Supporting Information

Substituted Quinolines as Noncovalent Proteasome Inhibitors

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Supporting Information

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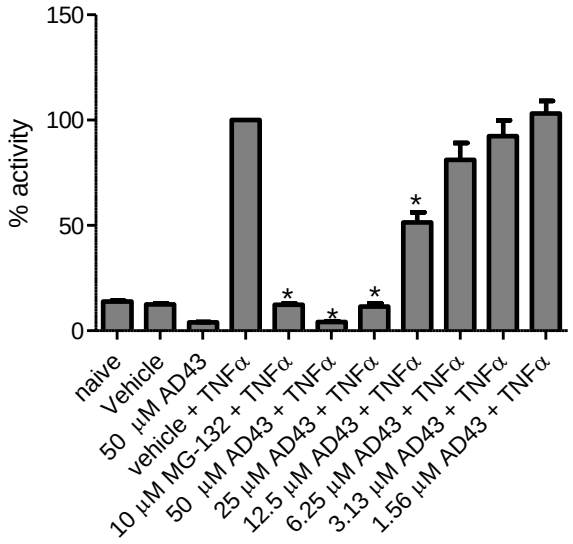
Fluorescence Quenching Control

During the measurements of 20S proteasomal activity using Suc-LLVY-AMC as the fluorogenic substrate, a fluorescence quenching control was run simultaneously with these experiments; one row of the 96 well plate was designated for this control. A buffer solution of 50 mM Tris-HCl pH 7.5 with 0.03% SDS was prepared. The test wells contained 100 µL total volume consisting of: 1 nM of purified human 20S proteasome, 50 µM of quinoline and buffer solution. Monitoring was done at 37 °C using a SpectraMax M5e multiwell plate reader at an excitation wavelength of 380 nm and emission wavelength of 460 nm to detect any fluorescence quenching stemming from the quinoline/label interactions. No interference was observed for any of the samples with the exception of **TM-124** (**quinoline #35**). **TM-124** exhibited fluorescence quenching, which lead to the perception that the quinoline inhibited the proteasome with an IC_{50} ~2.3 µM. The compound must not be as active as the measurement implies. Considering **TM-124** is similar in structure to **TM-080**, which is inactive, we assumed **TM-124** is also inactive.

Inhibition of NF-kB-luc activity



log(inhibitor) vs. response -- Variable slope (four parameters)	
Best-fit values	
Bottom	= 0.0
Top	= 100.0
$LogIC_{50}$	1.084
HillSlope	-2.373
IC_{50}	12.12
Span	= 100.0
Std. Error	
$LogIC_{50}$	0.02998
HillSlope	0.3480
95% Confidence Intervals	
$LogIC_{50}$	1.021 to 1.146
HillSlope	-3.095 to -1.652
IC_{50}	10.51 to 13.99
Goodness of Fit	
Degrees of Freedom	22
R square	0.9361
Absolute Sum of Squares	2402
Standard Deviation of Residuals	10.45
Constraints	
Bottom	Bottom = 0.0
Top	Top = 100.0
Number of points	
Analyzed	24

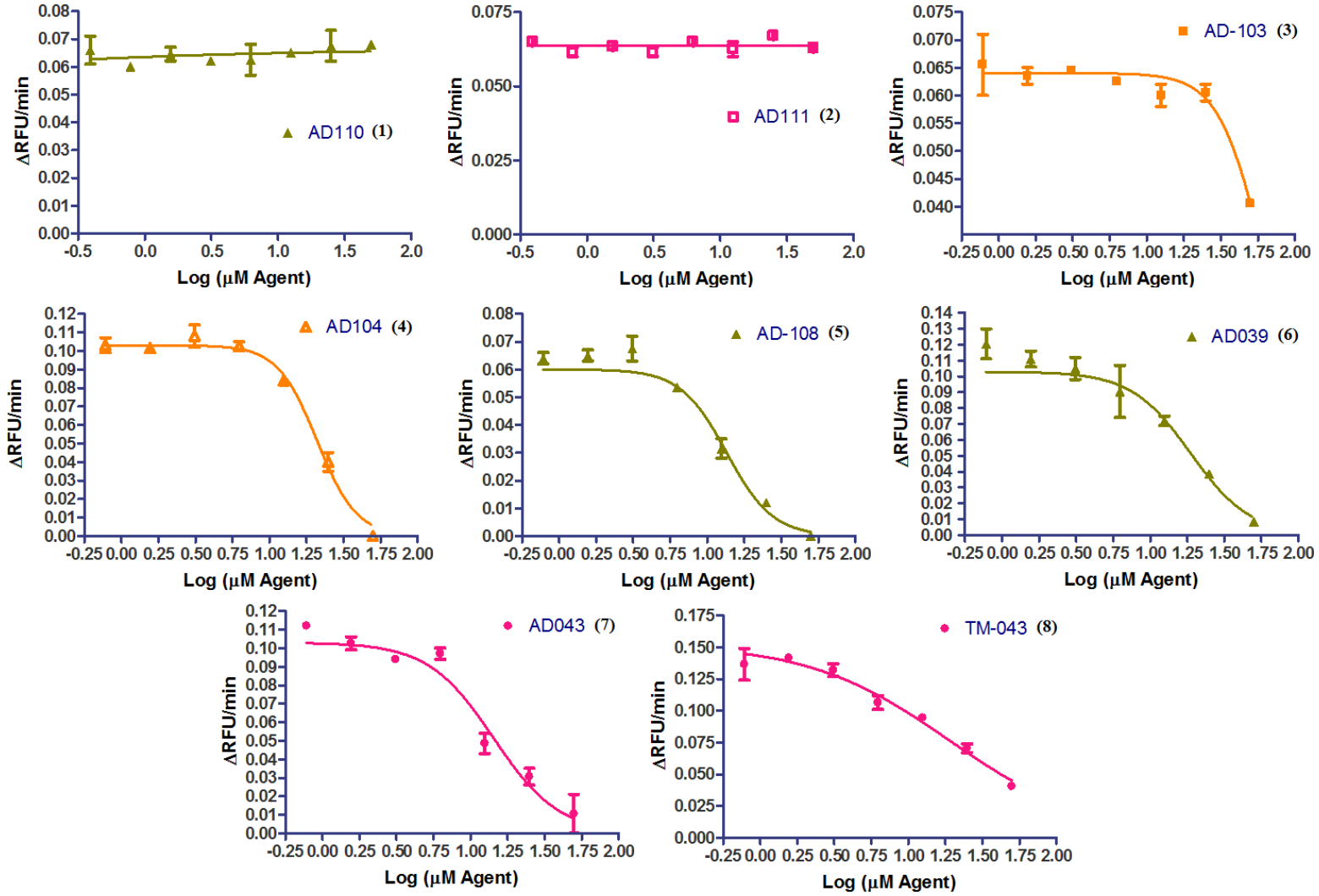


Figure S1: The inhibition of chymotryptic-like activity of purified human 20S proteasome.

(Quinolines 1 to 8)

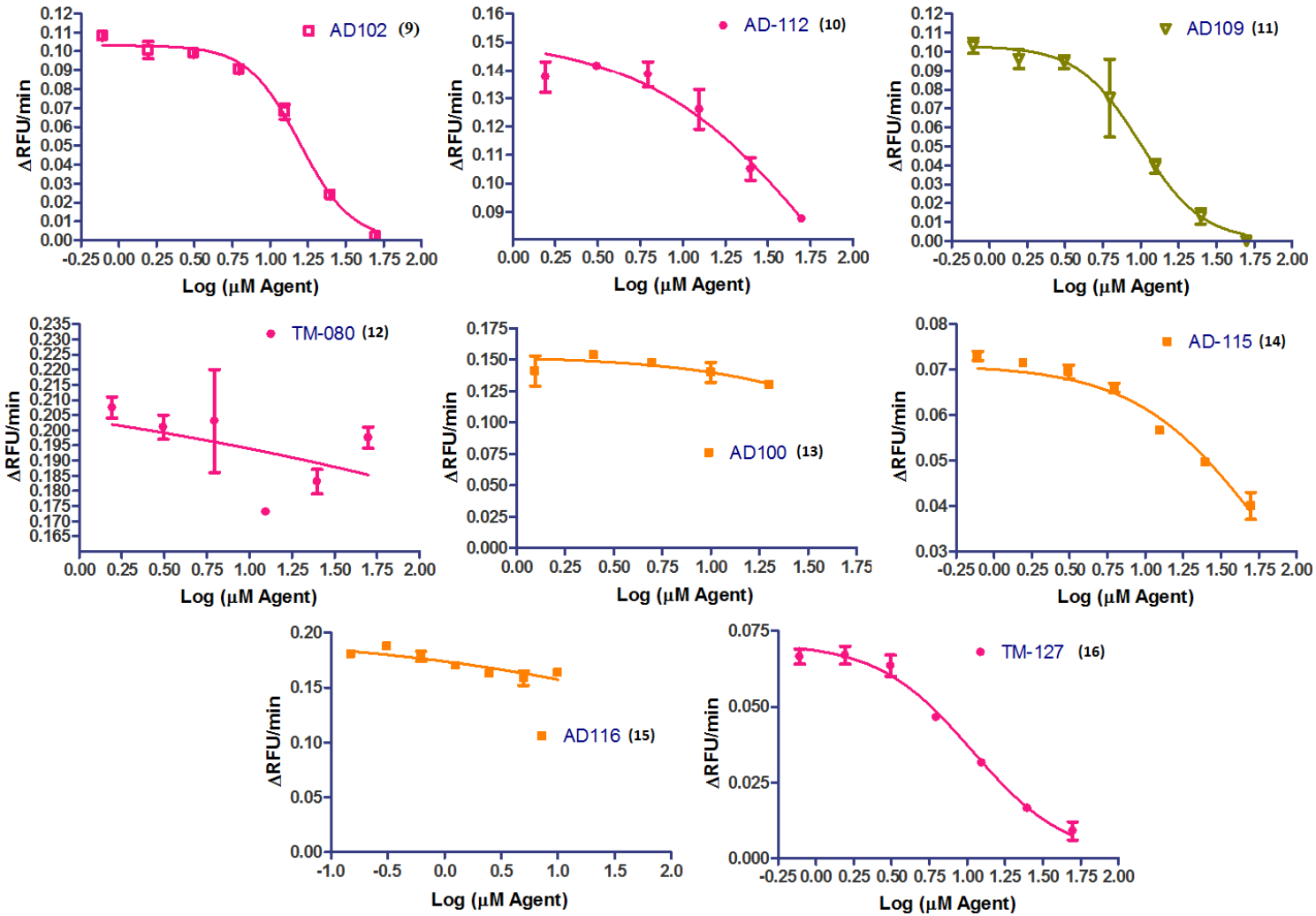


Figure S2: The inhibition of chymotryptic-like activity of purified human 20S proteasome.

(Quinolines 9 to 16)

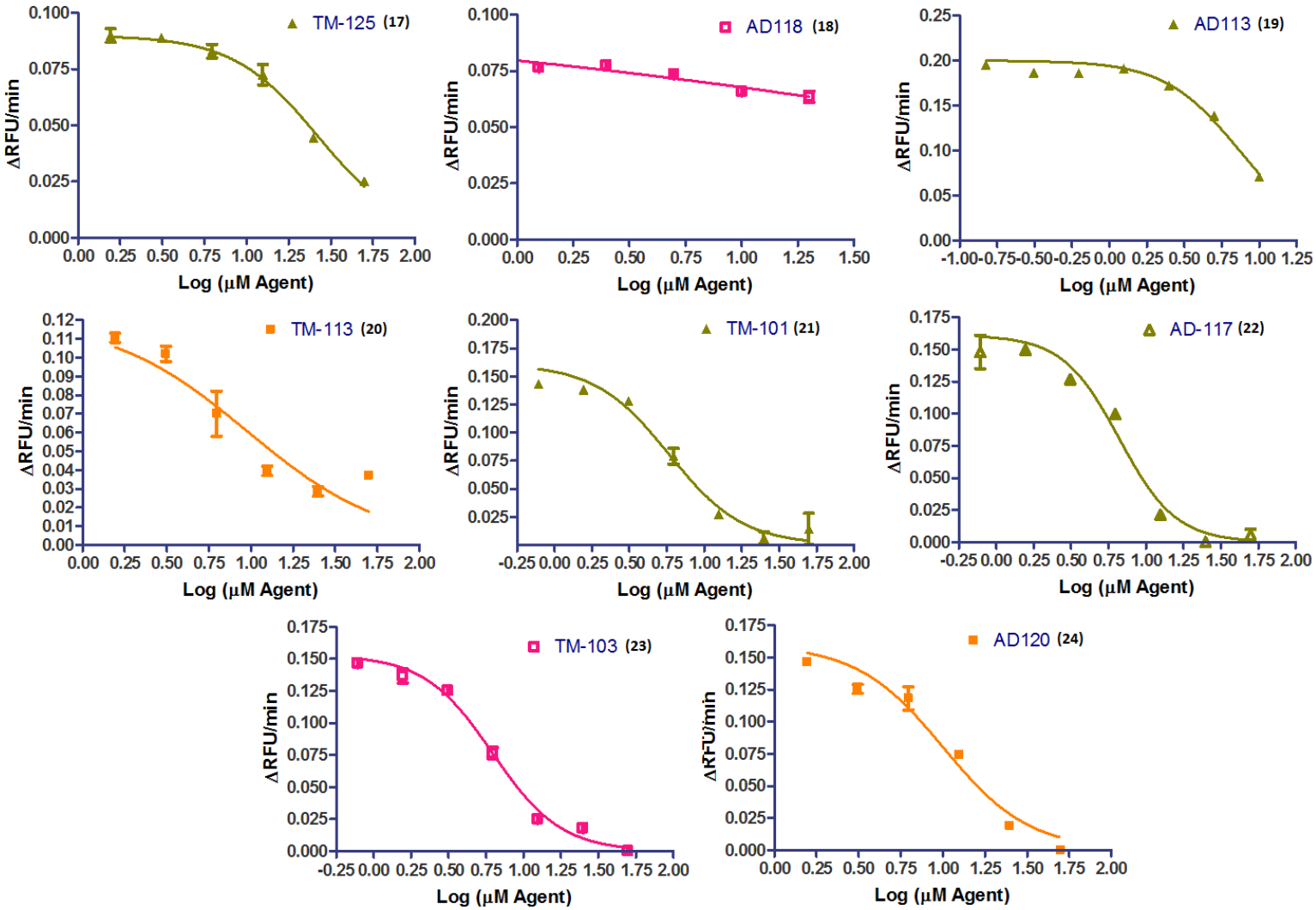


Figure S3: The inhibition of chymotryptic-like activity of purified human 20S proteasome.

(Quinolines 17 to 24)

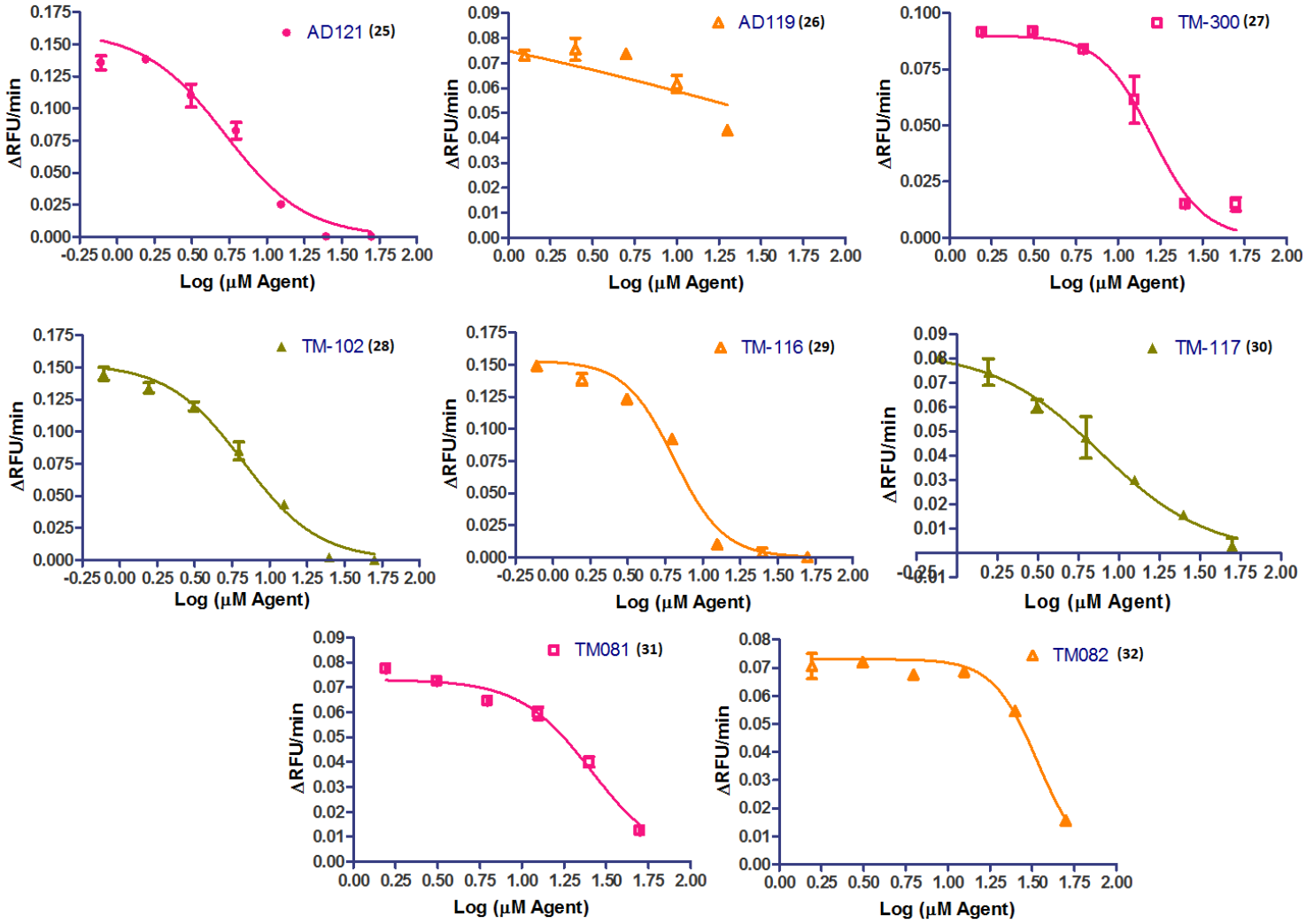


Figure S4: The inhibition of chymotryptic-like activity of purified human 20S proteasome.

(Quinolines 25 to 32)

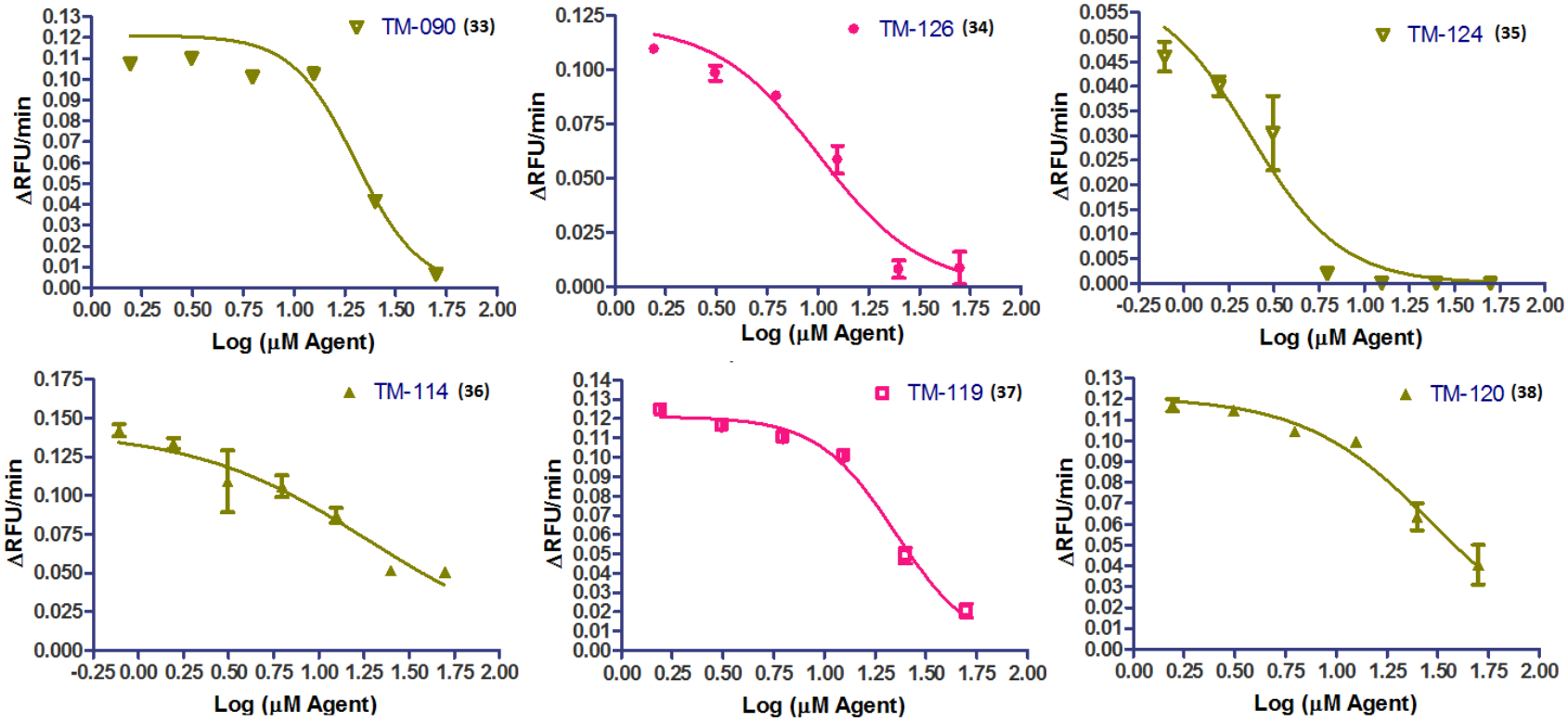


Figure S5: The inhibition of chymotryptic-like activity of purified human 20S proteasome.

(Quinolines 33 to 38)

	AD110 (1)	AD111 (2)	AD103 (3)	AD104 (4)	AD108 (5)
Sigmoidal dose-response (variable slope)					
Best-fit values					
BOTTOM	0	0	0	0	0
TOP	0.153	0.067	0.064	0.103	0.06
LOGIC$_{50}$	2.196	-5.753	1.908	1.322	1.132
HILLSLOPE	-0.8588	0.2058	-1.501	-3.259	-2.791
IC$_{50}$	156.9	1.77E-06	80.83	20.98	13.54
Std. Error					
LOGIC$_{50}$	0.587	3.835	0.07863	0.01787	0.03306
HILLSLOPE	0.4622	0.1341	0.2812	0.3861	0.5405
95% Confidence Intervals					
LOGIC$_{50}$	0.8420 to 3.549	-14.11 to 2.603	1.726 to 2.089	1.283 to 1.361	1.060 to 1.204
HILLSLOPE	-1.925 to 0.2070	-0.08633 to 0.4980	-2.149 to -0.8524	-4.101 to -2.418	-3.969 to -1.614
IC$_{50}$	6.951 to 3542	7.767e-015 to 401.1	53.24 to 122.7	19.18 to 22.95	11.47 to 15.98
Goodness of Fit					
Degrees of Freedom	8	12	8	12	12
R²	0.3591	0.1684	0.8968	0.9838	0.9631
Absolute Sum of Squares	0.0006809	5.94E-05	4.86E-05	0.0003347	0.0003402
Standard Deviation of Residuals	0.009225	0.002225	0.002464	0.005281	0.005325
Constraints					
BOTTOM	BOTTOM = 0.0	BOTTOM = 0.0	BOTTOM = 0.0	BOTTOM = 0.0	BOTTOM = 0.0
TOP	TOP = 0.1530	TOP = 0.0670	TOP = 0.0640	TOP = 0.1030	TOP = 0.0600
Data					
Number of X values	5	8	7	7	7
Number of Y replicates	2	2	2	2	2
Total number of values	10	14	10	14	14
Number of missing values	0	2	4	0	0

Table S1: Statistical analysis for the inhibition of chymotryptic-like activity of purified human 20S proteasome **(Quinolines 1 to 5)**

	AD039 (6)	AD043 (7)	TM-043 (8)	AD102 (9)	AD-112 (10)
Sigmoidal dose-response (variable slope)					
Best-fit values					
BOTTOM	0	0	0	0	0
TOP	0.103	0.103	0.153	0.103	0.152
$LOGIC_{50}$	1.273	1.155	1.28	1.195	1.86
HILLSLOPE	-2.143	-1.973	-0.9075	-2.524	-0.8281
IC_{50}	18.76	14.3	19.04	15.67	72.43
Std. Error					
$LOGIC_{50}$	0.04102	0.0408	0.0394	0.0159	0.07215
HILLSLOPE	0.3928	0.3294	0.08148	0.205	0.1027
95% Confidence Intervals					
$LOGIC_{50}$	1.182 to 1.365	1.067 to 1.244	1.194 to 1.366	1.160 to 1.230	1.699 to 2.021
HILLSLOPE	-3.018 to -1.268	-2.691 to -1.256	-1.085 to -0.7299	-2.971 to -2.078	-1.057 to -0.5993
IC_{50}	15.20 to 23.15	11.66 to 17.55	15.63 to 23.20	14.47 to 16.97	50.02 to 104.9
Goodness of Fit					
Degrees of Freedom	10	12	12	12	10
R^2	0.9429	0.9462	0.9545	0.9901	0.9129
Absolute Sum of Squares	0.000967	0.001062	0.0007929	0.0002062	0.0004356
Standard Deviation of Residuals	0.009834	0.009409	0.008129	0.004145	0.0066
Constraints					
BOTTOM	BOTTOM = 0.0	BOTTOM = 0.0	BOTTOM = 0.0	BOTTOM = 0.0	BOTTOM = 0.0
TOP	TOP = 0.1030	TOP = 0.1030	TOP = 0.1530	TOP = 0.1030	TOP = 0.1520
Data					
Number of X values	7	7	7	7	6
Number of Y replicates	2	2	2	2	2
Total number of values	12	14	14	14	12
Number of missing values	2	0	0	0	0

Table S2: Statistical analysis for the inhibition of chymotryptic-like activity of purified human 20S proteasome **(Quinolines 6 to 10)**

	AD109 (11)	TM-080 (12)	AD100 (13)	AD-115 (14)	AD116 (15)
Sigmoidal dose-response (variable slope)					
Best-fit values					
BOTTOM	0	0	0	0	0
TOP	0.103	0.226	0.153	0.071	0.2
LOGIC$_{50}$	0.9969	5.427	1.521	1.772	3.219
HILLSLOPE	-2.111	-0.1764	-2.711	-1.044	-0.2557
IC$_{50}$	9.93	267080	33.19	59.18	1655
Std. Error					
LOGIC$_{50}$	0.03965	3.202	0.265	0.04401	0.5925
HILLSLOPE	0.3594	0.1296	2.94	0.1044	0.05242
95% Confidence Intervals					
LOGIC$_{50}$	0.9105 to 1.083	-1.708 to 12.56	0.9100 to 2.132	1.676 to 1.868	1.928 to 4.510
HILLSLOPE	-2.894 to -1.328	-0.4653 to 0.1124	-9.491 to 4.069	-1.271 to -0.8161	-0.3699 to -0.1414
IC$_{50}$	8.138 to 12.12	0.0196 to 3.643e+12	8.128 to 135.6	47.46 to 73.81	84.66 to 32336
Goodness of Fit					
Degrees of Freedom	12	10	8	12	12
R^2	0.9524	0.1818	0.4787	0.9575	0.6998
Absolute Sum of Squares	0.001076	0.002017	0.002118	8.16E-05	0.0004621
Standard Deviation of Residuals	0.009469	0.0142	0.01627	0.002607	0.006206
Constraints					
BOTTOM	BOTTOM = 0.0	BOTTOM = 0.0	BOTTOM = 0.0	BOTTOM = 0.0	BOTTOM = 0.0
TOP	TOP = 0.1030	TOP = 0.2260	TOP = 0.1530	TOP = 0.0710	TOP = 0.2000
Data					
Number of X values	7	6	5	7	7
Number of Y replicates	2	2	2	2	2
Total number of values	14	12	10	14	14
Number of missing values	0	0	0	0	0

Table S3: Statistical analysis for the inhibition of chymotryptic-like activity of purified human 20S proteasome **(Quinolines 11 to 15)**

	TM-127 (16)	TM-125 (17)	AD118 (18)	AD113 (19)	TM-113 (20)
Sigmoidal dose-response (variable slope)					
Best-fit values					
BOTTOM	0	0	0	0	0
TOP	0.066	0.09	0.1	0.2	0.121
$LOGIC_{50}$	0.9586	1.426	2.188	0.8687	0.9798
HILLSLOPE	-1.665	-1.713	-0.2707	-1.738	-1.06
IC_{50}	9.092	26.66	154.3	7.39	9.545
Std. Error					
$LOGIC_{50}$	0.02059	0.01892	0.2231	0.02202	0.06701
HILLSLOPE	0.1177	0.1285	0.03594	0.1633	0.1818
95% Confidence Intervals					
$LOGIC_{50}$	0.9138 to 1.003	1.384 to 1.468	1.702 to 2.675	0.8207 to 0.9166	0.8305 to 1.129
HILLSLOPE	-1.921 to -1.408	-1.999 to -1.427	-0.3490 to -0.1924	-2.094 to -1.382	-1.465 to -0.6548
IC_{50}	8.199 to 10.08	24.19 to 29.37	50.40 to 472.7	6.618 to 8.254	6.768 to 13.46
Goodness of Fit					
Degrees of Freedom	12	10	12	12	10
R^2	0.9883	0.9839	0.8395	0.9673	0.8687
Absolute Sum of Squares	9.38E-05	0.0001164	0.0001311	0.0007973	0.001683
Standard Deviation of Residuals	0.002796	0.003412	0.003306	0.008151	0.01297
Constraints					
BOTTOM	BOTTOM = 0.0	BOTTOM = 0.0	BOTTOM = 0.0	BOTTOM = 0.0	BOTTOM = 0.0
TOP	TOP = 0.0660	TOP = 0.0900	TOP = 0.1000	TOP = 0.2000	TOP = 0.1210
Data					
Number of X values	7	6	7	7	6
Number of Y replicates	2	2	2	2	2
Total number of values	14	12	14	14	12
Number of missing values	0	0	0	0	0

Table S4: Statistical analysis for the inhibition of chymotryptic-like activity of purified human 20S proteasome **(Quinolines 16 to 20)**

	TM-101 (21)	AD-117 (22)	TM-103 (23)	AD120 (24)	AD121 (25)
Sigmoidal dose-response (variable slope)					
Best-fit values					
BOTTOM	0	0	0	0	0
TOP	0.161	0.161	0.142	0.16	0.16
LOGIC$_{50}$	0.7652	0.8222	0.6951	1.002	0.7207
HILLSLOPE	-1.756	-2.3	-1.5	-1.697	-1.612
IC$_{50}$	5.824	6.641	4.956	10.05	5.256
Std. Error					
LOGIC$_{50}$	0.03361	0.03003	0.03662	0.03567	0.03723
HILLSLOPE	0.212	0.325	0.186	0.214	0.1995
95% Confidence Intervals					
LOGIC$_{50}$	0.6920 to 0.8385	0.7568 to 0.8877	0.6123 to 0.7780	0.9229 to 1.082	0.6396 to 0.8018
HILLSLOPE	-2.218 to -1.294	-3.009 to -1.592	-1.921 to -1.079	-2.173 to -1.220	-2.047 to -1.178
IC$_{50}$	4.920 to 6.894	5.712 to 7.721	4.096 to 5.998	8.373 to 12.07	4.361 to 6.336
Goodness of Fit					
Degrees of Freedom	12	12	9	10	12
R^2	0.965	0.9701	0.9656	0.9614	0.9615
Absolute Sum of Squares	0.001572	0.00165	0.0008108	0.001403	0.001747
Standard Deviation of Residuals	0.01145	0.01173	0.009491	0.01185	0.01207
Constraints					
BOTTOM	BOTTOM = 0.0	BOTTOM = 0.0	BOTTOM = 0.0	BOTTOM = 0.0	BOTTOM = 0.0
TOP	TOP = 0.1610	TOP = 0.1610	TOP = 0.1420	TOP = 0.1600	TOP = 0.1600
Data					
Number of X values	7	7	7	7	7
Number of Y replicates	2	2	2	2	2
Total number of values	14	14	11	12	14
Number of missing values	0	0	3	2	0

Table S5: Statistical analysis for the inhibition of chymotryptic-like activity of purified human 20S proteasome **(Quinolines 21 to 25)**

	AD119 (26)	TM-300 (27)	TM-102 (28)	TM-116 (29)	TM-117 (30)
Sigmoidal dose-response (variable slope)					
Best-fit values					
BOTTOM	0	0	0	0	0
TOP	0.1	0.09	0.153	0.161	0.083
LOGIC$_{50}$	1.478	1.203	0.8245	0.8261	0.8826
HILLSLOPE	-0.3197	-2.842	-1.729	-2.45	-1.309
IC$_{50}$	30.04	15.94	6.675	6.7	7.631
Std. Error					
LOGIC$_{50}$	0.2461	0.03177	0.02508	0.03708	0.03269
HILLSLOPE	0.07391	0.5078	0.1535	0.4596	0.1192
95% Confidence Intervals					
LOGIC$_{50}$	0.9413 to 2.014	1.132 to 1.273	0.7698 to 0.8791	0.7435 to 0.9087	0.8114 to 0.9538
HILLSLOPE	-0.4807 to -0.1586	-3.973 to -1.711	-2.064 to -1.395	-3.474 to -1.426	-1.568 to -1.049
IC$_{50}$	8.737 to 103.3	13.54 to 18.76	5.886 to 7.570	5.539 to 8.103	6.477 to 8.992
Goodness of Fit					
Degrees of Freedom	12	10	12	10	12
R²	0.6228	0.9568	0.9827	0.9487	0.9727
Absolute Sum of Squares	0.000702	0.0005846	0.0007782	0.002236	0.000292
Standard Deviation of Residuals	0.007649	0.007646	0.008053	0.01495	0.004933
Constraints					
BOTTOM	BOTTOM = 0.0	BOTTOM = 0.0	BOTTOM = 0.0	BOTTOM = 0.0	BOTTOM = 0.0
TOP	TOP = 0.1000	TOP = 0.0900	TOP = 0.1530	TOP = 0.1610	TOP = 0.0830
Data					
Number of X values	7	6	7	7	7
Number of Y replicates	2	2	2	2	2
Total number of values	14	12	14	12	14
Number of missing values	0	0	0	2	0

Table S6: Statistical analysis for the inhibition of chymotryptic-like activity of purified human 20S proteasome **(Quinolines 26 to 30)**

	TM081 (31)	TM082 (32)	TM-090 (33)	TM-126 (34)	TM-124 (35)
Sigmoidal dose-response (variable slope)					(Autofluorescence)
Best-fit values					
BOTTOM	0	0	0	0	0
TOP	0.073	0.073	0.121	0.121	0.06
LOGIC$_{50}$	1.411	1.532	1.304	1.006	0.3684
HILLSLOPE	-2.053	-3.277	-2.762	-1.727	-1.709
IC$_{50}$	25.75	34.03	20.16	10.13	2.336
Std. Error					
LOGIC$_{50}$	0.02302	0.01729	0.03416	0.03981	0.05026
HILLSLOPE	0.2151	0.356	0.5267	0.2468	0.3146
95% Confidence Intervals					
LOGIC$_{50}$	1.359 to 1.462	1.493 to 1.570	1.228 to 1.381	0.9169 to 1.094	0.2589 to 0.4779
HILLSLOPE	-2.532 to -1.573	-4.070 to -2.484	-3.935 to -1.588	-2.277 to -1.177	-2.394 to -1.023
IC$_{50}$	22.88 to 28.98	31.14 to 37.19	16.92 to 24.02	8.258 to 12.42	1.815 to 3.006
Goodness of Fit					
Degrees of Freedom	10	10	10	10	12
R^2	0.9759	0.9739	0.9371	0.95	0.9139
Absolute Sum of Squares	0.000143	0.0001249	0.001193	0.001018	0.0004676
Standard Deviation of Residuals	0.003781	0.003534	0.01092	0.01009	0.006242
Constraints					
BOTTOM	BOTTOM = 0.0	BOTTOM = 0.0	BOTTOM = 0.0	BOTTOM = 0.0	BOTTOM = 0.0
TOP	TOP = 0.0730	TOP = 0.0730	TOP = 0.1210	TOP = 0.1210	TOP = 0.0600
Data					
Number of X values	6	6	6	6	7
Number of Y replicates	2	2	2	2	2
Total number of values	12	12	12	12	14
Number of missing values	0	0	0	0	0

