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Supporting Information

Ruthenium-Catalyzed *Ortho* C-H Bond Alkylation of Aromatic Amides with α,β-Unsaturated Ketones via a Bidentate-Chelation Assistance

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I. General Information

^{1}H NMR and ^{13}C NMR spectra were recorded on a JEOL ECS-400 spectrometer in $CDCl_3$ or DMSO-d_6 with tetramethylsilane as the internal standard. Data are reported as follows: chemical shift in ppm, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, brs = broad singlet, td = triplet of doublets and m = multiplet), coupling constant (Hz), and integration. Infrared spectra (IR) were obtained using a Jasco FT/IR-4200 spectrometer; absorptions are reported in reciprocal centimeters with the following relative intensities: s (strong), m (medium), or w (weak). Mass spectra were obtained using Shimadzu GCMS-QP 2014 and Shimadzu GCMS-QP 5000 instruments instrument with ionization voltages of 70 eV. High resolution mass spectra (HRMS) were obtained on a JEOL JMS-DX303 instrument. Analytical gas chromatography (GC) was carried out on Shimadzu GC-14B, Shimadzu GC-2014 and Shimadzu GC-8A gas chromatographs, equipped with a flame ionization detector. Melting points were determined using a Yamato melting point apparatus. Column chromatography was performed with SiO_2 (Silicycle SiliaFlash F60 (230-400 mesh)). Some compounds were purified by LC-908 HPLC (GPC).

II. Materials

$[RuCl_2(p\text{-cymene})]_2$, $RuCl_2(PPh_3)_3$, 3-Buten-2-one (**2a**), 3-pent-2-one (**2e**), vinyl magnesium bromide, methyl lithium, tributyl(vinyl)tin, tetrakis(triphenylphosphine)palladium, tetrachloroethane,[1] Bis(cyclopentadienyl)zirconium(IV) chloride hydride (Schwartz's reagent), methyl iodide and iodine were purchased from Sigma-Aldrich. NaOAc, and PPh_3 were purchased from Wako Pure Chemicals. 8-Aminoquinoline, o-toluoyl chloride, 2,5-dimethylbenzoic acid, 3-(trifluoromethoxy)benzoic acid, 2-(trifluoromethyl)benzoyl chloride, 2,5-difluorobenzoyl chloride, 5-bromo-2-methylbenzoic acid, 2-methoxybenzoyl chloride, 3-fluorobenzoic acid, 3-chlorobenzoyl chloride, 3-iodobenzoic acid, benzoyl chloride, cyclohexanecarboxaldehyde, 4-methoxybenzoyl chloride, 2-furoyl chloride, Methyl terephthalaldehydate, 4-(trifluoromethyl)benzaldehyde, 2-(methylthio)aniline, 4-fluorobenzoyl chloride, 2-naphthoyl chloride, 1-octen-3one (**2b**), and cinnamaldehyde were purchased from Tokyo Kasei Kogyo Co., Ltd. These reagents were used as received. Triethylamine[2] and sodium hydride (60 % oil suspension) were purchased from Nacalai Tesque Inc. Dess-Martin Periodinane was prepared according to a reported procedure.[3] Sodium pivalate was prepared by stirring pivalic acid with 1 equivalent of sodium hydroxide in refluxing methanol for 3 h, the resulting solid was then washed with Et_2O/MeOH (99/1) and dried under vacuum. Toluene, THF and Et_2O were dried on a Glass Contour solvent dispensing system (Nikko Hansen & Co., Ltd.).

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[1] Distilled from CaH_2
[2] Distilled from KOH
[3] a) M. Frigerio, M. Santagostino, S. Sputore, *J. Org. Chem.* **1999,** *64,* 4537; b) R. K. Boeckman, Jr., P. Shao, J. J. Mullins, *Org. Synth.* **2004**, *10*, 696.

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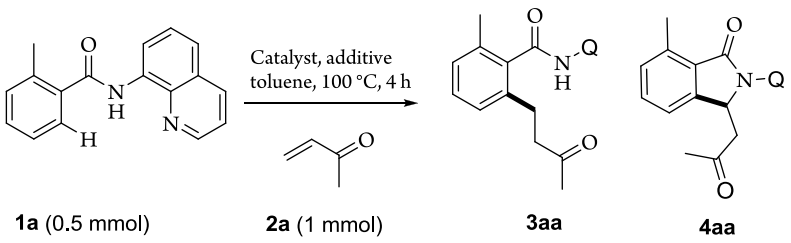
III.Optimization Studies

Formation of **3aa**: conditions screening



Catalyst[a]	Additive [mol %]	3aa [%]	4aa [%]	1a [%][b]
$RhCl(PPh_3)_3$	-	0	0	90
$ReBr(CO)_5$	-	0	0	90
$[IrCl_2(Cp^*)]_2$	-	0	0	94
$RuH_2(CO)(PPh_3)_3$	-	0	0	98
$RuH_2(PPh_3)_4$	-	0	0	95
$Ru_3(CO)_{12}$	-	6	6	68
$[RuCl_2(Cp^*)]_2$	-	0	0	89
$[RuCl_2(p\text{-cymene})]_2$	-	10	0	84
$[RuCl_2(p\text{-cymene})]_2$	$NaHCO_2$ [25]	12	0	78
$[RuCl_2(p\text{-cymene})]_2$	$NaHCO_2$ [25]/PPh_3 [30]	50	0	43
$[RuCl_2(p\text{-cymene})]_2$	NaOAc [25]/PPh_3 [30]	90	0	0
$[RuCl_2(p\text{-cymene})]_2$	NaOAc [25]	91	0	0
$RuCl_2(PPh_3)_3$	NaOAc [25]	94	0	0
$RuCl_2(PPh_3)_3$	NaOAc [200]	93	0	0

[a] 10 mol % were used, but 5 mol % were used in the case of $[RuCl_2(p\text{-cymene})]_2$ [b] recovered **1a**.

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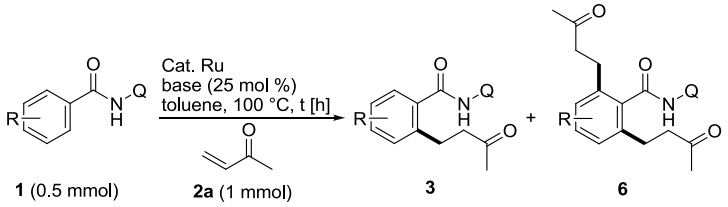
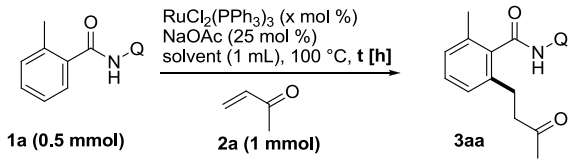
$[RuCl_2(p\text{-cymene})]_2$ *vs* $RuCl_2(PPh_3)_3$



Entry	R	Catalyst	t [h]	Base [25 mol %]	3 [%]	6 [%]	Recovered 1 [%]
1[a,e]	2-F	$RuCl_2(PPh_3)_3$	4	NaOAc	60	-	25
2[b,e]	2-F	$[RuCl_2(p\text{-cymene})]_2$	4	NaOAc	58	-	25
3[c,e]	2-F	$[RuCl_2(p\text{-cymene})]_2$	4	NaOAc	62	-	21
4[a,e]	2-OMe	$RuCl_2(PPh_3)_3$	4	NaOAc	36	-	61
5[b,e]	2-OMe	$[RuCl_2(p\text{-cymene})]_2$	4	NaOAc	63	-	23
6[c,e]	2-OMe	$[RuCl_2(p\text{-cymene})]_2$	4	NaOAc	38	-	55
7[a]	3-Me	$RuCl_2(PPh_3)_3$	6	NaOAc	77	17	0
8[b]	3-Me	$[RuCl_2(p\text{-cymene})]_2$	6	NaOAc	10	0	78
9[c]	3-Me	$[RuCl_2(p\text{-cymene})]_2$	6	NaOAc	58	22	17
10[a]	3-Br	$RuCl_2(PPh_3)_3$	6	NaOPiv	65	24	0
11[c]	3-Br	$[RuCl_2(p\text{-cymene})]_2$	6	NaOPiv	48	19	11
12[a]	3-NMe_2	$RuCl_2(PPh_3)_3$	6	NaOAc	61	0	22
13[b]	3-NMe_2	$[RuCl_2(p\text{-cymene})]_2$	6	NaOAc	19	0	66
14[c]	3-NMe_2	$[RuCl_2(p\text{-cymene})]_2$	6	NaOAc	49	0	39
15[a,d]	4-Me	$RuCl_2(PPh_3)_3$	6	NaOAc	0	98	0
16[b,d]	4-Me	$[RuCl_2(p\text{-cymene})]_2$	6	NaOAc	0	10	80
17[c,d]	4-Me	$[RuCl_2(p\text{-cymene})]_2$	6	NaOAc	0	93	4

[a] **1** (0.5 mmol), **MVK** (1 mmol), $RuCl_2(PPh_3)_3$ (10 mol %), base (25 mol %), toluene (1 mL), 100 ° C.
[b] **1** (0.5 mmol), **MVK** (1 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5 mol %), base (25 mol %), toluene (1 mL), 100 ° C.
[c] **1** (0.5 mmol), **MVK** (1 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5 mol %), PPh_3 (30 mol %), base (25 mol %), toluene (1 mL), 100 ° C.
[d] **MVK** (1.5 mmol).
[e] 24 h reaction time or 140 °C reaction temperature didn't improve yields.

Catalyst loading with $RuCl_2(PPh_3)_3$



Cata [mol %]	t [h]	Yield 3aa [%]	Recovered 1a [%]
10	4	94	0
5	4	61	31
5	15	90	trace

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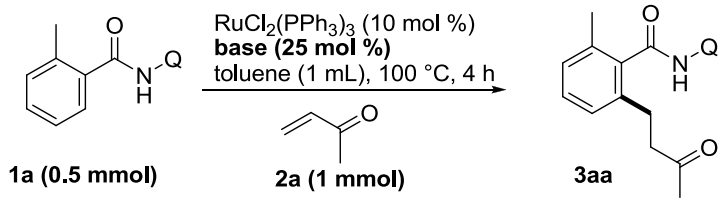
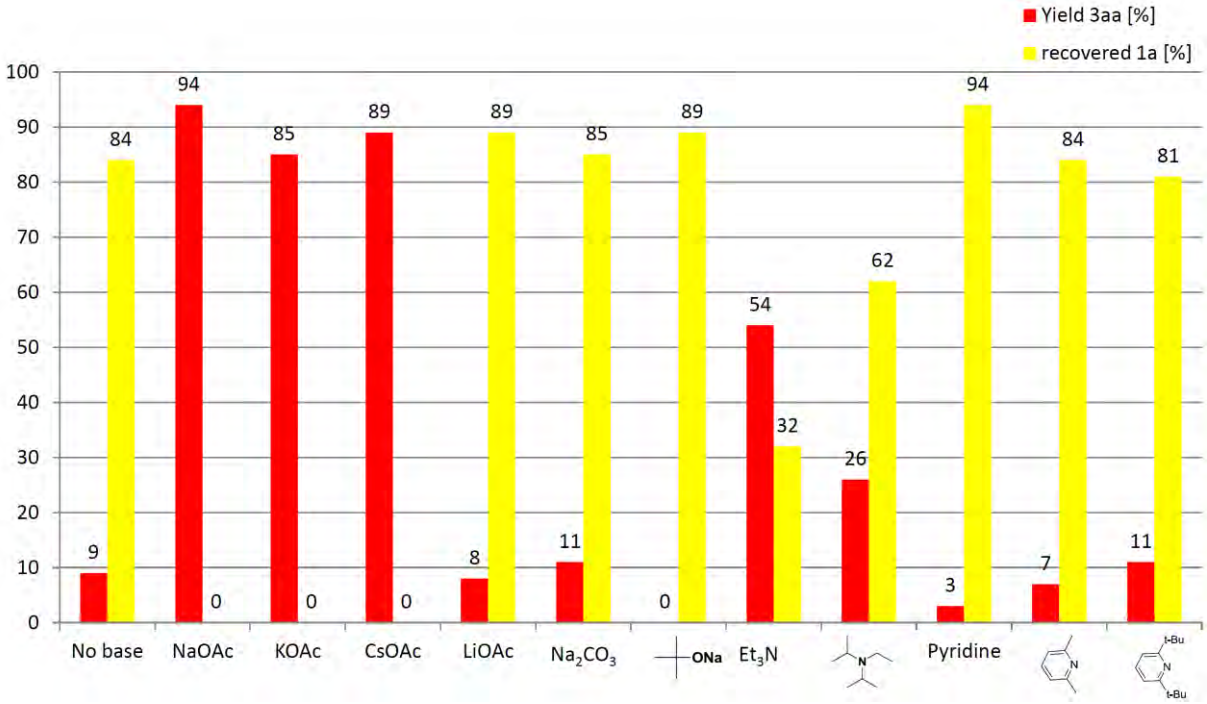
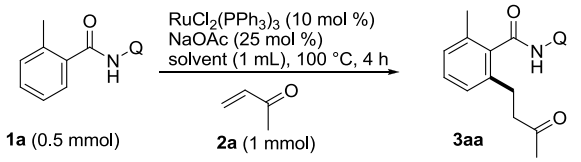
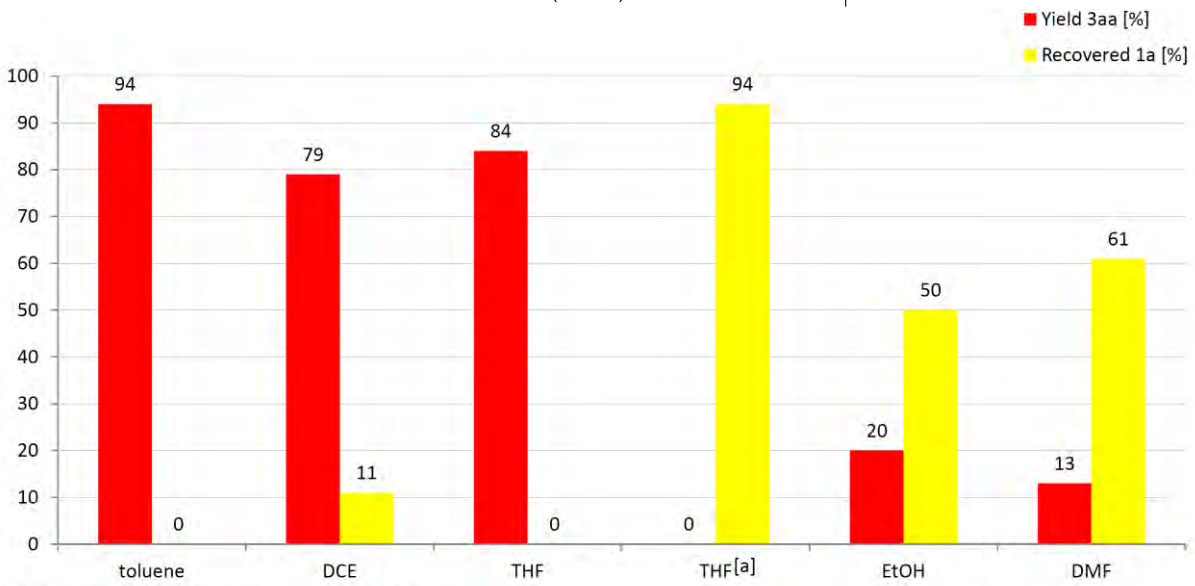
Base screening with $RuCl_2(PPh_3)_3$





Solvent screening with $RuCl_2(PPh_3)_3$





[a] 50 °C reaction temperature, 24 h reaction time

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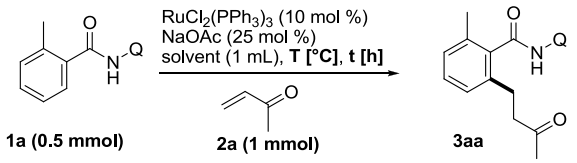
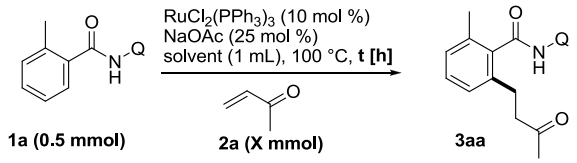
Temperature screening with $RuCl_2(PPh_3)_3$



T [°C]	t [h]	Yield 3aa [%]	Recovered 1a [%]
100	3	85	12
100	4	94	0
120	0.5	90	Trace
120	1	90	0
80	4	12	80
80	24	97	0
60	24	8	86

Variation of MVK equivalents with $RuCl_2(PPh_3)_3$



MVK [equiv.]	t [h]	Yield 3aa [%]	Recovered 1a [%]
1.1	4	58	34
1.1	15	83	9
2	3	85	12
2	4	94	0
6	4	95	0
6	0.5	91	0

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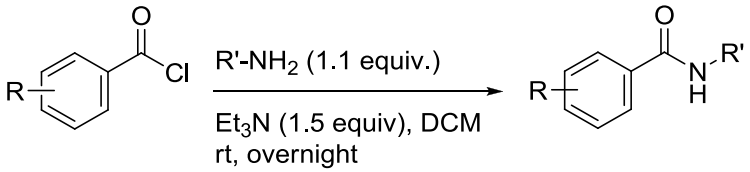
IV. Synthesis of Starting Amides

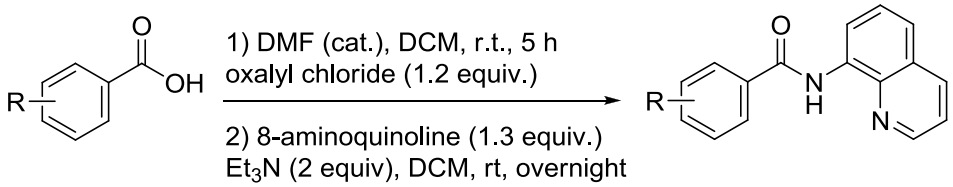
All amides bearing an 8-aminoquinoline moiety were synthesized by the reaction of 8-aminoquinoline with the corresponding acyl chloride. Amides **1a**, **I**, **F**, **1f**, **1h**, **1i**, **1l**, **1m**, **1o**, **1q**, **7d**, **7e**, **7f** [4], amides **1j**, **1k**, **7h**, **7g** [5], amides **1d** and **1g** [6] were already described.

General Procedure 1 for the Preparation of Starting Amides (GP1)[4]



To an oven-dried 100 mL three-necked flask, the amine (22 mmol, 1.1 equiv.), Et_3N (4.1 mL, 30 mmol, 1.5 equiv.) and DCM (40 mL) were added. The acid chloride (20 mmol, 1 equiv.) was slowly added to this solution at 0 °C and the mixture was then warmed to room temperature. After stirring overnight, the reaction system was quenched with sat. aq. $NaHCO_3$ (30 mL) and the organic layer was separated. The aqueous layer was extracted with DCM (2 x 20 mL). The combined organic layers were washed with 1 M HCl aq. (20 mL) and brine (30 mL), dried over $MgSO_4$, filtered and evaporated *in vacuo*. The obtained crude amide was purified by column chromatography on silica gel (hexane/EtOAc) to afford the desired amide. If necessary, an additional purification by recrystallisation (hexane/EtOAc) may be possible.

General Procedure 2 for the Preparation of Starting Amides (GP2)[4]



To an oven-dried 100 mL three-necked flask, the benzoic acid (20 mmol), DMF (5 drops) and DCM (40 mL) were added under a N_2 atmosphere. Oxalyl chloride (2 mL, 24 mmol, 1.2 equiv.) was added dropwise at 0 °C resulting in vigorous bubbling. The mixture was stirred for 5 h at room temperature, and the solvent was then removed *in vacuo*. The resulting acid chloride was used immediately without further purification.

To another oven-dried 100 mL three-necked flask, 8-aminoquinoline (3.75 g, 26 mmol, 1.3 equiv.), Et_3N (5.6 mL, 40 mmol, 2 equiv.) and DCM (40 mL) were added. A solution of the acid chloride in DCM (20 mL) was added dropwise to the solution at 0 °C, and the solution was then warmed to room temperature. After stirring overnight, the reaction system was quenched with sat. aq. $NaHCO_3$ (30 mL) and the organic layer was separated. The aqueous layer was extracted with DCM (2 x 20 mL). The combined organic layers were washed with 1 M HCl aq. (40 mL) and brine (30 mL), dried over $MgSO_4$, filtered and evaporated *in vacuo*.

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[4] Ano, Y.; Tobisu, M.; Chatani, N. *Org. Lett.* **2012**, *14*, 354.

[5] Y. Aihara, N. Chatani, *Chem. Sci.* **2013**, Advance Article.

[6] H.-P. Bi, Z.-H. Guan and Y.-M. Liang, *Org. Lett.* **2009**, *11*, 5726

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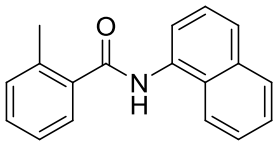
The obtained crude amide was purified by column chromatography on silica gel (hexane/EtOAc) to afford the desired amide. If necessary, an additional purification by recrystallisation (hexane/EtOAc) may be possible.

V. Spectroscopic Data for Starting Amides

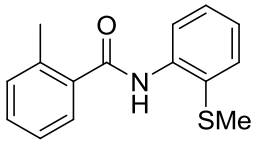
2-methyl-N-(naphthalen-1-yl)benzamide (G)



Synthesized according to **GP1** from o-toluoyl chloride (20 mmol, 2.60 mL), 1-naphthalenamine (22 mmol, 2.82 mL). Purification by column chromatography on silica gel (hexane/EtOAc = 85/15) followed by recrystallisation from hexane/EtOAc (80/20) afforded 4.17 g of **G** (80% yield).

Rf 0.2 (hexane/EtOAc = 90/10). White solid. **MP** = 190 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.58 (s, 3H), 7.32 (d, *J* = 6.4 Hz, 1H), 7.41 (t, *J* = 6.8 Hz, 1H), 7.51-7.55 (m, 3H), 7.63 (d, *J* = 5.2 Hz, 1H), 7.74 (d, *J* = 8Hz, 1H), 7.88-7.91 (m, 3H), 8.12 (d, *J* = 5.6 Hz, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 19.96, 120.47, 120.73, 125.75, 125.96 (2 overlapping peaks), 126.02, 126.38, 126.71, 127.00, 128.83, 130.35, 131.35, 132.24, 134.09, 136.33, 136.63, 168.56.
IR (neat) 3261 w, 2953 w, 1650 s, 1528 m, 1445 m, 1434 m, 1334 m, 1248 m, 1019 w, 839 s.
MS *m/z* (relative intensity, %) 261 (M^+, 34), 119 (100), 91 (33).
HRMS Calcd for $C_{18}H_{15}NO$: 261.1154; Found: 261.1156.

2-methyl-N-(2-(methylthio)phenyl)benzamide (H)



Synthesized according to **GP1** from o-toluoyl chloride (20 mmol, 2.60 mL), 2-(methylthio)aniline (22 mmol, 2.75 mL). Purification by column chromatography on silica gel (hexane/EtOAc = 90/10) followed by recrystallisation from hexane/EtOAc (90/10) afforded 4.62 g of **H** (90% yield).

Rf 0.37 (hexane/EtOAc = 90/10). White solid. **MP** = 65 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.38 (s, 3H), 2.57 (s, 3H), 7.12 (dt, *J* = 8, 1.6 Hz, 1H), 7.29 (t, *J* = 7.2 Hz, 1H), 7.35 (d, *J* = 8.4 Hz, 1H), 7.39 (dt, *J* = 8.4, 1.2 Hz, 1H), 7.52 (dd, *J* = 8, 1.6 Hz, 1H), 7.57 (d, *J* = 7.6 Hz, 1H), 8.51 (d, *J* = 7.6 Hz, 1H), 8.65 (brs, 1H).

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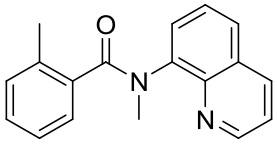
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 18.99, 20.10, 120.61, 124.60, 125.64, 126.01, 126.80, 128.85, 130.40, 131.41, 132.85, 136.20, 136.70, 138.39, 167.89.
IR (neat) 3338 w, 3059 w, 2923 w, 1677 m, 1577 m, 1505 s, 1428 s, 1303 m, 1242 w, 1038 w, 894 w, 840 w.
MS *m/z* (relative intensity, %) 257 (M^+, 17), 210 (37), 119 (100), 91 (39), 76 (16).
HRMS Calcd for $C_{15}H_{15}NOS$: 257.0874; Found:257.0874.

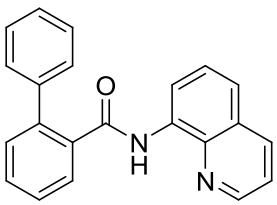
N,2-dimethyl-N-(quinolin-8-yl)benzamide (J)



To an oven-dried 1 neck round bottom flask, 2-methyl-N-(quinolin-8-yl)benzamide (**1a**) (2.62 g, 10 mmol) was dissolved in THF (20 mL) under a nitrogen atmosphere. At 0 °C, NaH (420 mg, 10.5 mmol, 1.05 equiv, 60 % oil dispersion) was added portionwise to this solution, then, the mixture was stirred 1 h at room temperature. MeI (2.49 mL, 40 mmol) was then added at room temperature and the reaction mixture was stirred overnight at room temperature. The reaction system was quenched with sat. aq. $NaHCO_3$ (20 mL) and the organic layer was separated. The aqueous layer was then extracted with Et_2O (2 x 20 mL) and the combined organic layers were dried over $MgSO_4$, filtered and evaporated *in vacuo*. The crude amide was purified by column chromatography on silica gel (hexane/EtOAc = 50/50) to afford the desired amide **J** as a brown solid (1.98 g, 72% yield).

Rf 0.32 (hexane/EtOAc = 50/50). White solid. **MP** = 100 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.46 (brs, 3H), 3.61 (brs, 3H), 6.61 (brs, 1H), 6.90 (brs, 3H), 7.30 (brs, 1H), 7.38 (d, J = 4 Hz, 1H), 7.40 (d, J = 4.4 Hz, 1H), 7.61 (d, J = 4.4 Hz, 1H), 8.06 (d, J = 6.4 Hz, 1H), 8.96 (dd, J = 4, 1.2 Hz, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 19.65, 37.47, 121.58, 124.22, 125.97, 126.63, 127.75, 128.25, 128.52, 128.98, 129.97, 135.51, 136.06, 136.62, 141.54, 144.00, 150.35, 171.90.
IR (neat) 3050 w, 2926 w, 1642 s, 1493 m, 1362 m, 1071 m, 912 w, 833 m.
MS *m/z* (relative intensity, %) 276 (M^+, 17), 275 (35), 248 (30), 158 (20), 157 (100), 129 (11), 119 (81), 91 (58), 65 (11).
HRMS Calcd for $C_{18}H_{16}N_2O$: 276.1263; Found:276.1250.

N-(quinolin-8-yl)biphenyl-2-carboxamide (1b)



Synthesized according to **GP2** from biphenyl-2-carboxylic acid (20 mmol, 3.96 g). Purification by column chromatography on silica gel (hexane/EtOAc = 80/20) afforded 4.67 g of **1b** (72% yield).

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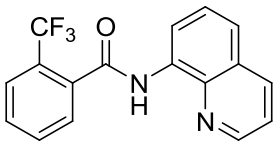
Rf 0.26 (hexane/EtOAc = 80/20). White solid. **Mp** = 123 °C.
1H NMR ($CDCl_3$, 399.78 MHz) δ 7.16 (t, J = 8.0 Hz, 1H), 7.28 (t, J = 8.0 Hz, 2H), 7.33 (dd, J = 8.0, 4.0 Hz, 1H), 7.43-7.58 (m, 7H), 7.91 (d, J = 8.0 Hz, 1H), 8.06 (dd, J = 8.0, 1.2 Hz, 1H), 8.52 (dd, J = 4.4, 1.2 Hz, 1H), 8.81 (dd, J = 8.0, 1.2 Hz, 1H), 9.79 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 116.07, 121.26, 121.39, 127.09, 127.47, 127.53, 128.24, 128.83, 129.04, 130.39, 130.56, 134.37, 135.83, 135.97, 138.20, 139.86, 140.11, 147.61, 167.68.
IR (KBr) 3316 m, 3058 w, 1662 s, 1594 w, 1521 s, 1482 m, 1465 m, 1423 m, 1380 m, 1324 m, 1267 m, 1126 w,. 894 w, 833m, 779 m, 742 m, 680 m.
MS m/z (relative intensity, %) 325 (10), 324 (M+, 41), 182 (14), 181 (100), 153 (23), 152 (27).
HRMS Calcd for $C_{22}H_{16}N_2O$: 324.1263; Found: 324.1265.

N-(quinolin-8-yl)-2-(trifluoromethyl)benzamide (**1c**)



Synthesized according to **GP1** from 2-(trifluoromethyl)benzoyl chloride (20 mmol, 2.9 mL) and 8-aminoquinoline (21 mmol, 3.02 g). Purification by column chromatography on silica gel (hexane/EtOAc = 80/20) followed by a recrystallisation from hexane/EtOAc (80/20) afforded 5.75 g of **1c** (91% yield).

Rf 0.34 (hexane/EtOAc = 80/20). White solid. **Mp** = 115 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 7.45 (dd, *J* = 6.4, 4.4 Hz, 1H), 7.58-7.64 (m, 3H), 7.68 (t, *J* = 7.2 Hz, 1H), 7.76 (d, *J* = 8 Hz, 1H), 7.8 (d, *J* = 8 Hz, 1H), 8.18 (dd, *J* = 8.4, 2 Hz, 1H), 8.75 (dd, *J* = 4, 1.6 Hz, 1H), 8.93 (dd, *J* = 6.8, 2 Hz, 1H), 10.17 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 116.73, 121.64, 122.22, 123.56 (q, *J* = 273 Hz), 126.53 (q, *J* = 4.7 Hz), 127.19, 127.44 (q, *J* = 31 Hz), 127.81, 128.33, 130.05, 132.08, 134.18, 135.98, 136.25, 138.26, 148.23, 165.81.
IR (neat) 3342 w, 1683 m, 1522 s, 1481 m, 1424 m, 1387 m, 1312 s, 1167 m, 1123 m, 1108 m,1035 m, 771 s.
MS *m/z* (relative intensity, %) 316 (M^+, 64), 173 (100), 171 (59), 145 (49).
HRMS Calcd for $C_{17}H_{11}F_3N_2O$: 316.0823; Found:316.0822.

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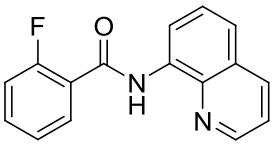
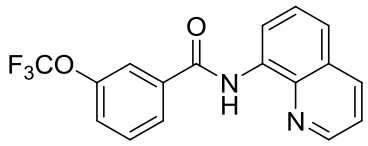
2-fluoro-N-(quinolin-8-yl)benzamide (**1e**)



Synthesized according to **GP2** from 2-Fluorobenzoic acid (20 mmol, 2.80 g). Purification by column chromatography on silica gel (hexane/EtOAc = 80/20) afforded 3.62 g of **1e** (68% yield).

R_f 0.23 (hexane/EtOAc = 5/1). White solid. **Mp** = 130°C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 7.22-7.28 (m, 1H), 7.31-7.36 (m, 1H), 7.45-7.61 (m, 4H), 8.16-8.24 (m, 1H), 8.86-8.89 (m, 1H), 8.98 (dd, J = 7.6, 1.6 Hz, 1H), 11.16 (d, J = 12.0 Hz, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 116.30 (d, J = 24.8 Hz), 117.21、121.64, 121.98(d, J = 8.6 Hz), 122.03, 124.81 (d, J = 2.9 Hz), 127.34, 127.92, 131.96, 133.54 (d, J = 8.6 Hz), 134.75, 136.26, 138.69, 148.43, 160. 44 (d, J = 234.8 Hz), 161.60.
IR (KBr) 3328 m, 1664 s, 1608 w, 1535 s, 1482 s, 1427 m, 1388 m, 1326 m, 1284 m, 1205 w, 823 m, 757 m.
MS *m/z* (relative intensity, %) 2674 (15), 266 (M^+, 86), 171 (33), 123 (100), 95 (22).
HRMS Calcd for $C_{16}H_{11}FN_2O$: 266.0855; Found: 266.0857.

N-(quinolin-8-yl)-3-(trifluoromethoxy)benzamide (**1n**)



Synthesized according to **GP2** from 3-(trifluoromethoxy)benzoic acid (20 mmol, 4.12 g). Purification by column chromatography on silica gel (hexane/EtOAc = 80/20) followed by a recrystallisation from hexane/EtOAc (99/1) afforded 4.64 g of **1n** (70% yield).

Rf 0.28 (hexane/EtOAc = 90/10). White solid. **Mp** = 70 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 7.38-7.59 (m, 5H), 7.93 (s, 2H), 8.08 (d, *J* = 8.4 Hz, 1H), 8.78 (s, 1H), 8.85 (d, *J* = 7.2 Hz, 1H), 10.66 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 116.46, 120.20, 120.37 (q, *J* = 258 Hz), 121.63, 121.93, 123.92, 124.95, 127.16, 127.78, 130.12, 133.96, 136.21, 137.04, 138.45, 148.24, 149.51, 163.42.
IR (neat) 3354 w, 2956 w, 1677 m, 1582 m, 1530 m, 1432 m, 1331 m, 1252 s, 1218 s, 1168 m, 836 m.
MS *m/z* (relative intensity, %) 332 (M^+, 87), 304 (13), 189 (100), 171 (61), 161 (23), 95 (35).
HRMS Calcd for $C_{17}H_{11}F_3N_2O_2$: 332.0773; Found: 332.0773.

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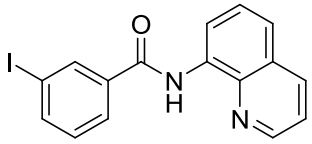
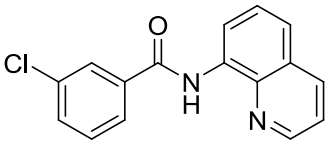
3-iodo-N-(quinolin-8-yl)benzamide (1p)



Synthesized according to **GP2** from 3-iodobenzoic acid (20 mmol, 4.96 g). Purification by column chromatography on silica gel (hexane/EtOAc = 90/10) followed by a recrystallisation from hexane/EtOAc (95/5) afforded 5.98 g of **1p** (80% yield).

Rf 0.25 (hexane/EtOAc = 90/10). White solid. **MP** = 110 °C
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 7.29 (t, *J* = 7.6 Hz, 1H), 7.49 (dd, *J* = 8.4, 4 Hz, 1H), 7.56 (dd, *J* = 8, 1.6 Hz, 1H), 7.60 (t, *J* = 8 Hz, 1H), 7.91 (dt, *J* = 8, 1.2 Hz, 1H), 8.02 (dt, *J* = 8, 1.2 Hz, 1H), 8.2 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.60 (t, *J* = 2 Hz, 1H), 8.86 (dd, *J* = 4, 1.2 Hz, 1H), 8.89 (dd, *J* = 7.2, 1.6 Hz, 1H), 10.67 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 94.61, 116.63, 121.75, 121.98, 126.18, 127.35, 127.89, 130.34, 134.16, 136.38, 136.44, 136.99, 138.59, 140.66, 148.36, 163.65.
IR (neat) 3347 w, 1674 m, 1529 s, 1487 m, 1425 m, 1387 m, 1328 m, 1258 m, 824 m.
MS *m/z* (relative intensity, %) 374 (M^+, 100), 231 (74), 203 (24), 171 (38), 76 (16).
HRMS Calcd for $C_{16}H_{11}IN_2O$: 373.9916; Found:373.9919.

3-chloro-N-(quinolin-8-yl)benzamide (1r)



Synthesized according to **GP1** from 3-chlorobenzoyl chloride (20 mmol, 2.56 mL) and 8-aminoquinoline (21 mmol, 3.02 g). Purification by column chromatography on silica gel (hexane/EtOAc = 90/10) followed by a recrystallisation from hexane/EtOAc (90/10) afforded 4.96 g of **1r** (88% yield).

Rf 0.25 (hexane/EtOAc = 90/10). White solid. **MP** = 90 °C .
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 7.46 (dd, *J* = 8, 2.8 Hz, 1H), 7.47 (d, *J* = 8 Hz, 1H), 7.53 (dd, *J* = 8.4, 0.8 Hz, 1H), 7.57 (t, *J* = 8.4 Hz, 1H), 7.93 (d, *J* = 7.6 Hz, 1H), 8.04 (t, *J* = 1.6 Hz, 1H), 8.17 (dd, *J* = 8, 1.2 Hz, 1H), 8.84 (dd, *J* = 4, 2 Hz, 1H), 8.88 (dd, *J* = 7.2, 1.6 Hz, 1H) 10.68 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 116.65, 121.74, 121.98, 125.21, 127.37, 127.66, 127.92, 130.04, 131.83, 134.18, 134.97, 136.41, 136.85, 138.63, 148.35, 163.95.
IR (neat) 3346 w, 1672 m, 1525 s, 1485 m, 1425 m, 1387 m, 1327 s, 1258 m, 1128 m, 1066 m 824 m.
MS *m/z* (relative intensity, %) 282 (M^+, 82), 254 (13), 171 (65), 141 (34), 139 (100), 111 (43).
HRMS Calcd for $C_{16}H_{11}ClN_2O$: 282.0560; Found: 282.0558.

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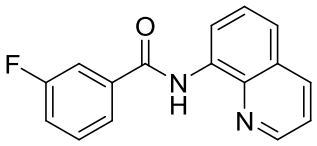
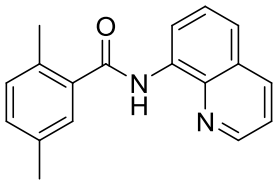
3-fluoro-N-(quinolin-8-yl)benzamide (**1s**)



Synthesized according to **GP2** from 3-fluorobenzoic acid (20 mmol, 2.8 g). Purification by column chromatography on silica gel (hexane/EtOAc = 90/10) followed by a recrystallisation from hexane/EtOAc (80/20) afforded 4 g of **1s** (75% yield).

Rf 0.25 (hexane/EtOAc = 90/10). Yellow solid. **MP** = 110 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 7.29 (dd, *J* = 8.4, 2.8 Hz, 1H), 7.47-7.61 (m, 4H), 7.78 (dt, *J* = 9.6, 2 Hz, 1H), 7.85 (d, *J* = 7.6 Hz, 1H), 8.19 (dd, *J* = 8.4, 2 Hz, 1H), 8.85 (dd, *J* = 4, 1.2 Hz, 1H), 8.90 (dd, *J* = 7.6, 1.6 Hz, 1H) 10.72 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 114.67 (d, *J* = 23 Hz), 116.63, 118.83 (d, *J* = 21 Hz), 121.75, 121.96, 122.69 (d, *J* = 2.9 Hz), 127.40, 127.93, 130.43 (d, *J* = 7.6 Hz), 134.21, 136.42, 137.36 (d, *J* = 7.2 Hz), 138.64, 148.34, 162.83 (d, *J* = 234 Hz), 164.13.
IR (neat) 3349 w, 1676 m, 1587 m, 1524 s, 1479 m, 1424 m, 1386 m, 1327 m, 1268 m, 848 m, 824 m.
MS *m/z* (relative intensity, %) 266 (M^+, 100), 238 (12), 171 (53), 123 (95), 95 (43).
HRMS Calcd for $C_{19}H_{11}FN_2O$: 266.0855; Found: 266.0854.

2,5-dimethyl-N-(quinolin-8-yl)benzamide (**7a**)



Synthesized according to **GP2** from 2,5-dimethylbenzoic acid (20 mmol, 3 g). Purification by column chromatography on silica gel (hexane/EtOAc = 80/20) followed by a recrystallisation from hexane/EtOAc (80/20) afforded 4.6 g of **7a** (83% yield).

Rf 0.34 (hexane/EtOAc = 90/10). White solid. **MP** = 85 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.40 (s, 3H), 2.55 (s, 3H), 7.20 (s, 2H), 7.45 (dd, *J* = 8.4, 4.8 Hz, 1H), 7.49 (s, 1H), 7.54 (d, *J* = 8 Hz, 1H), 7.60 (t, *J* = 8.4 Hz, 1H), 8.17 (dd, *J* = 8.4, 0.8 Hz, 1H), 8.78 (dd, *J* = 4, 1.2 Hz, 1H), 8.95 (d, *J* = 7.6 Hz, 1H), 10.18 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 19.69, 20.91, 116.49, 121.61, 121.67, 127.40, 127.81, 127.96, 130.98, 131.21, 133.28, 134.71, 135.56, 136.34, 136.50, 138.54, 148.20, 168.38.
IR (neat) 3357 w, 2957 w, 2919 w, 1675 m, 1520 s, 1480 m, 1422 m, 1378 m, 1320, 822 m, 774 s.
MS *m/z* (relative intensity, %) 276 (M^+, 32), 259 (21), 133 (100), 132 (29), 105 (33).
HRMS Calcd for $C_{18}H_{16}N_2O$: 276.1263; Found: 276.1262.

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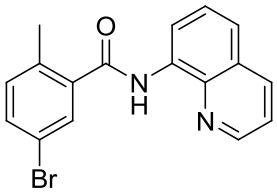
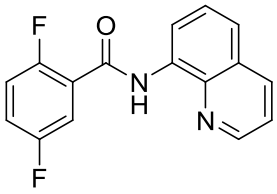
5-bromo-2-methyl-N-(quinolin-8-yl)benzamide (**7b**)



Synthesized according to **GP2** from 5-bromo-2-methylbenzoic acid (20 mmol, 4.3 g). Purification by column chromatography on silica gel (hexane/EtOAc = 90/10) followed by a recrystallisation from hexane/EtOAc (90/10) afforded 5.5 g of **7b** (81% yield).

Rf 0.31 (hexane/EtOAc = 90/10). White solid. **Mp** = 130 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.53 (s, 3H), 7.18 (d, *J* = 8 Hz, 1H), 7.47 (dd, *J* = 8, 4 Hz, 1H), 7.51 (dd, *J* = 8.4, 2 Hz, 1H), 7.57 (d, *J* = 8.8 Hz, 1H), 7.60 (t, *J* = 8 Hz, 1H), 7.79 (d, *J* = 2 Hz, 1H), 8.19 (d, *J* = 8.4 Hz, 1H), 8.80 (d, *J* = 4 Hz, 1H), 8.90 (d, *J* = 6 Hz, 1H), 10.16 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 19.64, 116.62, 119.37, 121.69, 122.05, 127.28, 127.89, 129.97, 132.89, 133.11, 134.27, 135.39, 136.35, 138.34, 138.40, 148.30, 166.47.
IR (neat) 3345 w, 1672 m, 1519 s, 1477 m, 1421 m, 1386 m, 1325 m, 1108 w, 902 w.
MS *m/z* (relative intensity, %) 340 (M^+, 57), 323 (54), 296 (29), 199 (100), 197 (99), 169 (42), 144 (71), 116 (23), 90 (50).
HRMS Calcd for $C_{17}H_{13}BrN_2O$: 340.0211; Found: 340.0214.

2,5-difluoro-N-(quinolin-8-yl)benzamide (**7c**)



Synthesized according to **GP1** from 2,5-difluorobenzoyl chloride (20 mmol, 2.47 mL), 8-aminoquinoline (21 mmol, 3.02 g). Purification by column chromatography on silica gel (hexane/EtOAc = 90/10) followed by a recrystallisation from hexane/EtOAc (90/10) afforded 4.37 g of **7c** (77% yield).

Rf 0.31 (hexane/EtOAc = 90/10). Yellow solid. **Mp** = 177 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 7.20-7.23 (m, 2H), 7.47 (dd, *J* = 7.6, 3.6 Hz, 1 H), 7.55-7.61 (m, 2H), 7.89-7.93 (m, 1H), (d, *J* = 8.18 Hz, 1 H), 8.86 (d, *J* = 4 Hz, 1 H), 8.94 (dd, *J* = 6.8, 2.4 Hz, 1 H), 11.18 (d, *J* = 12.4 Hz, 1 H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 117.30, 117.69 (dd, *J* = 27.8, 7.7 Hz), 118.08 (dd, *J* = 26, 2 Hz), 120.13 (dd, *J* = 25, 10 Hz), 121.67, 122.28, 123.35 (dd, *J* = 14.4, 7.6 Hz), 127.26, 127.88, 134.44, 136.22, 138.64, 148.48, 156.39 (d, *J* = 244.4 Hz), 158.83 (d, *J* = 244.4 Hz), 160.14.
IR (neat) 3337 w, 1671 m, 1535 m, 1482 m, 1326 m, 1264 m, 1220 m, 1166 m, 771 s.
MS *m/z* (relative intensity, %) 284 (M^+, 100), 171 (79), 141 (99), 113 (33).
HRMS Calcd for $C_{16}H_{10}F_2N_2O$: 284.0761; Found: 284.0763.

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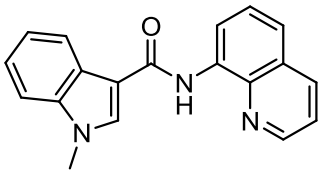
1-methyl-N-(quinolin-8-yl)-1H-indole-3-carboxamide (7i)



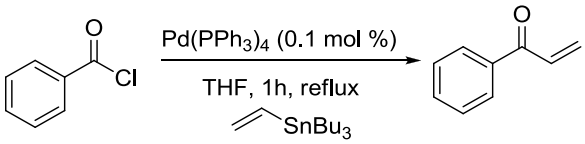
Synthesized according to **GP2** from 1-methylindole-3-carboxylic acid (20 mmol, 3.5 g). Purification by column chromatography on silica gel (EtOAc) afforded 4.27 g of **7i** (71% yield).

R_f 0.77 (EtOAc). White solid. **Mp** = 187 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 3.91 (s, 3H), 7.35-7.43 (m, 3H), 7.47-7.62 (m, 3H), 7.95 (s, 1H), 8.20 (dd, J = 8.0, 1.6 Hz, 1H), 8.48 (dd, J = 8.0, 1.6 Hz, 1H), 8.90 (dd, J = 4.4, 1.6 Hz, 1H), 8.96 (dd, J = 8.0, 0.8 Hz, 1H), 10.56 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 33.32, 110.00, 111.61, 116.12, 120.64, 120.71, 121.45, 121.74, 122.59, 125.42, 127.48, 127.94, 132.91, 135.23, 136.25, 137.31, 138.49, 148.05, 163.16.
IR (neat) 3382 w, 3357 w, 3112 w, 1646 m, 1523 s, 1484 s, 1421 m, 1376 m, 1324 m, 1222 m, 1149m, 1108 m, 873 w, 825 w, 738 m.
MS *m/z* (relative intensity, %) 301 (M^+, 25), 159 (11), 158 (100).
HRMS Calcd for $C_{19}H_{15}N_3O$: 301.1215; Found: 301.1214.

VI. Synthesis of α,β-Unsaturated Ketones

Two different procedures to synthesize not commercially available α,β-unsaturated ketones are suggested. The first one is a palladium catalyzed coupling with tributyl(vinyl)tin, which afforded α,β-unsaturated ketones in one step. However, sometimes some functional groups are not tolerated or products are contaminated by tin residues after purification. An alternative is proposed with a two steps procedure consisting in the synthesis of the corresponding alcohol, followed by a Dess-Martin oxidation.

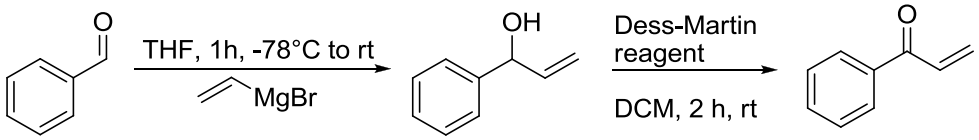
General Procedure 3. Palladium catalyzed coupling (GP3)



To an oven-dried 100 mL one-necked round bottom flask, acyl chloride (10 mmol) and tributyl(vinyl)tin (3.32 g, 10.5 mmol) were mixed in THF (20 mL) under N_2 atmosphere. Tetrakis(triphenylphosphine)palladium (11.55 g, 0.01 mmol) was then added and the solution

was refluxed for 1h. The reaction was cooled to room temperature and THF was evaporated *in vacuo* to afford a yellow crude mixture, immediately purified by column chromatography on silica gel (if necessary silica can be mixed with KF (500 mg KF/100 g silica) to remove tin residues).

General Procedure 4. Vinylation-Oxidation (GP4)

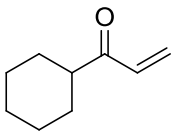


Step 1: The aldehyde (20 mmol) was dissolved in THF (50 mL) under a nitrogen atmosphere and the solution was cooled to -78°C, then vinylmagnesium bromide (22 mL, 22 mmol, 1 M in THF) was slowly added to this solution. The reaction mixture was allowed to reach room temperature and was stirred for 1 h. Reaction was then quenched with saturated NH_4Cl_{aq} (15 mL) and the organic layer was separated. Aqueous layer was extracted with diethyl ether (3x20 mL), combined organic layers were dried over $MgSO_4$ and solvent was evaporated *in vacuo*. Purification by column chromatography on silica gel afforded the expected alcohol.

Step 2: The alcohol was dissolved in DCM (100 mL) and Dess-Martin reagent (12.72 g, 30 mmol) was added at 0°C. The reaction was stirred at room temperature for 2 h and saturated $Na_2S_2O_{3aq}$ (20 mL) and saturated $NaHCO_{3aq}$ (20 mL) were then added at room temperature. The biphasic mixture was stirred for 1 h and then the organic layer was separated off. The aqueous layer was extracted with DCM (3x20mL), combined organic layers were dried over $MgSO_4$ and solvent was evaporated *in vacuo*. Column chromatography on silica gel afforded the expected α,β-unsaturated ketone.

VII. Spectroscopic Data for α,β-Unsaturated Ketones

1-cyclohexylprop-2-en-1-one (2c)

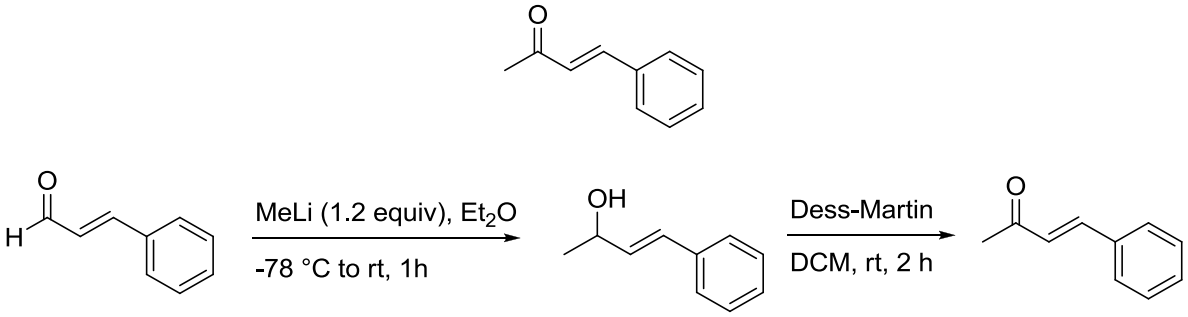


Synthesized according to **GP4** from cyclohexanecarboxaldehyde (20 mmol, 2.42 mL). Intermediate 1-cyclohexylprop-2-en-1-ol[7] was obtained in a quantitative yield and was used without further purifications. Filtration through a short path of silica (hexane/EtOAc = 95/5) followed by kugelrohr distillation (100 °C, 5 mmHg) afforded 1.65 g of **2c** (60% yield) as colorless liquid.

[7] Z. Shi, Q. Tong,W. W. Y. Leong, G. Zhong, *Chem. Eur. J.* **2012**, *18*, 9802.

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 1.17-1.40 (m, 5H), 1.66-1.83 (m, 5H), 2.56-2.63 (m, 1H), 5.73 (dd, *J* = 10.4, 1.2 Hz, 1H), 6.23 (dd, *J* = 17.2, 1.2 Hz, 1H), 6.41 (dd, *J* = 17.2, 10.4 Hz, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 25.63, 25.81, 28.47, 48.11, 127.75, 134.90, 203.54.
IR (neat) 2928 s, 2854 m, 1695 s, 1673 s, 1610 m, 1449 m, 1402 m, 1146 w, 975 m.
MS *m/z* (relative intensity, %) 138 (M^+, 27), 110 (14), 109 (19), 97 (27), 96 (31), 95 (12), 83 (75), 82 (15), 81 (17), 70 (17), 67 (22), 55 (100), 41 (38).
HRMS Calcd for $C_9H_{14}O$: 138.1045; Found:138.1041.

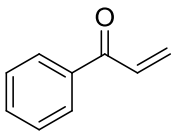
(E)-4-phenylbut-3-en-2-one (**2f**)



Intermediate alcohol was synthesized according to a reported procedure[8] from Cinnamaldehyde (20 mmol, 2.6 g). The expected alcohol was obtained in a quantitative yield and used without further purification according to **GP4**. Column chromatography on silica gel afforded 2.6 g of **2f** (89% yield from step1).

Rf 0.26 (hexane/EtOAc = 90/10). Yellow solid. **MP** = 35 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.38 (s, 3H), 6.72 (d, *J* = 16.4 Hz, 1H), 7.38-7.40 (m, 3H), 7.40-7.55 (m, 4H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 27.46, 127.08, 128.22, 128.93, 130.48, 134.35, 143.38, 198.33.
IR (neat) 1666 s, 1608 s, 1449 m, 1358 m, 1254 s, 1174 m, 974 s.
MS *m/z* (relative intensity, %) 146 (M^+, 74), 145 (58), 132 (10), 131 (100), 103 (72), 77 (31), 51 (16).
HRMS Calcd for $C_{10}H_{10}O$: 146.0732; Found: 146.0737.

1-phenylprop-2-en-1-one (**2g**)



Synthesized according to **GP3** from benzoyl chloride (10 mmol, 1.16 mL). Purification by column chromatography on silica gel (hexane/EtOAc = 95/5) afforded 1.05 g of **2g** (80% yield).

Rf 0.38 (hexane/EtOAc = 95/5). Colorless liquid.

[8] A. Shuji, H. Ryosuke, F. Noboru, K. Yasuyuki, E. Masahiro, *Org. Lett.* **2010**, 12, 4900.

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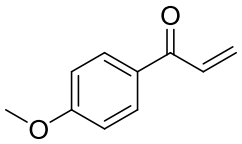
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 5.92 (dd, *J* = 10.8, 2 Hz, 1H), 6.43 (dd, *J* = 16.8, 1.2 Hz, 1H), 7.158 (dd, *J* = 16.8, 10.8 Hz, 1H), 7.45-7.49 (m, 2H), 7.57 (tt, *J* = 6.8, 1.2 Hz, 1H), 7.93-7.96 (m, 2H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 128.55, 128.63, 130.15, 132.28, 132.93, 137.17, 190.96.
IR (neat) 1671 s, 1608 m, 11448 m, 1403 s, 1230 s, 992 s.
MS *m/z* (relative intensity, %) 132 (M^+, 48), 105 (100), 77 (55), 51 (16).
HRMS Calcd for C_9H_8O: 132.0575; Found: 132.0574.

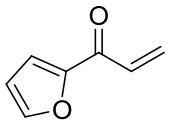
1-(4-methoxyphenyl)prop-2-en-1-one (**2h**)



Synthesized according to **GP3** from 4-methoxybenzoyl chloride (10 mmol, 1.35 mL). Purification by column chromatography on silica gel (hexane/EtOAc = 90/10) afforded 1.16 g of **2h** (72% yield).

Rf 0.25 (hexane/EtOAc = 90/10). White solid.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 3.88 (s, 3H), 5.87 (dd, *J* = 10.4, 2 Hz, 1H), 6.42 (dd, *J* = 17.2, 1.6 Hz, 1H), 6.96 (d, *J* = 9.2 Hz, 2H), 7.17 (dd, *J* = 17.6, 10.8 Hz, 1H), 7.96 (d, *J* = 8.4 Hz, 2H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 55.32, 113.70, 129.10, 130.02, 130.88, 131.95, 163.42, 189.02.
IR (neat) 1662 m, 1595 s, 1573 m, 1509 m, 1419 m, 1399 m, 1236 s, 1169 s, 991 m, 848 m.
MS *m/z* (relative intensity, %) 162 (M^+, 41), 135 (100), 92 (11), 77 (14).
HRMS Calcd for $C_{10}H_{10}O_2$: 162.0681; Found: 162.0683.

1-(furan-2-yl)prop-2-en-1-one (**2i**)



Synthesized according to **GP3** from 2-furoyl chloride (10 mmol, 0.98 mL). Purification by column chromatography on silica gel (hexane/EtOAc = 80/20) afforded 1.02 g of **2i** (84% yield).

Rf 0.37 (hexane/EtOAc = 80/20). White solid.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 5.88 (dd, *J* = 10.8, 1.6 Hz, 1H), 6.53 (d, *J* = 1.2 Hz, 1H), 6.56-6.58 (m, 1H), 7.07 (dd, *J* = 17.6, 10.8 Hz, 1H), 7.27 (dd, *J* = 3.6, 0.8 Hz, 1H), 7.64 (dd, *J* = 2.4, 1.2 Hz, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 112.44, 118.27, 129.53, 131.25, 146.93, 152.91, 178.03.
IR (neat) 1668 s, 1567 m, 1523 m, 1465 s, 1395 m, 1326 m, 1268 m, 1163 m, 1032 m, 882 m.
MS *m/z* (relative intensity, %) 122 (M^+, 58), 95 (100), 94 (11), 55 (10), 39 (12).
HRMS Calcd for $C_7H_6O_2$: 122.0368; Found: 122.0370.

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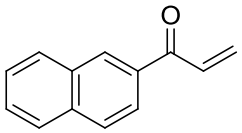
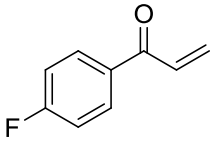
1-(naphthalen-2-yl)prop-2-en-1-one (**2j**)



Synthesized according to **GP3** from 2-naphthoyl chloride (10 mmol, 1.90 g). Purification by column chromatography on silica gel (hexane/EtOAc = 95/5) afforded 1.56 g of **2j** (86% yield).

Rf 0.42 (hexane/EtOAc = 90/10). White solid.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 5.97 (dd, *J* = 10.4, 1.2 Hz, 1H), 6.51 (dd, *J* = 17.2, 1.6 Hz, 1H), 7.32 (dd, *J* = 17.2, 10.8 Hz, 1H), 7.53-7.62 (m, 2H), 7.86-7.97 (m, 3H), 8.04 (dd, *J* = 8.8, 2 Hz, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 124.35, 126.76, 127.75, 128.45, 128.55, 129.48, 130.06, 130.35, 132.26, 132.39, 134.51, 135.47, 190.73.
IR (neat) 1667 s, 1627 m, 1607 m, 1523 m, 1468 m, 1401 m, 1277 m, 1222 m, 1180 m, 1125 m, 979 w, 866 w.
MS *m/z* (relative intensity, %) 182 (M^+, 61), 156 (12), 155 (100), 154 (18), 127 (78), 126 (12).
HRMS Calcd for $C_{13}H_{10}O$: 182.0732; Found: 182.0732.

1-(4-fluorophenyl)prop-2-en-1-one (**2k**)



Synthesized according to **GP3** from 4-fluorobenzoyl chloride (10 mmol, 1.18 mL). Purification by column chromatography on silica gel (hexane/EtOAc = 95/5) afforded 1.03 g of **2k** (69% yield).

Rf 0.28 (hexane/EtOAc = 95/5). White solid.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 5.94 (d, *J* = 10.4 Hz, 1H), 6.44 (d, *J* = 16.8 Hz, 1H), 7.12-7.17 (m, 3H), 7.98 (dd, *J* = 8, 5.6 Hz, 2H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 115.67 (d, *J* = 22 Hz), 130.28, 131.56 (d, *J* = 9.5 Hz), 131.85, 133.49 (d, *J* = 2.8 Hz), 165.60 (d, *J* = 255 Hz), 189.22.
IR (neat) 1670 m, 1594 m, 1410 m, 1227 s, 1156 m, 999 m, 853 m.
MS *m/z* (relative intensity, %) 150 (M^+, 45), 123 (100), 95 (45), 75 (12).
HRMS Calcd for C_9H_7FO: 150.0481; Found: 150.0488.

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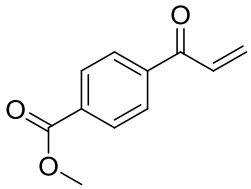
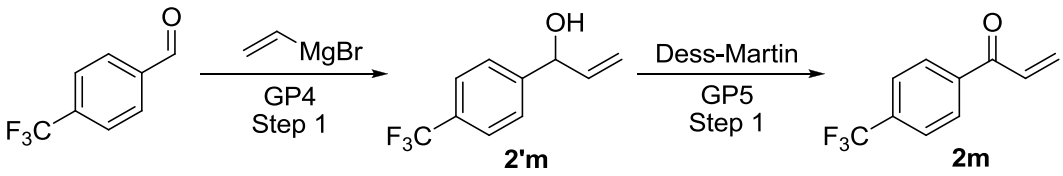
methyl 4-acryloylbenzoate (2l)



Synthesized according to **GP4** from methyl terephthalaldehydate (20 mmol, 3.28 g). Purification by column chromatography on silica gel (hexane/EtOAc = 90/10) afforded 3.42 g of **2l** (90% yield).

Rf 0.34 (hexane/EtOAc = 90/10). White solid.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 3.94 (s, 3H), 5.98 (dd, *J* = 8.8, 1.6 Hz, 1H), 6.44 (dd, *J* = 17.2, 1.6 Hz, 1H), 7.13 (dd, *J* = 17.6, 10.8 Hz, 1H), 7.97 (d, *J* = 8.4 Hz, 2H), 8.13 (d, *J* = 8.4 Hz, 2H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 52.44, 128.53, 129.79, 131.16, 132.18, 133.67, 140.56, 166.18, 190.62.
IR (neat) 1723 s, 1670 s, 1604 m, 1411 m, 1276 s, 1227 s, 1108 s, 999 s.
MS *m/z* (relative intensity, %) 190 (M^+, 24), 163 (100), 159 (20), 135 (18), 103 (13), 55 (10).
HRMS Calcd for $C_{11}H_{10}O_3$: 190.0630; Found: 190.0631.

1-(4-(trifluoromethyl)phenyl)prop-2-en-1-one (2m)

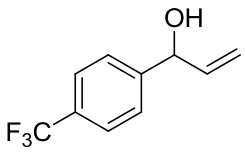


Synthesized according to **GP4** from:

Step 1: 4-(trifluoromethyl)benzaldehyde (20 mmol, 3.48 g). Purification by column chromatography on silica gel (hexane/EtOAc = 90/10) afforded 3.42 g of the intermediate 1-(4-(trifluoromethyl)phenyl)prop-2-en-1-ol **2'm** (90% yield).

Step 2: Dess-Martin periodinane (30 mmol, 12.7 g), **2'm** (17 mmol, 3.42g). Purification by column chromatography on silica gel (hexane/EtOAc = 95/5) afforded 2 g of **2m** (59% yield from step 2).

1-(4-(trifluoromethyl)phenyl)prop-2-en-1-ol (2'm)



Rf 0.18 (hexane/EtOAc = 90/10). Yellow oil.

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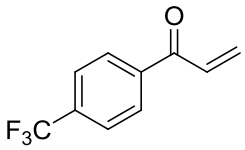
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 5.16 (d, *J* = 5.6 Hz, 1H), 5.2 (dd, *J* = 10.4, 0.8 Hz, 1H), 5.30 (dd, *J* = 16.8, 1.2 Hz, 1H), 5.91-5.99 (m, 1H), 7.43 (d, *J* = 8.4 Hz, 2H), 7.58 (d, *J* = 8.4 Hz, 2H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 74.67, 115.98, 124.11 (q, *J* = 259 Hz), 125.29, 126.51, 129.71 (q, *J* = 32.6 Hz), 139.41, 146.31.
IR (neat) 3348 w, 1326 s, 1165 m, 1125 m, 1067 m, 1015 w, 926 w.
MS *m/z* (relative intensity, %) 202 (M^+, 51), 183 (19), 175 (25), 173 (67), 160 (74), 159 (15), 146 (12), 145 (39), 133 (100), 127 (59), 115 (18), 105 (10), 91 (13), 77 (10), 55 (39).
HRMS Calcd for $C_{10}H_9F_3O$: 202.0605; Found: 202.0603.

1-(4-(trifluoromethyl)phenyl)prop-2-en-1-one (**2m**)



Rf 0.28 (hexane/EtOAc = 95/5). Yellow oil.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 6.01 (dd, *J* = 12.4, 1.6 Hz, 1H), 6.46 (dd, *J* = 17.2, 1.6 Hz, 1H), 7.12 (dd, *J* = 16.8, 10.4 Hz, 1H), 7.74 (d, *J* = 8.4 Hz, 2H), 8.02 (d, *J* = 8.4 Hz, 2H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 123.33 (q, *J* = 225 Hz), 125.65 (q, *J* = 4 Hz), 128.95, 131.48, 132.01, 134.19 (q, *J* = 57 Hz), 140.00, 190.20.
IR (neat) 1678 m, 1609 m, 1413 m, 1319 s, 1227 m, 1167 m, 1124 s, 1065 s, 999 m, 979 m, 860 m.
MS *m/z* (relative intensity, %) 200 (M^+, 32), 173 (100), 145 (61), 55 (13).
HRMS Calcd for $C_{10}H_7F_3O$: 200.0449; Found: 200.0448.

VIII. General Procedures for the *Ortho* C-H Bond Directed Alkylation

General procedures are described for the reaction of 2-methyl-N-(quinolin-8-yl)benzamide **1a** with MVK **2a**.

Variations of the general procedures:

- m-substituted amides were stirred 6 h at 100 °C (108 °C bath temperature).
- p-substituted amides were stirred 6 h at 100 °C (108 °C bath temperature) and 3 equiv of MVK were used to optimize the formation of the di-alkylated product, but, 1 equiv of MVK may be used if the formation of the mono-alkylated products is desired.
- If NaOPiv was used, the same procedures were followed by replacing NaOAc with NaOPiv.
- With acceptors **2d**, **2e** and **2f** reactions were run at 140°C (148 °C bath temperature).
- Amides **3ah-m** and products **9h-m** were isolated by HPLC.

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General Procedure 5 (GP5) with $RuCl_2(PPh_3)_3$ as catalyst.

To an oven-dried 5 mL screw-capped vial, 2-methyl-N-(quinolin-8-yl)benzamide **1a** (131 mg, 0.5 mmol, 1 equiv.), MVK **2a** (70 mg, 1 mmol, 2 equiv.), $RuCl_2(PPh_3)_3$ (48 mg, 0.05 mmol, 10 mol %), sodium acetate (10.25 mg, 0.125 mmol, 25 mol %) and toluene (1 mL) were added under a gentle stream of nitrogen. The mixture was stirred for 4 h at 100 °C (108 °C bath temperature) then cooled to room temperature and concentrated *in vacuo*. Purification by column chromatography on silica gel (hexane/EtOAc = 70/30) afforded 156 mg of **3aa** as a yellow oil (94% yield).

General Procedure 6 (GP6) with $[RuCl_2(p\text{-cymene})]_2$ as catalyst.

To an oven-dried 5 mL screw-capped vial, 2-methyl-N-(quinolin-8-yl)benzamide **1a** (131 mg, 0.5 mmol, 1 equiv.), MVK **2a** (70 mg, 1 mmol, 2 equiv.), $[RuCl_2(p\text{-cymene})]_2$ (15.30 mg, 0.025 mmol, 5 mol %), sodium acetate (10.25 mg, 0.125 mmol, 25 mol %) and toluene (1 mL) were added under a gentle stream of nitrogen. The mixture was stirred for 4 h at 100 °C (108 °C bath temperature) then cooled to room temperature and concentrated *in vacuo*. Purification by column chromatography on silica gel (hexane/EtOAc = 70/30) afforded 151 mg of **3aa** as a yellow oil (91% yield).

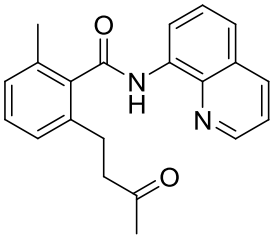
General Procedure 7 (GP7) with PPh_3/$[RuCl_2(p\text{-cymene})]_2$ as catalyst.

To an oven-dried 5 mL screw-capped vial, 2-methyl-N-(quinolin-8-yl)benzamide **1a** (131 mg, 0.5 mmol, 1 equiv.), MVK **2a** (70 mg, 1 mmol, 2 equiv.), $[RuCl_2(p\text{-cymene})]_2$ (15.30 mg, 0.025 mmol, 5 mol %), PPh_3 (39.30 mg, 0.15 mmol, 30 mol %), sodium acetate (10.25 mg, 0.125 mmol, 25 mol %) and toluene (1 mL) were added under a gentle stream of nitrogen. The mixture was stirred for 4 h at 100 °C (108 °C bath temperature) then cooled to room temperature and concentrated *in vacuo*. Purification by column chromatography on silica gel (hexane/EtOAc = 70/30) afforded 149 mg of **3aa** as a yellow oil (90% yield).

IX. Spectroscopic Data for Alkylated Products

2-methyl-6-(3-oxobutyl)-N-(quinolin-8-yl)benzamide (3aa)

See also part X for the cleavage of the 8-aminoquinoline moiety.



Rf 0.37 (hexane/EtOAc = 70/30). Yellow oil.

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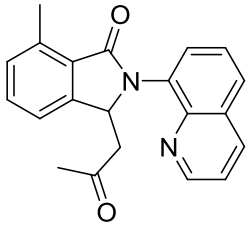
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.05 (s, 3H), 2.43 (s, 3H), 2.85 (t, *J* = 8 Hz, 2H), 2.97 (t, *J* = 8 Hz, 2H), 7.13 (d, *J* = 7.2 Hz, 1H), 7.14 (d, *J* = 7.6 Hz, 1H), 7.27 (t, *J* = 8 Hz, 1H), 7.46 (dd, *J* = 8, 4 Hz, 1H), 7.57 (d, *J* = 6.4 Hz, 1H), 7.61 (t, *J* = 8 Hz, 1H), 8.19 (d, *J* = 8 Hz, 1H), 8.74 (d, *J* = 4 Hz, 1H), 8.95 (dd, *J* = 7.2, 2 Hz, 1H), 9.96 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 19.30, 27.43, 29.67, 45.39, 116.64, 121.55, 121.98, 126.75, 127.13, 127.81, 128.13, 129.09, 134.01, 134.44, 136.21, 137.64 (two overlapping peaks), 138.26, 148.15, 168.40, 207.54.
IR (neat) 3348 w, 1712 m, 1671 m, 1518 s, 1481 s, 1423 m, 1385 m, 1324 m, 1263 m, 1161 w, 1127 w, 896 w.
HRMS Calcd for $C_{21}H_{20}N_2O_2$: 332.1525; Found: 332.1522.

7-methyl-3-(2-oxopropyl)-2-(quinolin-8-yl)isoindolin-1-one (**4aa**)



To an oven-dried 5 mL screw-capped vial, 2-methyl-N-(quinolin-8-yl)benzamide **1a** (131 mg, 0.5 mmol, 1 equiv.), MVK **2a** (70 mg, 1 mmol, 2 equiv.), $Ru_3(CO)_{12}$ (32 mg, 0.05 mmol, 10 mol %) and toluene (1 mL) were added under a gentle stream of nitrogen. The mixture was stirred for 4 h at 100 °C (108 °C bath temperature) then cooled to room temperature and concentrated *in vacuo*. Purification by column chromatography on silica gel (hexane/EtOAc = 50/50) afforded 10 mg of **4aa** as a yellow oil (6 % yield).

Rf 0.26 (hexane/EtOAc = 50/50). Yellow oil
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 1.87 (s, 3H), 2.70 (dd, *J* = 17.2, 7.6 Hz, 1H), 2.76 (s, 3H), 2.86 (dd, *J* = 17.2, 4.8 Hz, 1H), 6.24 (dd, *J* = 8, 4.8 Hz, 1H), 7.25 (d, *J* = 8.8 Hz, 1H), 7.30 (d, *J* = 7.6 Hz, 1H), 7.41(t, *J* = 4 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 1H), 7.62 (t, *J* = 8 Hz, 1H), 7.80 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.85 (dd, *J* = 8.4, 1.6 Hz, 1H), 8.19 (dd, *J* = 8.4, 1.6 Hz, 1H), 8.88 (dd, *J* = 4, 1.6 Hz, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 17.44, 30.52, 46.97, 58.23, 120.07, 121.52, 126.21, 128.08, 128.82, 129.32, 130.29, 131.52, 133.75, 136.29, 138.28, 144.77, 146.74, 150.37, 168.97, 205.83.
IR (neat) 2854 w, 1690 s, 1499 w, 1395 m, 1153 w, 891 w, 829 w.
MS *m/z* (relative intensity, %) 330 (M^+, 10), 288 (21), 287 (100).
HRMS Calcd for $C_{21}H_{18}N_2O_2$: 330.1368; Found: 330.1366.

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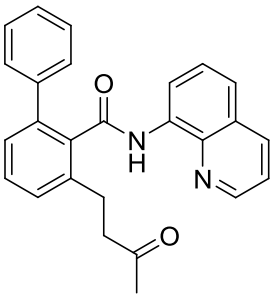
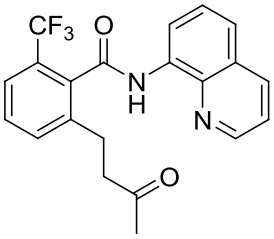
3-(3-oxobutyl)-N-(quinolin-8-yl)biphenyl-2-carboxamide (3ba)



Rf 0.34 (hexane/EtOAc = 70/30). brown solid. **MP** = 125 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.10 (s, 3H), 2.95 (t, *J* = 8 Hz, 2H), 3.07 (t, *J* = 8 Hz, 2H), 7.07 (t, *J* = 7.2 Hz, 1H), 7.20 (t, *J* = 7.2 Hz, 2H), 7.32-7.37 (m, 3H), 7.43-7.51 (m, 5H), 8.08 (dd, *J* = 8.4, 1.6 Hz, 1H), 8.59 (dd, *J* = 4.4, 1.2 Hz, 1H), 8.70 (dd, *J* = 6.8, 1.6 Hz, 1H), 9.60 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 27.80, 29.80, 45.61, 116.42, 121.35, 121.72, 127.04, 127.21, 127.61, 128.06, 128.50, 128.79, 129.39, 134.05, 136.03, 136.51, 138.10, 139.05, 139.73, 140.09, 147.81, 167.92, 207.81.
IR (neat) 3340 w, 3058 w, 1714 w, 1670 m, 1520 s, 1482 m, 1424 m, 1326 m, 1262 w, 1129 w, 826 m.
HRMS Calcd for $C_{26}H_{22}N_2O_2$: 394.1681; Found: 394.1679
Anal. Calcd for $C_{26}H_{22}N_2O_2$: C, 79.16; H, 5.62; N, 7.10. Found: C, 78.94; H, 5.55; N, 7.09.

2-(3-oxobutyl)-N-(quinolin-8-yl)-6-(trifluoromethyl)benzamide (3ca)



Rf 0.31 (hexane/EtOAc = 70/30). Brown solid. **MP** = 127 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.06 (s, 3H), 2.88 (m, 2H), 3.02 (m, 2H), 7.46 (dd, *J* = 8.4, 4.4 Hz, 1H), 7.50-7.56 (m, 2H), 7.59-7.63 (m, 3H), 8.20 (dd, *J* = 8.4, 1.6 Hz, 1H), 8.74 (dd, *J* = 4.4, 1.6 Hz, 1H), 8.90 (dd, *J* = 6, 2.8 Hz, 1H), 10.03 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 27.23, 29.76, 45.13, 116.97, 121.70, 122.43, 123.71 (q, *J* = 274 Hz), 124.17 (q, *J* = 5.02 Hz), 127.25, 127.31 (q, *J* = 31.16 Hz), 127.92, 129.48, 133.63 (d, *J* = 1.0 Hz), 133.92, 135.22 (q, *J* = 2.01 Hz), 136.32, 138.32, 139.98, 148.32, 165.40, 207.11.
IR (neat) 3335 w, 1714 m, 1677 m, 1522 s, 1484 m, 1318 s, 1220 m, 1161 m, 1124 s, 827 m.
HRMS Calcd for $C_{21}H_{17}F_3N_2O_2$: 386.1242; Found: 386.1241.
Anal. Calcd for $C_{21}H_{17}F_3N_2O_2$: C, 65.28; H, 4.43; N, 7.25. Found: C, 65.08; H, 4.40; N, 7.23.

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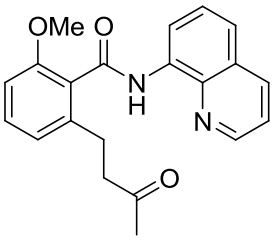
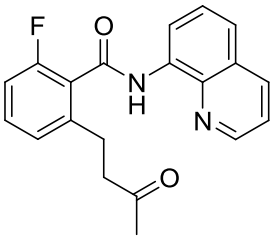
2-methoxy-6-(3-oxobutyl)-N-(quinolin-8-yl)benzamide (3da)



Rf 0.2 (hexane/EtOAc = 70/30). White solid. **MP** = 90 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.07 (s, 3H), 2.87 (t, *J* = 7.6 Hz, 2H), 2.99 (t, *J* = 7.6 Hz, 2H), 3.84 (s, 3H), 6.87 (d, *J* = 8.4 Hz, 1H), 6.90 (d, *J* = 7.6 Hz, 1H), 7.33 (t, *J* = 8 Hz, 1H), 7.44 (dd, *J* = 8, 4 Hz, 1H), 7.19 (d, *J* = 7.6 Hz, 2H), 7.59 (t, *J* = 8 Hz, 1H), 8.17 (dd, *J* = 8.0, 1.2 Hz, 1H), 8.75 (dd, *J* = 4, 1.6 Hz, 1H), 8.95 (dd, *J* = 7.6, 1.2 Hz, 1H), 10.13 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 25.59, 29.78, 45.41, 55.74, 109.02, 116.70, 121.50, 121.71, 122.01, 126.67, 127.31, 127.91, 130.39, 134.55, 136.23, 138.42, 140.56, 148.08, 156.37, 166.09, 207.86.
IR (neat) 3354 w, 1714 m, 1670 m, 1520 s, 1483 m, 1325 m, 1261 m, 1081 m, 896 m, 826 m.
HRMS Calcd for $C_{21}H_{20}N_2O_3$: 348.1474; Found: 348.1472.

2-fluoro-6-(3-oxobutyl)-N-(quinolin-8-yl)benzamide (3ea)



Rf 0.28 (hexane/EtOAc = 80/20). Yellow solid. **MP** = 65 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.10 (s, 3H), 2.89 (t, *J* = 7.2 Hz, 2H), 3.05 (t, *J* = 7.6 Hz, 2H), 7.05 (t, *J* = 8.0 Hz, 1H), 7.12 (d, *J* = 8.0 Hz, 1H), 7.36 (td, *J* = 8, 5.6 Hz, 1H), 7.45 (dd, *J* = 8.4, 4.8 Hz, 1H), 7.57 (d, *J* = 6.8 Hz, 1H), 7.60 (t, *J* = 8.4 Hz, 1H), 8.18 (dd, *J* = 8, 1.6 Hz, 1H), 8.77 (dd, *J* = 4.4, 2 Hz, 1H), 8.92 (dd, *J* = 6.4, 2.4 Hz, 1H), 10.17 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 27.42 (d, *J* = 1.9 Hz), 29.84, 45.18, 113.79 (d, *J* = 22 Hz), 116.83, 121.68, 122.24, 125.14 (d, *J* = 17.2 Hz), 125.73 (d, *J* = 2.8 Hz), 127.24, 127.91, 131.03 (d, *J* = 8.6 Hz), 134.13, 136.31, 138.32, 141.98 (d, *J* = 1.9 Hz), 148.30, 159.25 (d, *J* = 247 Hz), 163.25, 207.50.
IR (neat) 3342 w, 3049 w, 1714 w, 1673 m, 1523 s, 1484 m, 1326 m, 1247 w, 826 w.
HRMS Calcd for $C_{20}H_{17}FN_2O_2$: 336.1274; Found: 336.1272.

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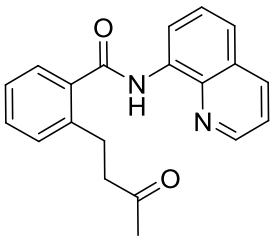
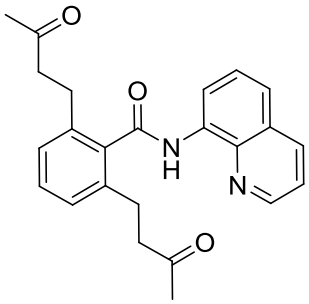
2-(3-oxobutyl)-N-(quinolin-8-yl)benzamide (3fa)



Rf 0.4 (hexane/EtOAc = 70/30); Yellow solid; **MP** = 90 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.10 (s, 3H), 2.91 (t, *J* = 7.6 Hz, 2H), 3.15 (t, *J* = 7.2 Hz, 2H), 7.30-7.34 (m, 2H), 7.39-7.43 (m, 2H), 7.52 (dd, *J* = 8.4, 2 Hz, 1H), 7.56 (t, *J* = 8 Hz, 1H), 7.65-7.67 (m, 1H), 8.13 (dd, *J* = 8.8, 1.2 Hz, 1H), 8.74 (dd, *J* = 4, 1.2 Hz, 1H), 8.90 (dd, *J* = 7.6, 1.6 Hz, 1H), 10.21 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 27.69, 29.77, 45.54, 116.34, 121.57, 121.79, 126.40, 127.08, 127.16, 127.81, 130.43, 130.68, 134.45, 136.23, 136.28, 138.34, 140.07, 148.14, 167.80, 207.87.
IR (neat) 3349 w, 3056 w, 1713 m, 1672 m, 1521 s, 1480 m, 1264 m, 826 m, 756 m.
MS *m/z* (relative intensity, %) 318 (M^+, 34), 276 (18), 275 (87), 175 (34), 145 (11), 144 (18), 133 (11), 132 (20), 131 (100), 103 (14), 77 (12), 43 (28).
HRMS Calcd for $C_{20}H_{18}N_2O_2$: 318.1368; Found: 318.1371.
Anal. Calcd for $C_{20}H_{18}N_2O_2$: C, 75.45; H, 5.70; N, 8.80. Found: C, 75.37; H, 5.61; N, 8.73.

2,6-bis(3-oxobutyl)-N-(quinolin-8-yl)benzamide (6fa)



Rf 0.38 (hexane/EtOAc = 50/50); Yellow oil.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.00 (s, 6H), 2.82 (t, *J* = 7.6 Hz, 4H), 2.95 (t, *J* = 8 Hz, 4H), 7.12 (d, *J* = 7.2 Hz, 2H), 7.27 (t, *J* = 8 Hz, 1H), 7.40 (dd, *J* = 8.4, 4.4 Hz, 1H), 7.53 (d, *J* = 6 Hz, 1H), 7.55 (t, *J* = 8.4 Hz, 1H), 8.14 (dd, *J* = 8.0, 1.2 Hz, 1H), 8.70 (dd, *J* = 4, 1.2 Hz, 1H), 8.88 (dd, *J* = 6.4, 2.8 Hz, 1H), 9.95 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 27.31, 29.64, 45.25, 116.72, 121.57, 122.13, 127.09, 127.26, 127.80, 129.32, 133.81, 136.23, 137.42, 137.71, 148.14, 168.09, 207.39.
IR (neat) 3339 w, 3058 w, 1712 m, 1669 m, 1519 s, 1481 m, 1423 m, 1325 m, 1161 m, 1125 m, 895 w, 826 m.
MS *m/z* (relative intensity, %) 388 (M^+, 41), 345 (74), 262 (19), 245 (62), 201 (100), 185 (13), 183 (12), 159 (17), 144 (36), 117 (15), 43 (46).
HRMS Calcd for $C_{24}H_{24}N_2O_3$: 388.1787; Found: 388.1788.

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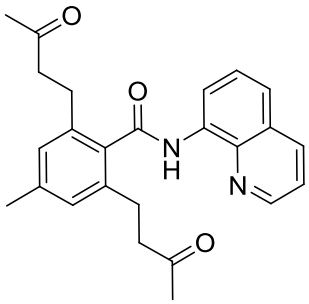
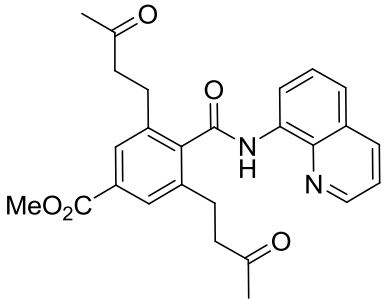
4-methyl-2,6-bis(3-oxobutyl)-N-(quinolin-8-yl)benzamide (6ga)



Rf 0.41 (hexane/EtOAc = 50/50). Yellow oil
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.02 (s, 6H), 2.32 (s, 3H), 2.80-2.85 (m, 4H), 2.90-2.94 (m, 4H), 6.95 (s, 2H), 7.41 (dd, *J* = 4, 8.4 Hz, 1H), 7.53-7.58 (m, 2H), 8.15 (dd, *J* = 1.2, 8 Hz, 1H), 8.71 (dd, *J* = 1.2, 4 Hz, 1H), 8.88 (dd, *J* = 2, 4.4 Hz, 1H), 9.93(brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 21.14, 27.38, 29.70, 45.43, 116.73, 121.61, 122.10, 127.20, 127.88, 128.06, 133.99, 134.84, 136.30, 137.80, 138.30, 139.23, 148.18, 168.46, 207.62.
IR (neat) 3348 w, 2951 w, 1713 m, 1670 m, 1518 s, 1482 m, 1324 m, 1160 m, 826 m.
HRMS Calcd for $C_{25}H_{26}N_2O_3$: 402.1943; Found: 402.1940.

methyl 3,5-bis(3-oxobutyl)-4-(quinolin-8-ylcarbamoyl)benzoate (6ha)



Rf 0.31 (hexane/EtOAc = 50/50). White solid. **MP** = 170 °C
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.04 (s, 6H), 2.85 (t, *J* = 8.4 Hz, 2H), 2.98 (t, *J* = 7.6 Hz, 2H), 3.92 (s, 3H), 7.44 (dd, *J* = 8, 4 Hz, 1H), 7.58 (d, *J* = 4.4 Hz, 2H), 7.82 (s, 2H), 8.17 (dd, *J* = 8.4, 1.6 Hz, 1H), 8.72 (dd, *J* = 4.4, 1.6 Hz, 1H), 8.86 ($quintet_{app}$, *J* = 4.4 Hz, 1H), 9.98(brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 27.25, 29.74, 45.03, 52.26, 117.07, 121.74, 122.51, 127.20, 127.94, 128.44, 130.91, 133.68, 136.41, 138.32, 138.42, 141.45, 148.35, 166.37, 167.35, 207.08.
IR (neat) 3342 w, 1712 m, 1669 m, 1519 s, 1481 m, 1424 m, 1323 m, 1263 m, 1219 s, 1132 m, 827 m.
HRMS Calcd for $C_{26}H_{26}N_2O_5$: 446.1842; Found: 446.1839;
Anal. Calcd for $C_{26}H_{26}N_2O_5$: C, 69.94; H, 5.87; N, 6.27. Found: C, 69.84; H, 5.86; N, 6.23.

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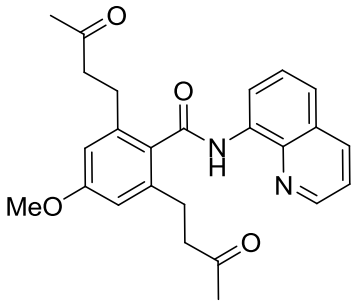
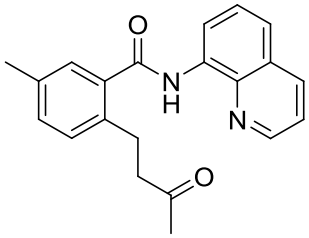
4-methoxy-2,6-bis(3-oxobutyl)-N-(quinolin-8-yl)benzamide (**6ia**)



Rf 0.32 (hexane/EtOAc = 50/50). Brown solid. **MP** = 110 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.01 (s, 6H), 2.83 (t, *J* = 9.6 Hz, 2H), 2.83 (t, *J* = 7.2 Hz, 2H), 2.93 (t, *J* = 9.2 Hz, 2H), 2.93 (t, *J* = 6.8 Hz, 2H), 3.79 (s, 3H), 6.67 (s, 2H), 7.41 (dd, *J* = 8.4, 4 Hz, 1H), 7.53 (d, *J* = 6.4 Hz, 1H), 7.56 (t, *J* = 8.4 Hz, 1H), 8.14 (dd, *J* = 8.4, 1.6 Hz, 1H), 8.71 (dd, *J* = 4.4, 1.6 Hz, 1H), 8.87 (dd, *J* = 6.8, 2.4 Hz, 1H), 9.92 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 27.63, 29.69, 45.27, 55.11, 112.65, 116.65, 121.60, 122.05, 127.18, 127.85, 130.44, 134.01, 136.28, 138.26, 139.76, 148.16, 159.88, 168.25, 207.44.
IR (neat) 3345 w, 1669 m, 1601 m, 1517 s, 1323 m, 1157 m, 824 m.
MS *m/z* (relative intensity, %) 418 (M^+, 17), 276 (17), 275 (100), 231 (23), 43 (13).
HRMS Calcd for $C_{25}H_{26}N_2O_4$: 418.1893; Found: 418.1898.

5-methyl-2-(3-oxobutyl)-N-(quinolin-8-yl)benzamide (**3ja**)

See also part X for the cleavage of the 8-aminoquinoline moiety.



Rf 0.31 (hexane/EtOAc = 80/20). Yellow oil.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.10 (s, 3H), 2.40 (s, 3H), 2.89 (t, *J* = 7.6 Hz, 2H), 3.10 (t, *J* = 8 Hz, 2H), 7.23 (s, 2H), 7.45-7.48 (m, 2H), 7.56 (dd, *J* = 4.4, 2 Hz, 1H), 7.59 (t, J = 8.4 Hz, 1H), 8.19 (dd, *J* = 8.4, 1.6 Hz, 1H), 8.78 (dd, *J* = 4, 1.6 Hz, 1H), 8.90 (d, *J* = 6.8 Hz, 1H), 10.18 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 20.96, 27.39, 29.90, 45.77, 116.58, 121.65, 121.86, 127.35, 127.75, 127.96, 130.67, 131.23, 134.58, 136.20, 136.35, 136.41, 136.89, 138.47, 148.22, 168.21, 208.25.
IR (neat) 3351 w, 2923 w, 1713 m, 1672 m, 1521 s, 1482 m, 1424 m, 1385 m, 1326 m, 826 m.
HRMS Calcd for $C_{21}H_{20}N_2O_2$: 332.1525; Found: 332.1522.

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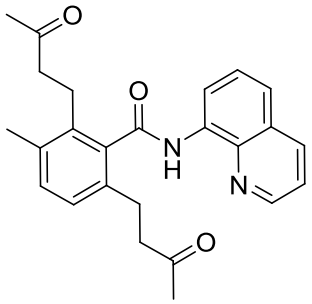
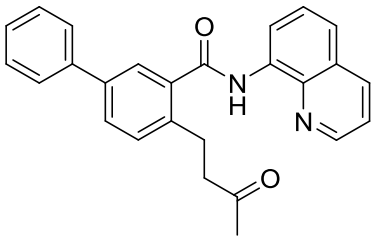
3-methyl-2,6-bis(3-oxobutyl)-N-(quinolin-8-yl)benzamide (6ja)



Rf 0.41 (hexane/EtOAc = 50/50). Yellow oil.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.02 (s, 6H), 2.31 (s, 3H), 2.80-2.83 (m, 4H), 2.90-2.94 (m, 4H), 7.07 (d, *J* = 7.6 Hz, 1H), 7.17 (d, *J* = 8.0 Hz, 1H), 7.44 (dd, *J* = 8, 4.4 Hz, 1H), 7.56 (d, *J* = 6 Hz, 1H), 7.59 (t, *J* = 8.4 Hz, 1H), 8.18 (dd, *J* = 8.4, 1.6 Hz, 1H), 8.72 (dd, *J* = 4.4, 2.0 Hz, 1H), 8.88 (dd, *J* = 6.4, 2.4 Hz, 1H), 9.91 (brs, 1H)
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 19.09, 24.91, 27.28, 29.64, 29.82, 44.18, 45.49, 116.97, 121.68, 122.23, 127.36, 127.99, 131.38, 133.98, 134.62, 135.33, 135.82, 136.47, 138.16, 138.34, 148.21, 168.75, 207.78 (two overlapping peaks)
IR (neat) 3345 w, 2955 w, 1714 m, 1672 m, 1520 s, 1482 m, 1424 m, 1385 m, 1326 m, 1270 w, 116 w, 827 m.
HRMS Calcd for $C_{25}H_{26}N_2O_3$: 402.1943; Found: 402.1946.

4-(3-oxobutyl)-N-(quinolin-8-yl)biphenyl-3-carboxamide (3ka)



Rf 0.28 (hexane/EtOAc = 80/20). White solid. **MP** = 100 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.14 (s, 3H), 2.96 (t, *J* = 7.6 Hz, 2H), 3.17 (t, *J* = 7.6 Hz, 2H), 7.35-7.48 (m, 5H), 7.57-7.65 (m, 5H), 7.88 (s, 1H), 8.20 (d, *J* = 8.4 Hz, 1H), 8.77 (d, *J* = 4.0 Hz, 1H), 8.93 (d, *J* = 7.20 Hz, 1H), 10.28 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 27.30, 29.76, 45.41, 116.43, 121.56, 121.87, 125.61, 126.82, 127.13, 127.44, 127.78, 128.74, 128.88, 131.13, 134.38, 136.21, 136.90, 138.30, 138.85, 139.30, 139.74, 148.17, 167.80, 207.75
IR (KBr) 3345 w, 3016 w, 1738 m, 1716 m, 1669 m, 1519 m, 1480 m, 1219 s.
HRMS Calcd for $C_{26}H_{22}N_2O_2$: 394.1681; Found: 394.1676
Anal. Calcd for $C_{26}H_{22}N_2O_2$: C, 79.16; H, 5.62; N, 7.10. Found: C, 78.90; H, 5.53; N, 7.04.

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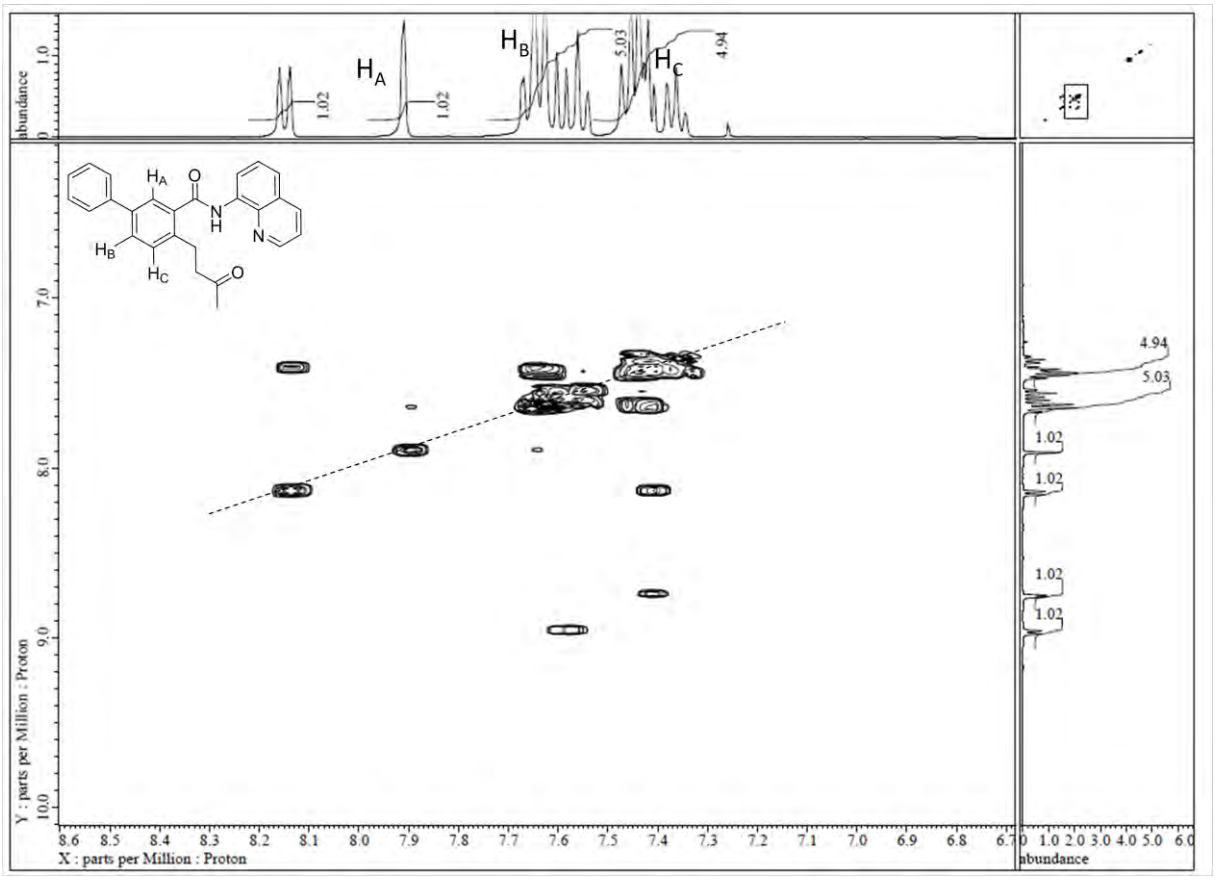
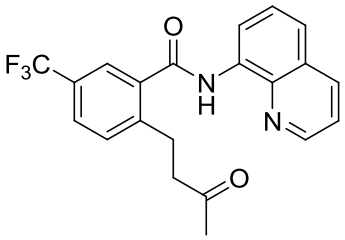
COSY



2-(3-oxobutyl)-N-(quinolin-8-yl)-5-(trifluoromethyl)benzamide (3la)



Rf 0.28 (hexane/EtOAc = 80/20). White solid. **MP** = 130 °C.

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.11 (s, 3H), 2.93 (t, *J* = 7.2 Hz, 2H), 3.17 (t, *J* = 7.6 Hz, 2H), 7.46 (dd, *J* = 8.4, 4 Hz, 1H), 7.48 (d, *J* = 7.2 Hz, 1H), 7.56-7.61(m, 2H), 7.66 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.89 (s, 1H), 8.18 (dd, *J* = 8.4, 1.6 Hz, 1H), 8.78 (dd, *J* = 4.4, 1.6 Hz, 1H), 8.87 (dd, *J* = 6, 2.8 Hz, 1H), 10.22 (brs, 1H)

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 27.51, 29.82, 45.00, 116.79, 121.77, 122.34, 123.71 (q, *J* = 272.2 Hz), 124.07 (q, *J* = 2.8 Hz), 127.00 (q, *J* = 2.8 Hz), 127.20, 127.92, 128.83 (q, *J* = 32.5 Hz), 131.34, 134.11, 136.41, 137.14, 138.37, 144.13, 148.39, 166.55, 207.22

IR (neat) 3339 w, 3058 w, 1715 m, 1675 m, 1523 s, 1484 m, 1326 m, 1168 m, 1125 s, 1080 m, 826 m.

HRMS Calcd for $C_{21}H_{17}F_3N_2O_2$: 386.1242; Found: 386.1242

Anal. Calcd for $C_{21}H_{17}F_3N_2O_2$: C, 65.28; H, 4.43; N, 7.25. Found: C, 65.14; H, 4.38; N, 7.25.

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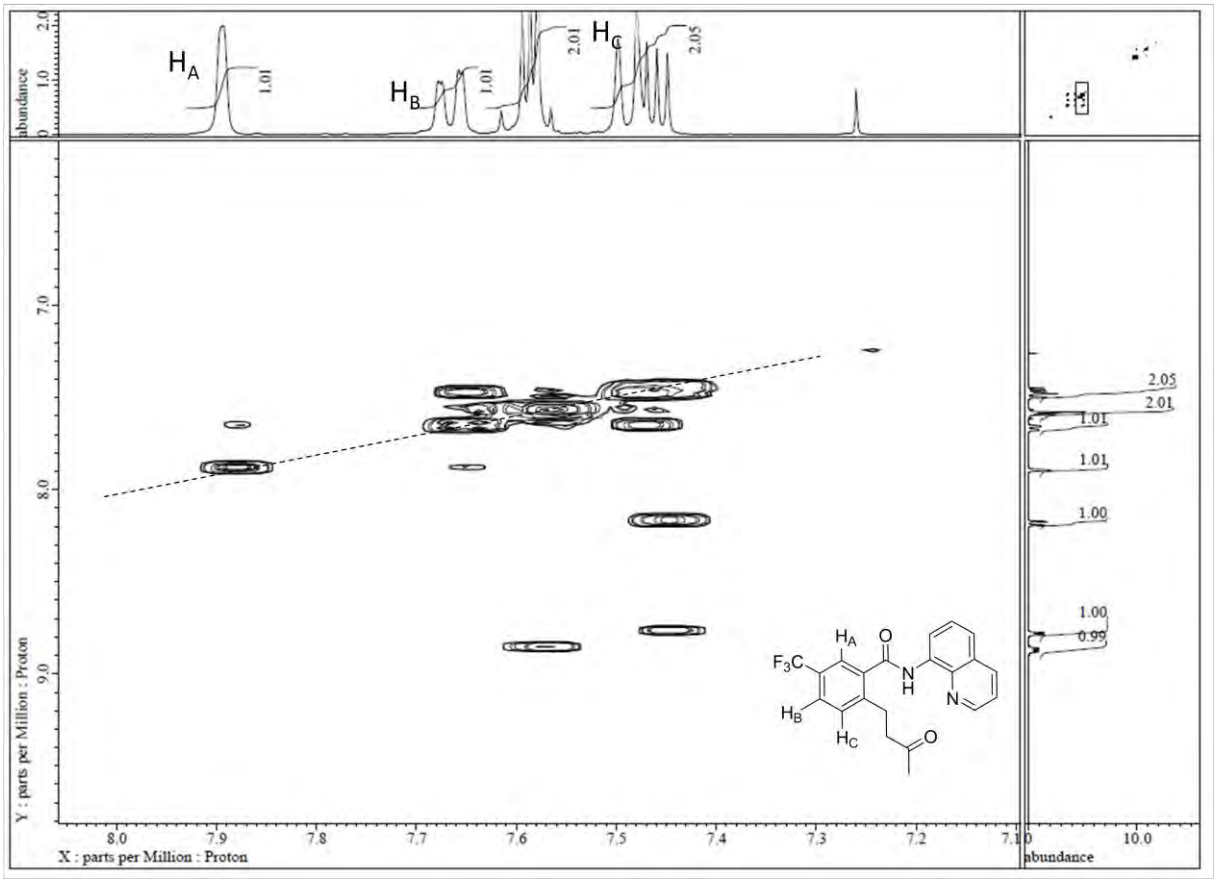
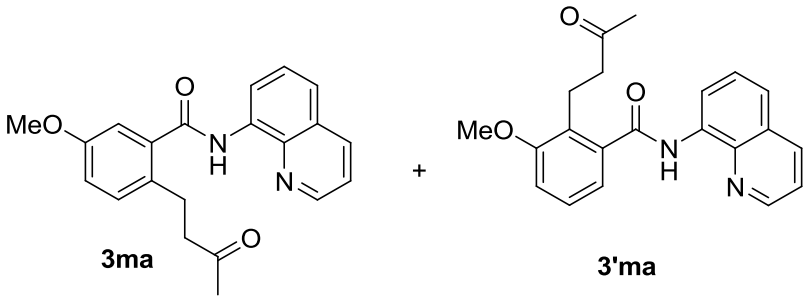


5-methoxy-2-(3-oxobutyl)-N-(quinolin-8-yl)benzamide (3ma), 3-methoxy-2-(3-oxobutyl)-N-(quinolin-8-yl)benzamide (3'ma).



mixture 3/1 : **3ma/3'ma**

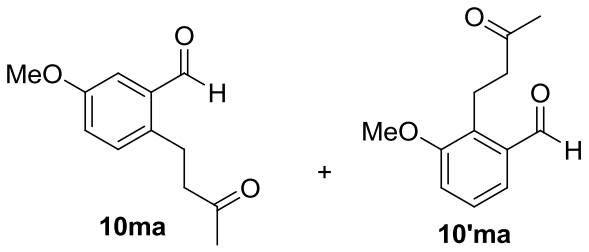
Rf 0.18 (hexane/EtOAc = 80/20). Yellow oil.

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.09 (s, 3H$_{ma}$), 2.13 (s, 1H'ma), 2.88 (t, *J* = 7.6 Hz, 2H$_{ma}$+0.7H'ma), 3.07 (t, *J* = 7.6 Hz, 2H$_{ma}$+0.7H'ma), 3.84 (s, 3H$_{ma}$), 3.86 (s, 1H'ma), 6.96 (dd, *J* = 8.4, 2.4 Hz, 1H$_{ma}$+0.3H'ma), 7.19 (d, *J* = 2.4 Hz, 1H$_{ma}$), 7.23-7.26 (m, 1H$_{ma}$+0.7H'ma), 7.31 (t, *J* = 8 Hz, 0.3H'ma), 7.45 (dd, *J* = 4.4, 8.4 Hz, 1H$_{ma}$+0.3H'ma), 7.52-7.61 (m, 2H$_{ma}$+0.7H'$_{ma}$), 8.17 (dd, *J* = 8.4, 1.6 Hz, 1H$_{ma}$+0.3H'ma), 8.77 (dd, *J* = 4.4, 2 Hz, 1H$_{ma}$+0.3H'ma), 8.89 (dd, *J* = 7.6, 2 Hz, 1Hma+0.3H'ma), 10.19 (brs, 1H$_{ma}$), 10.14 (brs, 1H'ma).

^{13}C NMR 3ma ($CDCl_3$, 100.53 MHz) δ 26.93, 28.85, 45.76, 55.40, 112.77, 115.86, 116.49, 121.64, 121.89, 127.23, 127.90, 131.69, 131.83, 134.46, 136.28, 137.27, 138.45, 148.24, 157.85, 167.69, 208.14.
^{13}C NMR 3'ma ($CDCl_3$, 100.53 MHz) δ 21.97, 29.58, 43.99, 55.52, 111.97, 118.93, 121.57, 121.80, 127.40, 128.16, 134.51, 138.25, 138.42, 148.14, 157.93, 167.81, 208.62, four peaks overlapped with A.
IR (neat) 3346 w, 2937 w, 1712 m, 1672 m, 1521 s, 1483 m, 1385 m, 1326 m, 1263 m, 1041 m, 826 m.
MS 3ma *m/z* (relative intensity, %) 348 (M^+, 26), 306 (12), 305 (54), 205 (19), 162 (17), 161 (100), 145 (12), 144 (15), 43 (11).
MS 3'ma *m/z* (relative intensity, %) 348 (M^+, 32), 306 (13), 305 (54), 290 (11), 205 (37), 163 (16), 162 (35), 161 (100), 145 (21), 144 (31), 43 (18).
HRMS 3ma Calcd for $C_{21}H_{20}N_2O_3$: 348.1474; Found: 348.1478.
HRMS 3'ma Calcd for $C_{21}H_{20}N_2O_3$: 348.1474; Found: 348.1468.

