Copper-Catalyzed Efficient Amidation of 2-Methylquinolines with Amines

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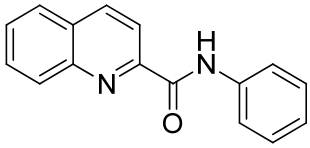
General information:

All reactions were carried out under an atmosphere of oxygen unless otherwise noted. Column chromatography was performed using silica gel (200-300 mesh). ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker-AV (400 and 100 MHz, respectively) instrument internally referenced to tetramethylsilane (TMS) or chloroform signals. Mass spectra was measured on Agilent 5975 GC-MS instrument (EI). High-resolution mass spectra were recorded at Institute of Chemistry, Chinese Academy of Sciences. The structure of known compounds was further corroborated by comparing their ^{1}H NMR, ^{13}C NMR data and MS data with those of literature. All reagents were obtained from commercial suppliers and used without further purification.

General procedure:

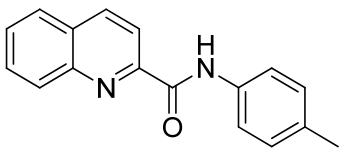
CuI (9.5 mg, 0.05 mmol) were added to a 25 mL oven-dried reaction vessel. The reaction vessel was purged with oxygen for three times and then was added 2-methylquinoline (**1a**, 70 μL, 0.5 mmol), aniline (**2a**, 90 μL, 1.0 mmol) and PivOH (0.8 mL) by syringe. The reaction vessel was stirred at 120 ^{o}C for 48 h. After cooling to room temperature, the volatiles were removed under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 20:1) to yield the desired product **3a** as white solid; yield 76%.

***N*-Phenylquinoline-2-carboxamide (3a, CAS: 7477-46-5)**[1]



^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 10.25 (s, 1H), 8,40 (q, J = 8.1 Hz, 2H), 8.20 (d, J = 8.4 Hz, 1H), 7.94-7.80 (m, 4H), 7.67 (t, J = 7.2 Hz, 1H), 7,43 (t, J = 8.0 Hz, 2H), 7.18 (t, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 162.2, 149.7, 146.3, 137.8, 137.8, 130.3, 129.7, 129.4, 129.1, 128.1, 127.8, 124.3, 119.8, 118.8; MS (EI) m/z (%) 248 (100), 207, 129, 101, 77.

***N*-(*p*-Tolyl)quinoline-2-carboxamide (3b, CAS: 110490-58-9)**[1]

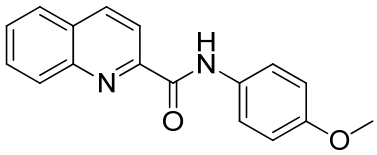


The reaction was conducted with 2-methylquinoline (**1a**, 70 μL, 0.5 mmol) and *p*-toluidine (**2b**,

107.0 mg, 1.0 mmol). The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 20:1) to give **3b** as white solid; yield 57%.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 10.22 (s, 1H), 8,39 (q, J = 8.1 Hz, 2H), 8.21 (d, J = 8.4 Hz, 1H), 7.92 (d, J = 8.0 Hz, 1H), 7.83-7.74 (m, 3H), 7.66 (t, J = 7.6 Hz, 1H), 7.22 (d, J = 8.0 Hz, 2H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 161.9, 149.8, 146.2, 137.9, 135.3, 133.9, 130.3, 129.7, 129.6, 129.4, 128.1, 127.8, 119.7, 118.8, 20.9; MS (EI) m/z (%) 262 (100), 207, 129, 101, 77.

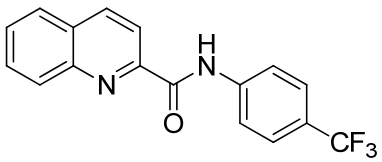
***N*-(4-Methoxyphenyl)quinoline-2-carboxamide (3c, CAS: 22765-52-2)**[1]



The reaction was conducted with 2-methylquinoline (**1a**, 70 μL, 0.5 mmol) and 4-methoxyaniline (**2c**, 125.0 mg, 1.0 mmol). The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 20:1) to give **3c** as orange solid; yield 49%.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 10.19 (s, 1H), 8.40 (q, J = 7.9 Hz, 2H), 8.21 (d, J = 8.4 Hz, 1H), 7.92 (d, J = 8.0 Hz, 1H), 7.84-7.77 (m, 3H), 7.66 (d, J = 7.6 Hz, 1H), 6.96 (d, J = 8.8 Hz, 2H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 161.8, 156.4, 149.8, 146.2, 137.8, 131.0, 130.3, 129.6, 129.3, 128.0, 127.8, 121.3, 118.7, 114.2, 55.5; MS (EI) m/z (%) 278 (100), 207, 129, 101, 77.

***N*-(4-(Trifluoromethyl)phenyl)quinoline-2-carboxamide (3d)**

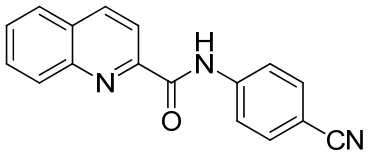


The reaction was conducted with 2-methylquinoline (**1a**, 70 μL, 0.5 mmol) and 4-(trifluoromethyl)aniline (**2d**, 125 μL, 1.0 mmol). The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 20:1) to give **3d** as white solid; yield 89%.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 10.45 (s, 1H), 8.41 (m, 2H), 8.22 (d, J = 8.4 Hz, 1H),

8.01-7.83 (m, 3H), 7.85 (t, J = 7.6 Hz, 1H), 7.71-7.67 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 162.4, 149.0, 146.2, 140.8 (q, J = 1.3 Hz), 138.0, 130.5, 129.6, 129.5, 128.4, 127.8, 126.3 (q, J = 3.8 Hz), 126.0 (q, J = 32.5 Hz), 124.2 (q, J = 269.8 Hz), 119.4, 118.7; HRMS calcd. for: $C_{17}H_{12}ON_2F_3$ $[M+H]^+$ 317.0907, found 317.0903.

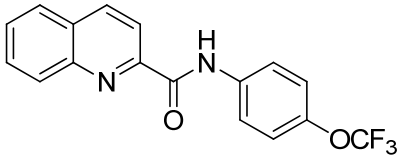
***N*-(4-Cyanophenyl)quinoline-2-carboxamide (3e, CAS: 22765-56-6)**



The reaction was conducted with 2-methylquinoline (**1a**, 70 μL, 0.5 mmol) and 4-aminobenzonitrile (**2e**, 120.0 mg, 1.0 mmol). The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 2:1) to give **3e** as gray solid; yield 86%.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 10.48 (s, 1H), 8.42-8.37 (m, 2H), 8.20 (d, J = 8.4 Hz, 1H), 8.01-7.94 (m, 3H), 7.85 (t, J = 7.6 Hz, 1H), 7.72-7.68 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 162.5, 148.7, 146.2, 141.7, 138.2, 138.2, 133.4, 130.7, 129.6, 129.6, 128.6, 127.9, 119.6, 118.7, 107.2; HRMS calcd. for: $C_{17}H_{12}ON_3$ $[M+H]^+$ 274.0986, found 274.0982.

***N*-(4-(Trifluoromethoxy)phenyl)quinoline-2-carboxamide (3f)**

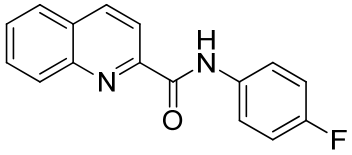


The reaction was conducted with 2-methylquinoline (**1a**, 70 μL, 0.5 mmol) and 4-(trifluoromethoxy)aniline (**2f**, 135 μL, 1.0 mmol). The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 20:1) to give **3f** as white solid; yield 86%.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 10.32 (s, 1H), 8.40 (m, 2H), 8.20 (d, J = 8.4 Hz, 1H), 7.94-7.89 (m, 3H), 7.83 (t, J = 7.6 Hz, 1H), 7.68 (t, J = 7.2 Hz, 1H), 7.27 (d, J = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 162.2, 149.2, 146.2, 145.3, 137.9, 136.5, 130.4, 129.6, 129.5, 128.3, 127.8, 121.8, 120.8, 120.5 (q, J = 255.3 Hz), 118.6; HRMS calcd. for: $C_{17}H_{12}O_2N_2F_3$

$[M+H]^+$ 333.0856, found 333.0853.

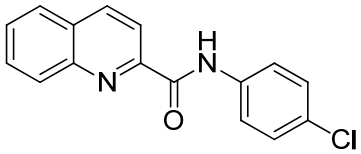
***N*-(4-Fluorophenyl)quinoline-2-carboxamide (3g, CAS: 22765-57-7)**[1]



The reaction was conducted with 2-methylquinoline (**1a**, 70 μL, 0.5 mmol) and 4-fluoroaniline (**2g**, 100 μL, 1.0 mmol). The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 20:1) to give **3g** as white solid; yield 85%.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 10.28 (s, 1H), 8.43-8.38 (m, 2H), 8.21 (d, J = 8.8 Hz, 1H), 7.94-7.82 (m, 4H), 7.68 (t, J = 7.8 Hz, 1H), 7.12 (t, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 162.1, 159.3 (d, J = 241.9 Hz), 149.4, 146.2, 137.9, 133.8 (d, J = 3.0 Hz), 130.4, 129.6, 129.4, 128.2, 127.8, 121.4 (d, J = 7.9 Hz), 118.7, 115.7 (d, J = 22.3 Hz); MS (EI) m/z (%) 266 (100), 207, 129, 101, 77.

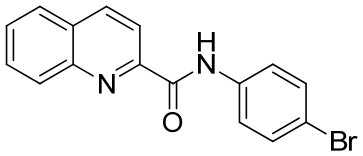
***N*-(4-Chlorophenyl)quinoline-2-carboxamide (3h, CAS: 7477-43-2)**[1]



The reaction was conducted with 2-methylquinoline (**1a**, 70 μL, 0.5 mmol) and 4-chloroaniline (**2h**, 127.5 mg, 1.0 mmol). The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 20:1) to give **3h** as white solid; yield 79%.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 10.28 (s, 1H), 8.39 (m, 2H), 8.20 (d, J = 8.0 Hz, 1H), 7.94-7.82 (m, 4H), 7.67 (t, J = 7.2 Hz, 1H), 7.38 (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 162.1, 149.2, 146.2, 138.0, 136.3, 130.4, 129.5, 129.4, 129.2, 129.1, 128.3, 127.8, 120.9, 118.7; MS (EI) m/z (%) 282 (100), 207, 129, 101, 77.

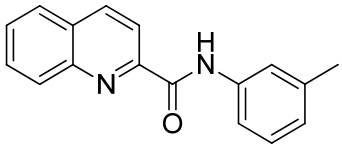
***N*-(4-Bromophenyl)quinoline-2-carboxamide (3i, CAS: 586985-01-5)**[1]



The reaction was conducted with 2-methylquinoline (**1a**, 70 μL, 0.5 mmol) and 4-bromoaniline (**2i**, 208.5 mg, 1.0 mmol). The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 20:1) to give **3i** as light-yellow solid; yield 72%.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 10.27 (s, 1H), 8.38 (m, 2H), 8.19 (d, J = 8.4 Hz, 1H), 7.92 (d, J = 8.0 Hz, 1H), 7.84-7.76 (m, 3H), 7.67 (t, J = 7.2 Hz, 1H), 7.52 (d, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 162.1, 149.2, 146.2, 137.9, 136.8, 132.0, 130.4, 129.6, 129.4, 128.3, 127.8, 121.2, 118.6, 116.8; MS (EI) m/z (%) 326 (100), 207, 129, 101, 77.

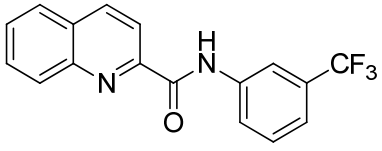
***N*-(*m*-Tolyl)quinoline-2-carboxamide (3j, CAS: 425389-17-9)**[1]



The reaction was conducted with 2-methylquinoline (**1a**, 70 μL, 0.5 mmol) and *m*-toluidine (**2j**, 108 μL, 1.0 mmol). The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 20:1) to give **3j** as white solid; yield 69%.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 10.25 (s, 1H), 8.40 (q, J = 7.3 Hz, 2H), 8,22 (d, J = 8.4 Hz, 1H), 7.93 (d, J = 8.0 Hz, 1H), 7.83 (t, J = 7.6 Hz, 1H), 7.73 (s, 1H), 7.69-7.65 (m, 2H), 7.31 (t, J = 8.0 Hz, 1H), 7.00 (d, J = 7.2 Hz, 1H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 162.1, 149.7, 146.3, 139.0, 137.9, 137.7, 130.3, 129.6, 129.4, 128.9, 128.1, 127.8, 125.2, 120.4, 118.8, 116.9, 21.6; MS (EI) m/z (%) 262 (100), 207, 129, 101, 77.

***N*-(3-(Trifluoromethyl)phenyl)quinoline-2-carboxamide (3k, CAS: 313241-23-5)**[1]

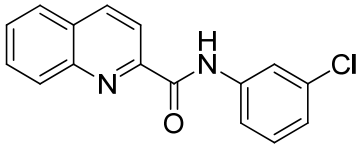


The reaction was conducted with 2-methylquinoline (**1a**, 70 μL, 0.5 mmol) and 3-(trifluoromethyl)aniline (**2k**, 125 μL, 1,0 mmol). The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 20:1) to give **3k** as white solid; yield

88%.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 10.39 (s, 1H), 8.40 (m, 2H), 8.21 (d, J = 8.4 Hz, 1H), 8.17 (s, 1H), 8.07 (d, J = 8.0 Hz, 1H), 7.94 (d, J = 8.0 Hz, 1H), 7.84 (t, J = 7.6 Hz, 1H), 7.68 (t, J = 7.6 Hz, 1H), 7.54 (t, J = 7.6 Hz, 1H), 7.44-7.42 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 162.4, 149.0, 146.2, 138.3, 138.0, 131.4 (q, J = 32.2 Hz), 130.4, 129.6, 129.5, 128.3, 127.8, 123.9 (q, J = 270.8 Hz), 122.7, 122.7, 120.8 (q, J = 3.9 Hz), 118.6, 116.4 (q, J = 4.0 Hz); MS (EI) m/z (%) 316 (100), 207, 129, 101, 77.

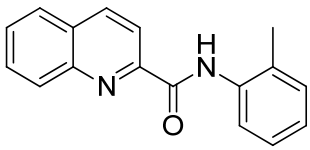
***N*-(3-Chlorophenyl)quinoline-2-carboxamide (3l, CAS: 22765-54-4)**[1]



The reaction was conducted with 2-methylquinoline (**1a**, 70 μL, 0.5 mmol) and 3-chloroaniline (**2l**, 106 μL, 1.0 mmol). The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 20:1) to give **3l** as white solid; yield 84%.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 10.28 (s, 1H), 8.39 (m, 2H), 8.19 (d, J = 8.4 Hz, 1H), 7.98 (s, 1H), 7.93 (d, J = 7.2 Hz, 1H), 7.83 (t, J = 7.2 Hz, 1H), 7.73-7.66 (m, 2H), 7.34 (t, J = 8.0 Hz, 1H), 7.15 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 162.2, 149.2, 146.2, 138.9, 137.9, 134.8, 130.4, 130.1, 129.6, 129.5, 128.3, 127.8, 124.3, 119.8, 118.7, 117.7; MS (EI) m/z (%) 282 (100), 207, 129, 101, 77.

***N*-(*o*-Tolyl)quinoline-2-carboxamide (3m, CAS: 298193-93-8)**[1]

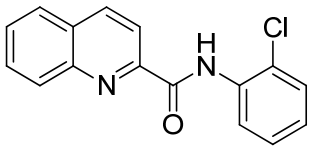


The reaction was conducted with 2-methylquinoline (**1a**, 70 μL, 0.5 mmol) and 4-acetylbenzonitrile (**2m**, 107 μL, 1.0 mmol). The residue was purified by column chromatography (silica gel, petroleum ether/ ethyl acetate = 20:1) to give **3m** as orange solid; yield 56%.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 10.37 (s, 1H), 8.43-8.33 (m, 3H), 8.18 (d, J = 8.0 Hz, 1H),

7.93 (d, J = 8.0 Hz, 1H), 7.83-7.79 (m, 1H), 7.68-7.64 (m, 1H), 7.33-7.26 (m, 2H), 7.13-7.10 (m, 1H), 2.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 161.9, 149.9, 146.2, 137.8, 135.9, 130.4, 130.2, 129.8, 129.4, 128.1, 128.0, 127.7, 126.9, 124.5, 121.2, 118.7, 17.7; MS (EI) m/z (%) 262 (100), 207, 129, 101, 77.

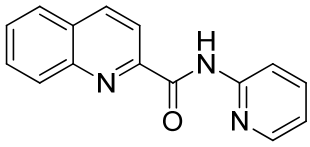
***N*-(2-Chlorophenyl)quinoline-2-carboxamide (3n, CAS: 22765-55-5)**[1]



The reaction was conducted with 2-methylquinoline (**1a**, 70 μL, 0.5 mmol) and 2-chloroaniline (**2n**, 105 μL, 1.0 mmol). The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 20:1) to give **3n** as white solid; yield 71%.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 11.02 (s, 1H), 8.70 (d, J = 7.6 Hz, 1H), 8.40 (m, 2H), 8.24 (d, J = 8.0 Hz, 1H), 7.93 (d, J = 7.6 Hz, 1H), 7.83 (t, J = 7.6 Hz, 1H), 7.68 (t, J = 6.8 Hz, 1H), 7.47 (d, J = 7.6 Hz, 1H), 7.37 (t, J = 7.2 Hz, 1H), 7.11 (t, J = 7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 162.3, 149.4, 146.3, 137.9, 134.8, 130.3, 130.0, 129.5, 129.2, 128.3, 127.8, 127.7, 124.6, 123.5, 121.0, 118.6; MS (EI) m/z (%) 282 (100), 247, 129, 101, 77.

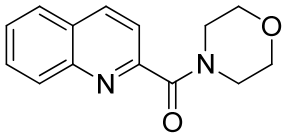
***N*-(Pyridin-2-yl)quinoline-2-carboxamide (3o)**



The reaction was conducted with 2-methylquinoline (**1a**, 70 μL, 0.5 mmol) and 4-chloroaniline (**2o**, 95.0 mg, 1.0 mmol). The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 20:1) to give **3o** as light-yellow solid; yield 81%.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 10.81 (s, 1H), 8.50 (d, J = 7.6 Hz, 1H), 8.42-8.38 (m, 3H), 8.21 (d, J = 7.6 Hz, 1H), 7.91 (d, J = 8.0 Hz, 1H), 7.79 (t, J = 7.6 Hz, 2H), 7.66 (t, J = 7.2 Hz, 1H), 7.12 (t, J = 6.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 162.7, 151.1, 148.8, 148.1, 146.3, 138.4, 137.7, 130.3, 129.8, 129.4, 128.3, 127.6, 119.8, 118.5, 113.9; HRMS calcd. for: $C_{15}H_{11}ON_3Na$ $[M+Na]^+$ 272.0805, found 272.0800.

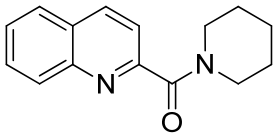
Morpholino(quinolin-2-yl)methanone (3p, CAS: 78224-46-1)[2]



The reaction was conducted with 2-methylquinoline (**1a**, 70 μL, 0.5 mmol) and morpholine (**2q**, 90 μL, 1.0 mmol). The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 20:1) to give **3p** as orange solid; yield 62%.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.31 (d, J = 8.0 Hz, 1H), 8.15 (d, J = 8.4 Hz, 1H), 7.88 (d, J = 8.0 Hz, 1H), 7.81-7.76 (m, 2H), 7.64 (t, J = 7.2 Hz, 1H), 3.90-3.87 (m, 4H), 3.75 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 167.5, 153.2, 146.5, 137.3, 130.1, 129.7, 128.1, 127.7, 127.6, 120.9, 67.0, 66.8, 47.8, 42.8; MS (EI) m/z (%) 242 (100), 156, 129, 101, 77.

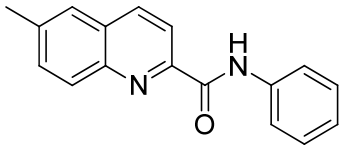
Piperidin-1-yl(quinolin-2-yl)methanone (3q) [2]



The reaction was conducted with 2-methylquinoline (**1a**, 70 μL, 0.5 mmol) and piperidine (**2r**, 100 μL, 1.0 mmol). The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 20:1) to give **3q** as orange solid; yield 42%.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.25 (d, J = 8.0 Hz, 1H), 8.12 (d, J = 8.4 Hz, 1H), 7.85 (d, J = 8.0 Hz, 1H), 7.76 (t, J = 7.6 Hz, 1H), 7.67-7.58 (m, 2H), 3.81 (m, 2H), 3.53-3.50 (m, 2H), 1.76 (m, 4H), 1.60 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 167.6, 154.3, 146.6, 137.0, 129.9, 129.5, 127.8, 127.5, 127.2, 120.2, 48.2, 43.2, 26.3, 25.4, 24.4; HRMS calcd. for: $C_{15}H_{16}ON_2Na$ $[M+Na]^+$ 263.1166, found 263.1162.