Table S7: Statistical analysis for the inhibition of chymotryptic-like activity of purified human 20S proteasome **(Quinolines 31 to 35)**

	TM-114 (36)	TM-119 (37)	TM-120 (38)
Sigmoidal dose-response (variable slope)			
Best-fit values			
BOTTOM	0	0	0
TOP	0.142	0.121	0.121
LOG(IC_{50})	1.276	1.352	1.471
HILLSLOPE	-0.8933	-2.257	-1.378
IC_{50}	18.87	22.5	29.59
Std. Error			
LOG(IC_{50})	0.06402	0.01827	0.03359
HILLSLOPE	0.1288	0.1983	0.1557
95% Confidence Intervals			
LOG(IC_{50})	1.136 to 1.415	1.311 to 1.393	1.396 to 1.546
HILLSLOPE	-1.174 to -0.6126	-2.699 to -1.815	-1.725 to -1.031
IC_{50}	13.69 to 26.02	20.49 to 24.71	24.90 to 35.15
Goodness of Fit			
Degrees of Freedom	12	10	10
R^2	0.8951	0.9844	0.9532
Absolute Sum of Squares	0.001766	0.0002785	0.0004617
Standard Deviation of Residuals	0.01213	0.005277	0.006795
Constraints			
BOTTOM	BOTTOM = 0.0	BOTTOM = 0.0	BOTTOM = 0.0
TOP	TOP = 0.1420	TOP = 0.1210	TOP = 0.1210
Data			
Number of X values	7	6	6
Number of Y replicates	2	2	2
Total number of values	14	12	12
Number of missing values	0	0	0

Table S8: Statistical analysis for the inhibition of chymotryptic-like activity of purified human 20S proteasome **(Quinolines 36 to 38)**

Selectivity of Quinoline 25

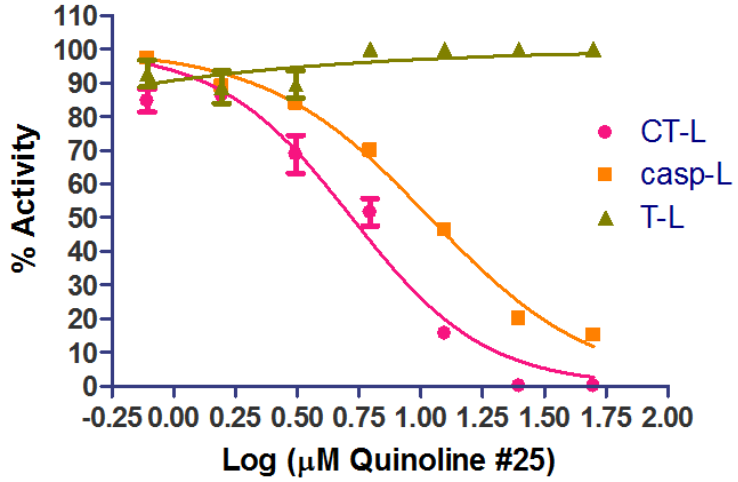
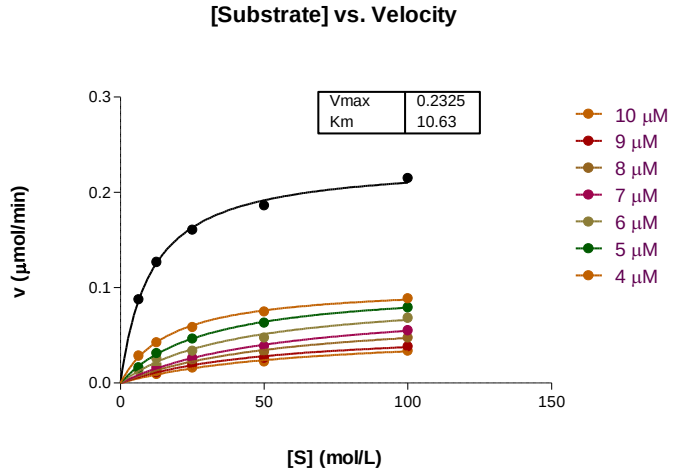
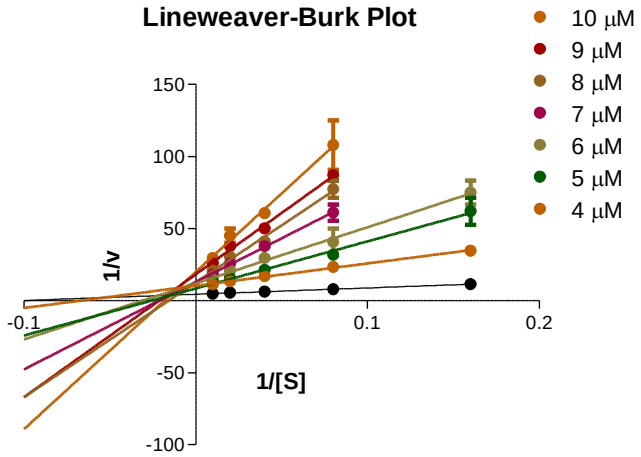


Figure S6: Quinoline **25** inhibits CT-L and Casp-L activity of the human proteasome. Fluorogenic substrates Suc-LLVY-AMC, Z-AAR-AMC and Z-LLE-AMC were used to measure CT-L, T-L and Casp-L activities of purified human 20S proteasome particles.

	CT-L	Casp-L	T-L
Sigmoidal dose-response (variable slope)			
Best-fit values			
BOTTOM	0	0	0
TOP	100	100	100
LOGEC50	0.7207	1.036	-1.92
HILLSLOPE	-1.612	-1.321	0.5137
IC50	5.256	10.87	**N/A**
Std. Error			
LOGIC50	0.03724	0.0181	1.292
HILLSLOPE	0.1995	0.06836	0.3109
95% Confidence Intervals			
LOGIC50	0.6395 to 0.8018	0.9967 to 1.076	-4.799 to 0.9583
HILLSLOPE	-2.047 to -1.178	-1.470 to -1.173	-0.1791 to 1.206
IC50	4.360 to 6.336	9.924 to 11.90	1.588e-005 to 9.085
Goodness of Fit			
Degrees of Freedom	12	12	10
R^2	0.9614	0.9903	0.3769
Absolute Sum of Squares	682.8	130.1	256.2
Standard Deviations of Residuals	7.543	3.293	5.061
Constraints			
BOTTOM	BOTTOM = 0.0	BOTTOM = 0.0	BOTTOM = 0.0
TOP	TOP = 100.0	TOP = 100.0	TOP = 100.0
Data			
Number of X values	25	25	25
Number of Y replicates	2	2	2
Total number of values	14	14	12
Number of missing values	36	36	38

Table S9: Statistical analysis for the inhibition of chymotryptic-like activity of purified human 20S proteasome. Quinoline **25** inhibits CT-L activity (IC_{50} = 5.26 μM) and Casp-L activity (IC_{50} = 10.87 μM), but not the T-L activities of the 20S catalytic core (IC_{50} = >25 μM).





	vehicle	10 µM	9 µM	8 µM	7 µM	6 µM	5 µM	4 µM
Michaelis-Menten [2]								
Best-fit values								
Vmax	0.2325	0.05414	0.05692	0.07422	0.08625	0.09304	0.1029	0.1030
Km	10.63	62.16	50.57	56.60	57.02	40.24	29.98	17.54
Std. Error								
Vmax	0.01587	0.008683	0.004206	0.006322	0.007711	0.009881	0.004568	0.003059
Km	2.601	19.61	7.917	9.805	10.34	9.609	3.308	1.557
95% Confidence Intervals								
Vmax	0.1959 to 0.2691	0.03289 to 0.07539	0.04663 to 0.06721	0.05875 to 0.08969	0.06738 to 0.1051	0.07026 to 0.1158	0.09235 to 0.1134	0.09590 to 0.1100
Km	4.633 to 16.63	14.18 to 110.1	31.20 to 69.94	32.61 to 80.59	31.72 to 82.32	18.08 to 62.39	22.35 to 37.61	13.95 to 21.13
Goodness of Fit								
Degrees of Freedom	8	6	6	6	6	8	8	8
R square	0.8711	0.9357	0.9799	0.9785	0.9760	0.9465	0.9862	0.9861
Absolute Sum of Squares	0.002912	4.387e-005	1.577e-005	2.837e-005	4.157e-005	0.0001981	6.980e-005	6.514e-005
Sy.x	0.01908	0.002704	0.001621	0.002174	0.002632	0.004977	0.002954	0.002853
Number of points								
Analyzed	10	8	8	8	8	10	10	10

Table S10. Kinetic analysis of quinoline 7 inhibition of purified 20S proteasome. Lineweaver-Burk plot using Suc-LLVY-AMC consistent with a model of "mixed-type inhibition". Proteasome activity was undetectable at the lowest amount of substrate thus these values are omitted in the L-B plot.

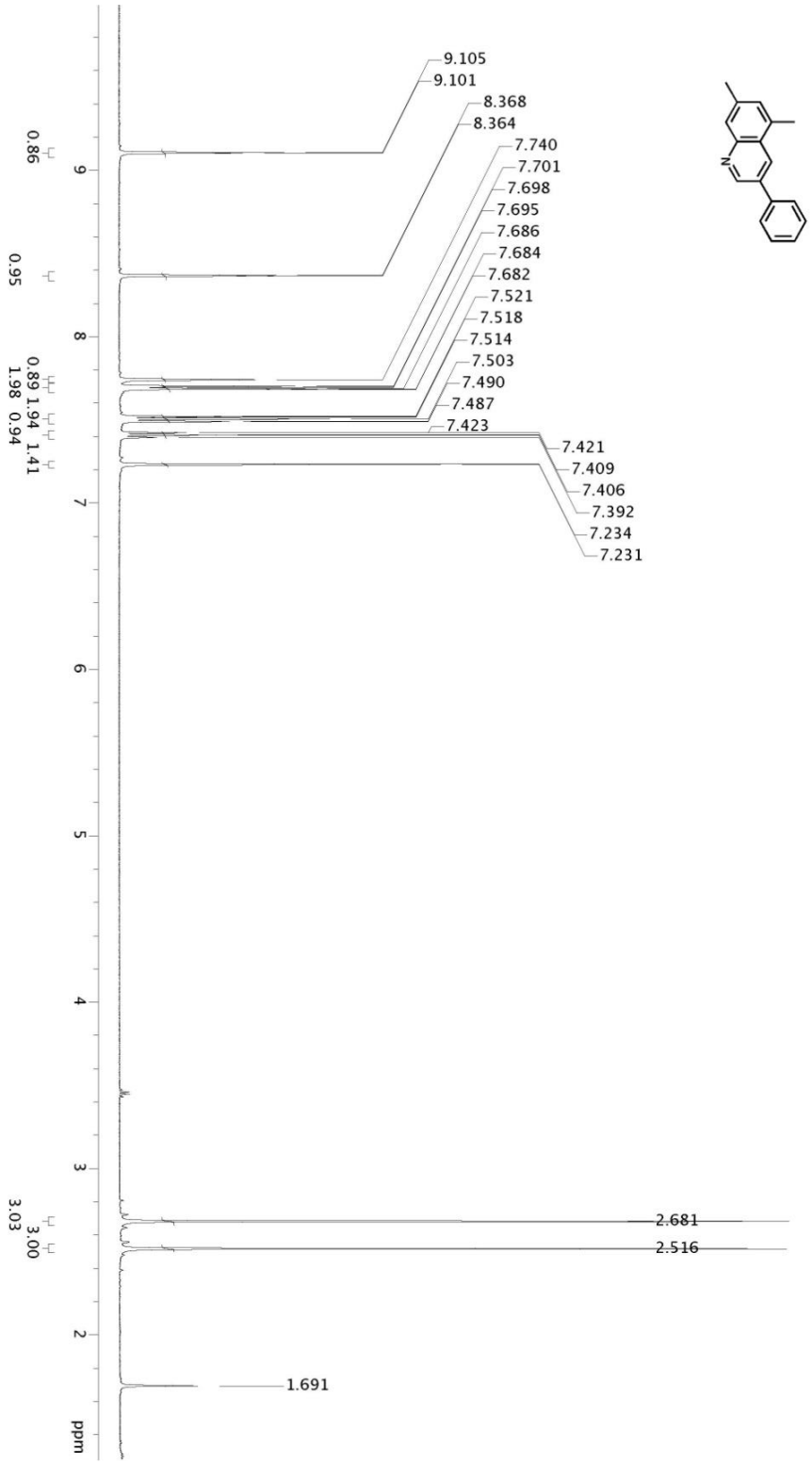


Figure S7: ^{1}H NMR spectrum for compound 5,7-dimethyl-3-phenylquinoline.

(AD104, Quinoline 4)

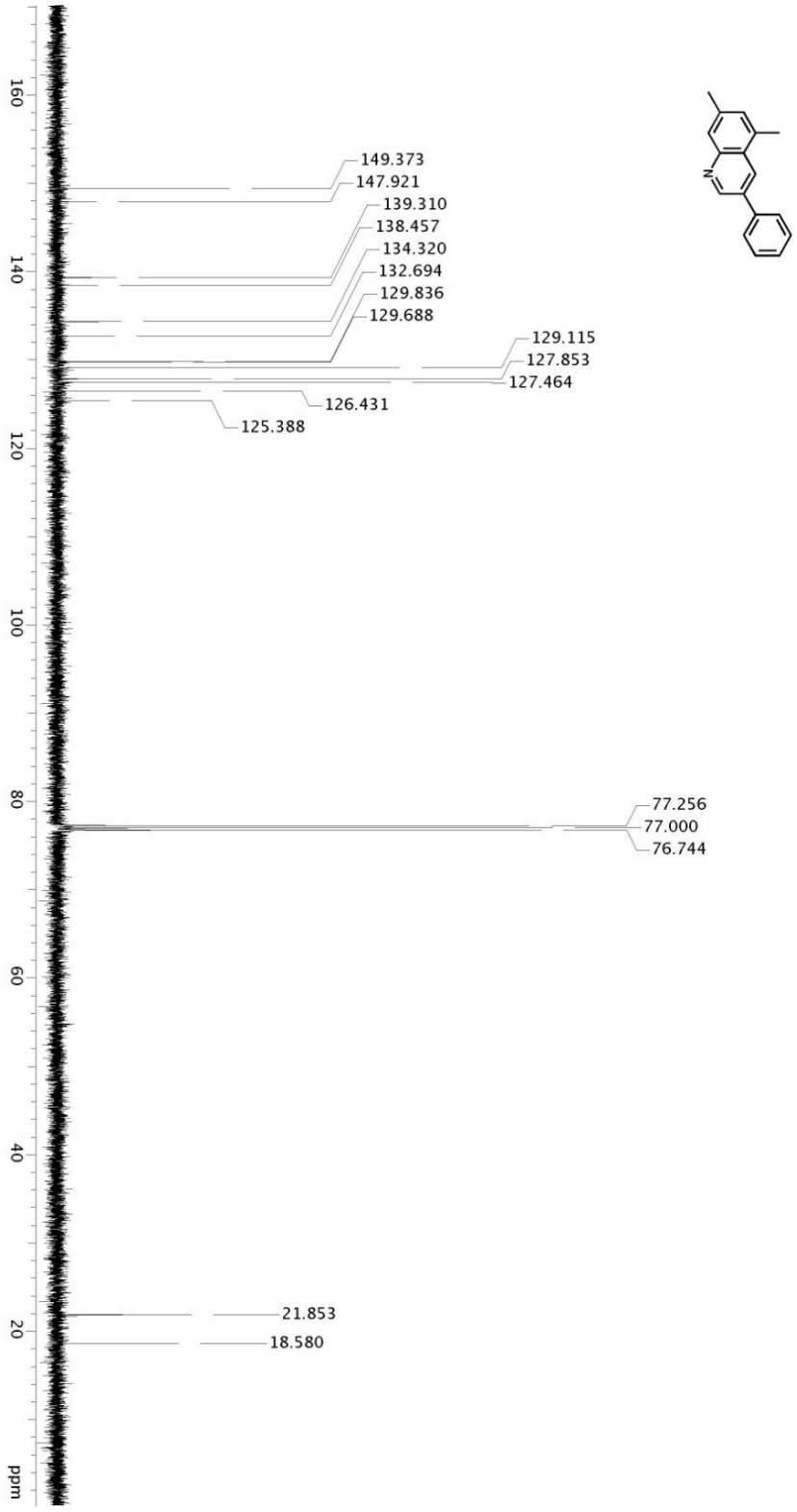


Figure S8: ^{13}C NMR spectrum for compound 5,7-dimethyl-3-phenylquinoline.

(AD104, Quinoline 4)

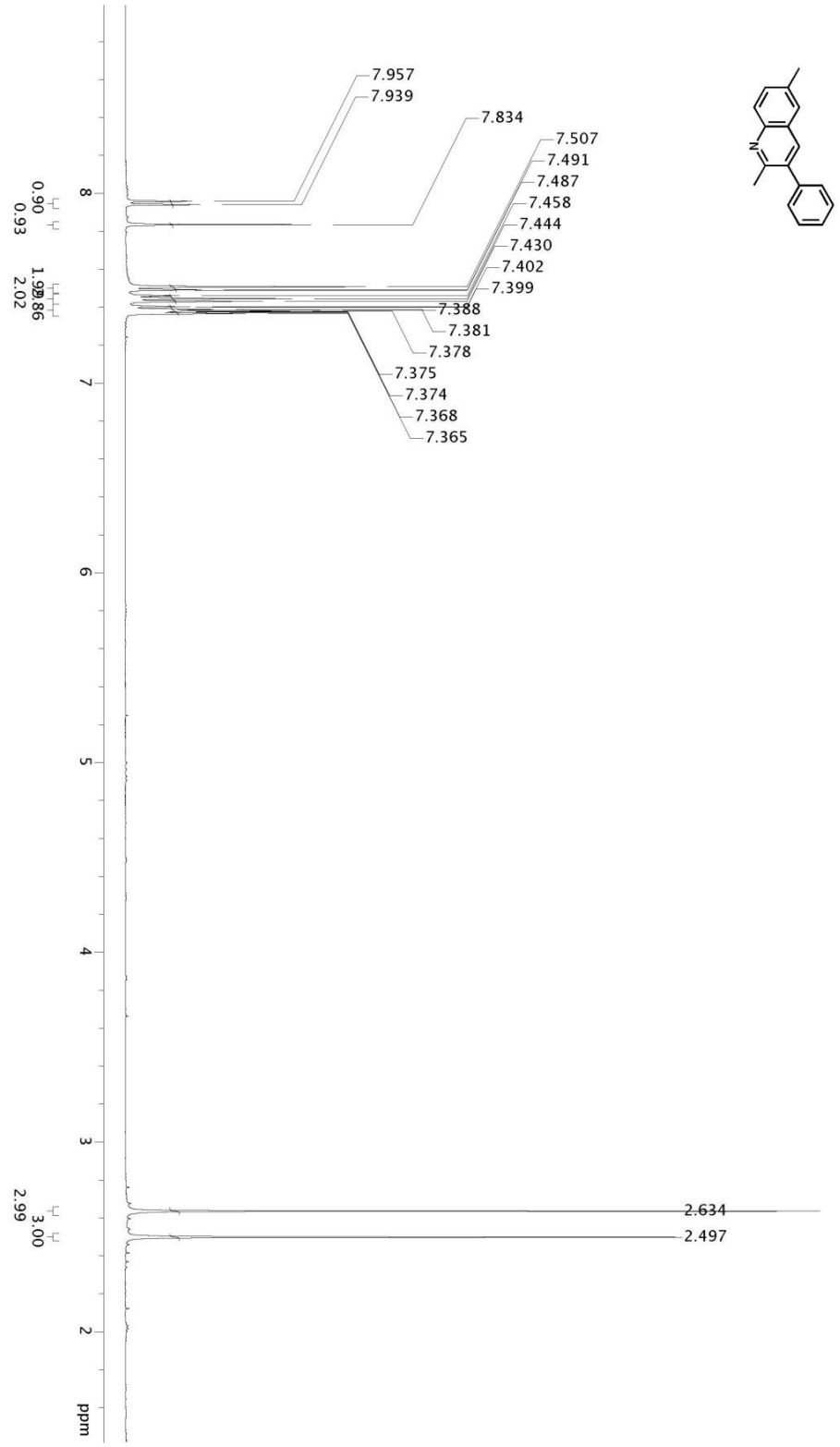


Figure S9: ^{1}H NMR spectrum for compound 2,6-dimethyl-3-phenylquinoline.

(AD108, Quinoline 5)

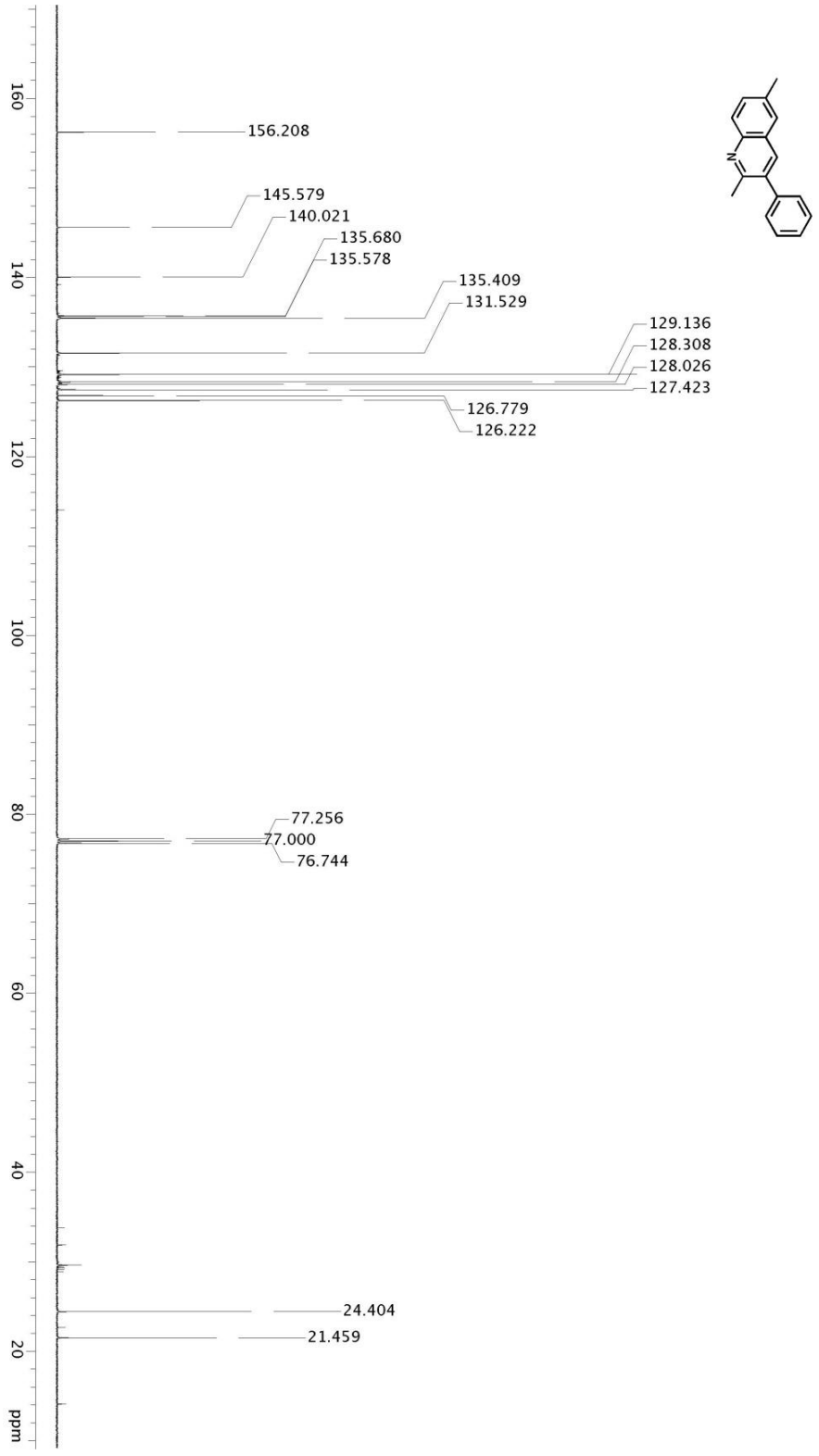


Figure S10: ^{13}C NMR spectrum for compound 2,6-dimethyl-3-phenylquinoline.

(AD108, Quinoline 5)

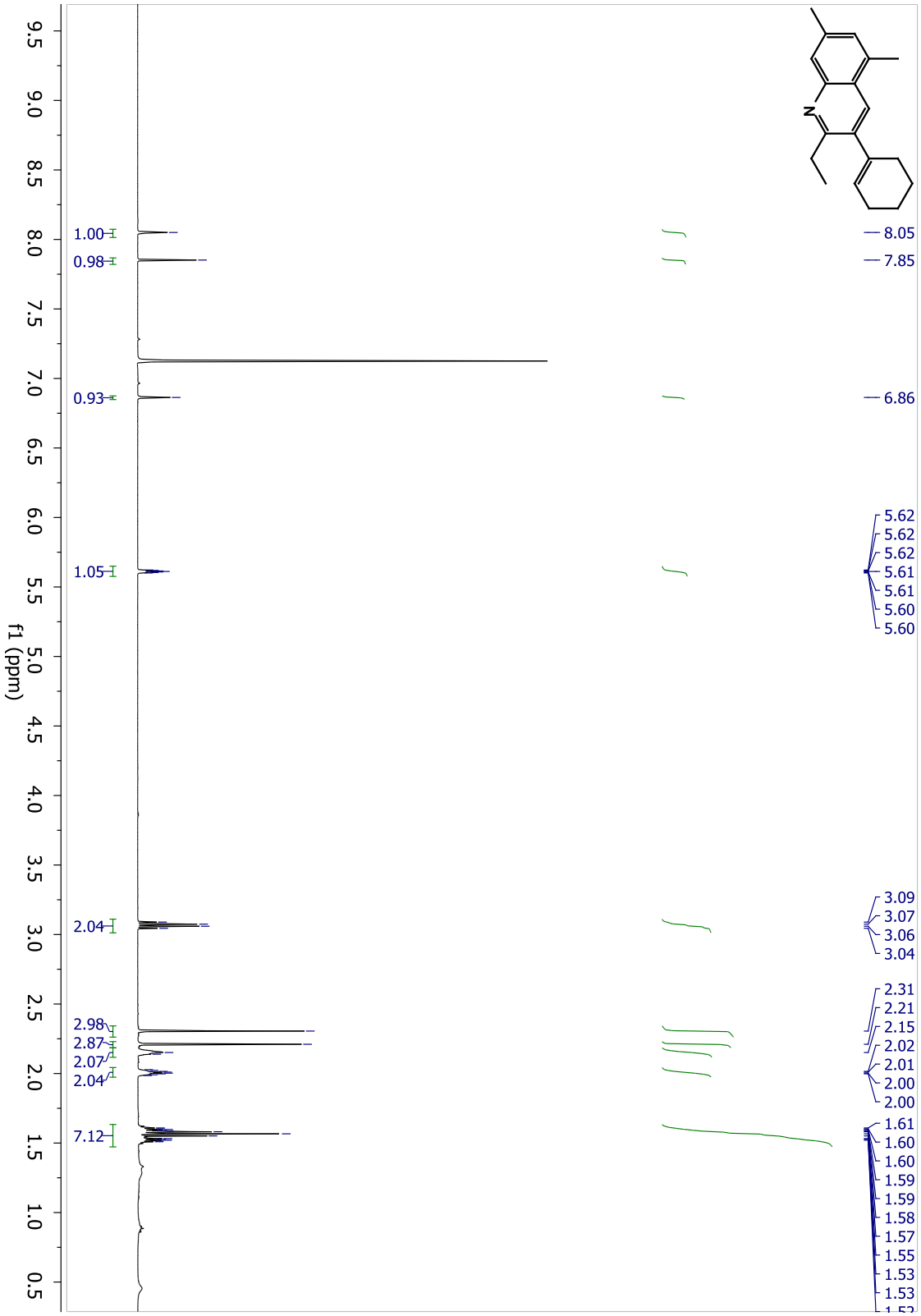


Figure S11: ^{1}H NMR spectrum for compound 2-ethyl-3-cyclohexenyl-5,7-dimethylquinoline.

(**TM-043, Quinoline 8)**

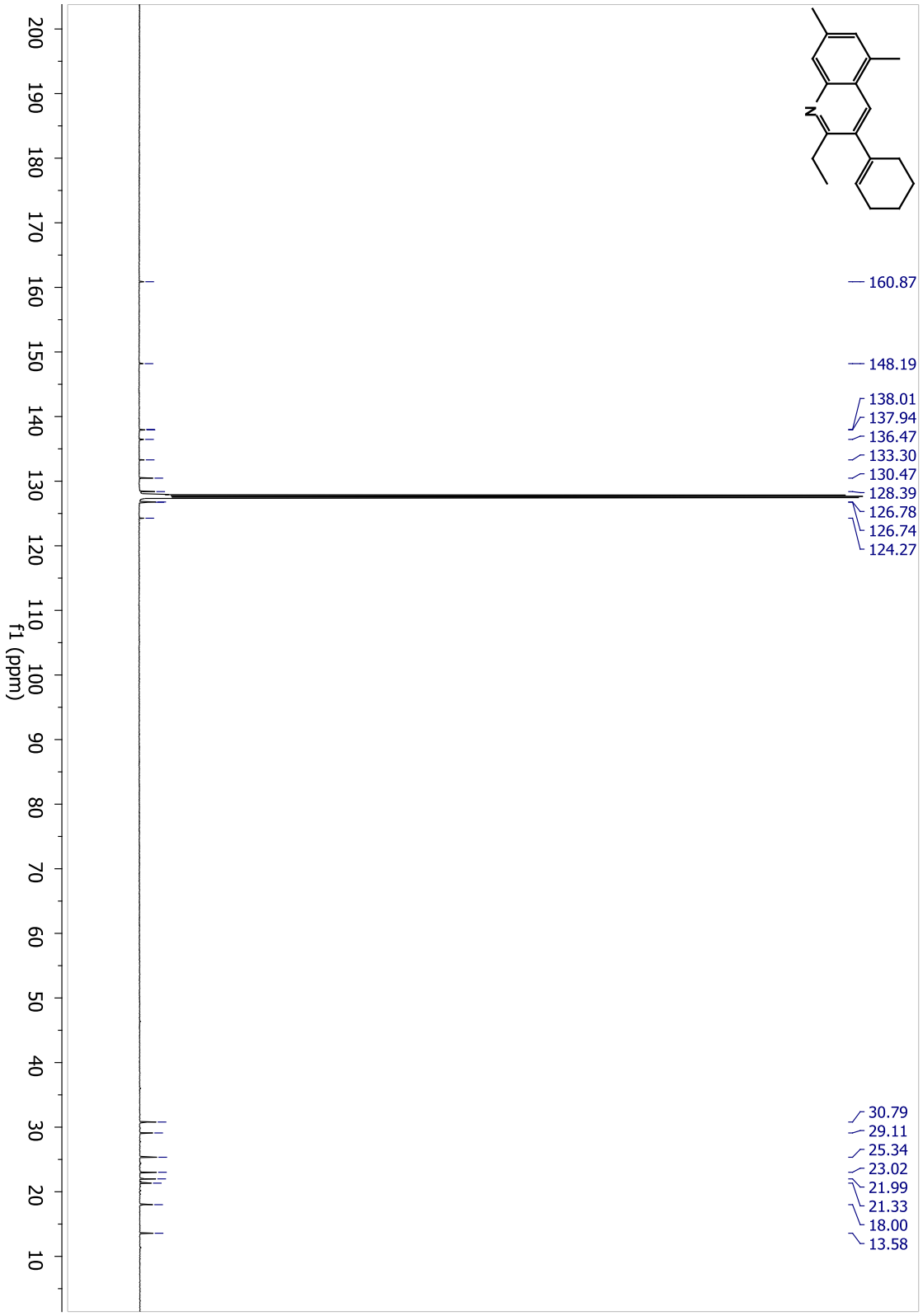


Figure S12: ^{13}C NMR spectrum for compound 2-ethyl-3-cyclohexenyl-5,7-dimethylquinoline.

(**TM-043, Quinoline 8)**

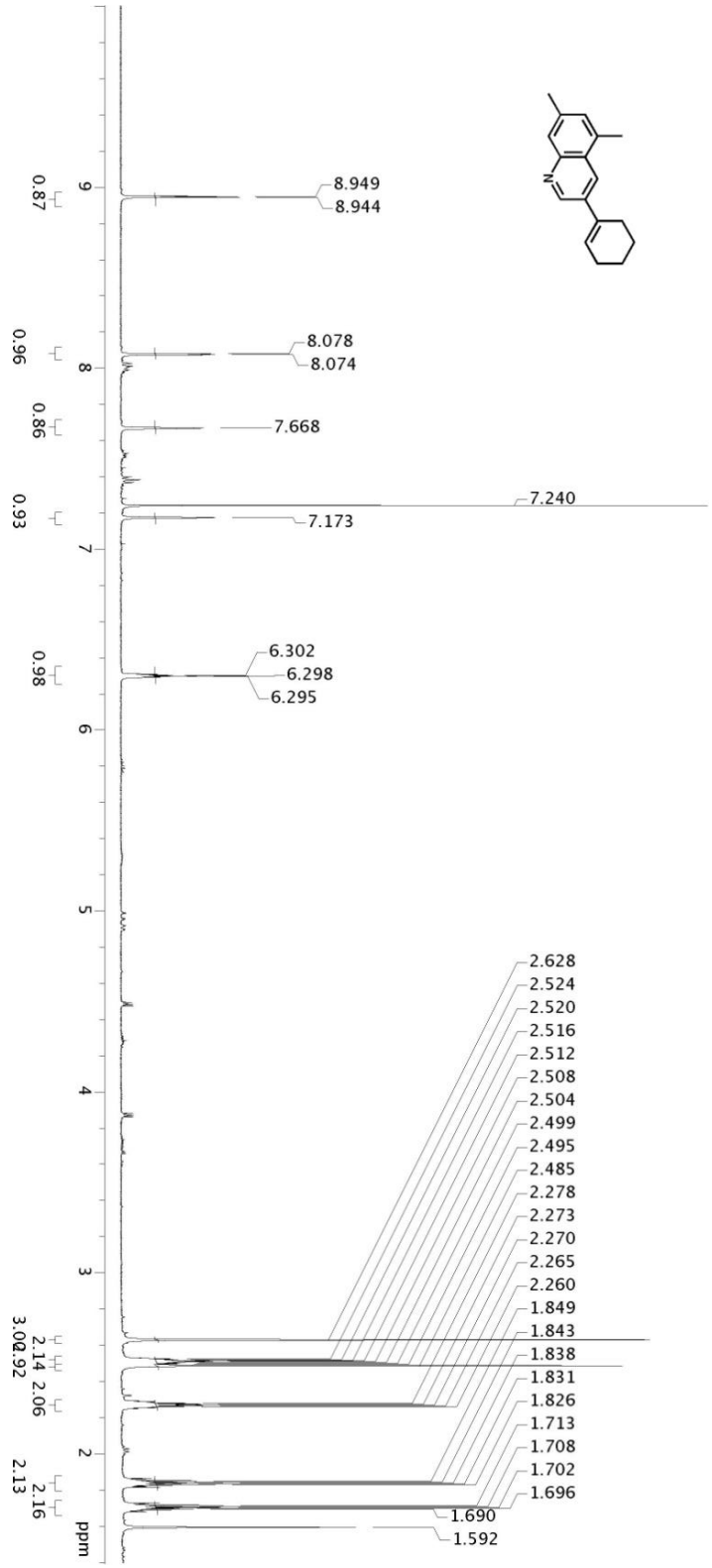


Figure S13: ^{1}H NMR spectrum for compound 3-cyclohexenyl-5,7-dimethylquinoline.

