Supporting Information

Nickel-catalyzed chelation-assisted direct arylation of unactivated C(sp^3)–H bonds with aryl halides

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I. General remarks

NMR spectra were obtained on a Bruker AV II-400 MHz spectrometer. The ^{1}H NMR (400 MHz) chemical shifts were measured relative to $CDCl_3$ or TMS as the internal reference ($CDCl_3$: δ = 7.26 ppm; TMS: δ = 0.00 ppm). The ^{13}C NMR (100 MHz) chemical shifts were given using $CDCl_3$ as the internal standard ($CDCl_3$: δ = 77.16 ppm). High-resolution mass spectra (HRMS) were obtained with a Waters-Q-TOF-Premier (ESI). Melting points were determined with XRC-1 and are uncorrected.

Unless otherwise noted, all reagents were obtained from commercial suppliers and used without further purification. $Ni(OAc)_2$ and $NiCl_2$ were purchased from Chengdu Kelong Chemical Engineering Reagent (China) CO., Ltd. 8-Aminoquinoline was purchased from Sichuan Xieli Biological & Chemical Reagent (China) CO., Ltd. The solvents were dried over CaH_2 (for DMF) or sodium (for 1,4-dioxane, toluene, and *t*-AmylOH). Starting materials **1** were prepared according to the literature procedure.[1,2]

II. Synthesis of nickel(II) trifluoromethanesulfonate[3]

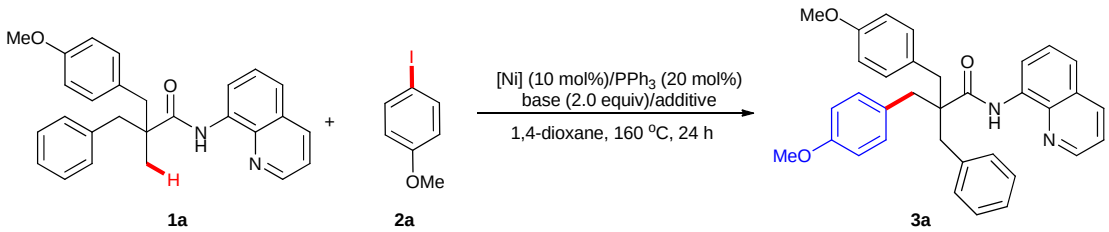
Trifluoromethanesulfonic acid (1.18 mL, 13.3 mmol) was added dropwise to the solution of $Ni(OAc)_2$ (0.72 g, 4.4 mmol) in CH_3CN (60 mL). The resulting mixture was stirred at room temperature for 2 h. Then the solvent was evaporated until around 15 mL solution was left. Diethyl ether (100 mL) was added. The suspension was decanted, and the residual powder was washed successively with diethyl ether and hexane, and dried under vacuum at 70 °C to afford $Ni(OTf)_2$ as a light green solid (0.94 g, 60% yield).

III. Optimization of the coupling of aliphatic amide 1a with aryl iodide 2a

An oven-dried Schlenk tube with a magnetic stir bar was charged with 2-benzyl-3-(4-methoxyphenyl)-2-methyl-*N*-(quinolin-8-yl)propanamide **1a** (82.1 mg, 0.2 mmol), 4-iodoanisole **2a** (93.6 mg, 0.4 mmol), Ni catalyst (0.02 mmol, 10 mol%), PPh_3 (10.4 mg, 0.04 mmol, if required), base (0.4 mmol), additive and 1,4-dioxane (1

mL) under an argon atmosphere. The tube was sealed with a teflon-coated cap and the mixture was stirred at 160 °C for 24 h. After being cooled to ambient temperature, the solution was diluted with 20 mL of EtOAc, filtered through a celite pad, and washed with 10-20 mL of EtOAc. The combined organic phases were concentrated and the residue was purified by column chromatography on silica gel (ethyl acetate/petroleum ether = 1/10, v/v) to give the desired product **3a**.

Table S1. Optimization of the nickel-catalyzed arylation of aliphatic amide **1a** with 1-iodo-4-methoxybenzene **2a**[a]



1a **2a** **3a**

Entry	Ni cat.	Base	Additive (equiv)	Yield[b]
1[c]	$Ni(OTf)_2$	K_2CO_3	none	24%
2[c]	$Ni(OTf)_2$	K_3PO_4	none	trace
3[c]	$Ni(OTf)_2$	Li_2CO_3	none	15%
4[c]	$Ni(OTf)_2$	Na_2CO_3	none	35%
5[c]	$Ni(OTf)_2$	Na_2CO_3	DMSO (7.0)	48%
6	$Ni(OTf)_2$	Na_2CO_3	DMSO (7.0)	57%
7	$Ni(OTf)_2$	Na_2CO_3	DMSO (3.5)	68%
8	$Ni(OTf)_2$	Na_2CO_3	PivOH (0.2)	52%
9	$Ni(OTf)_2$	Na_2CO_3	DMSO (3.5)/PivOH (0.2)	83%
10[d]	$Ni(OTf)_2$	Na_2CO_3	DMSO (3.5)/PivOH (0.2)	54%
11	$Ni(OTf)_2$	Na_2CO_3	DMSO (3.5)/PivOH (0.1)	76%
12	$Ni(OTf)_2$	Na_2CO_3	DMSO (3.5)/PivOH (0.4)	80%
13	$Ni(OAc)_2$	Na_2CO_3	DMSO (3.5)/PivOH (0.2)	61%
14	$NiCl_2$	Na_2CO_3	DMSO (3.5)/PivOH (0.2)	61%
15[e]	$Ni(cod)_2$	Na_2CO_3	DMSO (3.5)/PivOH (0.2)	62%
16	$Ni(cod)_2$	Na_2CO_3	DMSO (3.5)/PivOH (0.2)	50%
17[f]	$Ni(OTf)_2$	Na_2CO_3	DMSO (3.5)/PivOH (0.2)	85%

[a] Reactions were carried out using nickel catalyst (10 mol%), PPh_3 (20 mol%), additive, base (2.0 equiv), amide **1a** (0.2 mmol) and 1-iodio-4-methoxybenzene **2a** (2.0 equiv) in dry 1,4-dioxane (1 mL) at 160 °C for 24 h. [b] Isolated yields. [c] 140 °C. [d] In the absence of PPh_3. [e] PPh_3 (40 mol%). [f] 1-Iodo-4-methoxybenzene **2a** (3.0 equiv).

IV. General procedure for the coupling of aliphatic amides with aryl iodides

An oven-dried Schlenk tube with a magnetic stir bar was charged with aliphatic amide **1** (0.2 mmol, 1 equiv), aryl iodide **2** (0.4 mmol or 0.6 mmol), $Ni(OTf)_2$ (7.2 mg, 0.02 mmol), PPh_3 (10.4 mg, 0.04 mmol), Na_2CO_3 (42 mg, 0.4 mmol), and PivOH (4.2 mg, 0.04 mmol). The tube was then taken to a Schlenk line and DMSO (50 μL, 0.7 mmol) and 1,4-dioxane (1 mL) were added under an argon atmosphere. The tube was sealed with a teflon-coated cap and the resulting mixture was stirred at 160 ^oC for 36 h. After being cooled to ambient temperature, the solution was diluted with 20 mL of EtOAc, filtered through a celite pad, and washed with 10-20 mL of EtOAc. The combined organic phases were concentrated and the residue was purified by column chromatography on silica gel using hexane/ethyl acetate as the eluent to give the desired product.

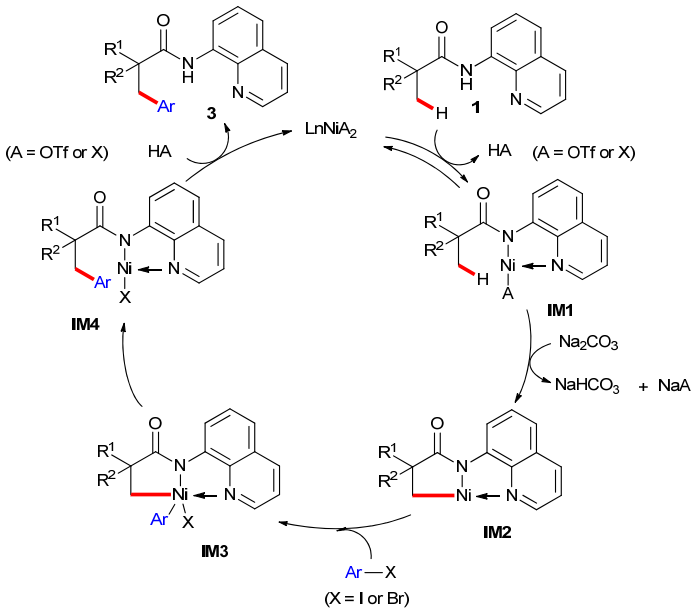
V. General procedure for the coupling of aliphatic amides with aryl bromides

An oven-dried Schlenk tube with a magnetic stir bar was charged with aliphatic amide **1** (0.2 mmol, 1 equiv), aryl bromide (0.8 mmol), $Ni(OTf)_2$ (7.2 mg, 0.02 mmol), PPh_3 (10.4 mg, 0.04 mmol), Na_2CO_3 (42 mg, 0.4 mmol), and PivOH (4.2 mg, 0.04 mmol) (6.7 mg, 0.04 mmol). The tube was then taken to a Schlenk line and DMSO (50 μL, 0.7 mmol) and 1,4-dioxane (1 mL) were added under an argon atmosphere. The tube was sealed with a teflon-coated cap and the resulting mixture was stirred at 160 ^oC for 36 h. After being cooled to ambient temperature, the solution was diluted with 20 mL of EtOAc, filtered through a celite pad, and washed with 10-20 mL of EtOAc. The combined organic phases were concentrated and the residue was purified by column chromatography on silica gel using hexane/ethyl acetate as the eluent to give the desired product.

VI. Plausible mechanism

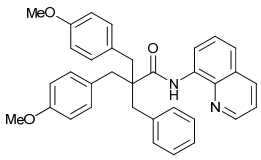
Although the detailed mechanism is not clear at this stage, a plausible catalytic cycle is proposed in Scheme S1. First, aliphatic amide **1** coordinates with nickel(II) complex via a chelation of an 8-aminoquinoline residue to generate the intermediate **IM1**,[3,4] which then undergoes an intramolecular $C(sp^3)$–H activation with the

assistance of Na_2CO_3 to form the metallocycle **IM2**. Subsequently, oxidative addition of **IM2** with aryl halide affords the key intermediate **IM3**.[3,5] Upon reductive elimination of **IM3**, the desired product **3** is obtained and the nickel catalyst is regenerated. When nickel(0) catalyst is used, we suspected that the oxidative addition of aryl iodide with Ni(0) might form Ar−Ni−I complex. The resulting Ni(II) species further reacts with the amide **1** to generate the intermediate **IM1**.[5]



Scheme S1 Plausible mechanism.

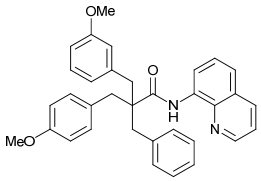
VII. Experimental data for the described substances



2-Benzyl-2-(4-methoxybenzyl)-3-(4-methoxyphenyl)-*N*-(quinolin-8-yl)propanamide (3a)

Following the general procedure except that the reaction time was 24 h. 2-Benzyl-3-(4-methoxyphenyl)-2-methyl-*N*-(quinolin-8-yl)propanamide (82.1 mg, 0.2 mmol) and 4-iodoanisole (93.6 mg, 0.4 mmol) were used. Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/10, v/v) afforded **3a**

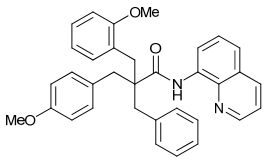
as a white solid (85 mg, 83% yield). When 4-bromoanisole (100 μL, 0.8 mmol) was used as the coupling partner, **3a** was obtained in 76% yield (79 mg). M.p.: 43-47 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.17 (s, 4H), 3.23 (s, 2H), 3.68 (s, 6H), 6.68-6.71 (m, 4H), 7.08-7.10 (m, 4H), 7.13-7.21 (m, 5H), 7.34 (dd, J = 8.4 Hz, 4.0 Hz, 1H), 7.48 (dd, J = 8.4 Hz, 0.8 Hz, 1H), 7.56 (t, J = 8.0 Hz, 1H), 8.09 (dd, J = 8.4 Hz, 1.6 Hz, 1H), 8.47 (dd, J = 4.0 Hz, 1.6 Hz, 1H), 8.84 (dd, J = 7.6 Hz, 0.8 Hz, 1H), 9.95 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 41.0, 41.5, 52.4, 55.2, 113.6, 116.3, 121.4, 121.5, 126.4, 127.5, 127.8, 128.2, 129.3, 130.7, 131.6, 134.3, 136.0, 137.6, 138.7, 147.9, 158.2, 174.2 ppm. HRMS (ESI$^+$): calcd for $C_{34}H_{32}N_2NaO_3$ $[M+Na]^+$ 539.2311, found 539.2313.



2-Benzyl-2-(3-methoxybenzyl)-3-(4-methoxyphenyl)-*N*-(quinolin-8-yl)propanamide (3b)

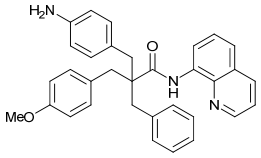
Following the general procedure. 2-Benzyl-3-(4-methoxyphenyl)-2-methyl-*N*-(quinolin-8-yl)propanamide (82.1 mg, 0.2 mmol) and 3-iodoanisole (71.4 μL, 0.6 mmol) were used. Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/10, v/v) afforded **3b** as an off-white solid (75 mg, 73% yield). When 3-bromoanisole (100.4 μL, 0.8 mmol) was used as the coupling partner, **3b** was obtained in 50% yield (51 mg). M.p.: 38-40 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.21 (s, 2H), 3.23 (s, 2H), 3.26 (s, 2H), 3.53 (s, 3H), 3.69 (s, 3H), 6.66-6.72 (m, 4H), 6.82 (d, J = 7.6 Hz, 1H), 7.09-7.12 (m, 3H), 7.15-7.23 (m, 5H), 7.34 (dd, J = 8.0 Hz, 4.0 Hz, 1H), 7.49 (dd, J = 8.4 Hz, 1.2 Hz, 1H), 7.57 (t, J = 8.0 Hz, 1H), 8.09 (dd, J = 8.4 Hz, 1.6 Hz, 1H), 8.48 (dd, J = 4.0 Hz, 1.6 Hz, 1H), 8.87 (d, J = 7.6 Hz, 1H), 9.99 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 41.1, 41.5, 41.9, 52.4, 55.0, 55.2, 112.5, 113.6, 115.8, 116.3, 121.4, 121.5, 123.0, 126.5, 127.4, 127.8, 128.2, 129.0, 129.2, 130.6, 131.6, 134.3, 136.0, 137.5, 138.6, 139.0, 148.0, 158.3, 159.3, 174.1 ppm.

HRMS (ESI$^+$): calcd for $C_{34}H_{32}N_2NaO_3$ $[M+Na]^+$ 539.2311, found 539.2317.



2-Benzyl-2-(2-methoxybenzyl)-3-(4-methoxyphenyl)-*N*-(quinolin-8-yl)propanamide (3c)

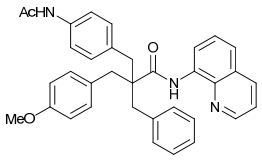
Following the general procedure. 2-Benzyl-3-(4-methoxyphenyl)-2-methyl-*N*-(quinolin-8-yl)propanamide (82.1 mg, 0.2 mmol) and 2-iodoanisole (78.0 μL, 0.6 mmol) were used. Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/15, v/v) afforded **3c** as an off-white solid (36 mg, 35% yield). M.p.: 44-47 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.14-3.33 (m, 6H), 3.50 (s, 3H), 3.69 (s, 3H), 6.58 (d, J = 8.4 Hz, 1H), 6.68-6.71 (m, 2H), 6.78 (td, J = 7.6 Hz, 1.2 Hz, 1H), 7.04-7.09 (m, 3H), 7.11-7.19 (m, 6H), 7.31 (dd, J = 8.4 Hz, 4.4 Hz, 1H), 7.45 (dd, J = 8.4 Hz, 1.2 Hz, 1H), 7.54 (t, J = 8.0 Hz, 1H), 8.07 (dd, J = 8.0 Hz, 1.6 Hz, 1H), 8.42 (dd, J = 4.4 Hz, 1.6 Hz, 1H), 8.85 (dd, J = 7.6 Hz, 1.2 Hz, 1H), 9.90 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 35.9, 40.7, 41.2, 52.0, 55.15, 55.23, 110.1, 113.5, 116.2, 120.1, 121.1, 121.4, 125.9, 126.3, 127.5, 127.7, 128.1, 129.8, 130.8, 131.5, 131.7, 134.6, 135.9, 138.0, 138.6, 147.8, 158.15, 158.22, 174.4 ppm. HRMS (ESI$^+$): calcd for $C_{34}H_{32}N_2NaO_3$ $[M+Na]^+$ 539.2311, found 539.2321.



2-(4-Aminobenzyl)-2-benzyl-3-(4-methoxyphenyl)-*N*-(quinolin-8-yl)propanamide (3d)

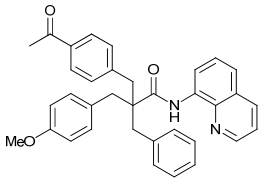
Following the general procedure. 2-Benzyl-3-(4-methoxyphenyl)-2-methyl-*N*-(quinolin-8-yl)propanamide (82.1 mg, 0.2 mmol) and 4-iodoaniline (131.4 mg, 0.6 mmol) were used. Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/3, v/v) afforded **3d** as an off-white solid (55 mg, 55%

yield). When 4-bromoaniline (137.6 mg, 0.8 mmol) was used as the coupling partner, **3d** was obtained in 46% yield (46 mg). M.p.: 70-74 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.14 (s, 2H), 3.16 (s, 2H), 3.22 (s, 2H), 3.53 (br. s, 2H), 3.68 (s, 3H), 6.50-6.52 (m, 2H), 6.68-6.71 (m, 2H), 6.96-6.98 (m, 2H), 7.08-7.11 (m, 2H), 7.13-7.21 (m, 5H), 7.33 (dd, J = 8.0 Hz, 4.0 Hz, 1H), 7.48 (dd, J = 8.4 Hz, 1.2 Hz, 1H), 7.56 (t, J = 8.0 Hz, 1H), 8.08 (dd, J = 8.4 Hz, 1.6 Hz, 1H), 8.50 (dd, J = 4.0 Hz, 1.6 Hz, 1H), 8.86 (dd, J = 7.6 Hz, 1.2 Hz, 1H), 9.99 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 40.8, 41.1, 41.6, 52.4, 55.2, 113.5, 115.0, 116.3, 121.3, 121.4, 126.4, 127.1, 127.5, 127.8, 128.1, 129.4, 130.7, 131.5, 131.6, 134.4, 136.0, 137.7, 138.7, 144.8, 147.9, 158.2, 174.4 ppm. HRMS (ESI$^+$): calcd for $C_{33}H_{31}N_3NaO_2$ $[M+Na]^+$ 524.2314, found 524.2314.



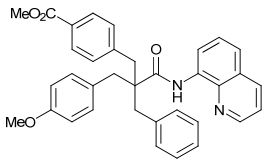
2-(4-Acetamidobenzyl)-2-benzyl-3-(4-methoxyphenyl)-*N*-(quinolin-8-yl)propana mide (3e)

Following the general procedure. 2-Benzyl-3-(4-methoxyphenyl)-2-methyl-*N*-(quinolin-8-yl)propanamide (82.1 mg, 0.2 mmol) and *N*-(4-iodophenyl)acetamide (156.6 mg, 0.6 mmol) were used. Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/1, v/v) afforded **3e** as an off-white solid (75 mg, 69% yield). M.p.: 82-88 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.06 (s, 3H), 3.15 (s, 2H), 3.18 (s, 2H), 3.21 (s, 2H), 3.66 (s, 3H), 6.67-6.69 (m, 2H), 7.05-7.10 (m, 4H), 7.12-7.17 (m, 5H), 7.30-7.33 (m, 3H), 7.46 (d, J = 7.6 Hz, 1H), 7.52 (t, J = 7.6 Hz, 1H), 7.70-7.72 (m, 1H), 8.06 (dd, J = 8.4 Hz, 1.2 Hz, 1H), 8.48 (dd, J = 4.4 Hz, 1.6 Hz, 1H), 8.81 (dd, J = 7.6 Hz, 1.2 Hz, 1H), 10.01 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.5, 41.0, 41.1, 41.6, 52.3, 55.2, 113.5, 116.3, 119.5, 121.47, 121.51, 126.5, 127.4, 127.8, 128.2, 129.1, 130.6, 131.0, 131.6, 133.1, 134.1, 136.0, 136.6, 137.3, 138.6, 148.0, 158.2, 168.6, 174.1 ppm. HRMS (ESI$^+$): calcd for $C_{35}H_{33}N_3NaO_3$ $[M+Na]^+$ 566.2420, found 566.2428.



