Stemona Alkaloid-Inspired Chemical Libraries: Methodology Development, Screening, and the Discovery of a Potent Class of Sigma Ligands

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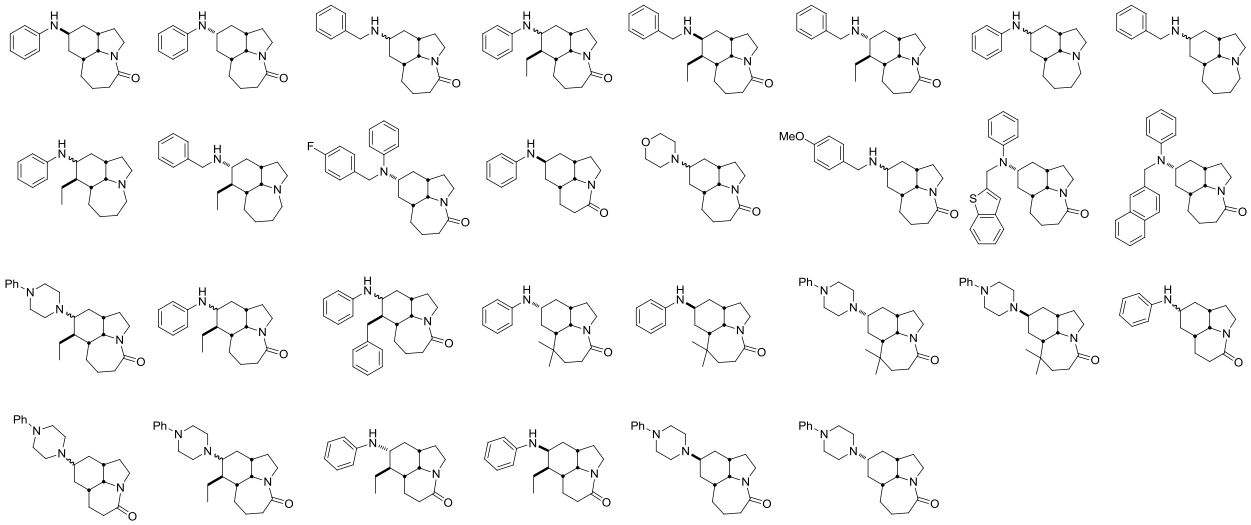
Contents:

Structures of the Initial 104 *Stemona* alkaloid analogues screened[a, b]

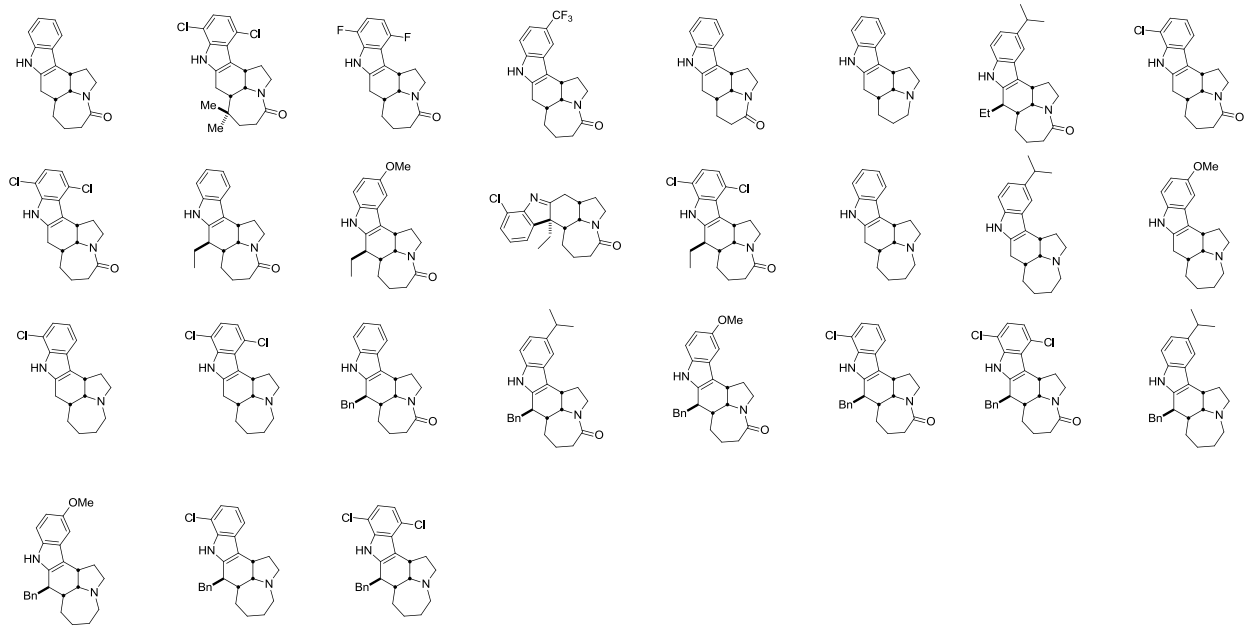
[a] Binding data can be found in Figure 3 of the manuscript (heatmap format) and in the supporting information data set (numerical Ki values with structures)

[b] To correlate the structures in this figure to the entries in the binding data tables above, read the structures left to right in rows

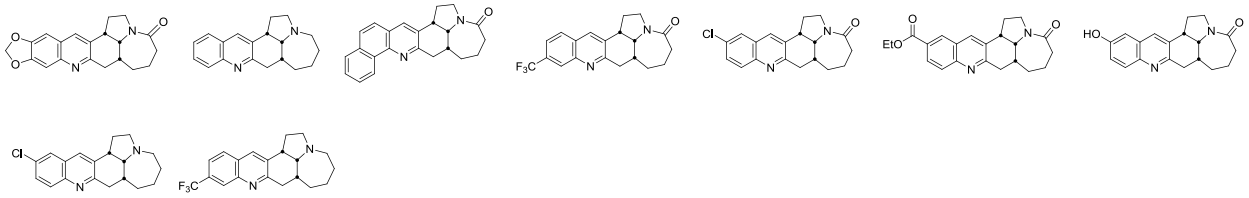
Reductive Amination Library Compounds:



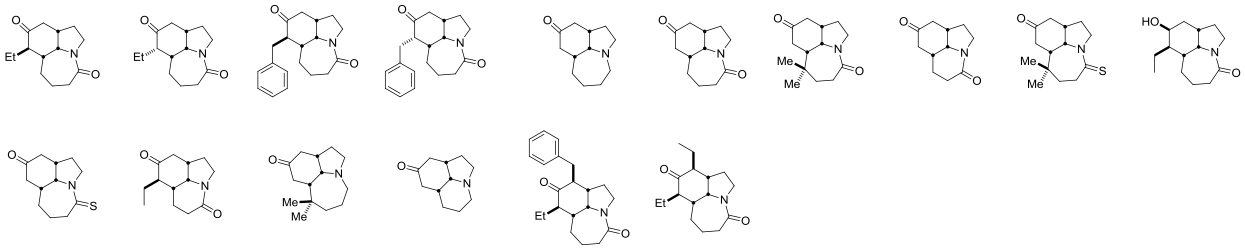
Indole Library Compounds:



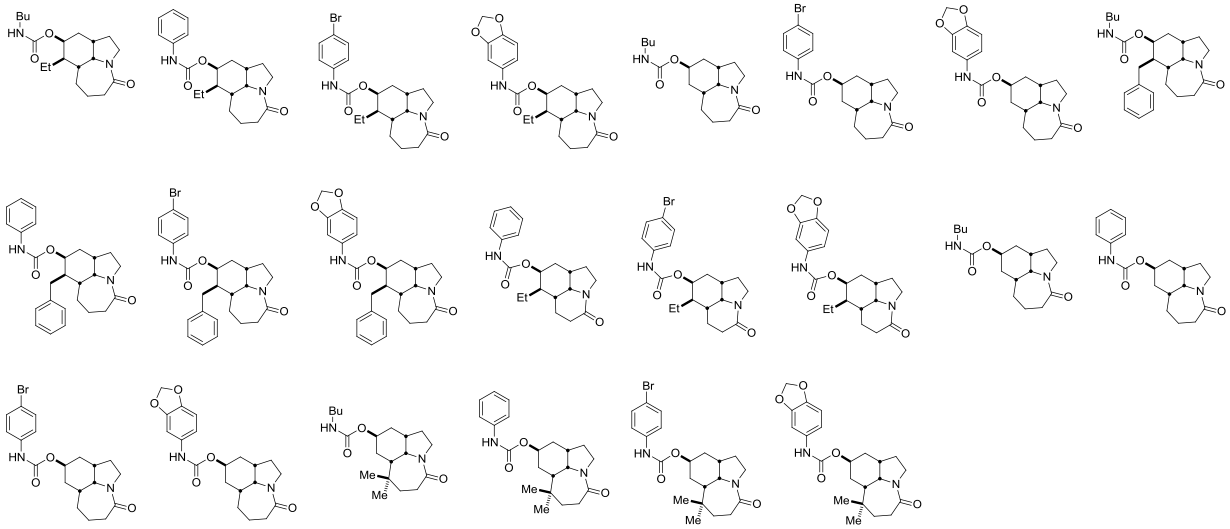
Quinoline Library Compounds:



Core Scaffold Analogue Compounds:



Carbamate Library Compounds:



Profile screening (secondary binding data) for compounds 10*{7}*, 10*{20}*, 10*{22}*

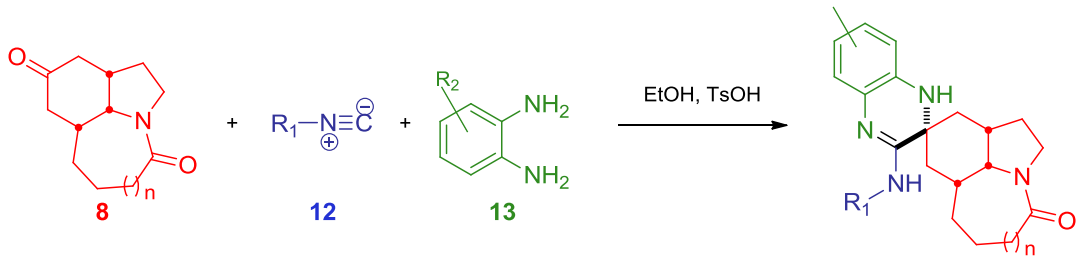
CMPD	5-HT1A	5-HT1B	5-HT1D	5-HT1E	5-HT2A	5-HT2B	5-HT2C	5-HT3	5-HT5A	5-HT6	5-HT7	Alpha1A	Alpha1B
10{7}													
10{20}	3,503.00												
10{22}	4,500.00												

CMPD	Alpha1D	Alpha2A	Alpha2B	Alpha2C	Beta1	Beta2	Beta3	D2	D4	DAT	DOR	H1	H2
10{7}		1,271.00	6,433.00	978.1					1,103.00			1,250.00	7,971.00
10{20}		906.7	8,222.00	1,060.00					1,274.00			1,574.00	
10{22}													

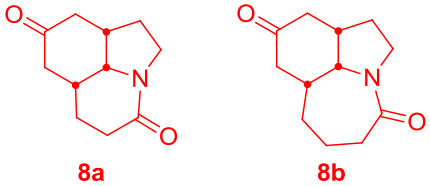
CMPD	H3	KOR	M1	M2	M3	M4	M5	MOR	NET	SERT	Sigma 1	Sigma 2
10{7}					2,686.00			516.9		1,941	5.8	124
10{20}		1,115.00			6,492.00			736.6			2	174.9
10{22}											12	288.1

Key:					
	Ki > 10 µM or primary screen missed		Ki = 5 to 10 µM		Ki = 1 to 5 µM
	Ki = 0.5 to 1 µM		Ki < 0.5 µM		no data or incomplete data

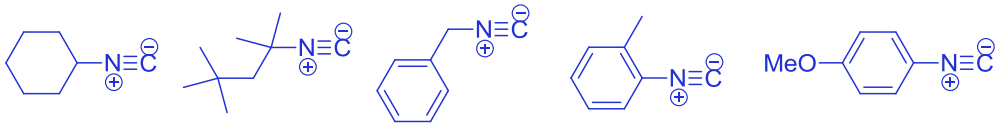
Synthesis and known secondary binding data for analogues 14



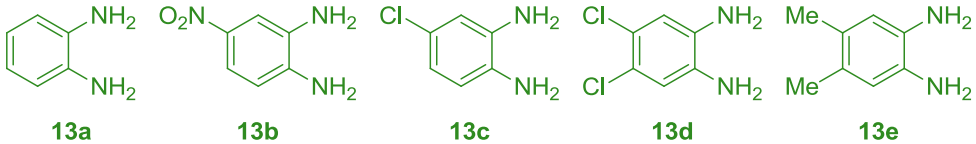
ketone scaffold



isocyanide fragment



diamine fragment



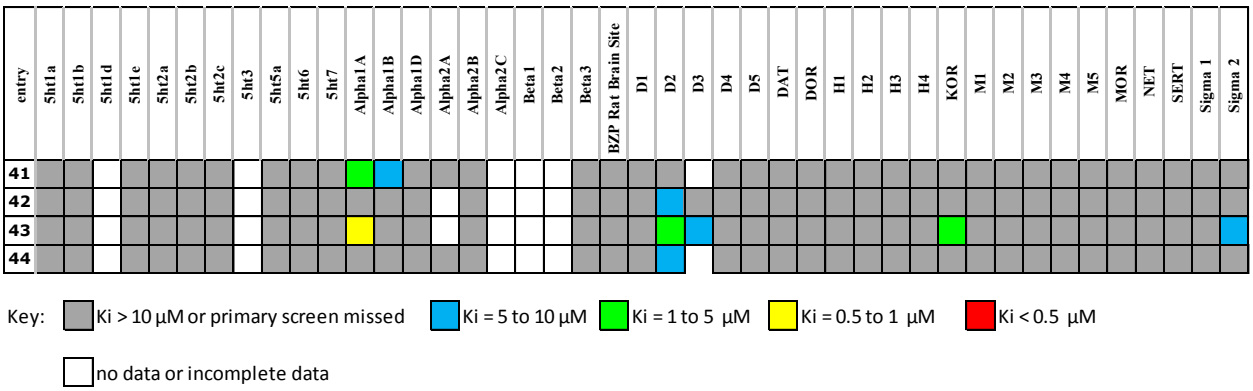
entry	ketone scaffold	isocyanide fragment	diamine fragment	yield[a] (%)	other known binding Ki (nM)	Sigma 1 Ki (nM)	Sigma 2 Ki (nM)
1	**8a**	**12a**	**13a**	29		3,037	> 10,000
2	**8a**	**12a**	**13b**	27		> 10,000	> 10,000
3	**8a**	**12a**	**13c**	30	KOR 2,948	> 10,000	> 10,000
4	**8a**	**12a**	**13d**	7		> 10,000	no data
5	**8a**	**12a**	**13e**	23		> 10,000	no data
6	**8a**	**12b**	**13a**	43		> 10,000	> 10,000
7	**8a**	**12b**	**13b**	16		3,885	> 10,000
8	**8a**	**12b**	**13c**	57		> 10,000	> 10,000
9	**8a**	**12b**	**13d**	30		> 10,000	760
10	**8a**	**12b**	**13e**	41	KOR 607	1,325	476
11	**8a**	**12c**	**13a**	33		867	280
12	**8a**	**12c**	**13b**	51		5,907	2,152
13	**8a**	**12c**	**13c**	40		1,117	> 10,000
14	**8a**	**12c**	**13d**	32	KOR 802	623	> 10,000
15	**8a**	**12c**	**13e**	54	KOR 407	1,158	> 10,000
16	**8a**	**12d**	**13a**	29		949	> 10,000
17	**8a**	**12d**	**13b**	8		> 10,000	no data
18	**8a**	**12d**	**13c**	6		> 10,000	no data
19	**8a**	**12d**	**13d**	7		> 10,000	no data
20	**8a**	**12d**	**13e**	35		> 10,000	> 10,000
21	**8b**	**12a**	**13a**	17		> 10,000	3,868

22	**8b**	**12a**	**13b**	45		6,613	> 10,000
23	**8b**	**12a**	**13c**	50		> 10,000	7,569
24	**8b**	**12a**	**13d**	15	KOR 3,614	> 10,000	3,160
25	**8b**	**12a**	**13e**	40		9,143	> 10,000
26	**8b**	**12b**	**13a**	42	$5HT_{1A}$ 431	4,415	6,798
27	**8b**	**12b**	**13b**	44	KOR 5,877	2,538	7,349
28	**8b**	**12b**	**13c**	60		> 10,000	4,137
29	**8b**	**12b**	**13d**	46		> 10,000	2,245
30	**8b**	**12b**	**13e**	61		> 10,000	> 10,000
31	**8a**	**12c**	**13a**	40	KOR 5,641	> 10,000	> 10,000
32	**8b**	**12c**	**13b**	27		> 10,000	> 10,000
33	**8b**	**12c**	**13c**	55	KOR 2,945	> 10,000	> 10,000
34	**8b**	**12c**	**13d**	28	KOR 7,412	3,628	1,622
35	**8b**	**12c**	**13e**	53		1,507	917
36	**8b**	**12d**	**13a**	24		4,133	1,014
37	**8b**	**12d**	**13b**	6		> 10,000	> 10,000
38	**8b**	**12d**	**13c**	24		1,253	769
39	**8b**	**12d**	**13d**	14		4,009	778
40	**8b**	**12d**	**13e**	35		3,744	749
41	**8b**	**12e**	**13b**	69	Alpha1A 1,156 Alpha1B 7,588	> 10,000	> 10,000
42	**8b**	**12e**	**13c**	73	D2 9,360	> 10,000	> 10,000
43	**8b**	**12e**	**13d**	23	KOR 3,080	> 10,000	7,526