(AD102, Quinoline 9)

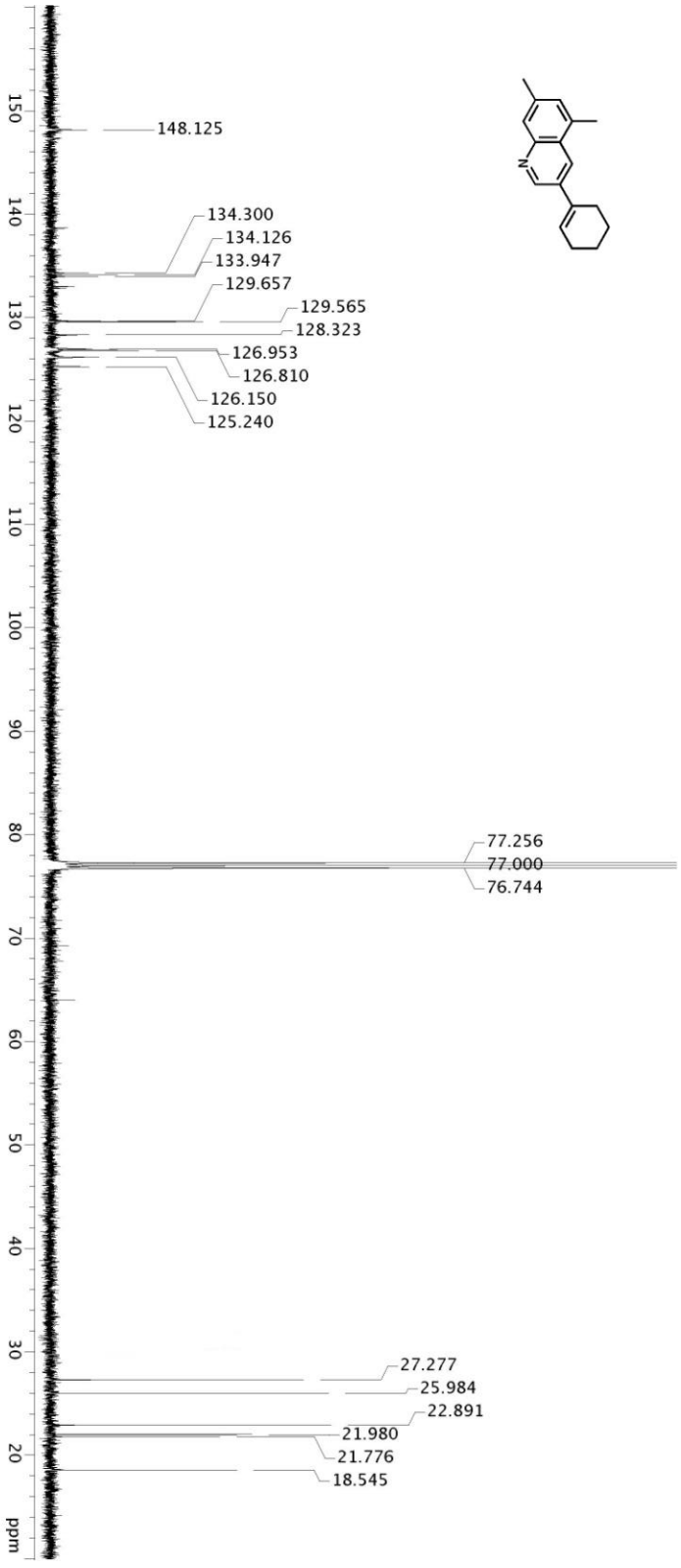


Figure S14: ^{13}C NMR spectrum for compound 3-cyclohexenyl-5,7-dimethylquinoline.

(AD102, Quinoline 9)

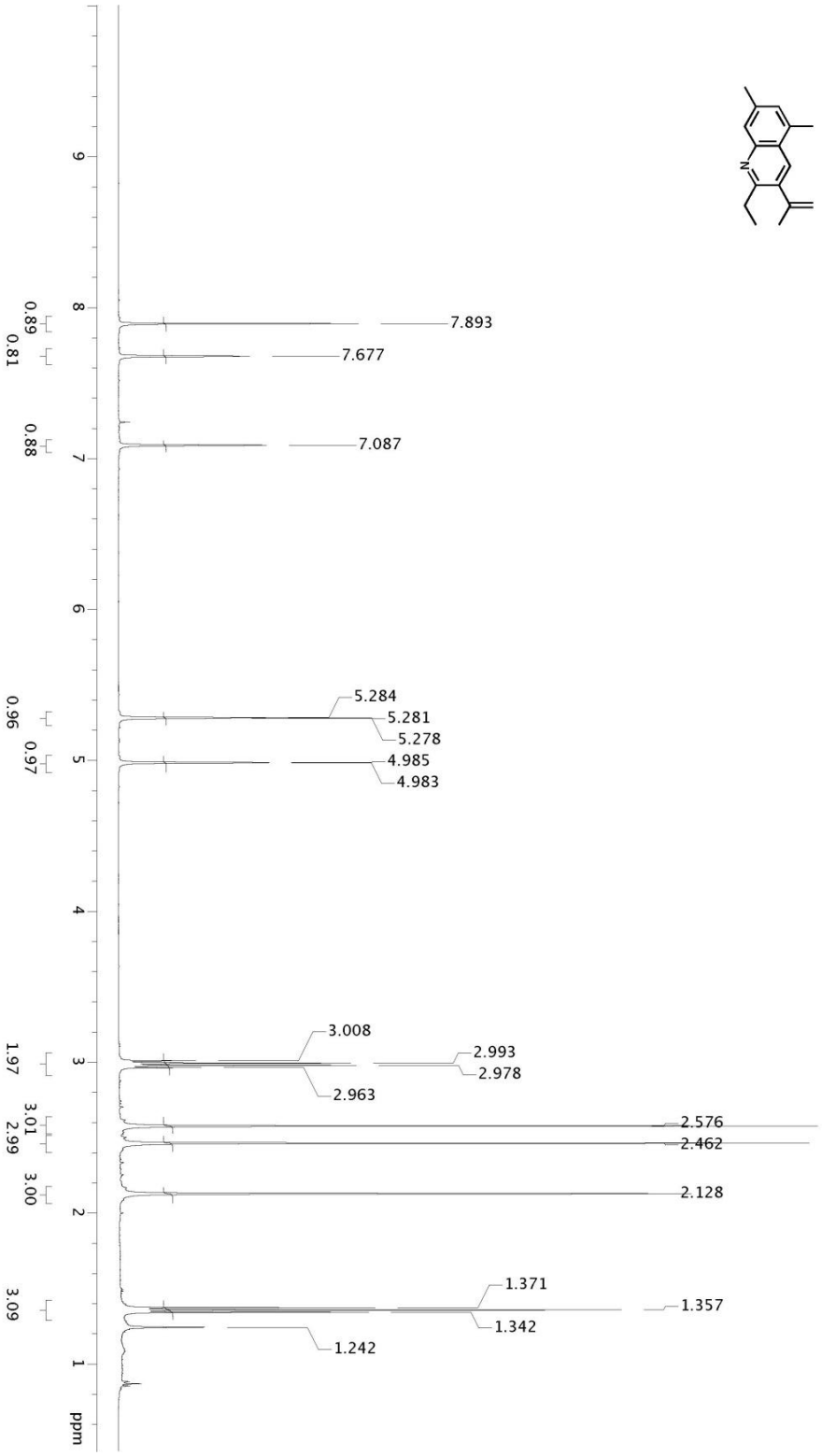


Figure S15: ^{1}H NMR spectrum for compound 2-ethyl-5,7-dimethyl-3-(prop-1-en-2-yl)quinoline.

(AD112, Quinoline 10)

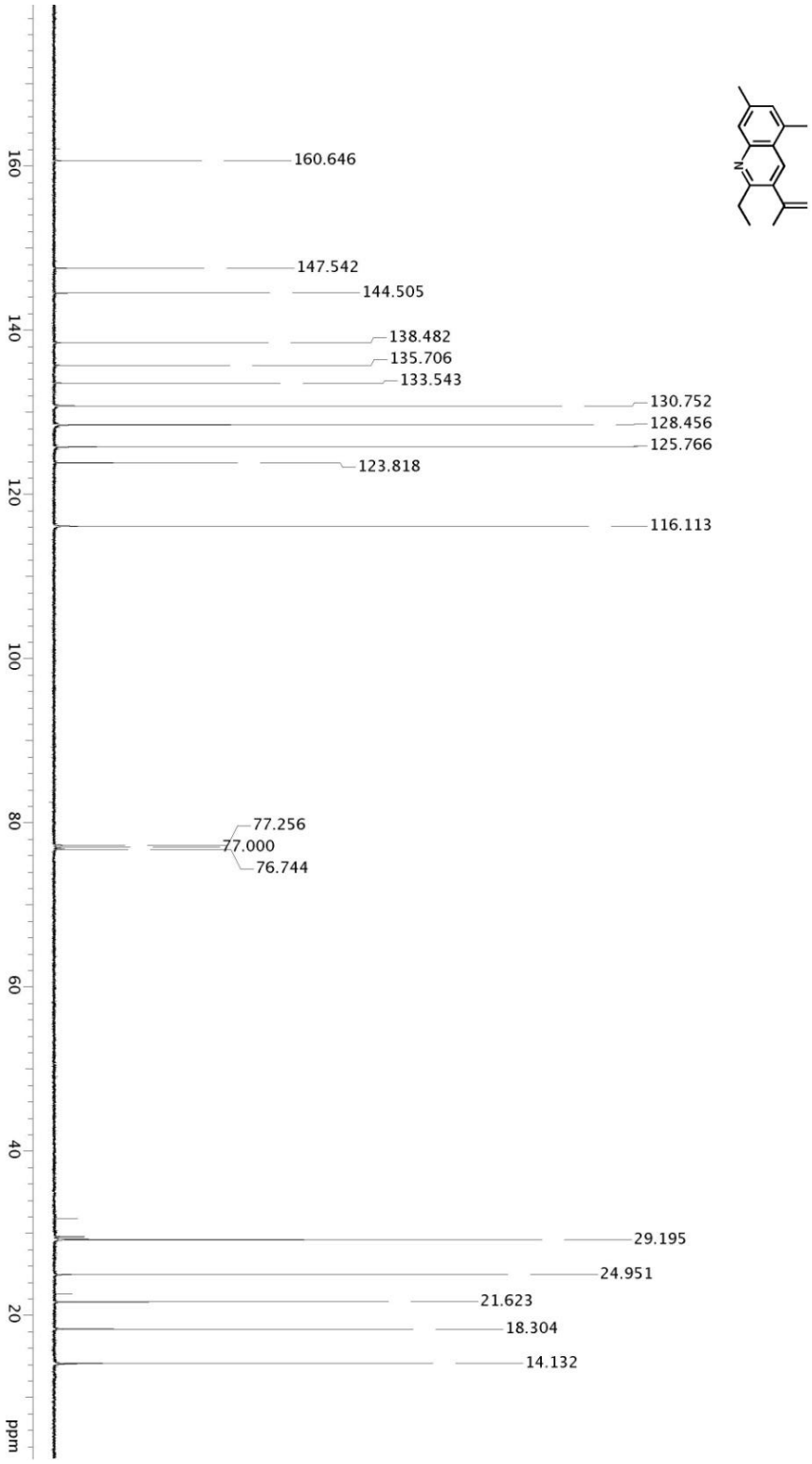


Figure S16: ^{13}C NMR spectrum for compound 2-ethyl-5,7-dimethyl-3-(prop-1-en-2-yl)quinoline.

(AD112, Quinoline 10)

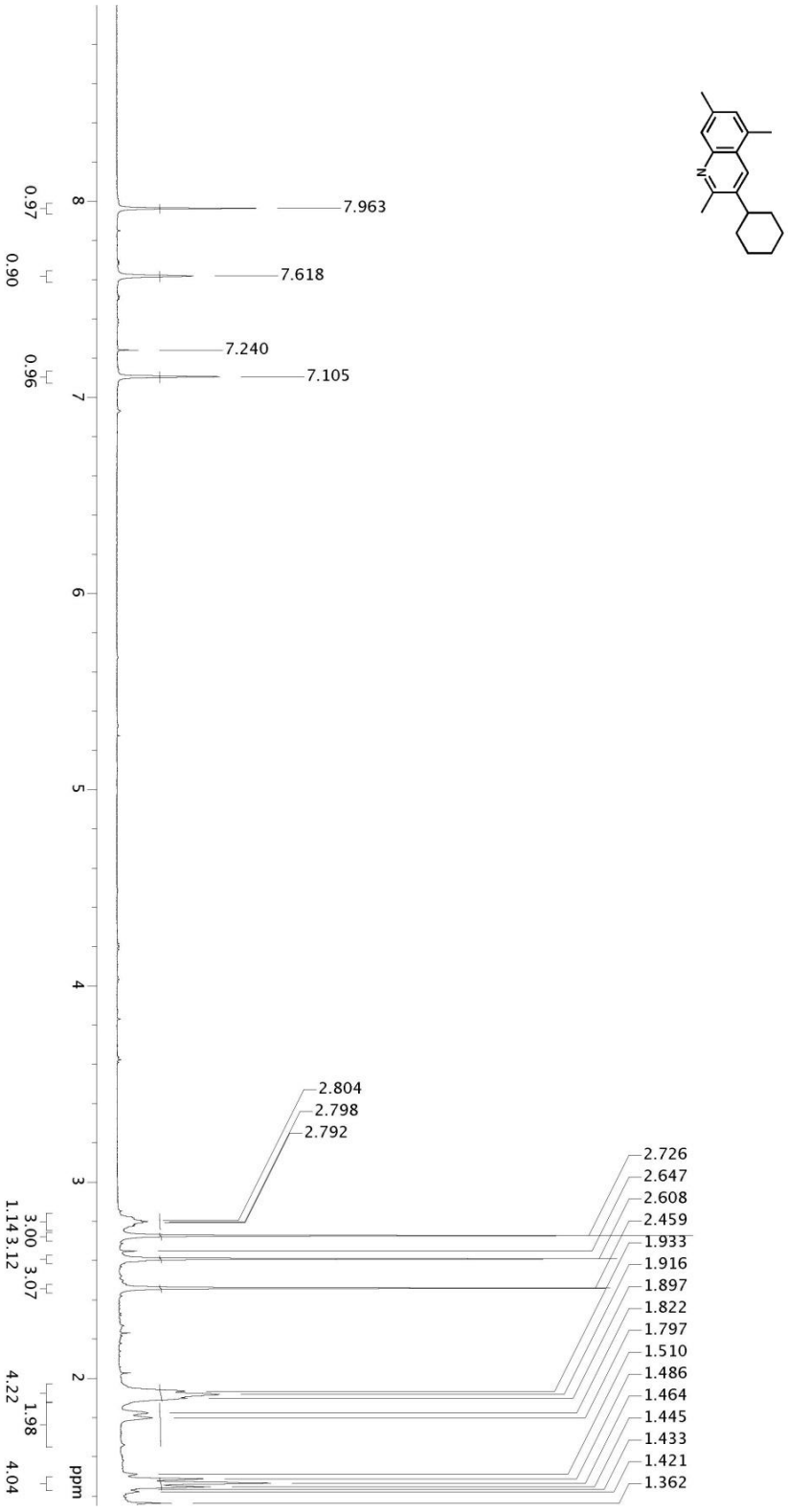


Figure S17: ^{1}H NMR spectrum for compound, 3-cyclohexyl-2,5,7-trimethylquinoline.

(AD109, Quinoline 11)

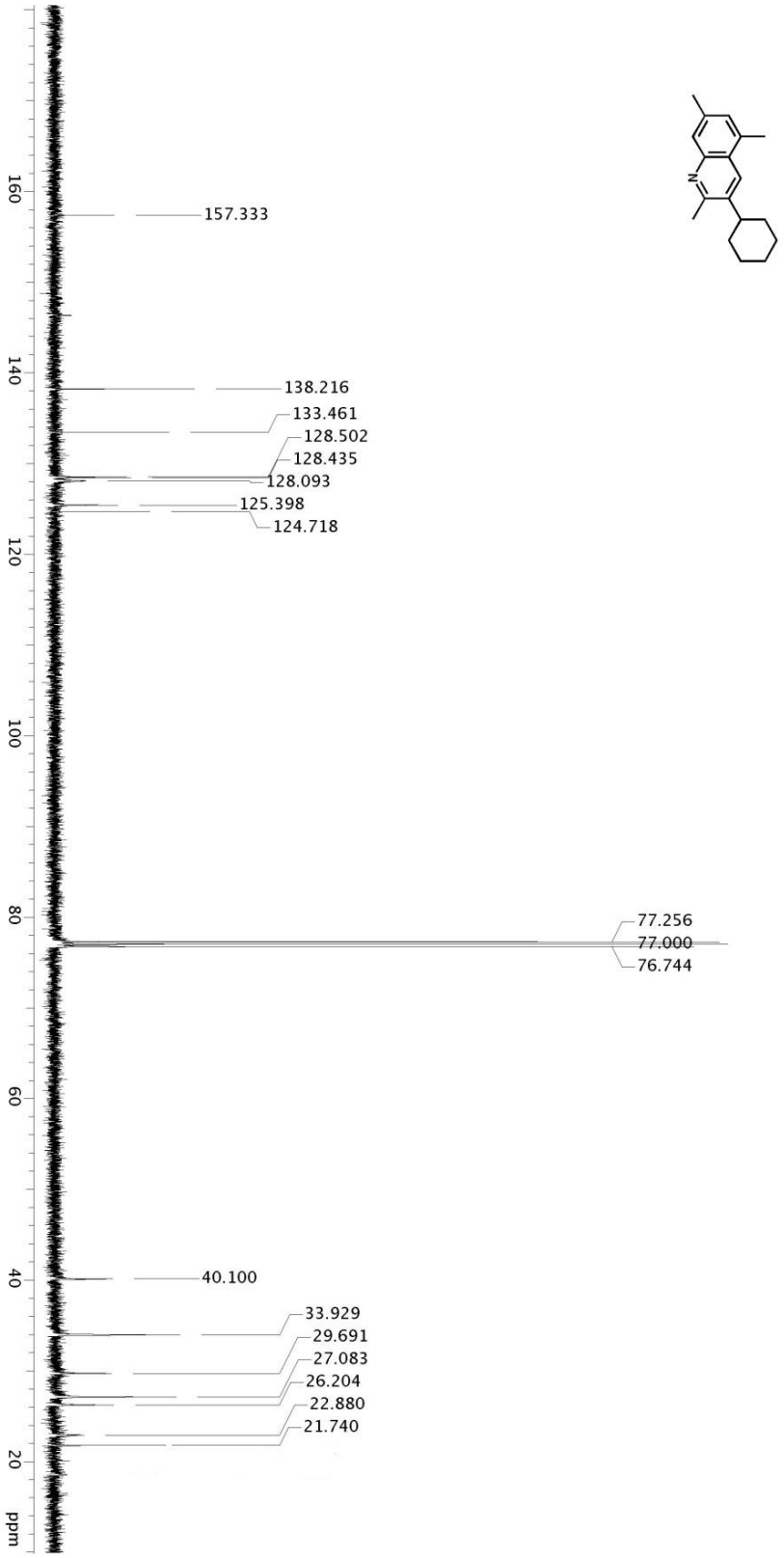


Figure S18: ^{13}C NMR spectrum for compound, 3-cyclohexyl-2,5,7-trimethylquinoline.

(AD109, Quinoline 11)

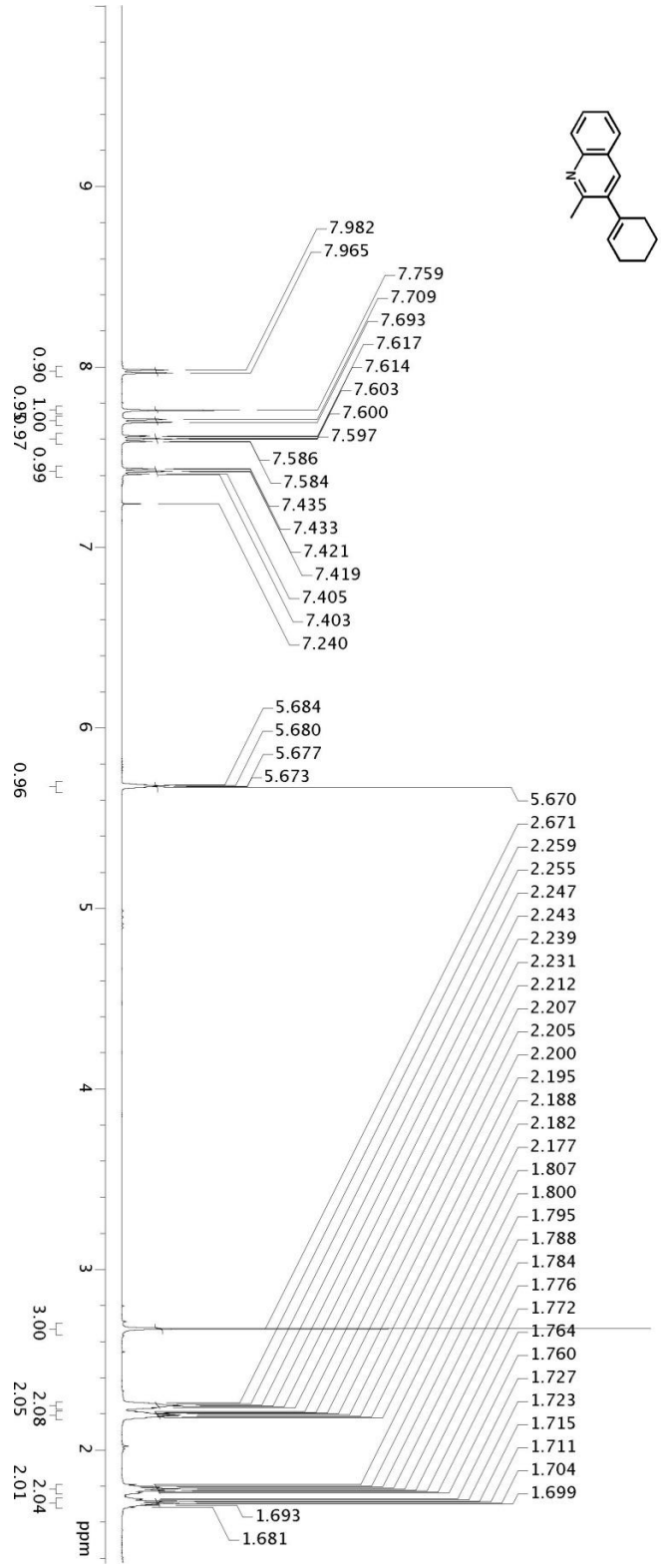


Figure S19: ^{1}H NMR spectrum for compound 3-cyclohexenyl-2-methylquinoline. **(AD100, Quinoline 13)**.

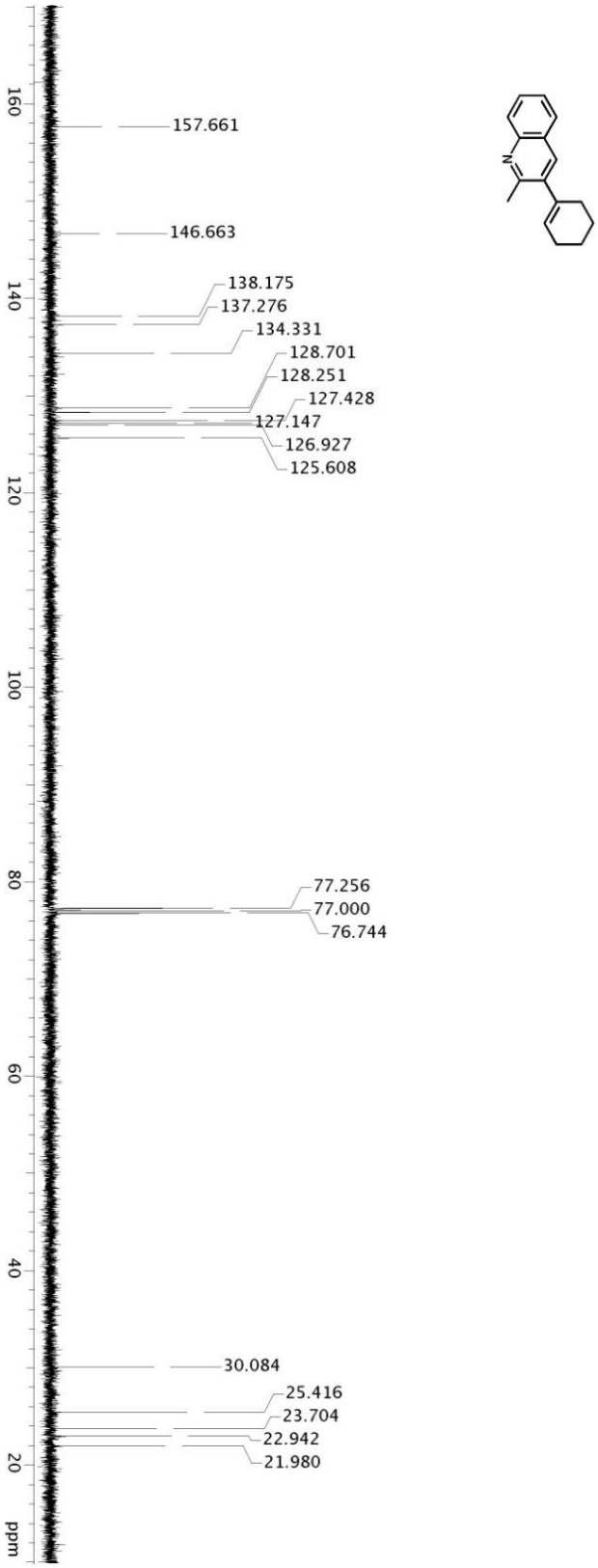


Figure S20: ^{13}C NMR spectrum for compound 3-cyclohexenyl-2-methylquinoline.

(AD100, Quinoline 13)

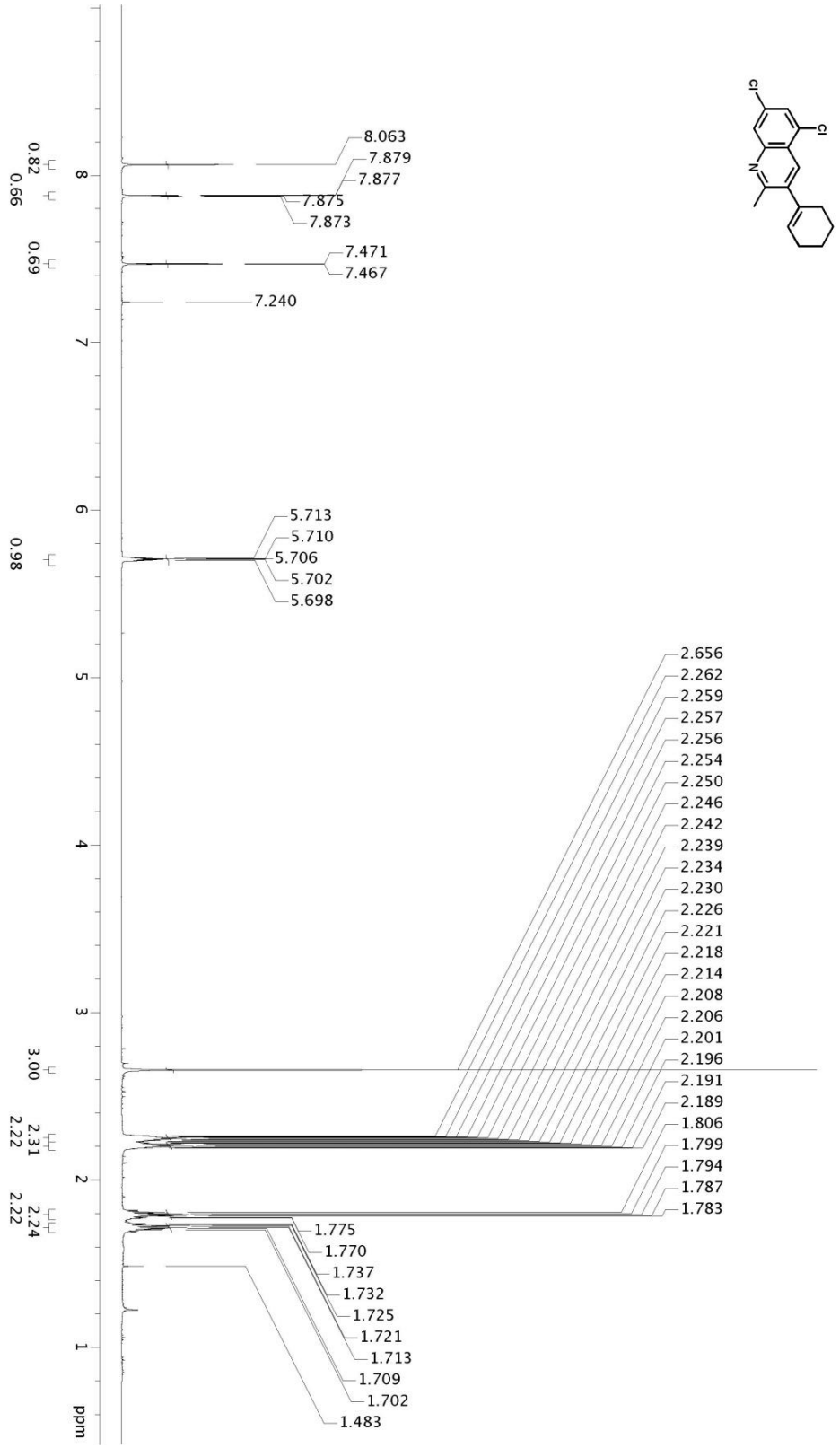


Figure S21: ^{1}H NMR spectrum for compound 5,7-dichloro-3-cyclohexenyl-2-methylquinoline.

(AD115, Quinoline 14)

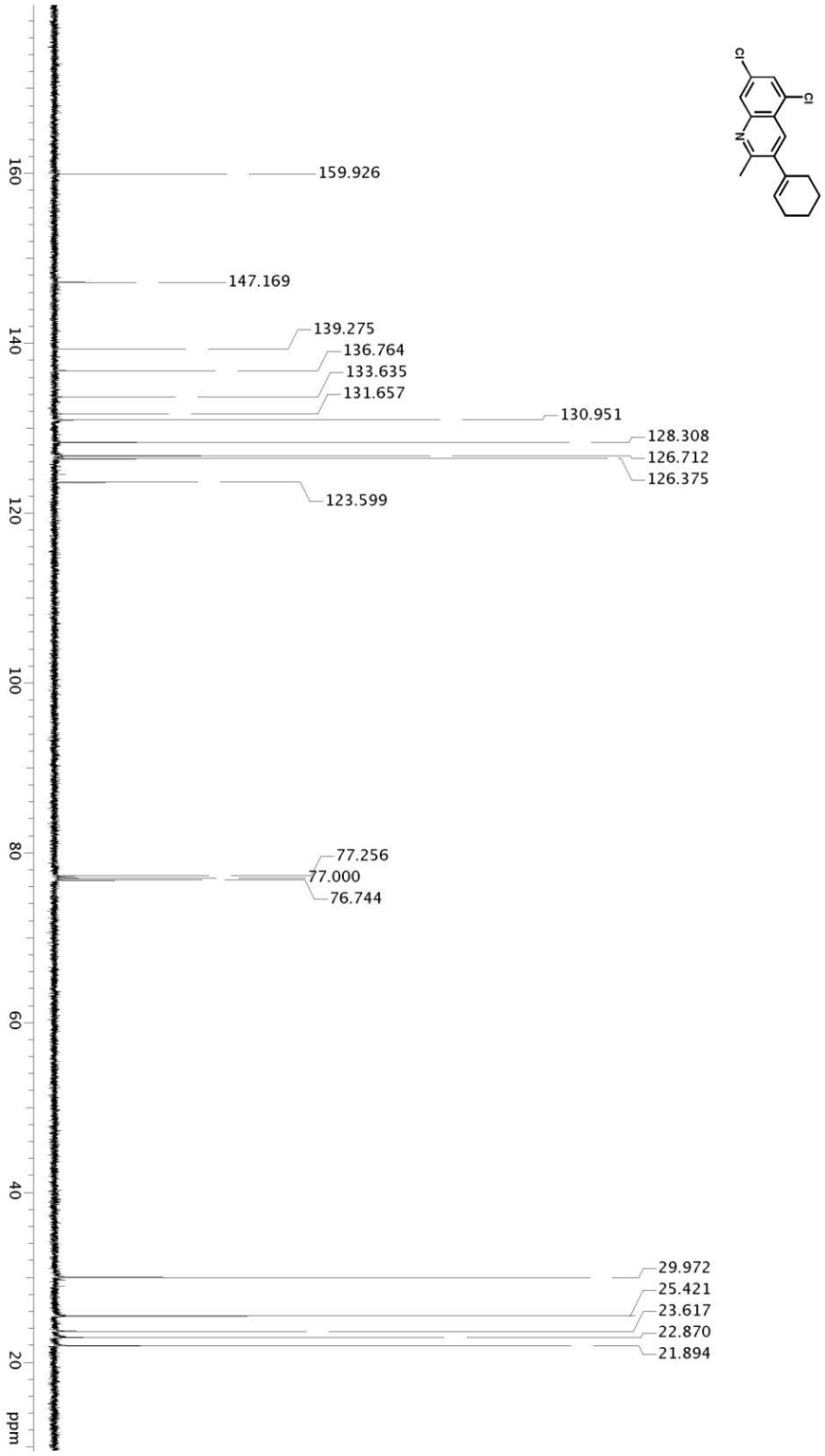


Figure S22: ^{13}C NMR spectrum for compound 5,7-dichloro-3-cyclohexenyl-2-methylquinoline.

