Supporting Information

Iron-Catalyzed, Chelation-Induced Remote C–H Allylation of Quinolines via an 8-Amido Assistance

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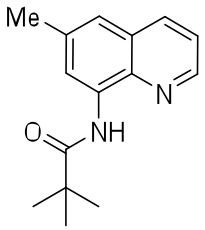
1. Materials and Methods

General. All reactions dealing with air- or moisture-sensitive compounds were carried out in a flame-dried, sealed Schlenk reaction tube under an atmosphere of nitrogen. Analytical thin-layer chromatography was performed on glass plates coated with 0.25 mm 230–400 mesh silica gel containing a fluorescent indicator (Merck). Flash silica gel column chromatography was performed on silica gel 60N (spherical and neutral, 140–325 mesh). NMR spectra were measured on a Bruker AV-400 spectrometer and reported in parts per million. ^{1}H NMR spectra were recorded at 400 MHz in $CDCl_3$ were referenced internally to tetramethylsilane as a standard, and ^{13}C NMR spectra were recorded at 100 MHz and referenced to the solvent resonance. The data is presented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet and/or multiplet resonances, br = broad), coupling constant in Hertz (Hz), and integration. High resolution (HR MS) mass spectra were recorded by ESI-TOF. Melting points were determined with a Hanon MP-300. Infrared spectra were collected on a Thermo Fisher Nicolet 6700 FT-IR spectrometer using ATR (Attenuated Total Reflectance) method. Absorption maxima (ν max) are reported in wave numbers (cm^{-1})

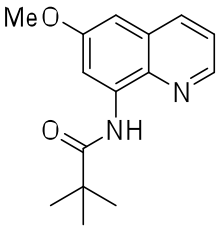
Materials. Unless otherwise noted, materials were purchased from Tokyo Chemical Industry Co., Aldrich Inc., and other commercial suppliers and used as received. Anhydrous iron(III) chloride (98% purity) was purchased from Acros Inc. $Fe(acac)_3$ (≥99.9% purity), $Fe(acac)_2$ (99.95% purity) and anhydrous $FeCl_2$ (98% purity) were purchased from Aldrich In. Solvents were dried over CaH_2 (for DCE and CH_3CN) or sodium (for toluene and dioxane) by refluxing for overnight and freshly distilled prior to use.

2. Preparation of Substrates

8-Aminoquinoline-bearing carboxamides were prepared from the reaction of 8-aminoquinolines with carboxylic acids or acyl chlorides according to the literatures.[1] *N*,2-Dimethyl-*N*-(quinolin-8-yl)-benzamide was synthesized by methylation of **1a** according to the literature.[2] Cinnamyl diethyl phosphate,[3] *tert*-butyl cinnamyl carbonate,[4] cinnamyl methyl ether,[5] and *Z*-allyl alcohol[4] were prepared according to the corresponding literatures.



***N*-(6-Methylquinolin-8-yl)pivalamide:** 6-Methylquinolin-8-amine (474.0 mg, 3.0 mmol) and triethylamine (0.63 mL, 4.5 mmol) were dissolved in anhydrous CH_2Cl_2 (10.0 mL) in a 50 mL round-bottom flask followed by dropwise addition of pivaloyl chloride (0.56 mL, 4.5 mmol) through syringe at 0 °C. The reaction mixture was stirred overnight at room temperature. After completion, the reaction was diluted with CH_2Cl_2 (10 mL), washed by $NaHCO_3$ (saturated aqueous solution, 10 mL), brine (10 mL), and dried over Na_2SO_4. The organic solvent was removed by evaporation. Purification by column chromatography in hexanes/EtOAc (20/1) afforded the title compound (661 mg, 91%) as a white solid. Melting point: 69–71 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.24 (brs, 1H), 8.73 (dd, J = 4.4, 1.6 Hz, 1H), 8.70 (d, J = 1.6 Hz, 1H), 8.04 (dd, J = 8.4, 1.6 Hz, 1H), 7.42–7.39 (m, 1H), 7.26 (d, J = 1.2 Hz, 1H), 2.52 (s, 3H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.2, 147.4, 137.71, 137.66, 135.7, 134.3, 128.1, 121.7, 120.3, 118.4, 40.5, 27.9, 22.5. IR (neat): 3365, 2961, 1679, 1532, 1479, 1426, 1381, 1333, 1241, 1179, 922, 853. HRMS (ESI^+): calcd for $C_{15}H_{19}N_2O$ $[M+H]^+$ 243.1497, found 243.1491.



***N*-(6-Methoxyquinolin-8-yl)pivalamide:** 6-Methoxyquinolin-8-amine (522.0 mg, 3.0 mmol) and triethylamine (0.63 mL, 4.5 mmol) were dissolved in anhydrous CH_2Cl_2 (10.0 mL) in a 50 mL round-bottom flask followed by dropwise addition of pivaloyl chloride (0.56 mL, 4.5 mmol) through syringe at 0 °C. The reaction mixture was stirred overnight at room temperature. After completion, the reaction was diluted with CH_2Cl_2 (10 mL), washed by $NaHCO_3$ (saturated aqueous solution, 10 mL), brine (10 mL), and dried over Na_2SO_4. The

organic solvent was removed by evaporation. Purification by column chromatography in hexanes/EtOAc (20/1) afforded the title compound (697 mg, 90%) as a slight yellow solid. Melting point: 83–85 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.24 (brs, 1H), 8.63 (dd, J = 4.0, 1.6 Hz, 1H), 8.55 (d, J = 2.8 Hz, 1H), 8.00 (dd, J = 8.4, 1.6 Hz, 1H), 7.40–7.37 (m, 1H), 6.78 (d, J = 3.4 Hz, 1H), 3.92 (s, 3H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.4, 158.6, 145.8, 135.7, 135.4, 135.1, 129.0, 122.1, 108.5, 99.9, 55.7, 40.5, 27.8. IR (neat): 3362, 2961, 1682, 1627, 1595, 1530, 1453, 1422, 1388, 1334, 1210, 1156, 1048, 922, 879, 831. HRMS (ESI$^+$): calcd for $C_{15}H_{19}N_2O_2$ $[M+H]^+$ 259.1447, found 259.1443.

3. Investigation of the Key Reaction Parameters for the C5-Allylation of Quinolines

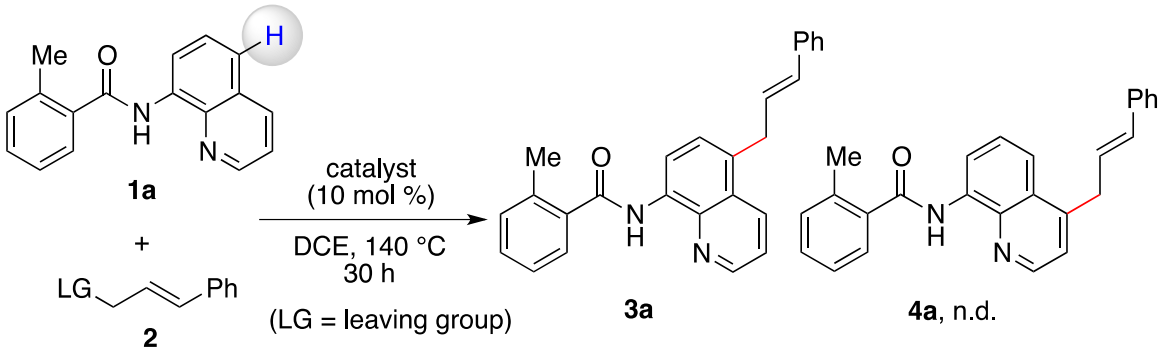


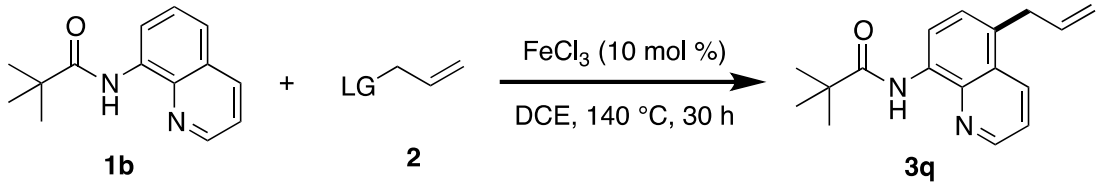
Table S1. *Investigation of the effect of catalysts and solvents for the synthesis of (E)-N-(5-cinnamylquinolin-8-yl)-2-methylbenzamide (**3a**)*[a,b]

Entry	LG	Catalyst	Solvent	Yield (**3a**)	Recovery (**1a**)[c]
1[d]	OH (**2a**)	[Ru(*p*-cymene)Cl_2]$_2$/$AgSbF_6$	DCE	53%	35%
2	OH	$AgSbF_6$	DCE	50%	36%
3	OH	$AgSbF_6$	Dioxane	42%	45%
4	OH	$AgSbF_6$	Toluene	18%	52%
5	OH	AgOTf	DCE	42%	46%
6	OH	$Cu(OTf)_2$	DCE	53%	40%
7	OH	$Ni(OTf)_2$	DCE	40%	47%
8	OH	$Fe(OTf)_2$	DCE	40%	49%
9	OH	$FeCl_3$	DCE	62%	28%
10	OH	$FeCl_3$	CH_3CN	30%	62%

11	OH	$FeCl_2$	DCE	trace	91%
12	OH	$Fe(acac)_3$	DCE	trace	90%
13	OMe	$FeCl_3$	DCE	57%	30%
14	OAc	$FeCl_3$	DCE	65%	26%
15	OCO_2t-Bu	$FeCl_3$	DCE	65%	28%
16	$OPO(OEt)_2$	$FeCl_3$	DCE	40%	38%

[a] Reaction conditions: **1a** (0.2 mmol), (*E*)-Cinnamic alcohol **2** (0.6 mmol), Catalyst (10 mol %), Solvent (1.0 mL), 140 ºC, 30 h. [b] Isolated yield. [c] The C4-allylated product **4a** was not detected by ^{1}H NMR and GC analyses. [d] $[Ru(p\text{-cymene})Cl_2]_2$ (2.5 mol %) and $AgSbF_6$ (10 mol %) were used.

Table S2. *Iron-catalyzed C5-allylation of quinolines using simple allyl oxygen electrophiles*[a,b]

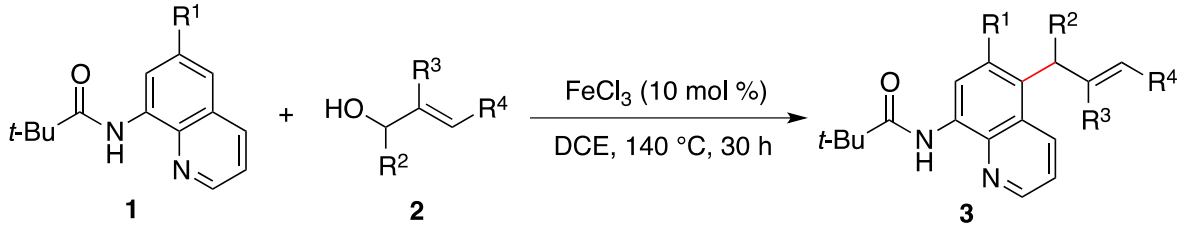


Entry	LG	Yield (**3q**)	Recovery (**1b**)
1	OPh	trace	92%
2	OBoc	trace	92%
3	OAc	trace	90%
4	$OPO(OEt)_2$	trace	88%

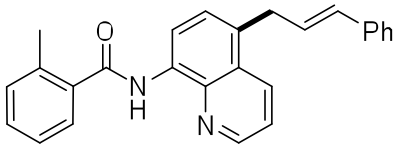
[a] Reaction conditions: **1b** (0.2 mmol), **2** (0.6 mmol), $FeCl_3$ (10 mol %), DCE (1.0 mL), 140 ºC, 30 h. [b] Isolated yield.

4. General Procedure for Iron-Catalyzed C5-Allylation of 8-Aminoquinolines with Allyl Alcohols

General Procedure

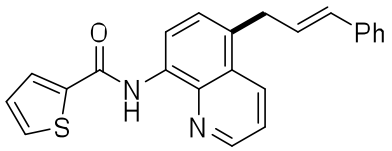


In a dried Schlenk flask were placed 8-Aminoquinolines **1** (0.2 mmol), allyl alcohols **2** (0.6 mmol), $FeCl_3$ (3.2 mg, 0.02 mmol). Then 1.0 mL of DCE was added with a syringe under nitrogen atmosphere. The resulting mixture was heated at 140 ºC for 30 h. After cooling to room temperature, the reaction mixture was diluted with 5.0 mL of CH_2Cl_2 and filtered through a plug of celite, followed by washing with 10–20 mL of CH_2Cl_2. The combined residue was concentrated under reduced pressure, and then the resulting crude product was purified by column chromatography on silica gel to provide the allylation product **3**.



(*E*)- 2-Methyl-*N*-(5-cinnamylquinolin-8-yl)benzamide (Table 2, 3a)

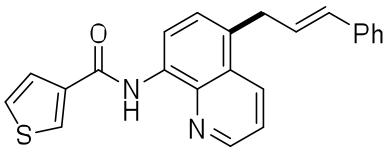
The general procedure was applied to 2-methyl-*N*-(quinolin-8-yl)benzamide (52.5 mg, 0.2 mmol), (*E*)-cinnamic alcohol (80.4 mg, 0.6 mmol) at 140 ºC for 30 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/40) to afford the title compound as a white solid (47 mg, 62% yield). Melting point: 173–175 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.24 (brs, 1H), 8.88 (d, J = 7.6 Hz, 1H), 8.77 (dd, J = 4.0, 1.2 Hz, 1H), 8.40 (dd, J = 8.4, 1.6 Hz, 1H), 7.68 (d, J = 7.6 Hz, 1H), 7.52–7.45 (m, 2H), 7.42–7.38 (m, 1H), 7.34–7.27 (m, 6H), 7.21–7.18 (m, 1H), 6.43 (dt, J = 16.0, 4.8 Hz, 1H), 6.38 (d, J = 16.0 Hz, 1H), 3.95 (d, J = 5.2 Hz, 2H), 2.61 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.3, 148.0, 139.2, 137.3, 136.9, 136.8, 133.8, 133.2, 131.7, 131.5, 130.6, 130.4, 128.70, 128.67, 127.8, 127.4, 127.0, 126.2, 126.1, 121.6, 116.5, 35.7, 20.4. IR (neat): 3349, 3025, 2924, 1673, 1599, 1519, 1494, 1455, 1386, 1326, 1260, 1100, 898, 843. HRMS (ESI$^+$): calcd for $C_{26}H_{23}N_2O$ $[M+H]^+$ 379.1810, found 379.1815.



(*E*)-*N*-(5-Cinnamylquinolin-8-yl)thiophene-2-carboxamide (Table 2, 3b)

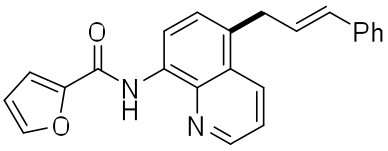
The general procedure was applied to *N*-(quinolin-8-yl)thiophene-2-carboxamide (50.8 mg, 0.2 mmol), (*E*)-cinnamic alcohol (80.4 mg, 0.6 mmol) at 140 ºC for 30 h. The crude product

was purified by column chromatography on silica gel (EtOAc/PE = 1/20) to afford the title compound as a white solid (45 mg, 61% yield). Melting point: 151–153 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.63 (brs, 1H), 8.85 (d, J = 3.6 Hz, 1H), 8.78 (d, J = 7.6 Hz, 1H), 8.40 (d, J = 8.8 Hz, 1H), 7.83 (s, 1H), 7.57 (d, J = 4.8 Hz, 1H), 7.47 (d, J = 8.0 Hz, 2H), 7.32–7.25 (m, 4H), 7.21–7.19 (m, 2H), 6.49–6.38 (m, 2H), 3.94 (d, J = 4.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.1, 148.0, 140.4, 139.1, 137.3, 133.4, 133.2, 131.7, 131.0, 130.5, 128.7, 128.6, 128.5, 128.0, 127.8, 127.4, 127.0, 126.2, 121.6, 116.5, 35.7. IR (neat): 3348, 3025, 2974, 2892, 1659, 1530, 1494, 1457, 1388, 1327, 1269, 1050, 966, 910, 850. HRMS (ESI$^+$): calcd for $C_{23}H_{19}N_2OS$ $[M+H]^+$ 371.1218, found 371.1216.



(*E*)-*N*-(5-Cinnamylquinolin-8-yl)thiophene-3-carboxamide (Table 2, 3c)

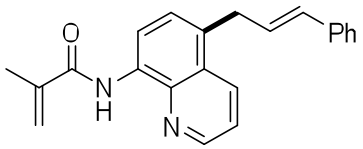
The general procedure was applied to *N*-(quinolin-8-yl)thiophene-3-carboxamide (50.8 mg, 0.2 mmol), (*E*)-cinnamic alcohol (80.4 mg, 0.6 mmol) at 140 ºC for 30 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/20) to afford the title compound as a white solid (43 mg, 58% yield). Melting point: 157–159 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.57 (brs, 1H), 8.84–8.81 (m, 2H), 8.40 (d, J = 8.8 Hz, 1H), 8.15 (s, 1H), 7.68 (d, J = 4.8 Hz, 1H), 7.48 (d, J = 8.0 Hz, 2H), 7.44–7.43 (m, 2H), 7.32–7.25 (m, 4H), 7.17 (t, J = 6.8 Hz, 1H), 6.49–6.38 (m, 2H), 3.94 (d, J = 4.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.1, 148.0, 139.2, 138.6, 137.3, 133.5, 133.2, 131.7, 130.4, 129.0, 128.7, 127.9, 127.4, 127.0, 126.8, 126.5, 126.2, 121.6, 116.4, 35.7. IR (neat): 3352, 3025, 2974, 2892, 1667, 1529, 1494, 1457, 1387, 1327, 1257, 1050, 967, 909, 851. HRMS (ESI$^+$): calcd for $C_{23}H_{19}N_2OS$ $[M+H]^+$ 371.1218, found 371.1218.



(*E*)-*N*-(5-Cinnamylquinolin-8-yl)furan-2-carboxamide (Table 2, 3d)

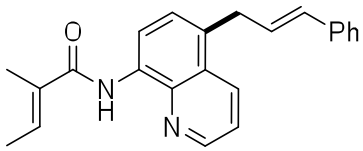
The general procedure was applied to *N*-(quinolin-8-yl)furan-2-carboxamide (47.6 mg, 0.2

mmol), (*E*)-cinnamic alcohol (80.4 mg, 0.6 mmol) at 140 ºC for 30 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/20) to afford the title compound as a white solid (36 mg, 51% yield). Melting point: 145–147 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.80 (brs, 1H), 8.88 (d, J = 2.8 Hz, 1H), 8.81 (d, J = 8.0 Hz, 1H), 8.40 (d, J = 8.8 Hz, 1H), 7.62 (s, 1H), 7.47 (d, J = 7.6 Hz, 2H), 7.30–7.25 (m, 5H), 7.17 (t, J = 7.2 Hz, 1H), 6.58 (s, 1H), 6.49–6.38 (m, 2H), 3.94 (d, J = 4.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.5, 148.6, 148.1, 144.6, 139.2, 137.3, 133.3, 133.1, 131.7, 130.6, 128.7, 128.6, 127.8, 127.4, 127.0, 126.2, 121.6, 116.6, 115.1, 112.6, 35.7. IR (neat): 3331, 3026, 2973, 1670, 1577, 1527, 1496, 1455, 1390, 1328, 1274, 1175, 1009, 967, 910, 842. HRMS (ESI$^+$): calcd for $C_{23}H_{19}N_2O_2$ $[M+H]^+$ 355.1447, found 355.1444.



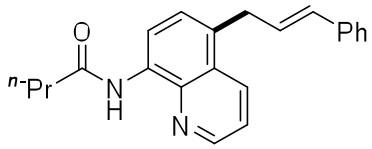
(*E*)-*N*-(5-Cinnamylquinolin-8-yl)methacrylamide (Table 2, 3e)

The general procedure was applied to *N*-(quinolin-8-yl)methacrylamide (42.4 mg, 0.2 mmol), (*E*)-cinnamic alcohol (80.4 mg, 0.6 mmol) at 140 ºC for 30 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/40) to afford the title compound as a white solid (43 mg, 65% yield). Melting point: 155–157 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.39 (brs, 1H), 8.80 (d, J = 4.0 Hz, 1H), 8.76 (d, J = 8.0 Hz, 1H), 8.37 (d, J = 8.8 Hz, 1H), 7.44 (d, J = 8.0 Hz, 2H), 7.31–7.24 (m, 4H), 7.17 (t, J = 6.8 Hz, 1H), 6.47 –6.36 (m, 2H), 6.04 (s, 1H), 5.54 (s, 1H), 3.91 (d, J = 5.2 Hz, 2H), 2.19 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.5, 147.9, 140.9, 139.3, 137.3, 133.5, 133.1, 131.6, 130.3, 128.7, 127.8, 127.4, 126.9, 126.2, 121.5, 120.7, 116.4, 35.7, 18.9. IR (neat): 3360, 3025, 2961, 1676, 1628, 1525, 1495, 1456, 1388, 1326, 1181, 966, 843. HRMS (ESI$^+$): calcd for $C_{22}H_{21}N_2O$ $[M+H]^+$ 329.1654, found 329.1652.



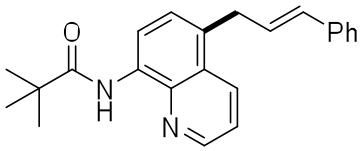
(*E*)-*N*-(5-Cinnamylquinolin-8-yl)-2-methylbut-2-enamide (Table 2, 3f)

The general procedure was applied to (*E*)-2-methyl-*N*-(quinolin-8-yl)but-2-enamide (45.2 mg, 0.2 mmol), (*E*)-cinnamic alcohol (80.4 mg, 0.6 mmol) at 140 ºC for 30 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/40) to afford the title compound as a white solid (43 mg, 63% yield). Melting point: 159–161 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.30 (brs, 1H), 8.80 (d, J = 3.2 Hz, 1H), 8.76 (d, J = 8.0 Hz, 1H), 8.36 (d, J = 8.4 Hz, 1H), 7.43 (d, J = 8.0 Hz, 2H), 7.31–7.24 (m, 4H), 7.16 (t, J = 7.6 Hz, 1H), 6.73 (q, J = 6.8 Hz, 1H), 6.47 –6.35 (m, 2H), 3.90 (d, J = 4.8 Hz, 2H), 2.07 (s, 3H), 1.87 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.6, 147.8, 139.3, 137.3, 133.8, 133.1, 133.0, 131.9, 131.6, 129.9, 128.7, 128.6, 127.8, 126.9, 126.2, 121.4, 116.3, 35.6, 14.4, 12.6. IR (neat): 3360, 3026, 2925, 1674, 1636, 1522, 1495, 1456, 1381, 1325, 1275, 966, 849. HRMS (ESI$^+$): calcd for $C_{23}H_{23}N_2O$ $[M+H]^+$ 343.1810, found 343.1806.



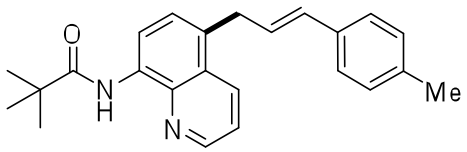
(*E*)-*N*-(5-Cinnamylquinolin-8-yl)butyramide (Table 2, 3g)

The general procedure was applied to *N*-(quinolin-8-yl)butyramide (42.8 mg, 0.2 mmol), (*E*)-cinnamic alcohol (80.4 mg, 0.6 mmol) at 140 ºC for 30 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/40) to afford the title compound as a white solid (44 mg, 67% yield). Melting point: 116–118 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.84 (brs, 1H), 8.80 (dd, J = 4.4, 1.6 Hz, 1H), 8.73 (d, J = 8.0 Hz, 1H), 8.39 (dd, J = 8.4, 1.6 Hz, 1H), 7.48–7.44 (m, 2H), 7.31–7.25 (m, 4H), 7.21–7.17 (m, 1H), 6.41 (dt, J = 16.0, 5.2 Hz, 1H), 6.36 (d, J = 16.0 Hz, 1H), 3.92 (d, J = 5.2 Hz, 2H), 2.53 (t, J = 7.6 Hz, 2H), 1.91–1.82 (m, 2H), 1.05 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.9, 147.8, 138.9, 137.3, 133.6, 133.2, 131.6, 130.0, 128.73, 128.66, 127.9, 127.4, 126.9, 126.2, 121.5, 116.4, 40.3, 35.7, 19.3, 14.0. IR (neat): 3355, 2962, 1685, 1598, 1520, 1494, 1457, 1388, 1324, 1266, 1187, 966, 844. HRMS (ESI$^+$): calcd for $C_{22}H_{23}N_2O$ $[M+H]^+$ 331.1810, found 331.1804. Crystals suitable for X-ray diffraction study of **3g** were obtained by slow evaporation of a mixed solution of hexane and ethyl acetate.



(*E*)-*N*-(5-Cinnamylquinolin-8-yl)pivalamide (Table 2, 3h)

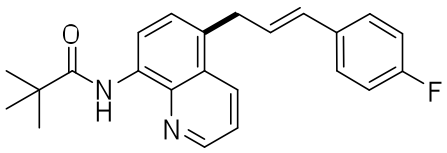
The general procedure was applied to *N*-(quinolin-8-yl)pivalamide (45.6 mg, 0.2 mmol), (*E*)-cinnamic alcohol (80.4 mg, 0.6 mmol) at 140 ºC for 30 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/40) to afford the title compound as a white solid (50 mg, 72% yield). Melting point: 163–165 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.31 (brs, 1H), 8.81 (dd, J = 4.0, 1.6 Hz, 1H), 8.73 (d, J = 8.0 Hz, 1H), 8.37 (dd, J = 8.4, 1.6 Hz, 1H), 7.48–7.43 (m, 2H), 7.31–7.25 (m, 4H), 7.21–7.17 (m, 1H), 6.41 (dt, J = 16.0, 5.6 Hz, 1H), 6.35 (d, J = 16.0 Hz, 1H), 3.92 (d, J = 5.6 Hz, 2H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.3, 147.9, 139.4, 137.3, 133.8, 133.1, 131.5, 129.9, 128.8, 128.7, 127.8, 127.4, 126.9, 126.2, 121.4, 116.1, 40.5, 35.6, 27.9. IR (neat): 3366, 2965, 1667, 1522, 1496, 1455, 1386, 1323, 1273, 1182, 966, 851. HRMS (ESI$^+$): calcd for $C_{23}H_{25}N_2O$ $[M+H]^+$ 345.1967, found 345.1961.



(*E*)-*N*-(5-(3-*p*-Tolylallyl)quinolin-8-yl)pivalamide (Table 3, 3i)

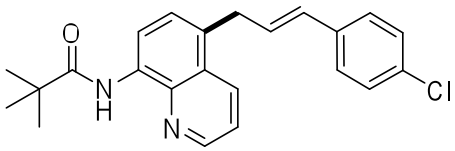
The general procedure was applied to *N*-(quinolin-8-yl)pivalamide (45.6 mg, 0.2 mmol), (*E*)-3-*p*-tolylprop-2-en-1-ol (88.8 mg, 0.6 mmol) at 140 ºC for 30 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/40) to afford the title compound as a white solid (37 mg, 52% yield). Melting point: 151–153 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.31 (brs, 1H), 8.81 (d, J = 4.0 Hz, 1H), 8.72 (d, J = 7.6 Hz, 1H), 8.38 (d, J = 8.4, 1.6 Hz, 1H), 7.47–7.42 (m, 2H), 7.19 (d, J = 8.0 Hz, 2H), 7.07 (d, J = 8.0 Hz, 2H), 6.42–6.31 (m, 2H), 3.90 (d, J = 4.8 Hz, 2H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.3, 147.9, 139.4, 137.2, 134.6, 133.7, 133.2, 131.4, 130.1, 129.4, 127.8, 127.7, 126.9, 126.1, 121.4, 116.1, 40.5, 35.7, 27.9, 21.3. IR (neat): 3370, 2958, 1679, 1524, 1495, 1384, 1325, 1181, 969, 929, 846. HRMS (ESI$^+$): calcd for $C_{24}H_{27}N_2O$ $[M+H]^+$ 359.2123, found

359.2116.



(*E*)-*N*-(5-(3-(4-Fluorophenyl)allyl)quinolin-8-yl)pivalamide (Table 3, 3j)

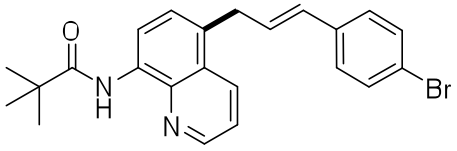
The general procedure was applied to *N*-(quinolin-8-yl)pivalamide (45.6 mg, 0.2 mmol), (*E*)-3-(4-fluorophenyl)prop-2-en-1-ol (91.2 mg, 0.6 mmol) at 140 ºC for 30 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/40) to afford the title compound as a slight yellow solid (65 mg, 90% yield). Melting point: 145–147 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.31 (brs, 1H), 8.82 (d, *J* = 4.0 Hz, 1H), 8.73 (d, *J* = 7.6 Hz, 1H), 8.36 (d, *J* = 8.4 Hz, 1H), 7.49–7.42 (m, 2H), 7.27–7.24 (m, 2H), 6.98–6.93 (m, 2H), 6.40–6.29 (m, 2H), 3.90 (d, *J* = 4.8 Hz, 2H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.4, 163.4, 161.0, 148.0, 139.4, 133.8, 133.5 (d, *J* = 3.0 Hz), 133.1, 130.4, 129.8, 128.5 (d, *J* = 2.0 Hz), 127.9, 127.7, 127.6, 126.9, 121.5, 116.1, 115.6, 115.4, 40.5, 35.5, 27.9; ^{19}F NMR (377 MHz, $CDCl_3$): δ = –115.51. IR (neat): 3364, 2963, 1677, 1601, 1524, 1508, 1385, 1325, 1228, 1157, 967, 910, 841. HRMS (ESI^+): calcd for $C_{23}H_{24}FN_2O$ $[M+H]^+$ 363.1873, found 363.1866.



(*E*)-*N*-(5-(3-(4-Chlorophenyl)allyl)quinolin-8-yl)pivalamide (Table 3, 3k)

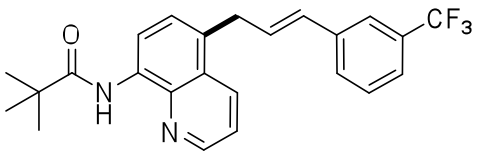
The general procedure was applied to *N*-(quinolin-8-yl)pivalamide (45.6 mg, 0.2 mmol), (*E*)-3-(4-chlorophenyl)prop-2-en-1-ol (100.8 mg, 0.6 mmol) at 140 ºC for 30 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/40) to afford the title compound as a white solid (62 mg, 82% yield). Melting point: 174–176 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.31 (brs, 1H), 8.82 (d, *J* = 4.0 Hz, 1H), 8.73 (d, *J* = 8.0 Hz, 1H), 8.35 (d, *J* = 8.4 Hz, 1H), 7.49–7.45 (m, 1H), 7.41 (d, *J* = 8.0 Hz, 1H), 7.24–7.20 (m, 4H), 6.38 (dt, *J* = 15.6, 6.0 Hz, 1H), 6.28 (d, *J* = 16.0 Hz, 1H), 3.90 (d, *J* = 6.0 Hz, 2H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.4, 148.0, 139.4, 135.8, 133.9, 133.0, 132.9, 130.3,

129.6, 129.5, 128.8, 127.9, 127.4, 126.8, 121.5, 116.1, 40.5, 35.6, 27.9. IR (neat): 3373, 2962, 1672, 1523, 1491, 1385, 1324, 1181, 1092, 1012, 968, 929, 840. HRMS (ESI^+): calcd for $C_{23}H_{24}ClN_2O$ $[M+H]^+$ 379.1577, found 379.1569.



