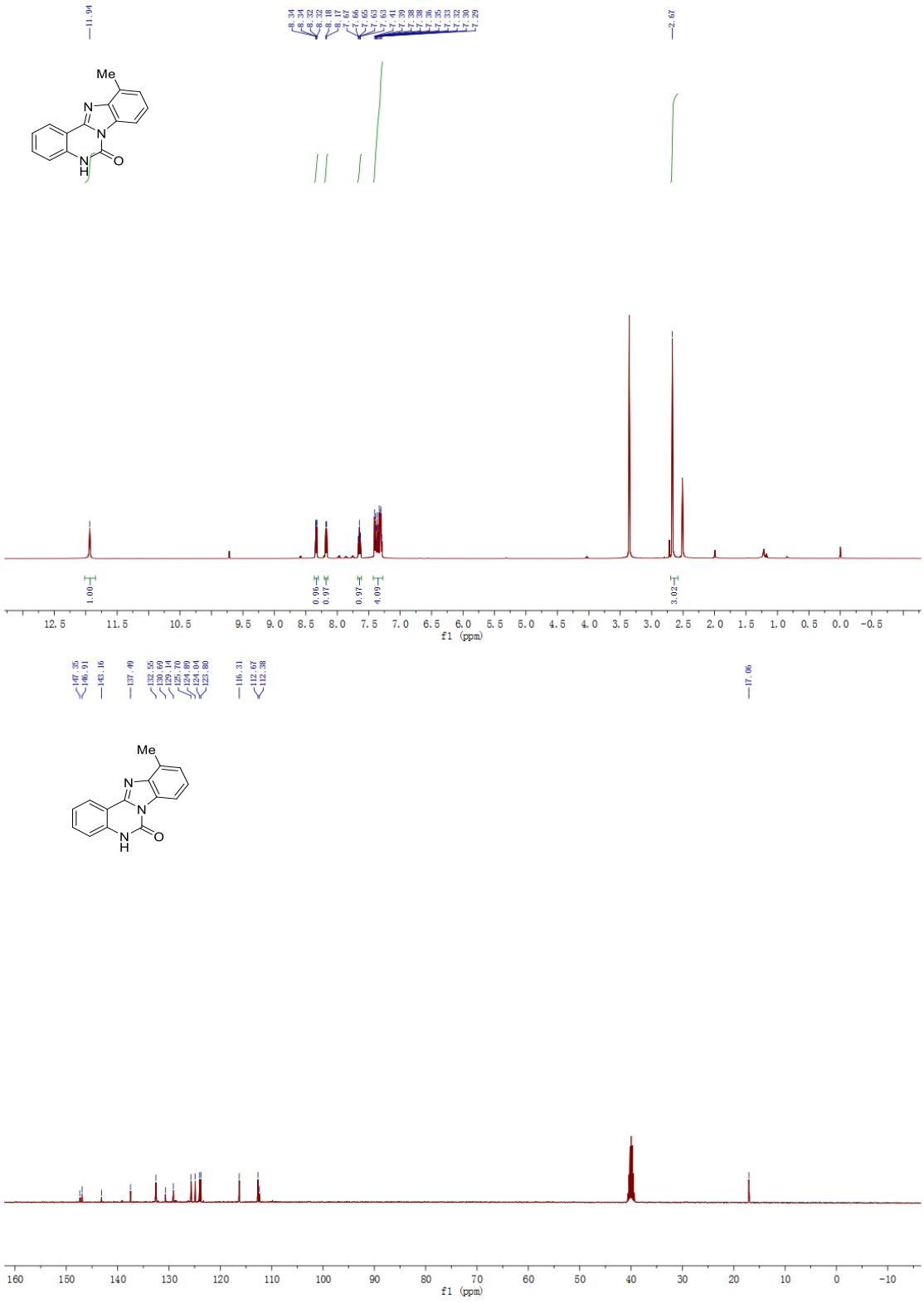

-57.25
F3CO
N
N
H
O
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

5-Methylbenzo[4,5]imidazo[1,2-c]quinazolin-6(5H)-one (3m)