(AD115, Quinoline 14)

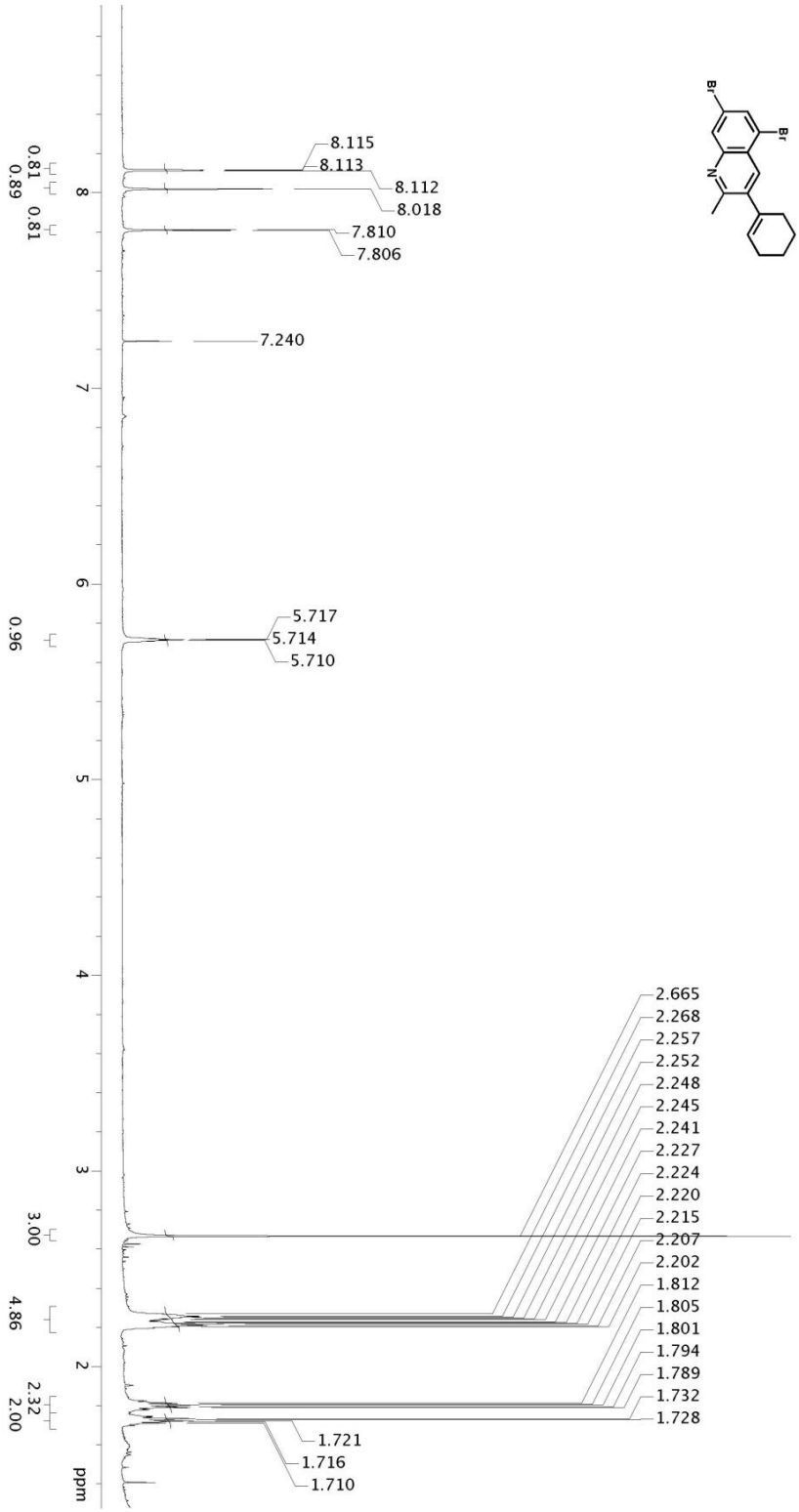


Figure S23:. ^{1}H NMR spectrum for compound 5,7-dibromo-3-cyclohexenyl-2-methylquinoline.

(AD116, Quinoline 15)

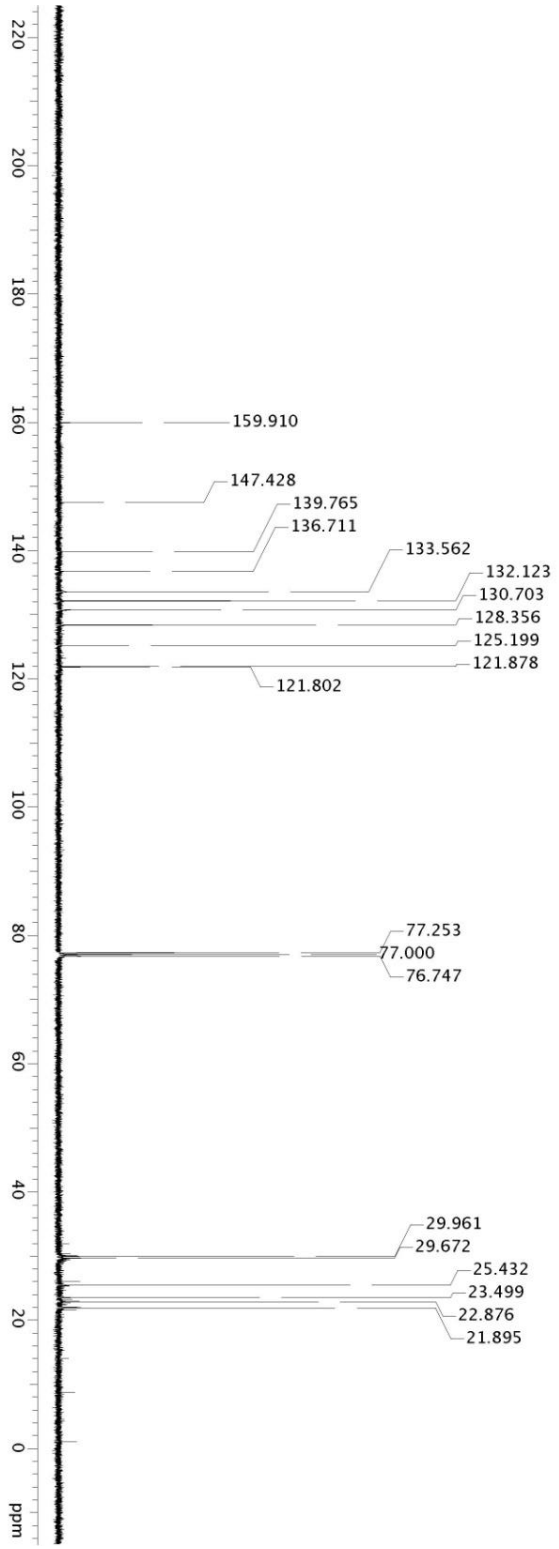


Figure S24: ^{13}C NMR spectrum for compound 5,7-dibromo-3-cyclohexenyl-2-methylquinoline.

(AD116, Quinoline 15)

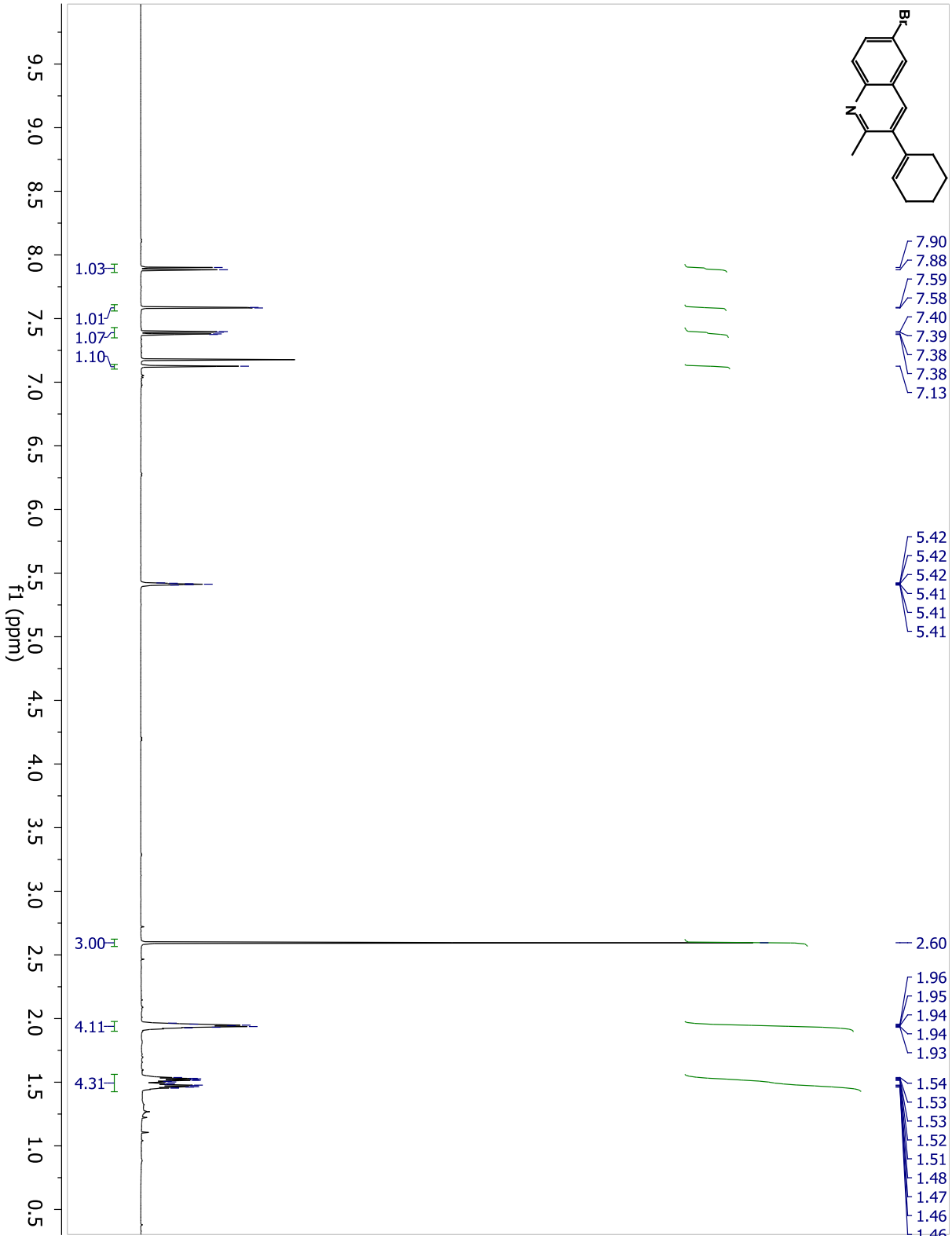


Figure S25: ^{1}H NMR spectrum for compound 6-bromo-3-cyclohexenyl-2-methylquinoline.

(TM127, Quinoline 16)

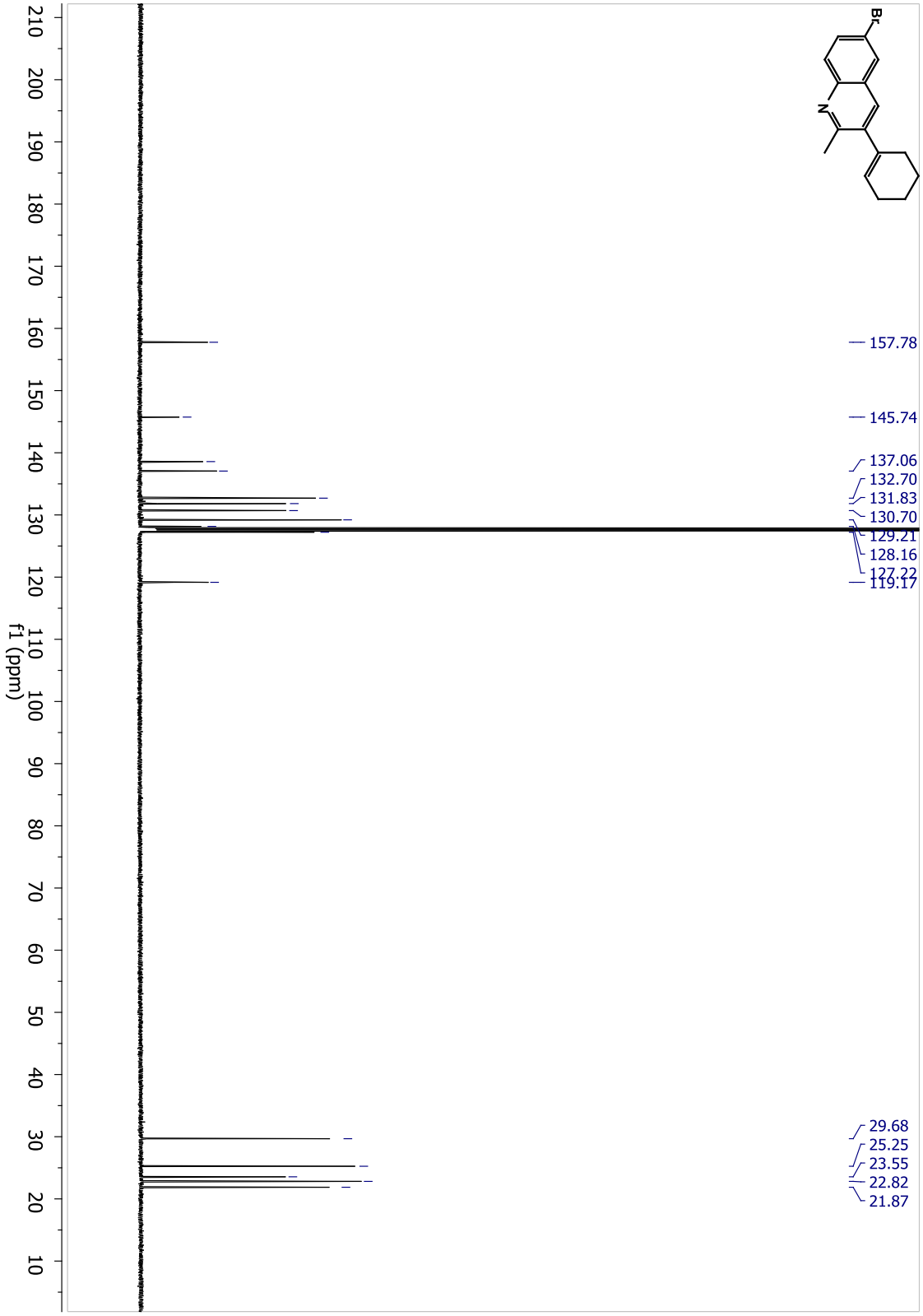


Figure S26: ^{13}C NMR spectrum for compound 6-bromo-3-cyclohexenyl-2-methylquinoline.

(TM127, Quinoline 16)

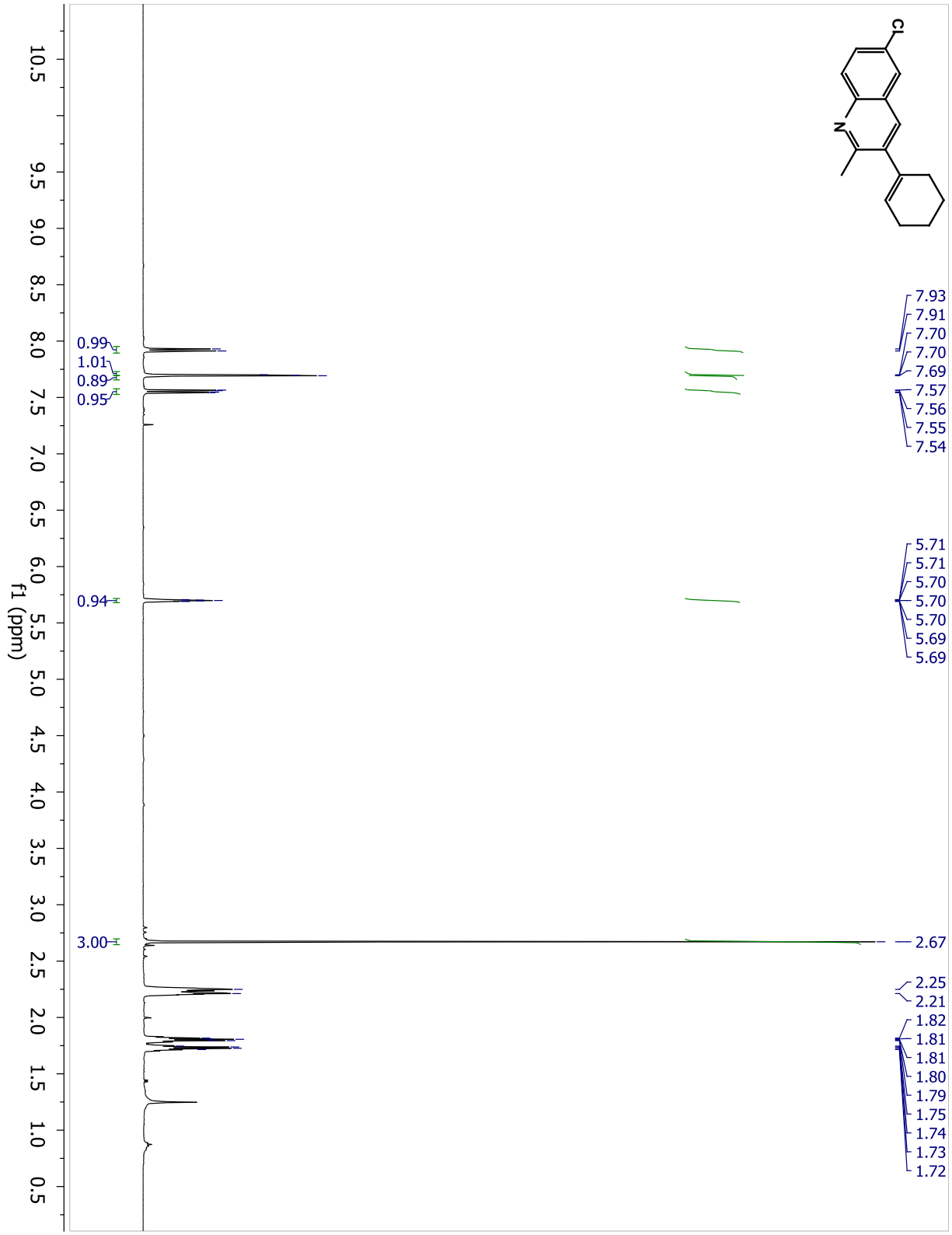


Figure S27: ^{1}H NMR spectrum for compound 6-chloro-3-cyclohexenyl-2-methylquinoline.

(TM-125, Quinoline 17)

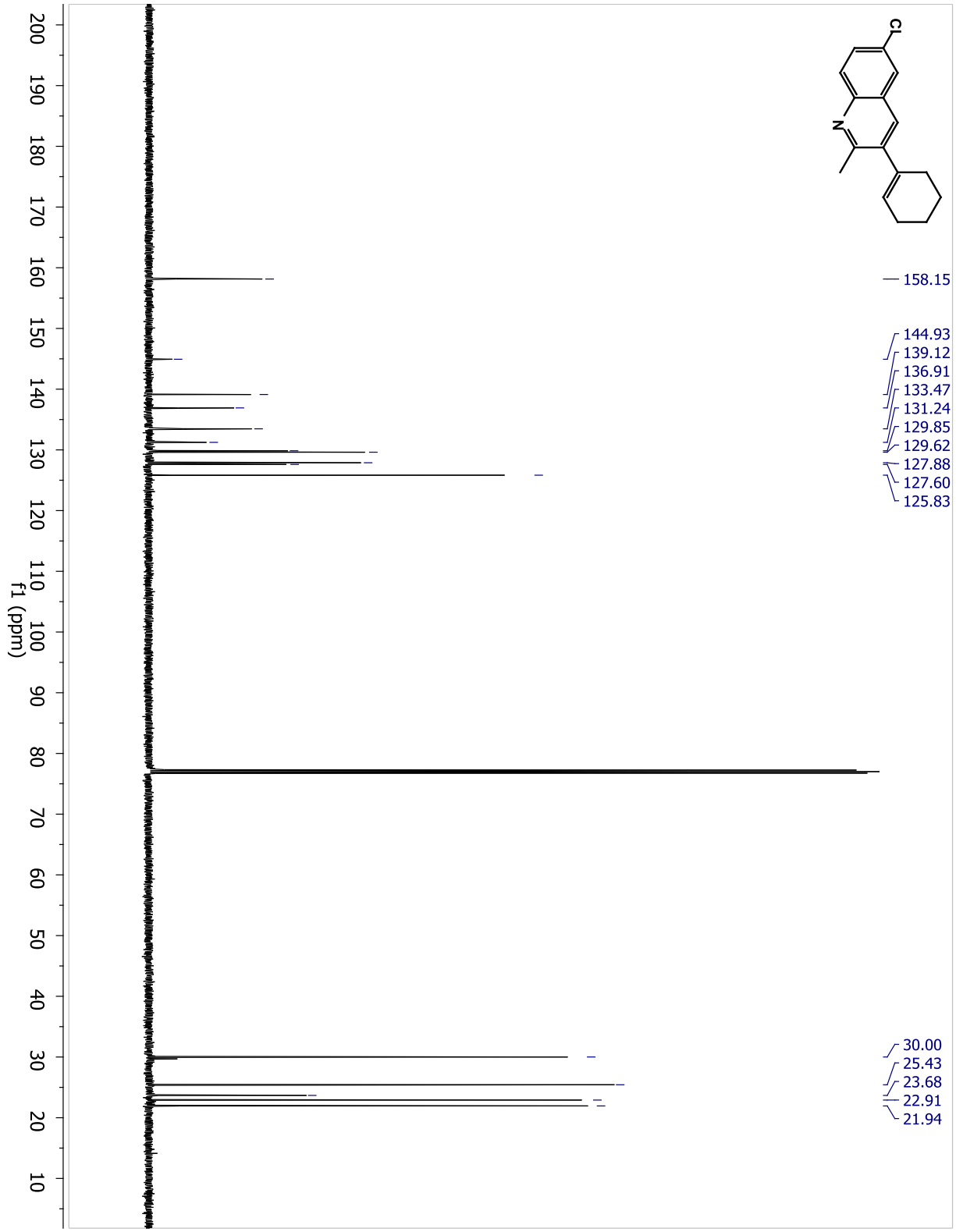


Figure S28: ^{13}C NMR spectrum for compound 6-chloro-3-cyclohexenyl-2-methylquinoline.

(TM-125, Quinoline 17)

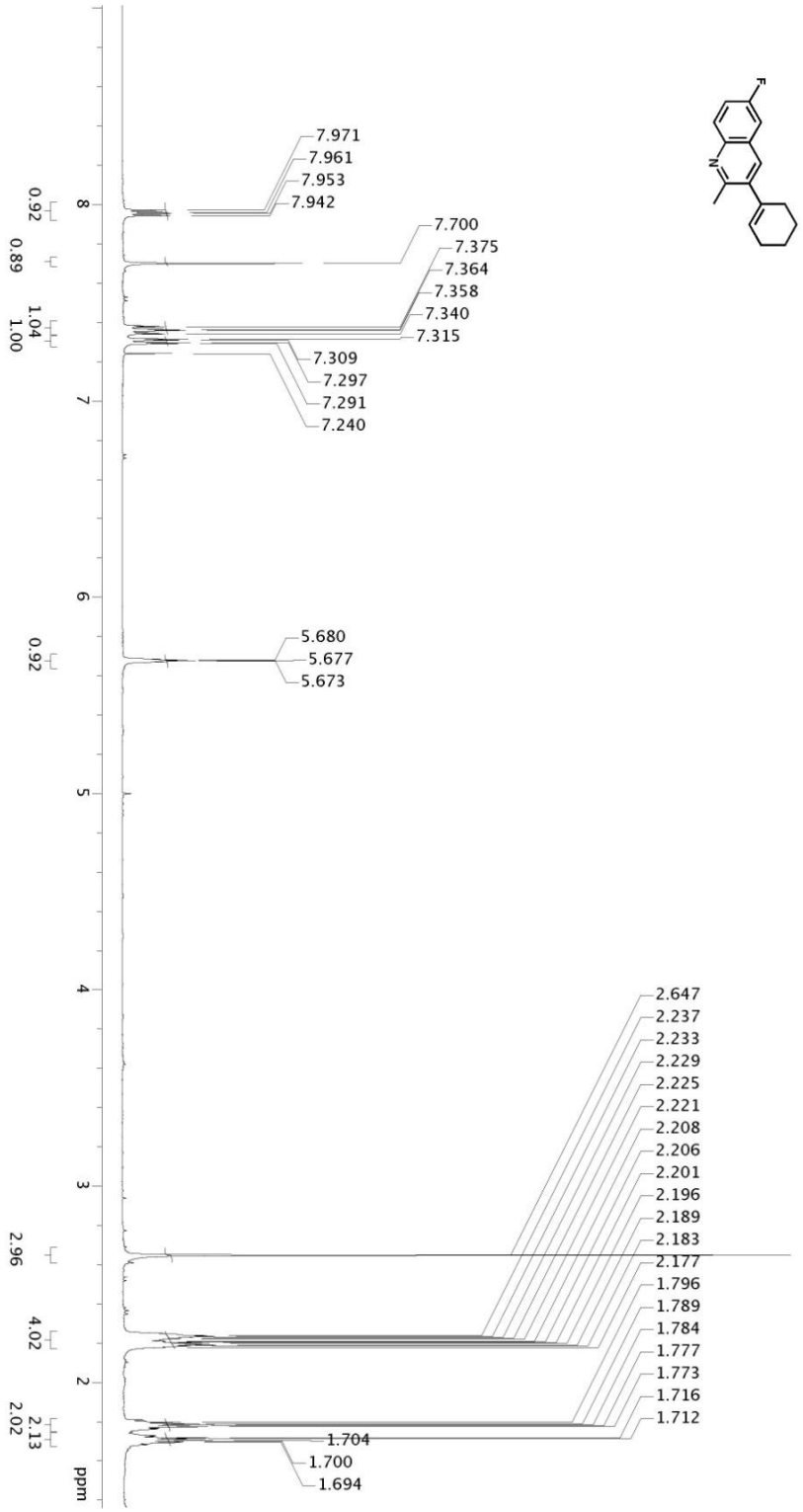


Figure S29: ^{1}H NMR spectrum for compound 3-cyclohexenyl-6-fluoro-2-methylquinoline**.**

(AD118, Quinoline 18).

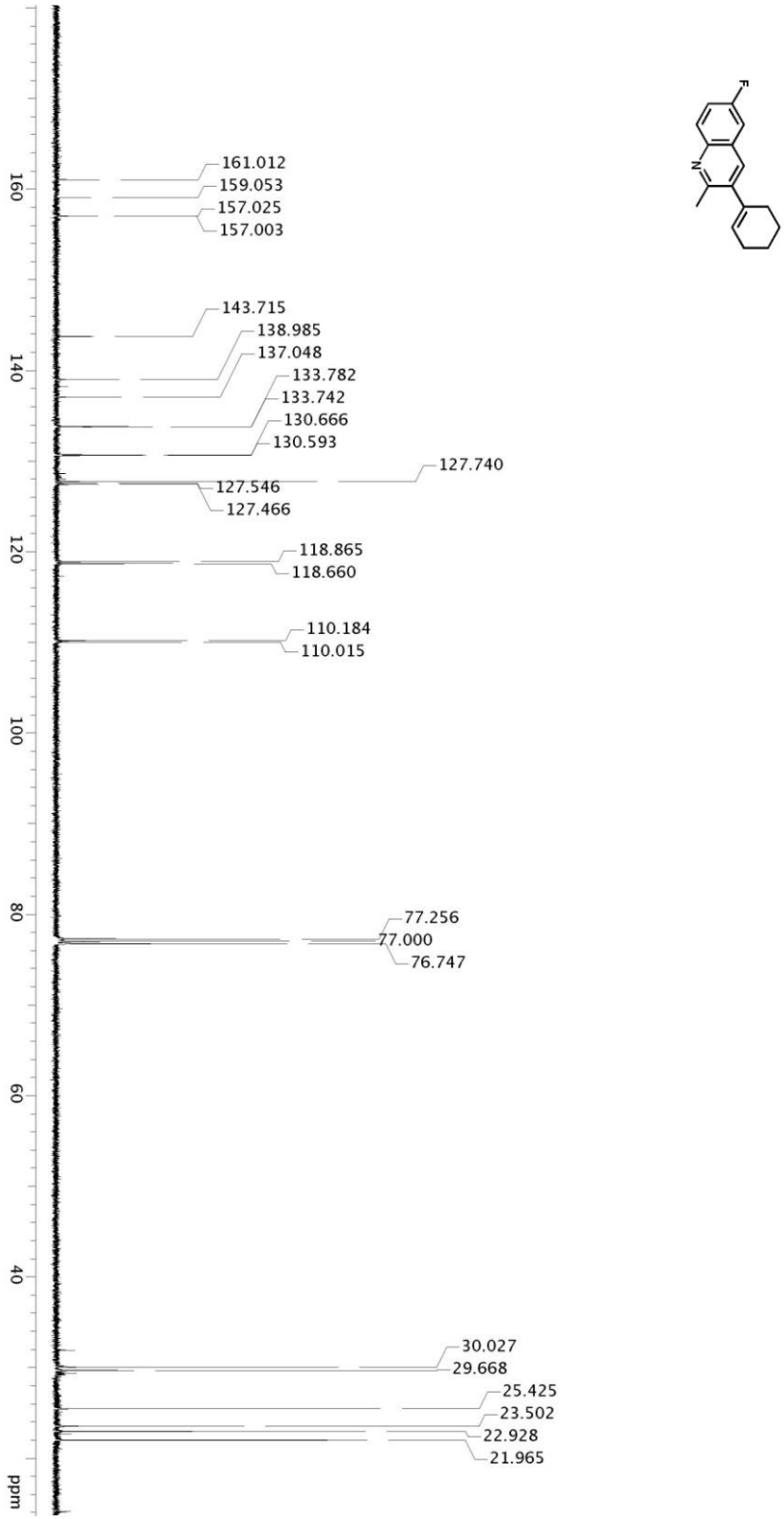


Figure S30: ^{13}C NMR spectrum for compound 3-cyclohexenyl-6-fluoro-2-methylquinoline**.** **(AD118, Quinoline 18)**.

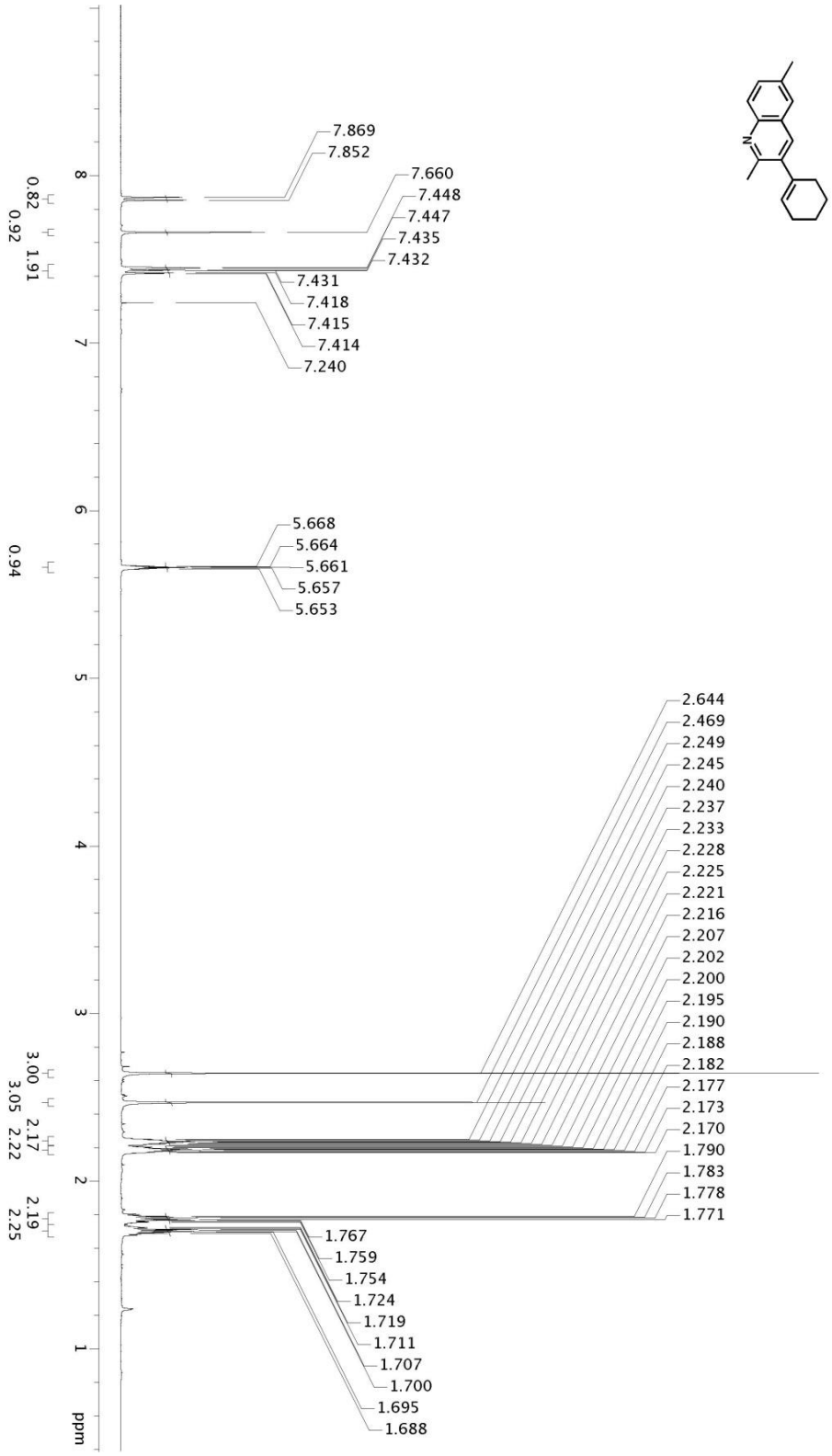


Figure S31: ^{1}H NMR spectrum for compound 3-cyclohexenyl-2,6-dimethylquinoline.

(AD113, Quinoline 19)

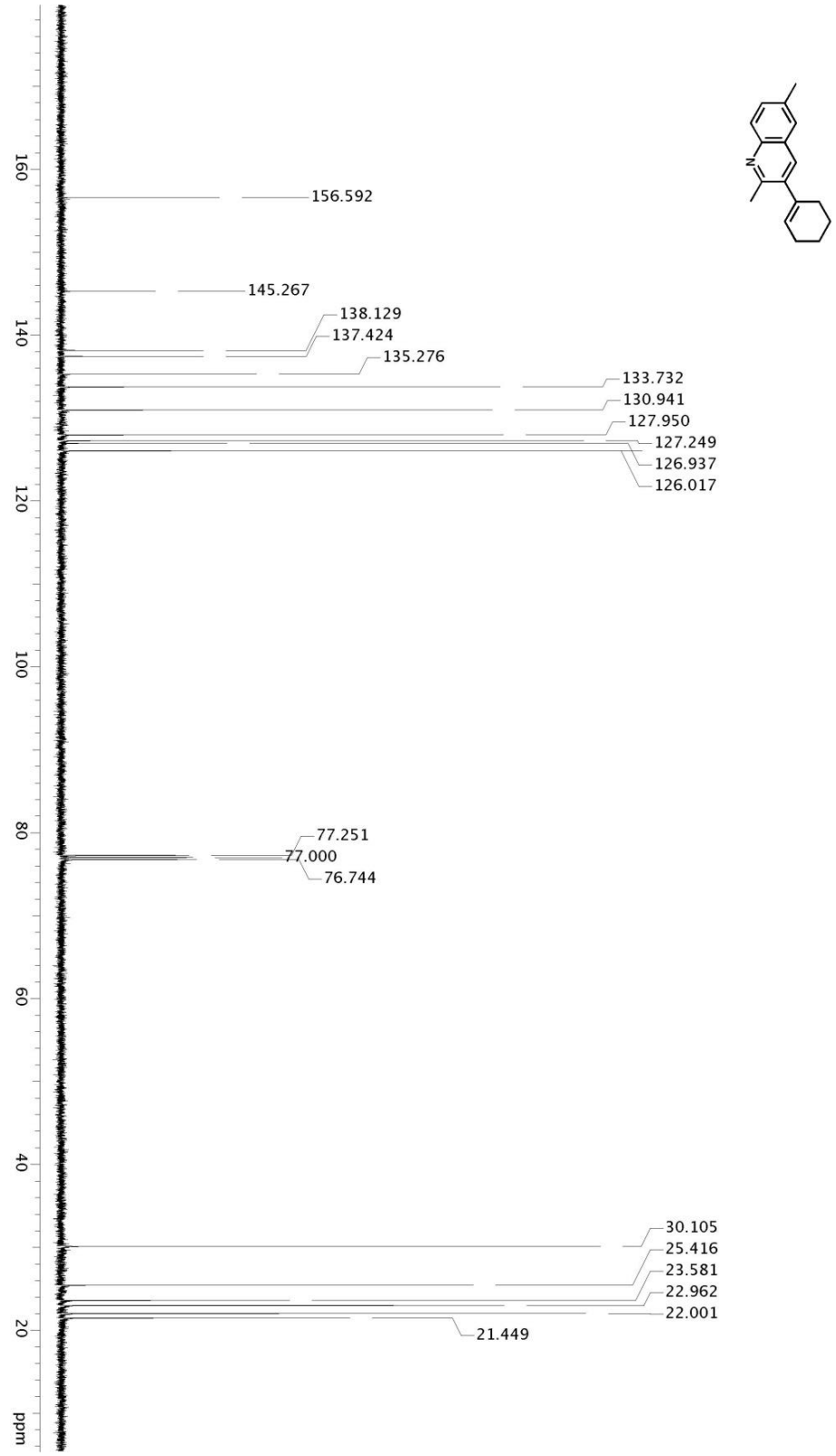


Figure S32: ^{13}C NMR spectrum for compound 3-cyclohexenyl-2,6-dimethylquinoline.