(*E*)-*N*-(5-(3-(4-Bromophenyl)allyl)quinolin-8-yl)pivalamide (Table 3, 3l)

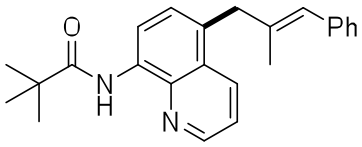
The general procedure was applied to *N*-(quinolin-8-yl)pivalamide (45.6 mg, 0.2 mmol), (*E*)-3-(4-bromophenyl)prop-2-en-1-ol (127.2 mg, 0.6 mmol) at 140 ºC for 30 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/40) to afford the title compound as a white solid (66 mg, 78% yield). Melting point: 171–173 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.30 (brs, 1H), 8.82 (d, J = 2.4 Hz, 1H), 8.73 (d, J = 7.6 Hz, 1H), 8.34 (d, J = 8.4 Hz, 1H), 7.48–7.37 (m, 4H), 7.14 (d, J = 7.6 Hz, 2H), 6.46–6.40 (m, 1H), 6.26 (d, J = 16.0 Hz, 1H), 3.89 (d, J = 6.0 Hz, 2H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.3, 148.0, 139.4, 136.3, 133.9, 133.0, 131.7, 130.4, 129.7, 129.5, 127.9, 127.8, 126.9, 121.5, 121.1, 116.1, 40.5, 35.6, 27.9. IR (neat): 3372, 2964, 1670, 1522, 1486, 1399, 1385, 1324, 1180, 1071, 1008, 968, 911, 839. HRMS (ESI^+): calcd for $C_{23}H_{24}BrN_2O$ $[M+H]^+$ 423.1072, found 423.1076.



(*E*)-*N*-(5-(3-(3-(Trifluoromethyl)phenyl)allyl)quinolin-8-yl)pivalamide (Table 3, 3m)

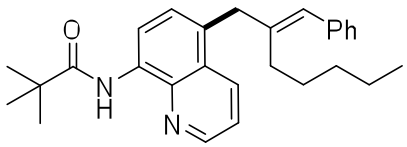
The general procedure was applied to *N*-(quinolin-8-yl)pivalamide (45.6 mg, 0.2 mmol), (*E*)-3-(3-(trifluoromethyl)phenyl)prop-2-en-1-ol (121.2 mg, 0.6 mmol) at 140 ºC for 30 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/40) to afford the title compound as a white solid (58 mg, 70% yield). Melting point: 141–143 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.32 (brs, 1H), 8.83 (d, J = 4.0 Hz, 1H), 8.75 (d, J = 8.0 Hz, 1H), 8.35 (d, J = 8.4, 1.6 Hz, 1H), 7.53 (s, 1H), 7.50–7.43 (m, 4H), 7.35 (t, J = 7.6 Hz, 1H), 6.50 (dt, J = 15.6, 6.0 Hz, 1H), 6.34 (d, J = 16.0 Hz, 1H), 3.94 (d, J = 6.0 Hz, 2H), 1.44 (s,

9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.4, 148.0, 139.4, 138.1, 134.0, 133.0, 131.2, 131.1, 130.9, 130.2, 129.33, 129.27, 129.1, 129.0, 128.0, 126.8, 125.6, 123.8 (q, J = 4.0 Hz), 122.8 (q, J = 3.0 Hz), 121.5, 116.1, 40.5, 35.5, 27.9; ^{19}F NMR (377 MHz, $CDCl_3$): δ = –62.78. IR (neat): 3363, 2965, 1678, 1525, 1496, 1385, 1328, 1165, 1126, 1072, 966, 911, 842. HRMS (ESI^+): calcd for $C_{24}H_{24}F_3N_2O$ $[M+H]^+$ 413.1841, found 413.1834.



(*E*)-*N*-(5-(2-Methyl-3-phenylallyl)quinolin-8-yl)pivalamide (Table 3, 3n)

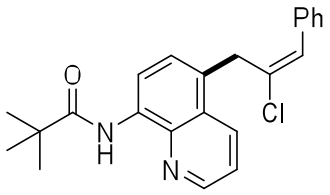
The general procedure was applied to *N*-(quinolin-8-yl)pivalamide (45.6 mg, 0.2 mmol), (*E*)-2-methyl-3-phenylprop-2-en-1-ol (88.8 mg, 0.6 mmol) at 140 ºC for 30 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/40) to afford the title compound as a white solid (57 mg, 80% yield). Melting point: 70–72 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.32 (brs, 1H), 8.80 (d, J = 4.0 Hz, 1H), 8.74 (d, J = 8.0 Hz, 1H), 8.41 (d, J = 8.8 Hz, 1H), 7.46–7.43 (m, 2H), 7.30–7.25 (m, 2H), 7.18–7.16 (m, 3H), 6.23 (s, 1H), 3.87 (s, 2H), 1.86 (s, 3H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.3, 147.9, 142.6, 139.3, 138.2, 137.8, 133.8, 133.3, 129.4, 128.9, 128.8, 128.2, 127.4, 127.1, 126.3, 121.3, 116.0, 43.3, 40.5, 27.9, 18.3. IR (neat): 3366, 2970, 1682, 1526, 1495, 1397, 1385, 1325, 1182, 1050, 929, 842. HRMS (ESI^+): calcd for $C_{24}H_{27}N_2O$ $[M+H]^+$ 359.2123, found 359.2115.



(*E*)-*N*-(5-(2-Benzylideneheptyl)quinolin-8-yl)pivalamide (Table 3, 3o)

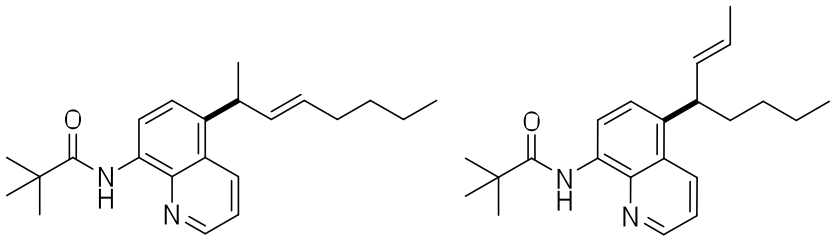
The general procedure was applied to *N*-(quinolin-8-yl)pivalamide (45.6 mg, 0.2 mmol), (*E*)-2-benzylideneheptan-1-ol (122.4 mg, 0.6 mmol) at 140 ºC for 30 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/40) to afford the title compound as a colorless oil (63 mg, 76% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.32 (brs, 1H), 8.80 (d, J = 4.0 Hz, 1H), 8.74 (d, J = 8.0 Hz, 1H), 8.37 (d, J = 8.4 Hz, 1H), 7.46–7.43 (m,

2H), 7.29–7.25 (m, 2H), 7.14 (t, J = 7.2 Hz, 1H), 7.10 (d, J = 8.0 Hz, 2H), 6.06 (s, 1H), 3.87 (s, 2H), 2.22 (t, J = 8.0 Hz, 2H), 1.58 (m. 2H), 1.44 (s, 9H), 1.29–1.27 (m. 4H), 0.86 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.3, 147.9, 142.6, 139.4, 138.2, 133.7, 133.4, 129.6, 128.9, 128.6, 128.2, 127.4, 127.3, 126.3, 121.3, 116.0, 40.5, 40.3, 32.1, 31.4, 28.3, 27.9, 22.6, 14.2. IR (neat): 3367, 2956, 1679, 1521, 1494, 1396, 1383, 1326, 1181, 932, 842. HRMS (ESI$^+$): calcd for $C_{28}H_{35}N_2O$ $[M+H]^+$ 415.2749, found 415.2742.



(*E*)-*N*-(5-(2-Chloro-3-phenylallyl)quinolin-8-yl)pivalamide (Table 3, 3p)

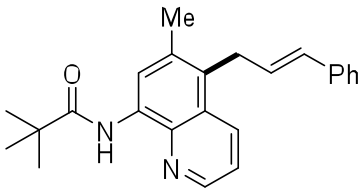
The general procedure was applied to *N*-(quinolin-8-yl)pivalamide (45.6 mg, 0.2 mmol), (*E*)-2-chloro-3-phenylprop-2-en-1-ol (100.8 mg, 0.6 mmol) at 140 ºC for 30 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/40) to afford the title compound as a colorless oil (35 mg, 46% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.33 (brs, 1H), 8.83 (d, J = 1.2 Hz, 1H), 8.77 (d, J = 7.6 Hz, 1H), 8.36 (d, J = 8.4 Hz, 1H), 7.52–7.48 (m, 4H), 7.31–7.21 (m, 3H), 6.29 (s, 1H), 4.17 (s, 2H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.4, 148.1, 139.3, 134.8, 134.6, 133.1, 132.9, 129.4, 129.1, 128.3, 127.9, 127.0, 126.9, 126.2, 121.7, 116.0, 43.6, 40.5, 27.9. IR (neat): 3365, 2965, 1682, 1522, 1495, 1385, 1325, 1181, 1142, 913, 842. HRMS (ESI$^+$): calcd for $C_{23}H_{24}ClN_2O$ $[M+H]^+$ 379.1577, found 379.1580.



(*E*)-*N*-[5-(Oct-3-en-2-yl)quinolin-8-yl]pivalamide (Table 3, 3r) and (*E*)-*N*-[5-(oct-2-en-4-yl)quinolin-8-yl]pivalamide (Table 3, 3s)

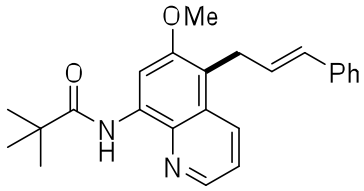
The general procedure was applied to *N*-(quinolin-8-yl)pivalamide (45.6 mg, 0.2 mmol), (*E*)-oct-3-en-2-ol (76.8 mg, 0.6 mmol) at 140 ºC for 30 h. The crude product was purified by

column chromatography on silica gel (EtOAc/PE = 1/40) to afford the title mixed compounds as a colorless oil (39 mg, 58% yield). The ratio of **3r**/**3s** (2.3/1) was determined by ^{1}H NMR. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.30 (brs, 1H), 8.79 (dd, J = 4.0, 1.2 Hz, 1H), 8.76–8.72 (m, 1H), 8.47–8.43 (m, 1H), 7.47–7.40 (m, 2H), 5.69–5.60 (m, 1H), 5.46–5.39 (m, 1H), 4.13–4.06 (m, 0.63H, **3r**), 3.90–3.85 (m, 0.28 H, **3s**), 2.03–1.98 (m, 1.39 H), 1.85–1.79 (m, 0.76 H), 1.65–1.63 (m, 1.73 H), 1.42 (m, 8H), 1.30–1.25 (m, 4H), 0.84 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.2, 147.7, 136.1, 135.3, 135.0, 134.6, 133.2, 132.8, 132.6, 130.3, 126.6, 126.4, 125.3, 125.1, 124.7, 121.1, 121.0, 116.2, 116.1, 43.0, 40.4, 36.9, 35.6, 32.3, 31.7, 30.1, 27.9, 22.9, 22.3, 21.2, 18.1, 14.2, 14.1.



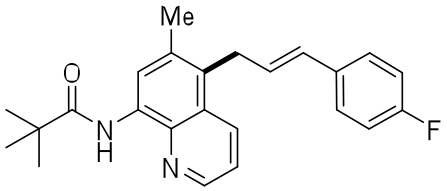
(*E*)-*N*-(5-Cinnamyl-6-methylquinolin-8-yl)pivalamide (Table 3, 3t)

The general procedure was applied to *N*-(6-methylquinolin-8-yl)pivalamide (48.4 mg, 0.2 mmol), (*E*)-cinnamic alcohol (80.4 mg, 0.6 mmol) at 140 ºC for 30 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/40) to afford the title compound as a white solid (56 mg, 78% yield). Melting point: 141–143 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.30 (brs, 1H), 8.74 (m, 2H), 8.31 (d, J = 8.8 Hz, 1H), 7.44–7.41 (m, 1H), 7.24–7.23 (m, 4H), 7.18–7.13 (m, 1H), 6.35 (dt, J = 15.6, 5.6 Hz, 1H), 6.21 (d, J = 16.4 Hz, 1H), 3.90 (d, J = 5.6 Hz, 2H), 2.53 (s, 3H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.5, 147.0, 138.3, 137.4, 135.8, 133.2, 132.8, 130.7, 128.6, 127.9, 127.3, 127.2, 126.4, 126.1, 121.6, 119.6, 40.5, 31.1, 27.9, 20.7. IR (neat): 3369, 2962, 1678, 1578, 1527, 1481, 1406, 1364, 1179, 966, 929, 891. HRMS (ESI$^+$): calcd for $C_{24}H_{27}N_2O$ $[M+H]^+$ 359.2123, found 359.2126.



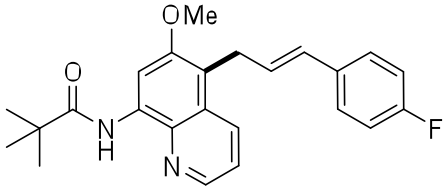
(*E*)-*N*-(5-Cinnamyl-6-methoxyquinolin-8-yl)pivalamide (Table 3, 3u)

The general procedure was applied to *N*-(6-methoxyquinolin-8-yl)pivalamide (51.6 mg, 0.2 mmol), (*E*)-cinnamic alcohol (80.4 mg, 0.6 mmol) at 140 ºC for 30 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/40) to afford the title compound as a slight yellow oil (59 mg, 79% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.39 (brs, 1H), 8.83 (s, 1H), 8.64 (d, *J* = 4.0 Hz, 1H), 8.25 (d, *J* = 8.4 Hz, 1H), 7.41–7.38 (m, 1H), 7.24–7.20 (m, 4H), 7.12 (t, *J* = 7.6 Hz, 1H), 6.34 (dt, *J* = 15.6, 5.6 Hz, 1H), 6.24 (d, *J* = 16.4 Hz, 1H), 4.02 (s, 3H), 3.90 (d, *J* = 5.6 Hz, 2H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.7, 155.2, 145.6, 137.6, 134.83, 134.80, 132.3, 130.2, 128.9, 128.5, 127.9, 127.0, 126.1, 122.0, 113.9, 104.4, 56.6, 40.5, 27.9, 27.7. IR (neat): 3361, 2961, 1677, 1617, 1578, 1522, 1483, 1455, 1401, 1349, 1212, 1169, 1113, 965, 937, 867. HRMS (ESI$^+$): calcd for $C_{24}H_{27}N_2O_2$ $[M+H]^+$ 375.2073, found 375.2077.



(*E*)-*N*-(5-(3-(4-Fluorophenyl)allyl)-6-methylquinolin-8-yl)pivalamide (Table 3, 3v)

The general procedure was applied to *N*-(6-methylquinolin-8-yl)pivalamide (48.4 mg, 0.2 mmol), (*E*)-3-(4-fluorophenyl)prop-2-en-1-ol (91.2 mg, 0.6 mmol) at 140 ºC for 30 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/40) to afford the title compound as a white solid (67 mg, 89% yield). Melting point: 141–143 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.29 (brs, 1H), 8.74 (m, 2H), 8.29 (d, *J* = 8.4 Hz, 1H), 7.44–7.41 (m, 1H), 7.16 (t, *J* = 6.0 Hz, 2H), 6.89 (t, *J* = 8.4 Hz, 2H), 6.25 (dt, *J* = 16.0, 5.6 Hz, 1H), 6.07 (d, *J* = 16.0 Hz, 1H), 3.87 (d, *J* = 5.2 Hz, 2H), 2.52 (s, 3H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.5, 163.3, 160.9, 147.0, 138.3, 135.8, 133.5 (d, *J* = 3.0 Hz), 133.2, 132.7, 129.5, 127.6 (d, *J* = 3.0 Hz), 127.5, 127.1, 126.3, 121.6, 119.6, 115.5, 115.3, 40.5, 31.0, 27.9, 20.6; ^{19}F NMR (377 MHz, $CDCl_3$): δ = –115.19. IR (neat): 3364, 2965, 1675, 1526, 1481, 1406, 1227, 1179, 967, 928, 842. HRMS (ESI$^+$): calcd for $C_{24}H_{26}FN_2O$ $[M+H]^+$ 377.2029, found 377.2032.

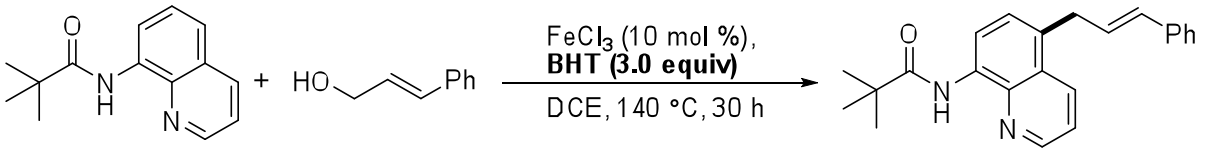


(*E*)-*N*-(5-(3-(4-Fluorophenyl)allyl)-6-methoxyquinolin-8-yl)pivalamide (Table 3, 3w)

The general procedure was applied to *N*-(6-methoxyquinolin-8-yl)pivalamide (51.6 mg, 0.2 mmol), (*E*)-3-(4-fluorophenyl)prop-2-en-1-ol (91.2 mg, 0.6 mmol) at 140 ºC for 30 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/40) to afford the title compound as a slight yellow solid (70 mg, 89% yield). Melting point: 121–123 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.38 (brs, 1H), 8.83 (s, 1H), 8.65 (d, J = 3.6 Hz, 1H), 8.24 (d, J = 8.4 Hz, 1H), 7.42–7.39 (m, 1H), 7.18 (t, J = 6.4 Hz, 2H), 6.89 (t, J = 8.4 Hz, 2H), 6.26 (dt, J = 15.6, 5.2 Hz, 1H), 6.19 (d, J = 16.0 Hz, 1H), 4.02 (s, 3H), 3.89 (d, J = 5.2 Hz, 2H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.7, 163.3, 160.8, 155.2, 145.6, 134.8 (d, J = 2.0 Hz), 133.8 (d, J = 3.0 Hz), 132.2, 129.0, 128.6 (d, J = 3.0 Hz), 127.9, 127.6, 127.5, 122.0, 115.5, 113.8, 104.4, 56.6, 40.6, 27.9, 27.6; ^{19}F NMR (377 MHz, $CDCl_3$): δ = –115.57. IR (neat): 3360, 2967, 1674, 1525, 1486, 1456, 1401, 1349, 1228, 1113, 967, 937, 841. HRMS (ESI$^+$): calcd for $C_{24}H_{26}FN_2O_2$ $[M+H]^+$ 393.1978, found 393.1976.

5. Preliminary Mechanistic Experiments

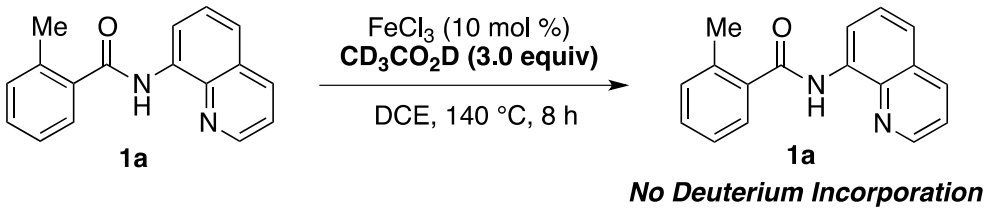
5.1 The Effect of Radical Scavenger on the Reaction of *N*-(quinolin-8-yl)pivalamide with Cinnamic Alcohol



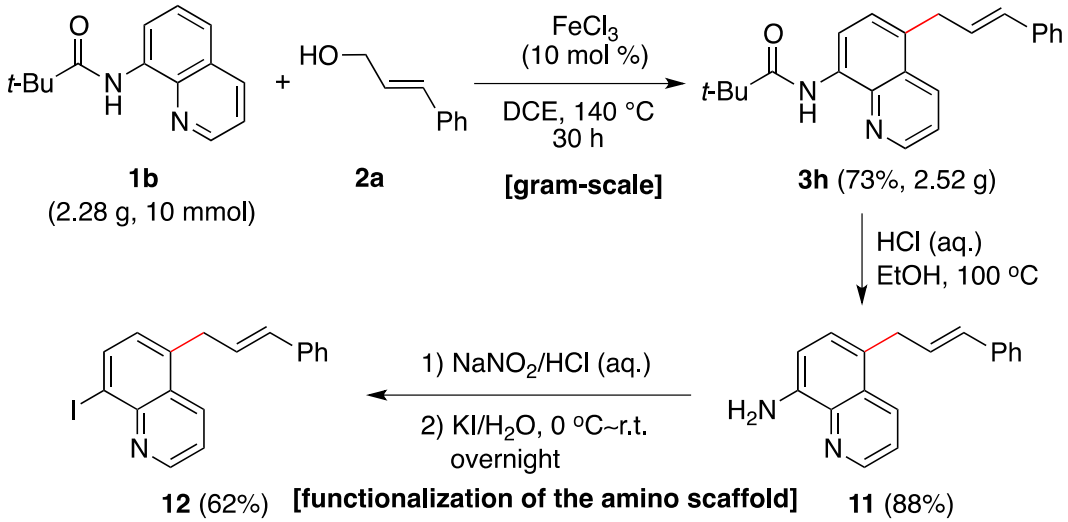
In a dried Schlenk flask were placed *N*-(quinolin-8-yl)pivalamide (45.6 mg, 0.2 mmol), (*E*)-cinnamic alcohol (80.4 mg, 0.6 mmol), butylated hydroxytoluene (132.0 mg, 0.6 mmol), and $FeCl_3$ (3.2 mg, 0.02 mmol). Then 1.0 mL of DCE was added with a syringe under molecular nitrogen atmosphere. The resulting mixture was heated at 140 ºC for 30 h. After cooling to room temperature, the reaction mixture was diluted with 5.0 mL of CH_2Cl_2 and

filtered through a plug of celite, followed by washing with 10–20 mL of CH_2Cl_2. The combined residue was concentrated under reduced pressure, and then the resulting crude product was purified by column chromatography on silica gel to provide the desired product **3h** (69%).

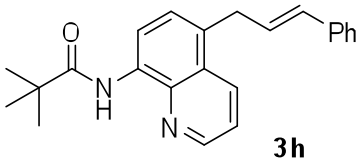
5.2 Deuterium Experiment



6. Gram-Scale C–H Allylation of 1b and Synthetic Application



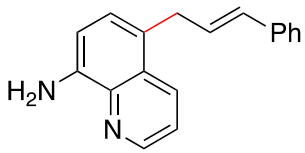
6.1 Synthesis of 3h



In a dried Schlenk flask were placed *N*-(quinolin-8-yl)pivalamide **1b** (2.28 g, 10.0 mmol), (*E*)-cinnamic alcohol **2a** (4.32 g, 30.0 mmol), $FeCl_3$ (162 mg, 1.0 mmol). Then 50 mL of DCE was added with a syringe under molecular nitrogen atmosphere. The resulting mixture was heated at 140 ºC for 30 h. After cooling to room temperature, the reaction mixture was diluted with 25 mL of CH_2Cl_2 and filtered through a plug of celite, followed by washing with

20–30 mL of CH_2Cl_2. The combined residue was concentrated under reduced pressure, and then the resulting crude product was purified by column chromatography on silica gel to provide the desired product **3h** (2.52 g, 73%).

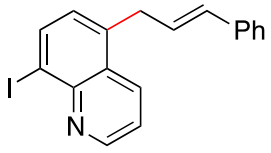
6.2 Synthesis of 11



11 (88%)

3h (1.03 g, 3 mmol) was dissolved in EtOH (20 mL) in a 100 mL tube then concentrated hydrochloric acid (7.5 mL) was added. The tube was sealed and stirred at 100 °C for 24 h. The resulting mixture was concentrated under vacuum and cooled to 0 °C. 3 N NaOH was added dropwise until the pH was alkaline. The solution was extracted with DCM, dried over Na_2SO_4, concentrated under reduced pressure and purified by silica gel chromatography to give **11** as a yellow oil (686 mg, 88 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.76 (d, J = 2.8 Hz, 1H), 8.28 (d, J = 8.4 Hz, 1H), 7.39–7.36 (m, 1H), 7.31–7.22 (m, 6H), 7.16 (t, J = 7.2 Hz, 1H), 6.88 (d, J = 7.6 Hz, 1H), 6.48–6.35 (m, 2H), 4.93 (brs, 2H), 3.84 (d, J = 5.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.2, 143.0, 139.1, 137.6, 132.7, 131.0, 129.6, 128.6, 127.8, 127.6, 126.2, 124.4, 121.2, 109.9, 35.5. IR (neat): 3473, 3373, 3024, 2894, 1610, 1588, 1506, 1477, 1367, 1337, 1124, 965, 822. HRMS (ESI$^+$): calcd for $C_{18}H_{17}N_2$ $[M+H]^+$ 261.1392, found 261.1392.

6.2 Synthesis of 12



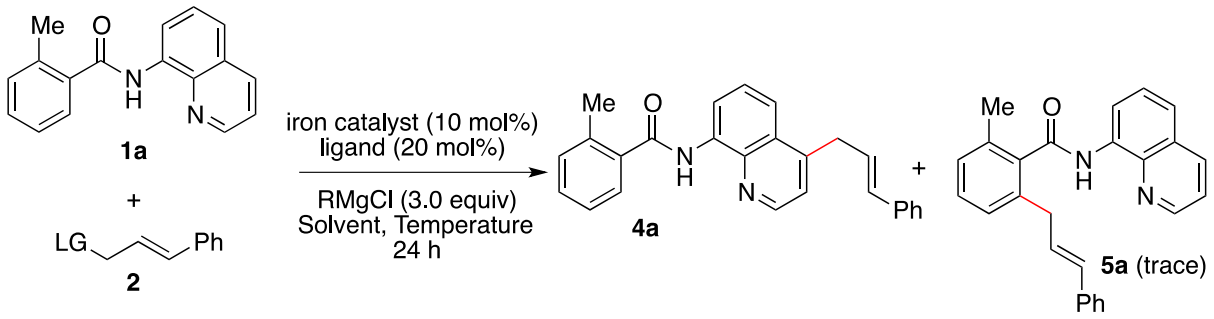
12

A mixture of **6** (156 mg, 0.6 mmol), water (3.0 ml) and concentrated HCl (1.0 mL) was cooled to 0 ^{o}C, and then a solution of $NaNO_2$ (69.0 mg, 1.0 mmol) in water (0.5 mL) was added dropwise. After stirring for 15 min, a solution of KI (166.0 mg, 1.0 mmol) in water (0.5 mL) was added slowly. Then the resulting mixture was warmed to room temperature and

stirred for overnight. The solution was neutralized by 3 N NaOH and the organic phase was extracted with CH_2Cl_2 (10 mL × 3). The combined organic layer was then washed with sodium sulfite aqueous, brine and dried over anhydrous Na_2SO_4. The crude product was purified by silica gel chromatography to give the desired **12** as a white solid (138 mg, 62 %). Melting point: 91–93 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.01 (d, J = 3.2 Hz, 1H), 8.35 (d, J = 8.4 Hz, 1H), 8.29 (d, J = 7.2 Hz, 1H), 7.48–7.45 (m, 1H), 7.31–7.26 (m, 4H), 7.20 (d, J = 7.6 Hz, 1H), 6.47–6.37 (m, 2H), 3.95 (d, J = 4.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.2, 147.5, 140.0, 138.0, 137.1, 133.3, 132.3, 128.7, 128.4, 128.0, 127.7, 127.6, 126.3, 121.9, 102.1, 35.6. IR (neat): 2924, 2853, 1595, 1495, 1453, 1275, 967, 900, 833. HRMS (ESI^+): calcd for $C_{18}H_{15}IN$ $[M+H]^+$ 372.0249, found 372.0253.

7. Investigation of the Key Reaction Parameters for the C4-Allylation of Quinolines

Table S3. *Investigation of the effect of iron catalysts, ligands, Grignard reagents and temperature for the synthesis of (E)-N-(4-cinnamylquinolin-8-yl)-2-methylbenzamide (**4a**)*[a,b]

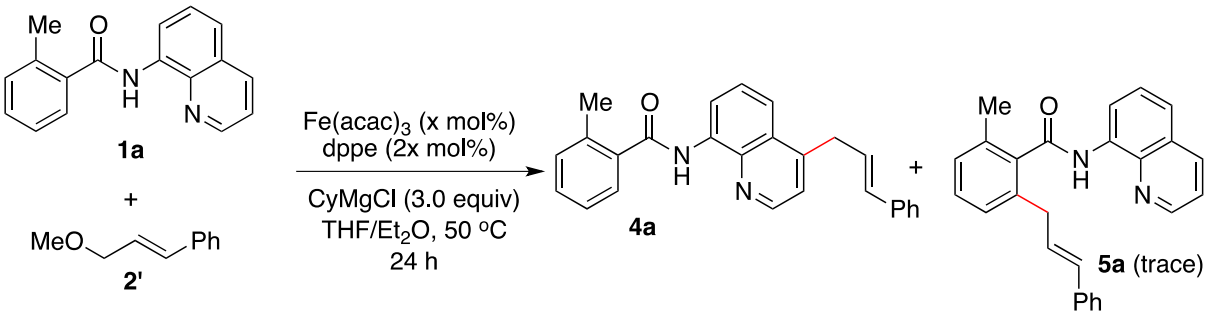


Entry	Iron Catalyst	LG	Ligand	RMgCl	Solvent	Temp (°C)	Yield (**4a**)[c]
1	$Fe(acac)_3$	$OPO(OEt)_2$	dppe	CyMgCl	THF	rt	33%
2	$Fe(acac)_2$	$OPO(OEt)_2$	dppe	CyMgCl	THF	rt	30%
3	$FeCl_2$	$OPO(OEt)_2$	dppe	CyMgCl	THF	rt	trace
4	$Fe(OTf)_2$	$OPO(OEt)_2$	dppe	CyMgCl	THF	rt	32%
5	$Fe(acac)_3$	$OPO(OEt)_2$	-	CyMgCl	THF	rt	trace
6	$Fe(acac)_3$	$OPO(OEt)_2$	dcype	CyMgCl	THF	rt	23%
7	$Fe(acac)_3$	$OPO(OEt)_2$	dppb	CyMgCl	THF	rt	trace
8	$Fe(acac)_3$	$OPO(OEt)_2$	dtbpy	CyMgCl	THF	rt	trace

9	$Fe(acac)_3$	$OPO(OEt)_2$	TMEDA	CyMgCl	THF	rt	trace
10	$Fe(acac)_3$	$OPO(OEt)_2$	dppe	*i*PrMgCl	THF	50	30%
11	$Fe(acac)_3$	$OPO(OEt)_2$	dppe	CyMgCl	Et_2O	rt	n.d.
12	$Fe(acac)_3$	$OPO(OEt)_2$	dppe	CyMgCl	THF	0	n.d.
13	**$Fe(acac)_3$**	**$OPO(OEt)_2$**	**dppe**	**CyMgCl**	**THF**	**50**	**36%**
14	$Fe(acac)_3$	$OPO(OEt)_2$	dppe	CyMgCl	THF	70	trace
15	**$Fe(acac)_3$**	**OMe**	**dppe**	**CyMgCl**	**THF**	**50**	**41%**

[a] Reaction conditions: **1a** (0.3 mmol), **2** (0.45 mmol), Catalyst (10 mol%), Ligand (20 mol %), RMgCl (3.0 equiv), Solvent (0.75 mL), 0-70 ºC, 24 h. [b] Isolated yield. [c] The C5-allylated product **3a** was not detected by ^{1}H NMR and GC analyses.