					Alpha1A 922 D2 3,530 D3 7,037		
44	**8b**	**12e**	**13e**	71	D2 8,170	> 10,000	> 10,000

(a) Yield refers to isolated material of the major isomer, when chromatographic separation was possible

Heatmap format of GPCR profile screening of compounds 14[a]



(a) Numerical data (K_i values) included in above table

Experimental Details:

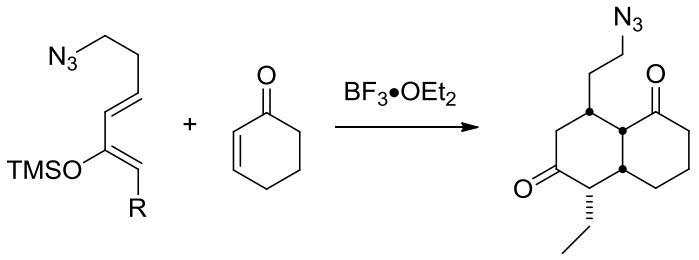
General. All chemicals were used as purchased from commercial suppliers unless otherwise stated. Methylene chloride, ethyl ether, toluene, acetonitrile and THF were dried by being passed through two packed columns of basic alumina under argon pressure prior to use. The azide-containing diene precursor to **7** and the ketoamide substrates **8a** and **8b** were synthesized as previously described.[i] The synthetic routes and representative characterization for the compounds in Table 2 of the manuscript have been previously described.[i]

Parallel syntheses were performed on the Bohdan Miniblock XT parallel solution phase synthesizer obtained from Mettler-Toledo Auto Chem. Automated weighing was performed using the Bohdan Balance Automator (Mettler-Toledo Auto Chem). Parallel evaporation was performed on the GeneVac EZ-2 plus evaporator system. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM 400 spectrometer (operating at 400 and 100 MHz respectively) in $CDCl_3$ with 0.03% TMS as an internal standard. Chemical shifts are reported in parts per million (ppm) downfield from TMS. ^{13}C multiplicities were determined with the aid of an APT pulse sequence, differentiating the signals for methyl and methane carbons as "d" from methylene and quarternary carbons as "u". The infrared (IR) spectra were acquired as thin on a PerkinElmer Spectrum 100 FT-IR spectrometer equipped with a universal ATR sampling accessory and the absorbtion frequencies are reported in cm^{-1}. Melting points were determined on an Electrothermal Mel-Temp model number 101D apparatus and are uncorrected.

HPLC analysis was carried out using an XBridge MS C-18 column (5 μM, 4.6 × 150 mm) with gradient elution (5% CH_3CN to 100% CH_3CN) on a Waters Alliance 2795 Separation Module with a Waters 2996 Photodiode Array UV detector and a Waters/Micromass LCT Premier (TOF) detector. Purification was carried out using an XBridge MS C-18 column (5 μM, 19 × 150 mm) with gradient elution (a narrow CH_3CN gradient was chosen based on the targets retention time from LCMS analysis of the crude sample) on a Mass Directed Fractionation instrument with a Waters 2767 sample manager, a Waters 2525 HPLC pump, a Waters 2487 dual λ absorbance detector, and a Waters/Micromass ZQ (quadrupole) detector. Fractions were triggered using an MS and/or UV threshold determined by an LCMS analysis of the crude sample. One of three aqueous mobile phases were chosen for both analysis and purification to promote the

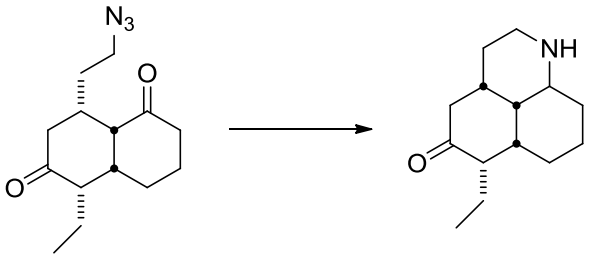
targets neutral state (water, 0.05% formic acid or pH 9.8 1mM HCO_2NH_4). High resolution mass spectra (HRMS) were obtained using a Waters/Micromass LCT Premier (TOF instrument).

Radio ligands for the radio ligand binding assays were purchased from Perkin-Elmer or GE Healthcare. Competition binding assays were performed using transfected or stably expressing cell membrane preparations as previously described.[ii, iii, iv] Detailed information such as radioligand identity, radioligand concentration, incubation buffer and incubation time for all assays are available online (http://pdsp.med.unc.edu/UNC-CH%20Protocol%20Book.pdf).



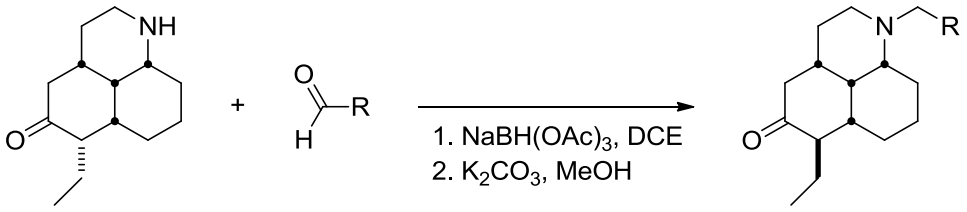
10-Ethyloctahydroazepino[3,2,1-hi]indole-4,9(1H,51H)-dione 7. To a solution of 2-cyclohexen-1-one (840 mg, 8.73 mmol) in CH_2Cl_2 (150 mL) and flame-dried 4 Å molecular sieve pellets (14.00 g) at -78 °C was added BF_3•OEt_2 (1.1 mL, 8.73 mmol, 1.0 equiv.). After stirring for 5 minutes at -78 °C, the azide-containing siloxydiene (3.13 g, 13.10 mmol, 1.5 equiv.) in CH_2Cl_2 (10 mL) was added portionwise over 15 minutes. The reaction was stirred overnight, slowly warming to rt. The reaction was worked up with saturated aqueous NH_4Cl and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried over anhydrous Na_2SO_4, concentrated and chromatographed to afford the bicyclic diketoazide intermediate (1.80 g, 6.84 mmol, 78% yield). TLC R_f = 0.43 (25% EtOAc in hexanes); ^{1}H NMR δ 0.83 (t, J = 7.6

Hz, 3 H), 1.40-1.52 (m, 2 H), 1.64 (m, 1 H), 1.85 (m, 2 H), 1.92-2.08 (complex, 3 H), 2.19-2.34 (complex, 3 H), 2.49 (m, 2 H), 2.68 (dd, J = 11.1, 14.4 Hz, 1 H), 2.78 (m, 1 H), 2.92 (m, 1 H), 3.27 (m, 1 H), 3.36 (m, 1 H); ^{13}C NMR δ d 11.9, 35.8, 42.3, 49.7, 55.1; u 19.7, 23.7, 25.3, 31.2, 41.3, 41.6, 49.2, 212.0, 213.0; IR 3397 (w), 2962 (s), 2876 (s), 2094 (s), 1715 (s), 1257 (s) cm^{-1}; HRMS calcd for $C_{14}H_{22}N_3O_2$ [M + H$^+$] 264.1712, found 264.1724.