(AD113, Quinoline 19)

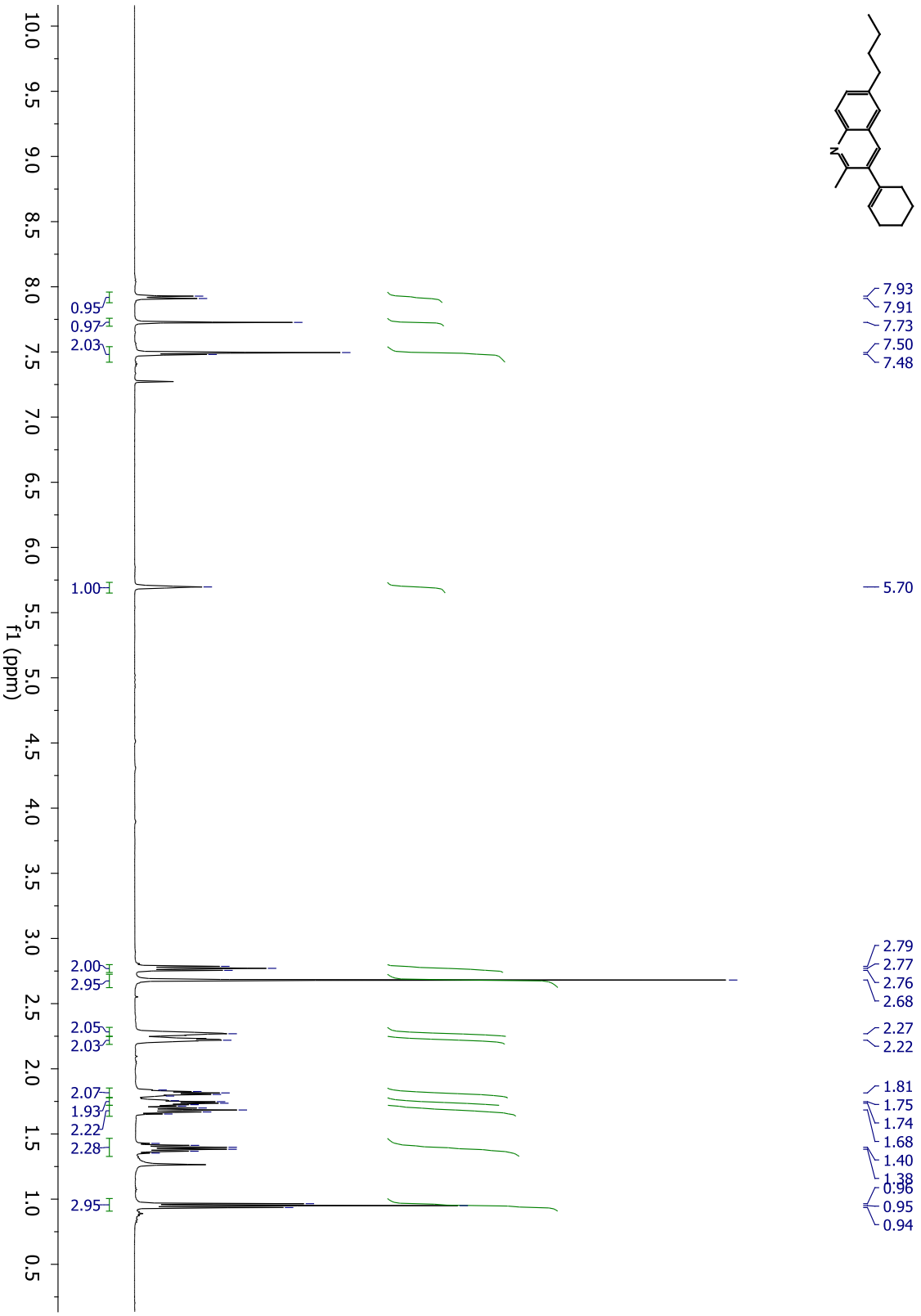


Figure S33: ^{1}H NMR spectrum for compound 6-butyl-3-cyclohexenyl-2-methylquinoline.

(TM-113, Quinoline 20)

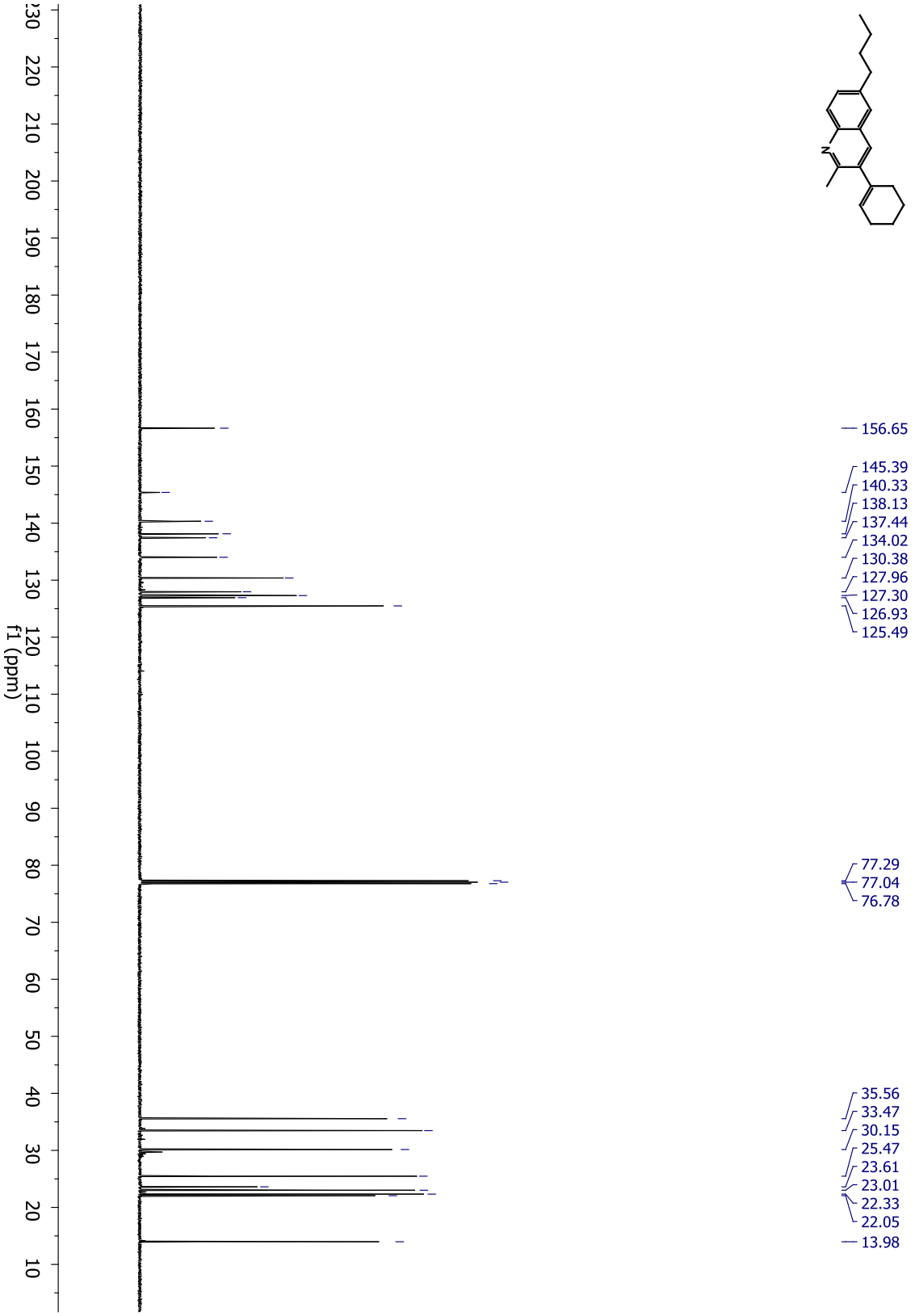


Figure S34: ^{13}C NMR spectrum for compound 6-butyl-3-cyclohexenyl-2-methylquinoline.

(TM-113, Quinoline 20)

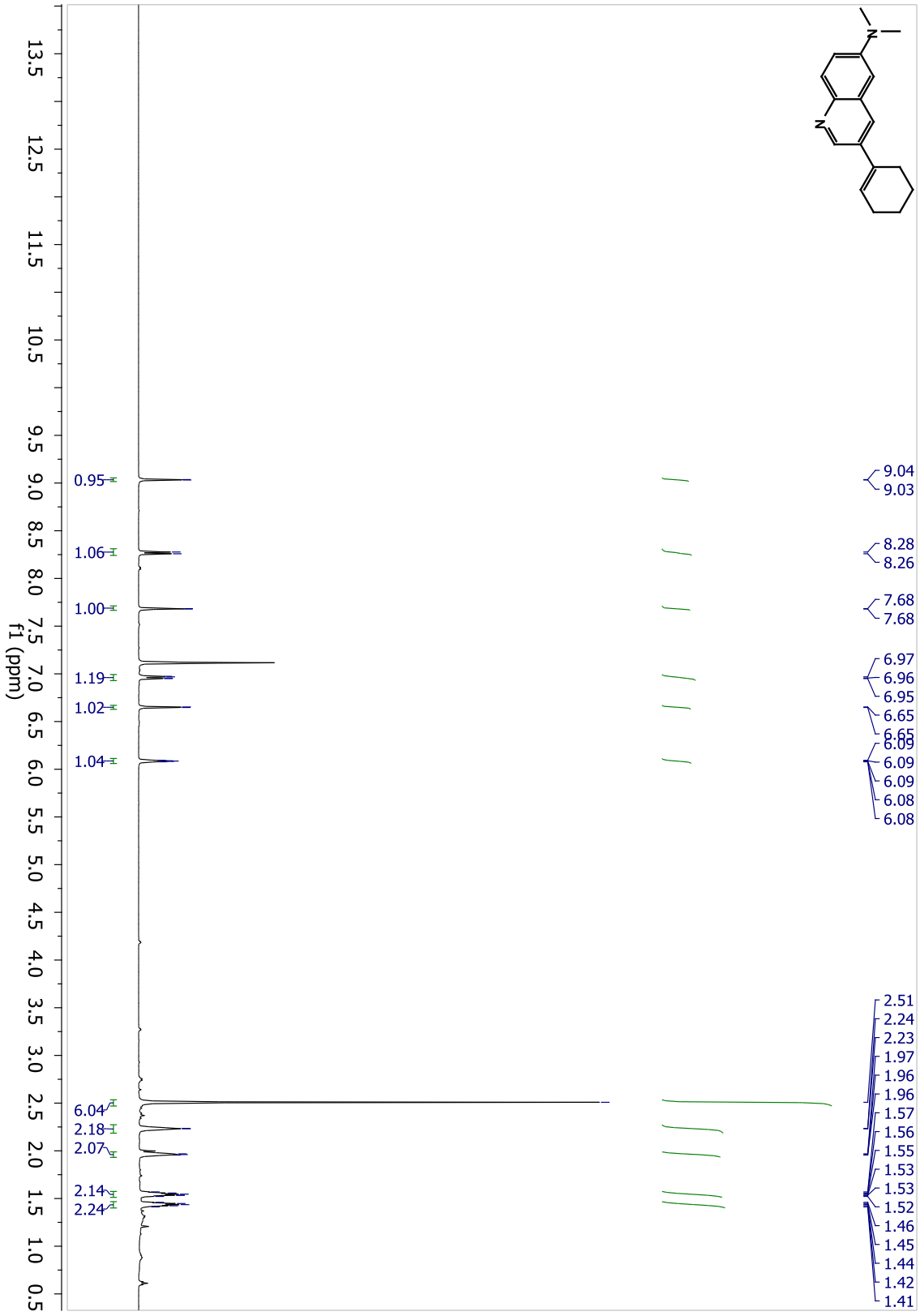


Figure S35: ^{1}H NMR spectrum for compound 3-cyclohexenyl-6-(N,N-dimethylamino)quinoline.

(**TM-101, Quinoline 21)**

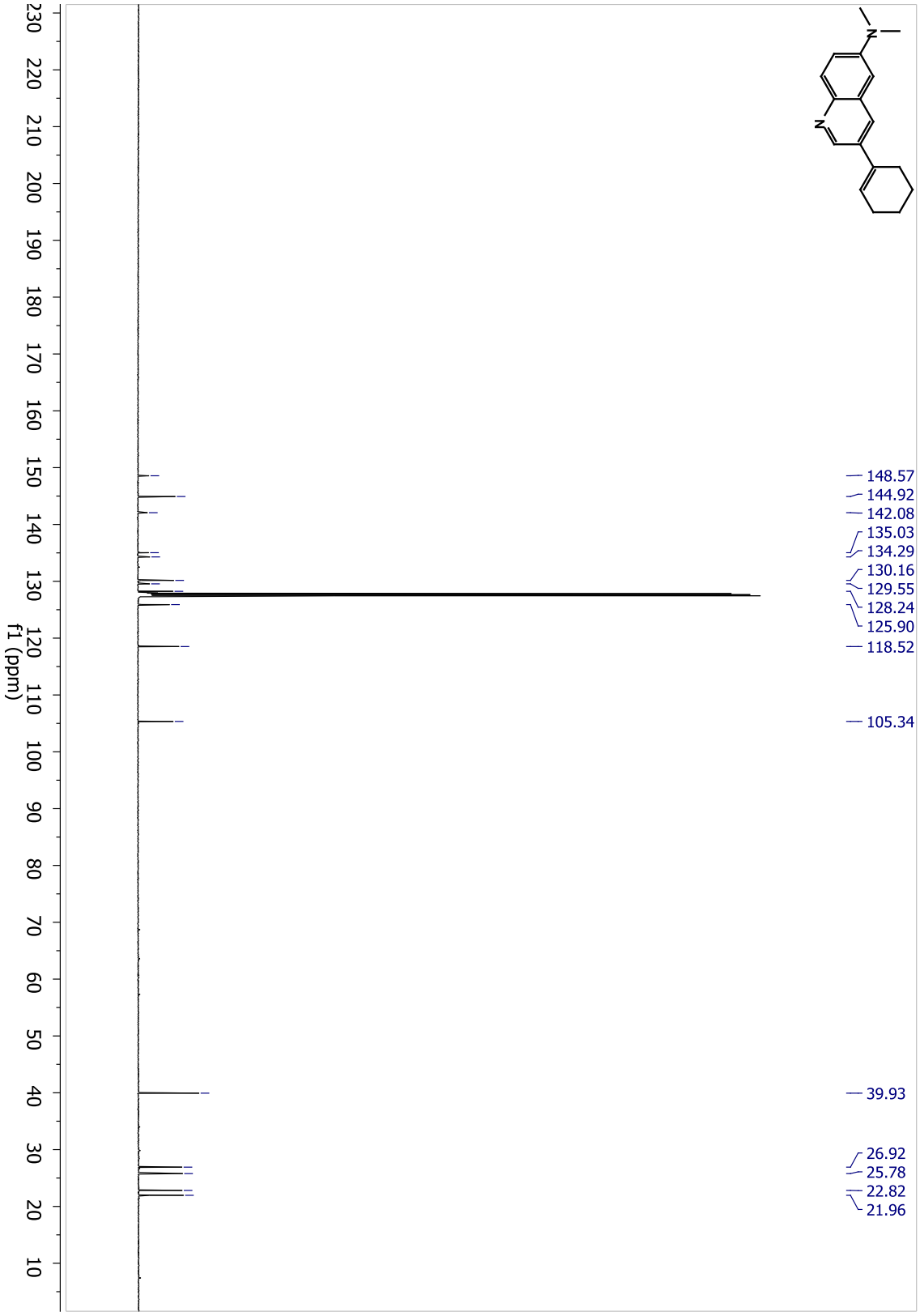


Figure S36: ^{13}C NMR spectrum for compound 3-cyclohexenyl-6-(N,N-dimethylamino)quinoline.

(**TM-101, Quinoline 21)**

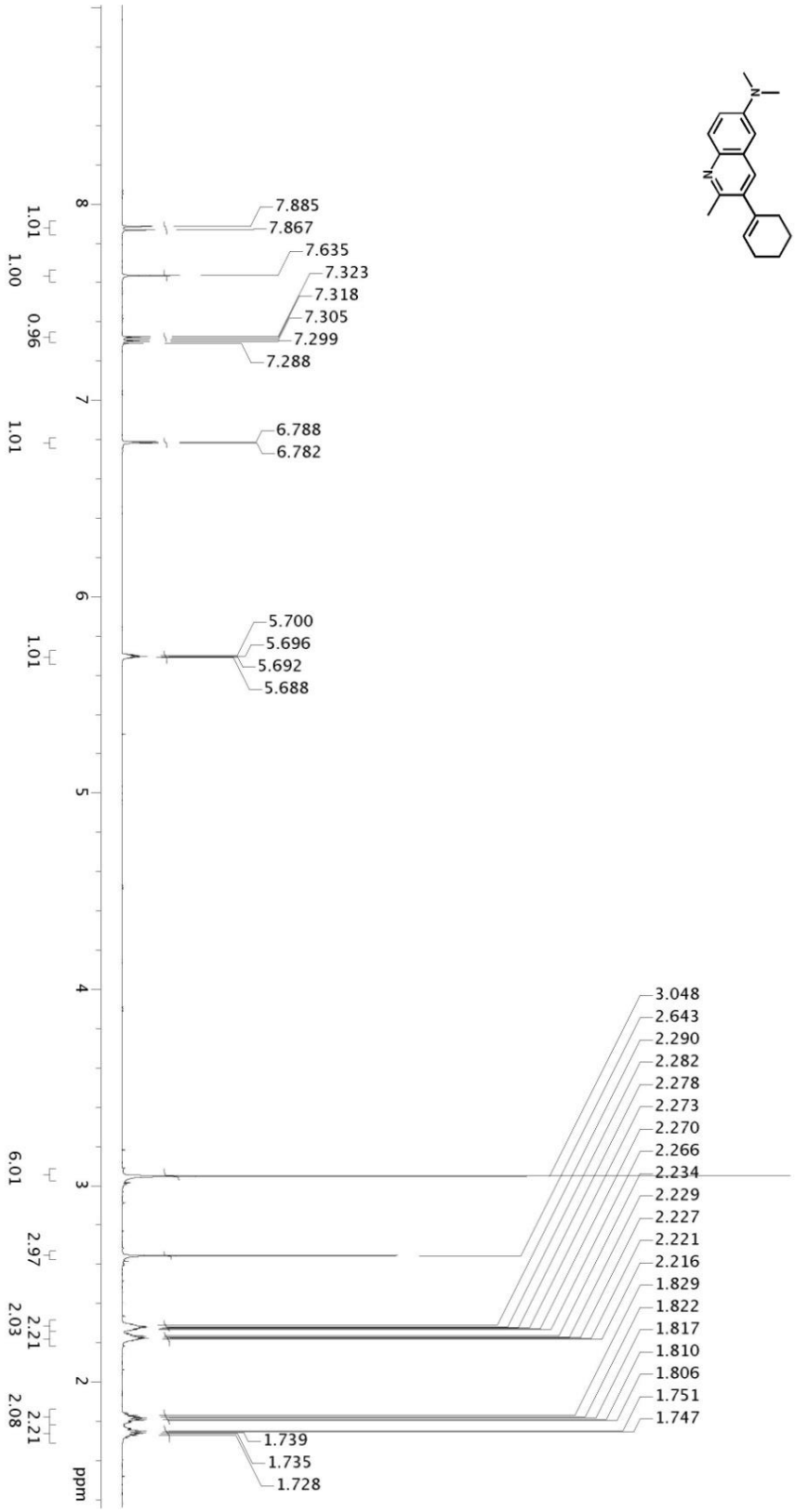


Figure S37: ^{1}H NMR spectrum for compound 3-cyclohexenyl-2-methyl-6-(N,N-dimethylamino)quinoline. **(AD117, Quinoline 22)***:*

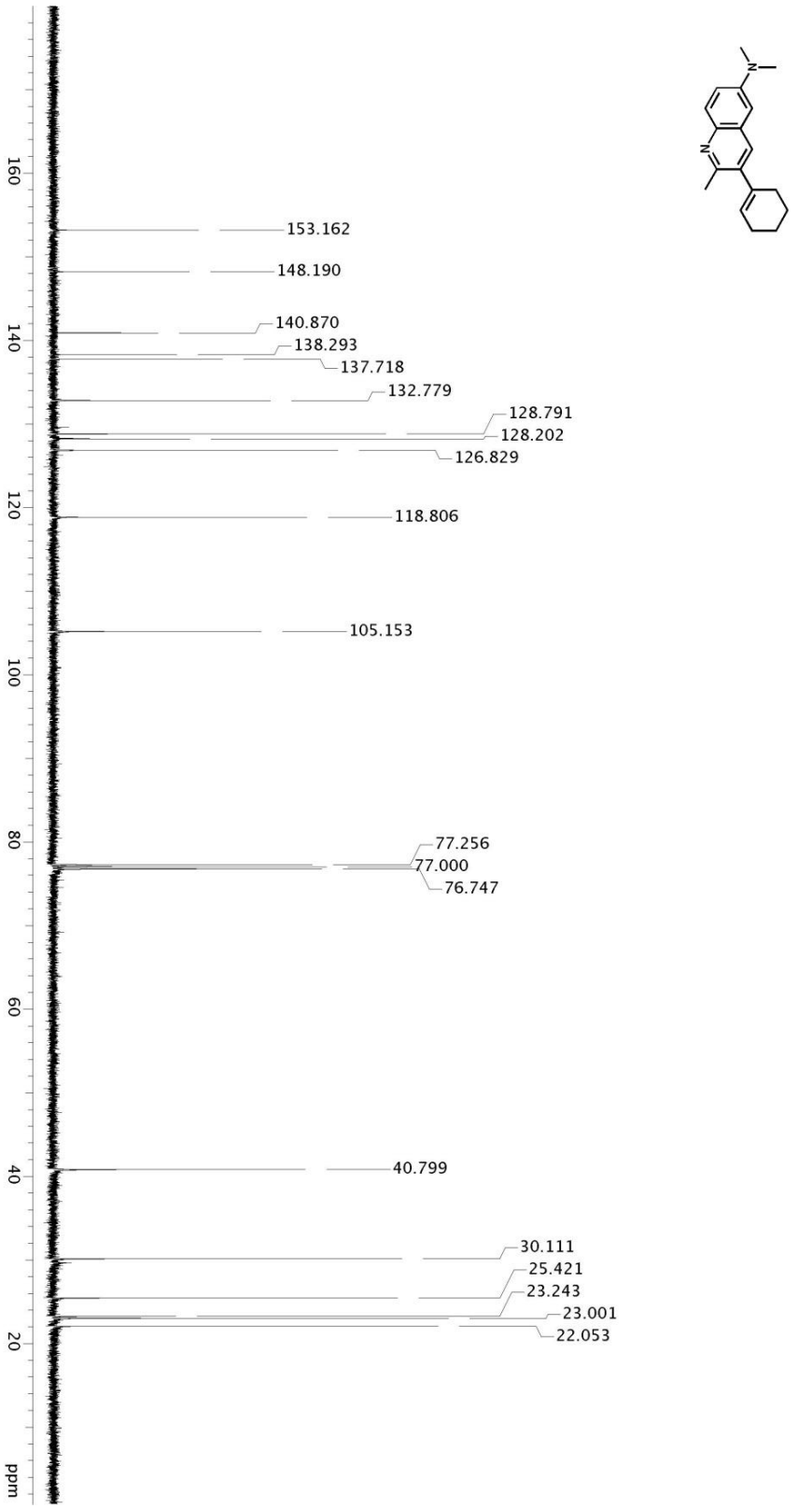


Figure S38: ^{13}C NMR spectrum for compound 3-cyclohexenyl-2-methyl-6-(N,N-dimethylamino)quinoline. **(AD117, Quinoline 22)***:*

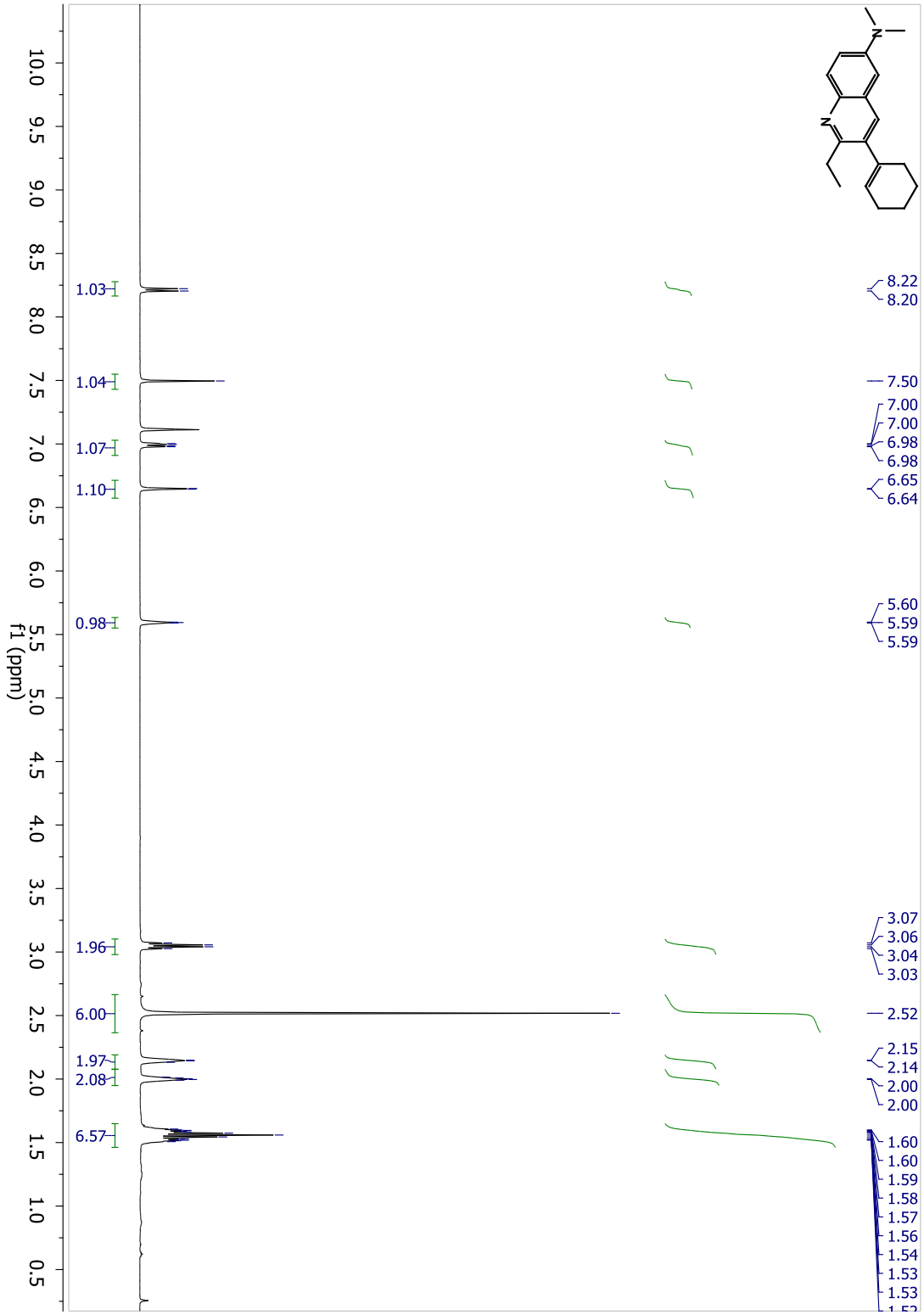


Figure S39: ^{1}H NMR spectrum for compound 3-cyclohexenyl-2-ethyl-6(N,N-dimethylamino)quinoline. (**TM-103, Quinoline 23)**

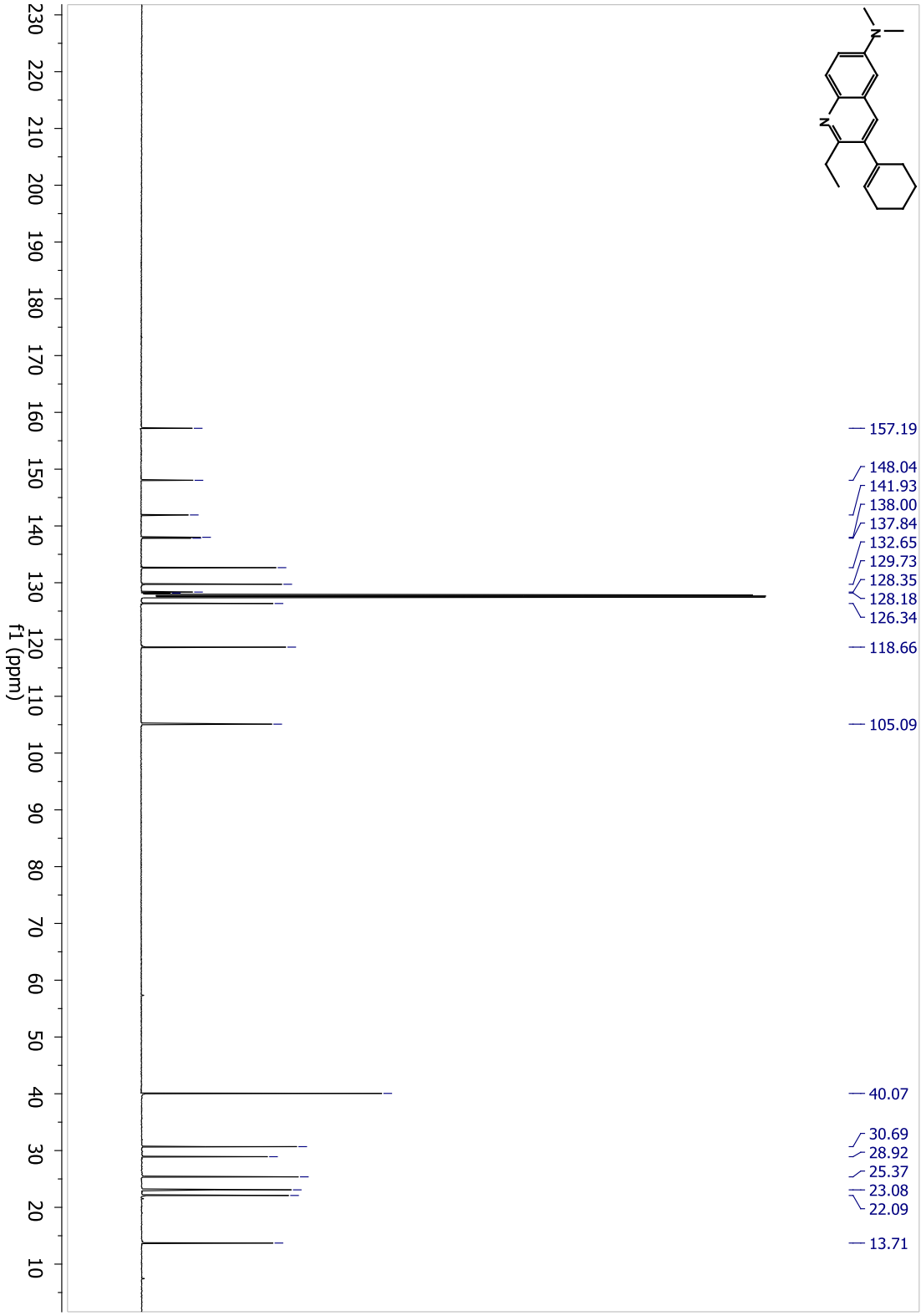


Figure S40:. ^{13}C NMR spectrum for compound 3-cyclohexenyl-2-ethyl-6(N,N-dimethylamino)quinoline. (**TM-103, Quinoline 23)**

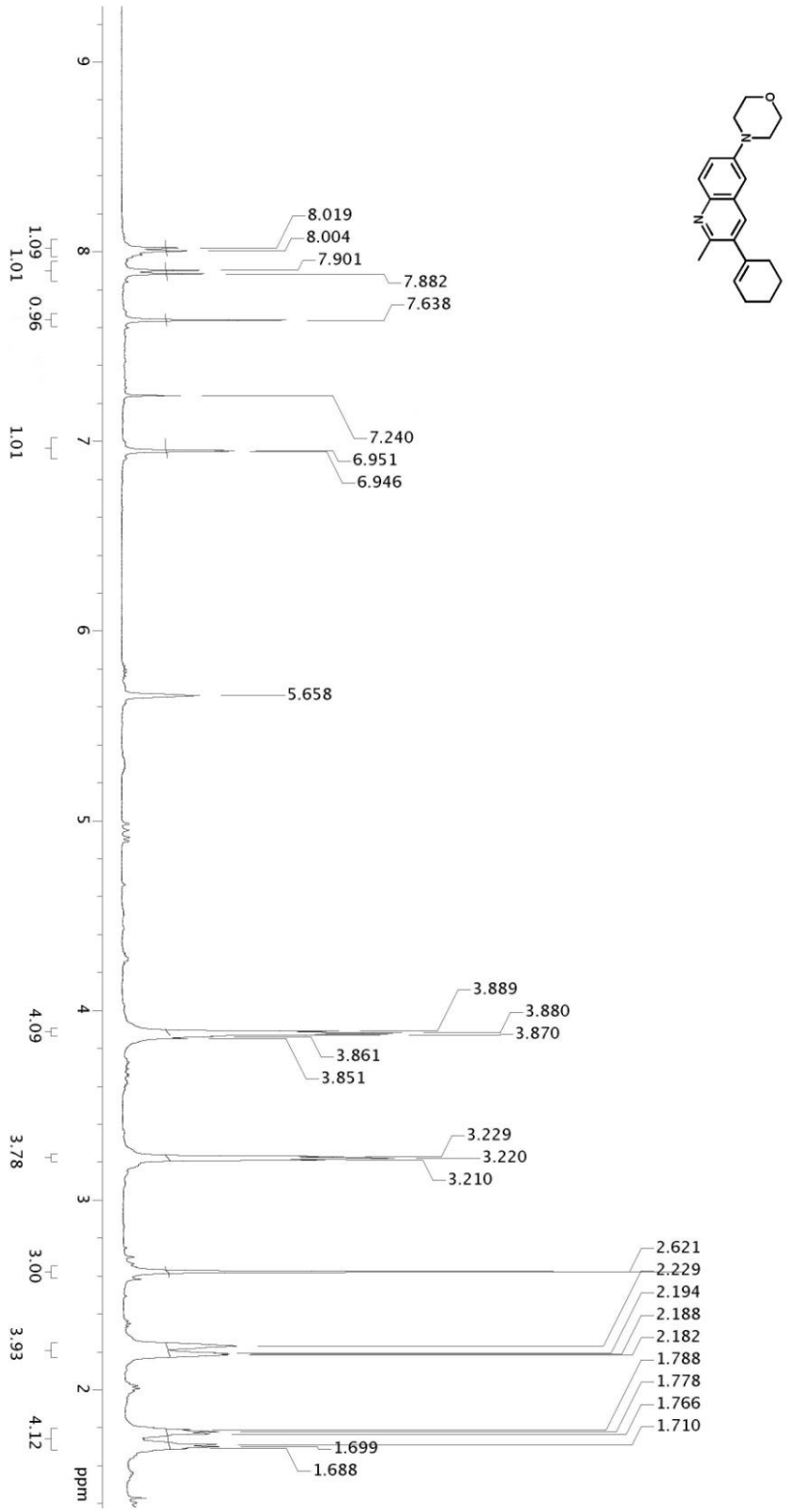


Figure S41: ^{1}H NMR spectrum for compound 3-cyclohexenyl-2-methyl-6-morpholinylquinoline.