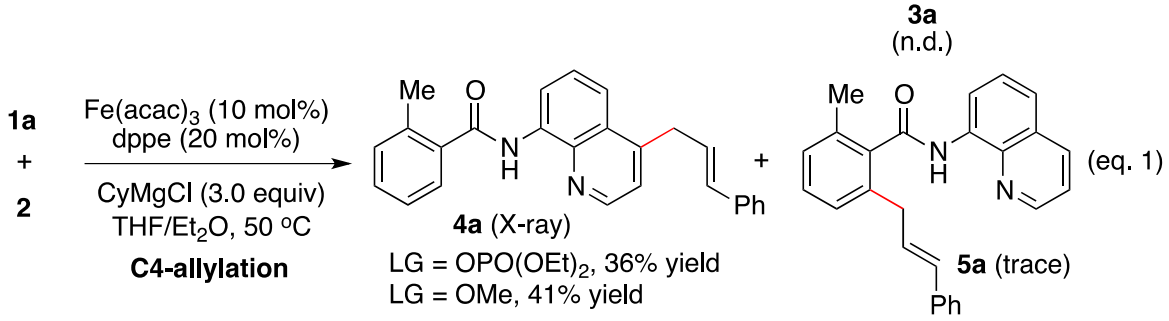
Table S4. *Investigation of the effect of the amount of iron catalyst for the synthesis of (E)-N-(4-cinnamylquinolin-8-yl)-2-methylbenzamide (**4a**)*[a]



Entry	x	**4a**[b]	Recovery (**1a**)[b]
1	10	41%[c]	48%
2	15	41%	46%
3	20	36%	54%
4	30	26%	59%

[a] Reaction conditions: **1a** (0.3 mmol), **2'** (0.45 mmol), $Fe(acac)_3$ (x mol%), dppe (2x mol %), CyMgCl (3.0 equiv), THF (0.75 mL), 50 ºC, 24 h. [b] ^{1}H NMR yield using 1,1,2,2-tetrachloroethane as an internal standard. [c] Isolated yield.

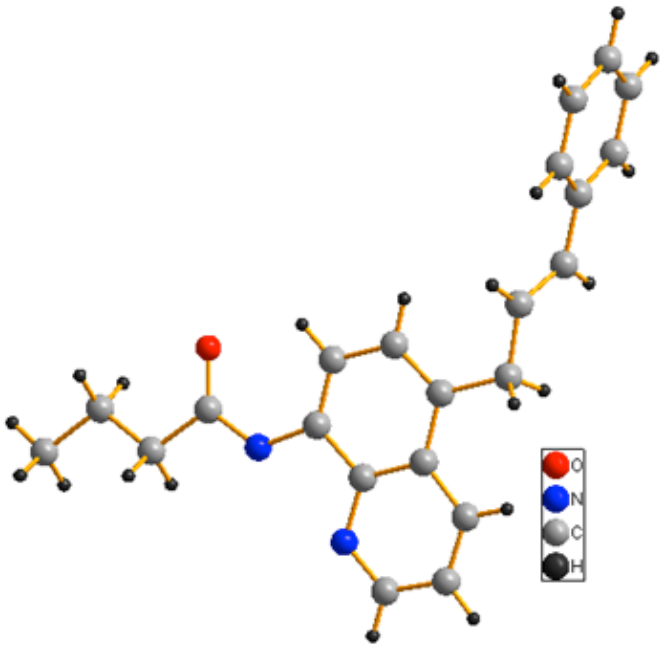
8. Iron-Catalyzed C4-Selective Allylation of 2-Methyl-N-(quinolin-8-yl)-benzamide with Cinnamyl Diethyl Phosphate or Cinnamyl Methyl Ether



In a 10 mL Schlenk tube were placed $Fe(acac)_3$ (10.6 mg, 0.03 mmol), 1,2-bis(diphenylphosphino)ethane (24.0 mg, 0.06 mmol), 2-methyl-*N*-(quinolin-8-yl)-benzamide (78.6 mg, 0.30 mmol), cinnamyl diethyl phosphate (121.5 mg, 0.45 mmol) or cinnamyl methyl ether (66.6 mg, 0.45 mmol), and THF (0.75 mL). To the mixture was added an Et_2O solution of CyMgCl (2.0 M, 0.45 mL, 0.90 mmol) dropwise at 0 °C. The reaction mixture was stirred at 50 °C for 24 h, and then quenched by the addition of saturated NH_4Cl aqueous solution (10.0 mL). The resulting mixture was stirred at room temperature for 10 min, and then extracted with ethyl acetate (3 x 10 mL). The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica gel chromatography (eluent: hexane/EtOAc = 40/1) to afford the title compound as a white solid **4a** (cinnamyl diethyl phosphate: 41 mg, 36%; cinnamyl methyl ether: 46 mg, 41%). Melting point: 165–167 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.34 (brs, 1H), 8.94 (d, J = 7.6 Hz, 1H), 8.69 (d, J = 4.4 Hz, 1H), 7.79 (dd, J = 8.4, 1.2 Hz, 1H), 7.68 (d, J = 7.6 Hz, 1H), 7.60 (t, J = 8.4 Hz, 1H), 7.42–7.28 (m, 8H), 7.20 (tt, J = 7.2, 1.2 Hz, 1H), 6.50 (d, J = 16.0 Hz, 1H), 6.41 (dt, J = 15.6, 6.0 Hz, 1H), 4.00 (d, J = 6.0 Hz, 2H), 2.61 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.4, 148.2, 146.9, 138.8, 137.0, 136.9, 136.8, 135.4, 133.0, 131.5, 130.4, 128.7, 127.7, 127.5, 127.4, 126.5, 126.3, 126.2, 121.9, 117.9, 116.4, 35.7, 20.4. IR (neat): 3315, 3022, 2927, 1665, 1595, 1522, 1479, 1414, 1387, 1333, 1255, 1096, 906, 823, 848. HRMS (ESI^+): calcd for $C_{26}H_{23}N_2O$ $[M+H]^+$ 379.1810, found 379.1803. Crystals suitable for X-ray diffraction study of **4a** were obtained by slow evaporation of a mixed solution of hexane and ethyl acetate.

9. X-ray Crystallographic Data of Compound 3g and Compound 4a

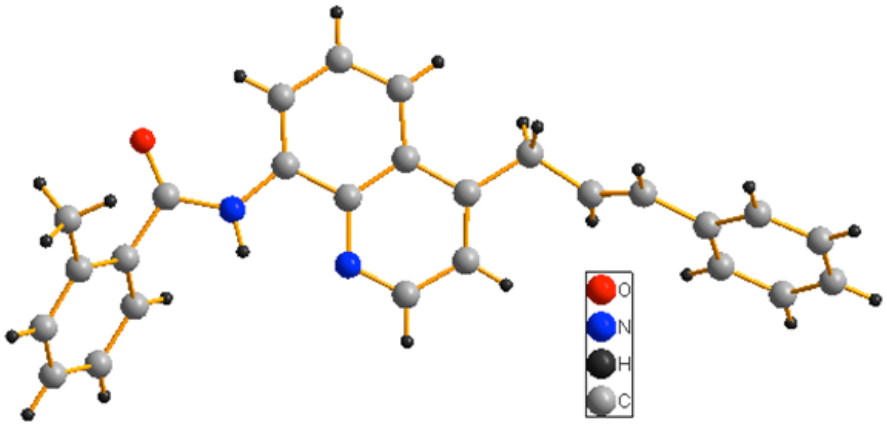
Table S5. Crystallography data and structure refinement for **3g** (CCDC 995433)



Identification code	1
Empirical formula	C22 H21 N2 O
Formula weight	329.41
Temperature	100(2) K
Wavelength	0.71073 A
Crystal system, space group	Monoclinic, P2(1)/c
Unit cell dimensions	a = 16.8889(13) A alpha = 90 deg.
	b= 5.4753(4) A beta = 108.5310(10) deg.
	c = 19.8420(15) A gamma = 90 deg.
Volume	1739.7(2) A^3
Z, Calculated density	4, 1.258 Mg/m^3
Absorption coefficient	0.078 mm^-1
F(000)	700
Theta range for data collection	2.13 to 27.36 deg.

Limiting indices	-17<=h<=21, -7<=k<=7, -25<=l<=25
Reflections collected / unique	21286 / 3923 [R(int) = 0.0210]
Completeness to theta = 27.36	99.9 %
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3923 / 0 / 227
Goodness-of-fit on F^2	1.007
Final R indices [I>2sigma(I)]	R1 = 0.0443, wR2 = 0.1178
R indices (all data)	R1 = 0.0534, wR2 = 0.1253
Largest diff. peak and hole	0.822 and -0.191 e.A^-3

Table S6. Crystallography data and structure refinement for **4a** (CCDC 995432)



Identification code	1
Empirical formula	C26 H22 N2 O
Formula weight	378.46
Temperature	100(2) K
Wavelength	0.71073 A
Crystal system, space group	Triclinic, P-1
Unit cell dimensions	a = 7.4266(9) A alpha = 95.7410(10) deg.
	b = 8.8041(11) A beta = 95.028(2) deg.
	c = 15.597(2) A gamma = 105.542(2) deg.
Volume	970.6(2) A^3
Z, Calculated density	2, 1.295 Mg/m^3
Absorption coefficient	0.079 mm^-1
F(000)	400
Crystal size	0.852 x 0.378 x 0.174 mm
Theta range for data collection	1.32 to 27.82 deg.
Limiting indices	-9<=h<=9, -11<=k<=11, -20<=l<=20
Reflections collected / unique	19765 / 4550 [R(int) = 0.0134]
Completeness to theta = 27.82	99.0 %
Refinement method	Full-matrix least-squares on F^2

Data / restraints / parameters	4550 / 0 / 263
Goodness-of-fit on F^2	1.046
Final R indices [I>2sigma(I)]	R1 = 0.0379, wR2 = 0.1046
R indices (all data)	R1 = 0.0402, wR2 = 0.1071
Largest diff. peak and hole	0.331 and -0.249 e.A^-3

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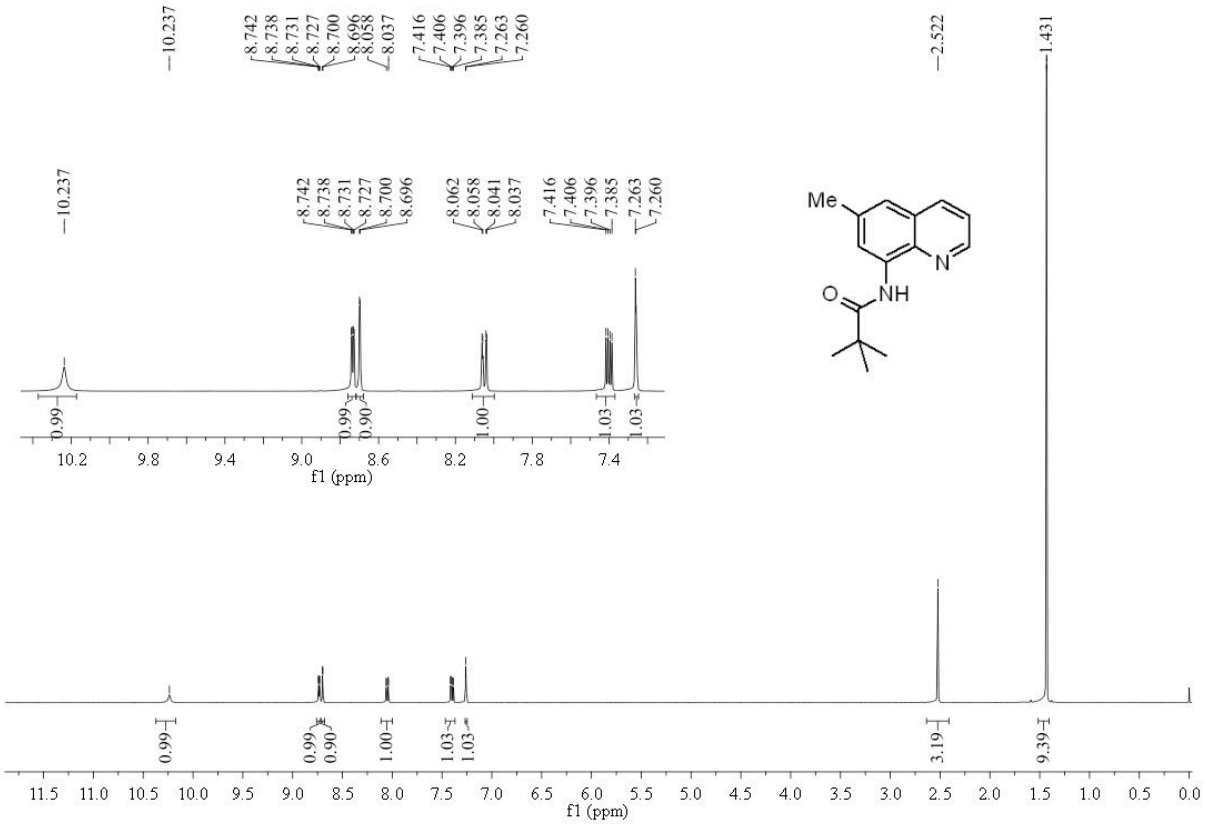
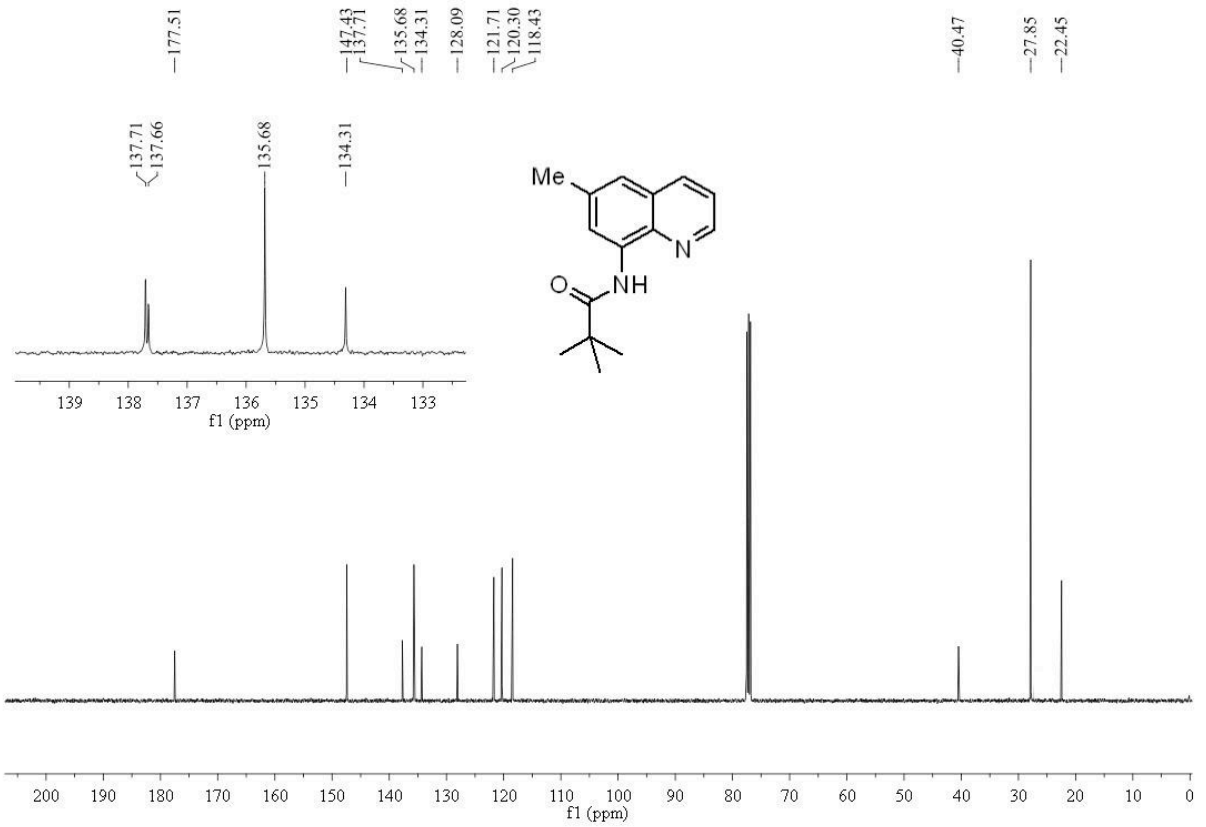
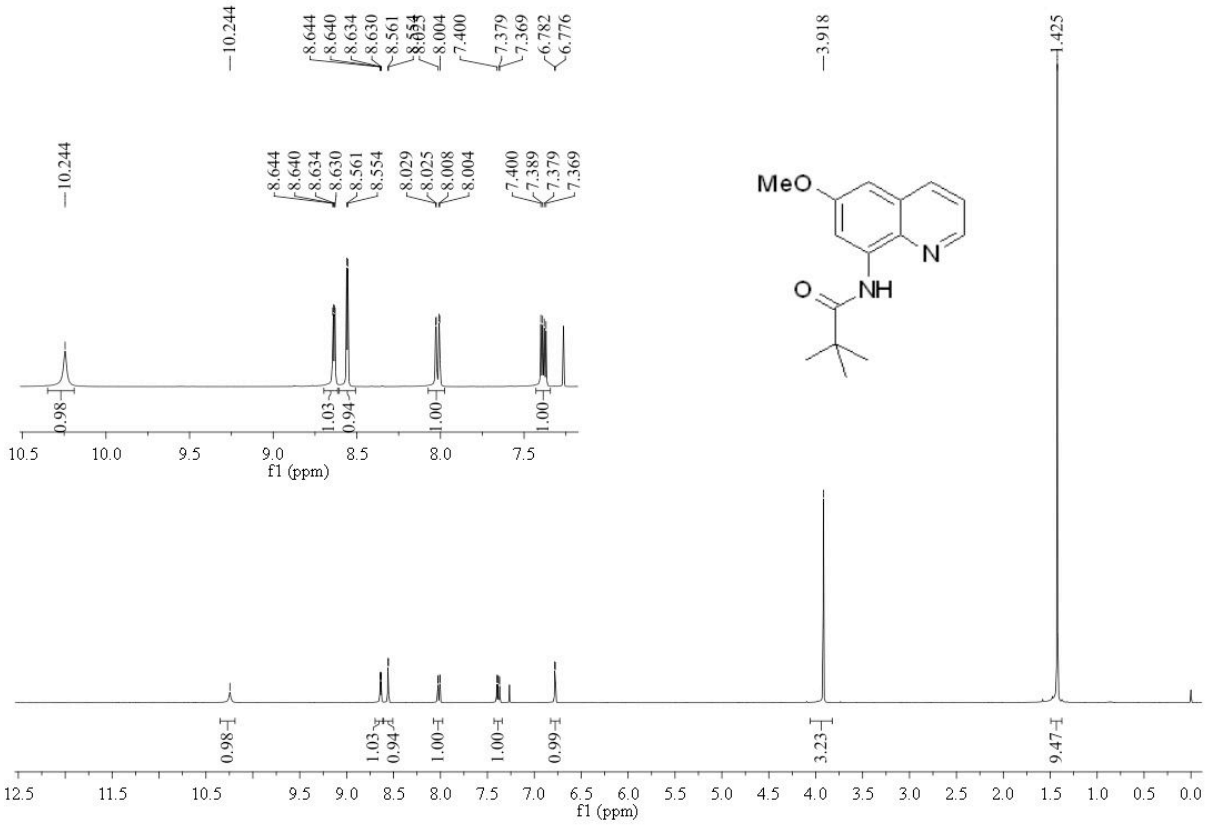
(5) Matsubara, R.; Jamison, T. F. *J. Am. Chem. Soc.* **2010**, *132*, 6880.

10. ^{1}H, ^{13}C and ^{19}F NMR Spectra



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N
O
NH
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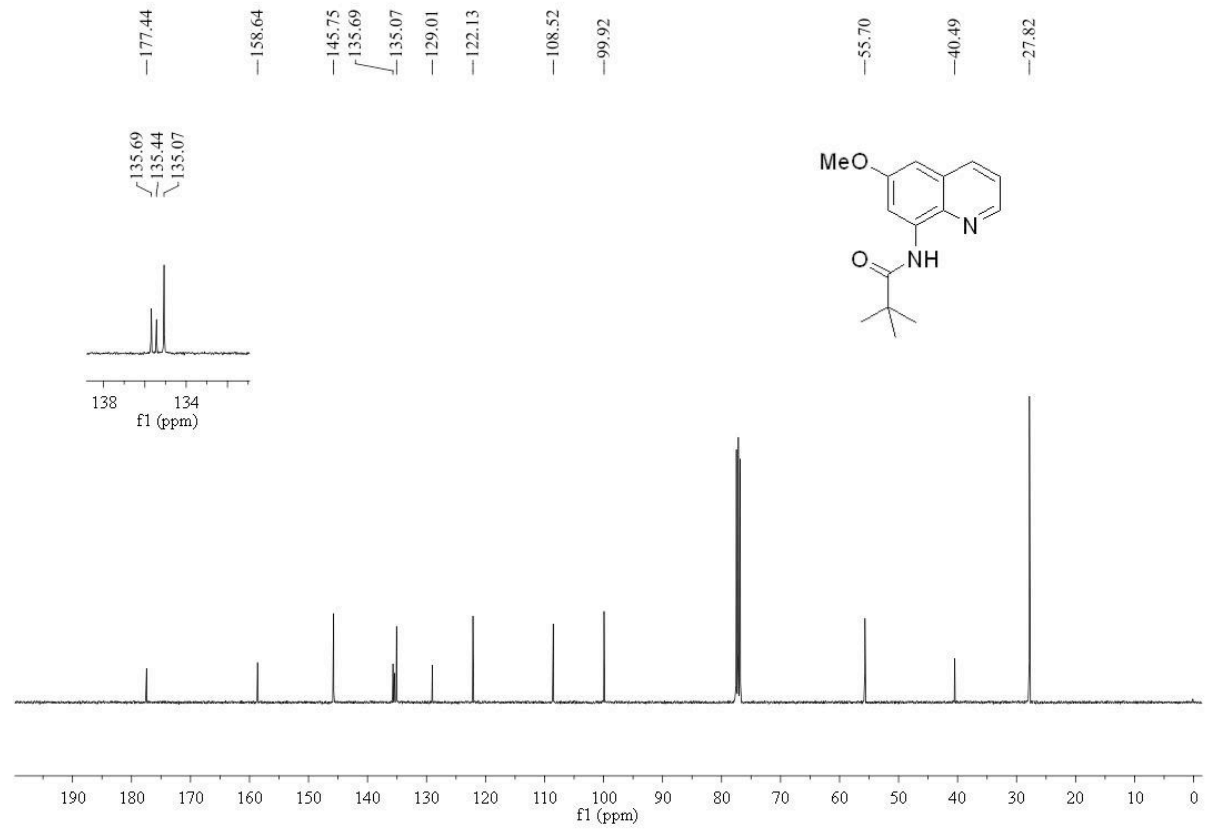
1.03
0.94
1.00
1.00
0.99
3.23
9.47
f1 (ppm)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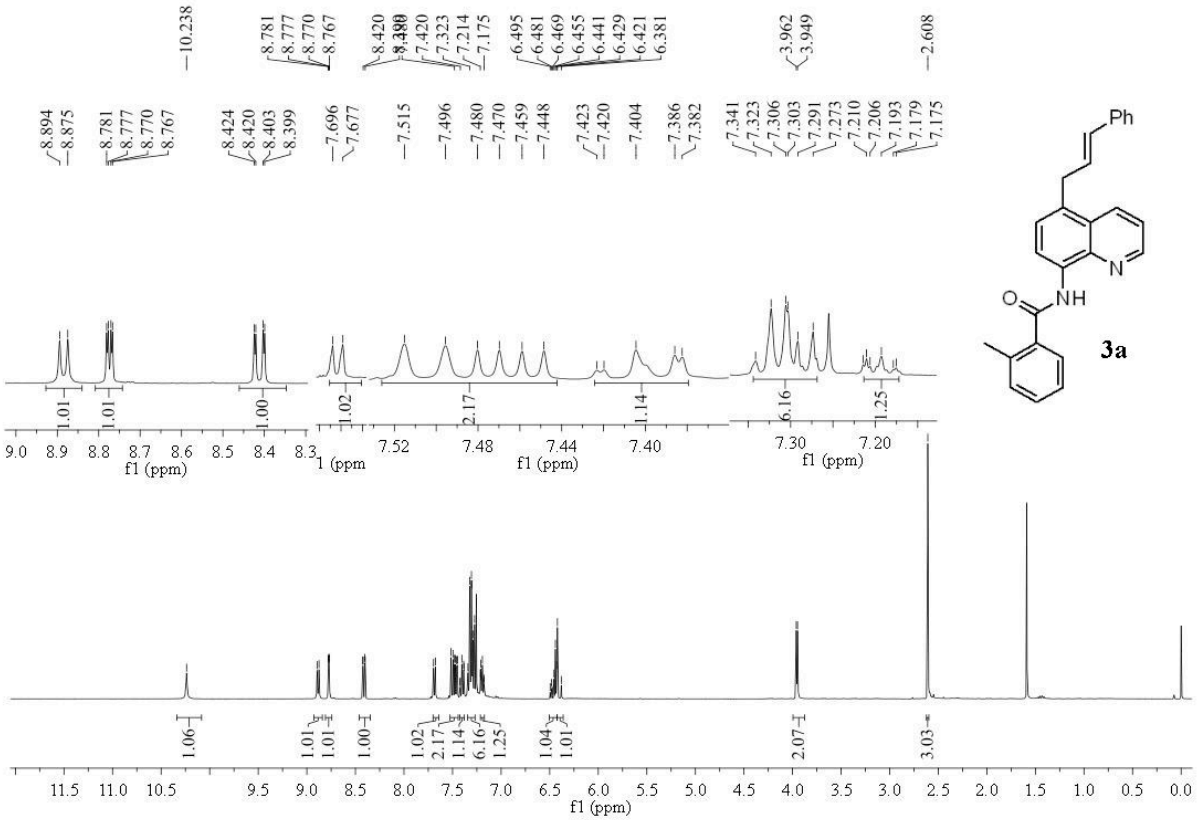
158.64
145.75
135.69
135.07
129.01
122.13
108.52
99.92
55.70
40.49
27.82
MeO
N
O
NH
f1 (ppm)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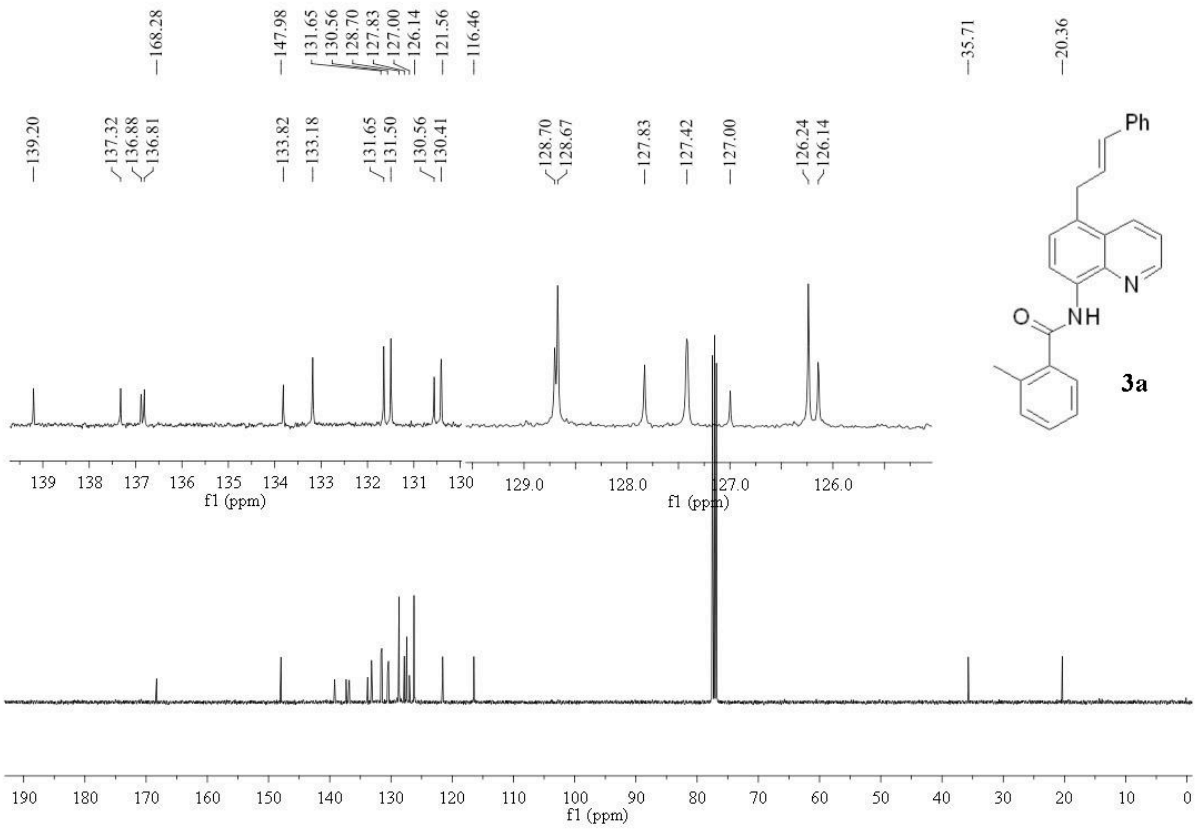
8.777
8.770
8.767
8.420
8.403
8.399
7.515
7.496
7.480
7.470
7.459
7.448
7.423
7.420
7.404
7.386
7.382
7.341
7.323
7.306
7.303
7.291
7.273
7.210
7.206
7.193
7.179
7.175
6.495
6.481
6.469
6.455
6.441
6.429
6.421
6.381
3.962
3.949
2.608
Ph
N
NH
O
3a
f1 (ppm)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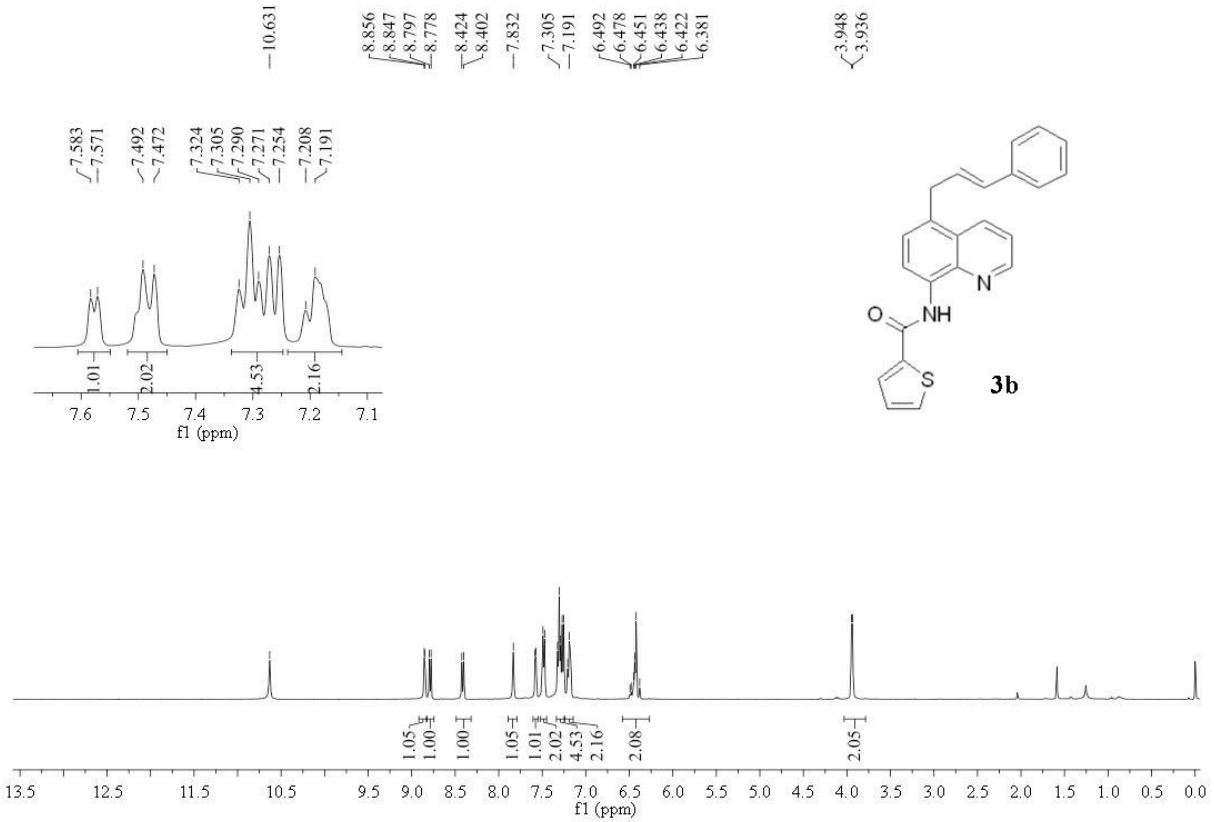
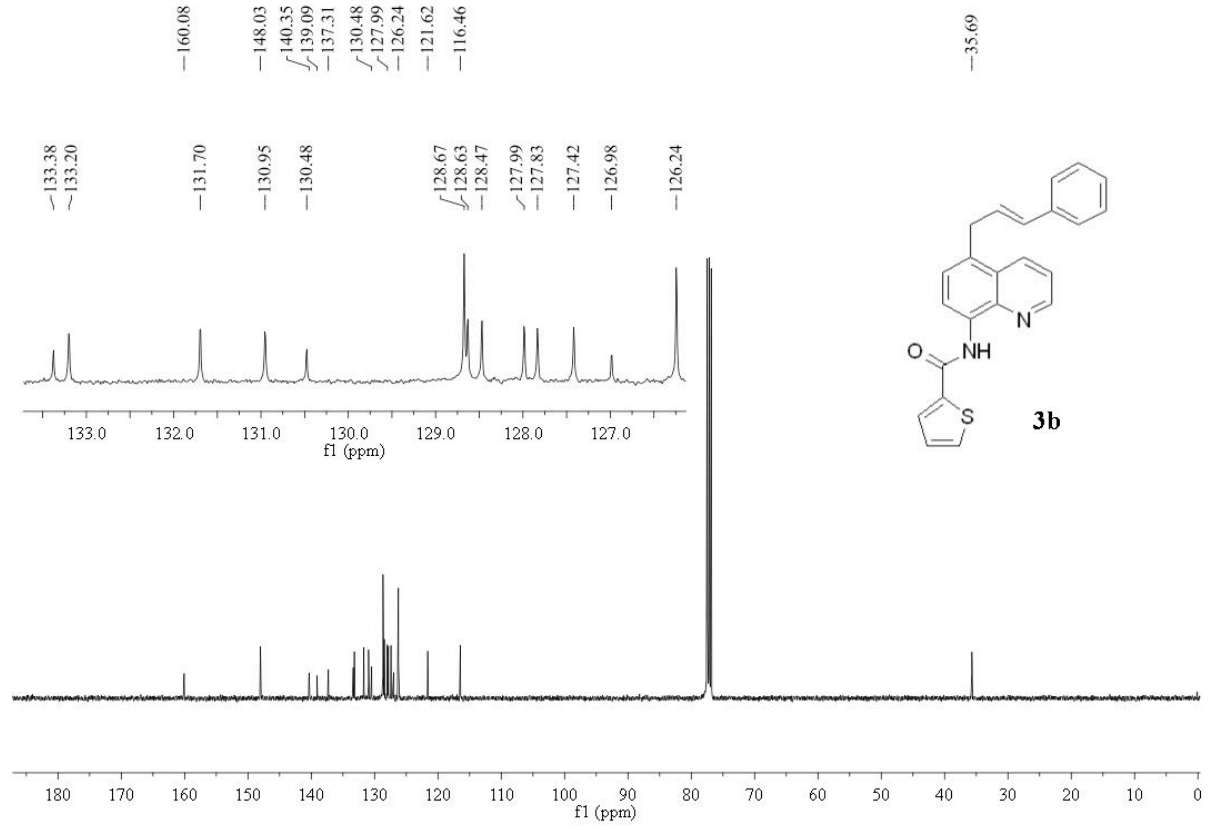
127.83
127.00
126.14
121.56
116.46
35.71
20.36
139.20
137.32
136.88
136.81
133.82
133.18
131.65
131.50
130.56
130.41
128.70
128.67
127.83
127.42
127.00
126.24
126.14
Ph
N
NH
O
3a
f1 (ppm)