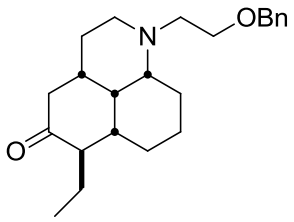
6-Ethyldecahydro-1H-benzo[de]quinolin-5(3a1H)-one 9. The diketoazide **7** (108 mg, 0.41 mmol) and polystyrene bound triphenyl phosphine (0.27 g resin, 0.82 mmol) in THF (8 mL) were stirred at rt for 14 h. The reaction was filtered through celite and concentrated. The residue was taken up in CH_2Cl_2 (5 mL) and $NaBH(OAc)_3$ (174 mg, 0.82 mmol) was added as a solid. The reaction was stirred 4 h at rt and partitioned between NaOH (1 N, 15 mL) and CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried (Na_2SO_4) and concentrated. The crude product was purified by filtration through a short alumina column, eluting with 1:1 acetone: CH_2Cl_2 to give the tricyclic amine **9** (65 mg, 0.29 mmol, 72% yield) as a yellow oil. R_f = 0.04 (1:1 acetone:CH_2Cl_2); ^{1}H NMR δ 0.81 (t, J = 7.3 Hz, 3 H), 1.21 (m, 2 H), 1.36-1.75 (complex, 11 H), 1.82 (m, 1 H), 2.14-2.32 (m, 3 H), 2.75 (dt, J = 2.8, 11.9 Hz, 1 H), 3.11 (ddd, J = 2.5, 4.3, 12.1 Hz, 1 H); ^{13}C NMR δ d 11.8, 42.3, 43.7, 46.1, 57.3, 61.0; u 19.6, 24.5, 29.2, 33.2, 34.3, 44.6,

46.5, 214.0; IR (neat) 2927, 2858, 1709 cm^{-1}; HRMS calcd for $C_{14}H_{24}NO$ [M + H] 222.1858, obsd 222.1851.

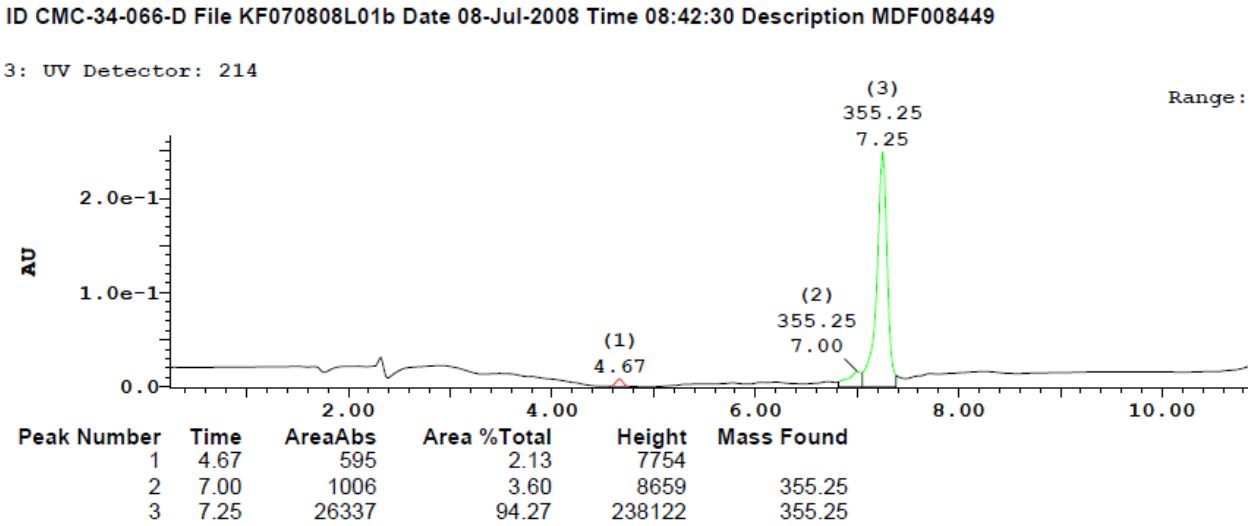


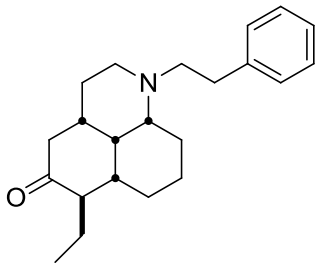
General procedure for the reductive amination of tricycle 9: The aldehyde component (0.50 mmol, 2.5 equiv) was charged as a neat oil or powder into individual reaction tubes of a Bohdan Miniblock XT parallel solution phase synthesizer. To each reaction tube was added a solution of the tricyclic amine **9** (45 mg, 0.20 mmol) in dichloroethane (3 mL) and solid sodium triacetoxyborohydride (170 mg, 0.80 mmol, 4 equiv). The reaction was stirred at rt for 14 h, diluted with aqueous sodium hydroxide (1 N, 6 mL), transferred to hydrophobic phase separator tubes and extracted with CH_2Cl_2 (2 × 3 mL). The combined organics were collected in a clean set of 17 × 110 mm reaction tubes and evaporated under vaccum in parallel to afford the crude tertiary amine products.

To each of the above crude tertiary amine products was added a magnetic stir bar, MeOH (4 mL) and K_2CO_3 (125 mg, 0.90 mmol, 4.5 equiv). The reactions were stirred for 16 h, filtered through fritted reaction tubes and evaporated under vacuum in parallel. The reaction residues were directly purified by mass-directed preparative HPLC purification to afford the pure epimerized tertiary amine products **10**.

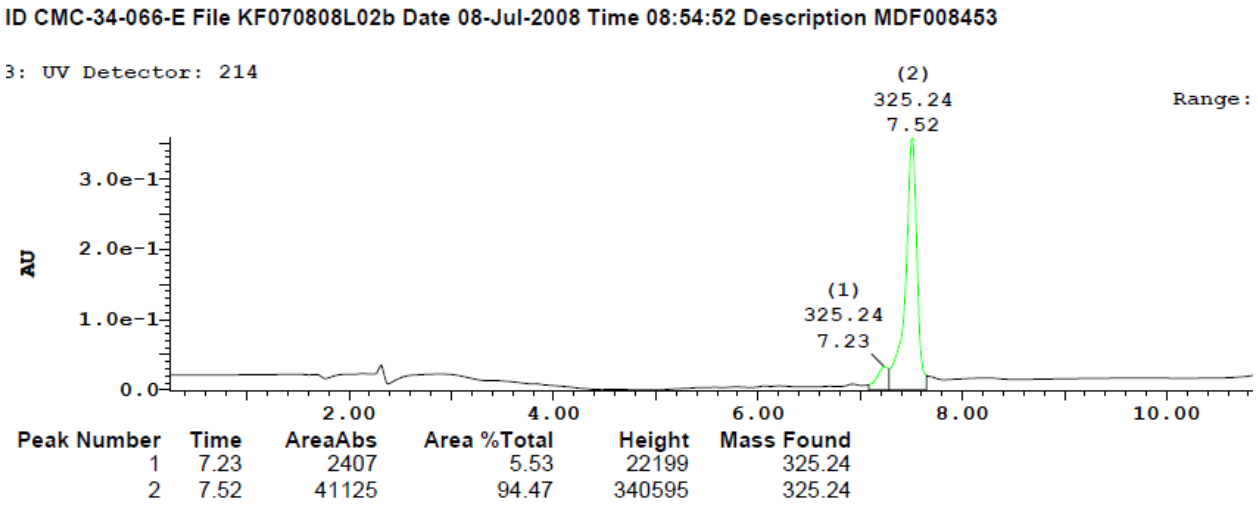


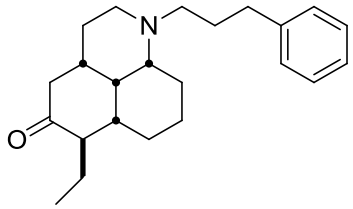
1-(2-(benzyloxy)ethyl)-6-ethyldecahydro-1H-benzo[de]quinolin-5(3a1H)-one 10*{1}*. The general procedure afforded **10*{1}*** (30.8 mg, 0.087 mmol, 44% yield) as a viscous light brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.84 (t, *J* = 8.0 Hz, 3 H), 1.02 (dq, *J* = 4.0, 12.0 Hz, 1 H), 1.12-1.35 (complex, 4 H), 1.40-1.69 (complex, 5 H), 1.84-2.04 (complex, 4 H), 2.14 (m, 2 H), 2.33 (dd, *J* = 4.0, 12.0 Hz, 1 H), 2.45 (m, 1 H), 2.76 (m, 1 H), 3.03 (m, 2 H), 3.59 (t, *J* = 8.0 Hz, 2 H), 4.51 (s, 2 H), 7.24-7.38 (complex, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ u: 17.9, 24.5, 30.0, 31.3, 33.1, 48.8, 52.1, 53.5, 67.3, 73.2, 138.3, 210.7; d 11.2, 41.4, 44.7, 50.7, 56.1, 64.5, 127.5, 127.6 (× 2), 128.3 (× 2); IR (neat) 2928, 2859, 1709 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{34}NO_2$ ($[M+H]^+$), 356.2590, found 356.2570.