2,4-Diptolylpyridine (3s)

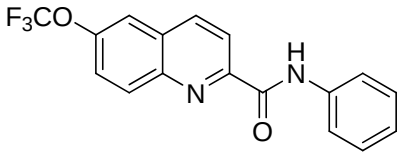


The reaction was conducted with 2,6-dimethylquinoline (**1c**, 81.0 mg, 0.5 mmol) and aniline (**2a**, 90 μL, 1.0 mmol). The residue was purified by column chromatography (silica gel, petroleum

ether/ethyl acetate = 20:1) to give **3s** as white solid; yield 78%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.25 (s, 1H), 8.38-8.36 (m, 1H), 8.28-8.26 (m, 1H), 8.09 (d, *J* = 8.4 HZ, 1H), 7.86 (d, *J* = 8.4 HZ, 2H), 7.67-7.63 (m, 2H), 7.44-7.40 (m, 2H), 7.17 (t, *J* = 6.4 Hz, 1H), 2.59 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) *δ* 162.2, 148.6, 144.7, 138.3, 137.8, 136.9, 132.6, 129.4, 129.2, 129.0, 126.5, 124.1, 119.6, 118.6, 21.7; HRMS calcd. for: $C_{17}H_{14}ON_2Na$ $[M+Na]^+$ 285.1009, found 285.1004.

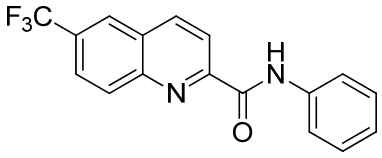
***N*-Phenyl-6-(trifluoromethoxy)quinoline-2-carboxamide (3t)**



The reaction was conducted with 2-methyl-6-(trifluoromethoxy)quinoline (**1d**, 114.0 mg, 0.5 mmol) and aniline (**2a**, 90 μL, 1.0 mmol). The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 20:1) to give **3t** as off-white solid; yield 86%.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) *δ* 10.16 (s, 1H), 8.47 (d, *J* = 8.4 Hz, 1H), 8.38 (d, *J* = 8.8 Hz, 1H), 8.26 (d, *J* = 9.2 Hz, 1H), 7.86 (d, *J* = 8.0 Hz, 2H), 7.74 (s, 1H), 7.67 (d, *J* = 9.2 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 2H), 7.19 (t, *J* = 7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) *δ* 161.6, 150.2, 148.1, 144.4, 137.7, 137.6, 132.0, 129.6, 129.2, 129.1, 124.5, 124.4, 120.5 (q, *J* = 257.1 Hz), 119.7, 117.4; HRMS calcd. for: $C_{17}H_{12}O_2N_2F_3$ $[M+H]^+$ 333.0856, found 333.0852.

***N*-Phenyl-6-(trifluoromethyl)quinoline-2-carboxamide (3u)**

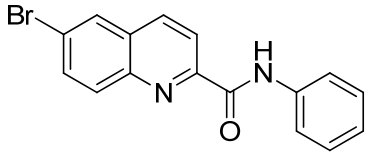


The reaction was conducted with 2-methyl-6-(trifluoromethyl)quinoline (**1e**, 106.0 mg, 0.5 mmol) and aniline (**2a**, 90 μL, 1.0 mmol). The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 20:1) to give **3u** as light-yellow solid; yield 88%.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) *δ* 10.20 (s, *J* = 8.0 Hz, 1H), 8.51 (q, *J* = 8.0 Hz, 2H), 8.35 (d, *J* = 8.8 Hz, 1H), 8.25 (s, 1H), 7.99 (d, *J* = 8.4 Hz, 1H), 7.86 (d, *J* = 8.0 Hz, 2H), 7.44 (t, *J* = 7.6 Hz, 2H), 7.20 (t, *J* = 7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) *δ* 161.3, 151.6, 147.1, 138.7,

137.5, 130.8, 129.8 (q, J = 32.7 Hz), 129.1, 128.2, 125.9 (q, J = 3.0 Hz), 125.7 (q, J = 4.4 Hz), 124.6, 123.7 (q, J = 270.9 Hz), 119.9, 119.7; HRMS calcd. for: $C_{17}H_{12}ON_2F_3$ $[M+H]^+$ 317.0907, found 317.0904.

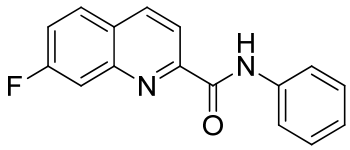
6-Bromo-*N*-phenylquinoline-2-carboxamide (3v)



The reaction was conducted with 6-bromo-2-methylquinoline (**1f**, 113.0 mg, 0.5 mmol) and aniline (**2a**, 90 μL, 1.0 mmol). The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 20:1) to give **3v** as a yellow solid; yield 44%.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 10.19 (s, 1H), 8.44 (d, J = 8.4 Hz, 1H), 8.30 (d, J = 8.4 Hz, 1H), 8.10-8.08 (m, 2H), 7.90-7.84 (m, 3H), 7.43 (t, J = 7.6 Hz, 2H), 7.18 (t, J = 7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 161.7, 150.0, 144.8, 137.6, 136.8, 133.9, 131.2, 130.4, 129.9, 129.1, 124.5, 122.4, 119.8, 119.7; HRMS calcd. for: $C_{16}H_{12}ON_2Br$ $[M+H]^+$ 327.0138, found 327.0136.

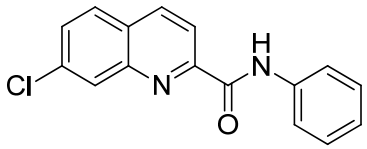
7-Fluoro-*N*-phenylquinoline-2-carboxamide (3w)



The reaction was conducted with 7-fluoro-2-methylquinoline (**1g**, 82.1 mg, 0.5 mmol) and aniline (**2a**, 90 μL, 1.0 mmol). The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 20:1) to give **3w** as orange solid; yield 81%.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 10.19 (s, 1H), 8.38 (m, 2H), 7.94-7.82 (m, 4H), 7.48-7.41 (m, 3H), 7.19 (t, J = 7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 163.4 (d, J = 250.3 Hz), 161.7, 150.6, 147.2 (d, J = 12.8 Hz), 137.8, 137.6, 129.9 (d, J = 9.9 Hz), 129.1, 126.4 (d, J = 1.0 Hz), 124.4, 119.7, 118.8 (d, J = 25.5 Hz), 118.2 (d, J = 2.5 Hz), 113.1 (d, J = 20.4 Hz); HRMS calcd. for: $C_{16}H_{12}ON_2F$ $[M+H]^+$ 267.0939, found 267.0935.

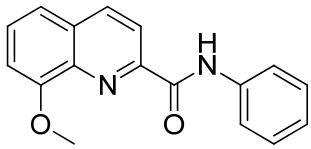
7-Chloro-*N*-phenylquinoline-2-carboxamide (3x)



The reaction was conducted with 7-chloro-2-methylquinoline (**1h**, 90.3 mg, 0.5 mmol) and aniline (**2a**, 90 μL, 1.0 mmol). The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 20:1) to give **3x** as orange solid; yield 47%.

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 10.19 (s, 1H), 8.39 (q, J = 9.2 Hz, 2H), 8.24 (s, 1H), 7.88-7.84 (m, 3H), 7.62 (d, J = 8.4 Hz, 1H), 7.43 (t, J = 7.2 Hz, 2H), 7.19 (t, J = 6.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 161.7, 150.5, 146.6, 137.8, 137.6, 136.3, 129.2, 129.1, 129.0, 128.5, 127.7, 124.5, 119.7, 119.0; HRMS calcd. for: $C_{16}H_{12}ON_2Cl$ $[M+H]^+$ 283.0644, found 283.0641.

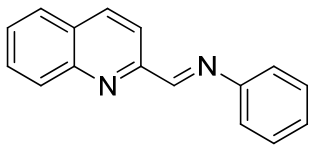
8-Methoxy-*N*-phenylquinoline-2-carboxamide (3y, CAS: 22765-62-4)



The reaction was conducted with 8-methoxy-2-methylquinoline (**1i**, 88.3 mg, 0.5 mmol) and aniline (**2a**, 90 μL, 1.0 mmol). The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 20:1) to give **3y** as gray solid; yield 88%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.30 (s, 1H), 8.45 (d, J = 8.4 Hz, 1H), 8.35 (d, J = 8.4 Hz, 1H), 7.87 (d, J = 7.6 Hz, 2H), 7.59 (t, J = 7.6 Hz, 1H), 7.50-7.40 (m, 3H), 7.19-7.14 (m, 2H), 4.13 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 162.4, 155.2, 148.5, 138.1, 137.8, 137.6, 130.5, 128.9, 128.5, 124.2, 120.0, 119.5, 119.3, 108.4, 55.9; MS (EI) m/z (%) 278 (100), 207, 159, 101, 77; HRMS calcd. for: $C_{17}H_{14}O_2N_2Na$ $[M+Na]^+$ 301.0959, found 301.0955.

(E)-*N*-(Quinolin-2-ylmethylene)aniline (4a, CAS: 22765-62-4)[3]



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (s, 1H), 8.36 (d, J = 8.4 Hz, 1H), 8.24 (d, J = 8.4 Hz, 1H),

8.17 (d, J = 8.4 Hz, 1H), 7.86 (d, J = 8.0 Hz, 1H), 7.76 (t, J = 7.6 Hz, 1H), 7.59 (t, J = 7.2 Hz, 1H), 7.46-7.25 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 160.8, 154.7, 150.7, 147.9, 136.6, 129.9, 129.6, 129.2, 128.8, 127.7, 127.7, 126.9, 121.2, 118.6; MS (EI) m/z (%) 232 (100), 204, 129, 102, 77.

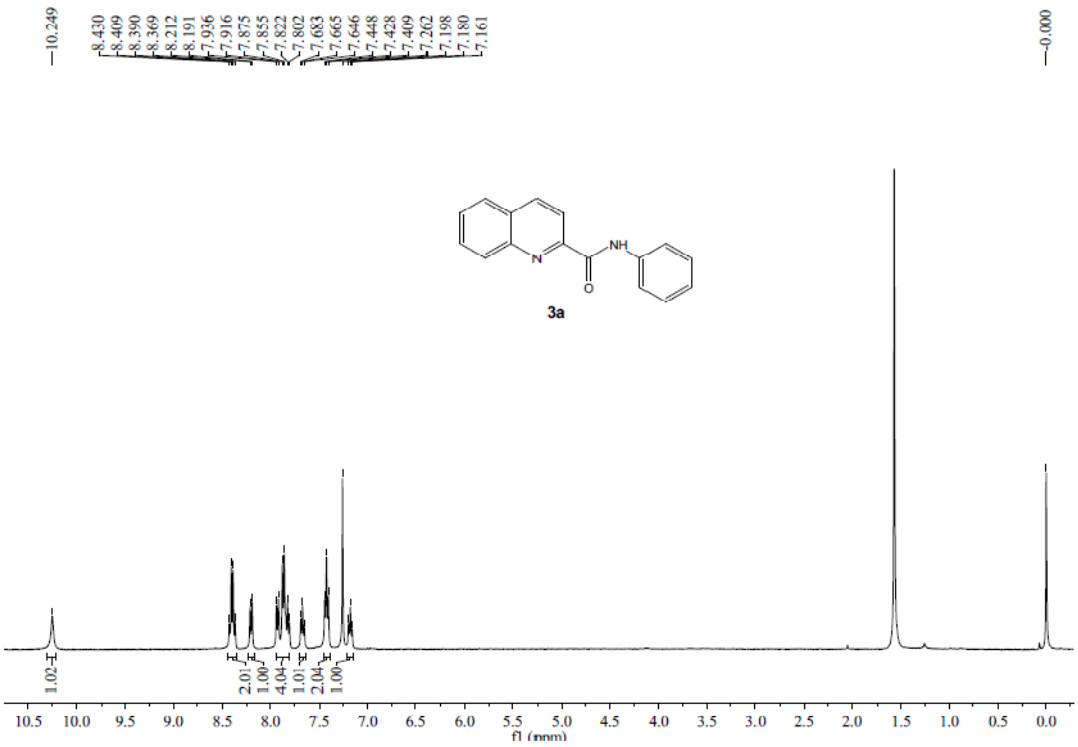
References

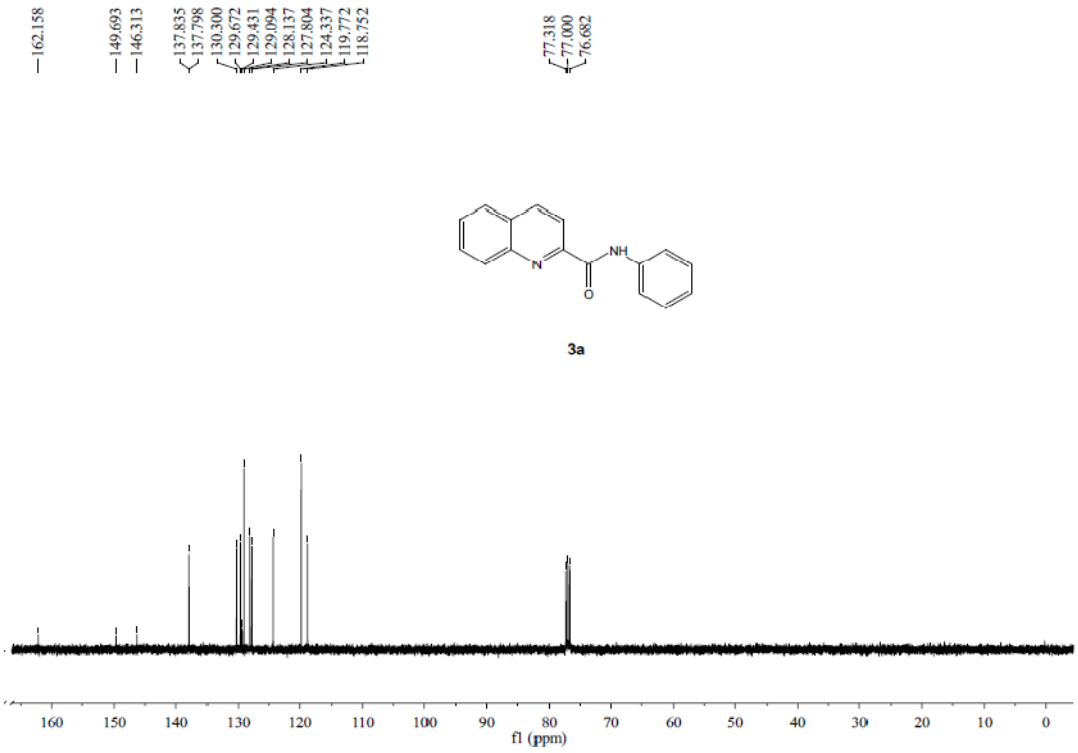
[1] T. Gonec, P. Bobal, J. Sujan, M. Pesko, J. Guo, K. Kralova, L. Pavlacka, L. Vesely, E. Kreckova, J. Kos, A. Coffey, P. Kollar, A. Imramovsky, L. Placek and J. Jampilek, *Molecules*, 2012, **17**, 613.

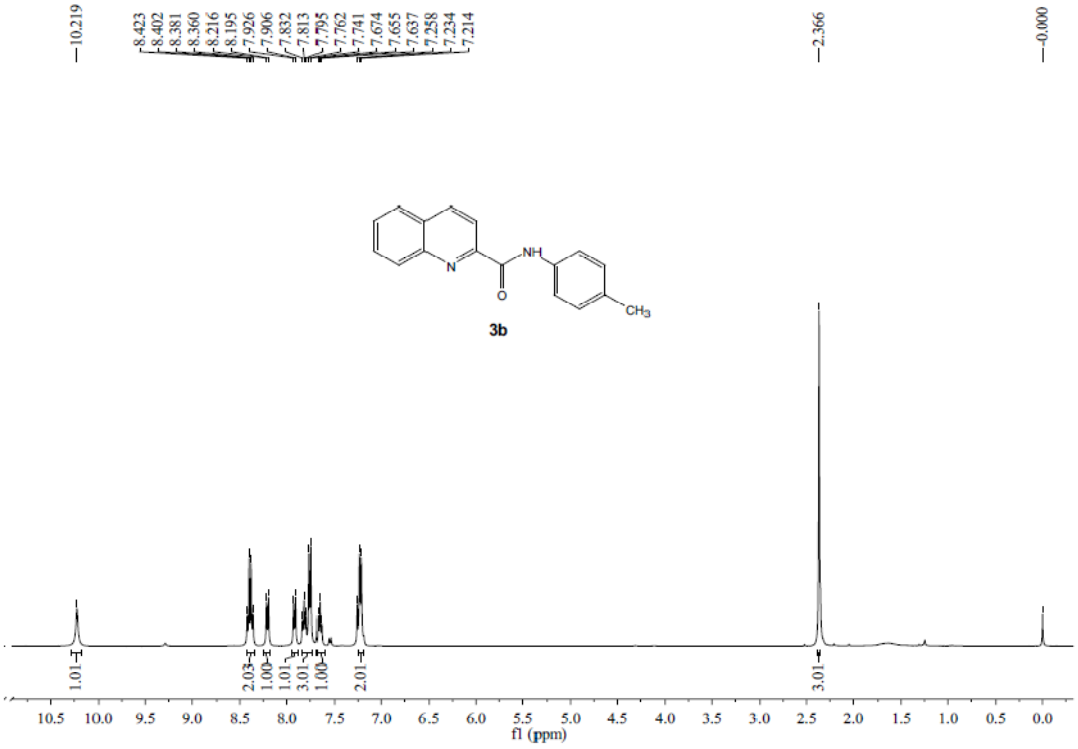
[2] Y. S. Bao, B. Zhaorigetu, B. Agula, M. H. Baiyin, M. L. Jia, *J. Org. Chem.,* 2014, **79**, 803.

[3] B. Zhang, S. F. Zhu, Q. L. Zhou, *Tetrahedron,* 2013, **69**, 2033.