10.631
8.856
8.847
8.797
8.778
8.424
8.402
7.832
7.583
7.571
7.492
7.472
7.324
7.305
7.290
7.271
7.254
7.208
7.191
7.305
7.191
6.492
6.478
6.451
6.438
6.422
6.381
3.948
3.936
1.01
2.02
4.53
2.16
f1 (ppm)
N
NH
O
S
3b
1.05
1.00
1.00
1.05
1.01
2.02
4.53
2.16
2.08
2.05
f1 (ppm)


160.08
148.03
140.35
139.09
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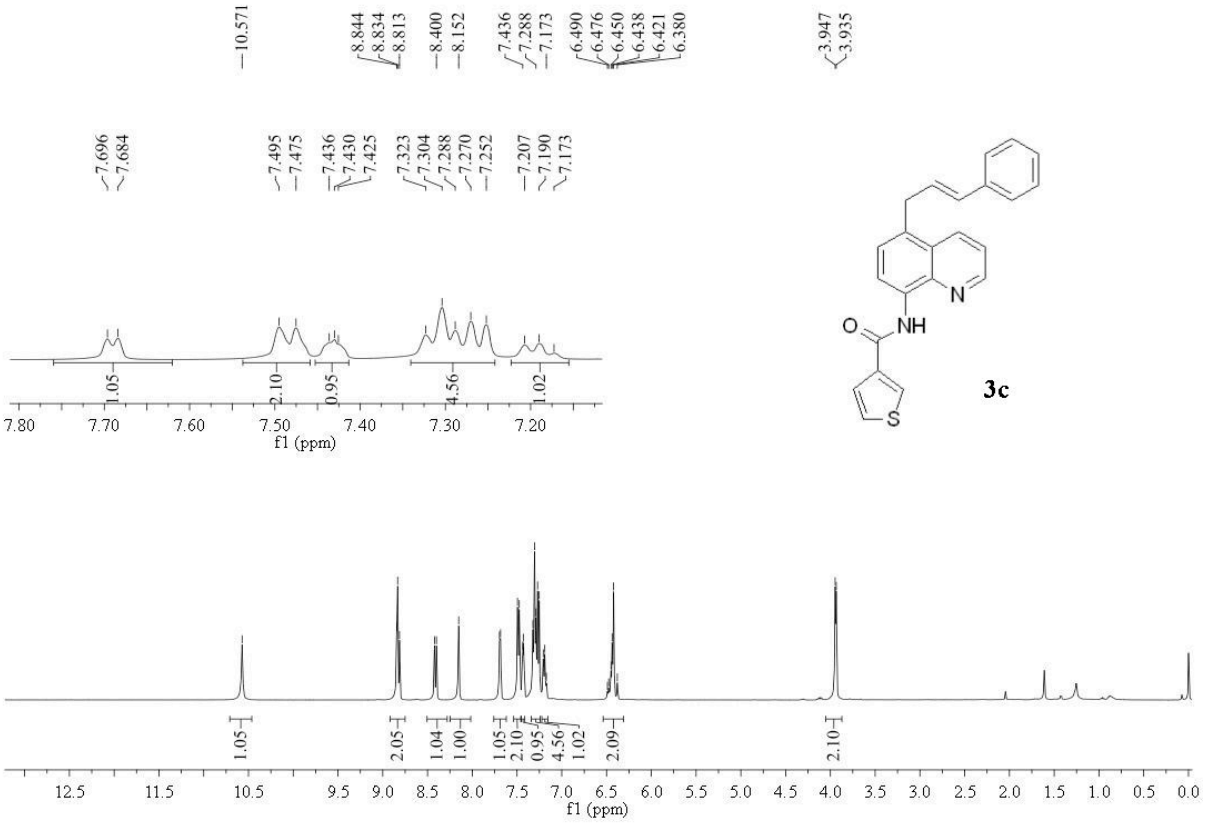
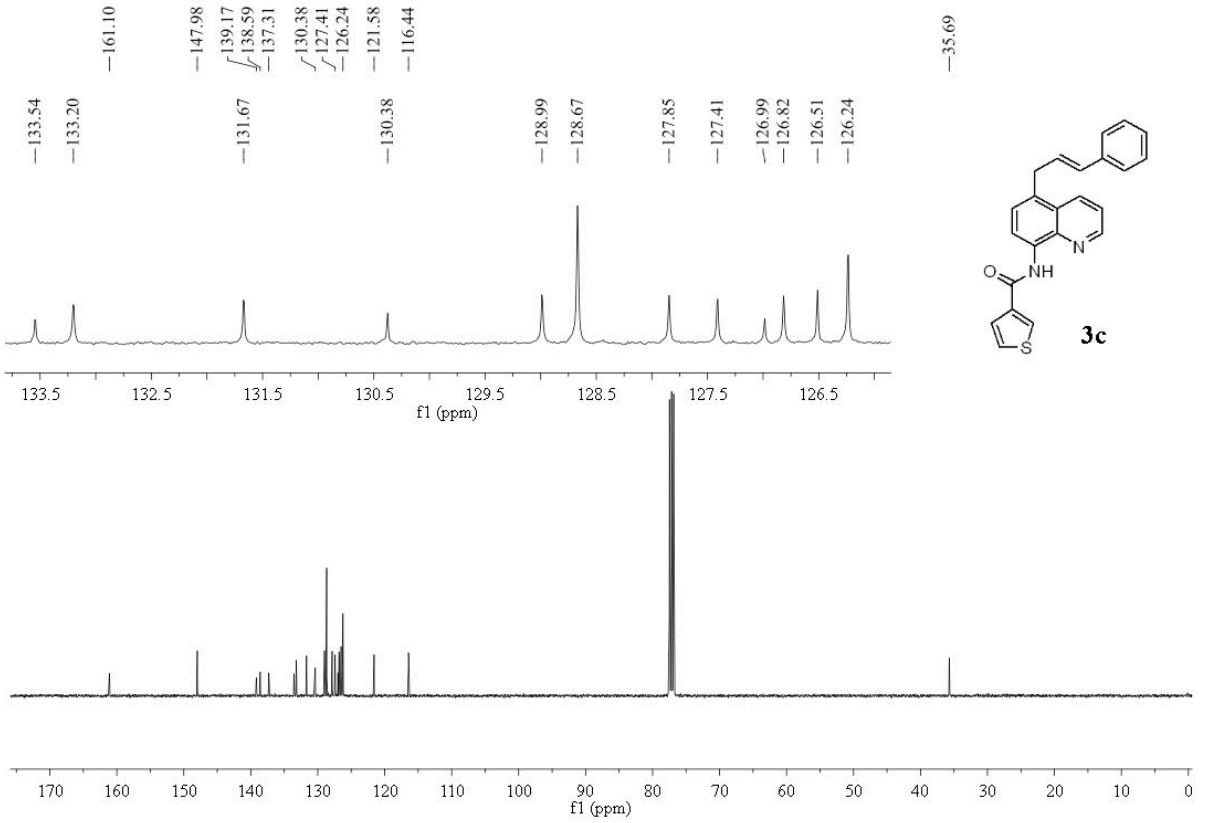
130.48
127.99
126.24
121.62
116.46
35.69
133.38
133.20
131.70
130.95
130.48
128.67
128.63
128.47
127.99
127.83
127.42
126.98
126.24
f1 (ppm)
N
NH
O
S
3b
f1 (ppm)


10.571
8.844
8.834
8.813
8.400
8.152
7.436
7.288
7.173
6.490
6.476
6.450
6.438
6.421
6.380
3.947
3.935
7.696
7.684
7.495
7.475
7.436
7.430
7.425
7.323
7.304
7.288
7.270
7.252
7.207
7.190
7.173
1.05
2.10
0.95
4.56
1.02
7.80
7.70
7.60
7.50
7.40
7.30
7.20
f1 (ppm)
N
NH
O
S
3c
1.05
2.05
1.04
1.00
1.05
2.10
0.95
4.56
1.02
2.09
2.10
12.5
11.5
10.5
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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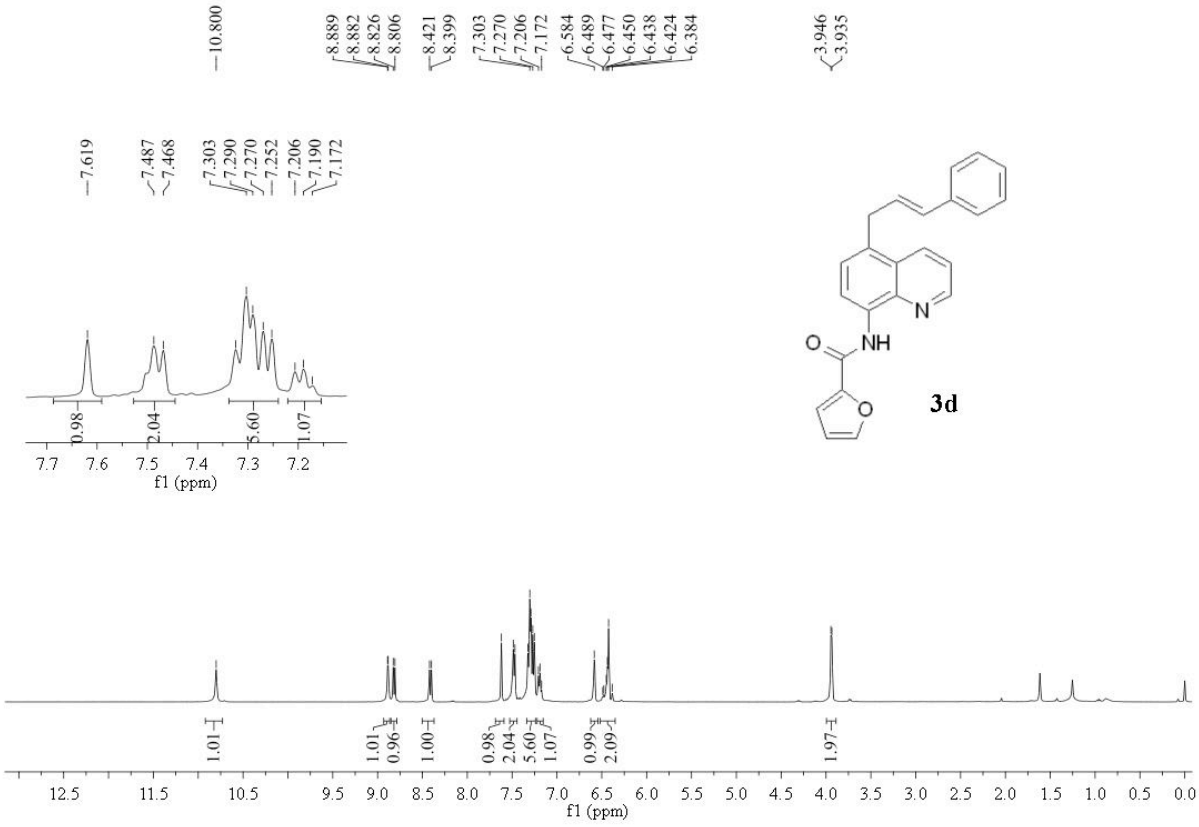
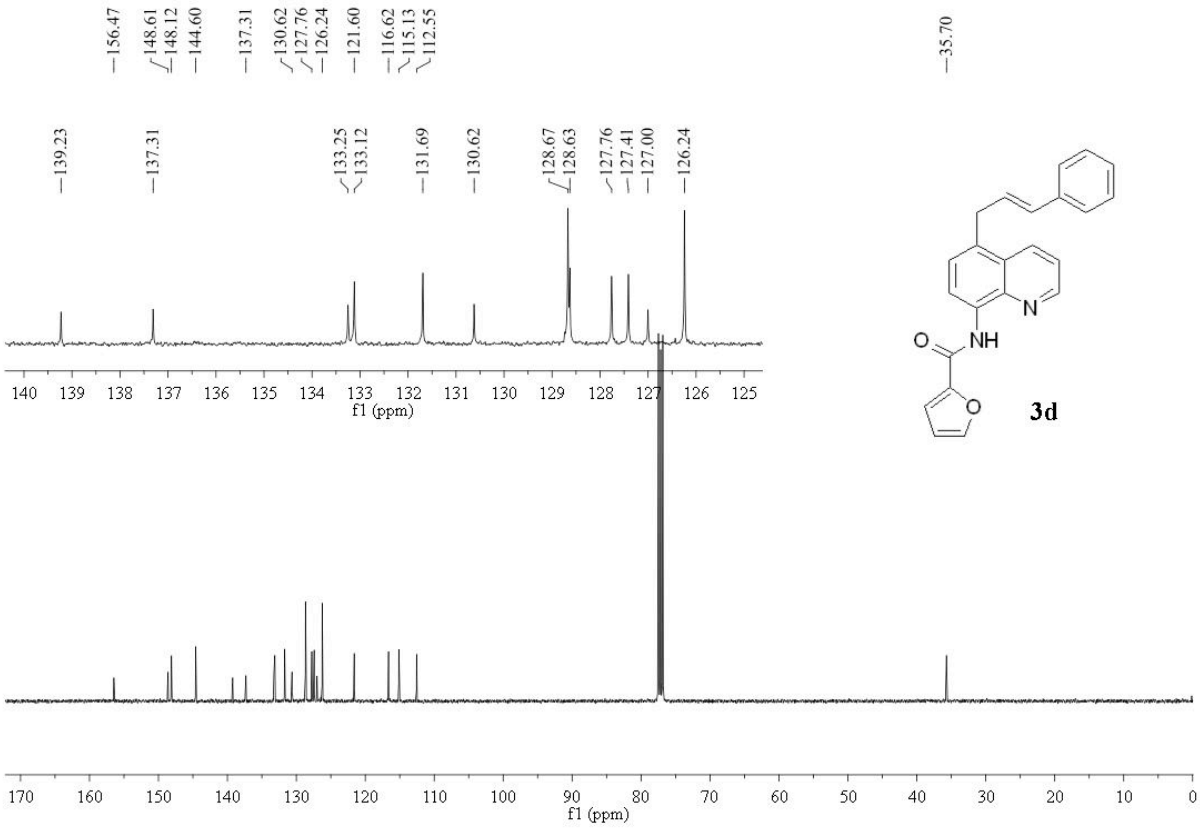
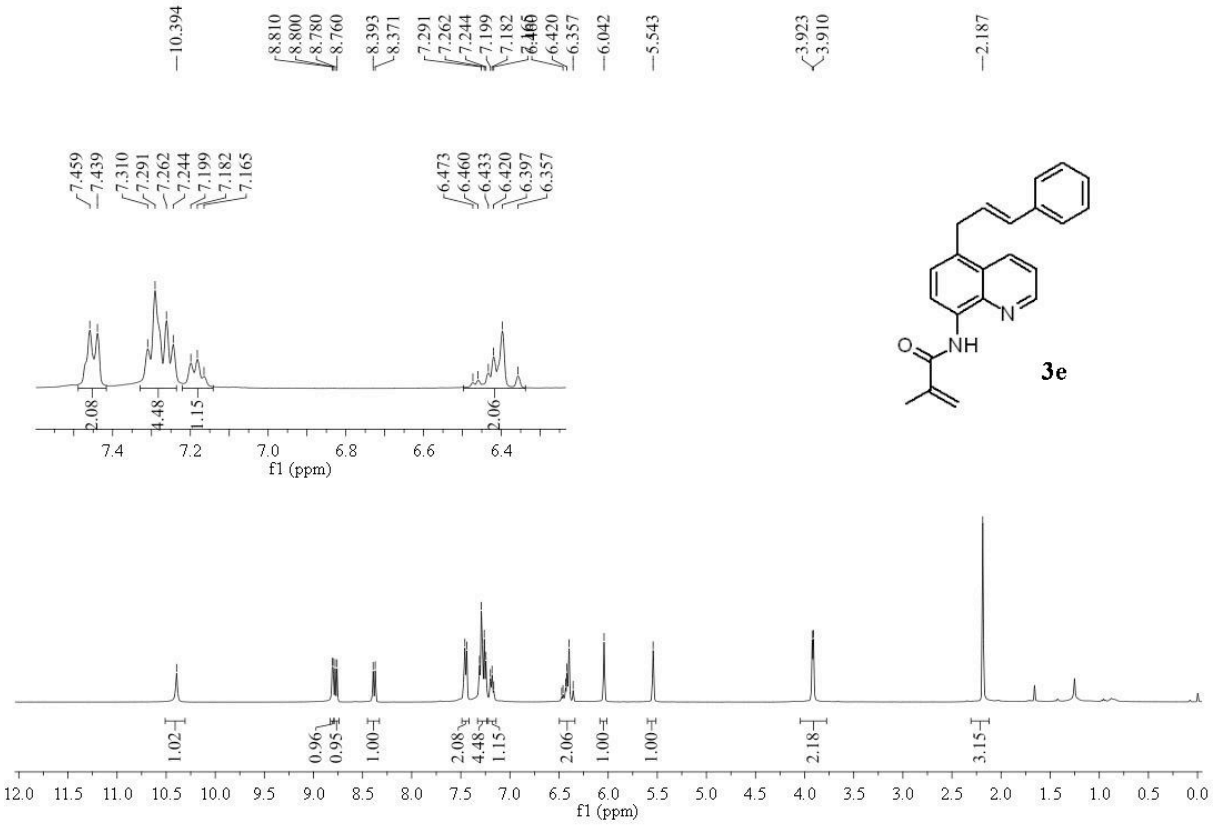
139.17
138.59
137.31
130.38
127.41
126.24
121.58
116.44
35.69
133.54
133.20
131.67
130.38
128.99
128.67
127.85
127.41
126.99
126.82
126.51
126.24
N
NH
O
S
3c
133.5
132.5
131.5
130.5
129.5
128.5
127.5
126.5
f1 (ppm)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


10.800
8.889
8.882
8.826
8.806
8.421
8.399
7.303
7.270
7.206
7.172
6.584
6.489
6.477
6.450
6.438
6.424
6.384
3.946
3.935
7.619
7.487
7.468
7.303
7.290
7.270
7.252
7.206
7.190
7.172
0.98
2.04
5.60
1.07
f1 (ppm)
NH
O
N
O
3d
1.01
1.01
0.96
1.00
0.98
2.04
5.60
1.07
0.99
2.09
1.97
f1 (ppm)


156.47
148.61
148.12
144.60
137.31
130.62
127.76
126.24
121.60
116.62
115.13
112.55
35.70
139.23
137.31
133.25
133.12
131.69
130.62
128.67
128.63
127.76
127.41
127.00
126.24
f1 (ppm)
NH
O
N
O
3d
f1 (ppm)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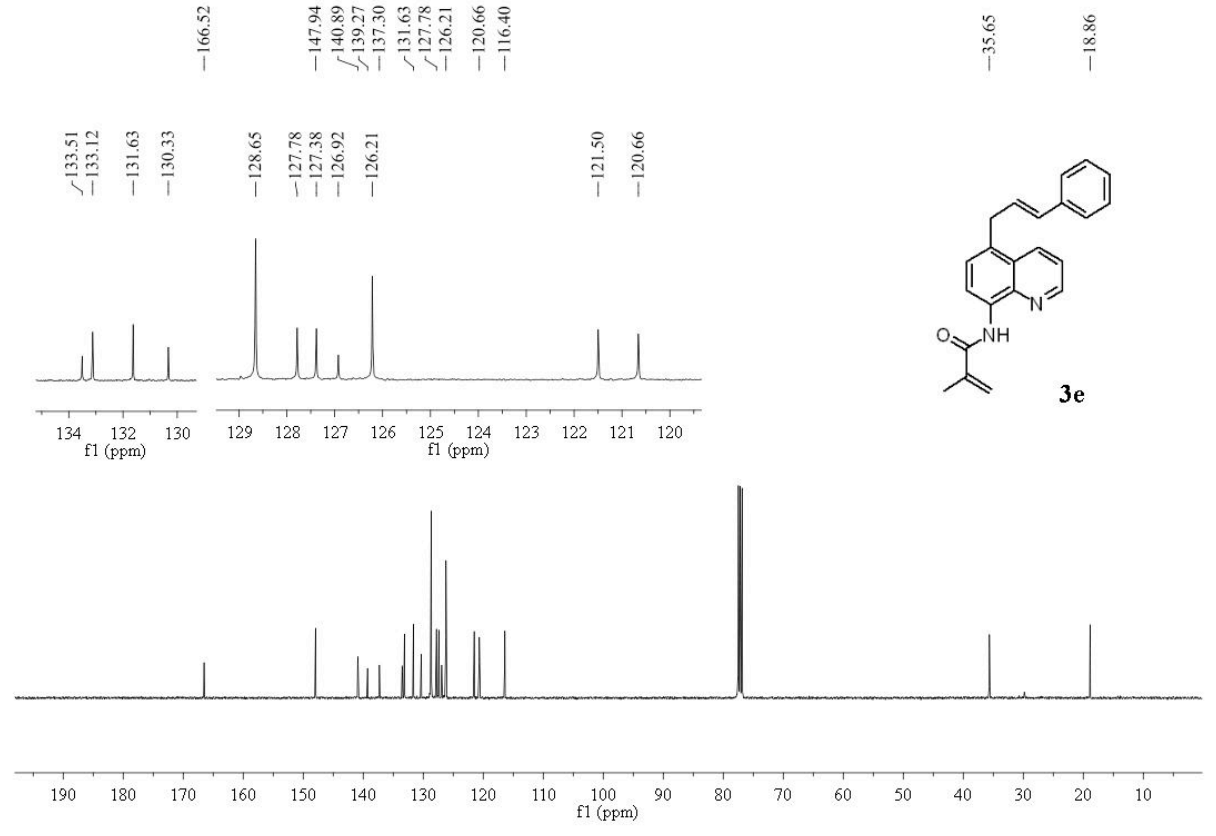
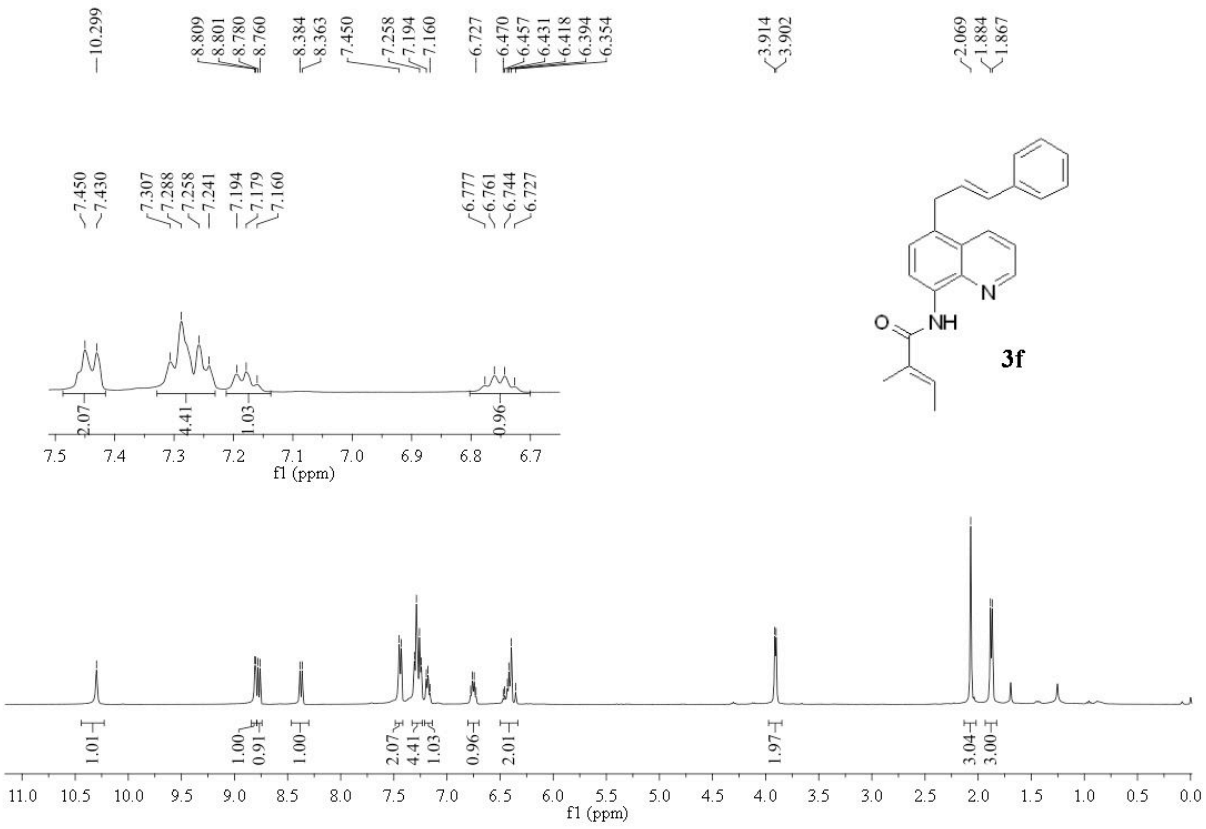
8.810
8.800
8.780
8.760
8.393
8.371
7.291
7.262
7.244
7.199
7.182
6.420
6.357
6.042
5.543
3.923
3.910
2.187
7.459
7.439
7.310
7.291
7.262
7.244
7.199
7.182
7.165
6.473
6.460
6.433
6.420
6.397
6.357
2.08
4.48
1.15
2.06
7.4
7.2
7.0
6.8
6.6
6.4
f1 (ppm)
NH
O
N
3e
1.02
0.96
0.95
1.00
2.08
4.48
1.15
2.06
1.00
1.00
2.18
3.15
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


166.52
147.94
140.89
139.27
137.30
131.63
127.78
126.21
120.66
116.40
35.65
18.86
133.51
133.12
131.63
130.33
128.65
127.78
127.38
126.92
126.21
121.50
120.66
134
132
130
f1 (ppm)
129
128
127
126
125
124
123
122
121
120
f1 (ppm)
NH
O
N
3e
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