2-(4-Acetylbenzyl)-2-benzyl-3-(4-methoxyphenyl)-*N*-(quinolin-8-yl)propanamide (3f)

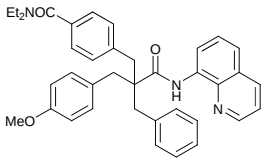
Following the general procedure. 2-Benzyl-3-(4-methoxyphenyl)-2-methyl-*N*-(quinolin-8-yl)propanamide (82.1 mg, 0.2 mmol) and 1-(4-iodophenyl)ethanone (147.6 mg, 0.6 mmol) were used. Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/8, v/v) afforded **3f** as a white solid (58 mg, 55% yield). When 2-(4-acetylbenzyl)-2-methyl-3-phenyl-*N*-(quinolin-8-yl)propanamide (84.5 mg, 0.2 mmol) and 4-iodoanisole (140.4 mg, 0.6 mmol) were used as the starting materials, **3f** was obtained in 71% yield (75 mg). M.p.: 65-68 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.48 (s, 3H), 3.19 (s, 2H), 3.25 (s, 4H), 3.69 (s, 3H), 6.68-6.72 (m, 2H), 7.06-7.09 (m, 2H), 7.14-7.19 (m, 5H), 7.26 (d, J = 8.4 Hz, 2H), 7.33 (dd, J = 8.4 Hz, 4.0 Hz, 1H), 7.50 (dd, J = 8.4 Hz, 1.2 Hz, 1H), 7.57 (t, J = 8.0 Hz, 1H), 7.74 (d, J = 8.4 Hz, 2H), 8.09 (dd, J = 8.4 Hz, 1.6 Hz, 1H), 8.45 (dd, J = 4.4 Hz, 1.6 Hz, 1H), 8.83 (dd, J = 7.6 Hz, 1.2 Hz, 1H), 9.95 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.6, 41.1, 41.6, 42.0, 52.4, 55.2, 113.7, 116.4, 121.5, 121.6, 126.7, 127.5, 127.8, 128.2, 128.3, 128.8, 130.6, 130.8, 131.6, 134.1, 135.4, 136.1, 137.1, 138.6, 143.6, 148.0, 158.4, 173.7, 198.0 ppm. HRMS (ESI^+): calcd for $C_{35}H_{33}N_2O_3$ $[M+H]^+$ 529.2491, found 529.2485.



Methyl 4-(2-benzyl-2-(4-methoxybenzyl)-3-oxo-3-(quinolin-8-ylamino)propyl) benzoate (3g)

Following the general procedure. 2-Benzyl-3-(4-methoxyphenyl)-2-methyl-*N*-(quinolin-8-yl)propanamide (82.1 mg, 0.2 mmol) and methyl 4-iodobenzoate (157.0

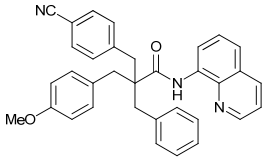
mg, 0.6 mmol) were used. Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/10, v/v) afforded **3g** as a white solid (65 mg, 60% yield). When methyl 4-(2-benzyl-2-methyl-3-oxo-3-(quinolin-8-ylamino)propyl) benzoate (87.7 mg, 0.2 mmol) and 4-iodoanisole (140.4 mg, 0.6 mmol) were used as the starting materials, **3g** was obtained in 50% yield (54 mg). M.p.: 55-59 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.19 (s, 2H), 3.24-3.26 (m, 4H), 3.68 (s, 3H), 3.86 (s, 3H), 6.70 (d, J = 8.4 Hz, 2H), 7.07 (d, J = 8.8 Hz, 2H), 7.13-7.18 (m, 5H), 7.25 (d, J = 8.8 Hz, 2H), 7.33 (dd, J = 8.4 Hz, 4.4 Hz, 1H), 7.49 (dd, J = 8.4 Hz, 1.2 Hz, 1H), 7.57 (t, J = 8.0 Hz, 1H), 7.83 (d, J = 8.4 Hz, 2H), 8.09 (dd, J = 8.4 Hz, 1.6 Hz, 1H), 8.46 (dd, J = 4.4 Hz, 1.6 Hz, 1H), 8.84 (dd, J = 7.6 Hz, 1.2 Hz, 1H), 9.96 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 41.2, 41.7, 41.8, 52.1, 52.4, 55.2, 113.7, 116.4, 121.5, 121.6, 126.6, 127.5, 127.9, 128.3, 128.4, 128.9, 129.4, 130.6, 130.7, 131.6, 134.1, 136.1, 137.2, 138.7, 143.3, 148.0, 158.4, 167.1, 173.7 ppm. HRMS (ESI$^+$): calcd for $C_{35}H_{33}N_2O_4$ $[M+H]^+$ 545.2440, found 545.2433.



4-(2-Benzyl-2-(4-methoxybenzyl)-3-oxo-3-(quinolin-8-ylamino)propyl)-*N,N*-dieth ylbenzamide (3h)

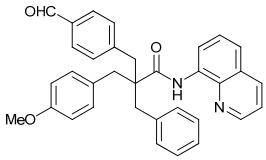
Following the general procedure. 2-Benzyl-3-(4-methoxyphenyl)-2-methyl-*N*-(quinolin-8-yl)propanamide (82.1 mg, 0.2 mmol) and *N,N*-diethyl-4-iodobenzamide (181.8 mg, 0.6 mmol) were used. Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/1, v/v) afforded **3h** as a white solid (72 mg, 62% yield). When 4-(2-benzyl-2-methyl-3-oxo-3-(quinolin-8-ylamino)propyl)-*N,N*-diethylbenzamide (95.9 mg, 0.2 mmol) and 4-iodoanisole (140.4 mg, 0.6 mmol) were used as the starting materials, **3h** was obtained in 73% yield (85 mg). M.p.: 39-40 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.97 (m, 3H), 1.19 (m, 3H), 3.09 (m, 2H), 3.18 (s, 2H), 3.23-3.28 (m, 4H), 3.49 (m, 2H), 3.67 (s, 3H), 6.67-6.70 (m, 2H), 7.05-7.09 (m, 2H), 7.13-7.18 (m, 5H), 7.21 (m, 4H), 7.34 (dd, J = 8.4 Hz, 4.4 Hz, 1H), 7.48 (dd, J =

8.4 Hz, 1.6 Hz, 1H), 7.56 (t, *J* = 8.0 Hz, 1H), 8.08 (dd, *J* = 8.0 Hz, 1.6 Hz, 1H), 8.49 (dd, *J* = 4.0 Hz, 1.6 Hz, 1H), 8.84 (dd, *J* = 7.6 Hz, 1.6 Hz, 1H), 9.99 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.0, 14.2, 41.2, 41.3, 41.6, 52.3, 55.2, 113.6, 116.3, 121.48, 121.53, 126.3, 126.5, 127.4, 127.8, 128.2, 129.0, 130.58, 130.60, 131.6, 134.2, 135.3, 136.0, 137.3, 138.6, 138.9, 148.1, 158.3, 171.3, 173.9 ppm. HRMS (ESI$^+$): calcd for $C_{38}H_{40}N_3O_3$ $[M+H]^+$ 586.3070, found 586.3074.



2-Benzyl-2-(4-cyanobenzyl)-3-(4-methoxyphenyl)-*N*-(quinolin-8-yl)propanamide (3i)

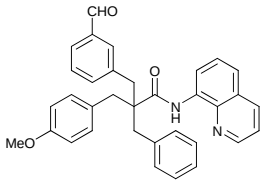
Following the general procedure. 2-Benzyl-3-(4-cyanophenyl)-2-methyl-*N*-(quinolin-8-yl)propanamide (81.1 mg, 0.2 mmol) and 4-iodoanisole (140.4 mg, 0.6 mmol) were used. Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/8, v/v) afforded **3i** as a white solid (60 mg, 59% yield). M.p.: 57-60 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.18 (s, 2H), 3.228 (s, 2H), 3.234 (s, 2H), 3.69 (s, 3H), 6.69-6.73 (m, 2H), 7.05-7.07 (m, 2H), 7.14-7.22 (m, 5H), 7.25-7.27 (m, 2H), 7.38 (dd, *J* = 8.0 Hz, 4.0 Hz, 1H), 7.42 (d, *J* = 8.0 Hz, 2H), 7.51 (dd, *J* = 8.0 Hz, 1.2 Hz, 1H), 7.57 (t, *J* = 8.0 Hz, 1H), 8.12 (dd, *J* = 8.0 Hz, 1.2 Hz, 1H), 8.49 (dd, *J* = 4.4 Hz, 1.6 Hz, 1H), 8.81 (dd, *J* = 7.6 Hz, 1.2 Hz, 1H), 9.94 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 41.2, 41.7, 42.3, 52.5, 55.2, 110.3, 113.7, 116.4, 119.0, 121.7, 121.8, 126.8, 127.5, 127.9, 128.4, 128.6, 130.5, 131.4, 131.6, 131.8, 133.9, 136.2, 136.9, 138.6, 143.7, 148.1, 158.5, 173.4 ppm. HRMS (ESI$^+$): calcd for $C_{34}H_{30}N_3O_2$ $[M+H]^+$ 512.2338, found 512.2336.



2-Benzyl-2-(4-formylbenzyl)-3-(4-methoxyphenyl)-*N*-(quinolin-8-yl)propanamide

(3j)

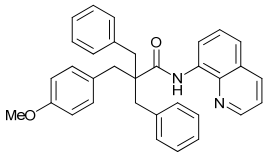
Following the general procedure. 2-Benzyl-3-(4-formylphenyl)-2-methyl-*N*-(quinolin-8-yl)propanamide (81.7 mg, 0.2 mmol) and 4-iodoanisole (140.4 mg, 0.6 mmol) were used. Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/8, v/v) afforded **3j** as a white solid (56 mg, 55% yield). M.p.: 50-52 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.20 (s, 2H), 3.26 (s, 2H), 3.27 (s, 2H), 3.69 (s, 3H), 6.69-6.72 (m, 2H), 7.06-7.08 (m, 2H), 7.14-7.21 (m, 5H), 7.32-7.35 (m, 3H), 7.50 (dd, J = 8.4 Hz, 1.2 Hz, 1H), 7.57 (t, J = 8.0 Hz, 1H), 7.66 (d, J = 8.0 Hz, 2H), 8.10 (dd, J = 8.0 Hz, 1.6 Hz, 1H), 8.45 (dd, J = 4.4 Hz, 1.6 Hz, 1H), 8.83 (dd, J = 7.6 Hz, 1.2 Hz, 1H), 9.87 (s, 1H), 9.96 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 41.2, 41.7, 42.3, 52.5, 55.2, 113.7, 116.4, 121.6, 121.7, 126.7, 127.5, 127.9, 128.3, 128.8, 129.6, 130.6, 131.3, 131.6, 134.1, 134.9, 136.1, 137.0, 138.6, 145.4, 148.0, 158.5, 173.6, 192.1 ppm. HRMS (ESI$^+$): calcd for $C_{34}H_{31}N_2O_3$ $[M+H]^+$ 515.2335, found 515.2338.



2-Benzyl-2-(3-formylbenzyl)-3-(4-methoxyphenyl)-*N*-(quinolin-8-yl)propanamide (3k)

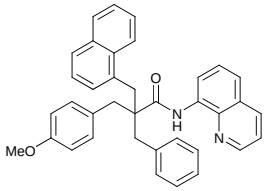
Following the general procedure. 2-Benzyl-3-(3-formylphenyl)-2-methyl-*N*-(quinolin-8-yl)propanamide (81.7 mg, 0.2 mmol) and 4-iodoanisole (140.4 mg, 0.6 mmol) were used. Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/8, v/v) afforded **3k** as a white solid (60 mg, 59% yield). M.p.: 48-50 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.19 (s, 2H), 3.24-3.27 (m, 4H), 3.69 (s, 3H), 6.69-6.73 (m, 2H), 7.07-7.10 (m, 2H), 7.13-7.21 (m, 5H), 7.30 (t, J = 7.6 Hz, 1H), 7.35 (dd, J = 8.0 Hz, 4.0 Hz, 1H), 7.45 (d, J = 7.6 Hz, 1H), 7.50 (dd, J = 8.0 Hz, 1.2 Hz, 1H), 7.57 (t, J = 8.0 Hz, 1H), 7.61-7.64 (m, 2H), 8.10 (dd, J = 8.4 Hz, 1.6 Hz, 1H), 8.45 (dd, J = 4.0 Hz, 1.6 Hz, 1H), 8.83 (dd, J = 7.6 Hz, 1.2 Hz, 1H), 9.76 (s,

1H), 9.97 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 41.2, 41.6, 41.9, 52.5, 55.3, 113.7, 116.4, 121.6, 121.7, 126.7, 127.4, 127.5, 127.9, 128.4, 128.8, 130.6, 131.6, 132.8, 134.1, 136.1, 136.3, 136.8, 137.1, 138.6, 138.8, 148.0, 158.4, 173.7, 192.4 ppm. HRMS (ESI$^+$): calcd for $C_{34}H_{31}N_2O_3$ $[M+H]^+$ 515.2335, found 515.2327.



2,2-Dibenzyl-3-(4-methoxyphenyl)-*N*-(quinolin-8-yl)propanamide (3l)

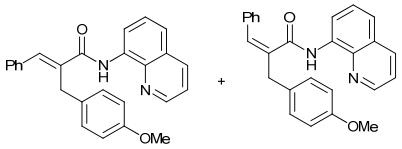
Following the general procedure. 2-Benzyl-2-methyl-3-phenyl-*N*-(quinolin-8-yl) propanamide (76.1 mg, 0.2 mmol) and 4-iodoanisole (140.4 mg, 0.6 mmol) were used. Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/10, v/v) afforded **3l** as an off-white solid (66 mg, 68% yield). M.p.: 39-42 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.19 (s, 2H), 3.25 (s, 4H), 3.68 (s, 3H), 6.67-6.71 (m, 2H), 7.08-7.10 (m, 2H), 7.12-7.20 (m, 10H), 7.33 (dd, J = 8.4 Hz, 4.0 Hz, 1H), 7.49 (dd, J = 8.4 Hz, 1.2 Hz, 1H), 7.57 (t, J = 8.0 Hz, 1H), 8.09 (dd, J = 8.0 Hz, 1.6 Hz, 1H), 8.47 (dd, J = 4.4 Hz, 1.6 Hz, 1H), 8.86 (dd, J = 7.6 Hz, 1.2 Hz, 1H), 9.97 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 41.2, 41.6, 52.3, 55.2, 113.6, 116.3, 121.4, 121.5, 126.5, 127.5, 127.8, 128.2, 129.2, 130.7, 131.6, 134.3, 136.0, 137.5, 138.7, 147.9, 158.3, 174.1 ppm. HRMS (ESI$^+$): calcd for $C_{33}H_{30}N_2NaO_2$ $[M+Na]^+$ 509.2205, found 509.2206.



2-Benzyl-2-(4-methoxybenzyl)-3-(naphthalen-1-yl)-*N*-(quinolin-8-yl)propanamide (3m)

Following the general procedure. 2-Benzyl-2-methyl-3-(naphthalen-1-yl)-*N*-(quinolin-8-yl)propanamide (86.1 mg, 0.2 mmol) and 4-iodoanisole (140.4 mg, 0.6 mmol) were used. Purification via column chromatography on silica gel (ethyl

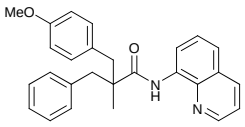
acetate/petroleum ether = 1/8, v/v) afforded **3m** as an off-white solid (84 mg, 79% yield). M.p.: 63-66 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.34 (s, 2H), 3.40 (d, J = 3.2 Hz, 2H), 3.59 (s, 2H), 3.67 (s, 3H), 6.66-6.69 (m, 2H), 7.08 (d, J = 8.4 Hz, 2H), 7.12-7.29 (m, 8H), 7.32 (t, J = 7.6 Hz, 1H), 7.40 (dd, J = 8.4 Hz, 1.2 Hz, 1H), 7.47 (d, J = 8.0 Hz, 1H), 7.50 (t, J = 8.0 Hz, 1H), 7.59 (t, J = 8.0 Hz, 2H), 7.95 (d, J = 8.4 Hz, 1H), 7.98 (dd, J = 8.0 Hz, 1.2 Hz, 1H), 8.22 (dd, J = 4.4 Hz, 1.6 Hz, 1H), 8.78 (dd, J = 7.6 Hz, 1.2 Hz, 1H), 9.74 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 37.7, 41.0, 41.6, 51.9, 55.2, 113.6, 116.1, 121.2, 123.8, 125.11, 125.13, 125.8, 126.5, 127.27, 127.29, 127.5, 127.6, 128.2, 128.4, 129.3, 130.8, 131.7, 133.3, 133.4, 133.9, 134.2, 135.7, 137.6, 138.4, 147.6, 158.3, 174.3 ppm. HRMS (ESI$^+$): calcd for $C_{37}H_{32}N_2NaO_2$ $[M+Na]^+$ 559.2361, found 559.2364.



2-(4-Methoxybenzyl)-3-phenyl-*N*-(quinolin-8-yl)acrylamide (4)

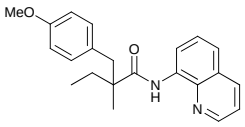
Following the general procedure. 2-Methyl-3-phenyl-*N*-(quinolin-8-yl)acrylamide (57.7 mg, 0.2 mmol), and 4-iodoanisole (140.4 mg, 0.6 mmol) were used. Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/10, v/v) afforded **4** as a mixture of (*E*)- and (*Z*)-isomers (46 mg, 58% yield). The ratio of (*E*)-**4**/(*Z*)-**4** was 8:1 as determined by ^{1}H NMR. ^{1}H NMR (400 MHz, $CDCl_3$, a mixture of two isomers) : δ = 3.77 (s, O$C\underline{H}_3$, major isomer), 3.83 (s, O$C\underline{H}_3$, minor isomer), 4.12 (s, major isomer), 4.21 (s, minor isomer), 6.60 (d, J = 8.8 Hz, minor isomer), 6.88 (d, J = 8.8 Hz, major isomer), 6.92 (d, J = 8.8 Hz, minor isomer), 7.18-7.23 (m), 7.28-7.44 (m), 7.48 (d, J = 8.4 Hz, major isomer), 7.53 (t, J = 7.6 Hz, major isomer), 7.91 (s, minor isomer), 7.93 (s, major isomer), 8.06 (dd, J = 8.4 Hz, 1.6 Hz, minor isomer), 8.12 (dd, J = 8.4 Hz, 1.6 Hz, major isomer), 8.53 (dd, J = 4.4 Hz, 1.6 Hz, minor isomer), 8.68 (dd, J = 4.0 Hz, 1.6 Hz, major isomer), 8.75 (d, J = 7.6 Hz, minor isomer), 8.83 (dd, J = 7.6 Hz, 1.2 Hz, major isomer), 9.58 (s, minor isomer), 10.40 (s,

major isomer) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 32.9, 33.8, 55.4, 55.5, 113.6, 114.2, 114.3, 116.7, 121.6, 121.7, 126.7, 127.5, 128.0, 128.3, 128.5, 128.7, 129.2, 129.5, 130.0, 130.2, 130.8, 130.9, 134.9, 135.4, 135.9, 136.3, 137.19, 137.23, 138.8, 148.1, 158.5, 167.0 ppm. HRMS (ESI$^+$): calcd for $C_{26}H_{22}N_2NaO_2$ $[M+Na]^+$ 417.1579, found 417.1575.



2-Benzyl-3-(4-methoxyphenyl)-2-methyl-*N*-(quinolin-8-yl)propanamide (5)

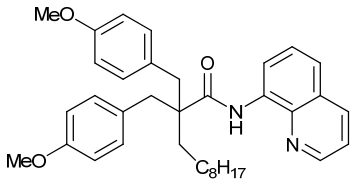
Following the general procedure except that the reaction temperature was 150 ^{o}C and 2-nitrobenzoic acid (6.7 mg, 0.04 mmol) instead of PivOH was added. 2,2-Dimethyl-3-phenyl-*N*-(quinolin-8-yl)propanamide (60.9 mg, 0.2 mmol) and 4-iodoanisole (140.4 mg, 0.6 mmol) were used. Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/20, v/v) afforded **5** as a white solid (49 mg, 60% yield). M.p.: 80-82 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.31 (s, 3H), 2.74 (d, J = 13.2 Hz, 1H), 2.78 (d, J = 13.2 Hz, 1H), 3.43 (d, J = 13.6 Hz, 1H), 3.49 (d, J = 13.2 Hz, 1H), 3.67 (s, 3H), 6.69-6.71 (m, 2H), 7.10-7.23 (m, 7H), 7.36 (dd, J = 8.4 Hz, 4.4 Hz, 1H), 7.48 (dd, J = 8.4 Hz, 1.2 Hz, 1H), 7.56 (t, J = 7.6 Hz, 1H), 8.09 (dd, J = 8.4 Hz, 1.6 Hz, 1H), 8.62 (dd, J = 4.4 Hz, 1.6 Hz, 1H), 8.88 (d, J = 7.6 Hz, 1H), 9.92 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.7, 45.9, 46.6, 50.2, 55.2, 113.5, 116.4, 121.49, 121.52, 126.5, 127.4, 127.9, 128.1, 129.7, 130.5, 131.4, 134.4, 136.2, 137.8, 138.8, 148.2, 158.3, 174.8 ppm. HRMS (ESI$^+$): calcd for $C_{27}H_{26}N_2NaO_2$ $[M+Na]^+$ 433.1892, found 433.1891.