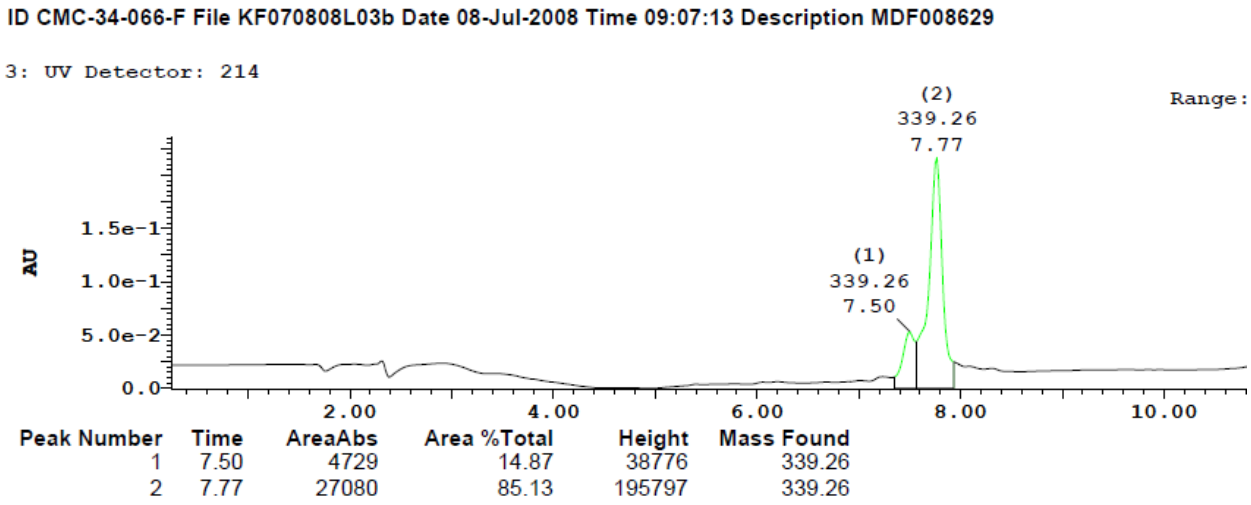


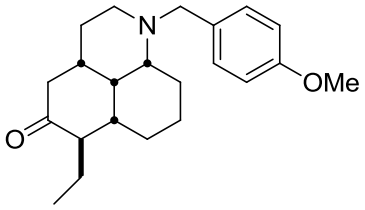
6-ethyl-1-phenethyldecahydro-1H-benzo[de]quinolin-5(3a1H)-one 10*{2}*. The general procedure afforded **10*{2}*** (20.9 mg, 0.064 mmol, 32% yield) as a viscous orange oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.85 (t, *J* = 8.0 Hz, 3 H), 1.07 (dt, *J* = 4.0, 12.0 Hz, 1 H), 1.19-1.38 (complex, 3 H), 1.44-1.72 (complex, 5 H), 1.87-2.25 (complex, 5 H), 2.36 (dd, *J* = 4.0, 12.0 Hz, 1 H), 2.51 (m, 1 H), 2.74 (m, 2 H), 2.91 (m, 2 H), 3.06 (td, *J* = 4.0, 12.0 Hz, 1 H), 7.16-7.22 (complex, 3 H), 7.29 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ u: 18.0, 24.7, 29.9, 30.7, 31.4, 33.3, 48.9, 52.6, 55.1, 140.5, 210.7; d: 11.2, 41.5, 44.7, 50.9, 56.2, 63.6, 126.0, 128.5 (× 2), 128.7 (× 2); IR (neat) 3398, 2932, 2859, 1710 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{22}H_{32}NO$ ($[M+H]^+$), 326.2484, found 326.2464.





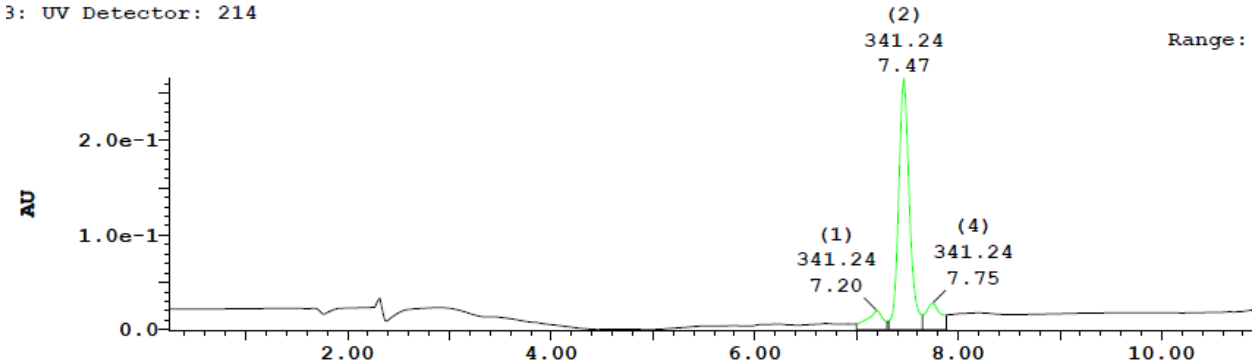
6-ethyl-1-(3-phenylpropyl)decahydro-1H-benzo[de]quinolin-5(3a1H)-one 10*{3}*. The general procedure afforded **10*{3}*** (37.6 mg, 0.111 mmol, 55% yield) as a viscous orange oil. HRMS (ESI) *m/z* calcd for $C_{23}H_{34}NO$ ($[M+H]^+$), 340.2640, found 340.2464.





6-Ethyl-1-(4-methoxybenzyl)decahydro-1H-benzo[de]quinolin-5(3a1H)-one 10*{4}*. The general procedure afforded **10*{4}*** (18.2 mg, 0.053 mmol, 27% yield) as a light yellow oil. HRMS (ESI) *m/z* calcd for $C_{22}H_{32}NO_2$ ($[M+H]^+$), 342.2433, found 342.2419.

ID CMC-34-066-J File KF070808L06 Date 08-Jul-2008 Time 09:44:19 Description MDF008615



Peak Number	Time	AreaAbs	Area %Total	Height	Mass Found
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2	7.47	29032	90.70	254689	341.24
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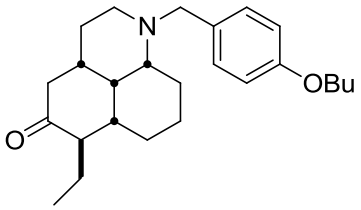
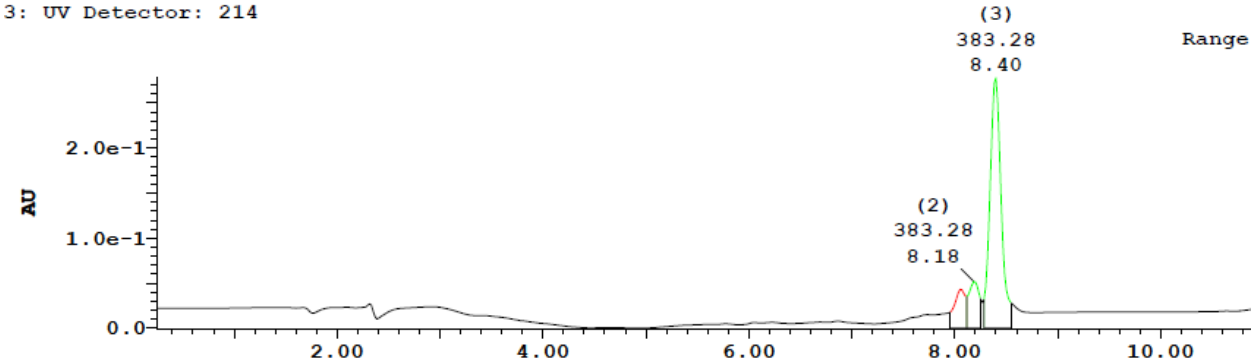


1-(4-butoxybenzyl)-6-ethyldecahydro-1H-benzo[de]quinolin-5(3a1H)-one 10*{5}*. The general procedure afforded **10*{5}*** (33.9 mg, 0.088 mmol, 44% yield) as a viscous colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.85 (t, *J* = 8.0 Hz, 3 H), 0.97 (t, *J* = 8.0 Hz, 3 H), 1.05-1.58 (complex, 11 H), 1.62-1.80 (complex, 4 H), 1.86-2.15 (complex, 5 H), 2.29 (d, *J* = 3.6 Hz, 1 H), 2.35 (m, 1 H), 2.84 (td, *J* = 3.6, 11.6 Hz, 1 H), 3.20 (d, *J* = 13.6 Hz, 1 H), 3.95 (t, *J* = 5.2 Hz, 2 H), 4.04 (d, *J* = 13.2 Hz, 1 H), 6.84 (d, *J* = 8.4 Hz, 2 H), 7.18 (d, *J* = 8.8 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ u: 17.9, 19.3, 24.6, 30.4, 31.4, 31.5, 33.1, 48.8, 52.5, 56.6, 67.6, 130.6, 158.1, 211.0; d: 11.2, 13.9, 41.6, 44.7, 50.9, 56.2, 65.0, 114.1 (× 2), 130.2 (× 2); IR (neat) 2930, 2862, 2789, 1710 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{25}H_{38}NO_2$ ($[M+H]^+$), 384.2903, found 384.2908.