Copies of ^{1}H and ^{13}C NMR spectra of all products



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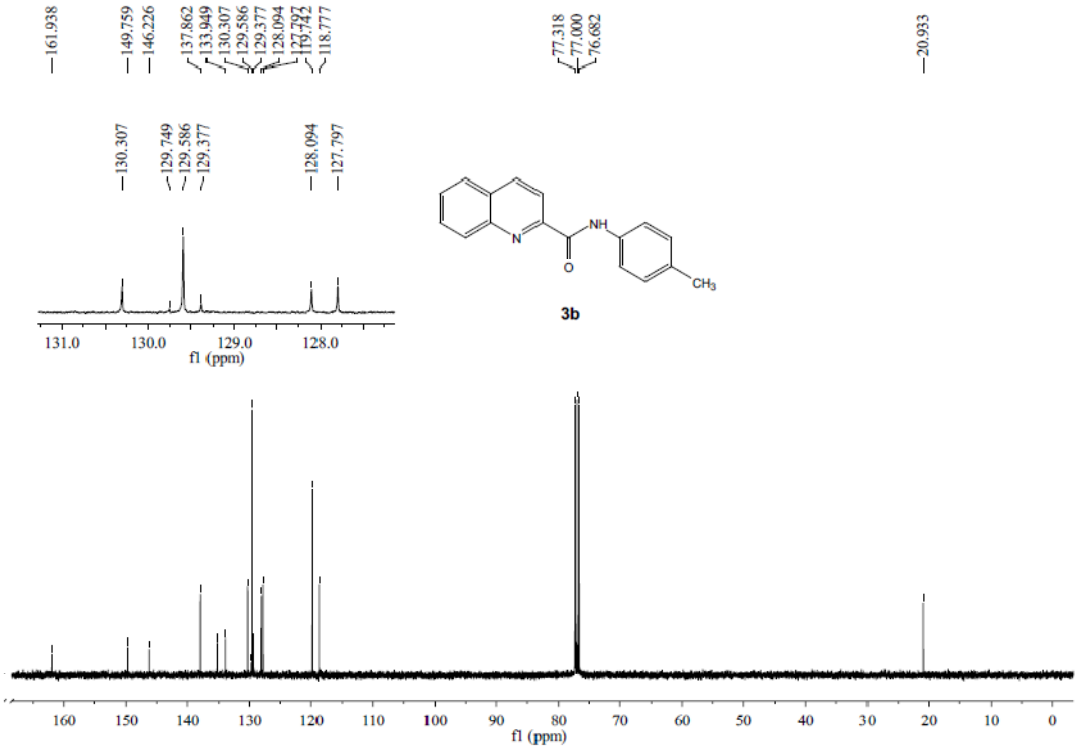
8.216
8.195
7.926
7.906
7.832
7.813
7.795
7.762
7.741
7.674
7.655
7.637
7.258
7.234
7.214
2.366
0.000
NH
N
O
CH3
3b
1.01
2.03
1.00
1.01
3.01
1.00
2.01
3.01
fl (ppm)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137.862
133.949
130.307
129.586
129.377
128.094
127.797
119.742
118.777
77.318
77.000
76.682
20.933
130.307
129.749
129.586
129.377
128.094
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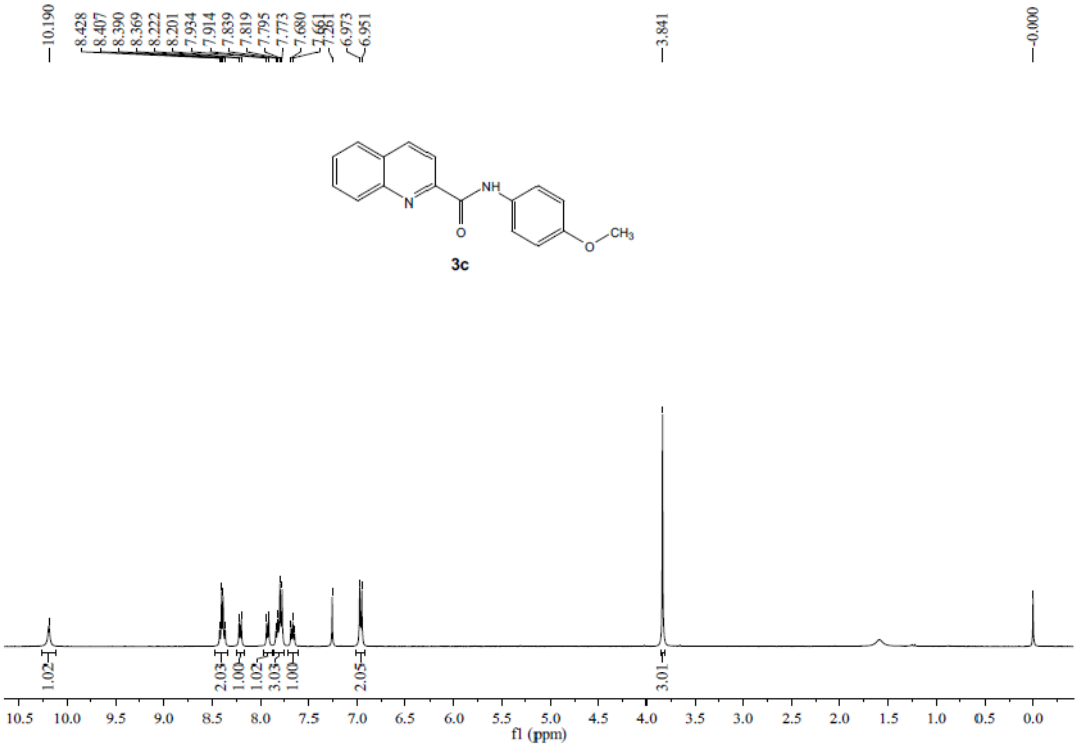
NH
N
O
CH3
3b
131.0
130.0
129.0
128.0
fl (ppm)
fl (ppm)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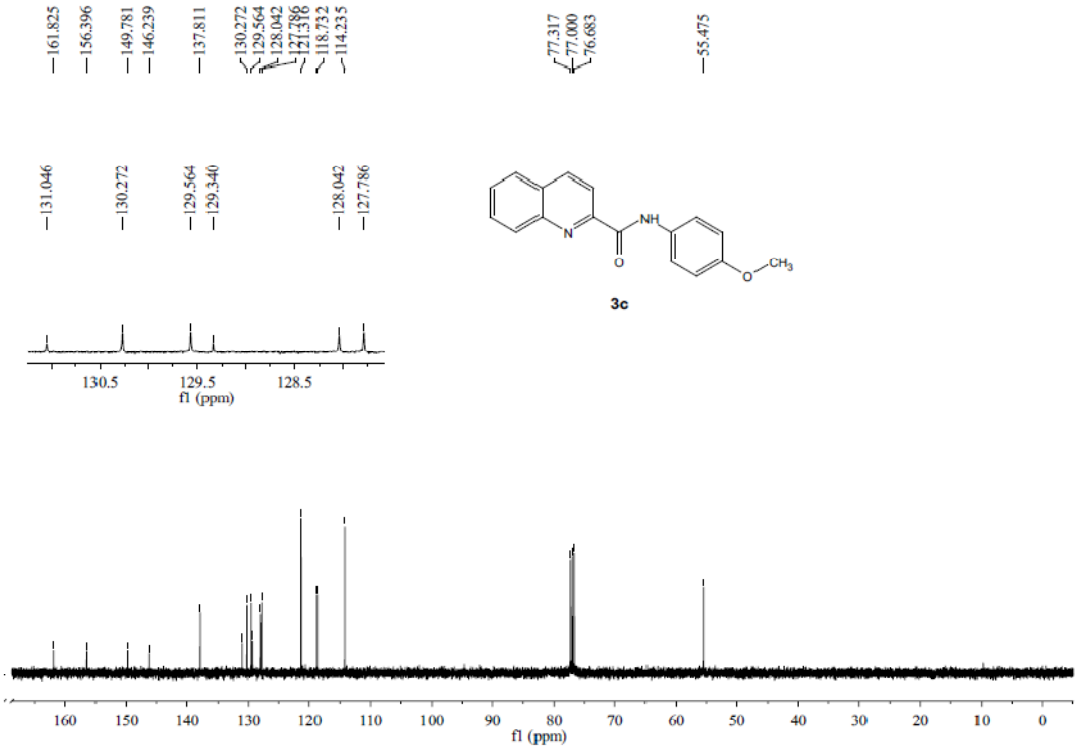
8.390
8.369
8.222
8.201
7.934
7.914
7.839
7.819
7.795
7.773
7.680
7.661
7.581
6.973
6.951
3.841
0.000
NH
O
N
O
CH3
3c
1.02
2.03
1.00
1.02
3.03
1.00
2.05
3.01
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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156.396
149.781
146.239
137.811
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128.042
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121.336
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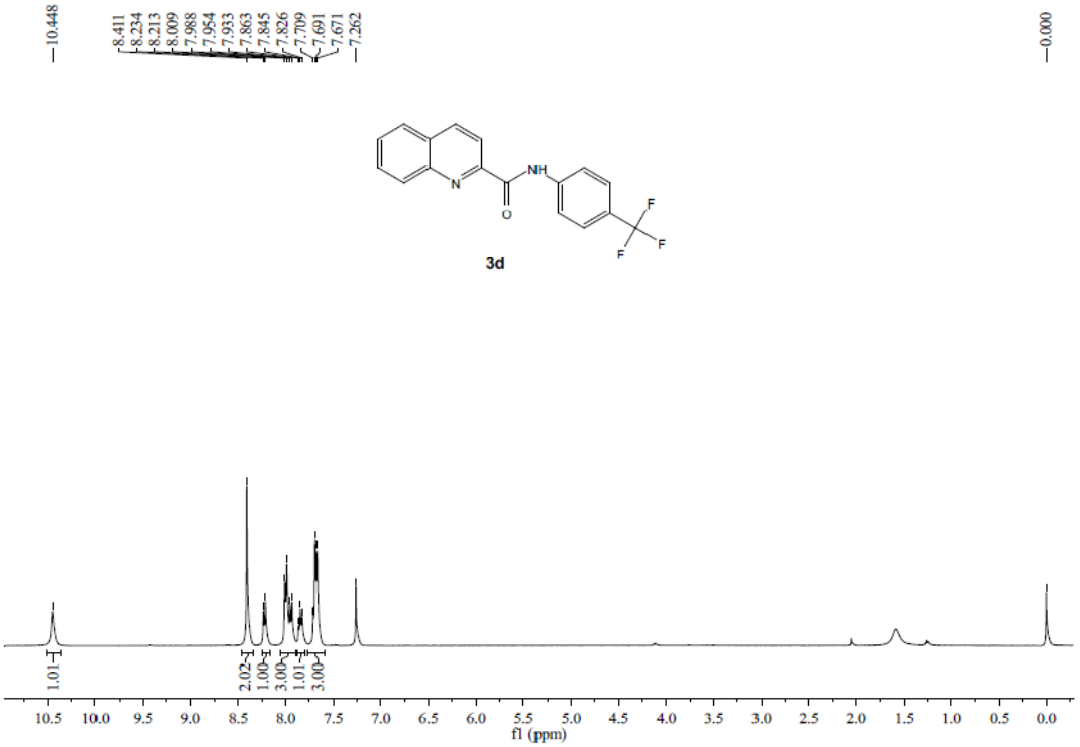
77.317
77.000
76.683
55.475
131.046
130.272
129.564
129.340
128.042
127.786
NH
O
N
O
CH3
3c
130.5
129.5
128.5
f1 (ppm)
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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7.691
7.671
7.262
0.000
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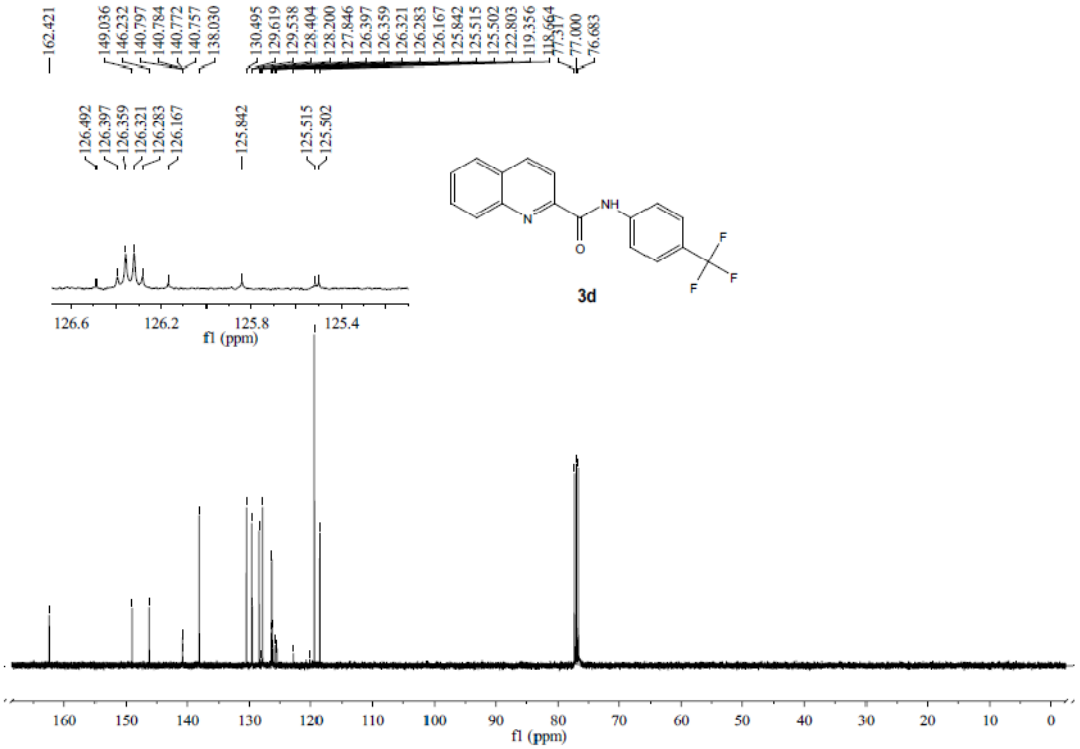
O
F
F
F
3d
1.01
2.02
1.00
3.00
1.01
3.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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140.772
140.757
138.030
130.495
129.619
129.538
128.404
128.200
127.846
126.397
126.359
126.321
126.283
126.167
125.842
125.515
125.502
122.803
119.356
118.564
77.317
77.000
76.683
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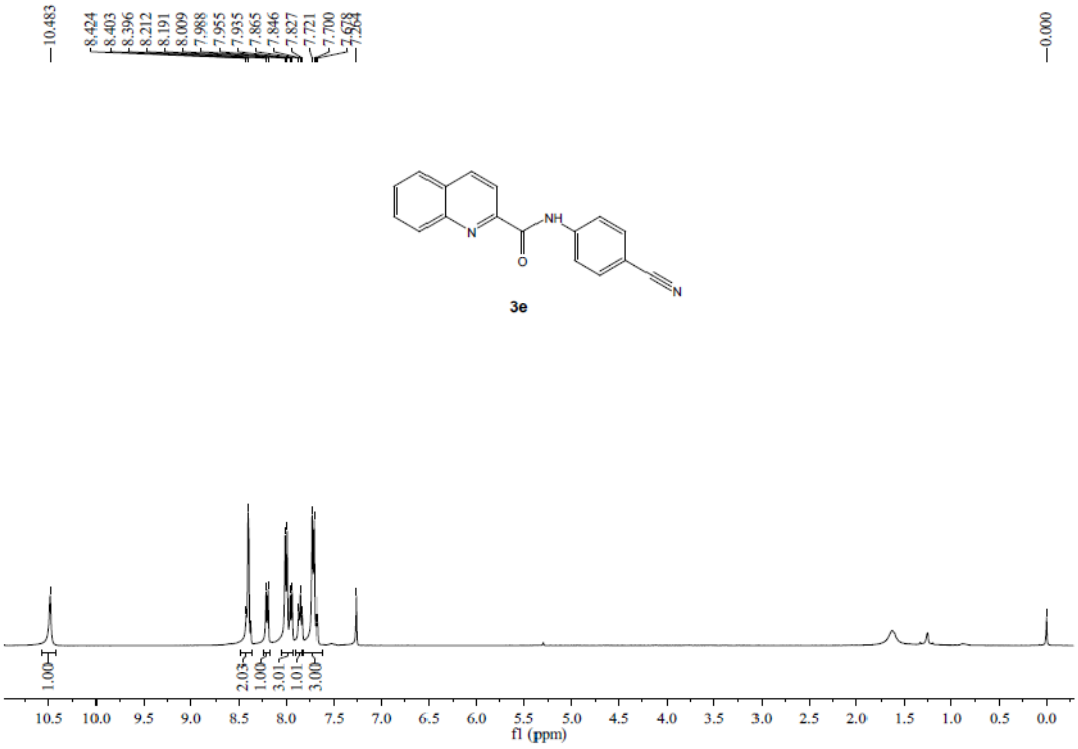
126.167
125.842
125.515
125.502
NH
O
F
F
F
3d
126.6 126.2 125.8 125.4
f1 (ppm)
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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8.191
8.009
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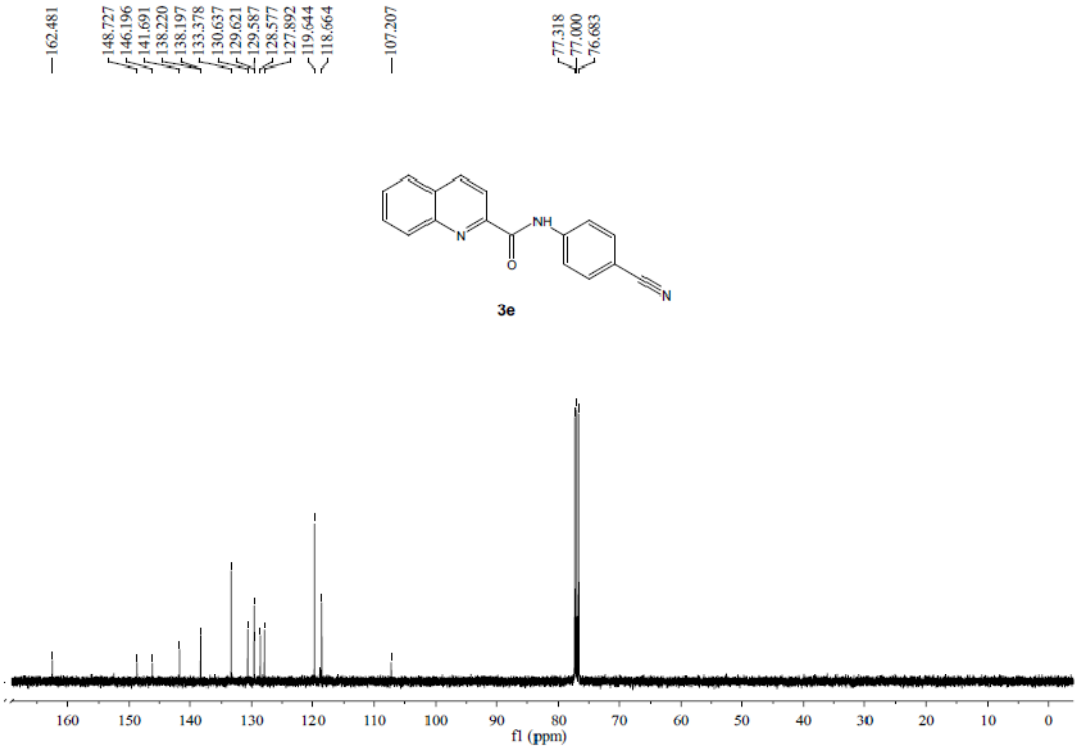
7.846
7.827
7.721
7.700
7.678
7.654
0.000
NH
N
O
N
3e
1.00
2.03
1.00
3.01
1.01
3.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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127.892
119.644
118.664
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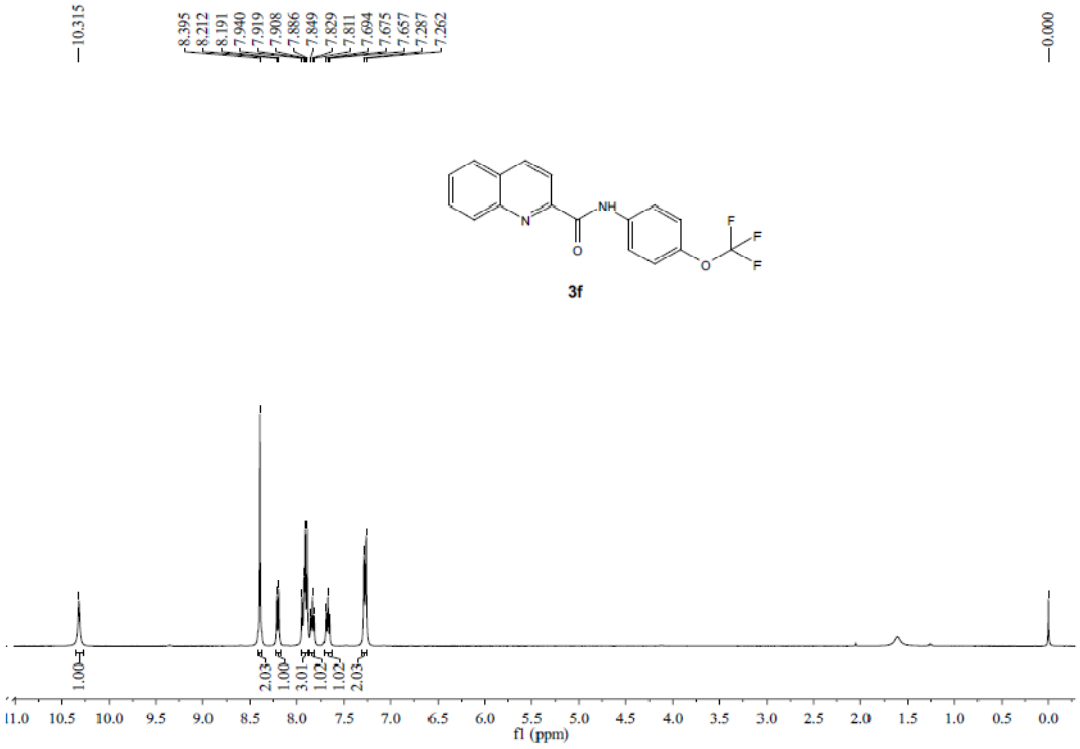
77.318
77.000
76.683
NH
N
O
N
3e
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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7.886
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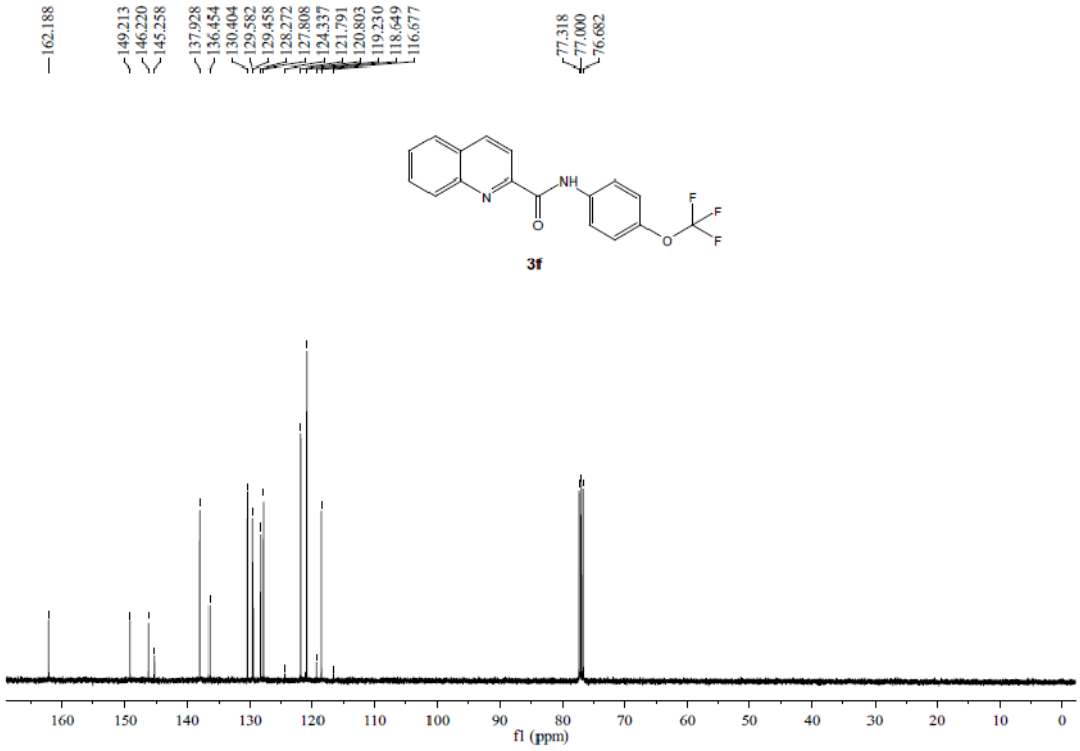