2-(4-Methoxybenzyl)-2-methyl-*N*-(quinolin-8-yl)butanamide (6)

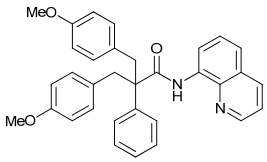
Following the general procedure except that the reaction temperature was 150 ^{o}C. 2,2-Dimethyl-*N*-(quinolin-8-yl)butanamide (48.5 mg, 0.2 mmol) and 4-iodoanisole (140.4 mg, 0.6 mmol) were used. Purification via column chromatography on silica

gel (ethyl acetate/petroleum ether = 1/20, v/v) afforded **6** as colourless oil (45 mg, 64% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.99 (t, J = 7.6 Hz, 3H), 1.34 (s, 3H), 1.54-1.63 (m, 1H), 2.00-2.09 (m, 1H), 2.77 (d, J = 13.2 Hz, 1H), 3.20 (d, J = 13.6 Hz, 1H), 3.68 (s, 3H), 6.69-6.73 (m, 2H), 7.09-7.11 (m, 2H), 7.41 (dd, J = 8.0 Hz, 4.0 Hz, 1H), 7.49 (dd, J = 8.4 Hz, 1.2 Hz, 1H), 7.55 (t, J = 7.6 Hz, 1H), 8.13 (dd, J = 8.0 Hz, 0.8 Hz, 1H), 8.74 (dd, J = 4.4 Hz, 1.6 Hz, 1H), 8.85 (d, J = 7.6 Hz, 1H), 10.12 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 9.3, 20.3, 32.8, 45.3, 49.2, 55.2, 113.5, 116.3, 121.4, 121.6, 127.5, 128.0, 130.0, 131.3, 134.6, 136.3, 138.9, 148.3, 158.2, 175.5 ppm. HRMS (ESI$^+$): calcd for $C_{22}H_{24}N_2NaO_2$ $[M+Na]^+$ 371.1735, found 371.1732.



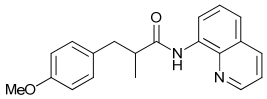
2,2-Bis(4-methoxybenzyl)-*N*-(quinolin-8-yl)undecanamide (7)

Following the general procedure. 2,2-Dimethyl-*N*-(quinolin-8-yl)undecanamide (68.1 mg, 0.2 mmol) and 4-iodoanisole (187.2 mg, 0.8 mmol) were used. Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/20, v/v) afforded **7** as colourless oil (64 mg, 58% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.89 (t, J = 6.8 Hz, 3H), 1.27-1.35 (m, 12H), 1.66 (m, 4H), 2.95 (d, J = 14.0 Hz, 2H), 3.23 (d, J = 14.0 Hz, 2H), 3.67 (s, 6H), 6.70 (d, J = 8.4 Hz, 4H), 7.12 (d, J = 8.4 Hz, 4H), 7.37 (dd, J = 8.4 Hz, 4.4 Hz, 1H), 7.49 (d, J = 8.0 Hz, 1H), 7.57 (t, J = 8.0 Hz, 1H), 8.11 (d, J = 8.4 Hz, 1H), 8.63 (d, J = 3.2 Hz, 1H), 8.87 (d, J = 7.2 Hz, 1H), 9.99 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.3, 22.8, 24.2, 29.4, 29.6, 29.7, 30.2, 32.0, 32.1, 41.3, 53.1, 55.1, 113.5, 116.3, 121.3, 121.5, 127.5, 127.9, 129.8, 131.2, 134.4, 136.1, 138.8, 148.1, 158.1, 174.8 ppm. HRMS (ESI$^+$): calcd for $C_{36}H_{44}N_2NaO_3$ $[M+Na]^+$ 575.3250, found 575.3242.



2-(4-Methoxybenzyl)-3-(4-methoxyphenyl)-2-phenyl-*N*-(quinolin-8-yl)propanamide (8)

Following the general procedure. 2-Methyl-2-phenyl-*N*-(quinolin-8-yl)propanamide (58.1 mg, 0.2 mmol) and 4-iodoanisole (187.2 mg, 0.8 mmol) were used. Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/10, v/v) afforded **8** as a white solid (57 mg, 57% yield). M.p.: 146-148 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.38-3.47 (m, 4H), 3.71 (s, 6H), 6.63-6.67 (m, 4H), 6.85-6.88 (m, 4H), 7.28-7.39 (m, 6H), 7.47 (dd, J = 8.4 Hz, 1.2 Hz, 1H), 7.54 (t, J = 8.0 Hz, 1H), 8.09 (dd, J = 8.4 Hz, 1.6 Hz, 1H), 8.54 (dd, J = 4.4 Hz, 1.6 Hz, 1H), 8.74 (dd, J = 7.6 Hz, 1.2 Hz, 1H), 9.87 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 41.1, 55.2, 58.4, 113.3, 116.2, 121.3, 121.6, 127.3, 127.5, 128.0, 128.3, 128.6, 129.3, 131.7, 134.6, 136.1, 138.7, 142.6, 148.2, 158.2, 174.0 ppm. HRMS (ESI$^+$): calcd for $C_{33}H_{30}N_2NaO_3$ $[M+Na]^+$ 525.2154, found 525.2154.



3-(4-Methoxyphenyl)-2-methyl-*N*-(quinolin-8-yl)propanamide (9)

Following the general procedure. *N*-(Quinolin-8-yl)isobutyramide (42.9 mg, 0.2 mmol) and 4-iodoanisole (140.4 mg, 0.6 mmol) were used. Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/20, v/v) afforded **9** as colourless oil (32 mg, 50% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.33 (d, J = 6.4 Hz, 3H), 2.74-2.79 (m, 1H), 2.81-2.90 (m, 1H), 3.14 (dd, J = 13.2 Hz, 7.2 Hz, 1H), 3.72 (s, 3H), 6.77-6.80 (m, 2H), 7.16-7.19 (m, 2H), 7.43 (dd, J = 8.4 Hz, 4.4 Hz, 1H), 7.48 (dd, J = 8.4 Hz, 1.6 Hz, 1H), 7.53 (t, J = 8.0 Hz, 1H), 8.14 (dd, J = 8.0 Hz, 1.6 Hz, 1H), 8.75 (dd, J = 4.4 Hz, 1.6 Hz, 1H), 8.79 (dd, J = 7.6 Hz, 1.6 Hz, 1H), 9.75 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.8, 39.6, 45.2, 55.3, 113.9, 116.6, 121.5, 121.6, 127.5, 128.0, 130.1, 131.8, 134.6, 136.4, 138.5, 148.2, 158.2, 174.7 ppm.

HRMS (ESI$^+$): calcd for $C_{20}H_{20}N_2NaO_2$ $[M+Na]^+$ 343.1422, found 343.1427.

VIII. References

1. R. Shang, L. Ilies, A. Matsumoto and E. Nakamura, *J. Am. Chem. Soc.*, 2013, **135**, 6030.

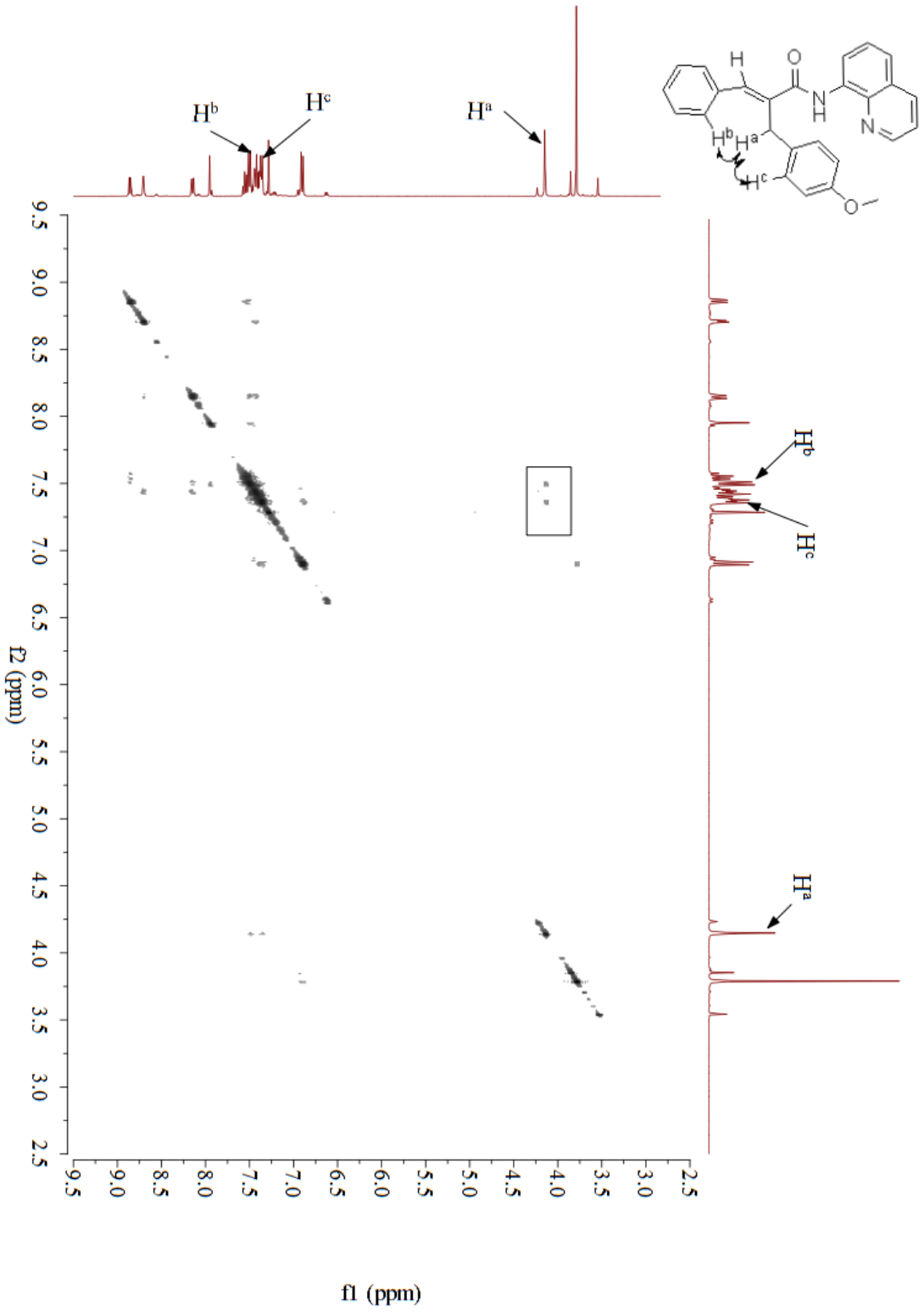
2. E. T. Nadres and O. Daugulis, *J. Am. Chem. Soc.*, 2012, **134**, 7.

3. Y. Aihara and N. Chatani, *J. Am. Chem. Soc.*, 2013, **135**, 5308.

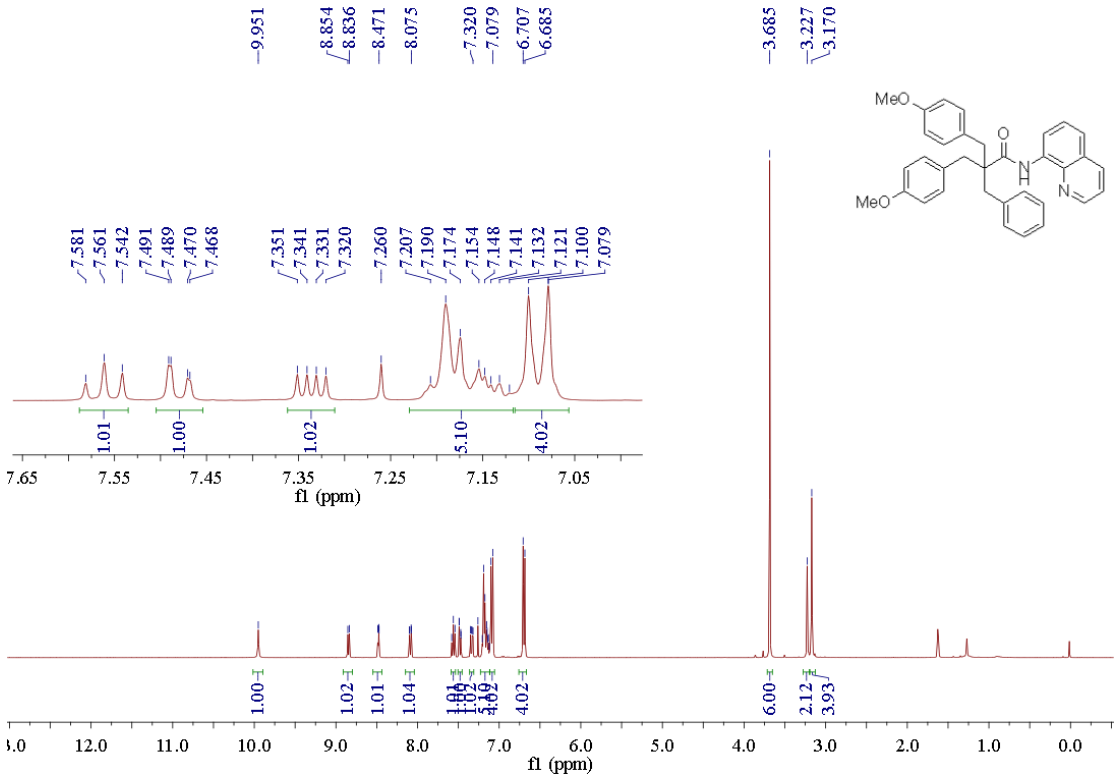
4. H. Shiota, Y. Ano, Y. Aihara, Y. Fukumoto and N. Chatani, *J. Am. Chem. Soc.*, 2011, **133**, 14952.

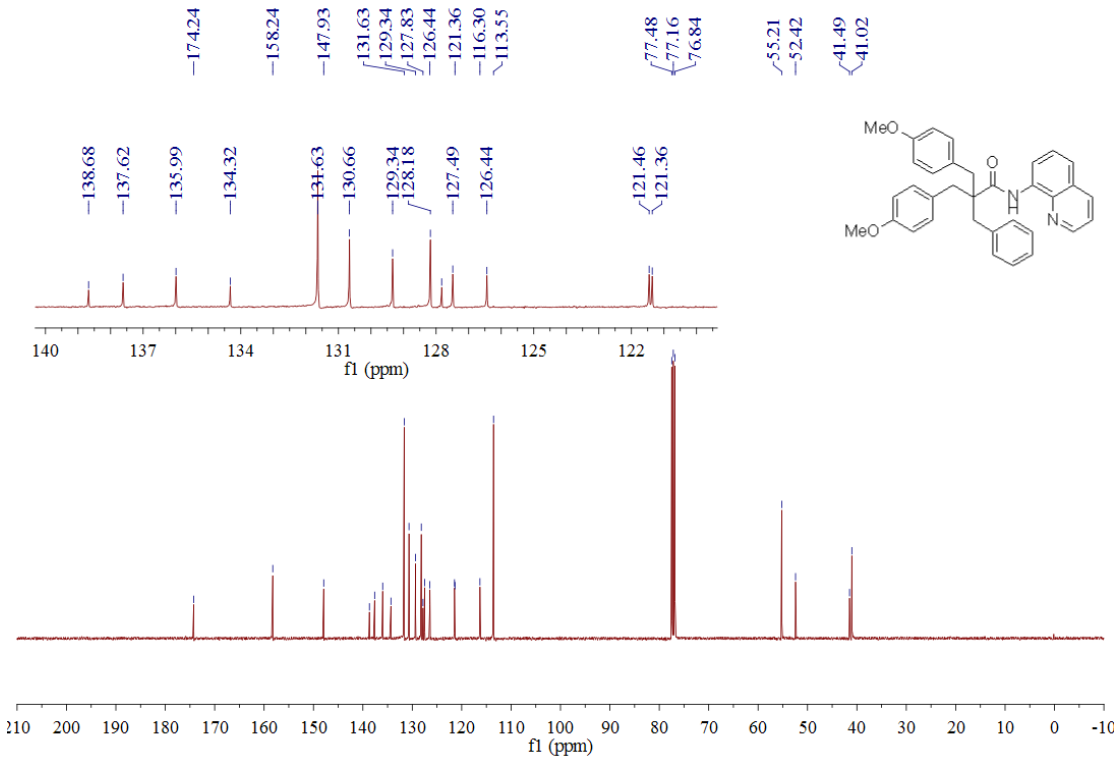
5. Y. Aihara and N. Chatani, *J. Am. Chem. Soc.*, 2014, **136**, 898.

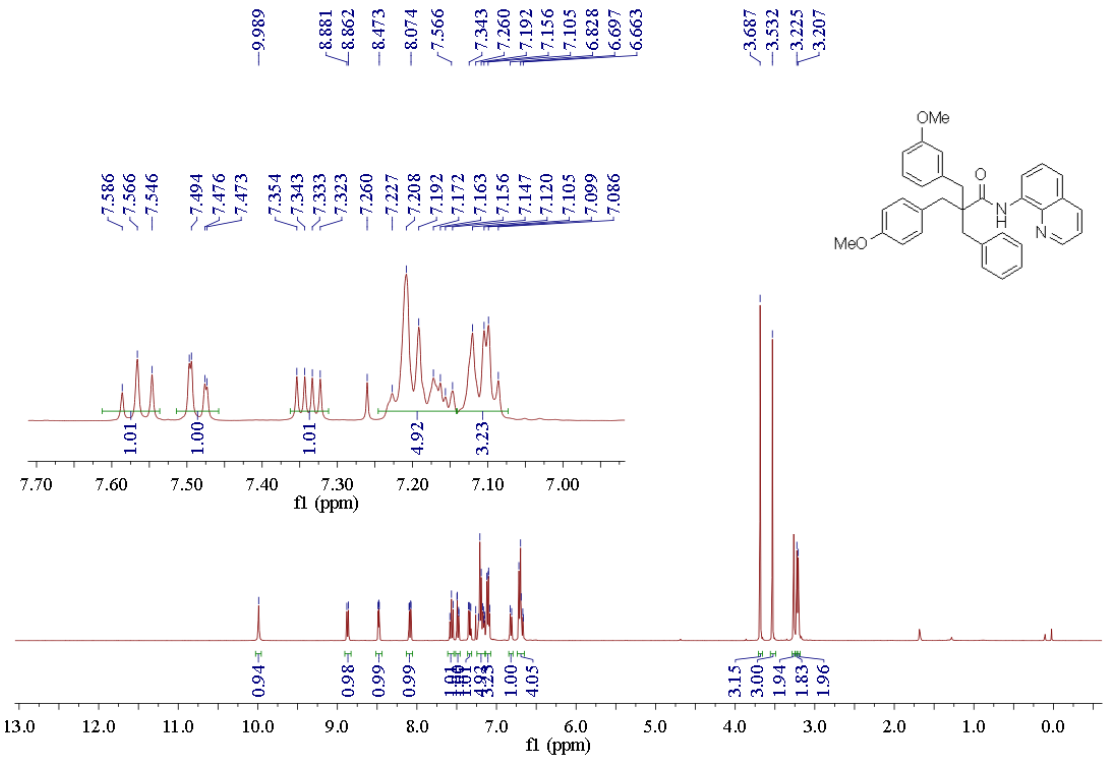
IX. Copy of ^{1}H-^{1}H NOESY spectrum of 4