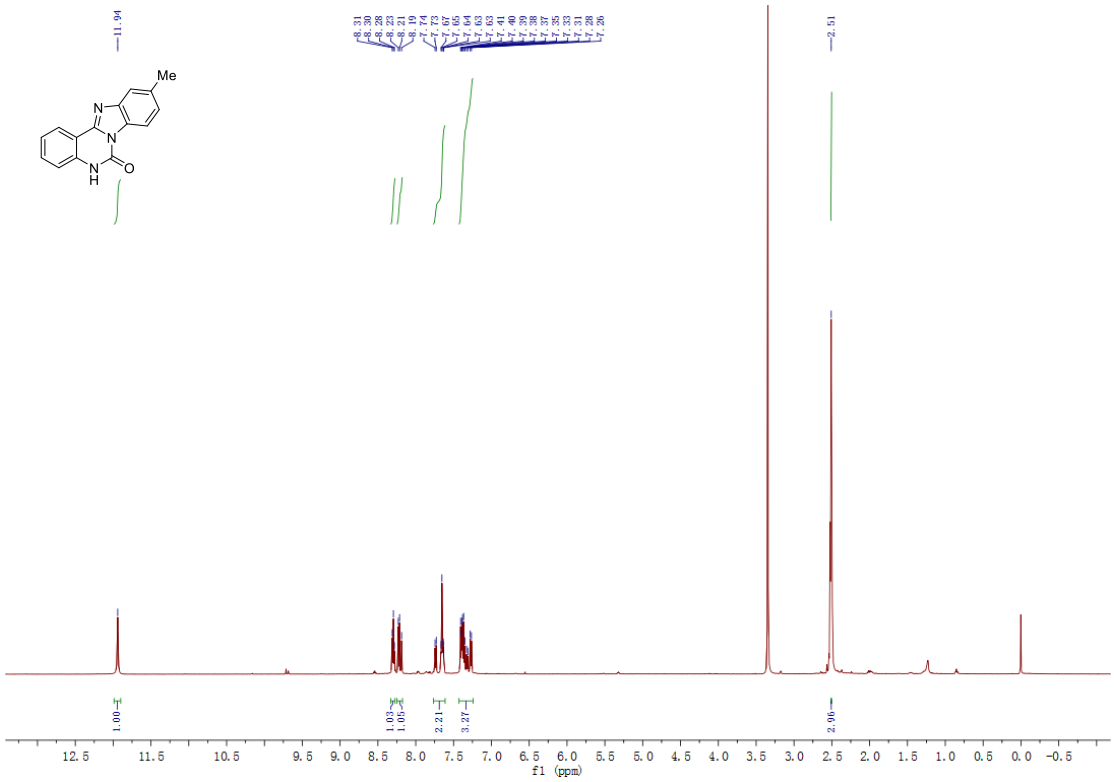


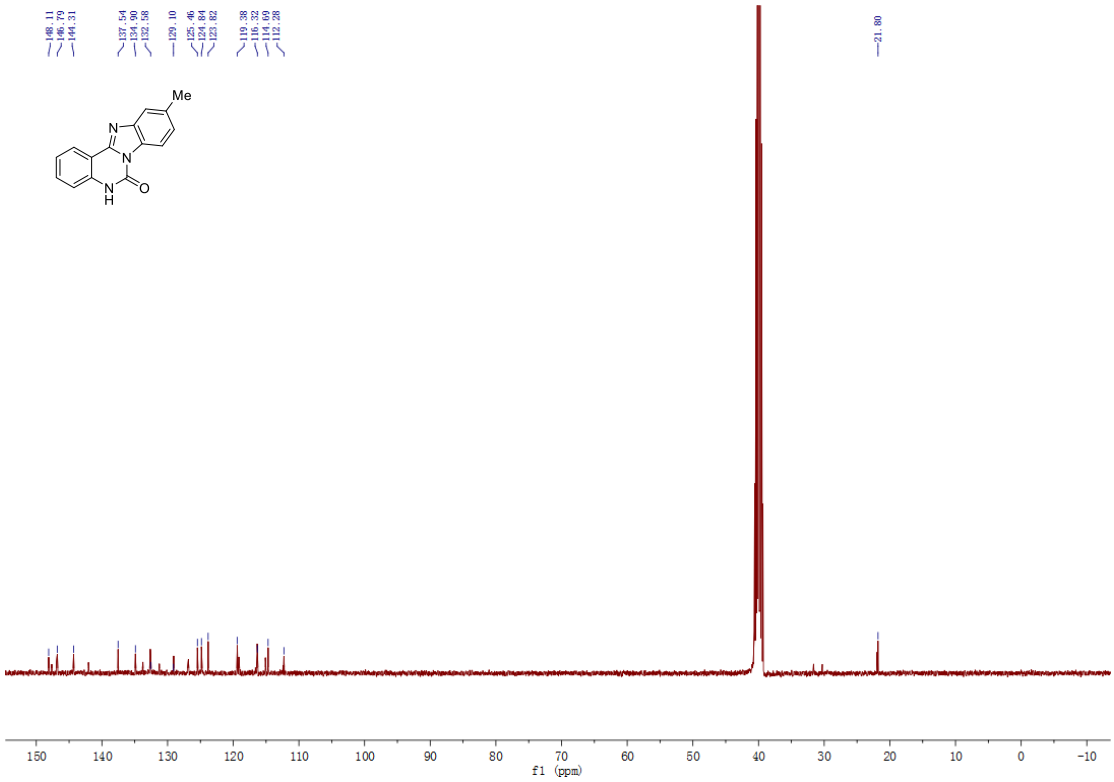


11-Methylbenzo[4,5]imidazo[1,2-c]quinazolin-6(5H)-one (3n)