ID CMC-34-066-K File KF070808L07 Date 08-Jul-2008 Time 09:56:39 Description MDF008540



Peak Number	Time	AreaAbs	Area %Total	Height	Mass Found
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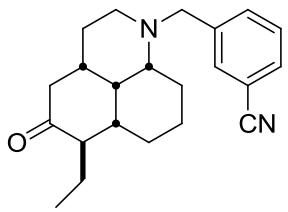
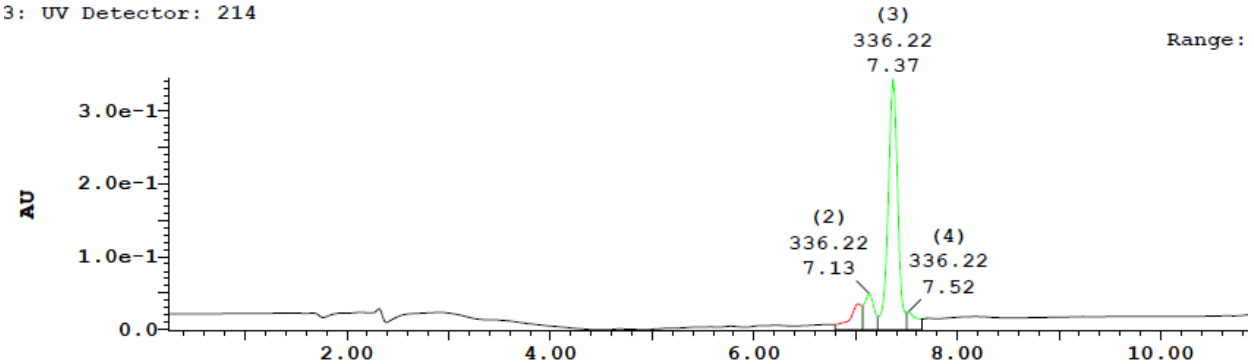
2	8.18	1954	6.35	22474	383.28
3	8.40	26942	87.58	248061	383.28

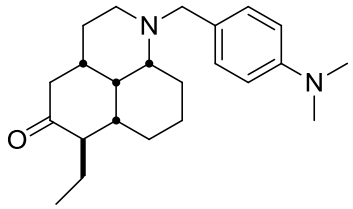


6-Ethyl-5-oxododecahydro-1H-benzo[de]quinolin-1-yl)methyl)benzonitrile 10*{6}*. The general procedure afforded **10*{6}*** (28.1 mg, 0.084 mmol, 42% yield) as an orange oil. HRMS (ESI) *m/z* calcd for $C_{22}H_{29}N_2O$ ($[M+H]^+$), 337.2280, found 337.2256.

ID CMC-34-066-L File KF070808L08 Date 08-Jul-2008 Time 10:09:02 Description MDF008543



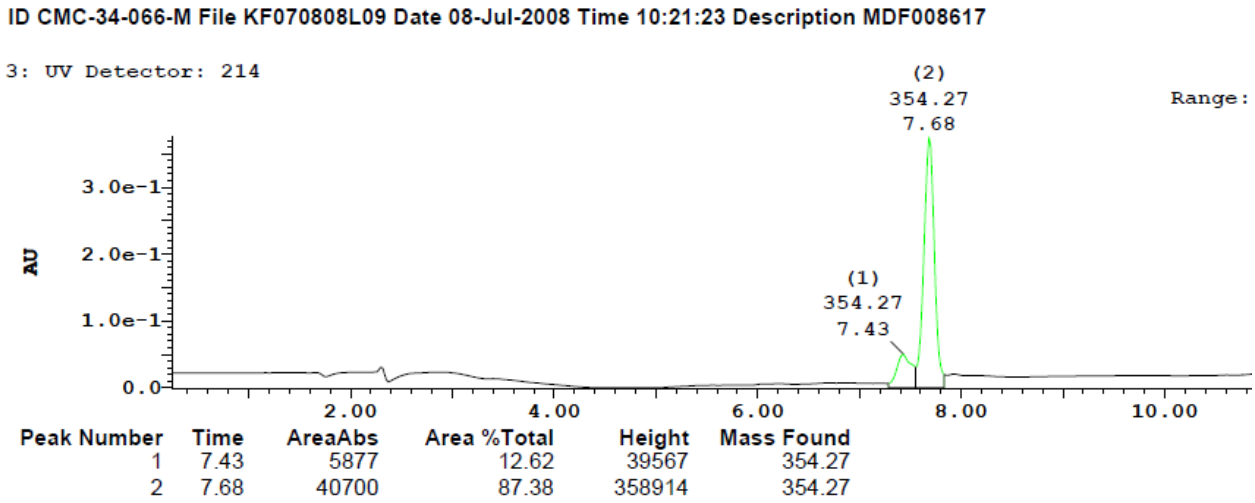
Peak Number	Time	AreaAbs	Area %Total	Height	Mass Found
1	7.02	2734	6.61	26337	
2	7.13	3980	9.62	39171	336.22
3	7.37	33980	82.15	331240	336.22
4	7.52	670	1.62	10405	336.22

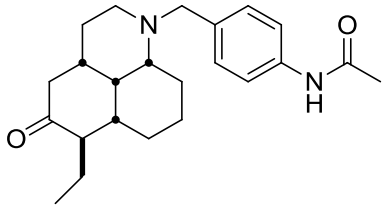


1-(4-(dimethylamino)benzyl)-6-ethyldecahydro-1H-benzo[de]quinolin-5(3a1H)-one 10*{7}*.

The general procedure afforded **10*{7}*** (18.4 mg, 0.052 mmol, 26% yield) as an orange oil.

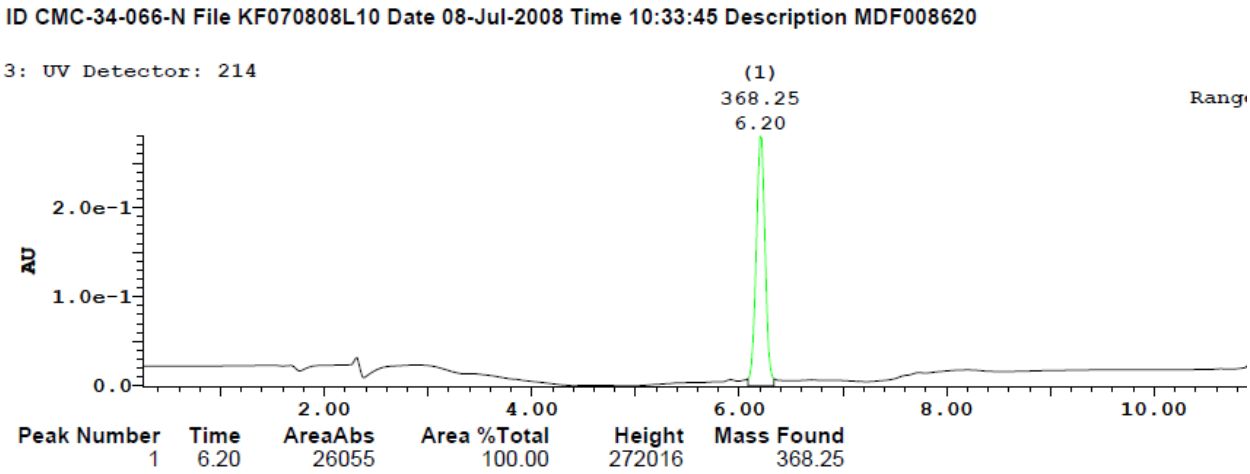
HRMS (ESI) *m/z* calcd for $C_{23}H_{35}N_2O$ ($[M+H]^+$), 355.2749, found 355.2733.