5-methoxy-2-(3-oxobutyl)benzaldehyde (10ma), 3-methoxy-2-(3-oxobutyl)benzaldehyde (10'ma)

8-aminoquinoline directing group was cleaved from the mixture **3ma**+**3'ma** to make the interpretation of the spectrum easier (see part X for a procedure) in order to have confirmation of the major regioisomer.



mixture 3/1 : **10ma**/**10'ma**

Rf 0.28 (hexane/EtOAc = 80/20). Yellow oil.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.12 (s, $3H_{ma}$), 2.16 (s, $1H'_{ma}$), 2.66 (t, *J* = 7.2 Hz, 0.7H'ma), 2.73 (t, *J* = 7.6 Hz, 2Hma), 3.2 (t, *J* = 7.2 Hz, $2H_{ma}$), 3.29 (t, *J* = 7.6 Hz, 0.7H'ma), 3.83 (s, $3H_{ma}$), 3.85 (s, 1H'ma), 7.05 (dd, *J* = 8, 2.8 Hz, $1H_{ma}$), 7.08 (d, *J* = 8 Hz, 0.33H'ma), 7.08 (d, *J* = 8 Hz, $1H_{ma}$), 7.31 (d, *J* = 2.8 Hz, 1Hma), 7.34 (t, *J* = 8 Hz, 0.33H'ma), 7.41 (d, *J* = 7.6 Hz, 0.33H'ma), 10.18 (s, $1H_{ma}$), 10.24 (s, 0.33H'ma).
^{13}C NMR 10ma ($CDCl_3$, 100.53 MHz) δ 25.83, 29.95, 45.31, 55.48, 116.28, 120.40, 132.46, 134.37, 135.73, 158.36, 192.15, 207.66.
^{13}C NMR 10'ma ($CDCl_3$, 100.53 MHz) δ 19.10, 29.68, 43.51, 55.77, 115.38, 124.10, 127.34, 131.96, 134.87, 157.81, 192.71, 208.23.
IR (neat) 2934 w, 1686 s, 1498 m, 1261 s, 1162 s, 1037 m, 871 w, 825 w.
MS 10ma *m/z* (relative intensity, %) 206 (M^+, 21), 188 (100), 163 (36), 149 (21), 148 (25), 145 (51), 121 (72), 105 (19), 91 (24), 77 (18), 43 (34).
MS 10'ma *m/z* (relative intensity, %) 206 (M^+, 11), 188 (100), 163 (30), 149 (17), 148 (42), 145 (44), 135 (25), 120 (28), 105 (22), 91 (50), 77 (24), 43 (33).
HRMS 10ma Calcd for $C_{12}H_{14}O_3$: 206.0943; Found: 206.0945.
HRMS 10'ma Calcd for $C_{12}H_{14}O_3$: 206.0943; Found: 206.0949.

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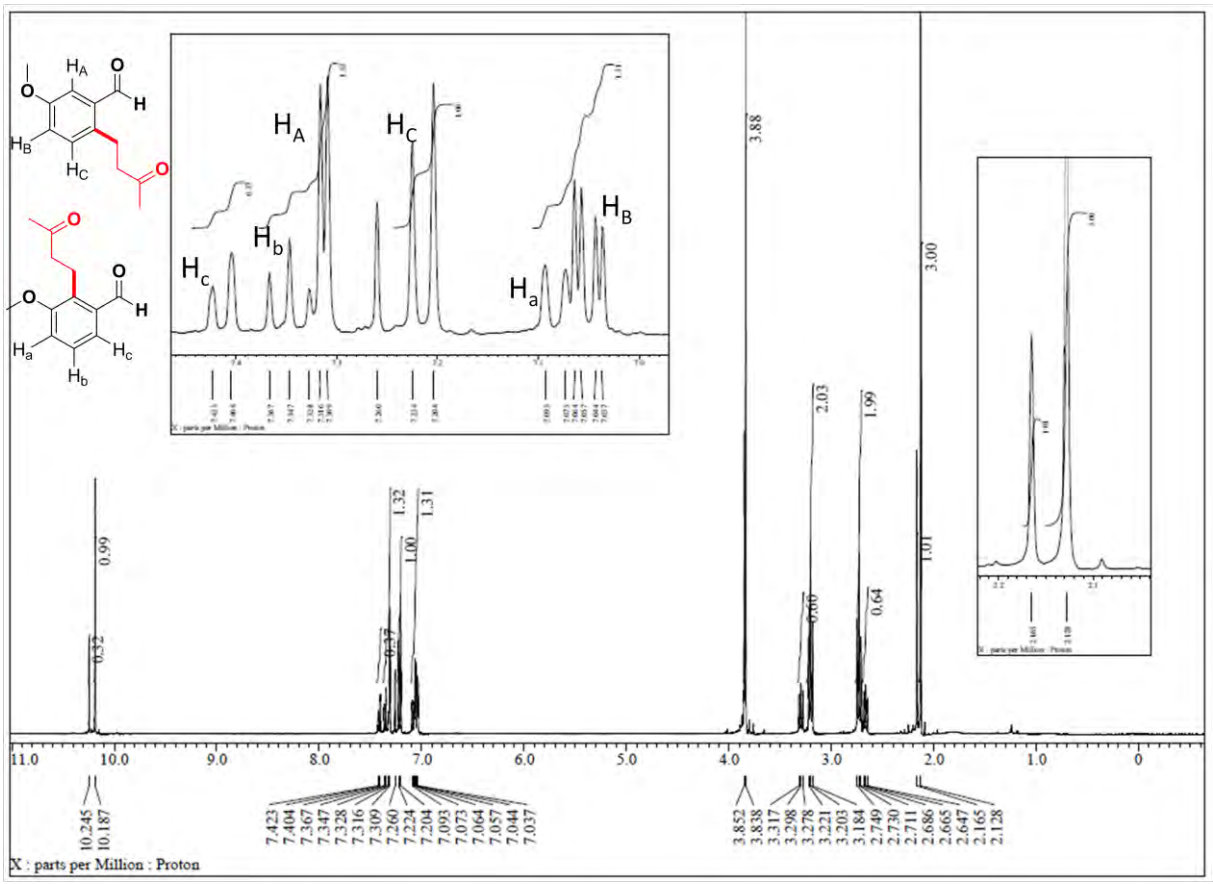
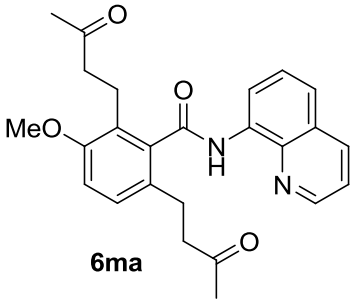


3-methoxy-2,6-bis(3-oxobutyl)-N-(quinolin-8-yl)benzamide (6ma)



6ma

Rf 0.18 (hexane/EtOAc = 60/40). Yellow oil
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.01 (s, 3H), 2.01 (s, 3H), 2.76-2.82 (m, 4H), 2.87-2.91 (m, 4H), 3.81 (s, 3H), 6.85 (d, *J* = 8.4 Hz, 1H), 7.12 (d, *J* = 8.8 Hz, 1H), 7.42 (dd, *J* = 8.4, 4.4 Hz, 1H), 7.54 (d, *J* = 5.6 Hz, 1H), 7.57 (t, *J* = 8 Hz, 1H), 8.16 (dd, *J* = 8.4, 1.6 Hz, 1H), 8.71 (dd, *J* = 4.4, 1.6 Hz, 1H), 8.87 (dd, *J* = 6.4, 2.8 Hz, 1H), 9.91 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 22.43, 26.85, 29.49, 29.80, 43.87, 45.58, 55.44, 111.09, 116.89, 121.63, 122.19, 126.08, 127.25, 127.92, 128.40, 129.24, 133.91, 136.39, 138.29, 138.70, 148.17, 155.89, 167.89, 207.94, 208.30.
IR (neat) 3351 w, 1711 m, 1671 m, 11669m, 1519 s, 1480 m, 1323 m, 1271 m, 1092 w.
HRMS Calcd for $C_{25}H_{26}N_2O_4$: 418.1893; Found: 418.1896.

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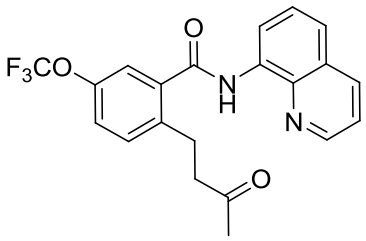
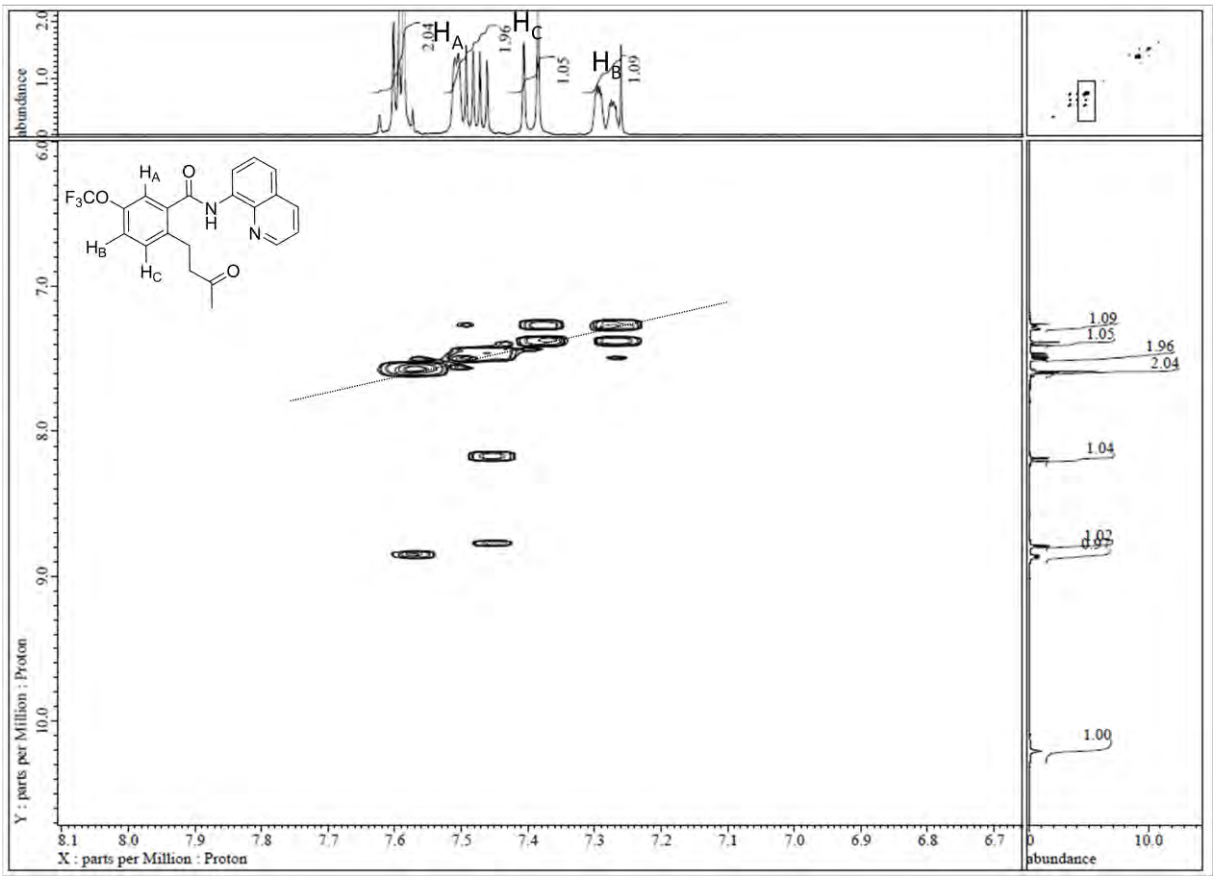
2-(3-oxobutyl)-N-(quinolin-8-yl)-5-(trifluoromethoxy)benzamide (3na)



Rf 0.28 (hexane/EtOAc = 80/20). White solid. **MP** = 108 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.11 (s, 3H), 2.91 (t, *J* = 7.6 Hz, 2H), 3.12 (t, *J* = 7.2 Hz, 2H), 7.27-7.29 (m, 1H), 7.39 (d, *J* = 8.4 Hz, 1H), 7.47 (dd, *J* = 8, 4 Hz, 1H), 7.50 (d, *J* = 2.4 Hz, 1H), 7.57-7.59 (m, 2H), 8.19 (dd, *J* = 8.4, 2 Hz, 1H), 8.79 (dd, *J* = 4, 1.2 Hz, 1H), 8.86 (dd, *J* = 6.0, 2.4 Hz, 1H), 10.20 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 27.07, 29.86, 45.31, 116.72, 119.90, 120.39 (q, *J* = 258 Hz), 121.79, 122.29, 122.77, 127.25, 127.95, 132.38, 134.19, 136.41, 137.92, 138.45, 138.79, 147.34 (d, *J* = 2 Hz), 148.42, 166.35, 207.51.
IR (neat) 3348 w, 1721 m, 1671 m, 1524 m, 1277 m, 1257 m, 1221 s, 1108 m, 999 m.
HRMS Calcd for $C_{21}H_{17}F_3N_2O_3$: 402.1191; Found: 402.1192.

COSY



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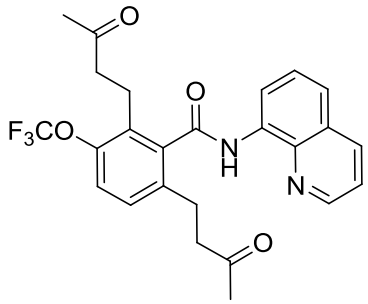
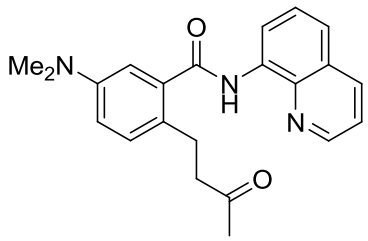
2,6-bis(3-oxobutyl)-N-(quinolin-8-yl)-3-(trifluoromethoxy)benzamide (6na)



Rf 0.48 (hexane/EtOAc = 50/50); Yellow oil
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.04 (s, 3H), 2.05 (s, 3H), 2.80-2.86 (m, 4H), 2.95-2.98 (m, 4H), 7.20-7.27 (m, 2H), 7.48 (dd, *J* = 8.0, 4.0 Hz, 1H), 7.61 (d, *J* = 4.4 Hz, 2H), 8.22 (d, *J* = 8.0 Hz, 1H), 8.76 (d, *J* = 3.2 Hz, 1H), 8.86 ($quintet_{app}$, *J* = 4.4 Hz, 1H), 9.99 (brs, 1H)
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 22.28, 27.03, 29.58, 29.87, 43.84, 45.14, 120.13 (q, *J* = 177 Hz), 120.93, 120.95, 121.80, 122.69, 127.44, 128.10, 129.00, 130.53, 133.61, 136.50, 136.81, 138.21, 139.63, 146.27 (d, *J* = 2 Hz), 148.26, 166.74, 207.02, 207.27
IR (neat) 3342 w, 2956 w, 1715 m, 1674 m, 1523 s, 1484 m, 1326 m, 1255 s, 1211 m, 1163 m, 827 m.
HRMS Calcd for $C_{25}H_{23}F_3N_2O_4$: 472.1610; Found: 472.1606.

5-(dimethylamino)-2-(3-oxobutyl)-N-(quinolin-8-yl)benzamide (3oa)



Rf 0.25 (hexane/EtOAc = 70/30). Brown solid. **Mp** = 112 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.09 (s, 3H), 2.86 (t, *J* = 7.2 Hz, 2H), 2.96 (s, 3H), 3.04 (t, *J* = 5.2 Hz, 1H), 6.79 (dd, *J* = 8.4, 2.8 Hz, 1H), 6.99 (d, *J* = 2.8 Hz, 1H), 7.18 (d, *J* = 8.4 Hz, 1H), 7.43 (dd, *J* = 8, 4 Hz, 1H), 7.53 (dd, *J* = 8, 1.2 Hz, 1H), 7.58 (t, *J* = 8 Hz, 1H), 8.15 (dd, *J* = 8.8, 1.6 Hz, 1H), 8.75 (dd, *J* = 4, 1.2 Hz, 1H), 8.91 (dd, *J* = 7.2, 0.8 Hz, 1H), 10.21 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 26.79, 29.85, 40.52, 45.95, 111.02, 114.50, 116.34, 121.56, 121.68, 126.87, 127.21, 127.85, 131.30, 134.60, 136.22, 137.01, 138.43, 148.15, 148.87, 168.63, 208.51.
IR (neat) 3345 w, 2924 w, 1711 m, 1672 m, 1608 m, 1519 s, 1481 s, 1325 m, 1220 m, 826 m.
MS *m/z* (relative intensity, %) 361 (M^+, 49), 218 (13), 217 (16), 189 (17), 175 (14), 174 (100), 146 (11).
HRMS Calcd for $C_{22}H_{23}N_3O_2$: 361.1790; Found: 361.1791.

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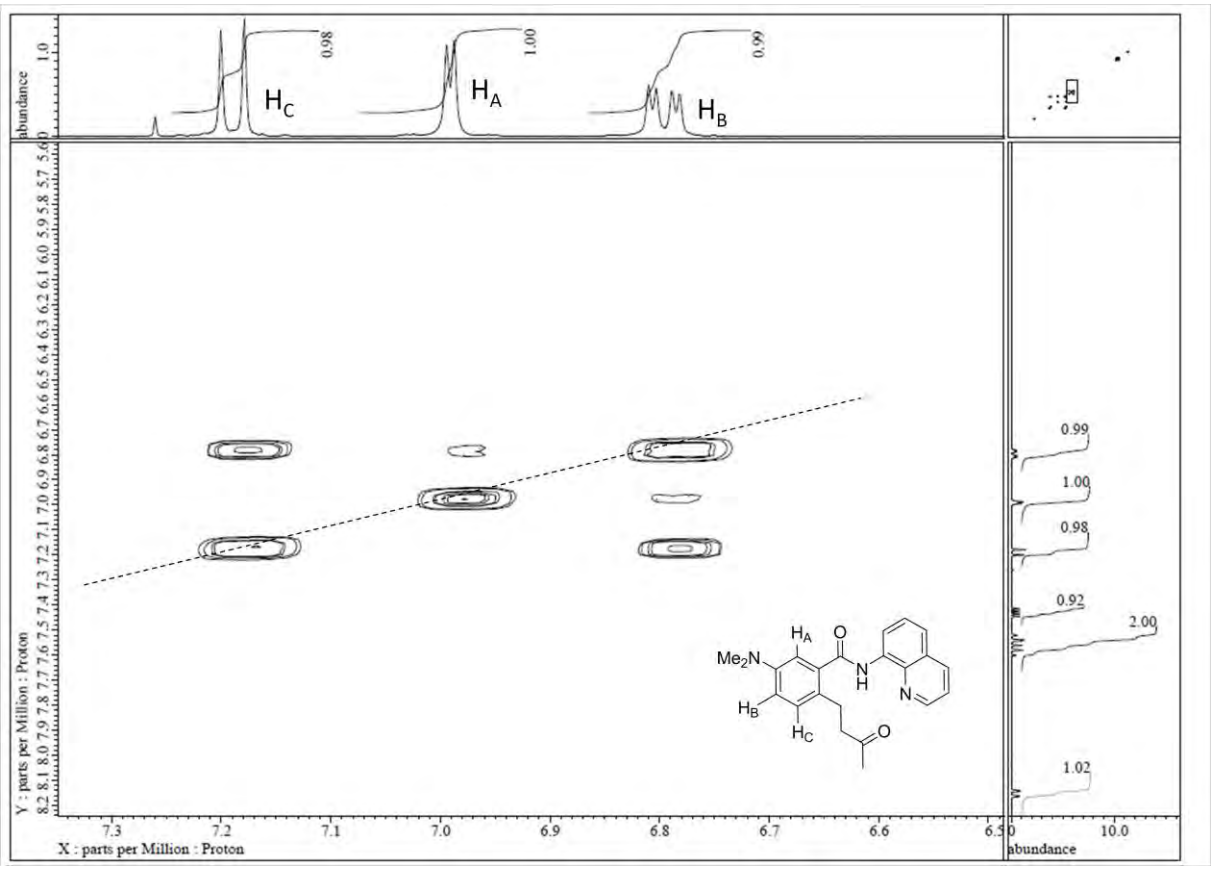
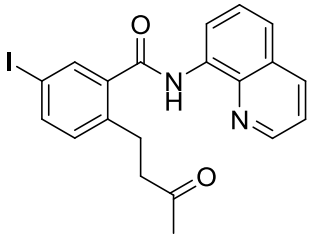
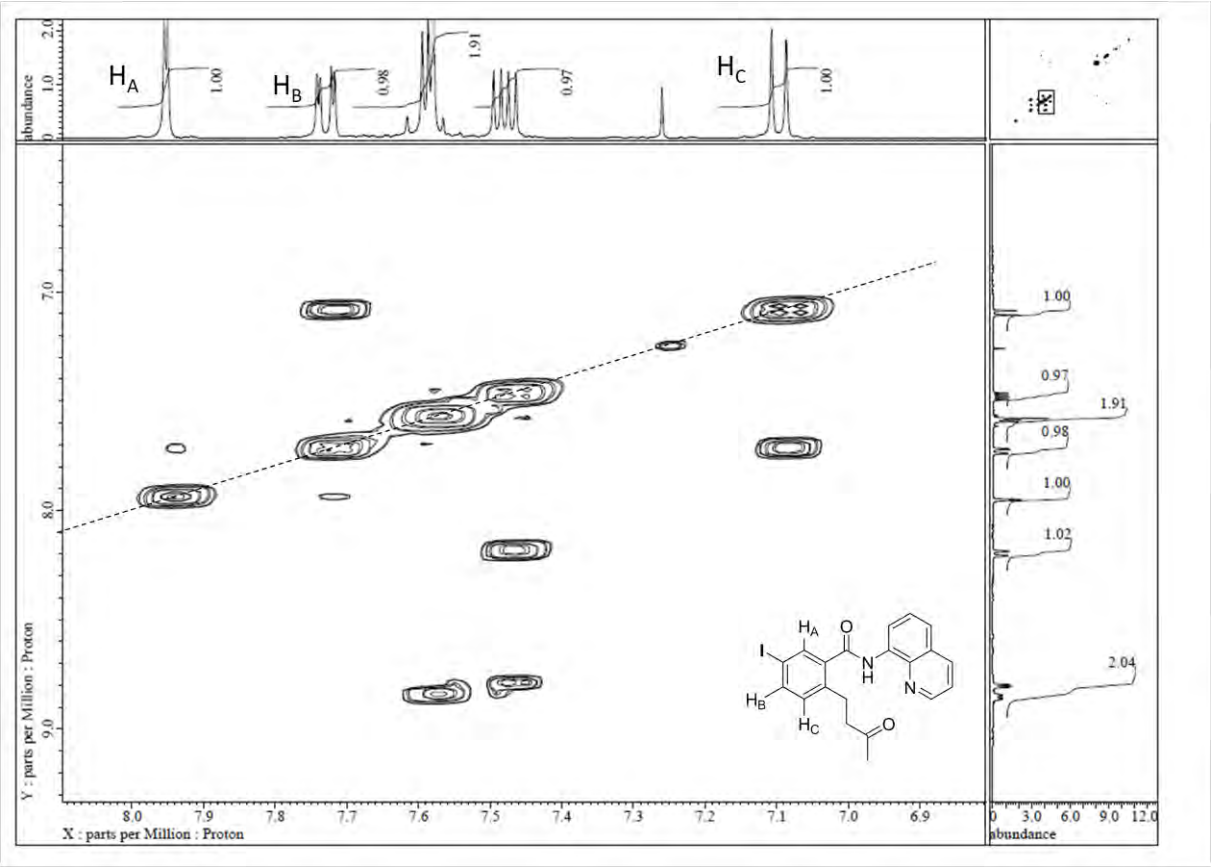


5-iodo-2-(3-oxobutyl)-N-(quinolin-8-yl)benzamide (3pa)

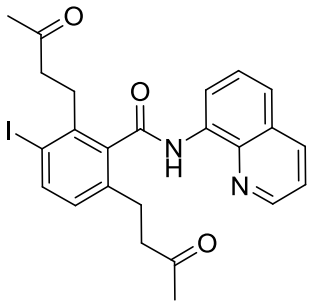


Rf 0.37(hexane/EtOAc = 70/30). White solid. **Mp** = 131°C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.10 (s, 3H), 2.88 (t, *J* = 7.6 Hz, 2H), 3.05 (t, *J* = 7.6 Hz, 1H), 7.09 (d, *J* = 8 Hz, 1H), 7.47 (dd, *J* = 8.4, 4 Hz, 1H), 7.58 (s_{app}, 1H), 7.59 (d_{app}, *J* = 3.2 Hz, 1H), 7.72 (dd, *J* = 8, 2 Hz, 1H), 7.95 (d, *J* = 1.6 Hz, 1H), 8.19 (dd, *J* = 8.4, 1.6 Hz, 1H), 8.80 (dd, *J* = 4, 1.6 Hz, 1H), 8.85 (dd, *J* = 6.4, 2.8 Hz, 1H), 10.16 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 27.27, 29.90, 45.23, 91.09, 116.84, 121.75, 122.24, 127.30, 127.95, 132.64, 134.18, 135.73, 136.52, 138.32, 138.60, 139.35, 139.61, 148.30, 166.26, 207.55.
IR (neat) 3332 w, 1711 w, 1671 m, 1520 s, 1483 m, 1325 m, 1165 w, 1042 w, 815 m.
MS *m/z* (relative intensity, %) 444 (M^+, 37), 401 (100), 301 (13), 257 (69), 144 (19), 102 (14), 43 (16)
HRMS Calcd for $C_{20}H_{17}IN_2O_2$: 444.0335; Found: 444.0337.

COSY



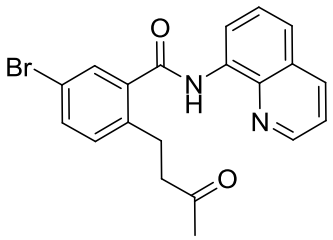
3-iodo-2,6-bis(3-oxobutyl)-N-(quinolin-8-yl)benzamide (6pa)



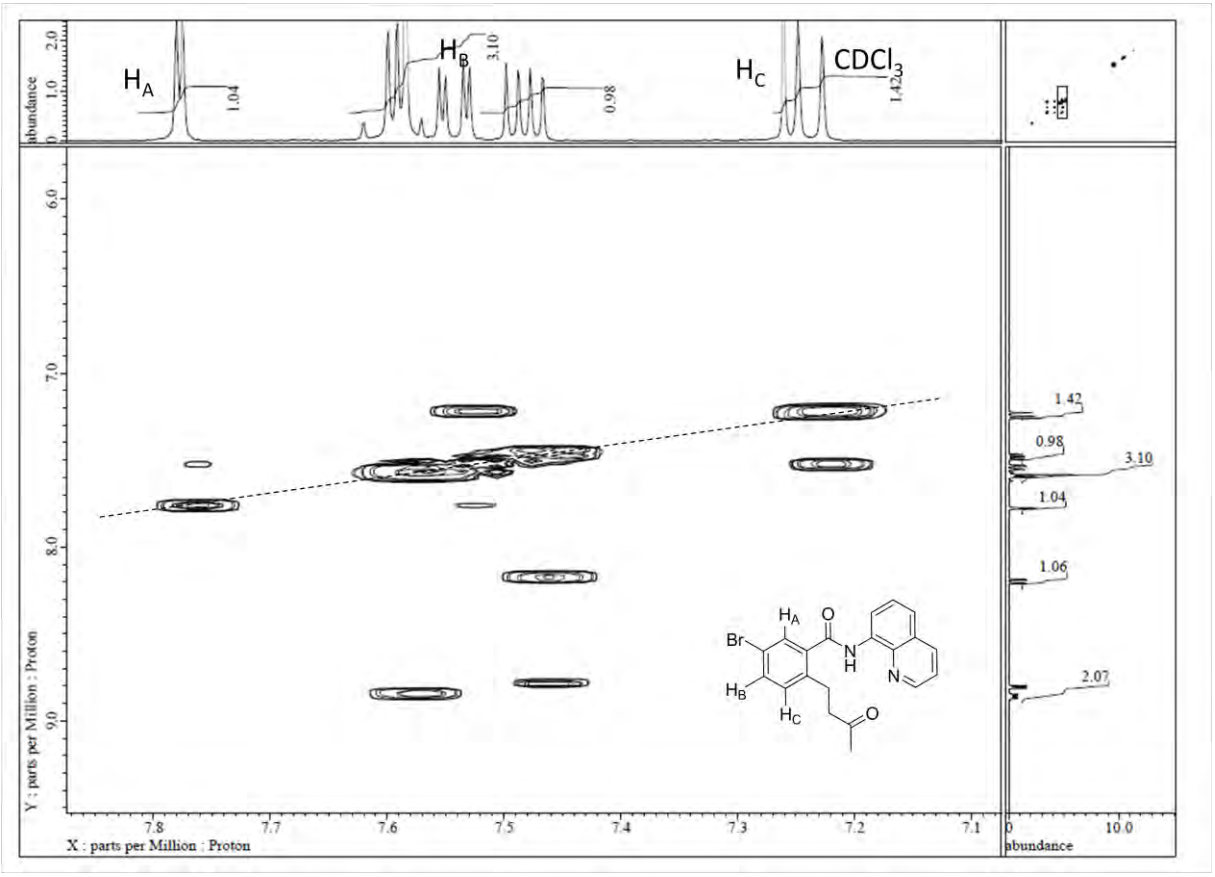
Rf 0.31(hexane/EtOAc = 60/40). Yellow oil.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.03 (s, 3H), 2.05 (s, 3H), 2.81-3.06 (m, 8H), 6.88 (d, *J* = 8.4 Hz, 1H), 7.45 (dd, *J* = 8.4, 4 Hz, 1H), 7.58 (d, *J* = 4.8 Hz, 2H), 7.82 (d, *J* = 8.4 Hz, 1H), 8.18 (dd, *J* = 8, 1.2 Hz, 1H), 8.73 (dd, *J* = 4.4, 1.6 Hz, 1H), 8.83 ($quintet_{app}$, *J* = 4.8 Hz, 1H), 9.91 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 27.05, 29.59, 29.81, 32.65, 43.63, 44.99, 98.45, 117.08, 121.76, 122.51, 127.27, 127.96, 129.37, 133.66, 136.47, 138.31 (two overlapping peaks), 138.67, 139.85, 140.51, 148.31, 167.15, 206.99, 207.17.
IR (neat) 3348 w, 1711 m, 1670 m, 1519 s, 1482 m, 1424 w, 1325 m, 1221 m, 1072 w, 893 w, 821 w.

MS *m/z* (relative intensity, %) 514 (M^+, 12), 471 (43), 456 (14), 371 (10), 327 (25), 200 (28), 182 (12), 157 (11), 144 (52), 116 (13), 43 (100).
HRMS Calcd for $C_{24}H_{23}IN_2O_3$: 514.0753; Found: 514.0759.

5-bromo-2-(3-oxobutyl)-N-(quinolin-8-yl)benzamide (3qa)



Rf 0.25 (hexane/EtOAc = 80/20). White solid. **MP** = 120 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.11 (s, 3H), 2.89 (t, *J* = 7.6 Hz, 2H), 3.07 (t, *J* = 7.6 Hz, 2H), 7.23 (d, *J* = 8.0 Hz, 1H), 7.48 (dd, *J* = 8.0, 4.0 Hz, 1H), 7.54 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.58 (s_{app}, 1H), 7.59 (d_{app}, *J* = 3.2 Hz, 1H), 7.77 (d, *J* = 2.4 Hz, 1H), 8.19 (dd, *J* = 8.4, 1.6 Hz, 1H), 8.80 (dd, *J* = 4.4, 2.0 Hz, 1H), 8.85 (dd, *J* = 6.0, 2.8 Hz, 1H), 10.16 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 27.19, 29.90, 45.25, 116.69, 119.98, 121.78, 122.23, 127.25, 127.93, 129.97, 132.52, 133.40, 134.24, 136.39, 138.29, 138.45, 139.03, 148.40, 166.38, 207.61.
IR (neat) 3339 w, 1715 m, 1671 m, 1521 s, 1476 m, 1325 m, 823 m, 774 m.
HRMS Calcd for $C_{20}H_{17}BrN_2O_2$: 396.0473; Found: 396.0471
Anal. Calcd for $C_{20}H_{17}BrN_2O_2$: C, 60.47; H, 4.31; N, 7.05. Found: C, 60.36; H, 4.17; N, 7.09.
COSY



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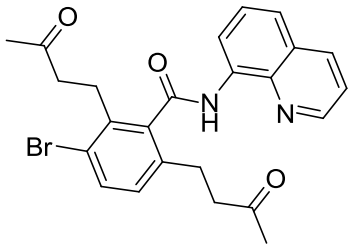
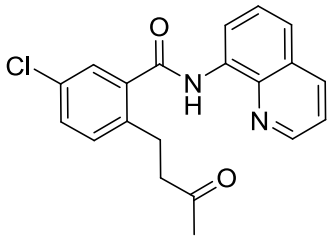
3-bromo-2,6-bis(3-oxobutyl)-N-(quinolin-8-yl)benzamide (6qa)



Rf 0.31(hexane/EtOAc = 60/40); Yellow oil
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.02 (s, 6H), 2.31 (s, 3H), 2.80-2.83 (m, 4H), 2.90-2.94 (m, 4H), 7.07 (d, *J* = 8.0 Hz, 1H), 7.17 (d, *J* = 8.0 Hz, 1H), 7.44 (dd, *J* = 4.0, 8.4 Hz, 1H), 7.57-7.59 (m, 2H), 8.18 (dd, *J* = 1.6, 8.0 Hz, 1H), 8.72 (dd, *J* = 2.0, 4.4 Hz, 1H), 8.88 (dd, *J* = 2.4, 6.4 Hz, 1H), 9.91(brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 19.09, 24.91, 27.28, 29.64, 28.92, 44.18, 45.50, 116.98, 121.69, 122.24, 127.35, 127.37, 127.99, 131.39, 133.99, 134.63, 135.34, 135.83, 136.48, 138.17, 138.34, 148.21, 168.75, 207.79.
IR (neat) 3339 w, 2961 w, 1714 m, 1667 m, 1597 m, 1520 s, 1483 s, 1423 m, 1325 m, 1241 m, 1170 m, 897 m.
HRMS Calcd for $C_{24}H_{23}BrN_2O_3$: 466.0892; Found: 466.0893.

5-chloro-2-(3-oxobutyl)-N-(quinolin-8-yl)benzamide (3ra)



Rf 0.42 (hexane/EtOAc = 70/30). White solid. **MP** = 60 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.10 (s, 3H), 2.89 (t, *J* = 7.6 Hz, 1H), 3.08 (t, *J* = 7.6 Hz, 1H), 7.28 (d, *J* = 8.4 Hz, 1H), 7.38 (dd, *J* = 8, 1.6 Hz, 2H), 7.46 (dd, *J* = 8.8.4.8 Hz, 1H), 7.57 (s_{app}, 1H), 7.58 (d_{app}, *J* = 4.4 Hz, 1H), 7.62 (d, *J* = 2.4 Hz, 1H), 8.18 (dd, *J* = 8, 1.2 Hz, 1H), 8.73 (dd, *J* = 4.4, 1.6 Hz, 1H), 8.83 (t_{app}, *J* = 4.8 Hz, 1H), 8.18 (dd, *J* = 8.4, 2 Hz, 1H), 8.79 (dd, *J* = 4.4, 2 Hz, 1H), 8.85 (dd, *J* = 6.4, 2.8 Hz, 1H), 10.17 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 27.11, 29.89, 45.32, 116.67, 121.75, 122.20, 127.12, 127.23, 127.91, 130.43, 132.11, 132.23, 134.20, 136.40, 137.88, 138.39, 138.52, 148.35, 166.49, 207.62.
MS *m/z* (relative intensity, %) 352 (M^+, 30), 309 (100), 311 (33), 291 (12), 209 (11), 165 (86), 144 (25), 43 (26).
IR (neat) 3341 w, 3055 w, 1713 m, 1673 m, 1522 s, 1481 m, 1326 m, 1162 w, 914 w, 825 m.
HRMS Calcd for $C_{20}H_{17}ClN_2O_2$: 352.0979; Found: 352.0979.

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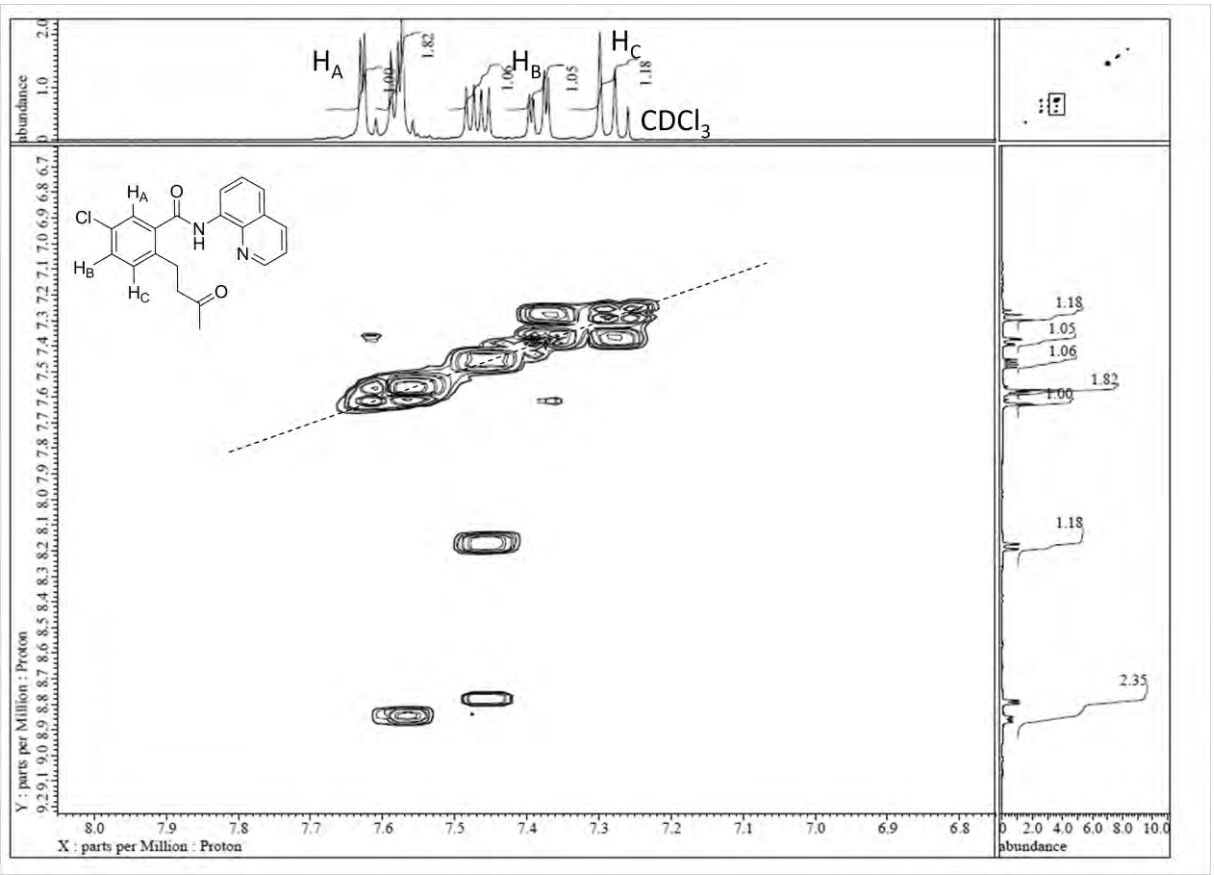
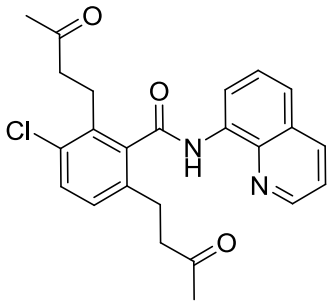


3-chloro-2,6-bis(3-oxobutyl)-N-(quinolin-8-yl)benzamide (**6ra**)



Rf 0.47 (hexane/EtOAc = 50/50). Yellow oil.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.03 (s, 3H), 2.04 (s, 3H), 2.80-3.03 (m, 8H), 7.12 (d, J = 8 Hz, 1H), 7.36 (d, J = 8.4 Hz, 1H), 7.45 (dd, J = 8.4, 4 Hz, 1H), 7.58 (d, J = 4.4 Hz, 2H), 8.18 (d, J = 8 Hz, 1H), 8.73 (d, J = 4.4 Hz, 1H), 8.851 (quintet$_{app}$, J = 4.8 Hz, 1H), 9.93 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 27.05, 29.59, 29.81, 32.65, 43.63, 44.99, 98.45, 117.08, 121.76, 122.51, 127.27, 127.96, 129.37, 133.66, 136.47, 138.31 (two overlapping peaks), 138.67, 139.85, 140.51, 148.31, 167.15, 206.99, 207.17.
IR (neat) 3338 w, 2963 w, 1713 m, 1671 m, 1519 s, 1482 m, 1454 w, 1325 m, 1163 w, 912 w, 826 m.
MS *m/z* (relative intensity, %) 422 (M^+, 40), 379 (100), 364 (16), 279 (19), 235 (80), 219 (14), 193 (12), 177 (21), 144 (56), 116 (11), 43 (56).
HRMS Calcd for $C_{24}H_{23}ClN_2O_3$: 422.1397; Found: 422.1395.

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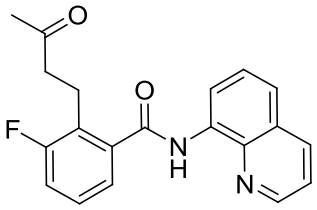
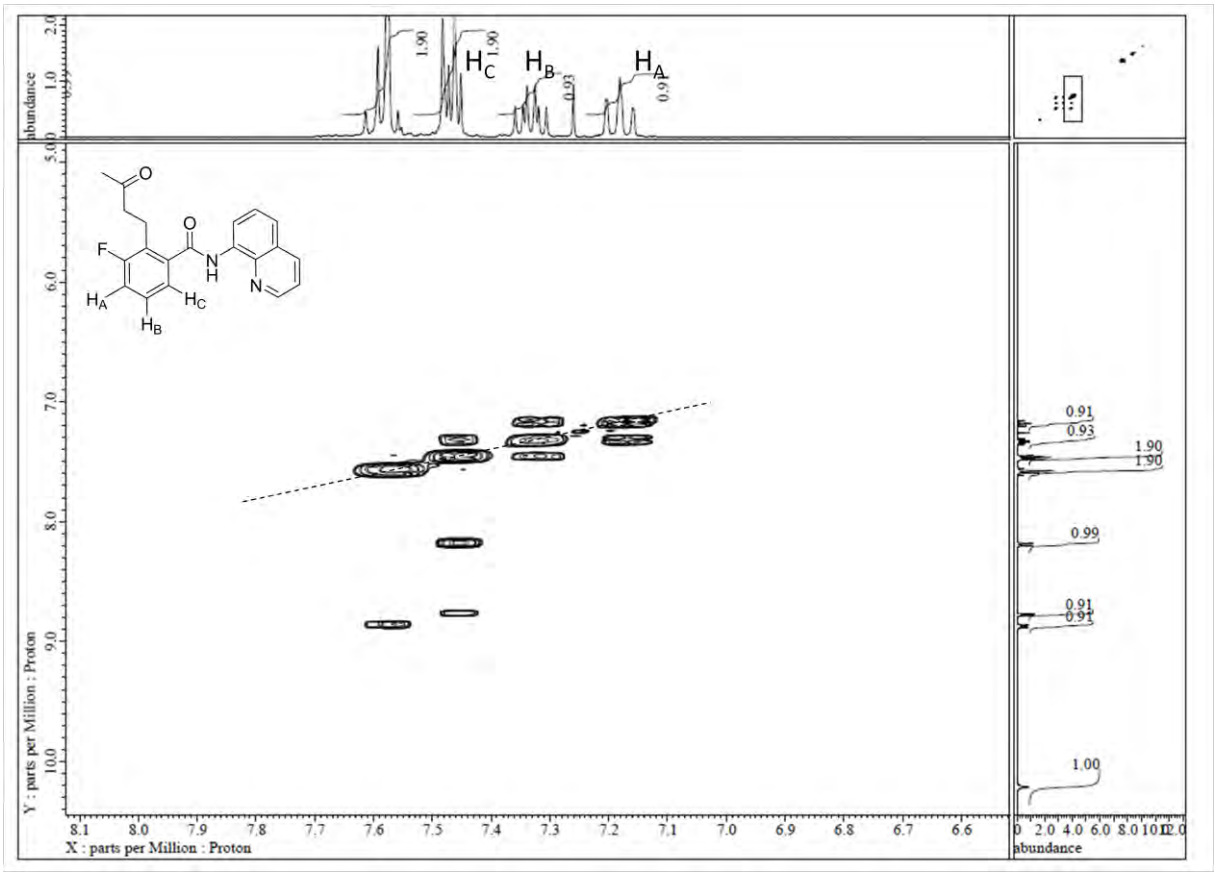
3-fluoro-2-(3-oxobutyl)-N-(quinolin-8-yl)benzamide (3'sa)

See also part X for the cleavage of the 8-aminoquinoline moiety.



Rf 0.45(hexane/EtOAc = 70/30). White solid. **Mp** = 110 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.14 (s, 3H), 2.92 (t, *J* = 8.8 Hz, 1H), 3.12 (t, *J* = 6.8 Hz, 1H), 7.18 (t, *J* = 8.8 Hz, 1H), 7.33 (dt, *J* = 8, 5.2 Hz, 1H), 7.46 (d, *J* = 8.4 Hz, 1H), 7.47 (d, *J* = 8 Hz, 1H), 7.56 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.59 (t, *J* = 8.8 Hz, 1H), 7.62 (d, *J* = 2.4 Hz, 1H), 8.18 (dd, *J* = 8, 1.2 Hz, 1H), 8.73 (dd, *J* = 4.4, 1.6 Hz, 1H), 8.83 (t_{app}, *J* = 4.8 Hz, 1H), 8.18 (dd, *J* = 8.4, 2 Hz, 1H), 8.79 (dd, *J* = 4.4, 2 Hz, 1H), 8.85 (dd, *J* = 6.4, 2.8 Hz, 1H), 10.17 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 20.86 (d, *J* = 2.8 Hz), 29.68, 44.12, 116.75, 117.35 (d, *J* = 23 Hz), 121.72, 122.14, 122.79 (d, *J* = 2.9 Hz), 127.34, 127.43 (d, *J* = 19 Hz), 127.89, 127.94 (d, *J* = 8.5 Hz), 134.30, 136.50, 138.39, 138.84 (d, *J* = 3.8 Hz), 148.26, 161.55 (d, *J* = 246 Hz), 166.61 (d, *J* = 3.9 Hz), 207.61.
IR (neat) 3342 w, 1712 m, 1672 m, 1521 s, 1484 m, 1424 w, 1326 m, 1265 m, 1161 w.
MS *m/z* (relative intensity, %) 336 (M^+, 37), 293 (100), 275 (15), 193 (14), 149 (97), 144 (25), 101 (12), 43 (21).
HRMS Calcd for $C_{20}H_{17}FN_2O_2$: 336.1274; Found: 336.1270.
COSY



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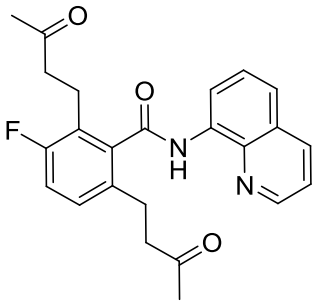
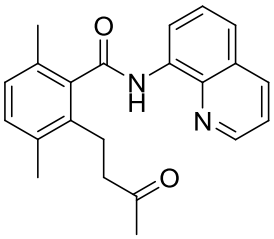
3-fluoro-2,6-bis(3-oxobutyl)-N-(quinolin-8-yl)benzamide (6sa)



Rf 0.45(hexane/EtOAc = 50/50); Yellow oil.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.03 (s, 6H), 2.80-2.96 (m, 8H), 7.04 (t, *J* = 9.2 Hz, 1H), 7.14 (dd, *J* = 8.8, 5.6 Hz, 1H), 7.45 (dd, *J* = 8, 4 Hz, 1H), 7.58 (d, *J* = 4.4 Hz, 2H), 8.2 (dd, *J* = 8.4, 2 Hz, 1H), 8.74 (dd, *J* = 4.4, 2 Hz, 1H), 8.86 (quintet, *J* = 4.4 Hz, 1H), 9.96 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 21.37, 26.91, 29.56, 29.83, 43.97, 45.32, 116.18 (d, *J* = 22 Hz), 117.12, 121.74, 122.49, 125.10 (d, *J* = 17.2 Hz), 127.28, 127.98, 129.12 (d, *J* = 7.7 Hz), 133.54 (d, *J* = 3.8 Hz), 133.70, 136.51, 138.28, 139.22 (d, *J* = 3.8 Hz), 148.28, 159.60 (d, *J* = 245 Hz), 166.76 (d, *J* = 2.9 Hz), 207.19, 207.44.
IR (neat) 3335 w, 1712 m, 1671 m, 1519 s, 1478 s, 1421 w, 1325 m, 1266 m, 1163 m, 826 m.
MS *m/z* (relative intensity, %) 406 (M^+, 39), 363 (100), 263 (13), 219 (81), 203 (12), 159 (20), 144 (35), 43 (36).
HRMS Calcd for $C_{24}H_{23}FN_2O_3$: 406.1693; Found: 406.1694.

3,6-dimethyl-2-(3-oxobutyl)-N-(quinolin-8-yl)benzamide (8aa)



Rf 0.35 (hexane/EtOAc = 70/30). Yellow oil.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.05 (s, 3H), 2.31 (s, 3H), 2.38 (s, 3H), 2.78-2.82 (m, 2H), 2.94 (t, *J* = 8.4 Hz, 2H), 7.05 (d, *J* = 8.0 Hz, 1H), 7.14 (d, *J* = 7.6 Hz, 1H), 7.44 (dd, *J* = 8.4, 4.4 Hz, 1H), 7.56 (d, *J* = 8 Hz, 1H), 7.60 (t, *J* = 8.4 Hz, 1H), 8.18 (dd, *J* = 8 Hz, 1H), 8.73 (d, *J* = 4 Hz, 1H), 8.93 (d, *J* = 7.2 Hz, 1H), 9.90 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 19.03, 19.15, 24.95, 29.65, 44.30, 116.84, 121.64, 122.03, 127.34, 127.96, 128.19, 131.10, 132.05, 133.89, 134.18, 135.70, 136.37, 138.38, 138.40, 148.21, 169.04, 207.92
IR (neat) 3345 w, 2953 w, 1715 w, 1673 m, 1520 s, 1483 m, 1424 w, 1326 w, 1163 w, 827 w.
HRMS Calcd for $C_{22}H_{22}N_2O_2$: 346.1681; Found: 346.1677.

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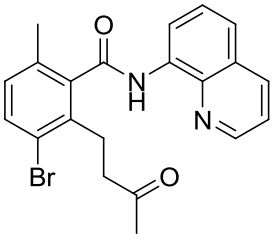
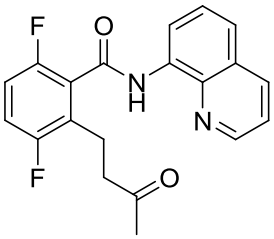
3-bromo-6-methyl-2-(3-oxobutyl)-N-(quinolin-8-yl)benzamide (8ba)



Rf 0.25 (hexane/EtOAc = 70/30). White solid. **MP** = 120 °C
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.06 (s, 3H), 2.36 (s, 3H), 2.85-2.89 (m, 2H), 3.05 (t, *J* = 8 Hz, 2H), 7.00 (d, *J* = 8.4 Hz, 1H), 7.43 (dd, *J* = 8, 4 Hz, 1H), 7.50 (d, *J* = 8.4 Hz, 1H), 7.56-7.60 (m, 2H), 8.16 (dd, *J* = 8.4, 1.6 Hz, 1H), 8.73 (dd, *J* = 4, 1.2 Hz, 1H), 8.88 (dd, *J* = 6, 2.8 Hz, 1H), 9.90 (brs, 1H)
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 19.08, 28.16, 29.55, 43.49, 116.91, 121.68, 122.11, 122.31, 127.20, 127.88, 129.84, 133.40, 133.77, 134.02, 136.36, 136.75, 138.28, 139.53, 148.28, 167.27, 207.21.
IR (neat) 3339 w, 1715 m, 1669 m, 1597 m, 1518 s, 1482 m, 1423 m, 1325 m, 1241 m, 1169 m, 826 m.
HRMS Calcd for $C_{21}H_{19}BrN_2O_2$: 410.0630; Found: 410.0627.
Anal. Calcd for $C_{21}H_{19}BrN_2O_2$: C, 61.33; H, 4.66; N, 6.81. Found: C, 61.32; H, 4.55; N, 6.80.

3,6-difluoro-2-(3-oxobutyl)-N-(quinolin-8-yl)benzamide (8ca)



Rf 0.2 (hexane/EtOAc = 70/30). White solid. **MP** = 132 °C
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.09 (s, 3H), 2.87-2.89 (m, 2H), 3.01 (t, *J* = 7.2 Hz, 2H), 7.00 (td, *J* = 9.2, 4.4 Hz, 1H), 7.08 (td, *J* = 8.8, 4.4 Hz, 1H), 7.41 (dd, *J* = 8.4, 4.4 Hz, 1H), 7.53-7.57 (m, 2H), 8.13 (dd, *J* = 8.0, 1.2 Hz, 1H), 8.74 (dd, *J* = 4.4, 1.6 Hz, 1H), 8.86 (dd, *J* = 5.2, 3.2 Hz, 1H), 10.18 (brs, 1H)
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 21.28, 29.54, 43.63, 114.84 (dd, *J* = 25.1, 9.0 Hz), 116.87, 117.47 (dd, *J* = 26.1, 9.0 Hz), 121.68, 122.41, 126.45 (dd, *J* = 20.1, 4.0 Hz), 127.12, 127.83, 128.49 (dd, *J* = 19.1, 3.0 Hz), 133.81, 136.29, 138.19, 148.29, 154.83 (dd, *J* = 221.1, 3.0 Hz), 157.2 (dd, *J* = 220.1, 2.0 Hz), 161.81 (d, *J* = 3.0 Hz), 207.02.
IR (neat) 3336 w, 1672 m, 1523 s, 1472 m, 1325 m, 1261 m, 824 m.
HRMS Calcd for $C_{20}H_{16}F_2N_2O_2$: 354.1180; Found: 354.1180.
Anal. Calcd for $C_{20}H_{16}F_2N_2O_2$: C, 67.79; H, 4.55; N, 7.91. Found: C, 67.92; H, 4.54; N, 7.86.

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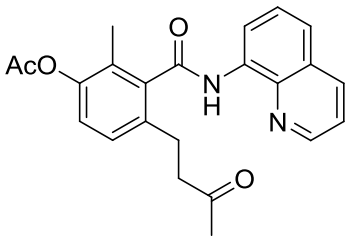
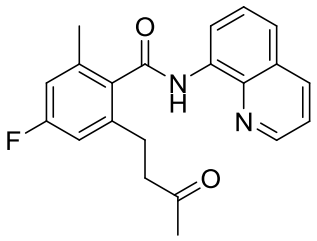
2-methyl-4-(3-oxobutyl)-3-(quinolin-8-ylcarbamoyl)phenyl acetate (8da)



Rf 0.34 (hexane/EtOAc = 60/40). White solid. **MP** = 130 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.04 (s, 3H), 2.23 (s, 3H), 2.33 (s, 3H), 2.84 (t, *J* = 7.2 Hz, 2H), 2.95 (t, *J* = 7.2 Hz, 2H), 7.05 (d, *J* = 8.0 Hz, 1H), 7.17 (d, *J* = 8.4 Hz, 1H), 7.45 (dd, *J* = 8.4, 4.4 Hz, 1H), 7.56-7.62 (m, 2H), 8.17 (d, *J* = 8.4 Hz, 1H), 8.74 (dd, *J* = 3.4, 0.8 Hz, 1H), 8.92 (dd, *J* = 6.0, 2.4 Hz, 1H), 9.97 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 13.24, 20.79, 27.19, 29.84, 45.44, 116.88, 121.74, 122.28, 122.93, 127.03, 127.24, 127.94, 128.12, 134.00, 135.65, 136.31, 138.41, 139.20, 147.68, 148.37, 167.45, 169.36, 207.62.
IR (neat) 3342 w, 3016 w, 1760 m, 1714 m, 1672 m, 1520 s, 1483 m, 1424 m, 1325 m, 1201 s, 897 w, 826 w.
HRMS Calcd for $C_{23}H_{22}N_2O_4$: 390.1580; Found: 390.1580
Anal. Calcd for $C_{23}H_{22}N_2O_4$: C, 70.75; H, 5.68; N, 7.17. Found: C, 70.64; H, 5.61; N, 7.12.

4-fluoro-2-methyl-6-(3-oxobutyl)-N-(quinolin-8-yl)benzamide (8ea)



Rf 0.28 (hexane/EtOAc = 70/30). Yellow oil.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.06 (s, 3H), 2.42 (s, 3H), 2.82-2.87 (m, 2H), 2.92-2.97 (m, 2H), 6.82 (s, 1H), 6.85 (s, 1H), 7.45 (dd, *J* = 8.0, 4.0 Hz, 1H), 7.57-7.60 (m, 2H), 8.18 (dd, *J* = 8.0, 1.6 Hz, 1H), 8.75 (dd, *J* = 4.0, 1.6 Hz, 1H), 8.91 (dd, *J* = 6.4, 2.0 Hz, 1H), 9.93 (brs, 1H)
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 19.62, 27.45, 29.85, 45.10, 113.63 (d, *J* = 21.1 Hz), 115.02 (d, *J* = 21.1 Hz), 116.86, 121.74, 122.24, 127.31, 127.99, 134.00, 134.03, 136.42, 137.54 (d, *J* = 9.0 Hz), 138.41, 140.70 (d, *J* = 8.0 Hz), 148.34, 162.62 (d, *J* = 247.3 Hz), 167.84, 207.30
IR (neat) 3344 w, 2925 w, 1714 m, 1671 m, 1598 m, 1519 s, 1482 m, 1325 m, 1140 m, 979 w, 826 m.
HRMS Calcd for $C_{21}H_{19}FN_2O_2$: 350.1431; Found: 350.1430.

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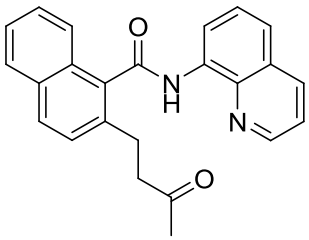
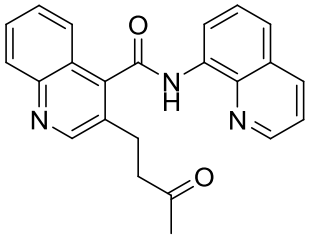
2-(3-oxobutyl)-N-(quinolin-8-yl)-1-naphthamide (8fa)



Rf 0.25 (hexane/EtOAc = 70/30). White solid. **MP** = 140 °C
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.08 (s, 3H), 2.95 (t, *J* = 7.6 Hz, 2H), 3.16 (t, *J* = 7.6 Hz, 2H), 7.40-7.50 (m, 4H), 7.60 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.65 (t, *J* = 8 Hz, 1H), 7.84-7.89 (m, 2H), 7.98-8.02 (m, 1H), 8.17 (dd, *J* = 8.4, 1.6 Hz, 1H), 8.66 (dd, *J* = 4.4, 2.0 Hz, 1H), 9.10 (dd, *J* = 7.6, 1.6 Hz, 1H), 10.16 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 27.95, 29.84, 45.43, 116.94, 121.67, 122.22, 124.77, 125.82, 127.11, 127.34, 127.39, 127.98, 127.98, 129.56, 130.17, 131.98, 134.22, 134.27, 135.57, 136.34, 138.37, 148.23, 168.06, 207.54.
IR (neat) 3343 w, 3049 w, 1714 m, 1670 m, 1518 s, 1482 m, 1423 m, 1325 m, 1155 w, 889 w, 825 m.
HRMS Calcd for $C_{24}H_{20}N_2O_2$: 368.1525; Found: 368.1528.
Anal. Calcd for $C_{24}H_{20}N_2O_2$: C, 78.24; H, 5.47; N, 7.60. Found: C, 78.21; H, 5.37; N, 7.59.

3-(3-oxobutyl)-N-(quinolin-8-yl)quinoline-4-carboxamide (8ga)



Rf 0.28 (EtOAc). Yellow solid. **MP** = 167 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.08 (s, 3H), 2.95 (t, *J* = 7.6 Hz, 2H), 3.16 (t, *J* = 7.6 Hz, 2H), 7.42 (dd, *J* = 8.4, 4 Hz, 1H), 7.53-7.55 (m, 1H), 7.60-7.72 (m, 3H), 7.97 (dd, *J* = 8, 0.8 Hz, 1H), 8.14 (d, *J* = 8 Hz, 1H), 8.18 (dd, *J* = 8.4, 2 Hz, 1H), 8.66 (dd, *J* = 4.4, 2.0 Hz, 1H), 8.91 (s, 1H), 9.01 (dd, *J* = 6.8, 2.4 Hz, 1H), 10.19 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 25.26, 29.87, 44.90, 117.18, 121.88, 122.77, 124.22, 124.68, 127.29, 127.81, 128.01, 129.40, 129.60, 129.86, 133.78, 136.42, 138.37, 141.18, 146.89, 148.50, 152.31, 165.46, 206.80.
IR (neat) 3060 w, 2953 w, 1583 m, 1523 m, 1461 m, 1425 m, 1266 m, 1128 m, 839 s, 754 s.
HRMS Calcd for $C_{23}H_{19}N_3O_2$: 369.1477; Found: 369.1479
Anal. Calcd for $C_{23}H_{19}N_3O_2$: C, 74.78; H, 5.18; N, 11.37. Found: C, 74.46; H, 5.17; N, 11.35.

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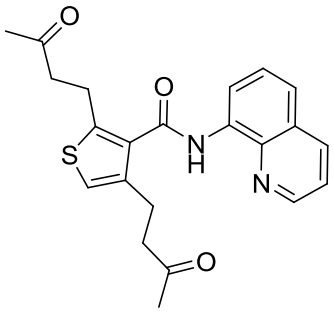
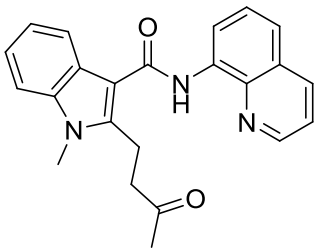
2,4-bis(3-oxobutyl)-N-(quinolin-8-yl)thiophene-3-carboxamide (8ha)



Rf 0.4 (hexane/EtOAc = 50/50). Yellow oil.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.02 (s, 3H), 2.05 (s, 3H) 2.77 (t, *J* = 7.2 Hz, 2H), 2.88 (t, *J* = 7.2 Hz, 2H), 3.00 (t, *J* = 7.6 Hz, 2H), 3.25 (t, *J* = 7.6 Hz, 2H), 6.80 (s, 1H), 7.39 (dd, *J* = 8.0, 4.0 Hz, 1H), 7.48-7.54 (m, 2H), 8.11 (dd, *J* = 8.0, 1.6 Hz, 1H), 8.72 (dd, *J* = 4.0, 1.6 Hz, 1H), 8.83 (dd, *J* = 6.8, 1.6 Hz, 1H), 10.06 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 22.89, 23.52, 29.59, 43.66, 44.87, 116.46, 119.33, 121.53, 121.86, 127.01, 127.74, 133.98, 134.73, 136.16, 138.26, 139.78, 144.94, 148.12, 163.81, 206.43, 207.49.
IR (neat) 3353 w, 2922 w, 1714 m, 1665 m, 1520 s, 1483 m, 1424 m, 1326 m, 1163 w, 827 w.
HRMS Calcd for $C_{22}H_{22}N_2O_3S$: 394.1351; Found: 394.1353.

1-methyl-2-(3-oxobutyl)-N-(quinolin-8-yl)-1H-indole-3-carboxamide (8ia)



A further recrystallisation from EtOAc was done to remove trace of impurity.

Rf 0.44 (hexane/EtOAc = 50/50). brown solid. **MP** = 145 °C
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.19 (s, 3H), 3.03 (t, *J* = 8 Hz, 2H), 3.50 (t, *J* = 8 Hz, 2H), 3.80 (s, 3H), 7.29-7.50 (m, 5H), 7.58 (t, *J* = 7.6 Hz, 1H), 8.16 (dd, *J* = 8, 1.6 Hz, 1H), 8.36 (d, *J* = 7.6 Hz, 1H), 8.84 (dd, *J* = 4, 1.2 Hz, 1H), 8.93 (dd, *J* = 7.2, 0.8 Hz, 1H), 10.62 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 19.81, 29.64, 29.88, 43.09, 108.14, 109.90, 116.03, 119.24, 120.76, 121.47, 121.72, 122.00, 124.78, 127.41, 128.00, 135.47, 136.22, 136.54, 138.70, 146.42, 148.13, 164.05, 207.69.
IR (neat) 3372 w, 3052 w, 1714 m, 1648 m, 1518 s, 1472 m, 1325 m, 1108 m, 824 m.
HRMS Calcd for $C_{23}H_{21}N_3O_2$: 371.1634; Found: 371.1632.

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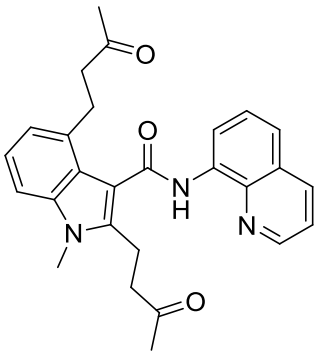
1-methyl-2,5-bis(3-oxobutyl)-N-(quinolin-8-yl)-1H-indole-3-carboxamide (8'ia)



Obtained as side product of product **8ia**

Rf 0.25 (hexane/EtOAc = 50/50). Yellow oil.

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 1.84 (s, 3H), 2.11 (s, 3H), 2.76 (t, *J* = 8.0 Hz, 2H), 2.97 (t, *J* = 8.4 Hz, 2H), 3.25 (t, *J* = 8.4 Hz, 2H), 3.27 (t, *J* = 9.2 Hz, 2H), 3.76 (s, 3H), 7.00 (dd, *J* = 6.4, 1.2 Hz, 1H), 7.19 (t, *J* = 8.8 Hz, 1H), 7.23 (dd, *J* = 8.4, 2 Hz, 1H), 7.44 (dd, *J* = 8, 4 Hz, 1H), 7.55 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.60 (t, *J* = 8 Hz, 1H), 8.18 (dd, *J* = 8, 1.2 Hz, 1H), 8.70 (dd, *J* = 4, 1.6 Hz, 1H), 8.94 (d, *J* = 7.6 Hz, 1H), 10.07 (brs, 1H).

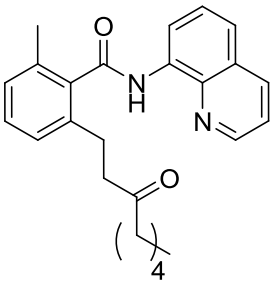
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 19.39, 28.38, 29.48, 29.89 (two overlapping peaks), 43.57, 44.63, 107.71, 111.28, 116.59, 121.60, 121.71, 121.98, 122.28, 123.44, 127.58, 128.06, 133.25, 134.47, 136.68, 136.92, 138.14, 140.25, 147.97, 166.07, 206.81, 208.43.

IR (neat) 3359 w, 230 w, 1714 m, 1659 m, 1518 s, 1481 m, 1425 w, 1324 w, 1161 w, 828 w.

MS *m/z* (relative intensity, %) 441 (M^+, 21), 298 (100), 254 (47), 212 (11), 196 (13), 170 (37), 43 (12)

HRMS Calcd for $C_{27}H_{27}N_3O_3$: 441.2052; Found: 441.2053.

2-methyl-6-(3-oxooctyl)-N-(quinolin-8-yl)benzamide (3ab)



Rf 0.42 (hexane/EtOAc = 80.20). Yellow oil.

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 0.81 (t, *J* = 8.0 Hz, 3H), 1.09-1.22 (m, 4H), 1.45 (quintet, *J* = 7.6 Hz, 2H), 2.27 (t, *J* = 7.6 Hz, 2H), 2.43 (s, 3H), 2.81 (t, *J* = 7.8 Hz, 2H), 2.97 (t, *J* = 8 Hz, 2H), 7.19 (d, *J* = 7.2 Hz, 1H), 7.19 (d, *J* = 7.2 Hz, 1H), 7.27 (t, *J* = 7.6 Hz, 1H), 7.45 (dd, *J* = 8, 4 Hz, 1H), 7.57 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.60 (t, *J* = 8.4 Hz, 1H), 8.18 (dd, *J* = 8.4, 2 Hz, 1H), 8.73 (dd, *J* = 4.0, 1.6 Hz, 1H), 8.95 (dd, *J* = 7.2, 2.0 Hz, 1H), 9.94 (brs, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 13.84, 19.44, 22.31, 23.40, 27.73, 31.25, 42.74, 44.61, 116.83, 121.67, 122.07, 126.98, 127.35, 127.99, 128.22, 129.21, 134.19, 134.64, 136.37, 137.79, 137.96, 138.44, 148.26, 168.59, 210.31.

IR (neat) 3346 w, 2953 w, 2929 w, 1712 m, 1674 m, 1520 s, 1482 m, 1325 m, 1127 m, 826 m.

HRMS Calcd for $C_{25}H_{28}N_2O_2$: 388.2151; Found: 388.2154.

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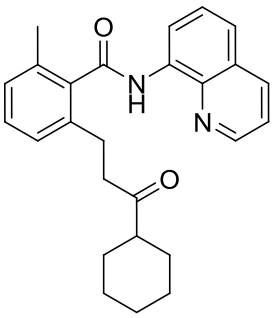
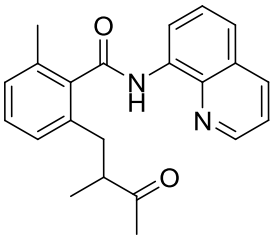
2-(3-cyclohexyl-3-oxopropyl)-6-methyl-N-(quinolin-8-yl)benzamide (3ac)



Rf 0.42 (hexane/EtOAc = 80.20). Yellow oil.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 1.06-1.22 (m, 5H), 1.55-1.69 (m, 5H), 2.19 (tt, *J* = 10.8, 3.2 Hz, 1H), 2.43 (s, 3H), 2.83 (t, *J* = 7.6 Hz, 2H), 2.95 (t, *J* = 8.4 Hz, 2H), 7.13 (d, *J* = 7.2 Hz, 1H), 7.13 (d, *J* = 7.2 Hz, 1H), 7.27 (t, *J* = 7.6 Hz, 1H), 7.45 (dd, *J* = 8.4, 4.4 Hz, 1H), 7.55-7.62 (m, 2H), 8.18 (dd, *J* = 8.4, 1.6 Hz, 1H), 8.73 (dd, *J* = 4.4, 2 Hz, 1H), 8.95 (dd, *J* = 7.2, 1.6 Hz, 1H), 9.95 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 19.40, 25.48, 25.69, 27.82, 28.19, 42.61, 50.69, 116.79, 121.64, 122.03, 126.97, 127.32, 127.96, 128.16, 129.18, 134.19, 134.59, 136.33, 137.79, 138.12, 138.40, 148.23, 168.59, 213.00.
IR (neat) 3348 w, 2929 w, 2849 w, 1673 m, 1519 s, 1481 m, 1325 m, 1263 w, 1127 w, 826 w.
HRMS Calcd for $C_{26}H_{28}N_2O_2$: 400.2151; Found: 400.2148.

2-methyl-6-(2-methyl-3-oxobutyl)-N-(quinolin-8-yl)benzamide (3ad)



Rf 0.28 (hexane/EtOAc = 80/20). Yellow oil.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 1.04 (d, *J* = 6.8 Hz, 3H), 2.02 (s, 3H), 2.43 (s, 3H), 2.60 (dd, *J* = 14.0, 8.0 Hz, 1H), 3.03 (sextet, *J* = 6.8 Hz, 1H), 3.17 (dd, *J* = 13.6, 6.0 Hz, 1H), 7.08 (d, *J* = 7.6 Hz, 1H), 7.15 (d, *J* = 7.6 Hz, 1H), 7.27 (t, *J* = 7.6 Hz, 1H), 7.46 (dd, *J* = 8.0, 4.0 Hz, 1H), 7.57-7.64 (m, 2H), 8.19 (dd, *J* = 8.4, 1.6 Hz, 1H), 8.74 (dd, *J* = 4.4, 1.6 Hz, 1H), 8.97 (dd, *J* = 7.2, 1.6 Hz, 1H), 9.96 (brs, 1H)
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 16.05, 19.43, 28.76, 36.22, 48.11, 116.65, 121.65, 122.05, 127.24, 127.63, 127.90, 128.38, 128.88, 134.10, 134.60, 136.29, 136.37, 137.93, 138.34, 148.26, 168.46, 212.02.
IR (neat) 3345 w, 2975 w, 1672 m, 1519 s, 1481 m, 1325 m, 12220 w, 1127 w, 826 w.
HRMS Calcd for $C_{22}H_{22}N_2O_2$: 346.1681; Found: 346.1681.

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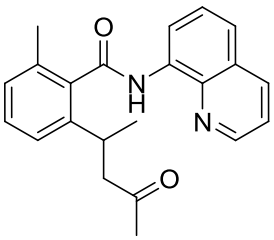
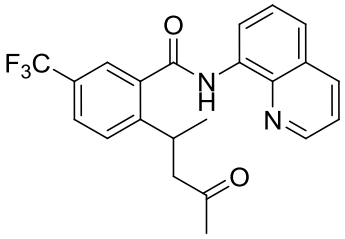
2-methyl-6-(4-oxopentan-2-yl)-N-(quinolin-8-yl)benzamide (3ae)



Rf 0.20 (hexane/EtOAc = 80/20). Yellow oil.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 1.29 (d, *J* = 6.8 Hz, 3H), 2.00 (s, 3H), 2.42 (s, 3H), 2.63 (dd, *J* = 16.4, 8.0 Hz, 1H), 2.94 (dd, *J* = 16.0, 6.0 Hz, 1H), 3.53 (sextet, *J* = 6.8 Hz, 1H), 7.12 (d, *J* = 7.6 Hz, 1H), 7.16 (d, *J* = 7.16 Hz, 1H), 7.31 (t, *J* = 7.6 Hz, 1H), 7.42 (dd, *J* = 8.0, 4.0 Hz, 1H), 7.56 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.60 (t, *J* = 8.4 Hz, 1H), 8.16 (dd, *J* = 8.4, 1.6 Hz, 1H), 8.74 (dd, *J* = 4.4, 1.6 Hz, 1H), 9.00 (dd, *J* = 7.6, 1.6 Hz, 1H), 10.06 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 19.46, 22.12, 29.76, 32.32, 51.92, 116.83, 121.60, 122.00, 123.11, 127.28, 127.94, 128.19, 129.27, 134.24, 134.54, 136.25, 137.27, 138.46, 142.62, 148.24, 168.61, 207.35.
IR (neat) 3339 w, 2965 w, 1671 m, 1519 s, 1482 m, 1325 m, 1218 w, 1165 w, 827 w.
MS *m/z* (relative intensity, %) 346 (M^+, 31), 303 (55), 288 (29), 203 (57), 159 (100), 143 (85), 128 (12), 115 (16), 91 (14), 43 (36).
HRMS Calcd for $C_{22}H_{22}N_2O_2$: 346.1681; Found: 346.1681.

2-(4-oxopentan-2-yl)-N-(quinolin-8-yl)-5-(trifluoromethyl)benzamide (3ce)



Rf 0.25 (hexane/EtOAc = 80/20). Yellow oil.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 1.34 (d, *J* = 6.8 Hz, 3H), 2.07 (s, 3H), 2.72 (dd, *J* = 16.4, 7.6 Hz, 1H), 2.99 (dd, *J* = 16.8, 6.8 Hz, 1H), 3.9 (sextet, *J* = 7.6 Hz, 1H), 7.45 (dd, *J* = 8, 4 Hz, 1H), 7.49 (d, *J* = 8 Hz, 1H), 7.57-7.62 (m, 2H), 7.69 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.85 (s, 1H), 8.18 (dd, *J* = 8.4, 2.0 Hz, 1H), 8.78 (dd, *J* = 4, 1.2 Hz, 1H), 8.92 (dd, *J* = 6.4, 2.4 Hz, 1H), 10.30 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 21.80, 29.89, 31.51, 51.50, 116.97, 116.97, 121.73, 122.32, 123.70 (q, *J* = 271 Hz), 124.16 (d, *J* = 4 Hz), 126.98 (d, *J* = 2.8 Hz), 127.22, 127.96, 128.64 (q, *J* = 32.5 Hz), 134.27, 136.36, 137.30, 138.48, 148.38, 148.45, 166.96, 206.79.
IR (neat) 3341 w, 2966 w, 1715 m, 1675 m, 1524 s, 1485 m, 1335m, 1326 m, 1170 m, 1124 m, 826 m.
MS *m/z* (relative intensity, %) 400 (M^+, 25), 357 (100), 213 (64), 145 (53), 116 (10), 43 (25).
HRMS Calcd for $C_{23}H_{19}F_3N_2O_2$: 400.1399; Found: 400.1401.

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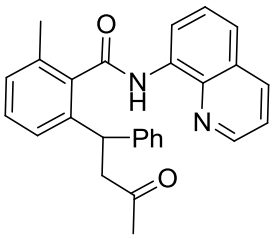
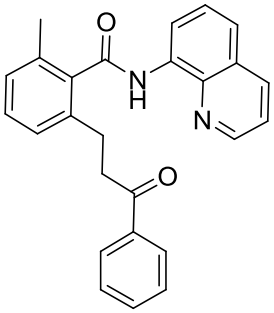
2-methyl-6-(3-oxo-1-phenylbutyl)-N-(quinolin-8-yl)benzamide (3af)



Rf 0.25 (hexane/EtOAc = 70/30). Yellow oil.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.03 (s, 3H), 2.42 (s, 3H), 3.19 (dd, *J* = 16.4, 8.4 Hz, 1H), 3.27 (dd, *J* = 17.2, 7.6 Hz, 1H), 4.89 (t, *J* = 11.6 Hz, 1H), 6.96-7.30 (m, 8H), 7.42 (dd, *J* = 8, 4.4 Hz, 1H), 7.57 (dd, *J* = 5.6, 1.2 Hz, 1H), 7.64 (t, *J* = 3.6 Hz, 1H), 8.16 (dd, *J* = 8.0, 1.2 Hz, 1H), 8.6 (d, *J* = 2.8 Hz, 1H), 9.02 (dd, *J* = 8, 1.6 Hz, 1H), 9.88 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 19.51, 29.79, 42.91, 50.07, 116.80, 121.50, 121.98, 124.73, 126.18, 127.27, 127.60, 127.86, 128.31, 128.48, 129.17, 134.20, 134.81, 136.16, 137.66, 138.38, 140.44, 142.61, 148.07, 168.41, 206.47.
IR (neat) 3342 w, 3061 w 2953 w, 1714 m, 1672 m, 1521 s, 1483 m, 1326 m, 1161 w, 898 w, 827 m.
MS *m/z* (relative intensity, %) 408 (M^+, 36), 365 (35), 221 (100), 207 (86), 178 (15), 145 (16).
HRMS Calcd for $C_{27}H_{24}N_2O_2$: 408.1838; Found: 408.1842.

2-methyl-6-(3-oxo-3-phenylpropyl)-N-(quinolin-8-yl)benzamide (3ag)



Rf 0.3 (hexane/EtOAc = 85/15). White solid. **MP** = 130 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.45 (s, 3H), 3.14 (t, *J* = 8.4 Hz, 2H), 3.40 (t, *J* = 7.6 Hz, 2H), 7.16 (d, *J* = 7.6 Hz, 1H), 7.21 (d, *J* = 7.6 Hz, 1H), 7.28-7.33 (m, 3H), 7.44-7.47 (m, 2H), 7.56-7.63 (m, 2H), 7.82 (d, *J* = 7.2 Hz, 1H), 8.19 (dd, *J* = 8.4, 1.6 Hz, 1H), 8.71(dd, *J* = 4.4, 1.6 Hz, 1H), 8.97 (dd, *J* = 7.2, 2.0 Hz, 1H), 10.02 (brs, 1H)
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 19.47, 28.47, 41.14, 116.95, 121.66, 122.11, 127.16, 127.35, 127.98, 128.09, 128.33, 128.38, 129.31, 132.90, 134.16, 134.66, 136.41, 136.51, 137.88, 138.03, 138.38, 148.26, 168.69, 199.21
IR (neat) 3345 w, 3060 w, 1675 m, 1520 s, 1482 m, 1325 m, 1127 w, 898 w, 826 m.
HRMS Calcd for $C_{26}H_{22}N_2O_2$: 394.1681; Found: 394.1680
Anal. Calcd for $C_{26}H_{22}N_2O_2$: C, 79.16; H, 5.62; N, 7.10. Found: C, 78.89; H, 5.58; N, 7.31.

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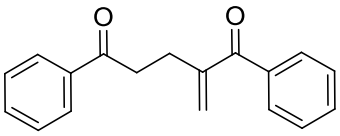
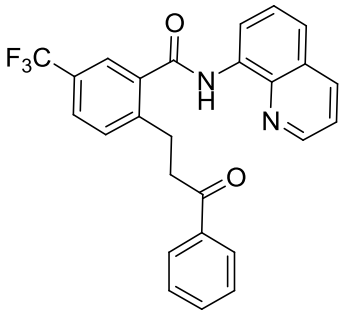
2-methylene-1,5-diphenylpentane-1,5-dione (9g)



Rf 0.42 (hexane/EtOAc = 85/15). Yellow oil
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.91 (t, *J* = 7.2 Hz, 2H), 3.24 (t, *J* = 7.2 Hz, 2H), 5.67 (s, 1H), 5.96 (d, *J* = 0.8 Hz, 1H), 7.41-7.47 (m, 4H), 7.51-7.57 (m, 2H), 7.73 (d, *J* = 8.4 Hz, 2H), 7.97 (d, *J* = 8.4 Hz, 2H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 27.32, 37.18, 127.30 (vinylic CH_2), 128.06, 128.18, 128.59, 129.46, 132.21, 133.08, 136.70, 137.71, 146.71, 198.11, 199.23.
IR (neat) 1683 s, 1652 s, 1447 m, 1274 m, 1177 w, 973 m, 824 m.
HRMS Calcd for $C_{18}H_{16}O_2$: 264.1150; Found: 264.1150.

2-(3-oxo-3-phenylpropyl)-N-(quinolin-8-yl)-5-(trifluoromethyl)benzamide (3cg)



Rf 0.34 (hexane/EtOAc = 85/15). White solid. **MP** = 140 °C
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 3.37 (t, *J* = 8 Hz, 2H), 3.50 (t, *J* = 7.6 Hz, 2H), 7.37 (t, *J* = 7.6 Hz, 2H), 7.44 (dd, *J* = 8.4, 4.4 Hz, 1H), 7.50 (t, *J* = 7.2 Hz, 1H), 7.56-7.59 (m, 3H), 7.69 (d, *J* = 8 Hz, 1H), 7.93 (s, 2H), 7.95 (s, 1H), 8.17 (dd, *J* = 8.4, 1.2 Hz, 1H), 8.74 (dd, *J* = 4, 1.2 Hz, 1H), 8.90 (dd, *J* = 6.8, 2.8 Hz, 1H), 10.26 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 28.14, 40.39, 116.80, 121.75, 122.33, 123.74 (q, *J* = 271 Hz), 124.10(d, *J* = 3.8 Hz), 127.02 (d, *J* = 2.8 Hz), 127.20, 127.90, 128.02, 128.44, 128.87 (q, *J* = 33 Hz), 131.48, 133.03, 134.15, 136.35, 136.46, 137.33, 138.41, 144.21, 148.40, 166.64, 198.63.
IR (neat) 3348 w, 3061 w, 1664 m, 1597 m, 1524 m, 1325 m, 1239 s, 1169 s, 1124 m, 992 m, 827 m.
HRMS Calcd for $C_{26}H_{19}F_3N_2O_2$: 448.1399; Found: 448.1400.
Anal. Calcd for $C_{26}H_{19}F_3N_2O_2$: C, 69.64; H, 4.27; N, 6.25. Found: C, 69.73; H, 4.19; N, 6.33.

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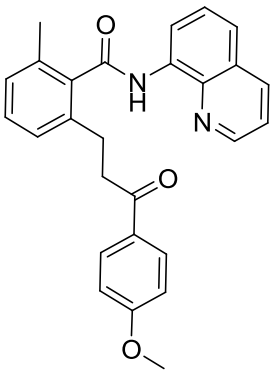
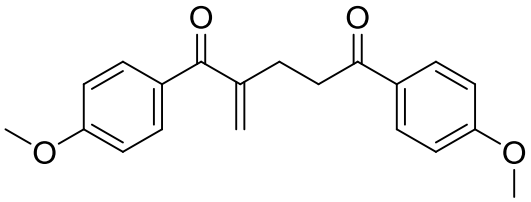
2-(3-(4-methoxyphenyl)-3-oxopropyl)-6-methyl-N-(quinolin-8-yl)benzamide (3ah)



Rf 0.2 (hexane/EtOAc = 80/20). White solid. **Mp** = 143 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.45 (s, 3H), 3.12 (t, *J* = 8.4 Hz, 2H), 3.33 (t, *J* = 7.2 Hz, 1H), 3.79 (s, 3H), 6.75 (d, *J* = 8.4 Hz, 2H), 6.16 (d, *J* = 7.6 Hz, 1H), 7.21 (d, *J* = 7.6 Hz, 1H), 7.30 (t, *J* = 8 Hz, 1H), 7.43 (dd, *J* = 8.4, 4.8 Hz, 1H), 7.57 (d, *J* = 6.8 Hz, 1H), 7.60 (t, *J* = 8.4 Hz, 2H), 7.87 (d, *J* = 8.8 Hz, 2H), 8.18 (d, *J* = 8 Hz, 1H), 8.71 (d, *J* = 4.8 Hz, 1H), 8.98 (d, *J* = 7.2 Hz, 1H), 10.00 (s, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 19.46, 28.81, 40.88, 55.34, 113.47, 116.94, 121.67, 122.08, 127.18, 127.35, 127.99, 128.28, 129.31, 129.63, 130.40, 134.22, 134.64, 136.38, 137.86, 138.14, 138.42, 148.29, 163.25, 168.76, 197.90.
IR (neat) 3335 w, 1672 m, 1598 m, 1520 s, 1482 m, 1259 m, 826 m.
MS *m/z* (relative intensity, %) 424 (M^+, 20), 289 (34), 281 (47), 145 (42), 144 (18), 135 (100).
HRMS Calcd for $C_{27}H_{24}N_2O_3$: 424.1787; Found: 424.1788.

(E)-1,6-bis(4-methoxyphenyl)hex-2-ene-1,6-dione (9h)



Isolated by HPLC in 8 % yield as a side product of the reaction of **2h** with **1a**.

Rf 0.24 (hexane/EtOAc = 80/20). Green solid. **Mp** = 70 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.88 (t, *J* = 7.2 Hz, 2H), 3.16 (t, *J* = 7.6 Hz, 1H), 3.85 (s, 3H), 3.86 (s, 3H), 5.57 (s, 1H), 5.84 (d, *J* = 0.8 Hz, 1H), 6.91 (d, *J* = 9.2 Hz, 4H), 7.78 (d, *J* = 12 Hz, 2H), 7.95 (d, *J* = 9.2 Hz, 2H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 28.04, 36.82, 55.43, 113.47, 113.69, 124.85, 129.83, 130.16, 130.37, 131.97, 147.00, 163.14, 163.43, 196.98, 197.88.
IR (neat) 2929 w, 2837 w, 1673 m, 1597 s, 1508 m, 1254 s, 1219 m, 1167 s, 1027 m, 980 w.
MS *m/z* (relative intensity, %) 324 (M^+, 15), 189 (55), 135 (100), 77 (12).
HRMS Calcd for $C_{20}H_{20}O_4$: 324.1362; Found: 324.1360.

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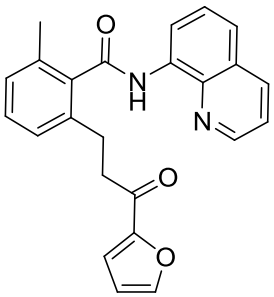
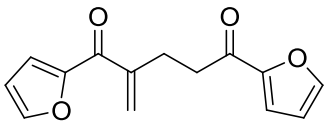
2-(3-(furan-2-yl)-3-oxopropyl)-6-methyl-N-(quinolin-8-yl)benzamide (3ai)



Rf 0.17 (hexane/EtOAc = 80/20). White solid. **Mp** = 120 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.44 (s, 3H), 3.11-3.16 (m, 2H), 3.20-3.25 (m, 2H), 6.34-6.36 (m, 1H), 7.10-7.19 (m, 3H),7.24-7.29 (m, 1H), 7.36-7.41 (m, 2H), 7.53-7.59 (m, 2H), 8.11-8.14 (m, 1H), 8.67-8.70 (m, 1H), 8.97 (dd, *J* = 7.2, 1.6 Hz, 1H), 10.00 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 19.33, 28.18, 40.58, 111.85, 116.63, 117.34, 121.55, 121.99, 126.97, 127.10, 127.80, 128.25, 129.17, 134.05, 134.45, 136.19, 137.47, 137.68, 138.26, 146.17, 148.16, 152.10, 168.44, 188.04.
IR (neat) 3343 w, 1671 s, 1520 s, 1482 m, 1468 m, 1326 m, 1127 w, 898 w, 826 m.
MS *m/z* (relative intensity, %) 384 (M^+, 55), 289 (38), 274 (23), 241 (65), 197 (10), 145 (70), 129 (14), 115 (11), 95 (100).
HRMS Calcd for $C_{24}H_{20}N_2O_3$: 384.1474; Found: 384.1477.

1,5-di(furan-2-yl)-2-methylenepentane-1,5-dione (9i)



Isolated by HPLC in 23 % yield as a side product of the reaction of **2i** with **1a**.

Rf 0.17 (hexane/EtOAc = 80/20). Yellow oil
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.82 (t, *J* = 7.2 Hz, 2H), 3.01 (t, *J* = 7.2 Hz, 2H), 5.82 (s, 1 H), 5.98 (s, 1H), 7.09 (d, *J* = 3.6 Hz, 1H), 6.48 (dd, *J* = 4, 2 Hz, 1H), 6.49 (dd, *J* = 3.6, 2 Hz, 1H), 7.17 (d, *J* = 3.6 Hz, 1H), 7.53 (d, *J* = 0.8 Hz, 1H), 7.61 (d, *J* = 3.6 Hz, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 19.33, 28.18, 40.58, 111.85, 116.63, 117.34, 121.55, 121.99, 126.97, 127.10, 127.80, 128.25, 129.17, 134.05, 134.45, 136.19, 137.47, 137.68, 138.26, 146.17, 148.16, 152.10, 168.44, 188.04.
IR (neat) 3133 w, 2924 w, 1672 s, 1645 m, 1466 s, 1392 m, 1159 w, 1027 m, 883 m.
MS *m/z* (relative intensity, %) 244 (M^+, 12), 149 (36), 95 (100).
HRMS Calcd for $C_{14}H_{12}O_4$: 244.0736; Found: 244.0736.

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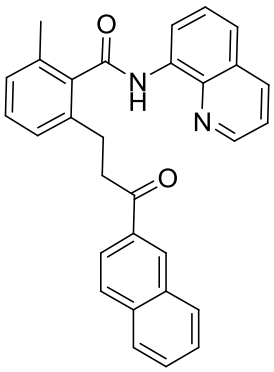
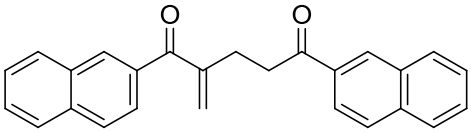
2-methyl-6-(3-(naphthalen-2-yl)-3-oxopropyl)-N-(quinolin-8-yl)benzamide (3aj)



Rf 0.44 (hexane/EtOAc = 80/20). Brown solid. **Mp** = 147 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.48 (s, 3H), 3.22 (t, *J* = 8.4 Hz, 2H), 3.55 (dt, *J* = 7.2, 3.6 Hz, 2H), 7.18 (d, *J* = 7.2 Hz, 1H), 7.26 (d, *J* = 6.8 Hz, 1H), 7.32 (t, *J* = 7.2 Hz, 1H), 7.38 (dd, *J* = 8.4, 4.4 Hz, 1H), 7.49-7.58 (m, 4H), 7.77 (d, *J* = 8.4 Hz, 2H), 7.81 (t, *J* = 7.6 Hz, 1H), 7.97 (dd, *J* = 8, 1.2 Hz, 1H), 8.13 (dd, *J* = 8, 1.2 Hz, 1H), 8.45 (s, 1H), 8.68 (dd, *J* = 4, 2.0 Hz, 1H), 8.99 (dd, *J* = 6.8, 1.6 Hz, 1H), 10.04 (brs, 1H)
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 19.47, 28.66, 41.18, 116.93, 121.60, 122.08, 123.75, 126.50, 127.20, 127.28, 127.59, 127.93, 128.16, 128.24, 128.34, 129.32, 129.48, 129.91, 132.38, 133.82, 134.12, 134.63, 135.40, 136.33, 137.86, 138.09, 138.33, 148.20, 168.72, 199.12.
IR (neat) 3343 w, 3061 w, 1675 s, 1521 s, 1483 m, 1326 m, 1124 w, 826 w.
MS *m/z* (relative intensity, %) 444 (M^+, 43), 301 (34), 289 (52), 257 (11), 155 (100), 144 (27), 145 (54), 127 (46).
HRMS Calcd for $C_{30}H_{24}N_2O_2$: 444.1838; Found: 444.1836.

2-methylene-1,5-di(naphthalen-2-yl)pentane-1,5-dione (9j)



Isolated by HPLC in 23 % yield as a side product of the reaction of **2j** with **1a**.

Rf 0.45 (hexane/EtOAc = 80/20). Brown solid. **Mp** = 127 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 3.05(t, *J* = 7.2 Hz, 2H), 3.43 (t, *J* = 7.2 Hz, 2H), 5.76 (s, 1H), 6.04 (s, 1H), 7.53 (t, *J* = 7.2 Hz, 2H), 7.59 (t, *J* = 6.4 Hz, 2H), 7.85-7.90 (m, 6H), 7.94 (d, *J* = 8.4 Hz, 1H), 8.06 (dd, *J* = 8.4, 1.6 Hz, 1H), 8.24 (s, 1H), 8.51 (s, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 27.76, 37.26, 123.81, 125.35, 126.71, 126.73, 127.17, 127.72 (two overlapping peaks), 128.16, 128.22, 128.43, 128.47, 129.34, 129.57, 129.86, 131.14, 132.16, 132.50, 134.06, 134.89, 135.16, 135.57, 146.90, 198.12, 199.27.
IR (neat) 1714 w, 1677 m, 1651 m; 1520 m, 1326 w, 1278 w, 1220 s, 1121 m, 863 w.
MS *m/z* (relative intensity, %) 364 (M^+, 25), 209 (56), 194 (14), 166 (18), 155 (100), 127 (70).
HRMS Calcd for $C_{26}H_{20}O_2$: 364.1463; Found: 364.1462.

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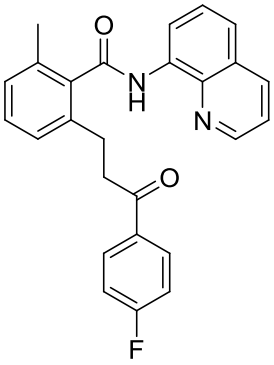
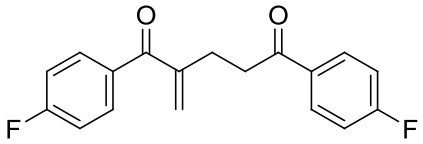
2-(3-(4-fluorophenyl)-3-oxopropyl)-6-methyl-N-(quinolin-8-yl)benzamide (3ak)



Rf 0.28 (hexane/EtOAc = 80/20). Yellow oil
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.47 (s, 3H), 3.15 (t, *J* = 8 Hz, 2H), 3.37 (t, *J* = 7.2 Hz, 2H), 6.94 (t, *J* = 8.8 Hz, 2H), 7.16 (d, *J* = 8 Hz, 1H), 7.21 (d, *J* = 7.2 Hz, 1H), 7.30 (d, *J* = 8 Hz, 1H), 7.40 (dd, *J* = 8.4, 4.4 Hz, 1H), 7.55 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.59 (t, *J* = 8 Hz, 1H), 7.88-7.92 (m, 2H), 8.14 (dd, *J* = 8, 1.2 Hz, 1H), 8.69 7.40 (dd, *J* = 4, 1.6 Hz, 1H), 8.99 (dd, *J* = 7.2, 1.2 Hz, 1H), 10.02 (s, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 19.36, 28.50, 40.94, 115.29 (d, *J* = 21 Hz), 116.71, 121.59, 122.07, 127.13 (d, *J* = 10 Hz), 127.85, 128.30, 129.24, 130.56, 130.66, 132.83 (d, *J* = 3 Hz), 134.05, 134.53, 136.25, 137.75 (two overlapping peaks), 138.28, 148.20, 165.40 (d, *J* = 254 Hz), 168.57, 197.46.
IR (neat) 3344 w, 3066 w, 1681 m, 1597 m, 1521 s, 1483 m, 1326 m, 1229 m, 1156 m, 980 w, 827 w.
MS *m/z* (relative intensity, %) 412 (M^+, 36), 289 (46), 269 (50), 145 (50), 123 (100), 95 (15).
HRMS Calcd for $C_{26}H_{21}FN_2O_2$: 412.1587; Found: 412.1586.

1,5-bis(4-fluorophenyl)-2-methylenepentane-1,5-dione (9k)



Isolated by HPLC in 30 % yield as a side product of the reaction of **2k** with **1a**.

Rf 0.4 (hexane/EtOAc = 80/20). Brown solid. **Mp** = 92 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.87 (t, *J* = 6.8 Hz, 2H), 3.19 (t, *J* = 7.2 Hz, 2H), 5.62 (s, 1H), 5.93 (s, 1H), 7.07-7.12 (m, 4H), 7.75-7.78 (m, 2H), 7.96-8.00 (m, 2H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 27.35, 37.01, 115.31 (d, *J* = 22 Hz),115.64 (d, *J* = 22 Hz), 126.79, 130.65 (d, *J* = 9.6 Hz), 131.02 (d, *J* = 9.6 Hz), 133.02 (d, *J* = 2.8 Hz), 133.73 (d, *J* = 2.9 Hz), 146.49, 165.22 (d, *J* = 254 Hz), 165.67 (d, *J* = 255 Hz), 196.50, 197.46.
IR (neat) 2926 w, 1683 m, 1656 m, 1598 s, 1523 m, 1506 m, 1484 w, 1411 w, 1228 m, 1156 m, 847 m.
MS *m/z* (relative intensity, %) 300 (M^+, 6), 177 (58), 123 (100), 95 (29).
HRMS Calcd for $C_{18}H_{14}F_2O_2$: 300.0962; Found: 300.0963.

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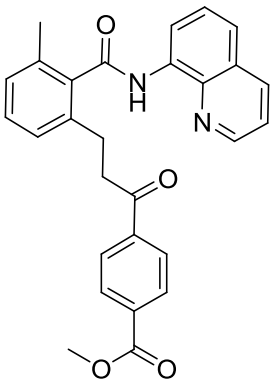
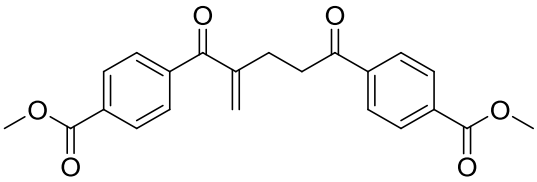
methyl 4-(3-(3-methyl-2-(quinolin-8-ylcarbamoyl)phenyl)propanoyl)benzoate (3al)



Rf 0.28 (hexane/EtOAc = 80/20). White solid. **Mp** = 122 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.45 (s, 3H), 3.14 (t, *J* = 8.4 Hz, 2H), 3.42 (t, *J* = 7.2 Hz, 2H), 3.92 (s, 3H), 7.17 (d, *J* = 8 Hz, 1H), 7.21 (d, *J* = 7.2 Hz, 1H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.43 (dd, *J* = 8, 4 Hz, 1H), 7.57 (dd, *J* = 8, 2 Hz, 1H), 7.60 (t, *J* = 8.4 Hz, 1H), 7.92 (d, *J* = 8.8 Hz, 2H), 7.97 (d, *J* = 8.8 Hz, 2H), 8.17 (dd, *J* = 8, 1.2 Hz, 1H), 8.70 (dd, *J* = 4, 1.6 Hz, 1H), 8.95 (dd, *J* = 6.8, 2 Hz, 1H), 9.98 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 19.48, 28.38, 41.48, 52.39, 116.92, 121.69, 122.18, 127.20, 127.35, 128.00, 128.46, 129.36, 129.63, 133.60, 134.13, 134.73, 136.41, 137.76 (two overlapping peaks), 137.88, 138.41, 139.73, 148.29, 166.18, 168.65, 198.72.
IR (neat) 3348 w, 1682 s, 1522 s, 1328 m, 1279 m, 1109 w, 823 m.
MS *m/z* (relative intensity, %) 452 (M^+, 24), 309 (47), 289 (66), 274 (10), 163 (100), 145 (65), 135 (14).
HRMS Calcd for $C_{28}H_{24}N_2O_4$: 452.1736; Found: 452.1741.

2-methylene-1,5-bis(4-(methylester)phenyl)pentane-1,5-dione (9l)



Isolated by HPLC in 29 % yield as a side product of the reaction of **2l** with **1a**.

Rf 0.22 (hexane/EtOAc = 80/20). White solid. **Mp** = 175 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.91 (t, *J* = 7.6 Hz, 2H), 3.28 (t, *J* = 6.8 Hz, 2H), 3.94 (s, 3H), 5.70 (s, 1H), 6.05 (s, 1H), 7.74 (d, *J* = 8 Hz, 2H), 8.02 (d, *J* = 8.8 Hz, 2H), 8.09 (d, *J* = 8.8 Hz, 2H), 8.11 (d, *J* = 10.4 Hz, 2H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 26.85, 37.54, 52.43, 52.46, 127.97, 128.93, 129.20, 129.42, 129.86, 133.03, 133.91, 139.81, 141.46, 146.38, 166.16, 166.25, 197.34, 198.58.
IR (neat) 1678 s, 1514 s, 1255 m, 1101 w, 820 m.
MS *m/z* (relative intensity, %) 380 (M^+, 8), 349 (14), 217 (65), 163 (100), 135 (17), 103 (11).
HRMS Calcd for $C_{22}H_{20}O_6$: 380.1260; Found: 380.1264.

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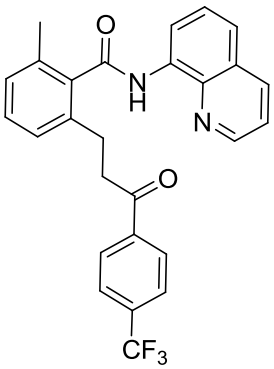
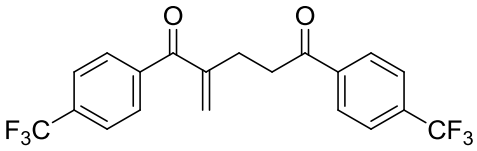
2-methyl-6-(3-oxo-3-(4-(trifluoromethyl)phenyl)propyl)-N-(quinolin-8-yl)benzamide (3am)



Rf 0.45 (hexane/EtOAc = 80/20). Yellow oil
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.46 (s, 3H), 3.14 (t, *J* = 8 Hz, 2H), 3.42 (t, *J* = 7.6 Hz, 2H), 7.18 (d, *J* = 14 Hz, 1H), 7.20 (d, *J* = 14.8 Hz, 1H), 7.31 (t, *J* = 8 Hz, 1H), 7.43 (dd, *J* = 8, 4 Hz, 1H), 7.53-7.6 (m, 4H), 7.98 (d, *J* = 8.4 Hz, 2H), 8.18 (dd, *J* = 8, 1.2 Hz, 1H), 8.70 (dd, *J* = 4.4, 1.6 Hz, 1H), 8.96 (dd, *J* = 7.6, 2 Hz, 1H), 10.00 (s, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 19.47, 28.52, 41.41, 116.89, 121.70, 122.22, 123.51 (q, *J* = 271 Hz), 125.42 (q, *J* = 3.8 Hz), 127.21, 127.32, 128.00, 128.43, 128.52, 129.38, 134.09 (q, *J* = 129.5 Hz), 134.12, 134.74, 136.41, 137.62, 137.86, 138.39, 139.10, 148.30, 168.65, 198.28.
IR (neat) 3348 w, 1672 s, 1520 s, 1482 m, 1323 s, 1167 m, 1126 s, 1065 m, 826 m.
MS *m/z* (relative intensity, %) 462 (M^+, 42), 319 (65), 289 (66), 275 (11), 173 (100), 145 (85).
HRMS Calcd for $C_{27}H_{21}F_3N_2O_2$: 462.1555; Found: 462.1554.

2-methylene-1,5-bis(4-(trifluoromethyl)phenyl)pentane-1,5-dione (9m)



Isolated by HPLC in 38 % yield as a side product of the reaction of **2m** with **1a**.

Rf 0.54 (hexane/EtOAc = 80/20). White solid. **Mp** = 102 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.91 (t, *J* = 7.2 Hz, 2H), 3.28 (t, *J* = 7.6 Hz, 2H), 5.70 (s, 1H), 6.06 (s, 1H), 7.67 (d, *J* = 8.4 Hz, 1H), 7.67 (d, *J* = 8.4 Hz, 1H), 7.79 (d, *J* = 8 Hz, 1H), 8.06 (d, *J* = 8 Hz, 1H.
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 26.76, 37.42, 123.51 (q, *J* = 272 Hz), 123.57 (q, *J* = 272 Hz), 125.22 (q, *J* = 3.8 Hz), 125.67 (q, *J* = 3.8 Hz), 128.36, 128.99, 129.56, 133.49 (q, *J* = 23 Hz), 134.38 (q, *J* = 23 Hz), 139.21, 140.77, 146.22, 196.77, 198.00.
IR (neat) 2932 w, 1685 m, 1644 m, 1409 m, 1326 s, 1173 m, 1131 s, 1067 m, 996 w, 852 m.
MS *m/z* (relative intensity, %) 400 (M^+, 6), 227 (62), 173 (100), 145 (43).
HRMS Calcd for $C_{20}H_{14}F_6O_2$: 400.0896; Found: 400.0898.