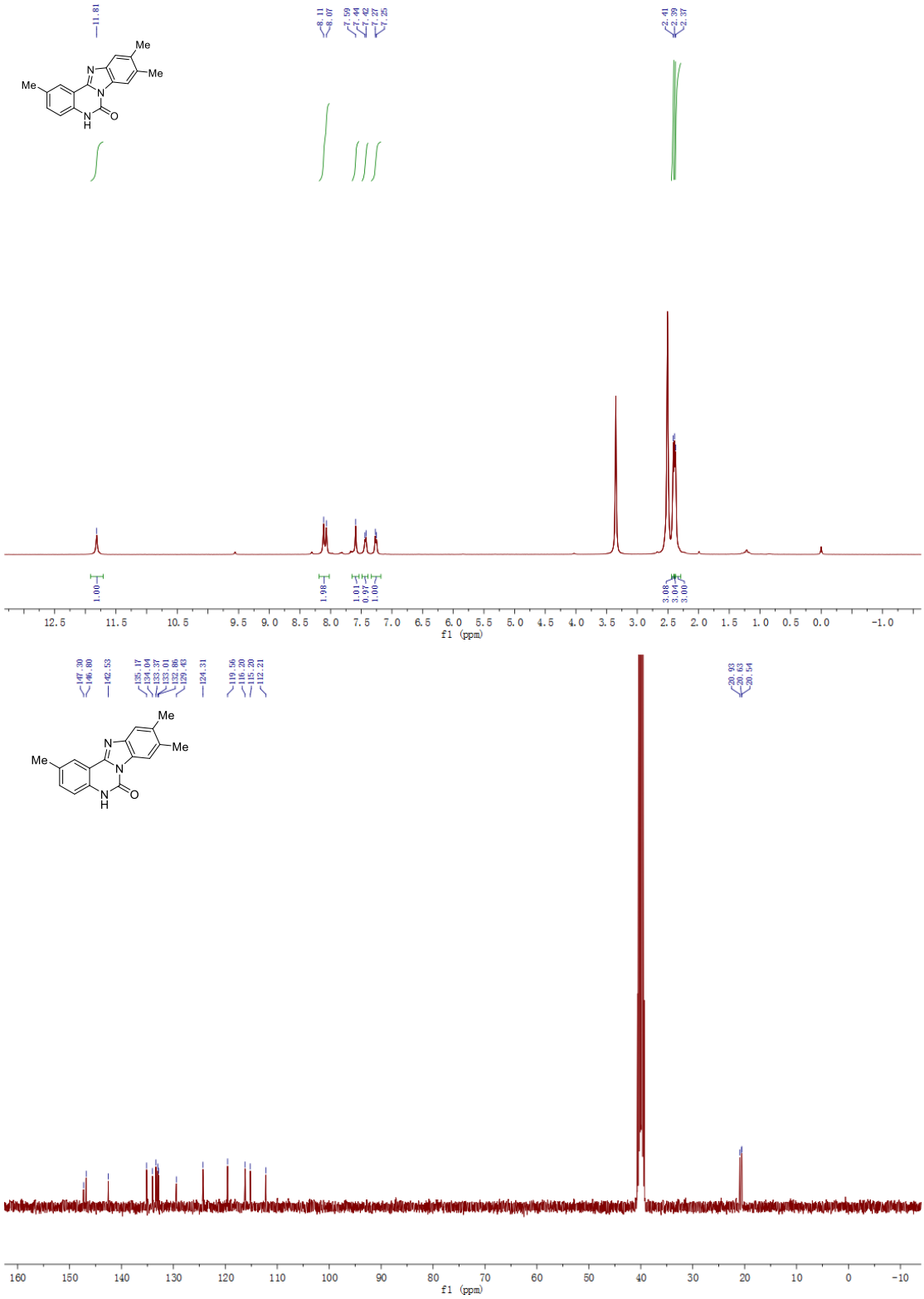
10-Methylbenzo[4,5]imidazo[1,2-c]quinazolin-6(5H)-one (3o)