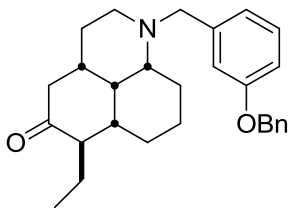




6-Ethyl-5-oxododecahydro-1H-benzo[de]quinolin-1-yl)methyl)phenyl)acetamide 10*{8}*. The general procedure afforded **10*{8}*** (17.5 mg, 0.049 mmol, 25% yield) as a viscous brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.85 (t, *J* = 7.2 Hz, 3 H), 1.07 (dt, *J* = 3.2, 11.2 Hz, 1 H), 1.19-1.47 (complex, 5 H), 1.55 (m, 2 H), 1.67 (m, 1 H), 1.89-2.22 (complex, 6 H), 2.17 (s, 3 H), 2.31 (dd, *J* = 3.6, 13.2 Hz, 2 H), 2.45 (m, 1 H), 2.84 (td, *J* = 3.2, 10.4 Hz, 1 H), 3.22 (d, *J* = 13.6 Hz, 1 H),

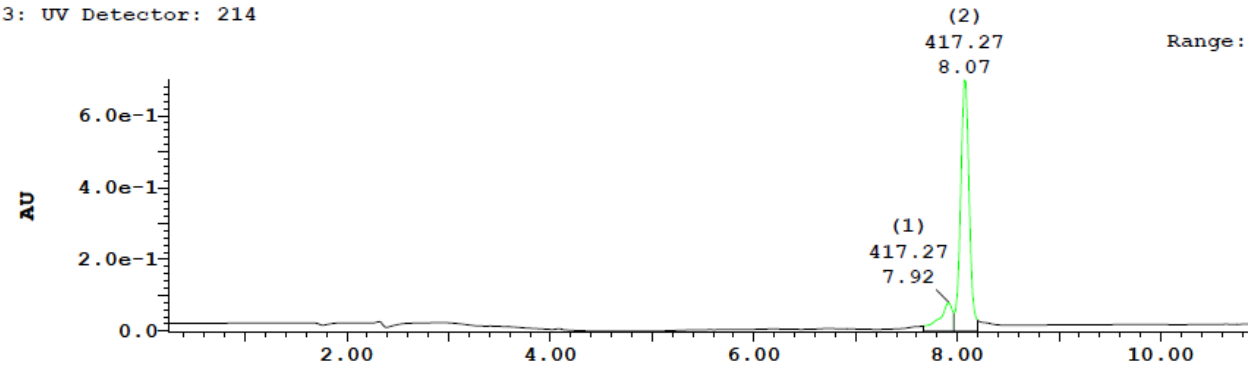
4.07 (d, J = 13.6 Hz, 1 H), 7.24 (d, J = 8.4 Hz, 2 H), 7.44 (d, J = 8.4 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ u: 17.9, 24.6, 30.4, 31.4, 31.4, 33.0, 48.8, 52.7, 56.7, 136.6, 168.2, 210.8; d: 11.2, 41.5, 44.7, 47.5, 50.8, 56.2, 65.2, 119.7 (× 2), 129.6 (× 2); IR (neat) 3307, 2935, 2860, 2791, 1707, 1670 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{35}N_2O$ ($[M+H]^+$), 355.2749, found 369.2527.





1-**(3-(benzyloxy)benzyl)-6-ethyldecahydro-1H-benzo[de]quinolin-5(3a1H)-one 10*{9}***. The general procedure afforded **10*{9}*** (34.6 mg, 0.083 mmol, 41% yield) as a sticky brown oil. HRMS (ESI) *m/z* calcd for $C_{28}H_{36}NO_2$ ($[M+H]^+$), 418.2746, found 418.2732.

ID CMC-34-066-O File KF070808L11 Date 08-Jul-2008 Time 10:46:07 Description MDF008550



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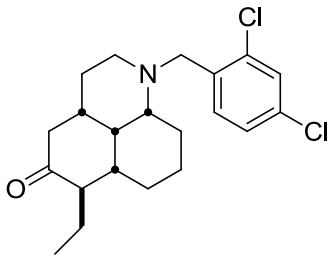
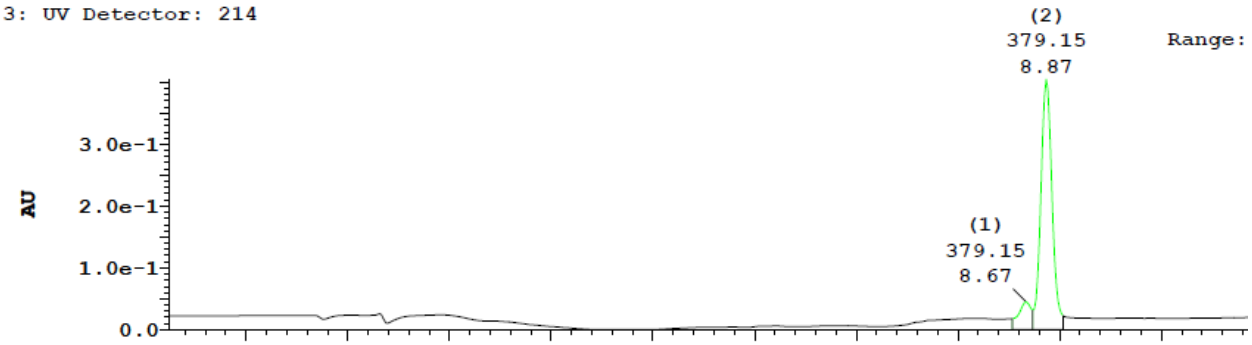
2	8.07	62296	90.66	673435	417.27

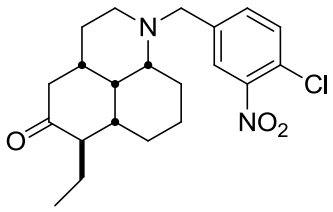


1-(2,4-dichlorobenzyl)-6-ethyldecahydro-1H-benzo[de]quinolin-5(3a1H)-one 10*{10}*. The general procedure afforded **10*{10}*** (31.6 mg, 0.083 mmol, 42% yield) as a viscous orange oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.86 (t, *J* = 7.2 Hz, 3 H), 0.96-1.20 (m, 2 H), 1.27-1.71 (complex, 9 H), 1.85 (m, 1 H), 1.92-2.24 (complex, 6 H), 2.34 (dd, *J* = 3.6, 12.8 Hz, 1 H), 2.81 (td, *J* = 3.2, 11.2 Hz, 1 H), 3.28 (d, *J* = 15.2 Hz, 1 H), 4.08 (d, *J* = 15.2 Hz, 1 H), 7.21 (dd, *J* = 2.0, 8.4 Hz, 1 H), 7.34 (d, *J* = 2.0 Hz, 1 H), 7.53 (d, *J* = 8.4 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ u: 18.0, 24.6, 30.6, 31.5, 33.2, 48.8, 53.7, 53.9, 132.5, 134.0, 136.8, 210.7; d: 11.2, 41.5, 44.7, 51.0, 56.2, 66.1, 126.8, 128.9, 131.2; IR (neat) 2928, 2859, 2797, 1711 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{21}H_{28}Cl_2NO$ ($[M+H]^+$), 380.1548, found 380.1541.

ID CMC-34-066-P File KF070808L12 Date 08-Jul-2008 Time 10:58:29 Description MDF008623



Peak Number	Time	AreaAbs	Area %Total	Height	Mass Found
1	8.67	2657	5.51	25900	379.15
2	8.87	45563	94.49	384270	379.15

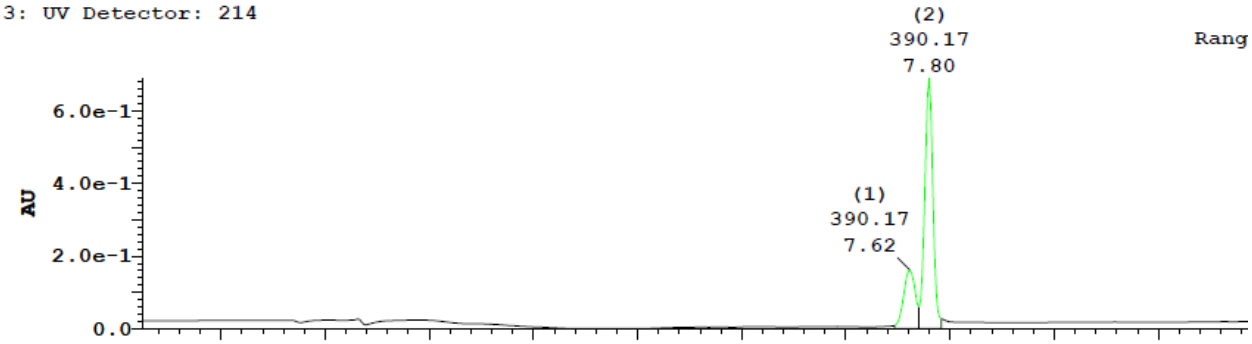


1-(4-Chloro-3-nitrobenzyl)-6-ethyldecahydro-1H-benzo[de]quinolin-5(3a1H)-one 10*{11}*.