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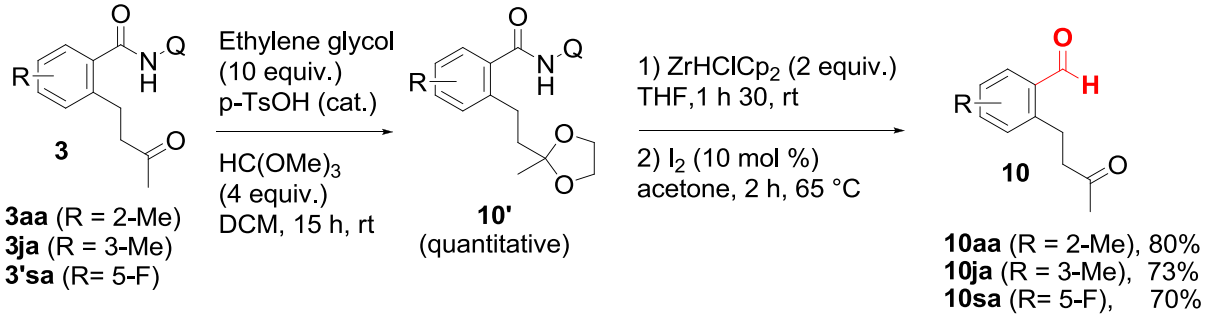
X. Removal of the 8-Aminoquinoline Directing Group

a) General procedure for the formation of the aldehyde (GP8)



3

3aa (R = 2-Me)
3ja (R = 3-Me)
3'sa (R= 5-F)

10'
(quantitative)

10

10aa (R = 2-Me), 80%
10ja (R = 3-Me), 73%
10sa (R= 5-F), 70%

Step 1: Alkylated amine **3** (1 mmol, 1 equiv.), ethylene glycol (620 mg, 10 mmol, 10 equiv.) and trimethyl orthoformate (424 mg, 4 mmol, 4 equiv.) were dissolved in 5 mL of DCM. Then p-toluenesulfonic acid (9.5 mg, 0.05 mmol, 5 mol %) was added at room temperature. The solution was stirred overnight at room temperature then satNaHCO$_3$aq (10 mL) was added and the organic layer was separated. Aqueous layer was extracted with DCM (2 x 10 mL) and the combined organic layers evaporated *in vacuo*. The intermediate dioxolane **10'** was purified by column chromatography through silica gel (hexane/EtOAc) then put to react in step 2.

Step 2: In an oven-dried one neck round bottom flask, dioxolane **10'** (1 mmol) was dissolved in THF (10 mL) and Bis(cyclopentadienyl)zirconium(IV) chloride hydride (ZrHClCp$_2$) (515 mg, 2 mmol, 2 equiv.) was added at 0 °C.[9] The solution was then stirred 1 h 30 at room temperature until forming a clear and limpid solution. HCl 1M (5 mL) was then added, the biphasic mixture was stirred 10 min and the organic layer separated. Aqueous layer was then extracted with Et$_2$O (2 x 10 mL) and combined organic layers evaporated in vacuo.
Then, the resulting oil was dissolved in dried acetone (10 mL) and iodine (13 mg, 0.1 mmol, 10 mol %) was added. A reported procedure was followed.[10] The solution was refluxed 2 h to ensure the complete cleavage of the dioxolane protecting group. If the reaction doesn't go at completion, then iodine (10%) can be added again. Aldehyde **10** was purified by column chromatography through silica gel (hexane/EtOAc).

[9] If the amide is not sterically hindered, formation of a small amount of the corresponding benzylic alcohol may be observed if too much equivalents of zirconium reagent are used.

[10] J. Sun, Y. Dong, L. Cao, X. Wang, S. Wang, Y. Hu, *J. Org. Chem.* **2004**, *69*, 8932.

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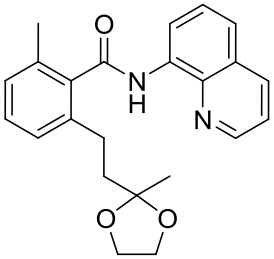
b) Spectroscopic Data of Aldehydes 10

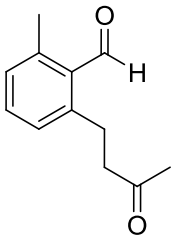
2-methyl-6-(2-(2-methyl-1,3-dioxolan-2-yl)ethyl)-N-(quinolin-8-yl)benzamide (10'aa)



Synthesized according to **GP8** (step 1) from amide **3aa** (1mmol, 332 mg). Purification by column chromatography through silica gel (hexane/EtOAc = 80/20) afforded 375 mg of **10'aa** (quantitative yield).

Rf 0.24 (hexane/EtOAc = 80/20). Yellow oil
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 1.22 (s, 3H), 2.02 (td, *J* = 8.8, 4.4 Hz, 2H), 2.43 (s, 3H), 2.82 (td, *J* = 8.4, 4.4 Hz, 2H), 3.69-3.80 (m, 4H), 7.12 (d, *J* = 7.6 Hz, 1H), 7.15 (d, *J* = 7.2 Hz, 1H), 7.27 (t, *J* = 8 Hz, 1H), 7.42 (dd, *J* = 8, 4 Hz, 1H), 7.55 (d, *J* = 7.6 Hz, 1H), 7.60 (t, *J* = 7.6 Hz, 1H), 8.16 (dd, *J* = 8.4, 1.2 Hz, 1H), 8.72 (dd, *J* = 4, 1.2 Hz, 1H), 8.99 (d, *J* = 7.2 Hz, 1H), 9.94 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 19.40, 23.41, 28.29, 40.92, 64.35, 109.32, 116.68, 121.57, 121.84, 126.79, 127.32, 127.83, 127.86, 129.06, 134.27, 134.50, 136.24, 137.71, 138.38, 138.76, 148.16, 168.58.
IR (neat) 3345 w, 2879 w, 1673 m, 1519 s, 1481 s, 1325 m, 1127 w, 1054 m, 908 m, 826 m.
MS *m/z* (relative intensity, %) 376 (M^+, 15), 289 (15), 189 (22), 145 (26), 144 (23), 87 (100), 43 (18).
HRMS Calcd for $C_{23}H_{24}N_2O_3$: 376.1787; Found: 376.1785.

2-methyl-6-(3-oxobutyl)benzaldehyde (10aa)



10'aa (1 mmol) was put to react according to **GP8** (step 2). Purification by column chromatography through silica gel (hexane/EtOAc = 80/20) afforded 152 mg of **10aa** (80 % yield).

Rf 0.27 (hexane/EtOAc = 85/15). Yellow oil
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.09 (s, 3H), 2.56 (s, 3H), 2.70 (t, *J* = 8 Hz, 2H), 3.11 (t, *J* = 7.6 Hz, 2H), 7.05 (d, *J* = 4.8 Hz, 1H), 7.07 (d, *J* = 4.4 Hz, 1H), 7.29 (t, *J* = 8 Hz, 1H), 10.52 (s, 1H).

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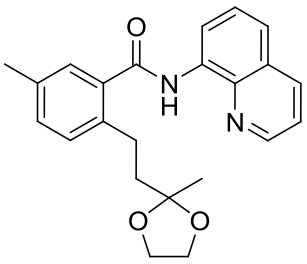
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 20.03, 27.63, 29.69, 45.20, 129.13, 129.94, 131.91, 133.07, 141.49, 143.60, 193.13, 207.56.
IR (neat) 2961 w, 1714 s, 1467 m, 1239 m, 1120 w, 1075 w.
HRMS Calcd for $C_{12}H_{14}O_2$: 190.0994; Found: 188.0839 (M^+-2H)

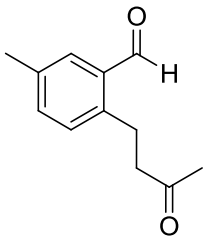
5-methyl-2-(2-(2-methyl-1,3-dioxolan-2-yl)ethyl)-N-(quinolin-8-yl)benzamide (10'ja)



Synthesized according to **GP8** (step 1) from amide **3ja** (1mmol, 332 mg). Purification by column chromatography through silica gel (hexane/EtOAc = 80/20) afforded 375 mg of **10'ja** (quantitative yield).

Rf 0.28 (hexane/EtOAc = 80/20). Brown solid. **Mp** = 115 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 1.30 (s, 3H), 2.01 (td, *J* = 8.8, 4.8 Hz, 2H), 2.39 (s, 3H), 2.96 (td, *J* = 8.8, 5.2 Hz, 2H), 3.81-3.89 (m, 4H), 7.23 (d, *J* = 0.8 Hz, 2H), 7.44 (s, 1H), 7.46 (dd, *J* = 8, 4 Hz, 1H), 7.55 (dd, *J* = 8.4, 2 Hz, 1H), 7.60 (t, *J* = 8.4 Hz, 1H), 8.19 (dd, *J* = 8.4, 1.6 Hz, 1H), 8.78 (dd, *J* = 4, 1.6 Hz, 1H), 8.95 (d, *J* = 6.8 Hz, 1H), 10.14 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 20.91, 23.58, 27.82, 40.80, 64.48, 109.58, 116.54, 121.57, 121.65, 127.39, 127.75, 127.91, 130.27, 131.00, 134.71, 135.74, 136.33, 136.61, 137.52, 138.46, 148.13, 168.32.
IR (neat) 3353 w, 2878 w, 1673 m, 1520 s, 1482 m, 1325 m, 1053 m, 826 m.
MS *m/z* (relative intensity, %) 376 (M^+, 30), 331 (13), 289 (22), 189 (12), 145 (38), 144 (22), 87 (100), 43 (15).
HRMS Calcd for $C_{23}H_{24}N_2O_3$: 376.1787; Found: 376.1780.

5-methyl-2-(3-oxobutyl)benzaldehyde (10ja)

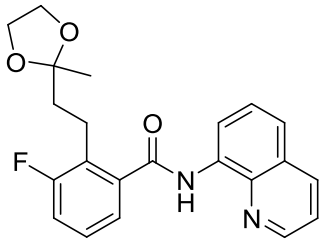


10'ja (1 mmol) was put to react according to **GP8** (step 2). Purification by column chromatography through silica gel (hexane/EtOAc = 80/20) afforded 138 mg of **10ja** (80 % yield).

Rf 0.34 (hexane/EtOAc = 80/20). Yellow oil.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.13 (s, 3H), 2.38 (s, 3H), 2.73 (t, *J* = 7.6 Hz, 2H), 3.23 (t, *J* = 7.2 Hz, 2H), 7.19 (d, *J* = 8 Hz, 1H), 7.31 (dd, *J* = 8, 1.6 Hz, 1H), 7.59 (s, 1H), 10.14 (s, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 20.71, 26.68, 29.90, 45.00, 131.31, 133.53, 134.18, 134.62, 136.62, 140.46, 193.04, 207.79.
IR (neat) 2925 w, 1713 s, 1690 s, 1612 w, 1361 w, 1161w, 823 w.
MS *m/z* (relative intensity, %) 190 (M^+, 8), 172 (100), 147 (75), 132 (68), 119 (36), 105 (40), 91 (30), 77 (19), 43 (51).
HRMS Calcd for $C_{12}H_{14}O_2$: 190.0994; Found: 190.0986.

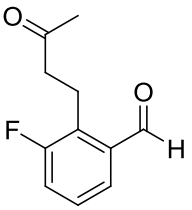
3-fluoro-2-(2-(2-methyl-1,3-dioxolan-2-yl)ethyl)-N-(quinolin-8-yl)benzamide (10'sa)



Synthesized according to **GP8** (step 1) from amide **3'sa** (1mmol, 336 mg). Purification by column chromatography through silica gel (hexane/EtOAc = 80/20) afforded 334 mg of **10'sa** (quantitative yield).

Rf 0.34 (hexane/EtOAc = 80/20). White solid. **Mp** = 95 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 1.34 (s, 3H), 2.04 (td, *J* = 8.8, 5.2 Hz, 2H), 2.98-3.02 (m, 2H), 3.82-3.89 (m, 4H), 7.16 (td, *J* = 9.6, 0.8 Hz, 1H), 7.29 (td, *J* = 7.6, 4.8 Hz, 1H), 7.42 (d, *J* = 2.8 Hz, 1H), 7.44 (t, *J* = 4 Hz, 1H), 7.54 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.58 (t, *J* = 8.4 Hz, 1H), 8.16(dd, *J* = 8.4, 2 Hz, 1H), 8.76 (dd, *J* = 4, 1.6 Hz, 1H), 8.95 (d, *J* = 6.8 Hz, 1H), 10.14 (brs, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 21.21 (d, *J* = 3 Hz), 23.38, 38.94, 64.40, 109.43, 116.55, 117.11 (d, *J* = 23 Hz), 121.65, 121.92, 122.68 (d, *J* = 3.8 Hz), 127.29, 127.53 (d, *J* = 8.6 Hz), 127.86, 128.17 (d, *J* = 17.2 Hz), 134.39, 136.31, 138.37, 138.85 (d, *J* = 4 Hz), 148.23, 161.47 (d, *J* = 246 Hz), 166.72 (d, *J* = 2.8 Hz).
IR (neat) 3345 w, 2982 w, 2881 w, 1674 m, 1520 s, 1485 m, 1384 m, 1326 m, 1265 m, 1049 m, 865 m, 825 m.
MS *m/z* (relative intensity, %) 380 (M^+, 36), 335 (33), 293 (24), 149 (29), 144 (25), 87 (100), 43 (23).
HRMS Calcd for $C_{22}H_{21}FN_2O_3$: 380.1536; Found: 380.1536.

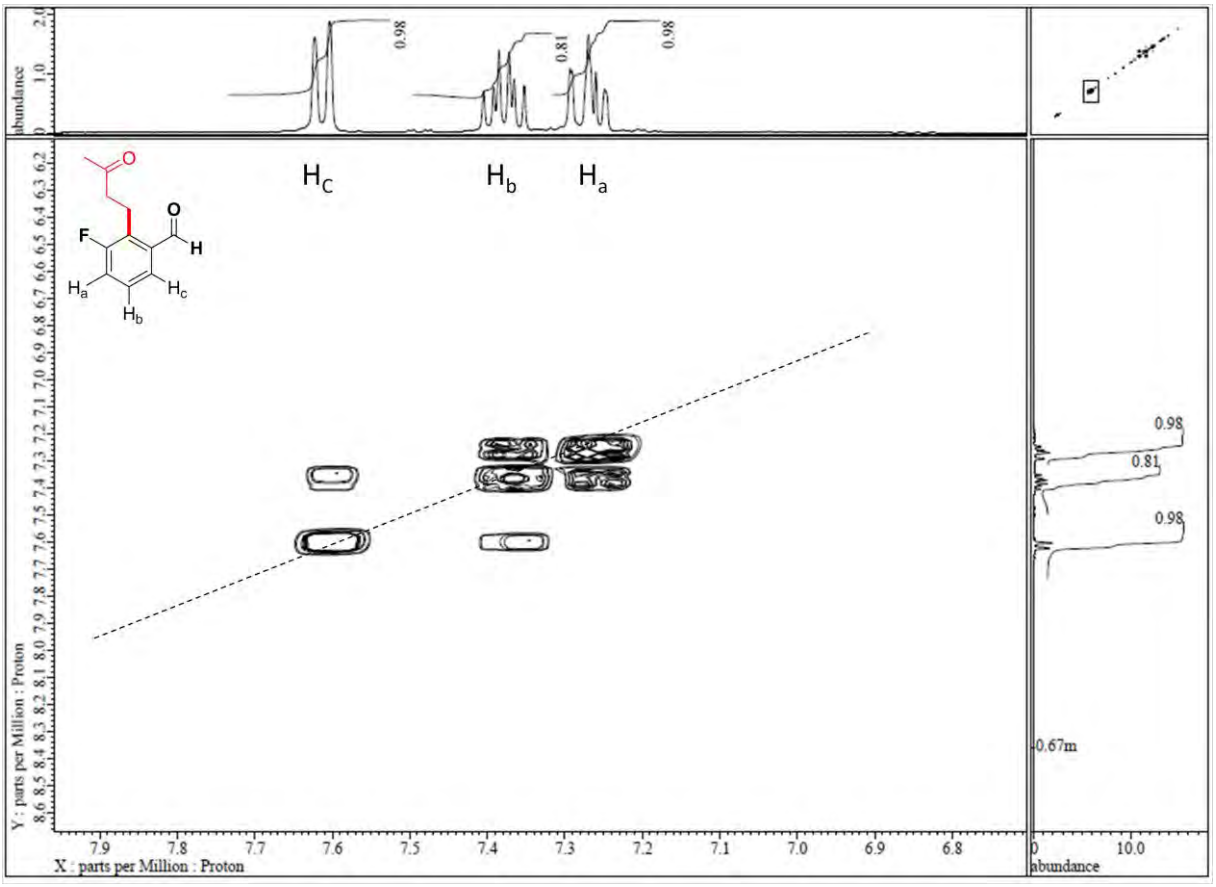
3-fluoro-2-(3-oxobutyl)benzaldehyde (10sa)



10'sa (1 mmol) was put to react according to **GP8** (step 2). Purification by column chromatography through silica gel (hexane/EtOAc = 80/20) afforded 135 mg of **10sa** (70 % yield).

Rf 0.28 (hexane/EtOAc = 80/20). Yellow oil

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.16 (s, 3H), 2.72 (t, *J* = 8.4 Hz, 2H), 3.29 (td, *J* = 8, 1.2 Hz, 2H), 7.27 (td, *J* = 9.2, 0.8 Hz, 1H), 7.37 (td, *J* = 7.6, 4.8 Hz, 1H), 7.61 (d, *J* = 7.2 Hz, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 18.47 (d, *J* = 4.8 Hz), 29.68, 43.43, 120.65 (d, *J* = 24 Hz), 127.89 (d, *J* = 8.6 Hz), 128.73 (d, *J* = 2.8 Hz), 130.07 (d, *J* = 16.3 Hz), 135.64 (d, *J* = 3.8 Hz), 161.30 (d, *J* = 246 Hz), 191.78 (d, *J* = 2.8 Hz), 207.23.
IR (neat) 2898 w, 1699 s, 1462 m, 1245 s, 1164 m, 824 w.
MS *m/z* (relative intensity, %) 194 (M^+, 2), 176 (26), 151 (45), 136 (36), 134 (14), 133 (19), 123 (12), 109 (25), 108 (11), 103 (19), 43 (100).
HRMS Calcd for $C_{11}H_{11}FO_2$: 194.0743; Found: 194.0741
COSY



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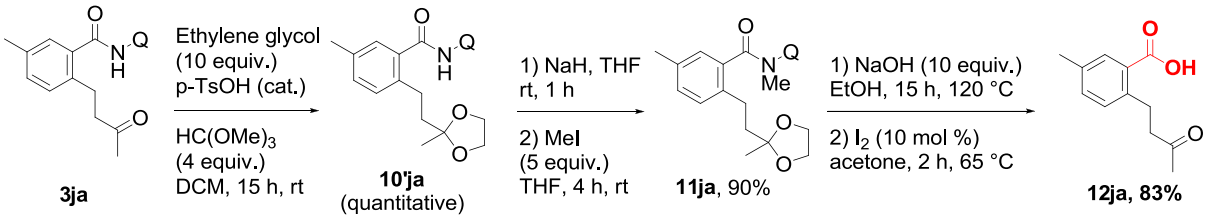
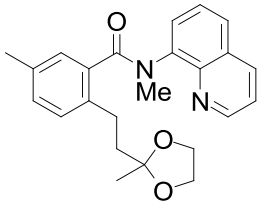
c) Synthesis of the carboxylic acid: representative procedure.



Methylation of 10'ja: 10'ja was synthesized as described above (see **GP8**). **10'ja** (1.37 mmol, 518 mg) was dissolved in THF (15 mL), then NaH (1.64 mmol, 1.2 equiv.) was added at 0°C to this solution. The mixture was then stirred at room temperature for 1 h. MeI (6.85 mmol, 0.42 mL) was added at 0°C and the solution stirred for 4 h at room temperature. H_2O (10 mL) was then added, the organic layer was separated and the aqueous layer extracted with Et_2O (3X). Combined organic layers were dried over Na_2SO_4 and solvent evaporated under vacuum. **11ja** was purified by column chromatography through silica gel (hexane/EtOAc: 30/70) and obtained as a yellow foam (480 mg, 90%).

Saponification+deprotection of 11ja: **11ja** (1 mmol, 390 mg) was dissolved in EtOH (10 mL) and NaOH (15 mmol, 600 mg) was added. The solution was heated for 15 h at 120 °C. After cooling at room temperature H_2O (15 mL) was added followed by DCM (10 mL). The DCM layer was separated (it contains the methylated aminoquinoline part). HCl_{aq} (10 mL, 4M) was added to the aqueous layer and the mixture of protected and deprotected caroboxylic acid **12ja** was extracted with DCM (3X). This mixture was dried over Na_2SO_4 and solvent was evaporated under vacuum. Then, the resulting oil was dissolved in dried acetone (10 mL) and iodine (13 mg, 0.1 mmol, 10 mol %) was added. A reported procedure was followed.[10] The solution was refluxed 2 h to ensure the complete cleavage of the dioxolane protecting group. If the reaction doesn't go at completion, then iodine (10%) can be added again. The reaction was cooled to room temperature and solvent evaporated under reduced pressure. **12ja** was purified by column chromatography through silica gel (hexane/EtOAc: 50/50) and was obtained as a yellow solid (171 mg, 83%).

N,5-dimethyl-2-(2-(2-methyl-1,3-dioxolan-2-yl)ethyl)-N-(quinolin-8-yl)benzamide (11ja)



Rf 0.2 (hexane/EtOAc = 30/70). Yellow foam
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 1.43 (s, 3H), 1.83-2.87 (massif of broad m, 7H), 3.60 (broad s, 3H), 4.00 (broad s, 4H), 6.72-6.81 (broad m, 2H), 7.29-7.82 (massif of broad m, 5H), 8.8 (broad s, 1H), 9.00 (dd, J = 3.6, 1.2 Hz, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 20.16, 23.55, 27.27, 37.26, 40.07, 64.36, 109.51, 121.28, 125.68, 127.19, 127.64, 128.20, 128.54, 128.75, 128.96, 133.55, 135.88, 136.24, 141.27, 143.84, 150.08, 171.50.
IR (neat) 2981 w, 2880 w, 1640 s, 1362 m, 1054 s, 911 m, 795, m, 684 s.

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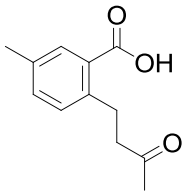
HRMS Calcd for $C_{24}H_{28}N_2O_3$: 390.1943; Found: 390.1946.

5-methyl-2-(3-oxobutyl)benzoic acid (12ja)



Rf 0.2 (hexane/EtOAc = 50/50). Yellow solid. **Mp** = 82 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.15 (s, 3H), 2.36 (s, 3H), 2.80 (t, *J* = 8 Hz, 2H), 3.21 (t, *J* = 8 Hz, 2H), 7.19 (d, *J* = 8 Hz, 1H), 7.29 (dd, *J* = 8, 0.8 Hz, 1H), 7.87 (d, *J* = 0.8 Hz, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 20.77, 28.51, 29.90, 45.36, 127.80, 131.39, 132.27, 134.00, 136.17, 140.85, 172.79, 208.68.
IR (neat) 2925 w, 1712 s, 1686 s, 1272 m, 1193 m, 734 m.
HRMS (CI+) Calcd for $C_{12}H_{15}O_3$ $(M+H^+)$: 207.1021; Found: 207.1019

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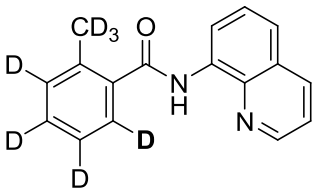
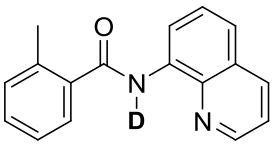
XI. Deuterium Labeling Experiments

Preparation of starting materials.



13

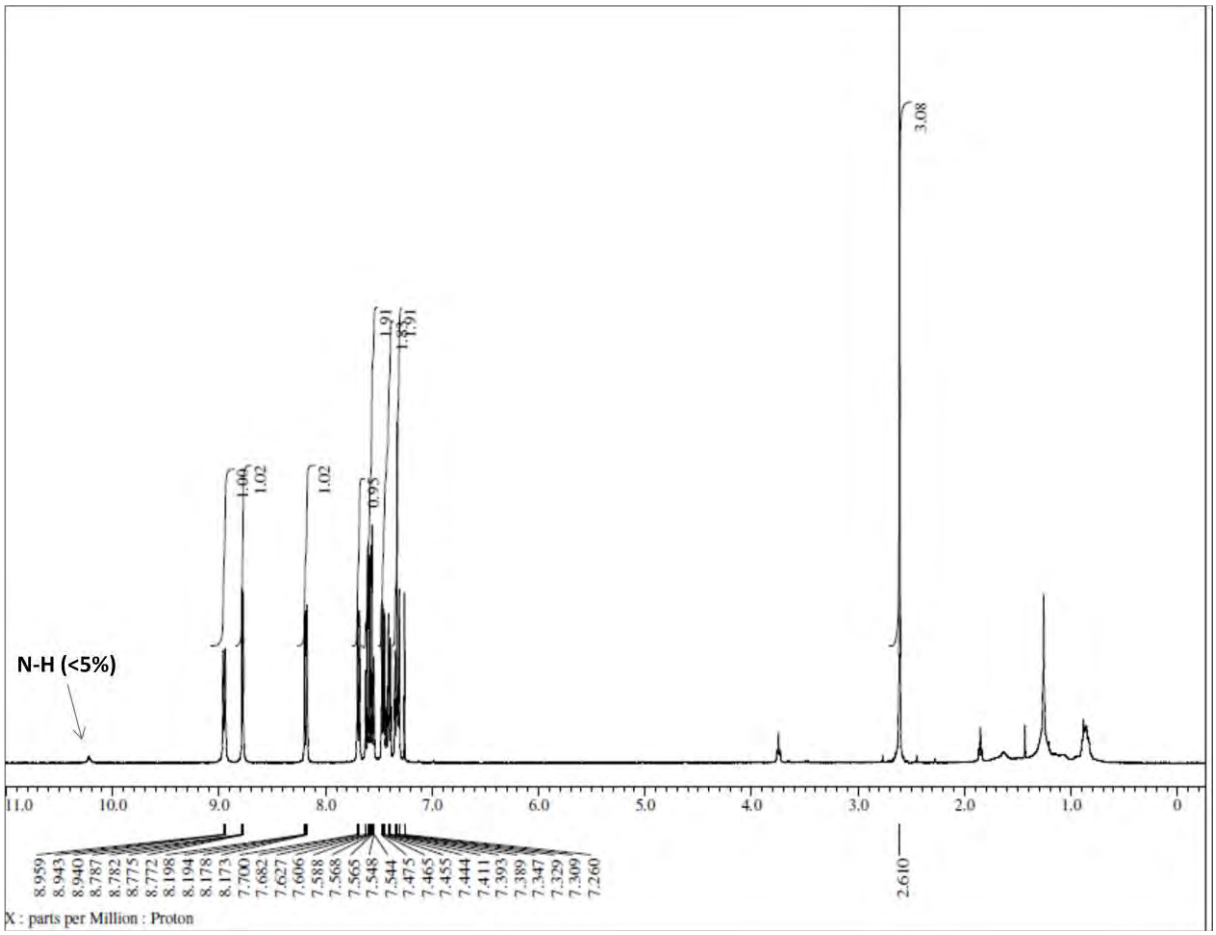
13 was prepared according to a reported procedure.[11]

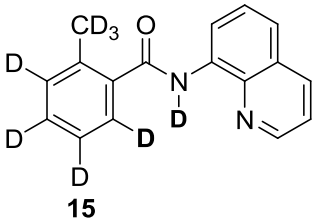


14

14 was prepared according to the following procedure: **1a** (1 mmol, 262 mg) was dissolved in 5 mL of THF, then NaH (1.2 mmol) was added at 0°C. The solution was allowed to reach room temperature and was stirred for 1 h. D_2O (0.5 mL) was then added at 0 °C and the solution was stirred 10 min at room temperature. Et_2O (dry, 10 mL) was added and the organic layer and the D_2O layer were then separated. Then, the organic layer washed with 0.5 mL of D_2O. Organic layer was then dried over Na_2SO_4 and the solvent evaporated under reduced pressure. The resulting solid (184 mg, 70%) was dried under vacuum for 10 h. According to ^1H NMR, the nitrogen contains 95% of deuterium. **14** was directly used without further purification.

White solid. **Mp** = 100 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.61 (s, 3H), 7.33 (t, 15.2 Hz, 2H), 7.40-7.48 (m , 2H), 7.55-7.63 (m, 2H), 7.69 (d, J = 7.6 Hz, 1H), 8.19 (dd, J = 8.4 , 2.0 Hz), 8.78 (dd, J = 4.0, 2.0 Hz, 1H), 8.95 (d, J = 7.6 Hz).
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 20.23, 116.41, 121.66, 121.77, 126.00, 127.23, 127.38, 127.96, 130.32, 131.37, 134.61, 136.33, 136.54, 136.67, 138.52, 148.26, 168.08.
IR (neat) 2925 w, 1666 s, 1500 s, 1471 s, 1405 s, 1359 s, 824 m, 790 m, 735 s.
HRMS Calcd for $C_{17}H_{13}DN_2O$: 263.1169; Found: 263.1142

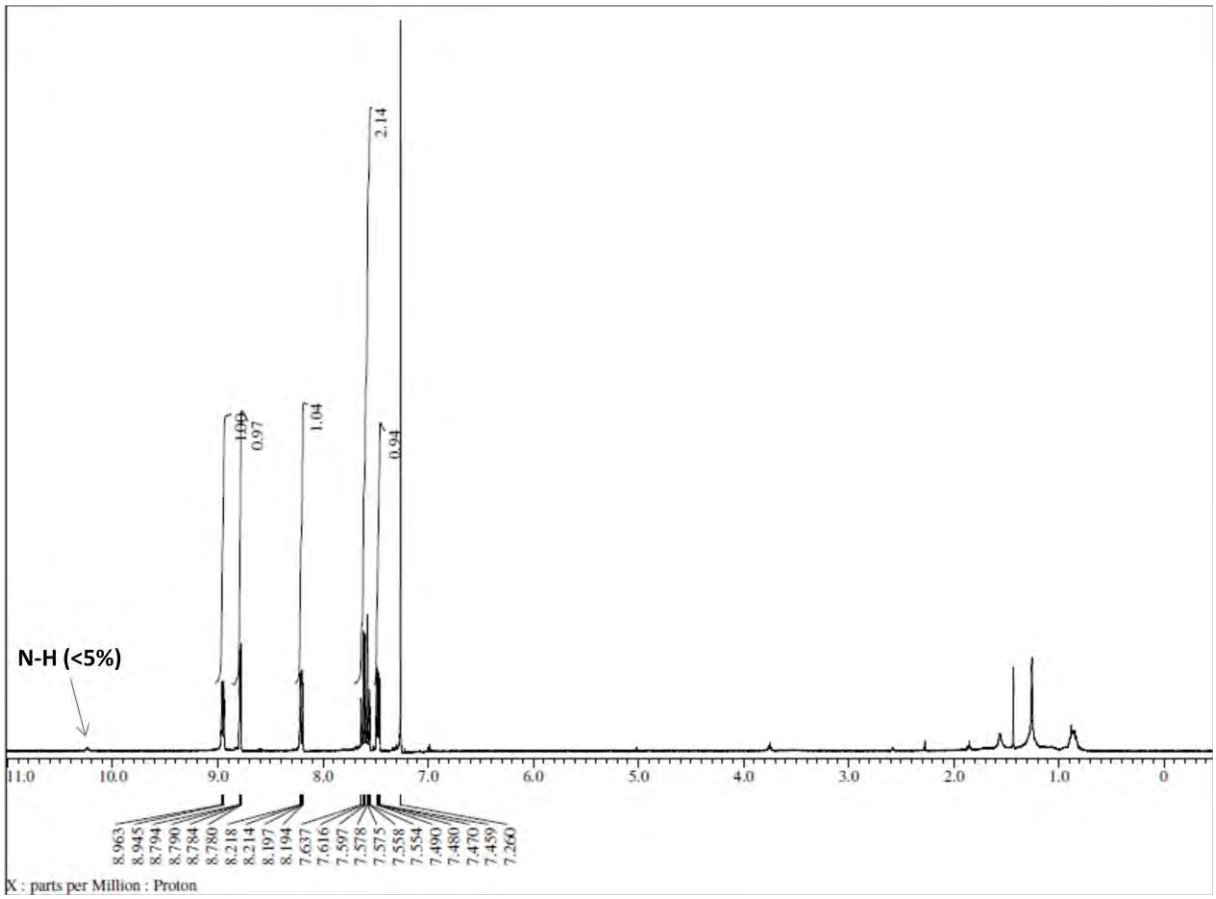




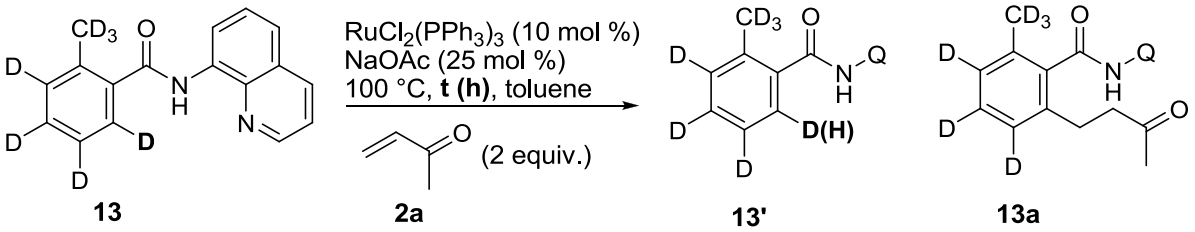
15

15 was prepared according to the following procedure: **13** (1 mmol, 269 mg) was dissolved in 5 mL of THF, then NaH (1.2 mmol) was added at 0°C. The solution was allowed to reach room temperature and was stirred for 1 h. D_2O (0.5 mL) was then added at 0 °C and the solution was stirred 10 min at room temperature. Et_2O (dry, 10 mL) was added and the organic layer and the D_2O layer were then separated. Then the organic layer washed with 0.5 mL of D_2O. Organic layer was then dried over Na_2SO_4 and the solvent evaporated under reduced pressure. The resulting solid (200 mg, 74%) was dried under vacuum for 10 h. According to ^1H NMR, the nitrogen contains 95% of deuterium. **15** was directly used without further purification.

White solid. **Mp** = 100 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 19.33 (septet, *J* = 19.2 Hz), 116.36, 121.61, 121.71, 125.45 (t, *J* = 24.4 Hz), 126.81 (t, *J* = 24.5 Hz), 127.35, 127.92, 129.78 (t, *J* = 24.0 Hz), 130.89 (t, *J* = 24.0 Hz), 134.64, 136.27 (two overlapping peaks), 136.43, 138.50, 148.22, 168.04.
IR (neat) 2924 w, 1668 s, 1518 s, 1415 s, 1167 w, 825 m, 791 m.
HRMS Calcd for $C_{17}H_6D_8N_2O$: 270.1608; Found: 270.1607



Deutrium labeling experiment: representative procedure.



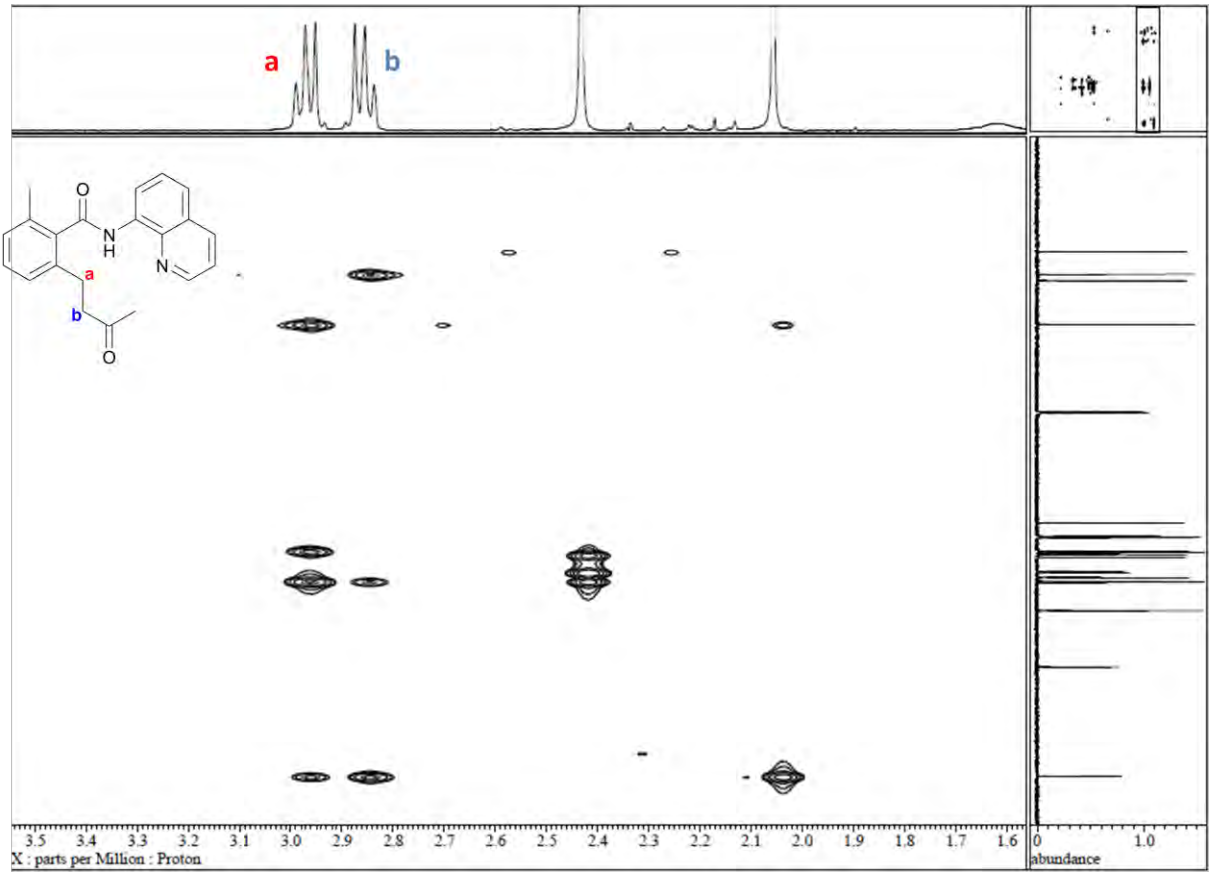
To an oven-dried 5 mL screw-capped vial, 2-methyl-N-(quinolin-8-yl)benzamide-***d*****$_7$** **11**[11] (134.5 mg, 0.5 mmol, 1 equiv.), MVK **2a** (70 mg, 1 mmol, 2 equiv.), $RuCl_2(PPh_3)_3$ (48 mg, 0.05 mmol, 10 mol %), sodium acetate (10.25 mg, 0.125 mmol, 25 mol %) and toluene (1 mL) were added under a gentle stream of nitrogen. The mixture was stirred for the appropriate time at 100 °C (108 °C bath temperature) then cooled to room temperature and concentrated *in vacuo*. Purification by column chromatography on silica gel afforded **13'** (hexane/EtOAc = 90/10) as a white solid, then **13a** as a yellow oil (hexane/EtOAc = 70/30). NMR ^{1}H of pure **13'** and **13a** gave an estimation of the rate of the H/D exchange.

*Experiments without **2a** were conducted in a similar way.*

[11] Synthesis of **11** : Ano, Y.; Tobisu, M.; Chatani, N. *Org. Lett*. **2012**, *14*, 354.

Preliminary studies

HMBC of 3aa



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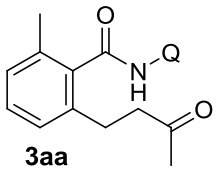
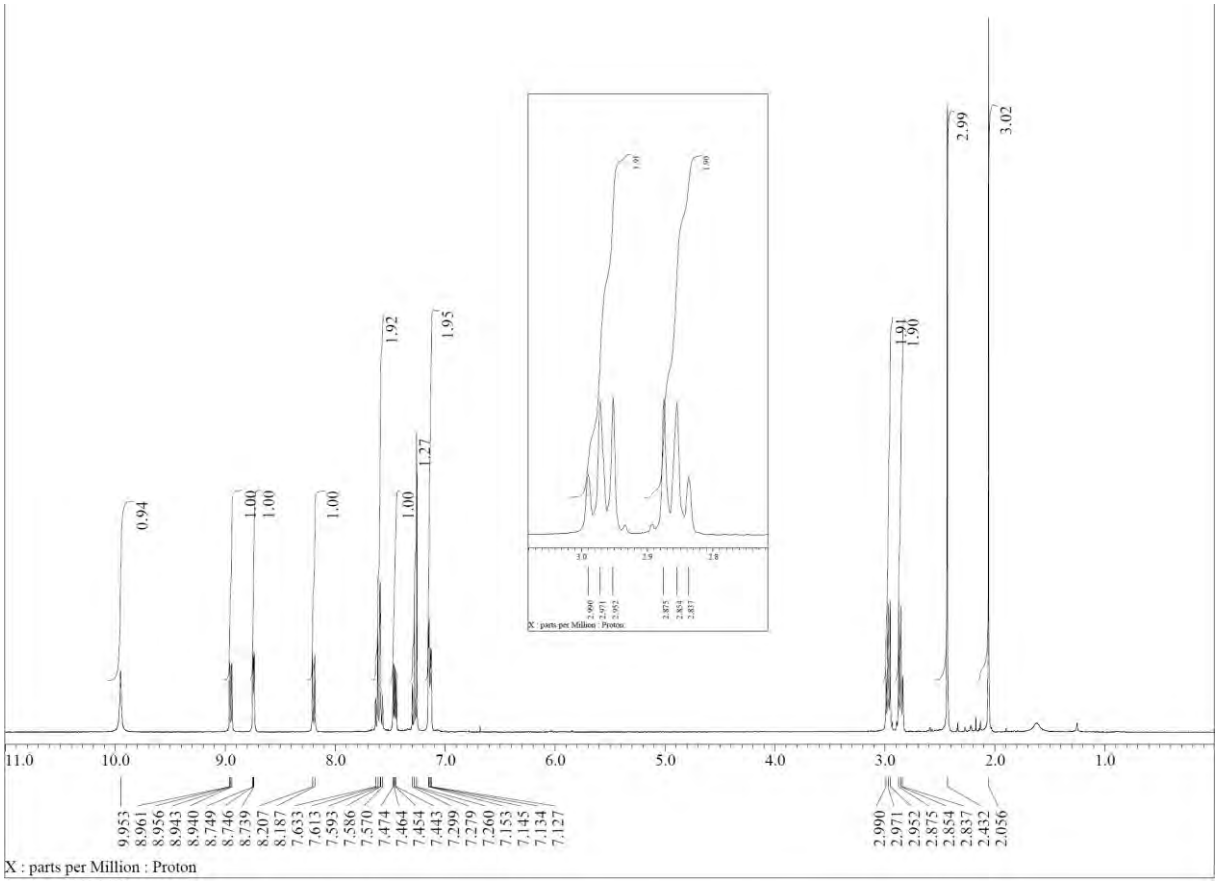
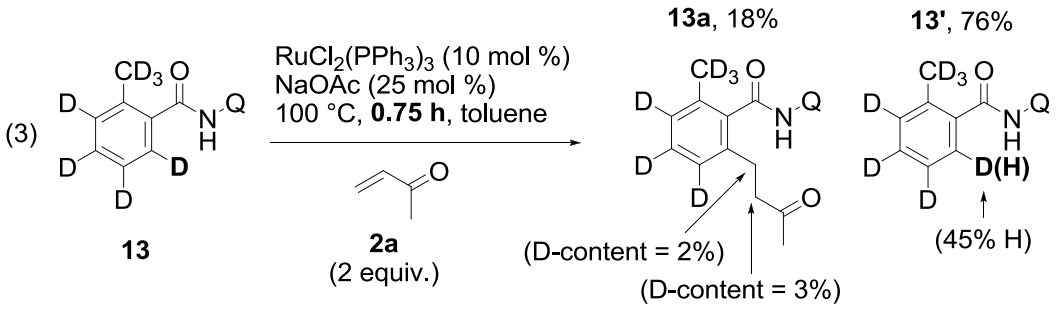
Reference ^{1}H NMR spectra for estimations of deuterium incorporation into the alkylated product.

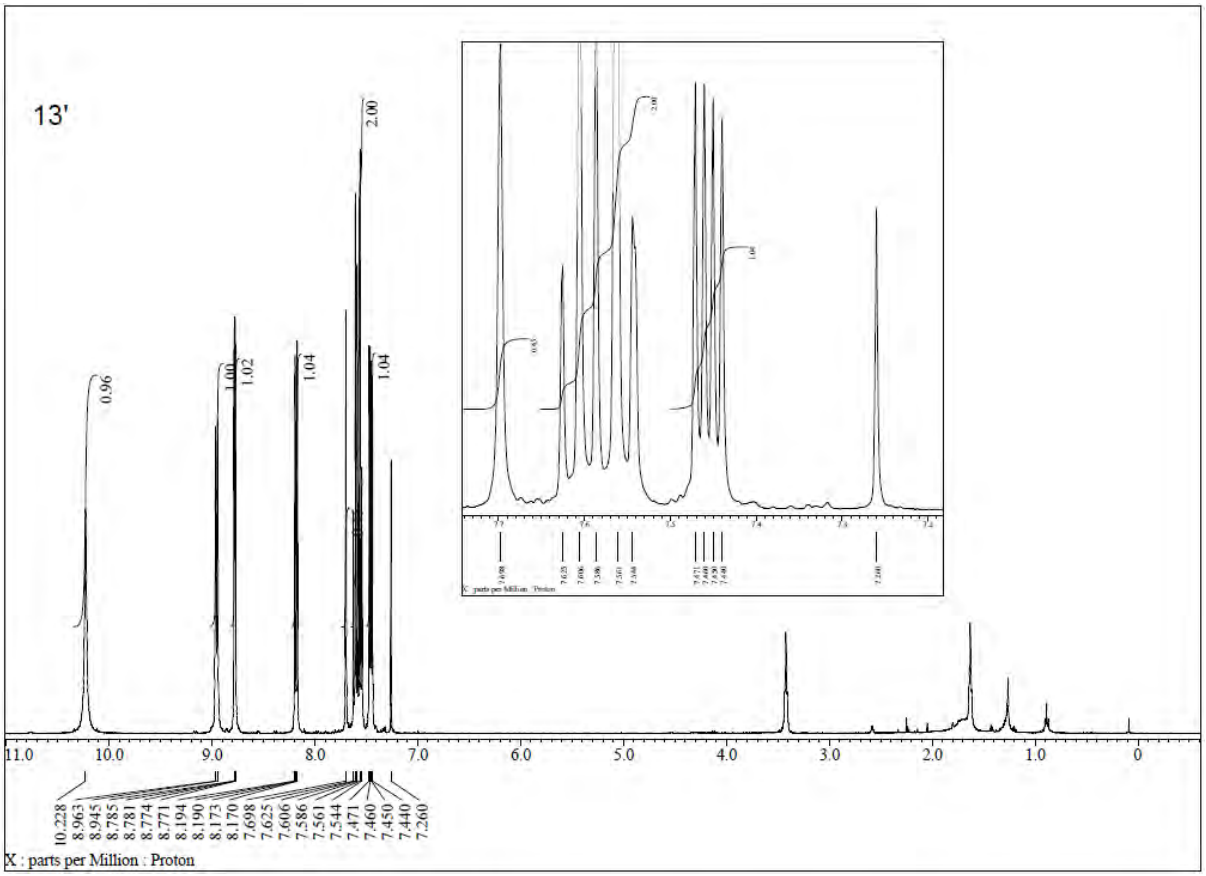


3aa



Deuterium Labeling Experiments: estimation of deuterium and hydrogen incorporation.





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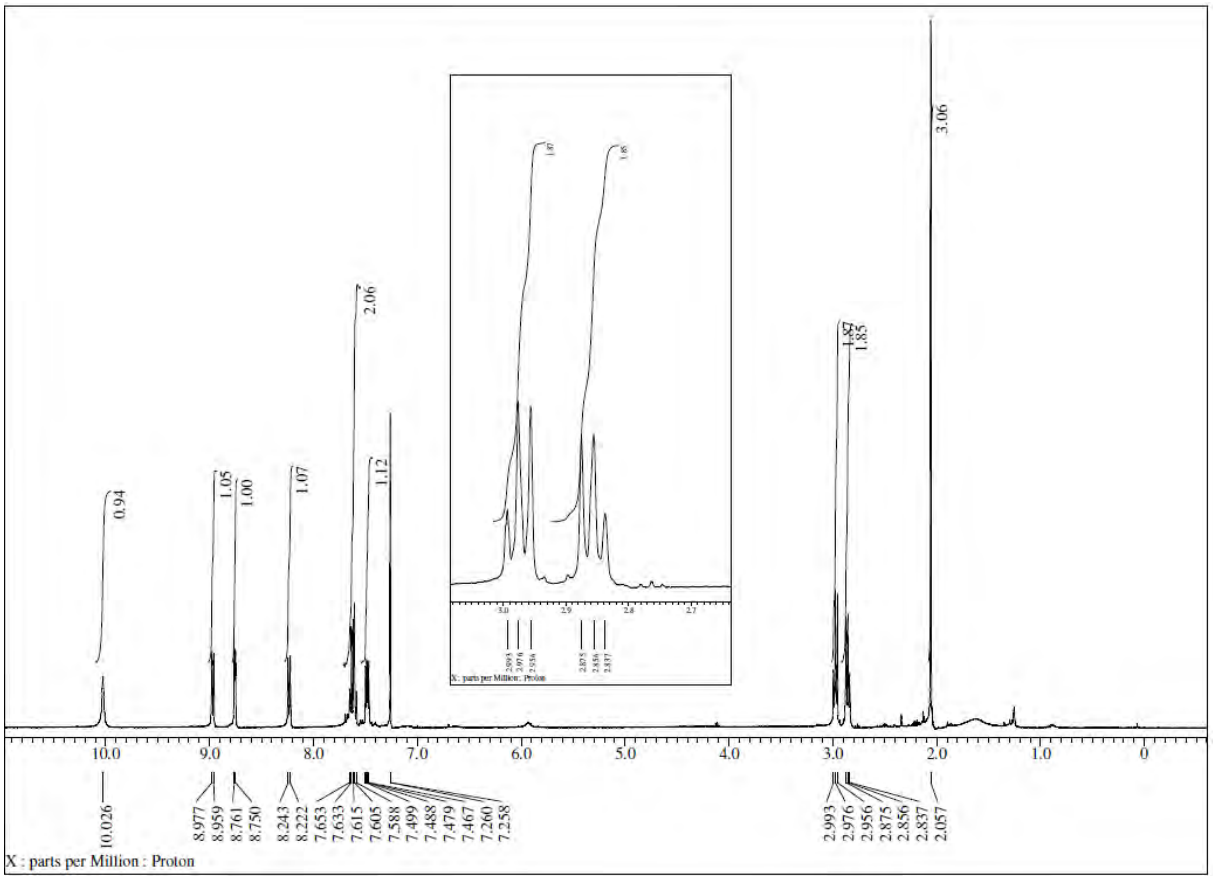
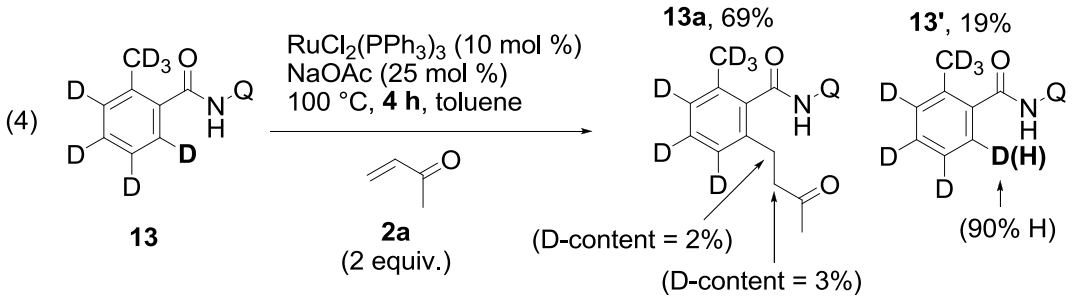
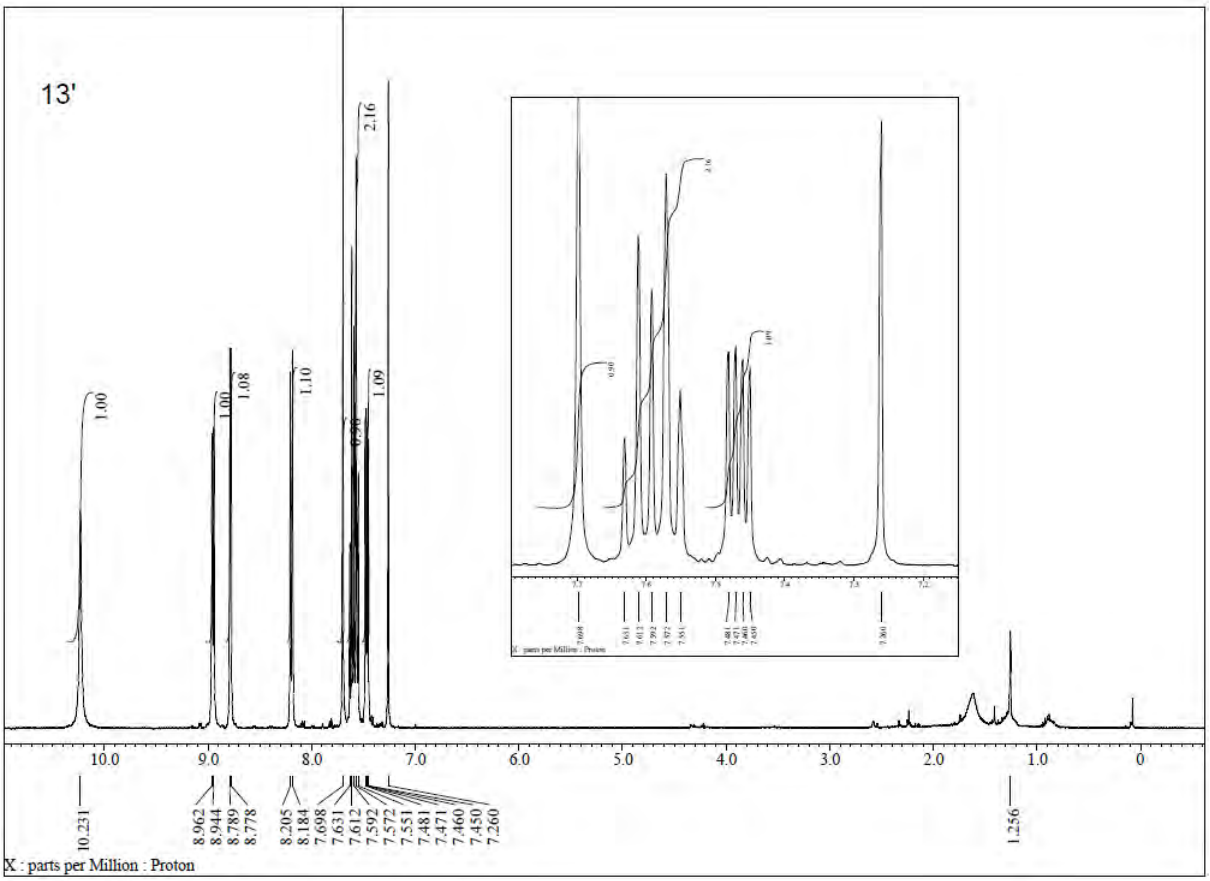
13a



C_a : 1.87/1.91=0.98. D-content = 2%
C_b : 1.85/1.90=0.97. D-content = 3%


(4)
CD3 O
D
D
D
D
N
H
Q
13
RuCl2(PPh3)3 (10 mol %)
NaOAc (25 mol %)
100 °C, 4 h, toluene
2a
(2 equiv.)
13a, 69%
(D-content = 2%)
(D-content = 3%)
13', 19%
D(H)
(90% H)


13'
1.00
1.00
1.08
1.10
0.96
2.16
1.09
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
10.231
8.962
8.944
8.789
8.778
8.205
8.184
7.698
7.631
7.612
7.592
7.572
7.551
7.481
7.471
7.460
7.450
7.260
1.256
X : parts per Million : Proton

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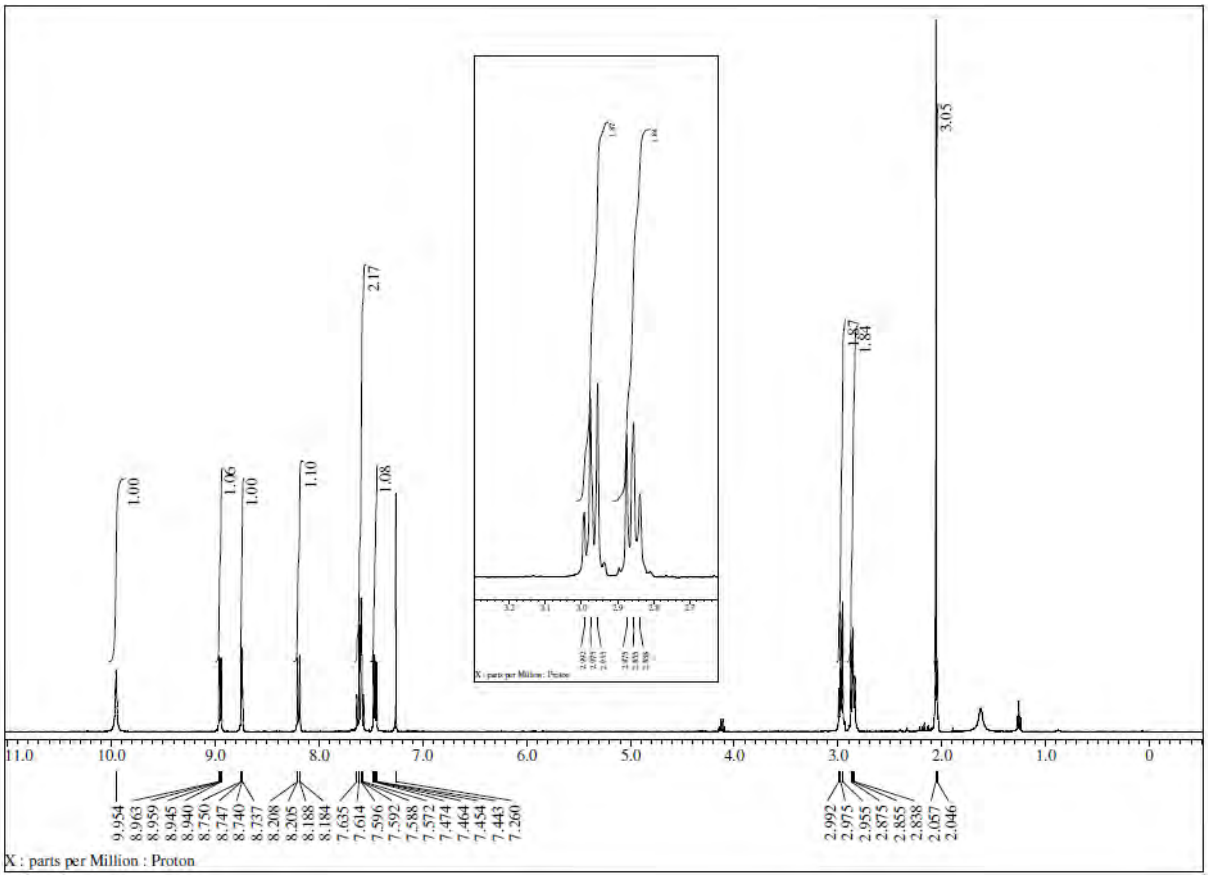
13a



C_a : 1.87/1.91=0.98. D-content = 2%
C_b : 1.84/1.90=0.97. D-content = 3%

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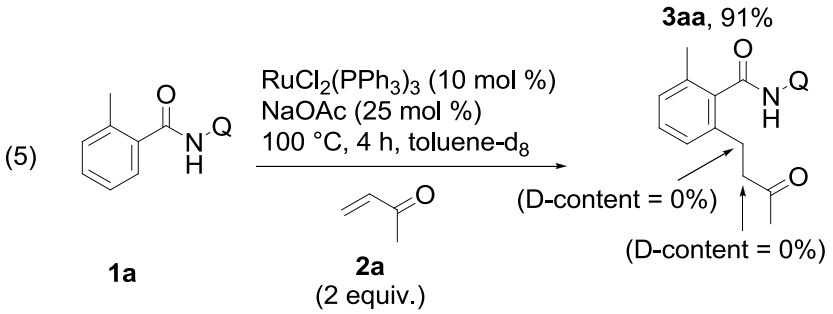

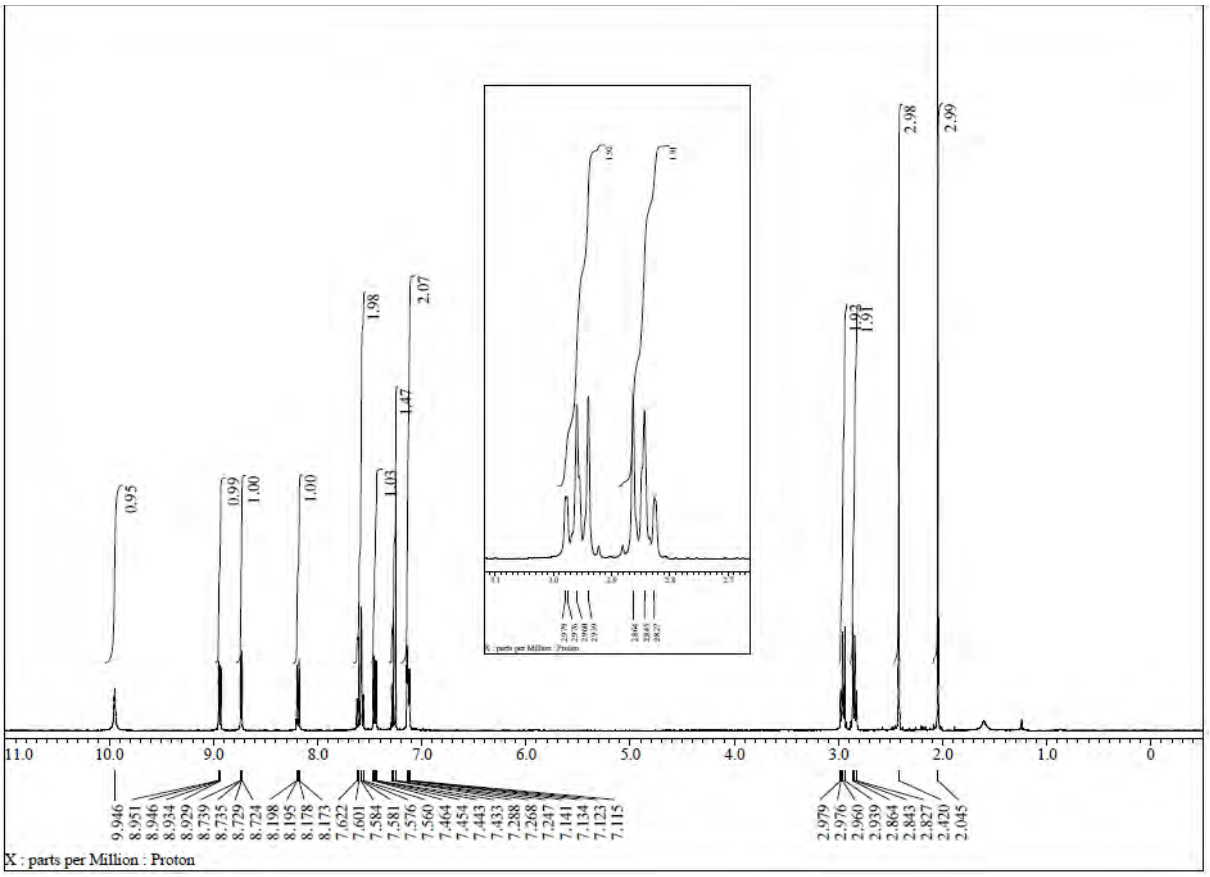

C_a : 1.92/1.91>1. D-content = 0%
C_b : 1.91/1.90>1. D-content = 0%

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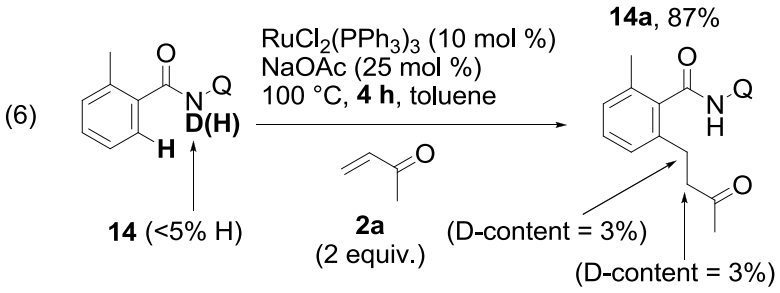
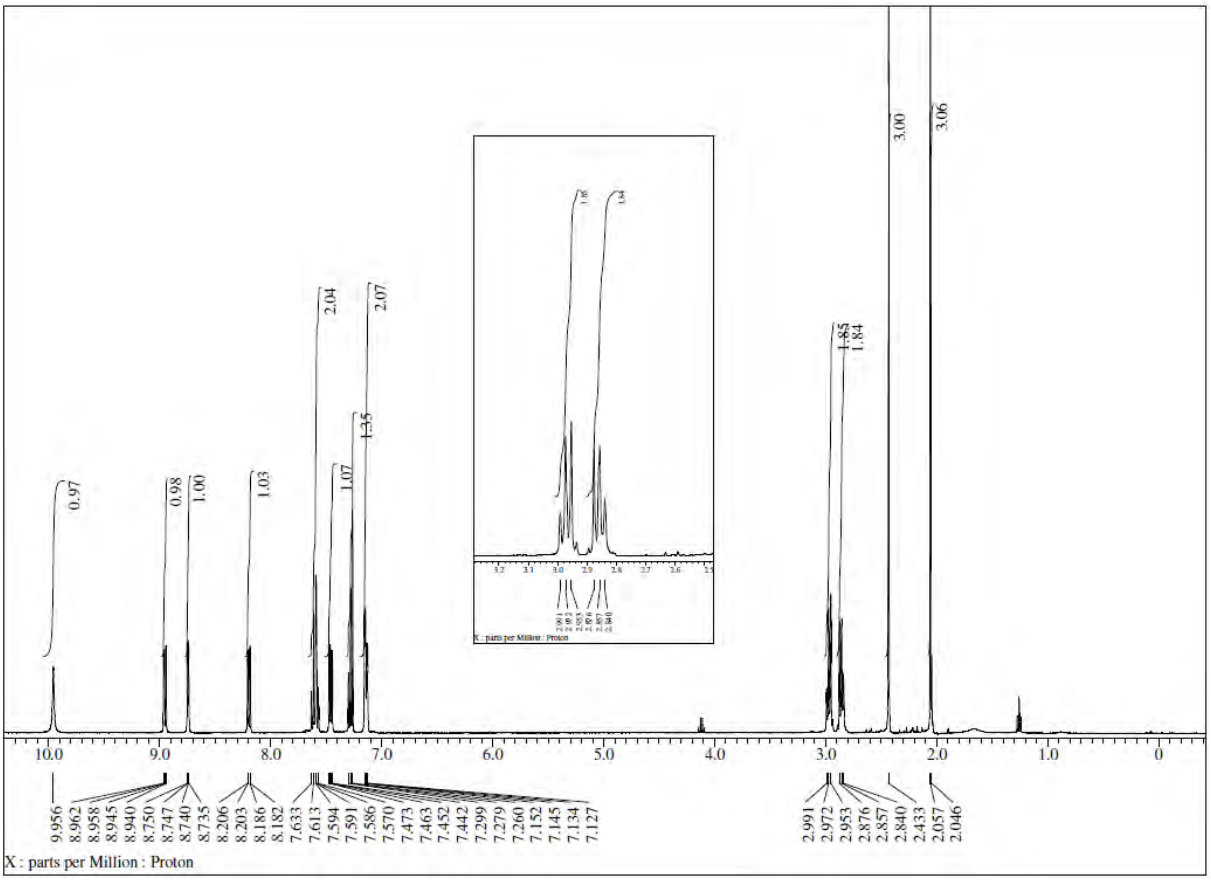
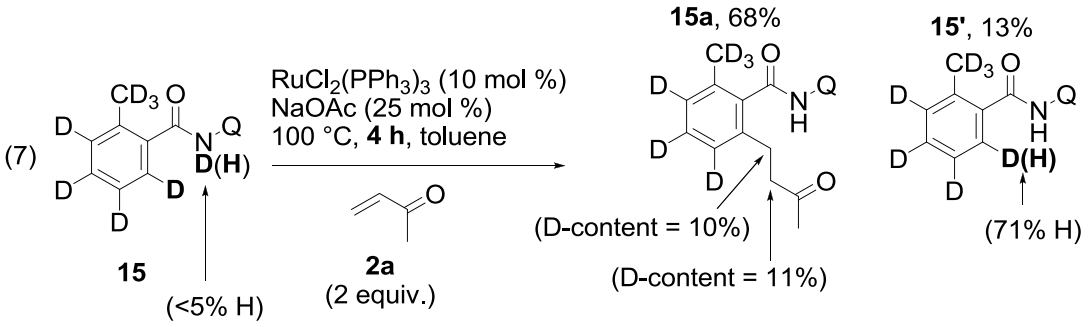
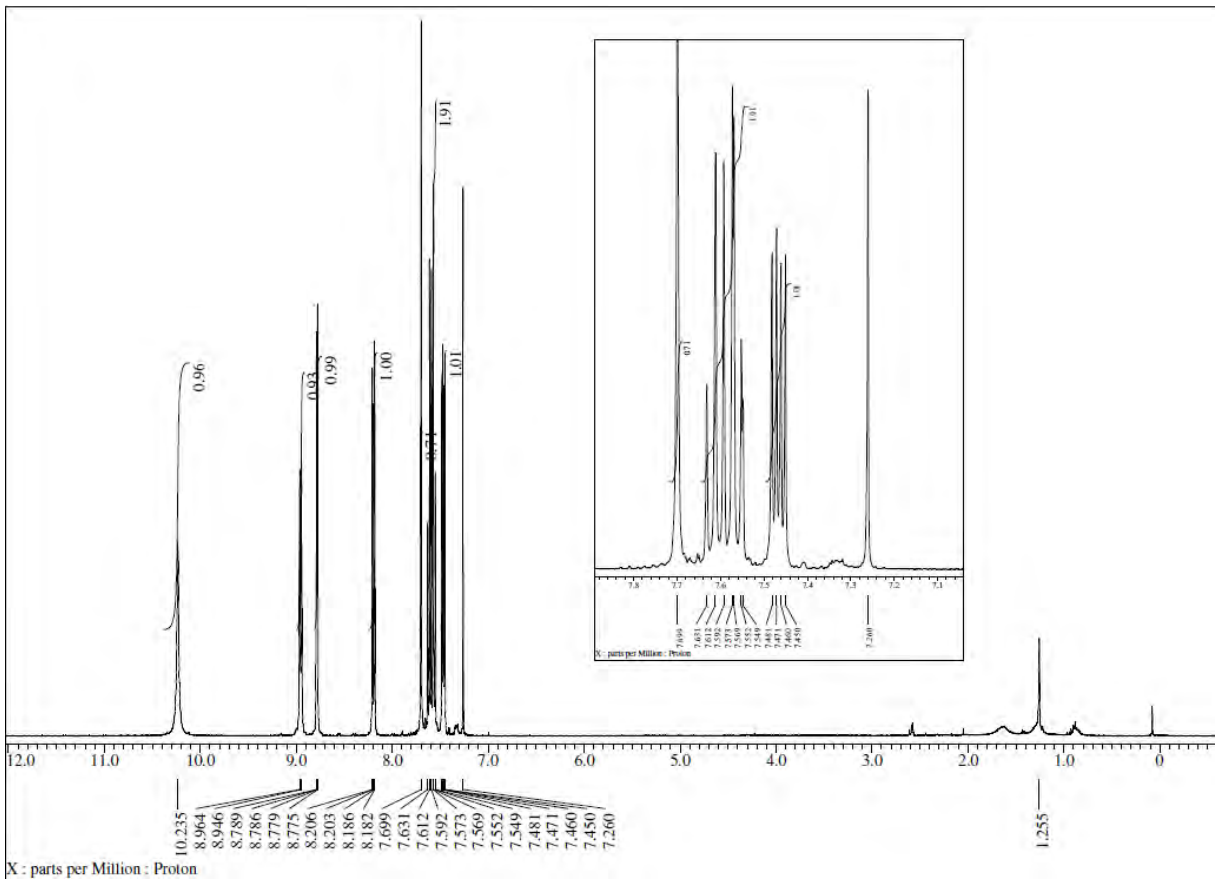




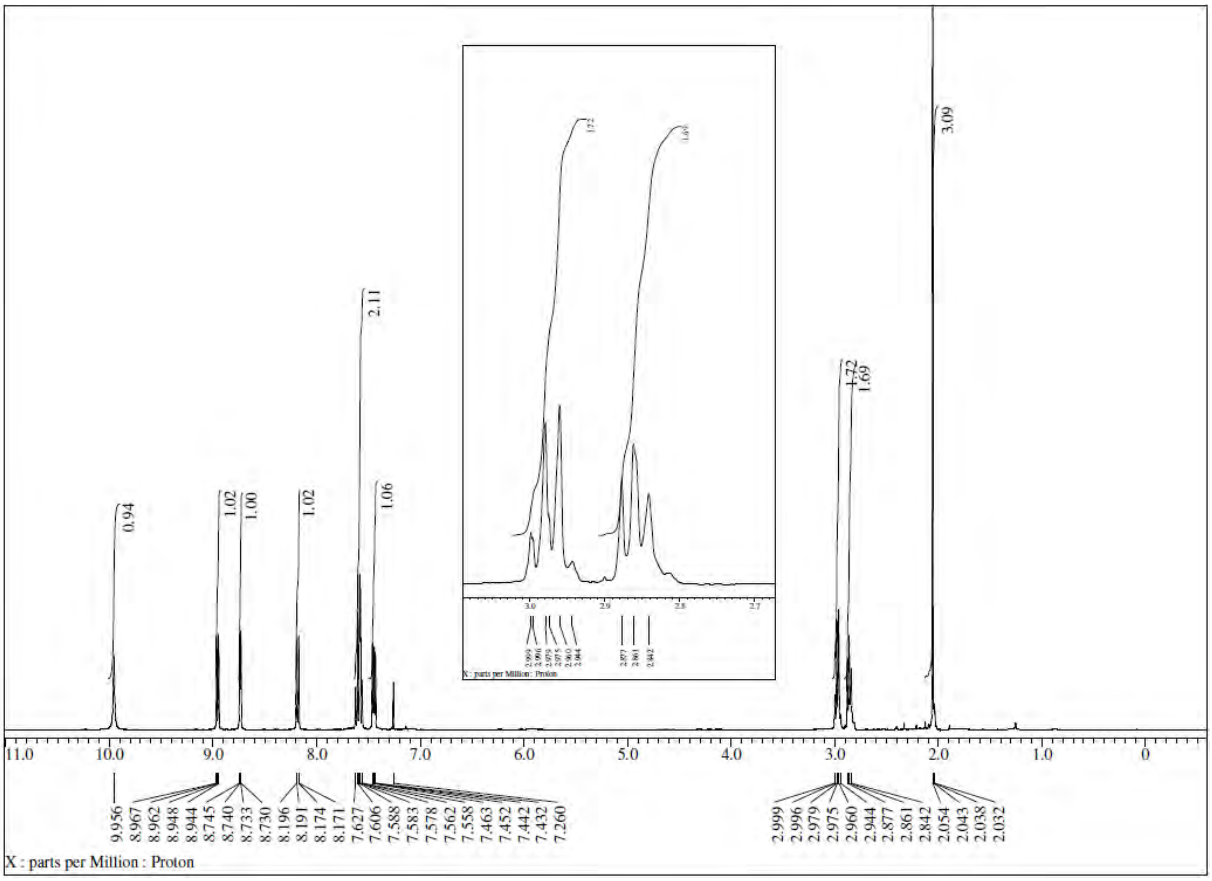
C_a : 1.85/1.91=0.97. D-content = %
C_b : 1.84/1.90=0.97. D-content = 3%


(7)
15
(<5% H)
RuCl2(PPh3)3 (10 mol %)
NaOAc (25 mol %)
100 °C, 4 h, toluene
2a
(2 equiv.)
15a, 68%
(D-content = 10%)
(D-content = 11%)
15', 13%
(71% H)

15'

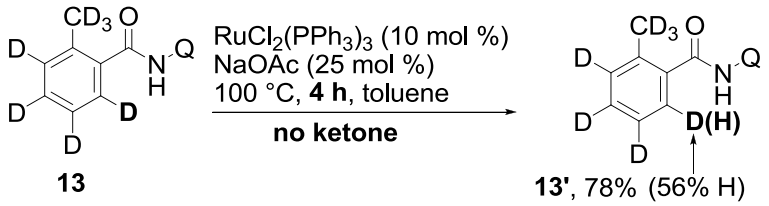

0.96
0.93
0.99
1.00
1.01
1.91
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
10.235
8.964
8.946
8.789
8.786
8.779
8.775
8.206
8.203
8.186
8.182
7.699
7.631
7.612
7.592
7.573
7.569
7.552
7.549
7.481
7.471
7.460
7.450
7.260
1.255
X : parts per Million : Proton

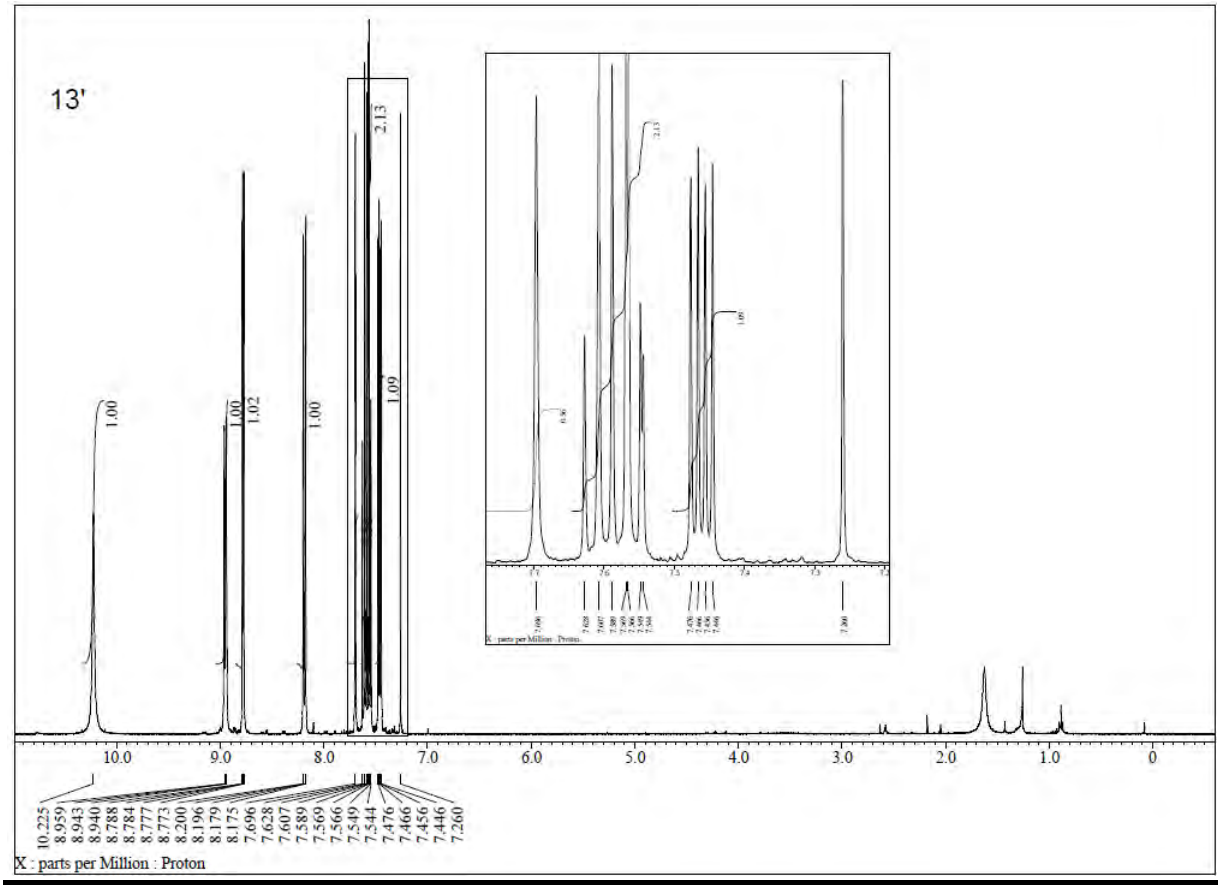
15a

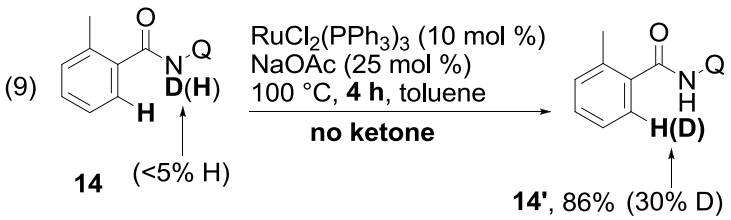


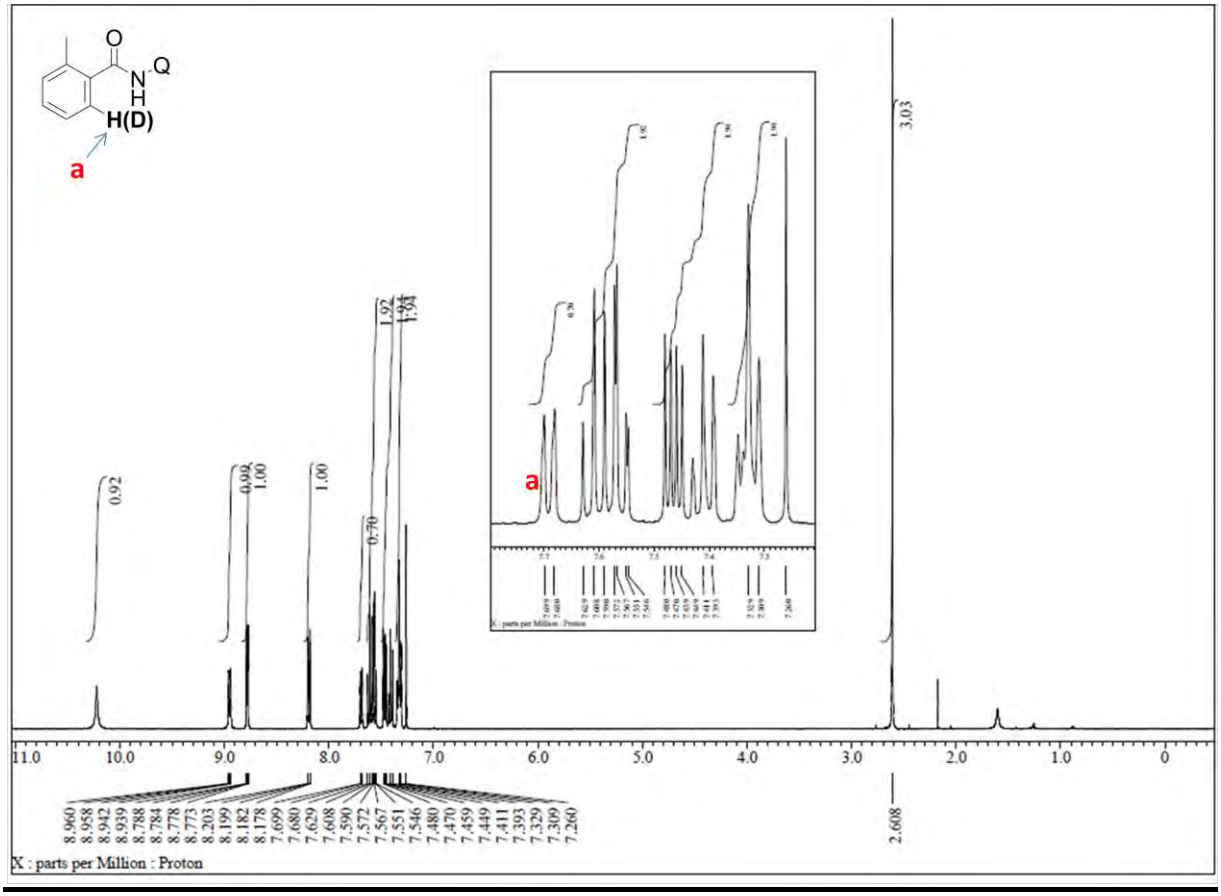
C_a : 1.72/1.91=0.90. D-content = 10%
C_b : 1.69/1.90=0.89. D-content = 11%

(8)


CD3 O
D
N
Q
H
D
D
D
13
RuCl2(PPh3)3 (10 mol %)
NaOAc (25 mol %)
100 °C, 4 h, toluene
no ketone
CD3 O
D
N
Q
H
D
D(H)
D
13', 78% (56% H)


13'
1.00
1.00
1.02
1.00
2.13
1.09
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
10.225
8.959
8.943
8.940
8.788
8.784
8.777
8.773
8.200
8.196
8.179
8.175
7.696
7.628
7.607
7.589
7.569
7.566
7.549
7.544
7.476
7.466
7.456
7.446
7.260
X : parts per Million : Proton


(9)
O
N
Q
D(H)
H
14
(<5% H)
RuCl2(PPh3)3 (10 mol %)
NaOAc (25 mol %)
100 °C, 4 h, toluene
no ketone
O
N
Q
H
H(D)
14', 86% (30% D)


O
N
Q
H
H(D)
a
0.92
0.99
1.00
1.00
0.70
1.92
1.94
3.03
2.608
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : Proton

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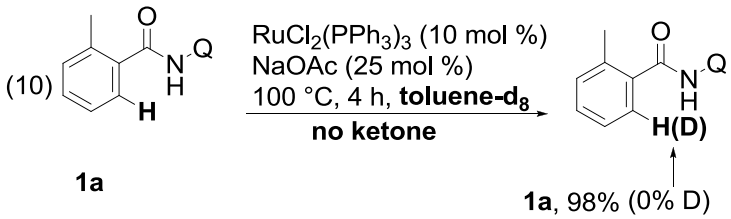
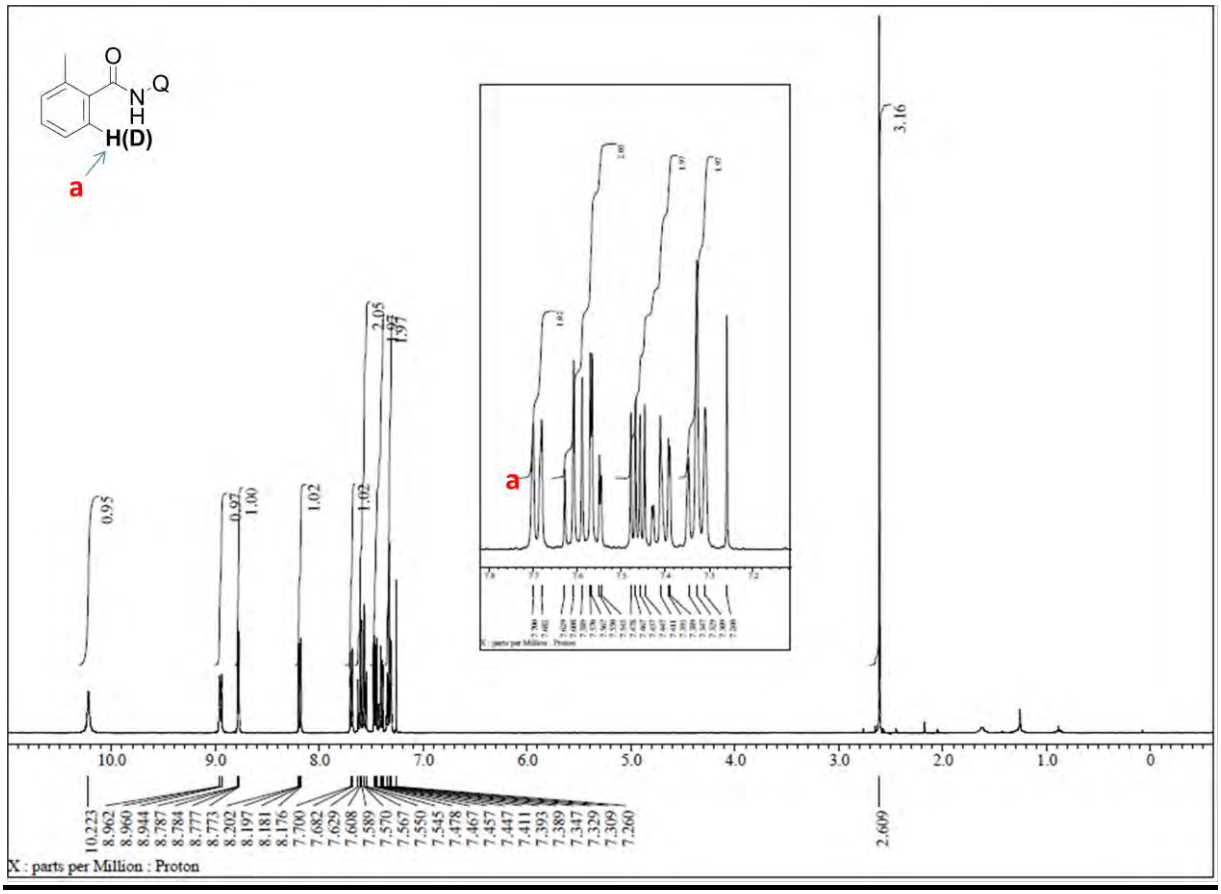
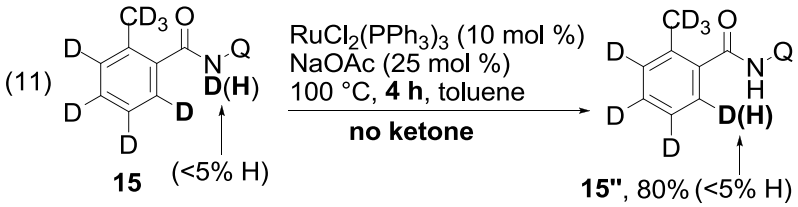
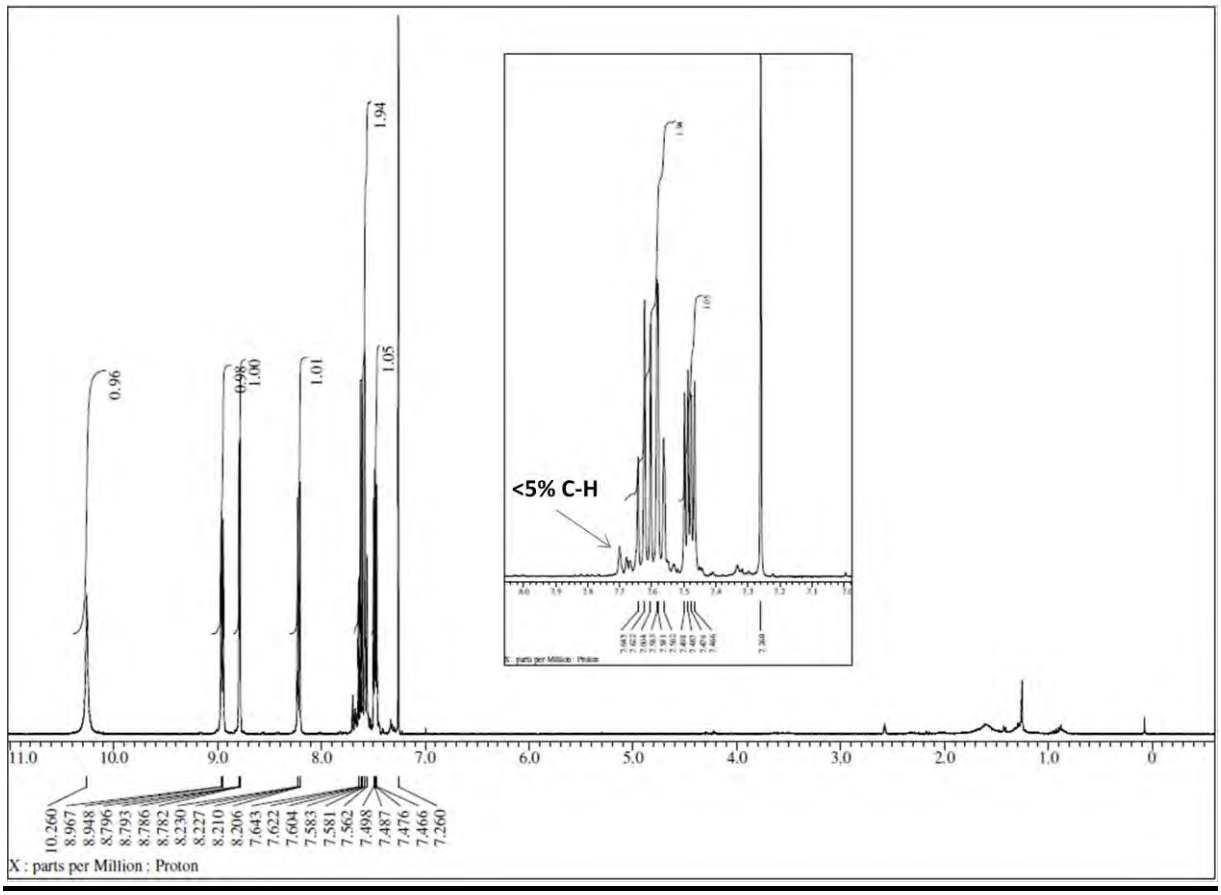





(11)
CD3 O
D
N
Q
D(H)
D
D
D
15
(<5% H)
RuCl2(PPh3)3 (10 mol %)
NaOAc (25 mol %)
100 °C, 4 h, toluene
no ketone
CD3 O
D
N
Q
H
D
D(H)
D
15", 80% (<5% H)


0.96
0.98
1.00
1.01
1.94
1.05
<5% C-H
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
10.260
8.967
8.948
8.796
8.793
8.786
8.782
8.230
8.227
8.210
8.206
7.643
7.622
7.604
7.583
7.581
7.562
7.498
7.487
7.476
7.466
7.260
X : parts per Million : Proton

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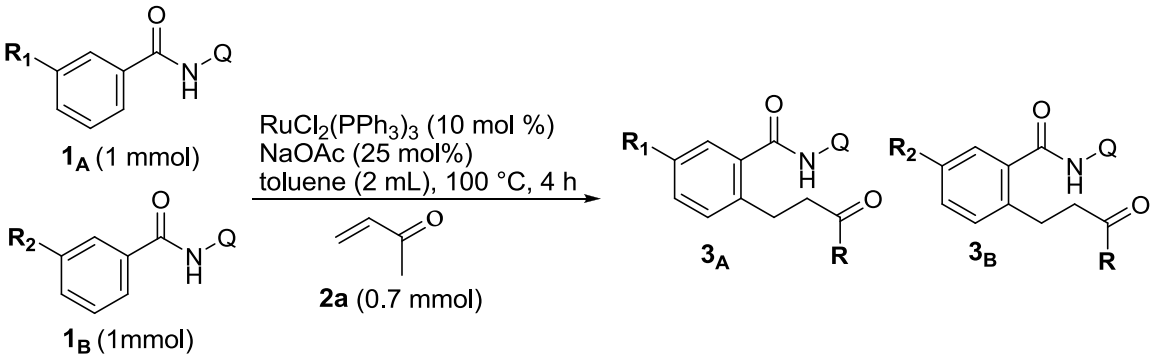
XII. Competition Experiments



To an oven-dried 5 mL screw-capped vial, amide **1A** (1 mmol), amide **1B** (1 mmol), MVK **2a** (49 mg, 0.7 mmol, 0.7 equiv), $RuCl_2(PPh_3)_3$ (96 mg, 0.1 mmol, 10 mol %), sodium acetate (20.5 mg, 0.25 mmol, 25 mol %) and toluene (2 mL) were added under a gentle stream of nitrogen. The mixture was stirred for 4 h at 100 °C (108 °C bath temperature) then cooled to room temperature and concentrated *in vacuo*. Yields were determined by NMR ^{1}H on the crude mixture with tetrachloroethane as internal standard.