7.829
7.811
7.694
7.675
7.657
7.287
7.262
0.000
NH
N
O
F
F
F
O
3f
1.00
2.03
1.00
3.01
1.02
1.02
2.03
f1 (ppm)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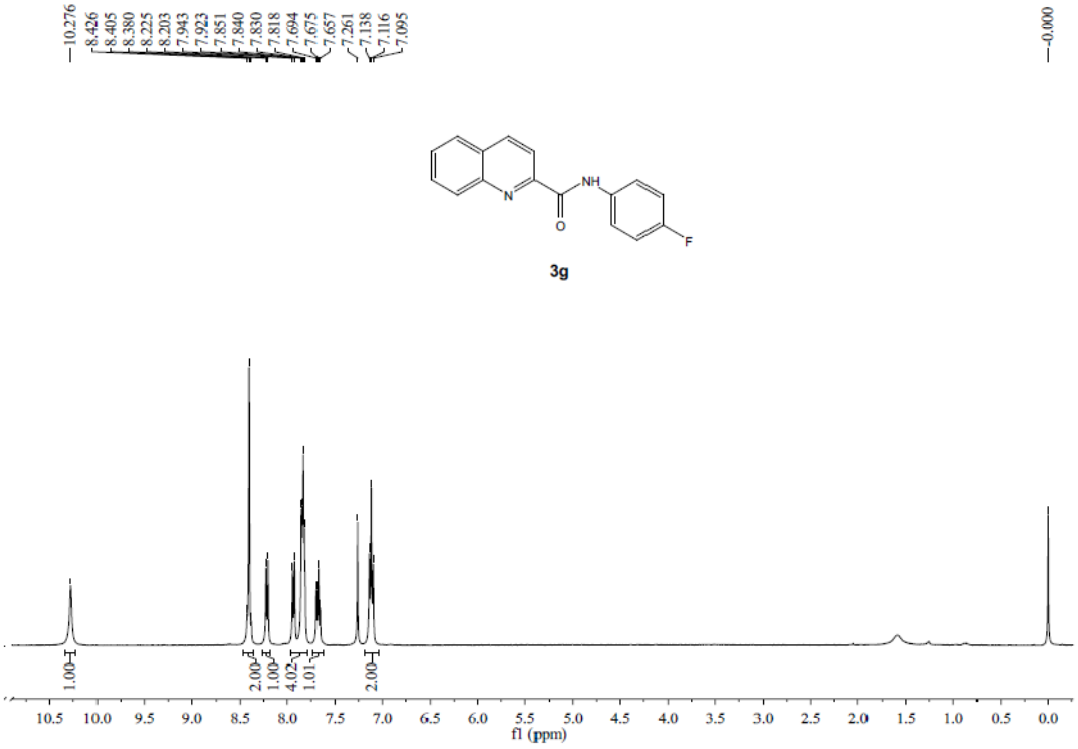
130.404
129.582
129.458
128.272
127.808
124.337
121.791
120.803
119.230
118.649
116.677
77.318
77.000
76.682
NH
N
O
F
F
F
O
3f
f1 (ppm)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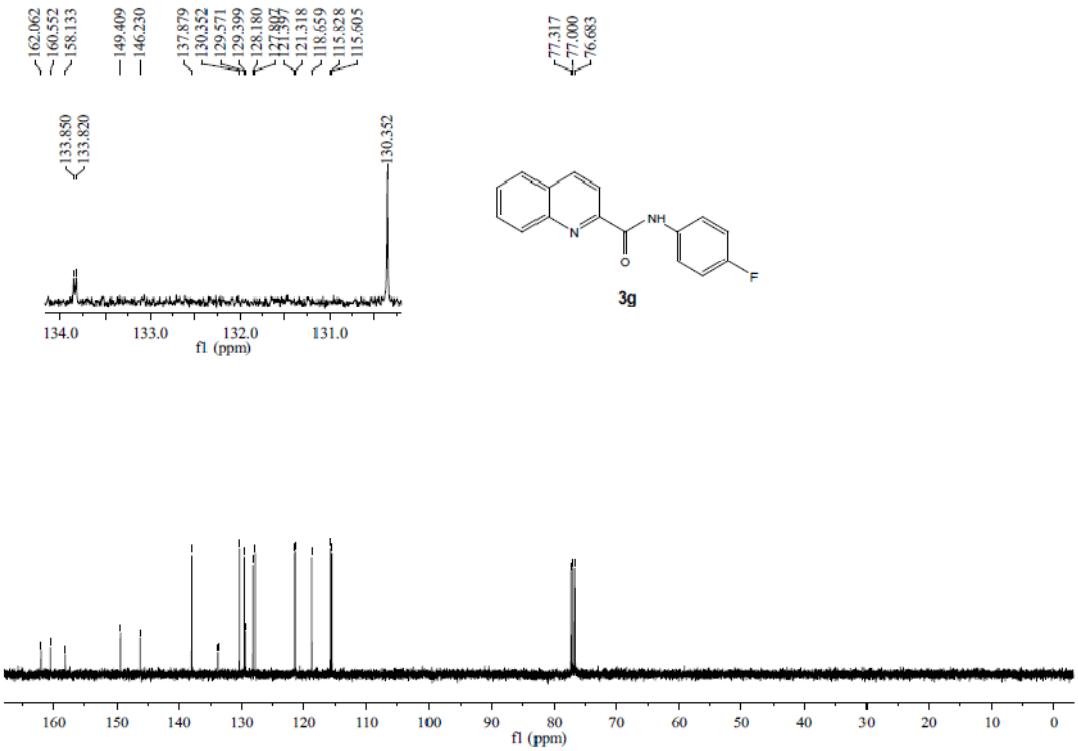
8.426
8.405
8.380
8.225
8.203
7.943
7.923
7.851
7.840
7.830
7.818
7.694
7.675
7.657
7.261
7.138
7.116
7.095
0.000
NH
N
O
F
3g
1.00
2.00
1.00
4.02
1.01
2.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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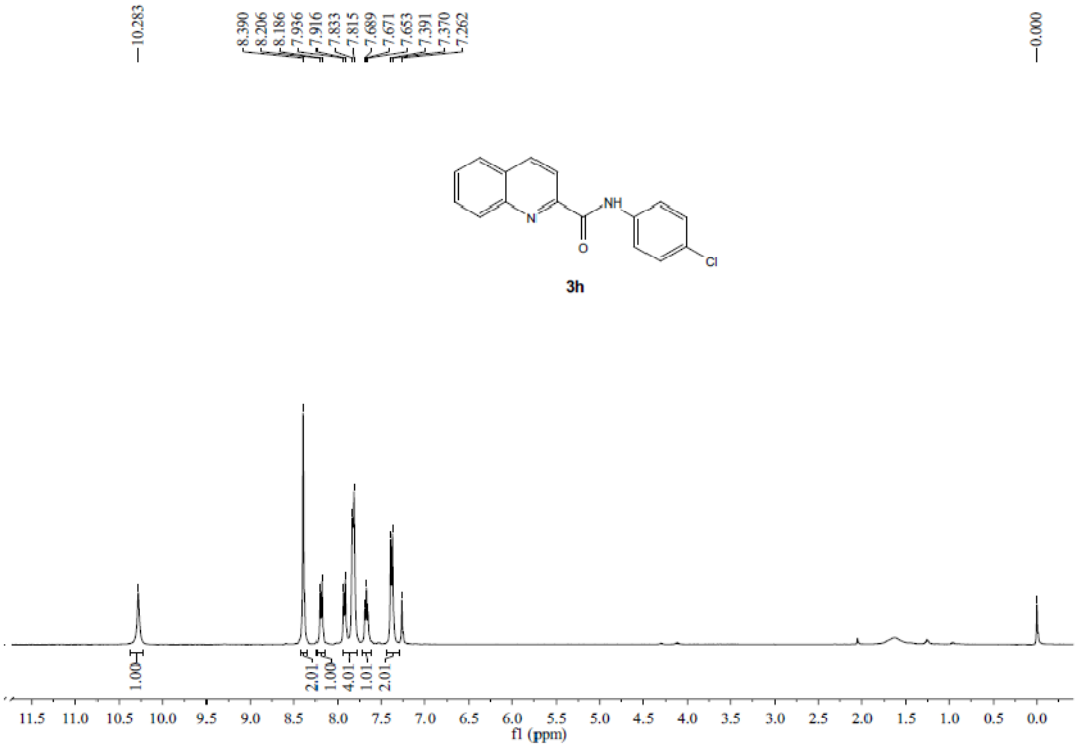
160.552
158.133
149.409
146.230
137.879
130.352
129.571
129.399
128.180
127.807
127.397
121.318
118.659
115.828
115.605
77.317
77.000
76.683
133.850
133.820
130.352
NH
N
O
F
3g
134.0 133.0 132.0 131.0
f1 (ppm)
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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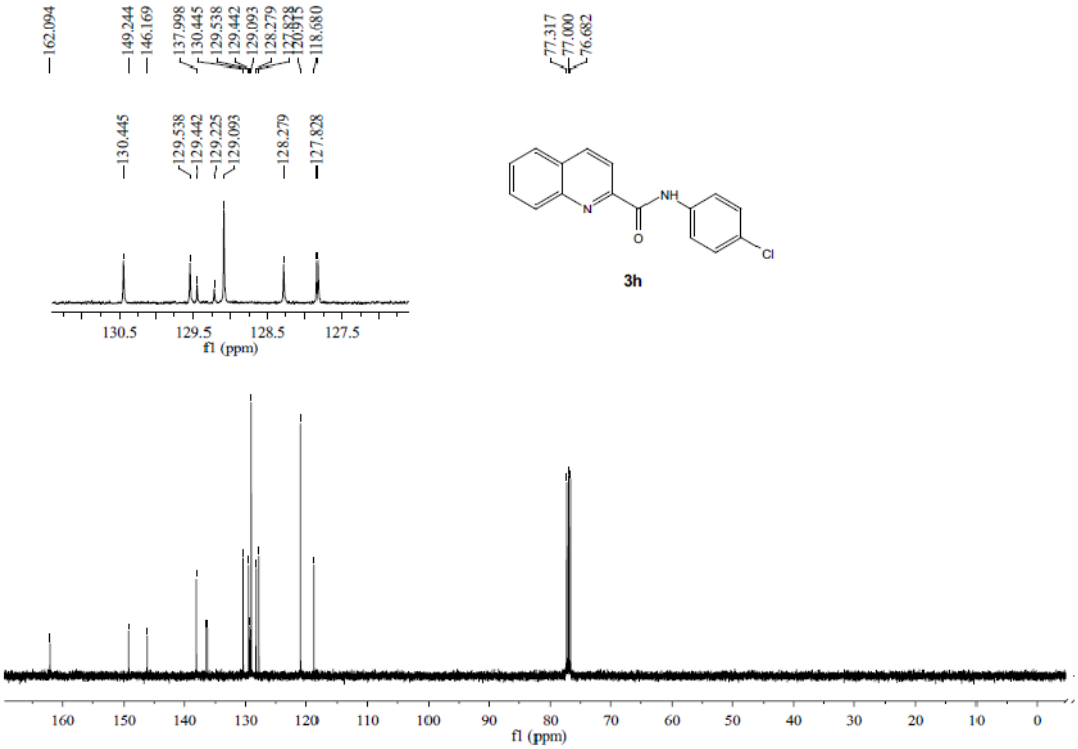
8.206
8.186
7.936
7.916
7.833
7.815
7.689
7.671
7.653
7.391
7.370
7.262
0.000
NH
N
O
Cl
3h
1.00
2.01
1.00
4.01
1.01
2.01
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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149.244
146.169
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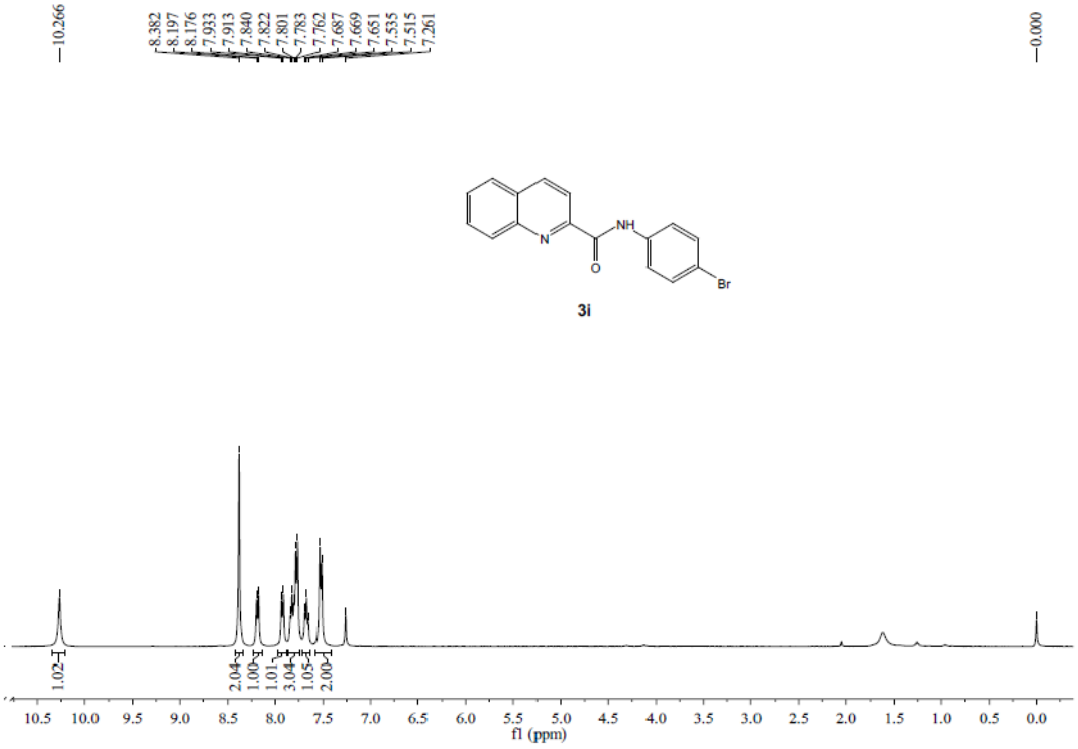
130.445
129.538
129.442
129.093
128.279
127.828
120.915
118.680
77.317
77.000
76.682
130.445
129.538
129.442
129.225
129.093
128.279
127.828
NH
N
O
Cl
3h
130.5 129.5 128.5 127.5
f1 (ppm)
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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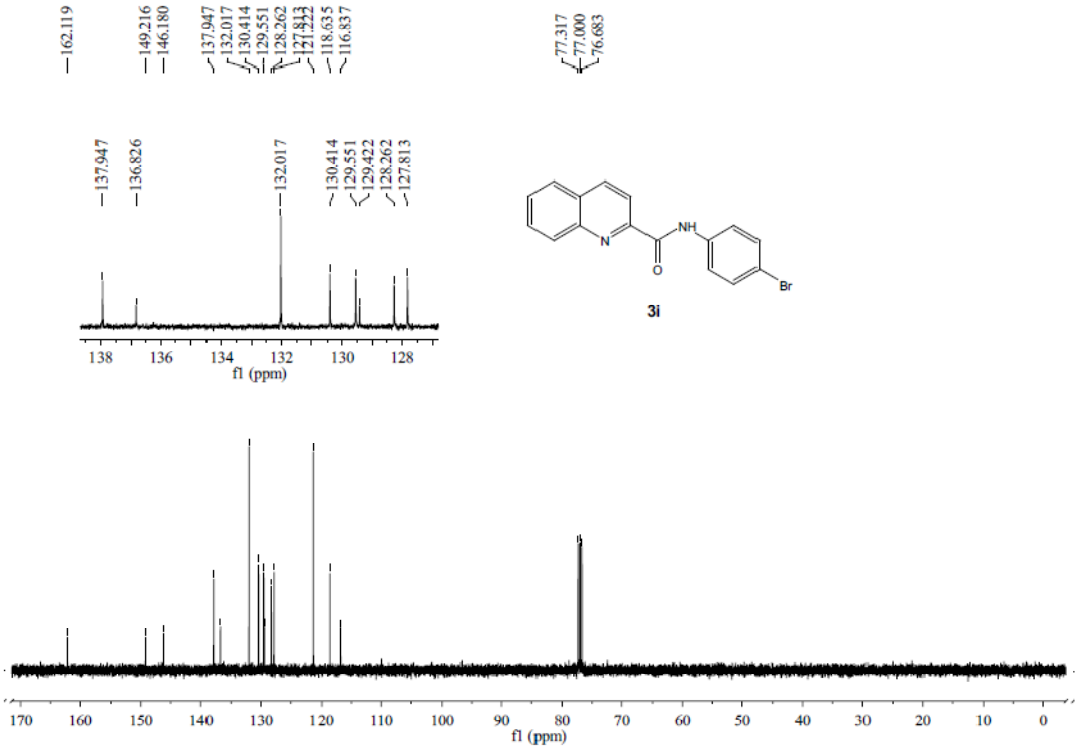
8.382
8.197
8.176
7.933
7.913
7.840
7.822
7.801
7.783
7.762
7.687
7.669
7.651
7.535
7.515
7.261
0.000
NH
N
O
Br
3i
1.02
2.04
1.00
1.01
3.04
1.05
2.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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149.216
146.180
137.947
132.017
130.414
129.551
128.262
127.843
121.222
118.635
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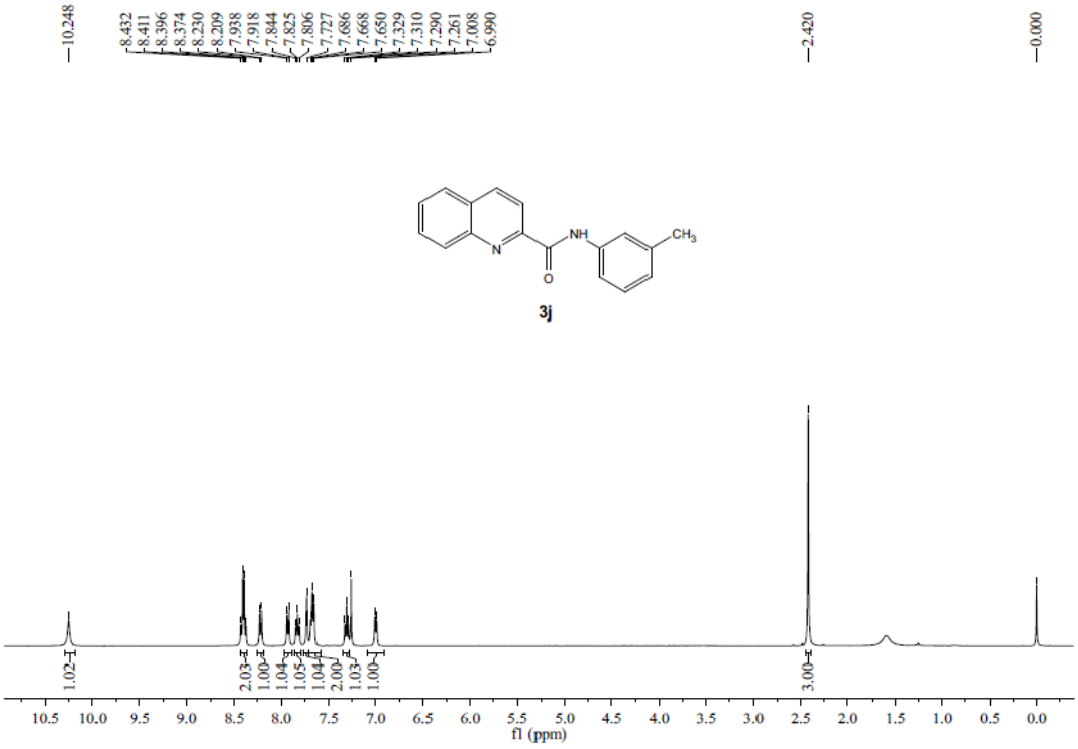
77.317
77.000
76.683
137.947
136.826
132.017
130.414
129.551
129.422
128.262
127.813
NH
N
O
Br
3i
138 136 134 132 130 128
f1 (ppm)
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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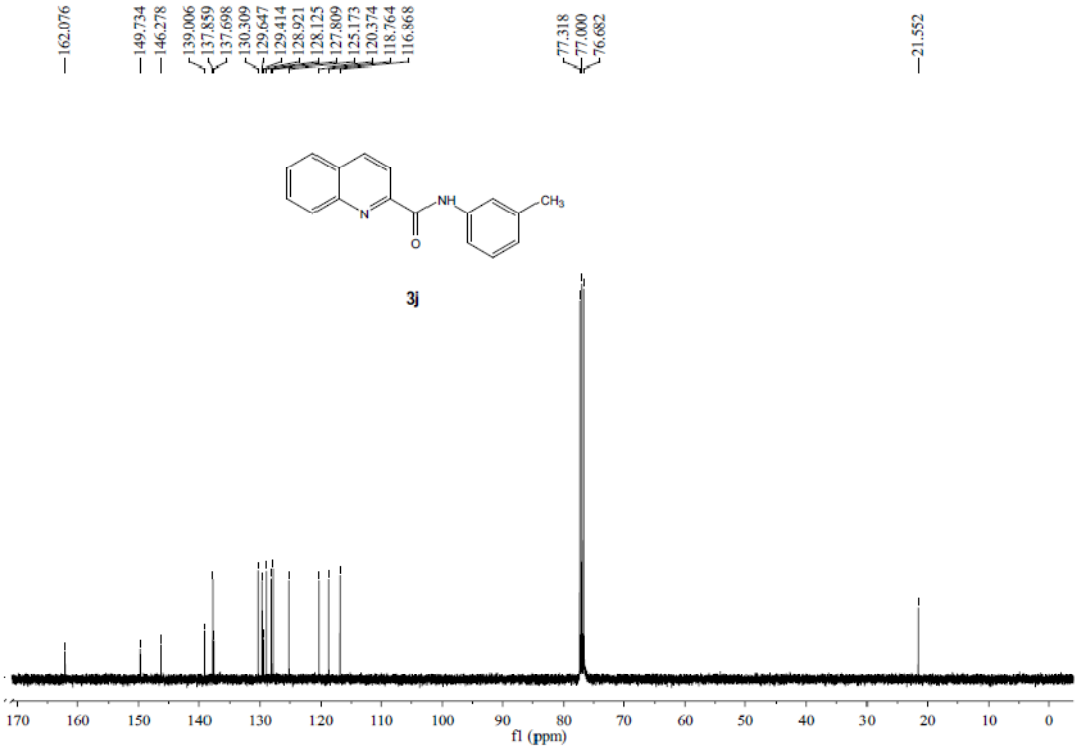
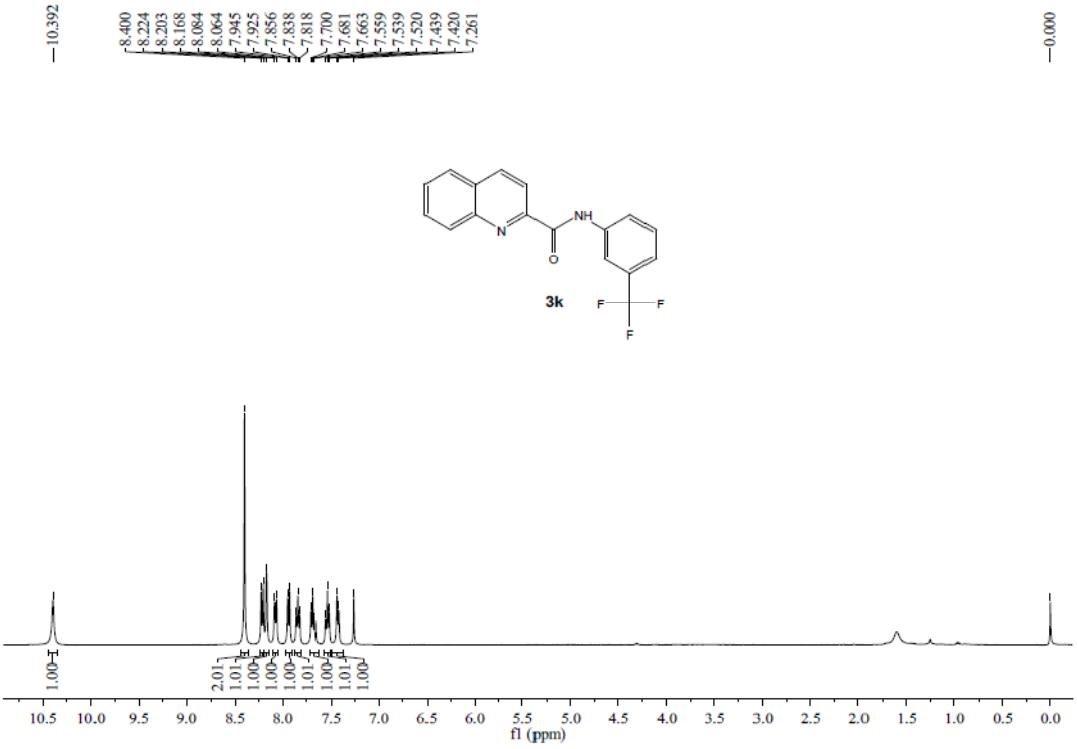
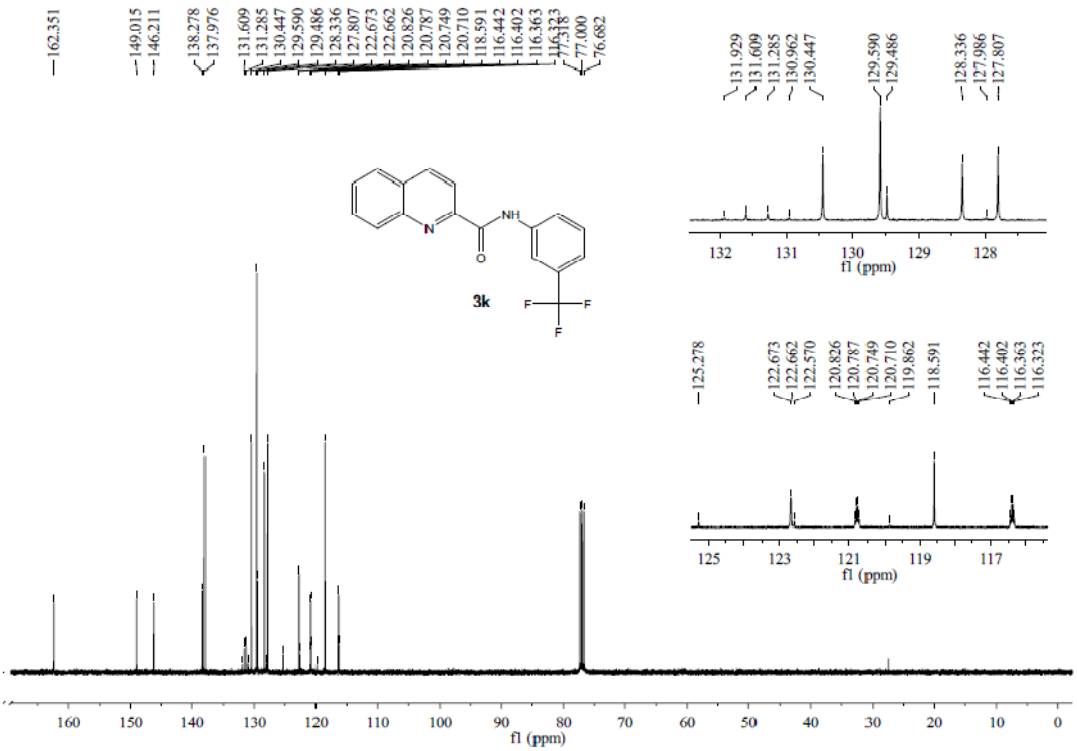
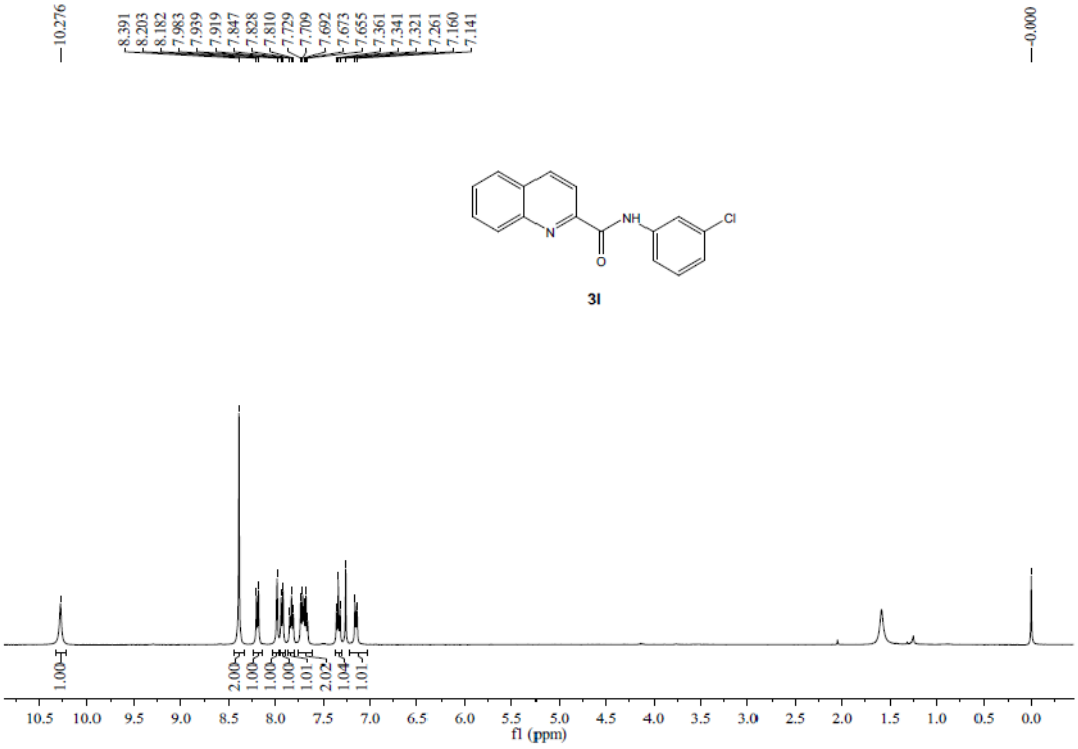
8.432
8.411
8.396
8.374
8.230
8.209
7.938
7.918
7.844
7.825
7.806
7.727
7.686
7.668
7.650
7.329
7.310
7.290
7.261
7.008
6.990
2.420
0.000
NH
CH3
O
N
3j
1.02
2.03
1.00
1.04
1.05
1.04
2.00
1.03
1.00
3.00
fl (ppm)