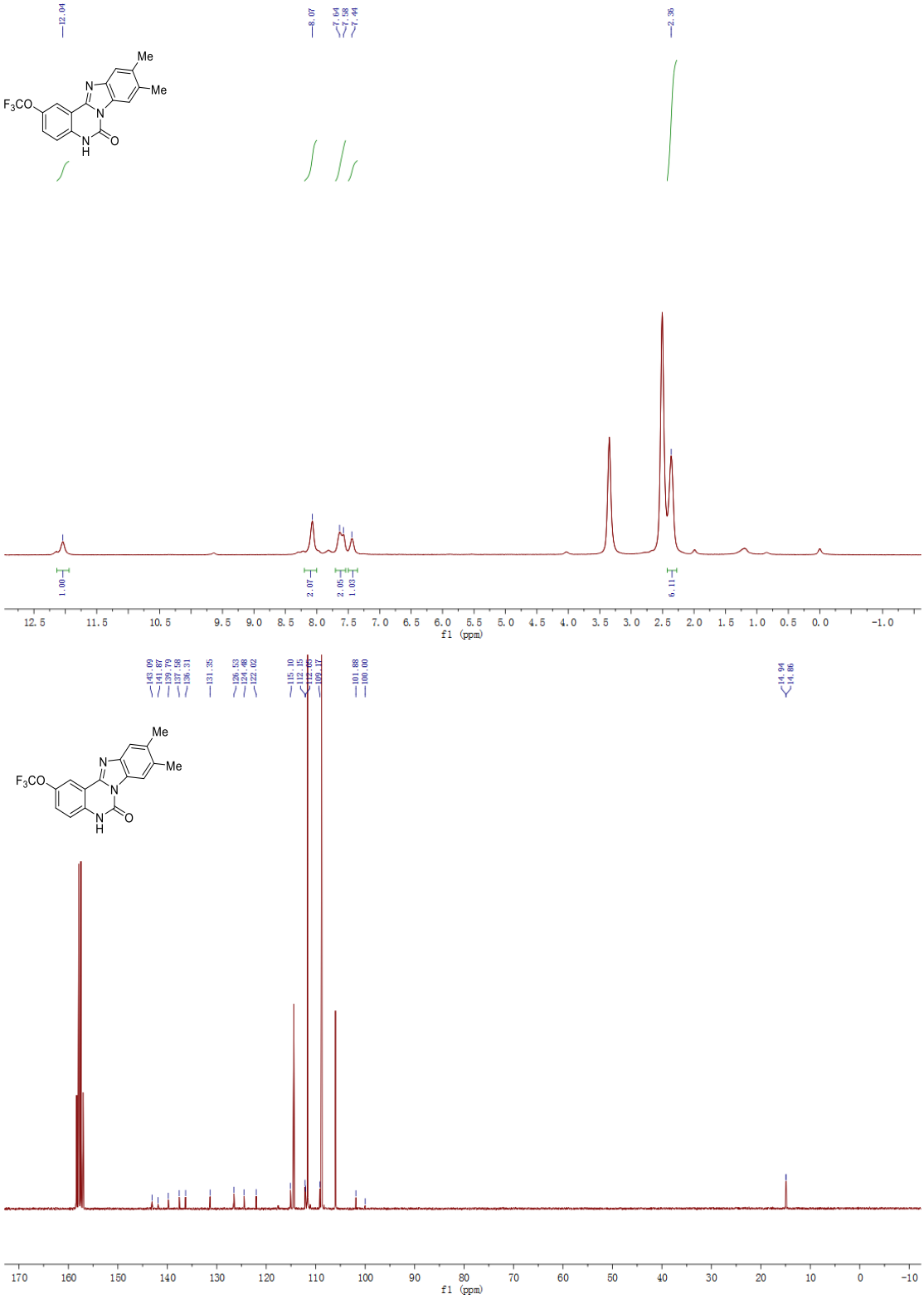


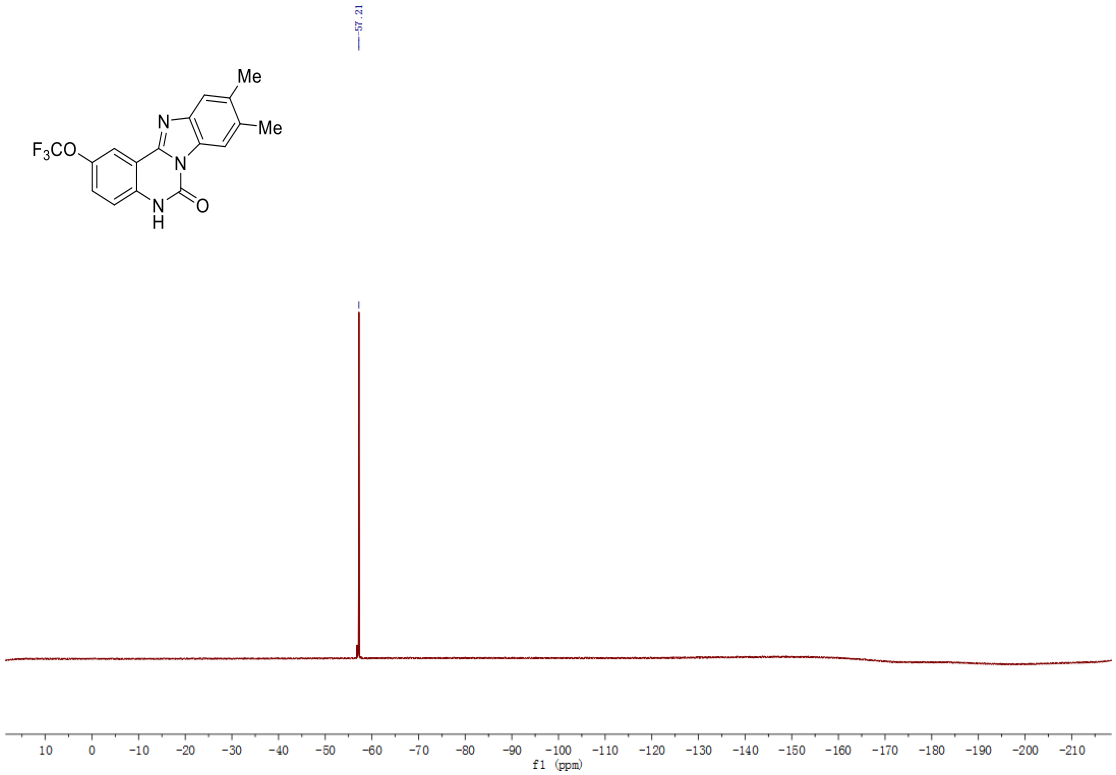
9,10-Dimethylbenzo[4,5]imidazo[1,2-c]quinazolin-6(5H)-one (3p)