X. Copies of ^{1}H and ^{13}C NMR spectra



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6.697
6.663
3.687
3.532
3.225
3.207
OMe
MeO
O
N
H
N
7.586
7.566
7.546
7.494
7.476
7.473
7.354
7.343
7.333
7.323
7.260
7.227
7.208
7.192
7.172
7.163
7.156
7.147
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7.105
7.099
7.086
1.01
1.00
1.01
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3.23
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7.50
7.40
7.30
7.20
7.10
7.00
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0.98
0.99
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1.96
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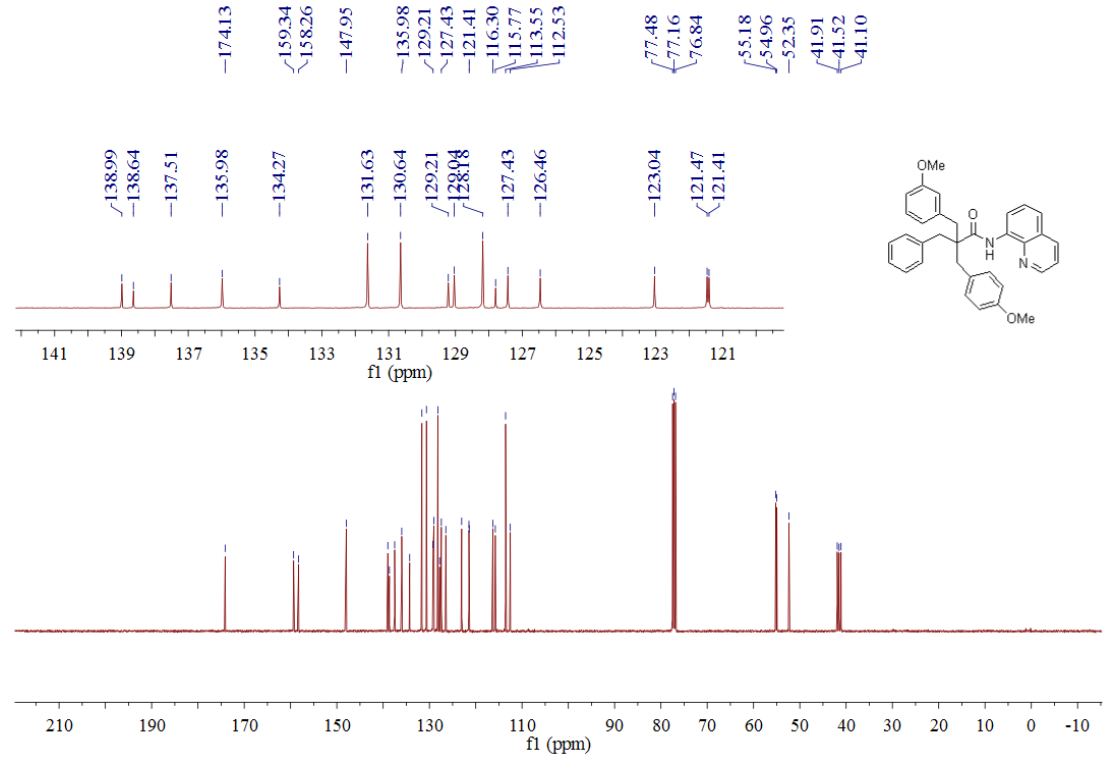
f1 (ppm)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76.84
55.18
54.96
52.35
41.91
41.52
41.10
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138.64
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127.43
126.46
123.04
121.47
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O
N
H
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141
139
137
135
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129
127
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123
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f1 (ppm)
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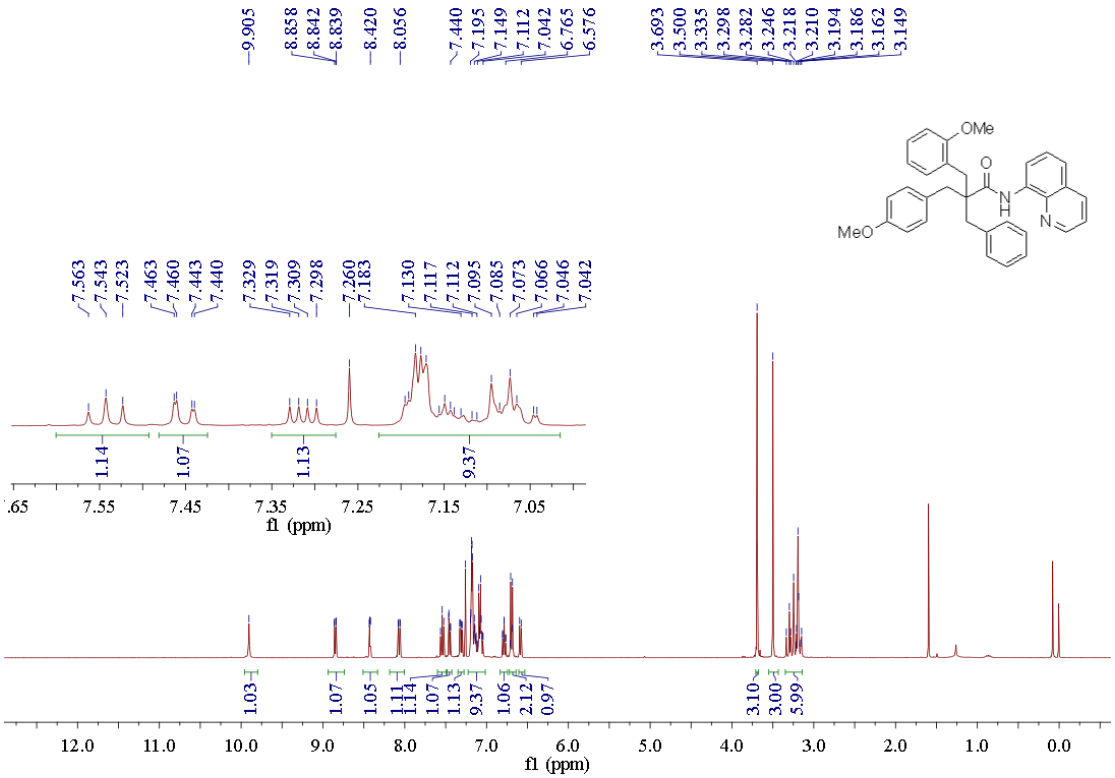
f1 (ppm)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6.576
3.693
3.500
3.335
3.298
3.282
3.246
3.218
3.210
3.194
3.186
3.162
3.149
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MeO
O
N
H
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7.543
7.523
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7.460
7.443
7.440
7.329
7.319
7.309
7.298
7.260
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7.130
7.117
7.112
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7.085
7.073
7.066
7.046
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1.07
1.13
9.37
fl (ppm)
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1.07