162.076
149.734
146.278
139.006
137.859
137.698
130.309
129.647
129.414
128.921
128.125
127.809
125.173
120.374
118.764
116.868
77.318
77.000
76.682
21.552
NH
CH3
O
N
3j
fl (ppm)


10.392
8.400
8.224
8.203
8.168
8.084
8.064
7.945
7.925
7.856
7.838
7.818
7.700
7.681
7.663
7.559
7.539
7.520
7.439
7.420
7.261
0.000
3k
1.00
2.01
1.01
1.00
1.00
1.00
1.01
1.00
1.01
1.00
fl (ppm)


162.351
149.015
146.211
138.278
137.976
131.609
131.285
130.447
129.590
129.486
128.336
127.807
122.673
122.662
120.826
120.787
120.749
120.710
118.591
116.442
116.402
116.363
116.323
77.318
77.000
76.682
3k
131.929
131.609
131.285
130.962
130.447
129.590
129.486
128.336
127.986
127.807
fl (ppm)
125.278
122.673
122.662
122.570
120.826
120.787
120.749
120.710
119.862
118.591
116.442
116.402
116.363
116.323
fl (ppm)
fl (ppm)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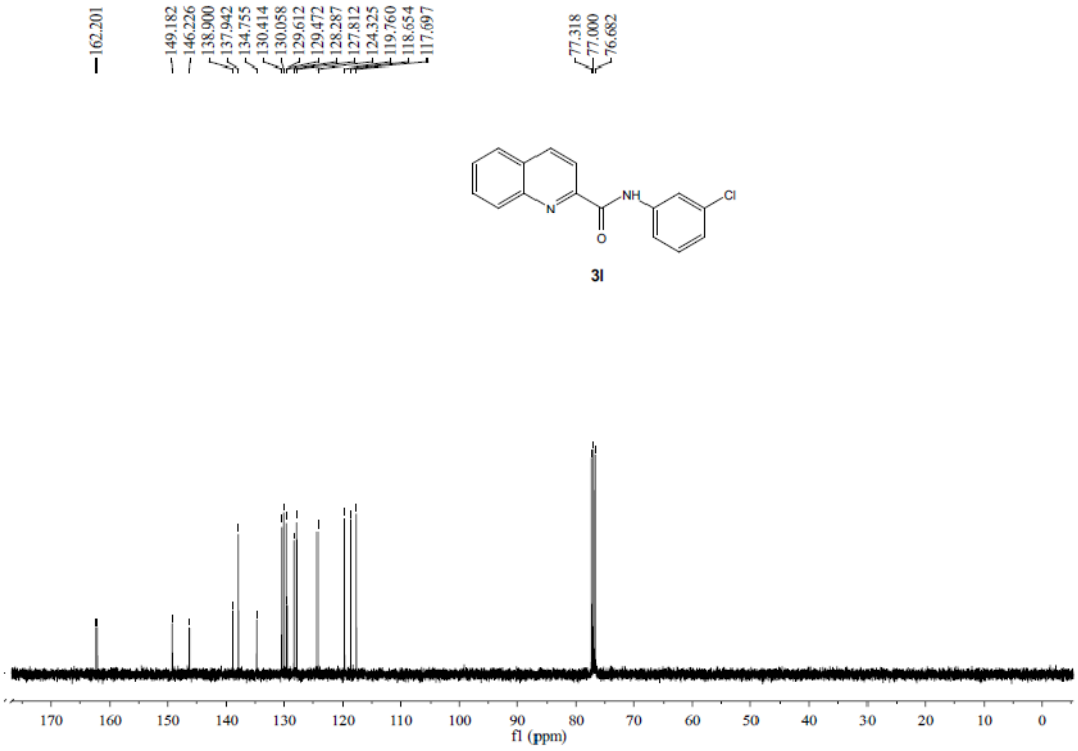
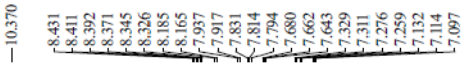
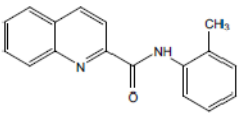
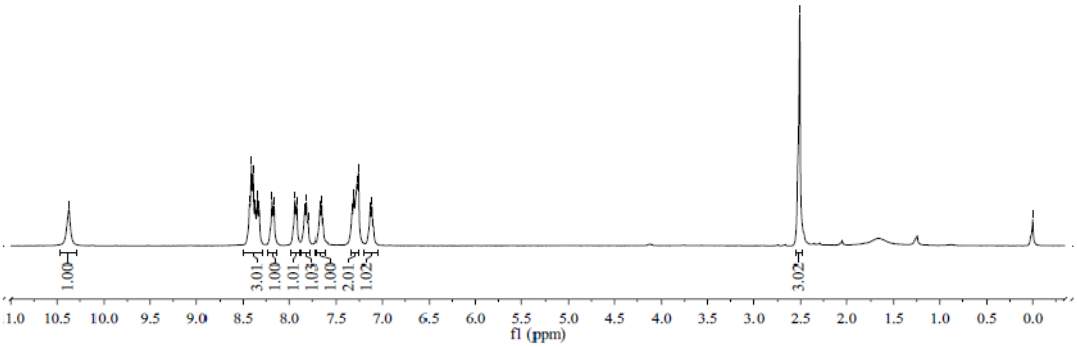
8.391
8.203
8.182
7.983
7.939
7.919
7.847
7.828
7.810
7.729
7.709
7.692
7.673
7.655
7.361
7.341
7.321
7.261
7.160
7.141
0.000
NH
N
O
Cl
3l
1.00
2.00
1.00
1.00
1.00
1.01
2.02
1.04
1.01
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

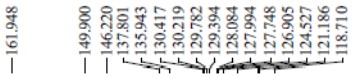

162.201
149.182
146.226
138.900
137.942
134.755
130.414
130.058
129.612
129.472
128.287
127.812
124.325
119.760
118.654
117.697
77.318
77.000
76.682
NH
N
O
Cl
3l
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


10.370
8.431
8.411
8.392
8.371
8.345
8.326
8.185
8.165
7.937
7.917
7.831
7.814
7.794
7.680
7.662
7.643
7.329
7.311
7.276
7.259
7.132
7.114
7.097
2.511
0.000


CH3
NH
N
O

3m


1.00
3.01
1.00
1.01
1.03
1.00
2.01
1.02
3.02
1.0 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)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146.220
137.801
135.943
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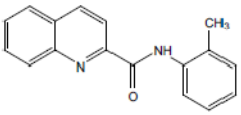
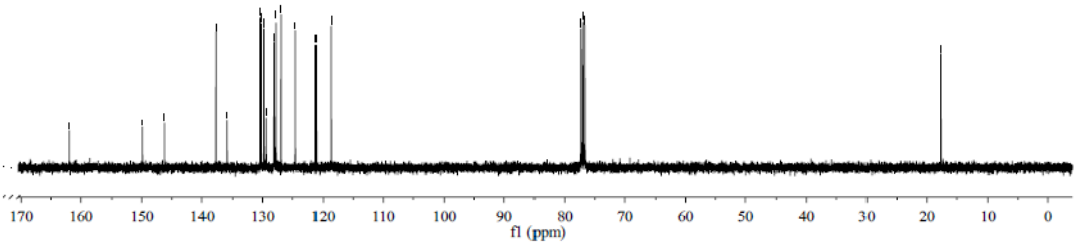
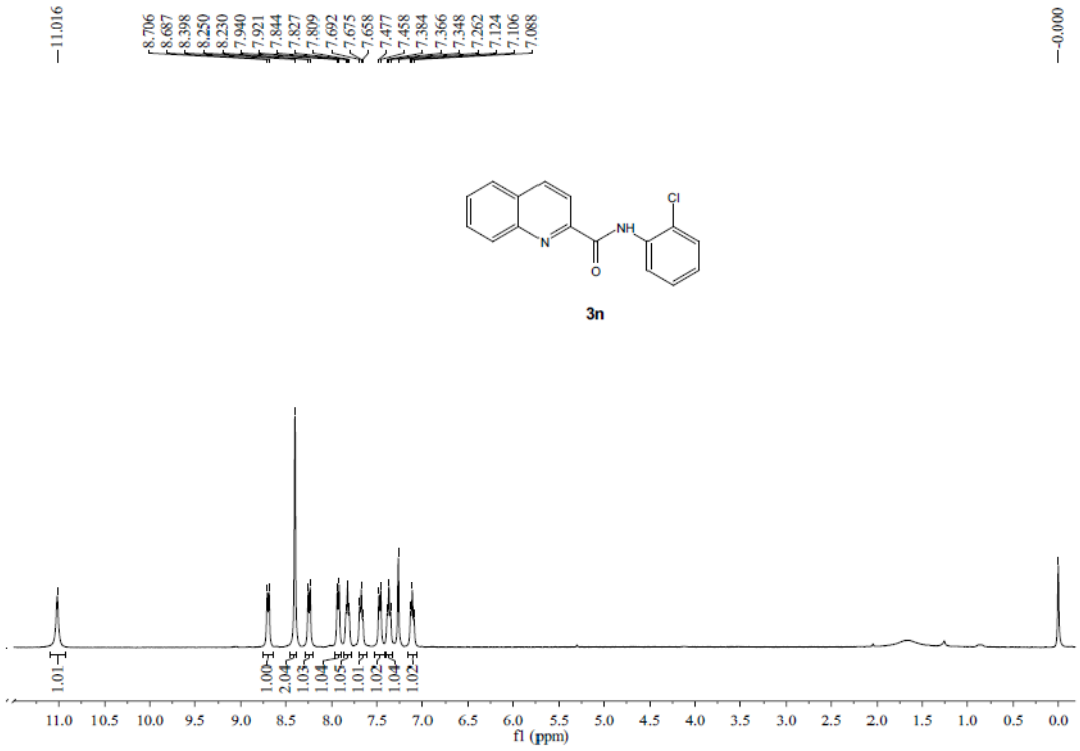
130.219
129.782
129.394
128.084
127.994
127.748
126.905
124.527
121.186
118.710
77.318
77.000
76.682
17.681