2,9,10-Trimethylbenzo[4,5]imidazo[1,2-c]quinazolin-6(5H)-one (3q)

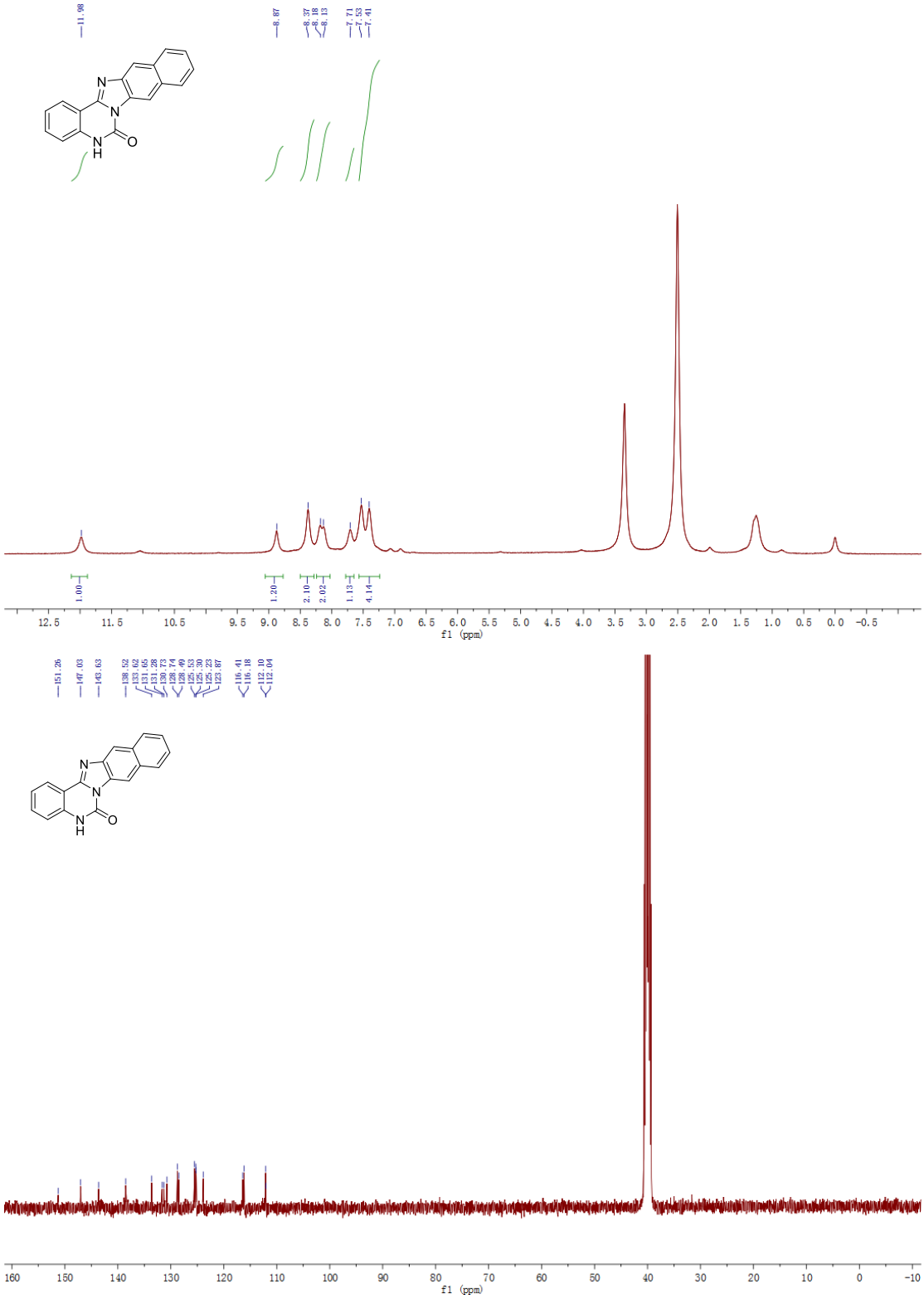


9,10-Dimethyl-2-(trifluoromethoxy)benzo[4,5]imidazo[1,2-c]quinazolin-6(5H)-one (3r)