10.299
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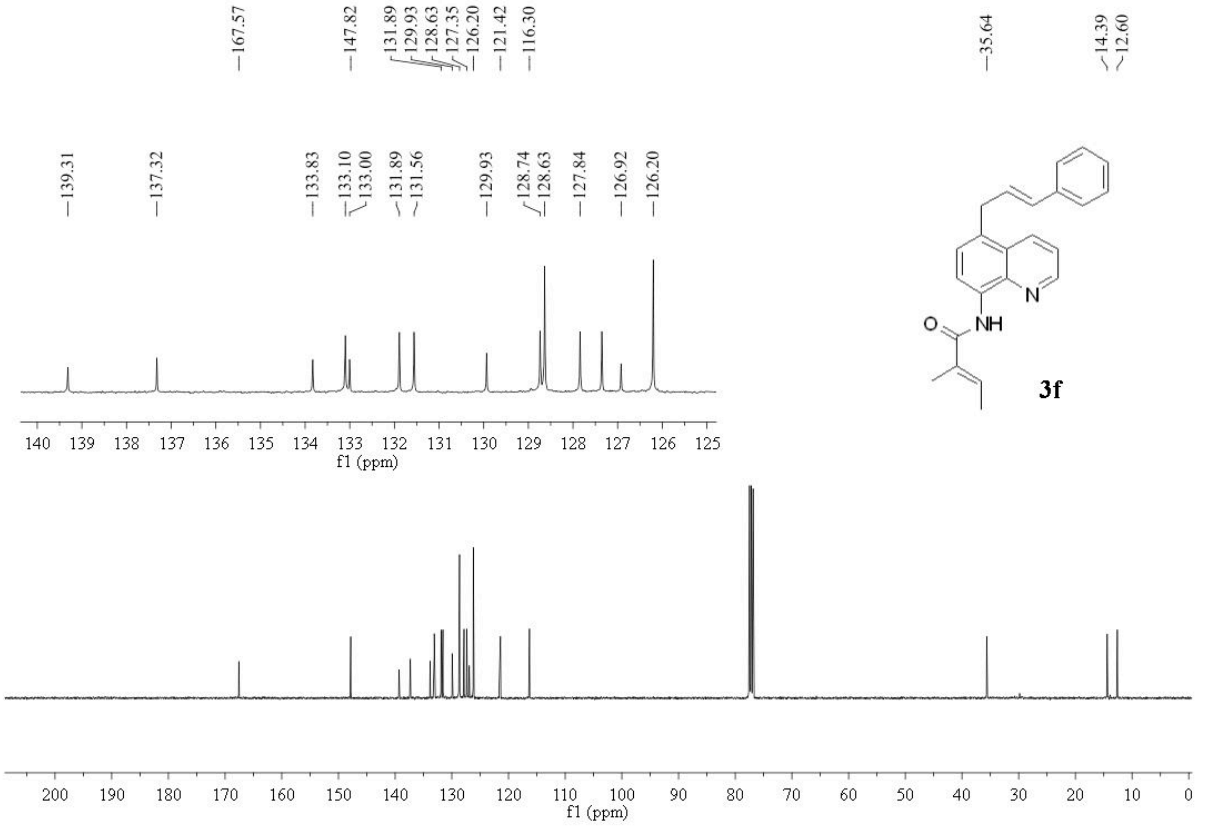
8.801
8.780
8.760
8.384
8.363
7.450
7.258
7.194
7.160
6.727
6.470
6.457
6.431
6.418
6.394
6.354
3.914
3.902
2.069
1.884
1.867
7.450
7.430
7.307
7.288
7.258
7.241
7.194
7.179
7.160
6.777
6.761
6.744
6.727
2.07
4.41
1.03
0.96
f1 (ppm)
O
NH
N
3f
1.01
1.00
0.91
1.00
2.07
4.41
1.03
0.96
2.01
1.97
3.04
3.00
f1 (ppm)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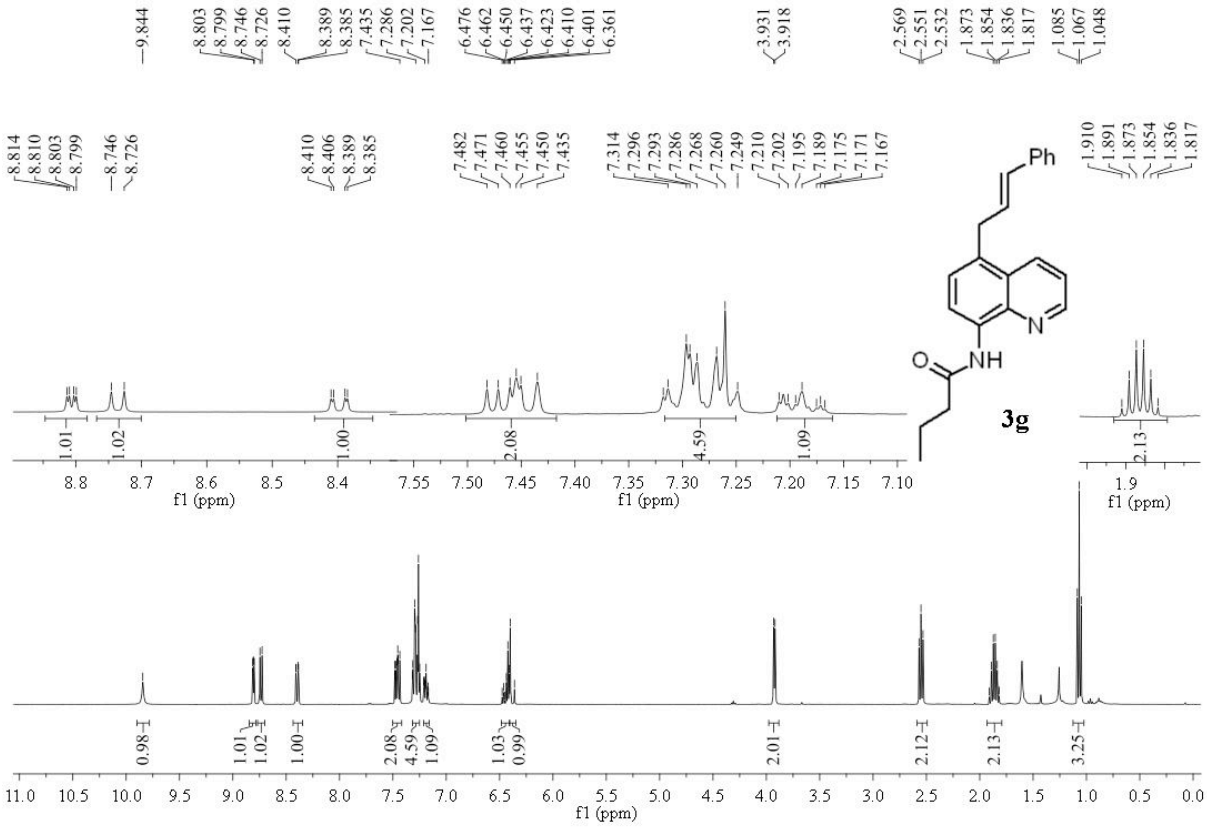
127.35
126.20
121.42
116.30
35.64
14.39
12.60
139.31
137.32
133.83
133.10
133.00
131.89
131.56
129.93
128.74
128.63
127.84
126.92
126.20
f1 (ppm)
O
NH
N
3f
f1 (ppm)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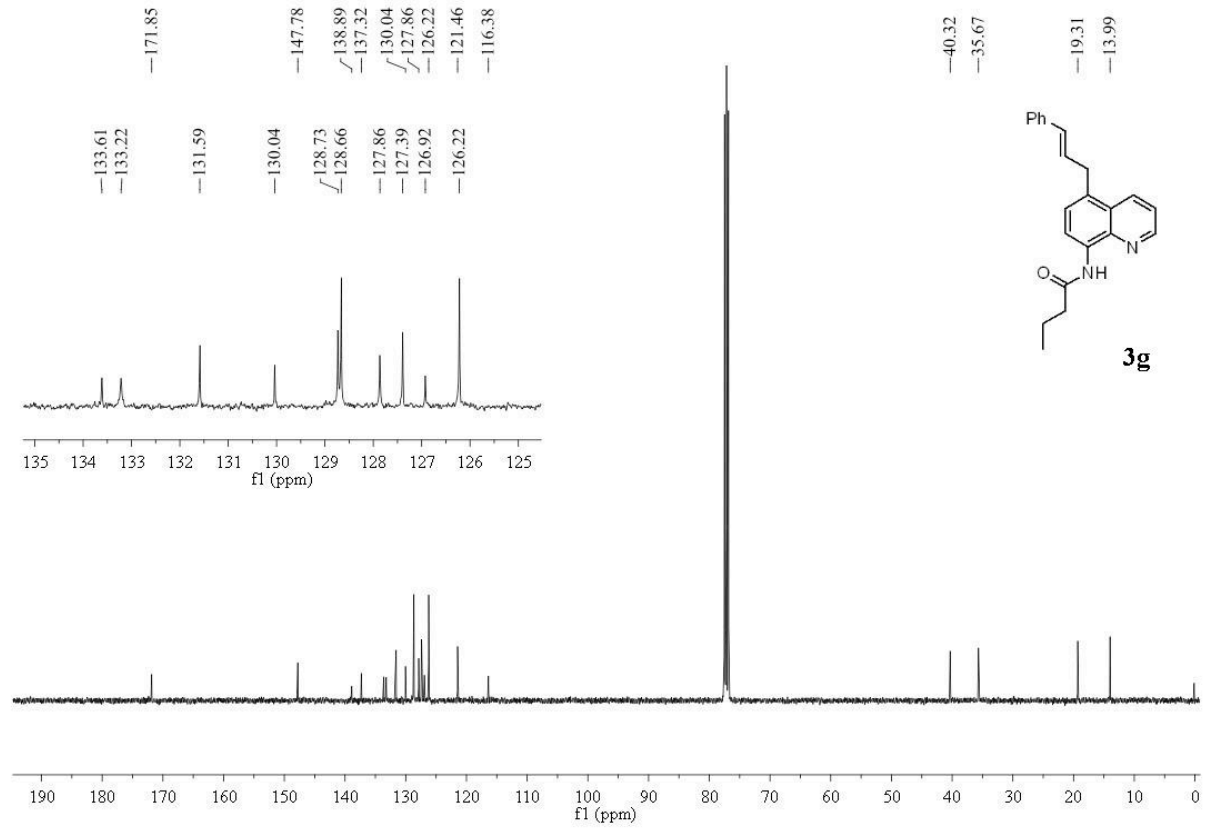
8.385
7.435
7.286
7.202
7.167
6.476
6.462
6.450
6.437
6.423
6.410
6.401
6.361
3.931
3.918
2.569
2.551
2.532
1.873
1.854
1.836
1.817
1.085
1.067
1.048
Ph
N
NH
O
3g
f1 (ppm)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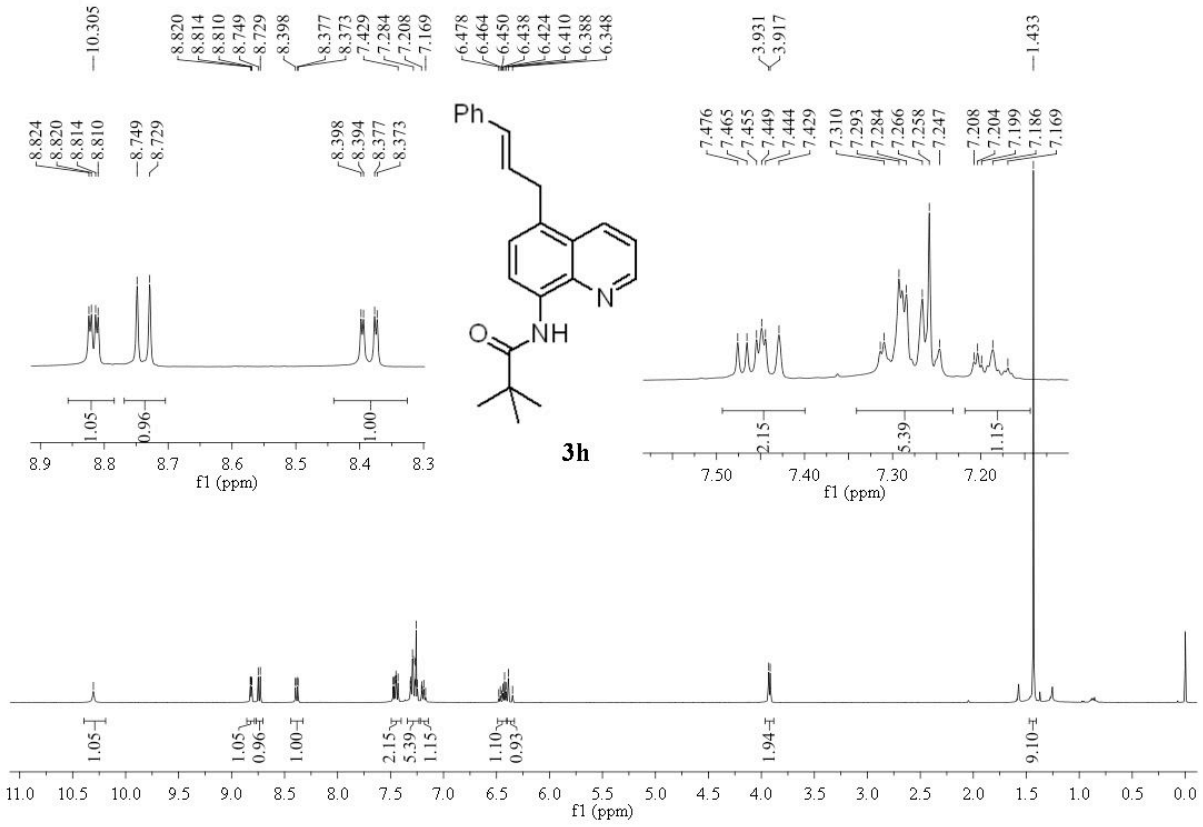
137.32
130.04
127.86
126.22
121.46
116.38
40.32
35.67
19.31
13.99
133.61
133.22
131.59
130.04
128.73
128.66
127.86
127.39
126.92
126.22
Ph
N
NH
O
3g
f1 (ppm)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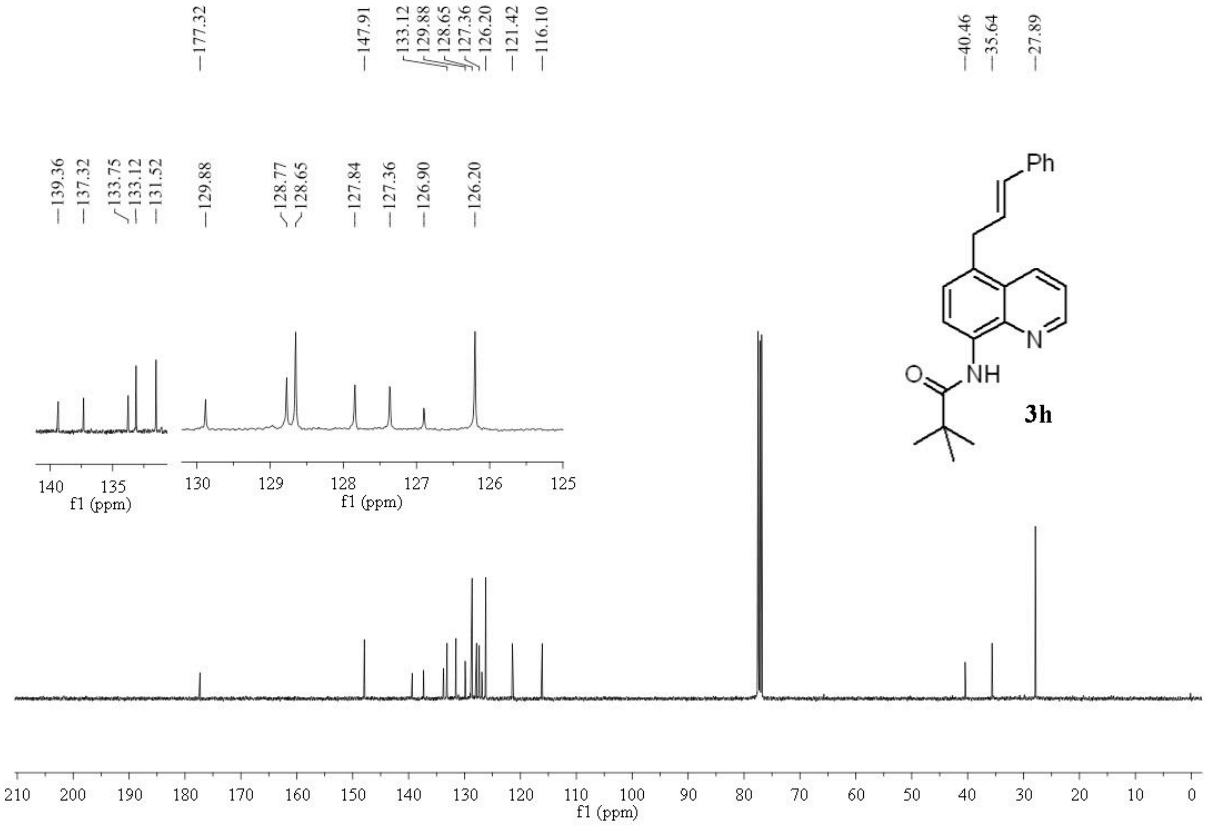
8.749
8.729
8.398
8.377
8.373
7.429
7.284
7.208
7.169
6.478
6.464
6.450
6.438
6.424
6.410
6.388
6.348
3.931
3.917
1.433
7.476
7.465
7.455
7.449
7.444
7.429
7.310
7.293
7.284
7.266
7.258
7.247
7.208
7.204
7.199
7.186
7.169
Ph
N
O
NH
3h
1.05
0.96
1.00
2.15
5.39
1.15
1.10
0.93
1.94
9.10
f1 (ppm)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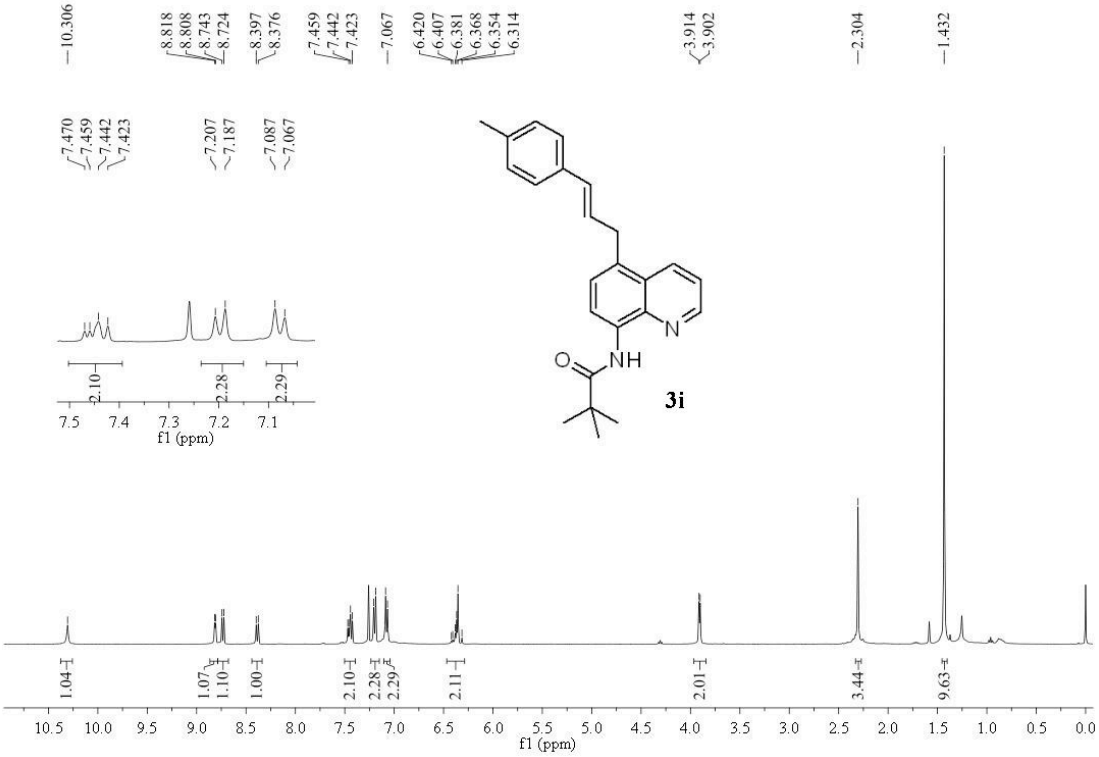
129.88
128.65
127.36
126.20
121.42
116.10
40.46
35.64
27.89
139.36
137.32
133.75
133.12
131.52
129.88
128.77
128.65
127.84
127.36
126.90
126.20
Ph
N
O
NH
3h
f1 (ppm)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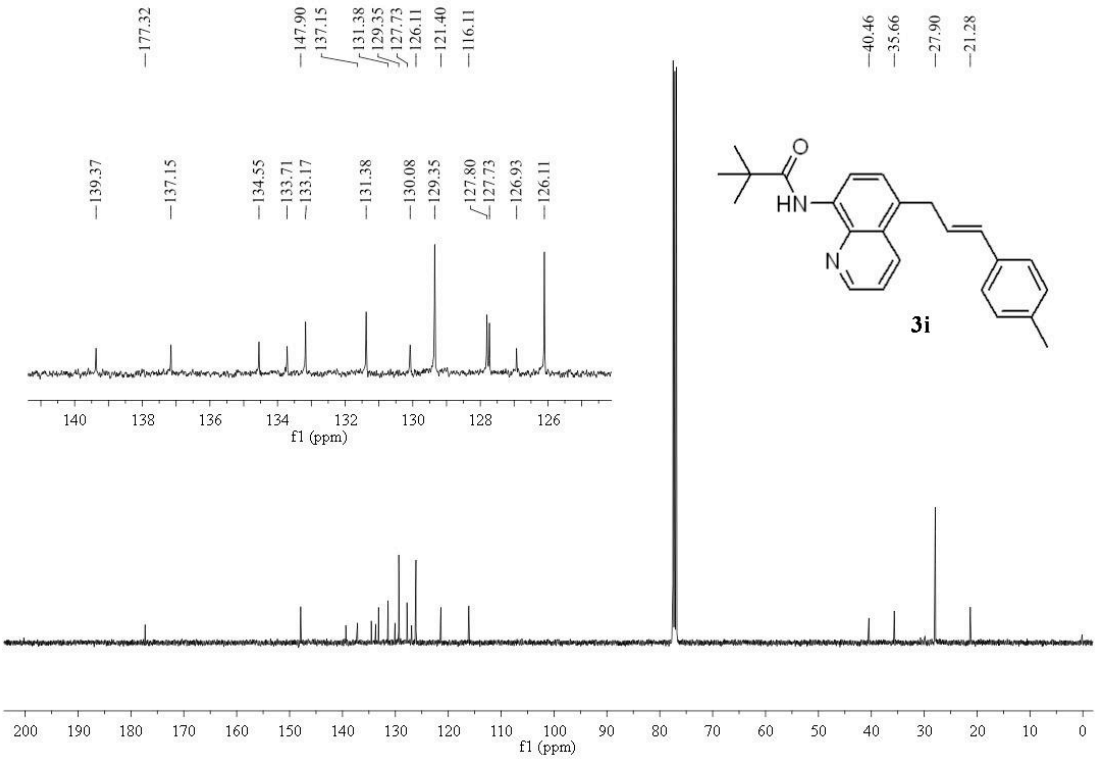
8.376
7.459
7.442
7.423
7.067
6.420
6.407
6.381
6.368
6.354
6.314
3.914
3.902
2.304
1.432
7.470
7.459
7.442
7.423
7.207
7.187
7.087
7.067
2.10
2.28
2.29
7.5 7.4 7.3 7.2 7.1
f1 (ppm)
O
NH
N
3i
1.04
1.07
1.10
1.00
2.10
2.28
2.29
2.11
2.01
3.44
9.63
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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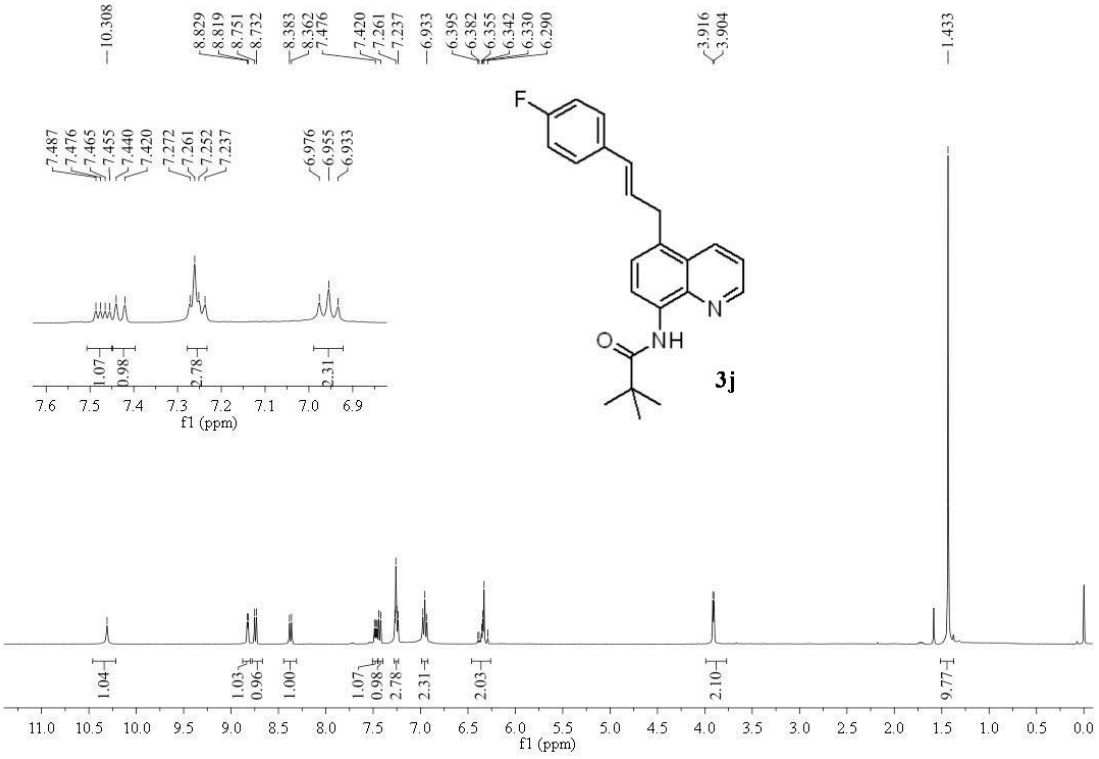
137.15
131.38
129.35
127.73
126.11
121.40
116.11
40.46
35.66
27.90
21.28
139.37
137.15
134.55
133.71
133.17
131.38
130.08
129.35
127.80
127.73
126.93
126.11
140 138 136 134 132 130 128 126
f1 (ppm)
O
HN
N
3i
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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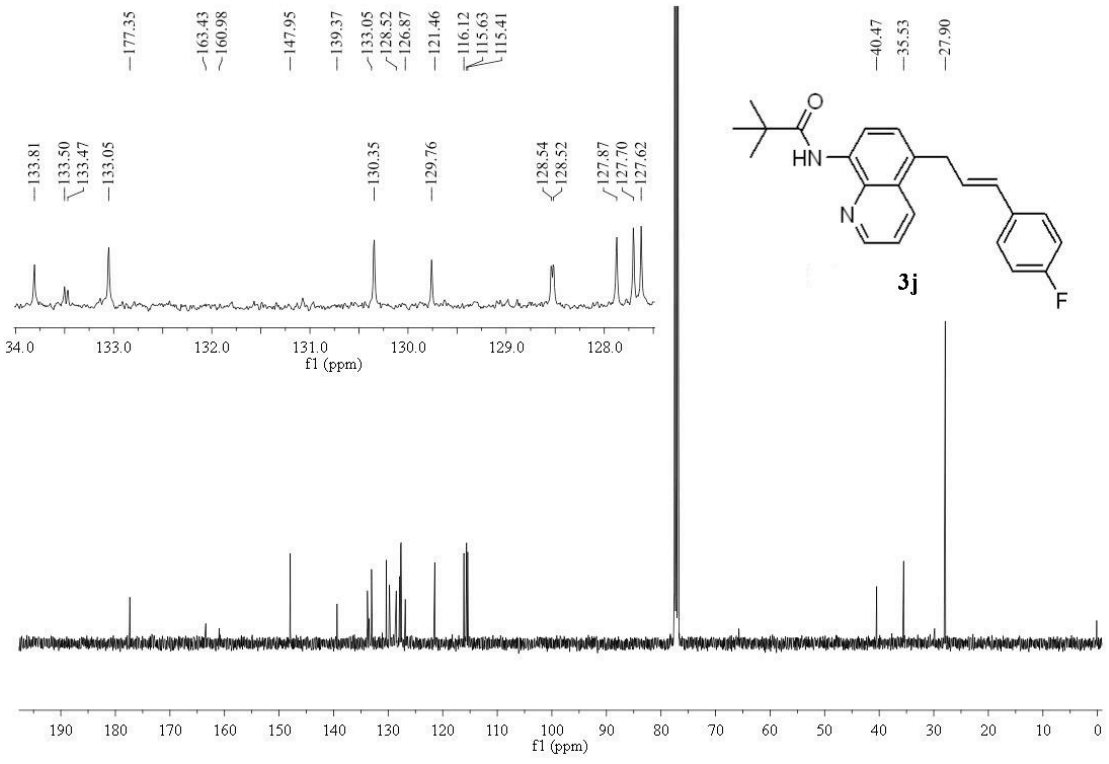
8.819
8.751
8.732
8.383
8.362
7.476
7.420
7.261
7.237
6.933
6.395
6.382
6.355
6.342
6.330
6.290
3.916
3.904
1.433
F
N
O
NH
3j
1.04
1.03
0.96
1.00
1.07
0.98
2.78
2.31
2.03
2.10
9.77
f1 (ppm)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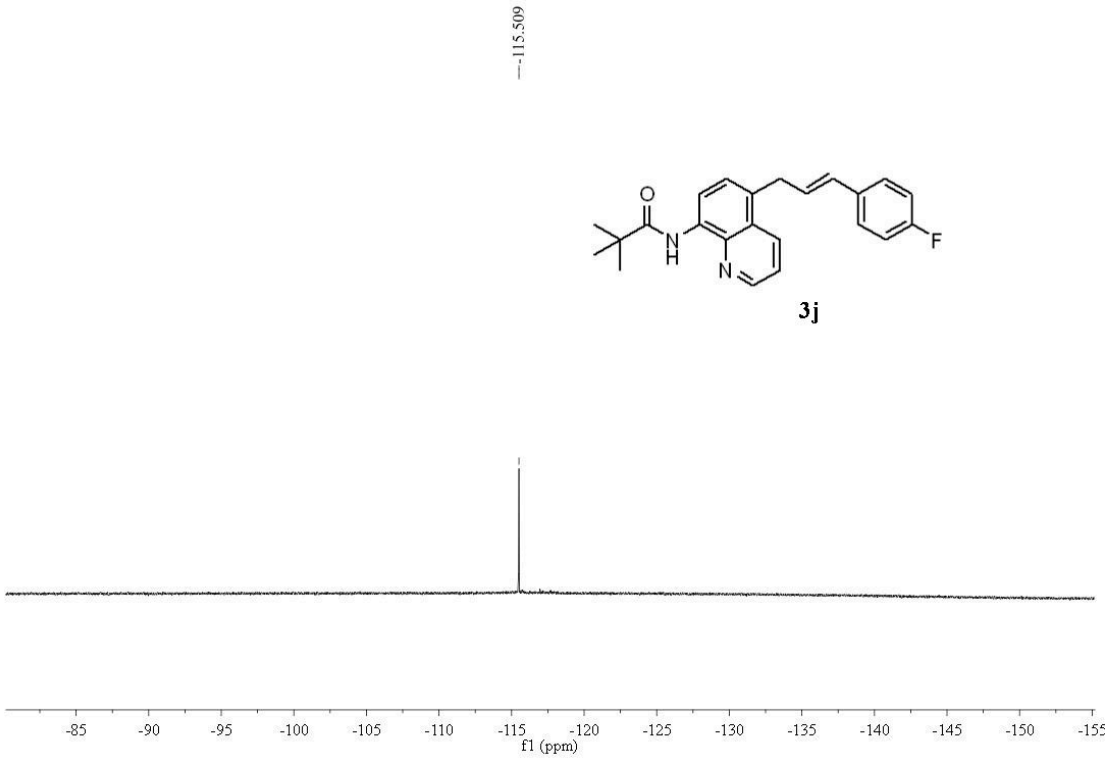
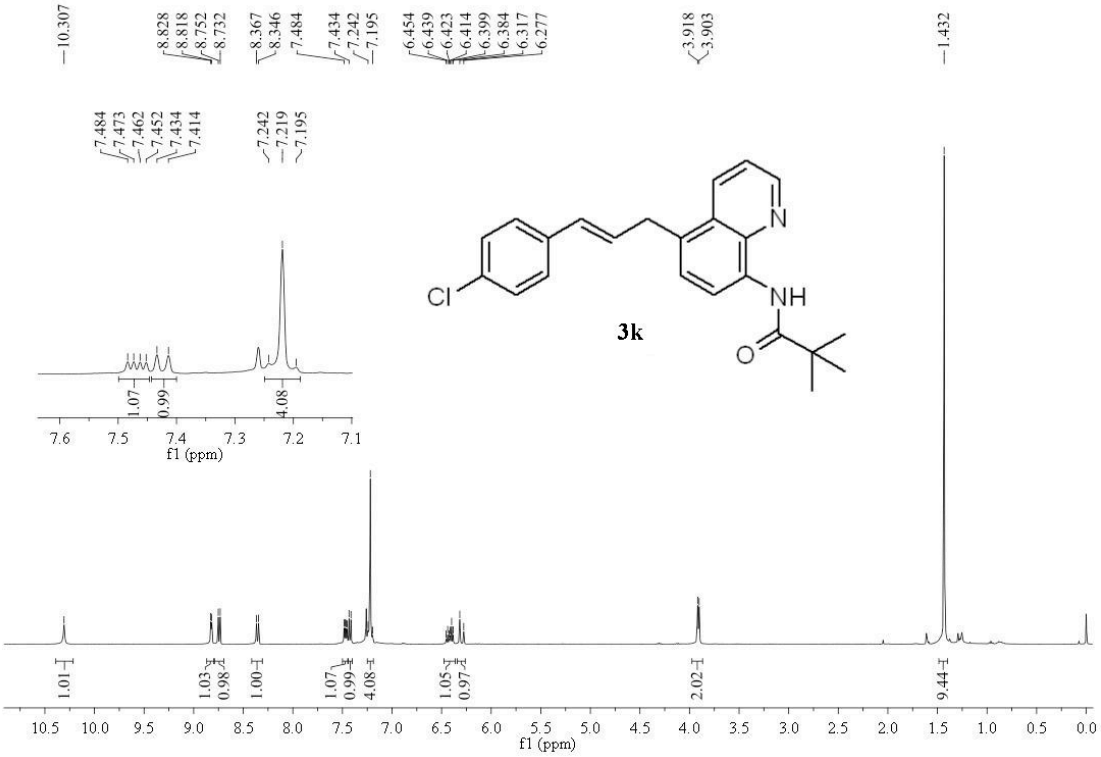
163.43
160.98
147.95
139.37
133.05
128.52
126.87
121.46
116.12
115.63
115.41
40.47
35.53
27.90
133.81
133.50
133.47
133.05
130.35
129.76
128.54
128.52
127.87
127.70
127.62
HN
O
N
F
3j
f1 (ppm)