CH3
NH
N
O

3m


170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


11.016
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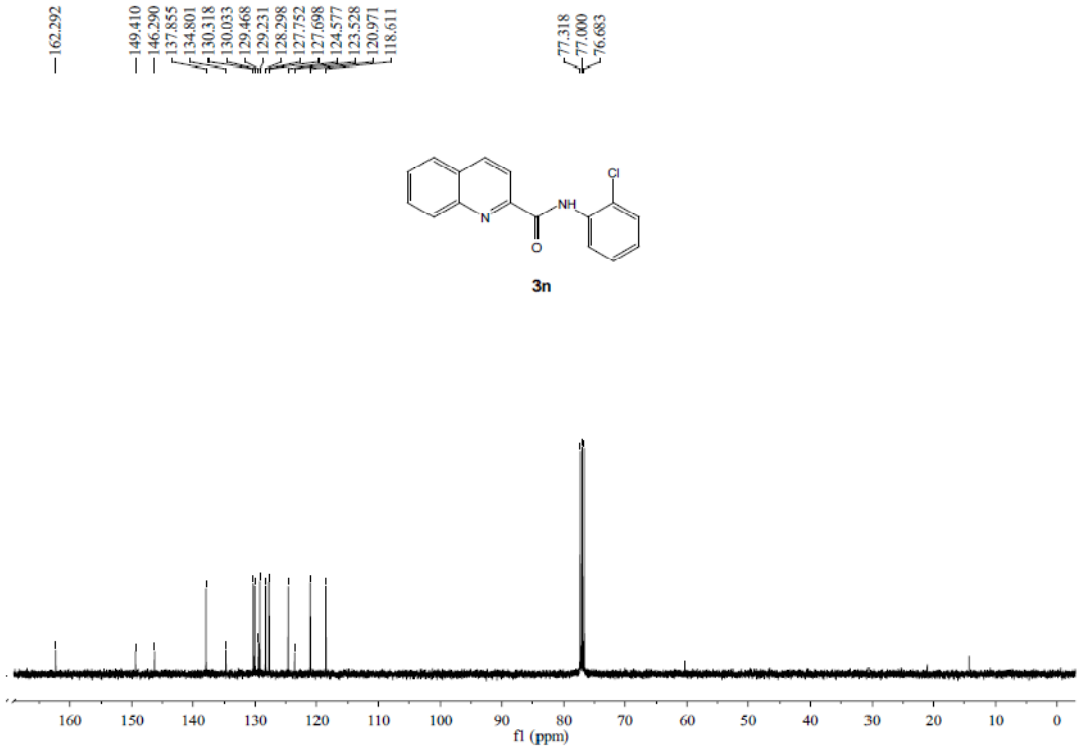
8.687
8.398
8.250
8.230
7.940
7.921
7.844
7.827
7.809
7.692
7.675
7.658
7.477
7.458
7.384
7.366
7.348
7.262
7.124
7.106
7.088
0.000
Cl
NH
N
O
3n
1.01
1.00
2.04
1.03
1.04
1.05
1.01
1.02
1.04
1.02
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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146.290
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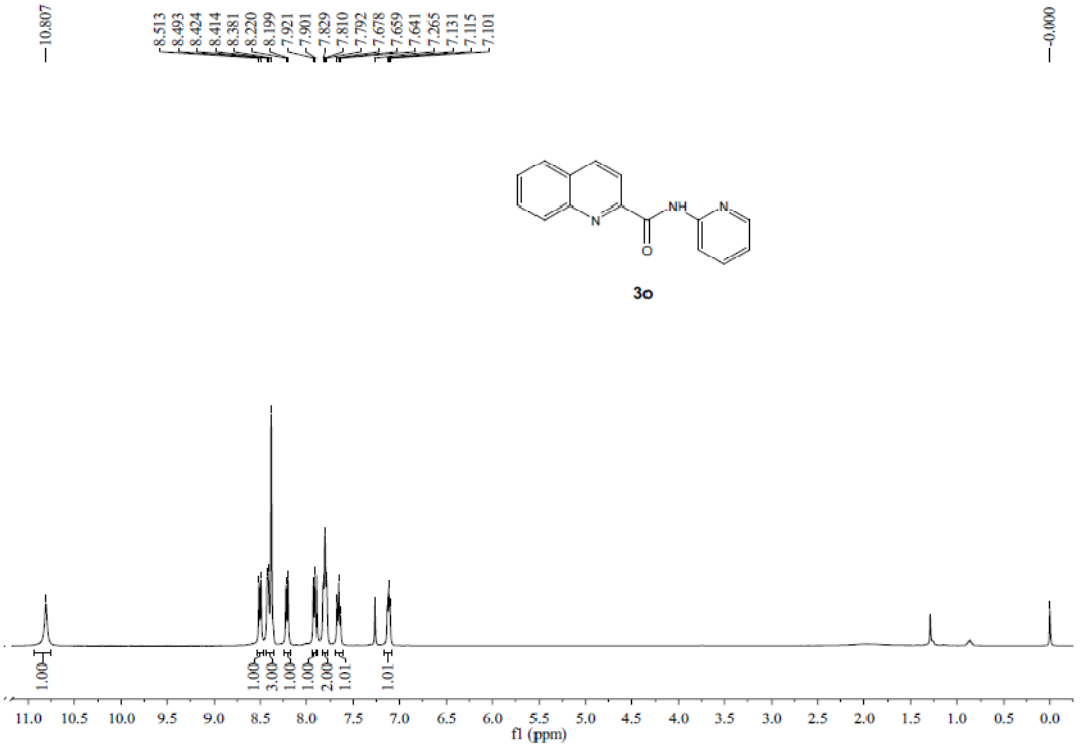
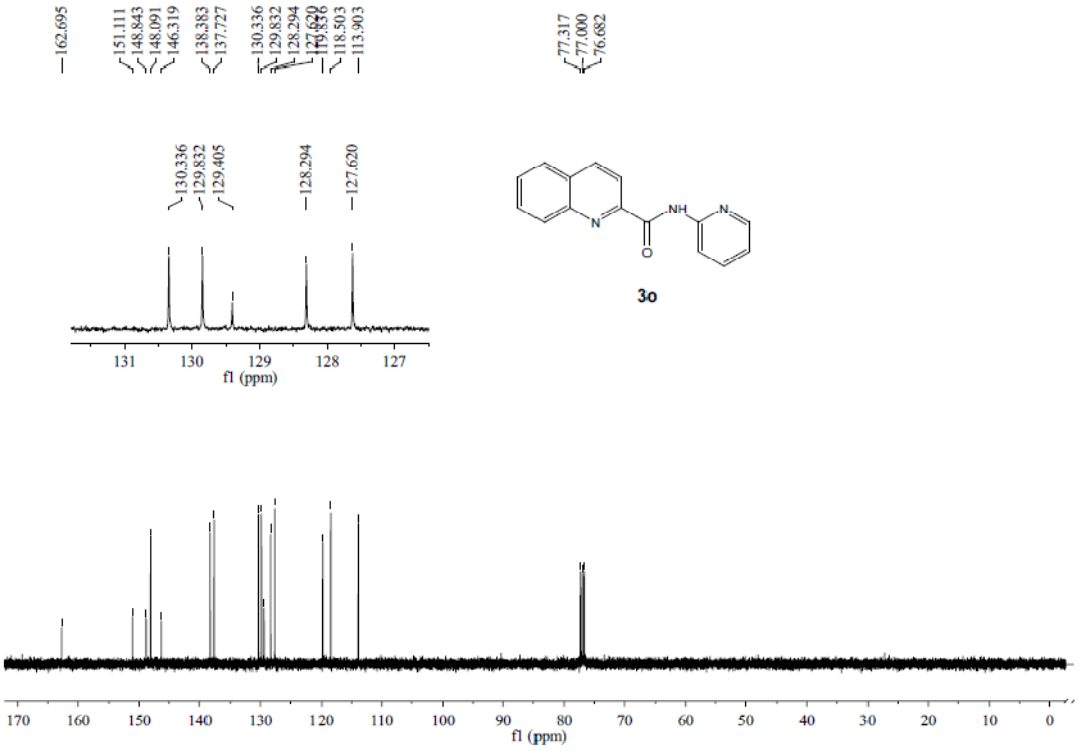
134.801
130.318
130.033
129.468
129.231
128.298
127.752
127.698
124.577
123.528
120.971
118.611
77.318
77.000
76.683
Cl
NH
N
O
3n
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


10.807
8.513
8.493
8.424
8.414
8.381
8.220
8.199
7.921
7.901
7.829
7.810
7.792
7.678
7.659
7.641
7.265
7.131
7.115
7.101
0.000
NH
N
O
3o
1.00
3.00
1.00
1.00
2.00
1.01
1.01
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)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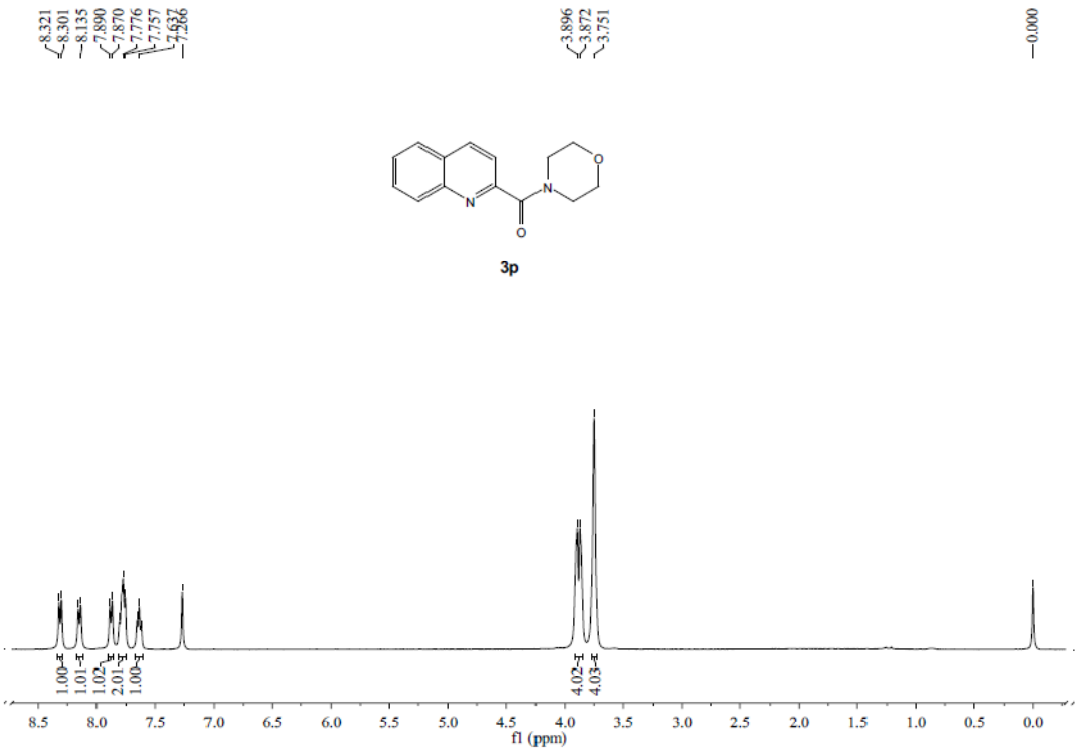
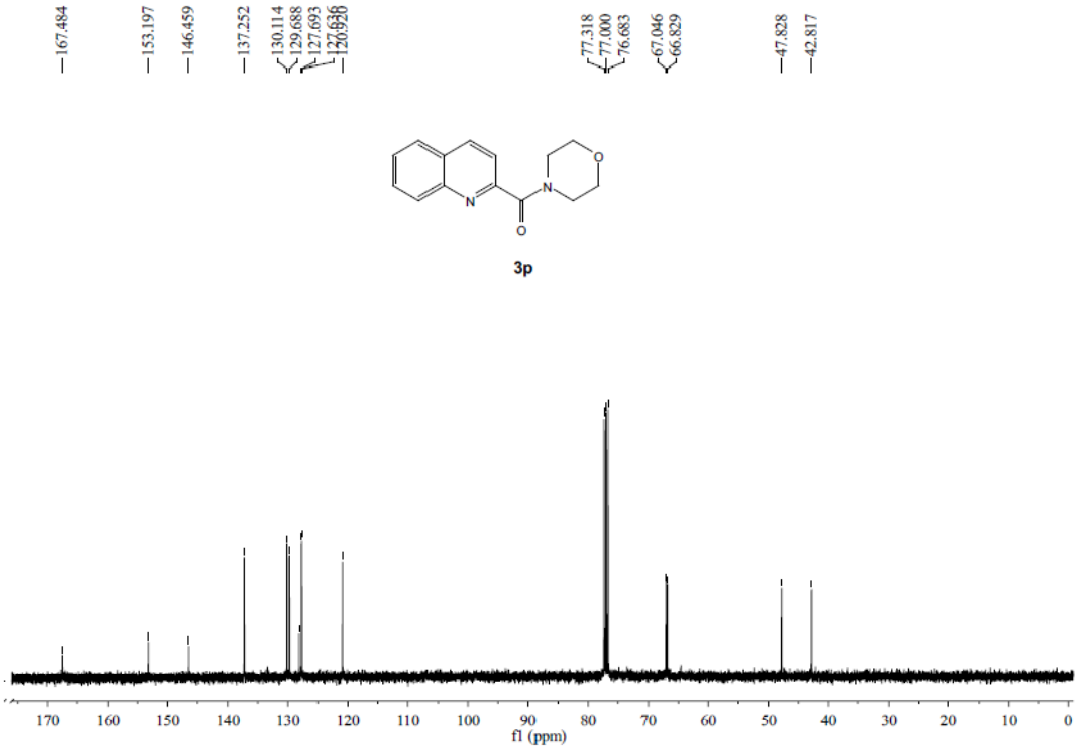
148.091
146.319
138.383
137.727
130.336
129.832
128.294
127.620
119.536
118.503
113.903
77.317
77.000
76.682
130.336
129.832
129.405
128.294
127.620
131 130 129 128 127
f1 (ppm)
NH
N
O
3o
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.321
8.301
8.135
7.890
7.870
7.776
7.757
7.637
7.266
3.896
3.872
3.751
0.000
3p
1.00
1.01
1.02
2.01
1.00
4.02
4.03
f1 (ppm)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153.197
146.459
137.252
130.114
129.688
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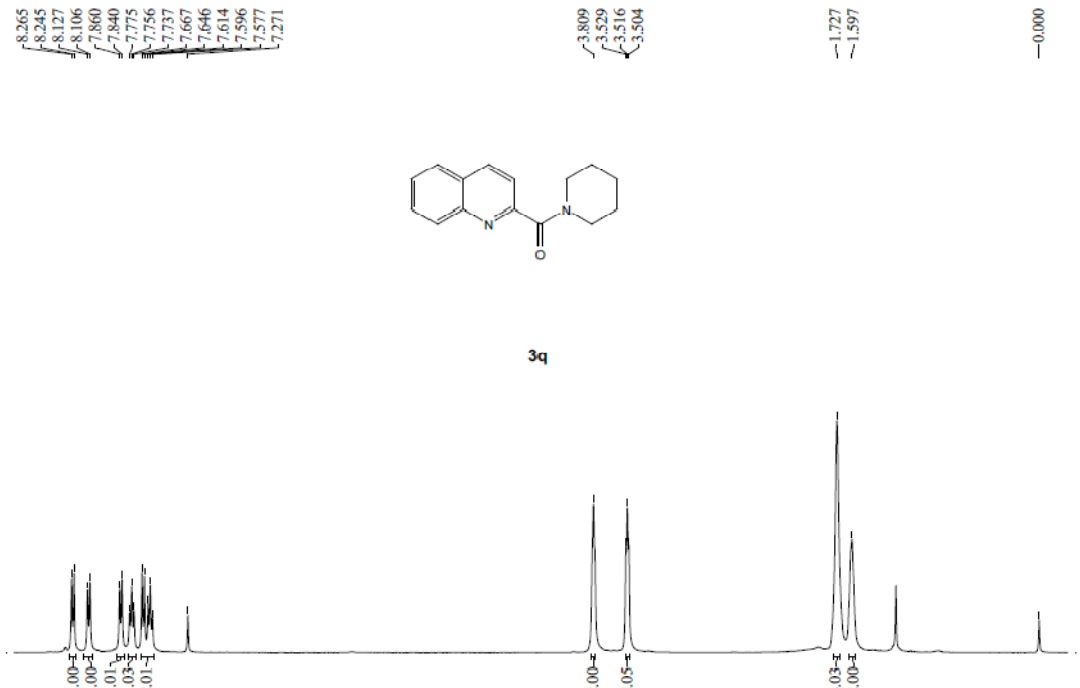
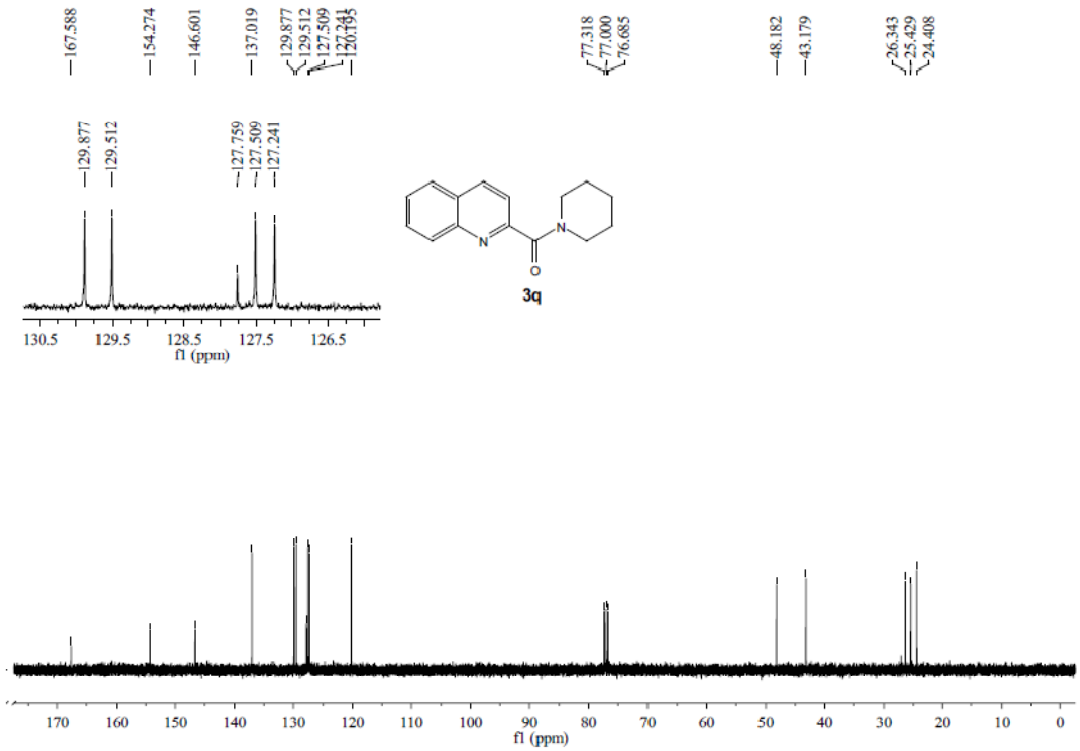
77.318
77.000
76.683
67.046
66.829
47.828
42.817
3p
f1 (ppm)


8.265
8.245
8.127
8.106
7.860
7.840
7.775
7.756
7.737
7.667
7.646
7.614
7.596
7.577
7.271
3.809
3.529
3.516
3.504
1.727
1.597
0.000
3q
1.00
1.00
1.01
1.03
2.01
2.00
2.05
4.03
2.00
fl (ppm)


167.588
154.274
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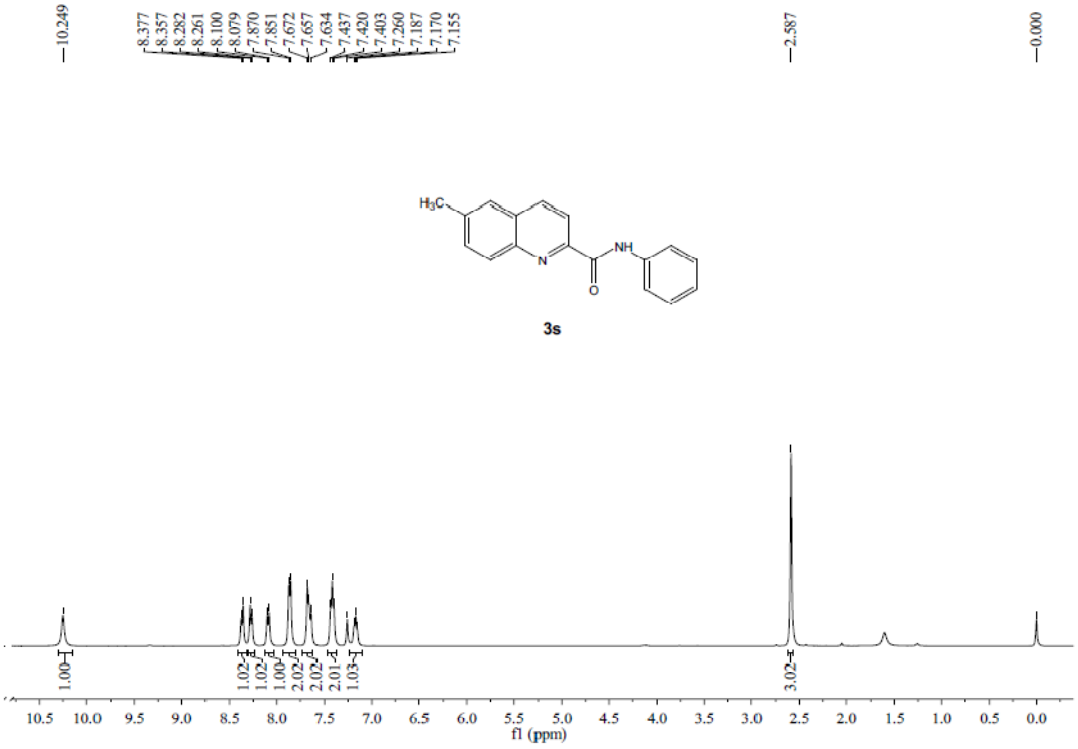
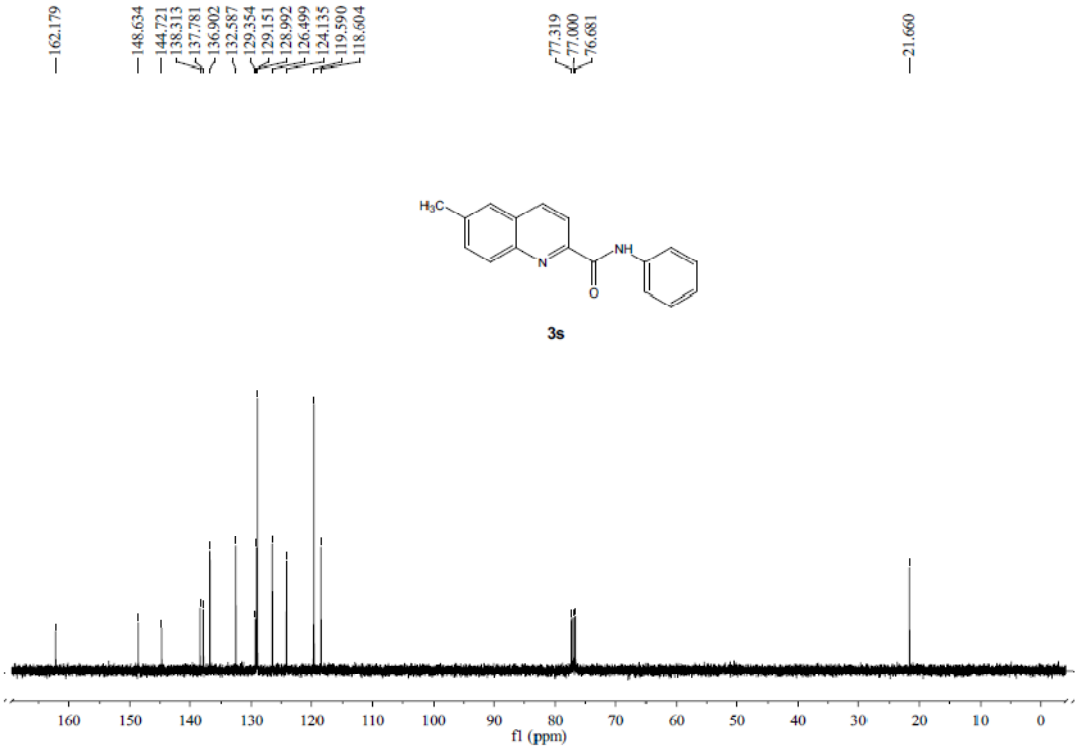
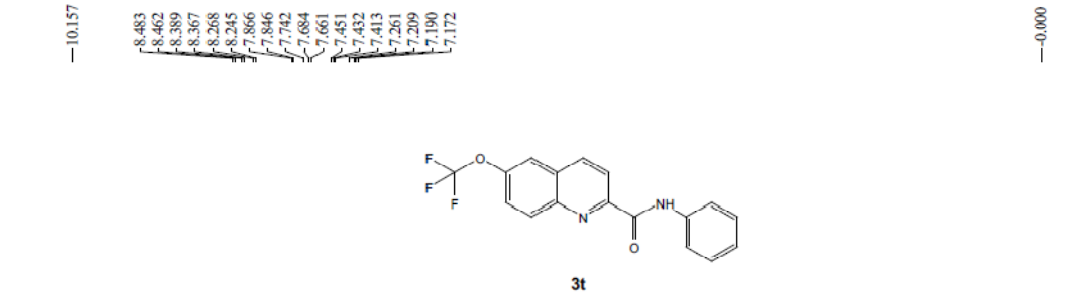
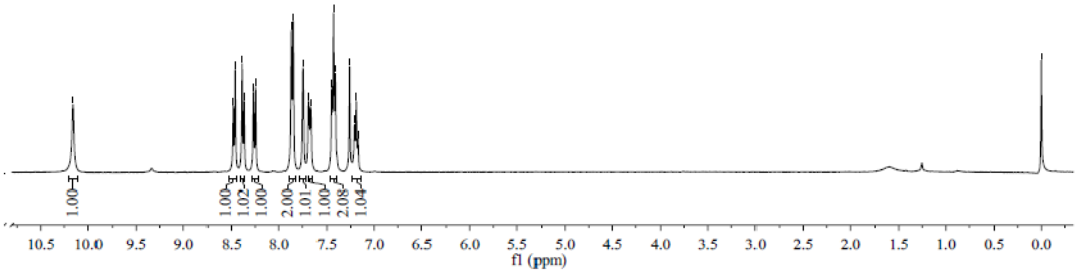
137.019
129.877
129.512
127.509
127.241
120.195
77.318
77.000
76.685
48.182
43.179
26.343
25.429
24.408
129.877
129.512
127.759
127.509
127.241
3q
fl (ppm)
fl (ppm)