(AD120, Quinoline 24)

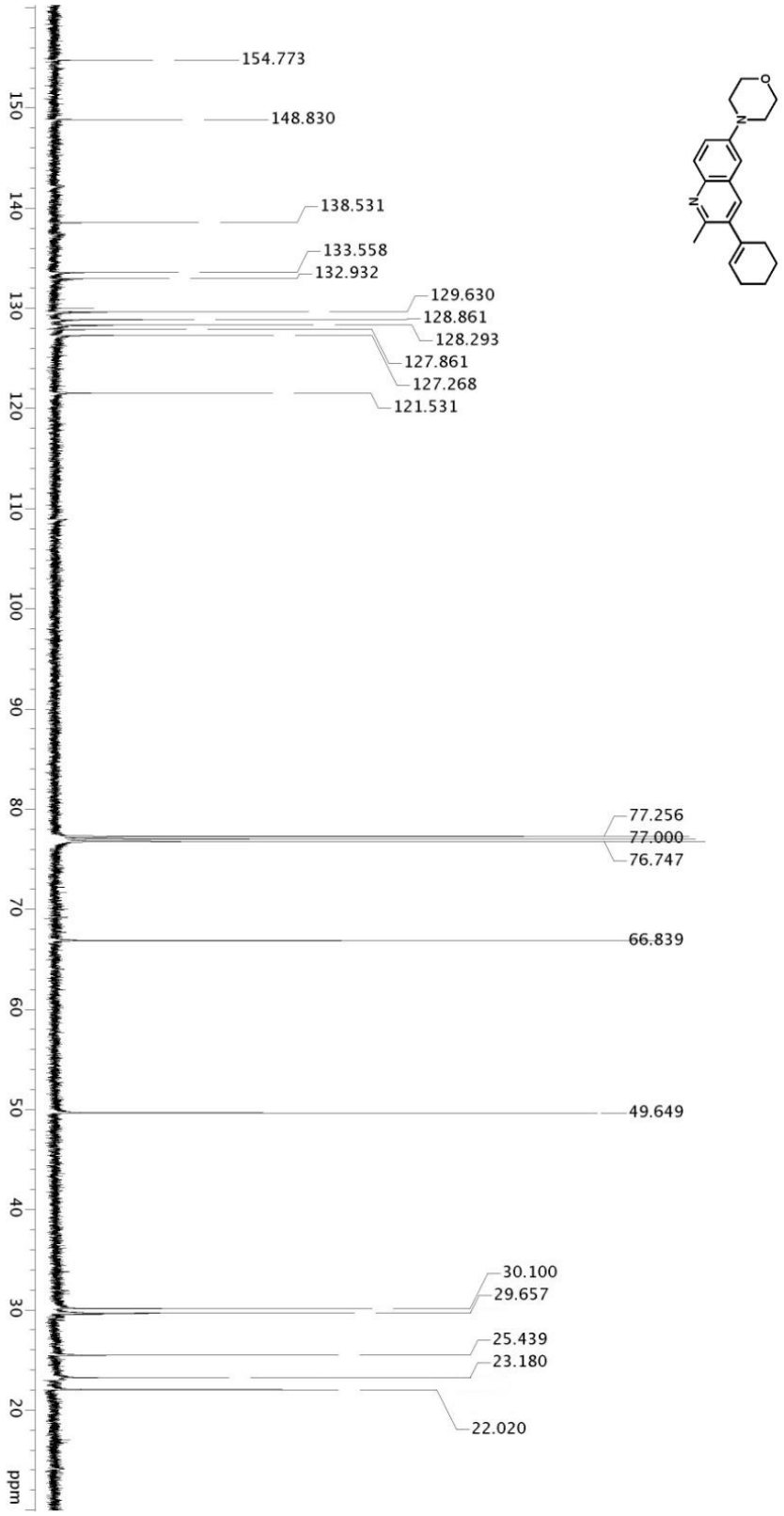


Figure S42: ^{13}C NMR spectrum for compound 3-cyclohexenyl-2-methyl-6-morpholinylquinoline.

(AD120, Quinoline 24)

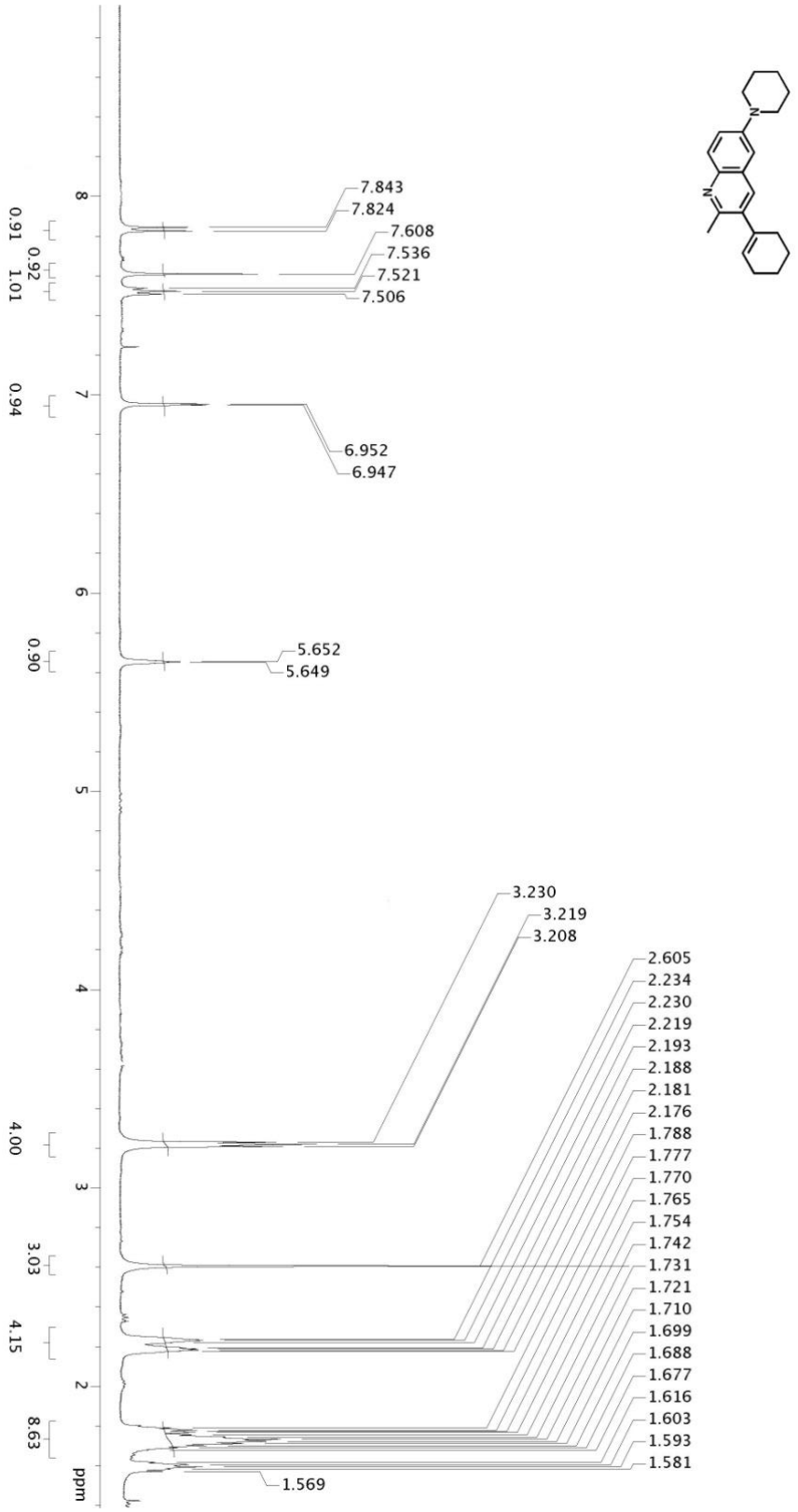


Figure S43: ^{1}H NMR spectrum for compound 3-cyclohexenyl-2-methyl-6-piperidinylquinoline.

(AD121, Quinoline 25)*:*

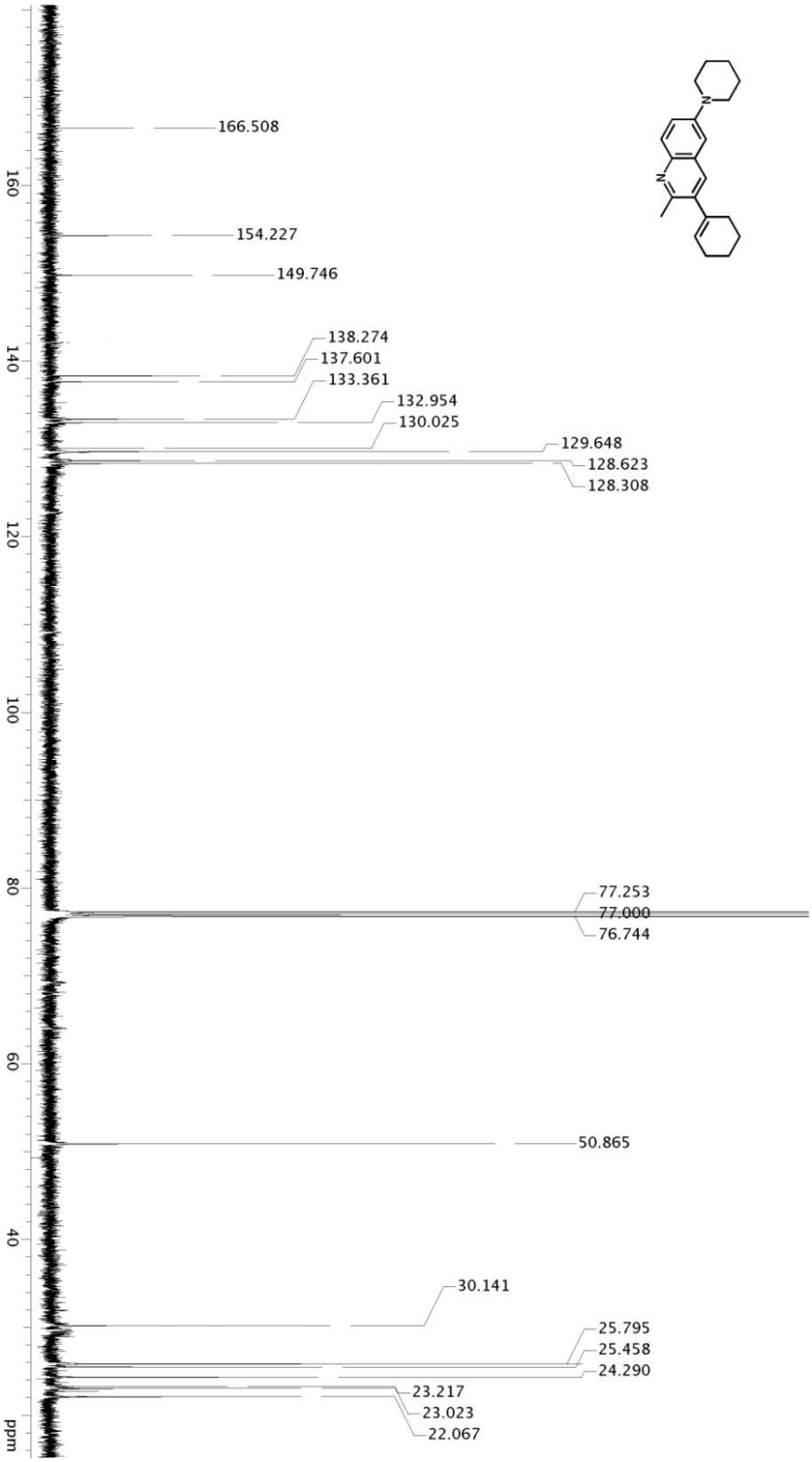


Figure S44: ^{13}C NMR spectrum for compound 3-cyclohexenyl-2-methyl-6-piperidinylquinoline. **(AD121, Quinoline 25)***:*

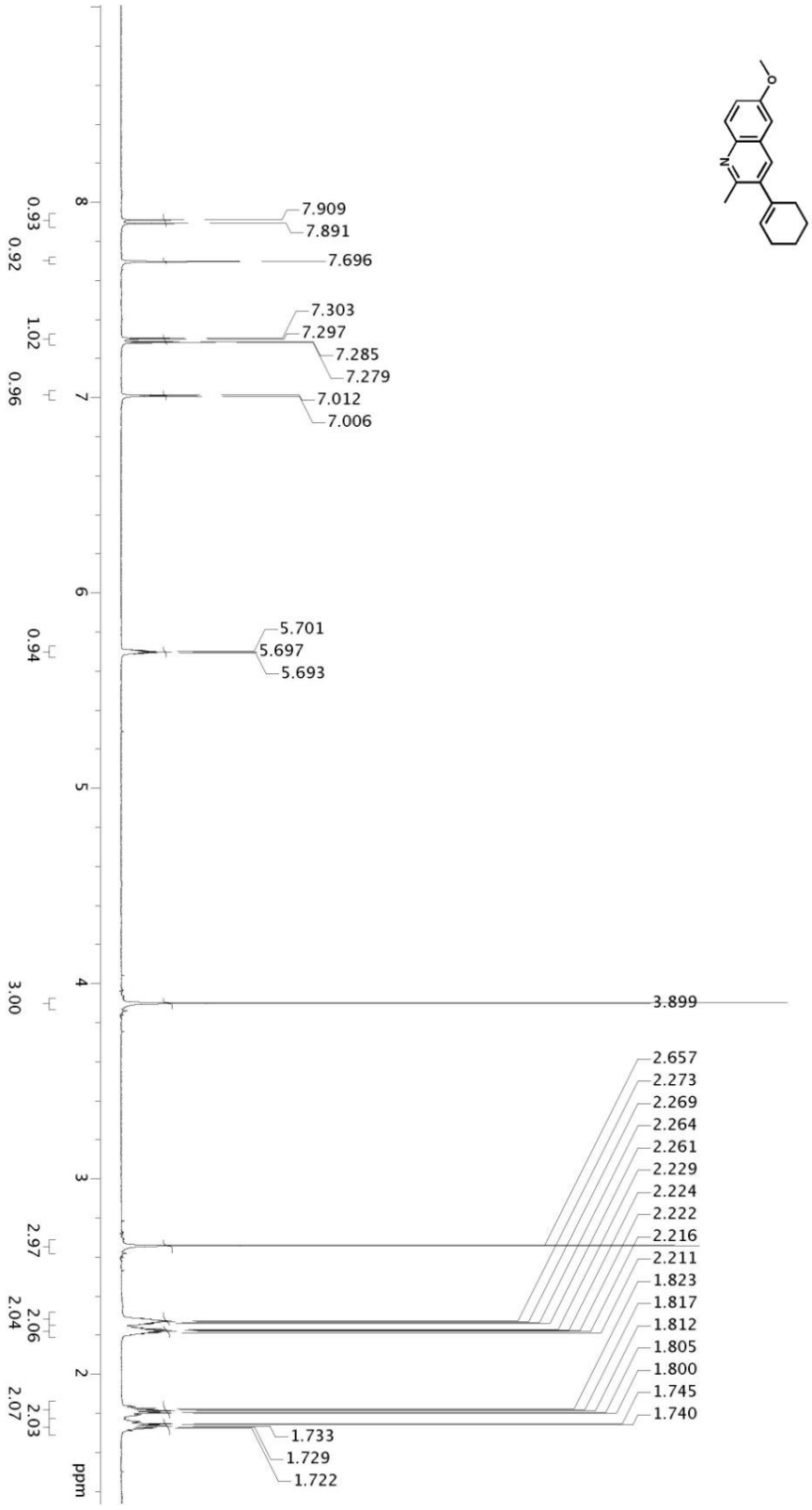


Figure S45: ^{1}H NMR spectrum for compound 3-cyclohexenyl-6-methoxy-2-methylquinoline.

(AD119, Quinoline 26)

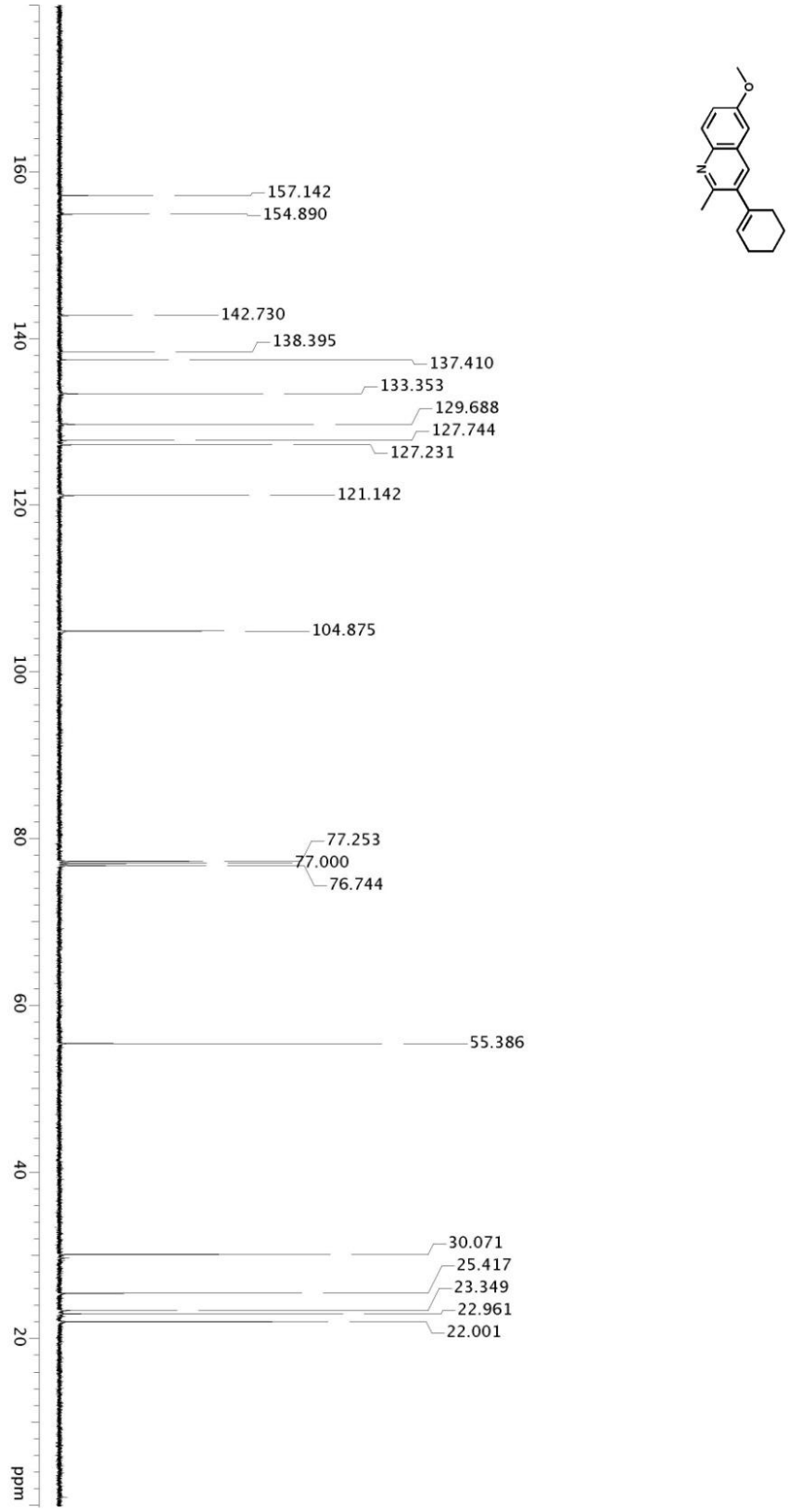


Figure S46: ^{13}C NMR spectrum for compound 3-cyclohexenyl-6-methoxy-2-methylquinoline.

(AD119, Quinoline 26)

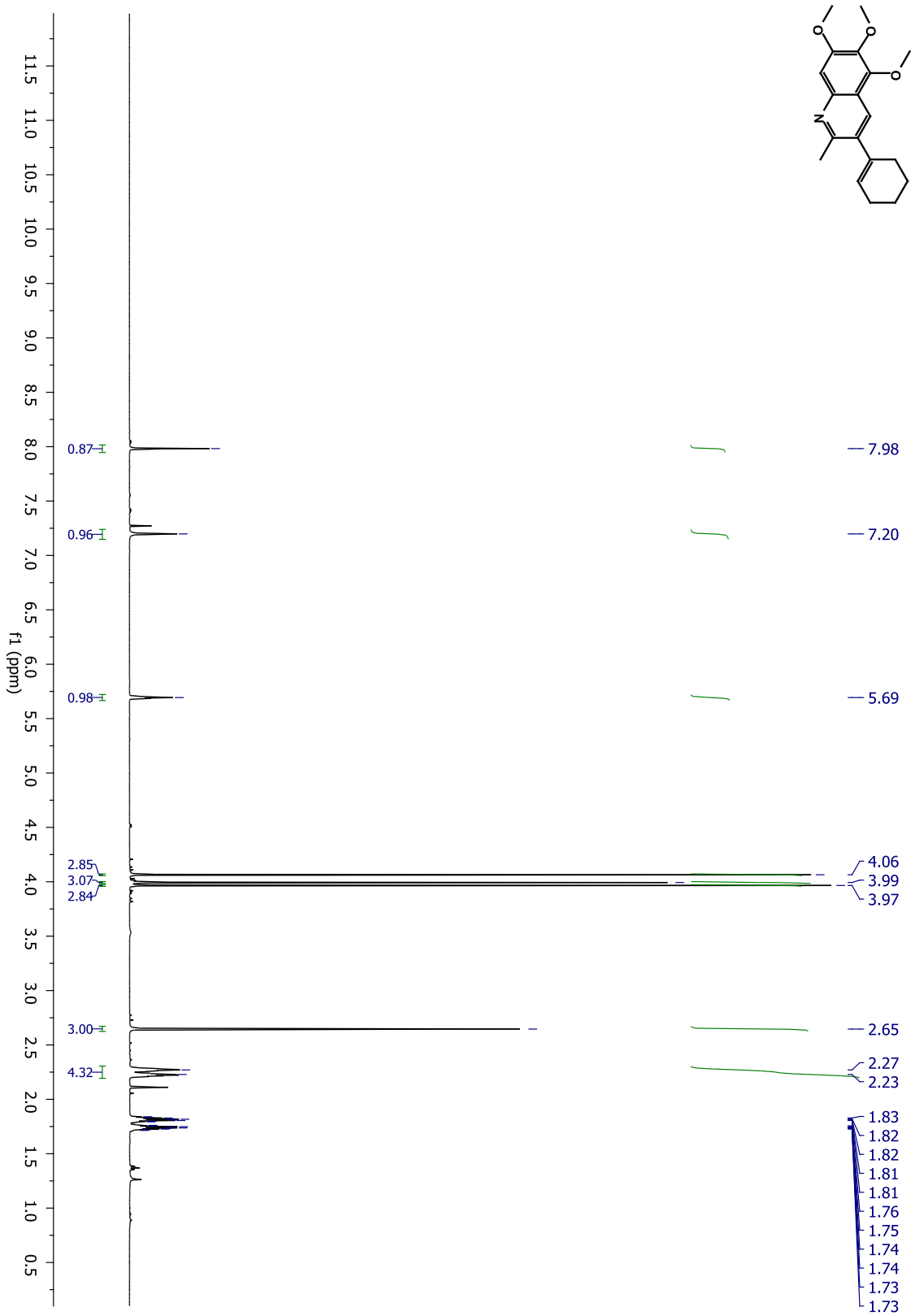


Figure S47: ^{1}H NMR spectrum for compound 3-cyclohexenyl-5,6,7-trimethoxy-2-methylquinoline. (**TM300, Quinoline 27)**

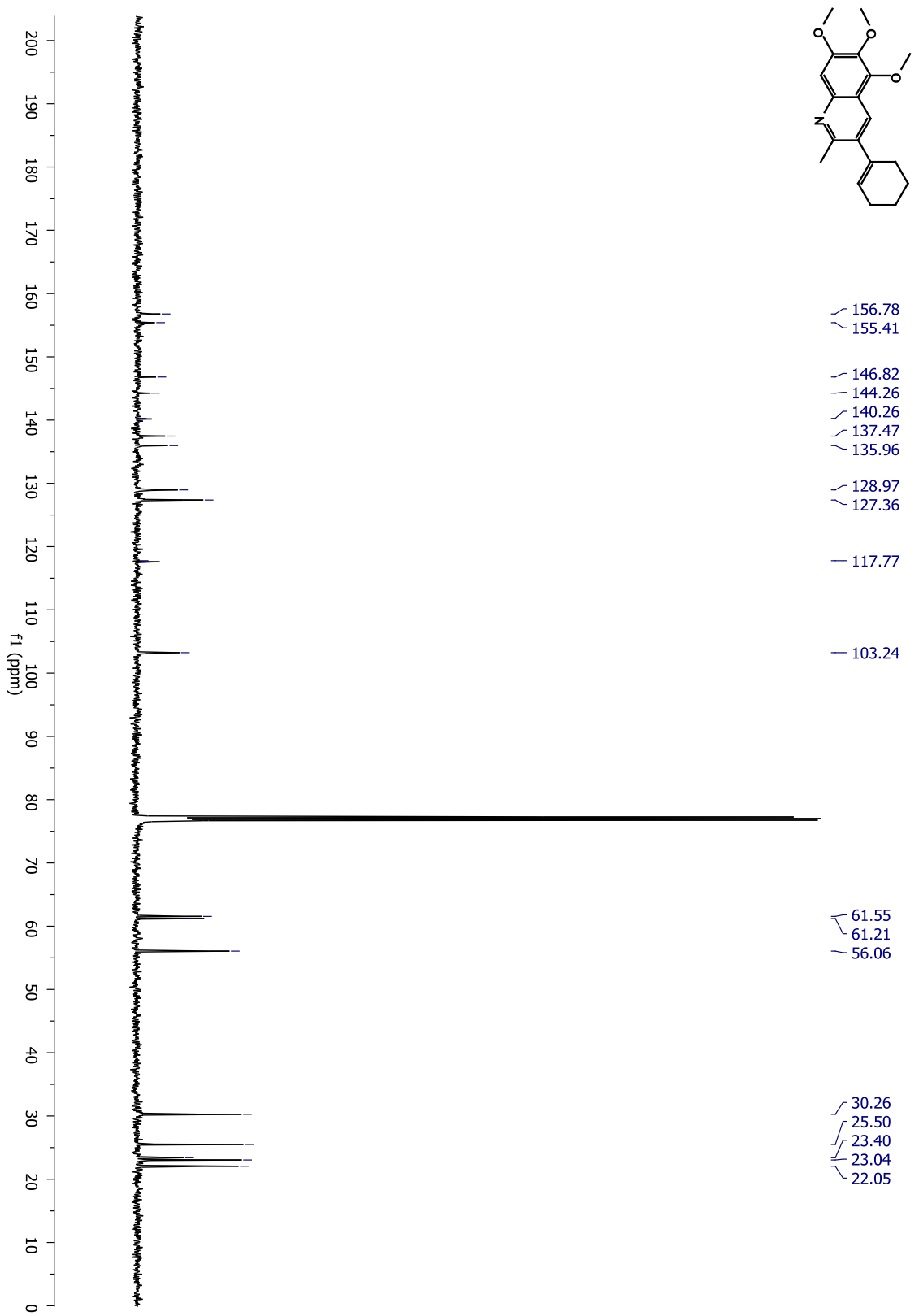


Figure S48: ^{13}C NMR spectrum for compound 3-cyclohexenyl-5,6,7-trimethoxy-2-methylquinoline.

(TM300, Quinoline 27)

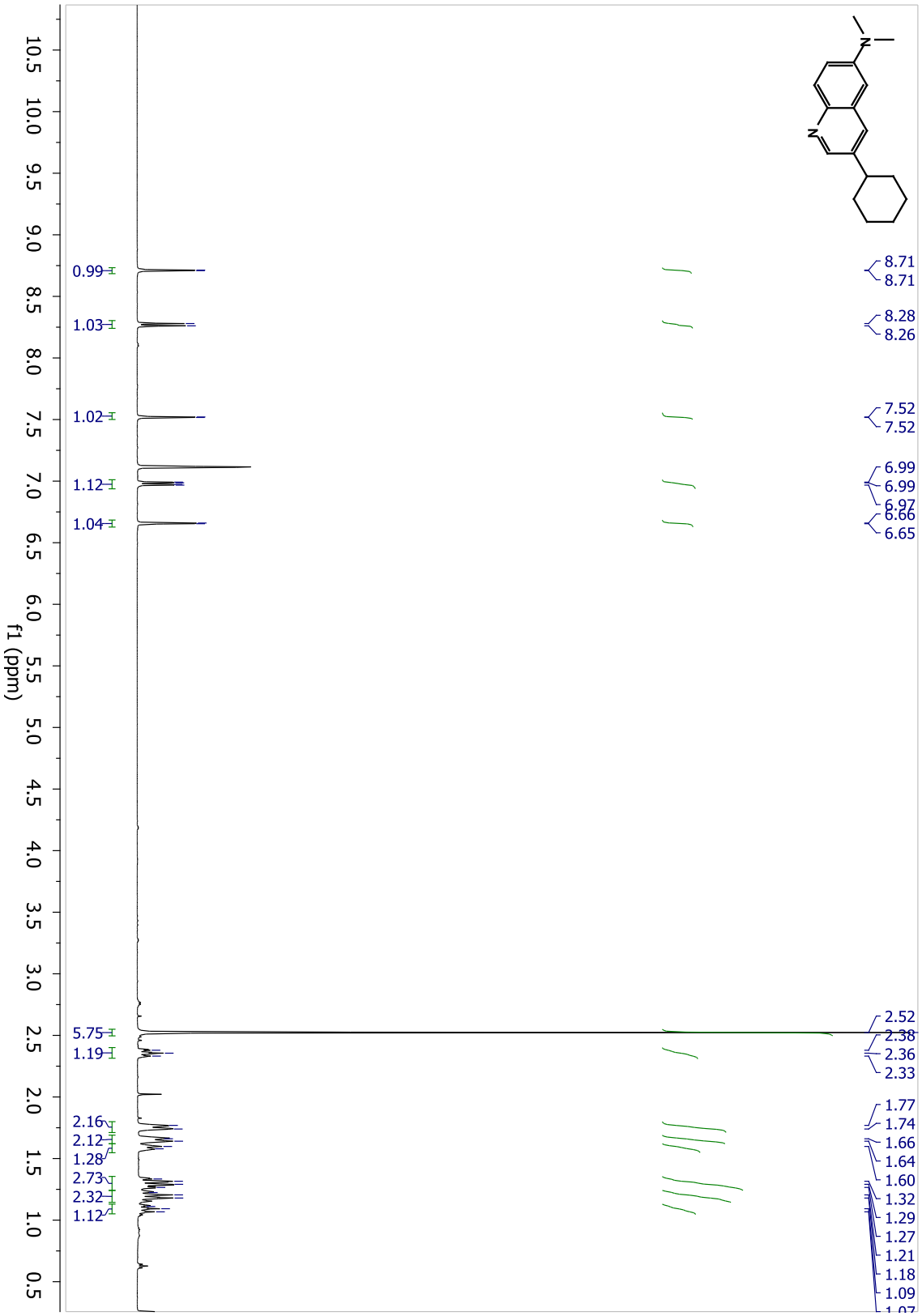


Figure S49: ^{1}H NMR spectrum for compound 3-cyclohexyl-6-(N,N-dimethylamino)quinoline.

(**TM-102, Quinoline 28)**

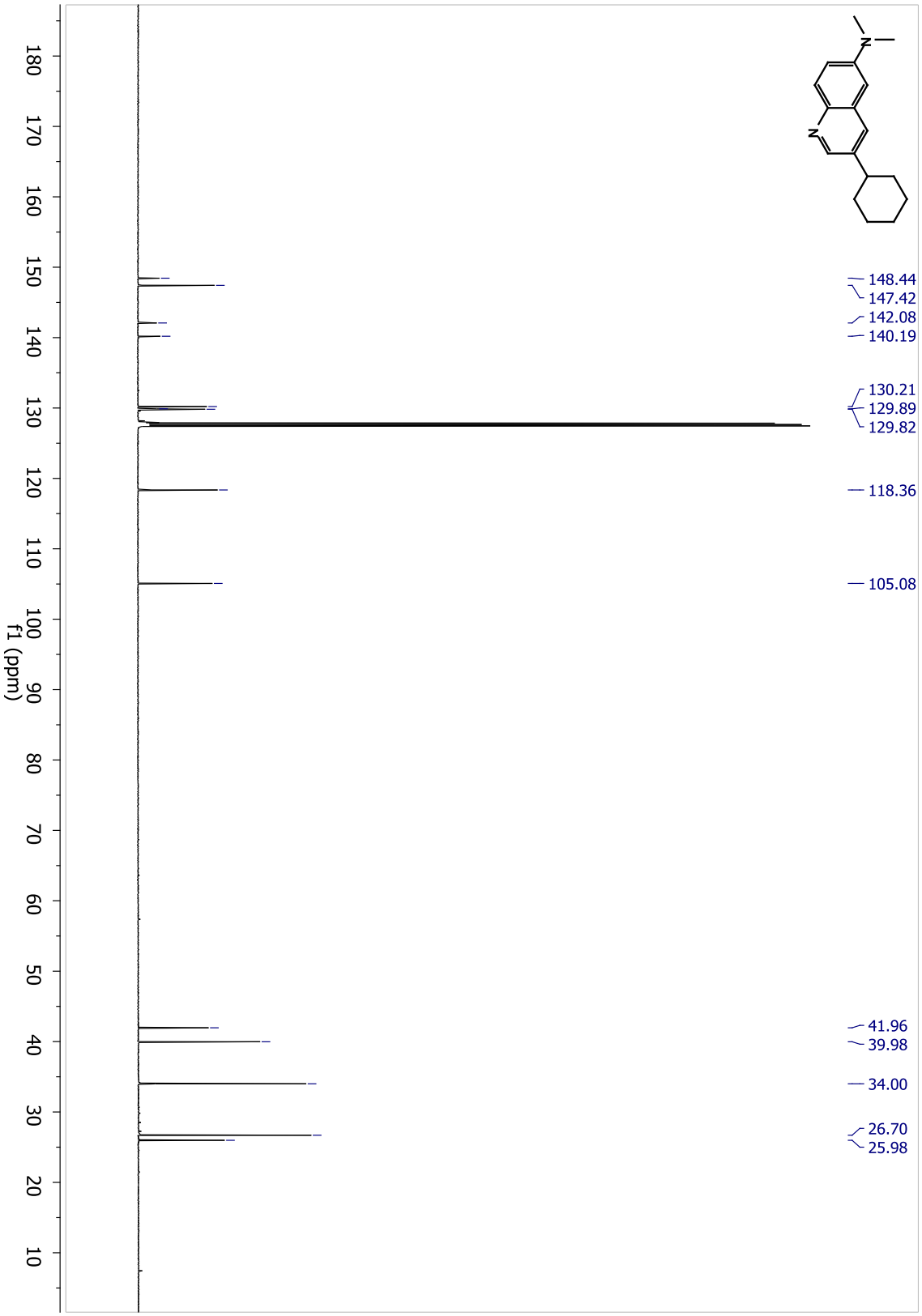


Figure S50: ^{13}C NMR spectrum for compound 3-cyclohexyl-6-(N,N-dimethylamino)quinoline.