1.05
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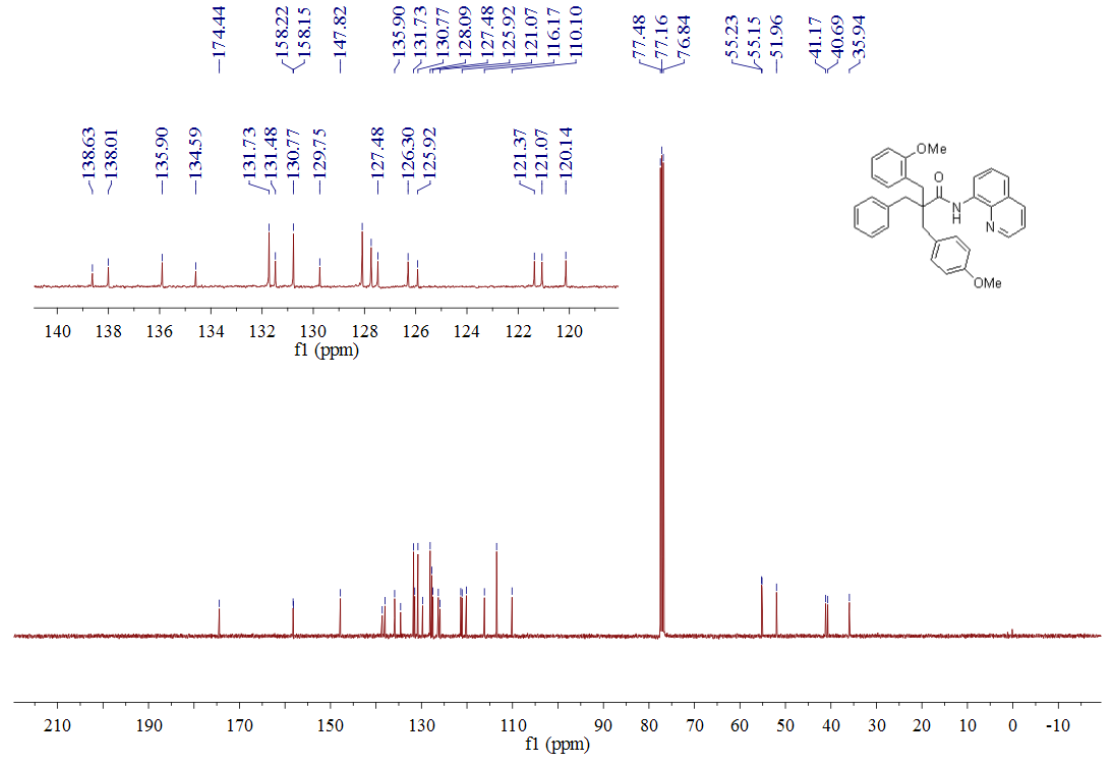
fl (ppm)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77.48
77.16
76.84
55.23
55.15
51.96
41.17
40.69
35.94
138.63
138.01
135.90
134.59
131.73
131.48
130.77
129.75
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125.92
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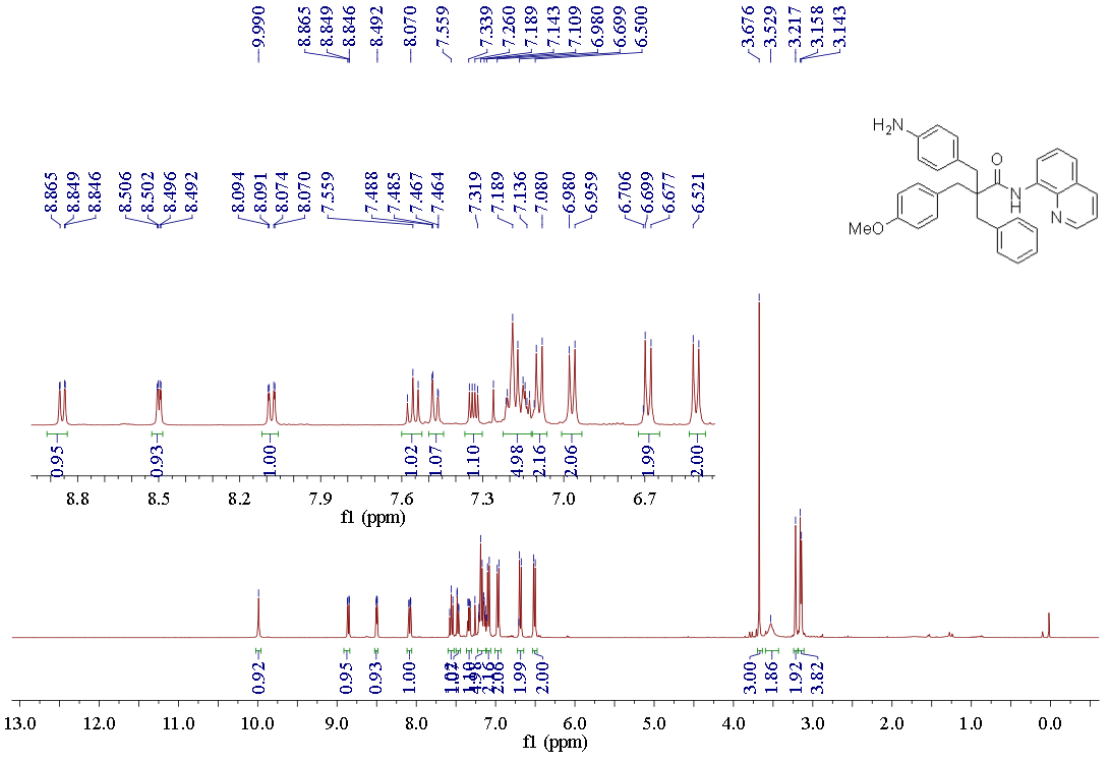
O
N
H
OMe
fl (ppm)
fl (ppm)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O
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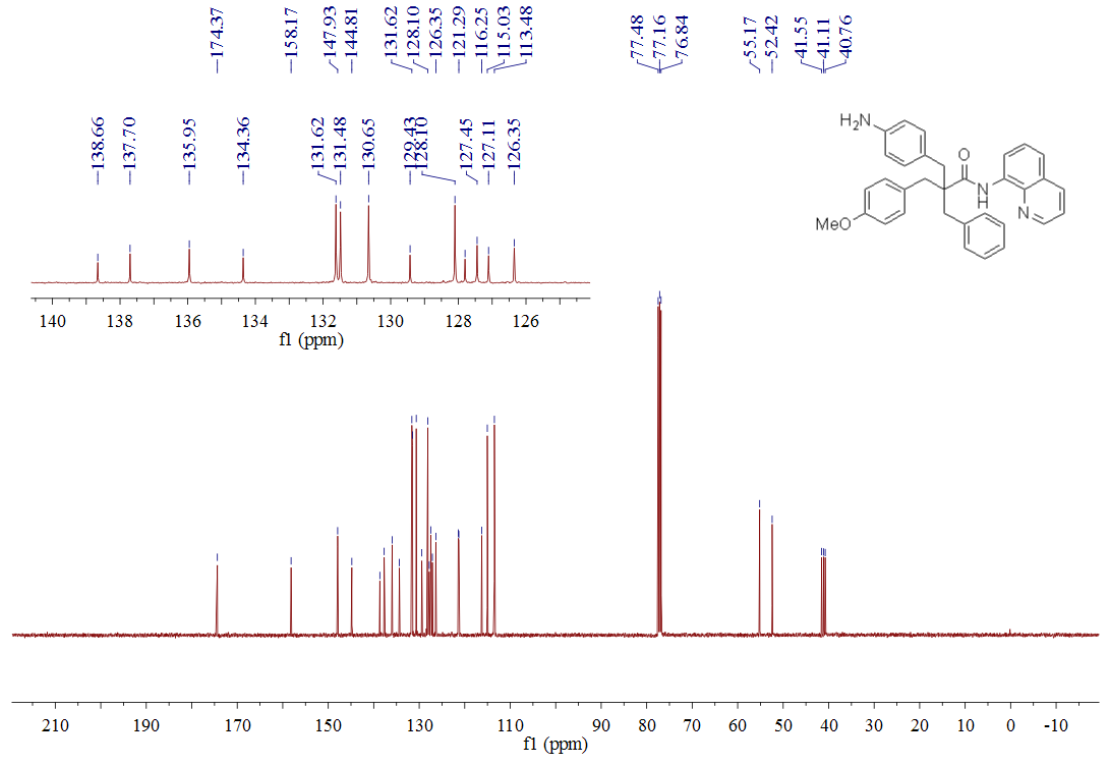
H
N
MeO
fl (ppm)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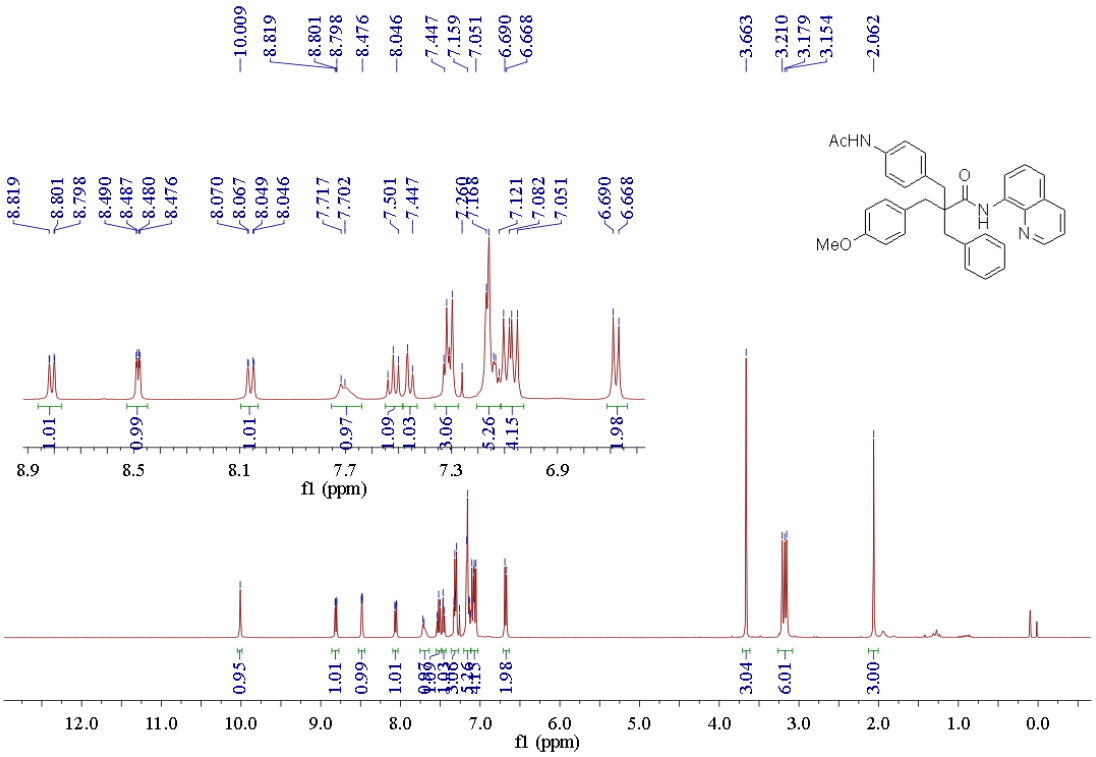
O
N
H
N
MeO
fl (ppm)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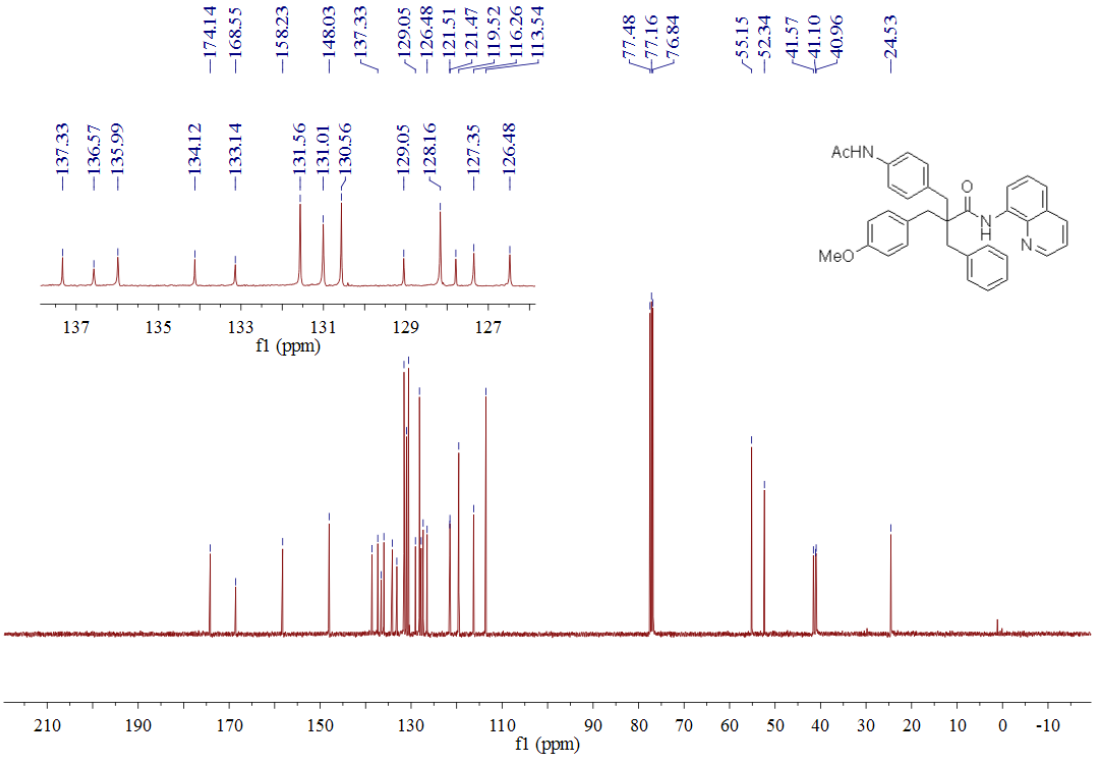
fl (ppm)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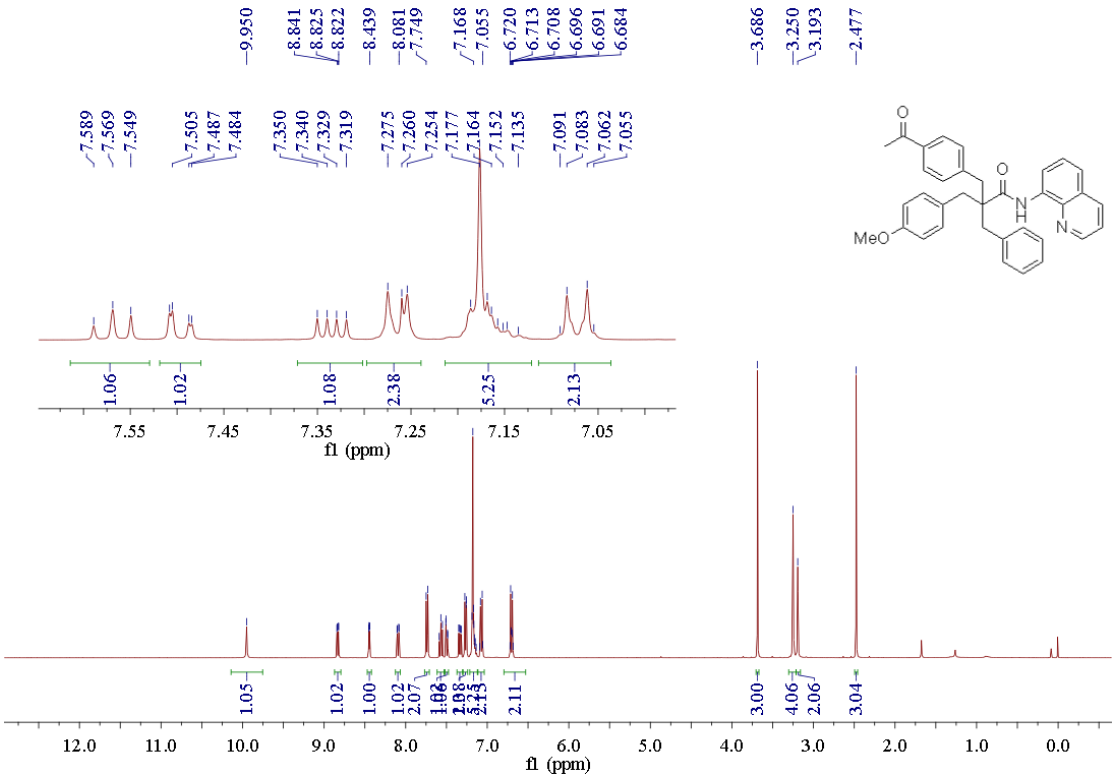
MeO
fl (ppm)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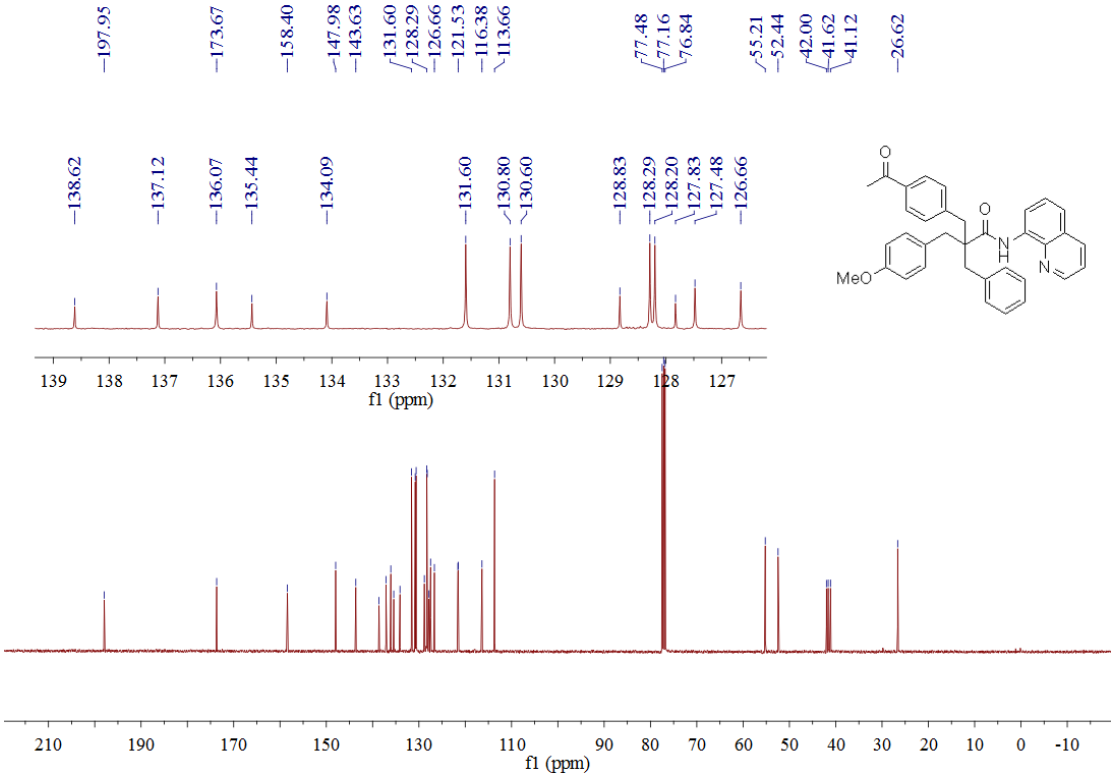
fl (ppm)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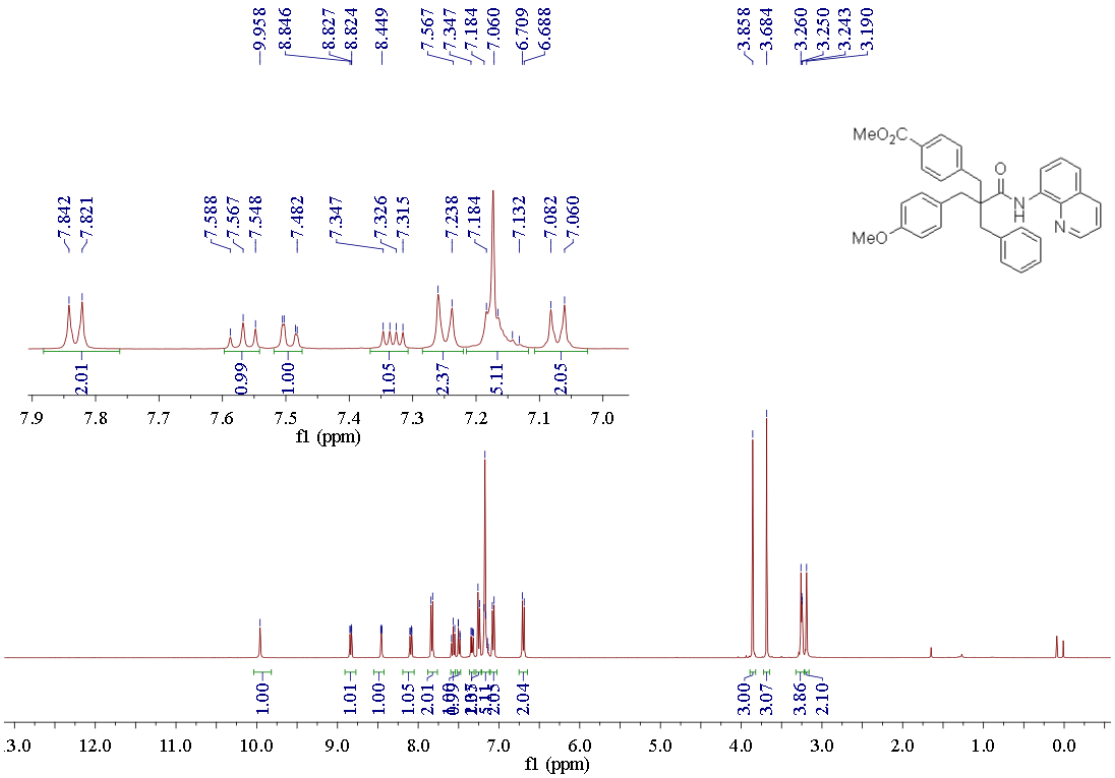
fl (ppm)
fl (ppm)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H
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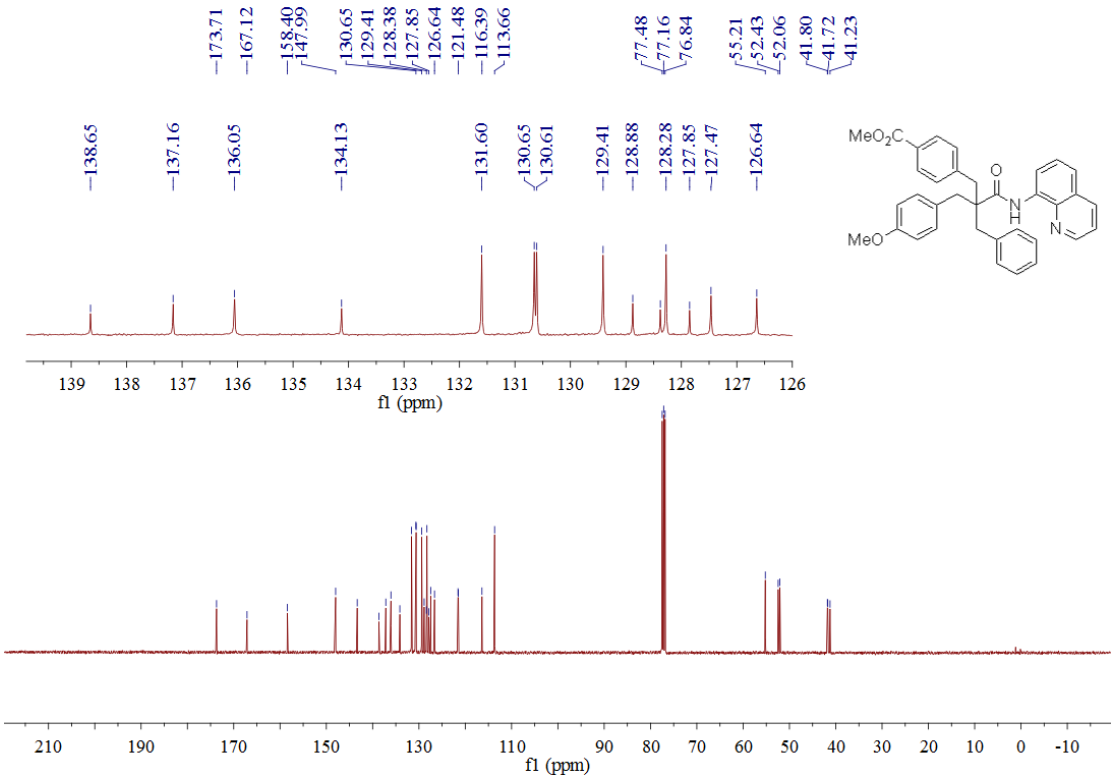
fl (ppm)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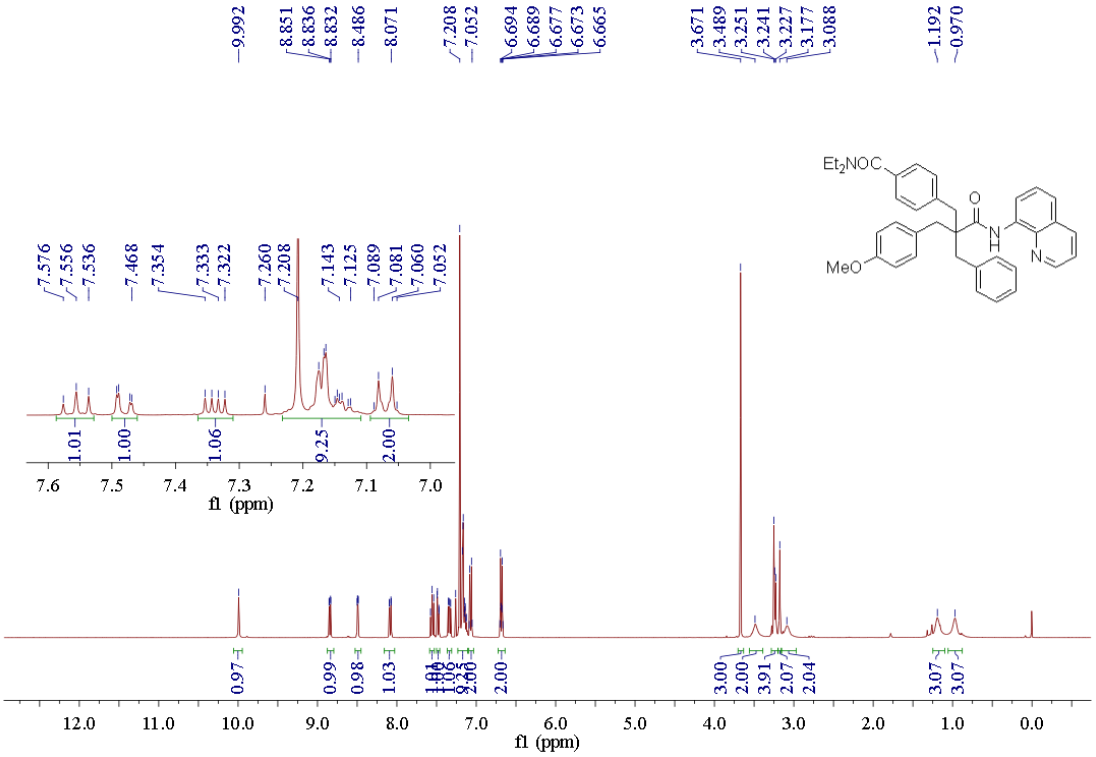
fl (ppm)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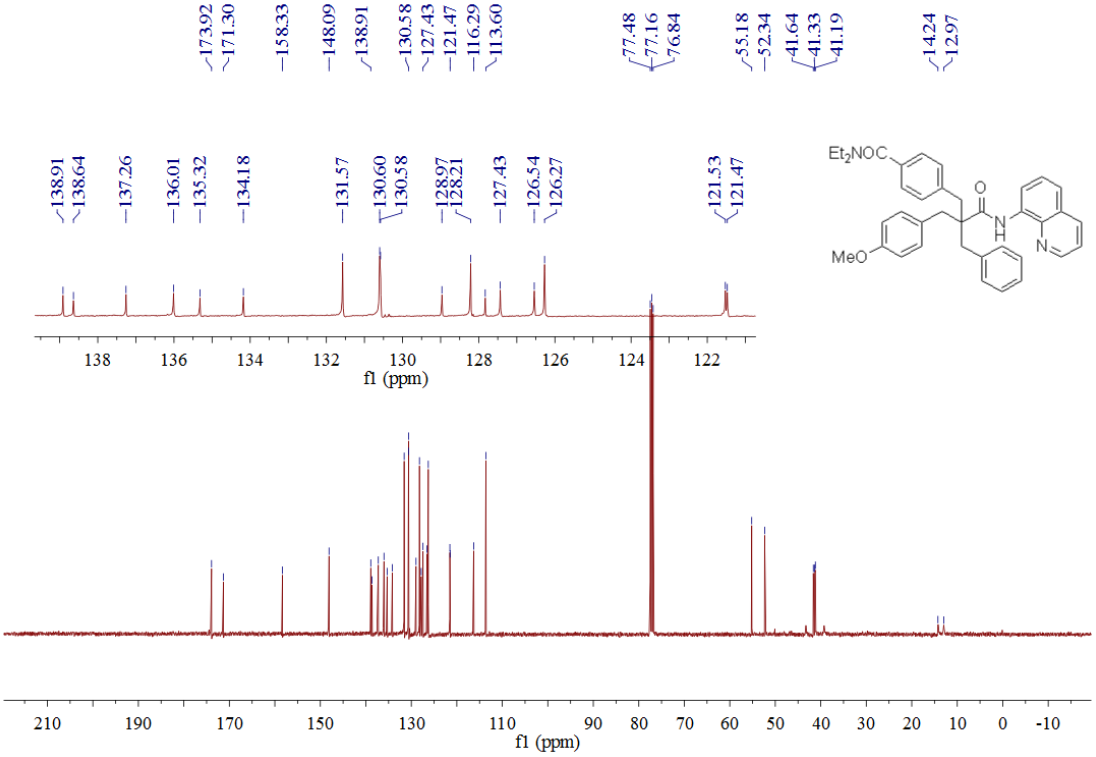
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f1 (ppm)
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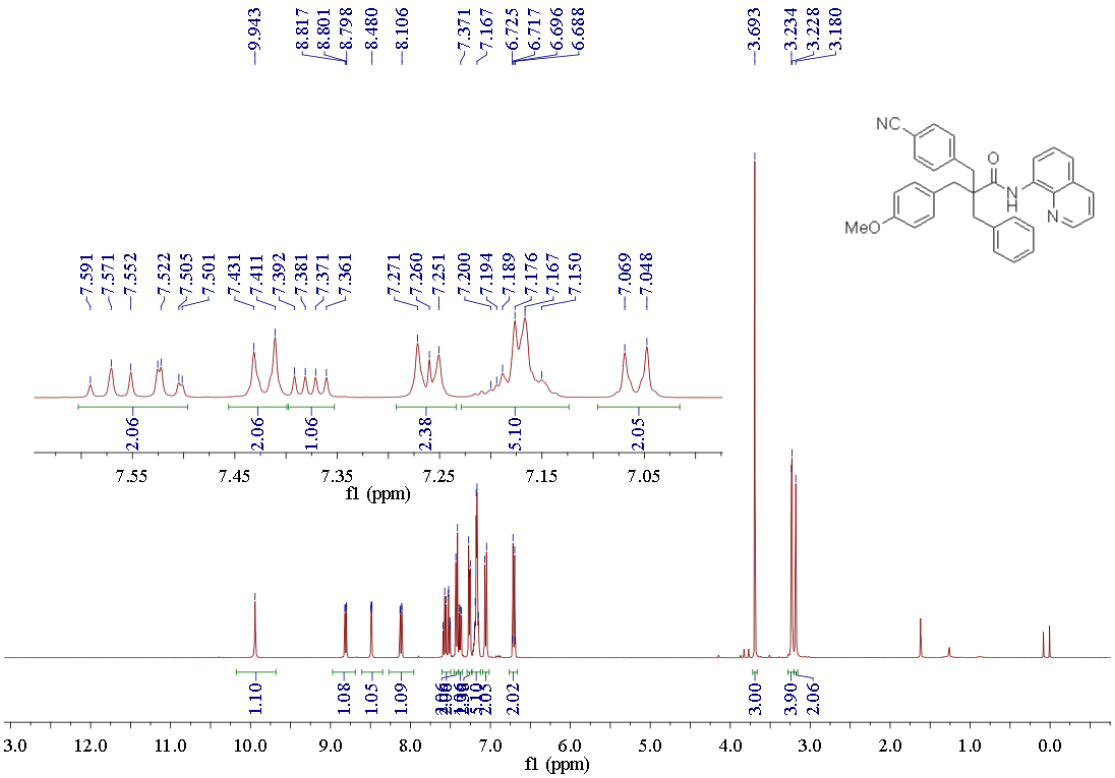
f1 (ppm)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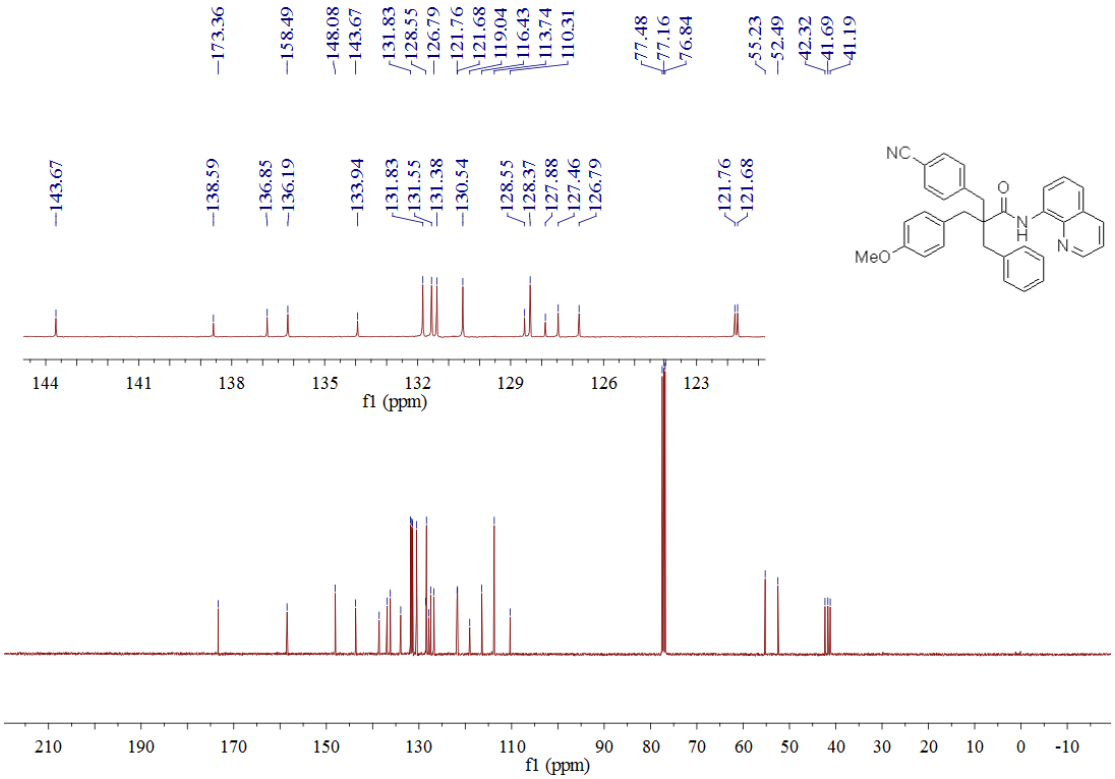
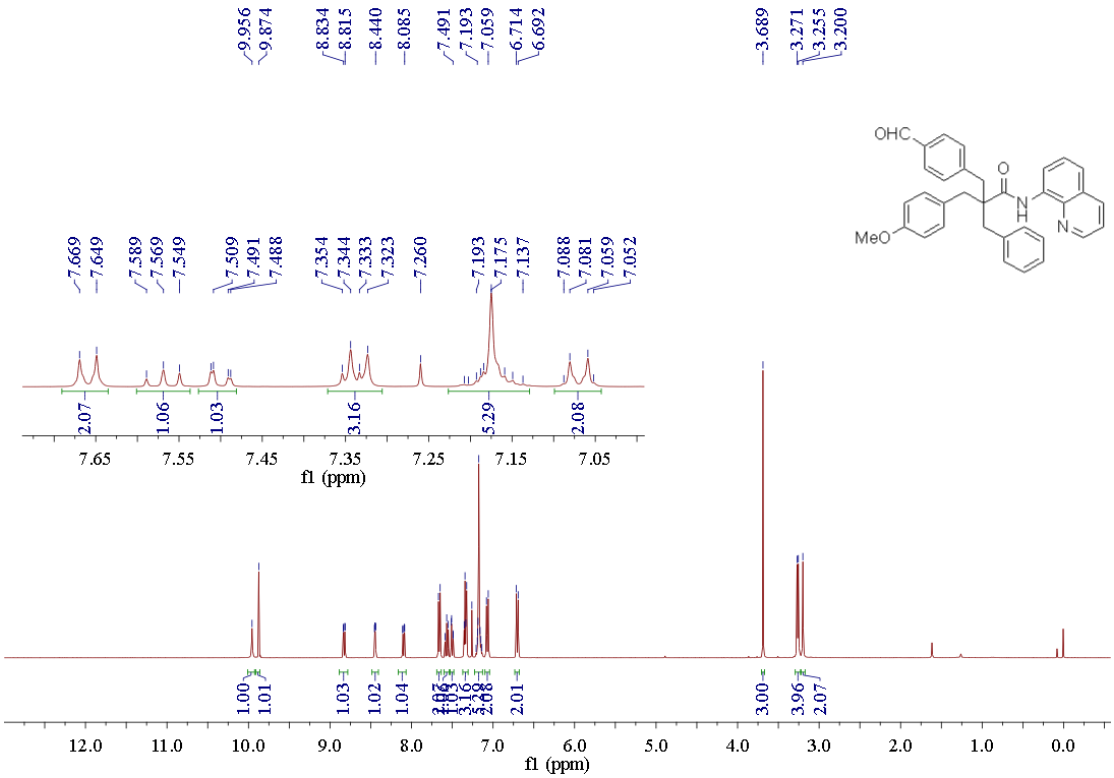
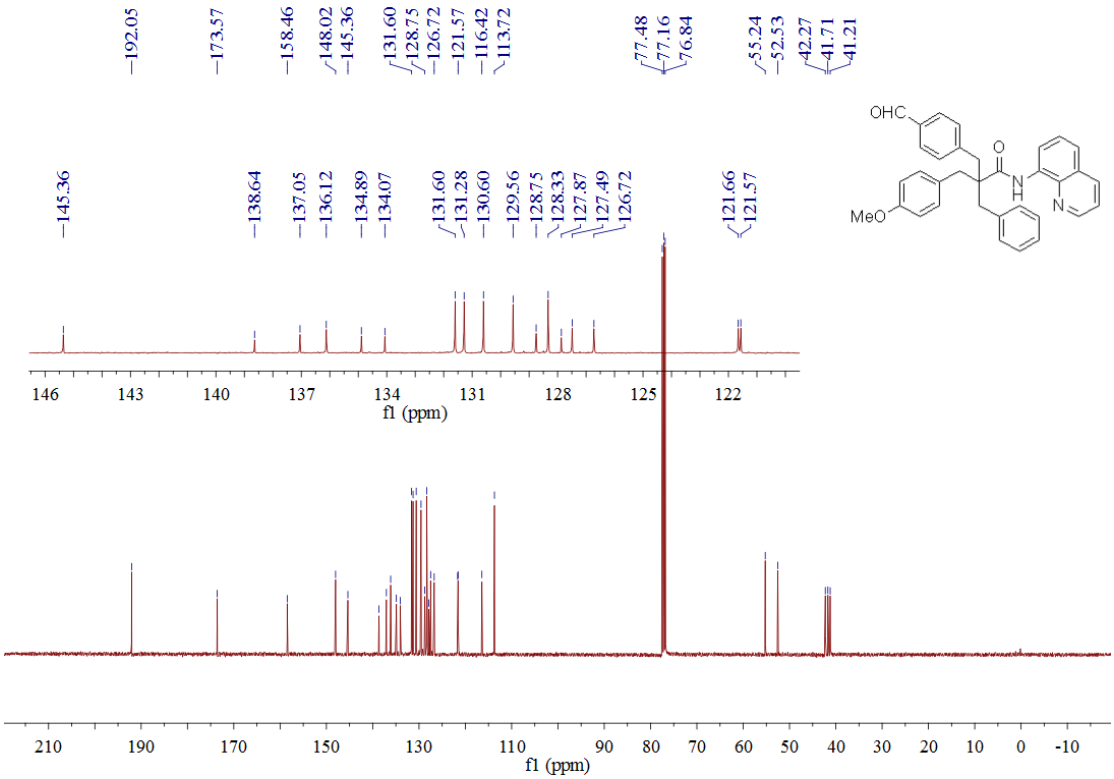
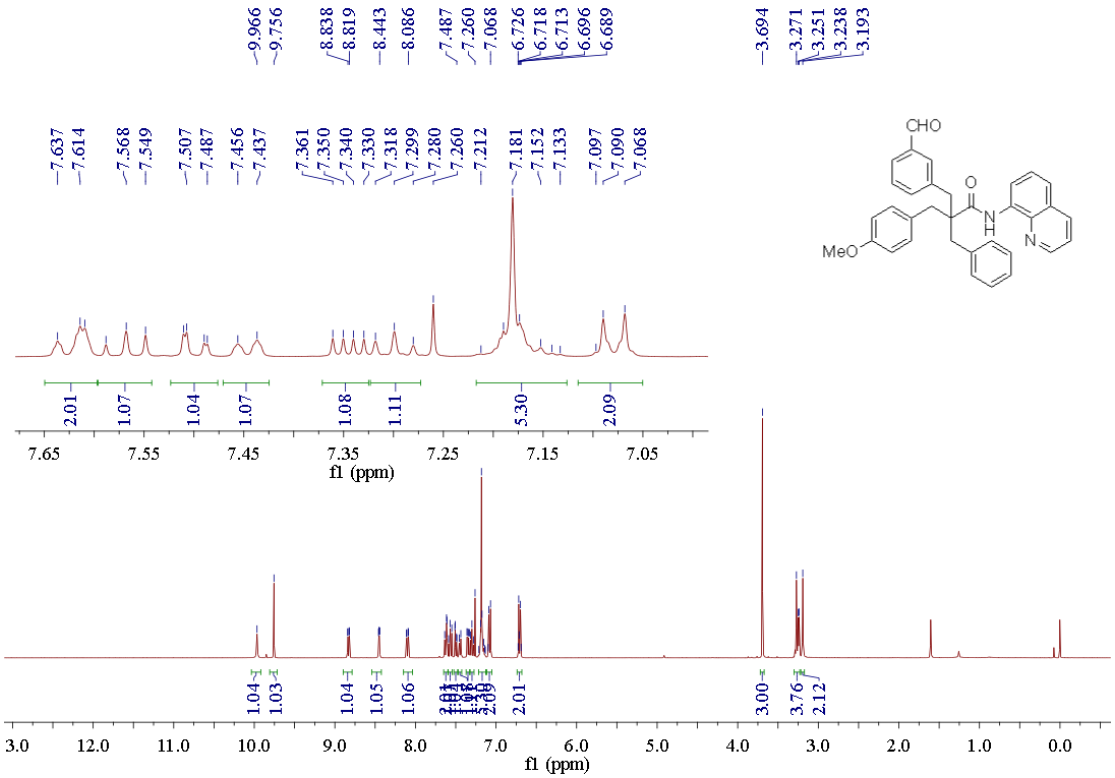
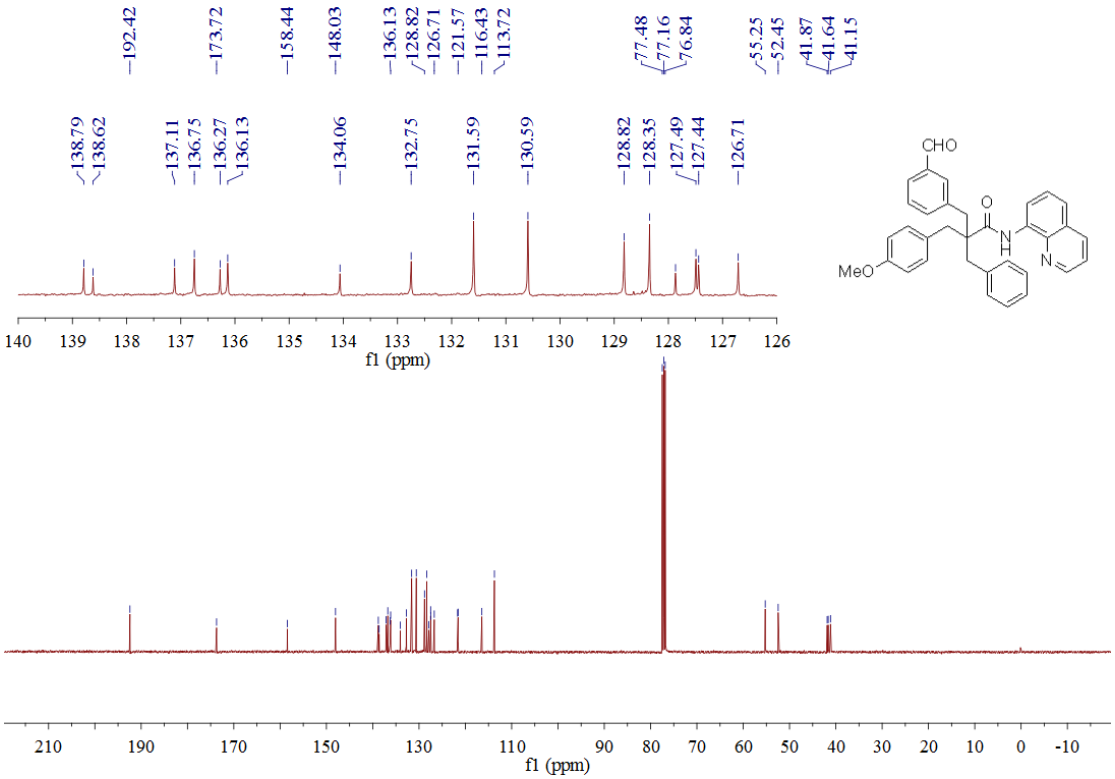
3.0
2.0
1.0
0.0
f1 (ppm)