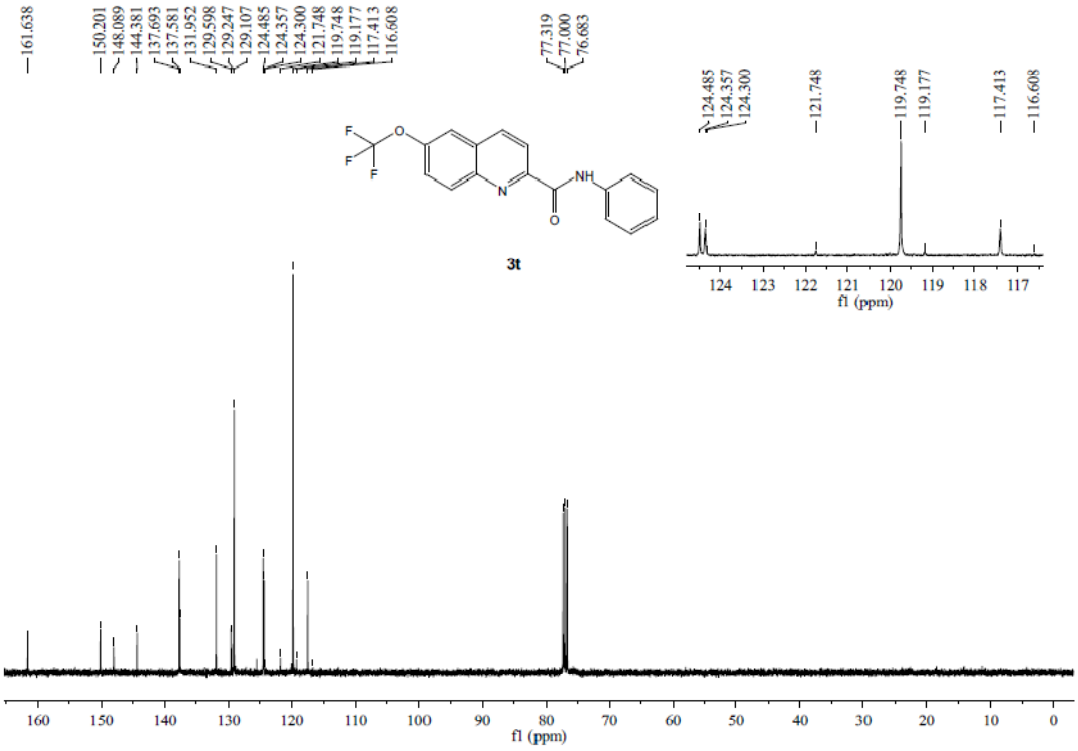

10.249
8.377
8.357
8.282
8.261
8.100
8.079
7.870
7.851
7.672
7.657
7.634
7.437
7.420
7.403
7.260
7.187
7.170
7.155
2.587
0.000
H3C
N
NH
O
3s
1.00
1.02
1.02
1.00
2.02
2.02
2.01
1.03
3.02
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


162.179
148.634
144.721
138.313
137.781
136.902
132.587
129.354
129.151
128.992
126.499
124.135
119.590
118.604
77.319
77.000
76.681
21.660
H3C
N
NH
O
3s
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

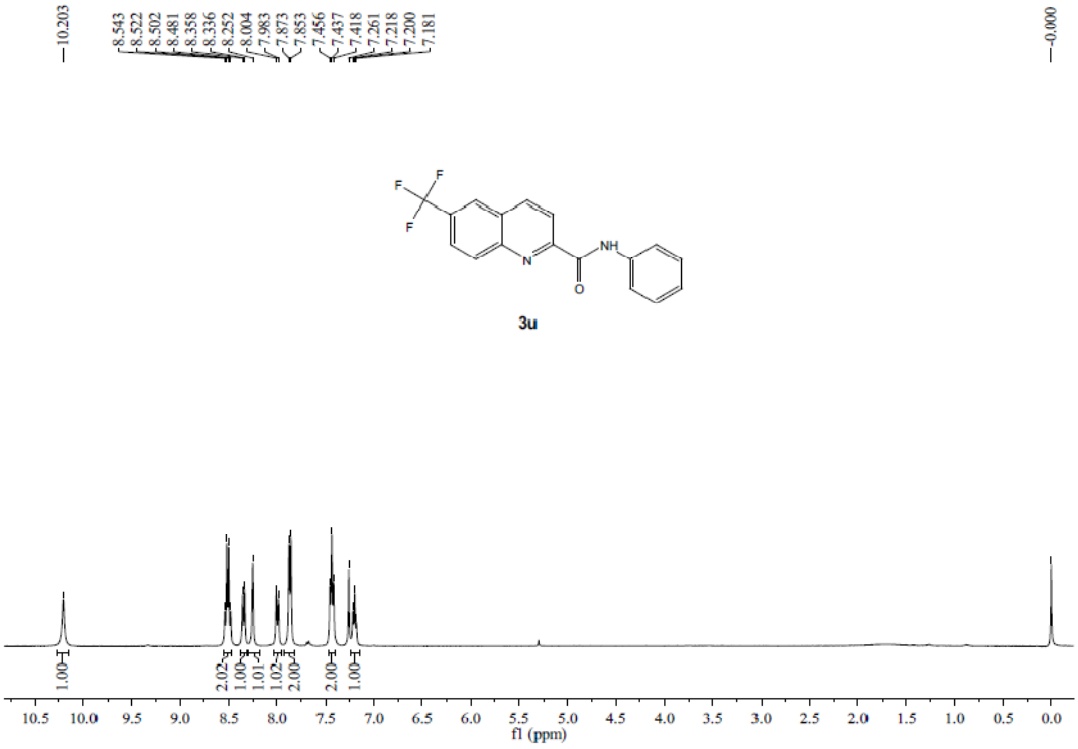

10.157
8.483
8.462
8.389
8.367
8.268
8.245
7.866
7.846
7.742
7.684
7.661
7.451
7.432
7.413
7.261
7.209
7.190
7.172
0.000
F
F
F
O
N
NH
O

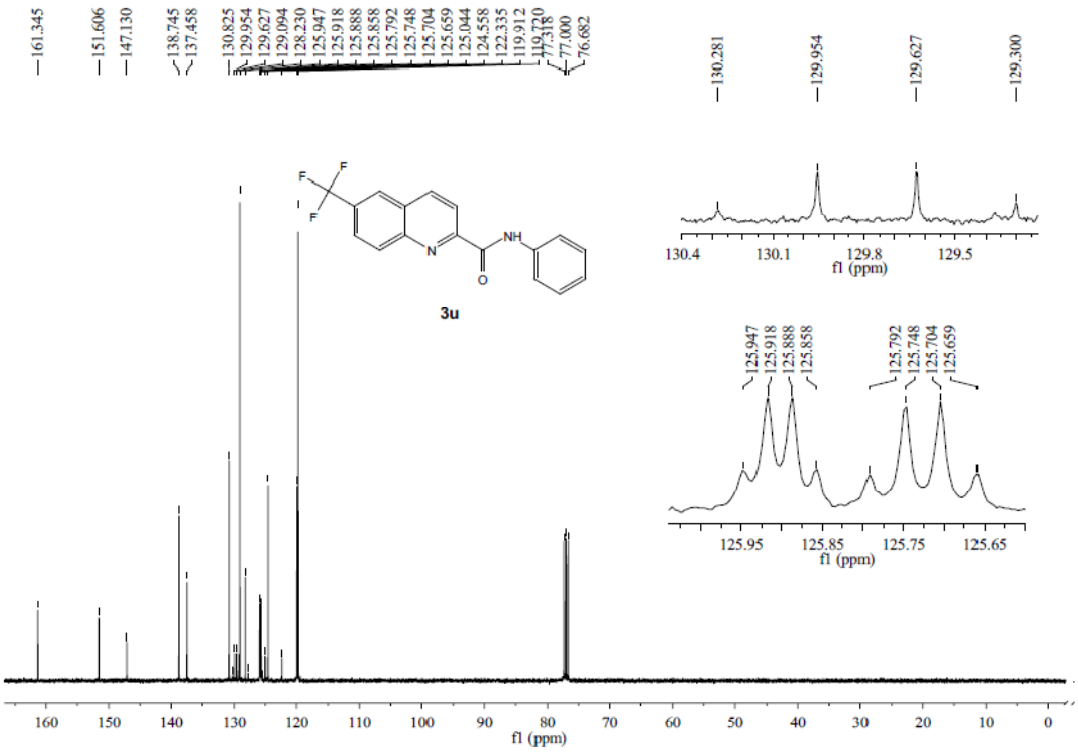
3t

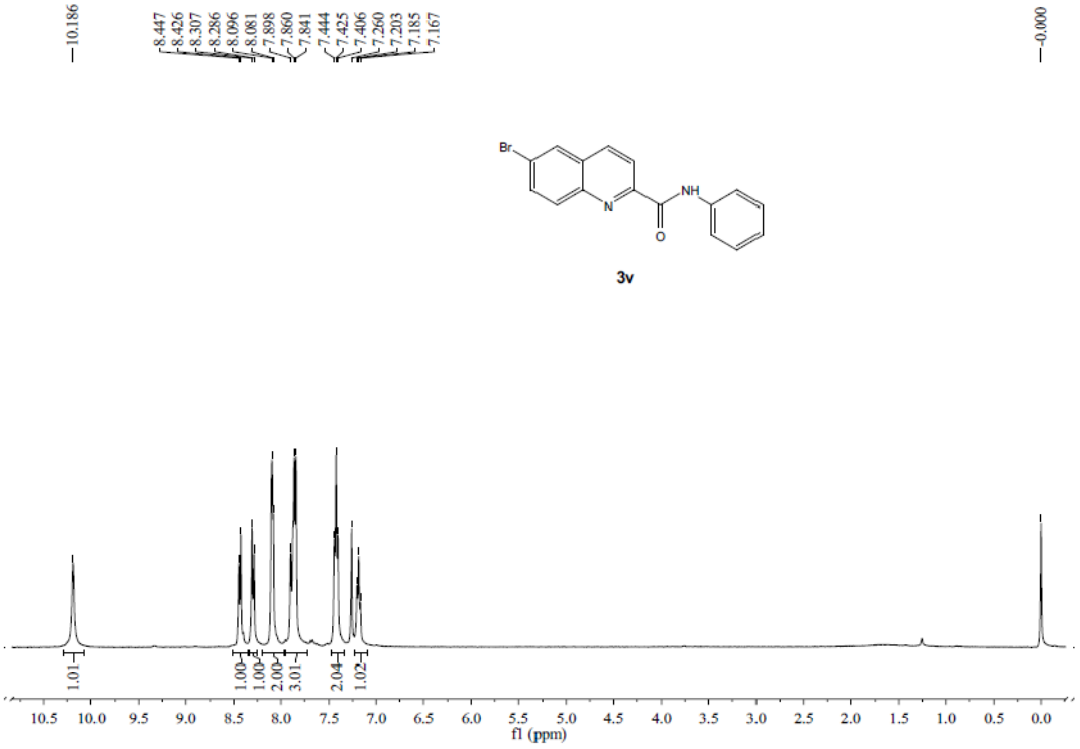

1.00
1.00
1.02
1.00
2.00
1.01
1.00
2.08
1.04
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

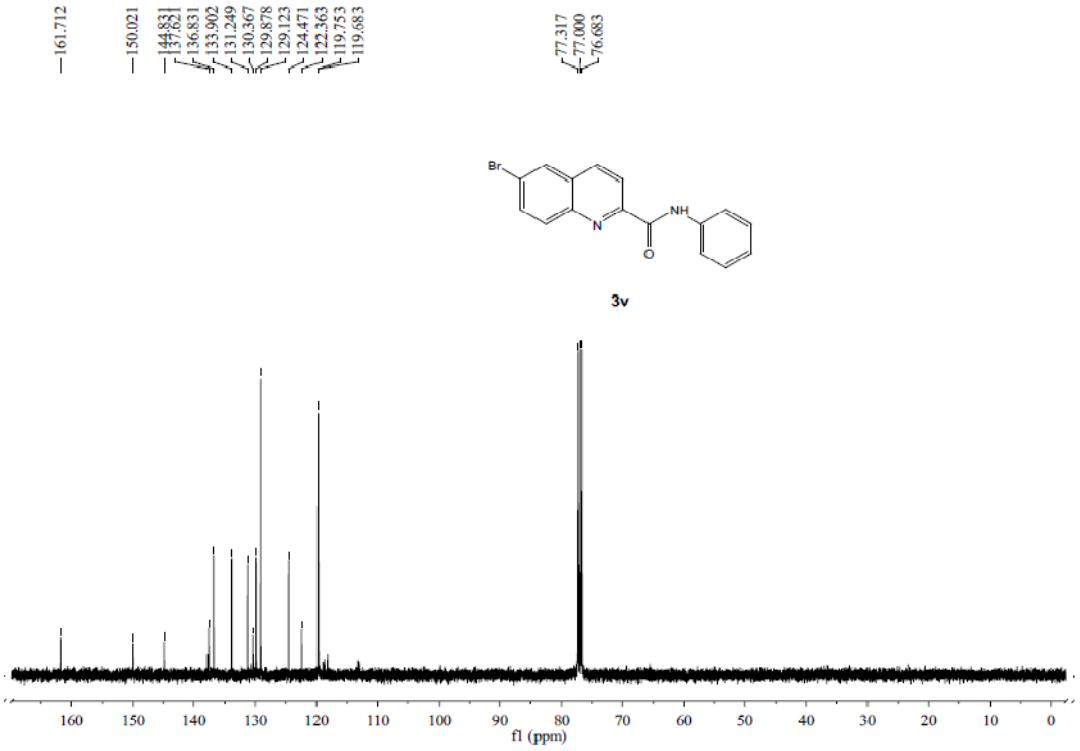

161.638
150.201
148.089
144.381
137.693
137.581
131.952
129.598
129.247
129.107
124.485
124.357
124.300
121.748
119.748
119.177
117.413
116.608
77.319
77.000
76.683
F
F
F
O
N
NH
O
124.485
124.357
124.300
121.748
119.748
119.177
117.413
116.608
124 123 122 121 120 119 118 117
f1 (ppm)
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

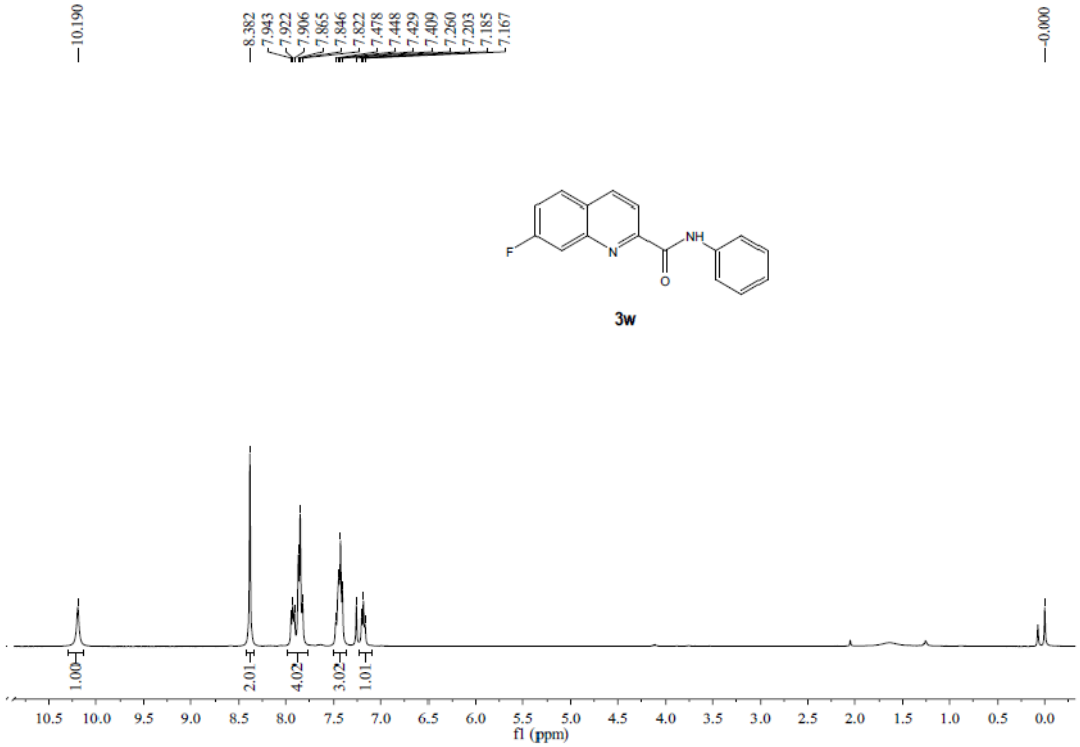
3t

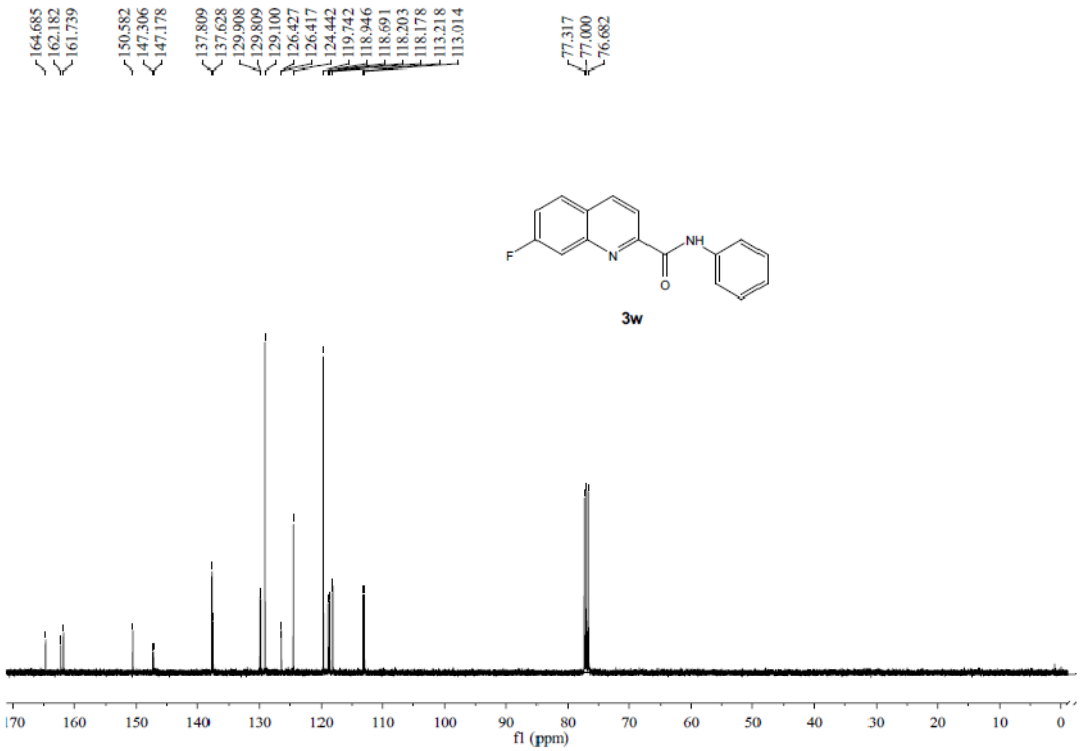

10.203
8.543
8.522
8.502
8.481
8.358
8.336
8.252
8.004
7.983
7.873
7.853
7.456
7.437
7.418
7.261
7.218
7.200
7.181
0.000
3u
1.00
2.02
1.00
1.01
1.02
2.00
2.00
1.00
fl (ppm)