(**TM-102, Quinoline 28)**

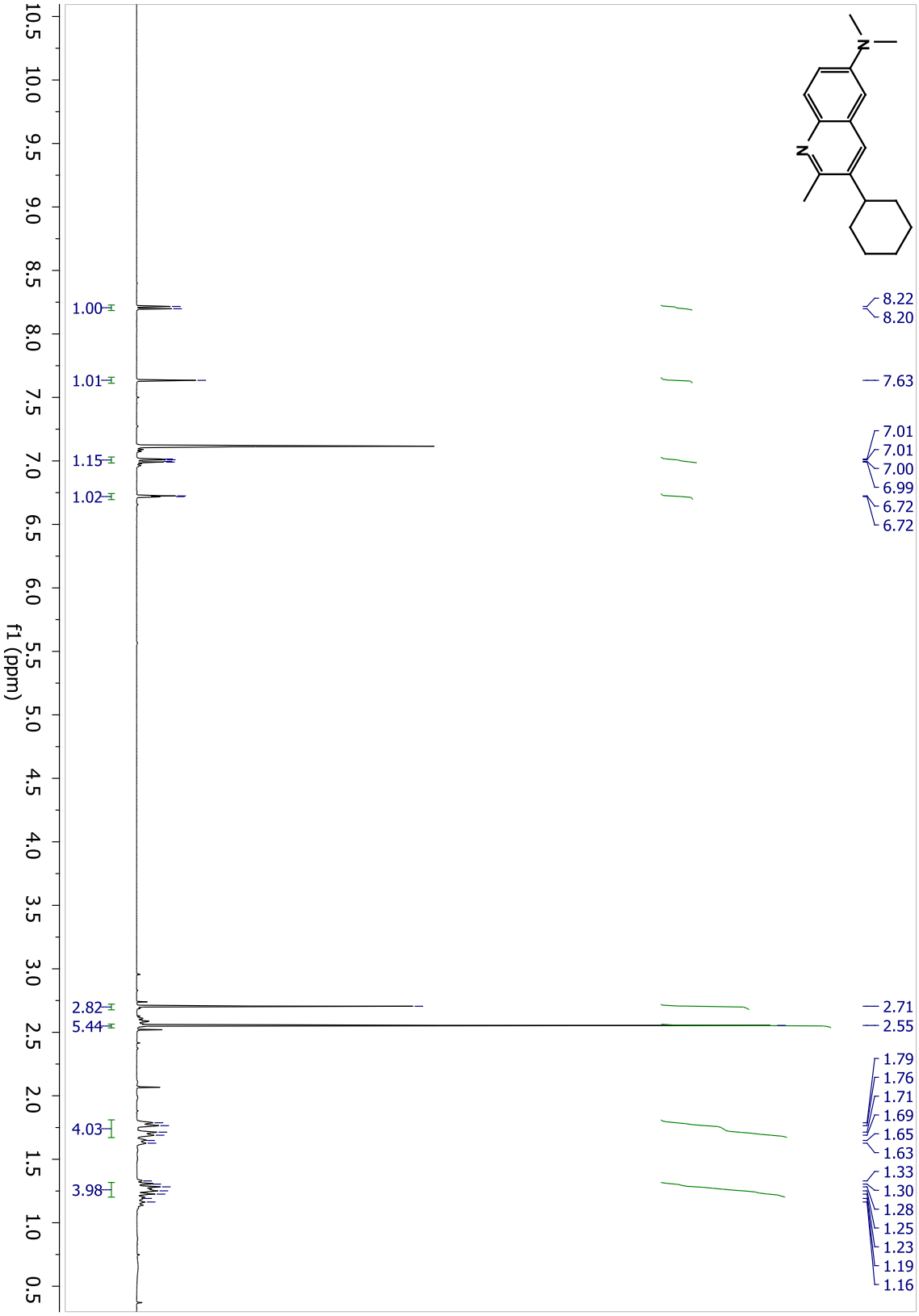


Figure S51: [1]H NMR spectrum for compound 3-cyclohexyl-2-methyl-6-(N,N-dimethylamino)quinoline.

(TM-116, Quinoline 29)

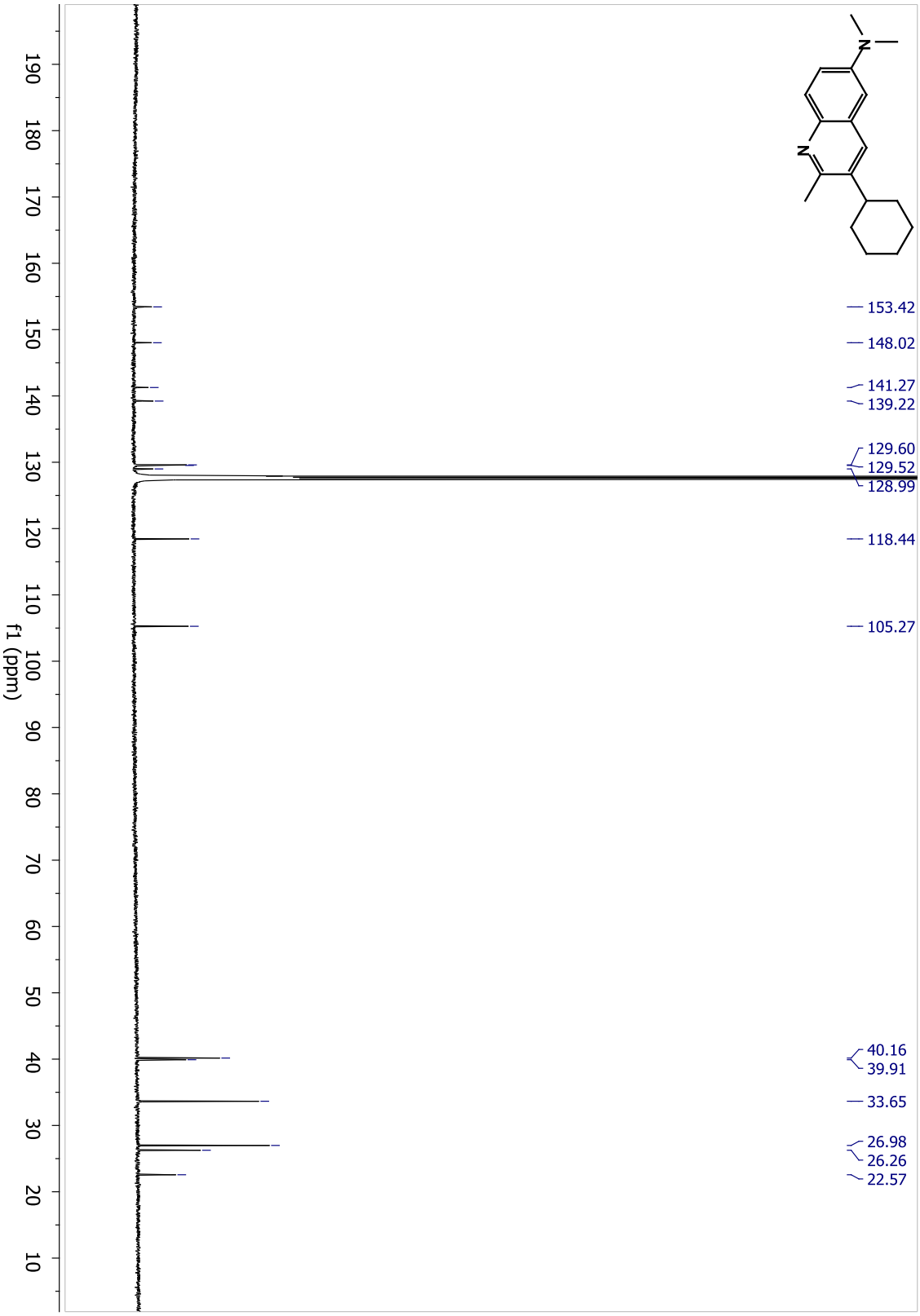


Figure S52: ^{13}C NMR spectrum for compound 3-cyclohexyl-2-methyl-6-(N,N-dimethylamino)quinoline.

(TM-116, Quinoline 29)

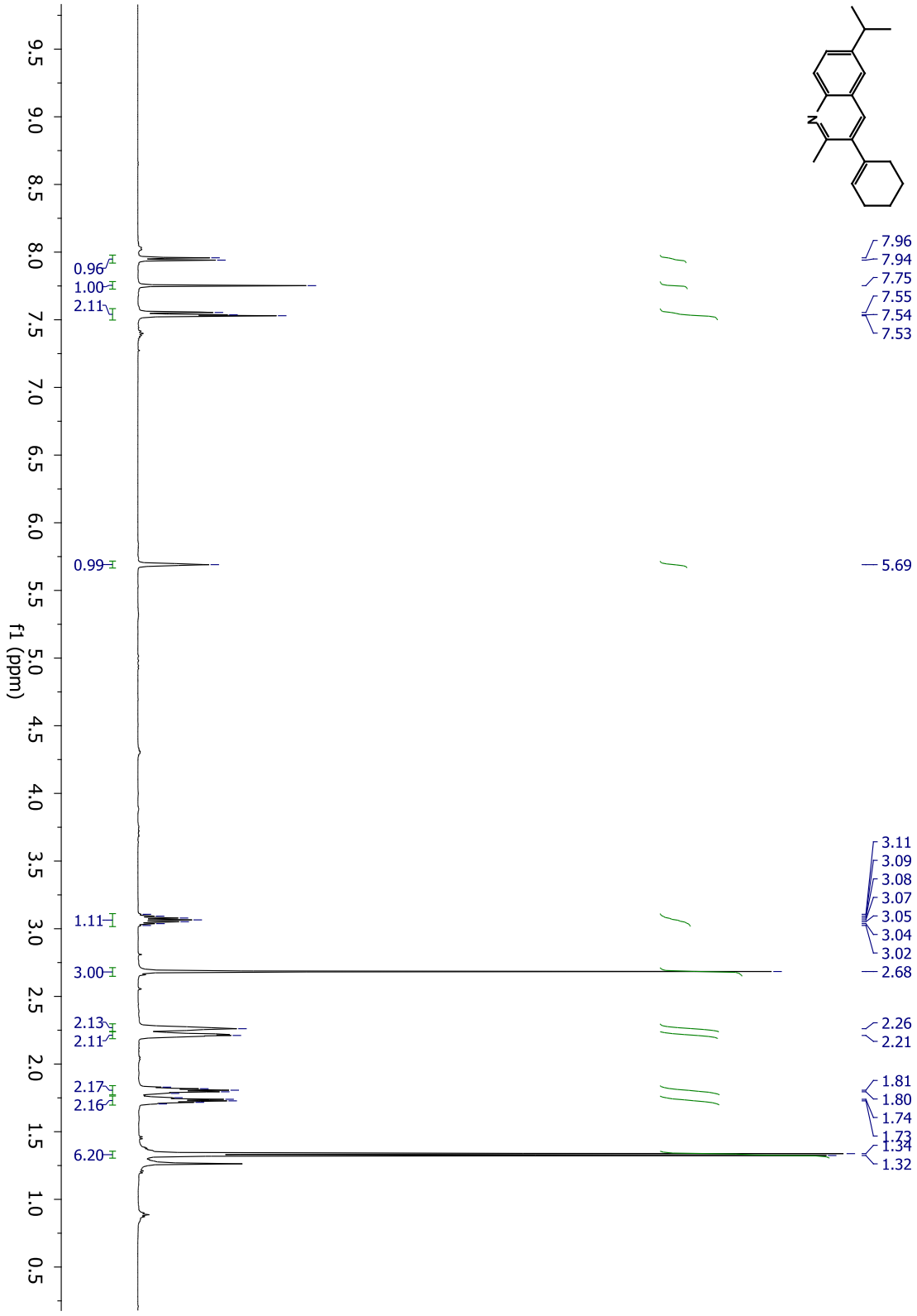


Figure S53: ^{1}H NMR spectrum for compound 3-cyclohexenyl-6-isopropyl-2-methylquinoline.

(**TM-117, Quinoline 30)**

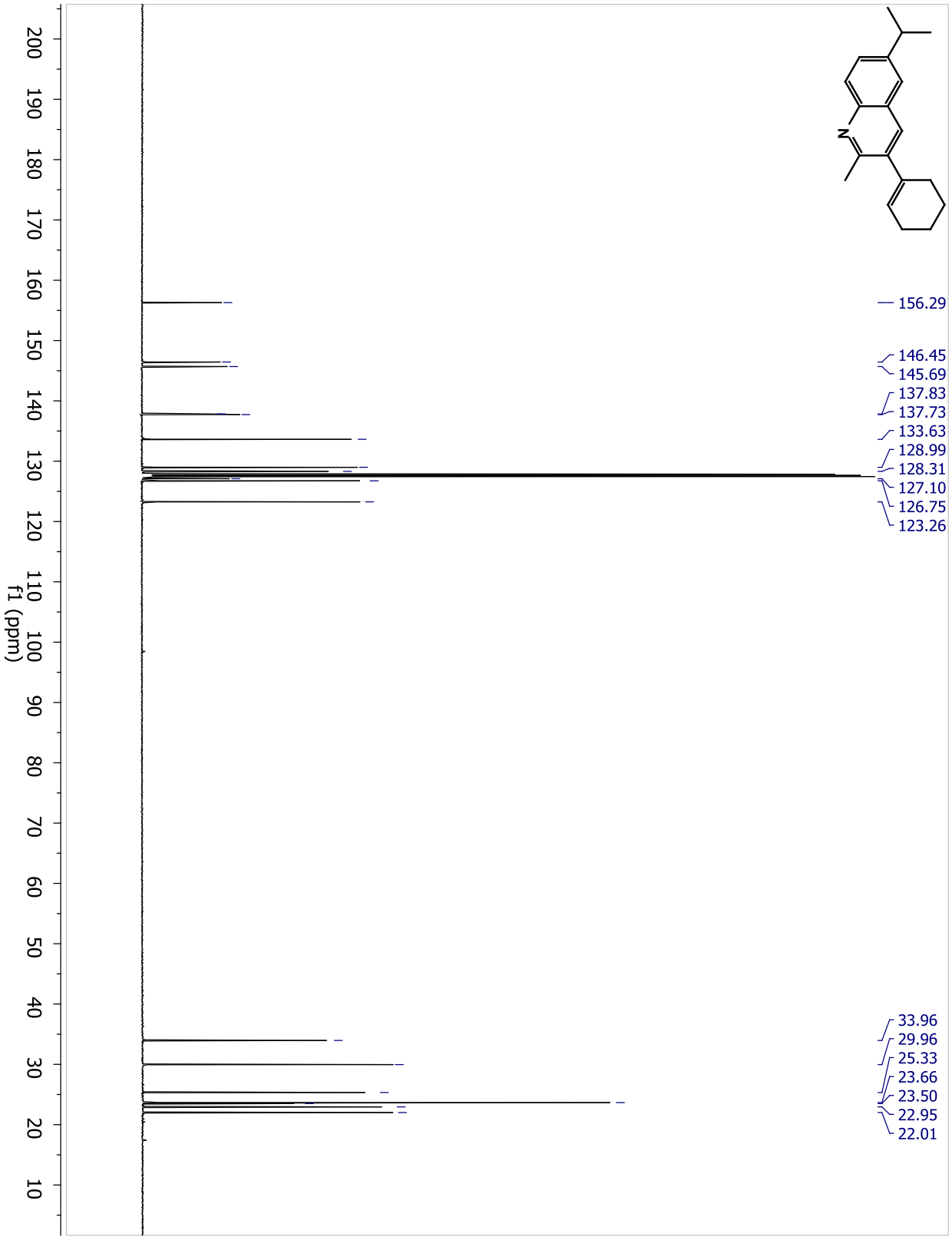


Figure S54: ^{13}C NMR spectrum for compound 3-cyclohexenyl-6-isopropyl-2-methylquinoline. (**TM-117, Quinoline 30)**

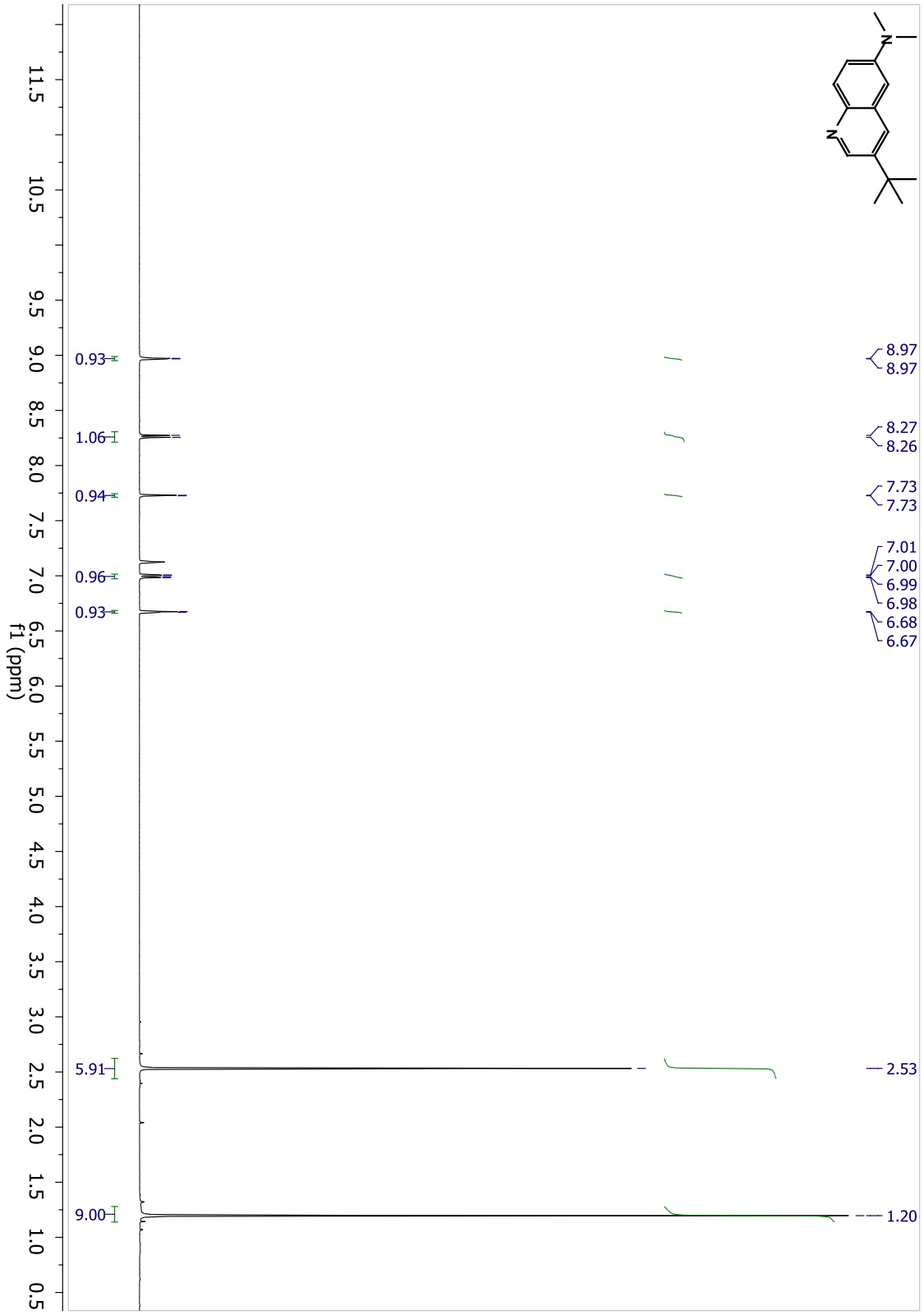


Figure S55: ^{1}H NMR spectrum for compound 3-*tert*-butyl-6-(N,N-dimethylamino)quinoline.

(**TM-081, Quinoline 31)**

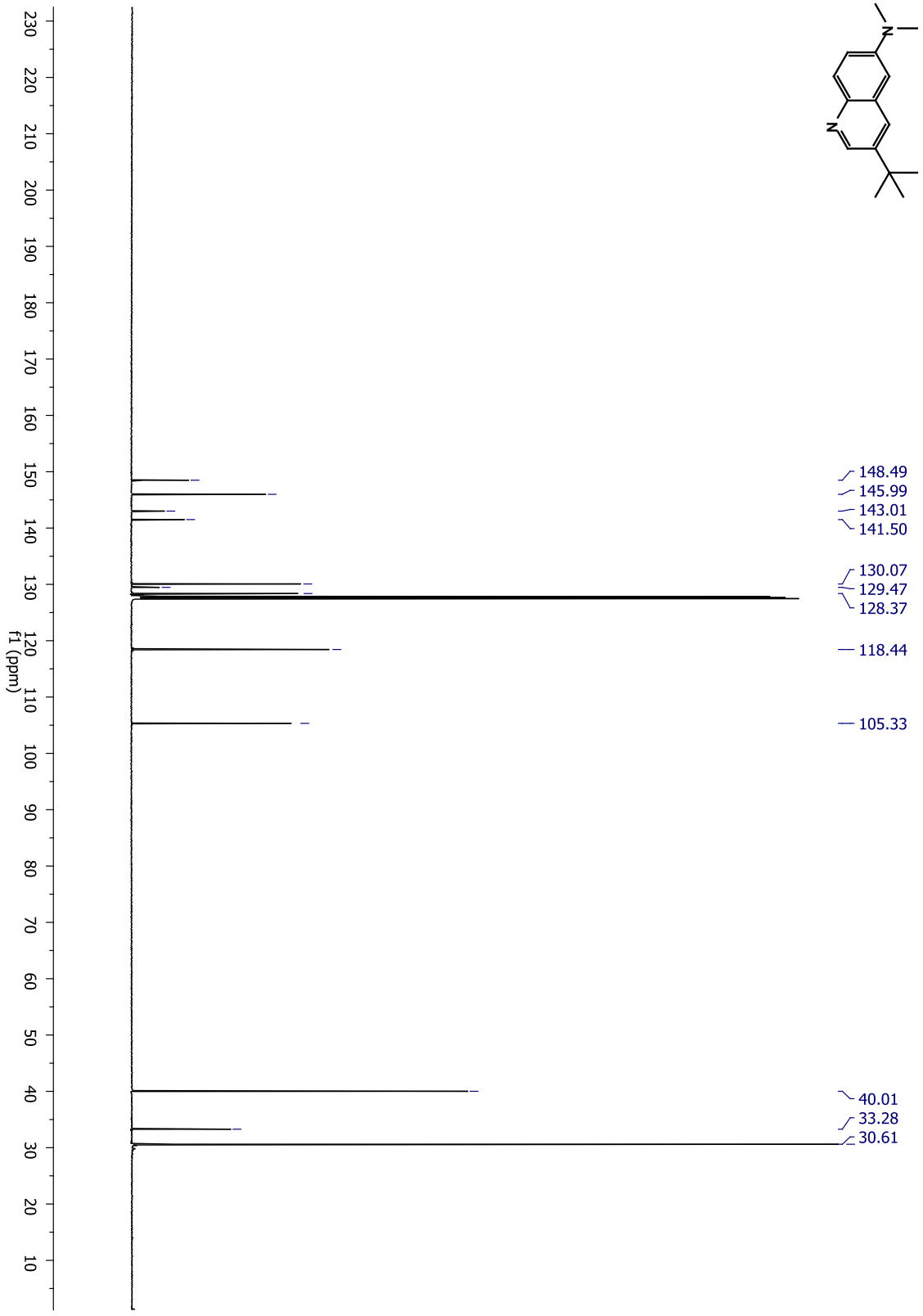


Figure S56: ^{13}C NMR spectrum for compound 3-*tert*-butyl-6-(N,N-dimethylamino)quinoline.

(**TM-081, Quinoline 31)**

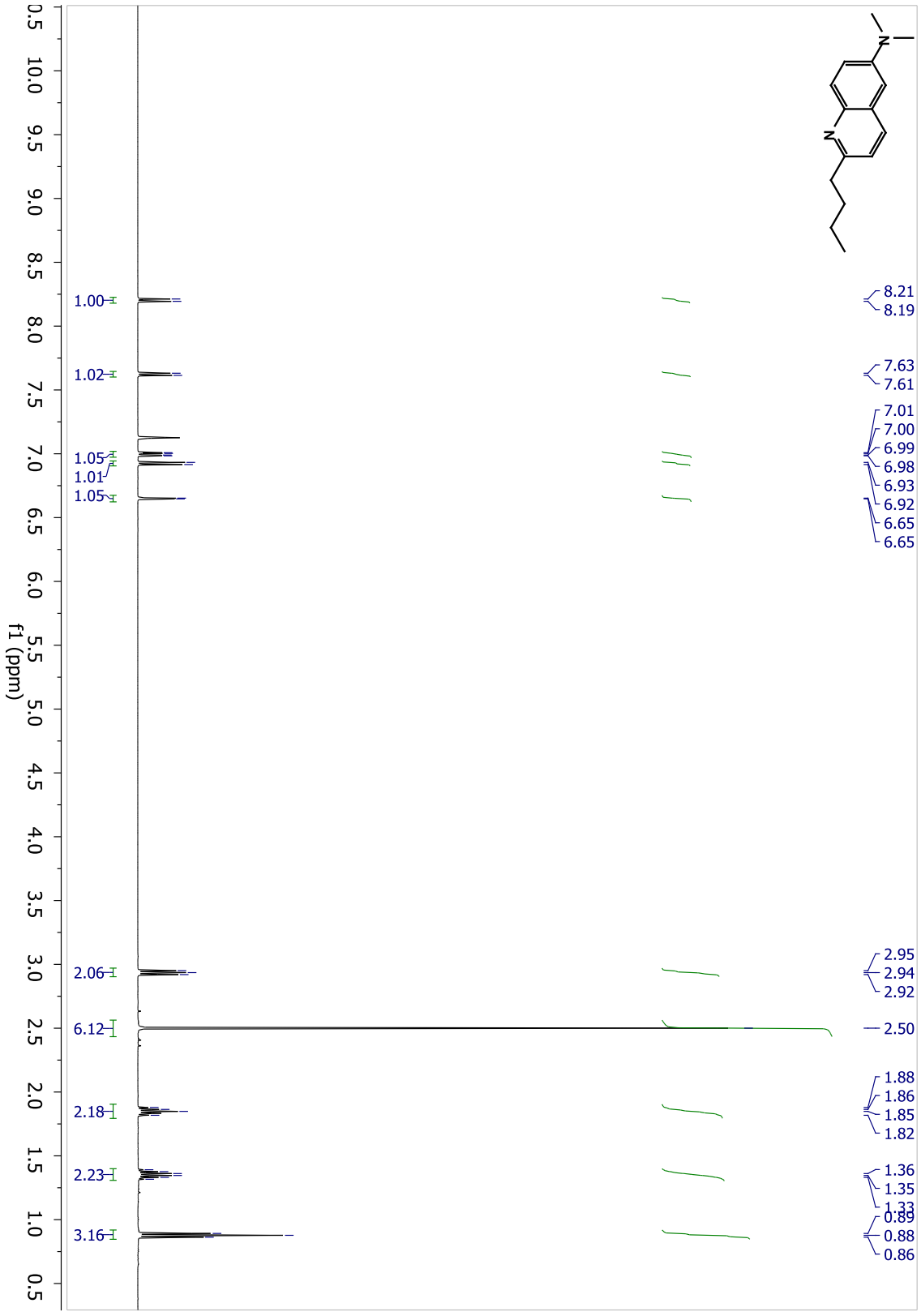


Figure S57: ^{1}H NMR spectrum for compound 2-butyl-6-(N,N-dimethylamino)quinoline.

(**TM-082, Quinoline 32)**

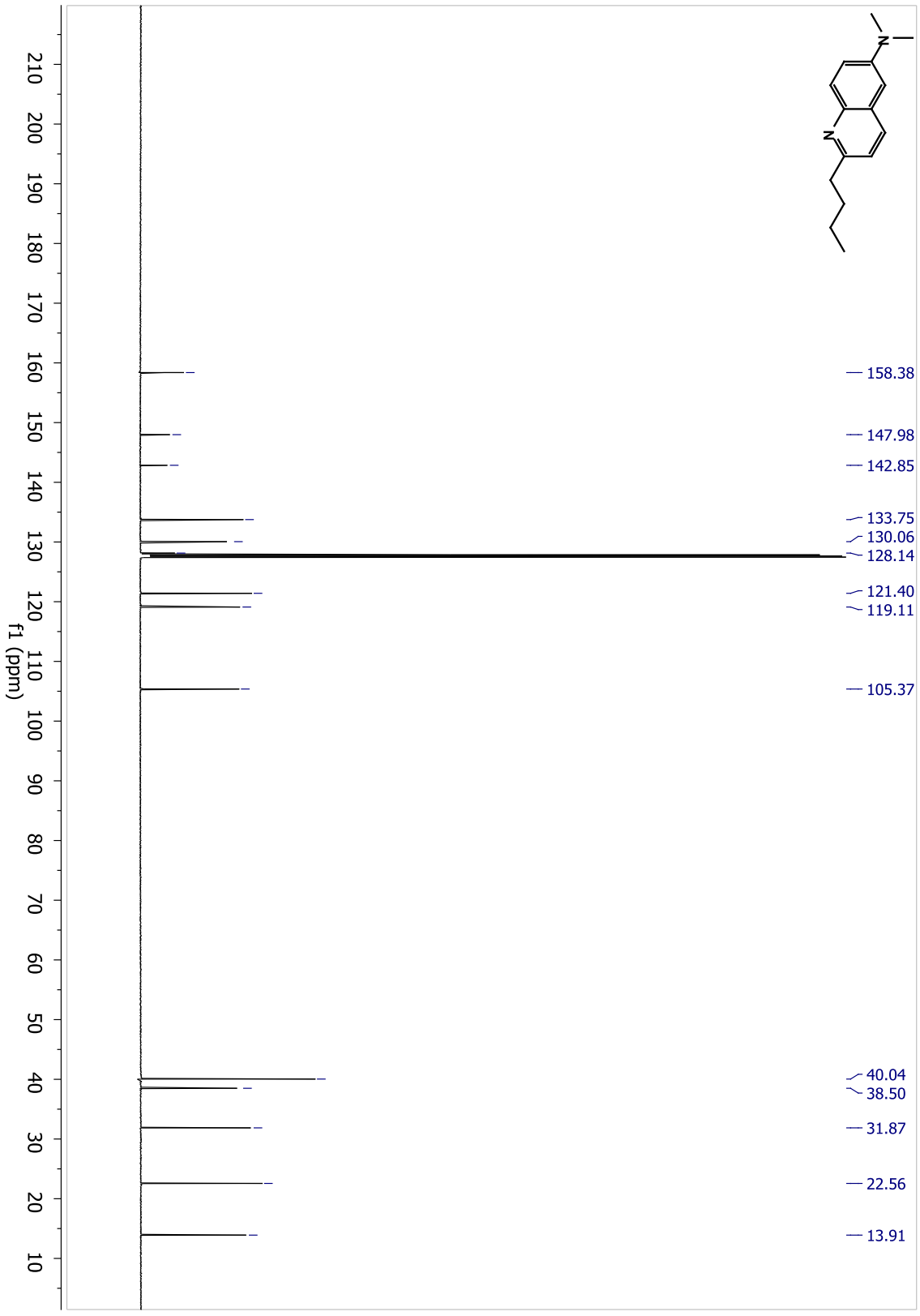


Figure S58: ^{13}C NMR spectrum for compound 2-butyl-6-(N,N-dimethylamino)quinoline.

(**TM-082, Quinoline 32)**

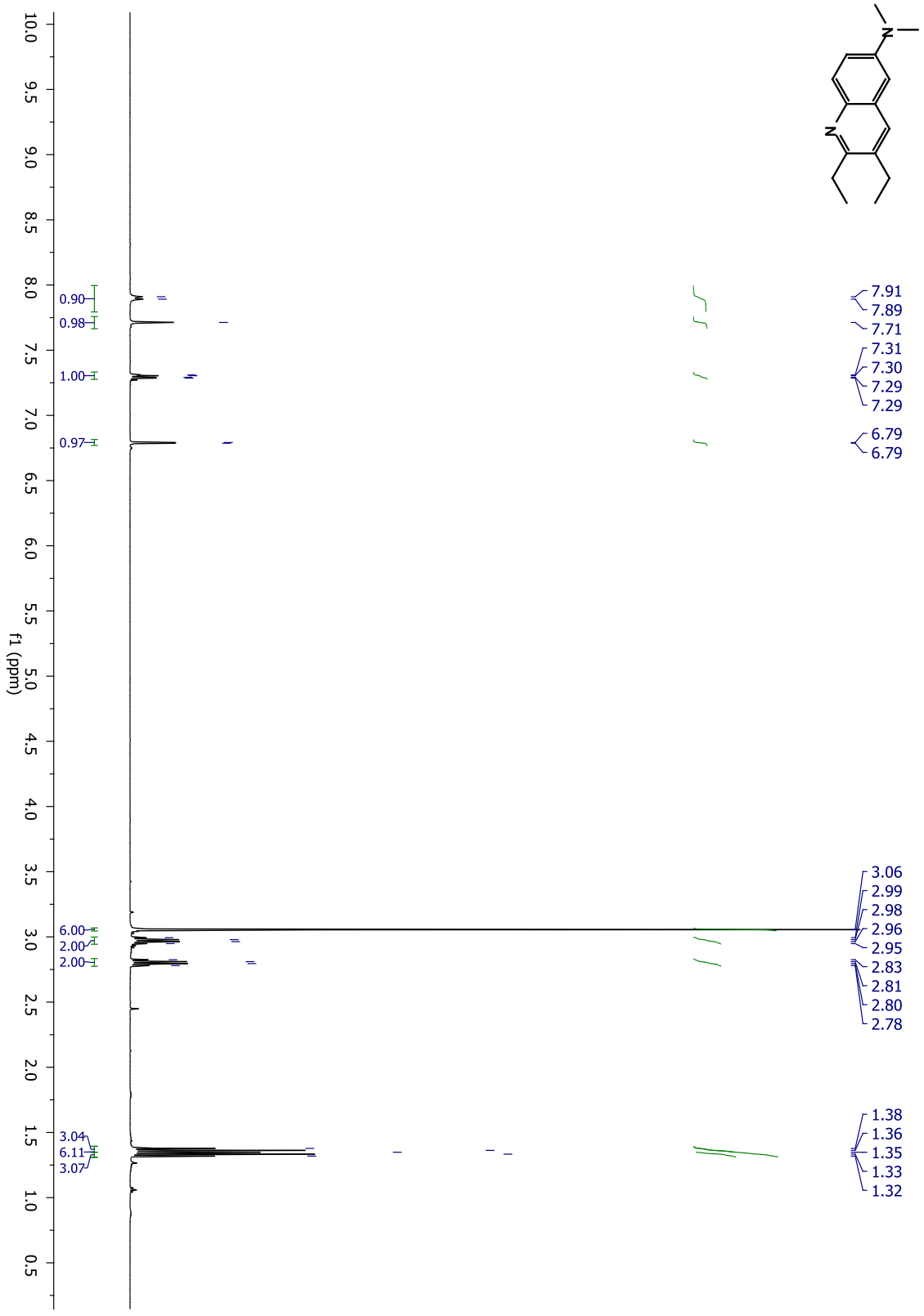


Figure S59: ^{1}H NMR spectrum for compound 2,3-diethyl-N,N-dimethylquinoline.