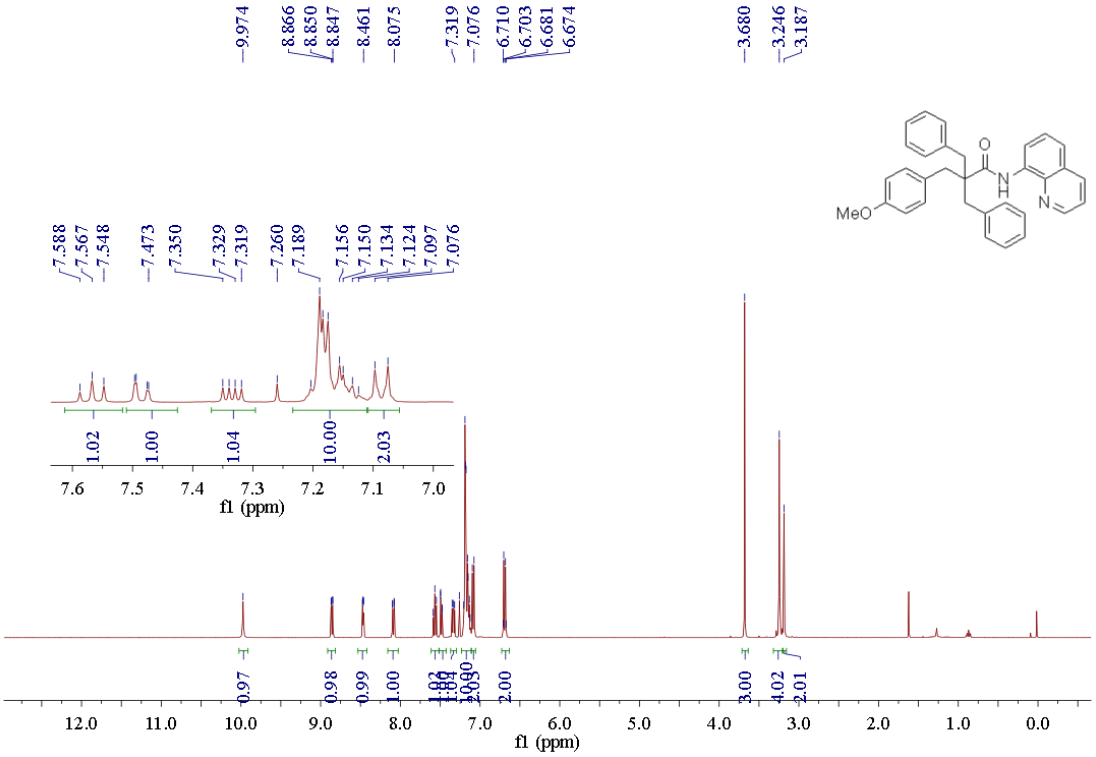

173.36
158.49
148.08
143.67
131.83
128.55
126.79
121.76
121.68
119.04
116.43
113.74
110.31
77.48
77.16
76.84
55.23
52.49
42.32
41.69
41.19
143.67
138.59
136.85
136.19
133.94
131.83
131.55
131.38
130.54
128.55
128.37
127.88
127.46
126.79
121.76
121.68
NC
O
N
H
N
MeO
144
141
138
135
132
129
126
123
f1 (ppm)
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

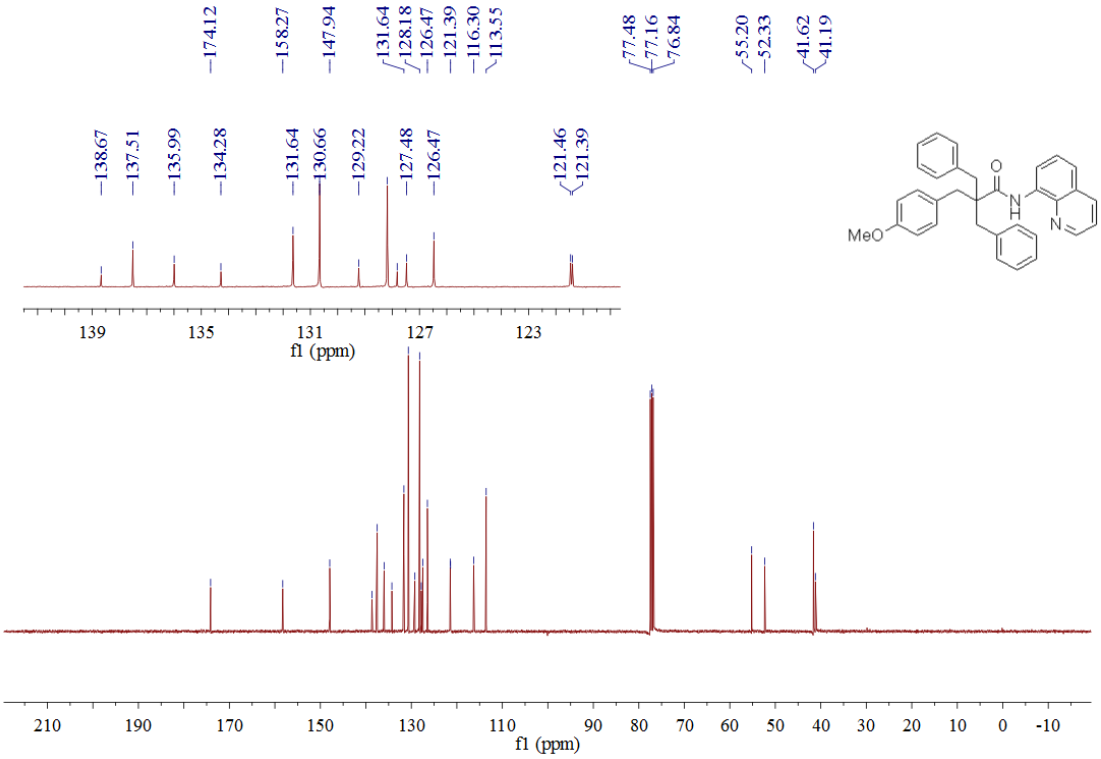

9.956
9.874
8.834
8.815
8.440
8.085
7.491
7.193
7.059
6.714
6.692
3.689
3.271
3.255
3.200
OHC
O
N
H
N
MeO
7.669
7.649
7.589
7.569
7.549
7.509
7.491
7.488
7.354
7.344
7.333
7.323
7.260
7.193
7.175
7.137
7.088
7.081
7.059
7.052
2.07
1.06
1.03
3.16
5.29
2.08
7.65
7.55
7.45
7.35
7.25
7.15
7.05
f1 (ppm)
1.00
1.01
1.03
1.02
1.04
2.01
3.00
3.96
2.07
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

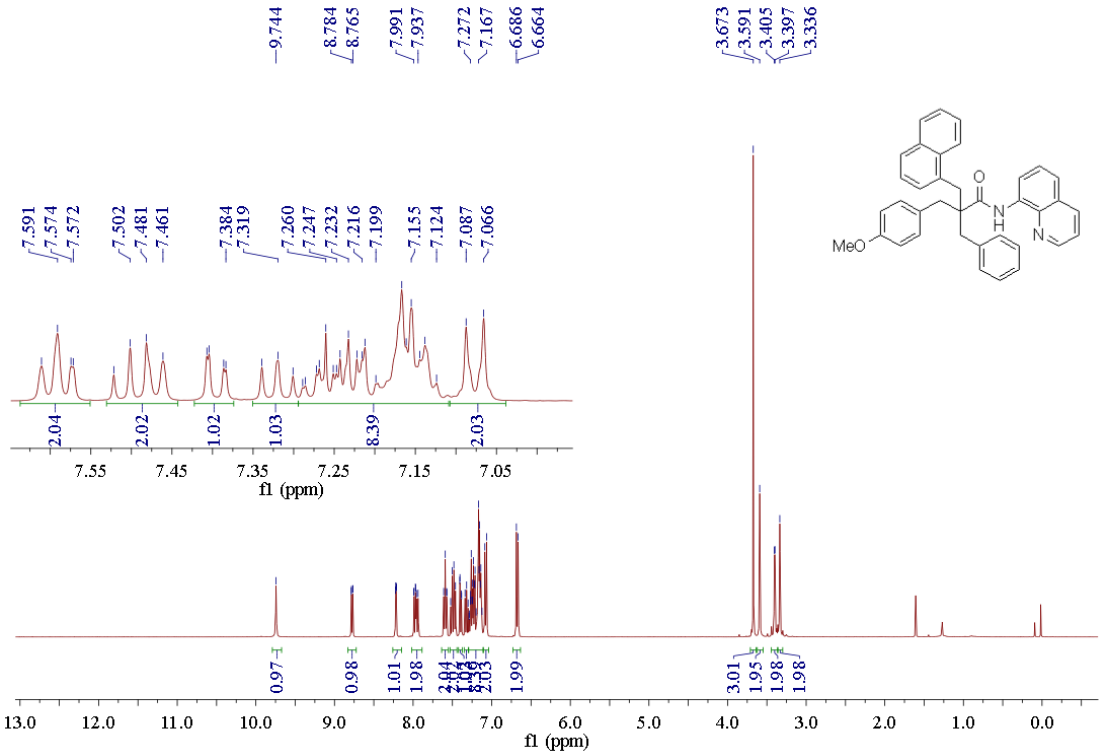

192.05
173.57
158.46
148.02
145.36
131.60
128.75
126.72
121.57
116.42
113.72
77.48
77.16
76.84
55.24
52.53
42.27
41.71
41.21
OHC
O
N
H
N
MeO
145.36
138.64
137.05
136.12
134.89
134.07
131.60
131.28
130.60
129.56
128.75
128.33
127.87
127.49
126.72
121.66
121.57
146
143
140
137
134
131
128
125
122
f1 (ppm)
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