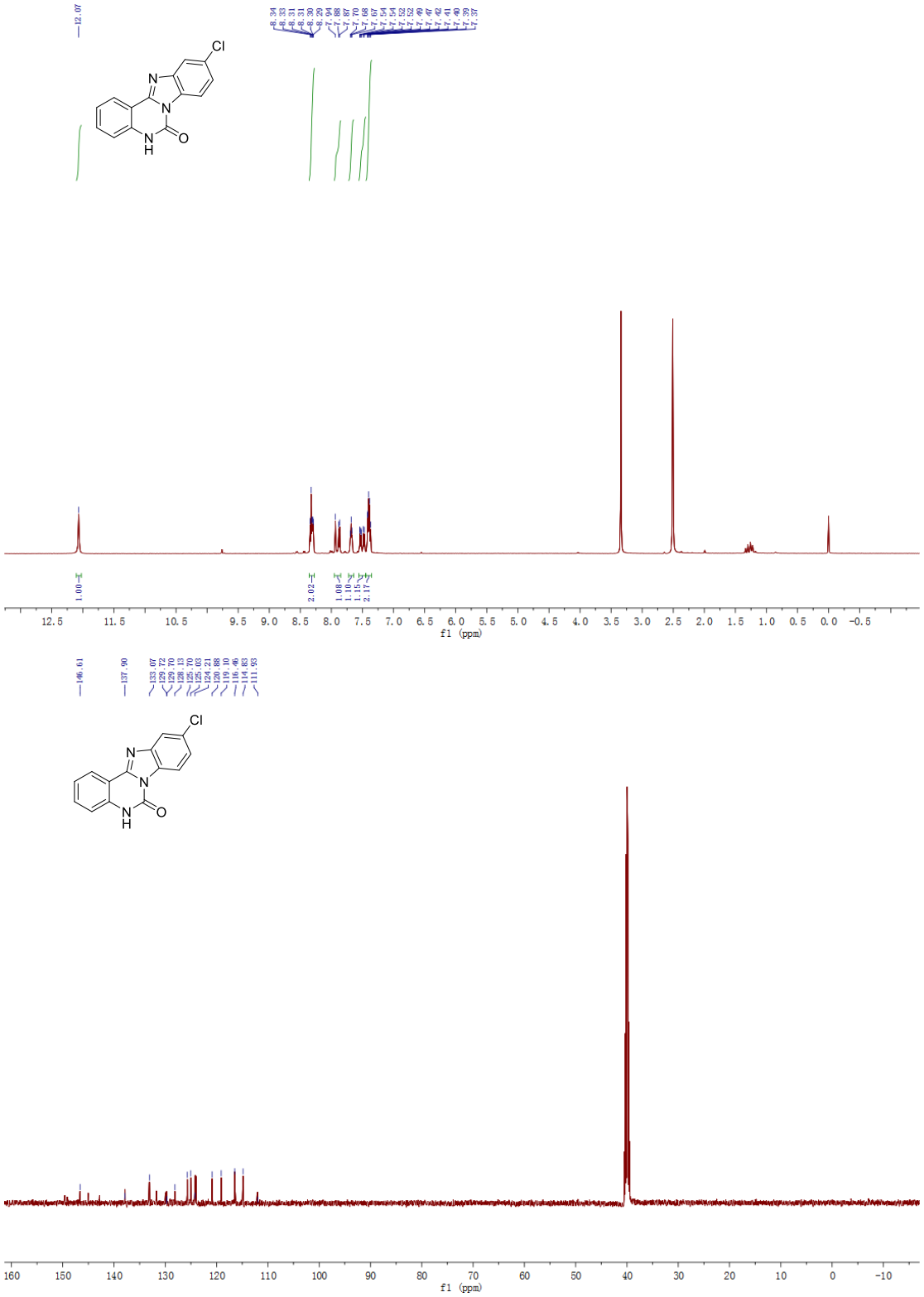



-57.21
Me
Me
F3CO
N
N
N
H
O
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