Entry	**1A**, R_1	**1B**, R_2	**Run**	**3A** [%]	**3B** [%]
1a	**1l**, CF_3	**1j**, Me	**run 1**	**3la**, 81	**3ja**, <6
1b			**run 2**	**3la**, 78	**3ja**, <6
1c			**run3**	**3la**, 82	**3ja**, <6
1d			**average**	**3la**, 80	**3ja**, <6
2a	**1k**, Ph	**1j**, Me	**run 1**	**3ka**, 56	**3ja**, 15
2b			**run 2**	**3ka**, 62	**3ja**, 14
2c			**run3**	**3ka**, 60	**3ja**, 14
2d			**average**	**3ka**, 59	**3ja**, 14
3a	**1l**, CF_3	**1m**, OMe	**run 1**	**3la**, 85	**3ma**, <6
3b			**run 2**	**3la**, 82	**3ma**, <6
3c			**run3**	**3la**, 76	**3ma**, <6
3d			**average**	**3la**, 81	**3ma**, <6
4a	**1l**, CF_3	**1o**, NMe_2	**run 1**	**3la**, 75	**3oa**, <6
4b			**run 2**	**3la**, 66	**3oa**, <6
4c			**run3**	**3la**, 73	**3oa**, <6
4d			**average**	**3la**, 71	**3oa**, <6
5a	**1o**, NMe_2	**1j**, Me	**run 1**	**3oa**, 27	**3ja**, 33
5b			**run 2**	**3oa**, 21	**3ja**, 38
5c			**run3**	**3oa**, 24	**3ja**, 30
5d			**average**	**3oa**, 24	**3ja**, 34

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XIII. Copies of ^{1}H and ^{13}C NMR Spectra

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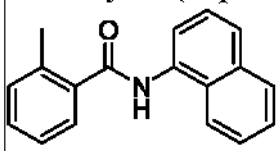
2-methyl-N-(naphthalen-1-yl)benzamide (G)



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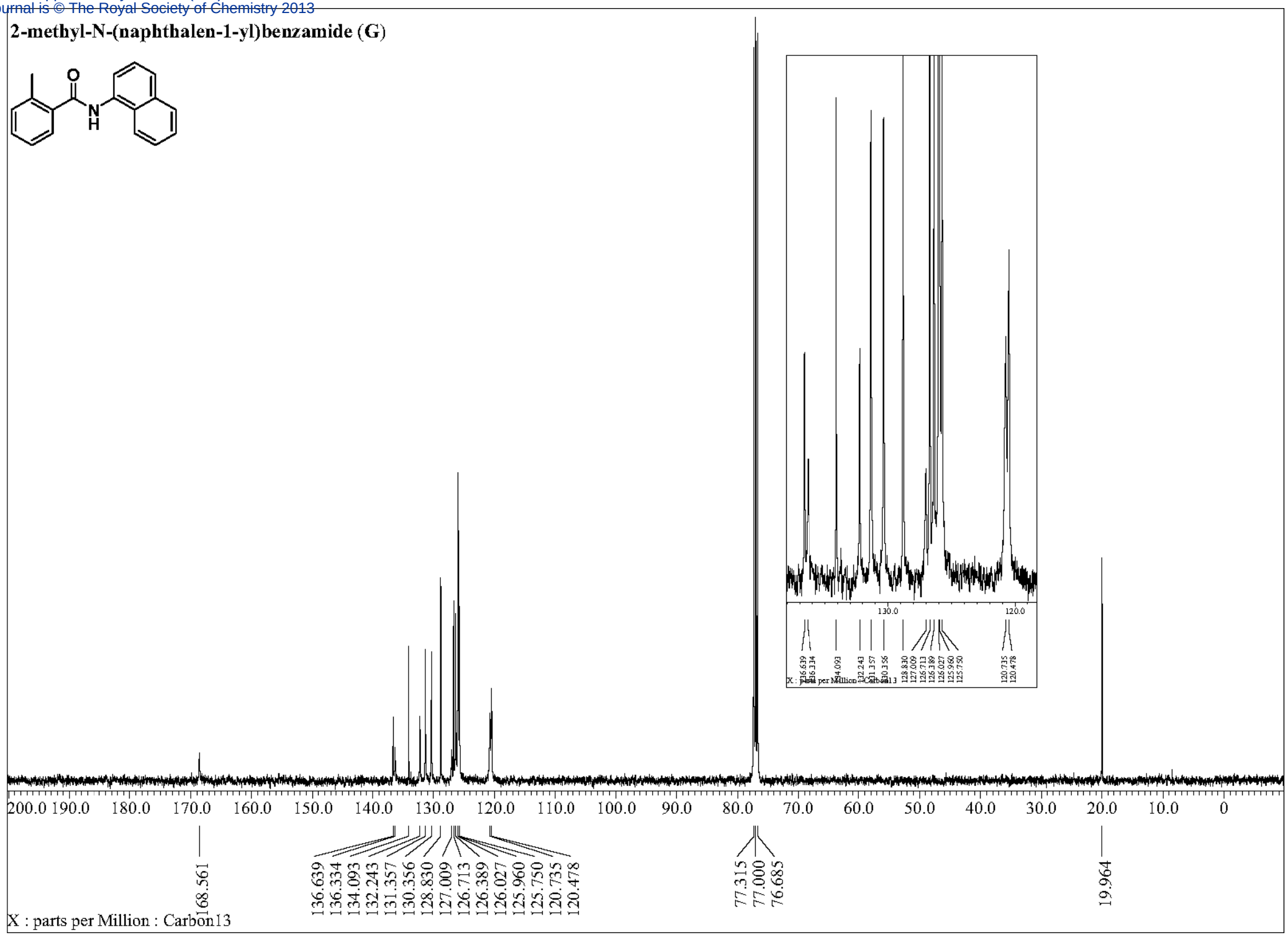

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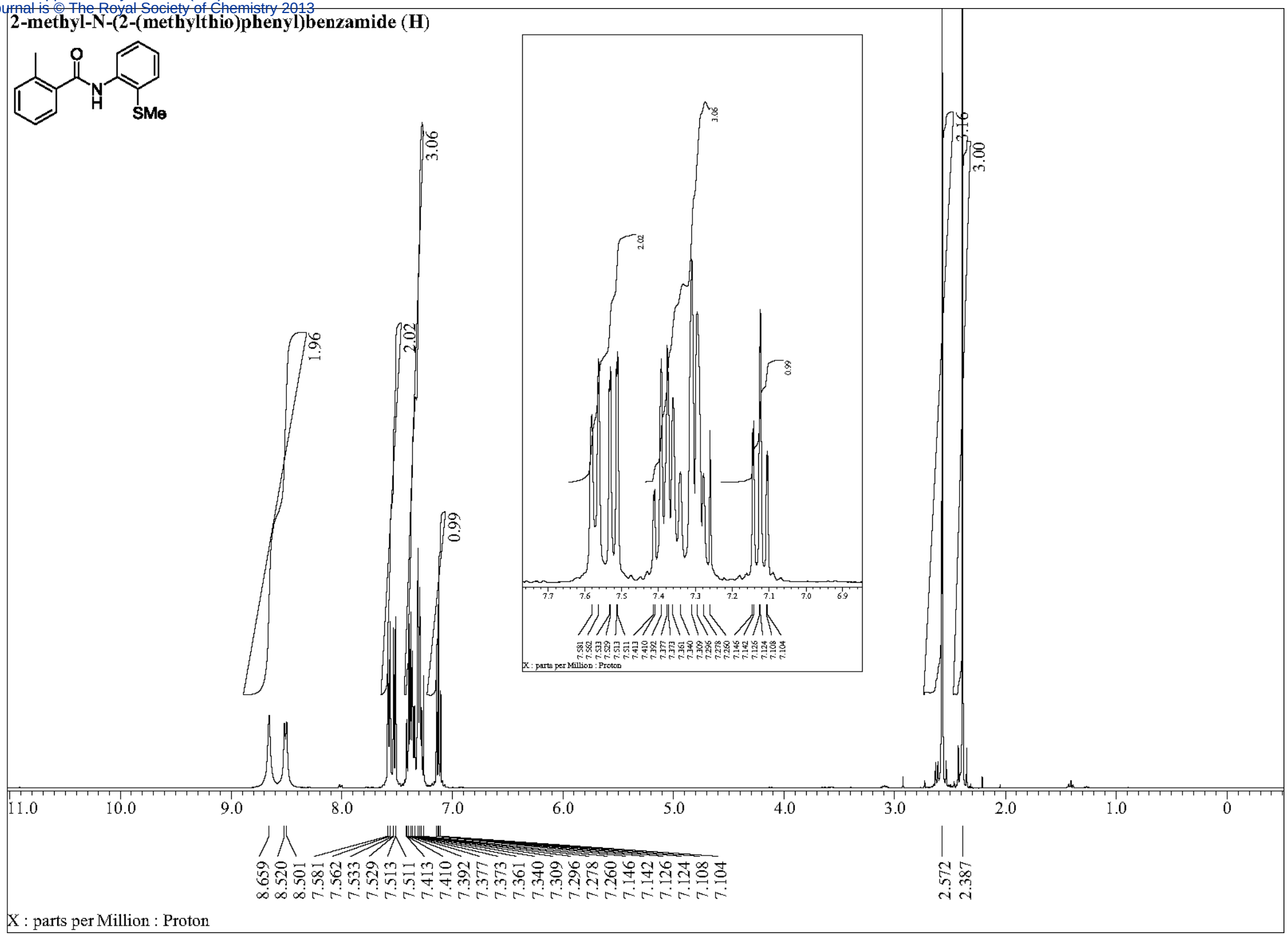

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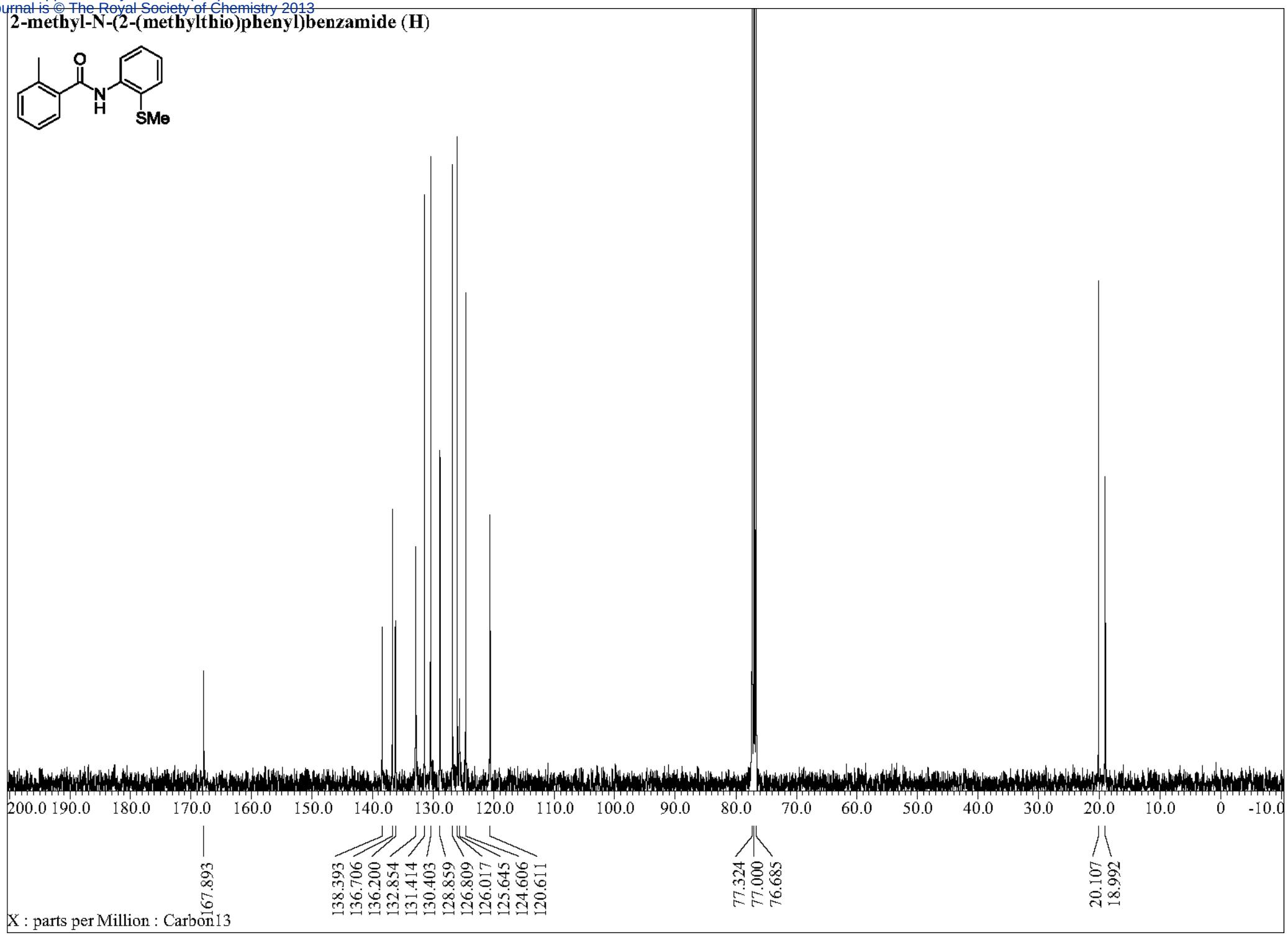

Electronic Supplementary Material (ESI) for Chemical Science
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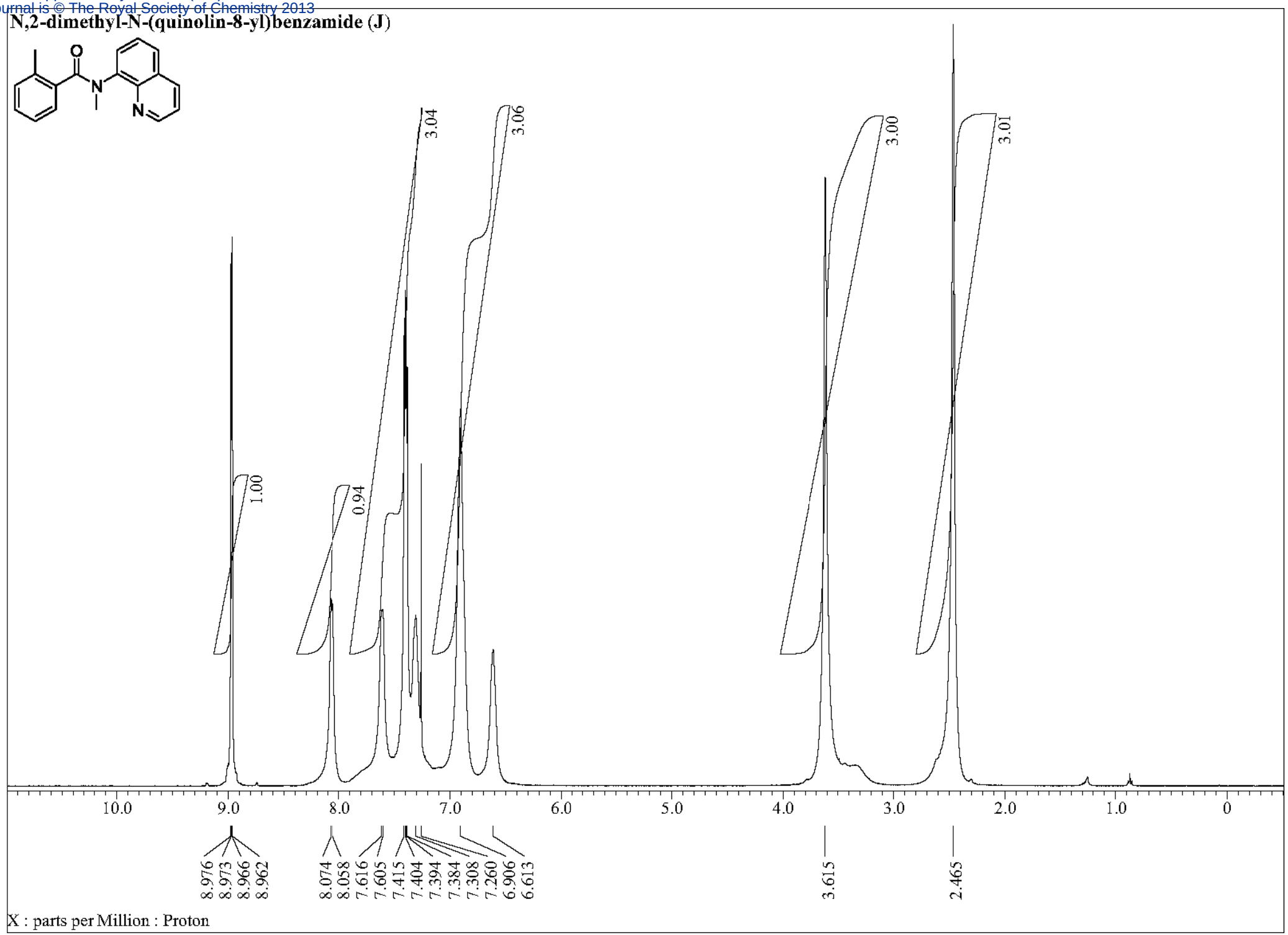

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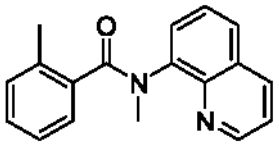
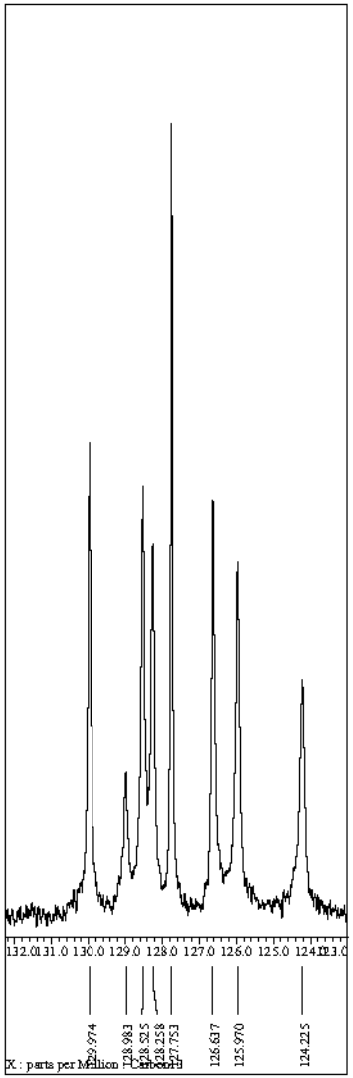
N,2-dimethyl-N-(quinolin-8-yl)benzamide (J)





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171.907
150.359
144.009
141.540
136.620
136.067
135.514
129.974
128.983
128.525
128.258
127.753
126.637
125.970
124.225
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77.315
77.000
76.676
37.479
19.659

X : parts per Million : Carbon13

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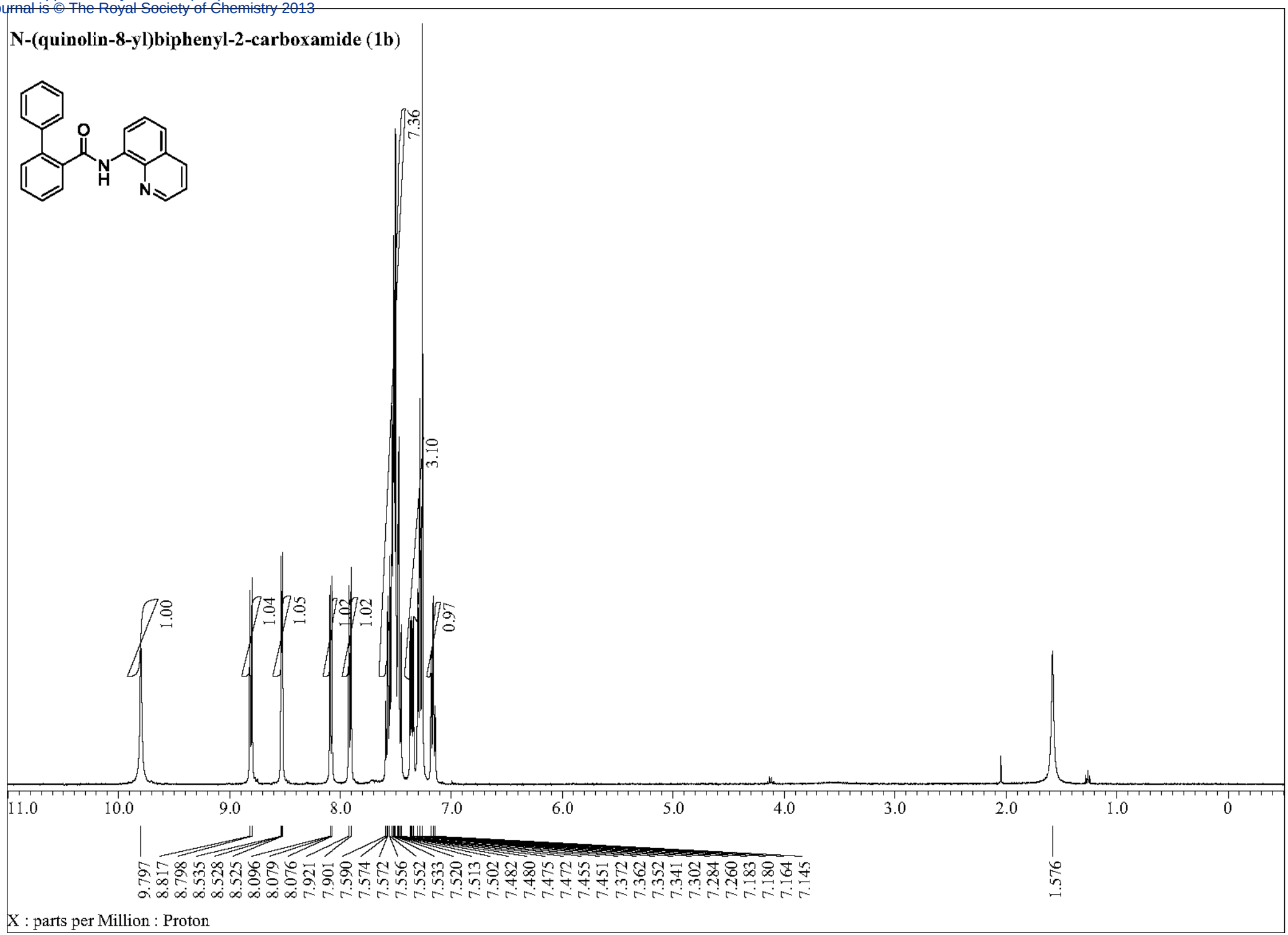

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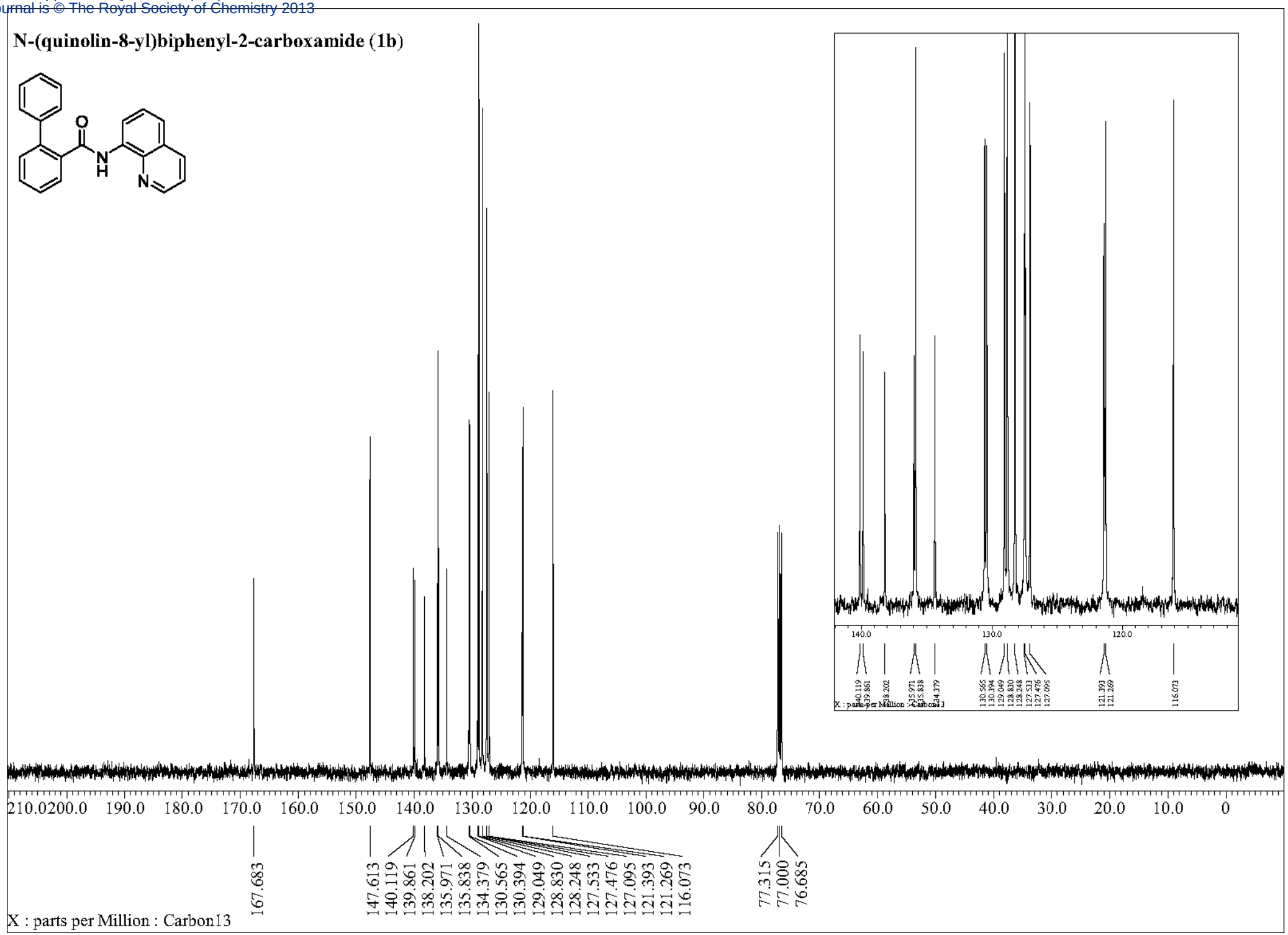

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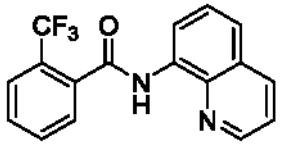
N-(quinolin-8-yl)-2-(trifluoromethyl)benzamide (1c)



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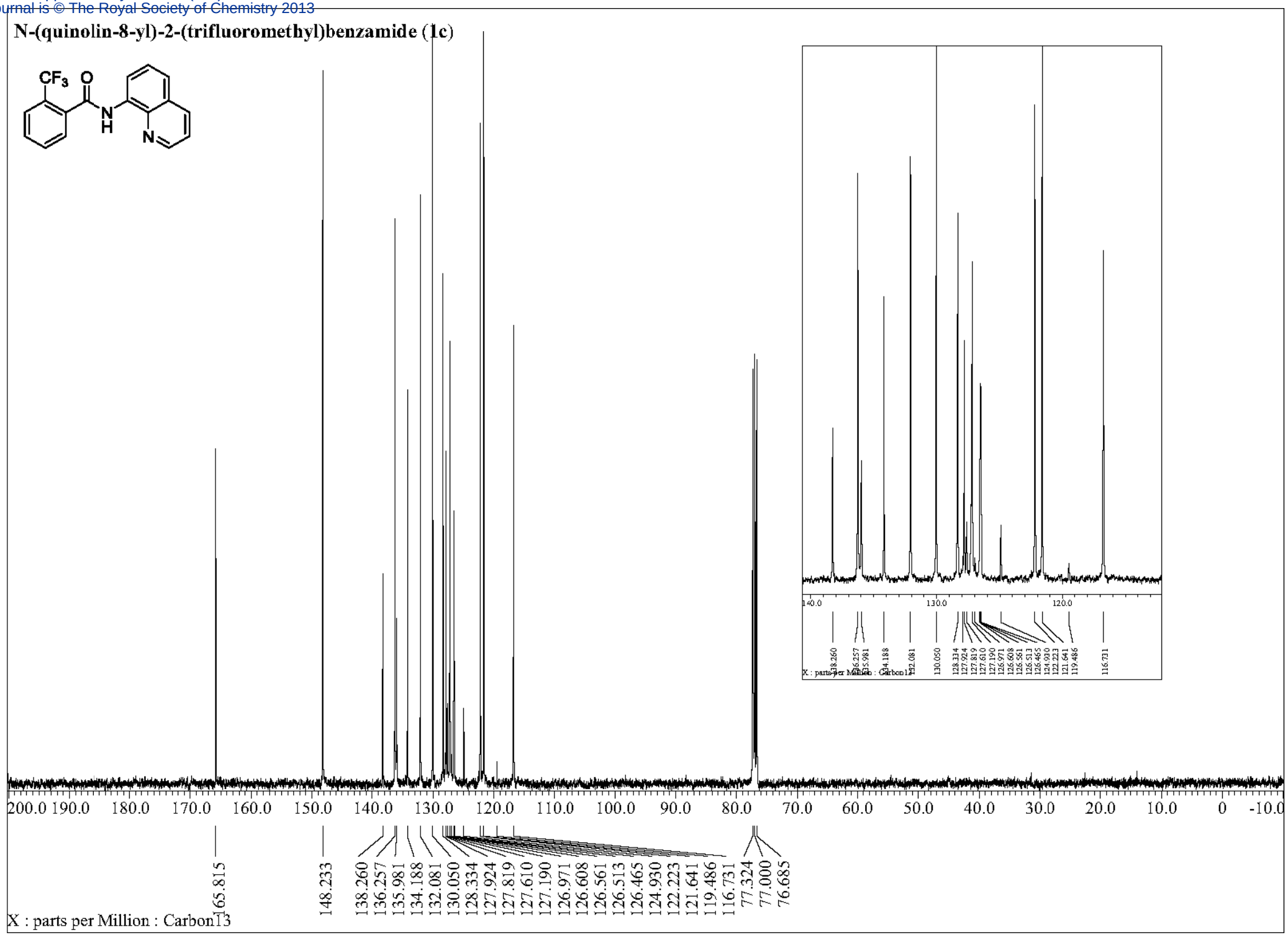

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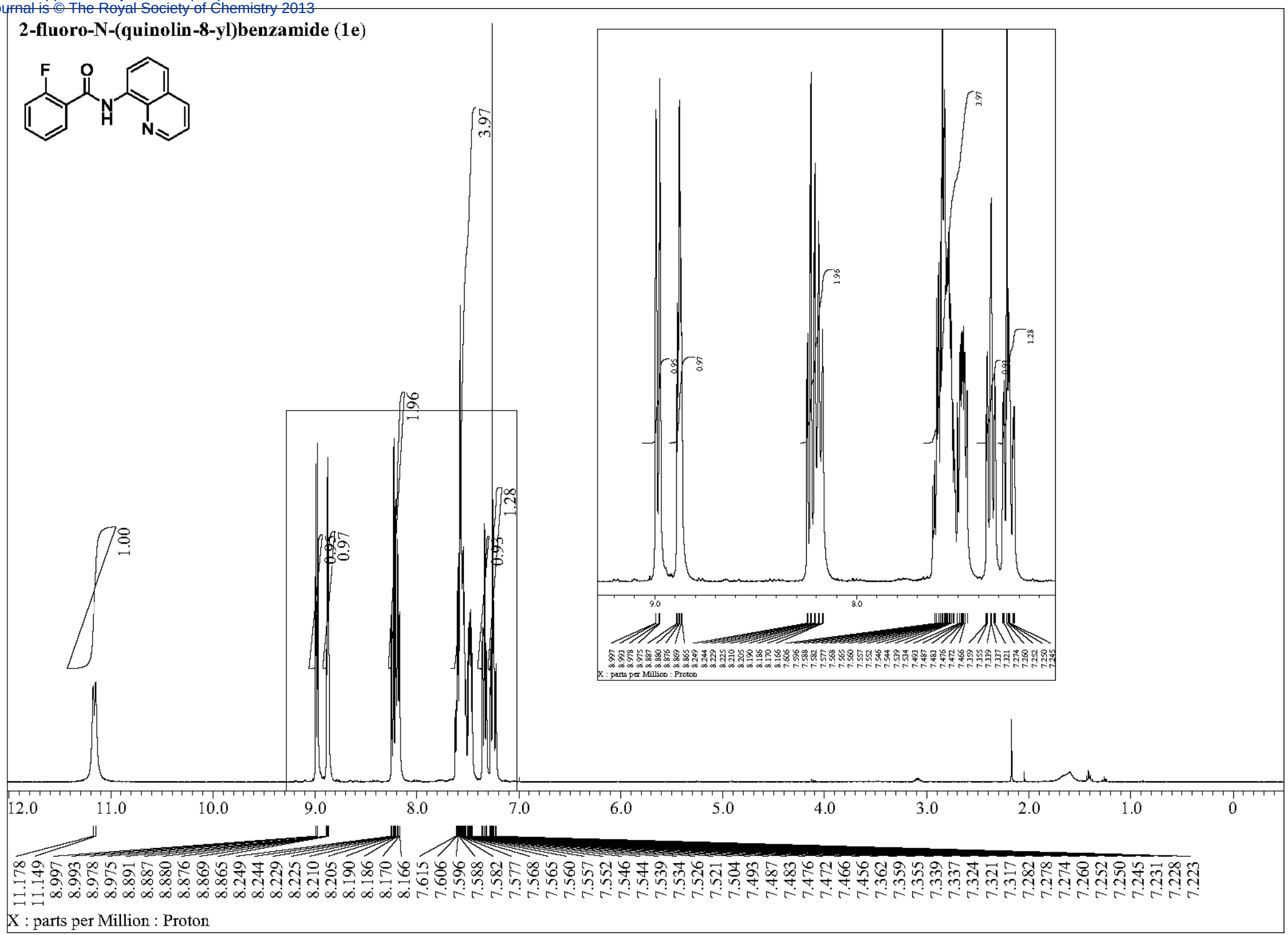

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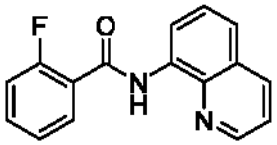
2-fluoro-N-(quinolin-8-yl)benzamide (1e)



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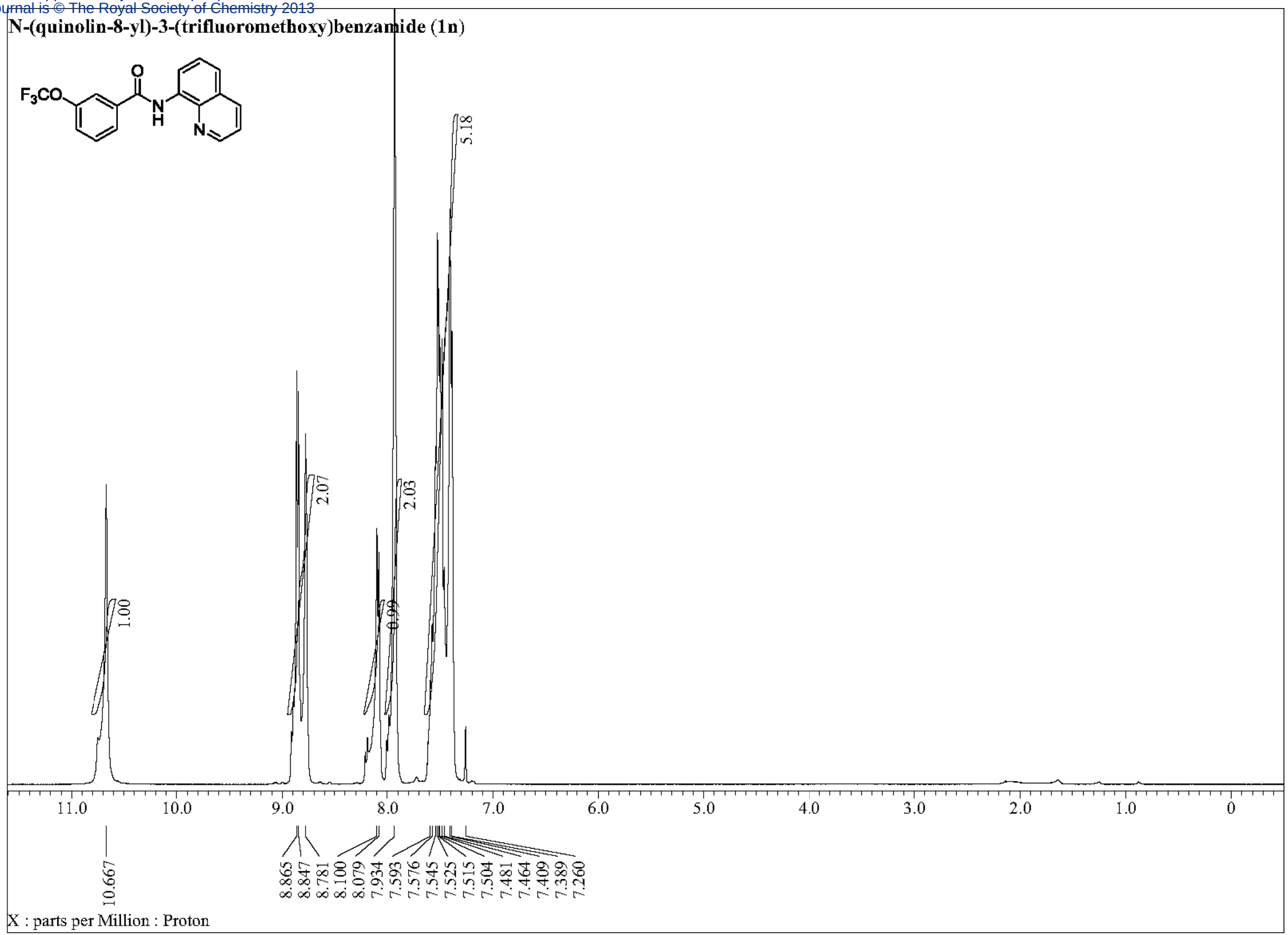

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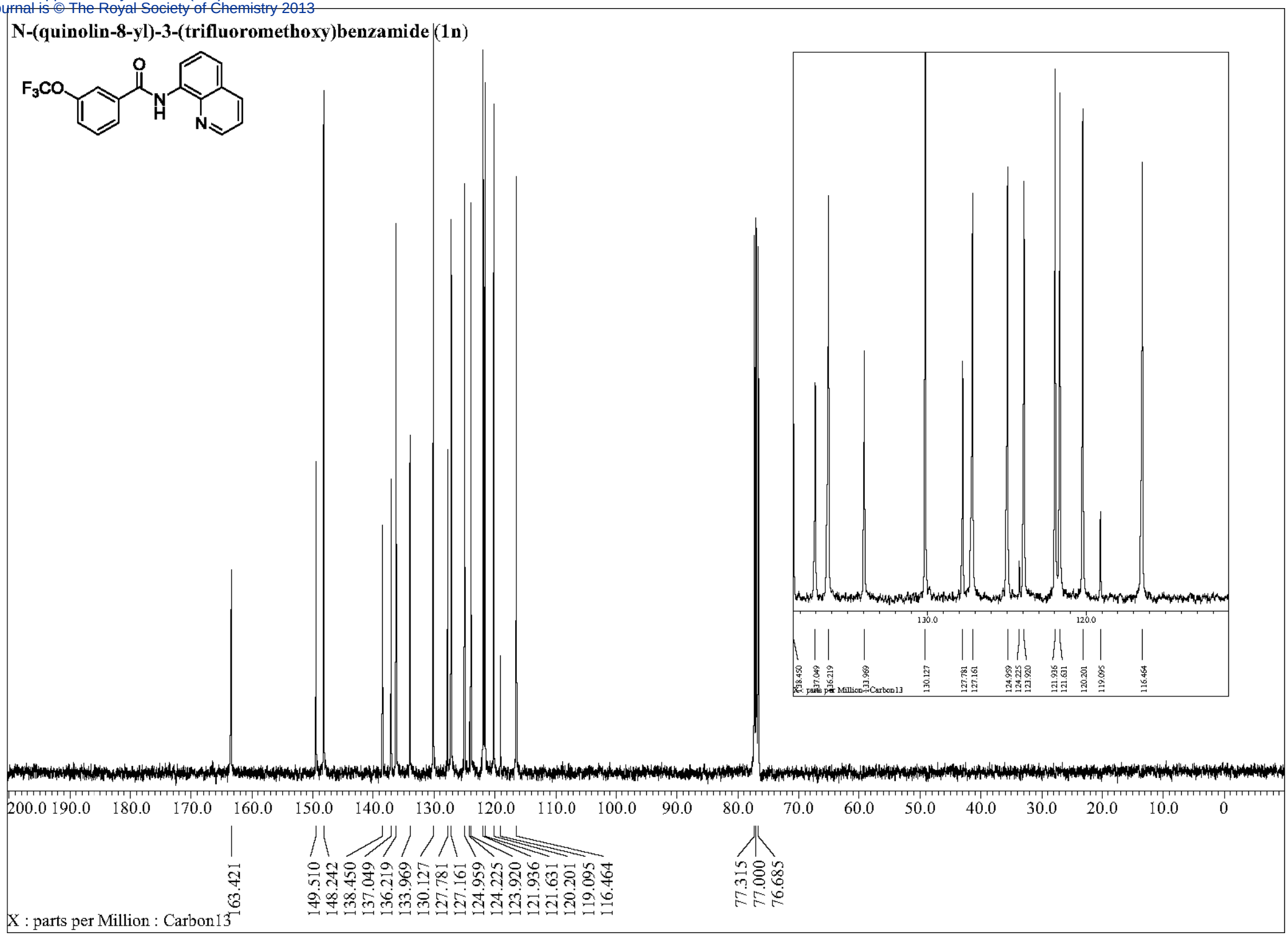

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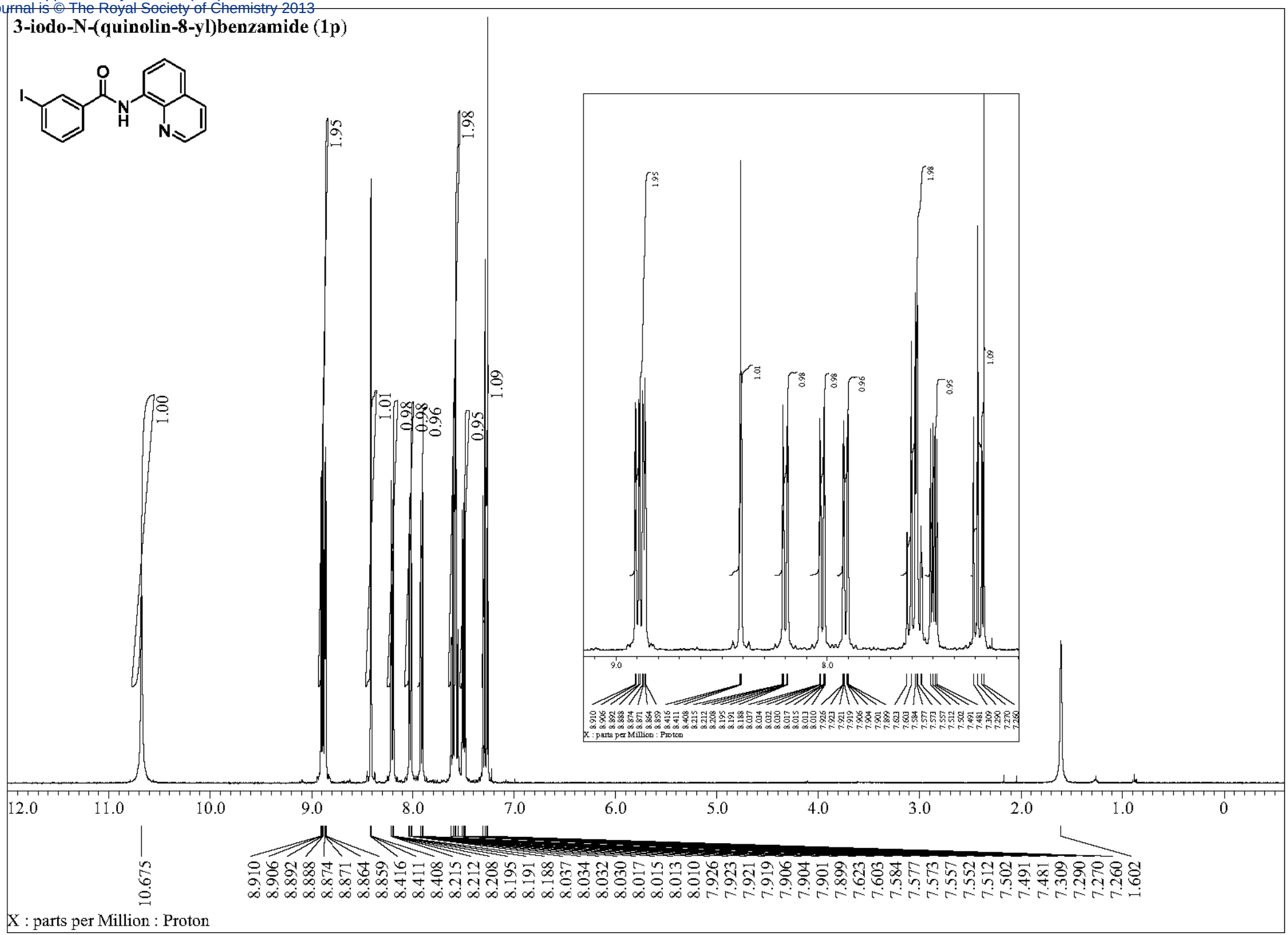

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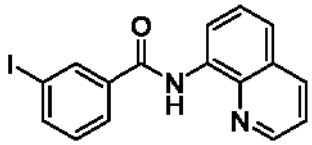
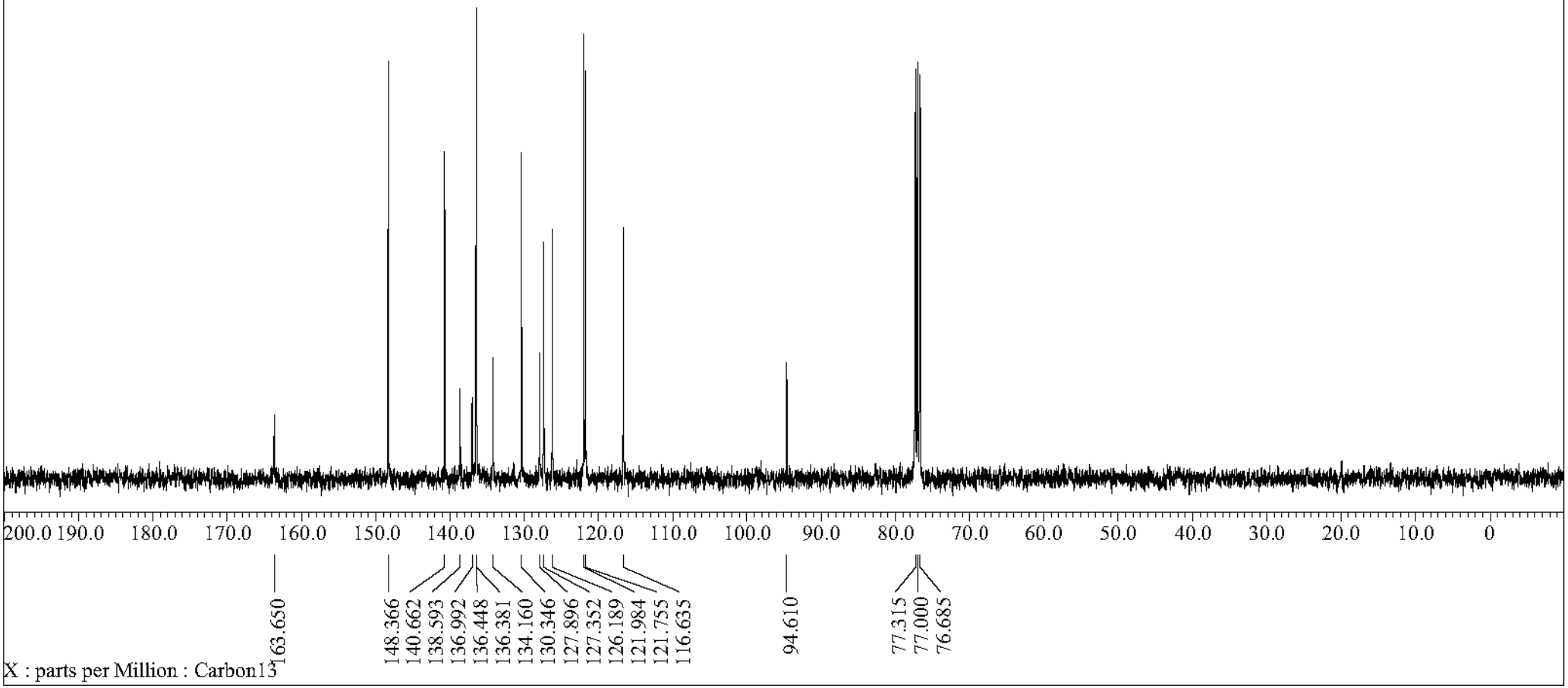
3-iodo-N-(quinolin-8-yl)benzamide (1p)





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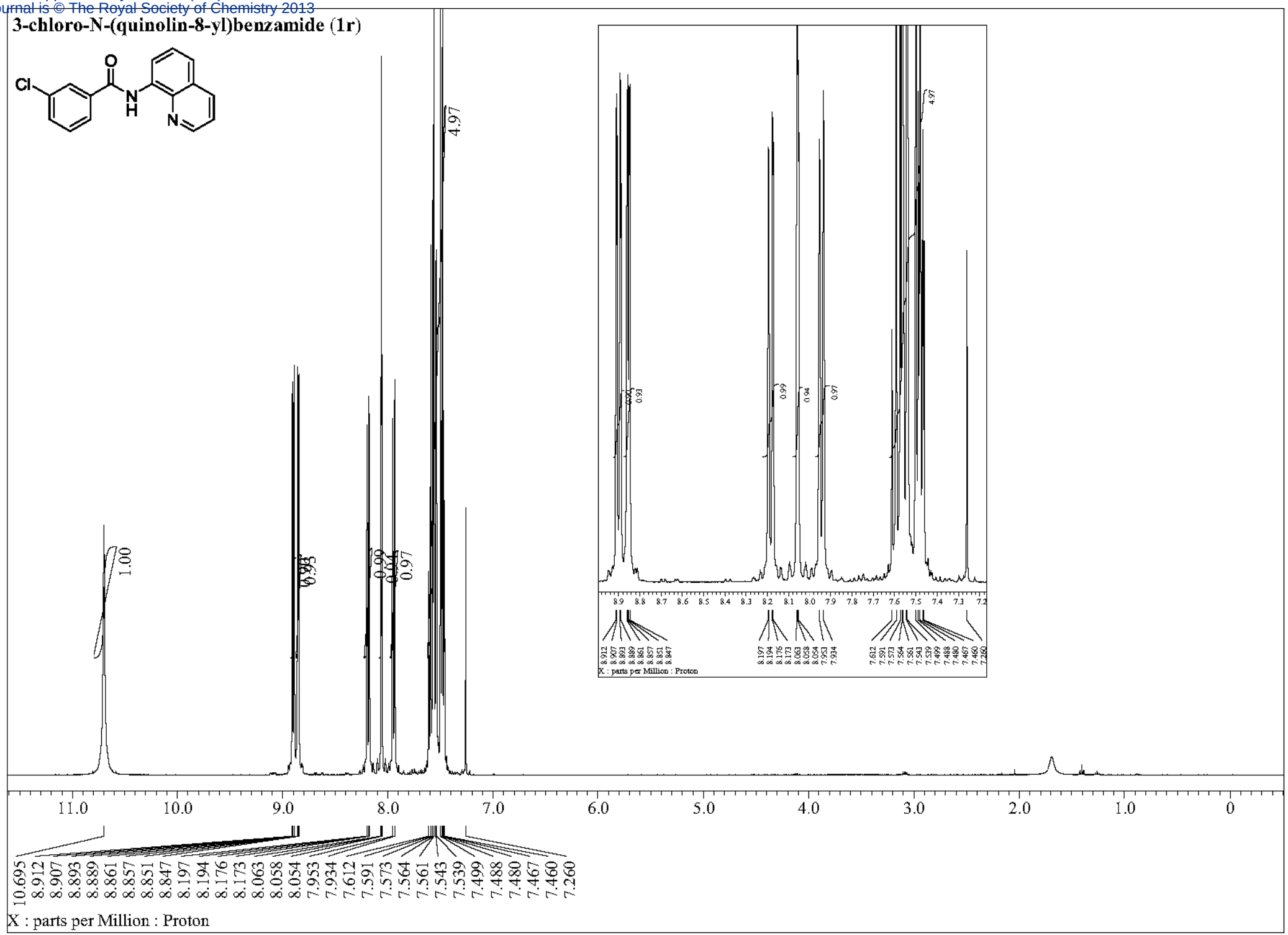

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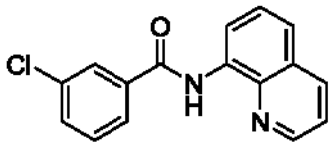
3-chloro-N-(quinolin-8-yl)benzamide (1r)



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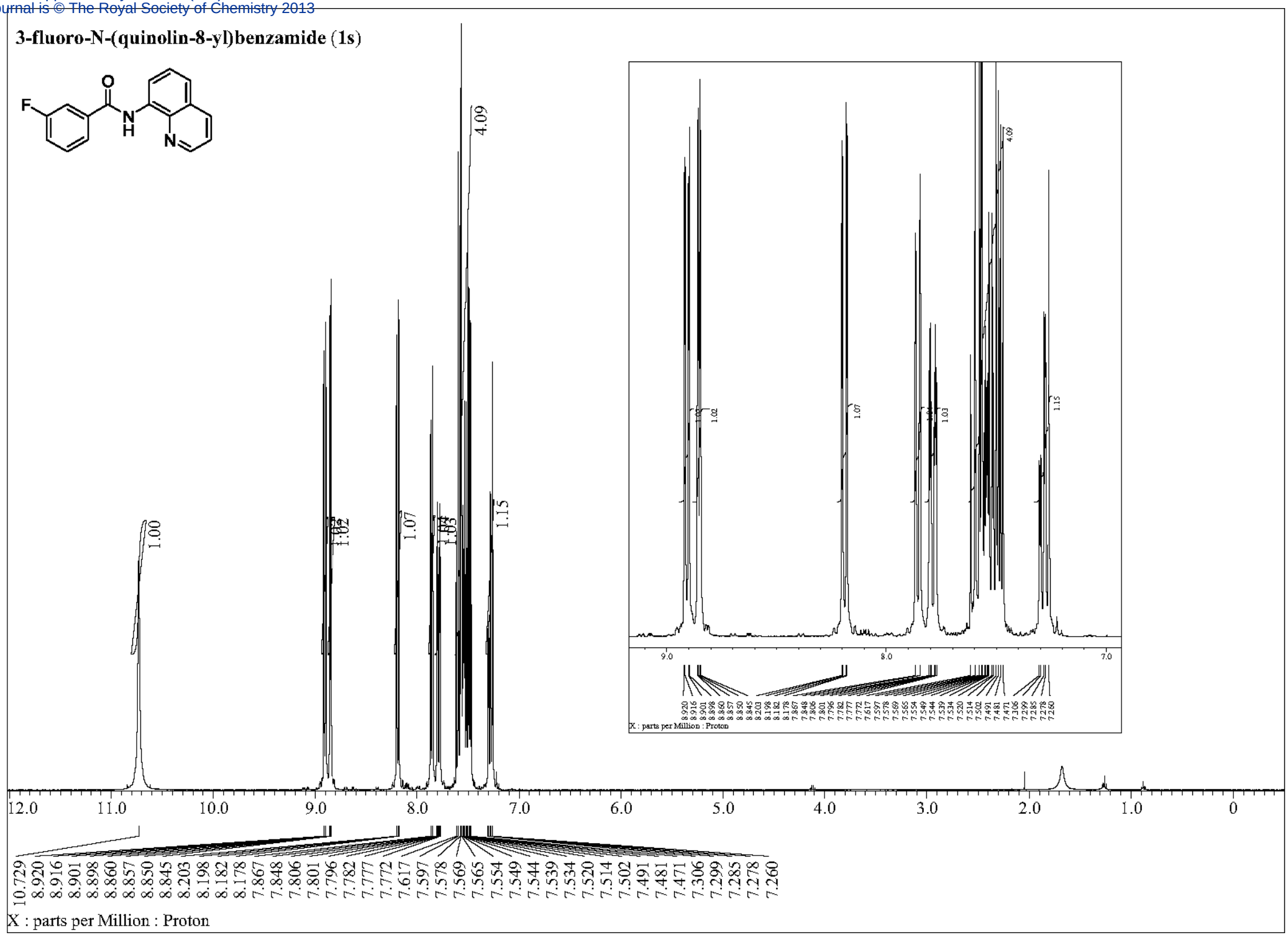

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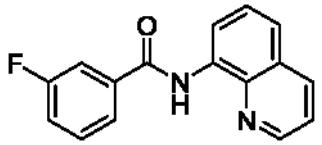
3-fluoro-N-(quinolin-8-yl)benzamide (1s)



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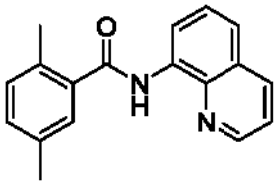
2,5-dimethyl-N-(quinolin-8-yl)benzamide (7a)



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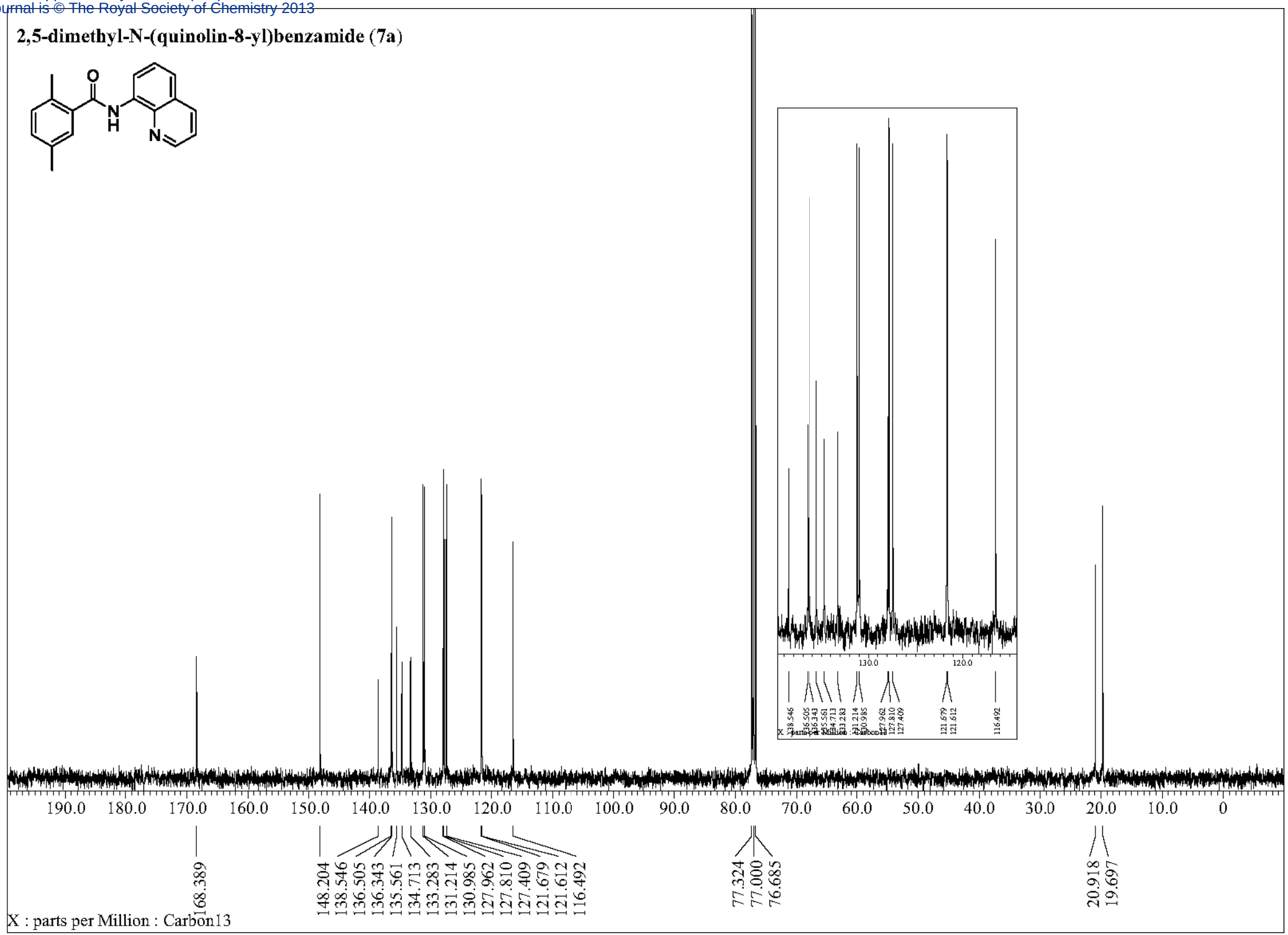

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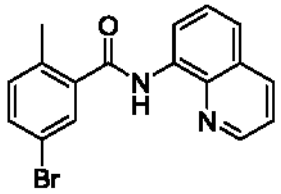
5-bromo-2-methyl-N-(quinolin-8-yl)benzamide (7b)



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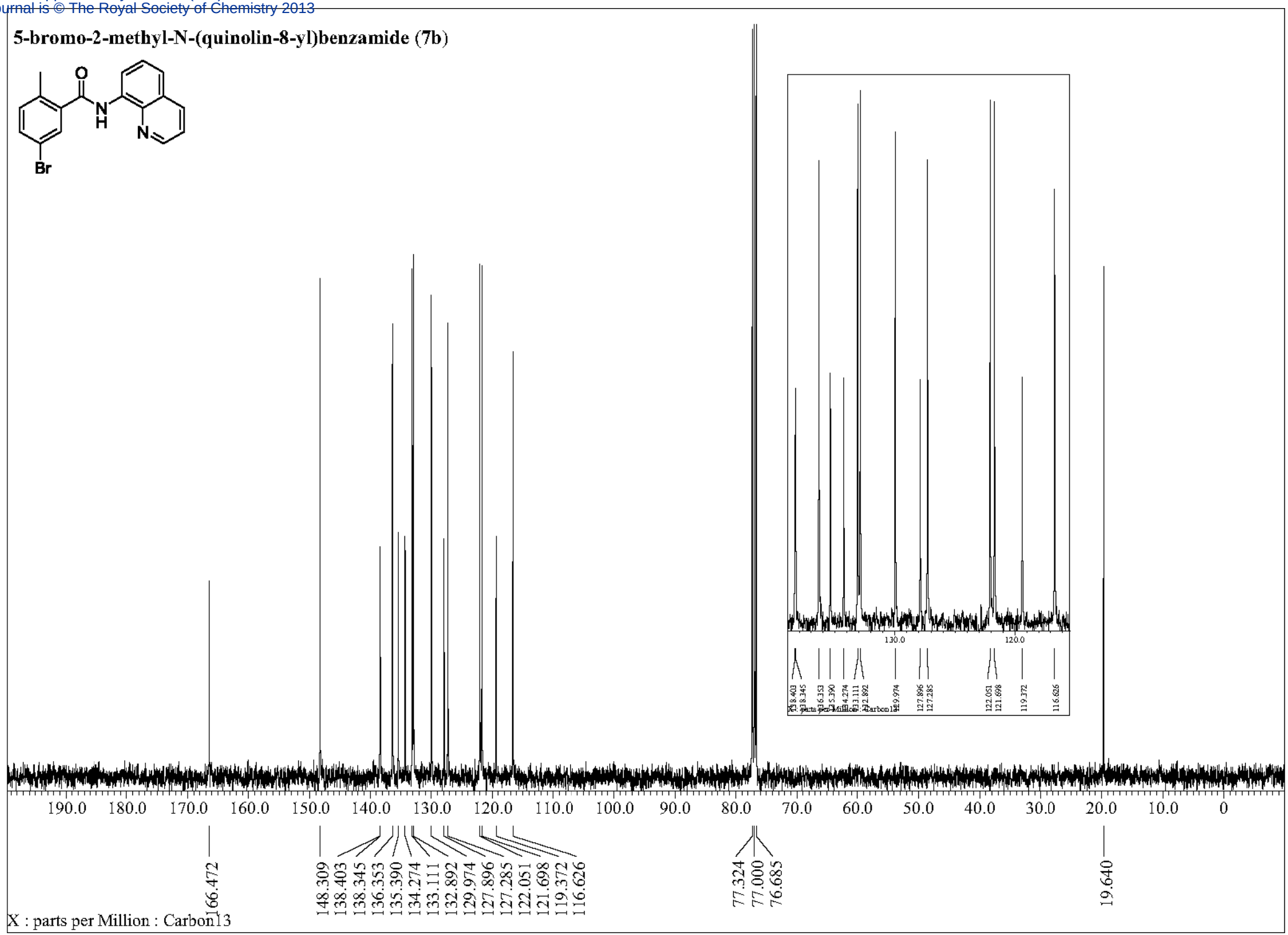

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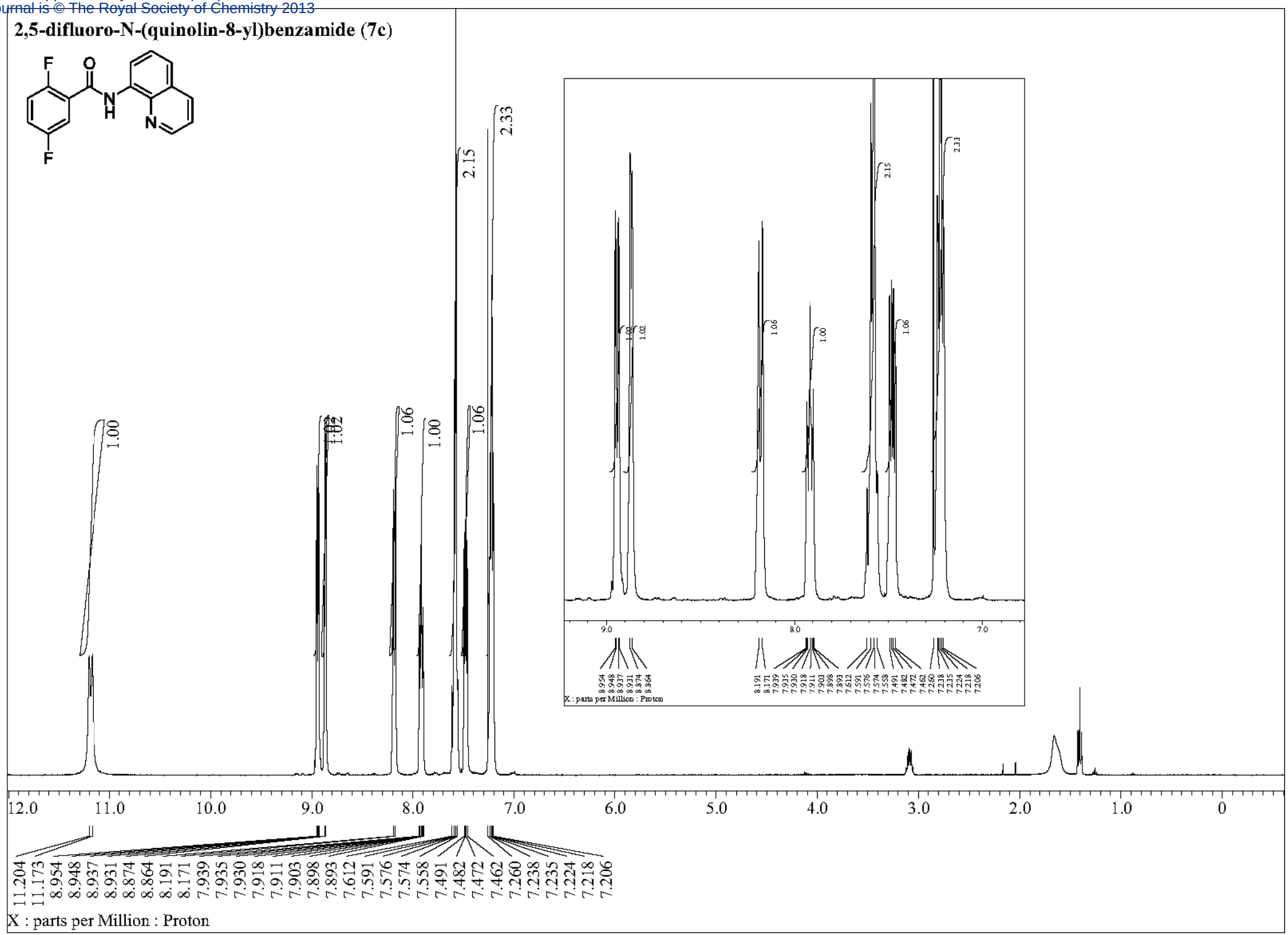

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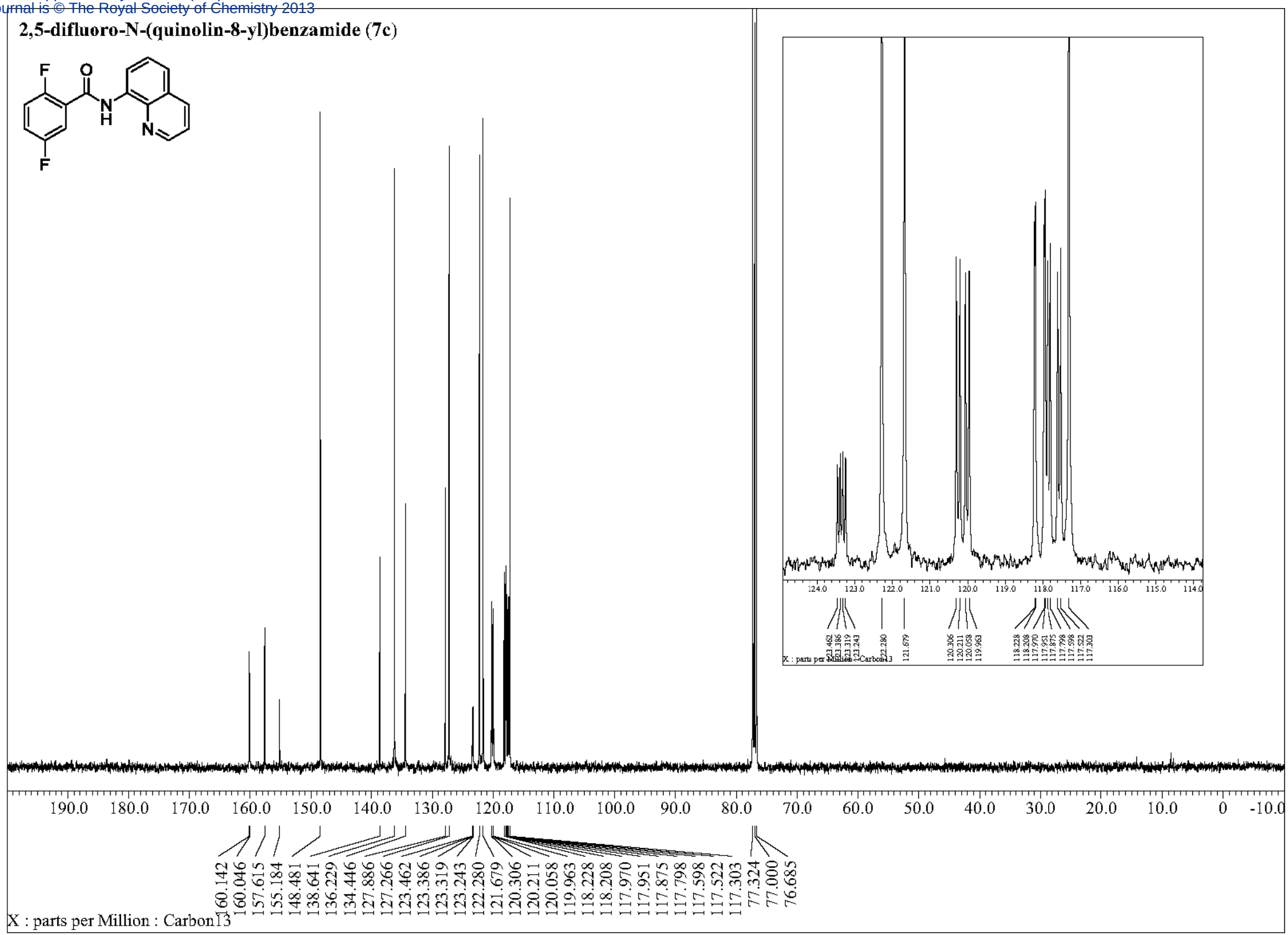

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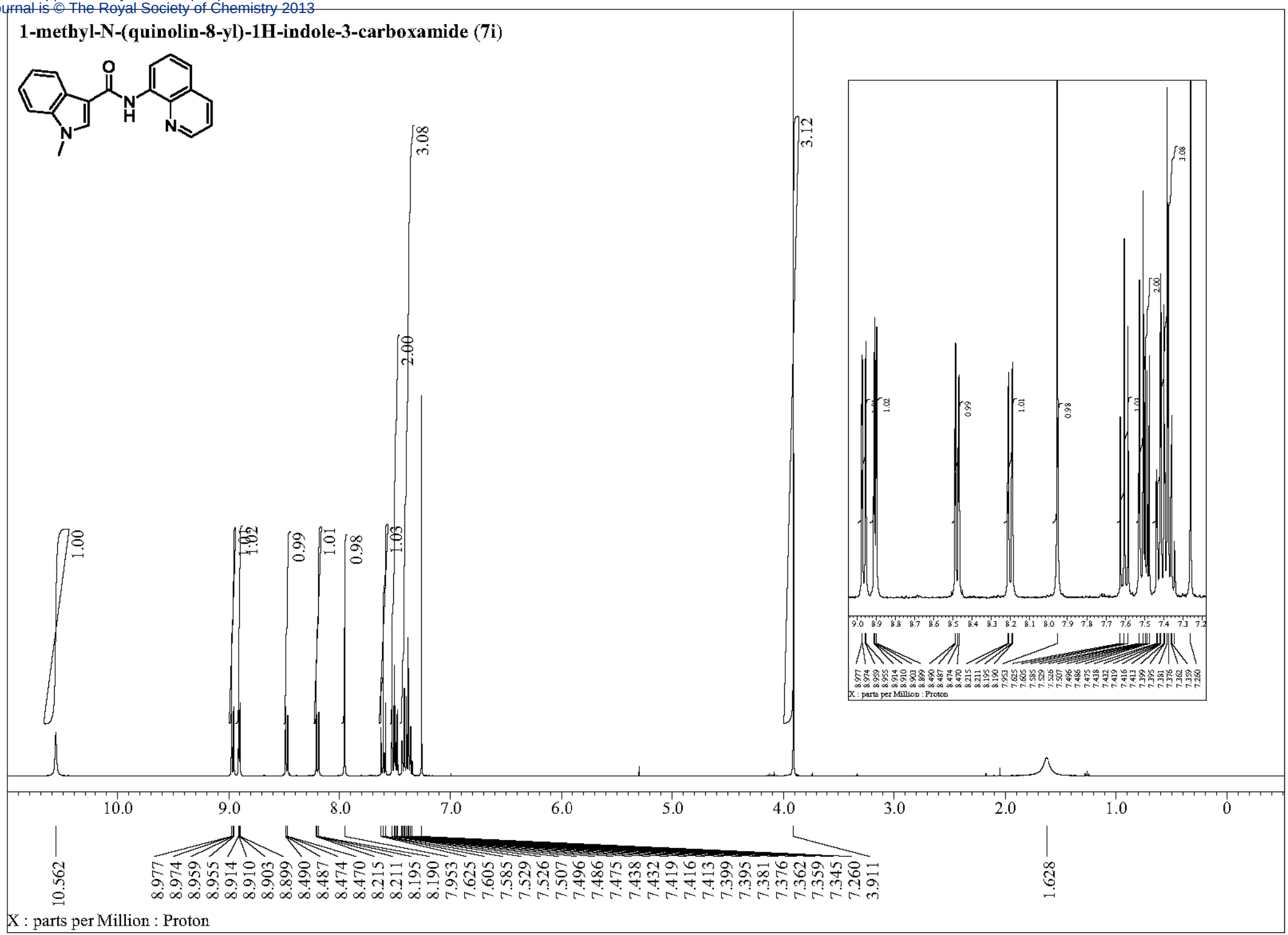

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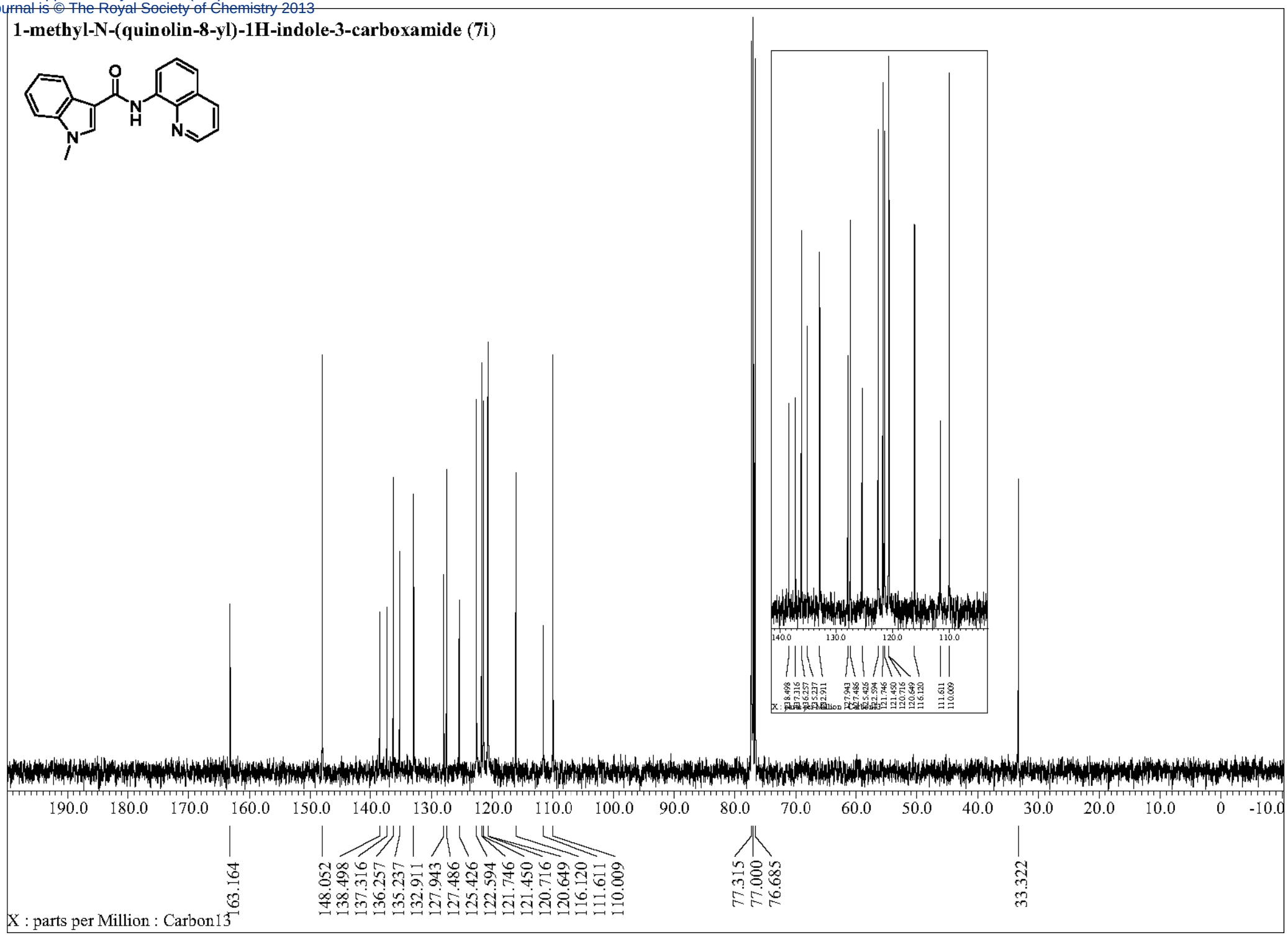

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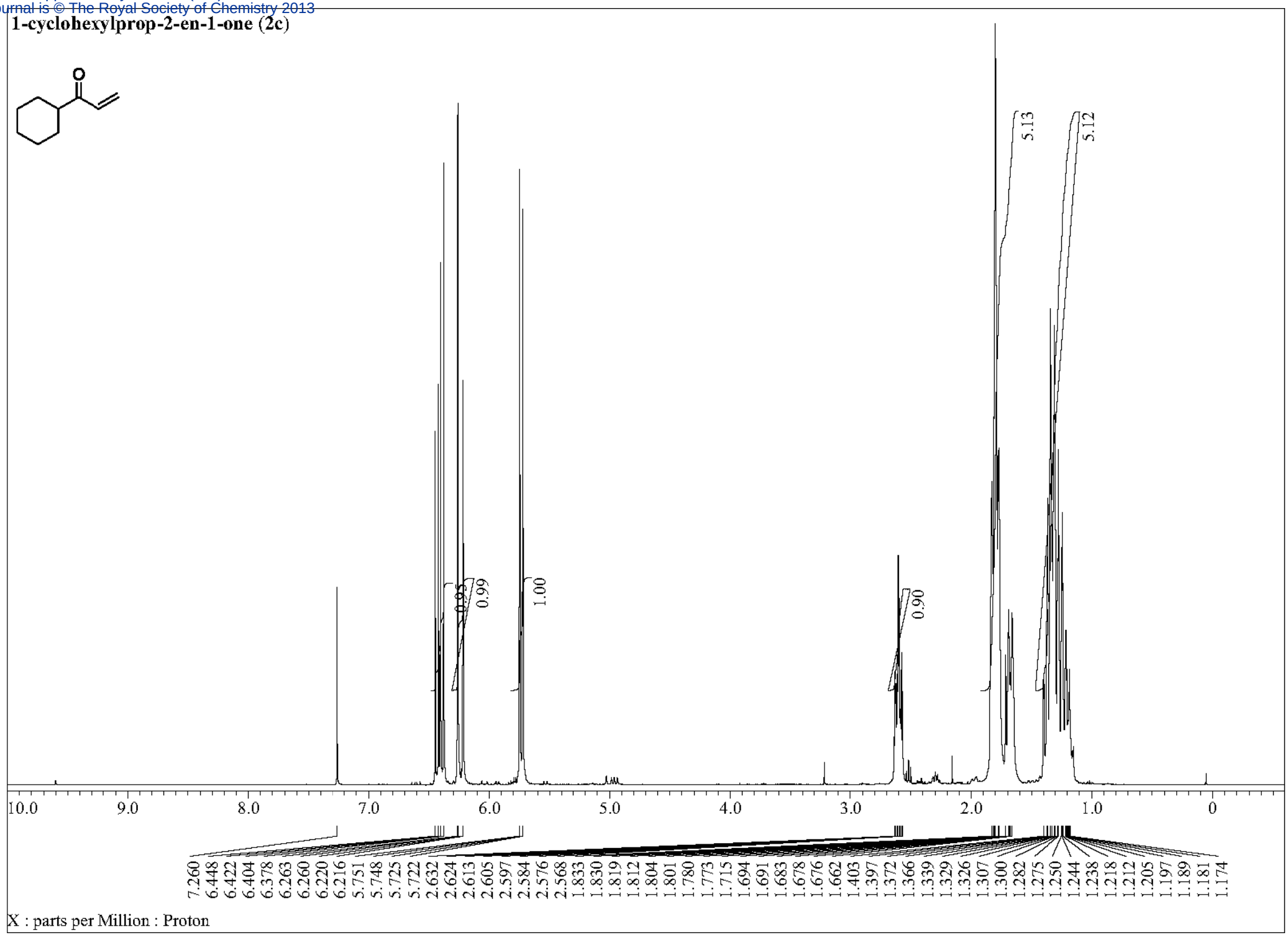

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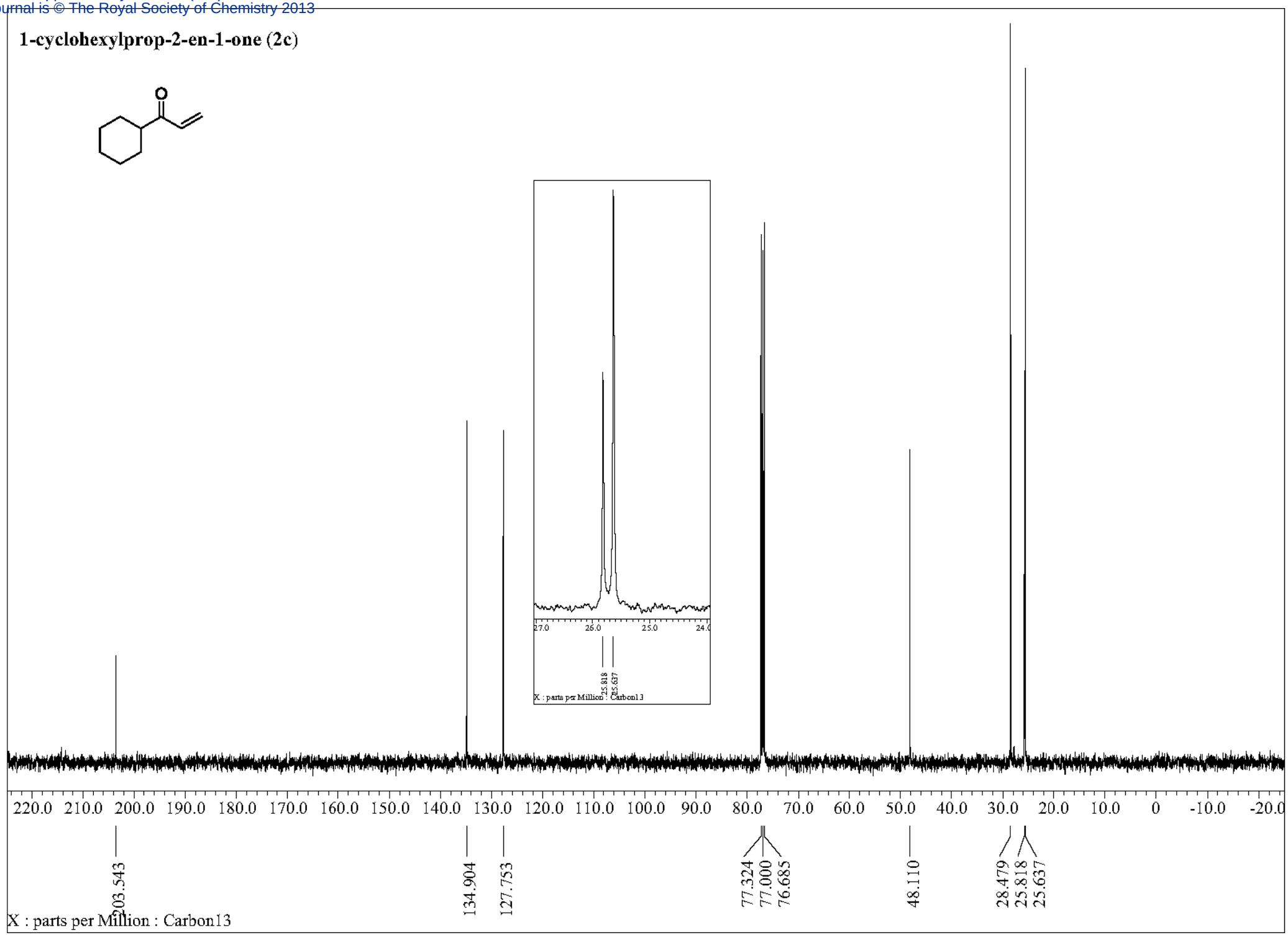

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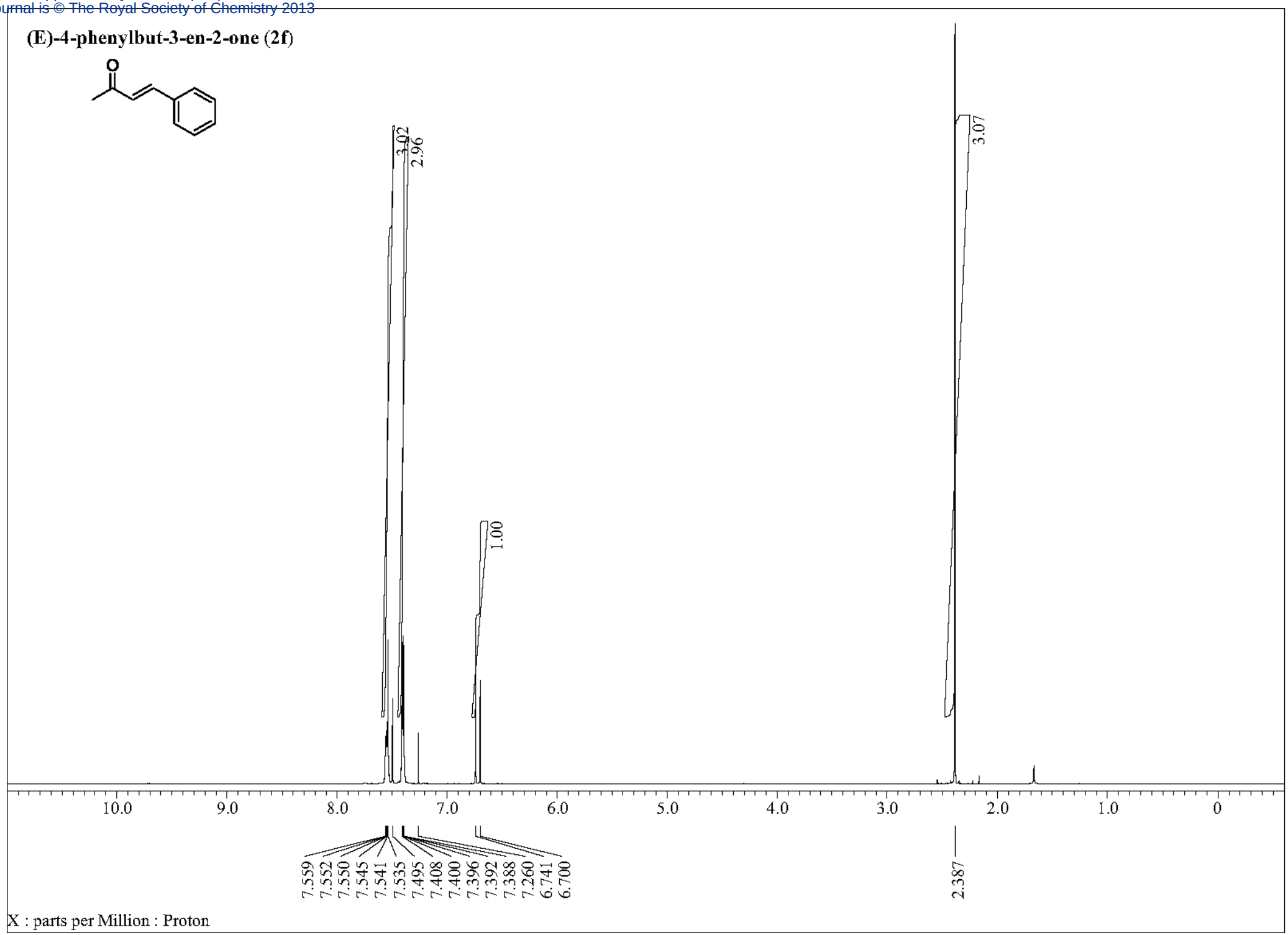

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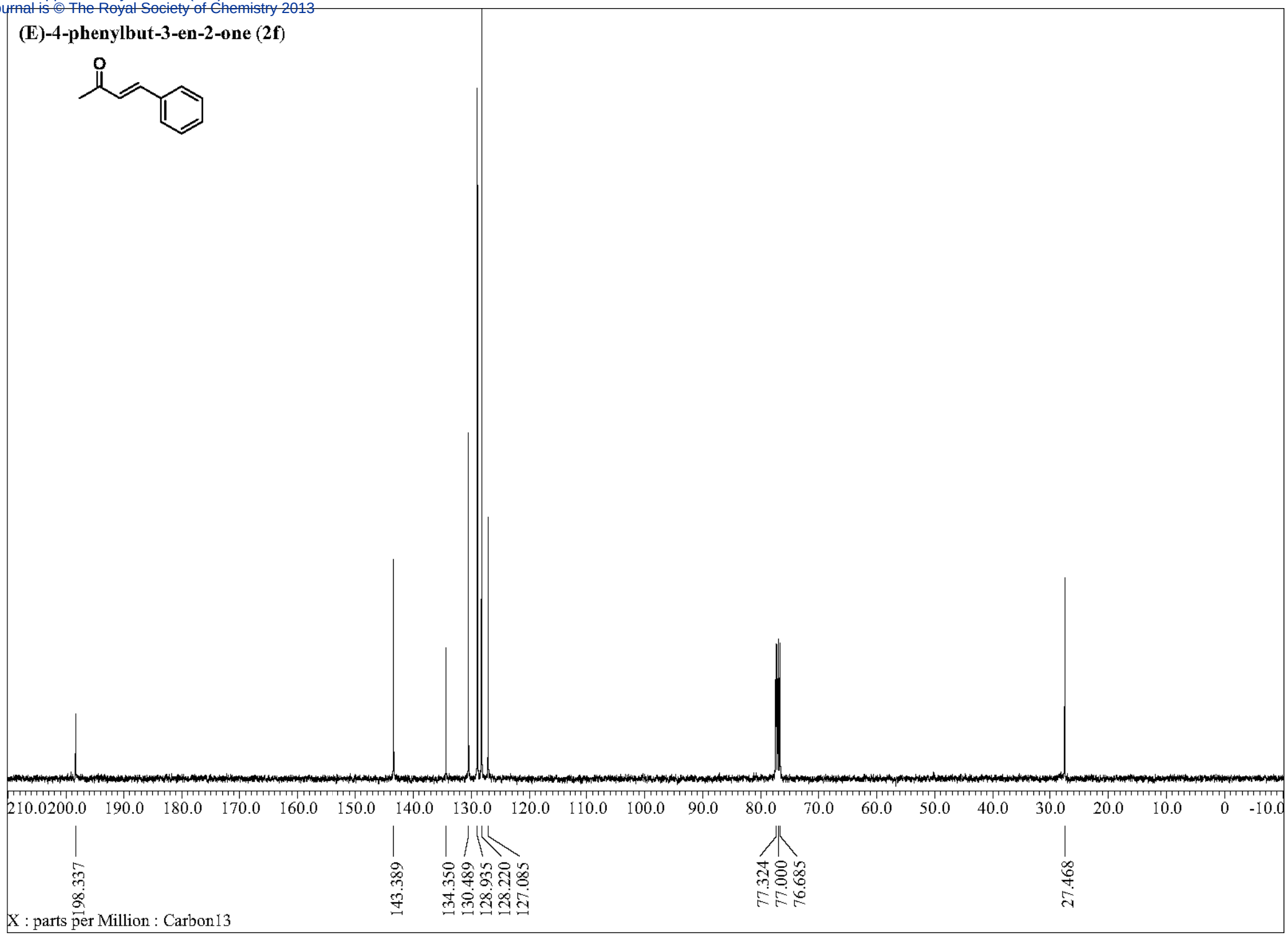

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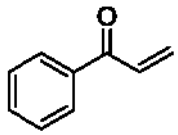
1-phenylprop-2-en-1-one (2g)



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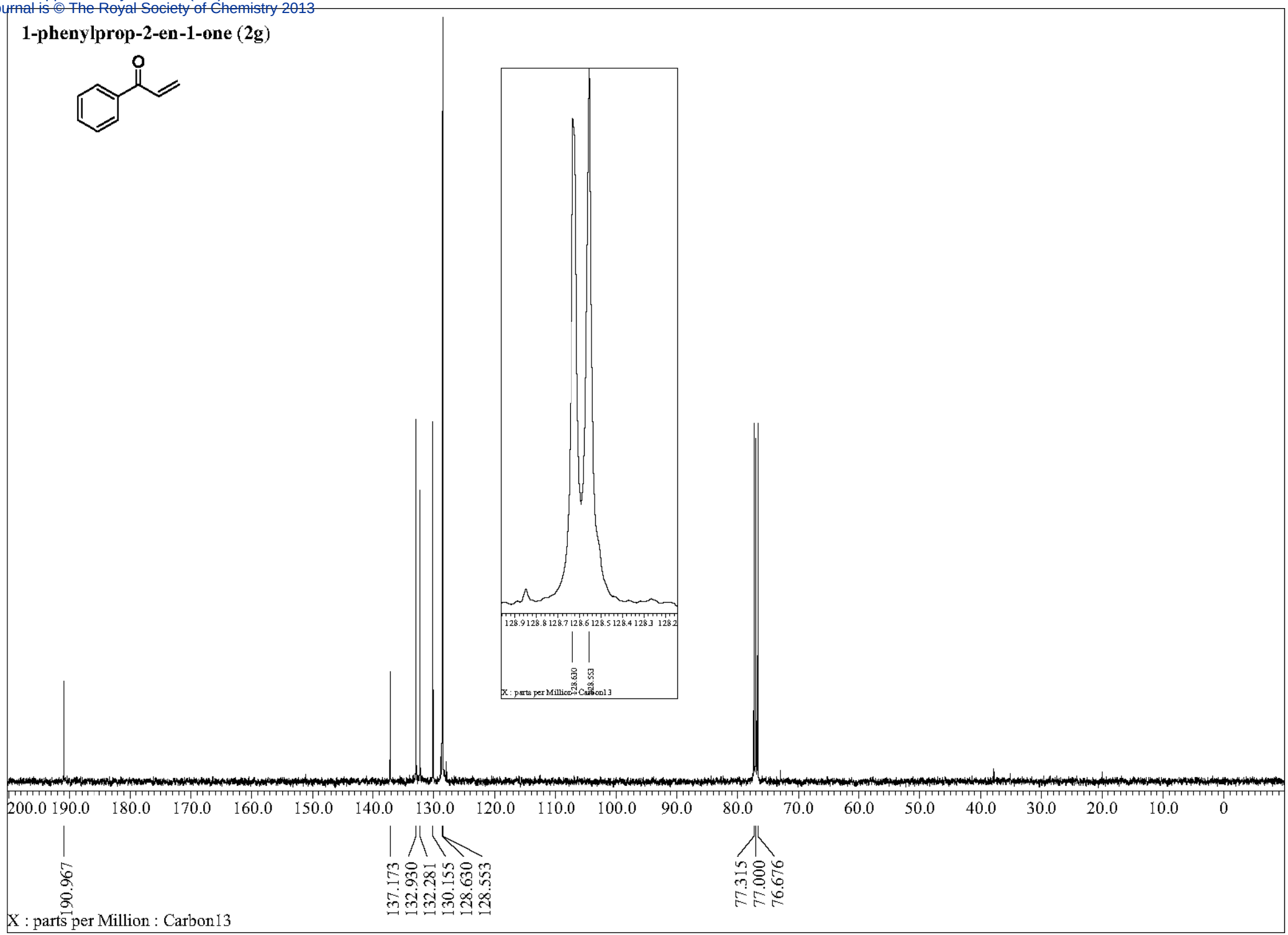

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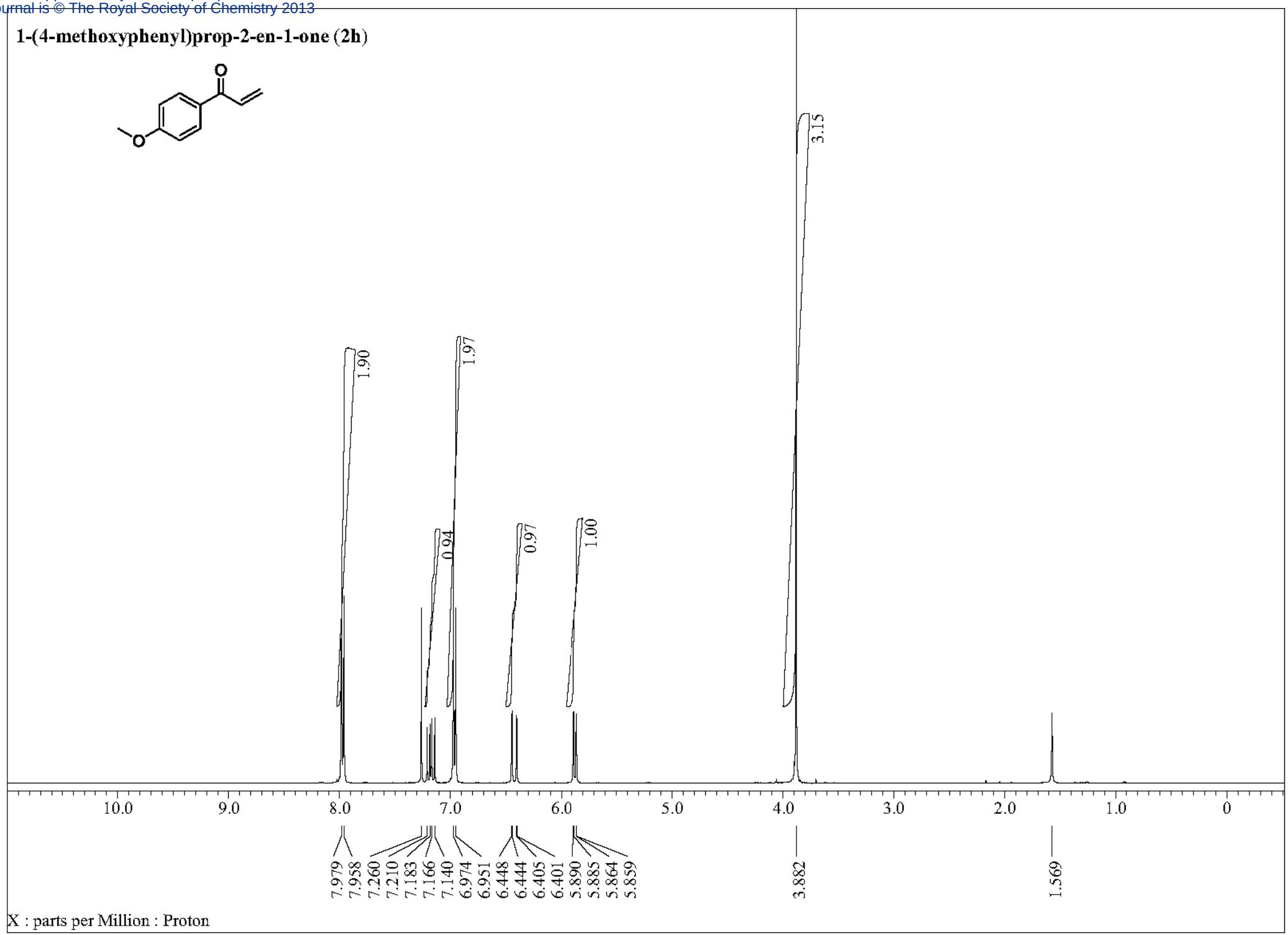

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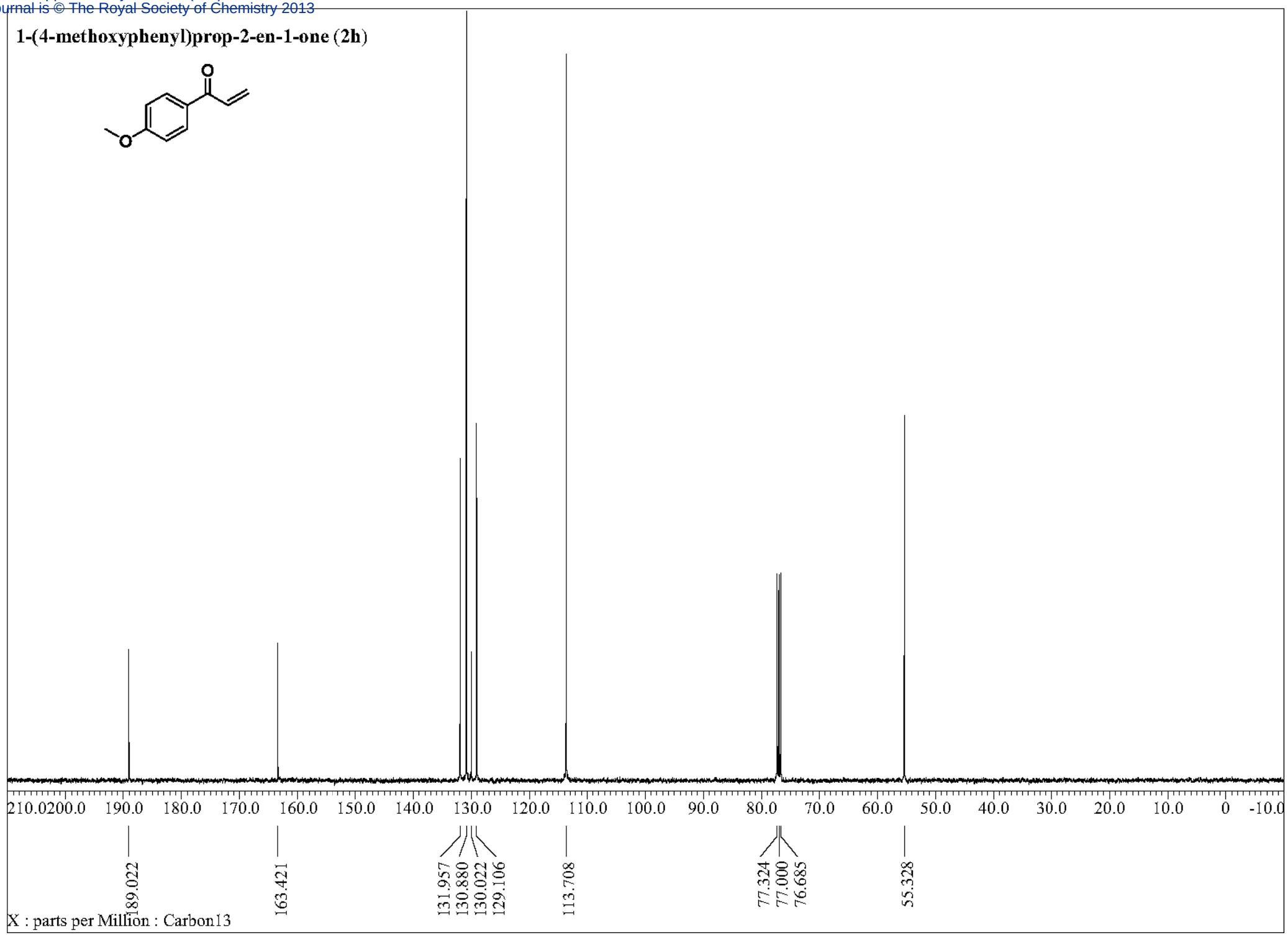

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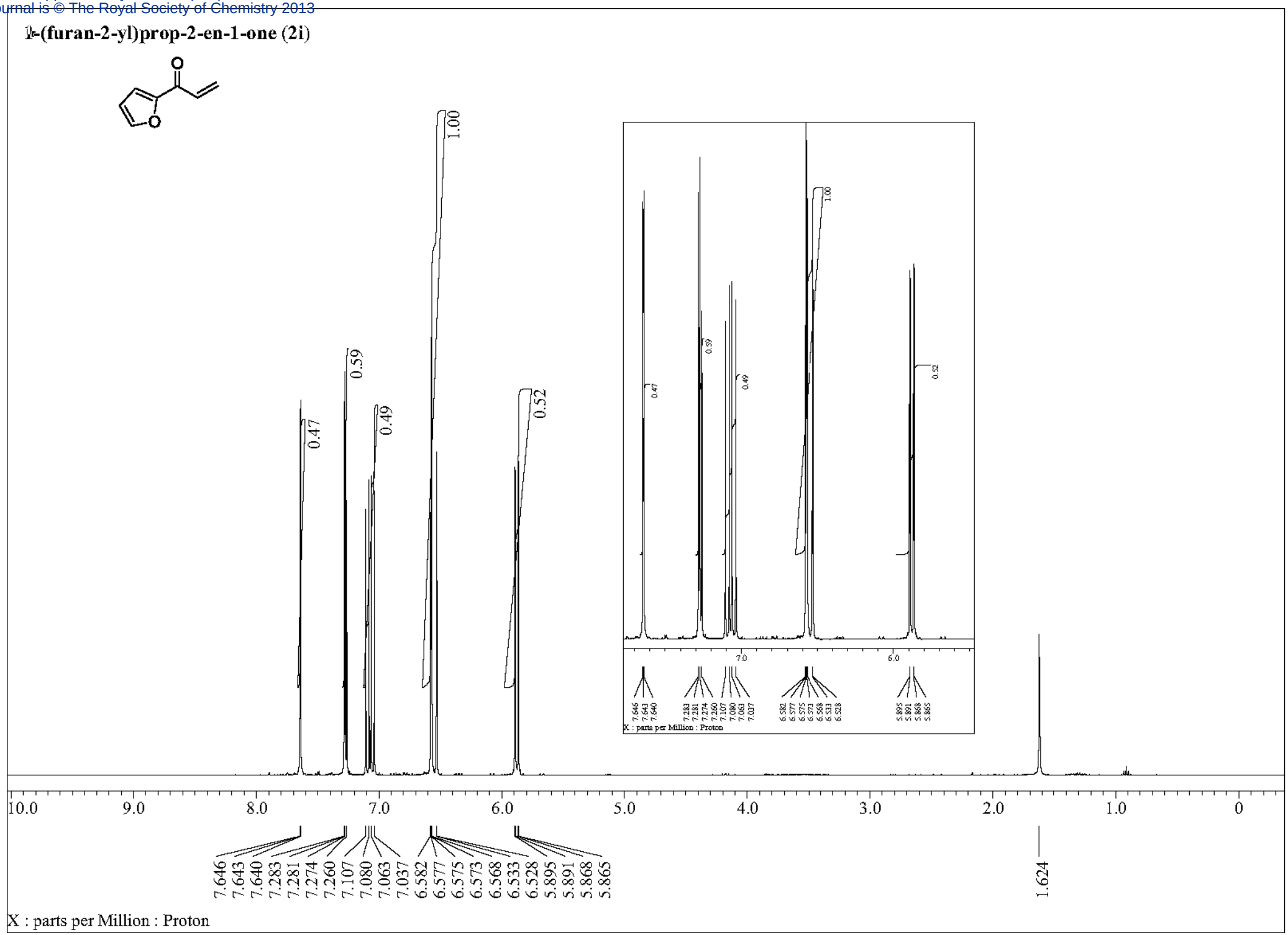

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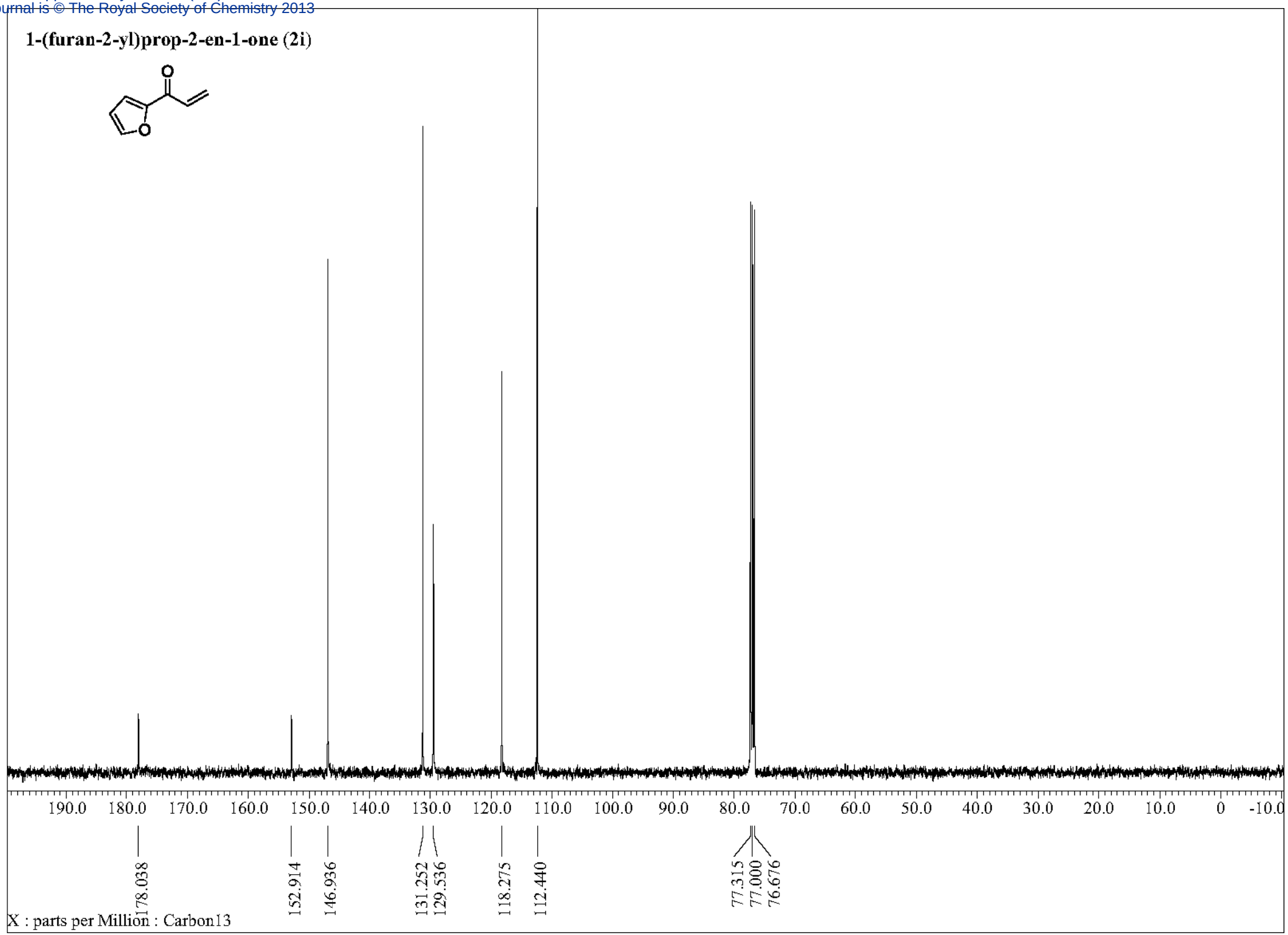

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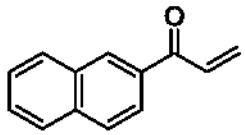
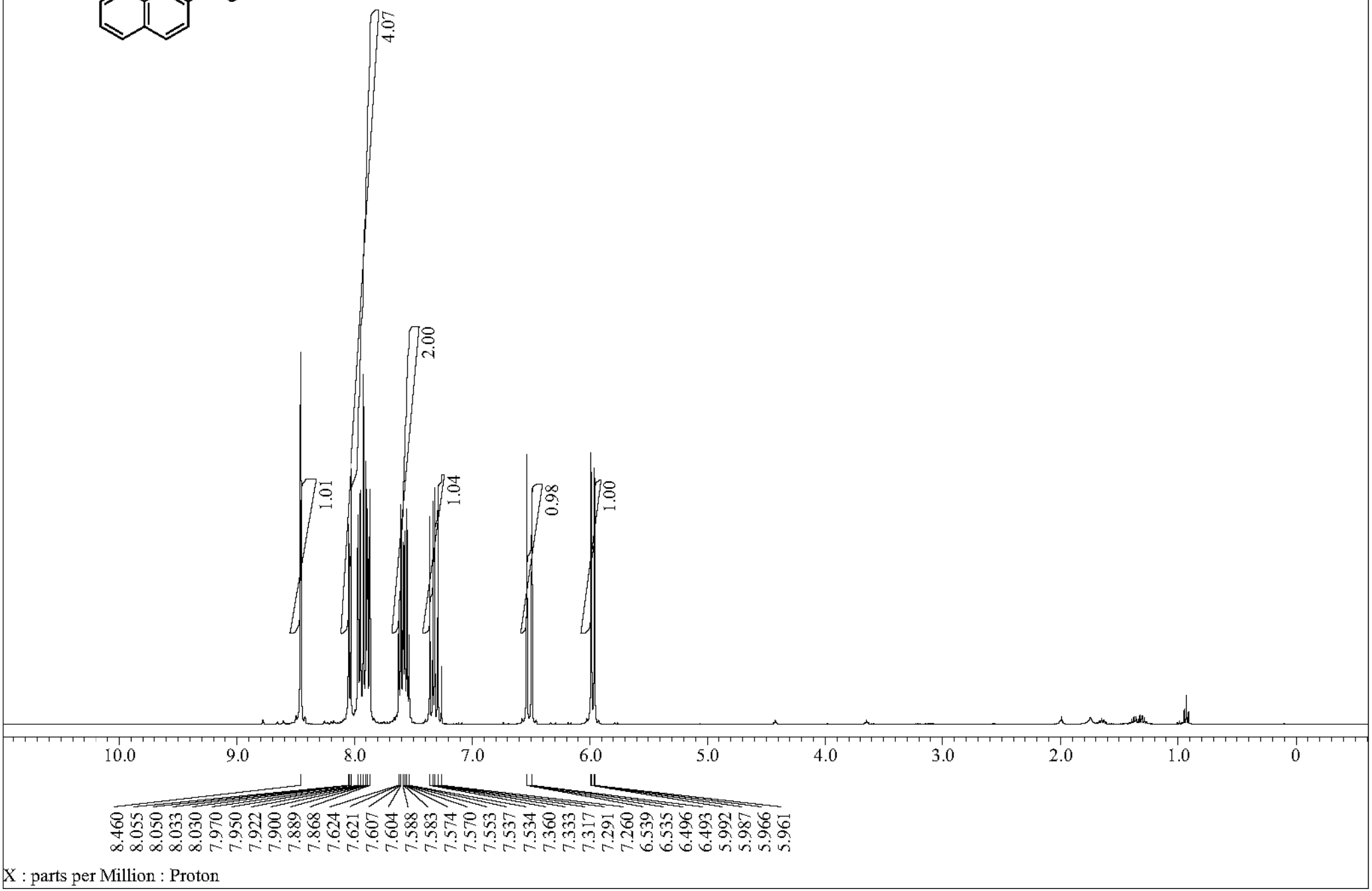
1-(naphthalen-2-yl)prop-2-en-1-one (2j)