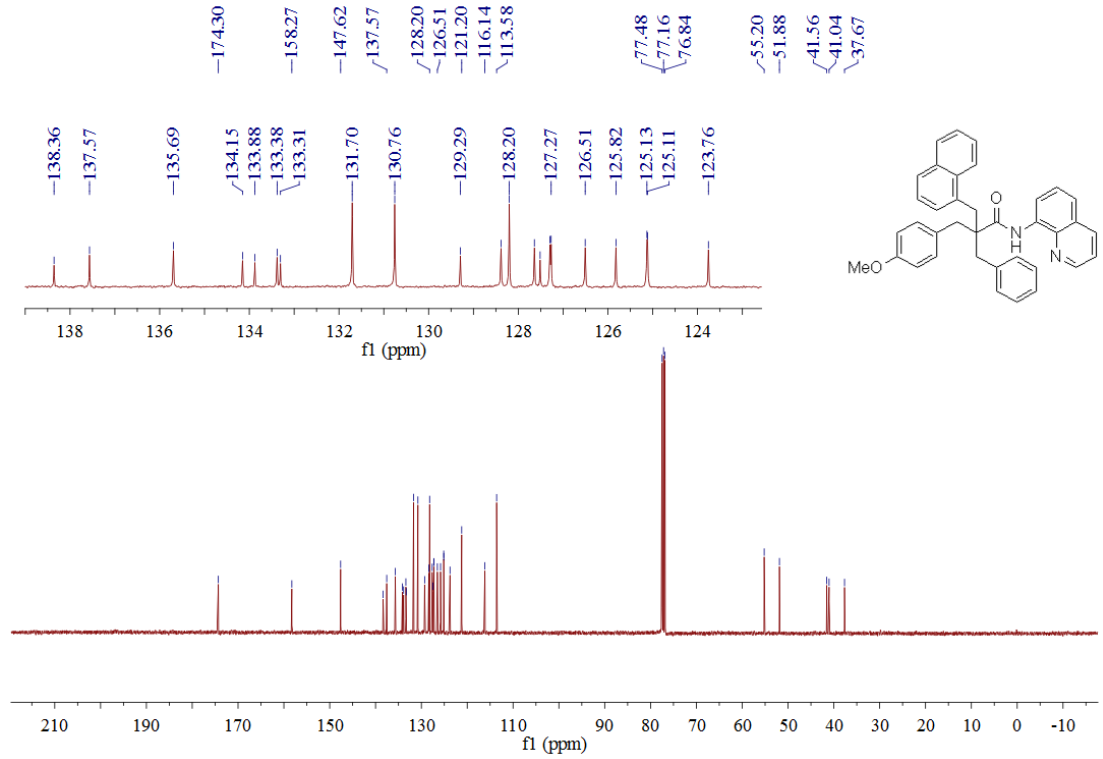

9.966
9.756
8.838
8.819
8.443
8.086
7.487
7.260
7.068
6.726
6.718
6.713
6.696
6.689
3.694
3.271
3.251
3.238
3.193
7.637
7.614
7.568
7.549
7.507
7.487
7.456
7.437
7.361
7.350
7.340
7.330
7.318
7.299
7.280
7.260
7.212
7.181
7.152
7.133
7.097
7.090
7.068
CHO
O
N
H
N
MeO
2.01
1.07
1.04
1.07
1.08
1.11
5.30
2.09
7.65
7.55
7.45
7.35
7.25
7.15
7.05
f1 (ppm)
1.04
1.03
1.04
1.05
1.06
2.01
3.00
3.76
2.12
3.0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

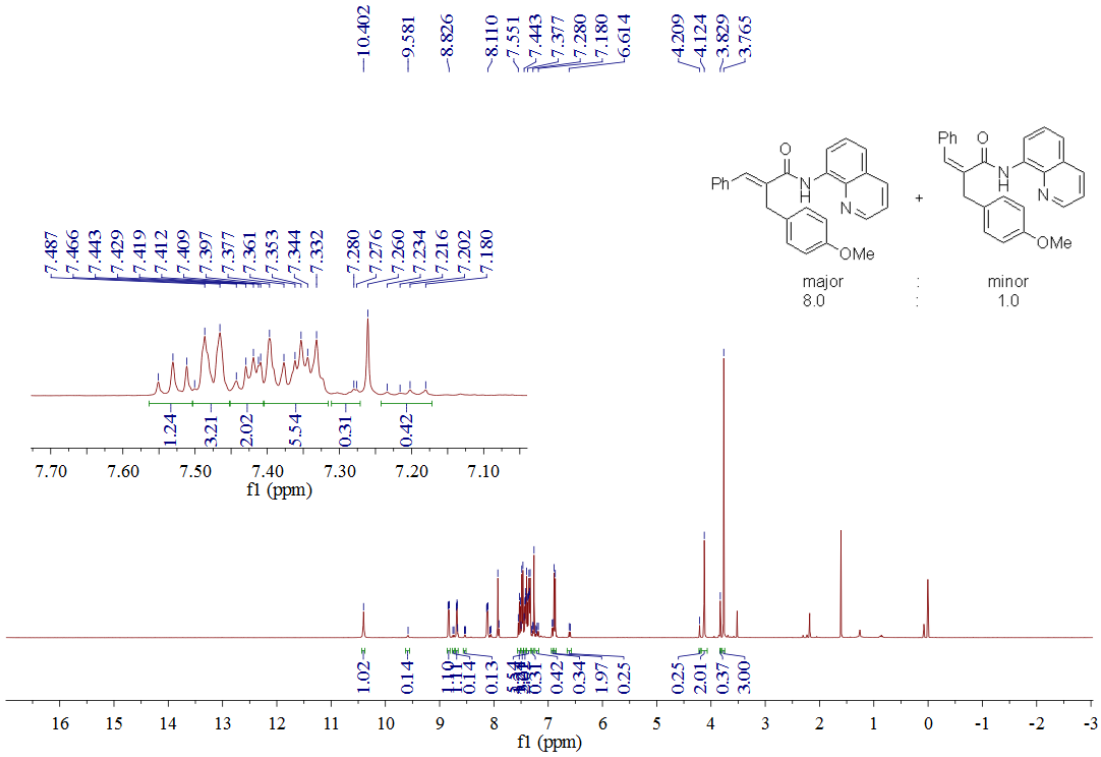

192.42
173.72
158.44
148.03
136.13
128.82
126.71
121.57
116.43
113.72
77.48
77.16
76.84
55.25
52.45
41.87
41.64
41.15
138.79
138.62
137.11
136.75
136.27
136.13
134.06
132.75
131.59
130.59
128.82
128.35
127.49
127.44
126.71
CHO
O
N
H
N
MeO
140
139
138
137
136
135
134
133
132
131
130
129
128
127
126
f1 (ppm)
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

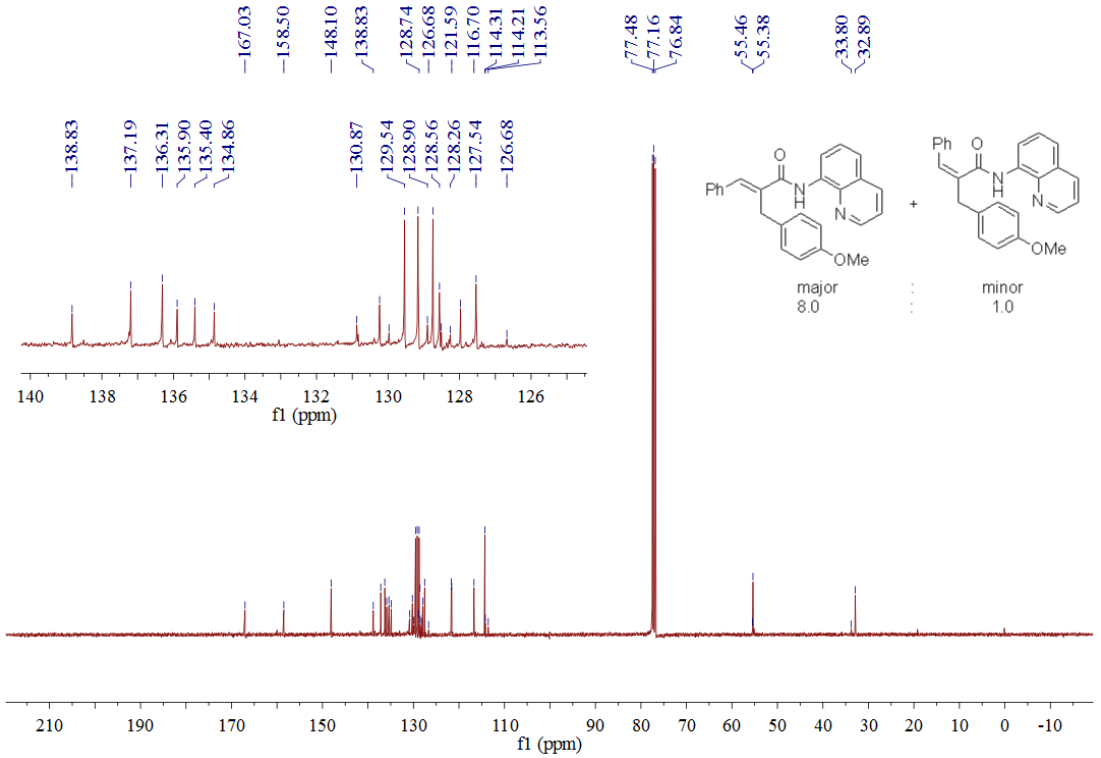

9.974
8.866
8.850
8.847
8.461
8.075
7.319
7.076
6.710
6.703
6.681
6.674
3.680
3.246
3.187
MeO
7.588
7.567
7.548
7.473
7.350
7.329
7.319
7.260
7.189
7.156
7.150
7.134
7.124
7.097
7.076
1.02
1.00
1.04
10.00
2.03
fl (ppm)
0.97
0.98
0.99
1.00
2.00
3.00
4.02
2.01
fl (ppm)

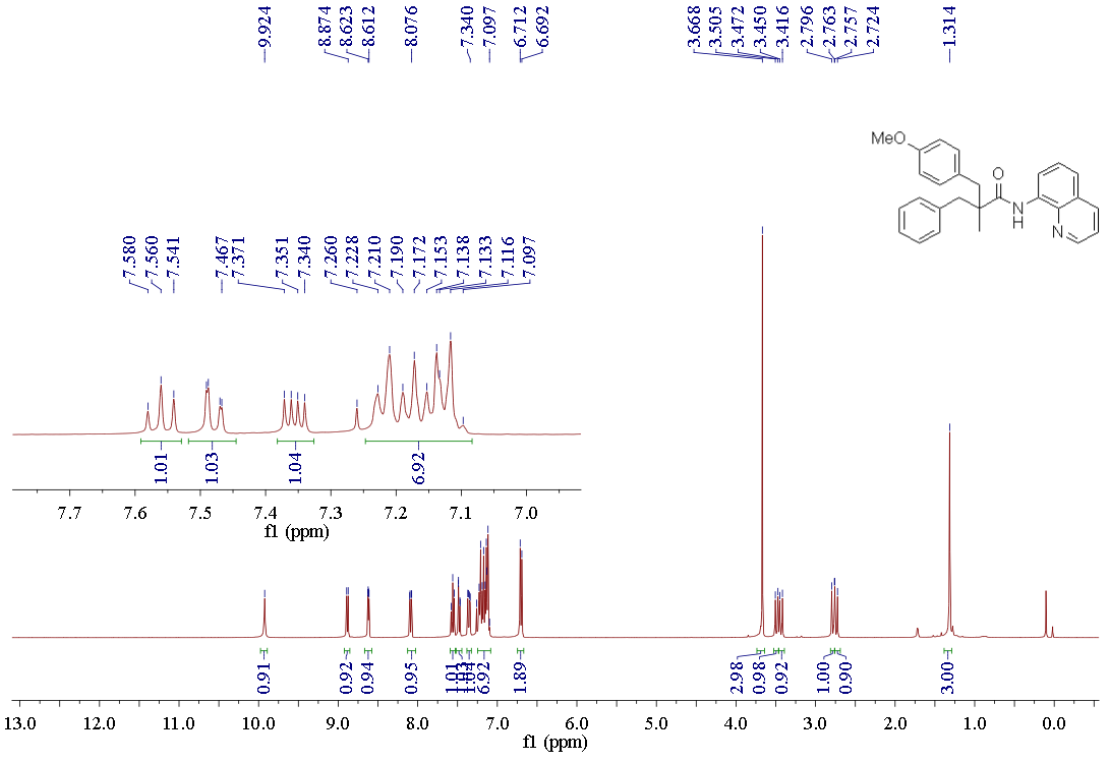

174.12
158.27
147.94
131.64
128.18
126.47
121.39
116.30
113.55
77.48
77.16
76.84
55.20
52.33
41.62
41.19
138.67
137.51
135.99
134.28
131.64
130.66
129.22
127.48
126.47
121.46
121.39
MeO
fl (ppm)
fl (ppm)

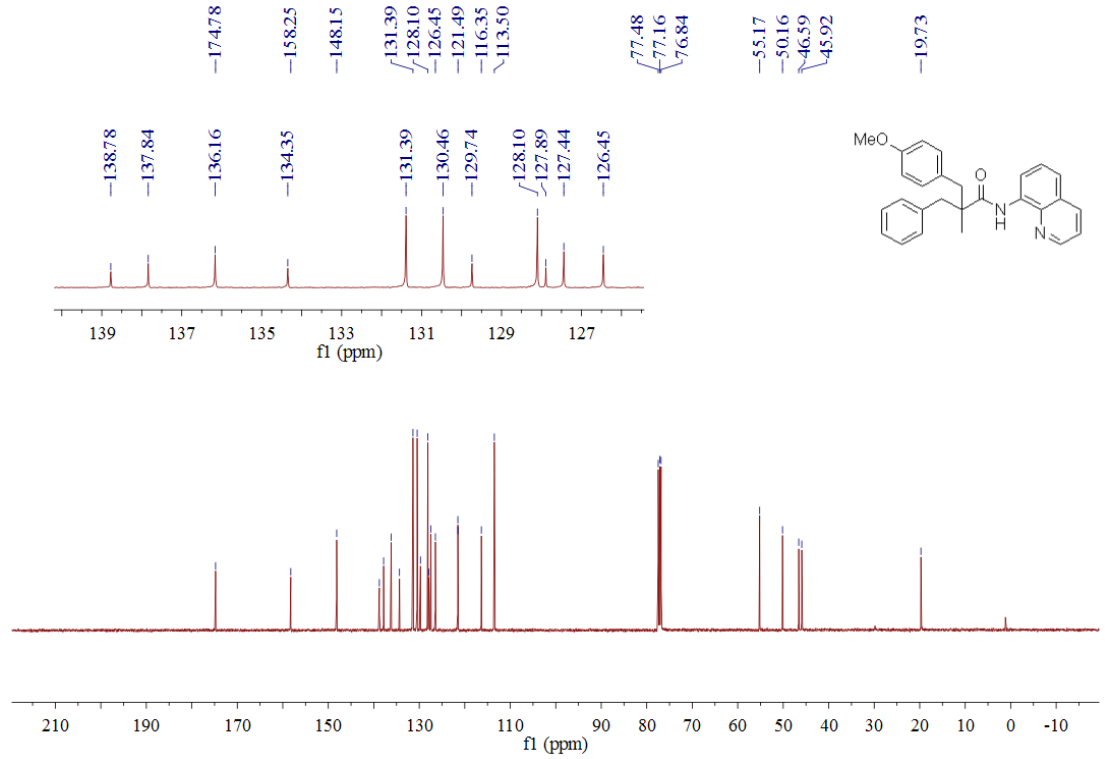

9.744
8.784
8.765
7.991
7.937
7.272
7.167
6.686
6.664
3.673
3.591
3.405
3.397
3.336
7.591
7.574
7.572
7.502
7.481
7.461
7.384
7.319
7.260
7.247
7.232
7.216
7.199
7.155
7.124
7.087
7.066
MeO
O
N
H
N
2.04
2.02
1.02
1.03
8.39
2.03
7.55
7.45
7.35
7.25
7.15
7.05
f1 (ppm)
0.97
0.98
1.01
1.98
2.04
2.07
2.06
2.03
1.99
3.01
1.95
1.98
1.98
13.0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

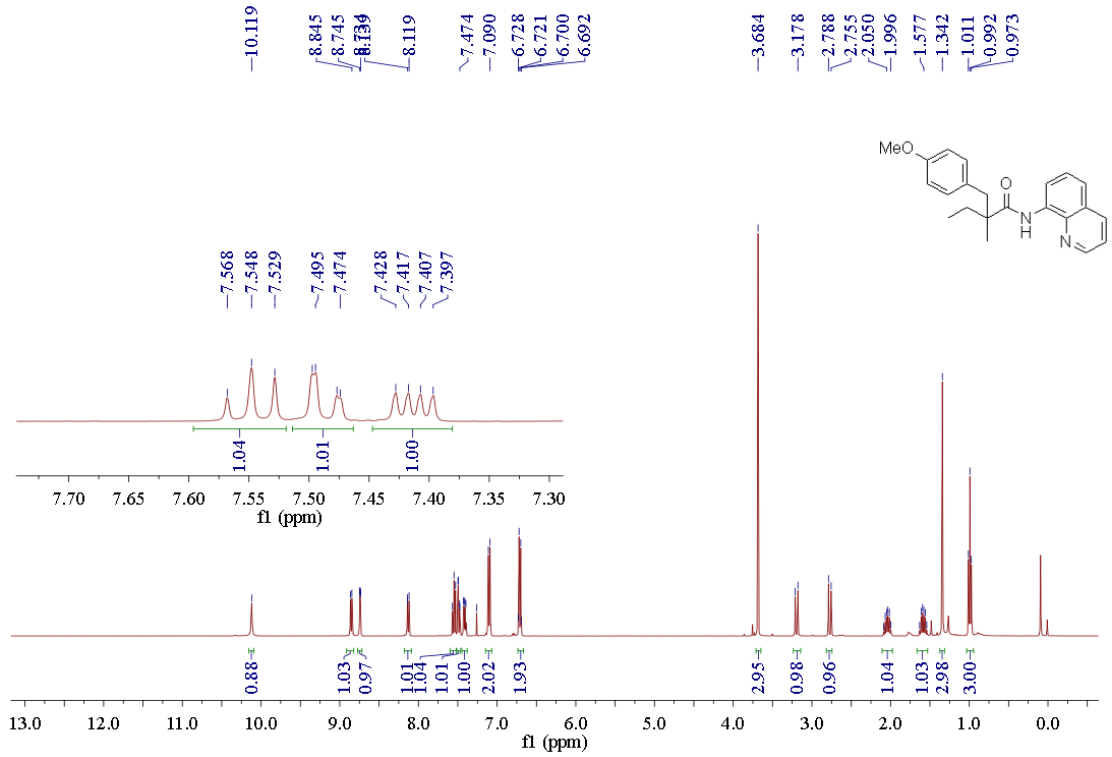

174.30
158.27
147.62
137.57
128.20
126.51
121.20
116.14
113.58
77.48
77.16
76.84
55.20
51.88
41.56
41.04
37.67
138.36
137.57
135.69
134.15
133.88
133.38
133.31
131.70
130.76
129.29
128.20
127.27
126.51
125.82
125.13
125.11
123.76
MeO
O
N
H
N
138
136
134
132
130
128
126
124
f1 (ppm)
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

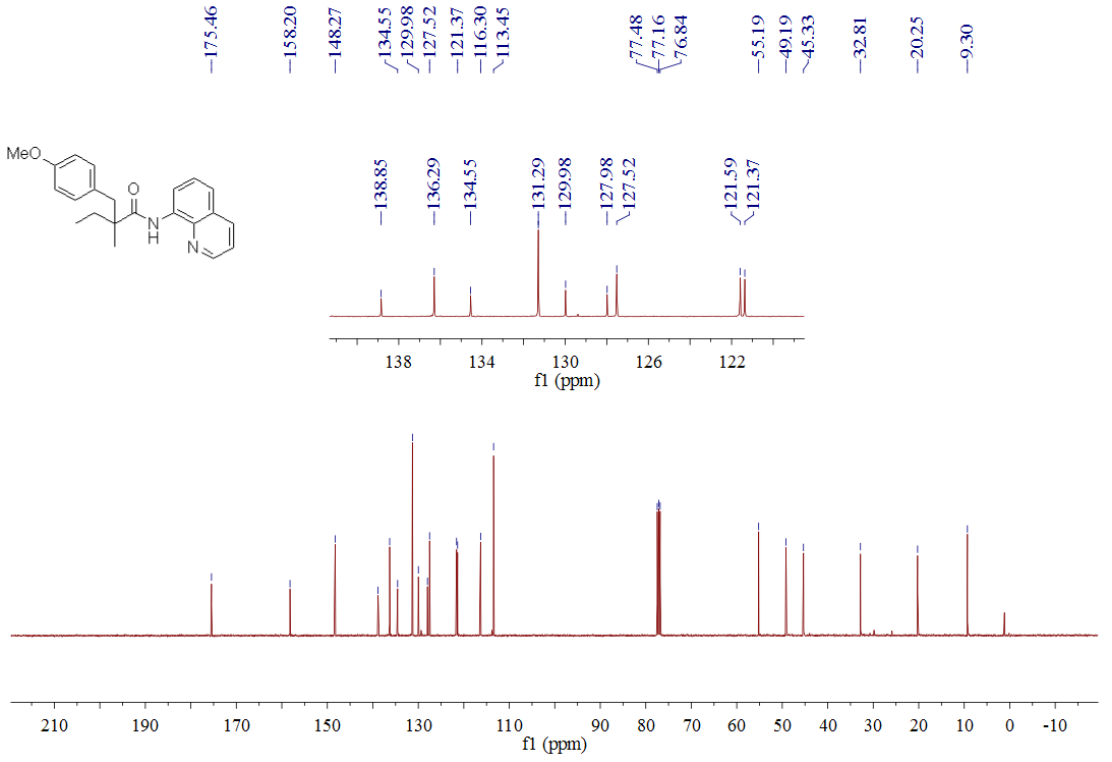

10.402
9.581
8.826
8.110
7.551
7.443
7.377
7.280
7.180
6.614
4.209
4.124
3.829
3.765
major
8.0
minor
1.0
f1 (ppm)