-115.509
O
N
H
N
F
-85
-90
-95
-100
-105
-110
-115
-120
-125
-130
-135
-140
-145
-150
-155
f1 (ppm)

3j


10.307
8.828
8.818
8.752
8.732
8.367
8.346
7.484
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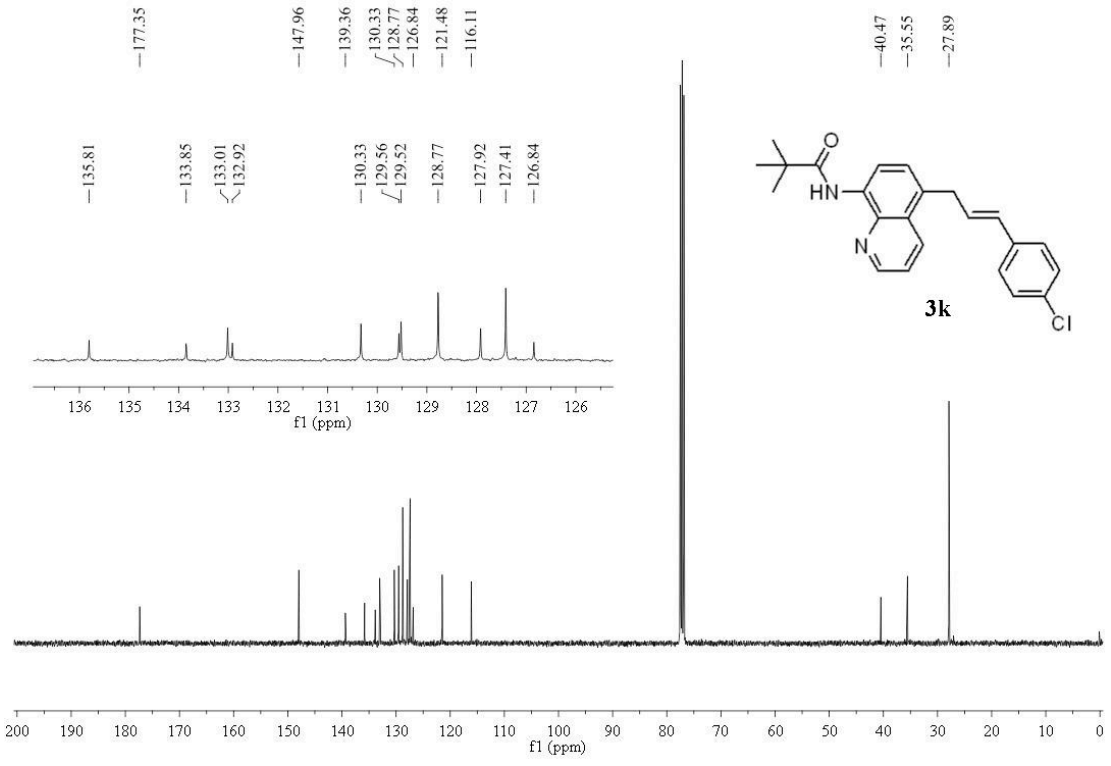
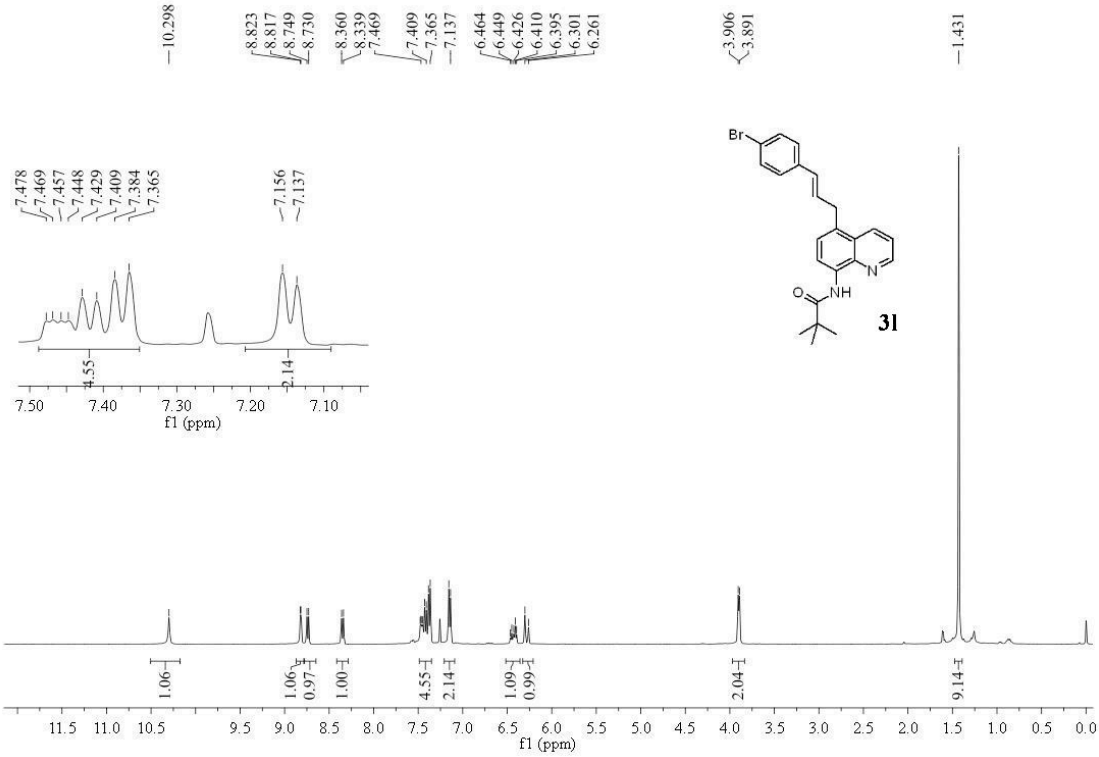
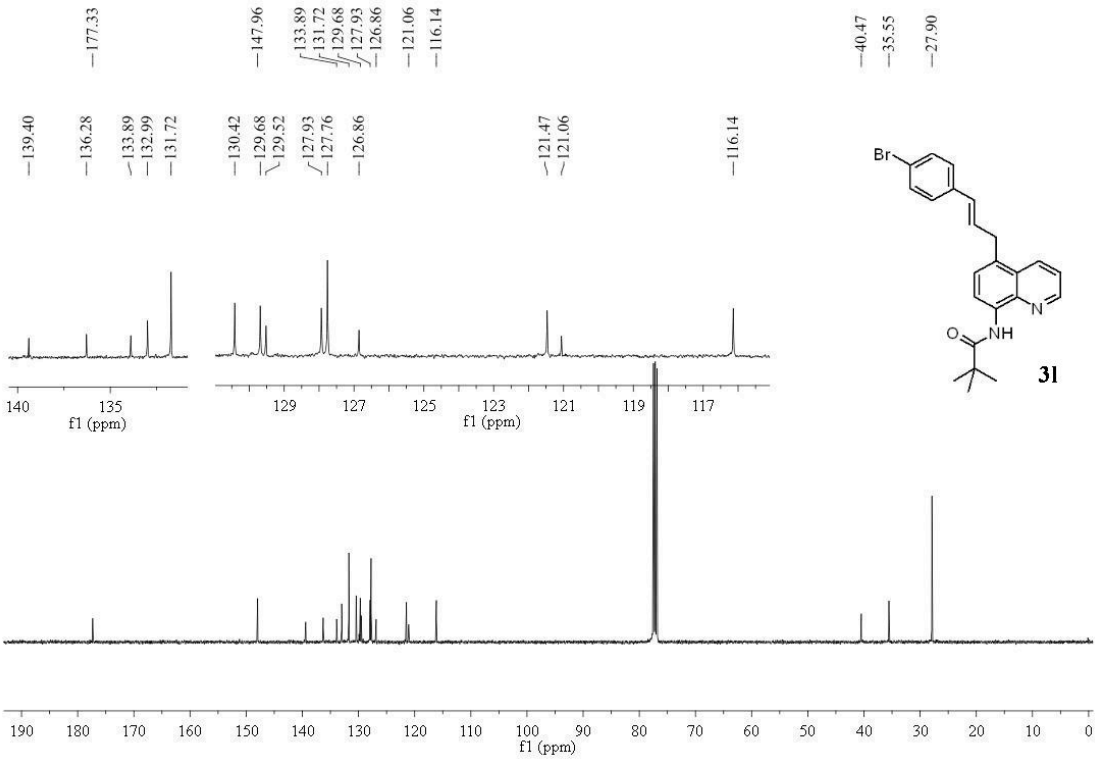
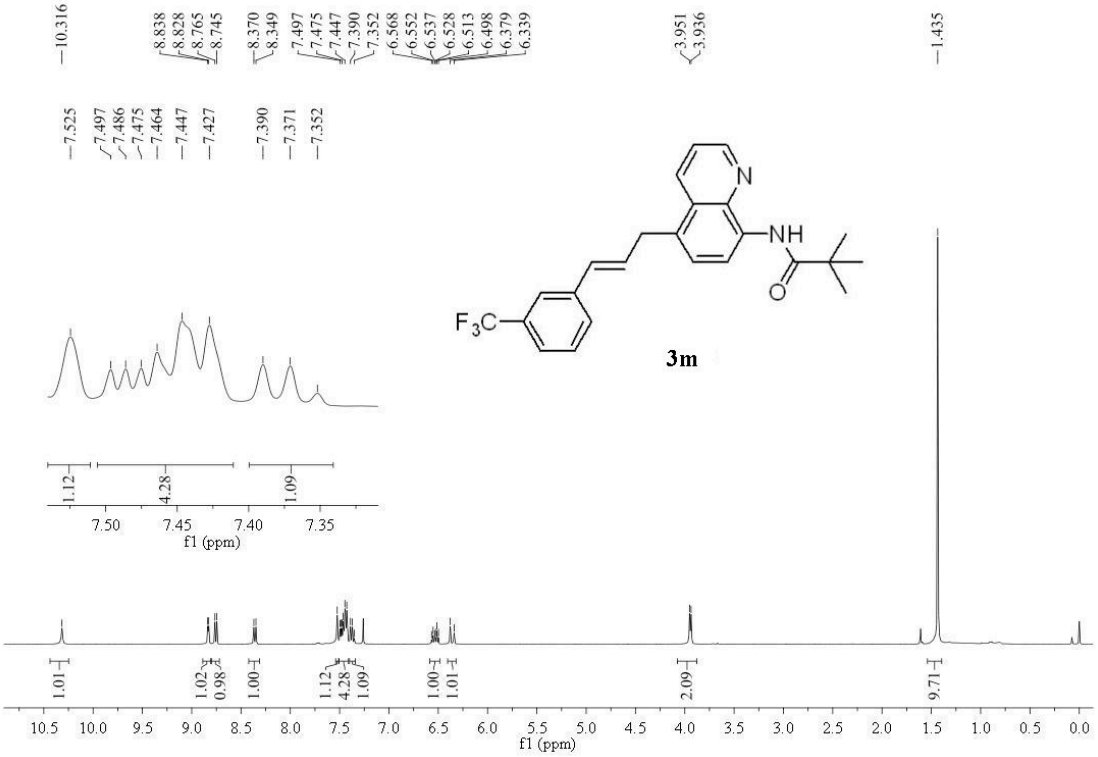
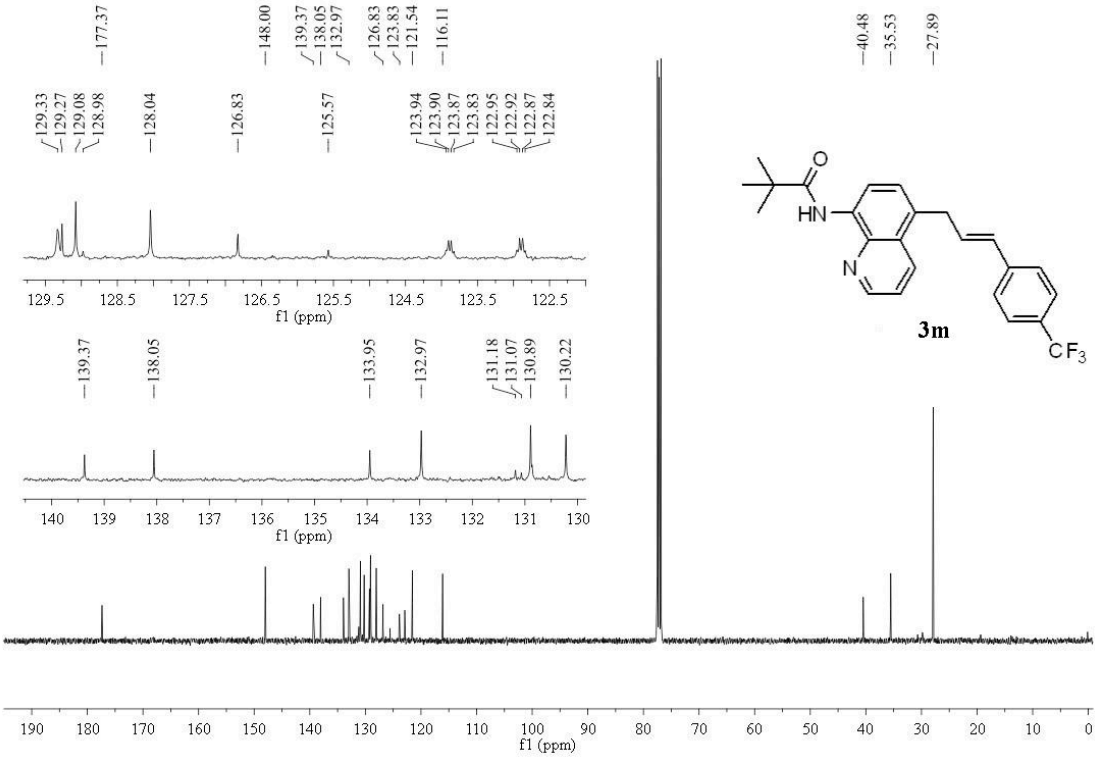
7.242
7.195
6.454
6.439
6.423
6.414
6.399
6.384
6.317
6.277
3.918
3.903
1.432
Cl
NH
O
N
3k
1.01
1.03
0.98
1.00
1.07
0.99
4.08
1.05
0.97
2.02
9.44
f1 (ppm)

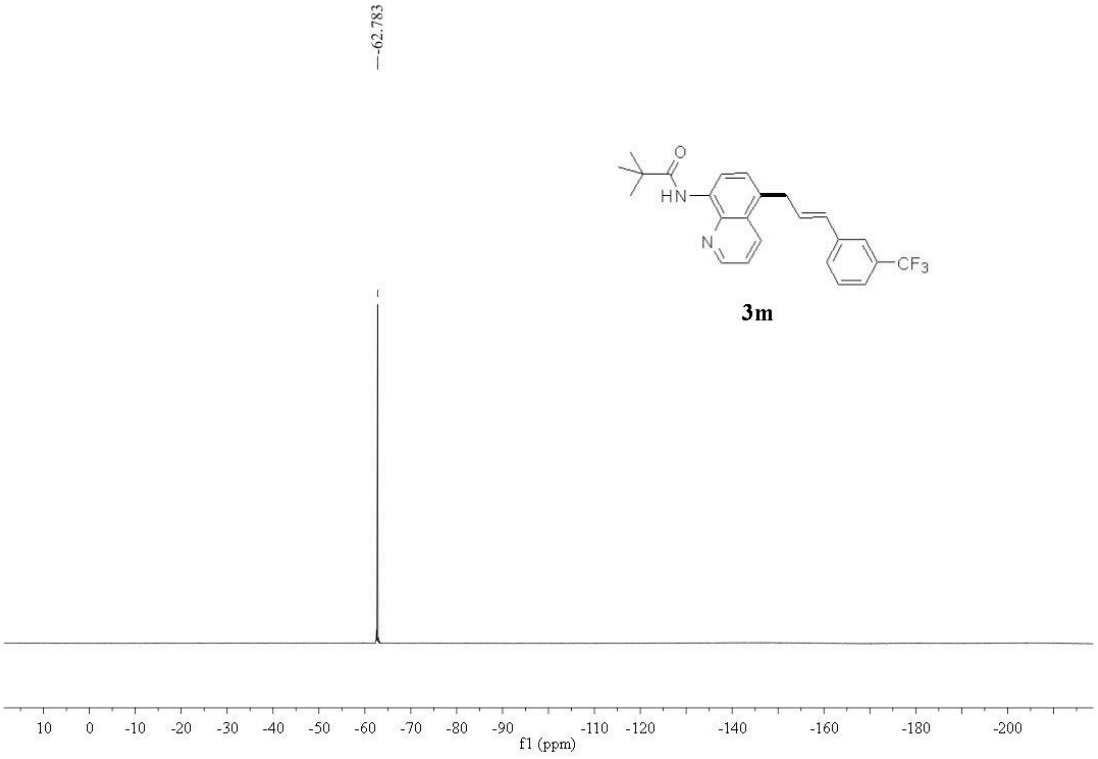

177.35
147.96
139.36
130.33
128.77
126.84
121.48
116.11
40.47
35.55
27.89
135.81
133.85
133.01
132.92
130.33
129.56
129.52
128.77
127.92
127.41
126.84
HN
O
N
Cl
3k
f1 (ppm)

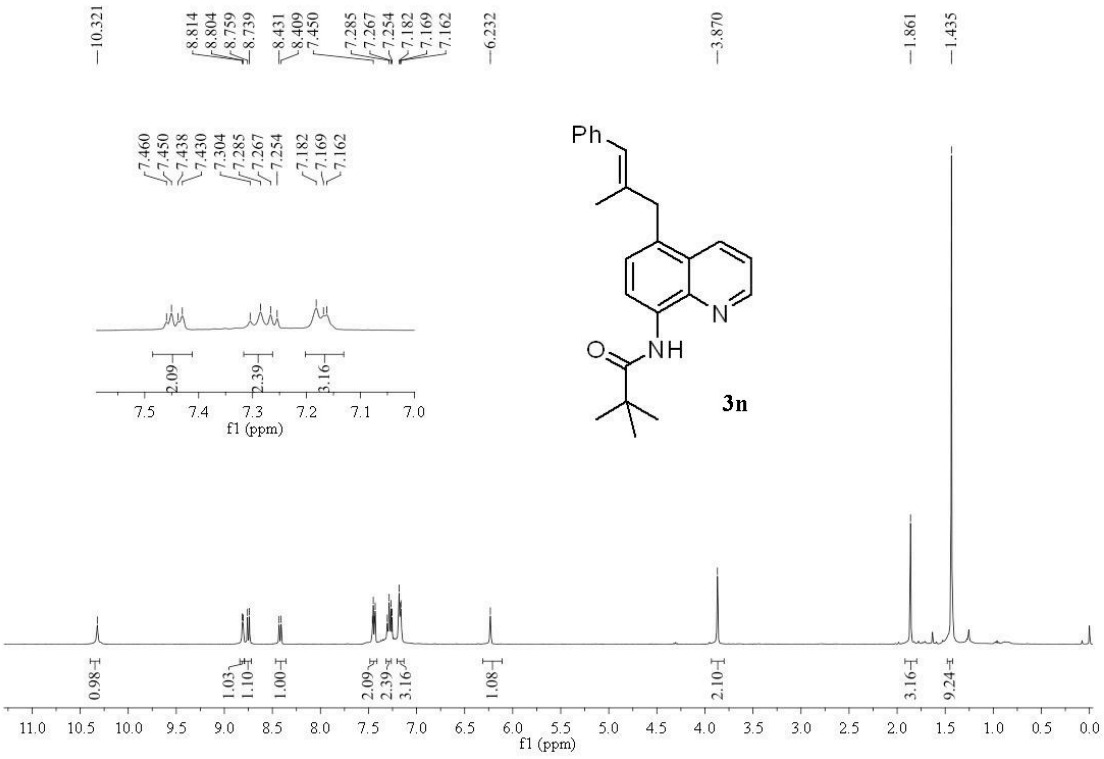

10.298
8.823
8.817
8.749
8.730
8.360
8.339
7.469
7.409
7.365
7.137
6.464
6.449
6.426
6.410
6.395
6.301
6.261
3.906
3.891
1.431
7.478
7.469
7.457
7.448
7.429
7.409
7.384
7.365
7.156
7.137
4.55
2.14
7.50
7.40
7.30
7.20
7.10
f1 (ppm)
Br
N
NH
O
3l
1.06
1.06
0.97
1.00
4.55
2.14
1.09
0.99
2.04
9.14
11.5 11.0 10.5 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)

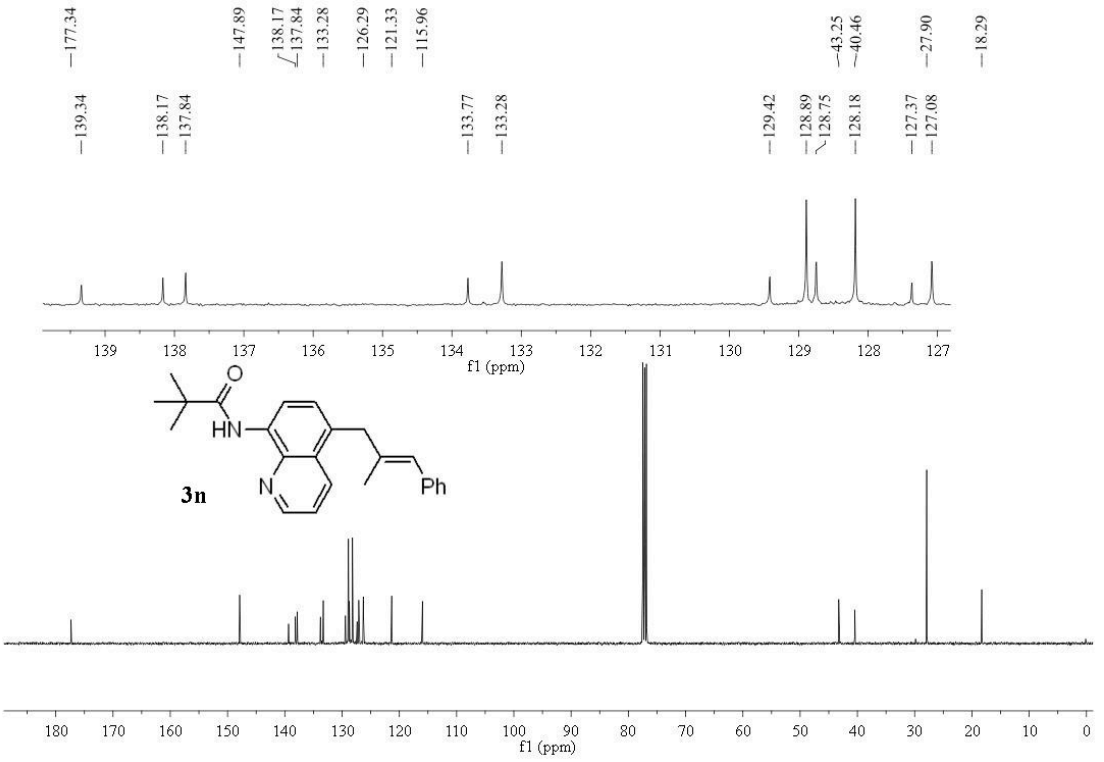

177.33
147.96
133.89
131.72
129.68
127.93
126.86
121.06
116.14
40.47
35.55
27.90
139.40
136.28
133.89
132.99
131.72
130.42
129.68
129.52
127.93
127.76
126.86
121.47
121.06
116.14
140
135
f1 (ppm)
129
127
125
123
121
119
117
f1 (ppm)
Br
N
NH
O
3l
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

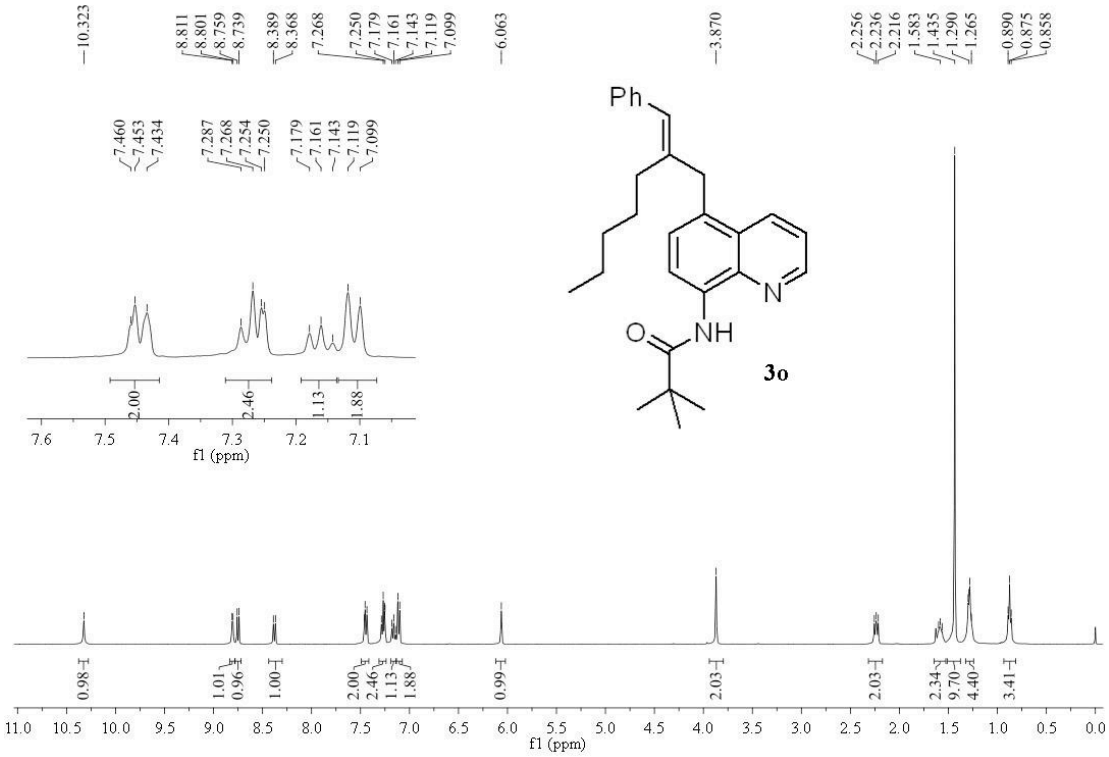

10.316
8.838
8.828
8.765
8.745
8.370
8.349
7.497
7.475
7.447
7.390
7.352
6.568
6.552
6.537
6.528
6.513
6.498
6.379
6.339
3.951
3.936
1.435
7.525
7.497
7.486
7.475
7.464
7.447
7.427
7.390
7.371
7.352
N
NH
O
F3C
3m
1.12
4.28
1.09
7.50
7.45
7.40
7.35
f1 (ppm)
1.01
1.02
0.98
1.00
1.12
4.28
1.09
1.00
1.01
2.09
9.71
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)

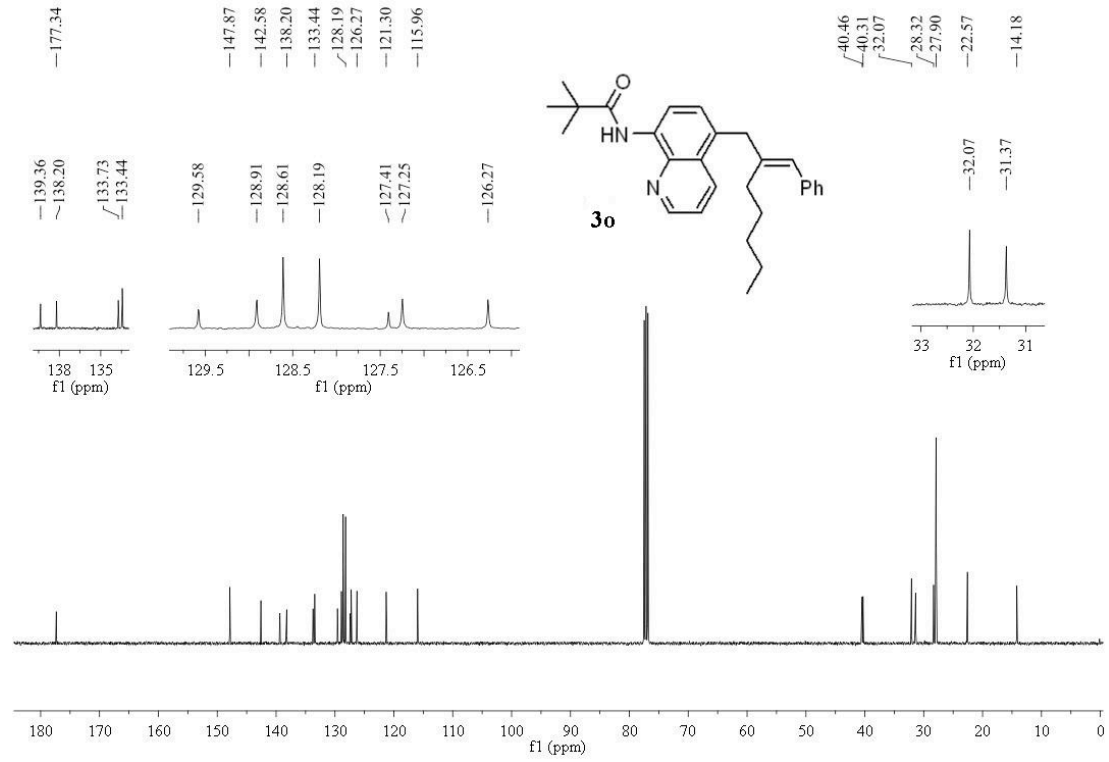

177.37
148.00
139.37
138.05
132.97
126.83
123.83
121.54
116.11
40.48
35.53
27.89
129.33
129.27
129.08
128.98
128.04
126.83
125.57
123.94
123.90
123.87
123.83
122.95
122.92
122.87
122.84
O
HN
N
3m
CF3
129.5 128.5 127.5 126.5 125.5 124.5 123.5 122.5
f1 (ppm)
139.37
138.05
133.95
132.97
131.18
131.07
130.89
130.22
140 139 138 137 136 135 134 133 132 131 130
f1 (ppm)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