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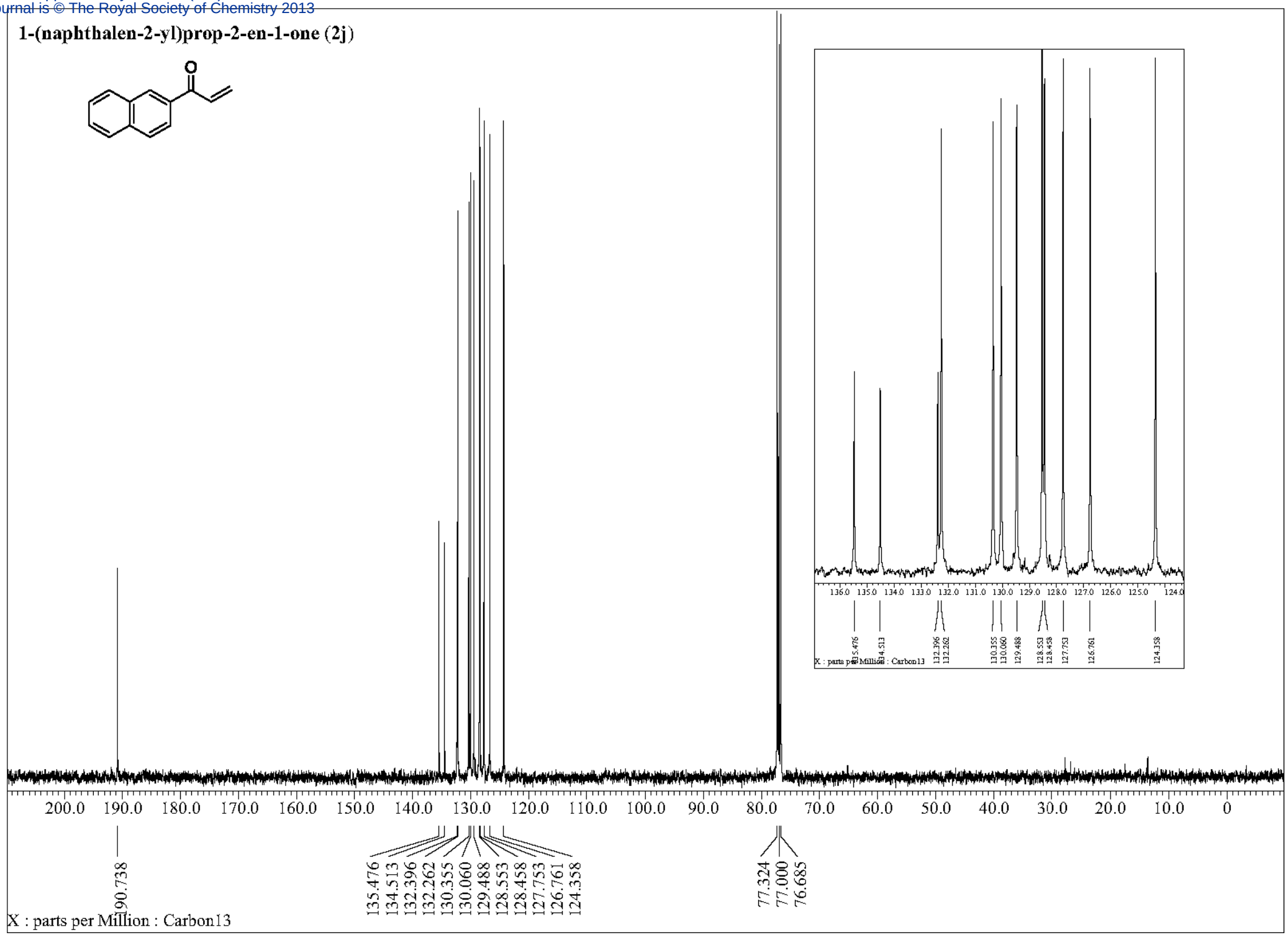

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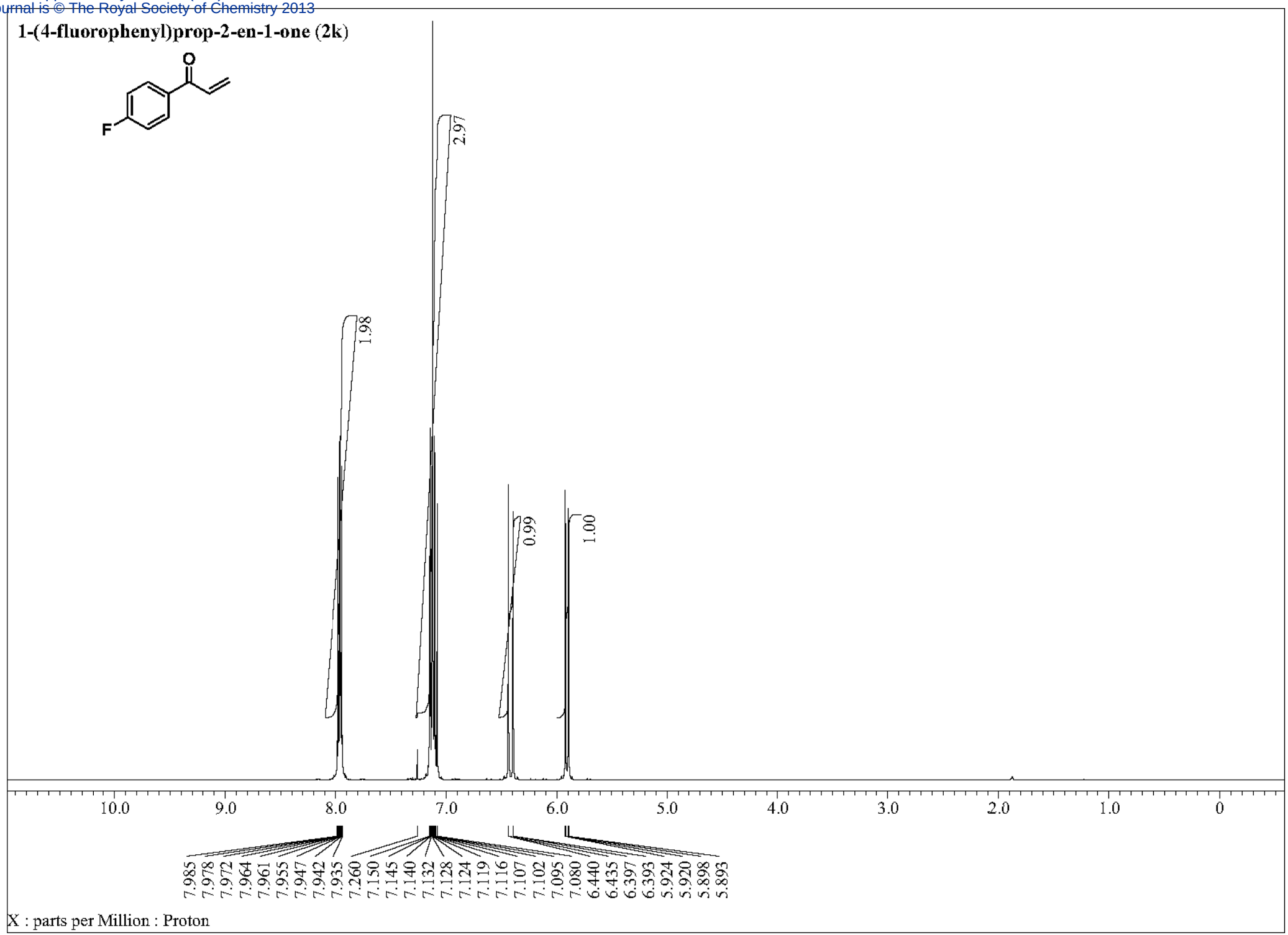

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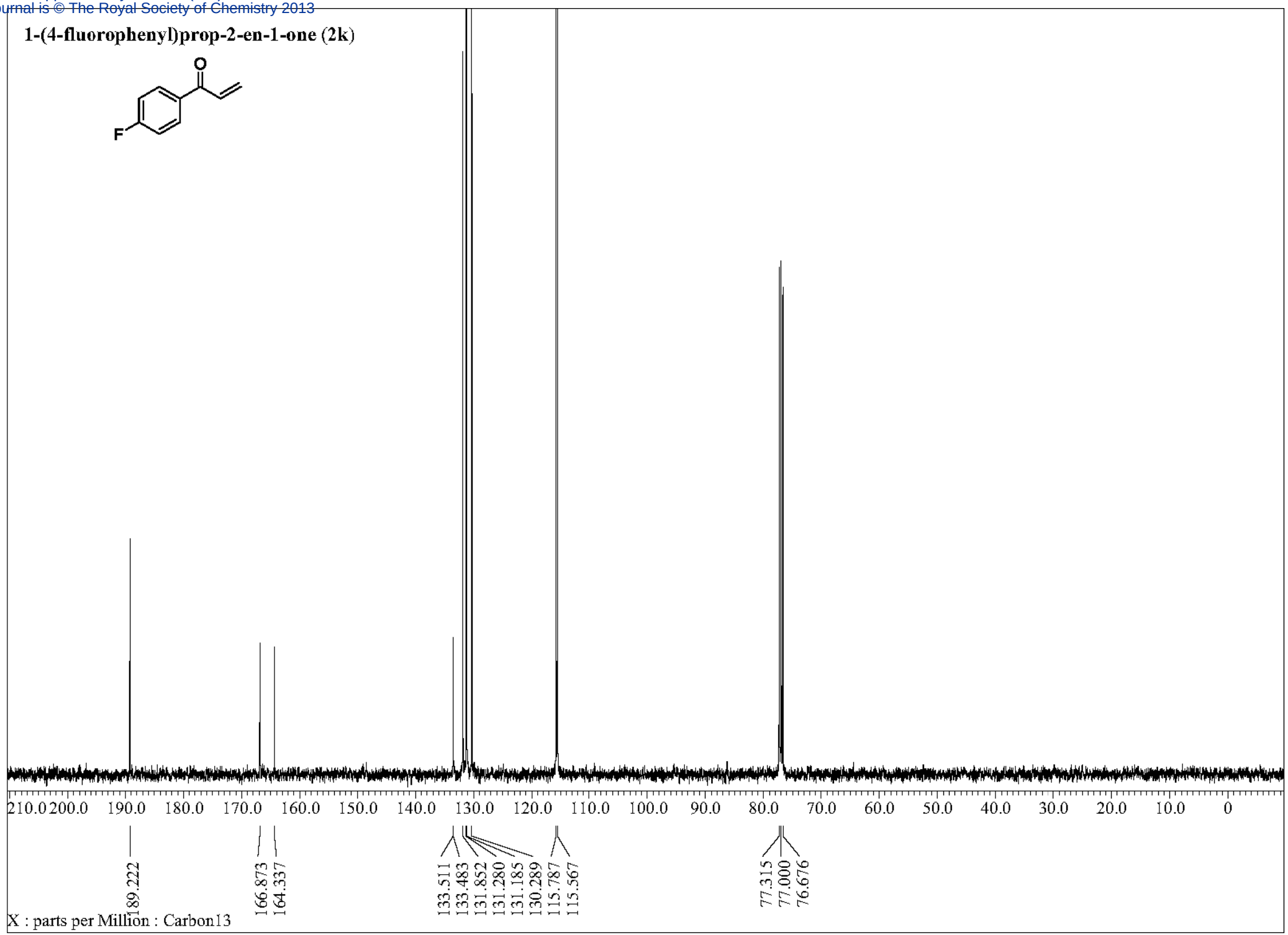

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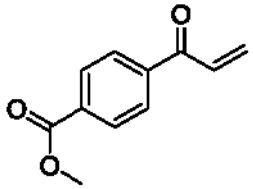
methyl 4-acryloylbenzoate (2l)



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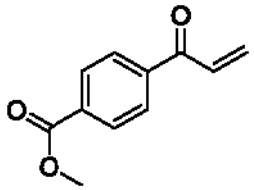
methyl 4-acryloylbenzoate (2l)



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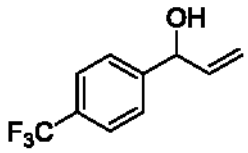
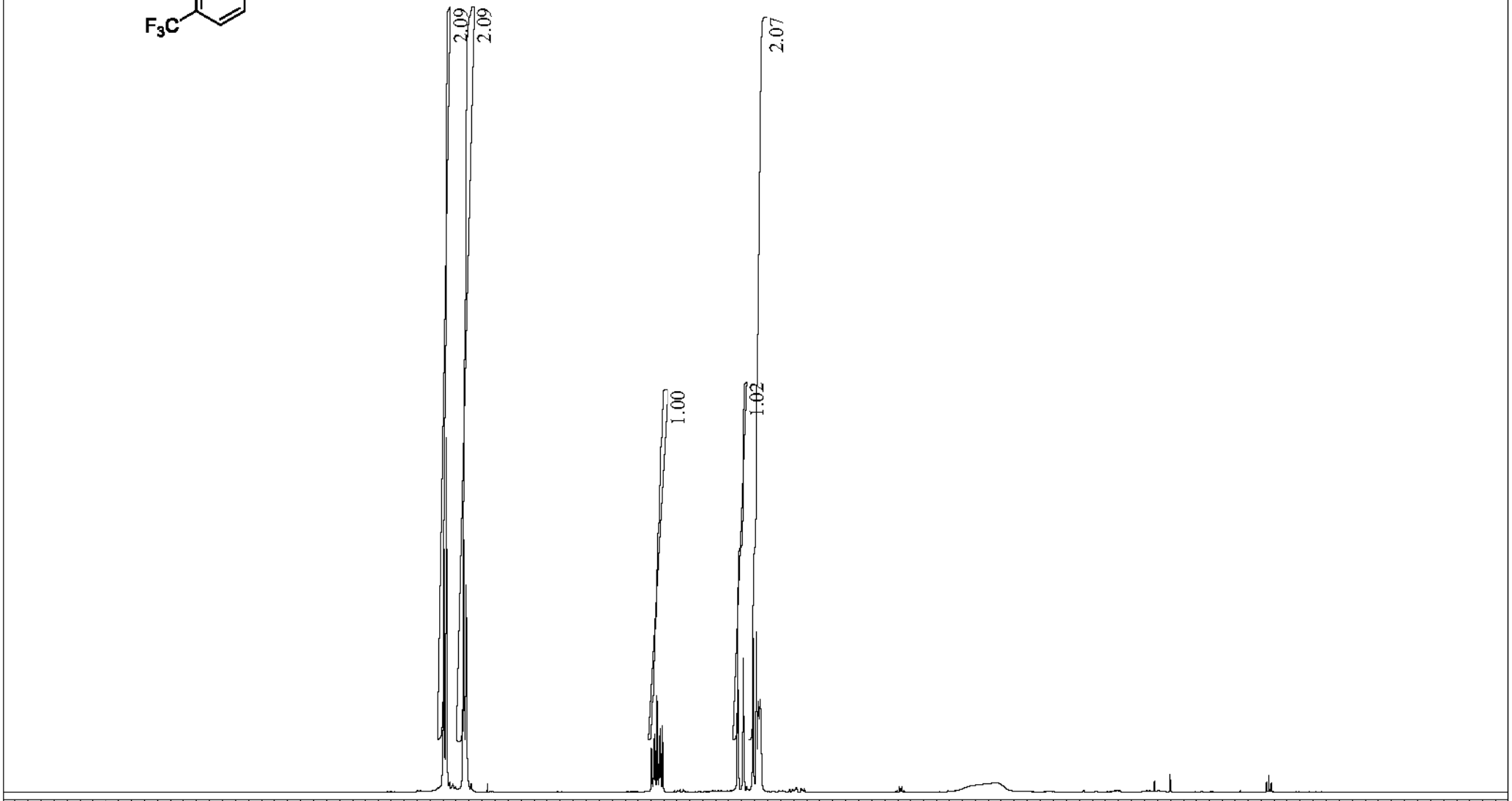
1-(4-(trifluoromethyl)phenyl)prop-2-en-1-ol (2'm)





1-(4-(trifluoromethyl)phenyl)prop-2-en-1-one (2m)

7.596 7.575 7.443 7.422 7.260 5.999 5.995 5.983 5.980 5.972 5.970 5.955 5.939 5.937 5.930 5.928 5.914 5.912 5.336 5.332 5.329 5.290 5.286 5.214 5.212 5.188 5.186 5.172 5.158

X : parts per Million : Proton

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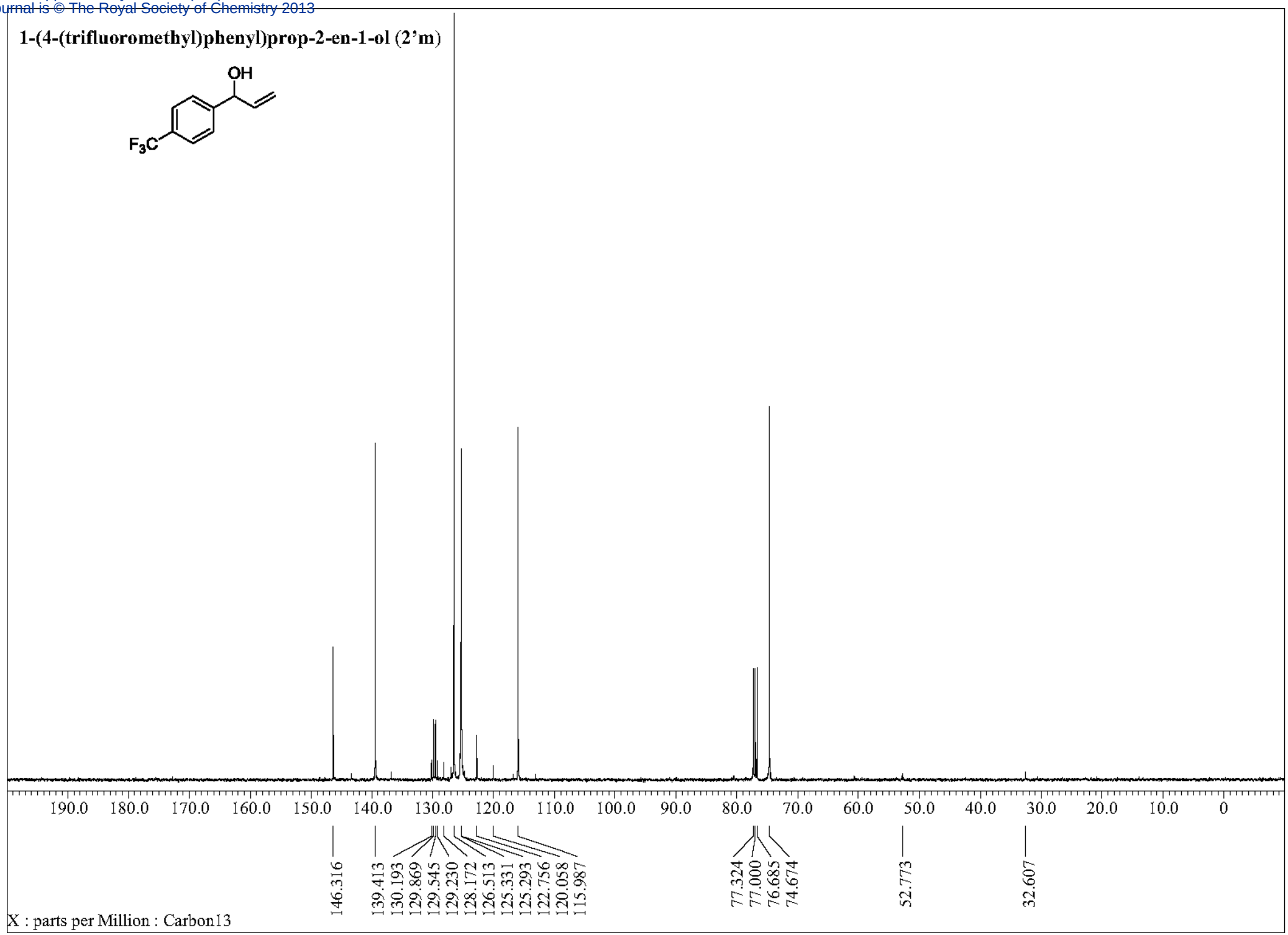

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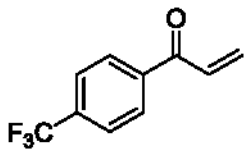
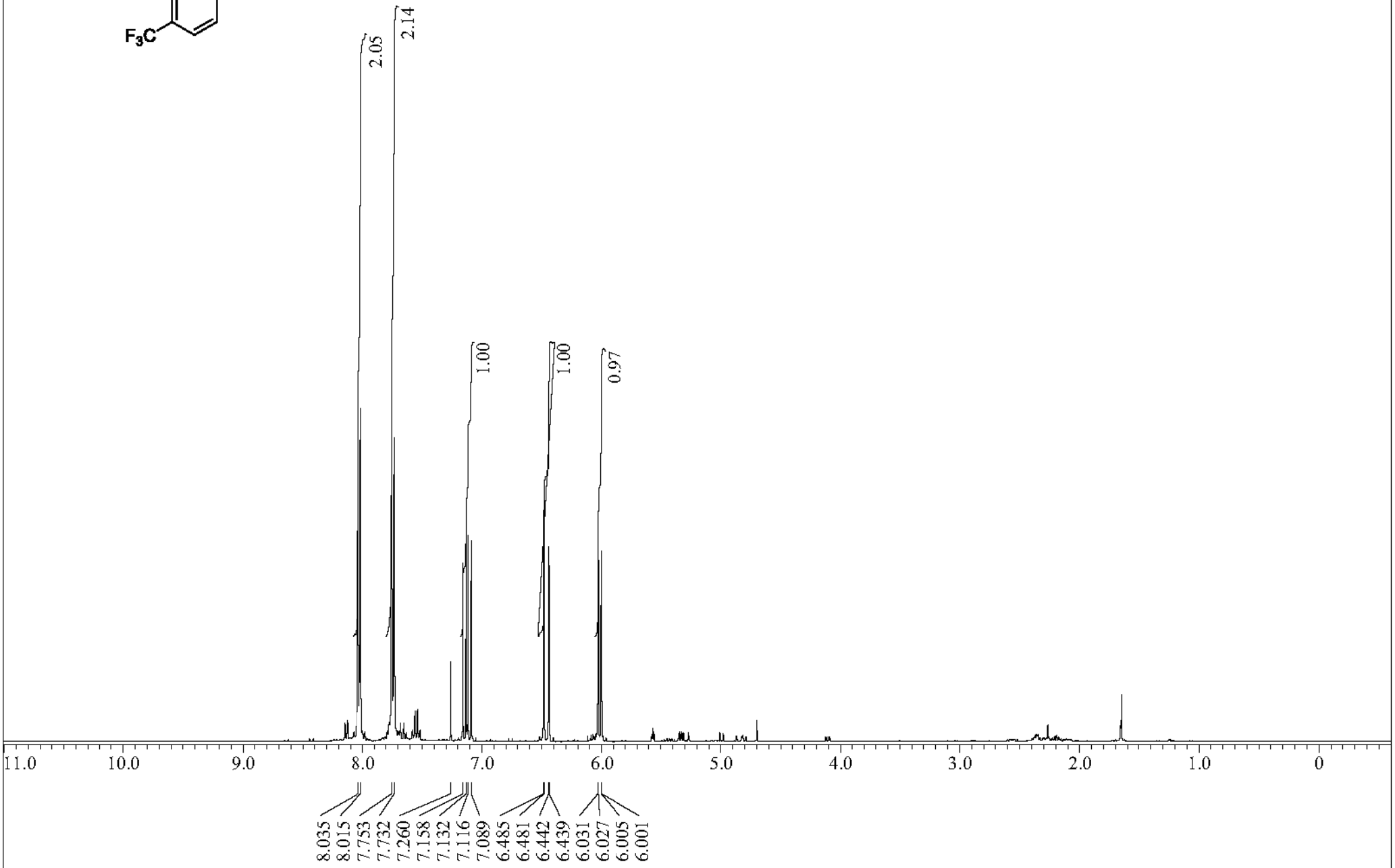
1-(4-(trifluoromethyl)phenyl)prop-2-en-1-one (2m)





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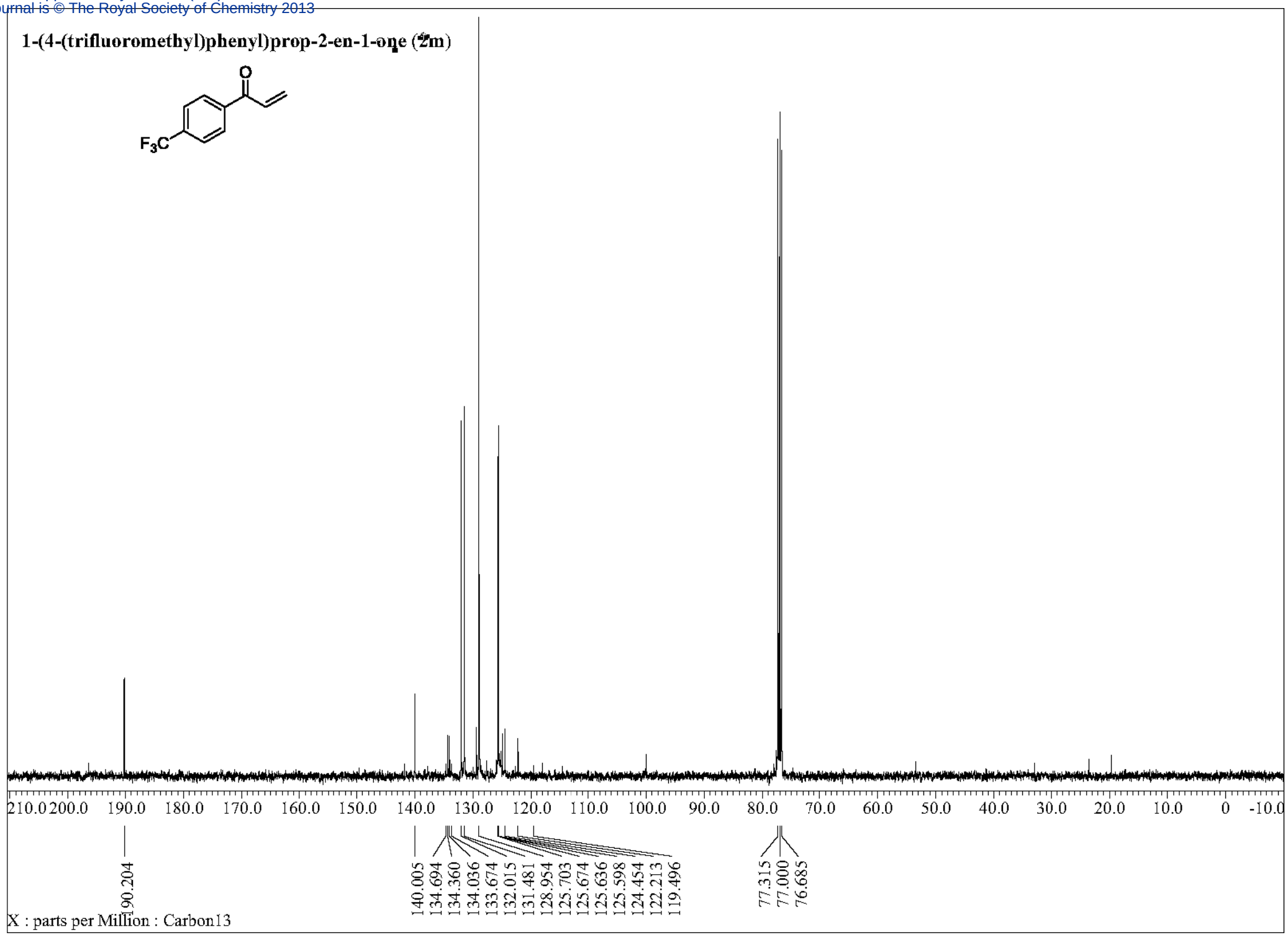

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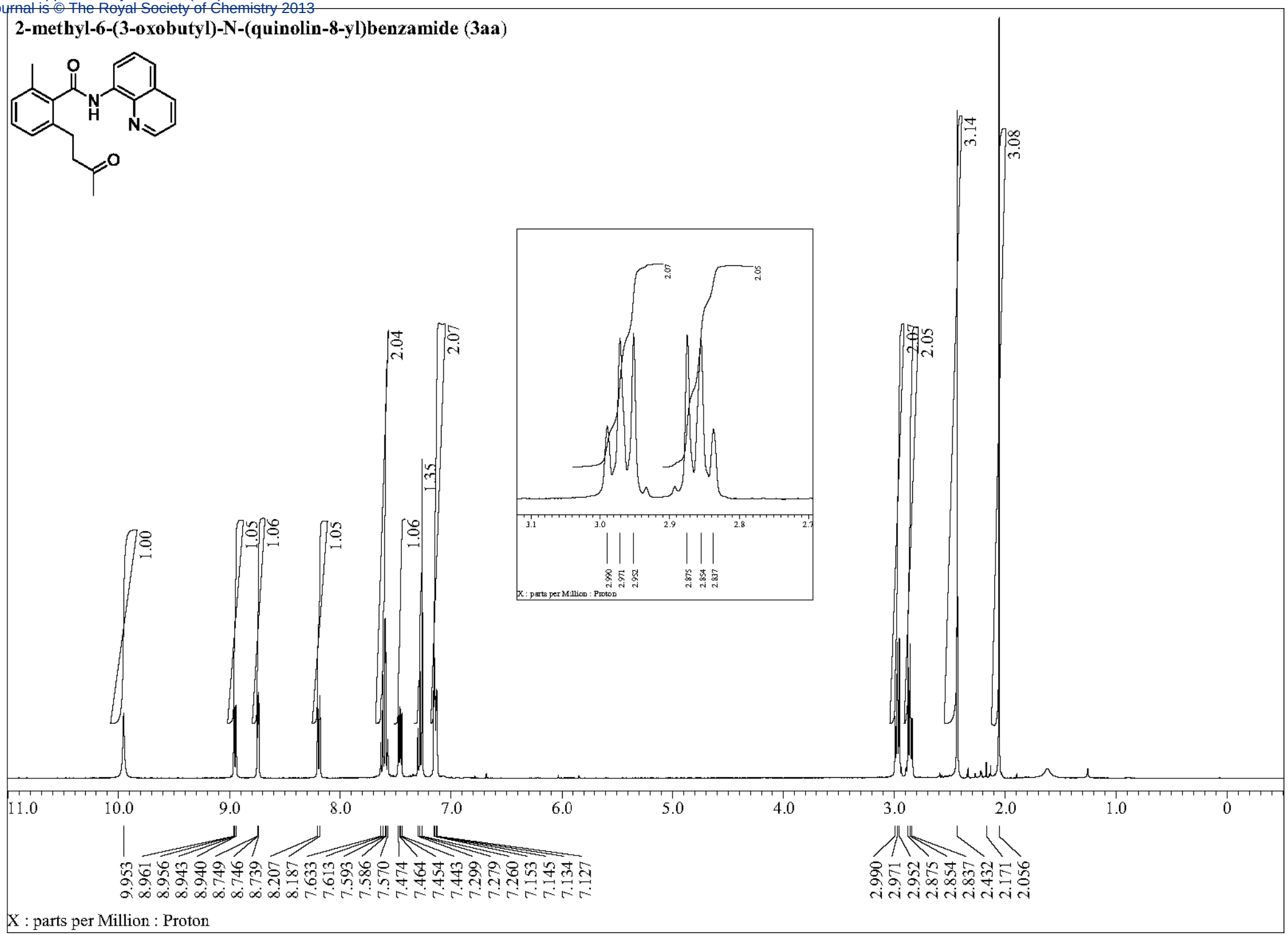

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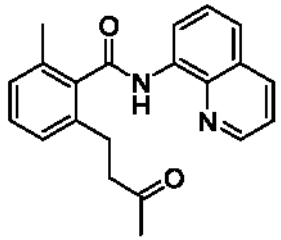
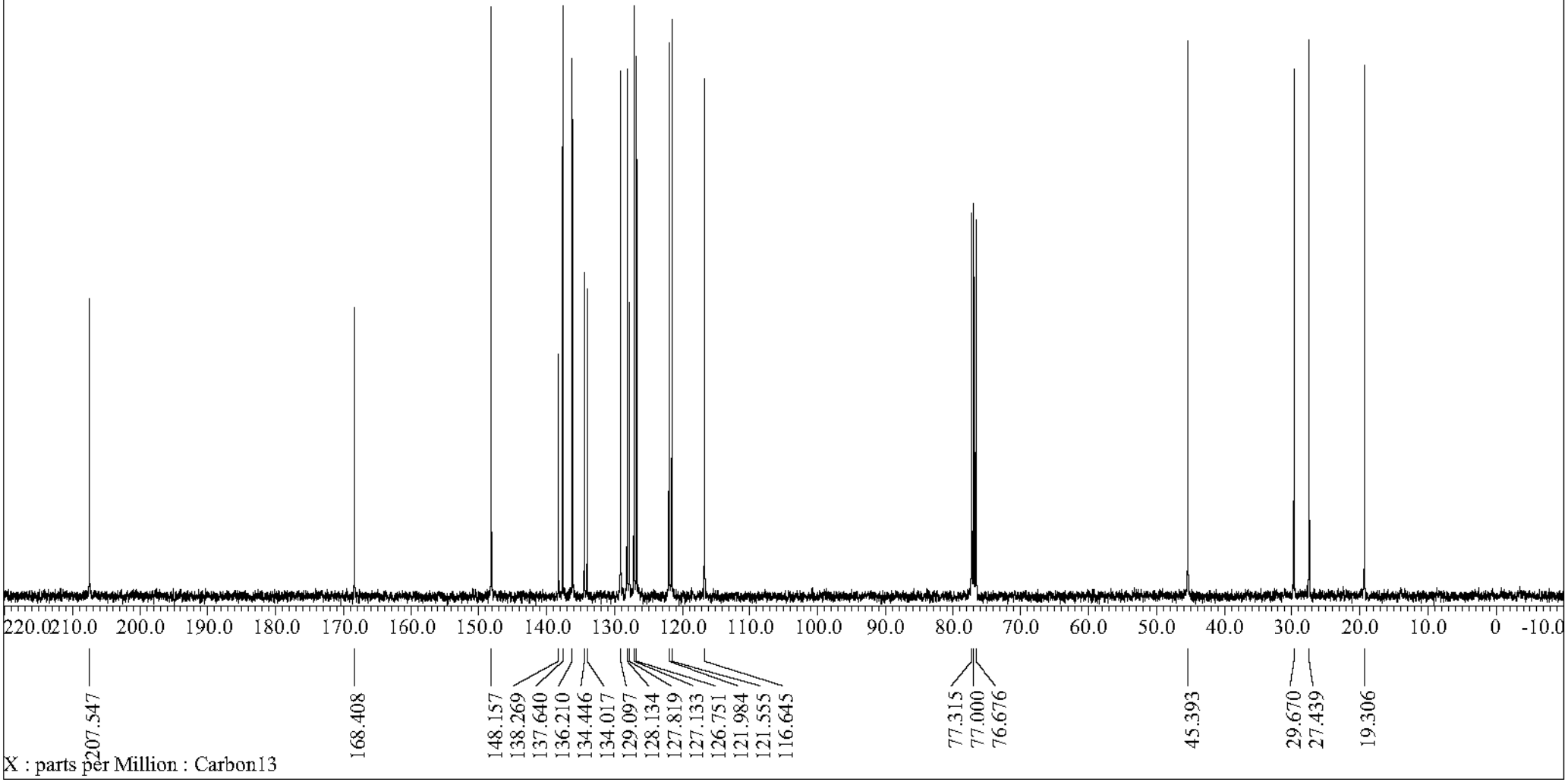
2-methyl-6-(3-oxobutyl)-N-(quinolin-8-yl)benzamide (3aa)





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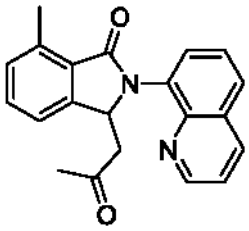
7-methyl-3-(2-oxopropyl)-2-(quinolin-8-yl)isoindolin-1-one (4aa)



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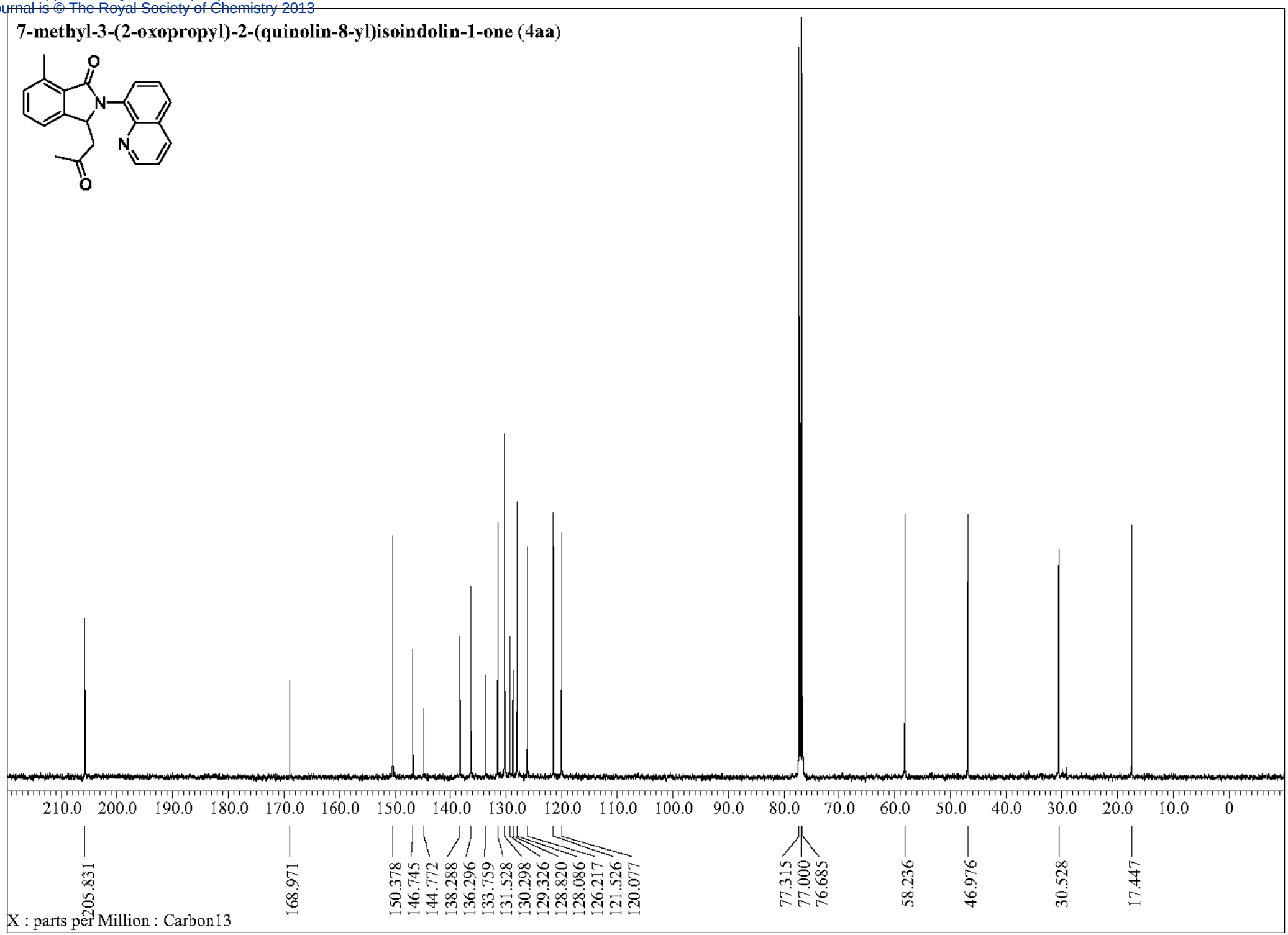

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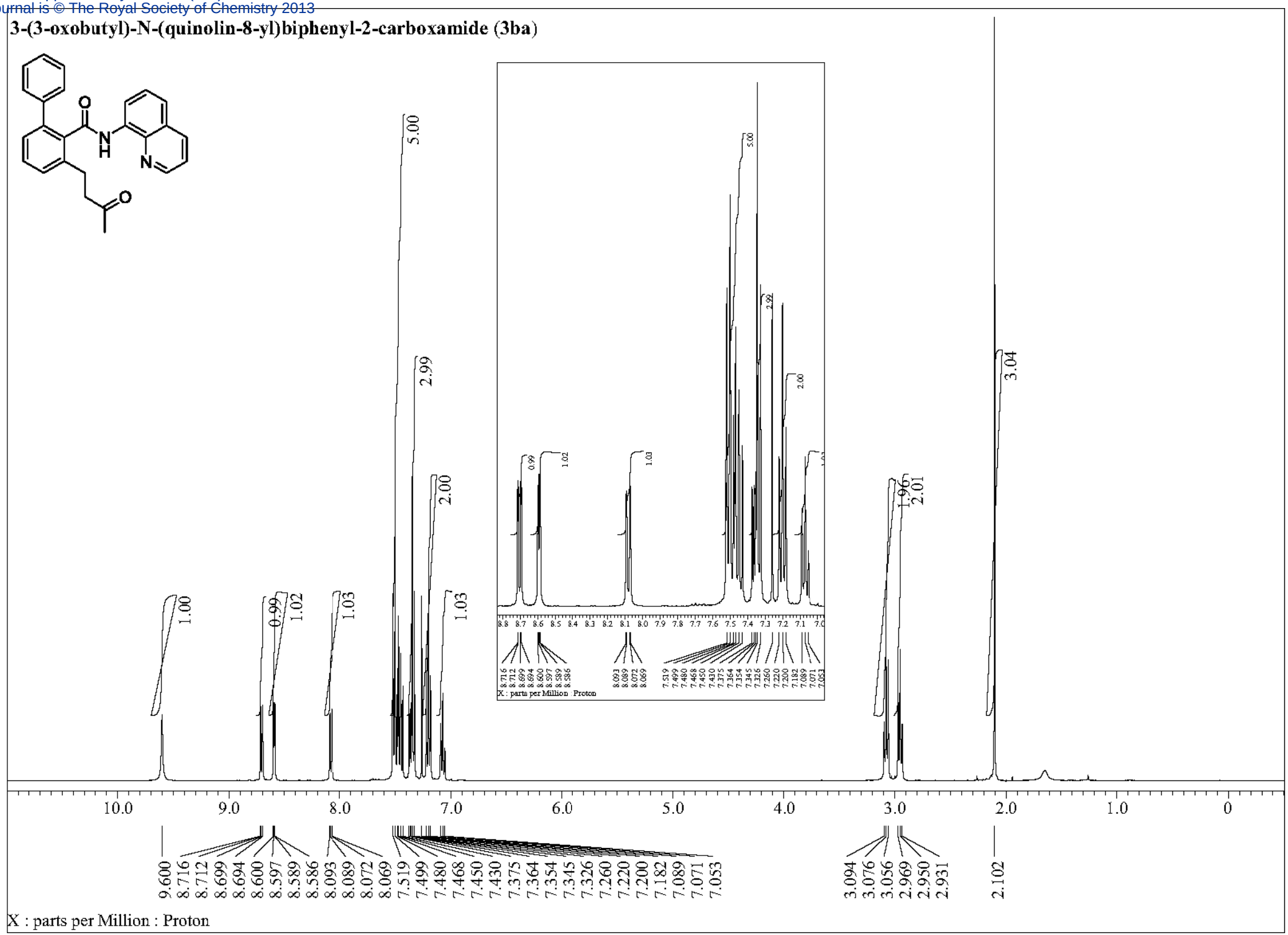

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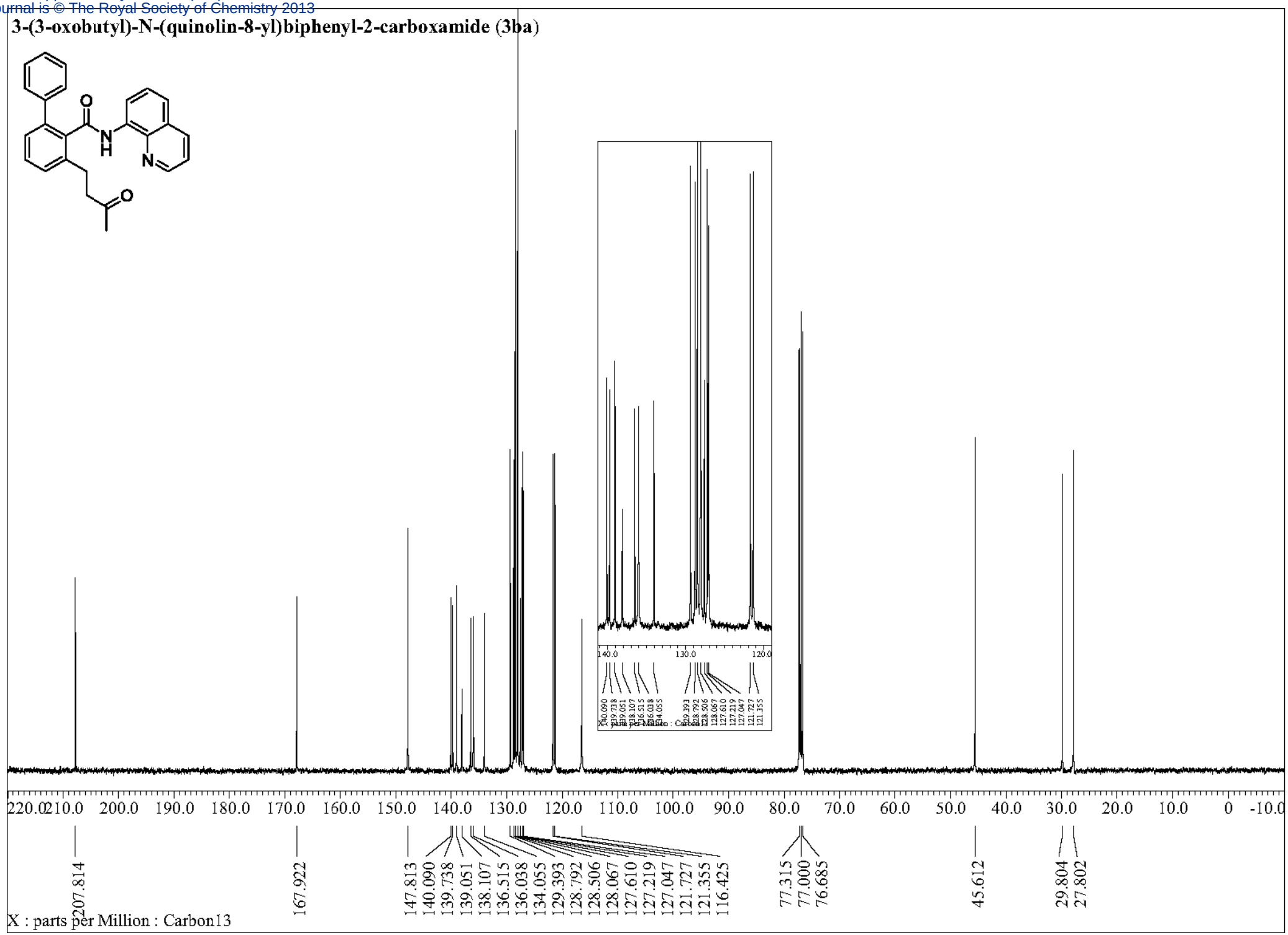

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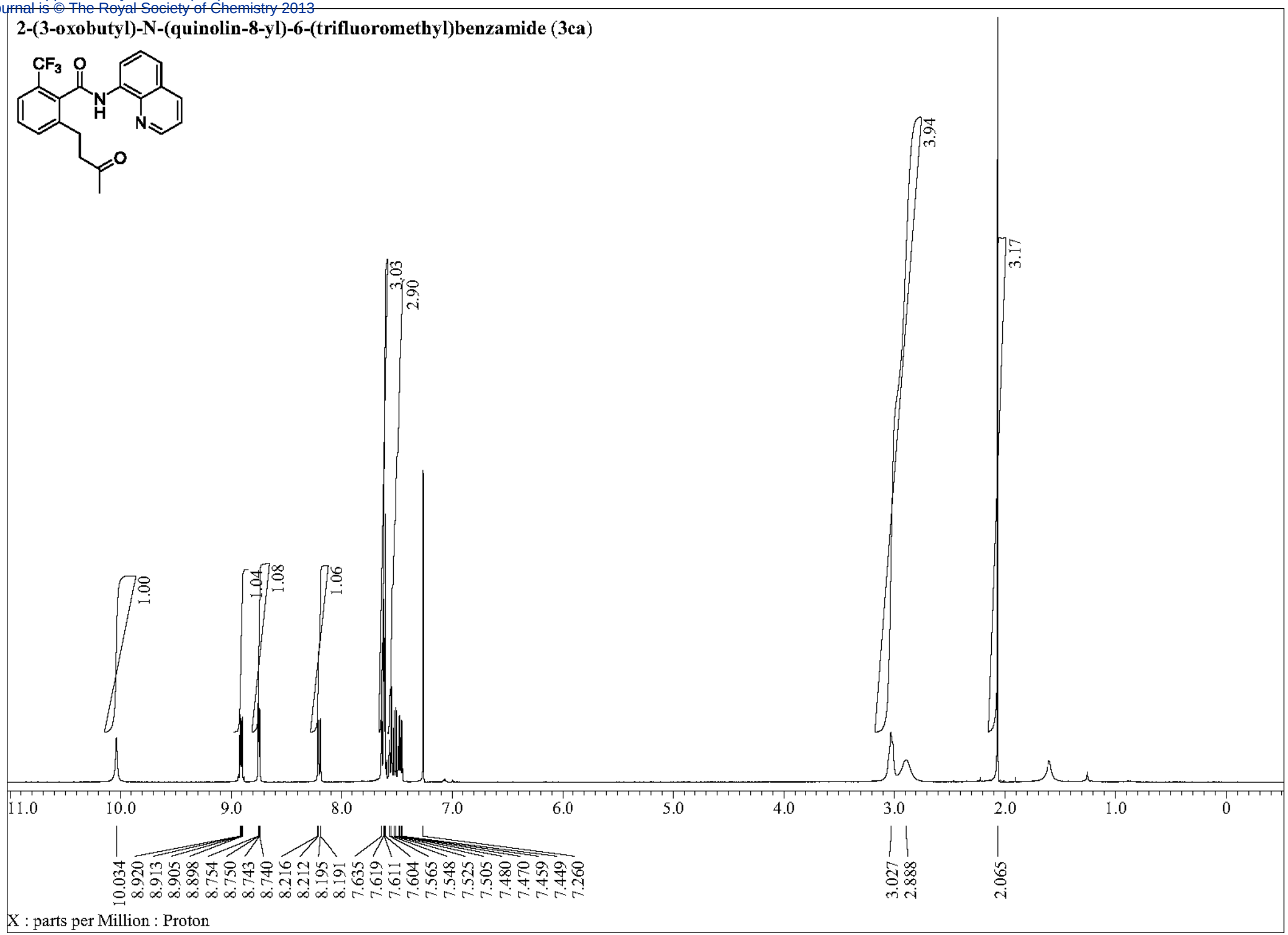

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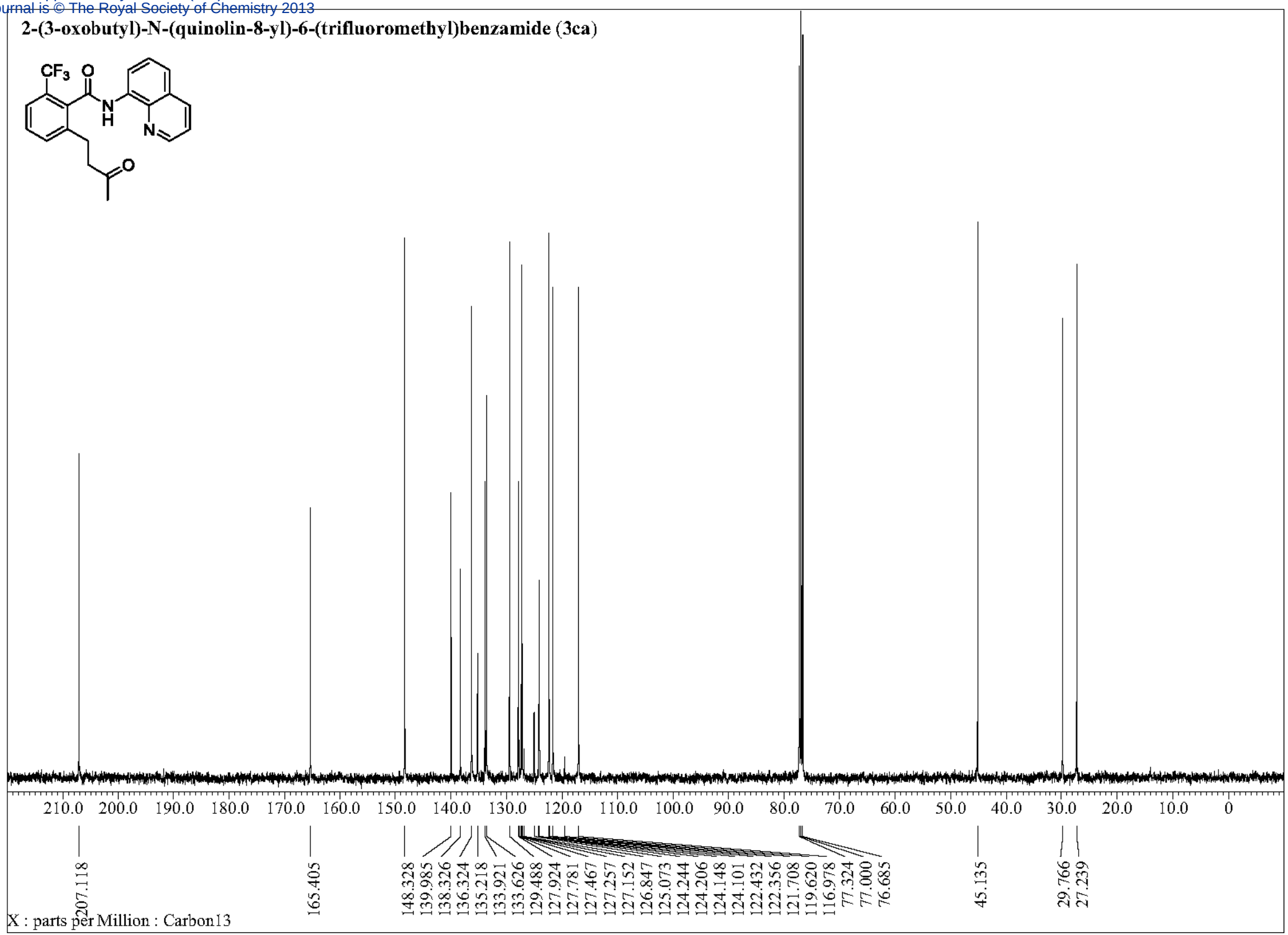

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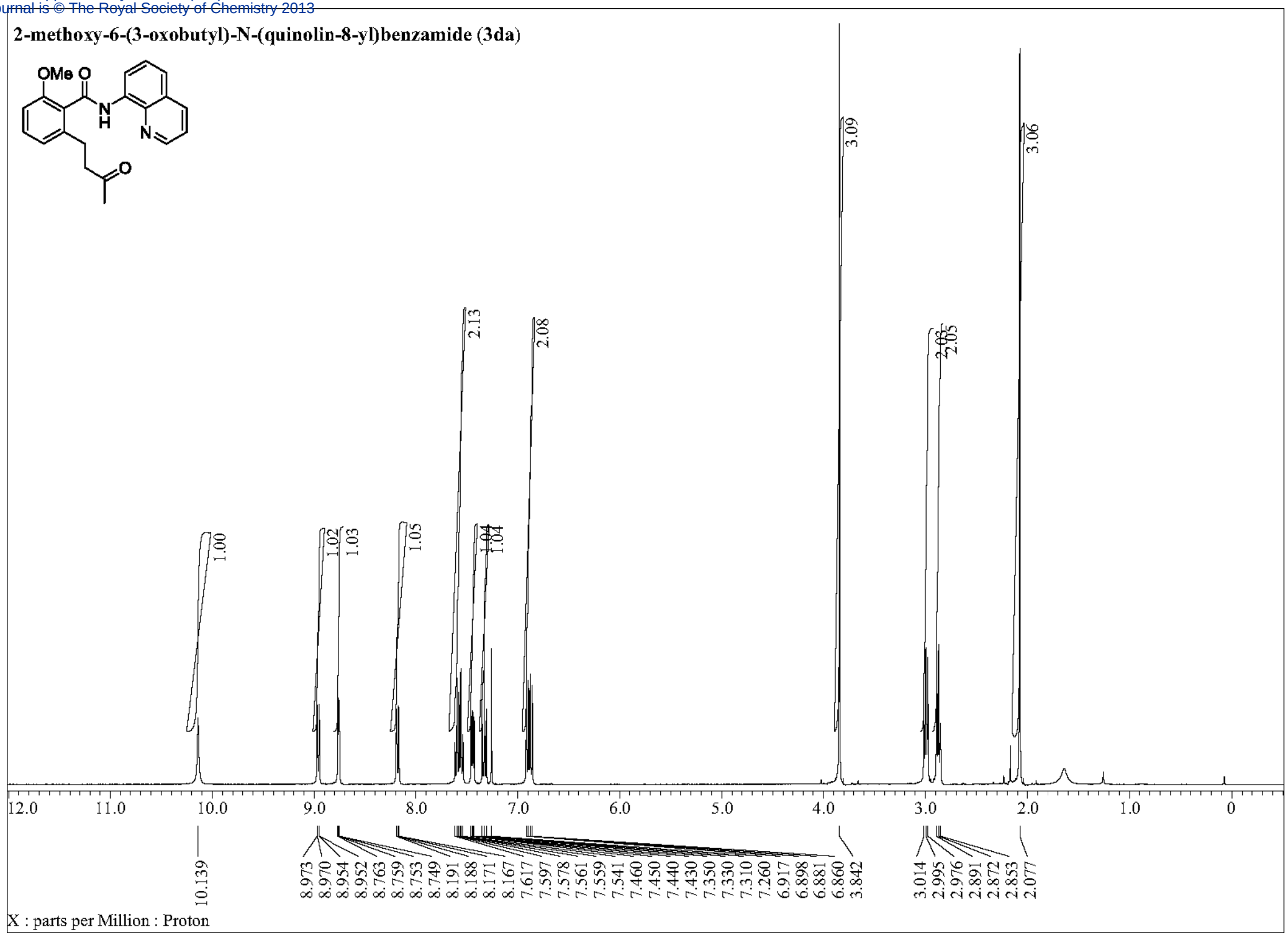

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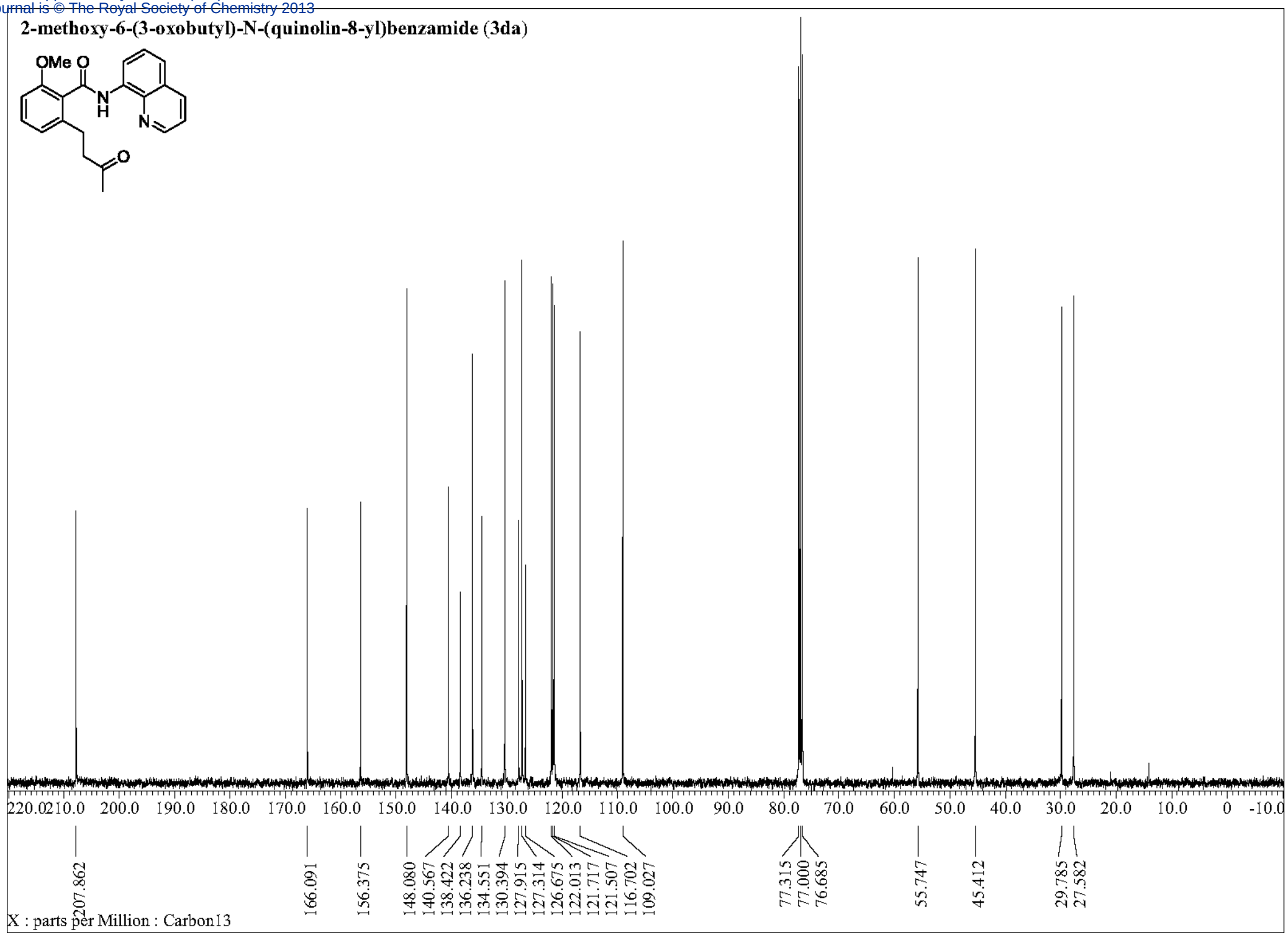

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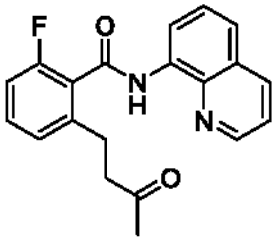
2-fluoro-6-(3-oxobutyl)-N-(quinolin-8-yl)benzamide (3ea)



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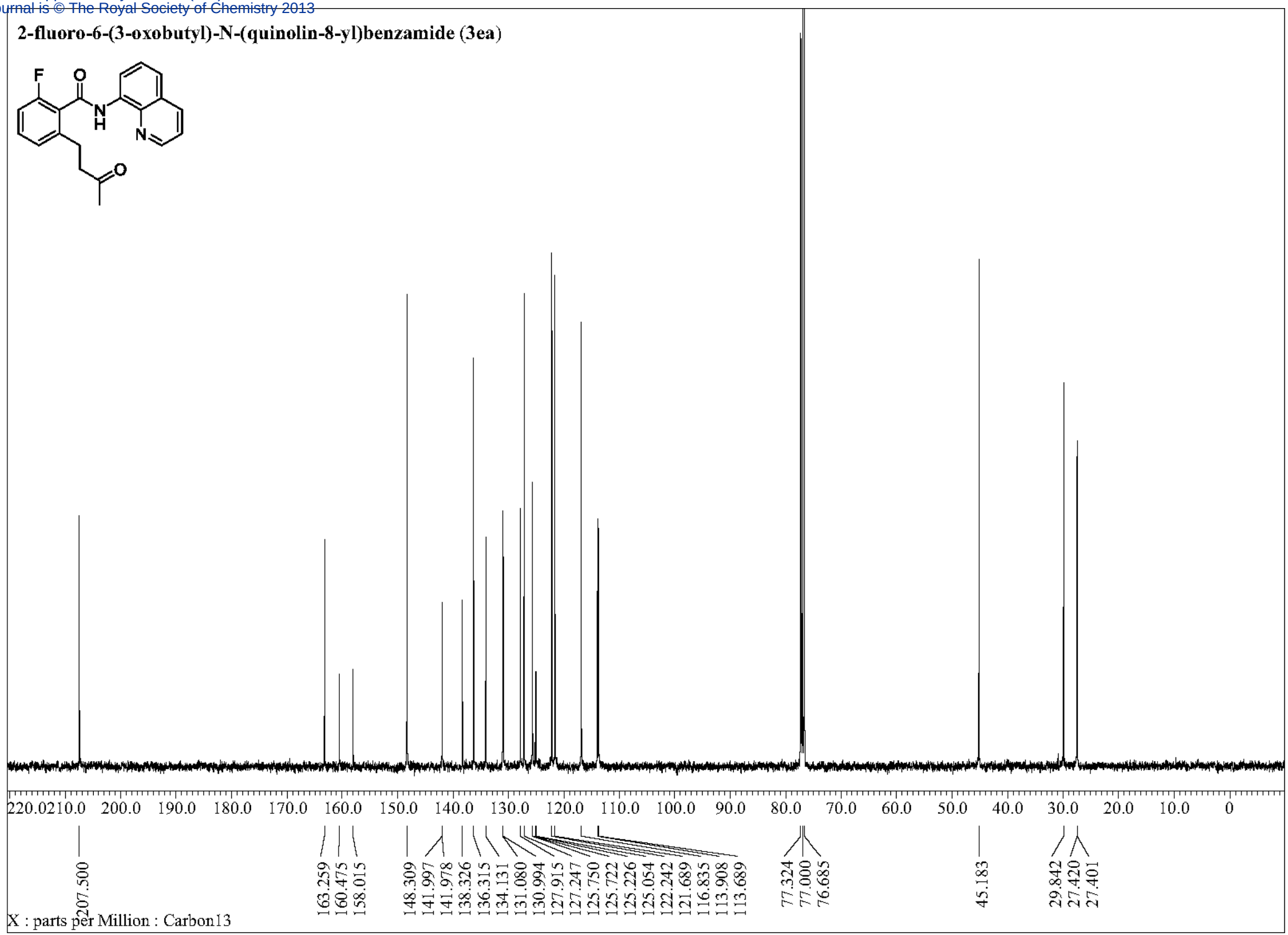

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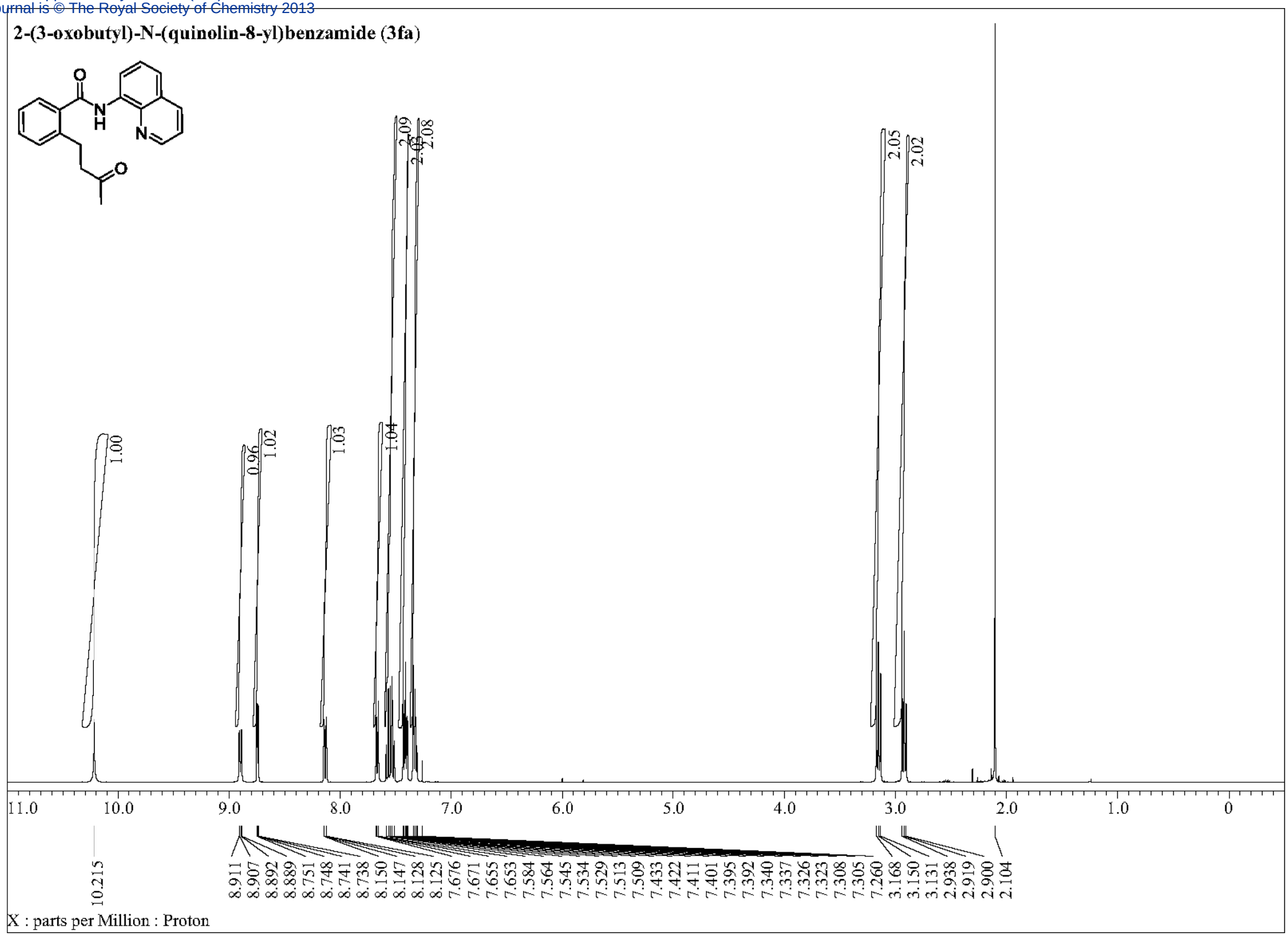

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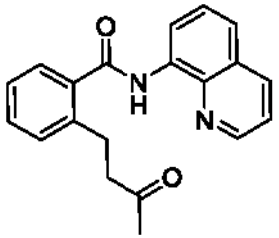
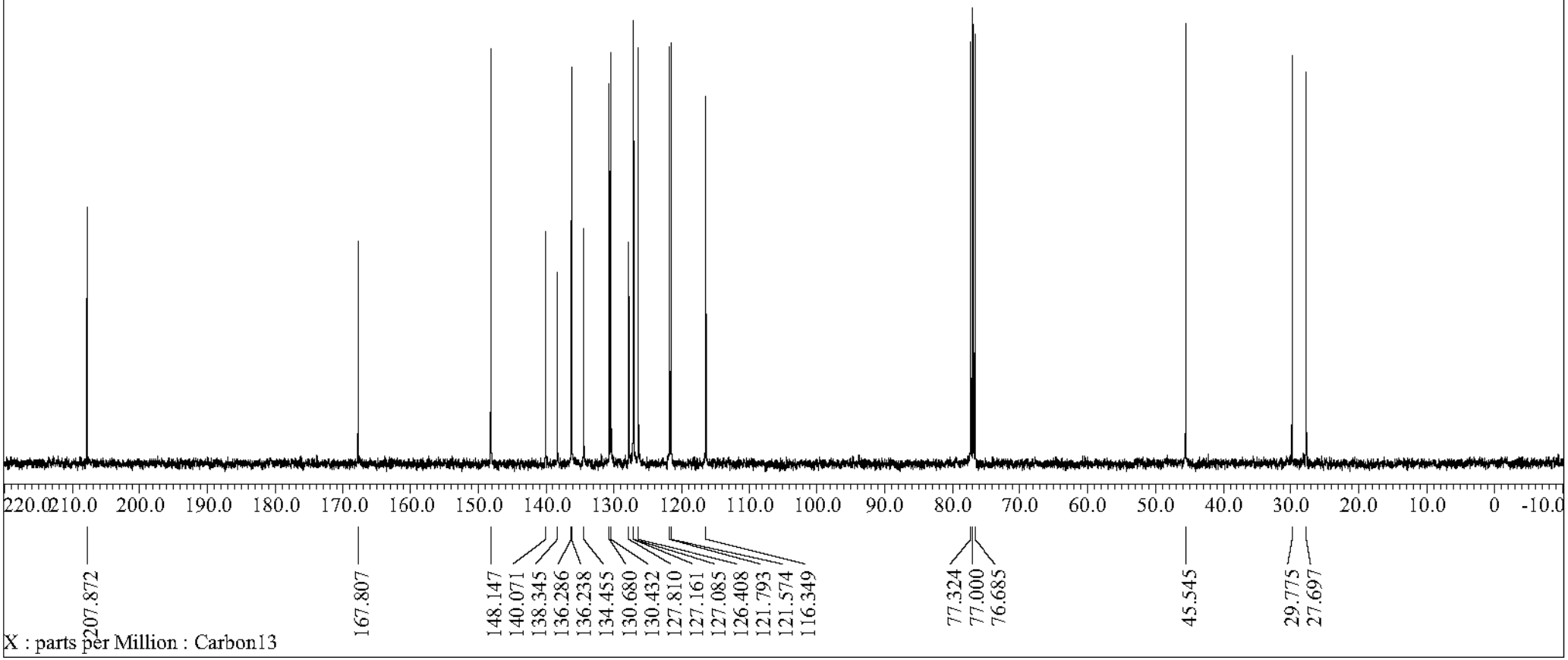
2-(3-oxobutyl)-N-(quinolin-8-yl)benzamide (3fa)





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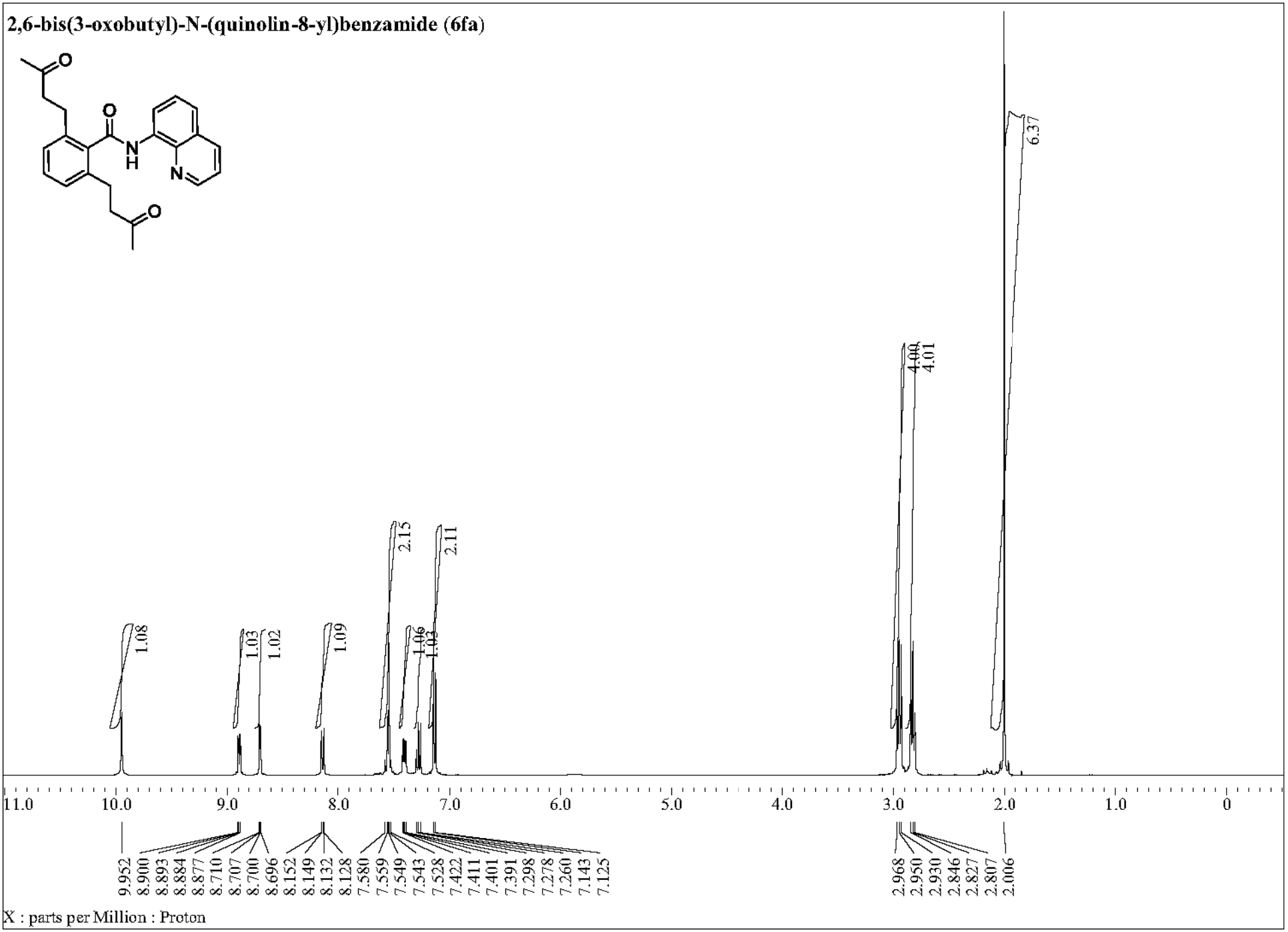

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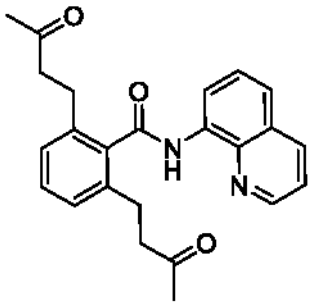
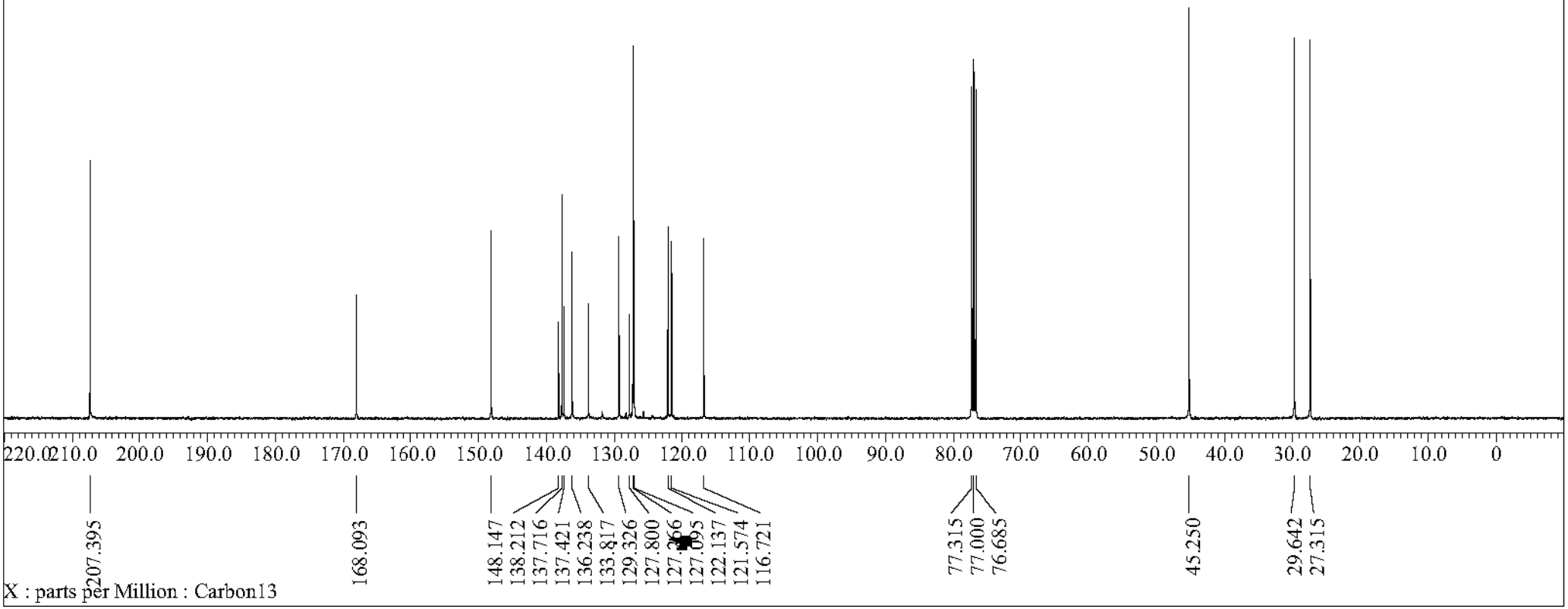
2,6-bis(3-oxobutyl)-N-(quinolin-8-yl)benzamide (6fa)





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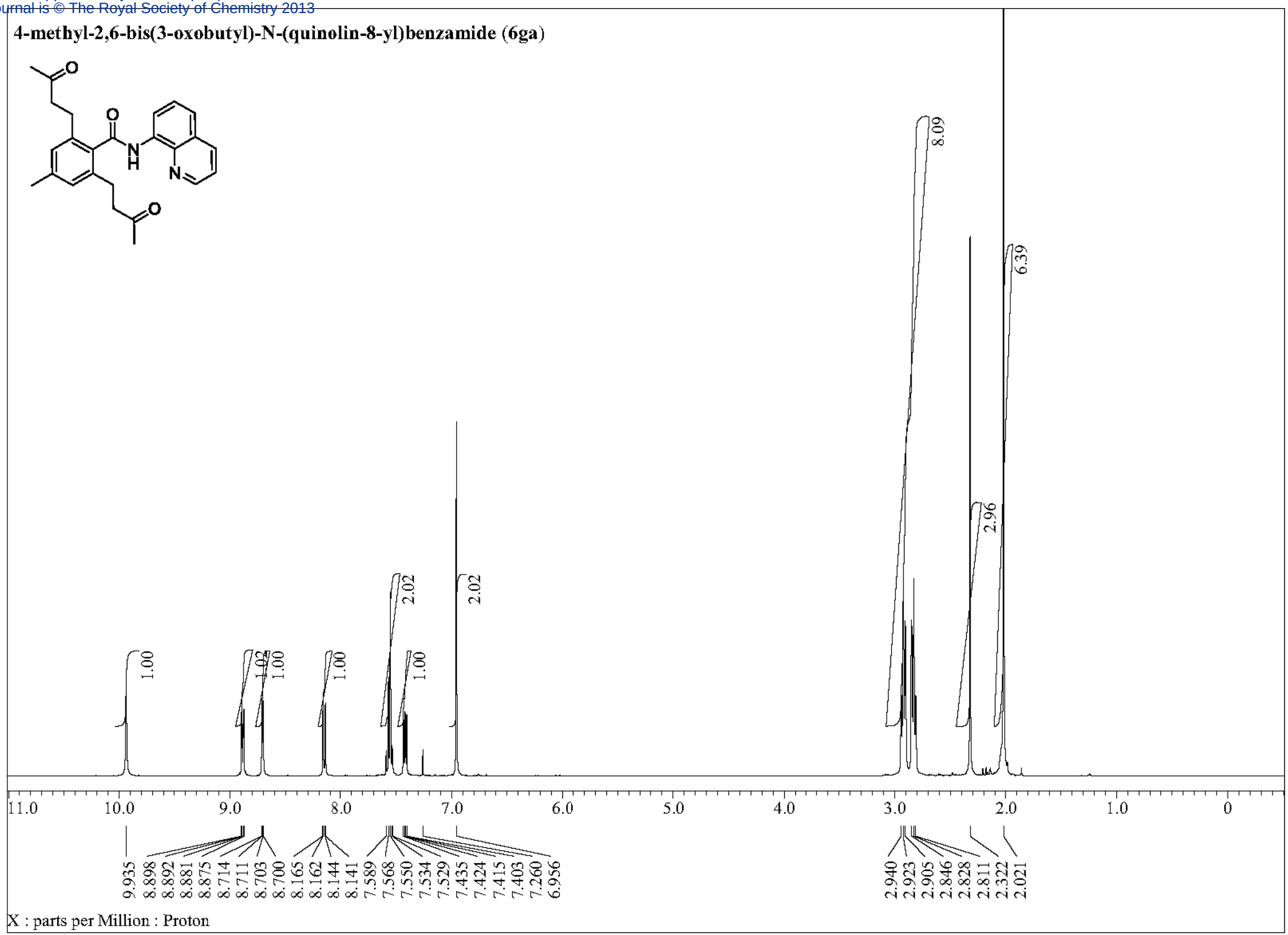

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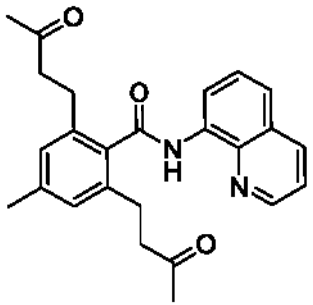
4-methyl-2,6-bis(3-oxobutyl)-N-(quinolin-8-yl)benzamide (6ga)



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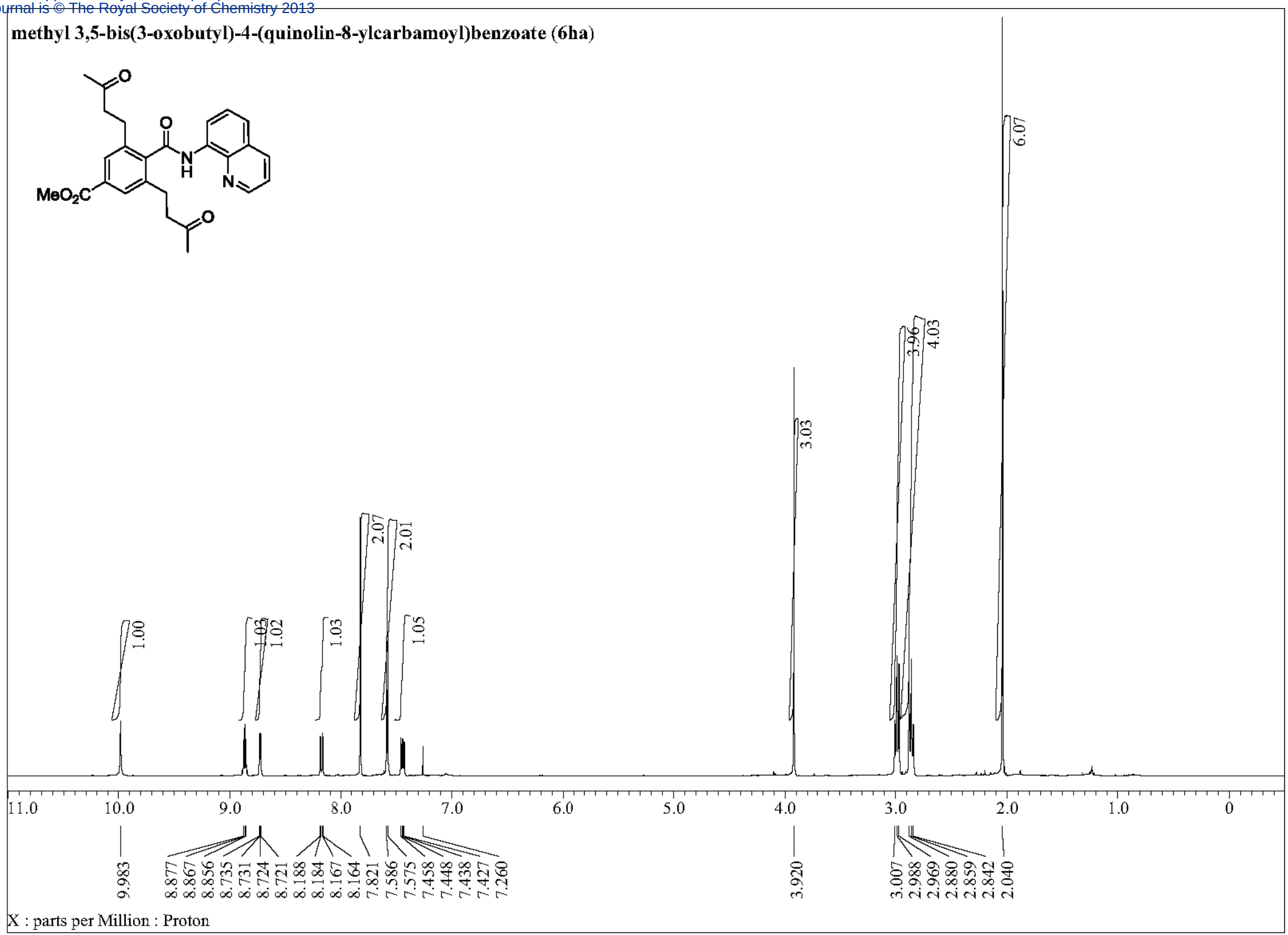

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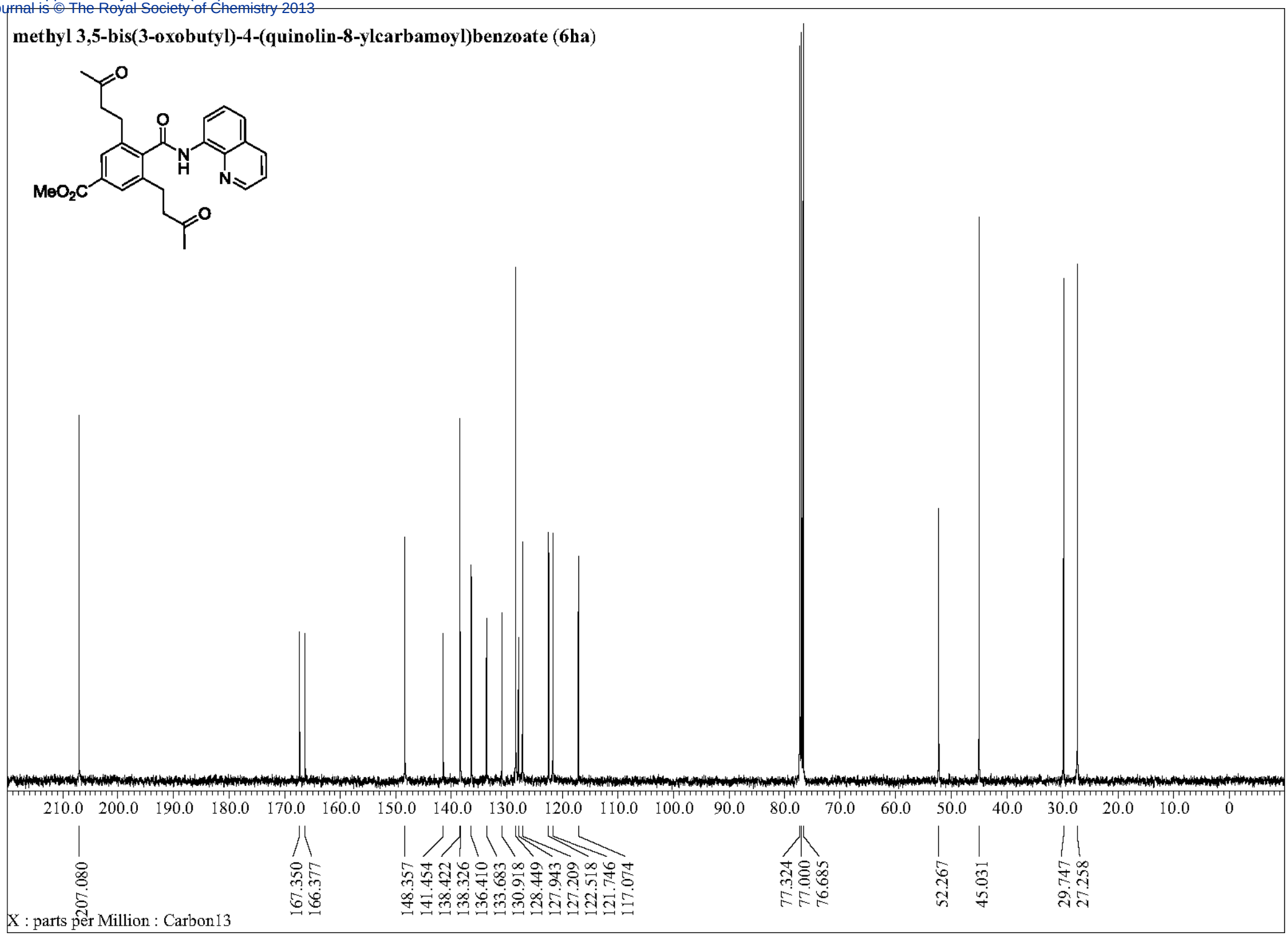

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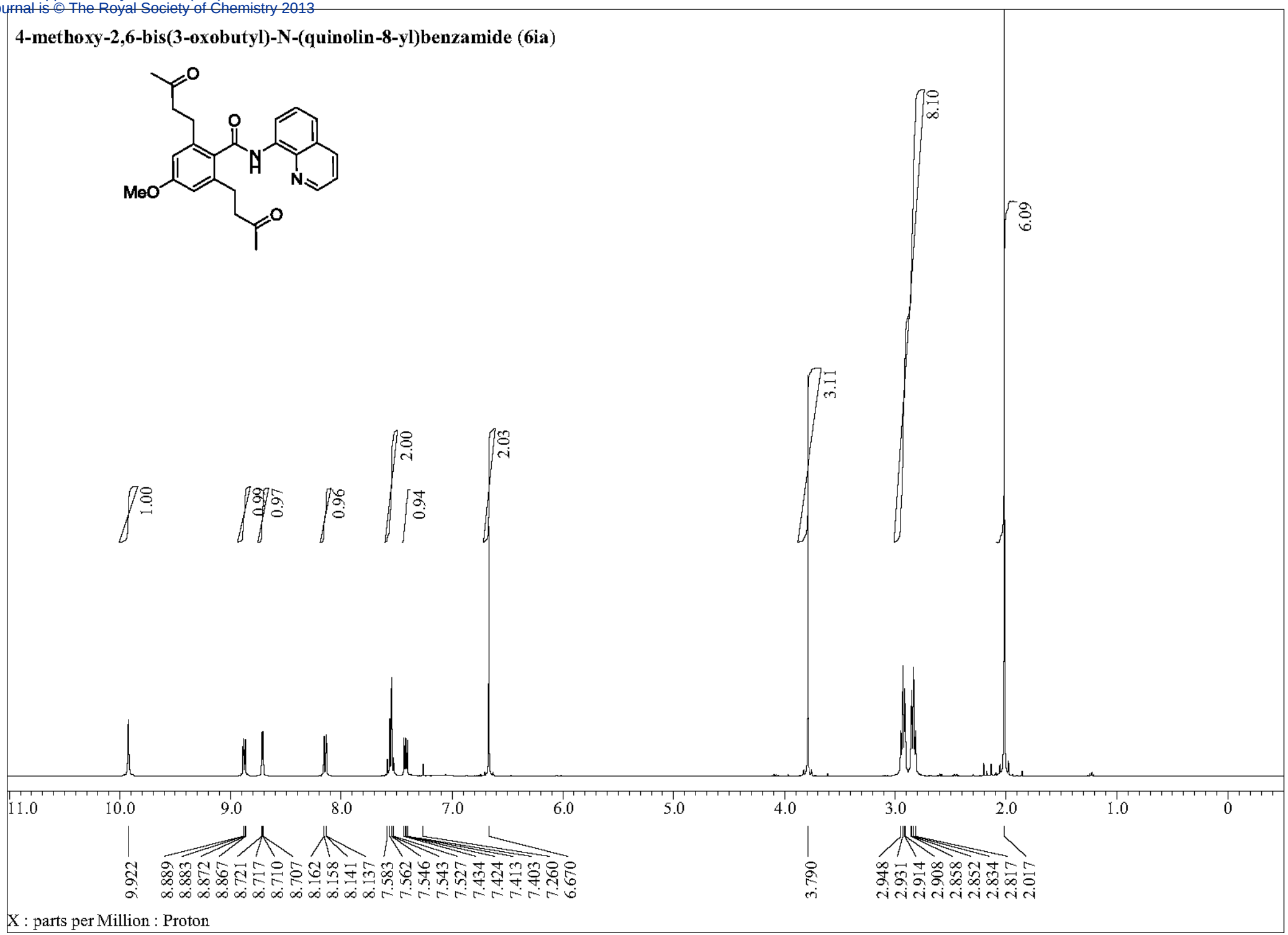

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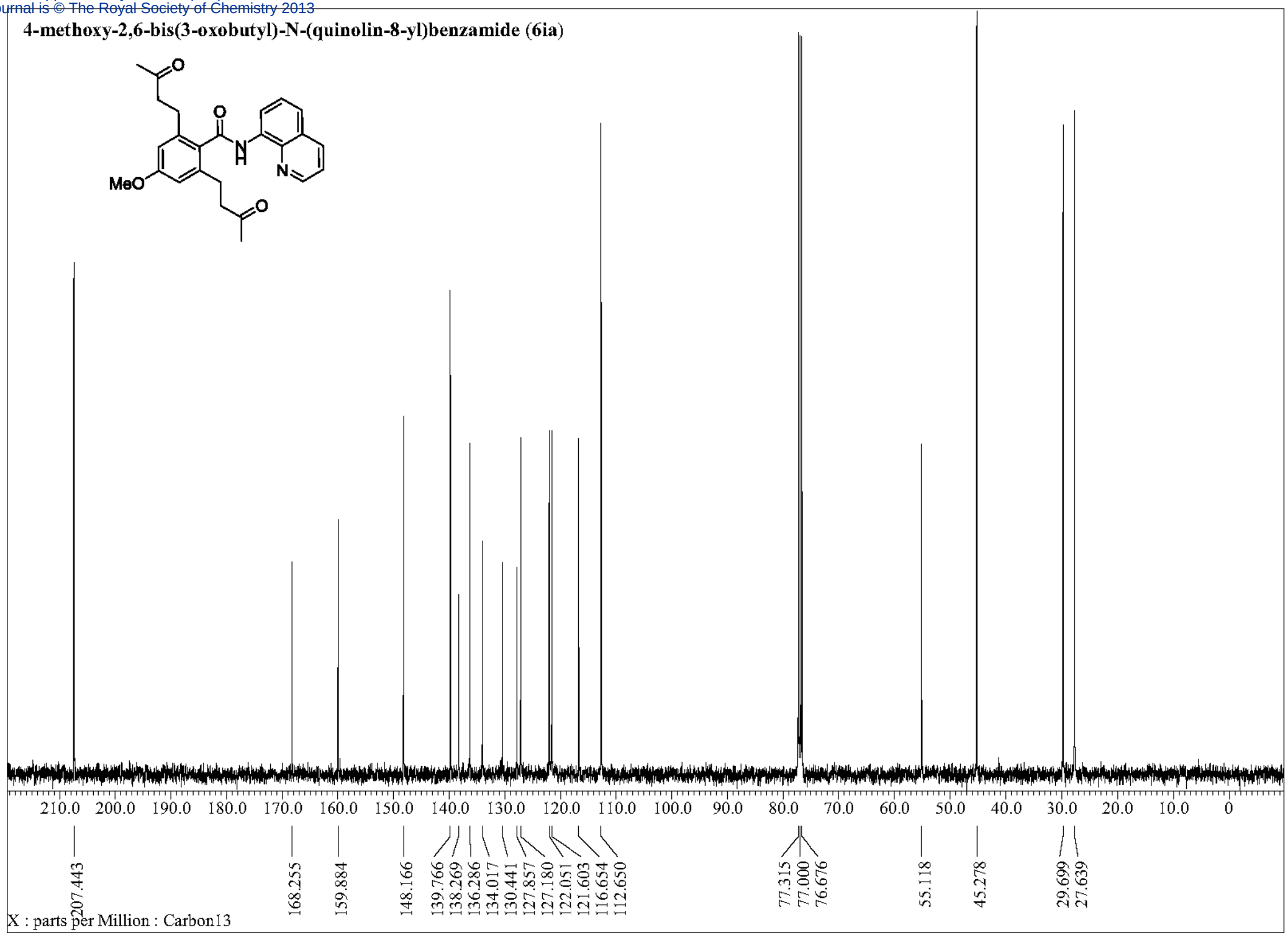

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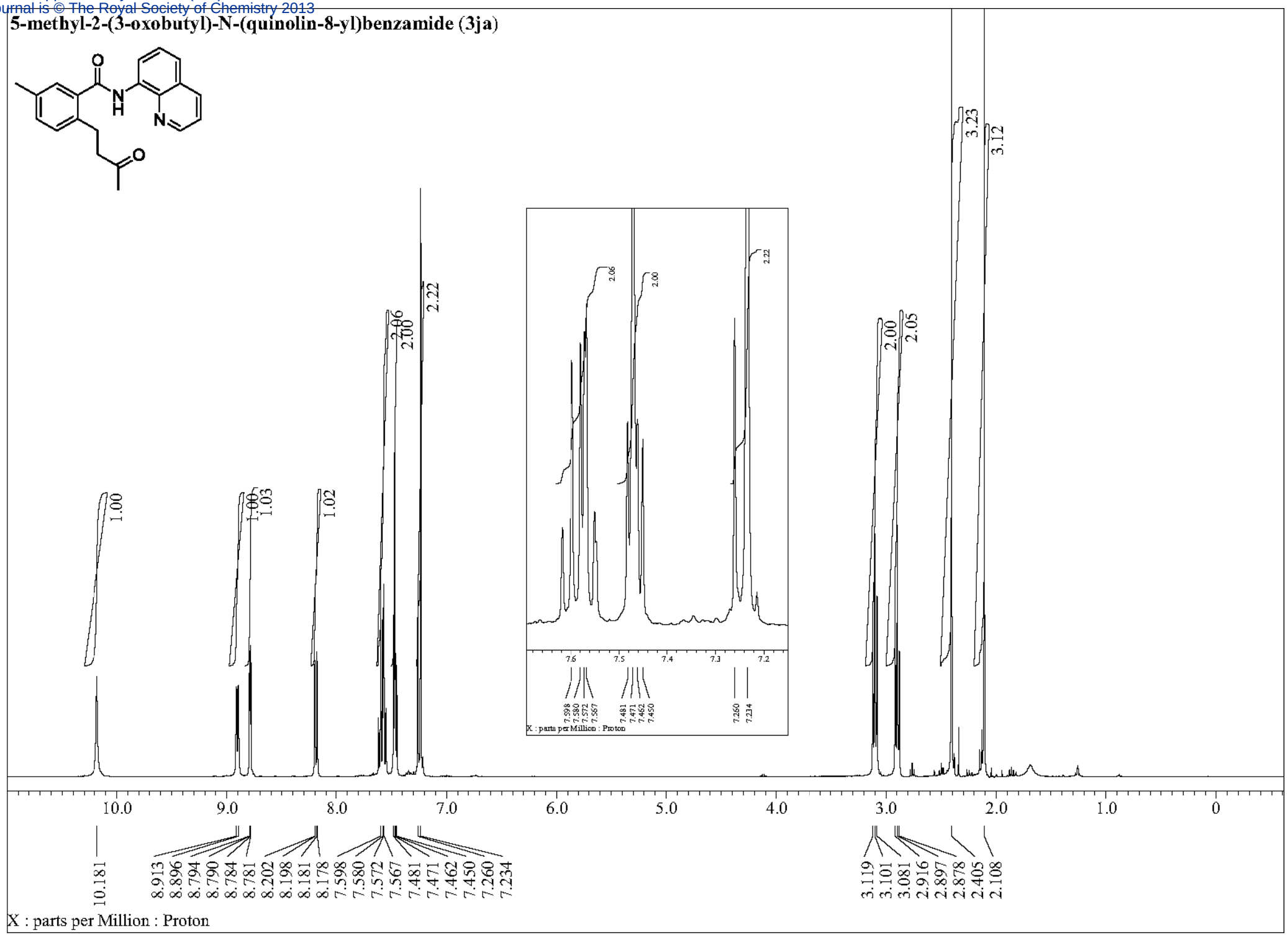

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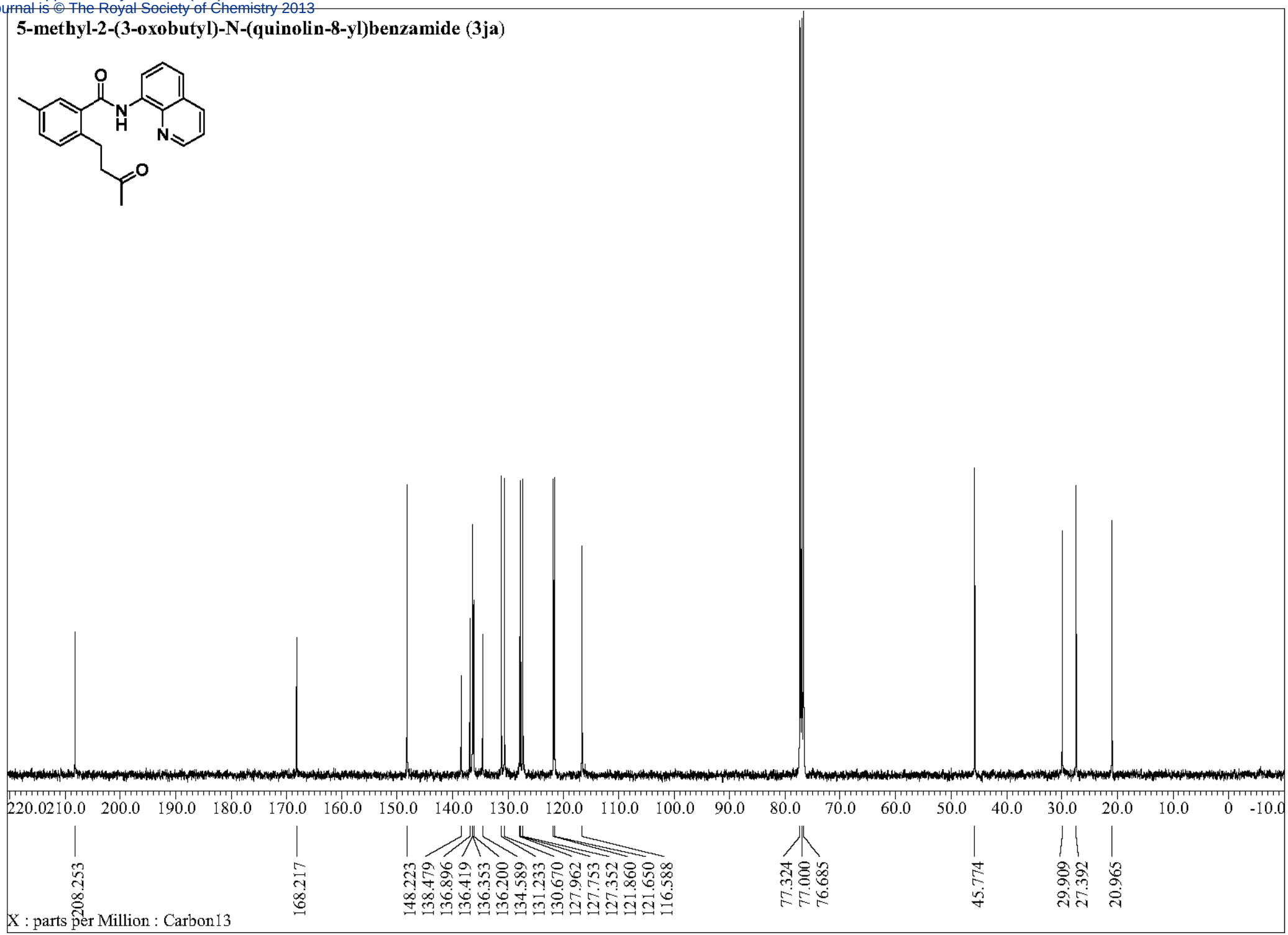