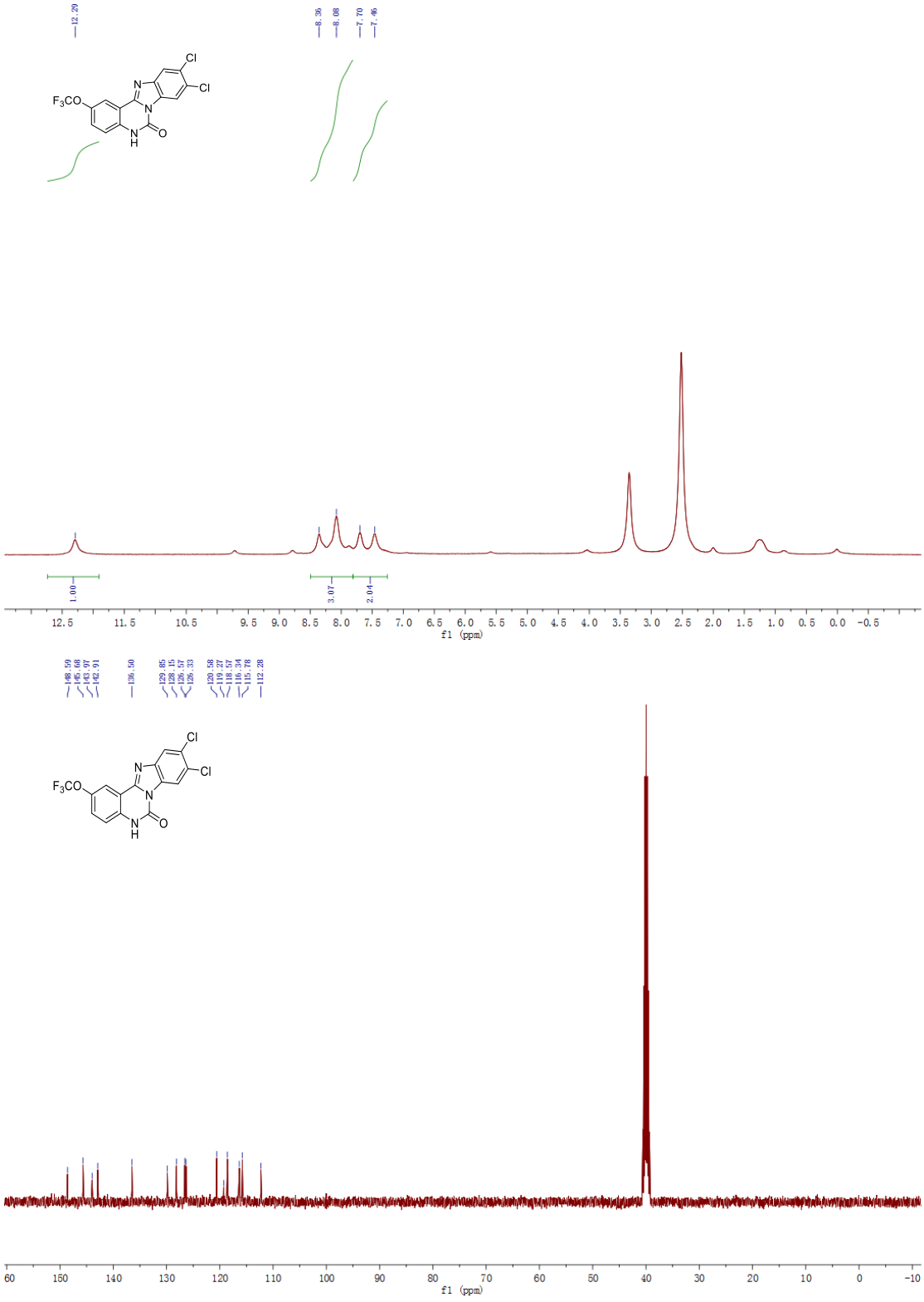
Naphtho[2',3':4,5]imidazo[1,2-c]quinazolin-6(5H)-one (3s)