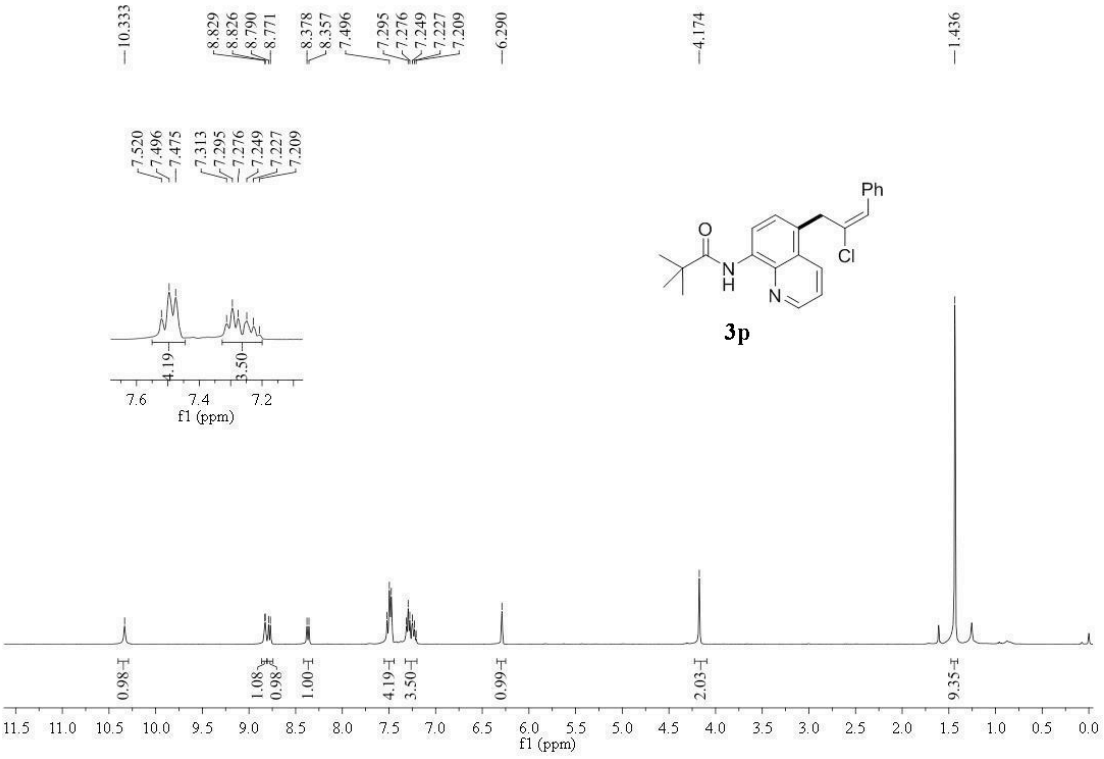

-62.783
O
HN
N
CF3
3m
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-110
-120
-140
-160
-180
-200
f1 (ppm)

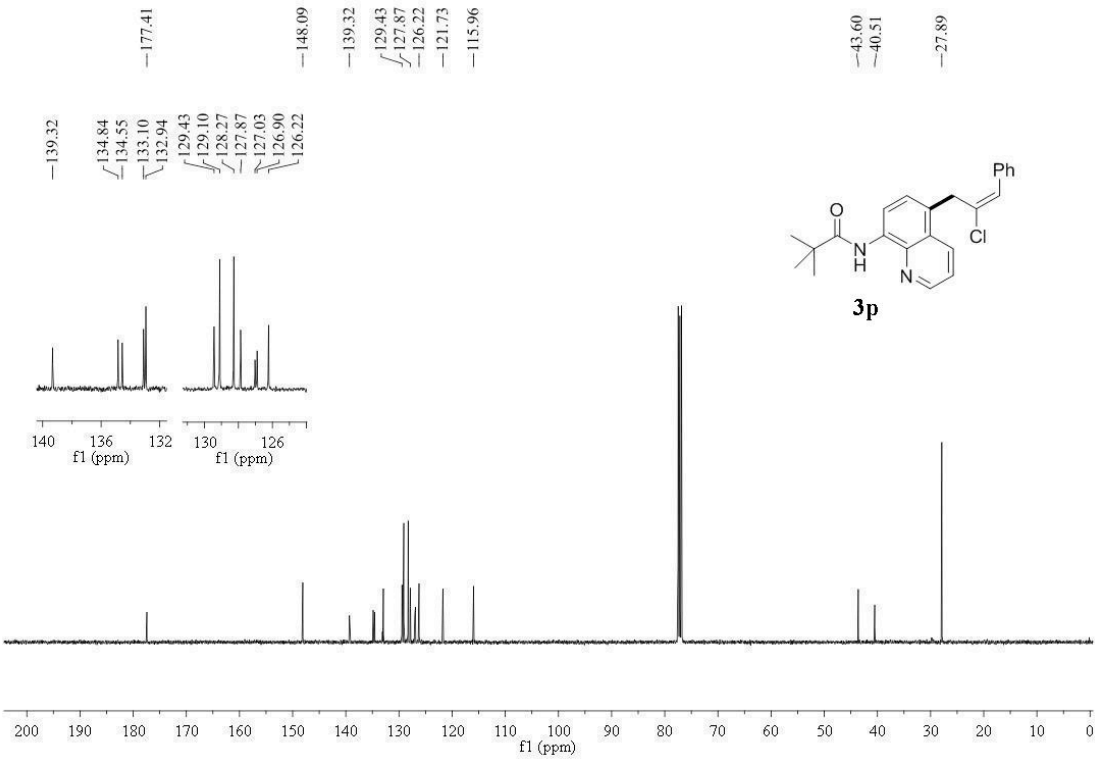

10.321
8.814
8.804
8.759
8.739
8.431
8.409
7.450
7.285
7.267
7.254
7.182
7.169
7.162
6.232
3.870
1.861
1.435
Ph
N
O
NH
3n
f1 (ppm)

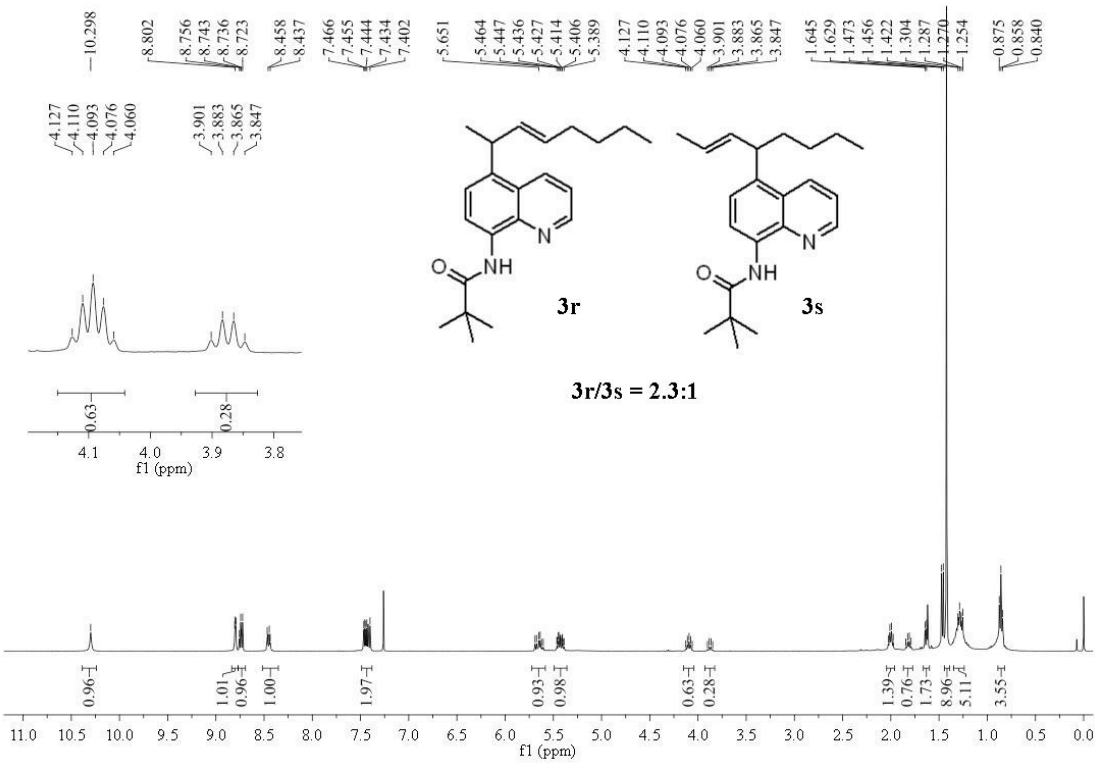

177.34
147.89
138.17
137.84
133.28
126.29
121.33
115.96
43.25
40.46
27.90
18.29
139.34
138.17
137.84
133.77
133.28
129.42
128.89
128.75
128.18
127.37
127.08
HN
O
N
Ph
3n
f1 (ppm)

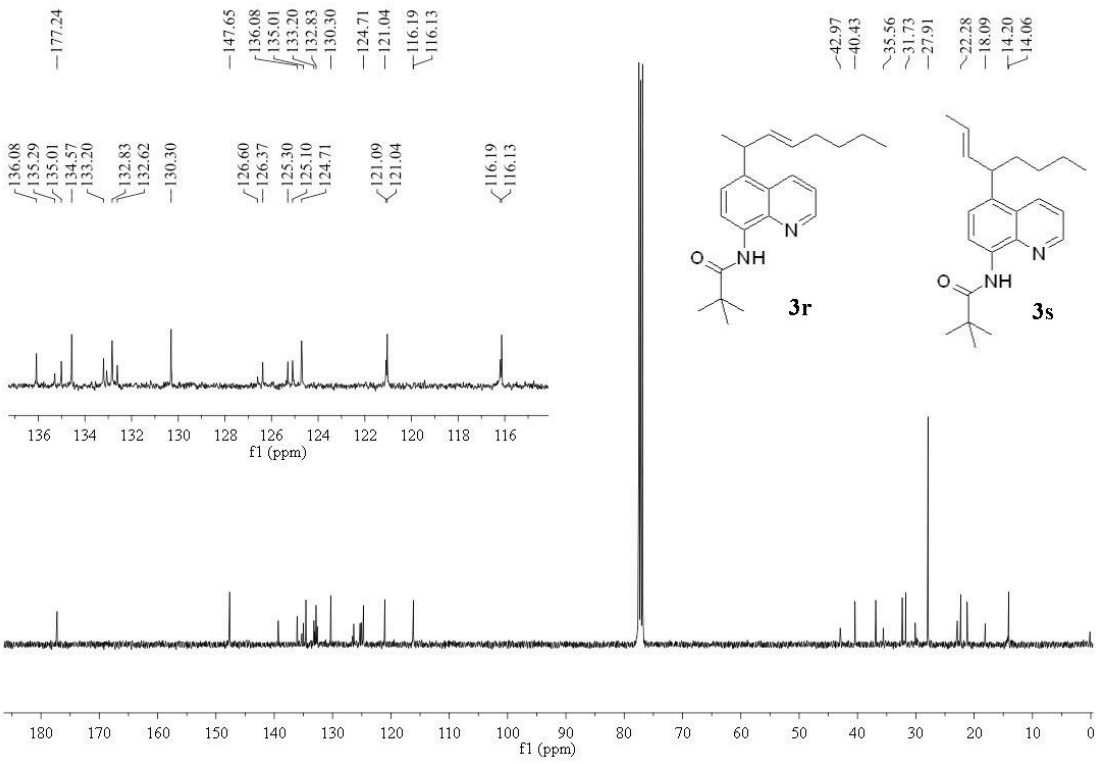

10.323
8.811
8.801
8.759
8.739
8.389
8.368
7.268
7.250
7.179
7.161
7.143
7.119
7.099
6.063
3.870
2.256
2.236
2.216
1.583
1.435
1.290
1.265
0.890
0.875
0.858
Ph
N
NH
O
3o
f1 (ppm)

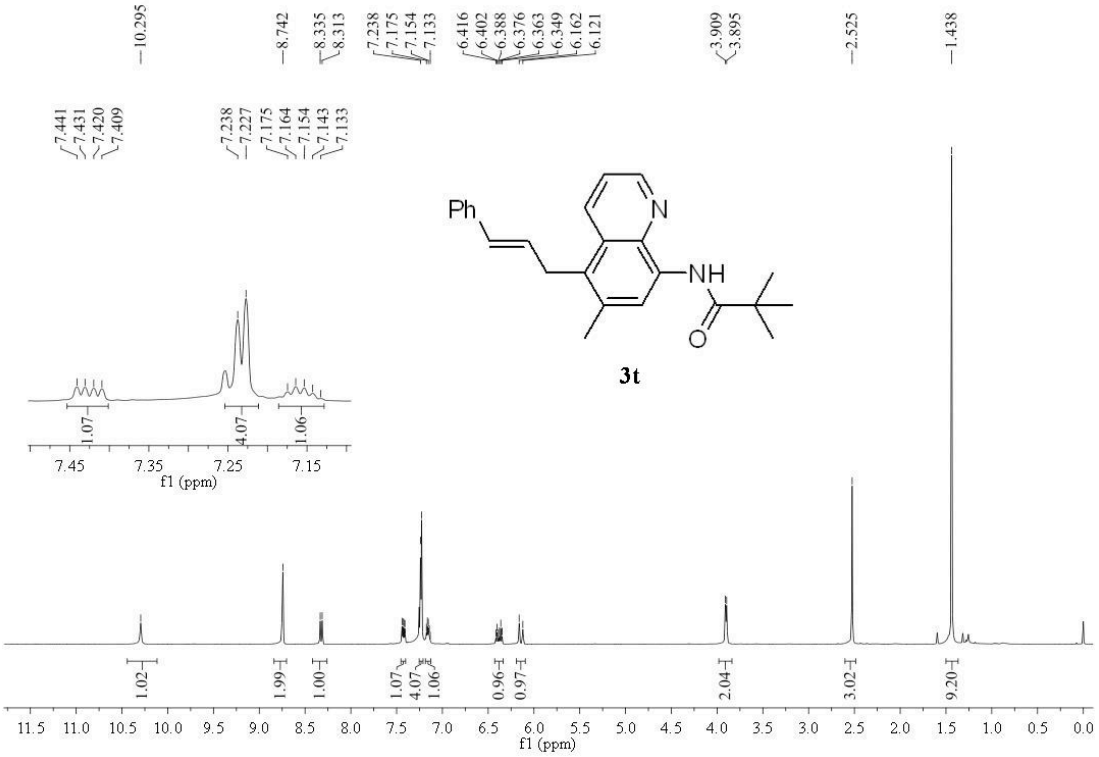

177.34
147.87
142.58
138.20
133.44
128.19
126.27
121.30
115.96
40.46
40.31
32.07
28.32
27.90
22.57
14.18
HN
O
N
Ph
3o
f1 (ppm)

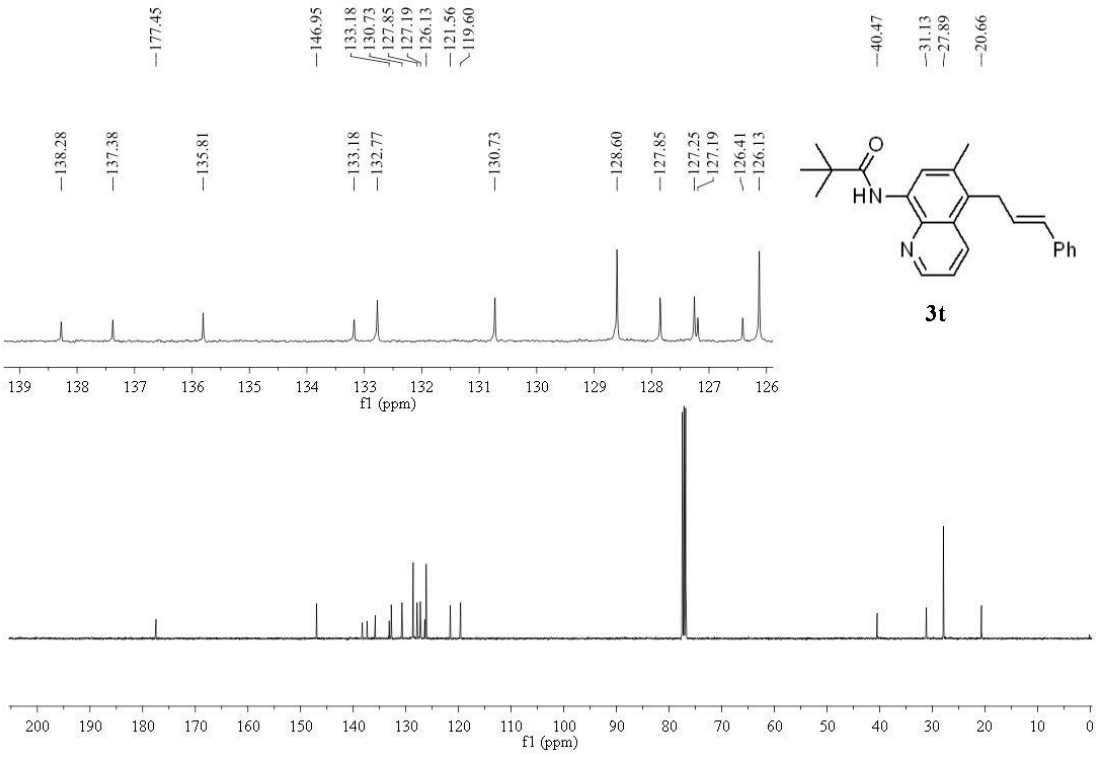

10.333
8.829
8.826
8.790
8.771
8.378
8.357
7.496
7.295
7.276
7.249
7.227
7.209
6.290
4.174
1.436
7.520
7.496
7.475
7.313
7.295
7.276
7.249
7.227
7.209
Ph
O
N
H
Cl
N
3p
4.19
3.50
7.6
7.4
7.2
f1 (ppm)
0.98
1.08
0.98
1.00
4.19
3.50
0.99
2.03
9.35
f1 (ppm)

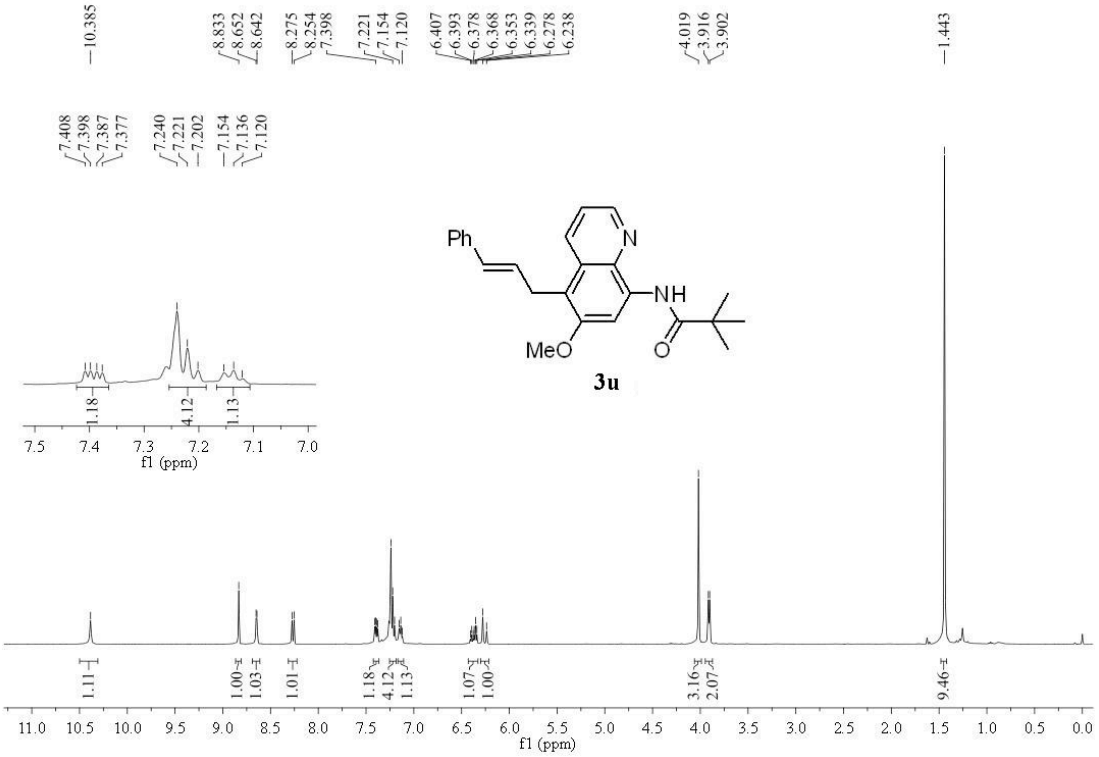

177.41
148.09
139.32
129.43
127.87
126.22
121.73
115.96
43.60
40.51
27.89
139.32
134.84
134.55
133.10
132.94
129.43
129.10
128.27
127.87
127.03
126.90
126.22
Ph
O
N
H
Cl
N
3p
140
136
132
f1 (ppm)
130
126
f1 (ppm)
f1 (ppm)

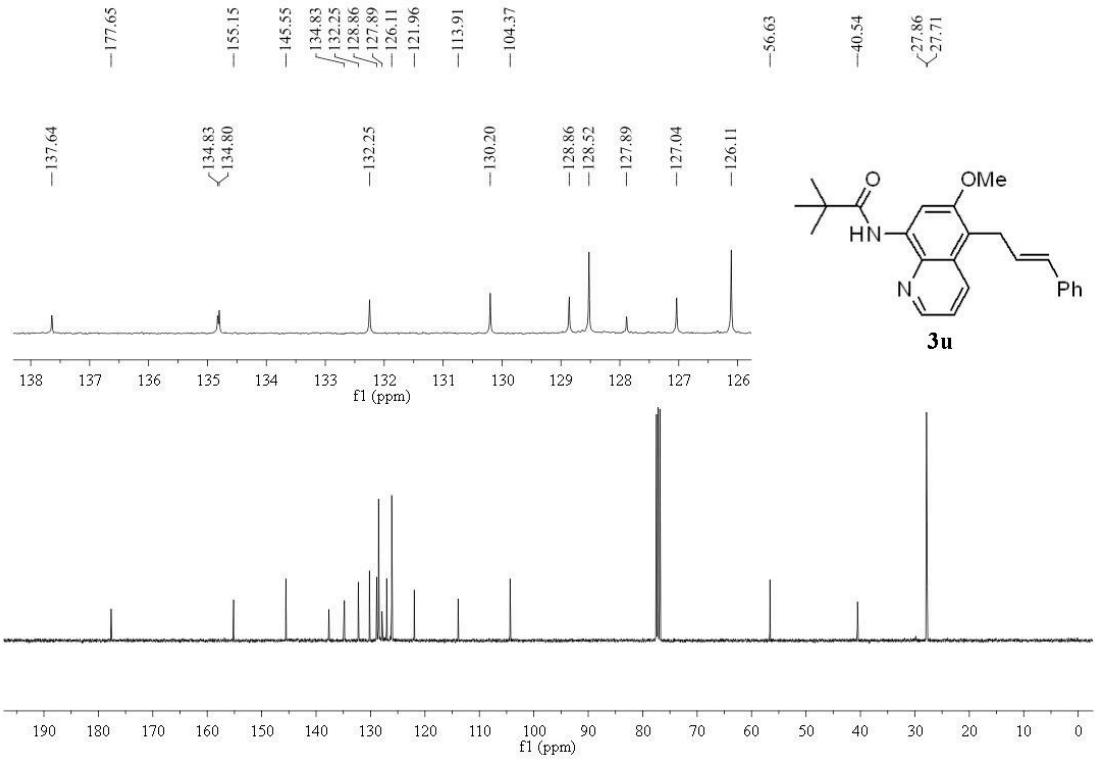

3r
3s
3r/3s = 2.3:1
f1 (ppm)

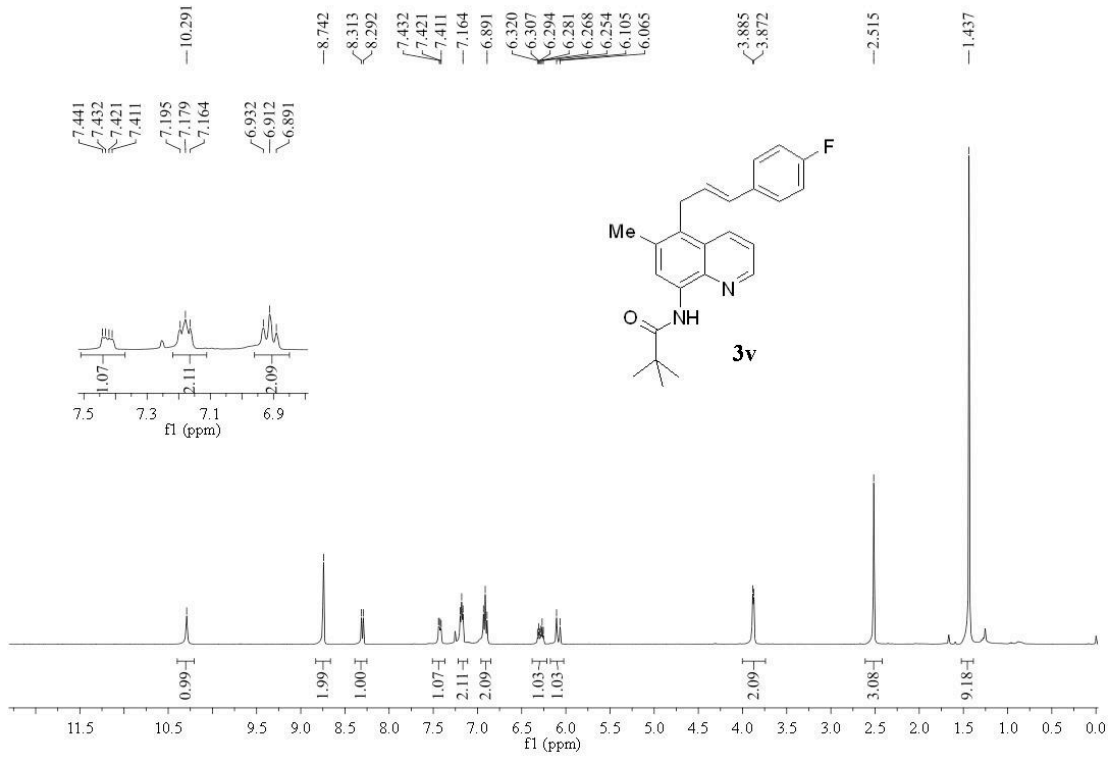

3r
3s
f1 (ppm)

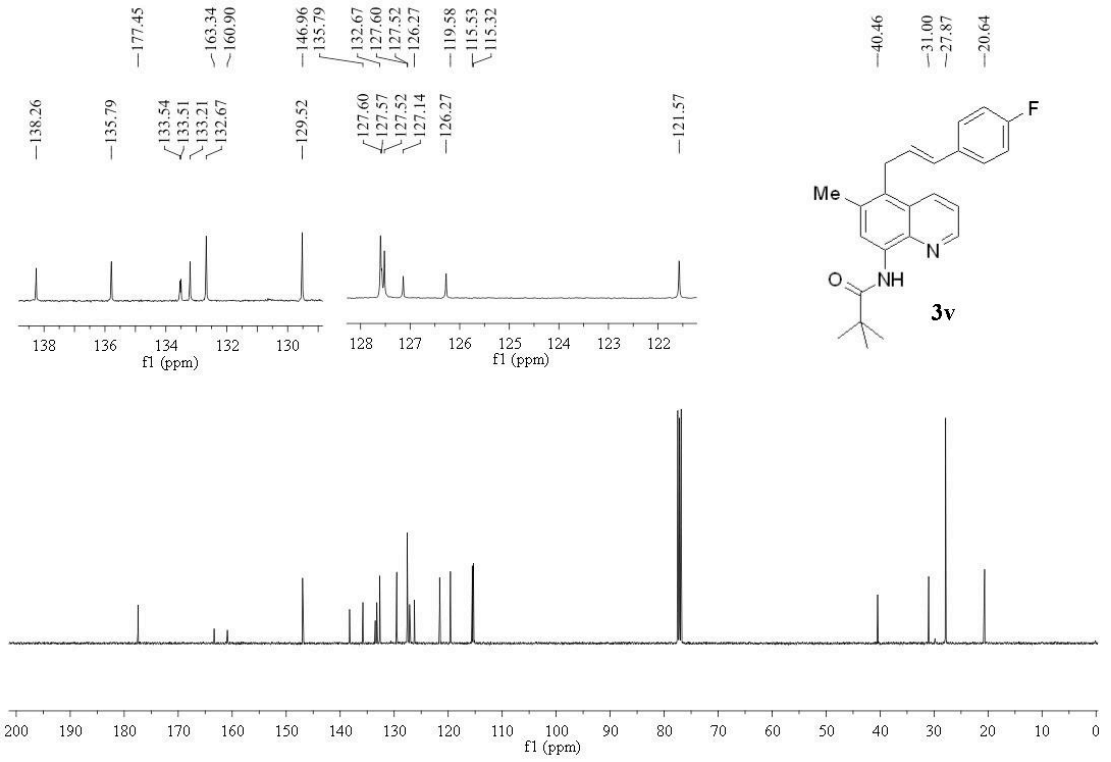

10.295
8.742
8.335
8.313
7.238
7.175
7.154
7.133
6.416
6.402
6.388
6.376
6.363
6.349
6.162
6.121
3.909
3.895
2.525
1.438
7.441
7.431
7.420
7.409
7.238
7.227
7.175
7.164
7.154
7.143
7.133
Ph
N
NH
O
3t
1.07
4.07
1.06
7.45
7.35
7.25
7.15
f1 (ppm)
1.02
1.99
1.00
1.07
4.07
1.06
0.96
0.97
2.04
3.02
9.20
11.5 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)

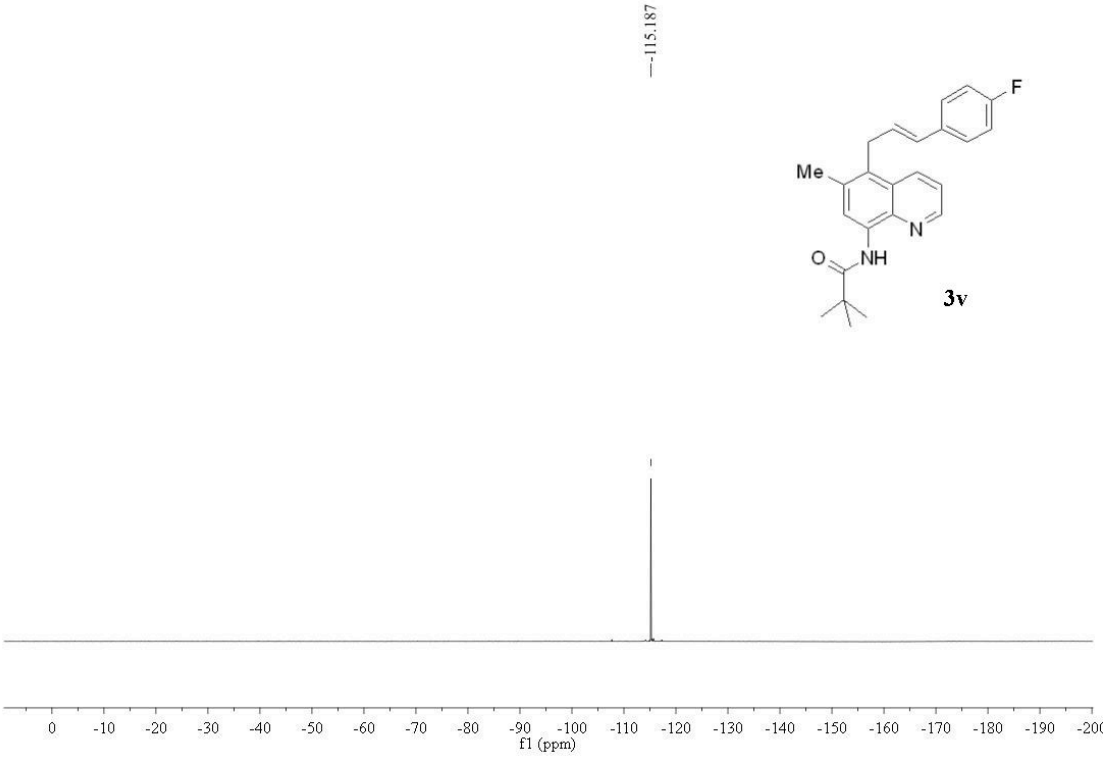

177.45
146.95
133.18
130.73
127.85
127.19
126.13
121.56
119.60
40.47
31.13
27.89
20.66
138.28
137.38
135.81
133.18
132.77
130.73
128.60
127.85
127.25
127.19
126.41
126.13
O
HN
N
Ph
3t
139 138 137 136 135 134 133 132 131 130 129 128 127 126
f1 (ppm)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