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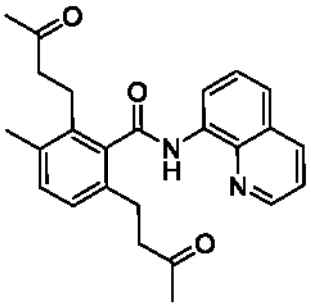
3-methyl-2,6-bis(3-oxobutyl)-N-(quinolin-8-yl)benzamide (6ja)



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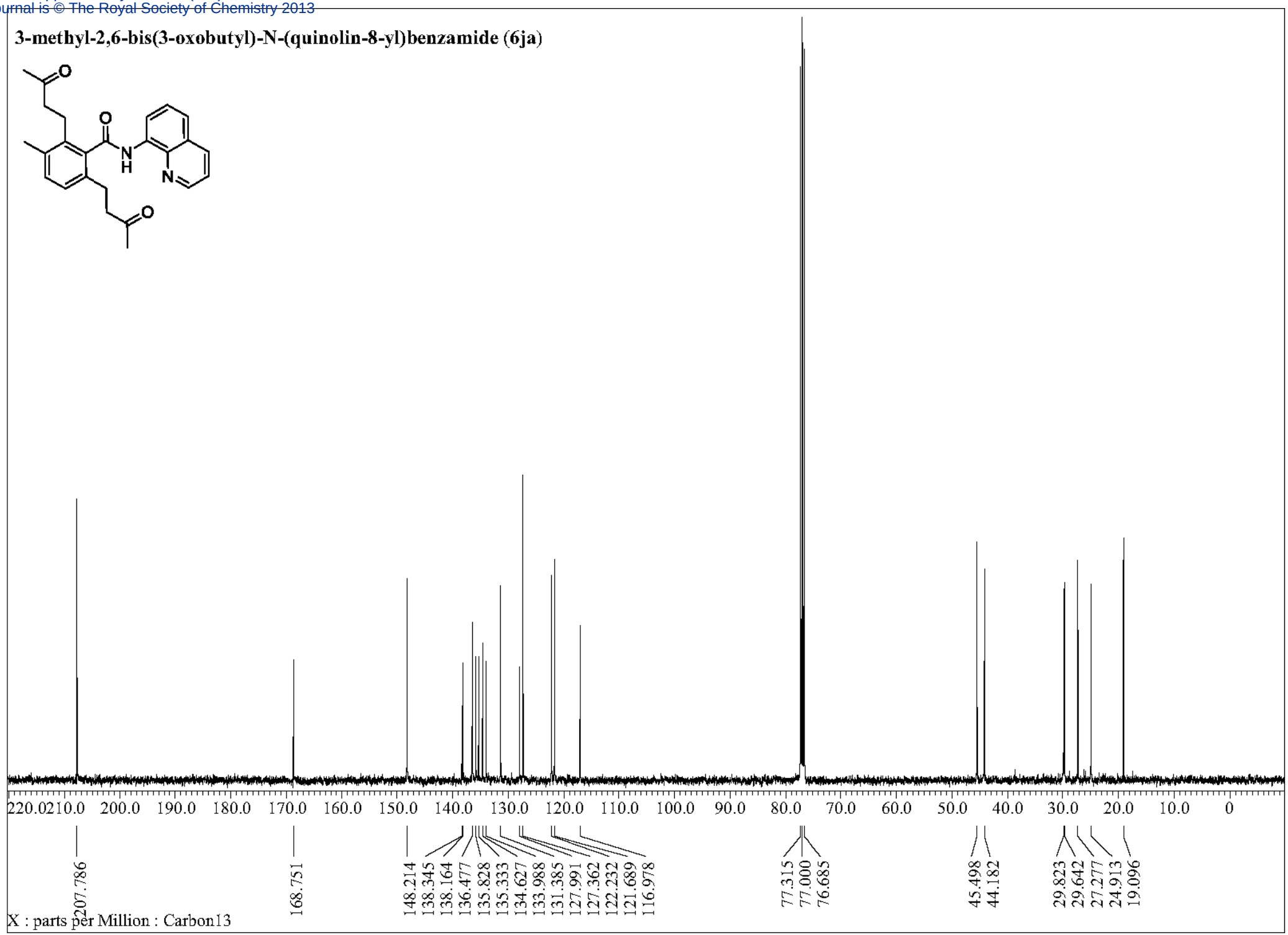

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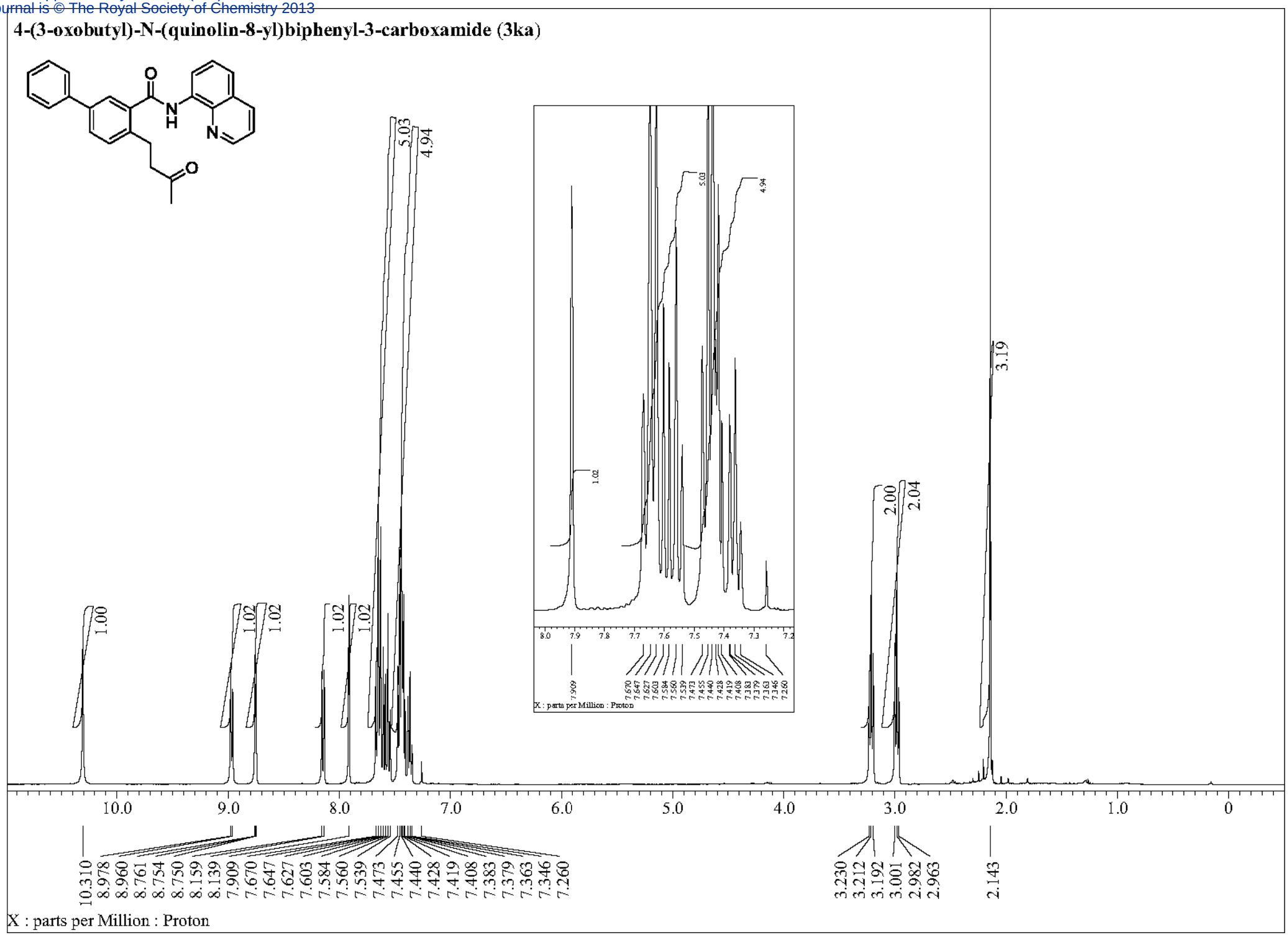

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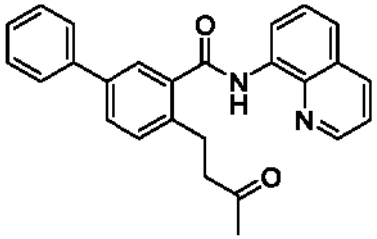
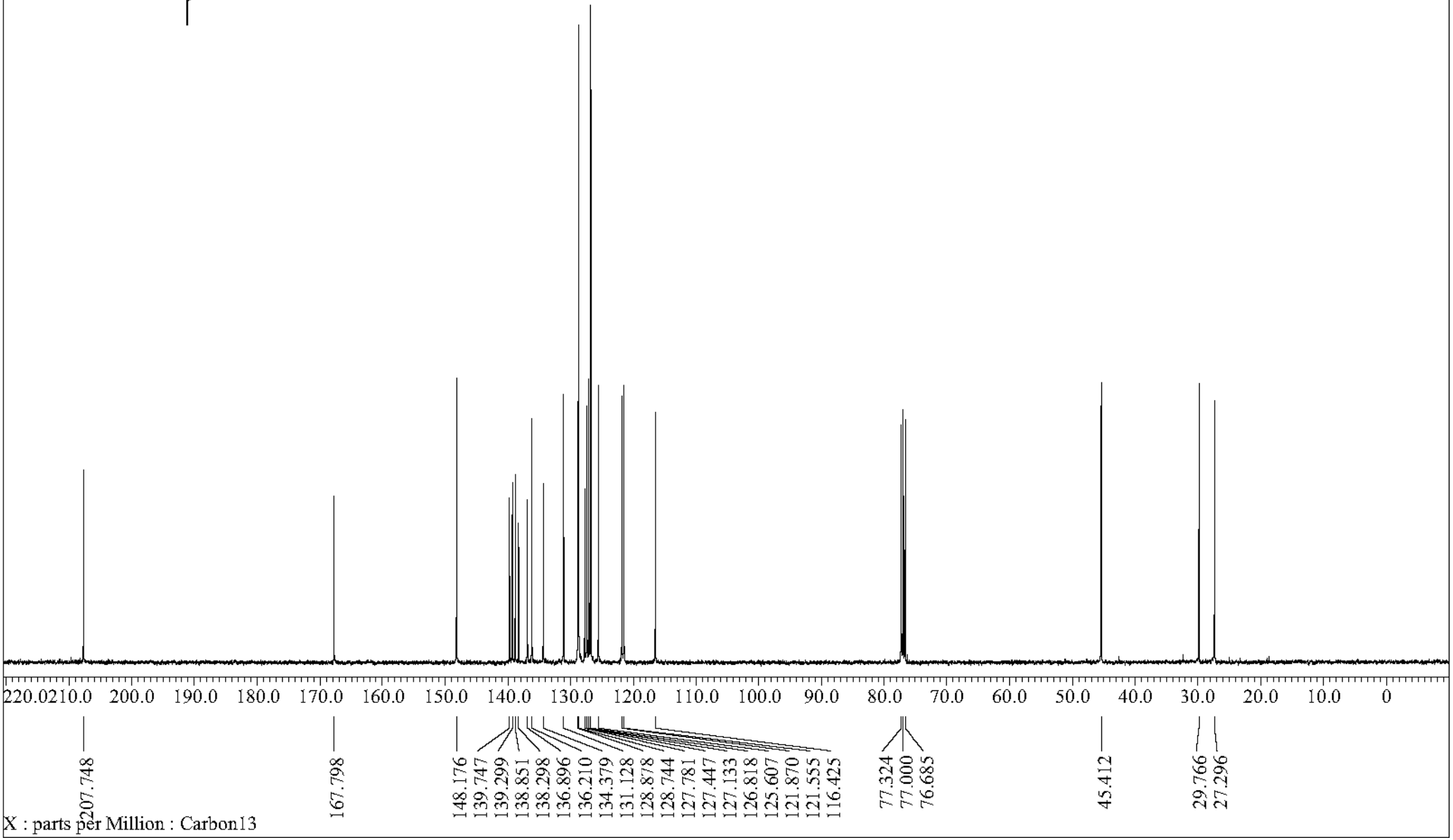
4-(3-oxobutyl)-N-(quinolin-8-yl)biphenyl-3-carboxamide (3ka)





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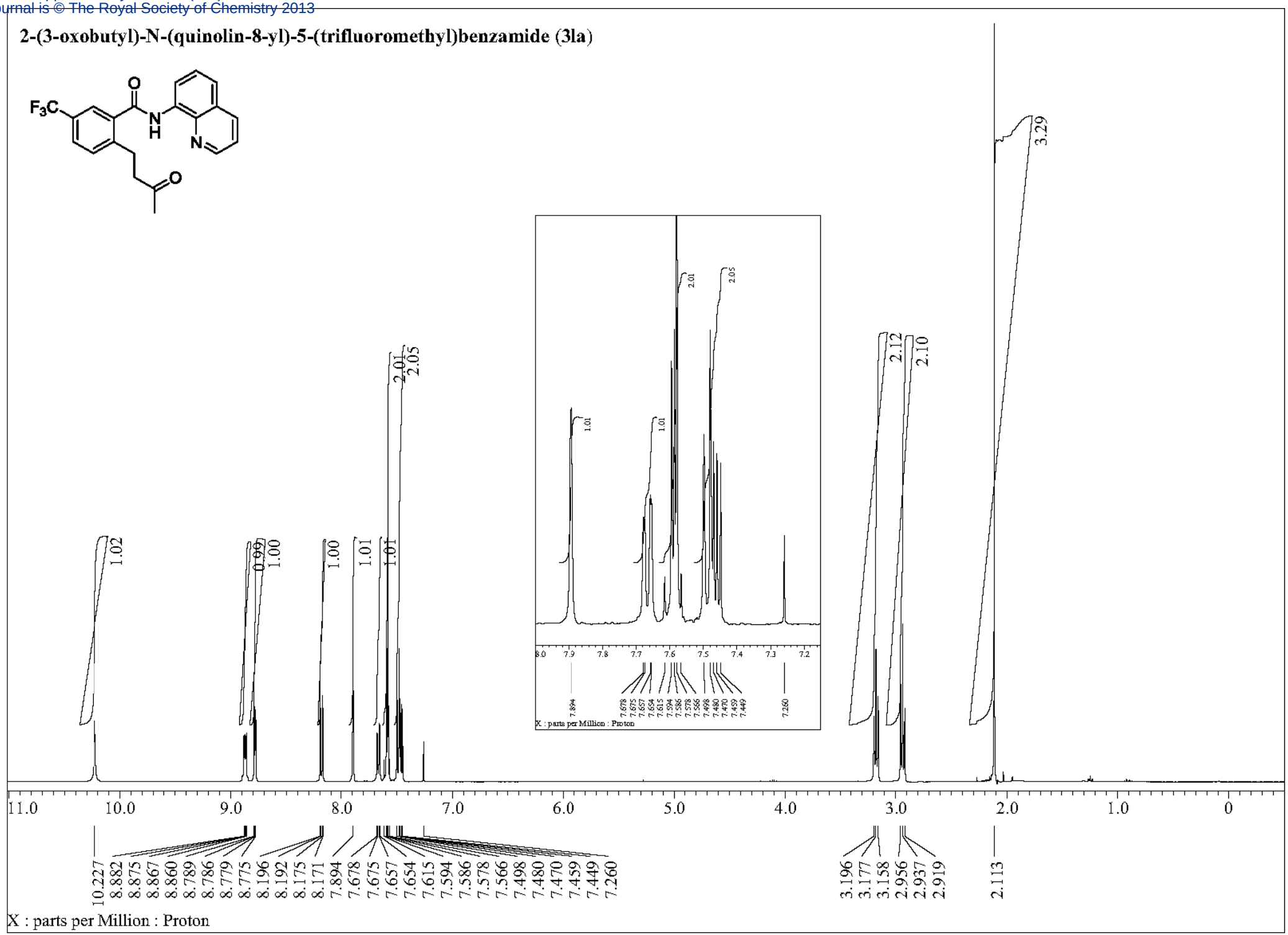

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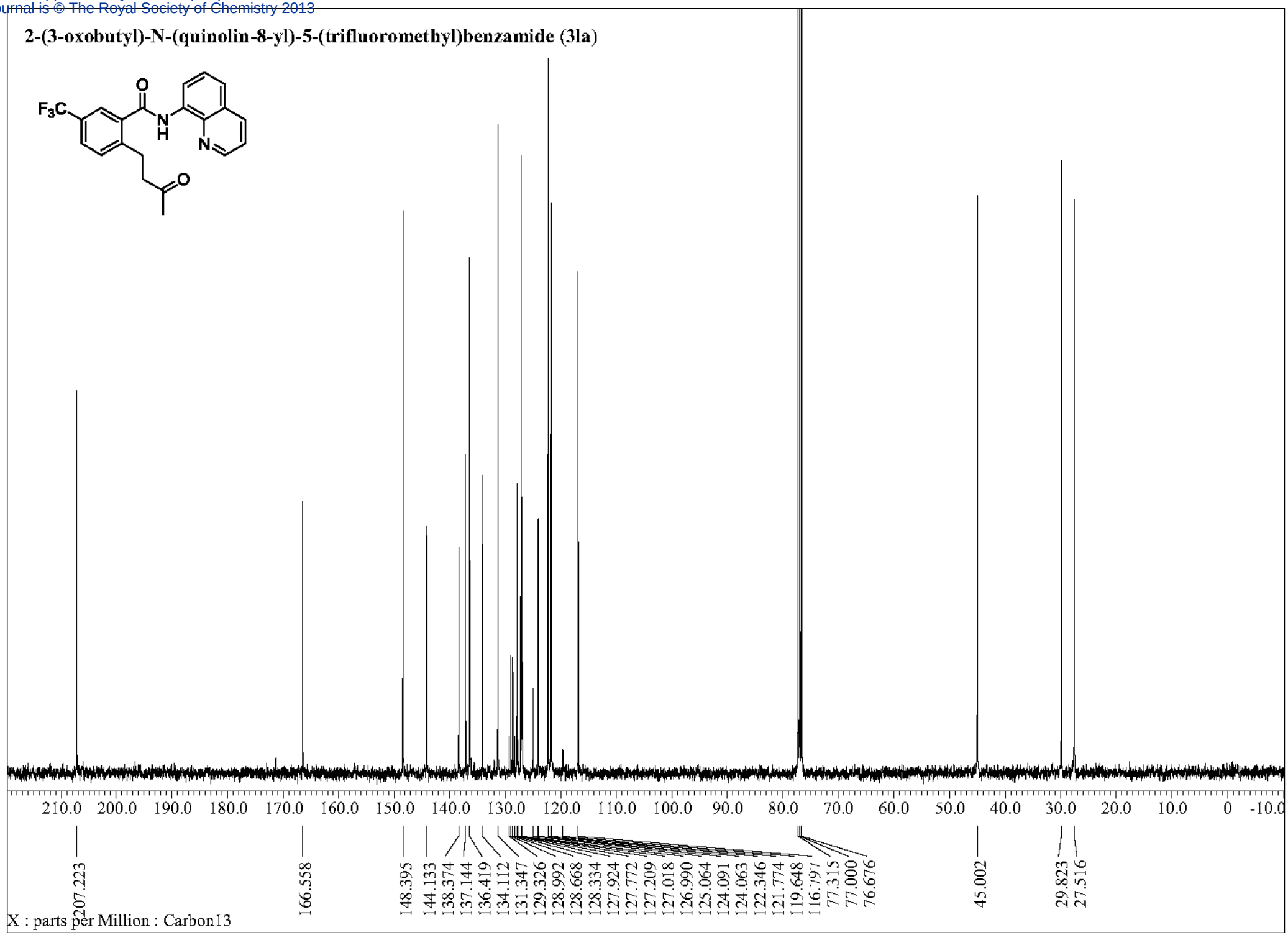

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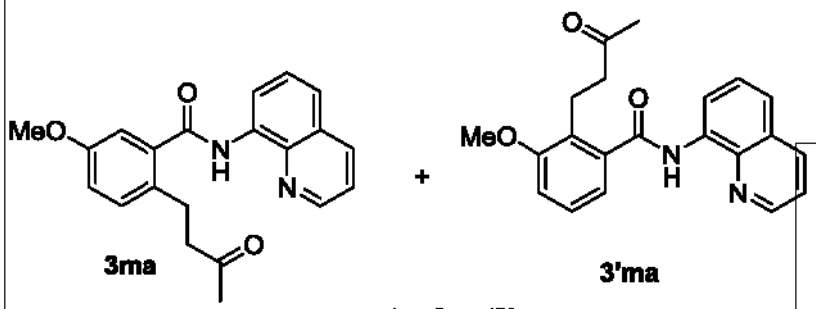
5-methoxy-2-(3-oxobutyl)-N-(quinolin-8-yl)benzamide (3ma), 3-methoxy-2-(3-oxobutyl)-N-(quinolin-8-yl)benzamide (3'ma).



mixture 3/1 : 3ma/3'ma

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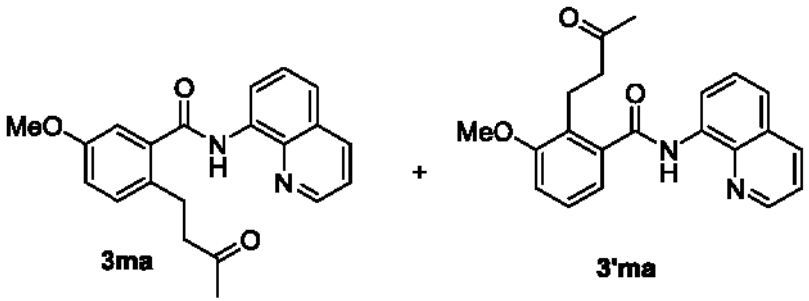
5-methoxy-2-(3-oxobutyl)-N-(quinolin-8-yl)benzamide (3ma), 3-methoxy-2-(3-oxobutyl)-N-(quinolin-8-yl)benzamide (3'ma).



mixture 3/1 : **3ma/3'ma**

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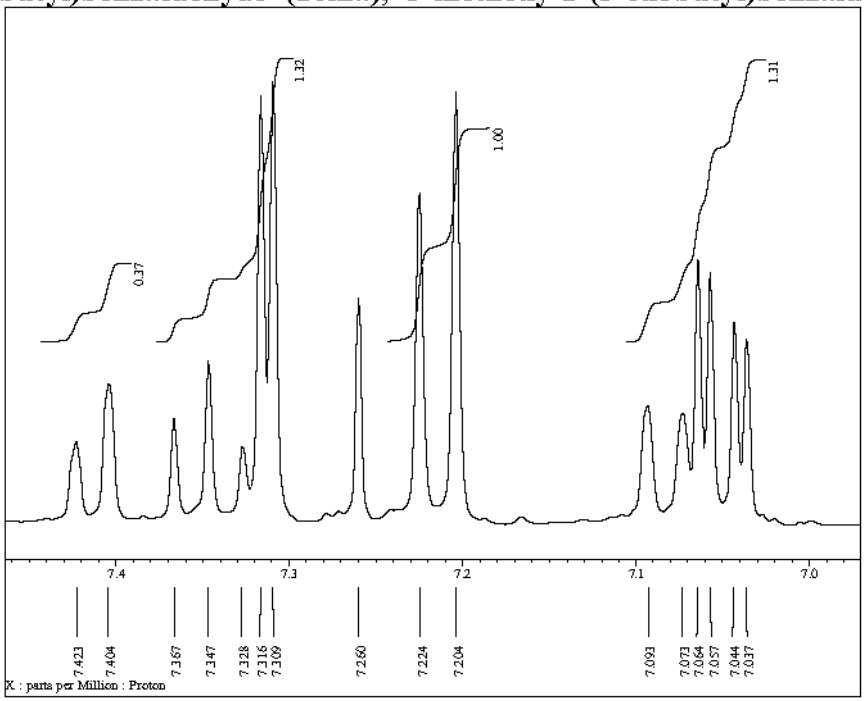

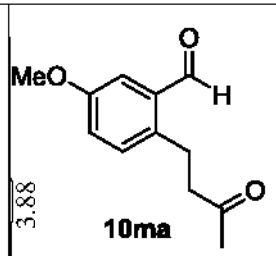

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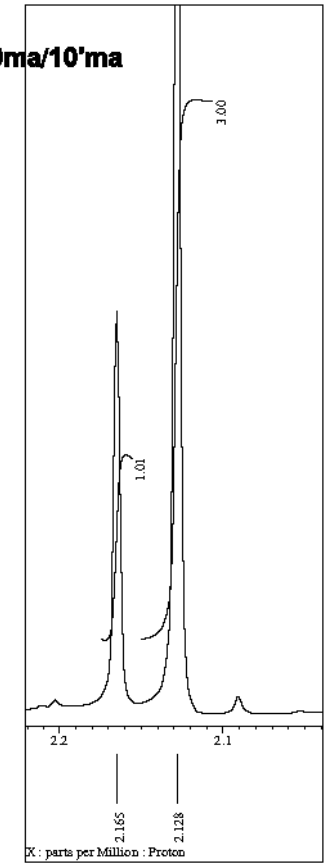

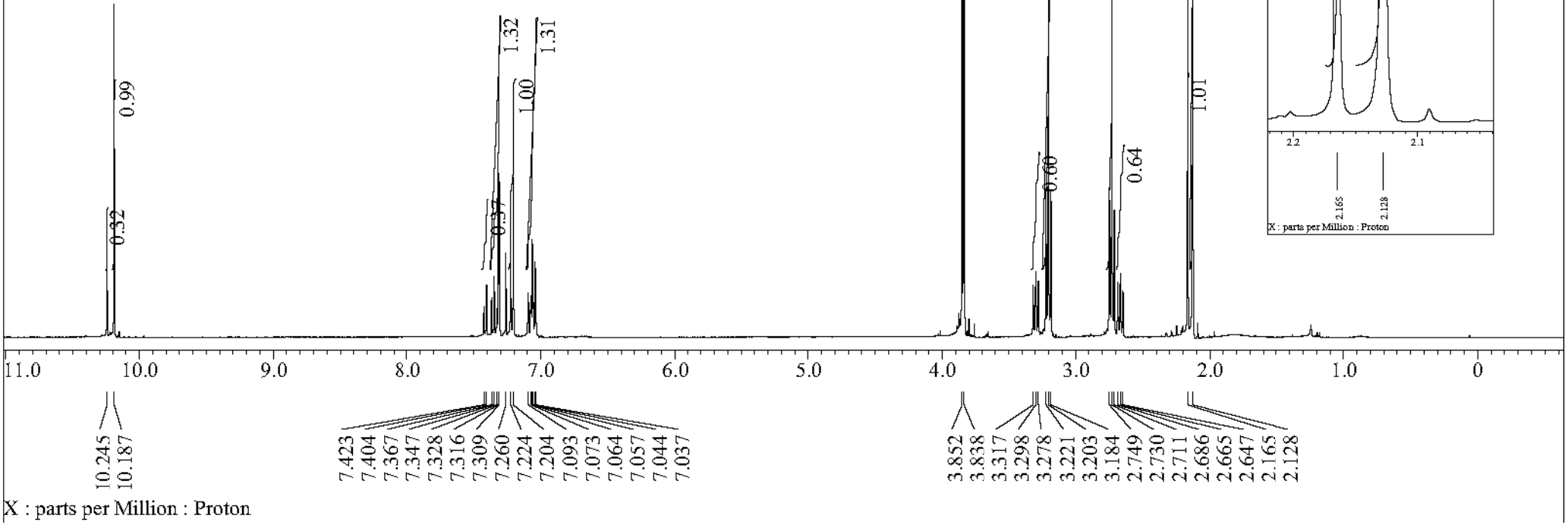

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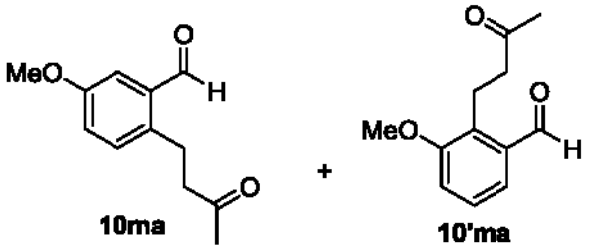
5-methoxy-2-(3-oxobutyl)benzaldehyde (10ma), 3-methoxy-2-(3-oxobutyl)benzaldehyde (10'ma)



mixture 3/1 : **10ma/10'ma**

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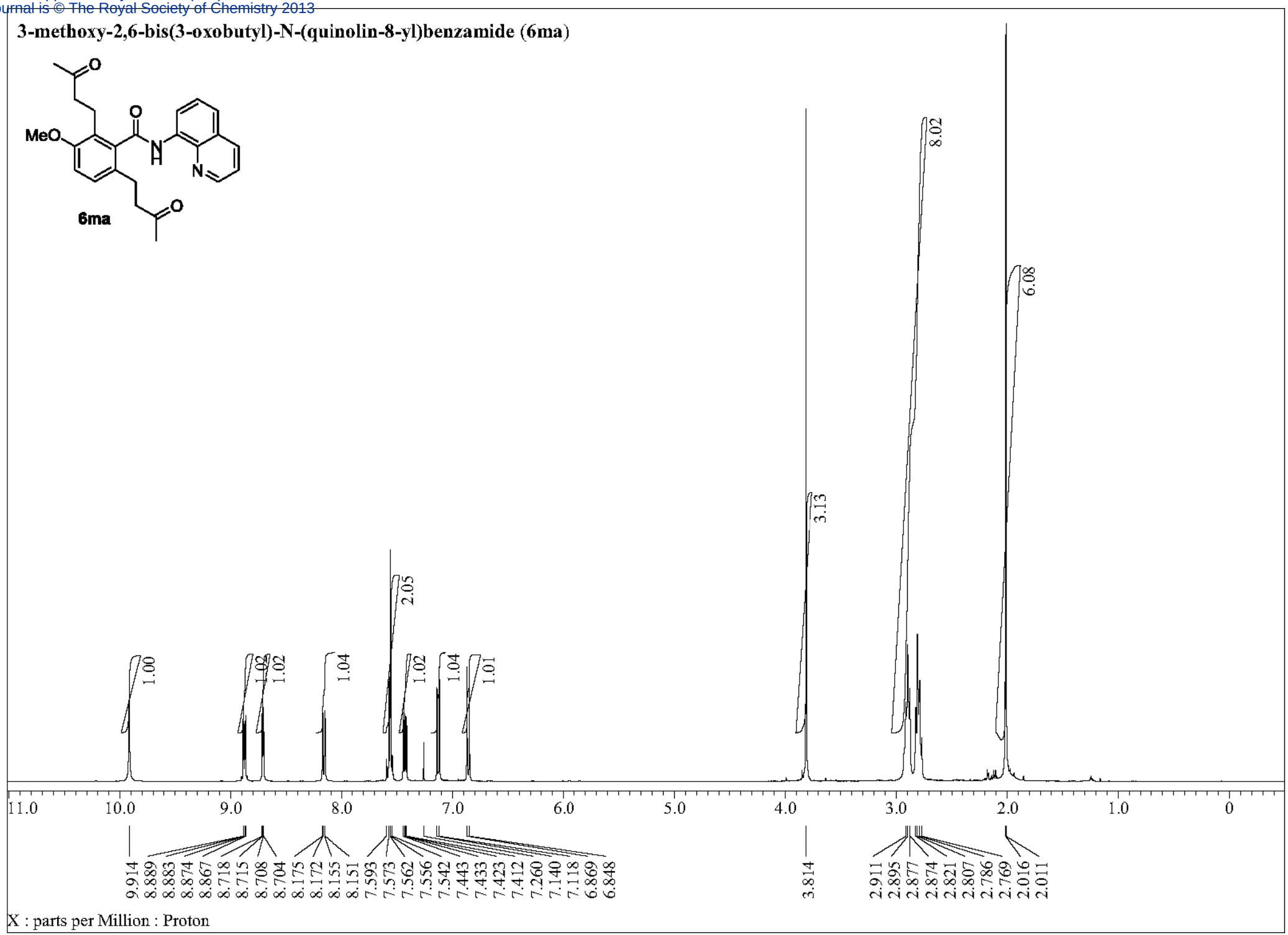

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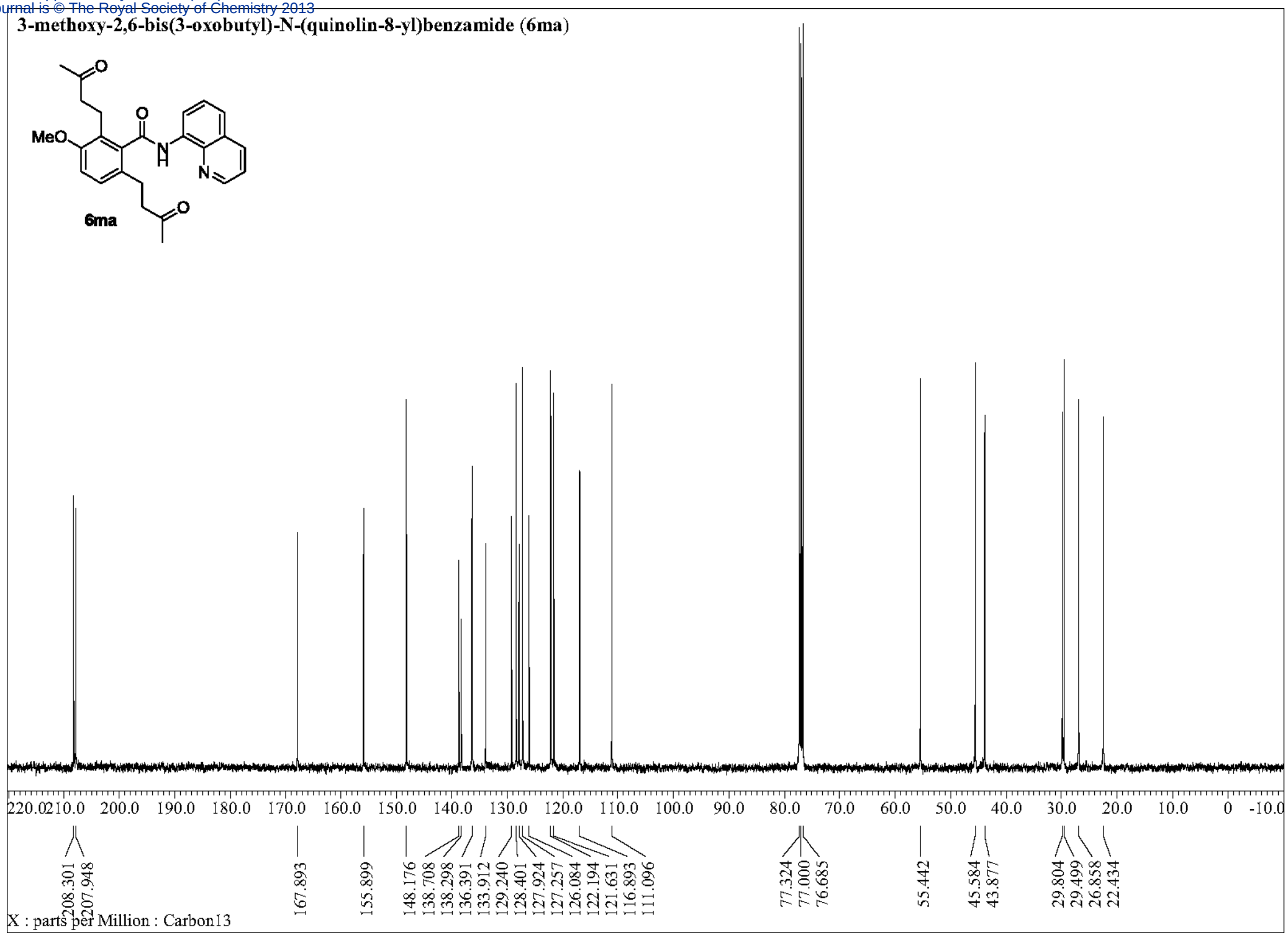

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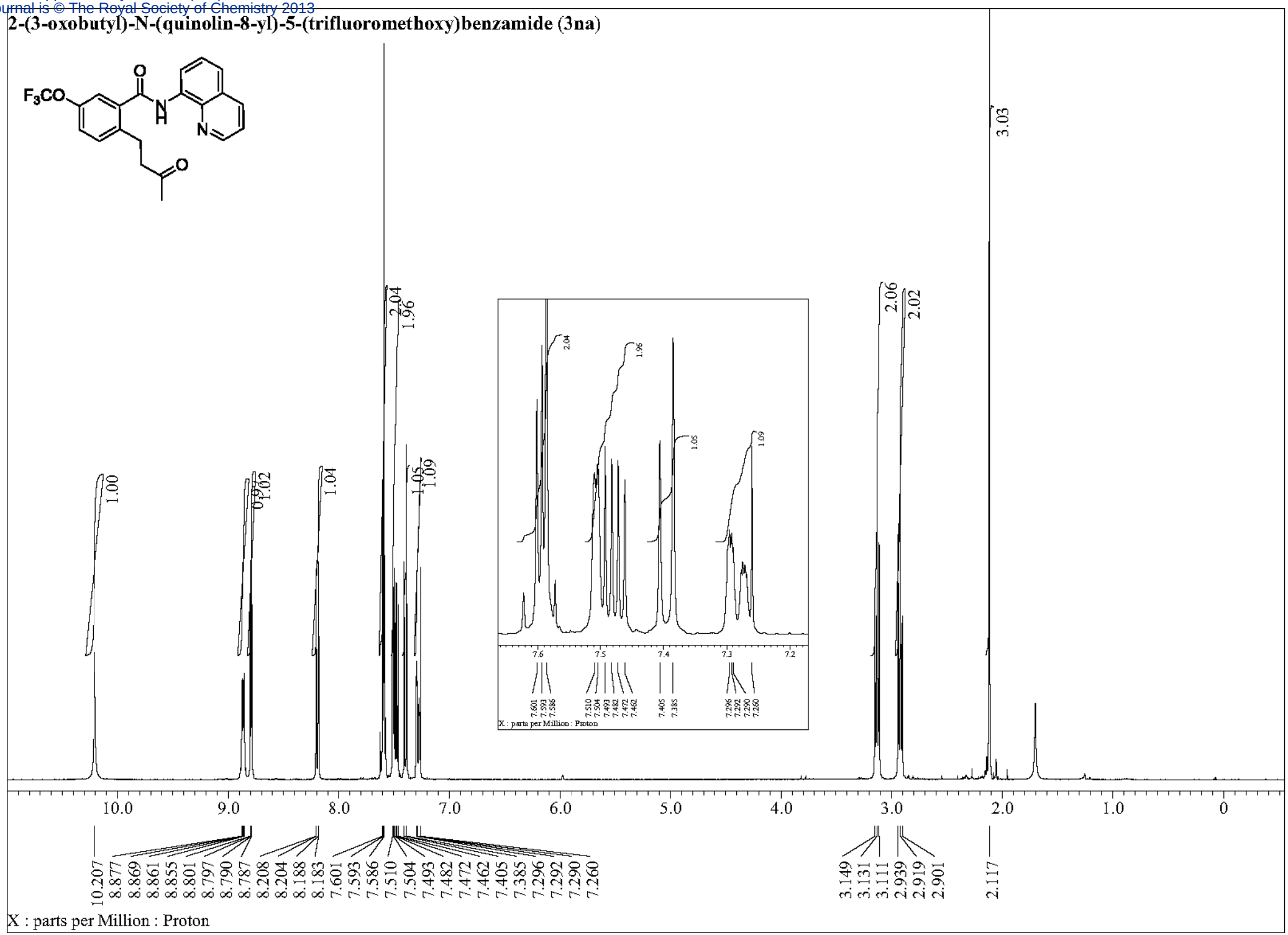

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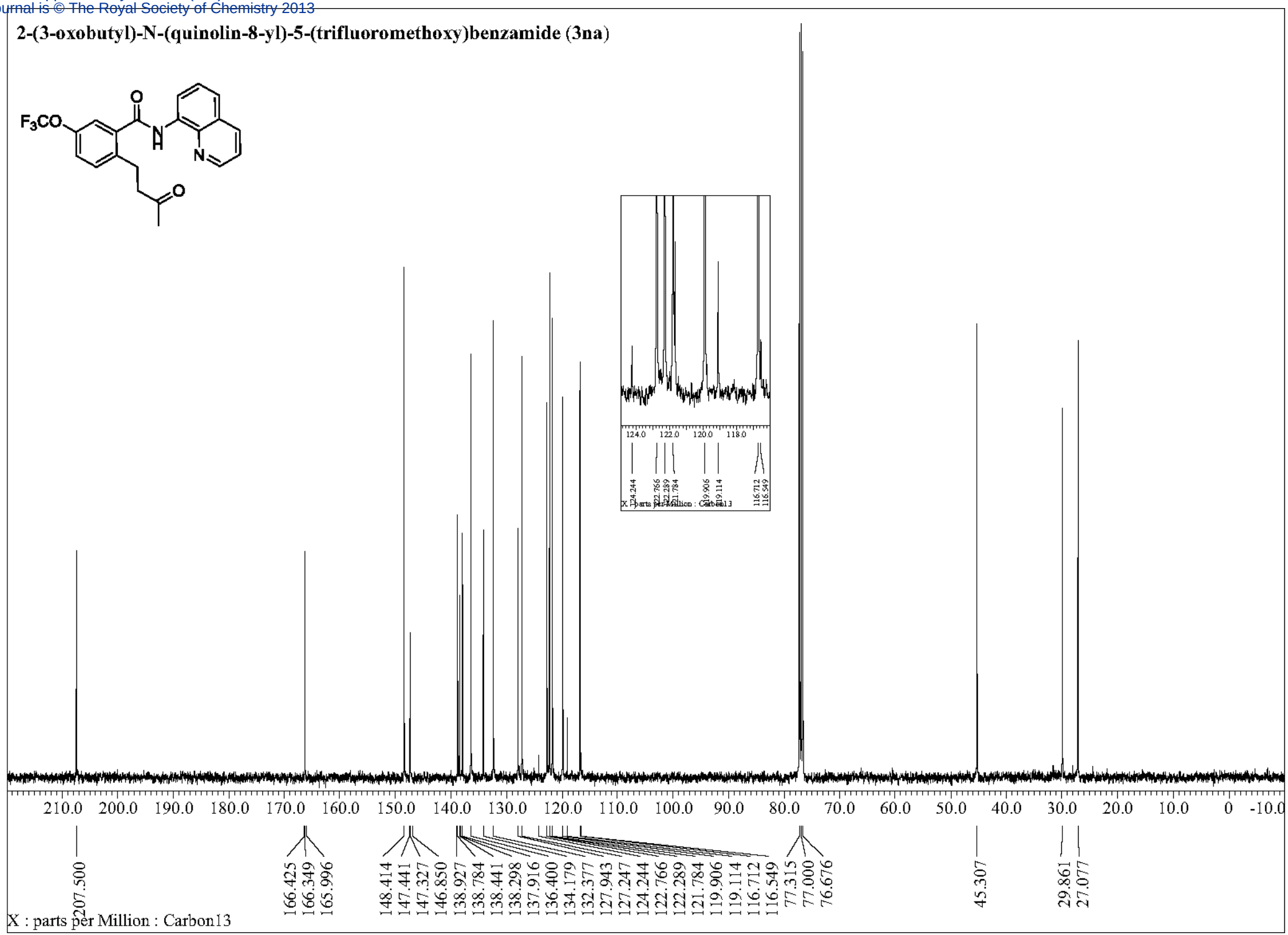

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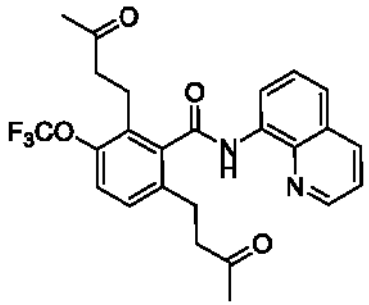
2,6-bis(3-oxobutyl)-N-(quinolin-8-yl)-3-(trifluoromethoxy)benzamide (6na)



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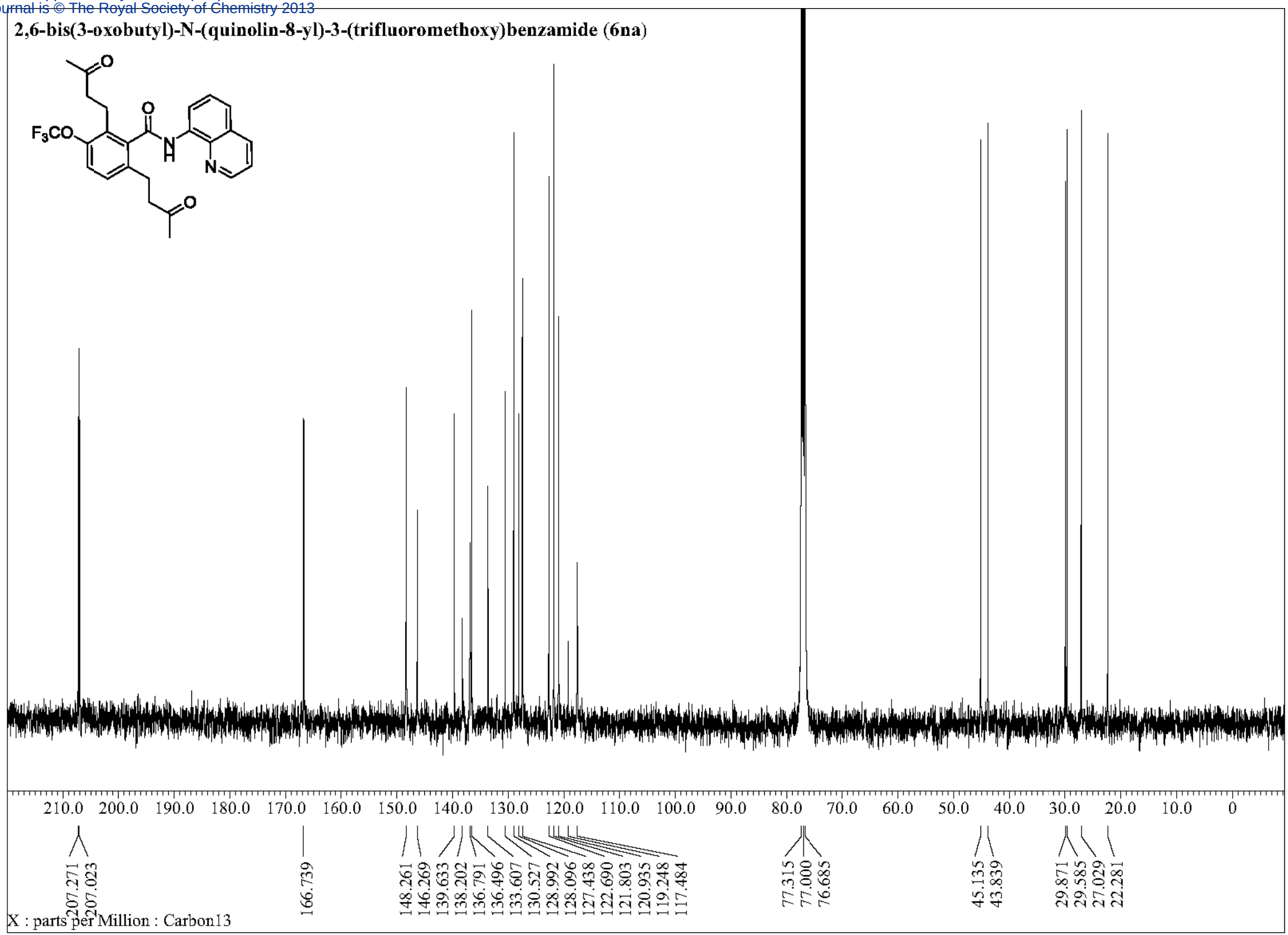

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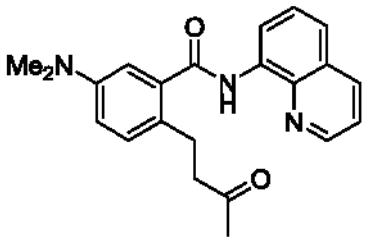
5-(dimethylamino)-2-(3-oxobutyl)-N-(quinolin-8-yl)benzamide (3oa)



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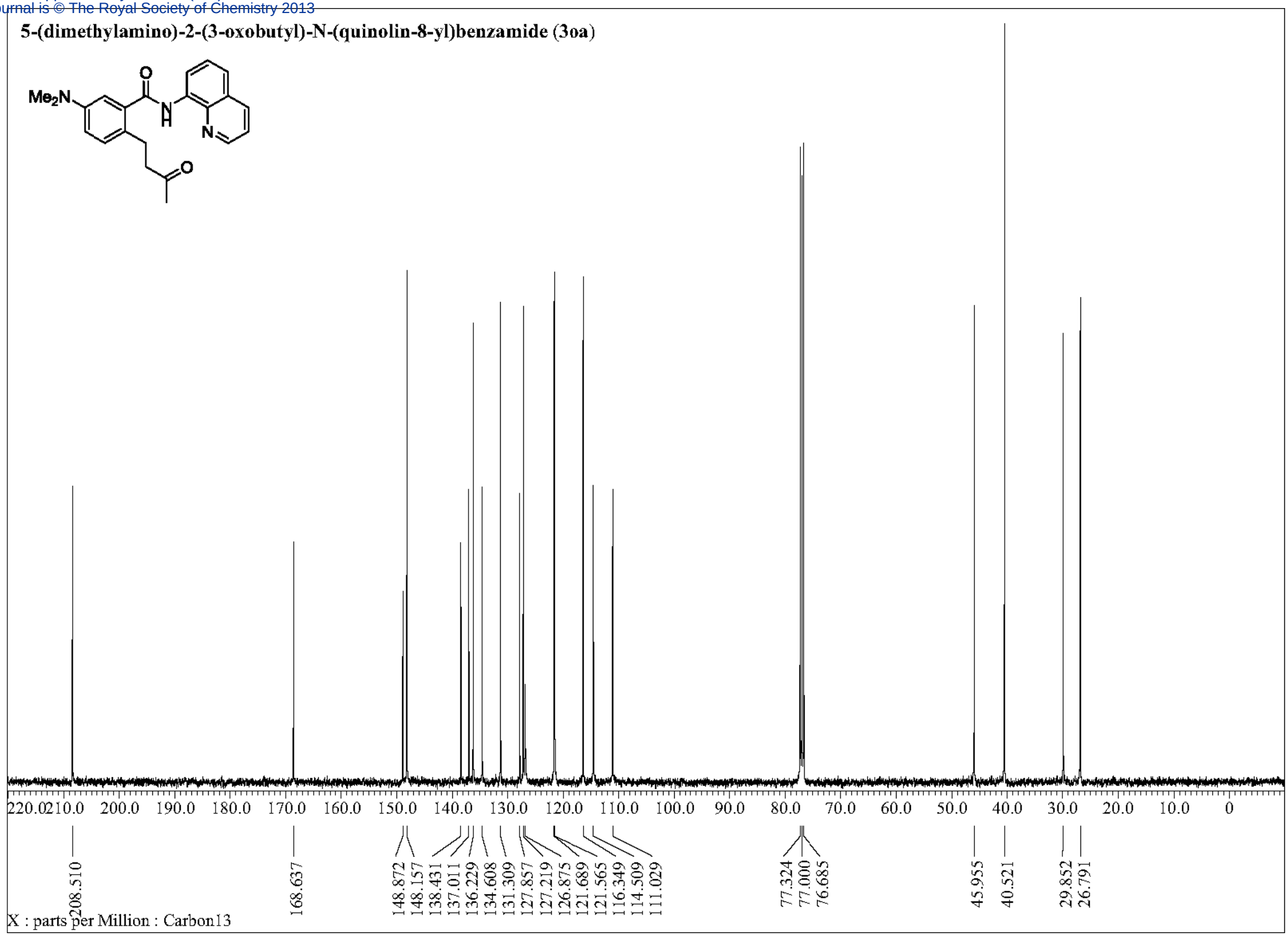

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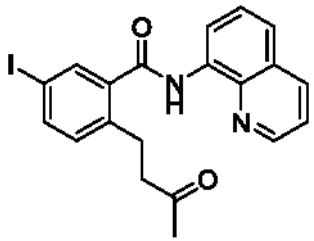
5-iodo-2-(3-oxobutyl)-N-(quinolin-8-yl)benzamide (3pa)



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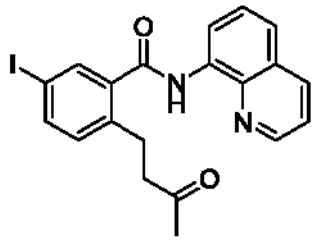
5-iodo-2-(3-oxobutyl)-N-(quinolin-8-yl)benzamide (3pa)



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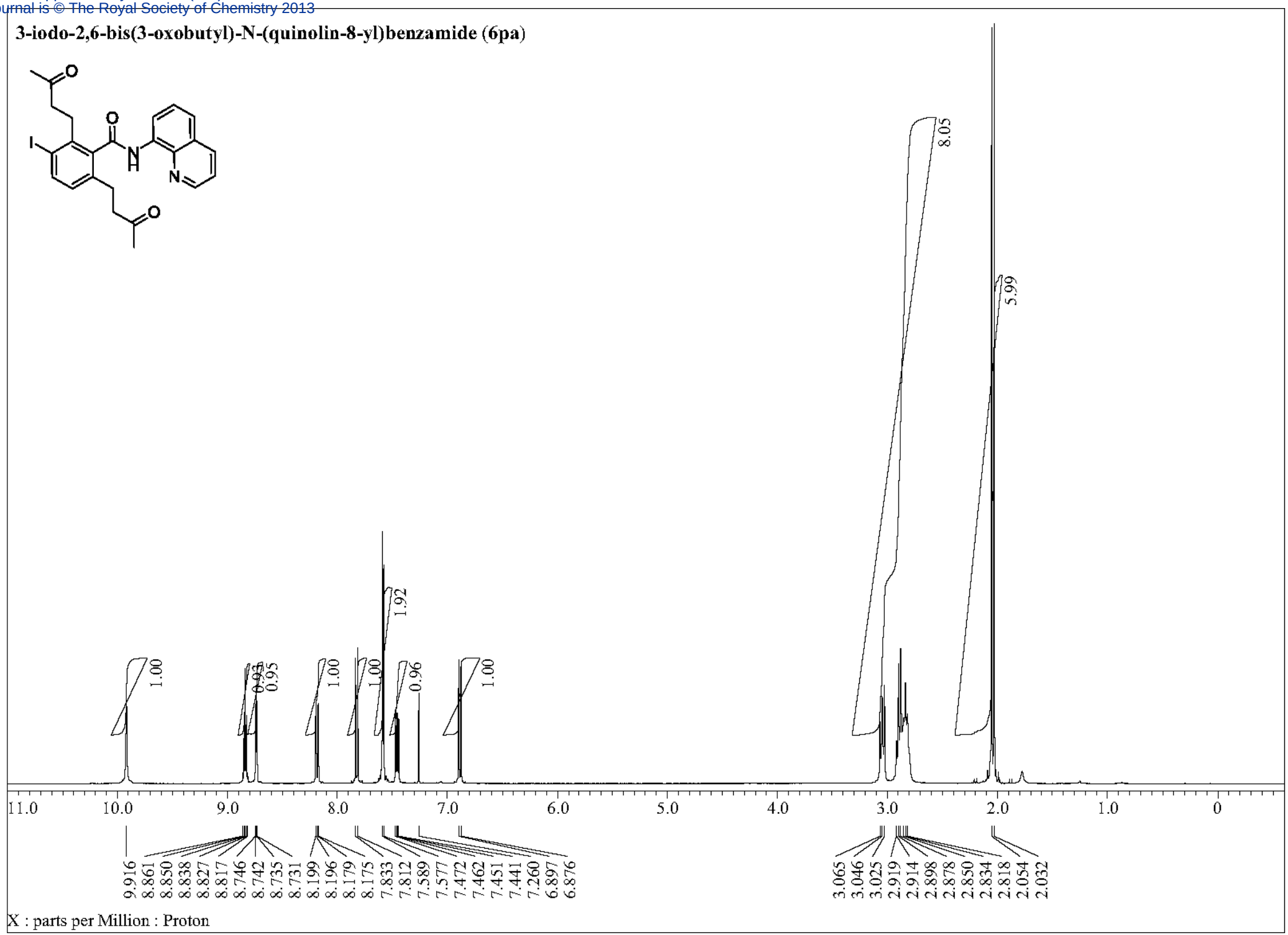

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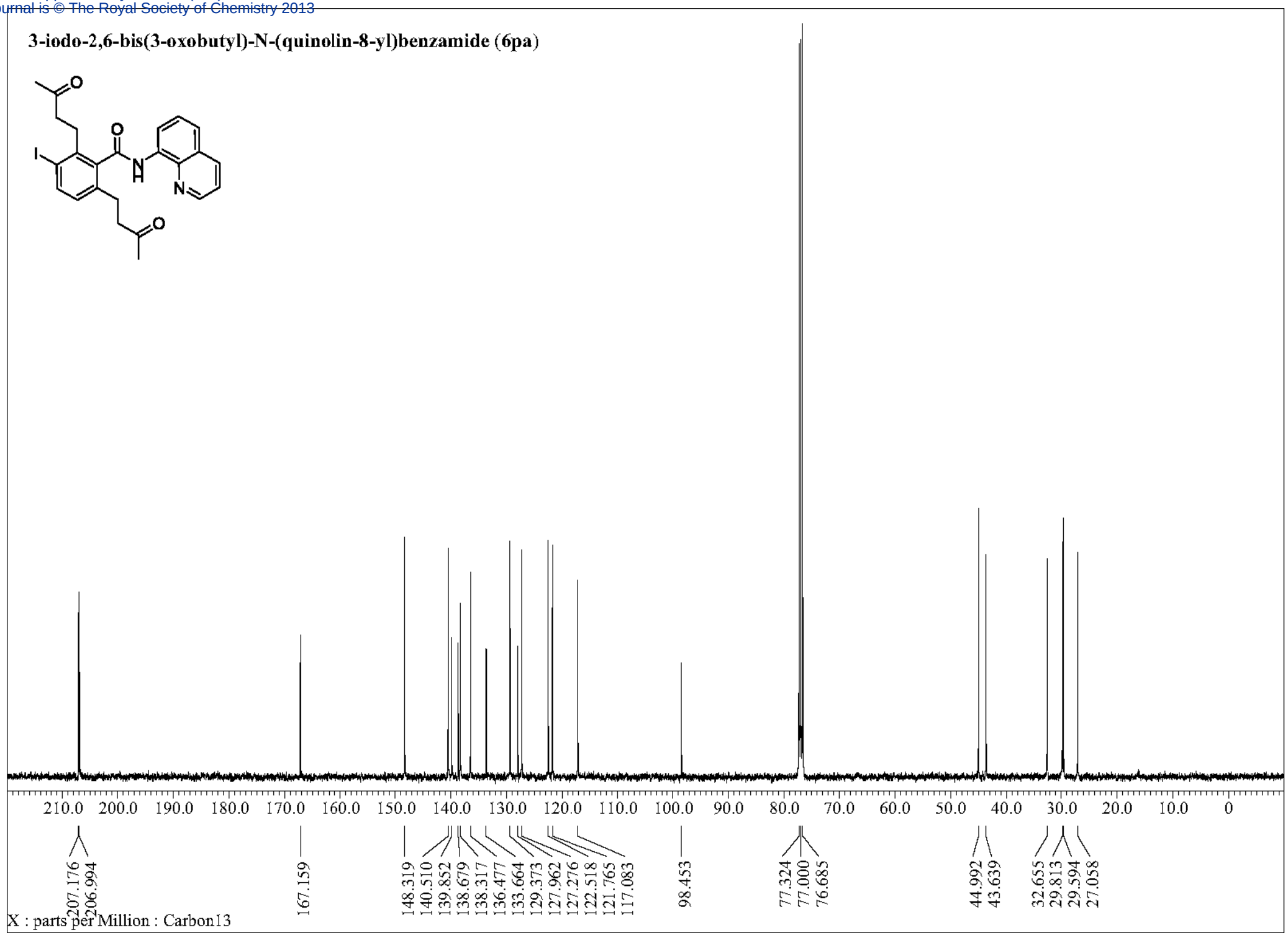

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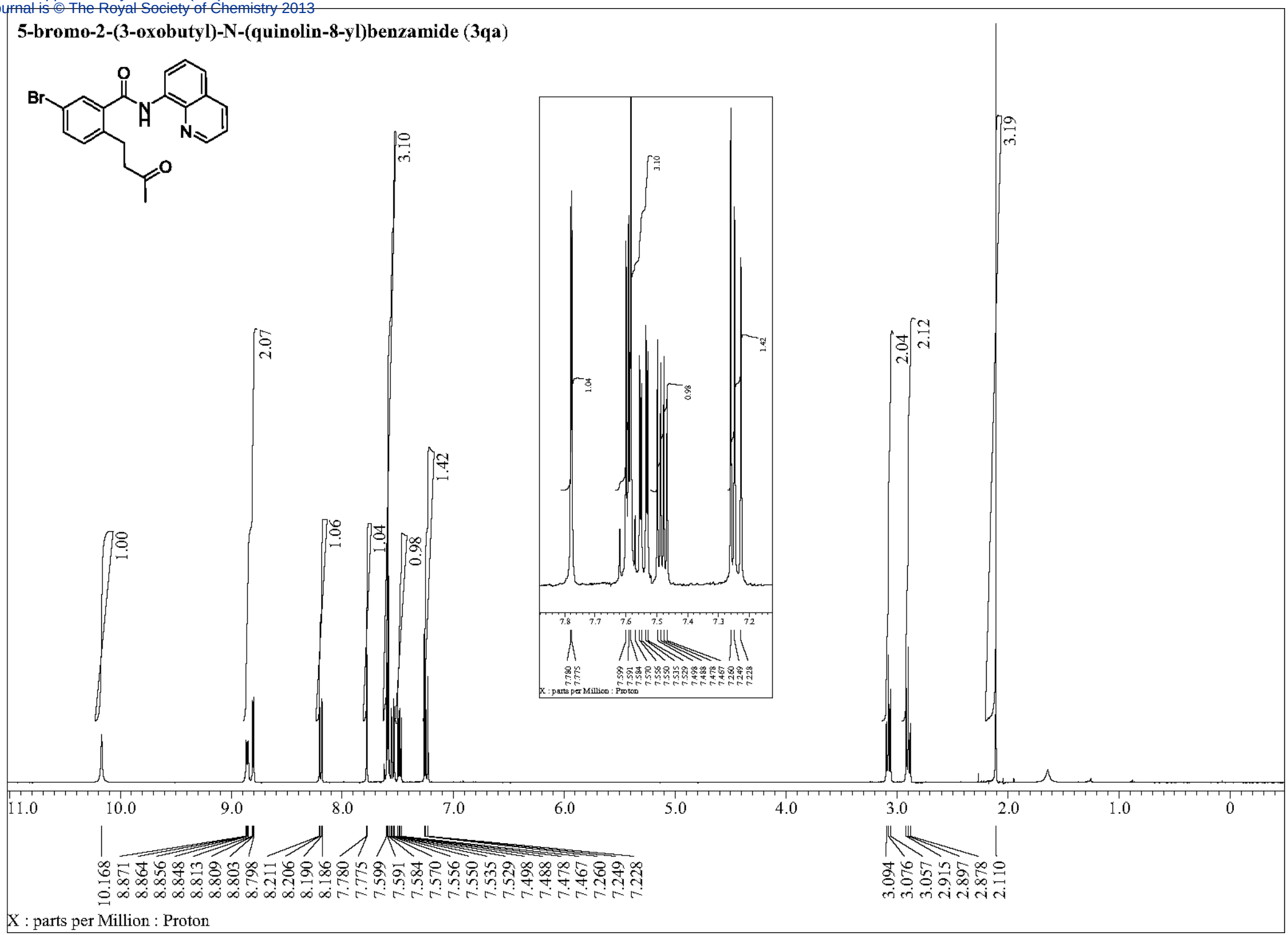

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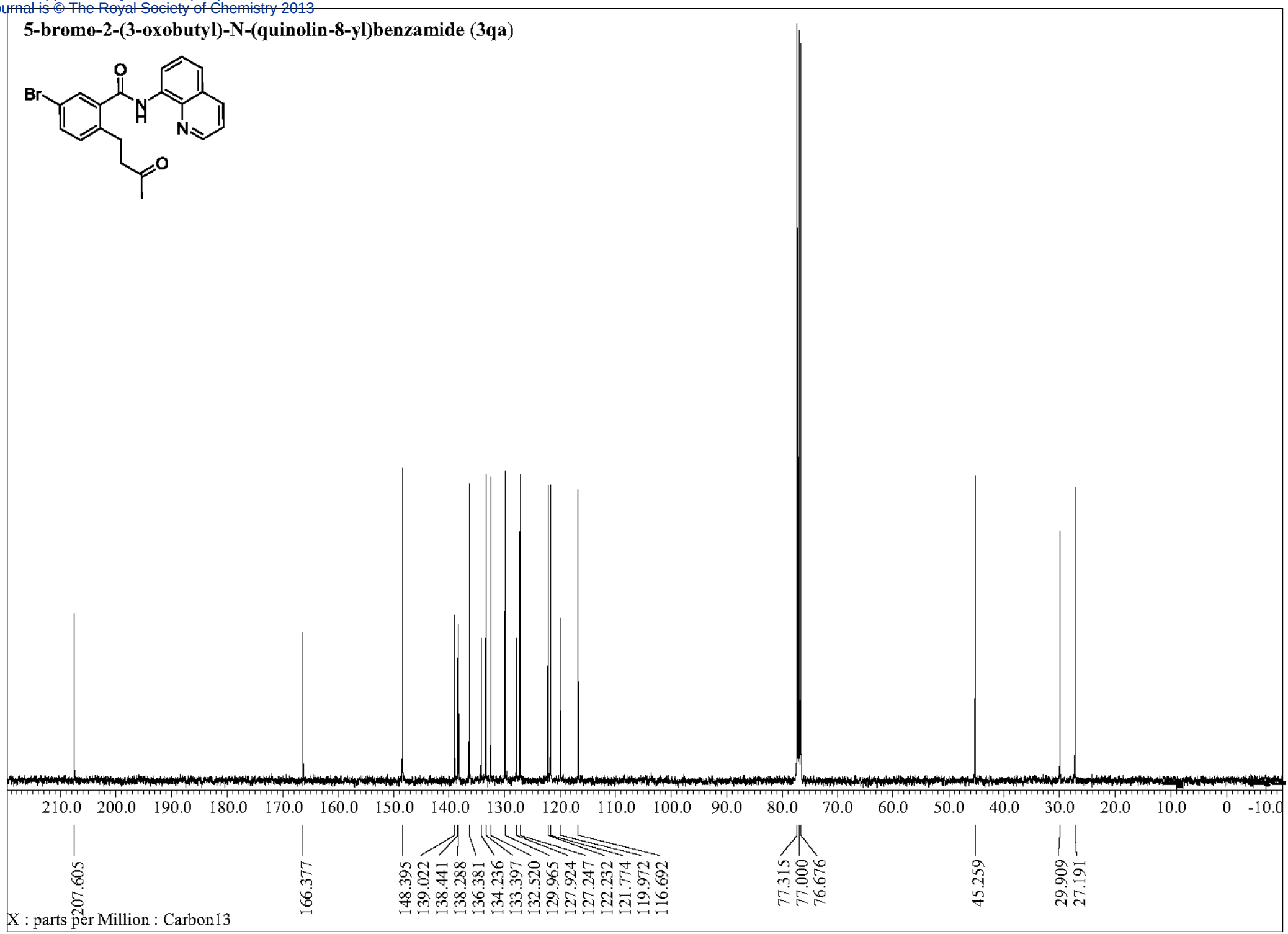

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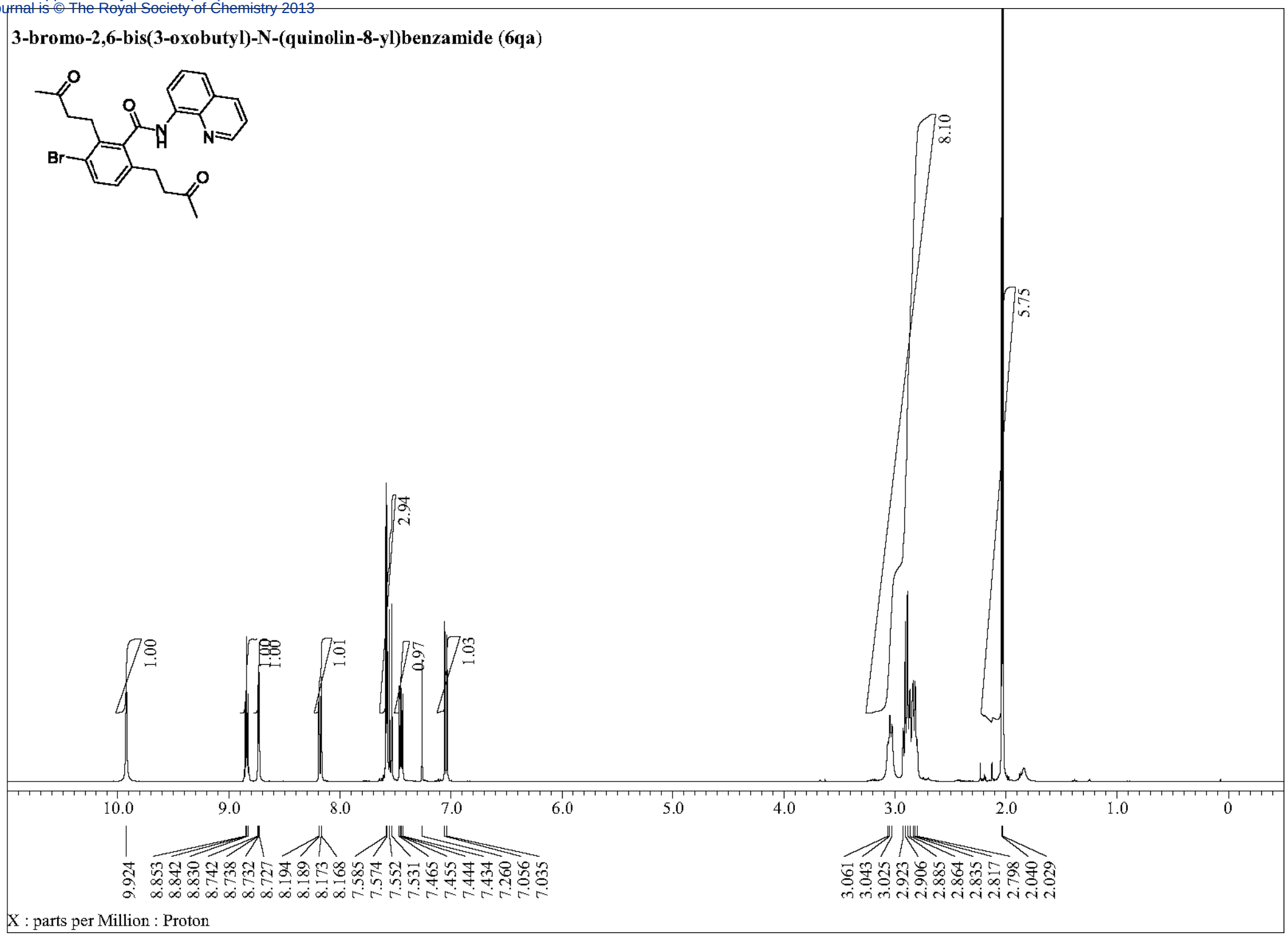

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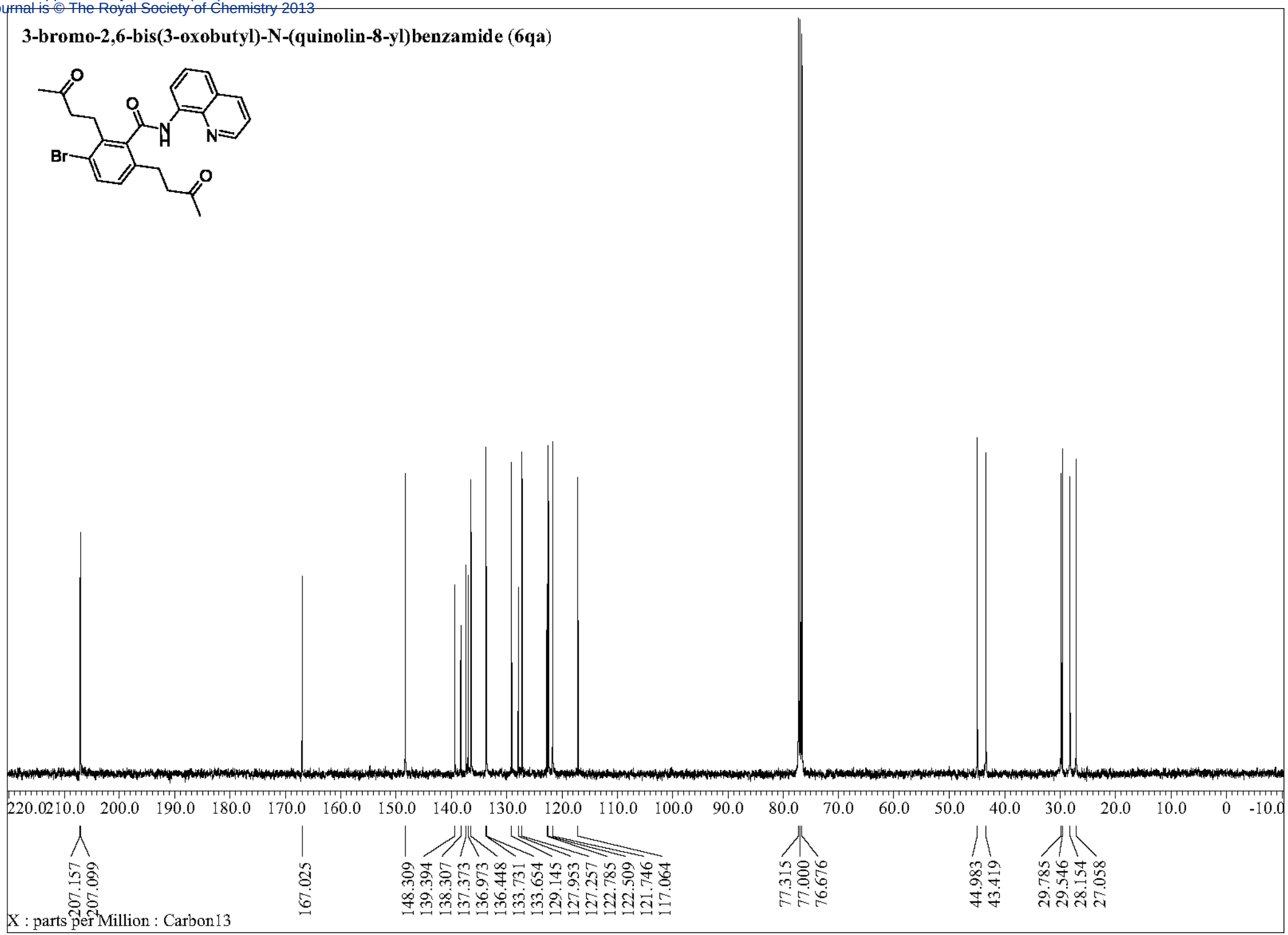

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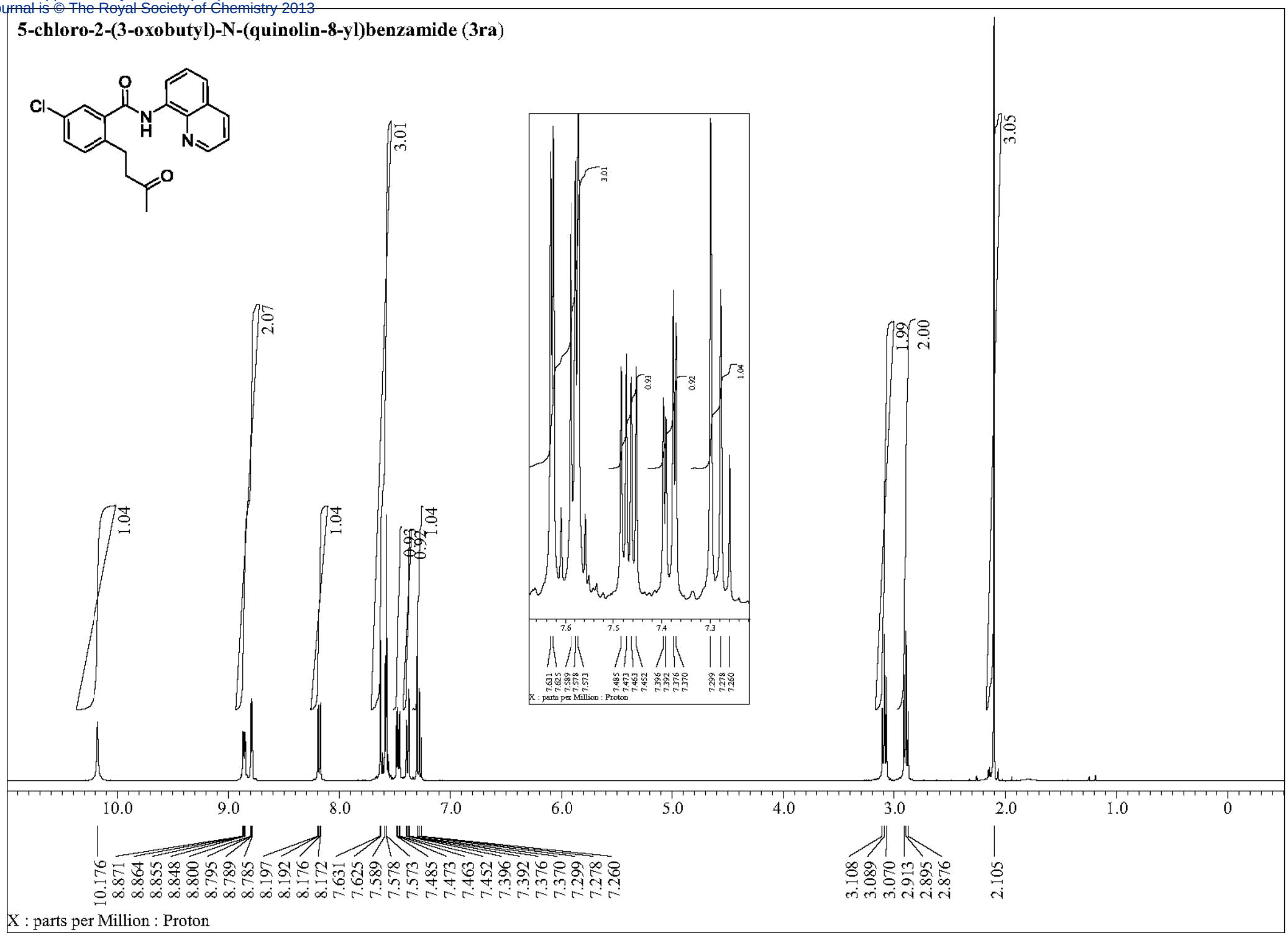

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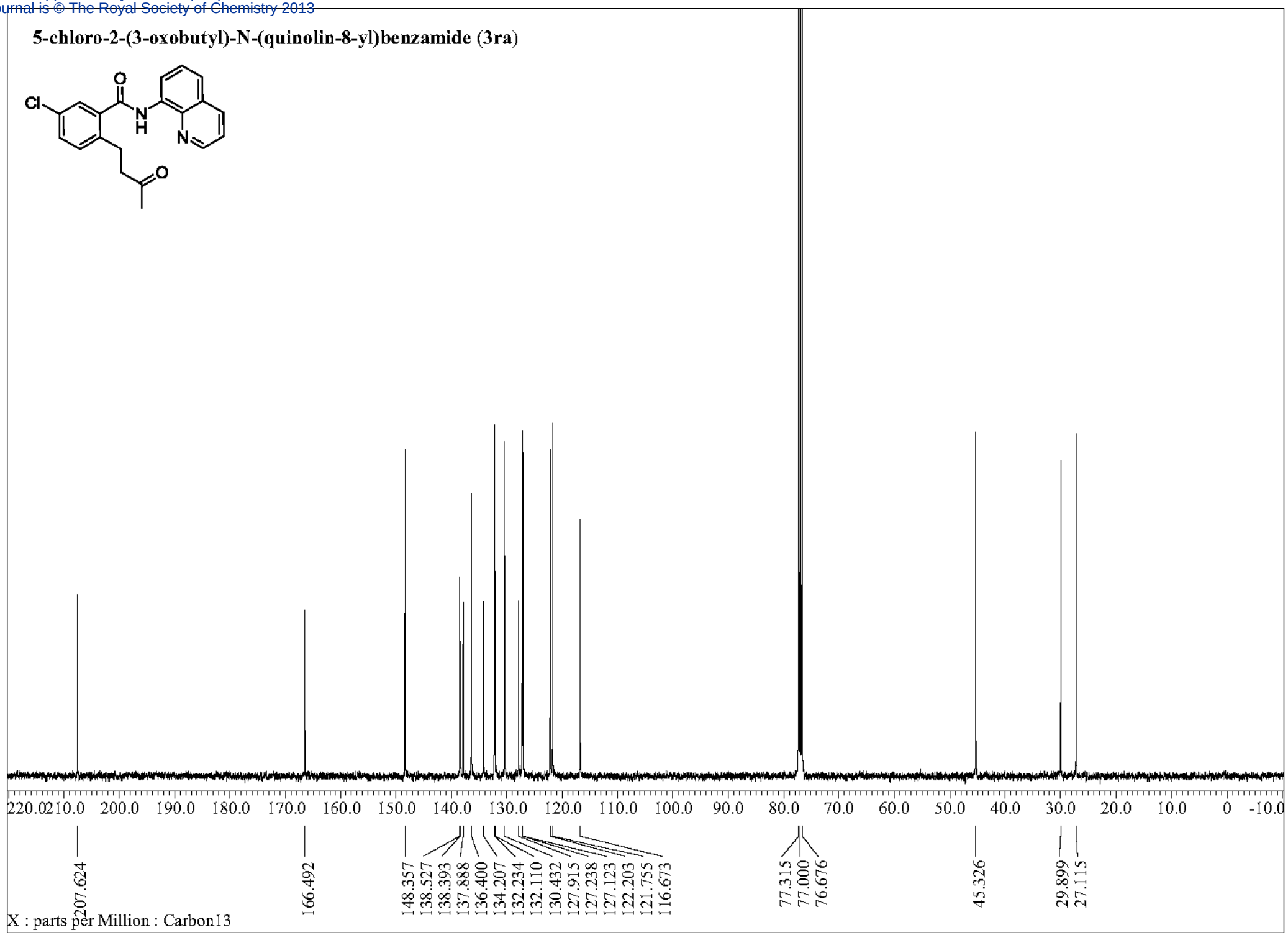

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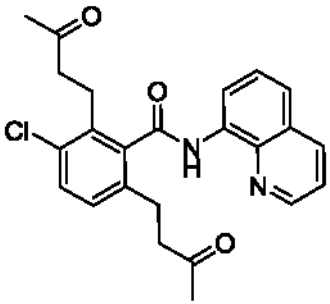
3-chloro-2,6-bis(3-oxobutyl)-N-(quinolin-8-yl)benzamide (6ra)



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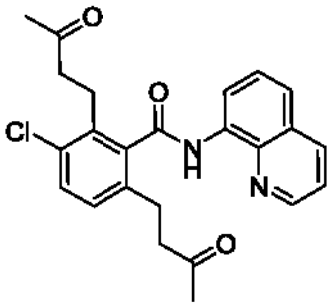

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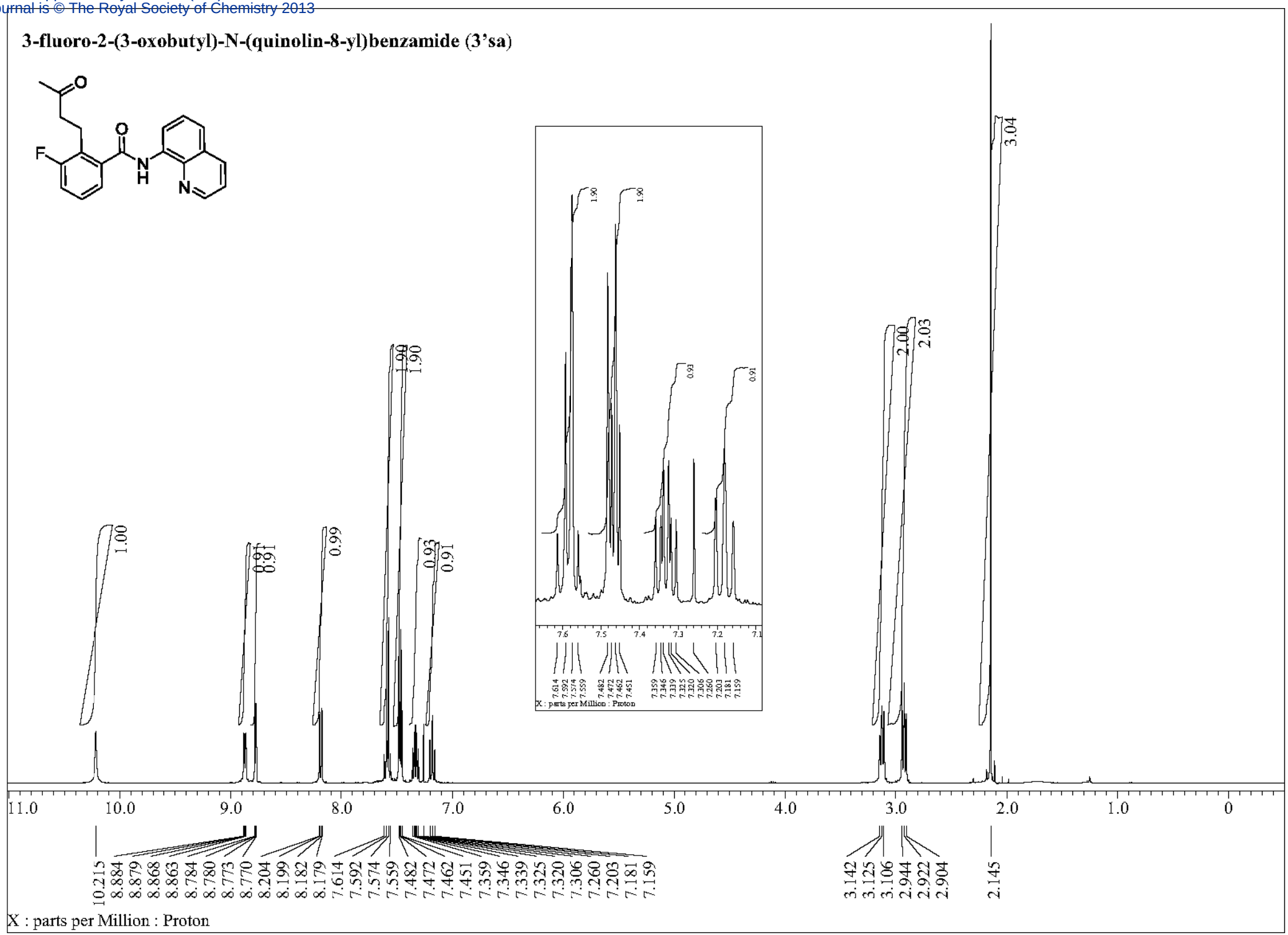

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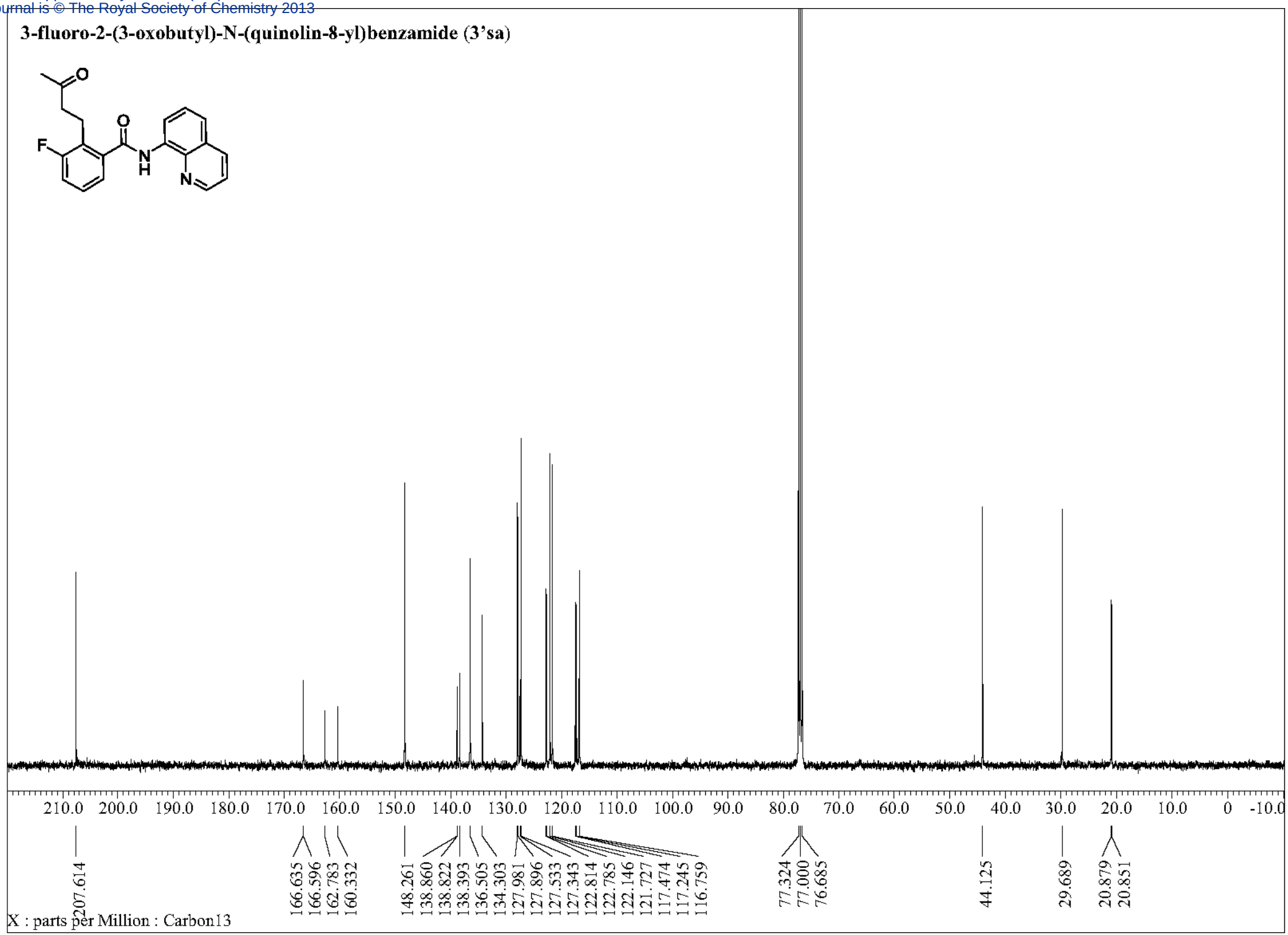

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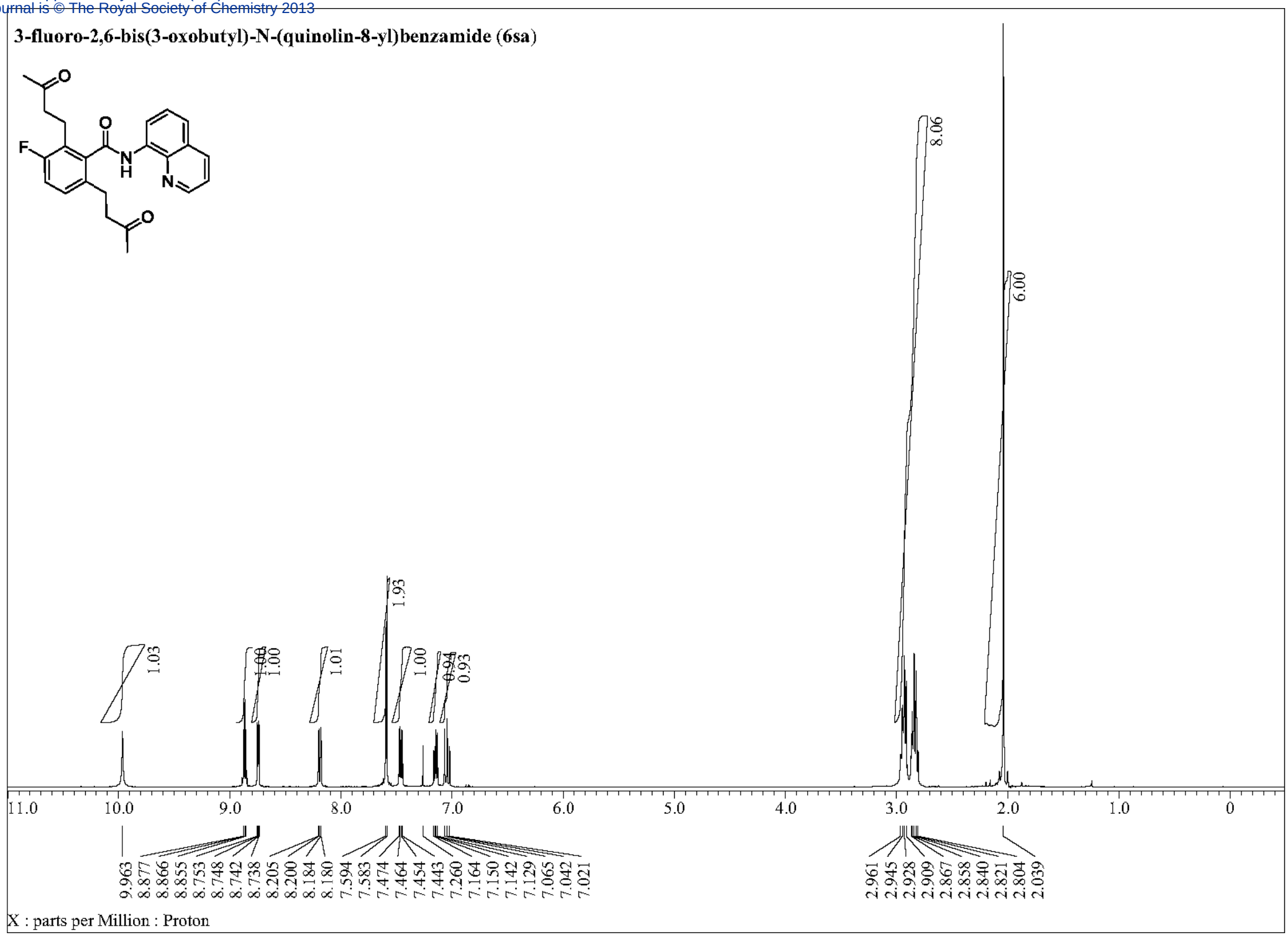

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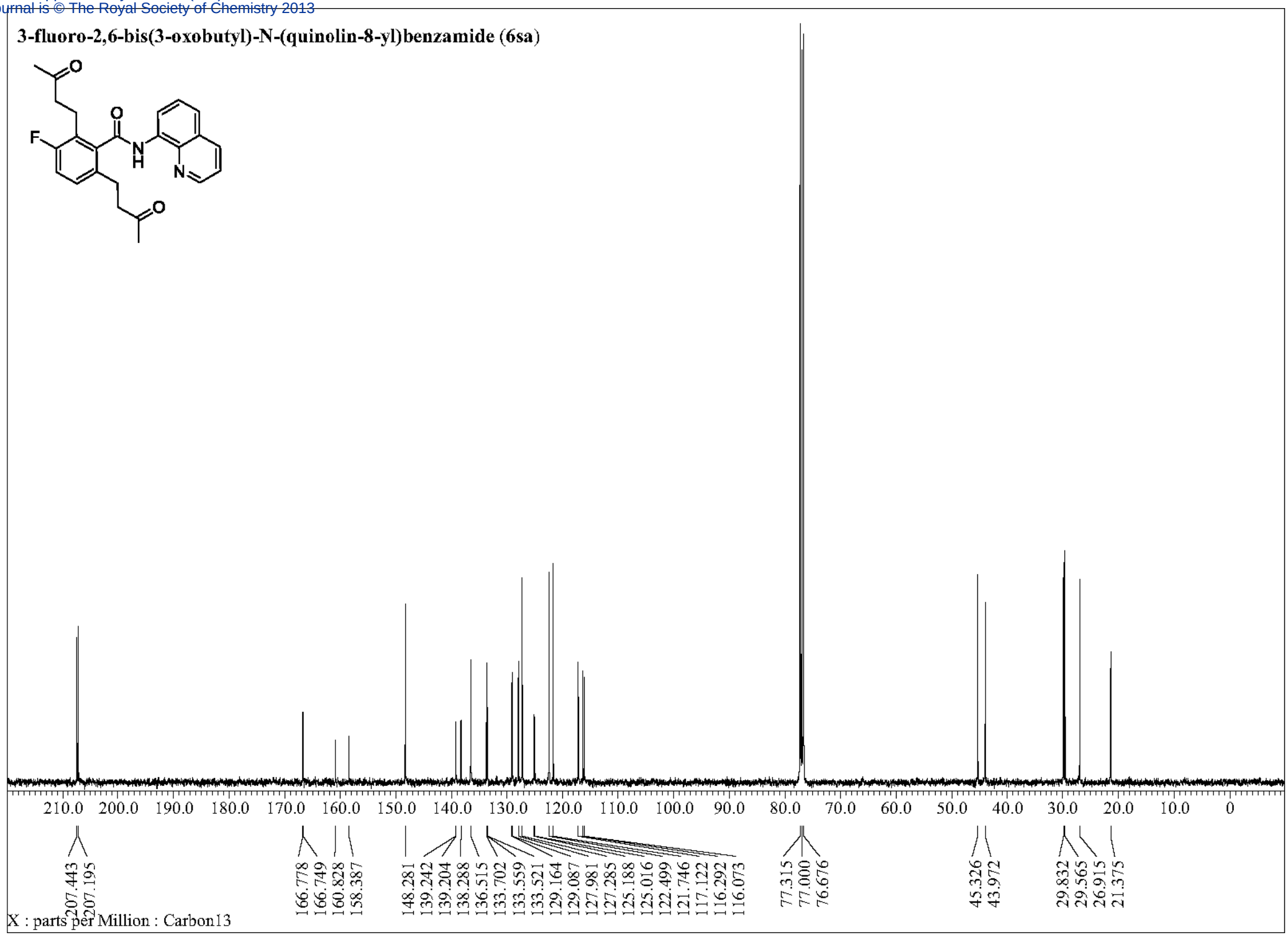

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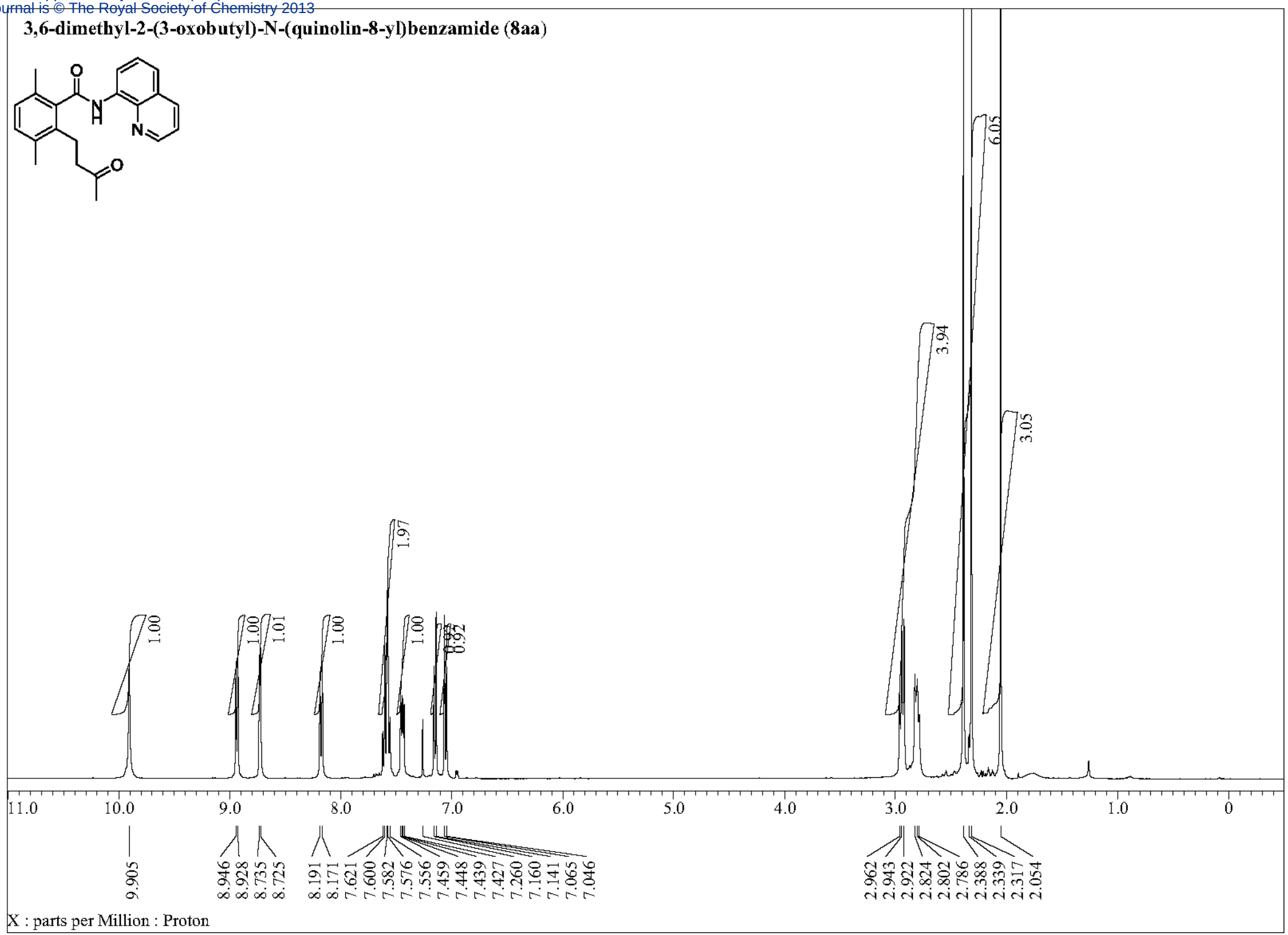

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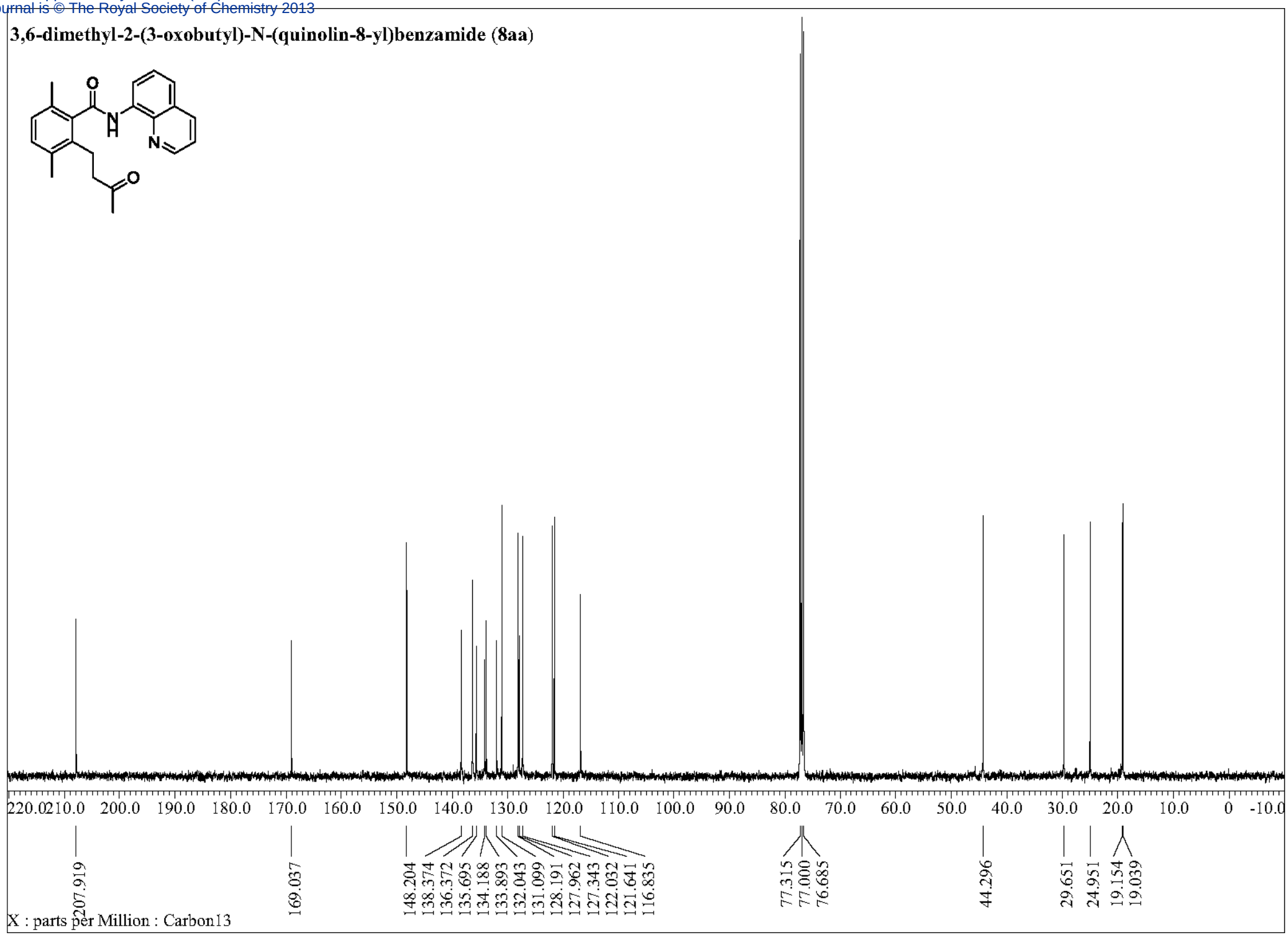