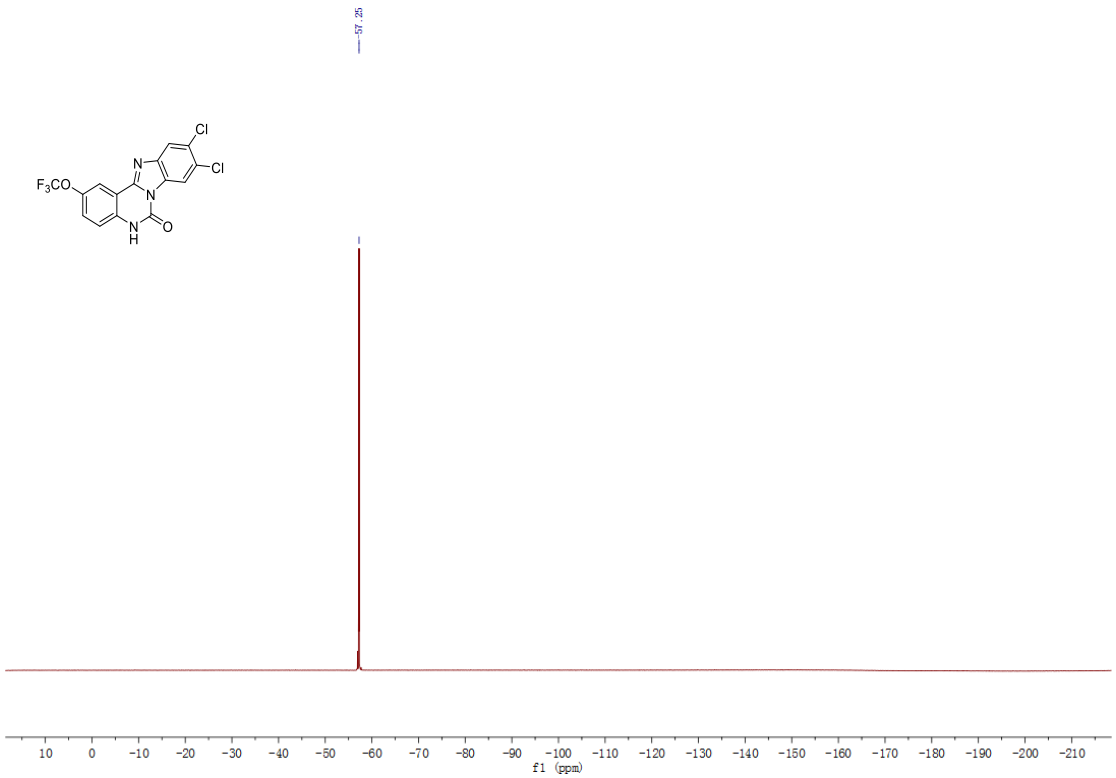


10-Chlorobenzo[4,5]imidazo[1,2-c]quinazolin-6(5H)-one (3t)

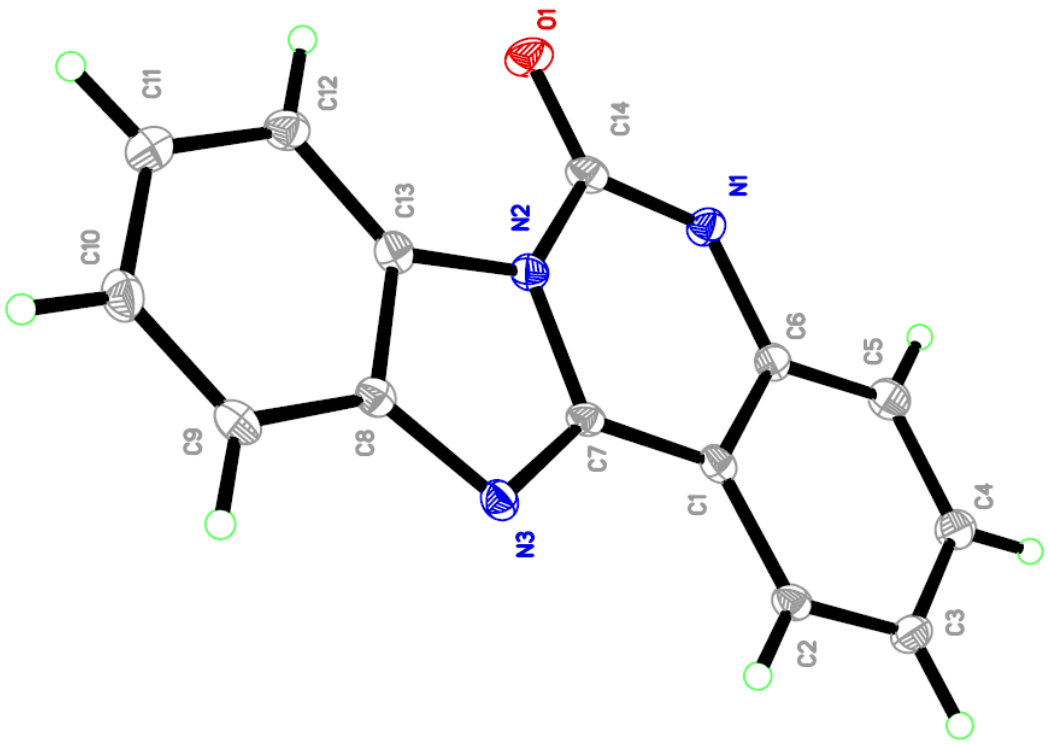


9,10-Dichloro-2-(trifluoromethoxy)benzo[4,5]imidazo[1,2-c]quinazolin-6(5H)-one (3u)




-57.25
Cl
Cl
N
N
F3CO
N
H
O
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

6. X-ray structure of 3a



CCDC1858811