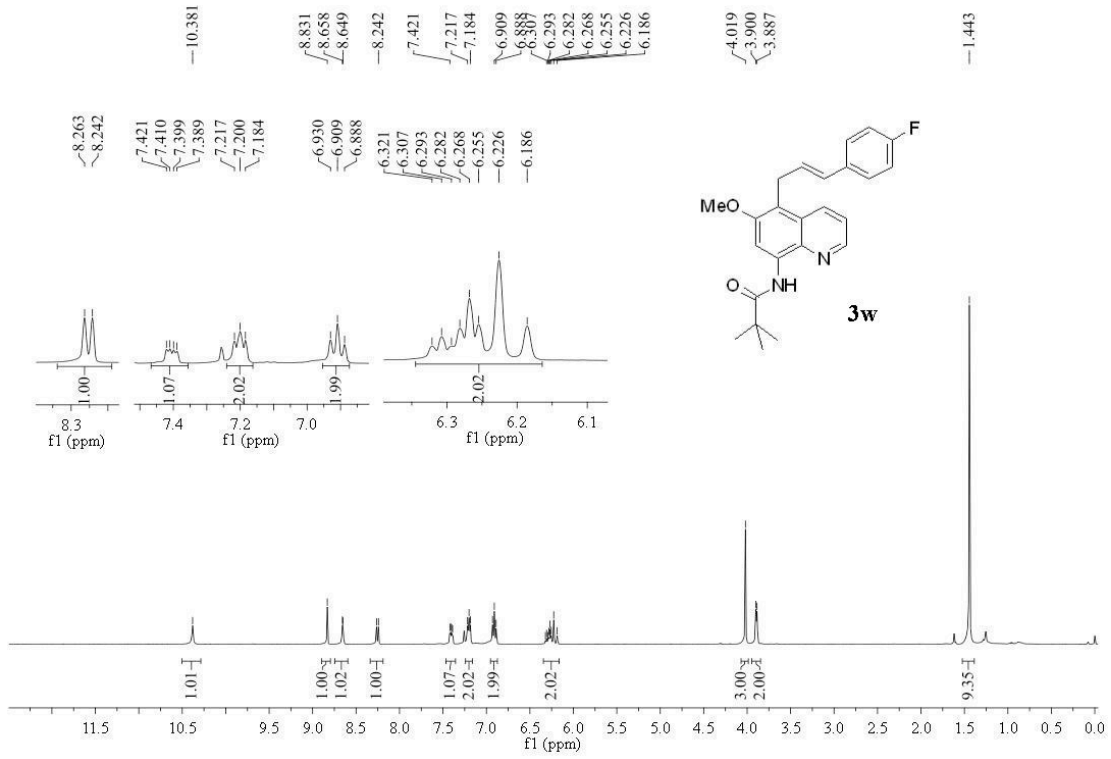

10.385
8.833
8.652
8.642
8.275
8.254
7.398
7.221
7.154
7.120
6.407
6.393
6.378
6.368
6.353
6.339
6.278
6.238
4.019
3.916
3.902
1.443
7.408
7.398
7.387
7.377
7.240
7.221
7.202
7.154
7.136
7.120
Ph
N
NH
MeO
O
3u
1.18
4.12
1.13
7.5 7.4 7.3 7.2 7.1 7.0
f1 (ppm)
1.11
1.00
1.03
1.01
1.18
4.12
1.13
1.07
1.00
3.16
2.07
9.46
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)

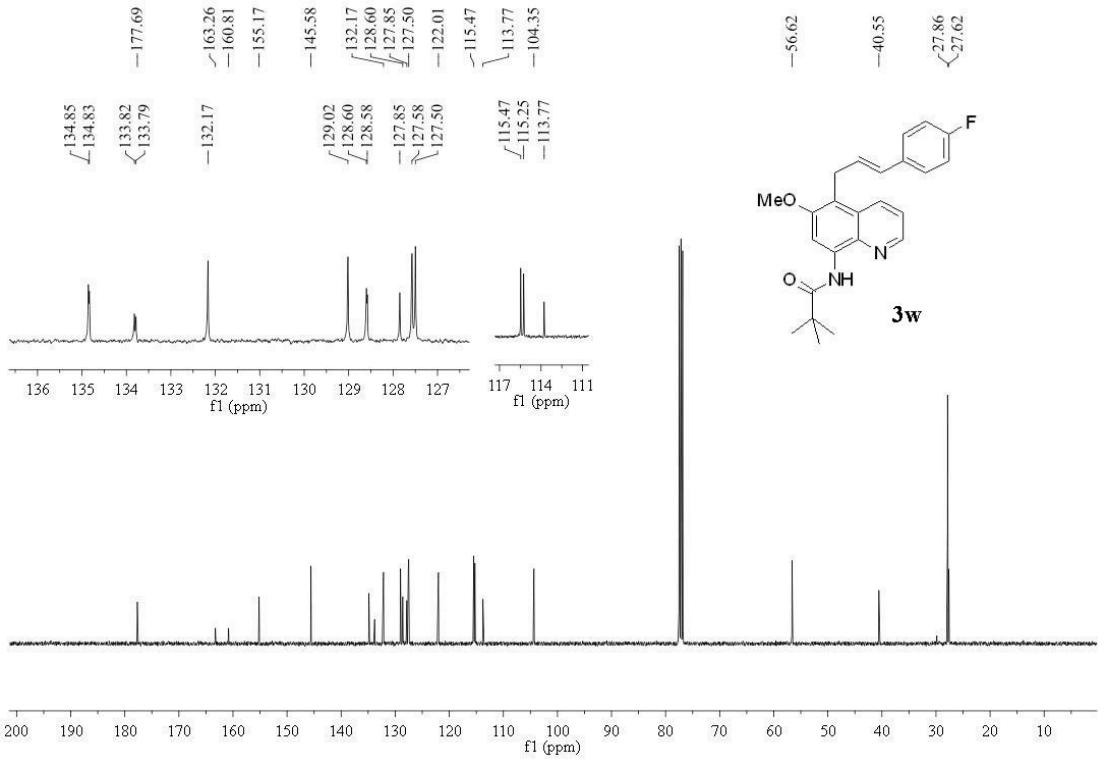

177.65
155.15
145.55
134.83
132.25
128.86
127.89
126.11
121.96
113.91
104.37
56.63
40.54
27.86
27.71
137.64
134.83
134.80
132.25
130.20
128.86
128.52
127.89
127.04
126.11
O
OMe
HN
N
Ph
3u
138 137 136 135 134 133 132 131 130 129 128 127 126
f1 (ppm)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

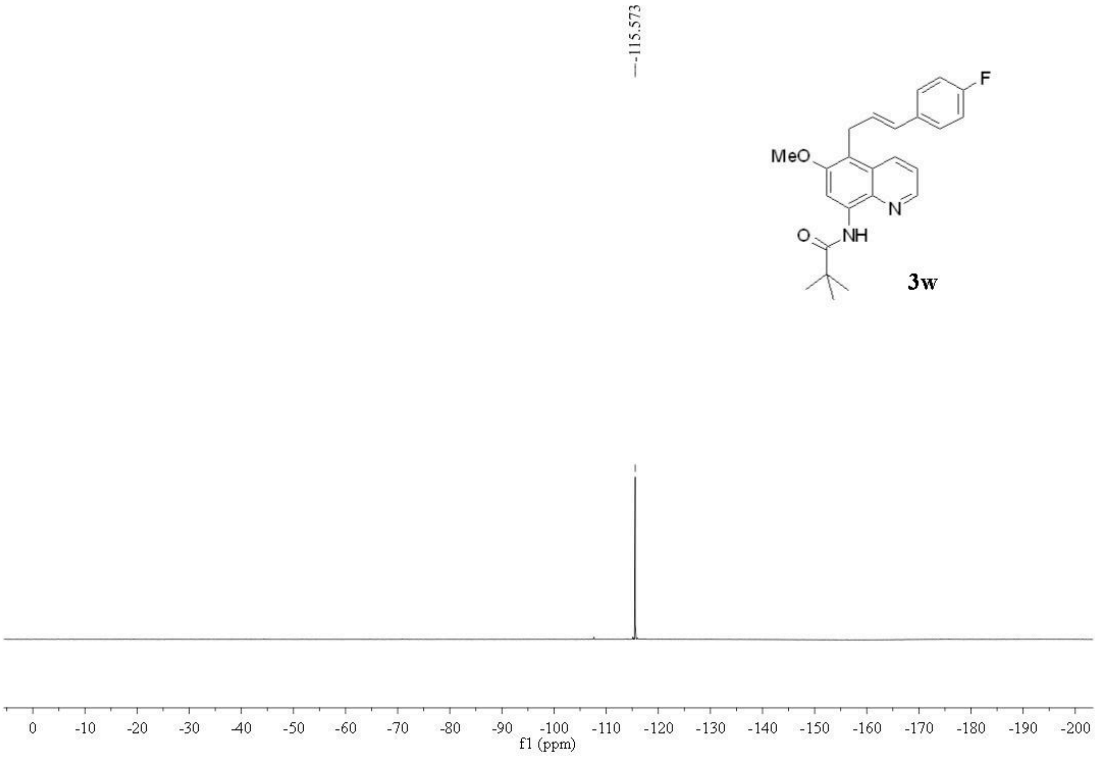

10.291
8.742
8.313
8.292
7.432
7.421
7.411
7.164
6.891
6.320
6.307
6.294
6.281
6.268
6.254
6.105
6.065
3.885
3.872
2.515
1.437
7.441
7.432
7.421
7.411
7.195
7.179
7.164
6.932
6.912
6.891
F
Me
N
O
NH
3v
1.07
2.11
2.09
7.5
7.3
7.1
6.9
f1 (ppm)
0.99
1.99
1.00
1.07
2.11
2.09
1.03
1.03
2.09
3.08
9.18
11.5
10.5
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)

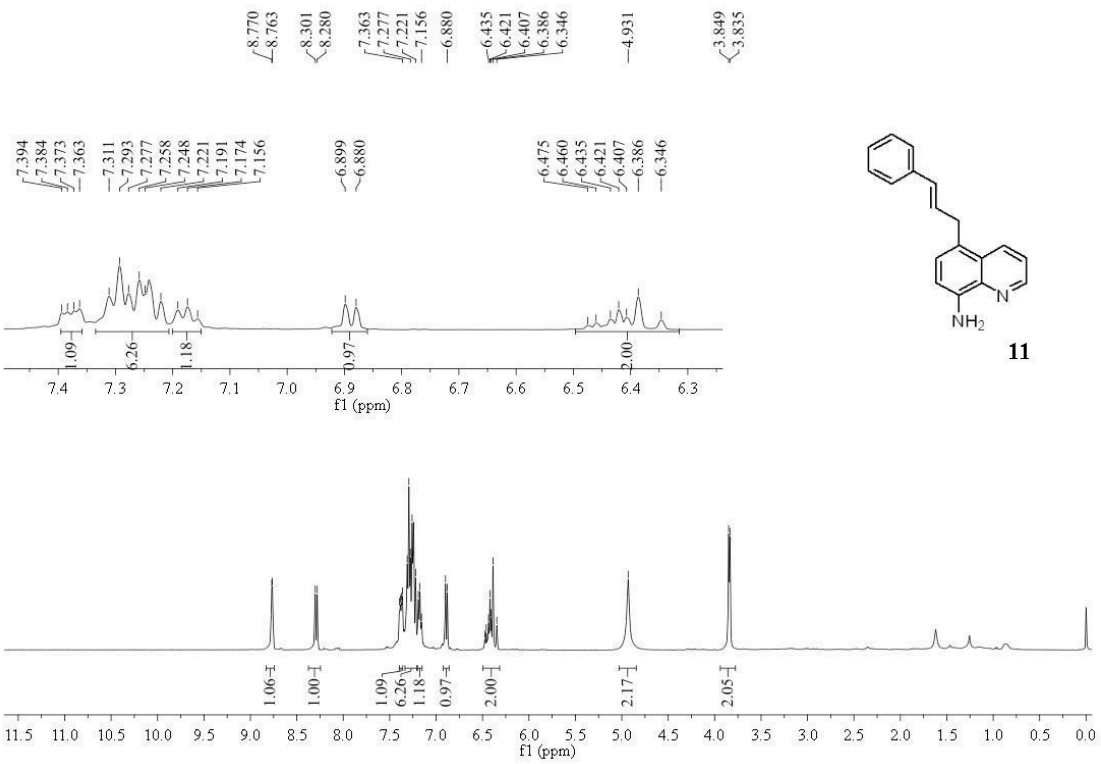

177.45
163.34
160.90
146.96
135.79
132.67
127.60
127.52
126.27
119.58
115.53
115.32
40.46
31.00
27.87
20.64
138.26
135.79
133.54
133.51
133.21
132.67
129.52
127.60
127.57
127.52
127.14
126.27
121.57
F
Me
N
O
NH
3v
138
136
134
132
130
f1 (ppm)
128
127
126
125
124
123
122
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

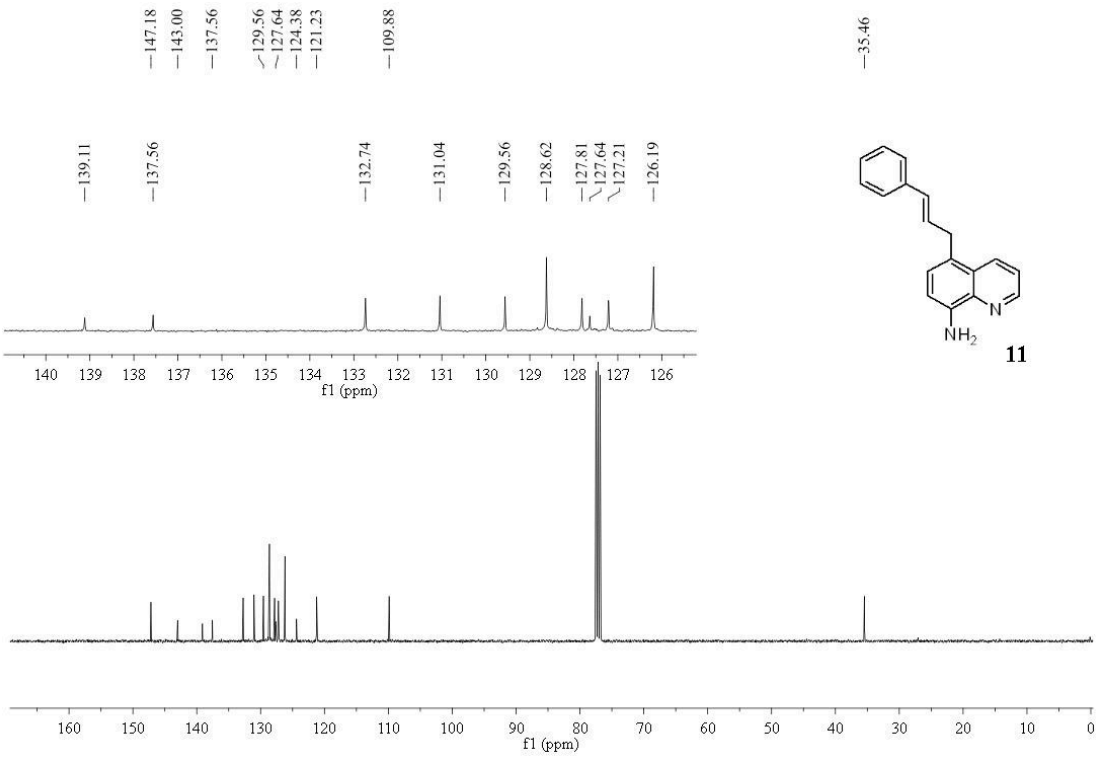

-115.187
F
Me
N
O
NH
3v
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

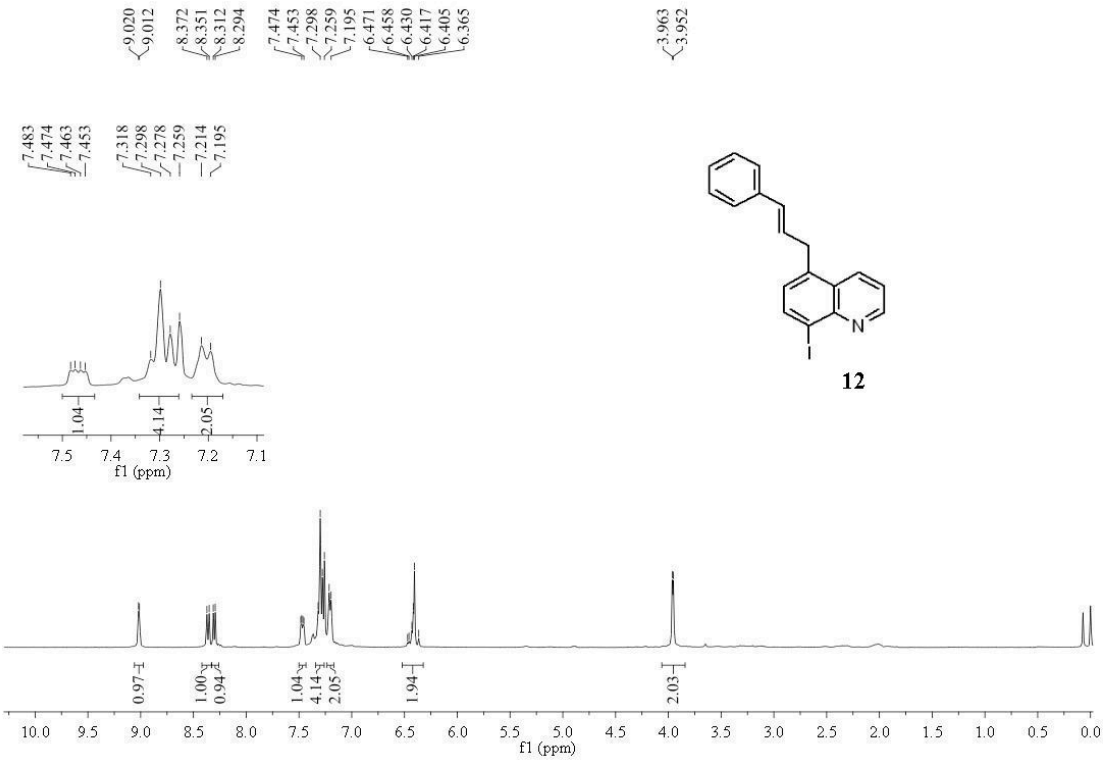

10.381
8.831
8.658
8.649
8.242
7.421
7.217
7.184
6.909
6.888
6.307
6.293
6.282
6.268
6.255
6.226
6.186
4.019
3.900
3.887
1.443
F
MeO
N
O
NH
3w
f1 (ppm)

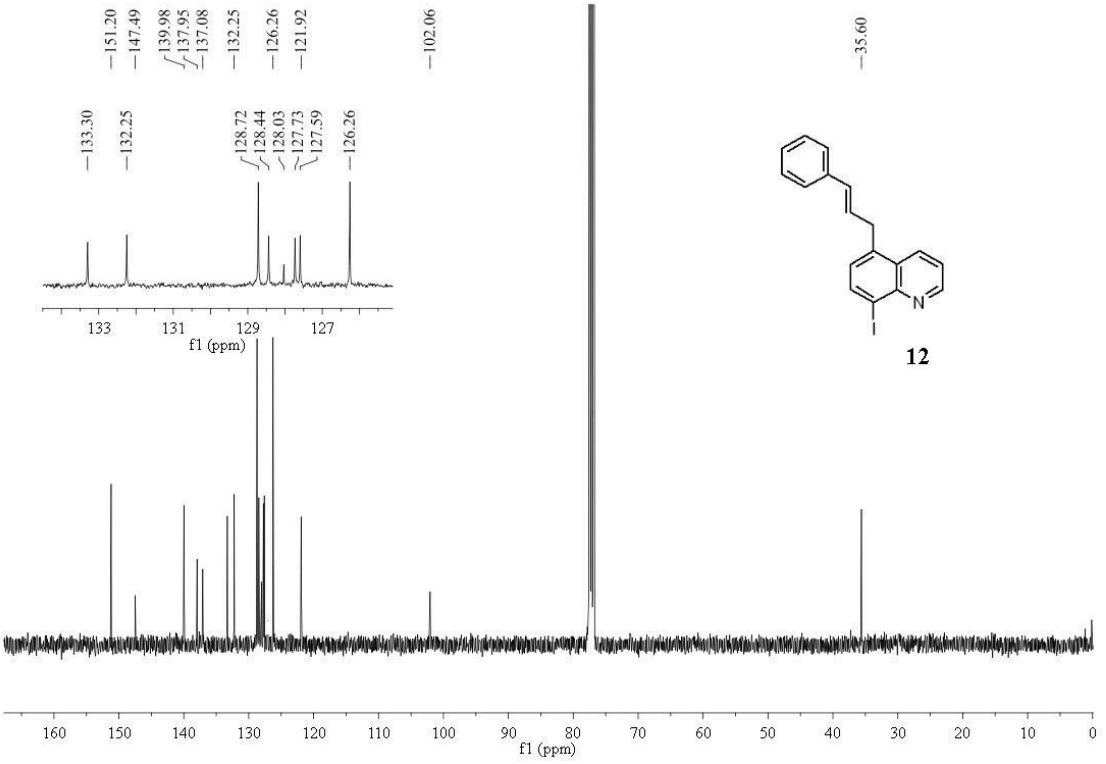

177.69
163.26
160.81
155.17
145.58
132.17
128.60
127.85
127.50
122.01
115.47
113.77
104.35
56.62
40.55
27.86
27.62
F
MeO
N
O
NH
3w
f1 (ppm)

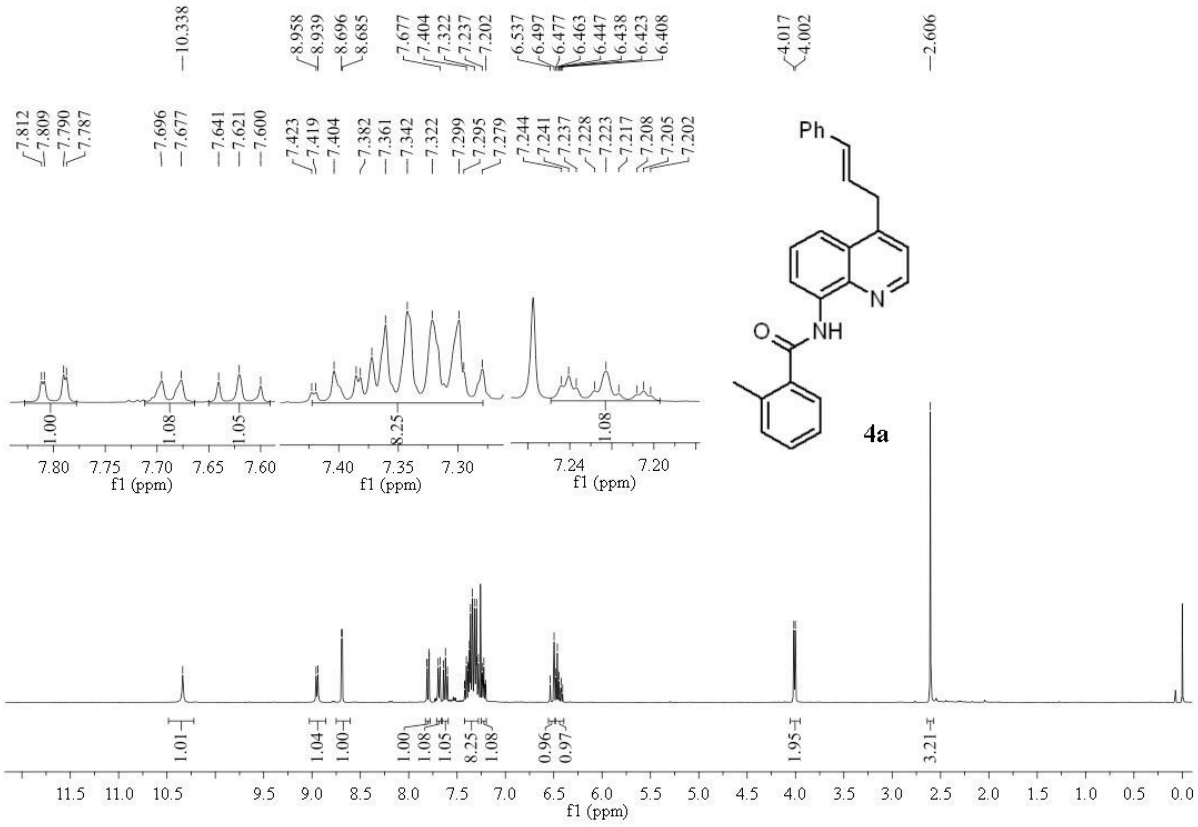

-115.573
F
MeO
N
O
NH
3w
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

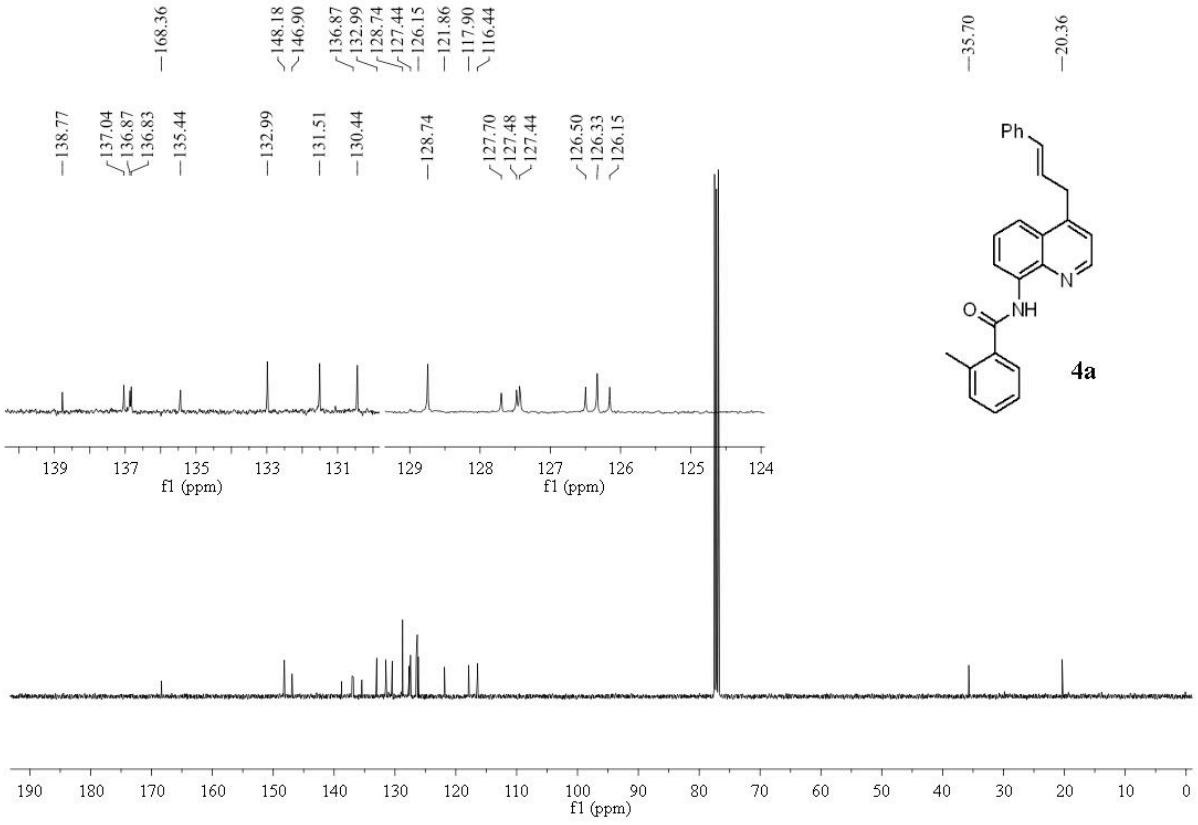

8.770
8.763
8.301
8.280
7.363
7.277
7.221
7.156
6.880
6.435
6.421
6.407
6.386
6.346
4.931
3.849
3.835
7.394
7.384
7.373
7.363
7.311
7.293
7.277
7.258
7.248
7.221
7.191
7.174
7.156
6.899
6.880
6.475
6.460
6.435
6.421
6.407
6.386
6.346
1.09
6.26
1.18
0.97
2.00
f1 (ppm)
NH2
11
1.06
1.00
1.09
6.26
1.18
0.97
2.00
2.17
2.05
f1 (ppm)


147.18
143.00
137.56
129.56
127.64
124.38
121.23
109.88
35.46
139.11
137.56
132.74
131.04
129.56
128.62
127.81
127.64
127.21
126.19
f1 (ppm)
NH2
11
f1 (ppm)


9.020
9.012
8.372
8.351
8.312
8.294
7.474
7.453
7.298
7.259
7.195
6.471
6.458
6.430
6.417
6.405
6.365
3.963
3.952
7.483
7.474
7.463
7.453
7.318
7.298
7.278
7.259
7.214
7.195
1.04
4.14
2.05
7.5 7.4 7.3 7.2 7.1
f1 (ppm)
N
I
12
0.97
1.00
0.94
1.04
4.14
2.05
1.94
2.03
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)


151.20
147.49
139.98
137.95
137.08
132.25
126.26
121.92
102.06
35.60
133.30
132.25
128.72
128.44
128.03
127.73
127.59
126.26
133 131 129 127
f1 (ppm)
N
I
12
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


10.338
8.958
8.939
8.696
8.685
7.677
7.404
7.322
7.237
7.202
6.537
6.497
6.477
6.463
6.447
6.438
6.423
6.408
4.017
4.002
2.606
7.812
7.809
7.790
7.787
7.696
7.677
7.641
7.621
7.600
7.423
7.419
7.404
7.382
7.361
7.342
7.322
7.299
7.295
7.279
7.244
7.241
7.237
7.228
7.223
7.217
7.208
7.205
7.202
Ph
N
O
NH
4a
1.00
1.08
1.05
8.25
1.08
f1 (ppm)
1.01
1.04
1.00
1.00
1.08
1.05
8.25
1.08
0.96
0.97
1.95
3.21
f1 (ppm)


168.36
148.18
146.90
136.87
132.99
128.74
127.44
126.15
121.86
117.90
116.44
35.70
20.36
138.77
137.04
136.87
136.83
135.44
132.99
131.51
130.44
128.74
127.70
127.48
127.44
126.50
126.33
126.15
Ph
N
O
NH
4a
f1 (ppm)
f1 (ppm)
f1 (ppm)