(**TM-090, Quinoline 33)**

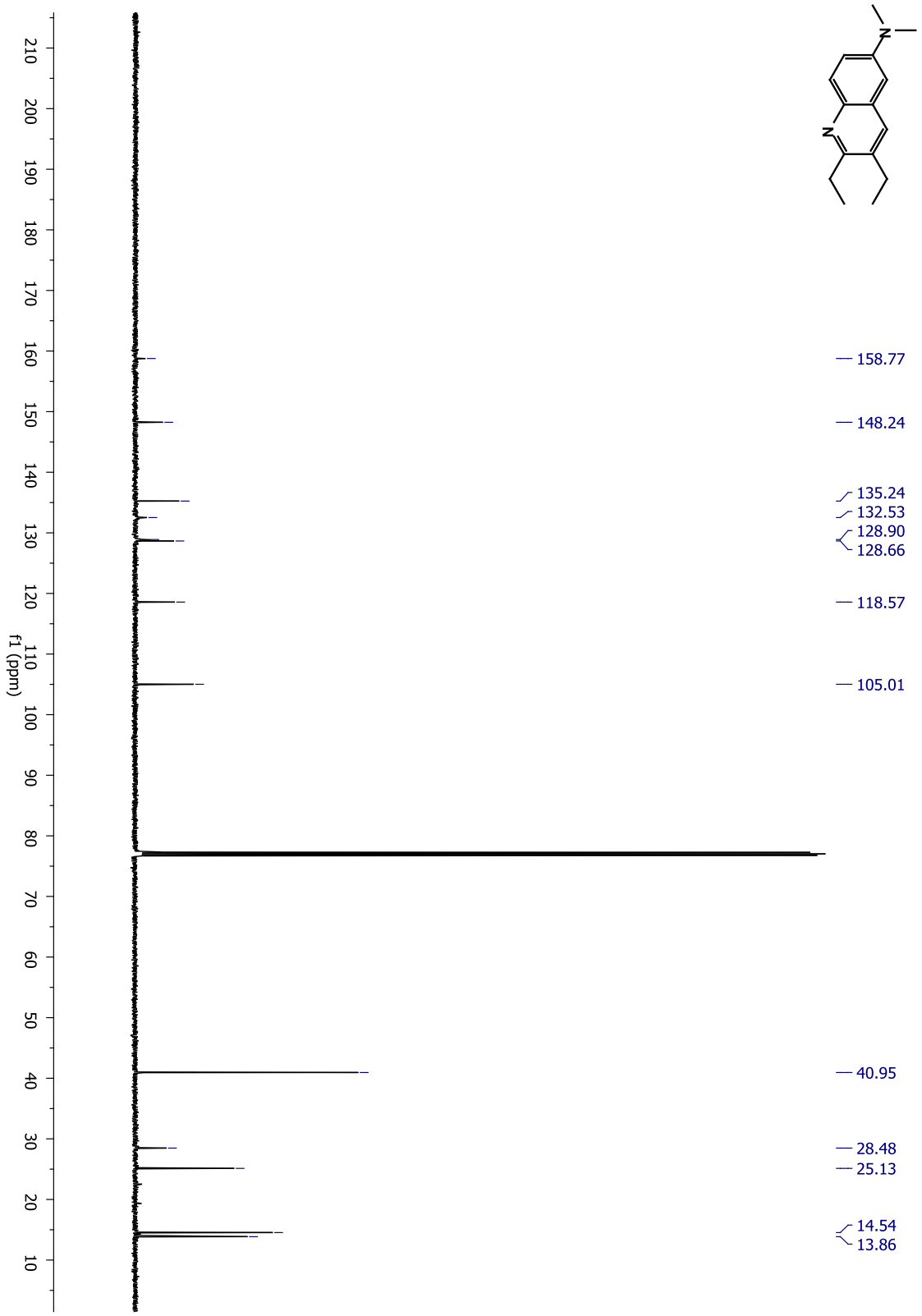


Figure S60: ^{13}C NMR spectrum for compound 2,3-diethyl-N,N-dimethylquinoline.

(**TM-090, Quinoline 33)**

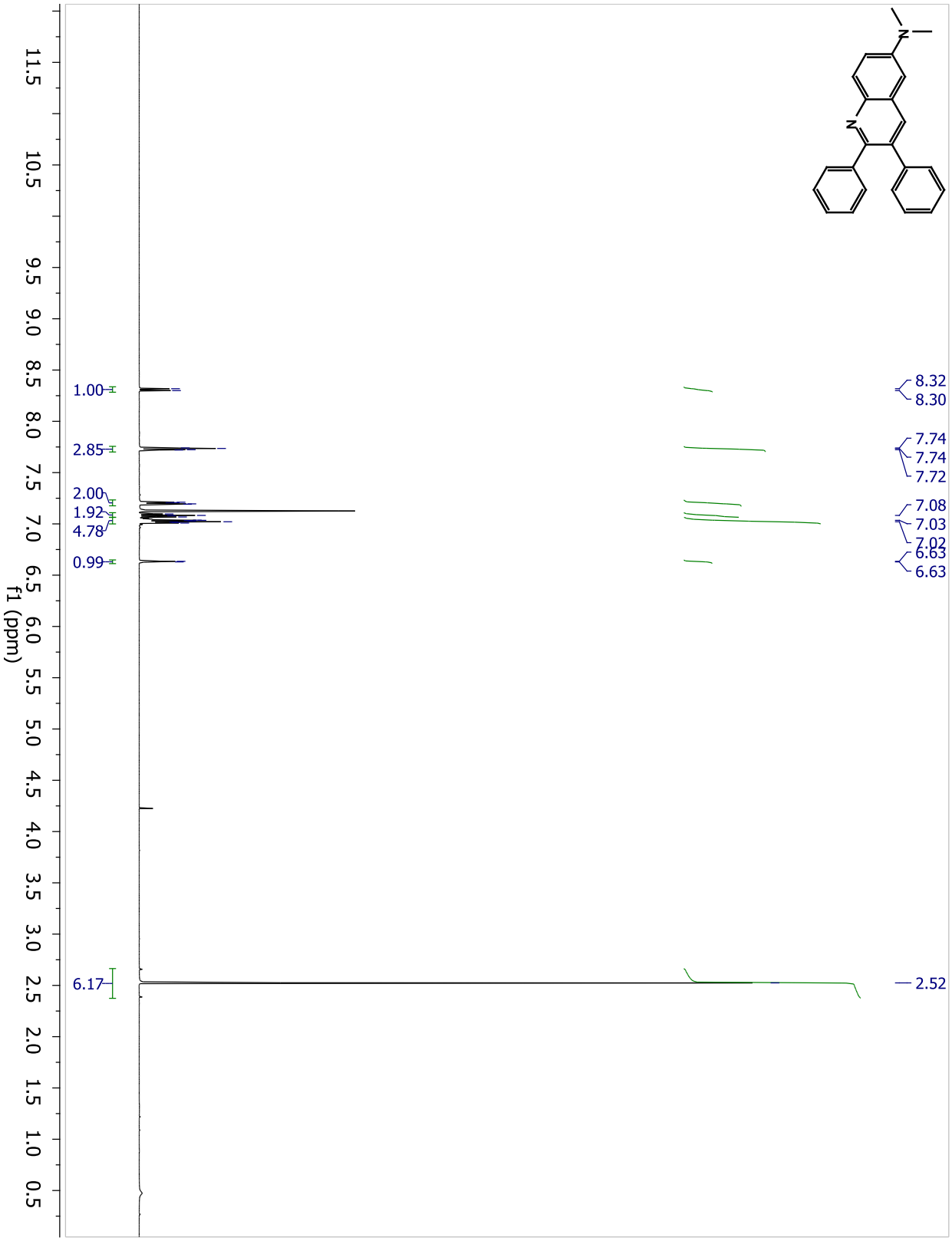


Figure S61: ^{1}H NMR spectrum for compound 2,3-diphenyl-6-(N,N-dimethylamino)quinoline.

(**TM-124, Quinoline 35)**

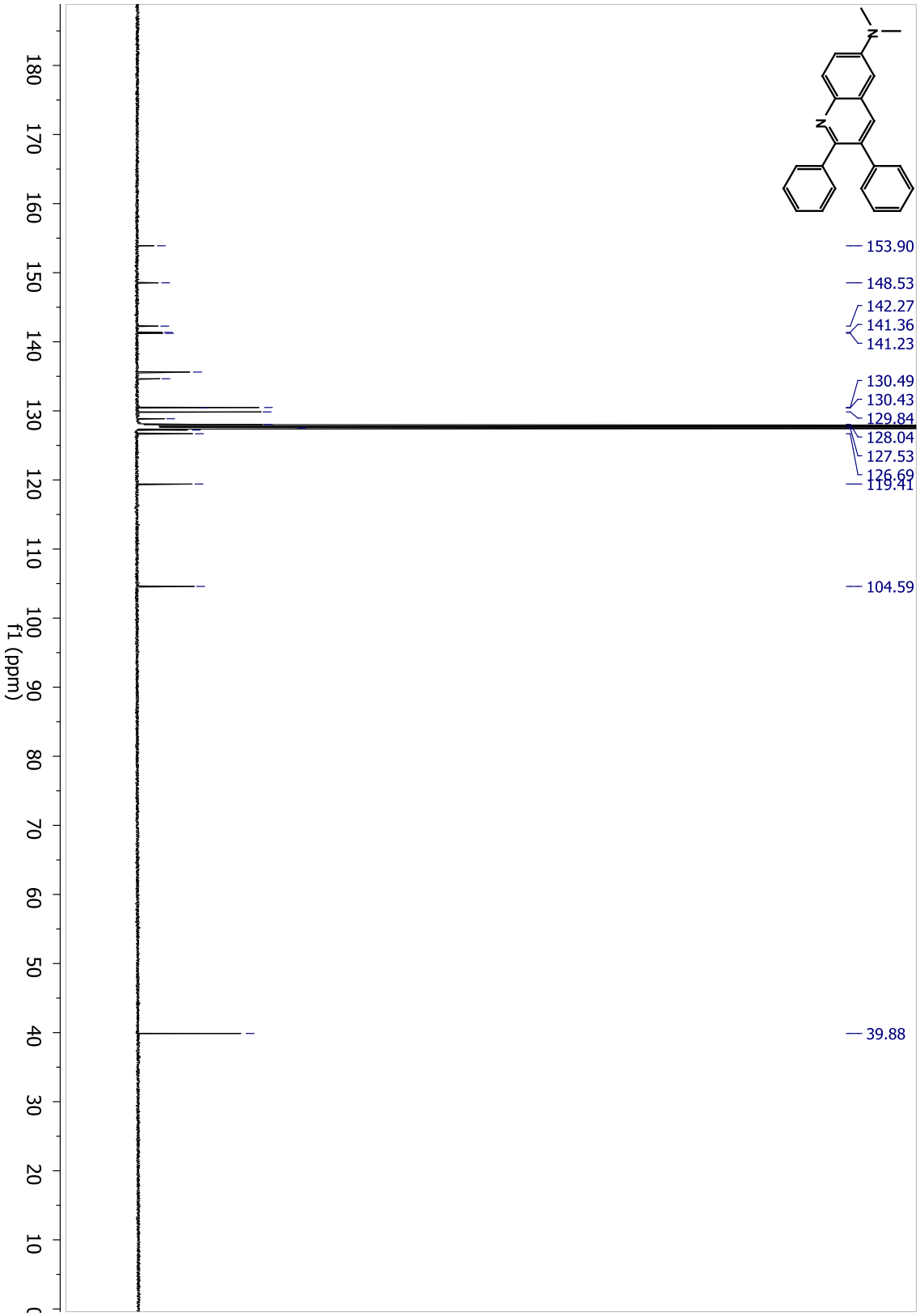


Figure S62: ^{13}C NMR spectrum for compound 2,3-diphenyl-6-(N,N-dimethylamino)quinoline.

(**TM-124, Quinoline 35)**

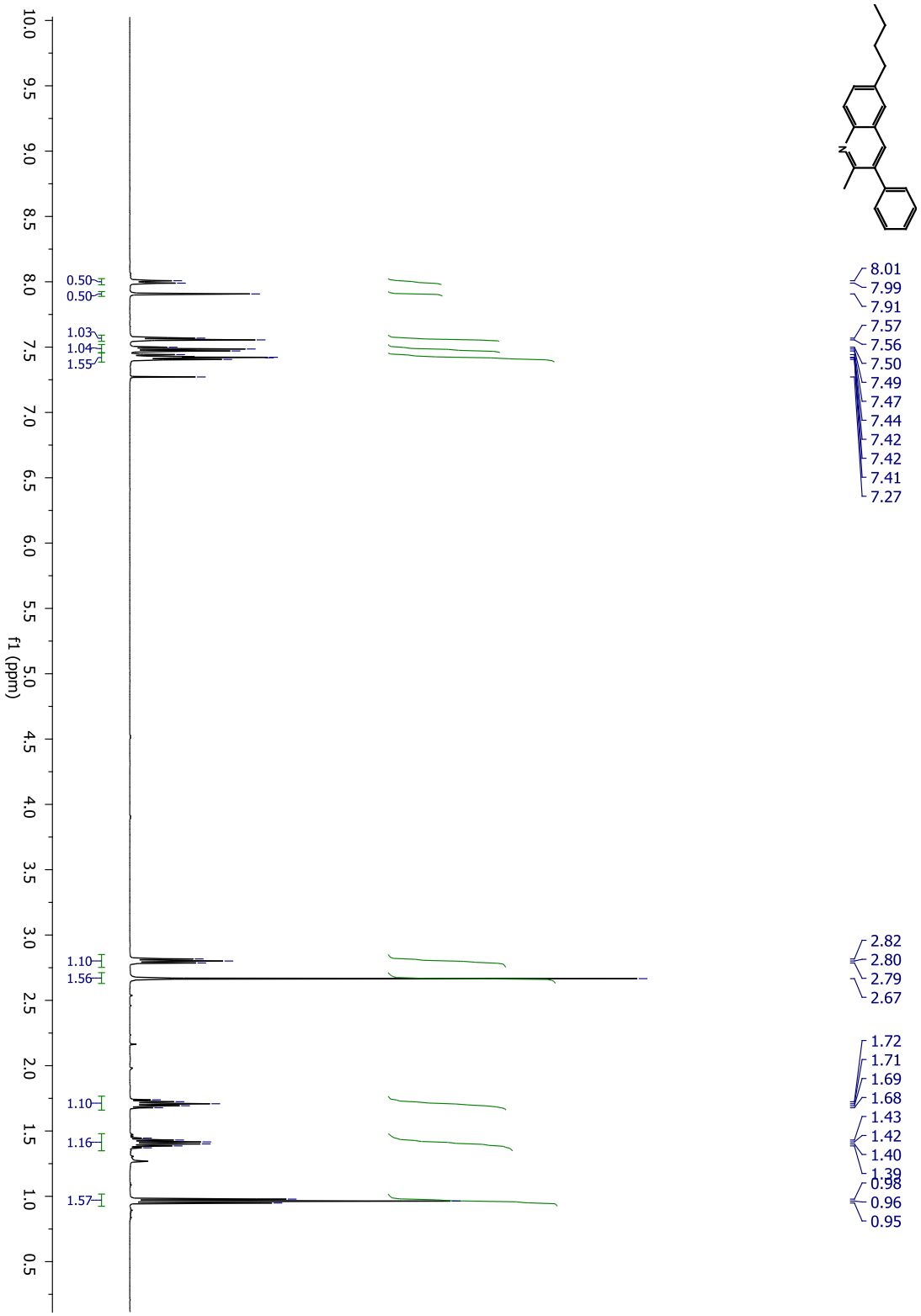


Figure S63: ^{1}H NMR spectrum for compound 6-butyl-2-methyl-3-phenylquinoline.

(**TM-114, Quinoline 36)**

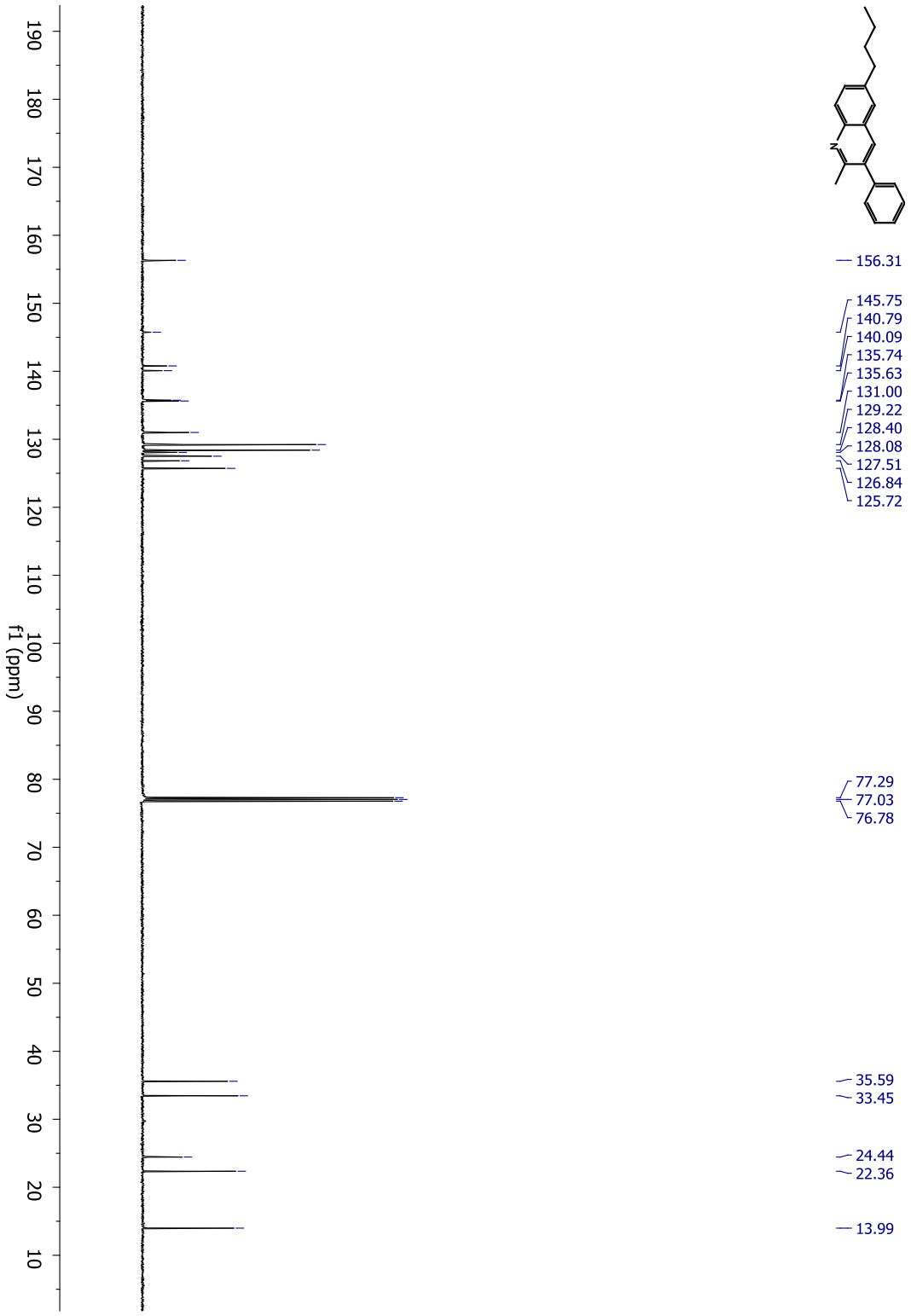


Figure S64: ^{13}C NMR spectrum for compound 6-butyl-2-methyl-3-phenylquinoline.

(**TM-114, Quinoline 36)**

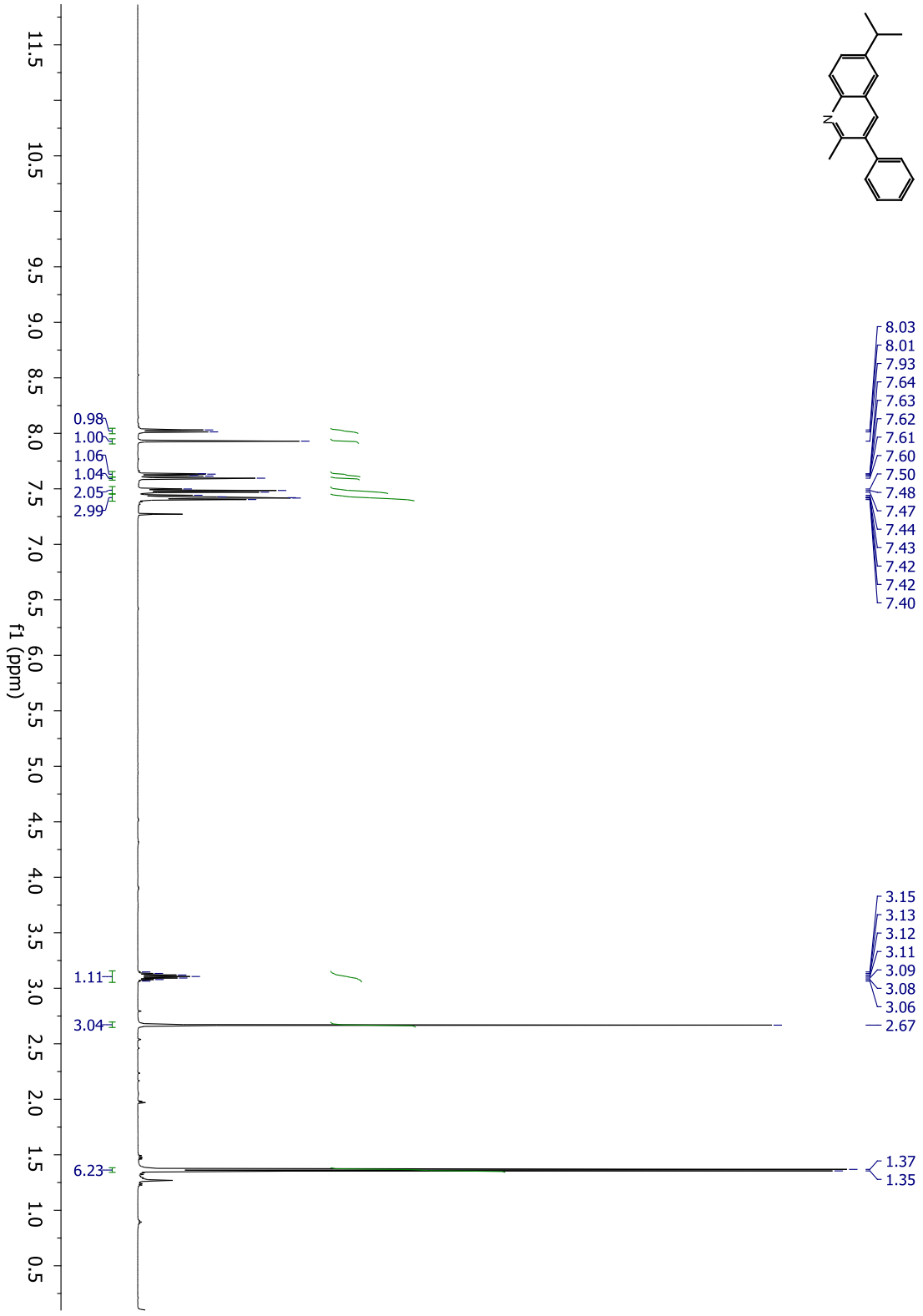


Figure S65: ^{1}H NMR spectrum for compound 6-isopropyl-2-methyl-3-phenylquinoline.

(**TM-119, Quinoline 37)**

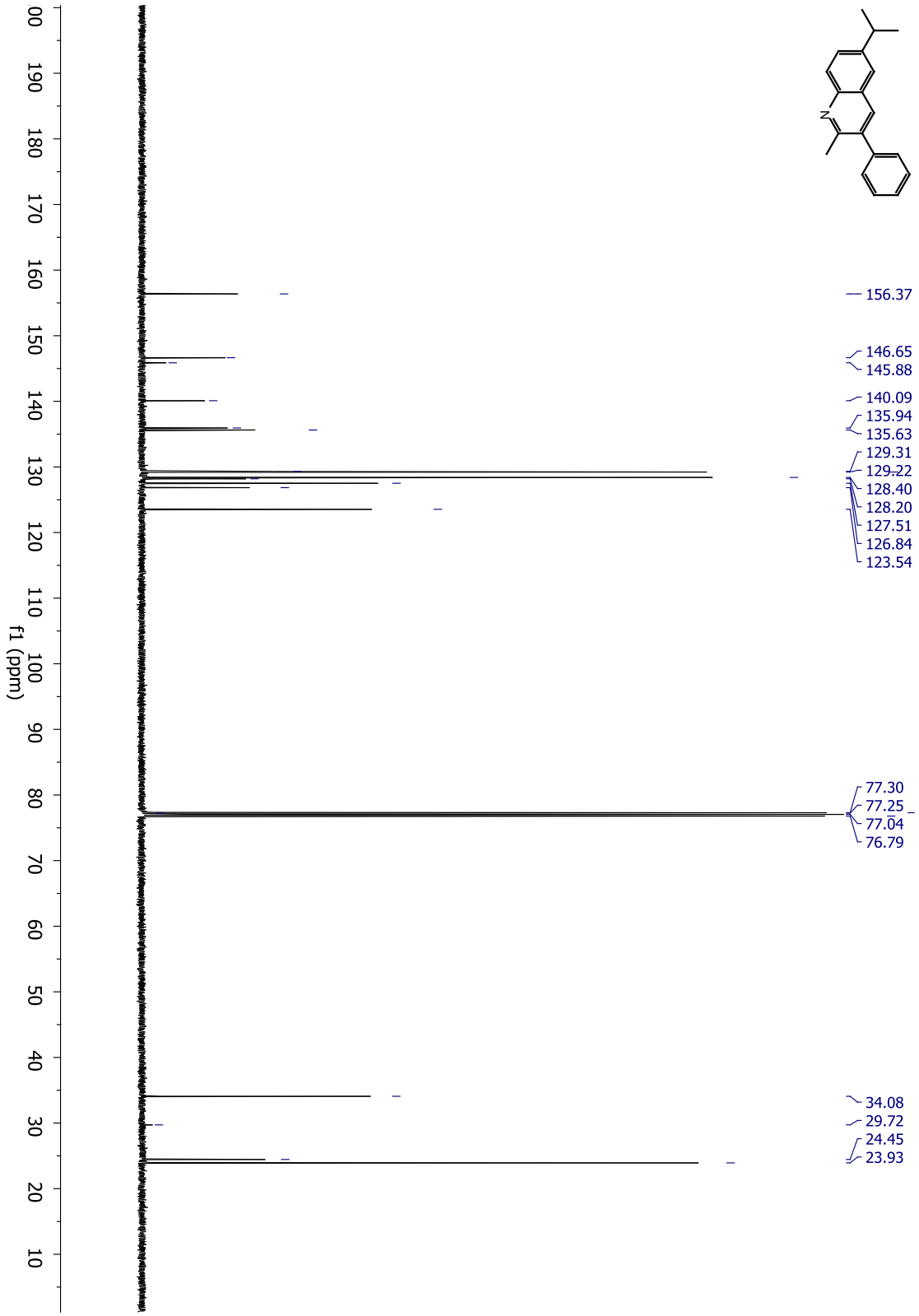


Figure S66: ^{13}C NMR spectrum for compound 6-isopropyl-2-methyl-3-phenylquinoline.

(**TM-119, Quinoline 37)**

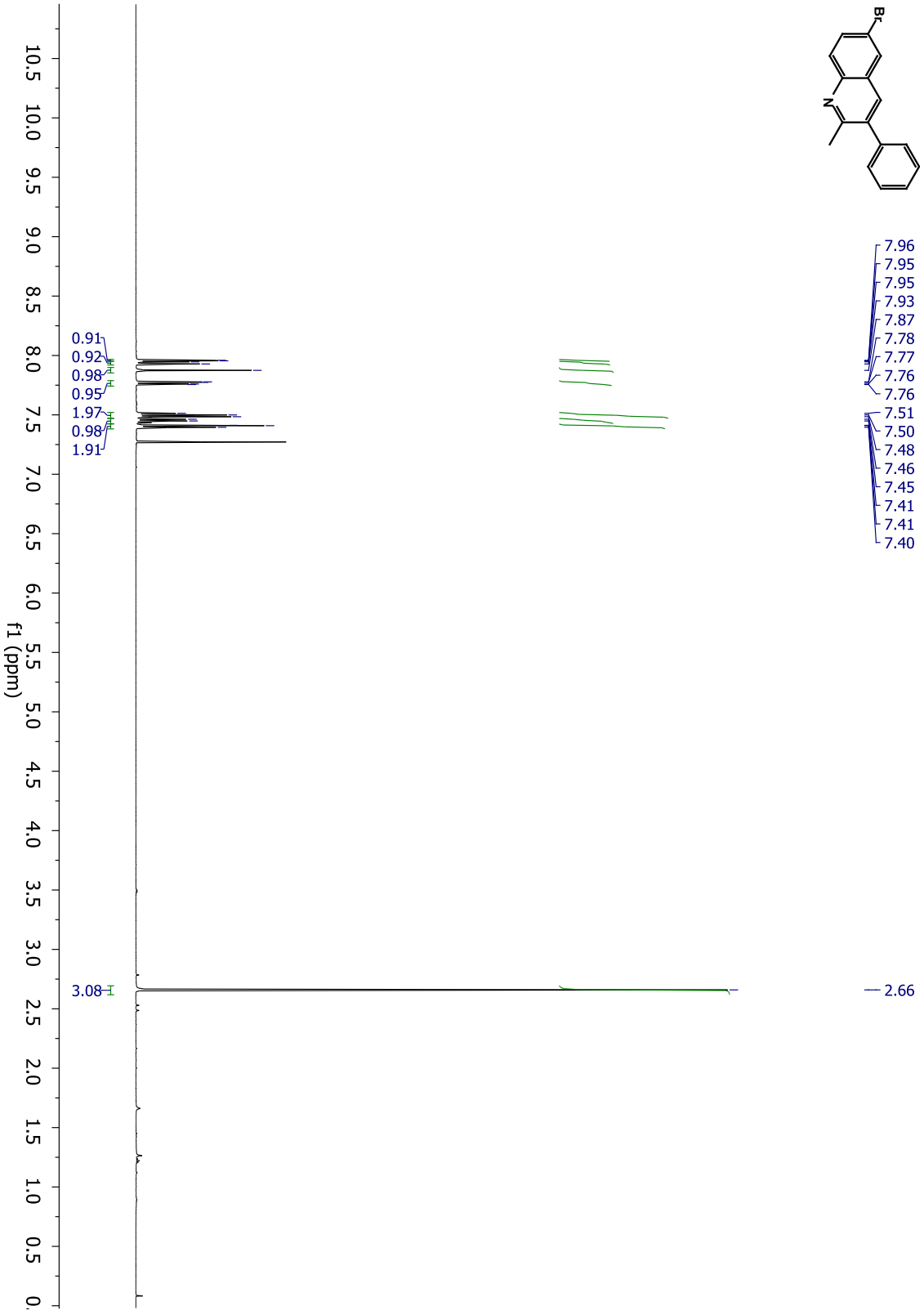


Figure S67: ^{1}H NMR spectrum for compound 6-bromo-2-methyl-3-phenylquinoline.

(TM-120, Quinoline 38)

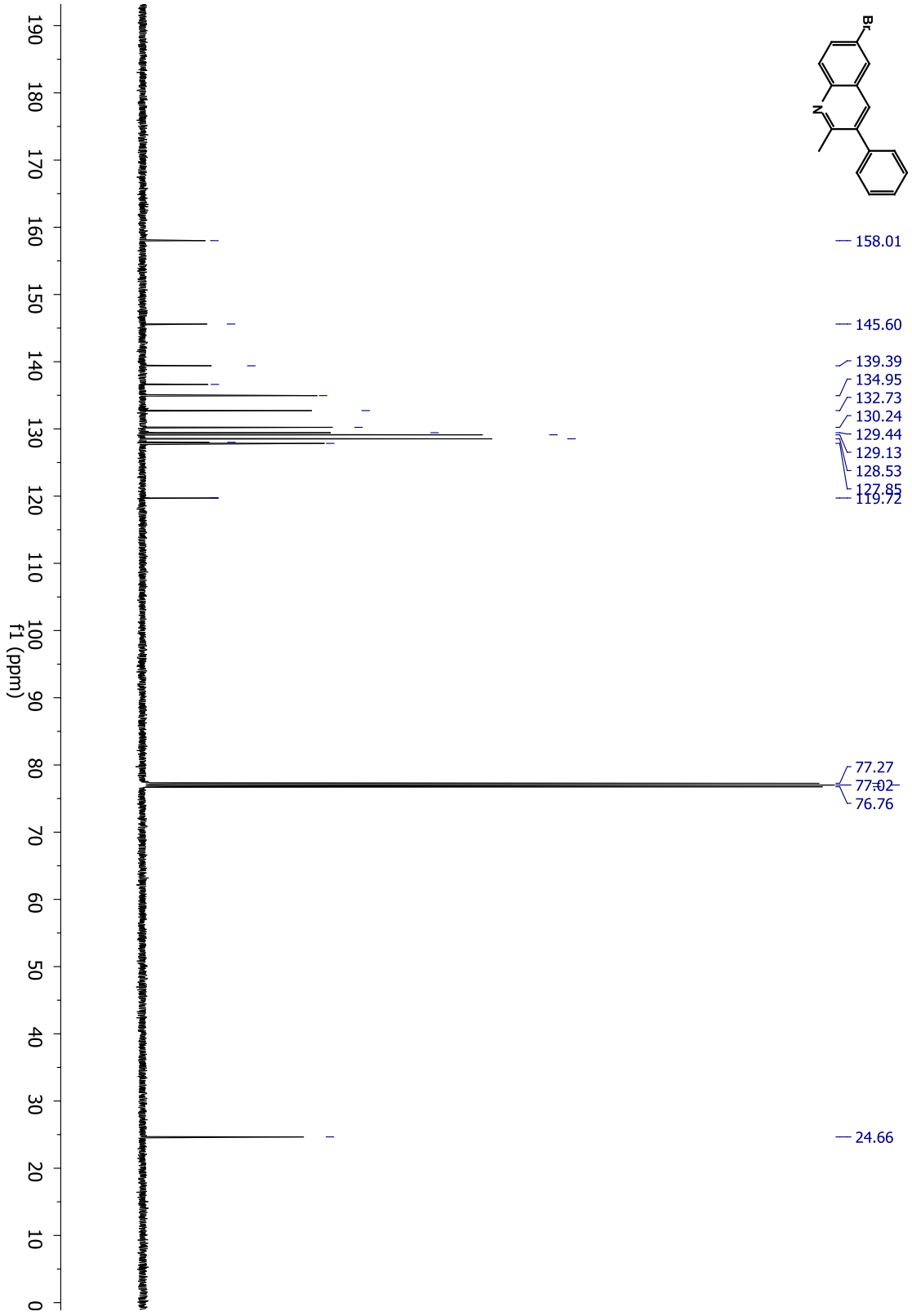


Figure S68: ^{13}C NMR spectrum for compound 6-bromo-2-methyl-3-phenylquinoline.

(TM-120, Quinoline 38)

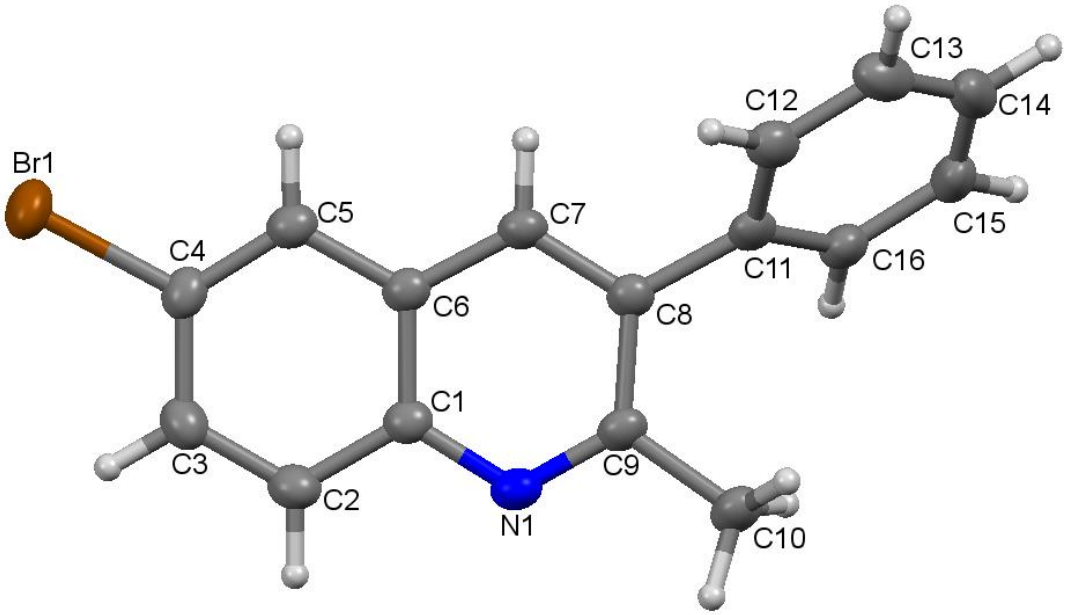


Figure 69: Crystal structure of 6-bromo-3-phenyl-2-methylquinoline.