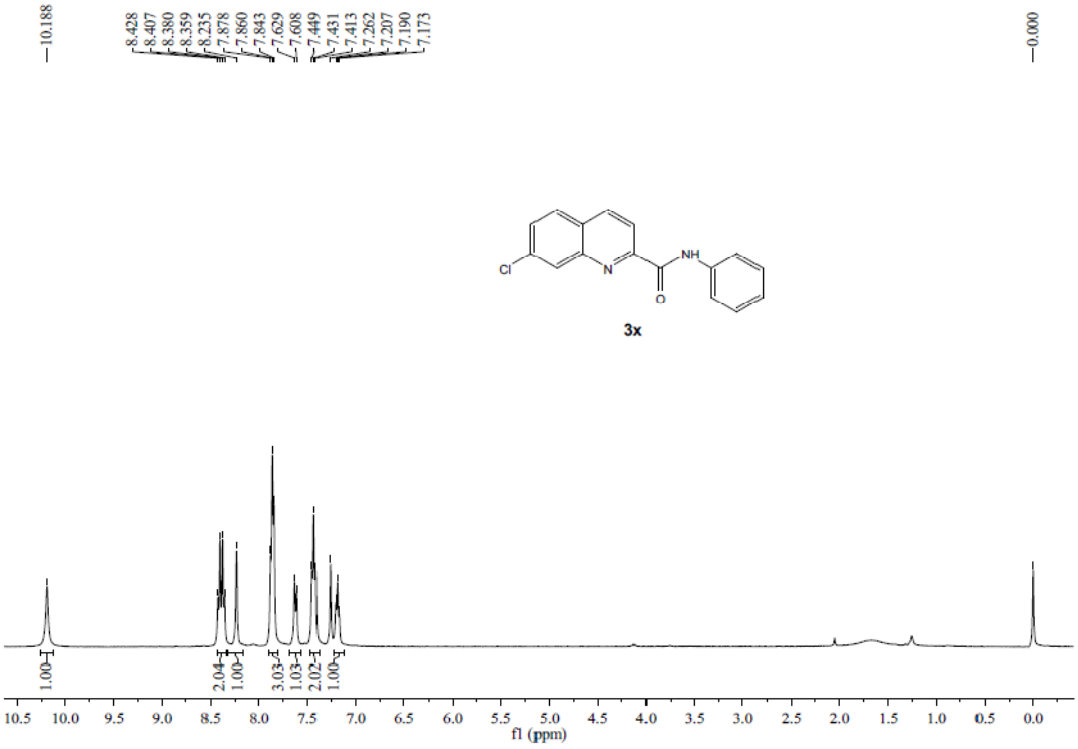

161.345
151.606
147.130
138.745
137.458
130.825
129.954
129.627
129.094
128.230
125.947
125.918
125.888
125.858
125.792
125.748
125.704
125.659
125.044
124.558
122.335
119.912
119.720
77.318
77.000
76.682
3u
130.281
129.954
129.627
129.300
130.4
130.1
129.8
129.5
fl (ppm)
125.947
125.918
125.888
125.858
125.792
125.748
125.704
125.659
125.95
125.85
125.75
125.65
fl (ppm)
fl (ppm)

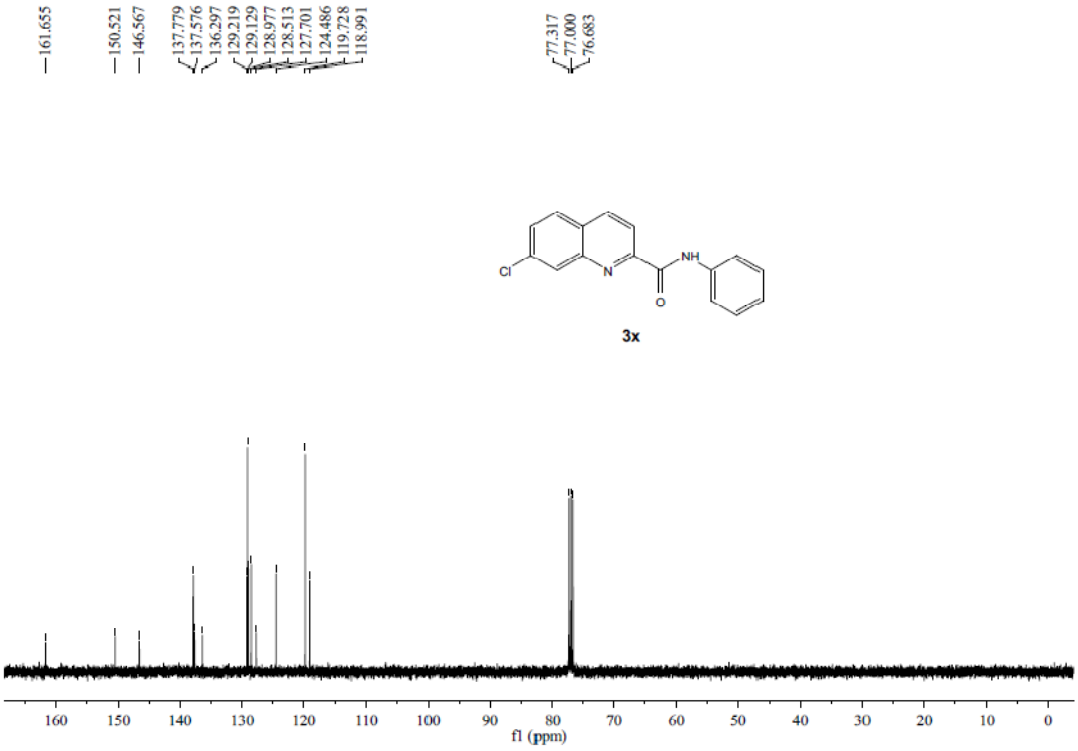

10.186
8.447
8.426
8.307
8.286
8.096
8.081
7.898
7.860
7.841
7.444
7.425
7.406
7.260
7.203
7.185
7.167
0.000
Br
N
NH
O
3v
1.01
1.00
1.00
2.00
3.01
2.04
1.02
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

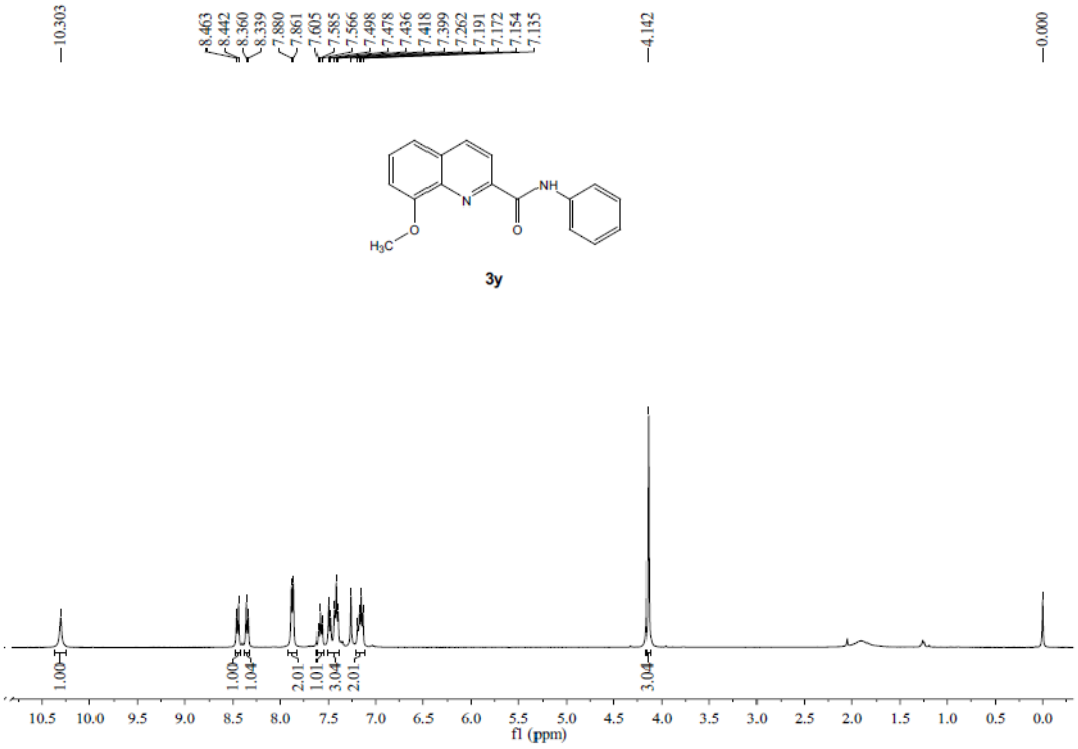

161.712
150.021
144.831
137.621
136.831
133.902
131.249
130.367
129.878
129.123
124.471
122.363
119.753
119.683
77.317
77.000
76.683
Br
N
NH
O
3v
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

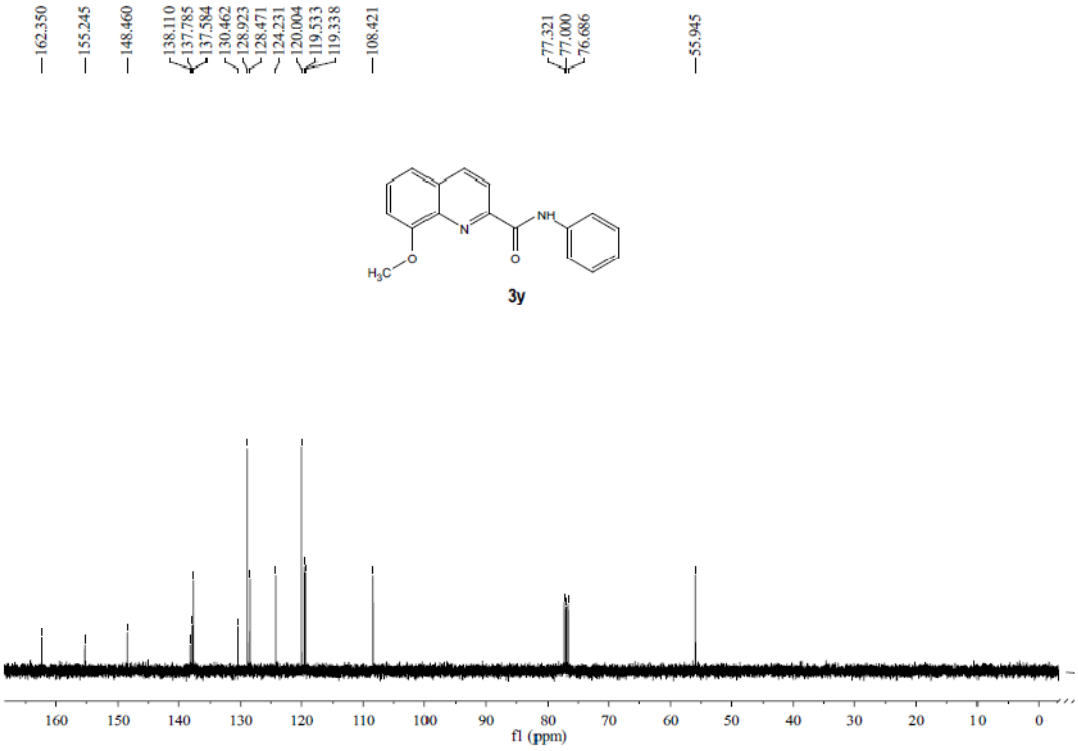

10.190
8.382
7.943
7.922
7.906
7.865
7.846
7.822
7.478
7.448
7.429
7.409
7.260
7.203
7.185
7.167
0.000
F
N
NH
O
3w
1.00
2.01
4.02
3.02
1.01
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


164.685
162.182
161.739
150.582
147.306
147.178
137.809
137.628
129.908
129.809
129.100
126.427
126.417
124.442
119.742
118.946
118.691
118.203
118.178
113.218
113.014
77.317
77.000
76.682
F
N
NH
O
3w
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


10.188
8.428
8.407
8.380
8.359
8.235
7.878
7.860
7.843
7.629
7.608
7.449
7.431
7.413
7.262
7.207
7.190
7.173
0.000
Cl
N
NH
O
3x
1.00
2.04
1.00
3.03
1.03
2.02
1.00
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)


161.655
150.521
146.567
137.779
137.576
136.297
129.219
129.129
128.977
128.513
127.701
124.486
119.728
118.991
77.317
77.000
76.683
Cl
N
NH
O
3x
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


10.303
8.463
8.442
8.360
8.339
7.880
7.861
7.605
7.585
7.566
7.498
7.478
7.436
7.418
7.399
7.262
7.191
7.172
7.154
7.135
4.142
0.000
NH
N
O
H3C
3y
1.00
1.00
1.04
2.01
1.01
3.04
2.01
3.04
fl (ppm)


162.350
155.245
148.460
138.110
137.785
137.584
130.462
128.923
128.471
124.231
120.004
119.533
119.338
108.421
77.321
77.000
76.686
55.945
NH
N
O
H3C
3y
fl (ppm)


8.794
8.373
8.352
8.249
8.228
8.180
8.159
7.866
7.846
7.777
7.759
7.739
7.611
7.593
7.574
7.458
7.440
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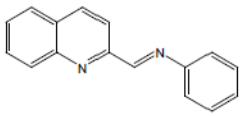
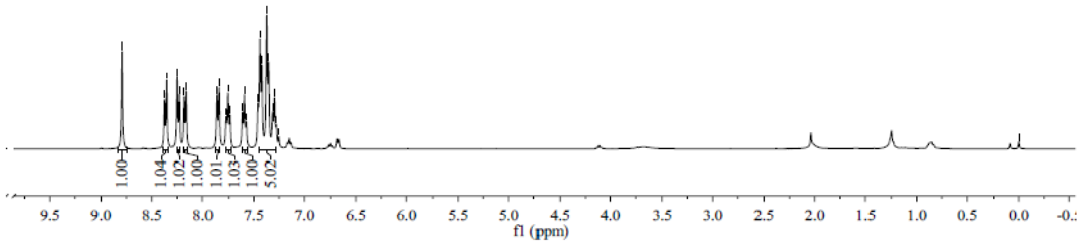
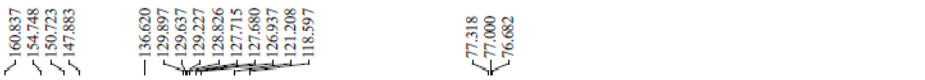
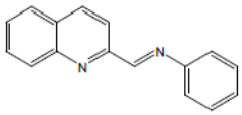
7.313
7.296
7.279
7.253
-0.000



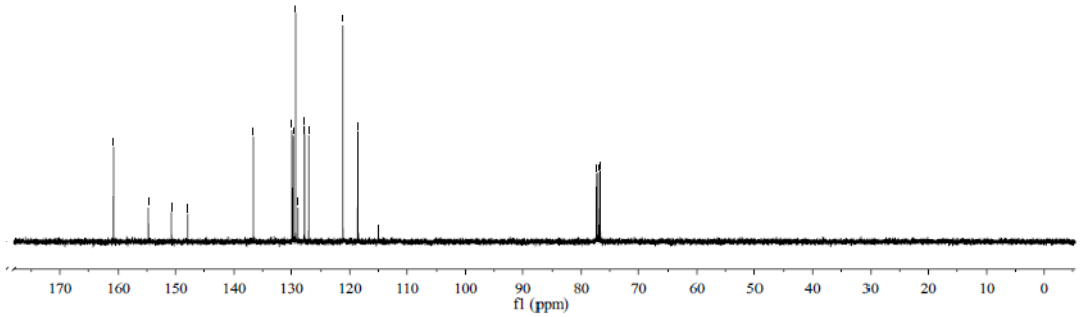
4a


1.00
1.04
1.02
1.00
1.01
1.03
1.00
5.02
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)

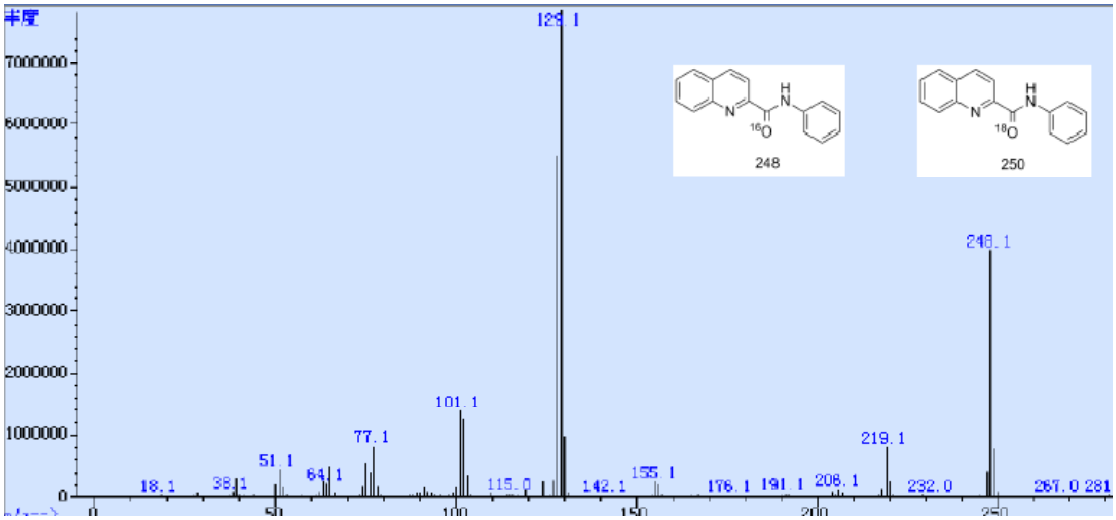

160.837
154.748
150.723
147.883
136.620
129.897
129.637
129.227
128.826
127.715
127.680
126.937
121.208
118.597
77.318
77.000
76.682



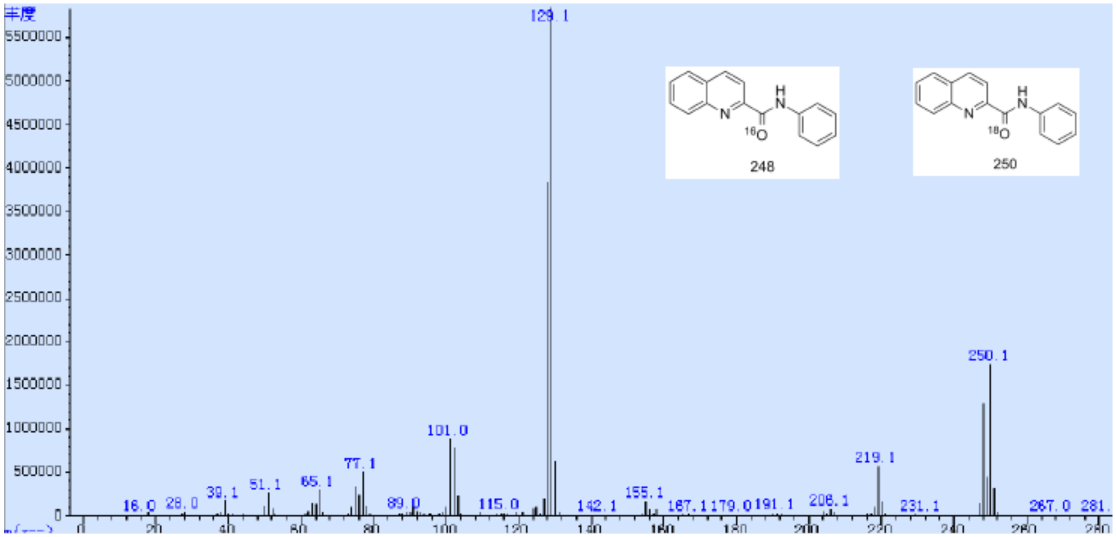
4a


170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

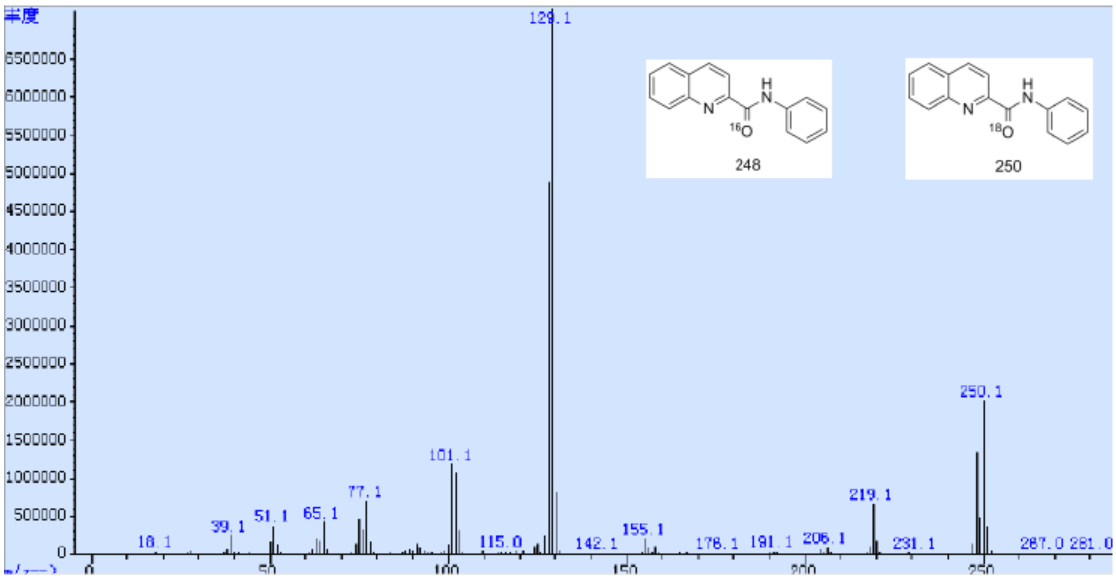
The MS spectra of ^{18}O labeling products



The MS spectra of desired product from **1a** and **2a** under $^{18}O_2$



The MS spectra of target product from **1a** and **2a** under $H_2{}^{18}O$



The MS spectra of desired product from **4a** under $H_2{}^{18}O$