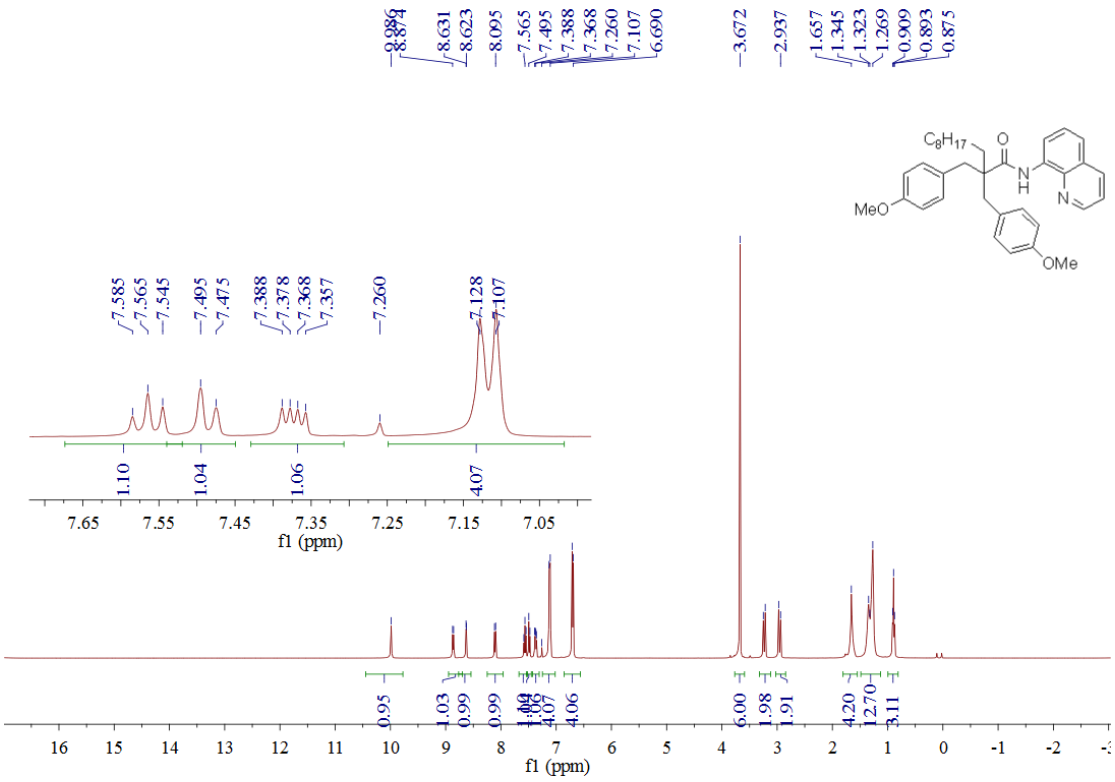

167.03
158.50
148.10
138.83
128.74
126.68
121.59
116.70
114.31
114.21
113.56
77.48
77.16
76.84
55.46
55.38
33.80
32.89
major
8.0
minor
1.0
f1 (ppm)

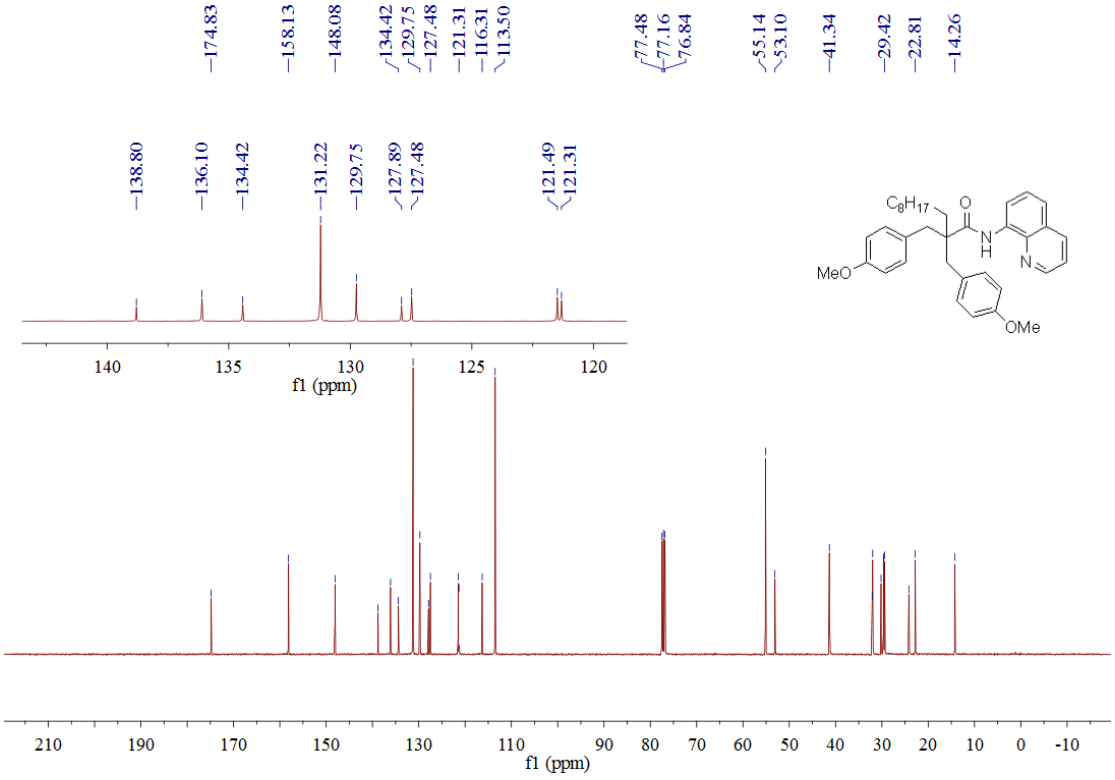

9.924
8.874
8.623
8.612
8.076
7.340
7.097
6.712
6.692
3.668
3.505
3.472
3.450
3.416
2.796
2.763
2.757
2.724
1.314
MeO
O
N
H
7.580
7.560
7.541
7.467
7.371
7.351
7.340
7.260
7.228
7.210
7.190
7.172
7.153
7.138
7.133
7.116
7.097
1.01
1.03
1.04
6.92
f1 (ppm)
0.91
0.92
0.94
0.95
1.89
2.98
0.98
0.92
1.00
0.90
3.00
f1 (ppm)

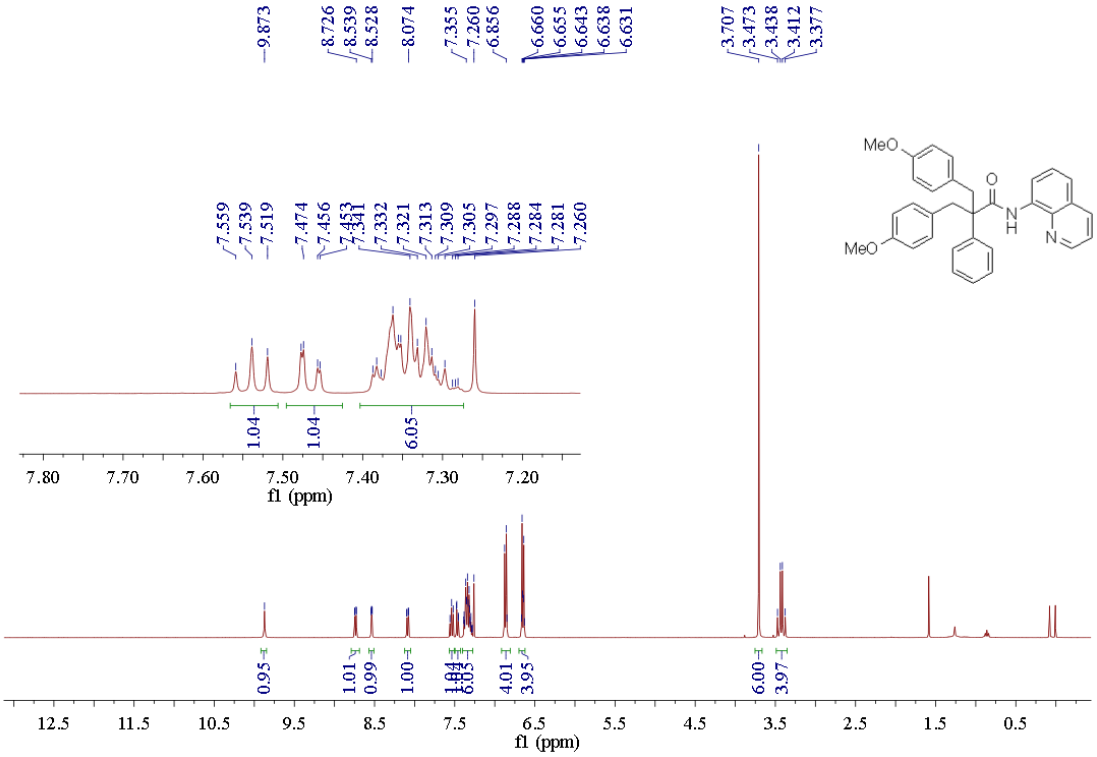

174.78
158.25
148.15
131.39
128.10
126.45
121.49
116.35
113.50
77.48
77.16
76.84
55.17
50.16
46.59
45.92
19.73
MeO
O
N
H
138.78
137.84
136.16
134.35
131.39
130.46
129.74
128.10
127.89
127.44
126.45
f1 (ppm)
f1 (ppm)

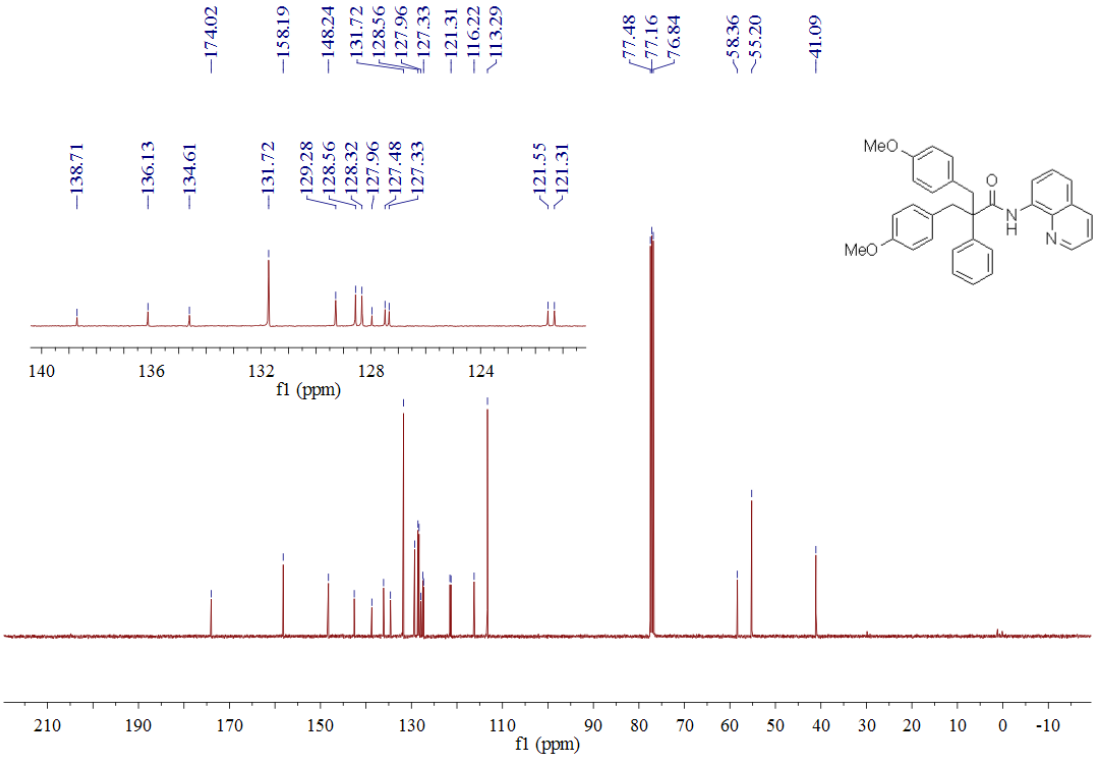

10.119
8.845
8.745
8.119
7.474
7.090
6.728
6.721
6.700
6.692
3.684
3.178
2.788
2.755
2.050
1.996
1.577
1.342
1.011
0.992
0.973
MeO
O
N
H
N
7.568
7.548
7.529
7.495
7.474
7.428
7.417
7.407
7.397
1.04
1.01
1.00
7.70 7.65 7.60 7.55 7.50 7.45 7.40 7.35 7.30
f1 (ppm)
0.88
1.03
0.97
1.01
1.04
1.01
1.00
2.02
1.93
2.95
0.98
0.96
1.04
1.03
2.98
3.00
13.0 12.0 11.0 10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0
f1 (ppm)

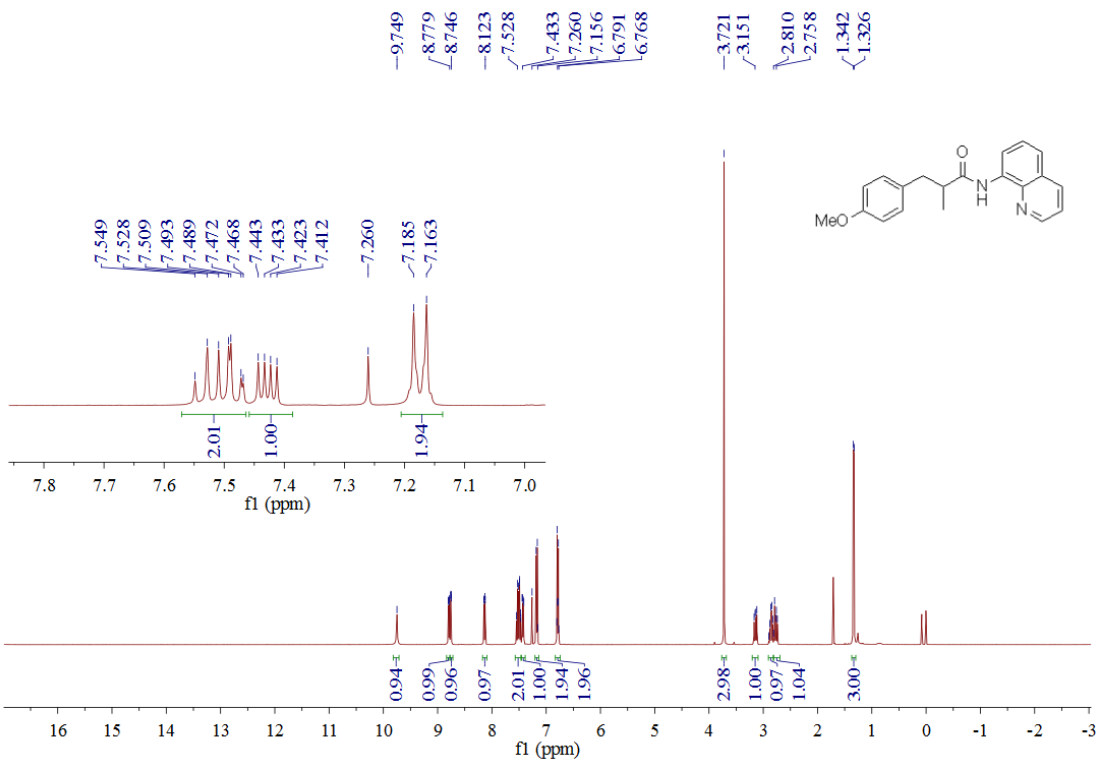

175.46
158.20
148.27
134.55
129.98
127.52
121.37
116.30
113.45
77.48
77.16
76.84
55.19
49.19
45.33
32.81
20.25
9.30
MeO
O
N
H
N
138.85
136.29
134.55
131.29
129.98
127.98
127.52
121.59
121.37
138 134 130 126 122
f1 (ppm)
210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

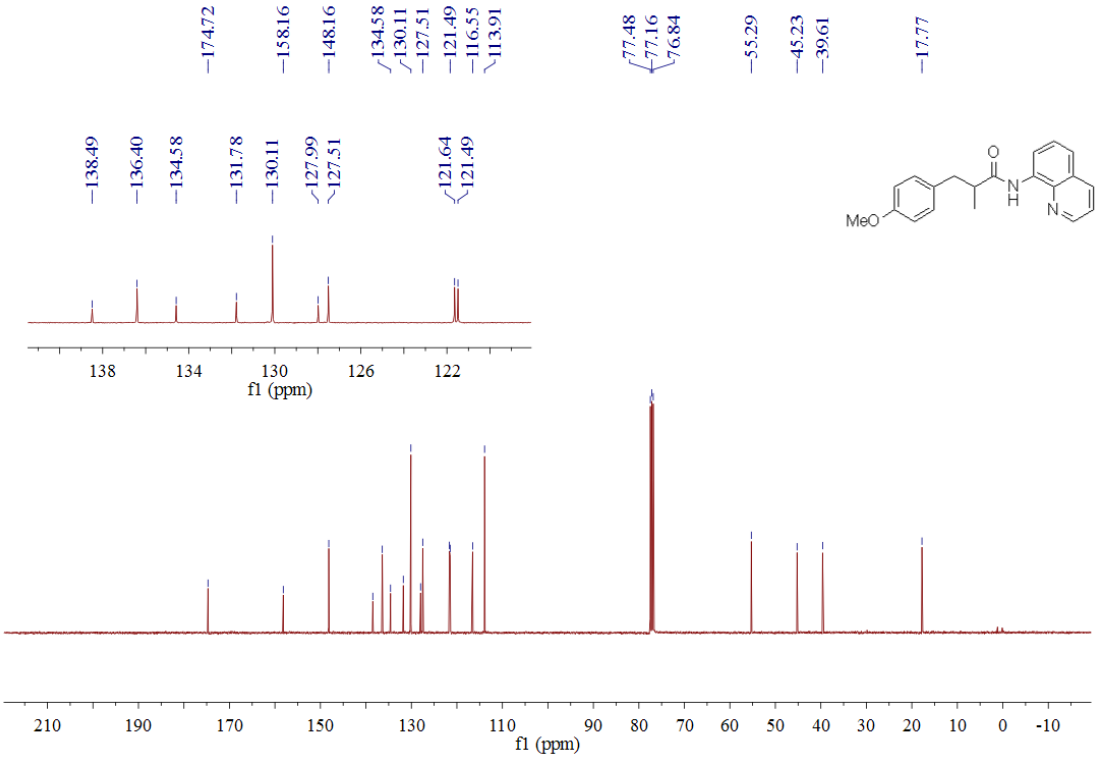

8.631
8.623
8.095
7.565
7.495
7.388
7.368
7.260
7.107
6.690
3.672
2.937
1.657
1.345
1.323
1.269
0.909
0.893
0.875
C8H17
O
N
H
MeO
OMe
7.585
7.565
7.545
7.495
7.475
7.388
7.378
7.368
7.357
7.260
7.128
7.107
1.10
1.04
1.06
4.07
f1 (ppm)
0.95
1.03
0.99
0.99
4.06
6.00
1.98
1.91
4.20
12.70
3.11


174.83
158.13
148.08
134.42
129.75
127.48
121.31
116.31
113.50
77.48
77.16
76.84
55.14
53.10
41.34
29.42
22.81
14.26
138.80
136.10
134.42
131.22
129.75
127.89
127.48
121.49
121.31
C8H17
O
N
H
MeO
OMe
f1 (ppm)


9.873
8.726
8.539
8.528
8.074
7.355
7.260
6.856
6.660
6.655
6.643
6.638
6.631
3.707
3.473
3.438
3.412
3.377
MeO
MeO
O
N
H
N
7.559
7.539
7.519
7.474
7.456
7.453
7.341
7.332
7.321
7.313
7.309
7.305
7.297
7.288
7.284
7.281
7.260
1.04
1.04
6.05
7.80
7.70
7.60
7.50
7.40
7.30
7.20
f1 (ppm)
0.95
1.01
0.99
1.00
1.04
1.03
4.01
3.95
6.00
3.97
12.5
11.5
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)


174.02
158.19
148.24
131.72
128.56
127.96
127.33
121.31
116.22
113.29
77.48
77.16
76.84
58.36
55.20
41.09
MeO
MeO
O
N
H
N
138.71
136.13
134.61
131.72
129.28
128.56
128.32
127.96
127.48
127.33
121.55
121.31
140
136
132
128
124
f1 (ppm)
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


9.749
8.779
8.746
8.123
7.528
7.433
7.260
7.156
6.791
6.768
3.721
3.151
2.810
2.758
1.342
1.326
MeO
f1 (ppm)


174.72
158.16
148.16
134.58
130.11
127.51
121.49
116.55
113.91
77.48
77.16
76.84
55.29
45.23
39.61
17.77
MeO
f1 (ppm)