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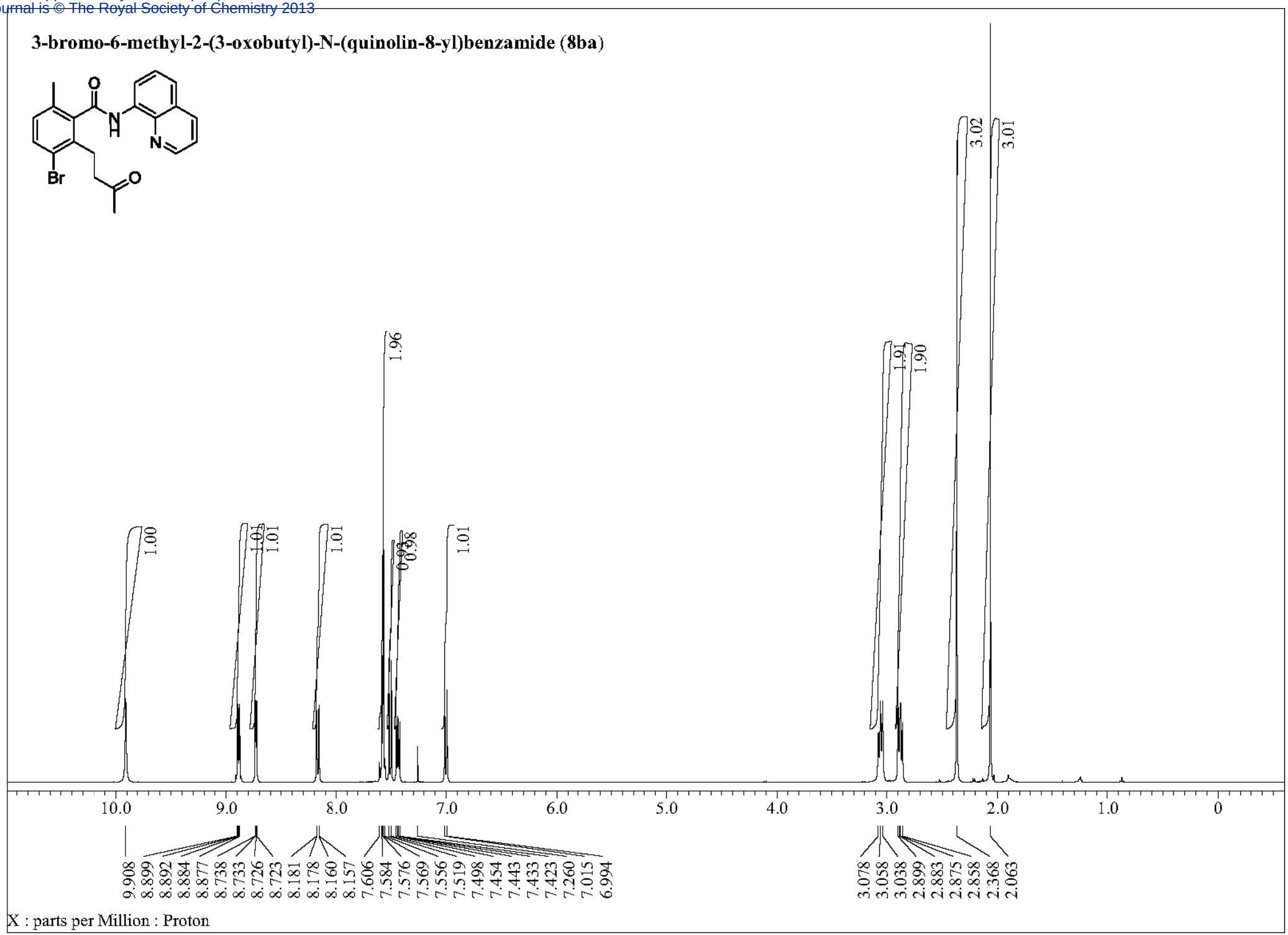

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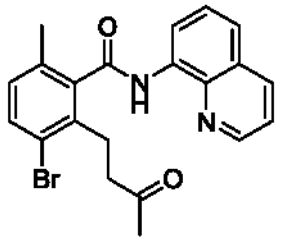
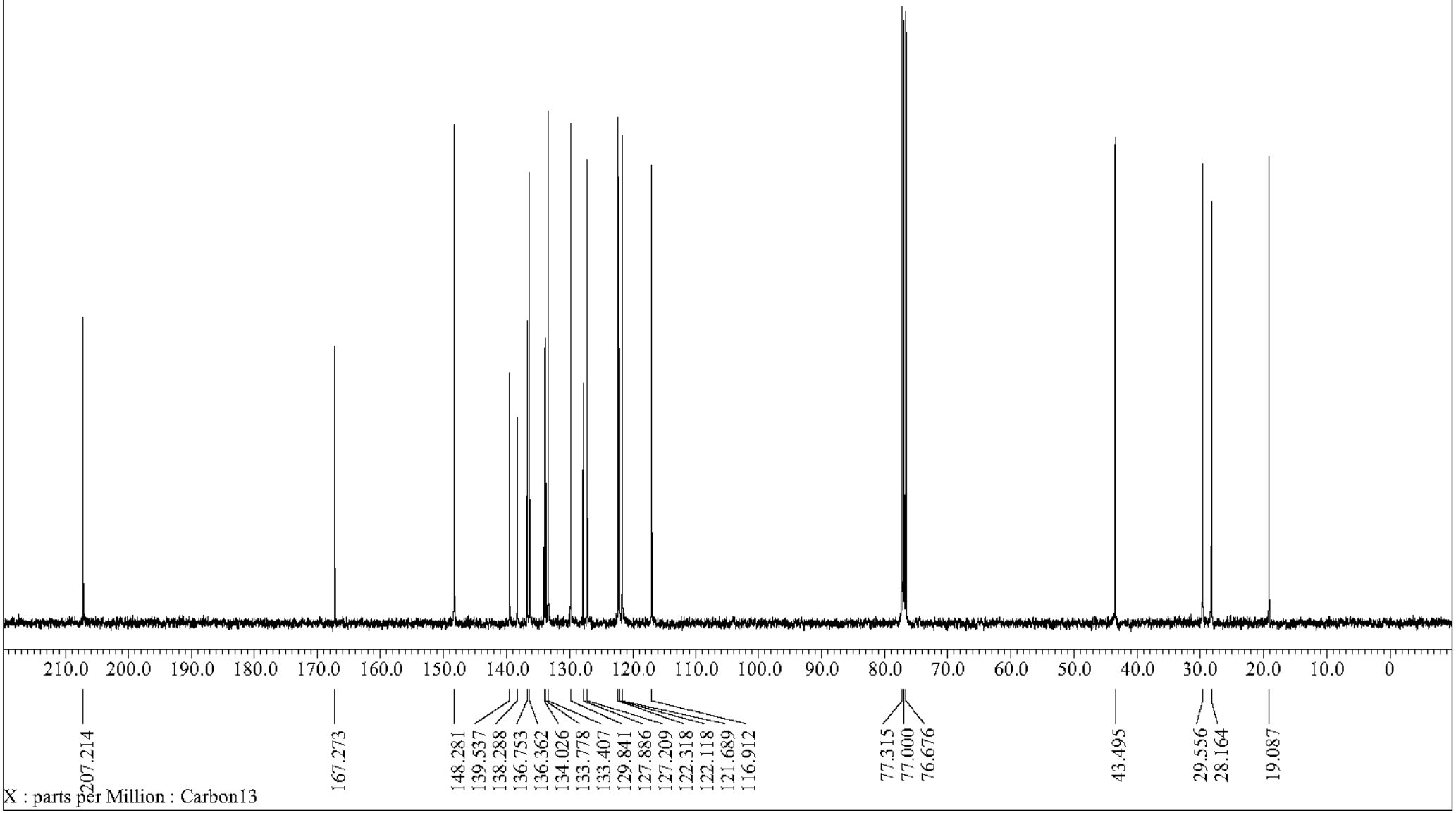
3-bromo-6-methyl-2-(3-oxobutyl)-N-(quinolin-8-yl)benzamide (8ba)





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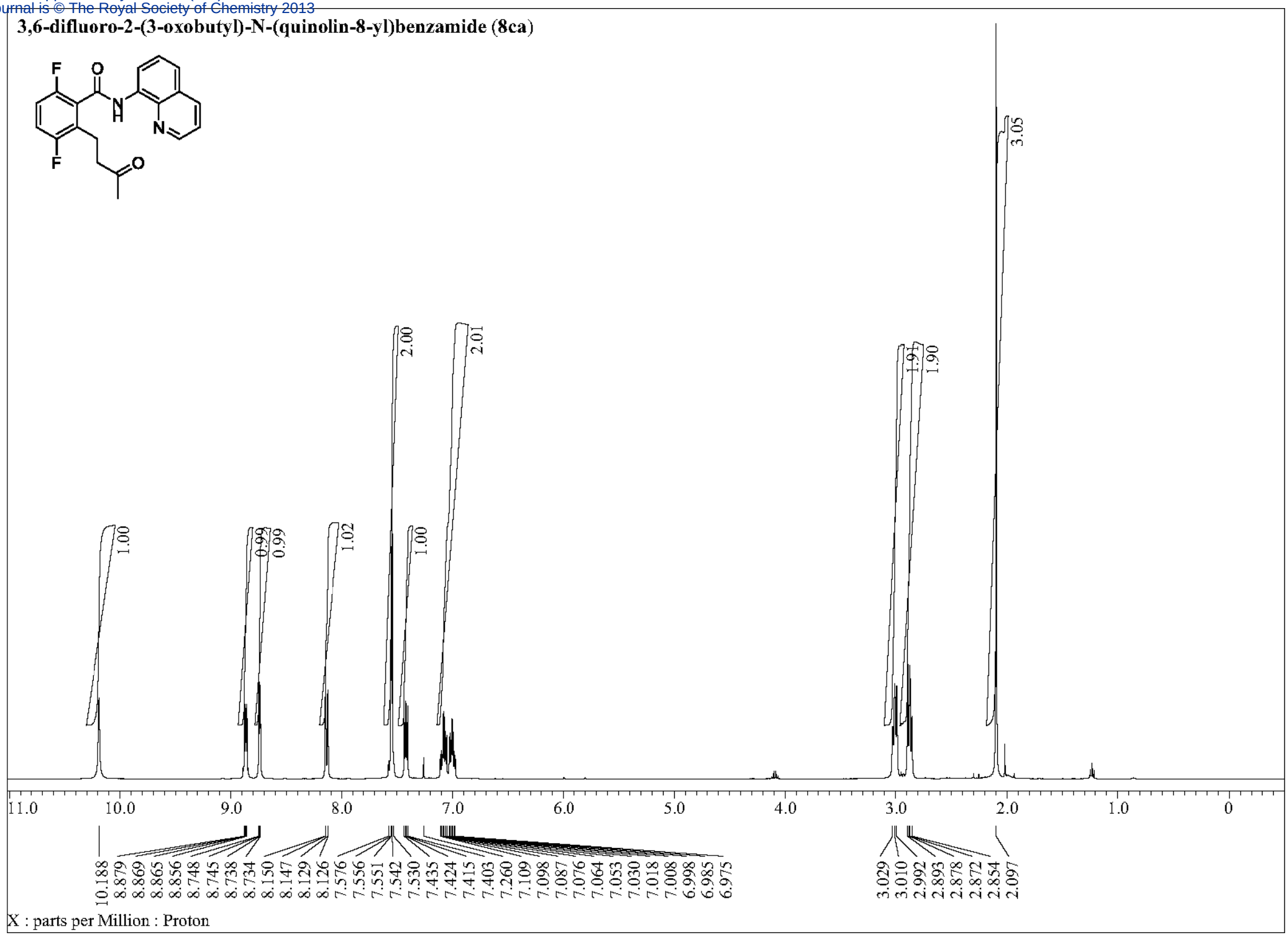

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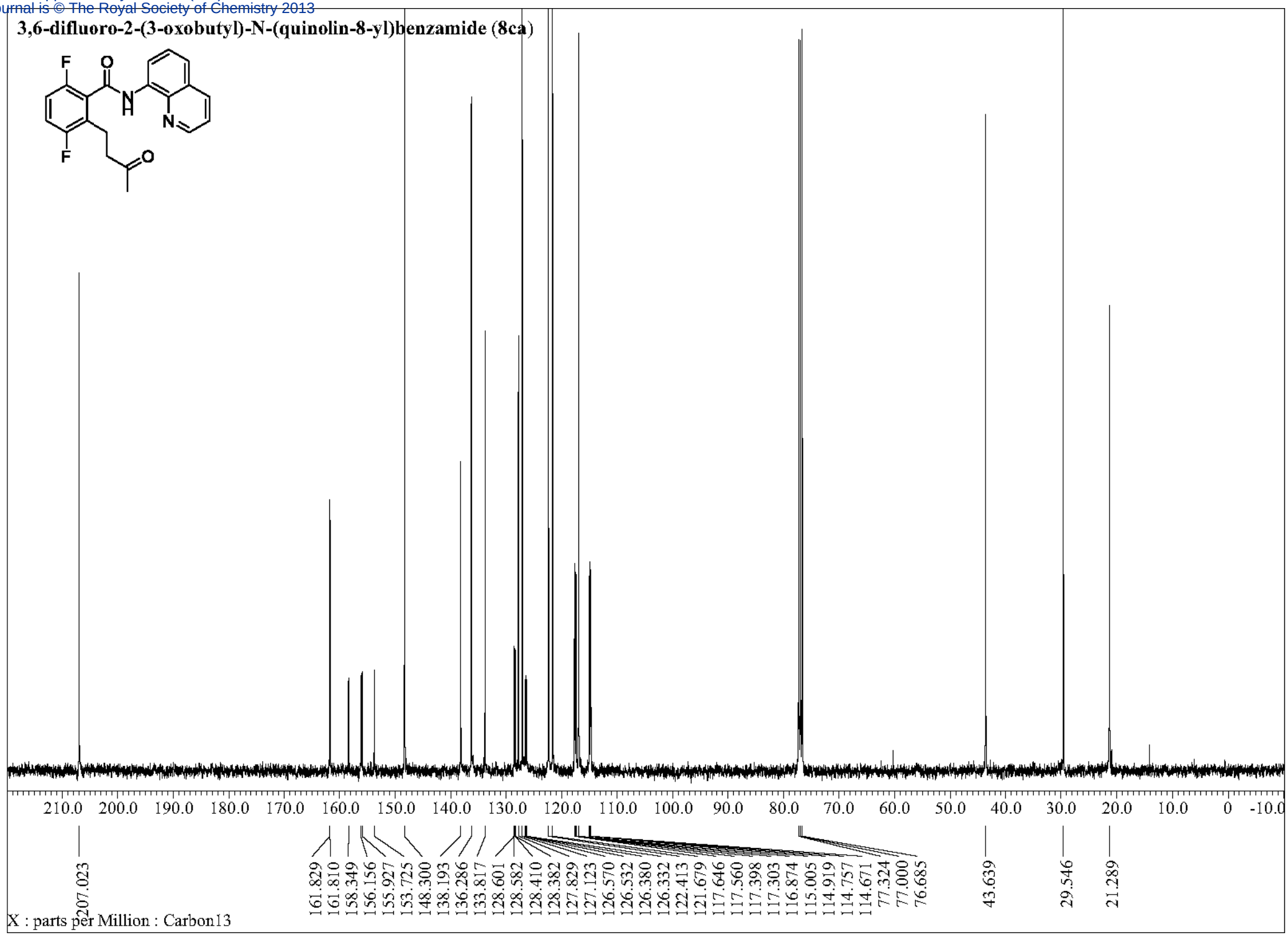

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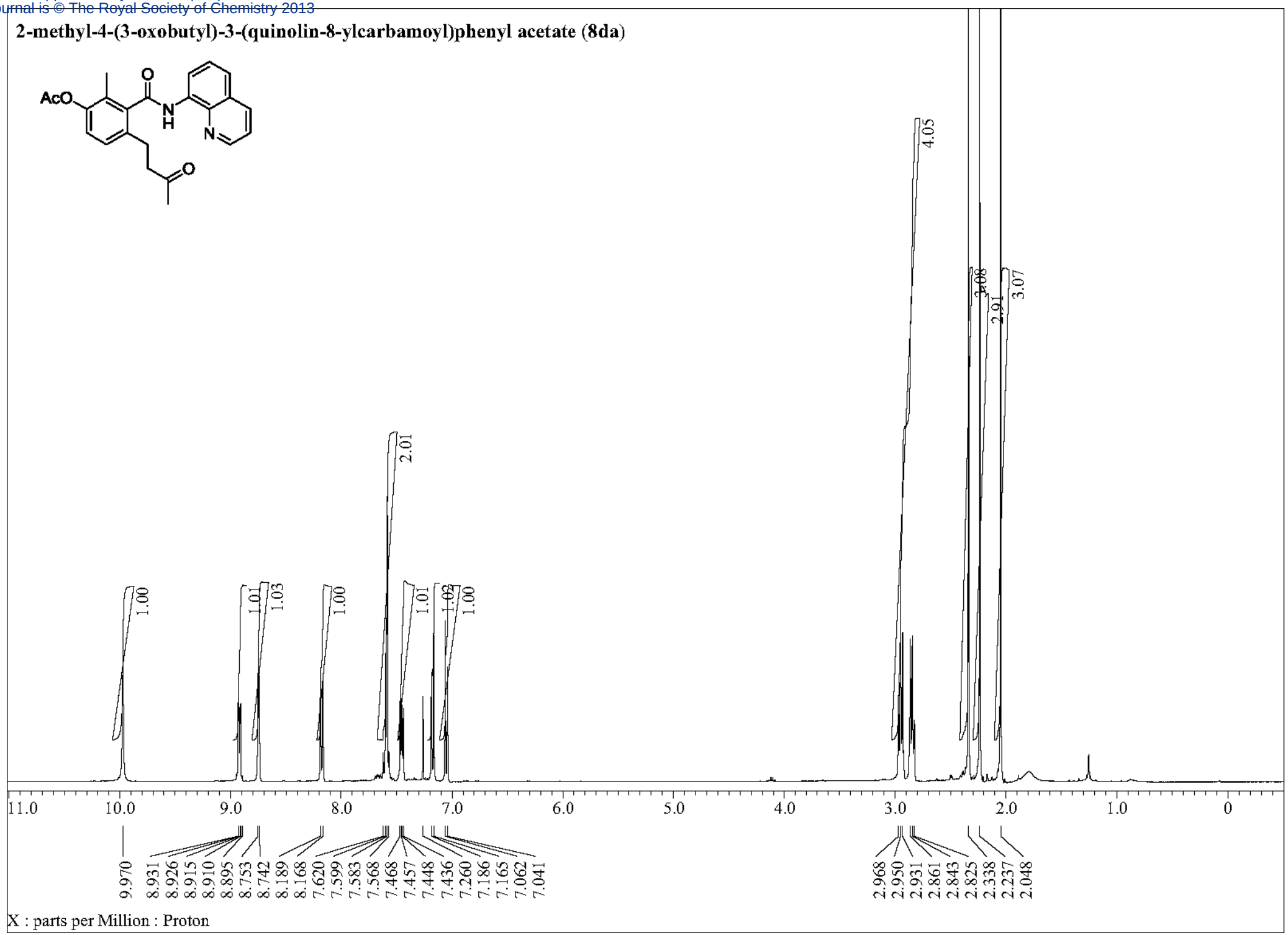

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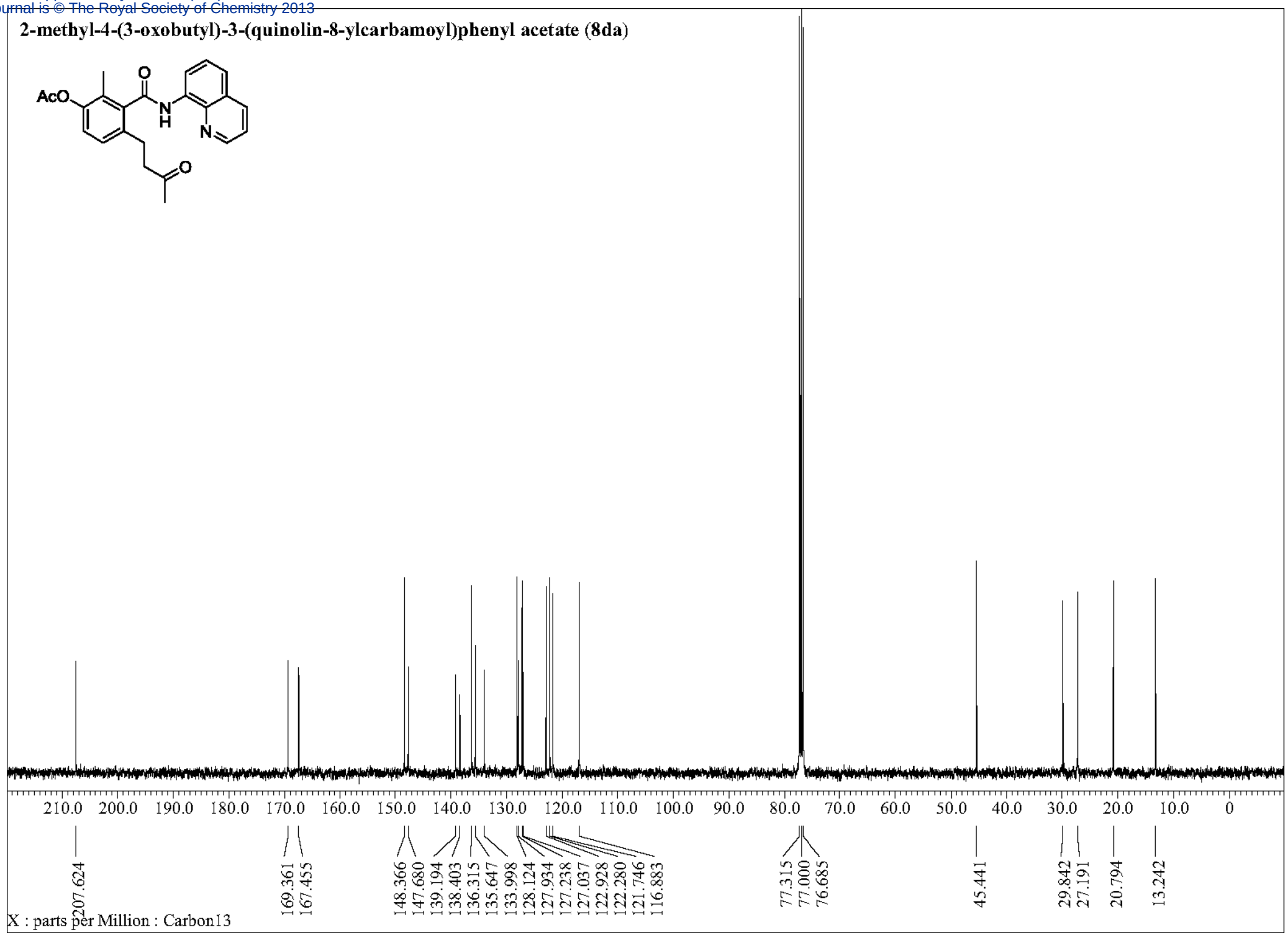

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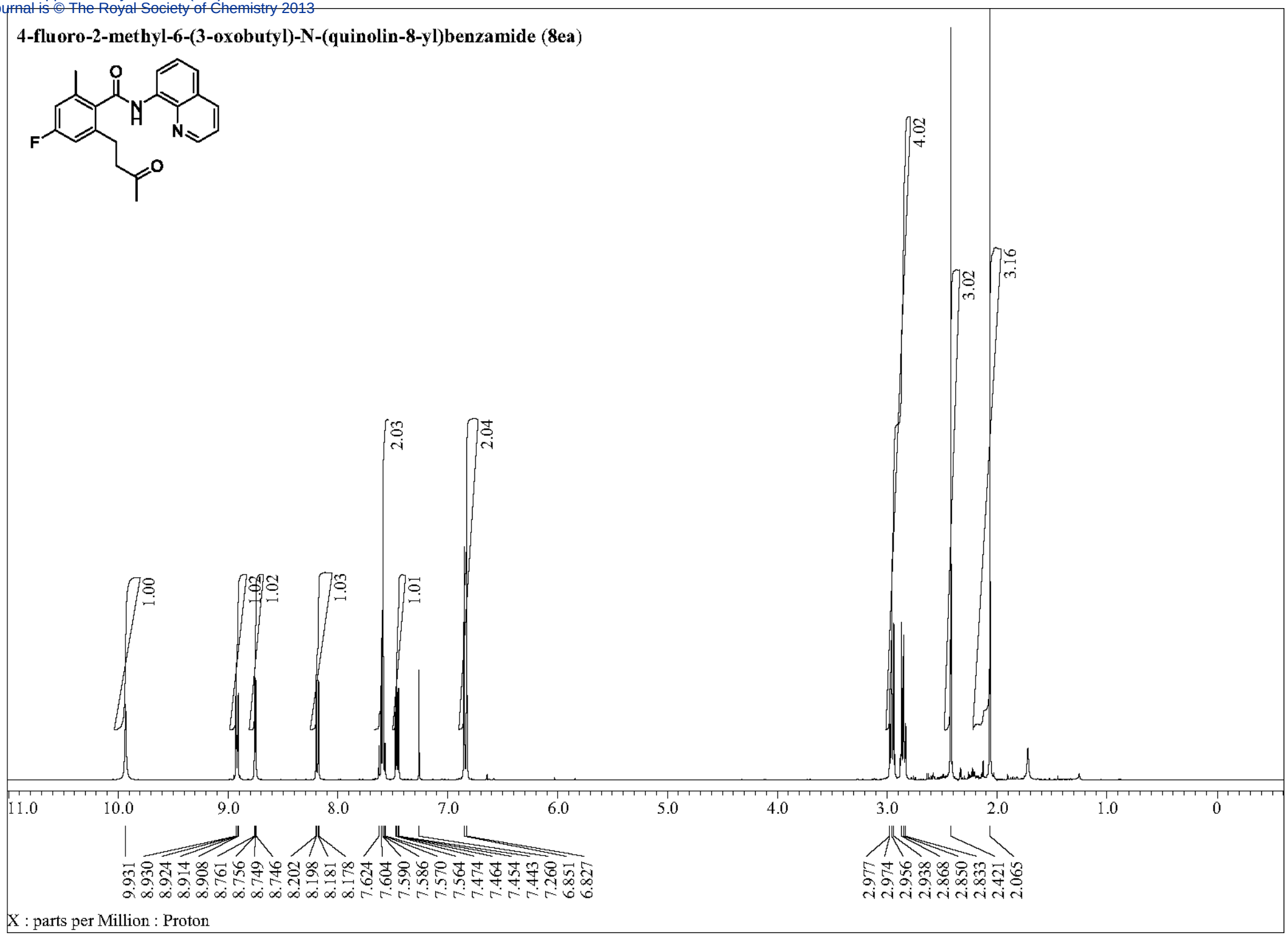

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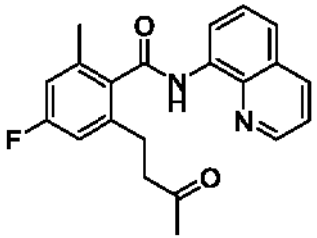
4-fluoro-2-methyl-6-(3-oxobutyl)-N-(quinolin-8-yl)benzamide (8ea)



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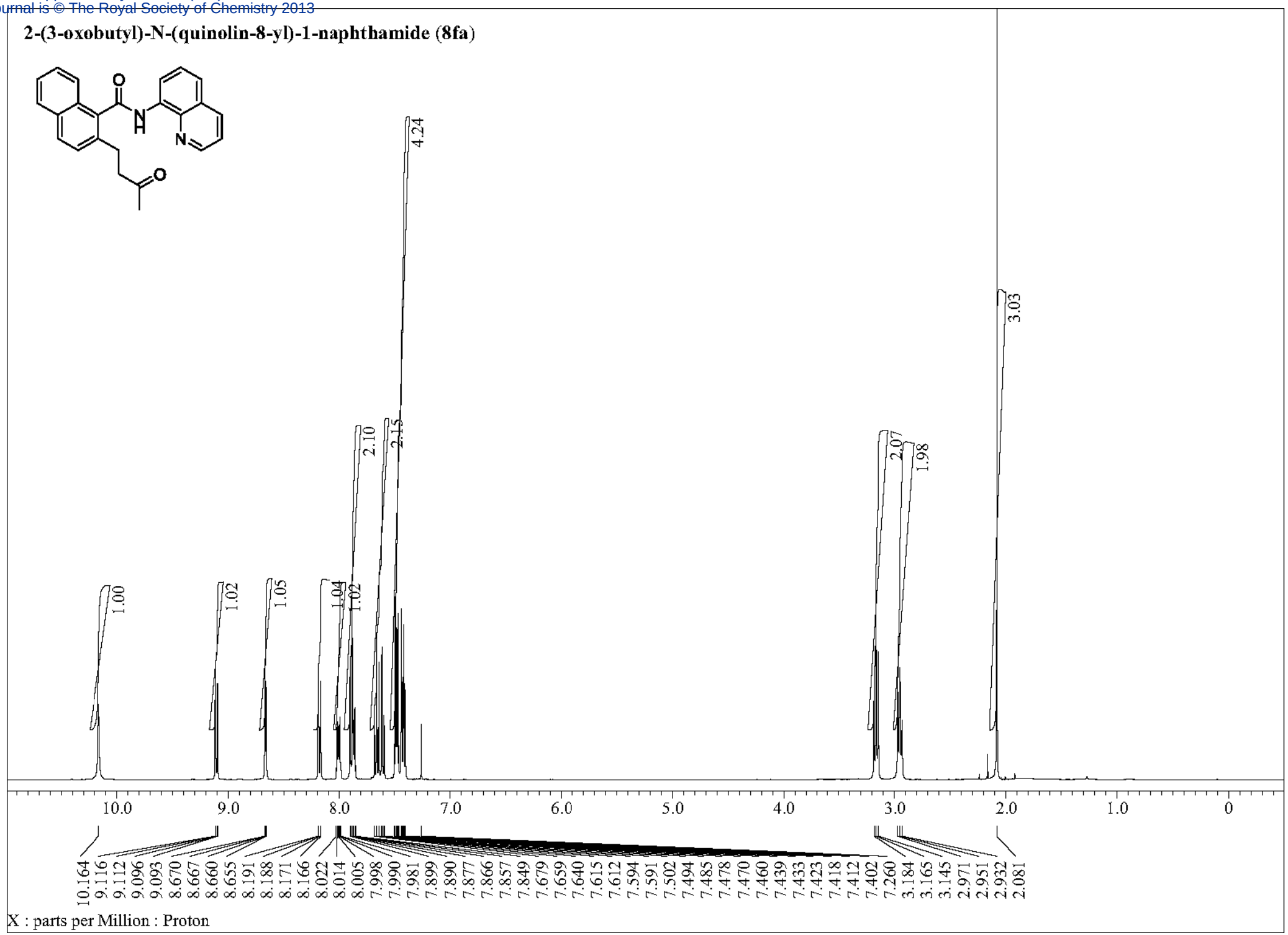

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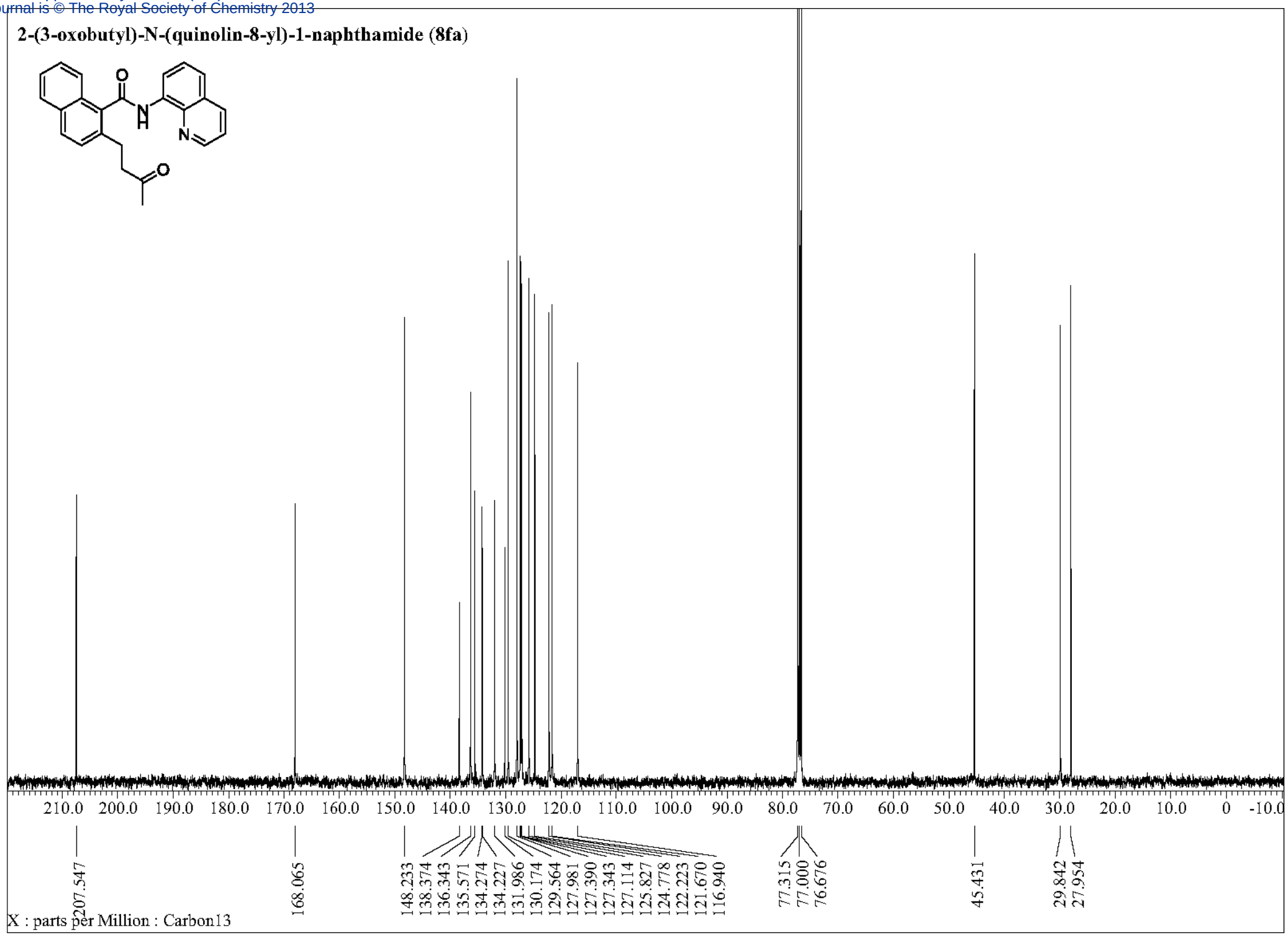

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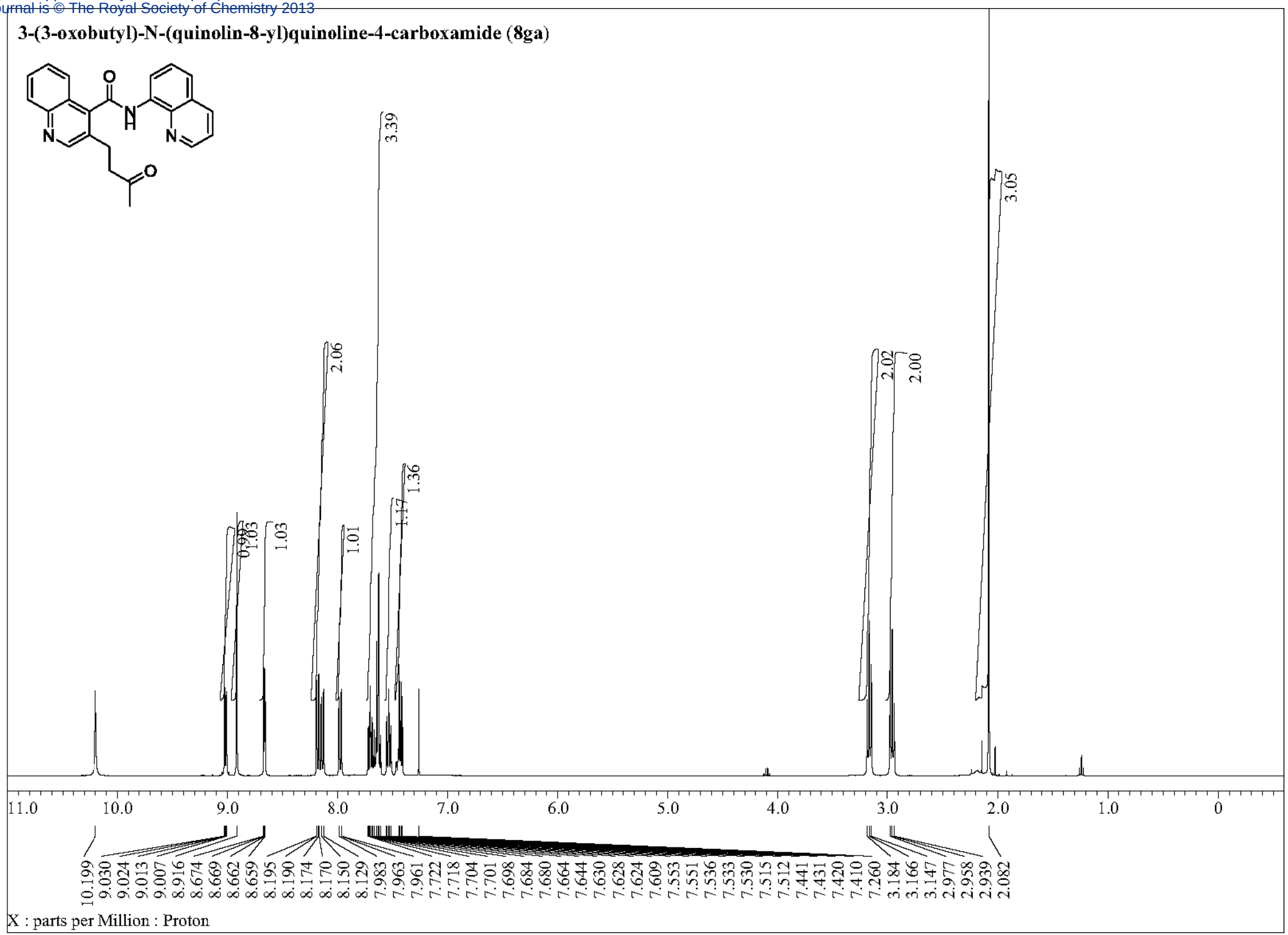

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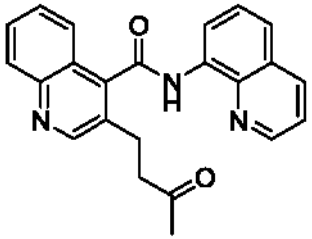
3-(3-oxobutyl)-N-(quinolin-8-yl)quinoline-4-carboxamide (8ga)



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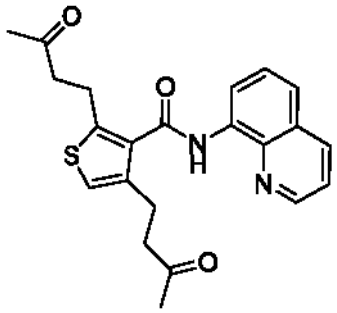
2,4-bis(3-oxobutyl)-N-(quinolin-8-yl)thiophene-3-carboxamide (8ha)



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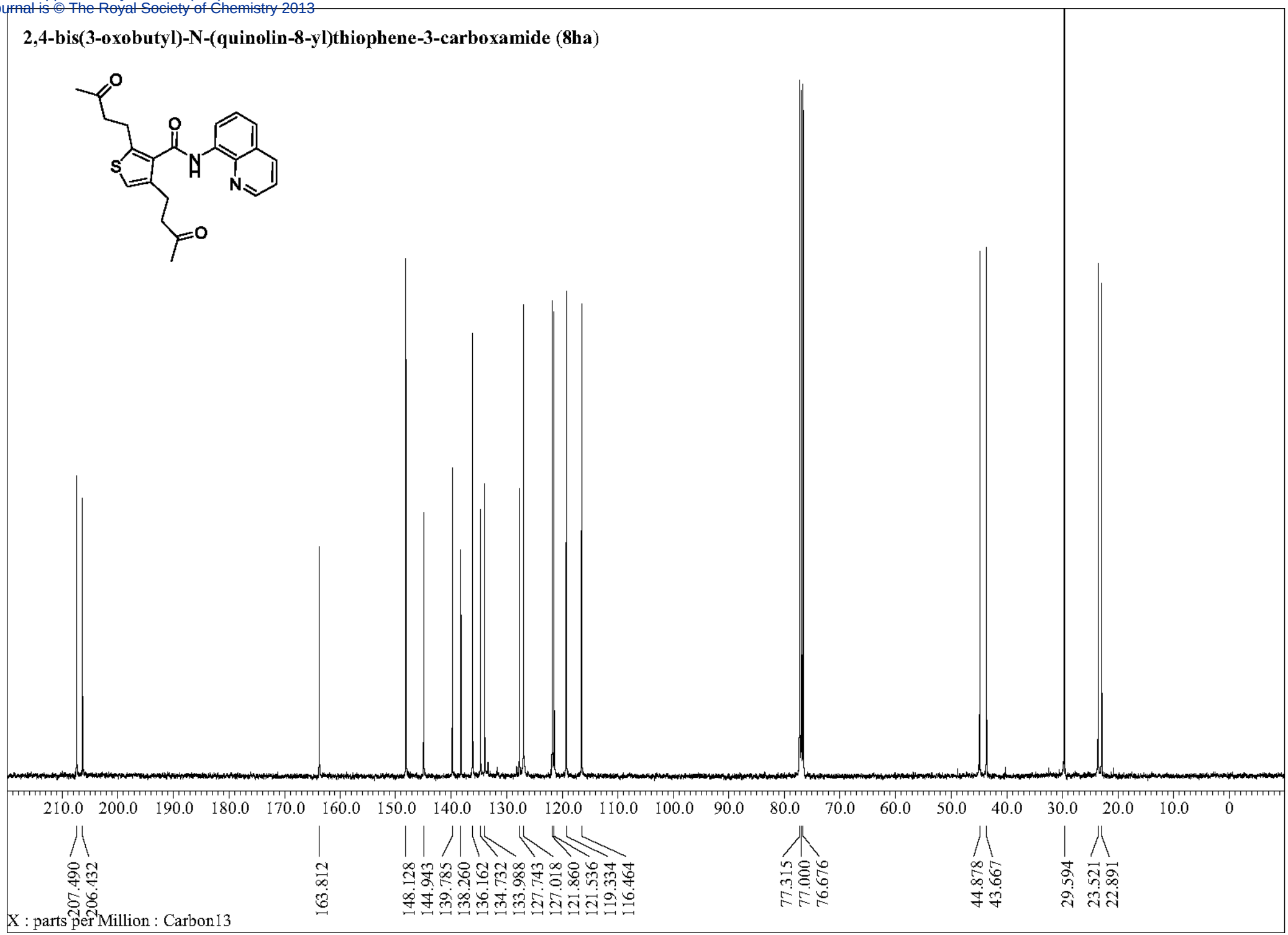

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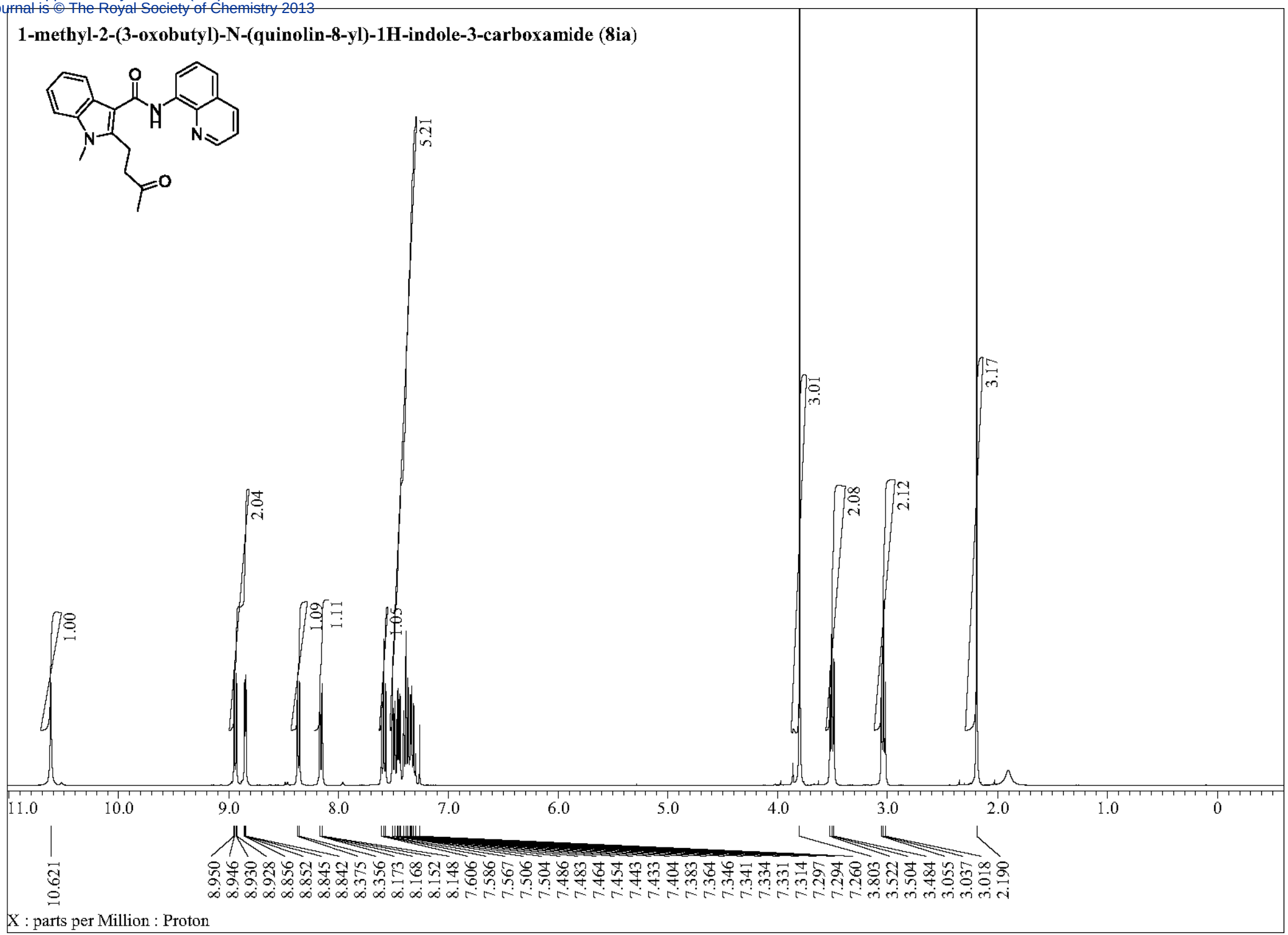

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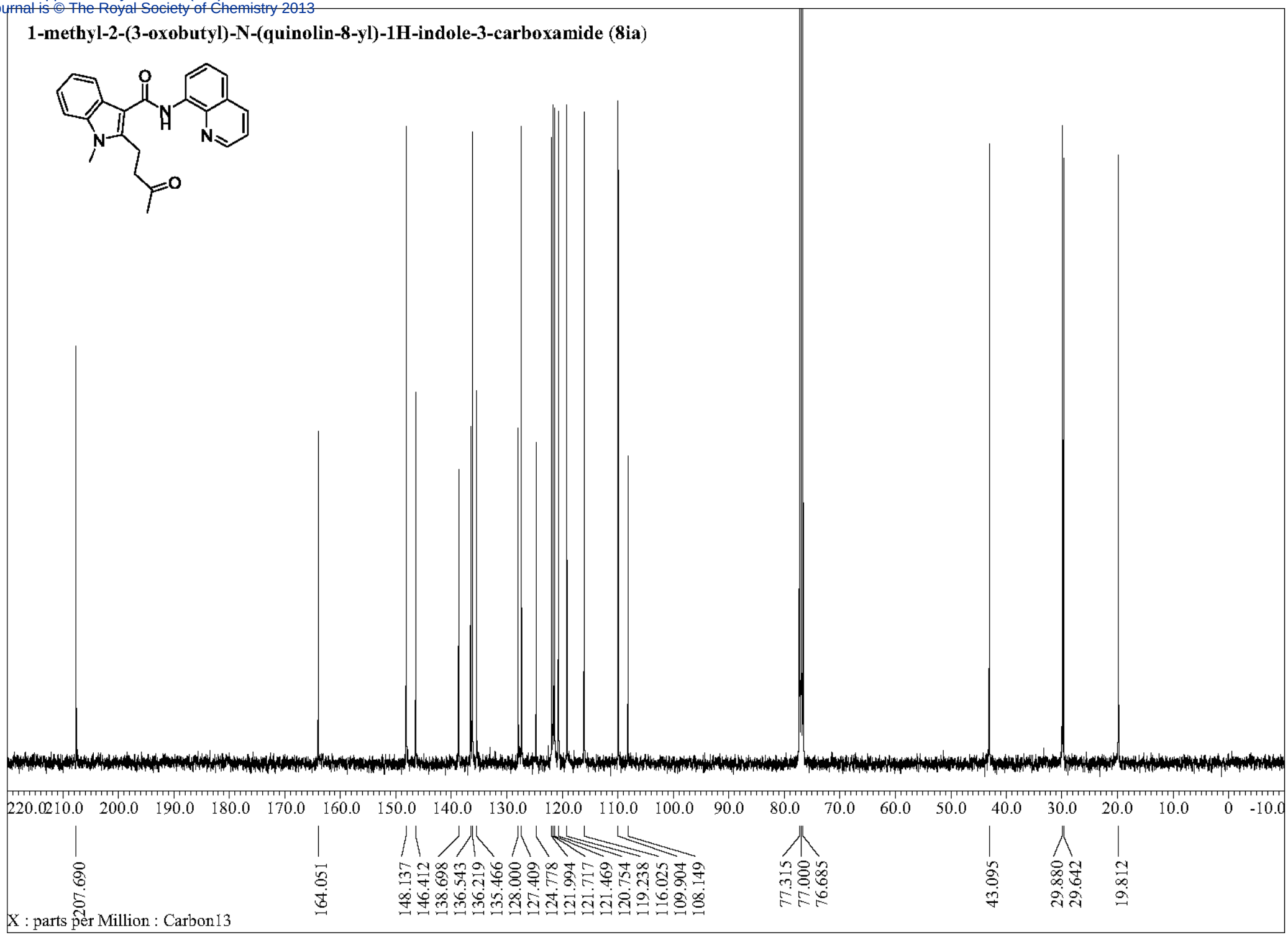

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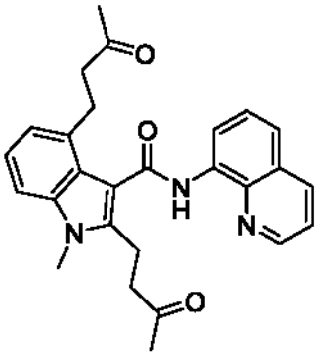
1-methyl-2,5-bis(3-oxobutyl)-N-(quinolin-8-yl)-1H-indole-3-carboxamide (8'ia)



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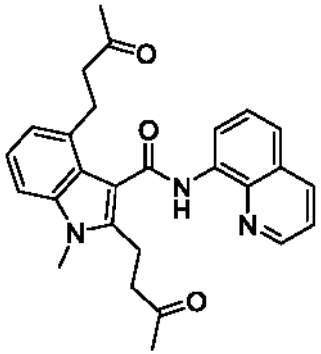
1-methyl-2,5-bis(3-oxobutyl)-N-(quinolin-8-yl)-1H-indole-3-carboxamide (8'ia)



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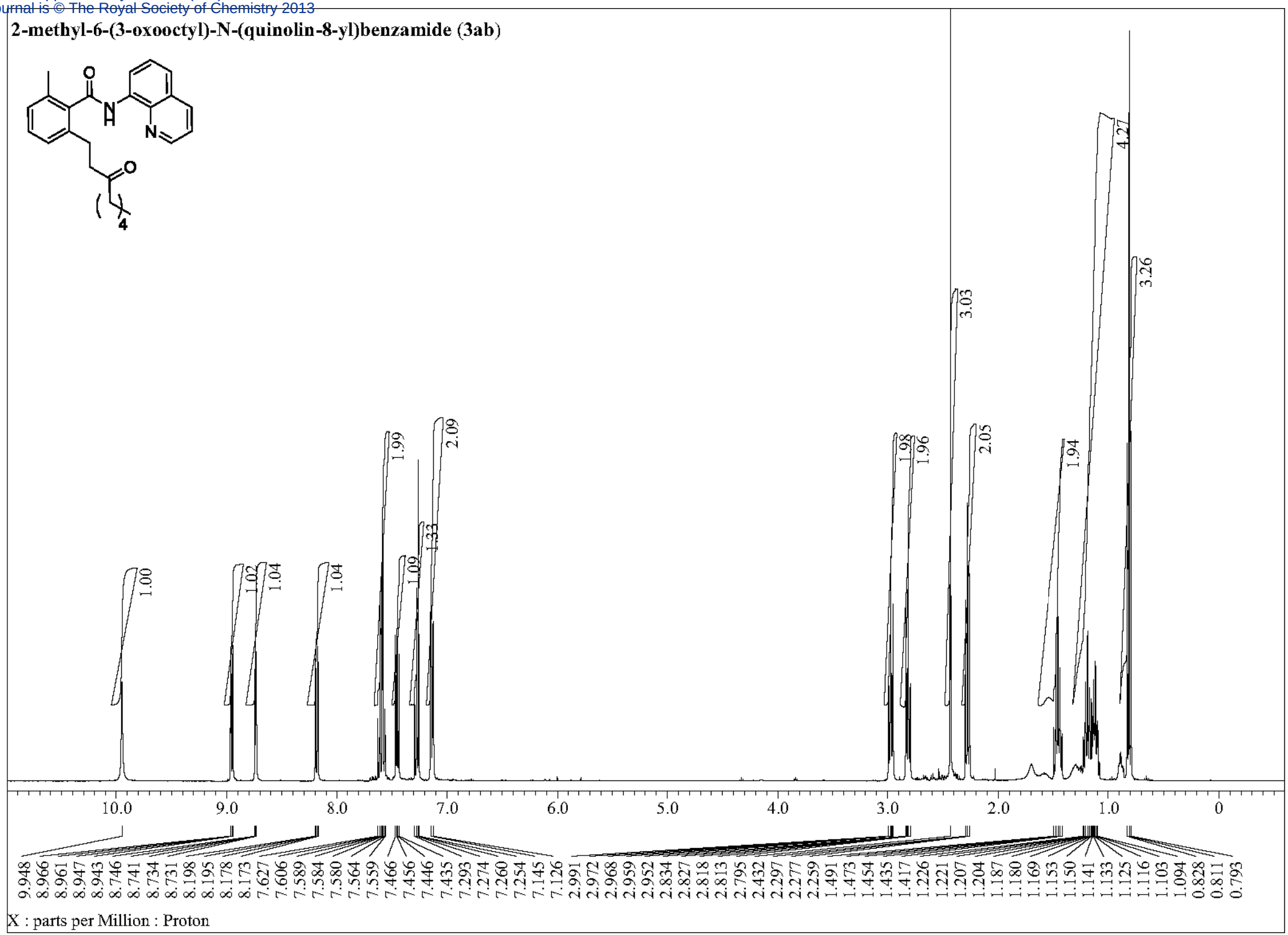

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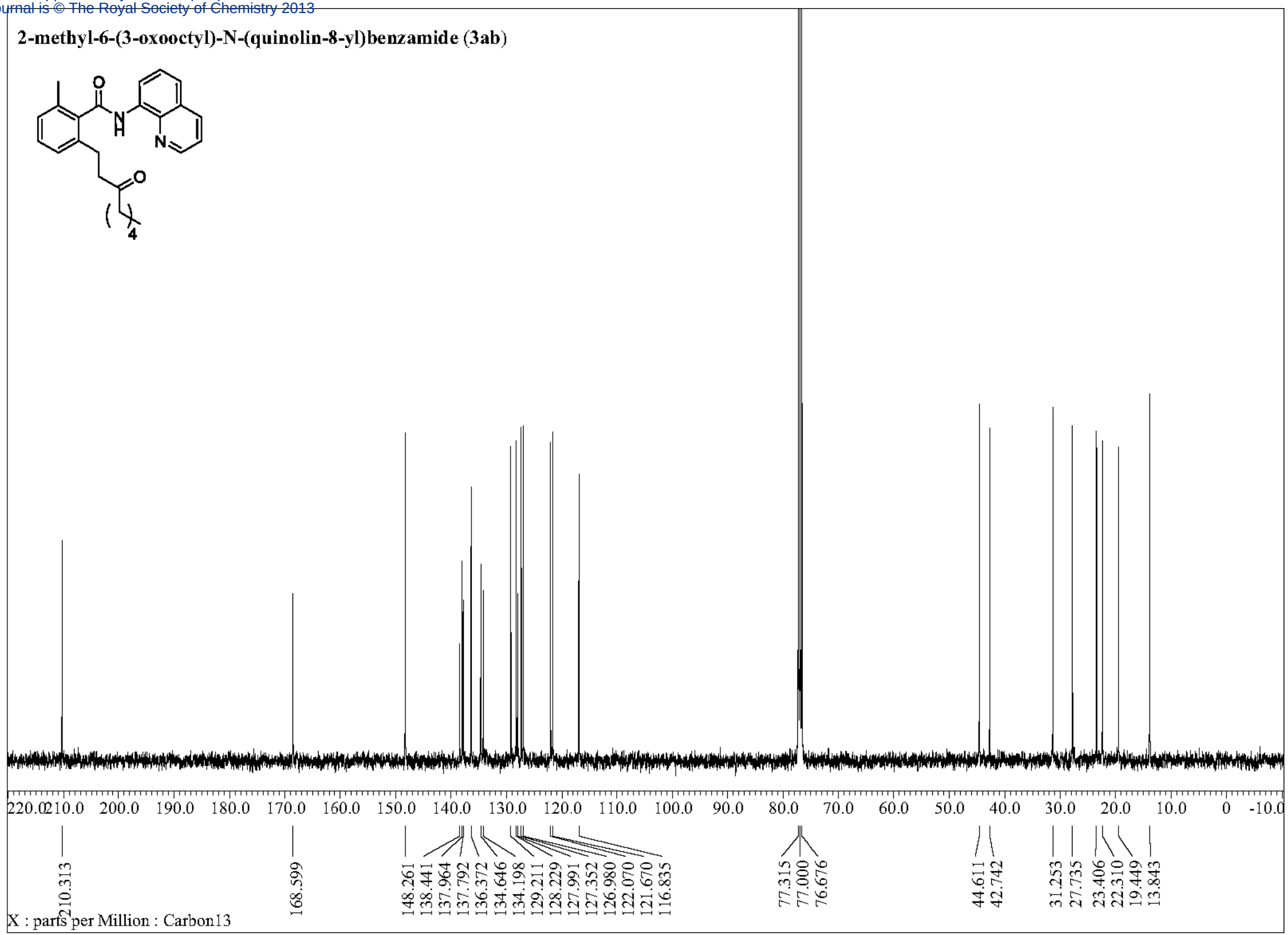

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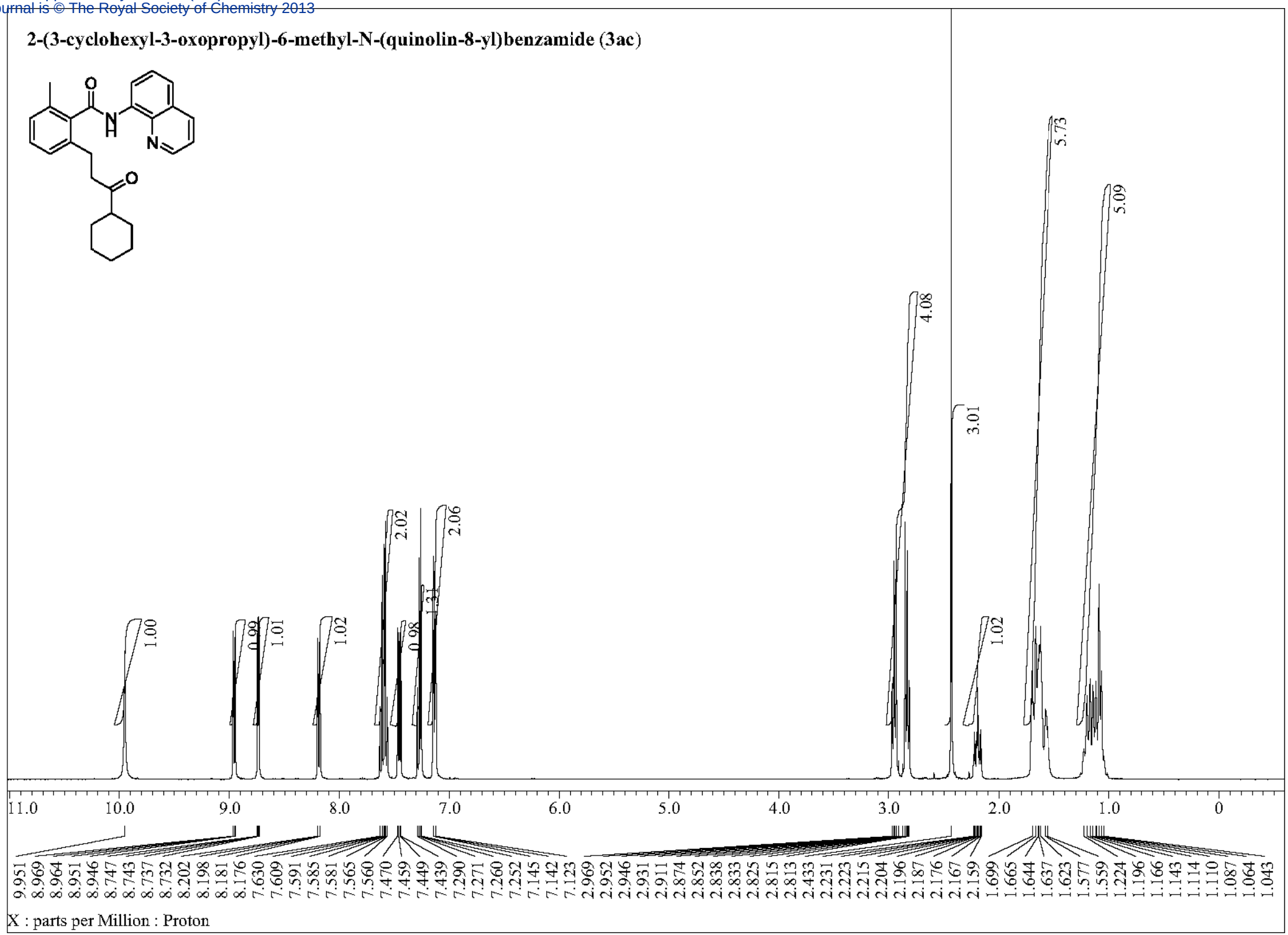

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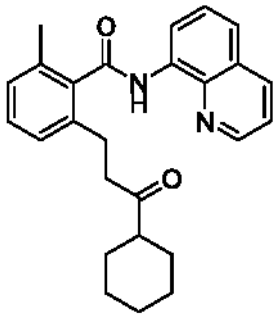
2-(3-cyclohexyl-3-oxopropyl)-6-methyl-N-(quinolin-8-yl)benzamide (3ac)



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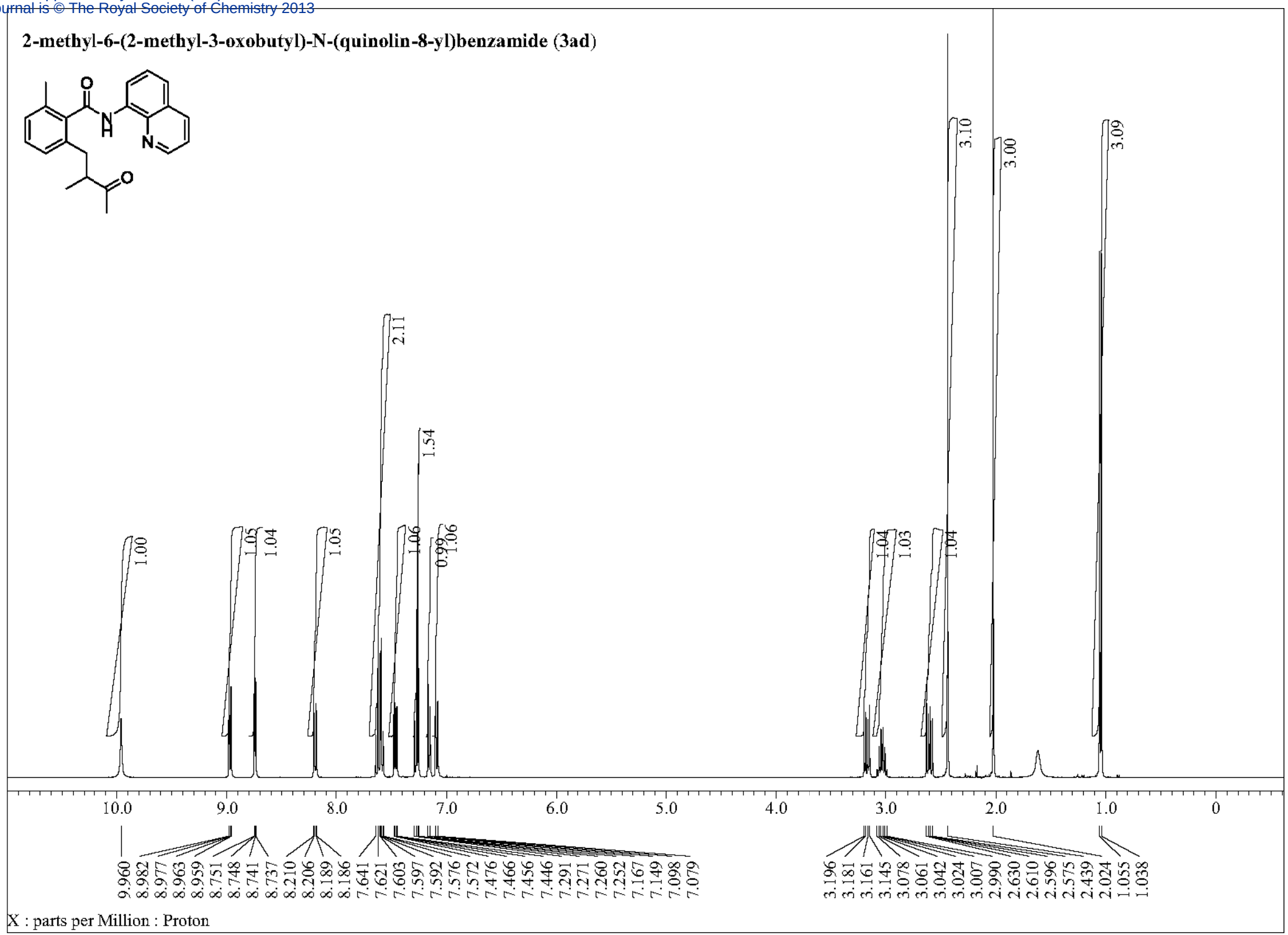

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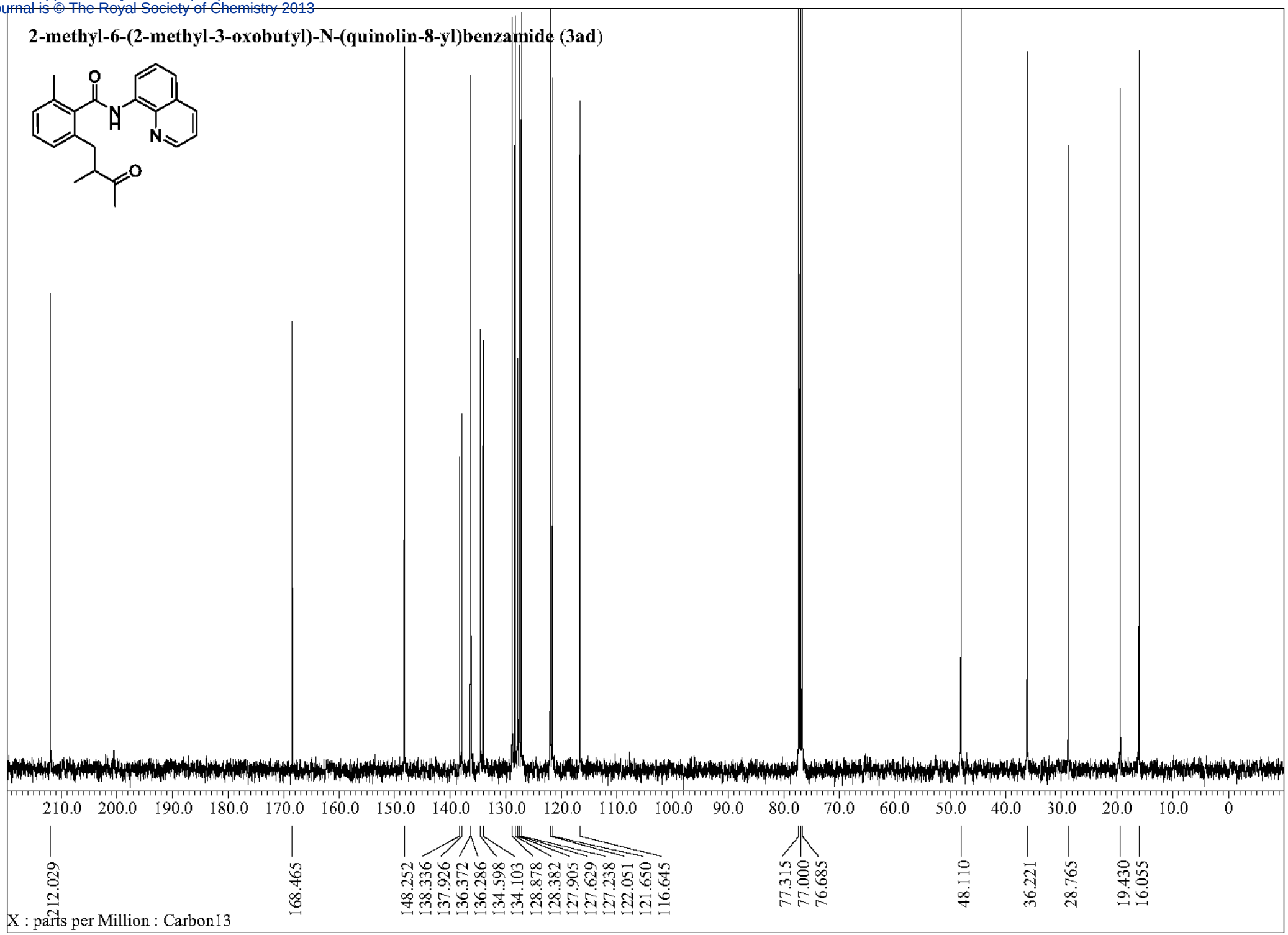

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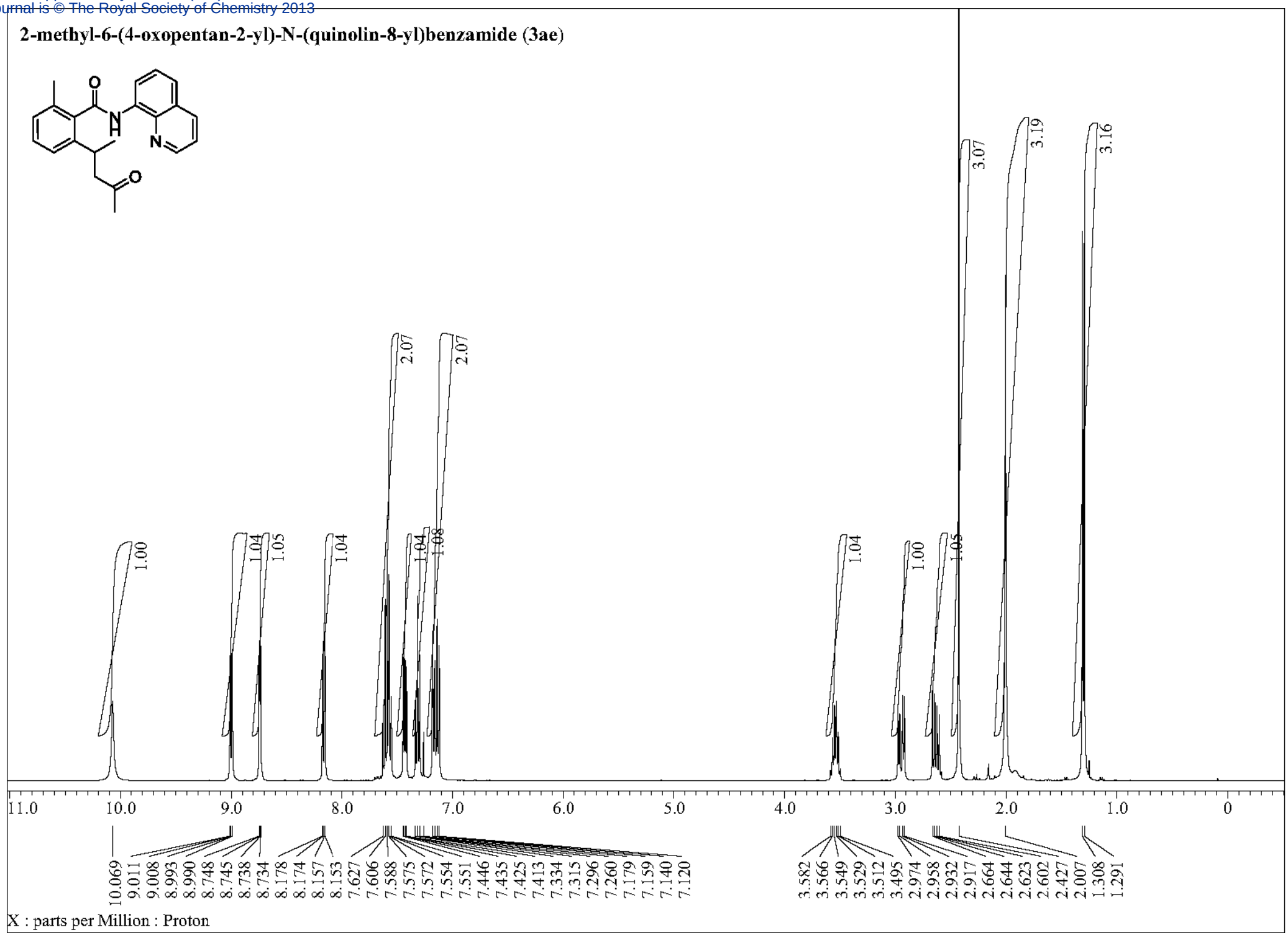

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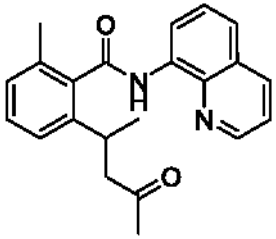
2-methyl-6-(4-oxopentan-2-yl)-N-(quinolin-8-yl)benzamide (3ae)



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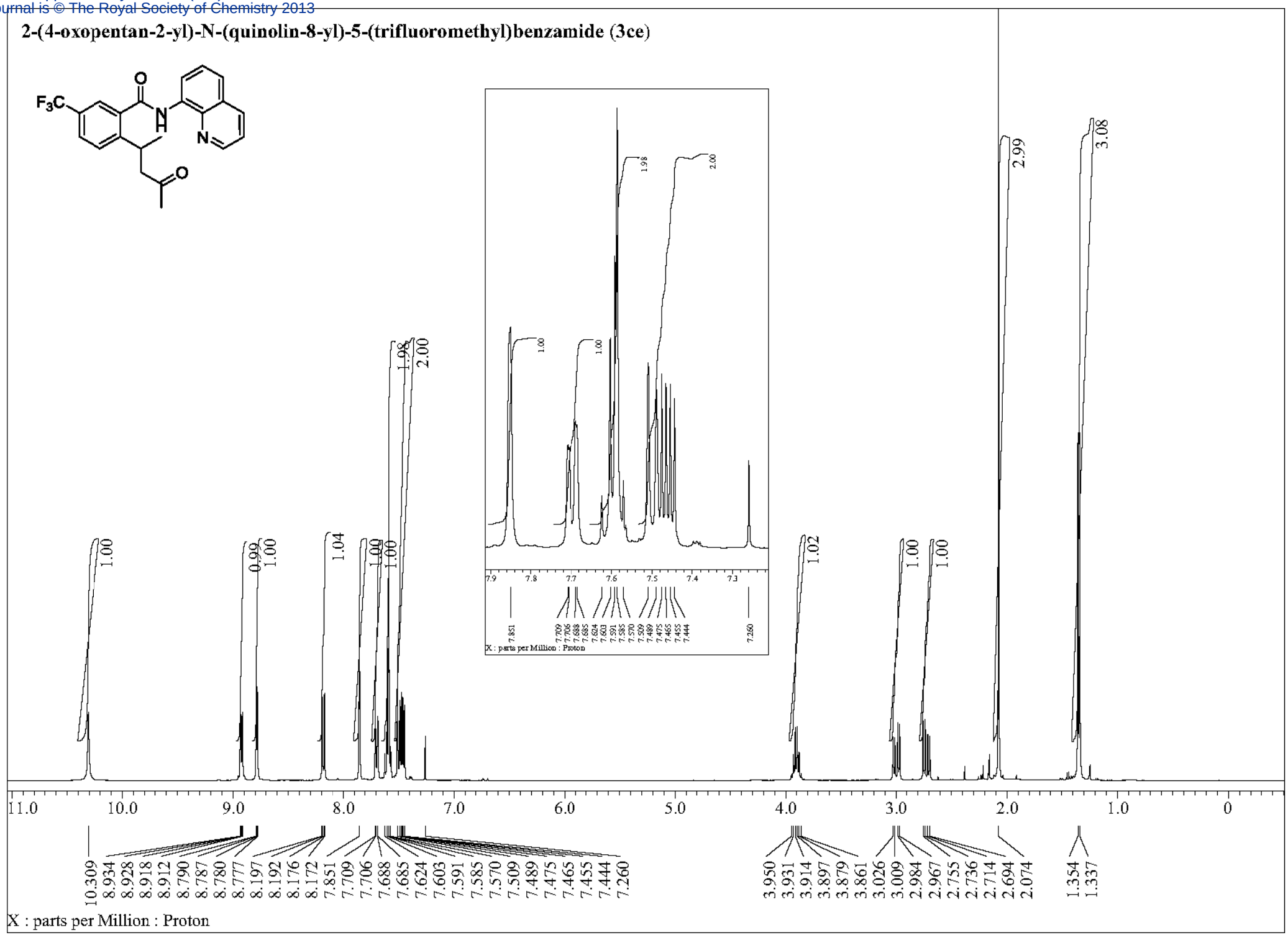

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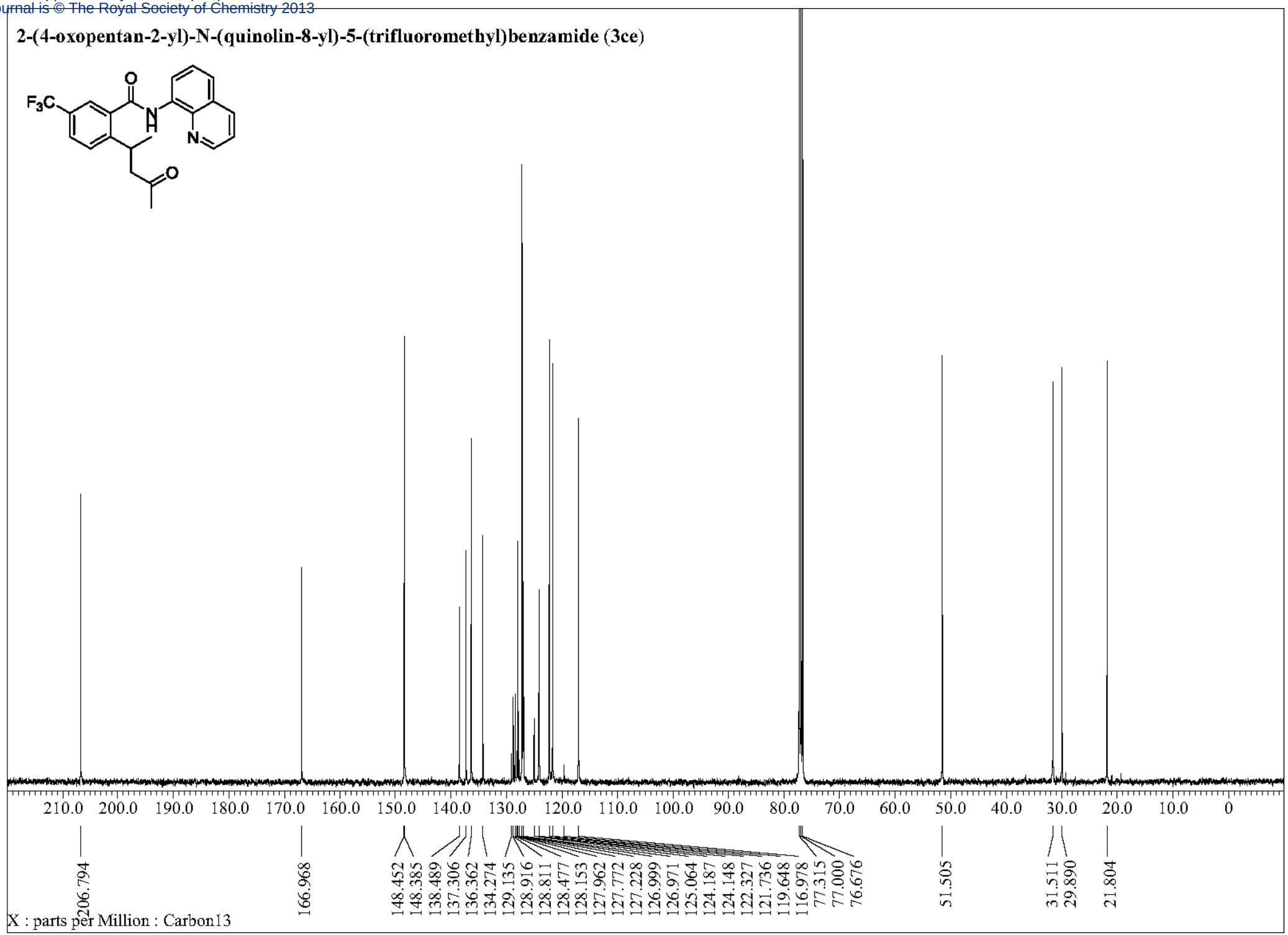

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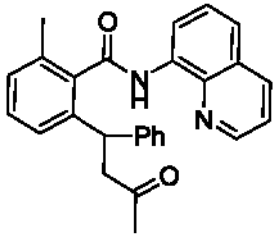
2-methyl-6-(3-oxo-1-phenylbutyl)-N-(quinolin-8-yl)benzamide (3af)



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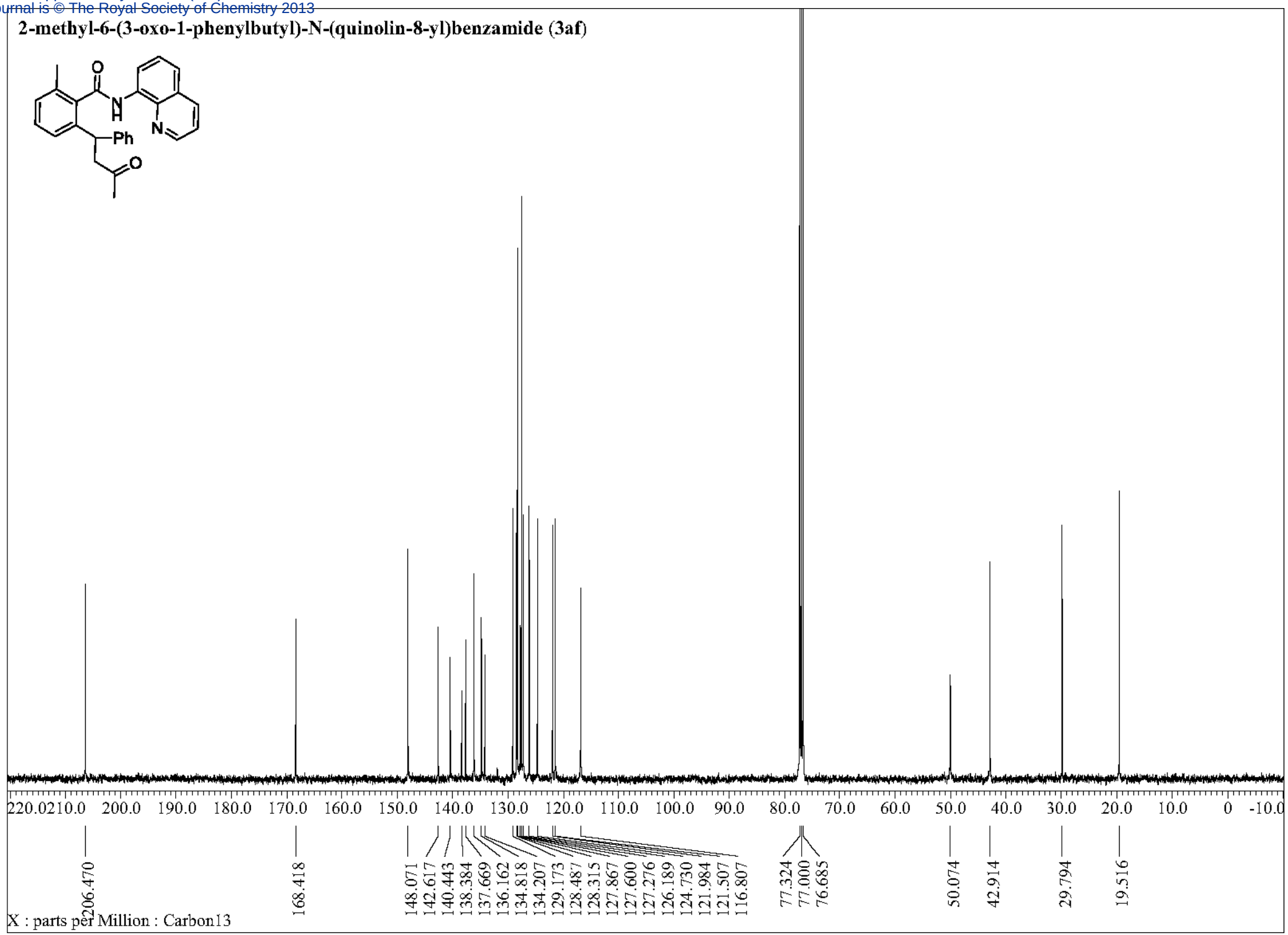

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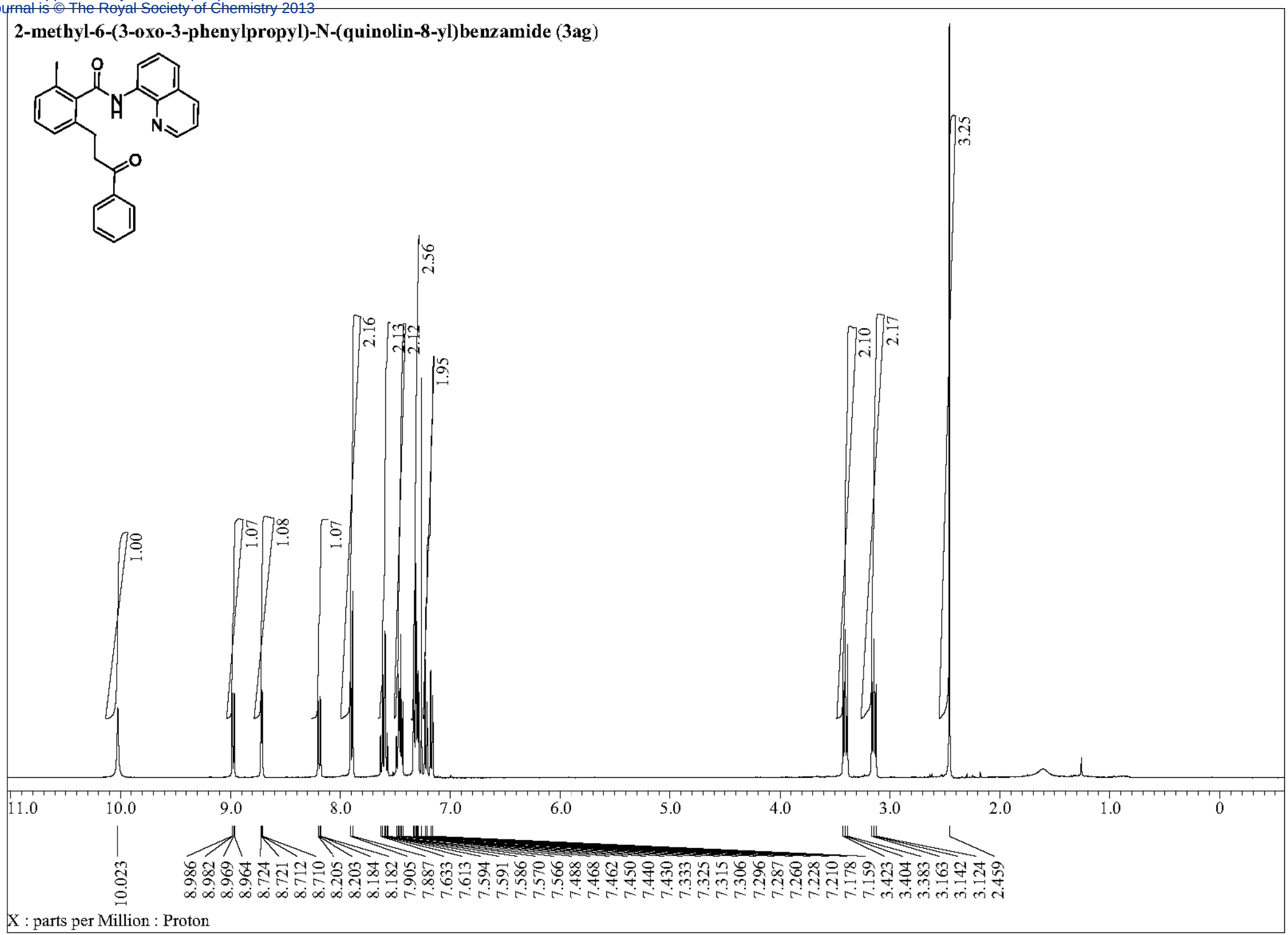

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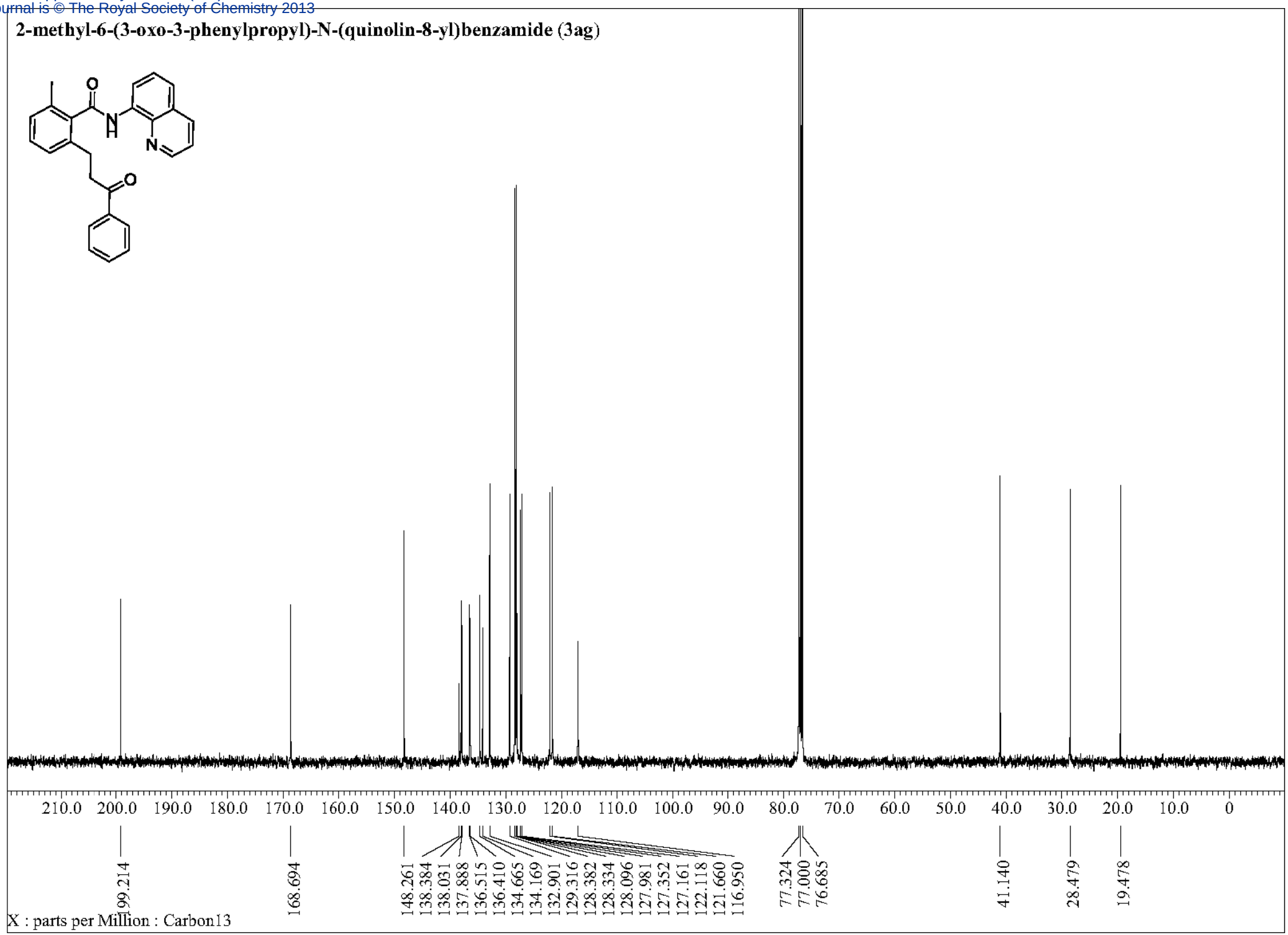

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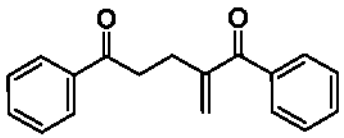
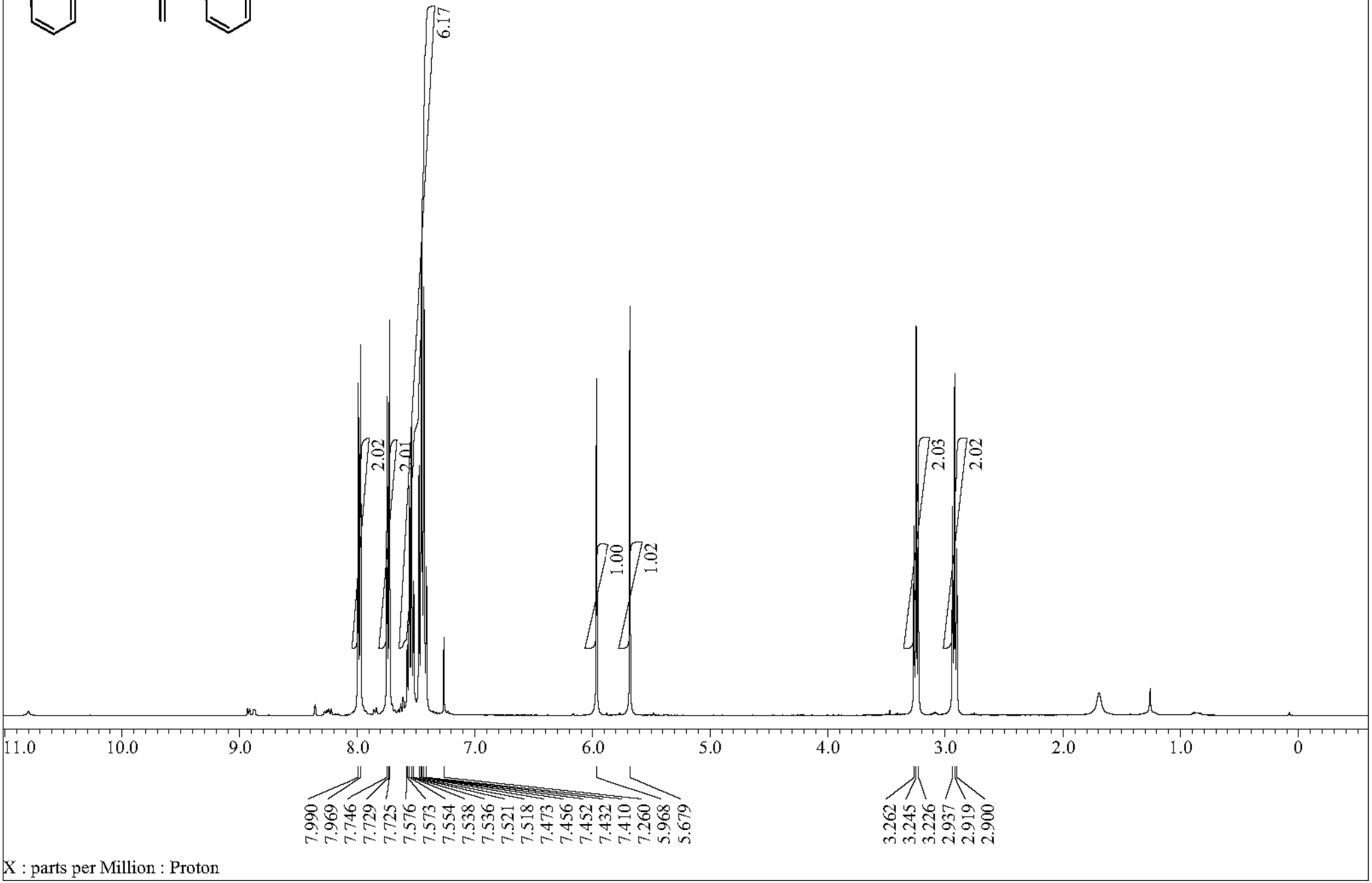
2-methylene-1,5-diphenylpentane-1,5-dione (9g)





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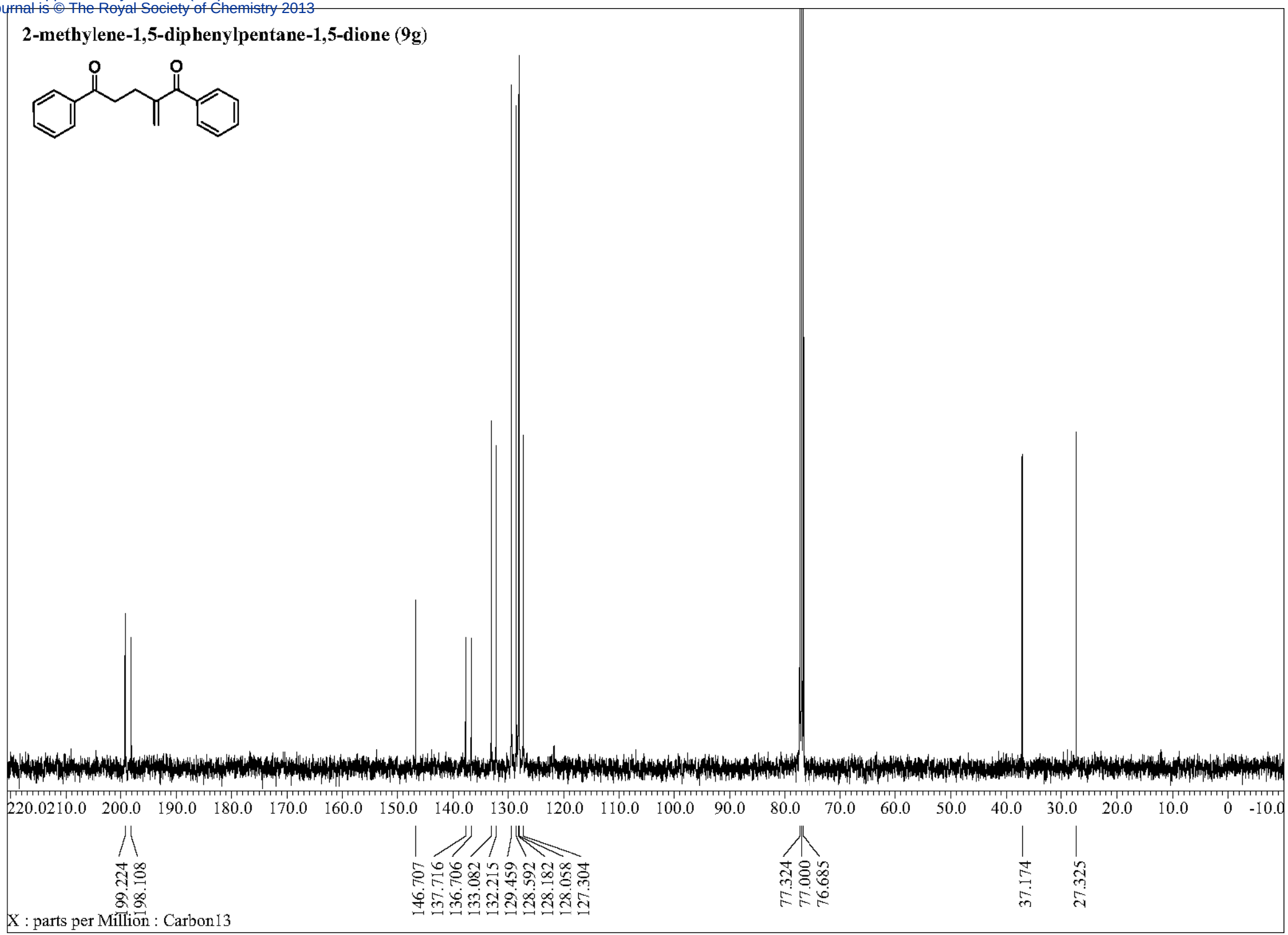

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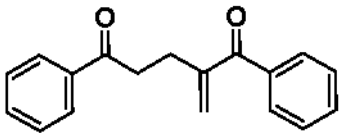
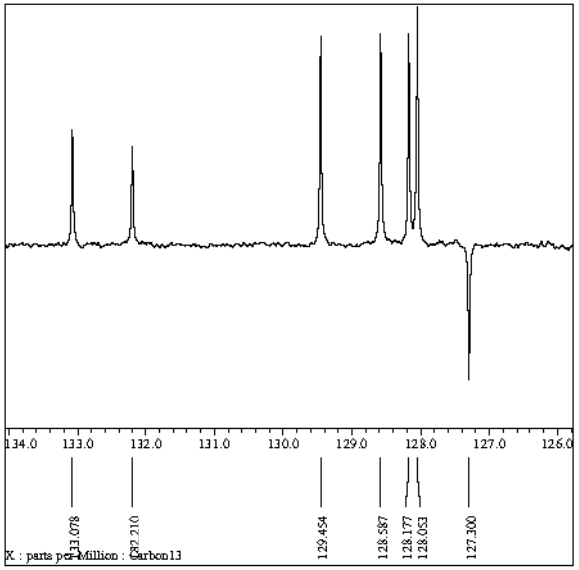
2-methylene-1,5-diphenylpentane-1,5-dione (9g)





160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0

133.078
132.210
129.454
128.587
128.177
128.053
127.300
37.169
27.320

X : parts per Million : Carbon13

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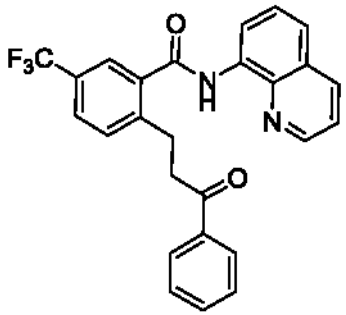
2-(3-oxo-3-phenylpropyl)-N-(quinolin-8-yl)-5-(trifluoromethyl)benzamide (3cg)



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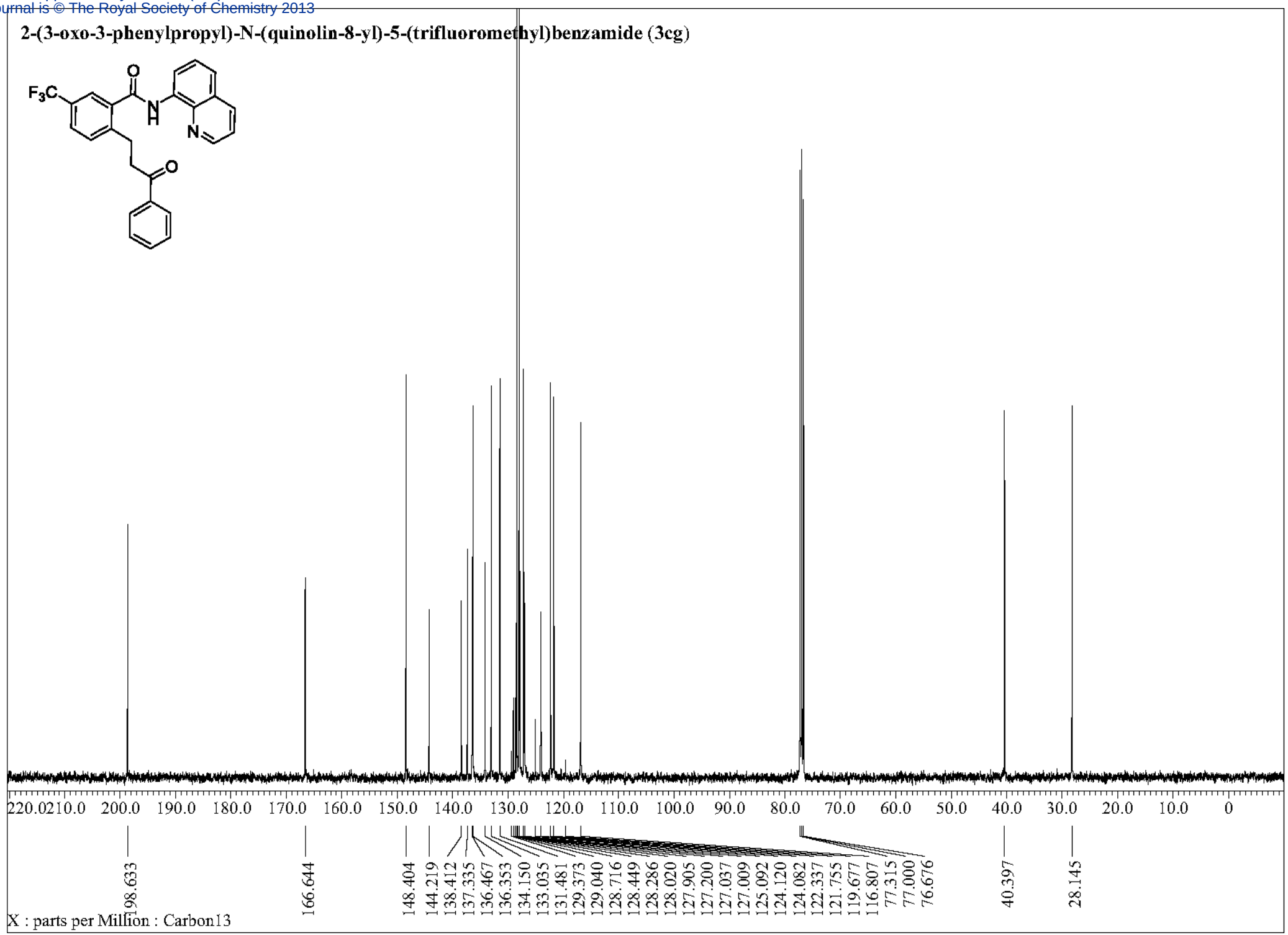

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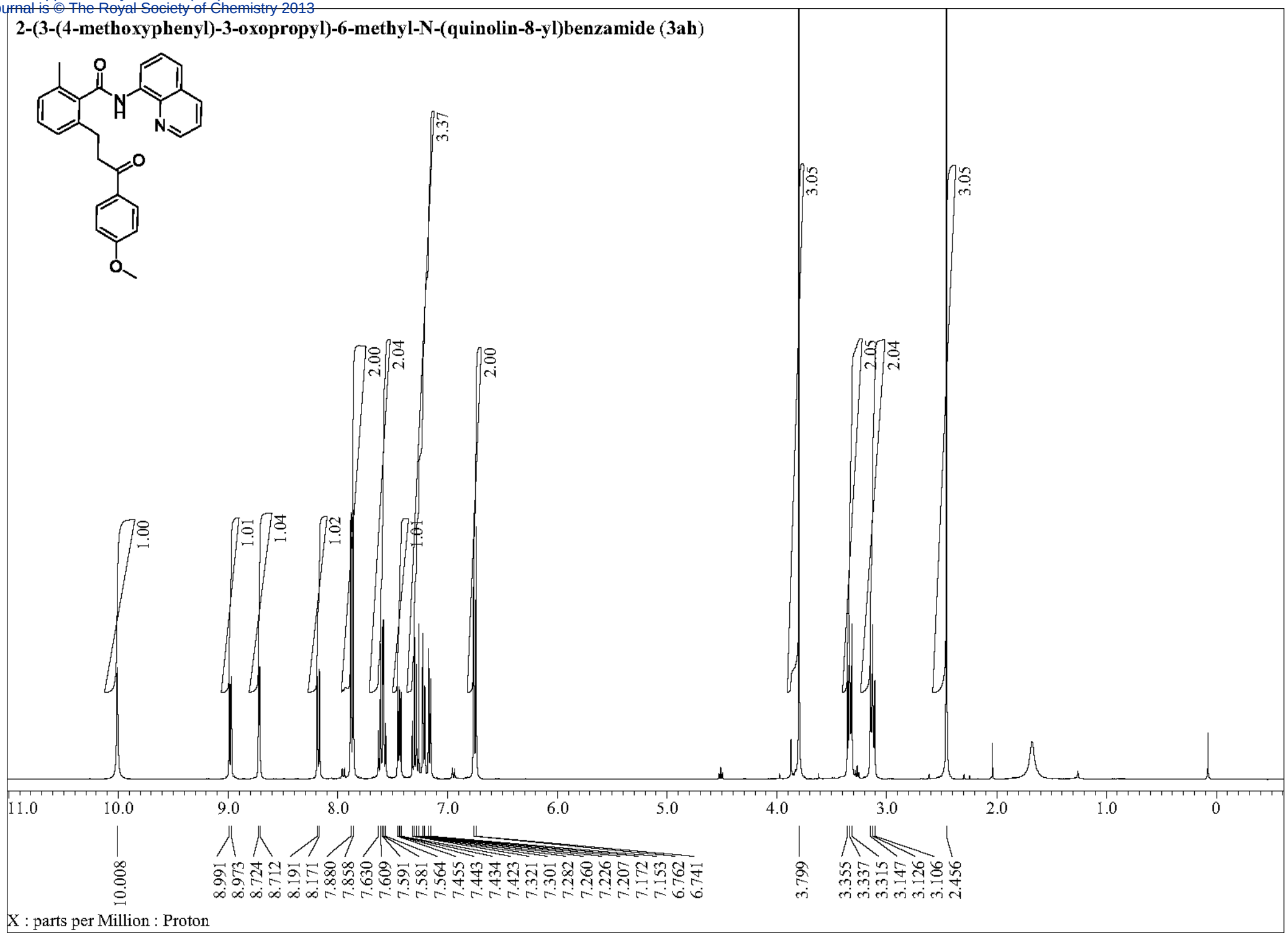

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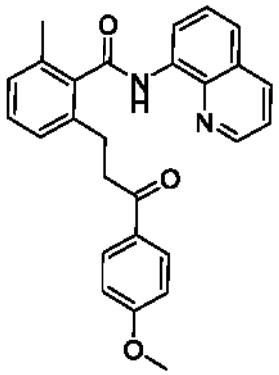
2-(3-(4-methoxyphenyl)-3-oxopropyl)-6-methyl-N-(quinolin-8-yl)benzamide (3ah)



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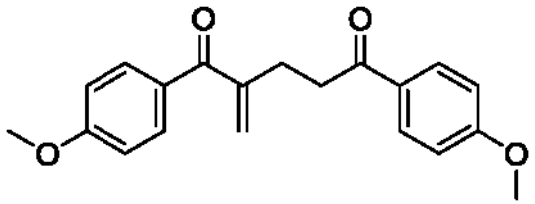
(E)-1,6-bis(4-methoxyphenyl)hex-2-ene-1,6-dione (9h)



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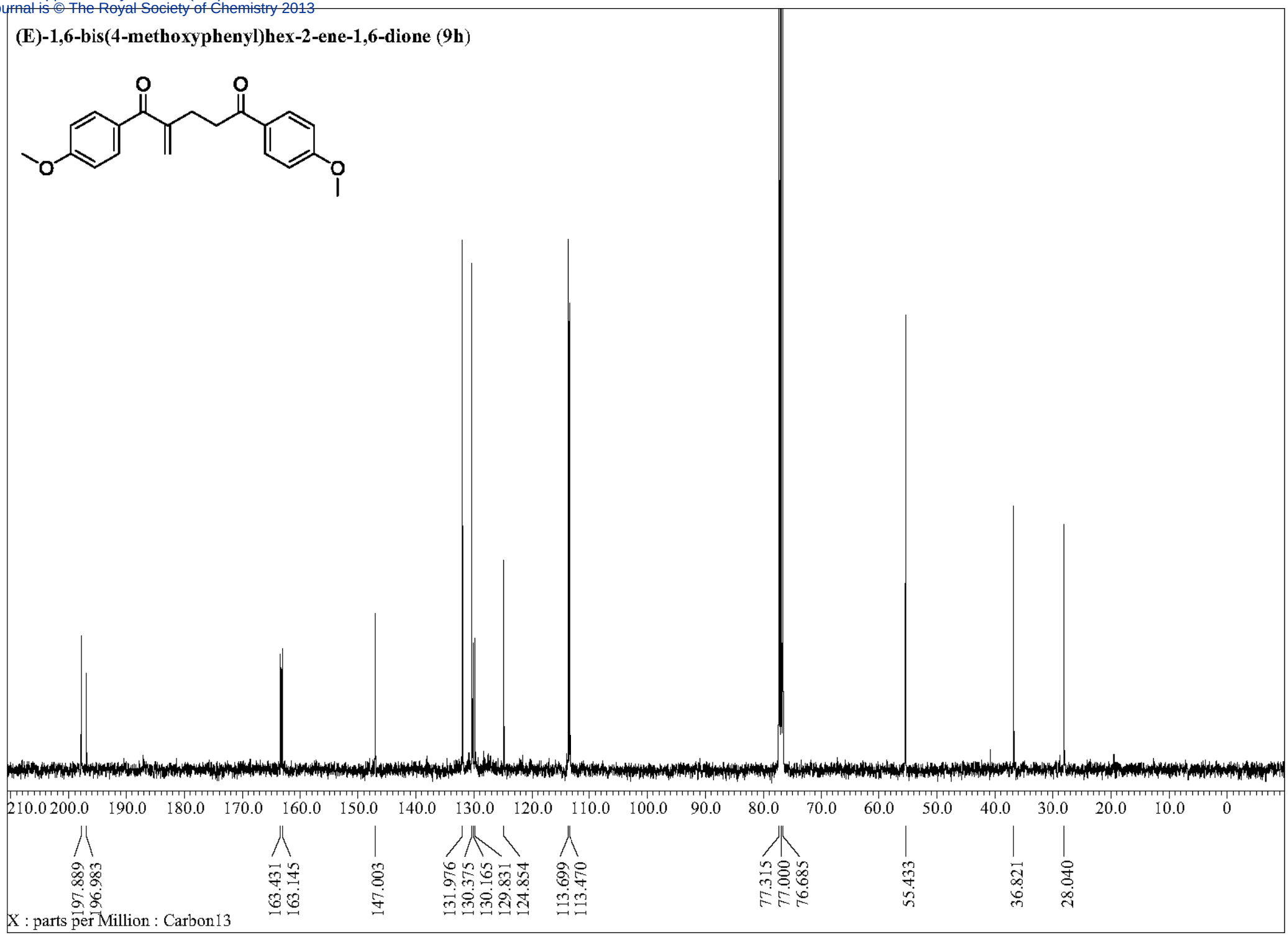

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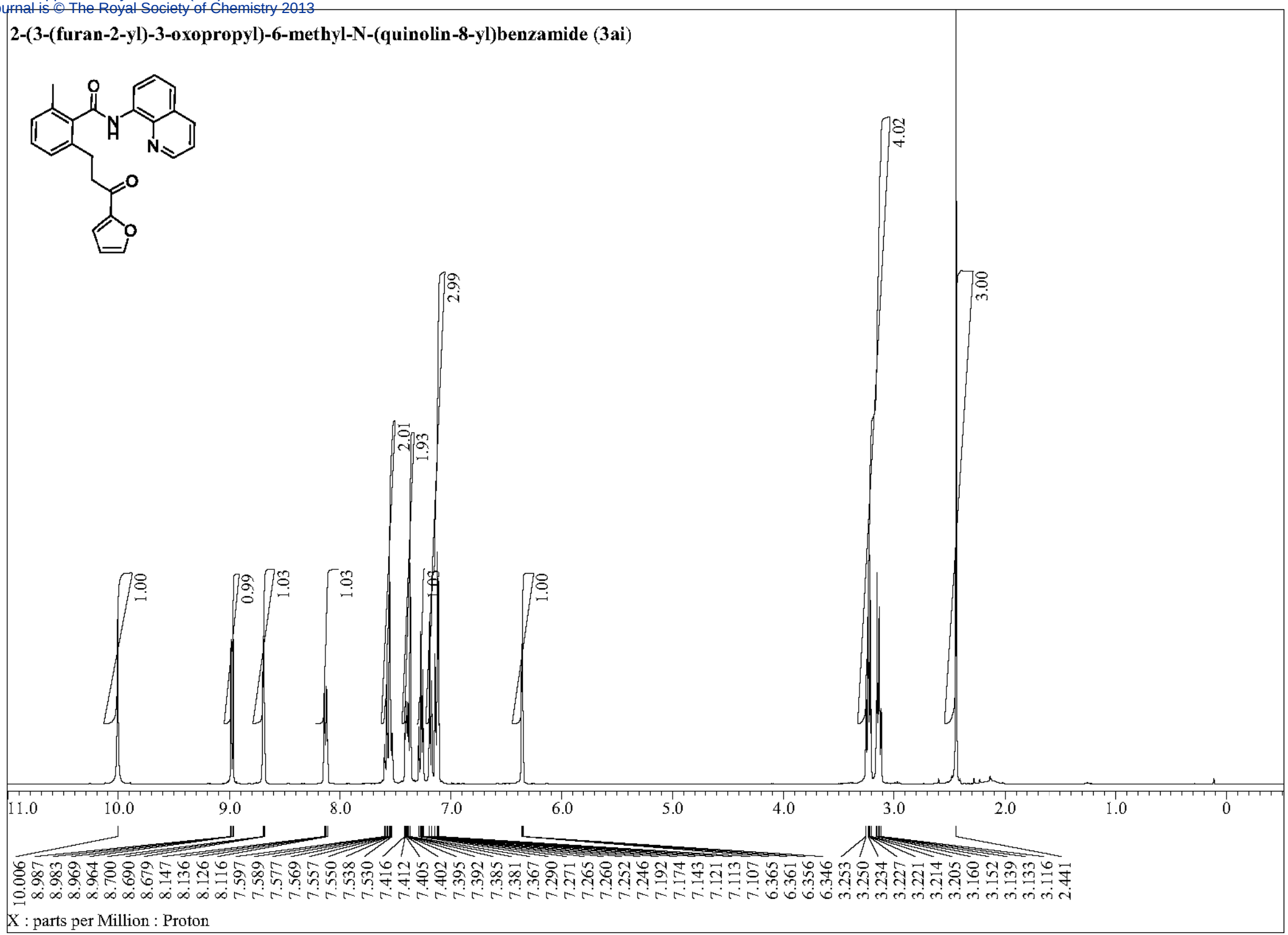

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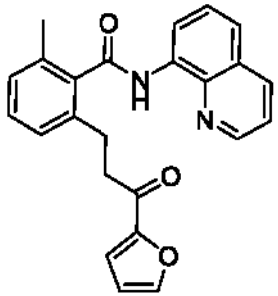
2-(3-(furan-2-yl)-3-oxopropyl)-6-methyl-N-(quinolin-8-yl)benzamide (3ai)



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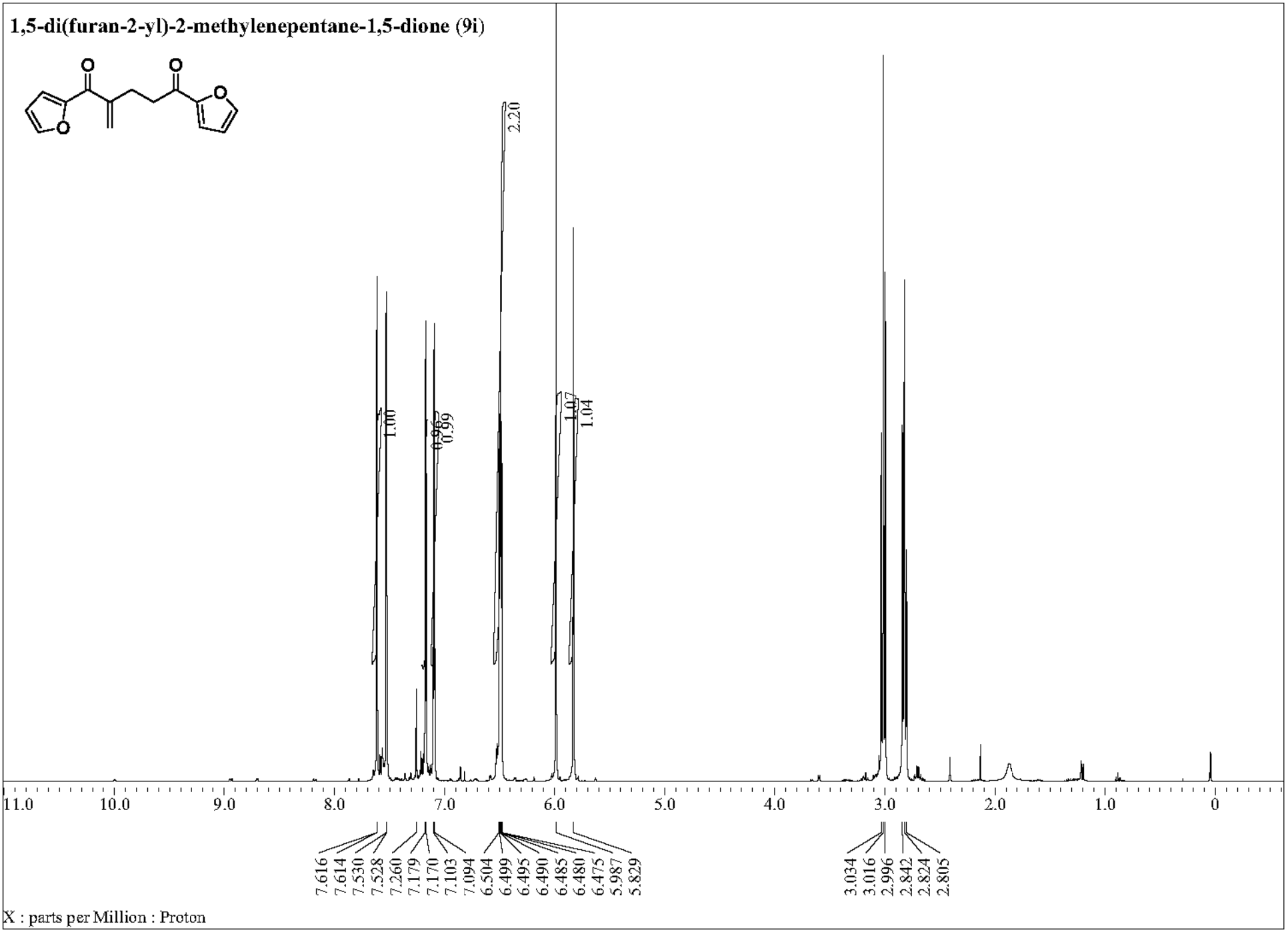

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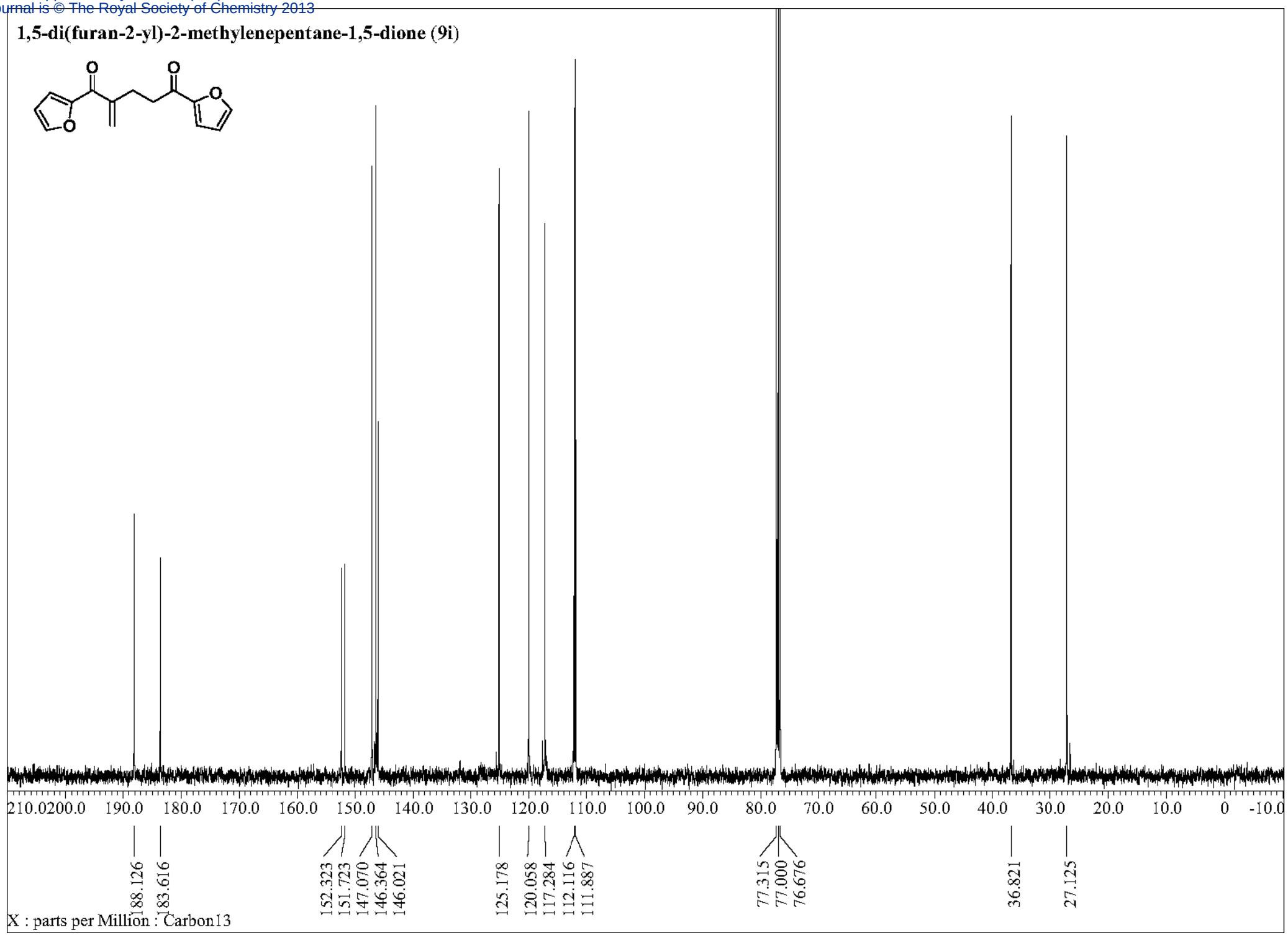

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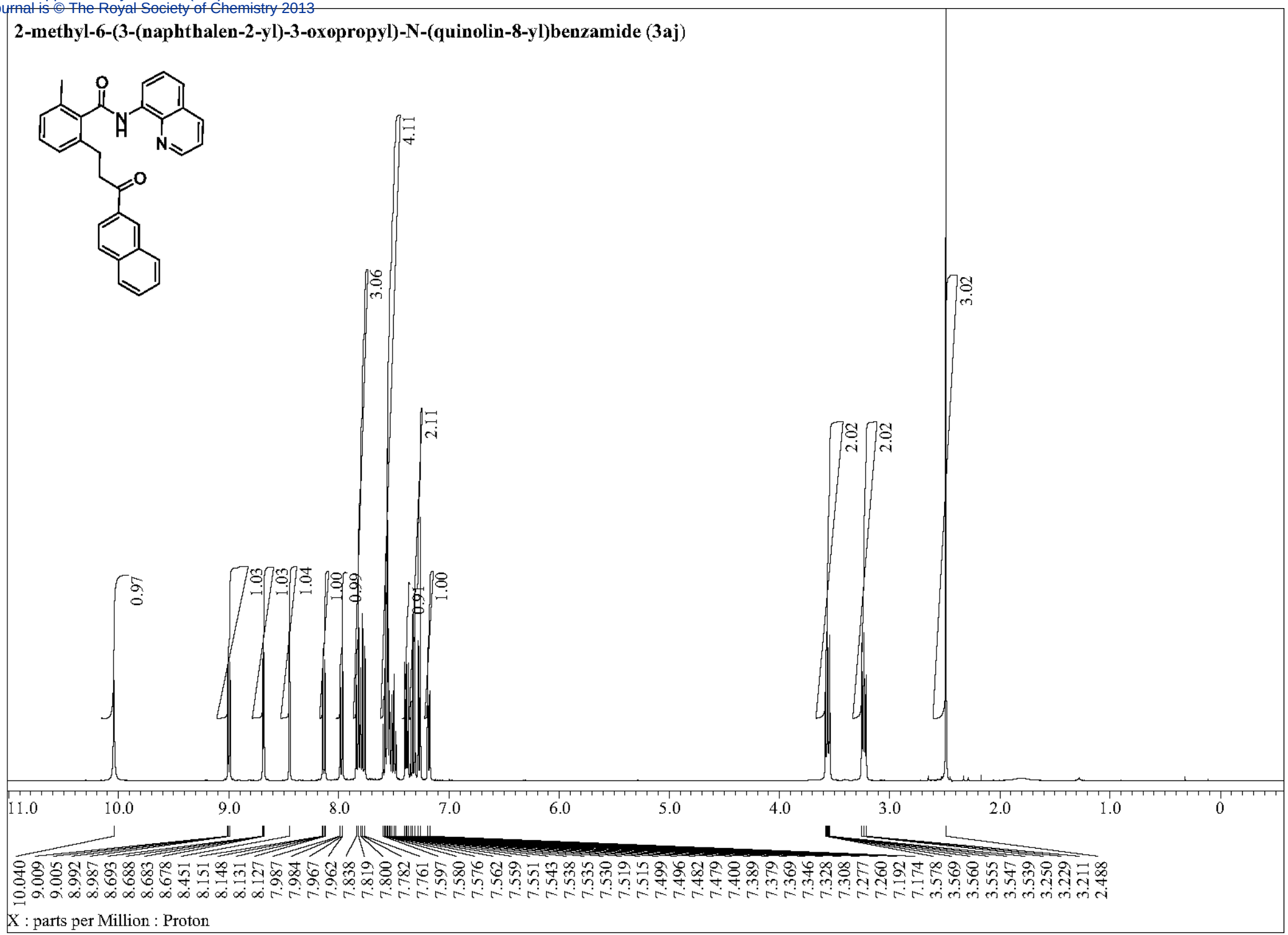

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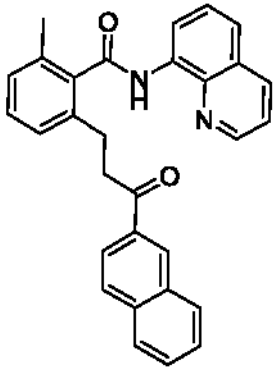
2-methyl-6-(3-(naphthalen-2-yl)-3-oxopropyl)-N-(quinolin-8-yl)benzamide (3aj)



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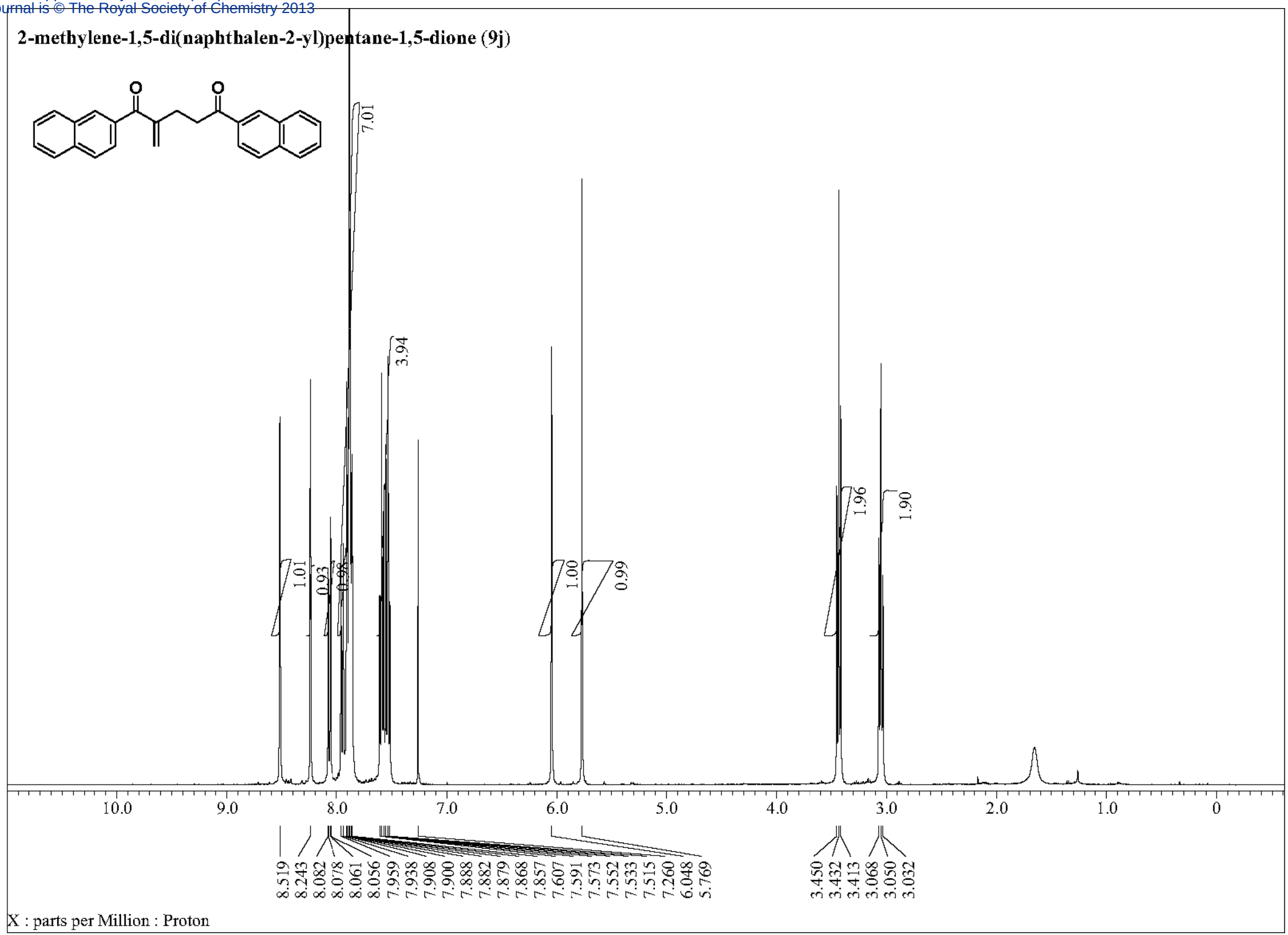

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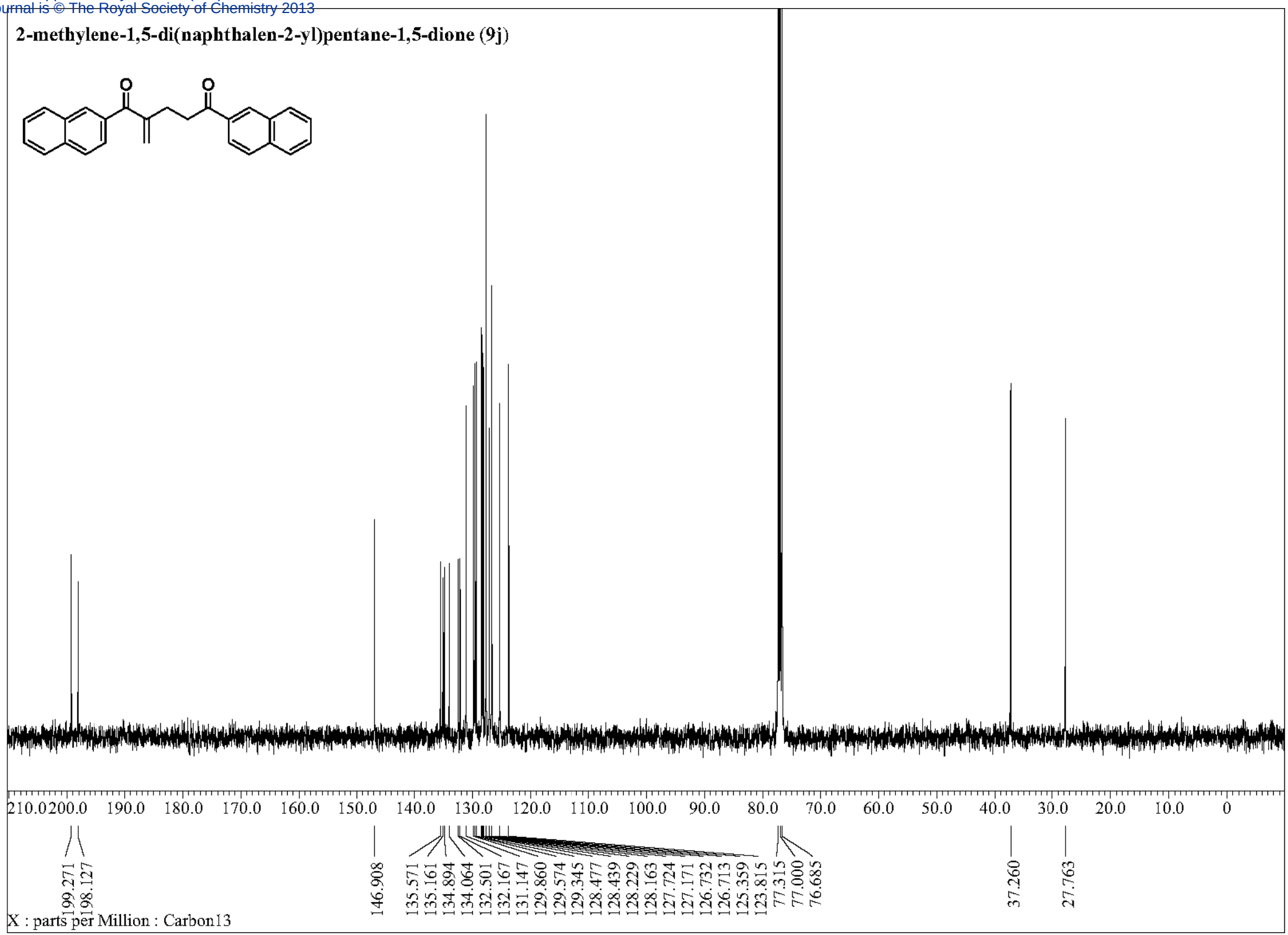

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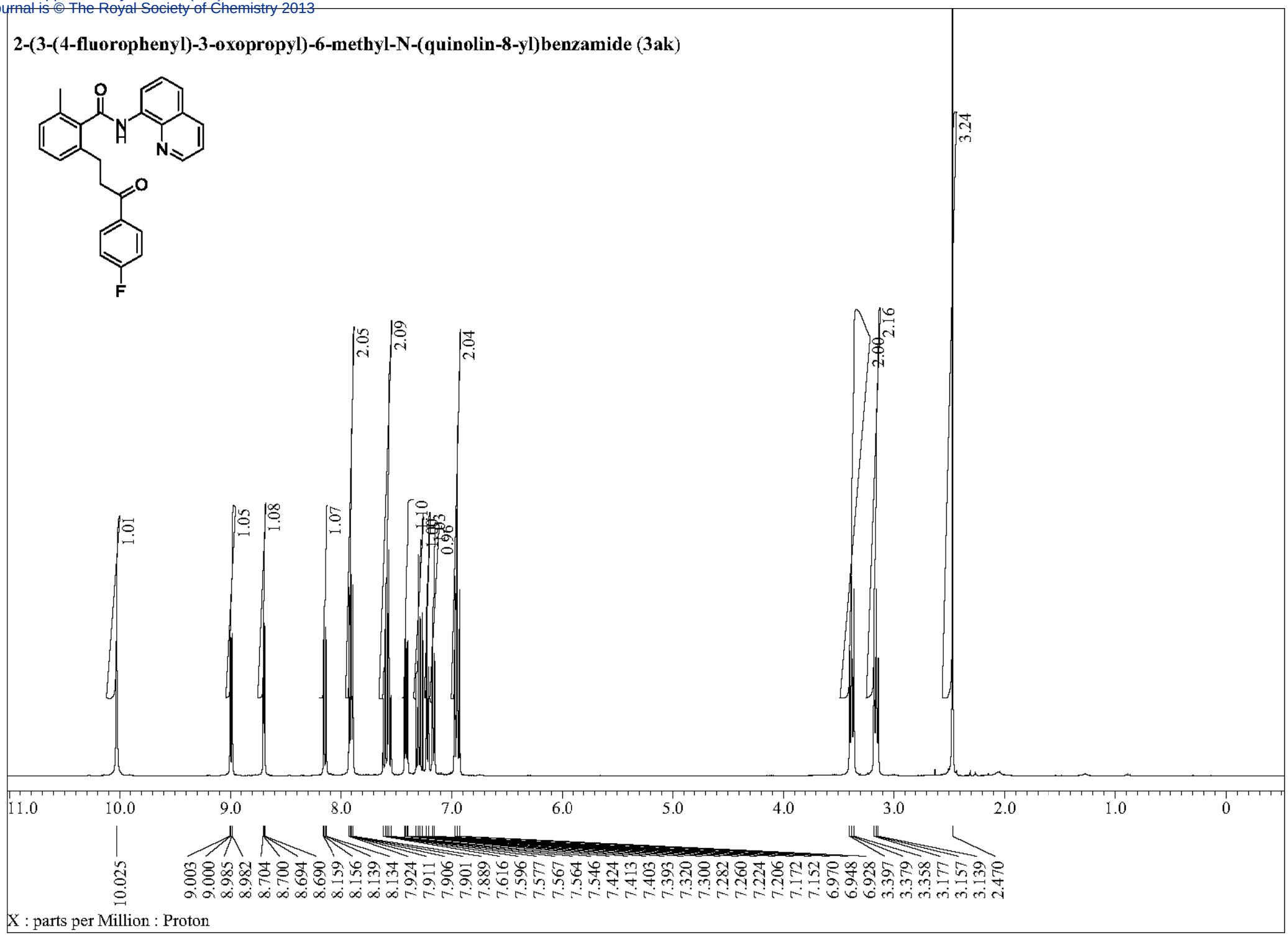

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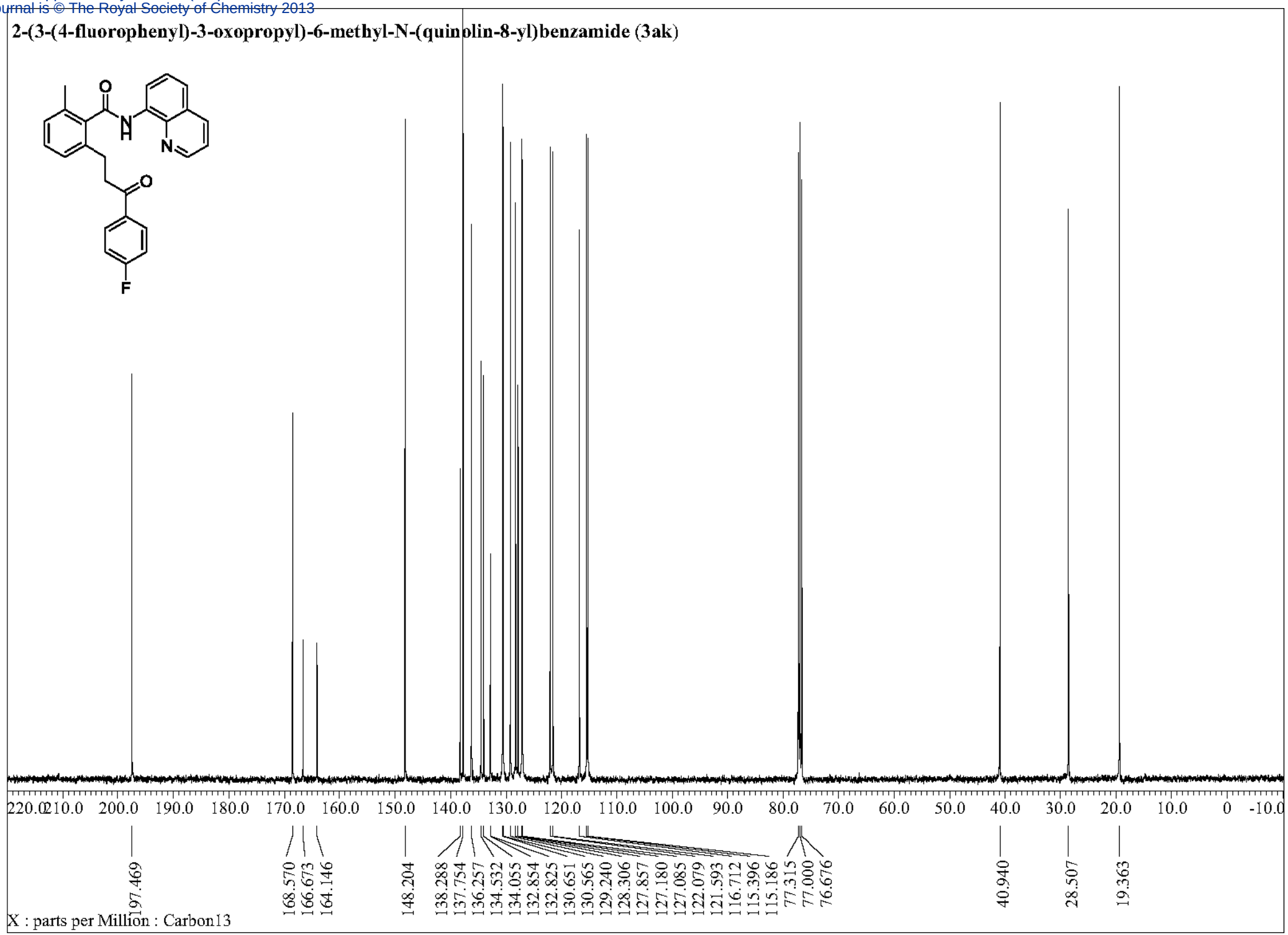

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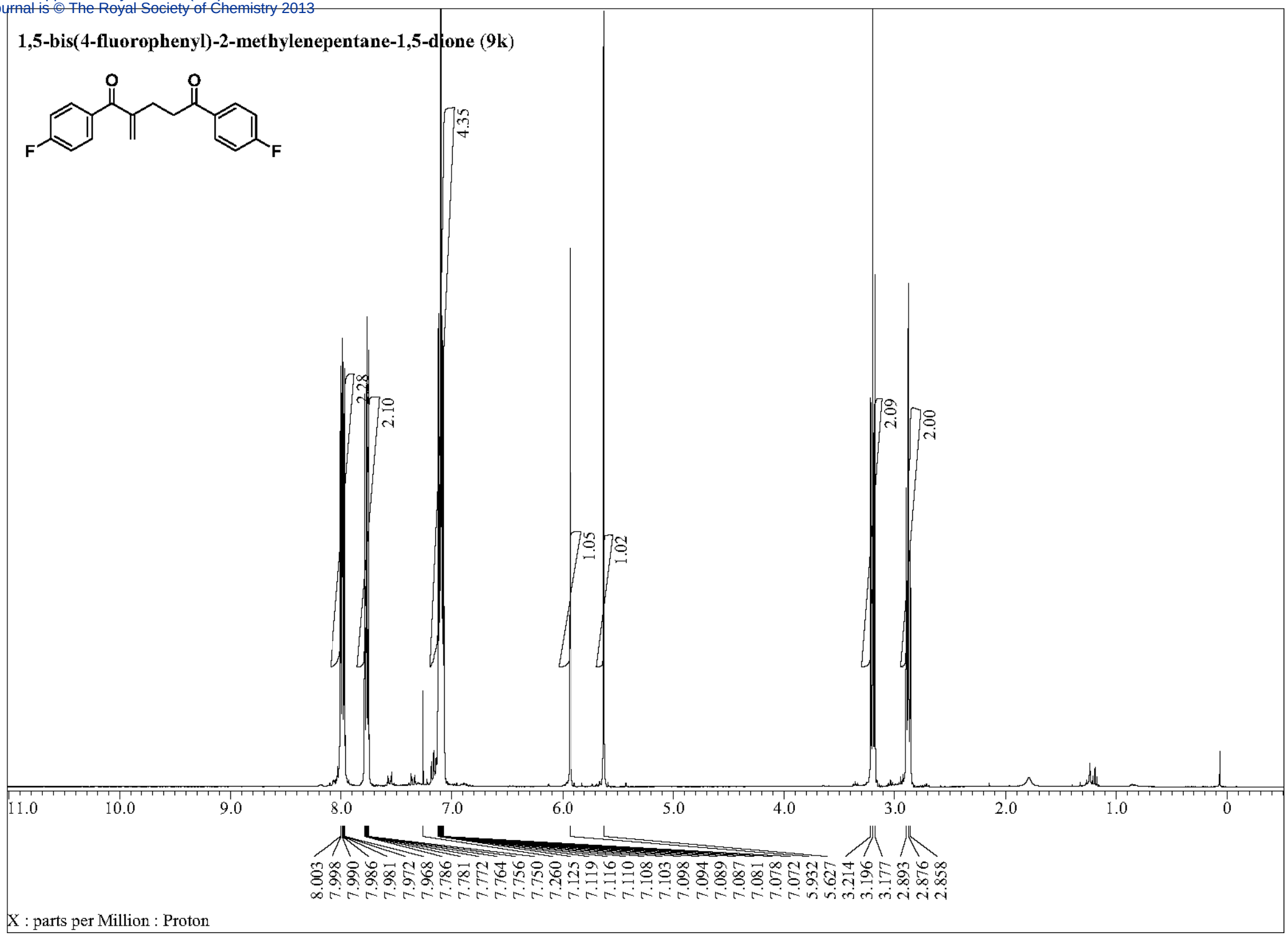

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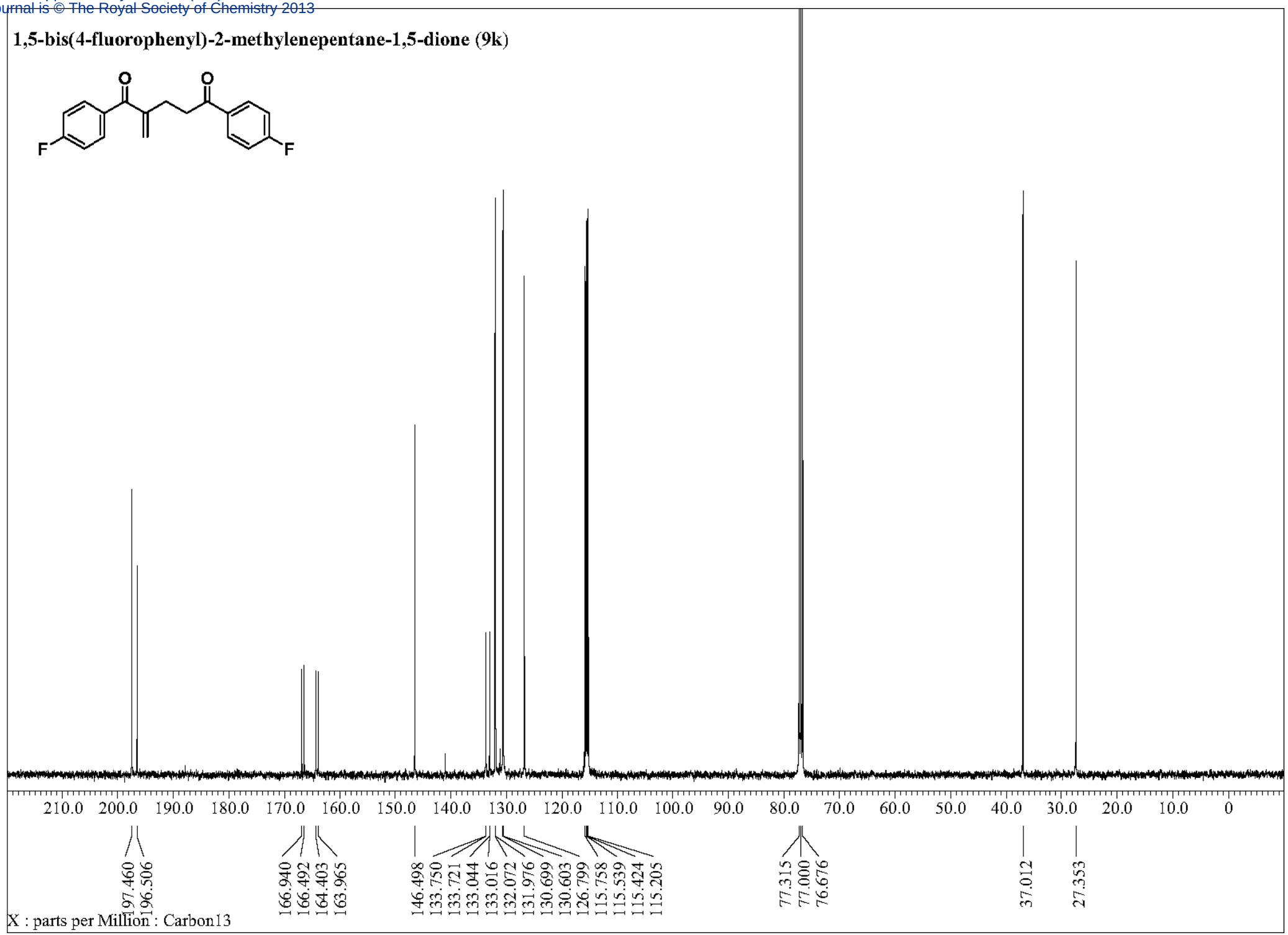

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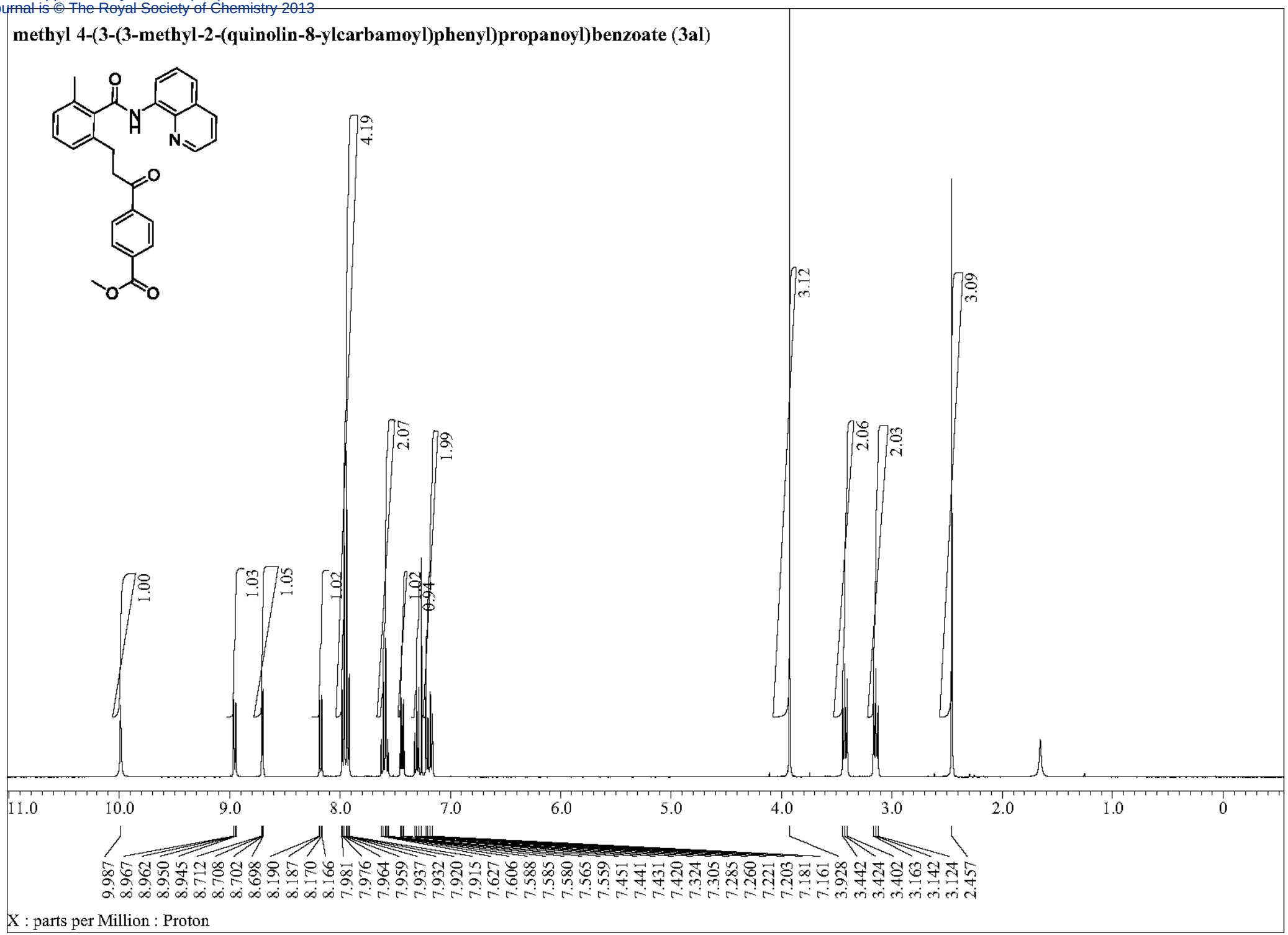

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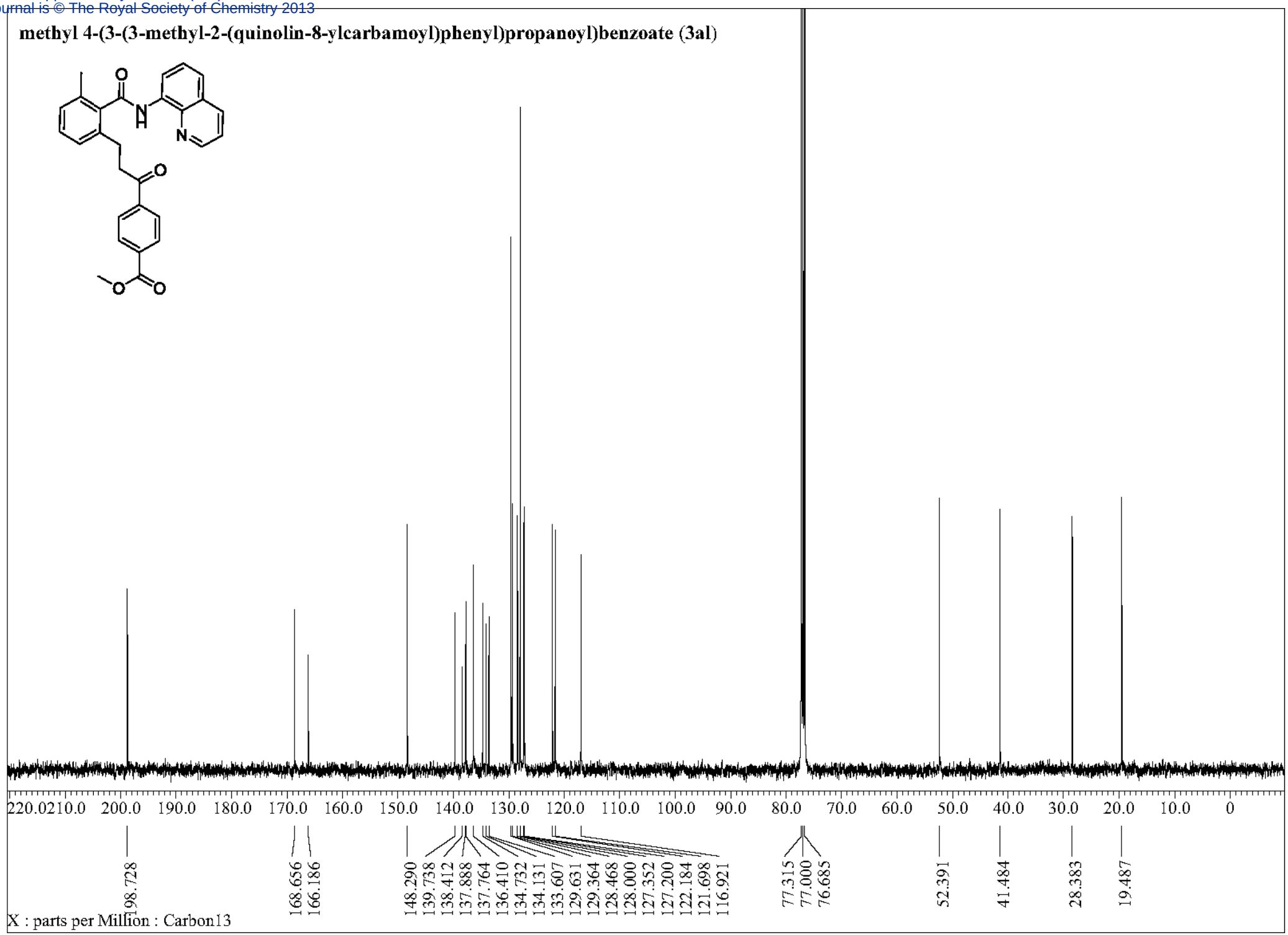

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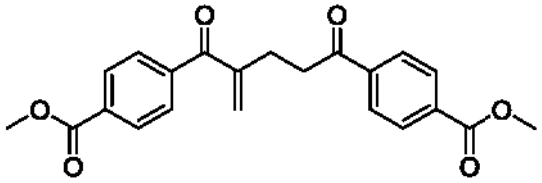
2-methylene-1,5-bis(4-(methylester)phenyl)pentane-1,5-dione (9l)



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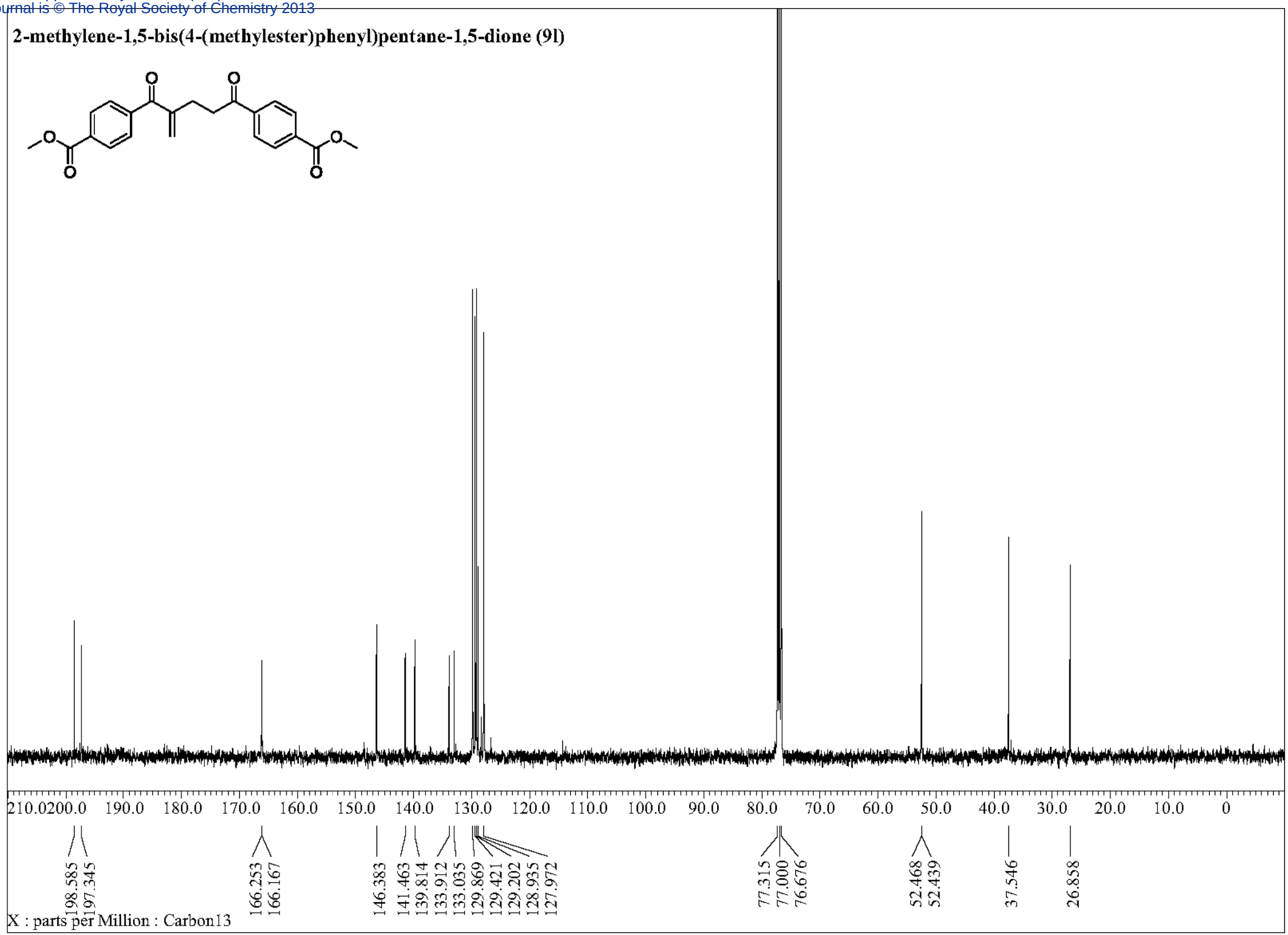

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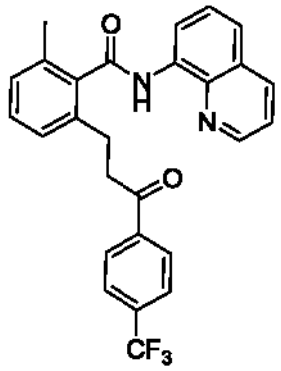
2-methyl-6-(3-oxo-3-(4-(trifluoromethyl)phenyl)propyl)-N-(quinolin-8-yl)benzamide (3am)



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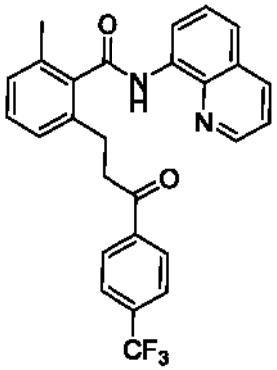
2-methyl-6-(3-oxo-3-(4-(trifluoromethyl)phenyl)propyl)-N-(quinolin-8-yl)benzamide (3am)



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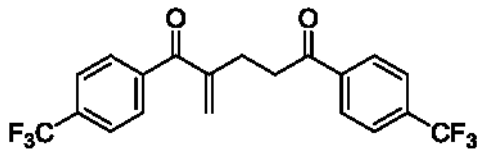
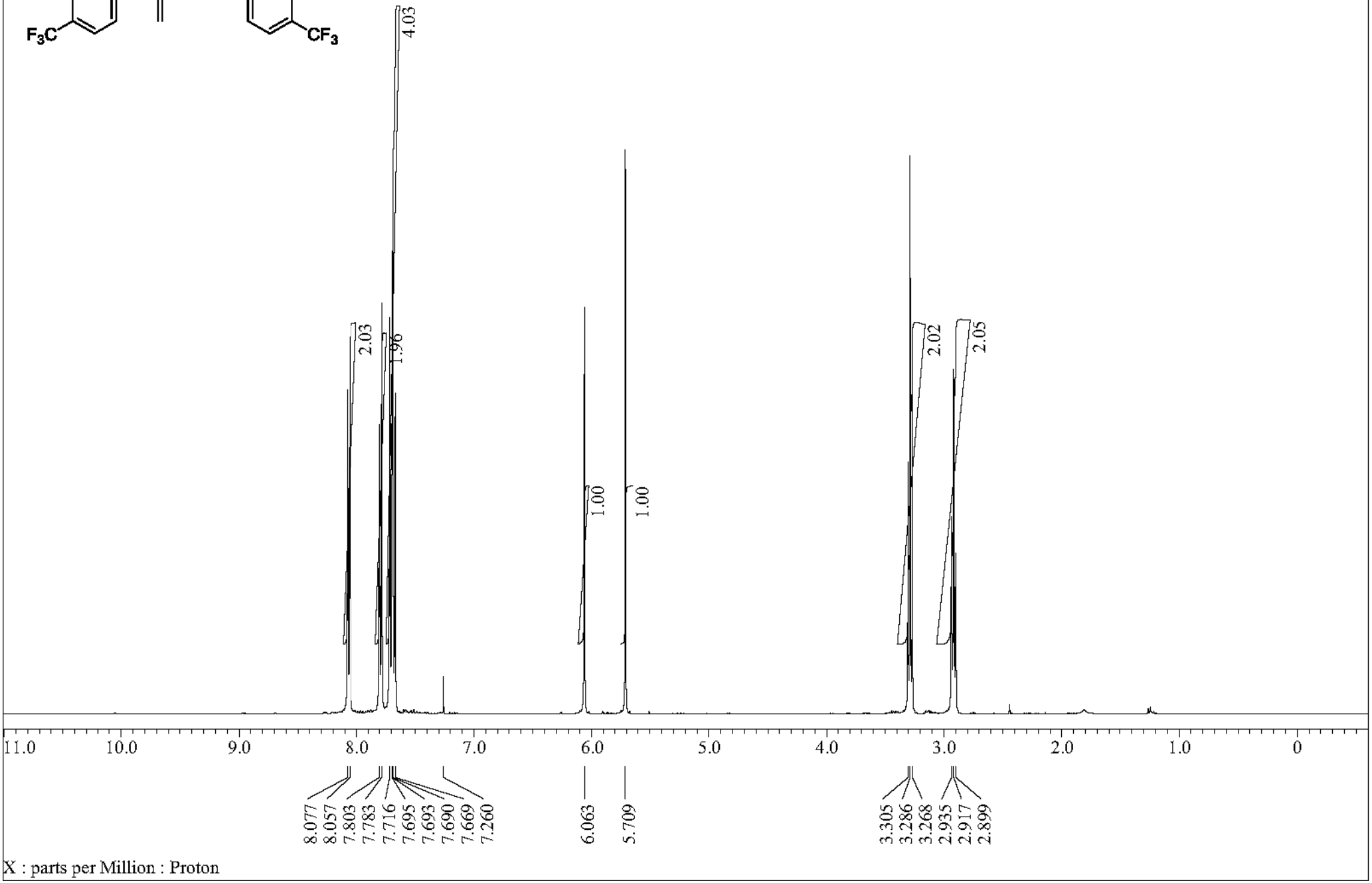
2-methylene-1,5-bis(4-(trifluoromethyl)phenyl)pentane-1,5-dione (9m)





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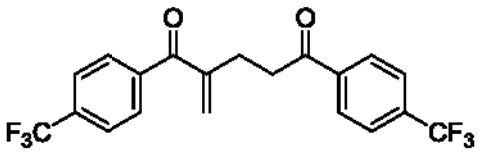
2-methylene-1,5-bis(4-(trifluoromethyl)phenyl)pentane-1,5-dione (9m)



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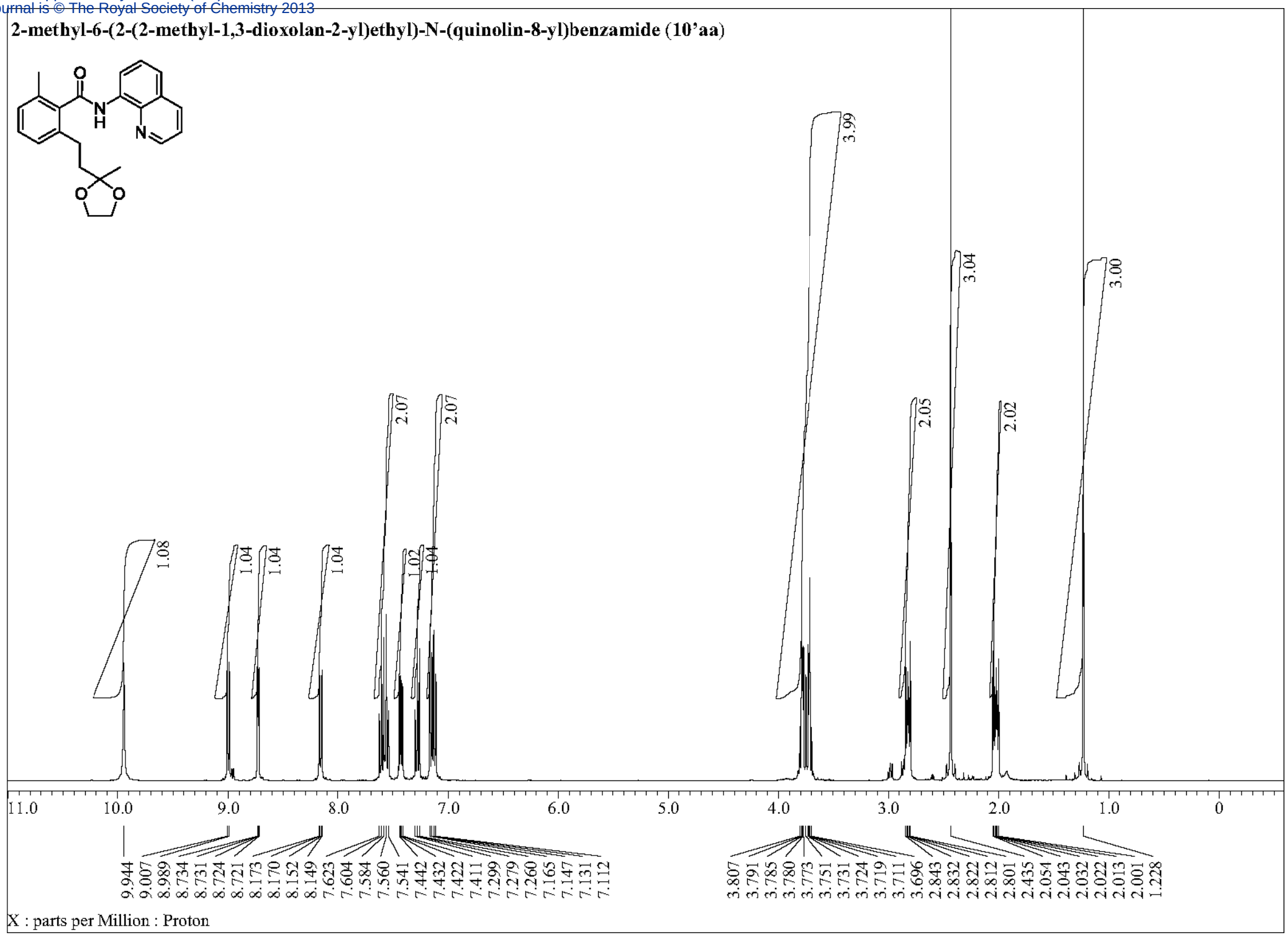

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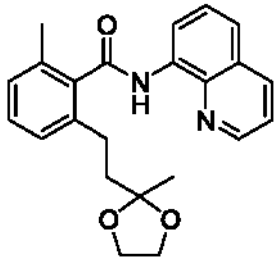
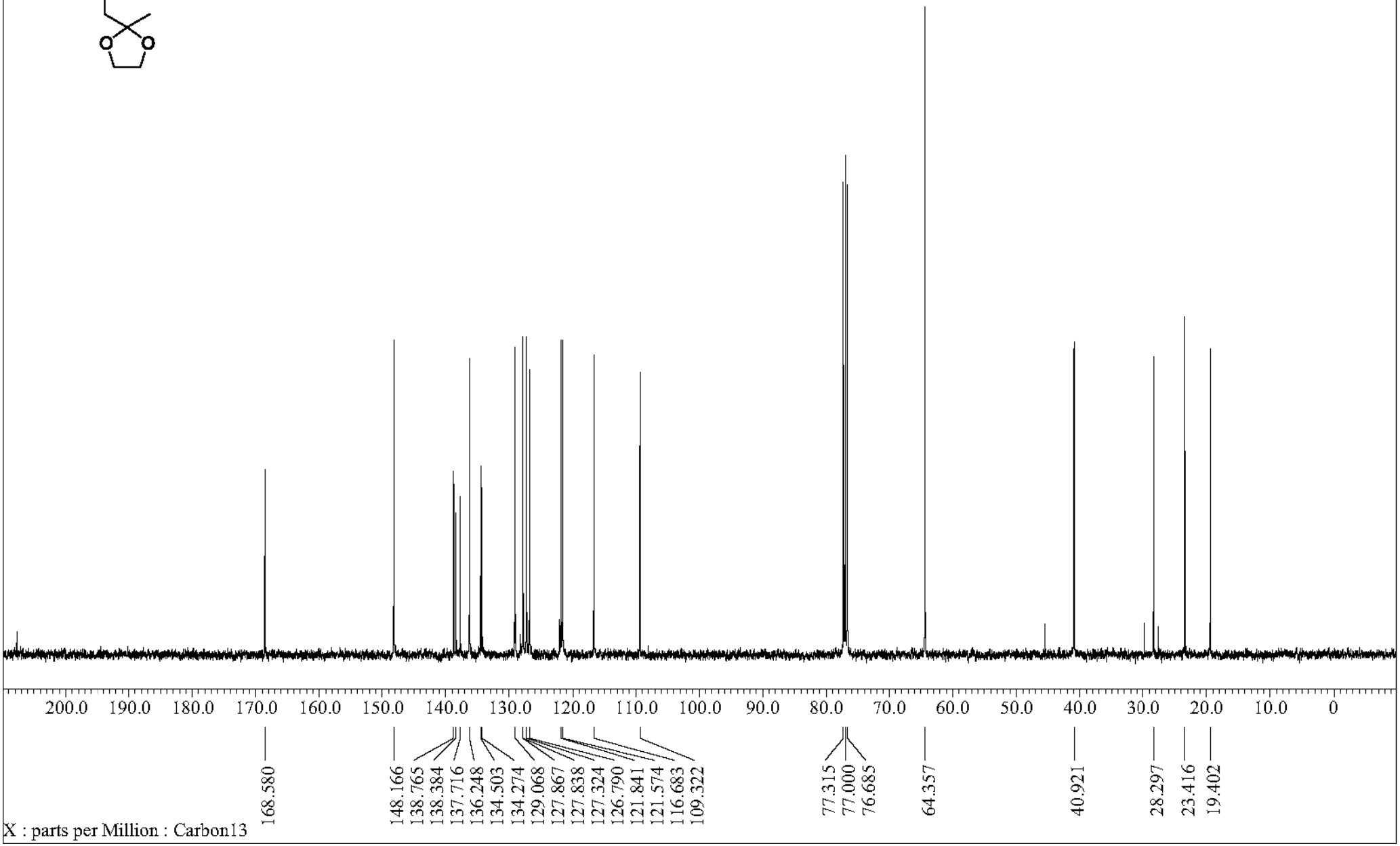
2-methyl-6-(2-(2-methyl-1,3-dioxolan-2-yl)ethyl)-N-(quinolin-8-yl)benzamide (10'aa)





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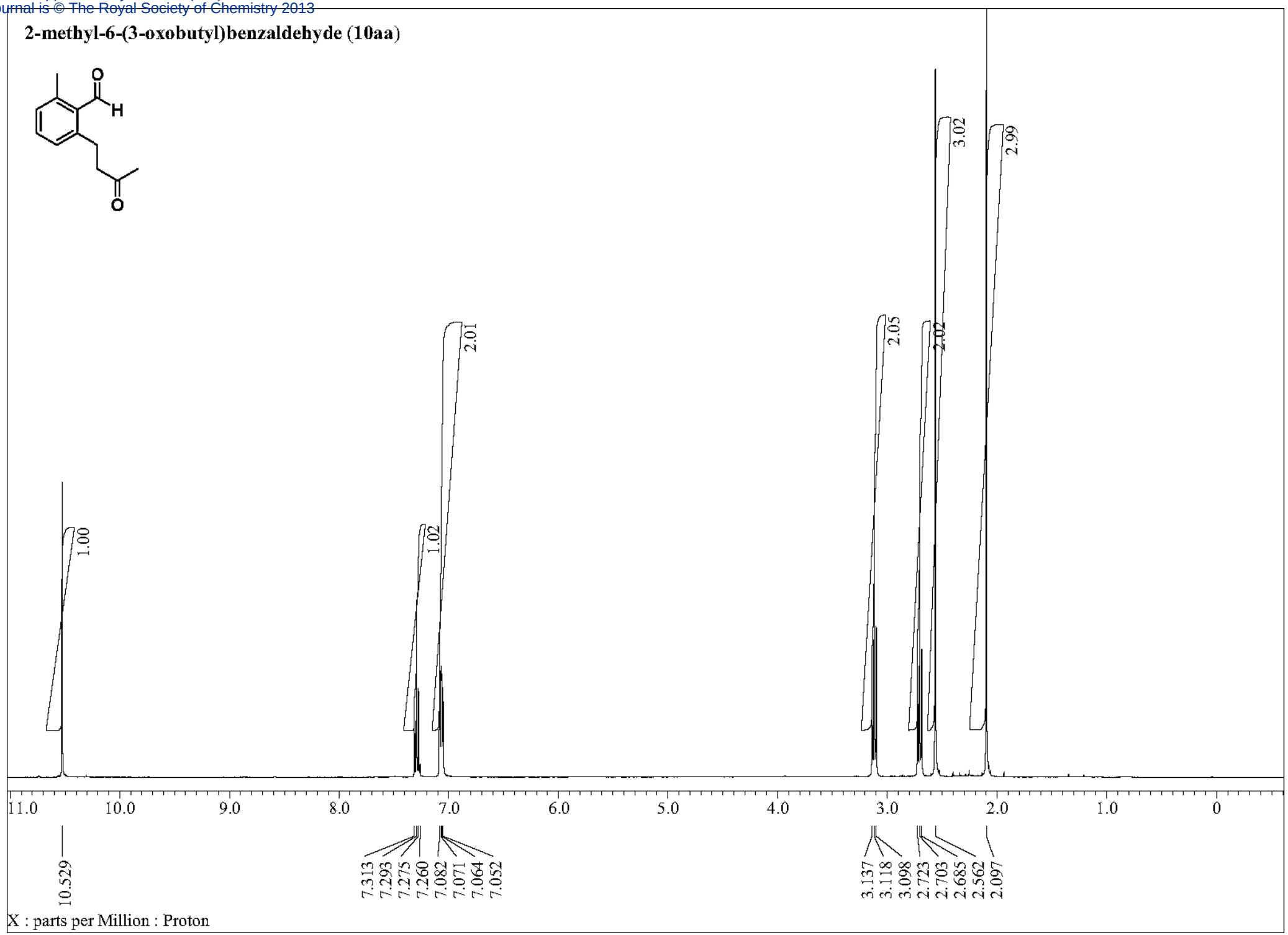

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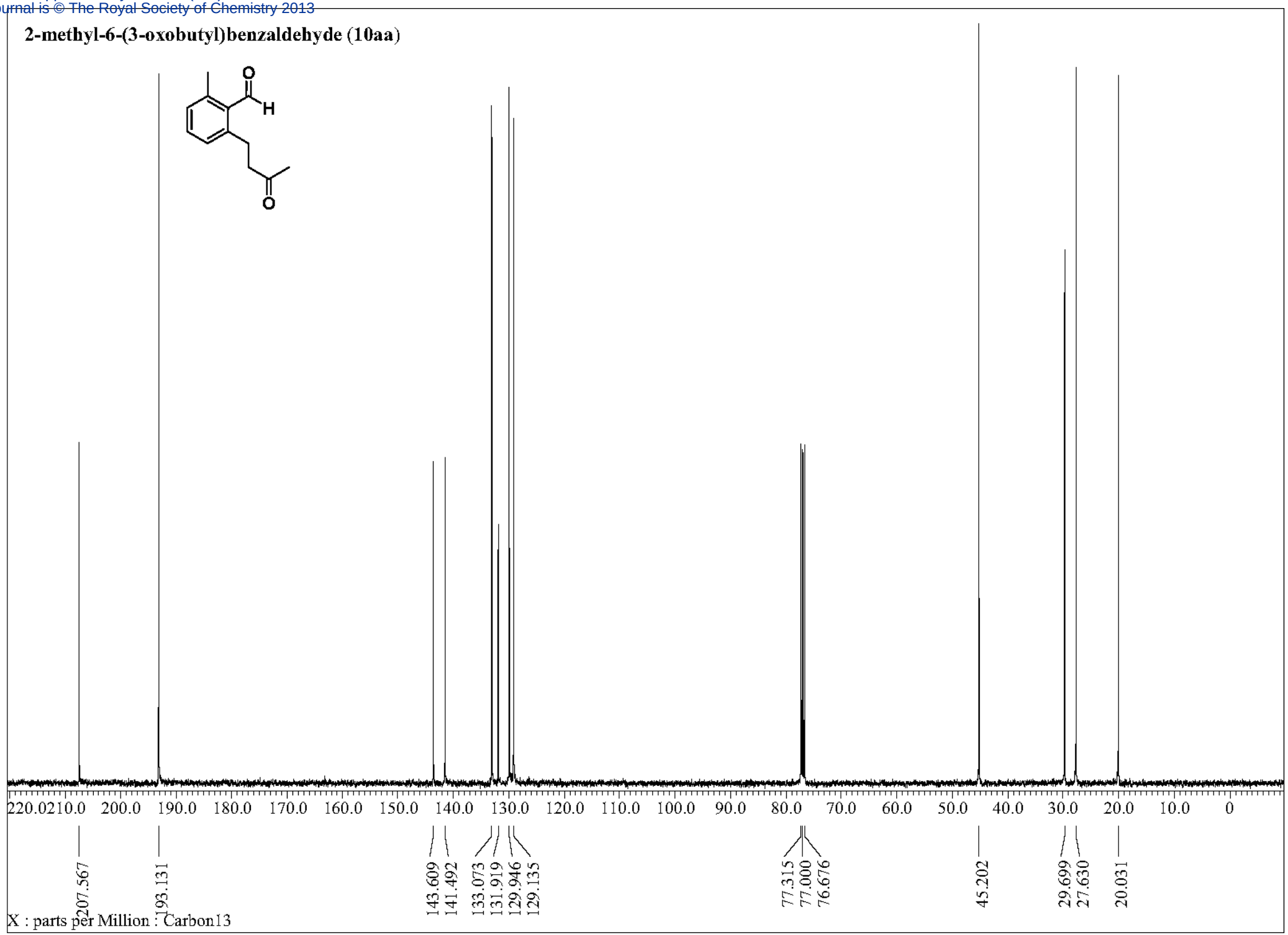

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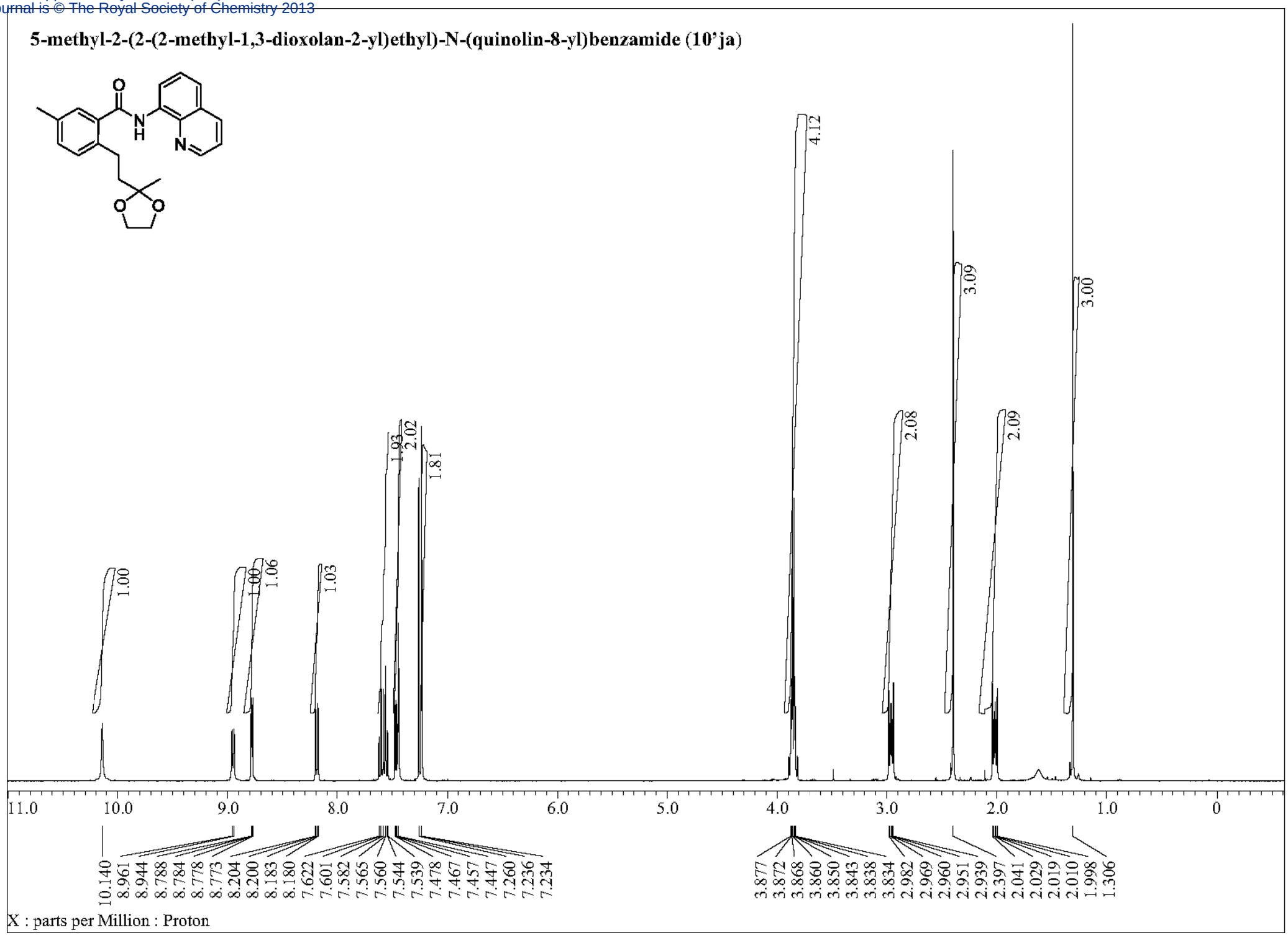

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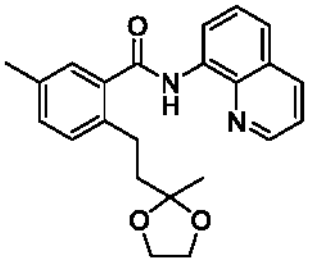
5-methyl-2-(2-(2-methyl-1,3-dioxolan-2-yl)ethyl)-N-(quinolin-8-yl)benzamide (10'ja)



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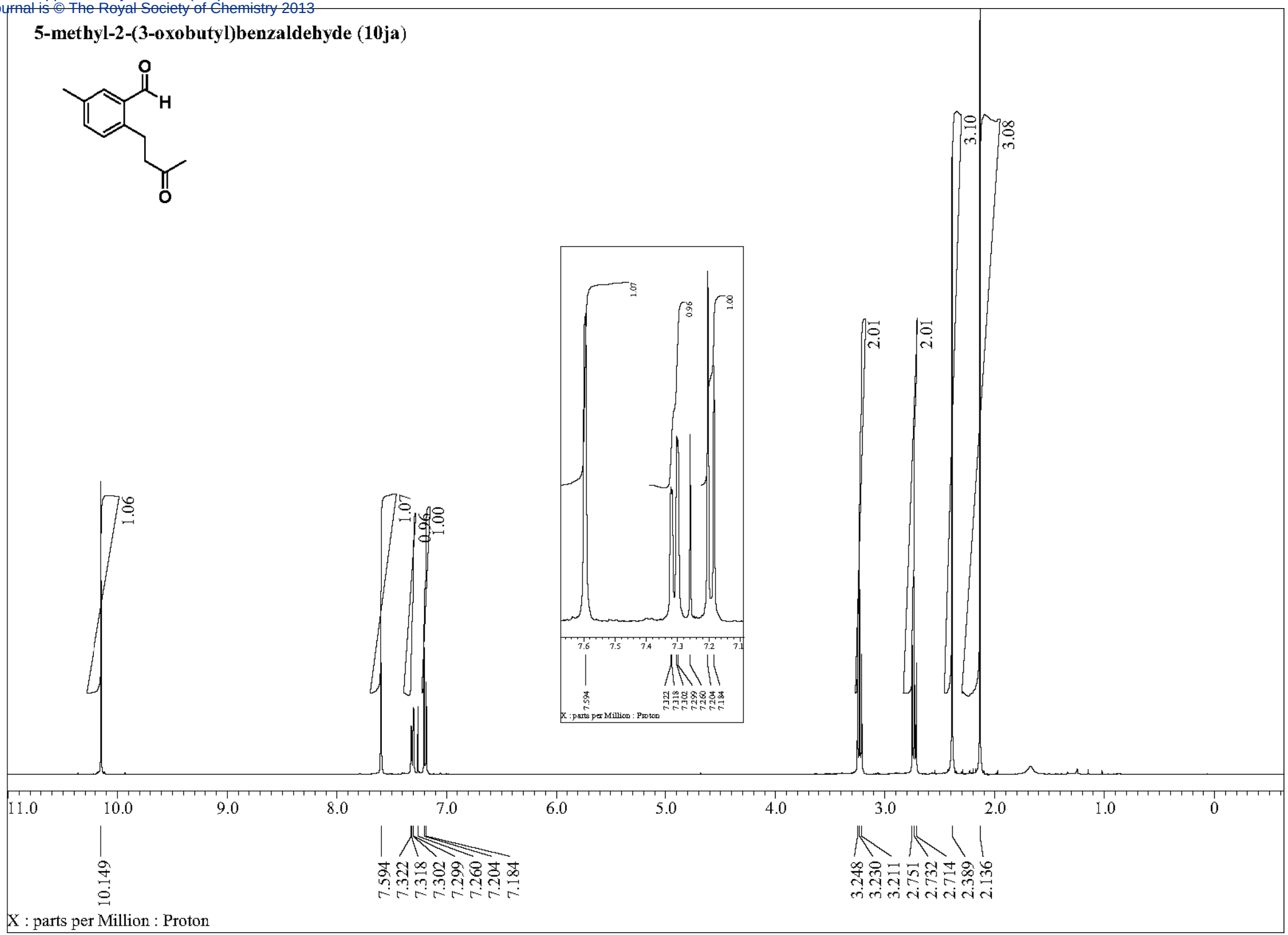

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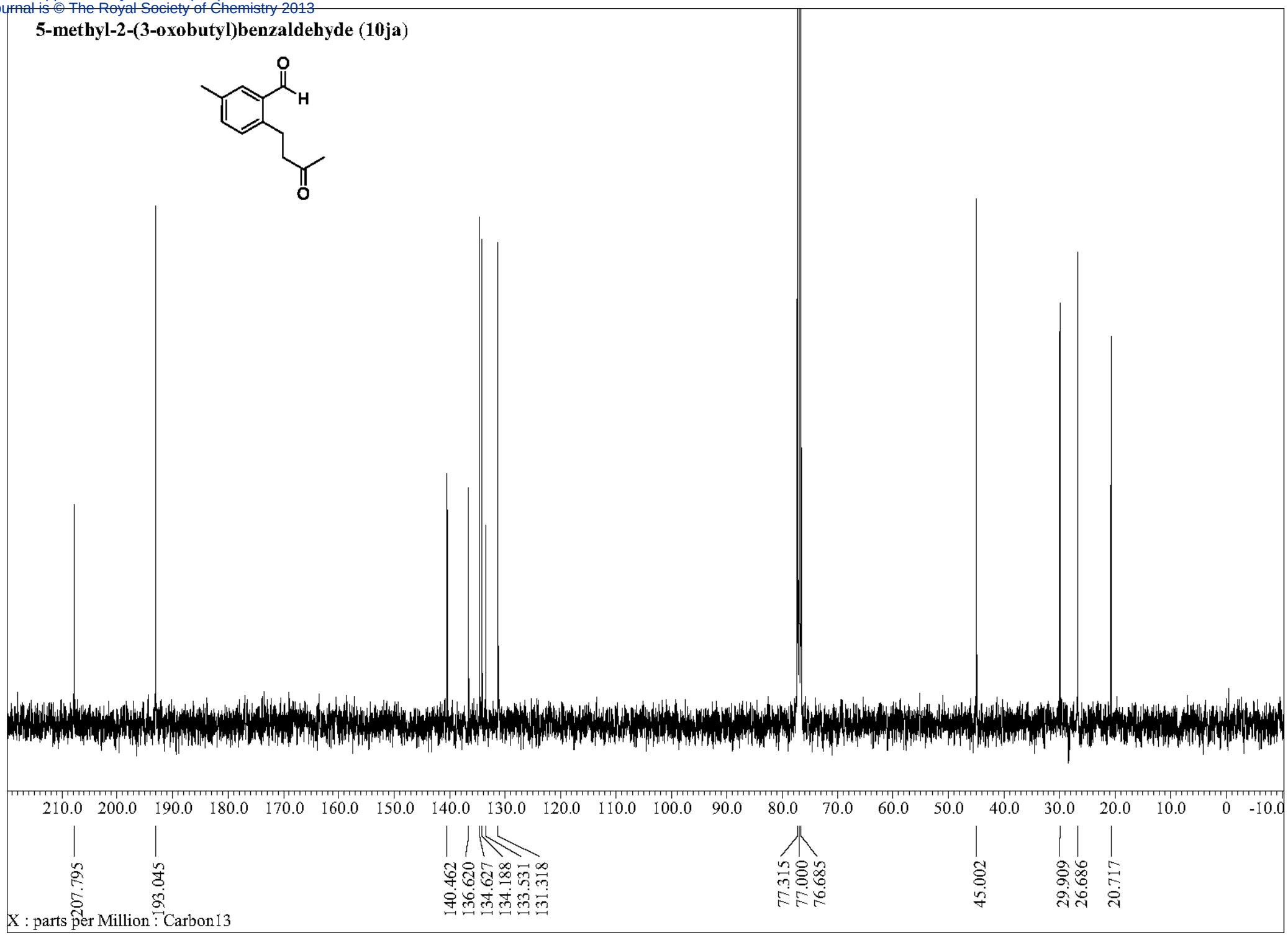

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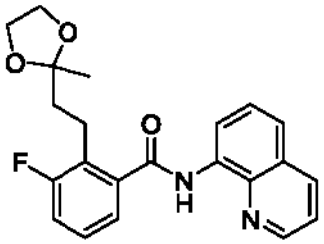
3-fluoro-2-(2-(2-methyl-1,3-dioxolan-2-yl)ethyl)-N-(quinolin-8-yl)benzamide (10'sa)



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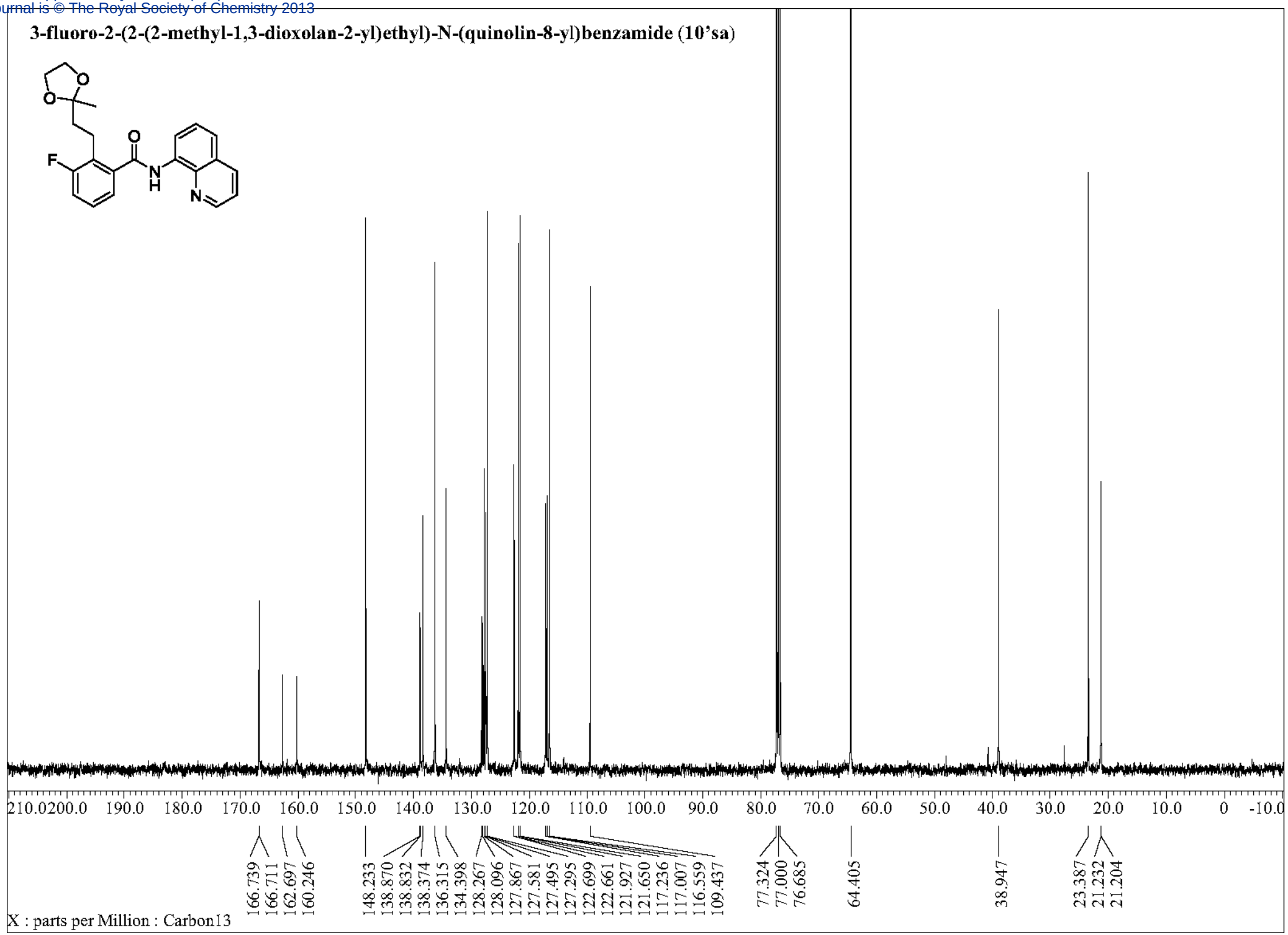

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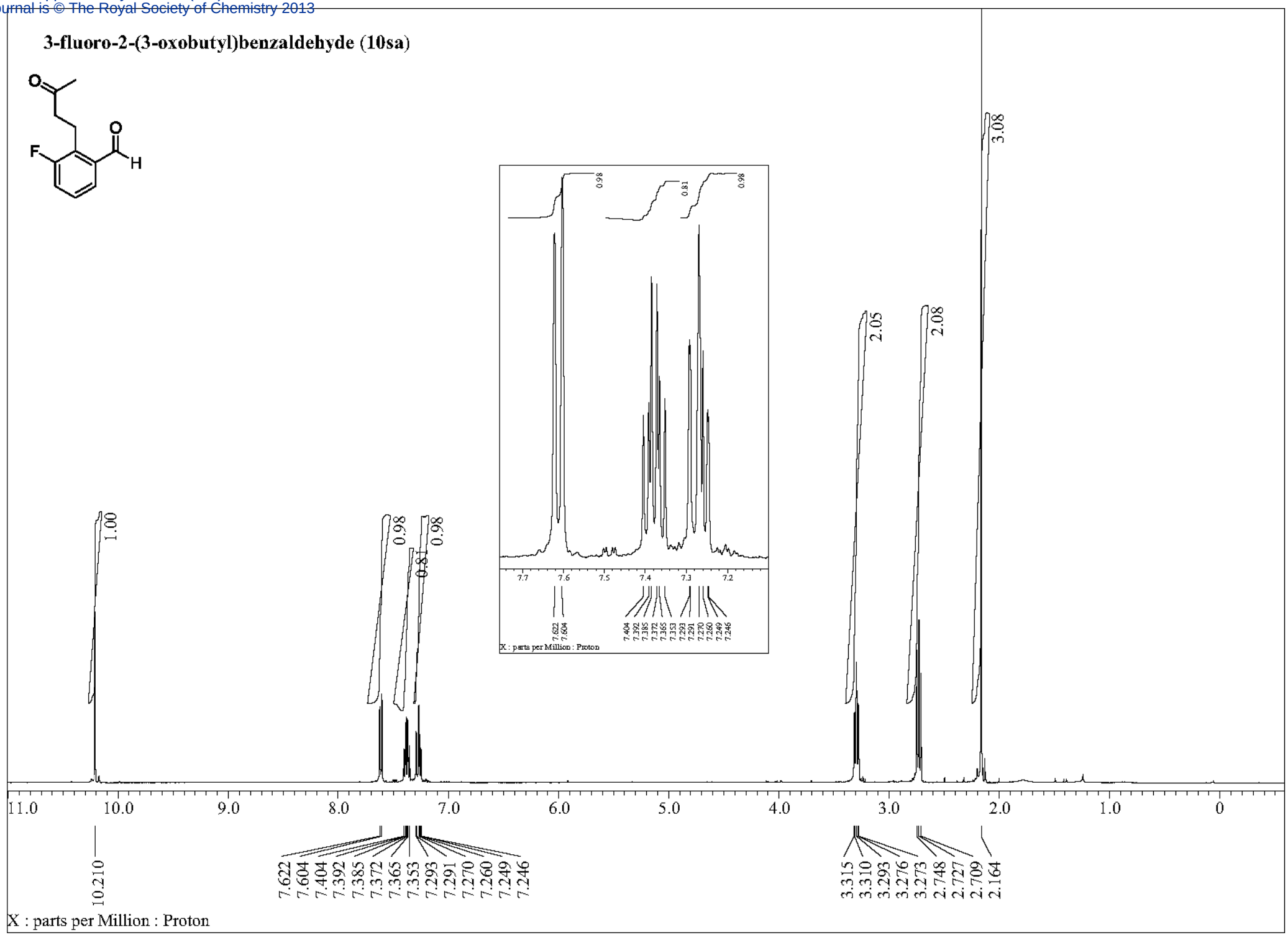

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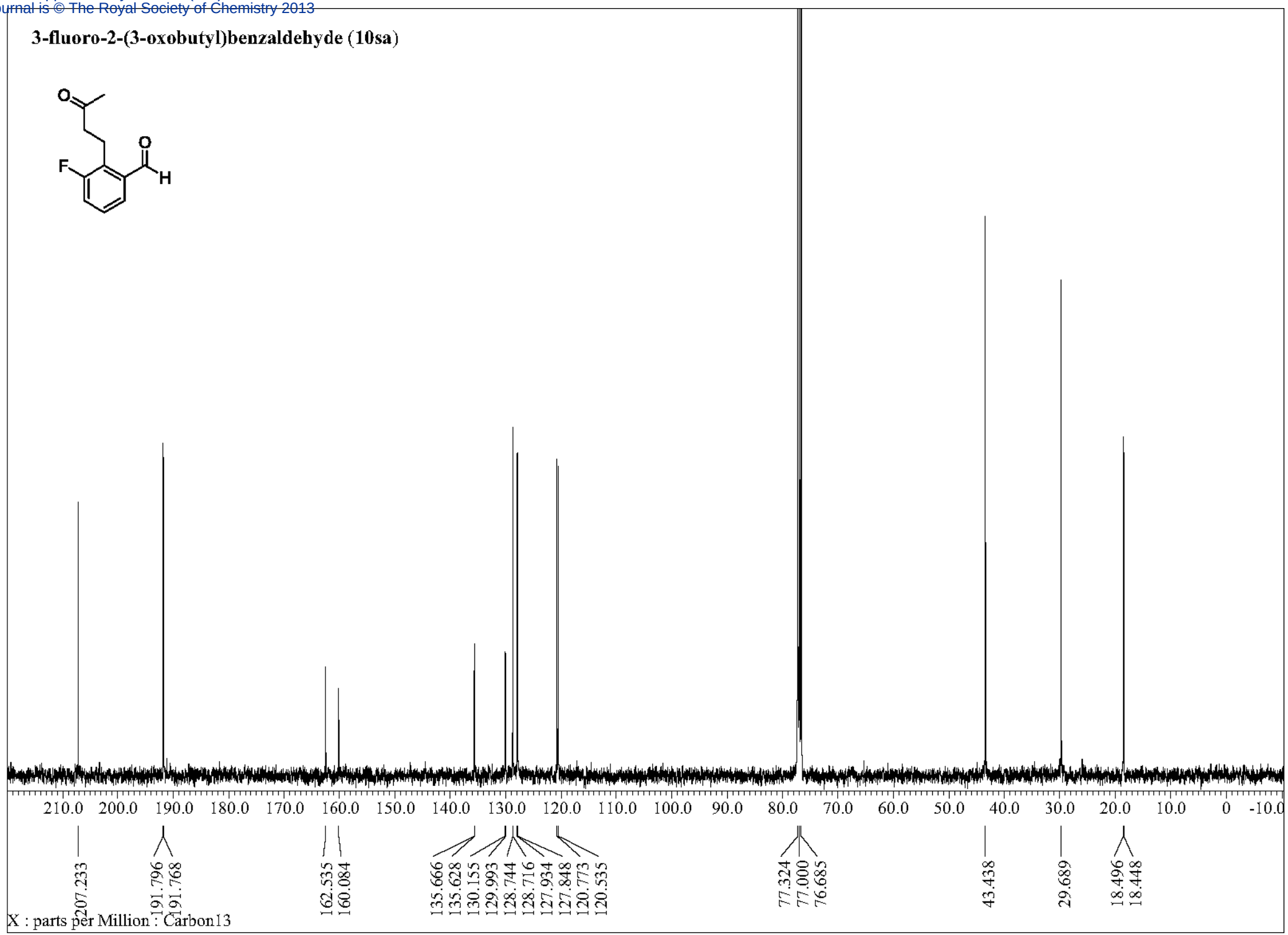

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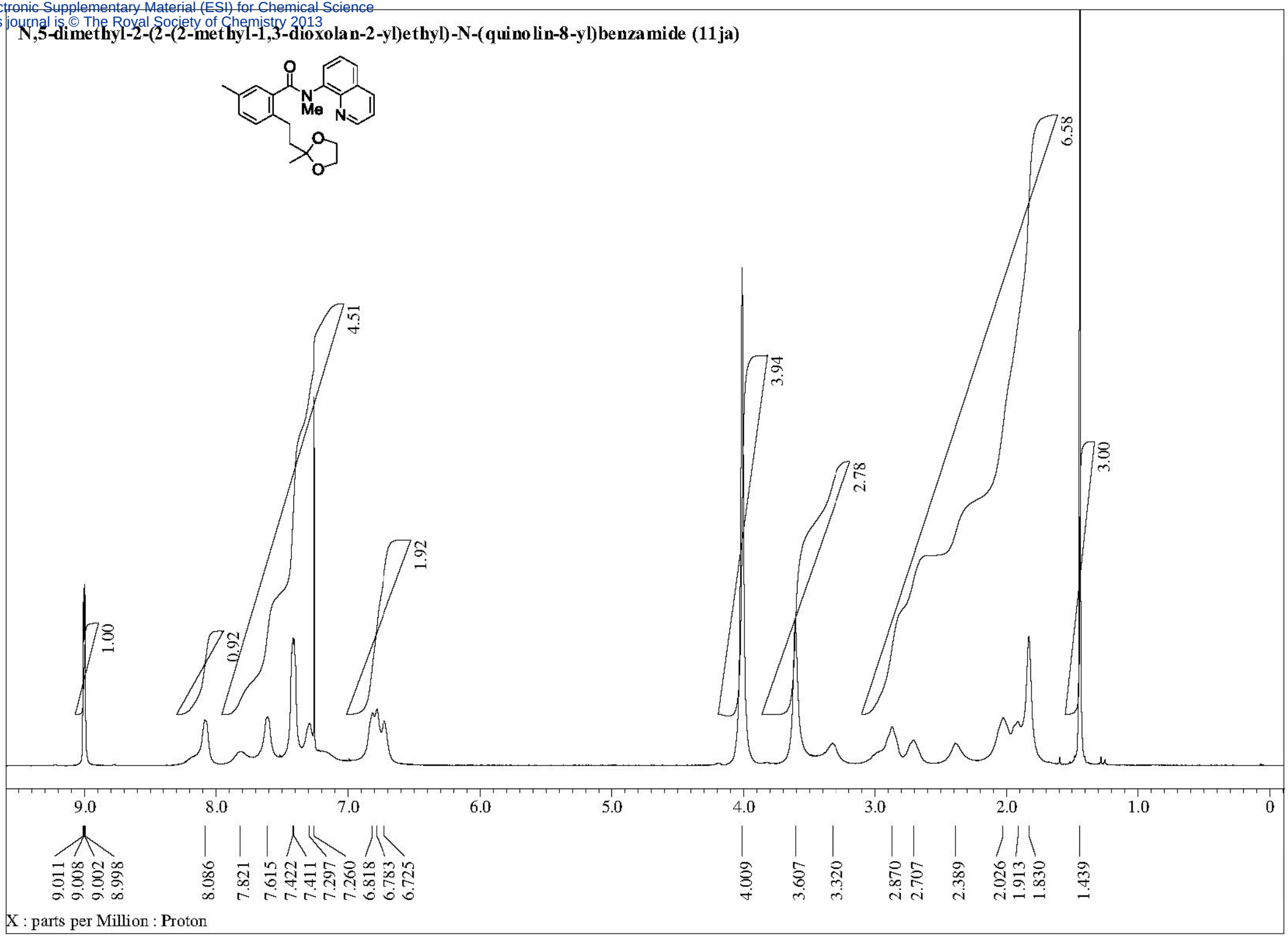

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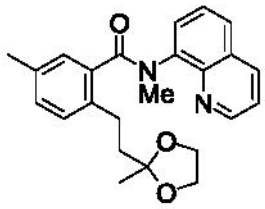
N,5-dimethyl-2-(2-(2-methyl-1,3-dioxolan-2-yl)ethyl)-N-(quinolin-8-yl)benzamide (11ja)



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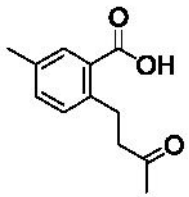
5-methyl-2-(3-oxobutyl)benzoic acid (12ja)



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5-methyl-2-(3-oxobutyl)benzoic acid (12ja)