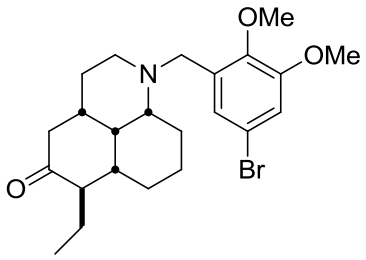
The general procedure afforded **10*{11}*** (34.7 mg, 0.089 mmol, 44% yield) as a sticky brown oil.

HRMS (ESI) *m/z* calcd for $C_{21}H_{28}ClN_2O_3$ ($[M+H]^+$), 391.1788, found 391.1777.

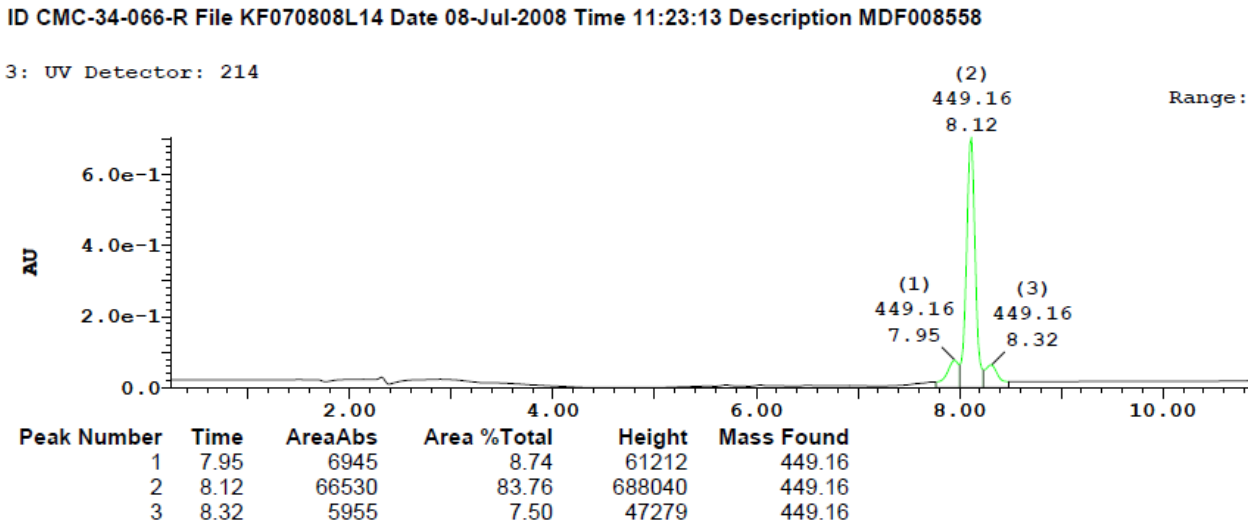
ID CMC-34-066-Q File KF070808L13 Date 08-Jul-2008 Time 11:10:51 Description MDF008625



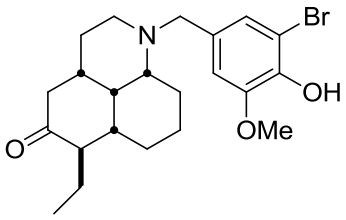
Peak Number	Time	AreaAbs	Area %Total	Height	Mass Found
1	7.62	17982	23.73	145100	390.17
2	7.80	57784	76.27	667368	390.17



1-(5-Bromo-2,3-dimethoxybenzyl)-6-ethyldecahydro-1H-benzo[de]quinolin-5(3a1H)-one 10*{12}*. The general procedure afforded **10*{12}*** (24.3 mg, 0.054 mmol, 27% yield) as a sticky orange oil. HRMS (ESI) *m/z* calcd for $C_{23}H_{33}BrNO_3$ ($[M+H]^+$), 450.1644, found 450.1635.



Peak Number	Time	AreaAbs	Area %Total	Height	Mass Found
1	7.95	6945	8.74	61212	449.16
2	8.12	66530	83.76	688040	449.16
3	8.32	5955	7.50	47279	449.16

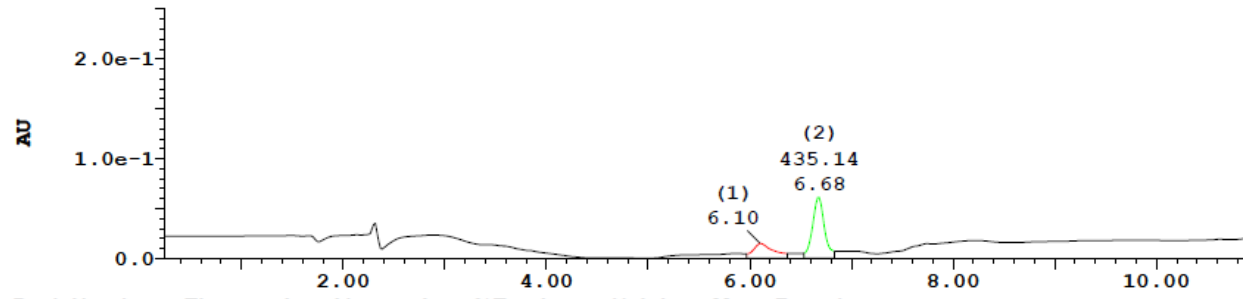


1-(3-Bromo-4-hydroxy-5-methoxybenzyl)-6-ethyldecahydro-1H-benzo[de]quinolin-5(3a1H)-one 10*{13}*. The general procedure afforded **10*{13}*** (3.7 mg, 0.008 mmol, 4% yield, 80% purity) as an orange oil. HRMS (ESI) *m/z* calcd for $C_{22}H_{31}BrNO_3$ ($[M+H]^+$), 436.1487, found 436.1470.

ID CMC-34-066-S File KF070808L15 Date 08-Jul-2008 Time 11:35:35 Description MDF008560

3: UV Detector: 214

Range:



Peak Number	Time	AreaAbs	Area %Total	Height	Mass Found
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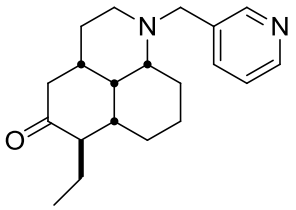
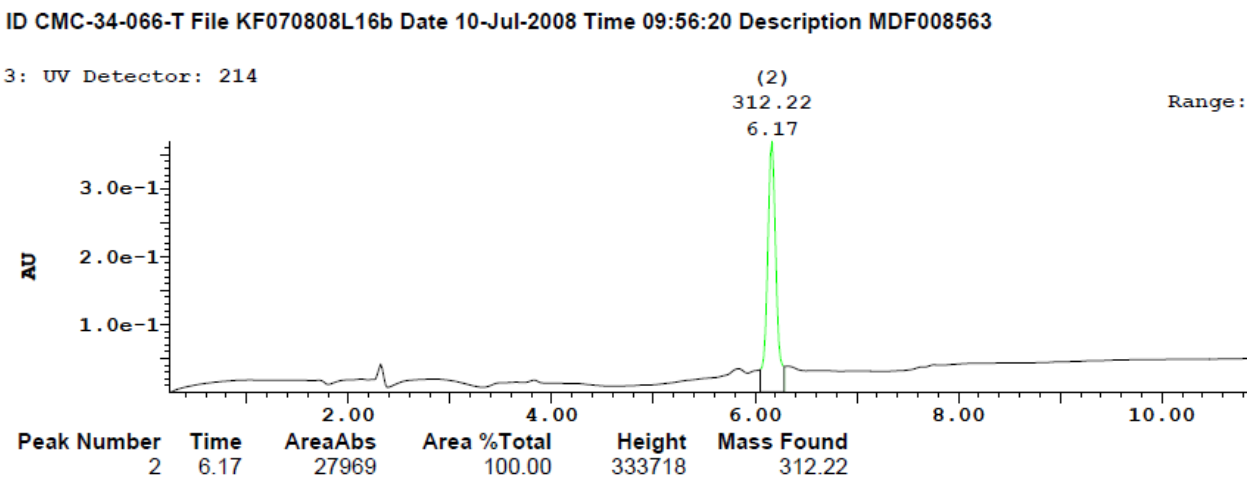
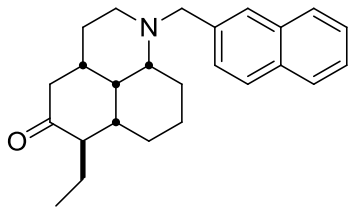
2	6.68	6530	79.71	55009	435.14



6-Ethyl-1-(pyridin-3-ylmethyl)decahydro-1H-benzo[de]quinolin-5(3a1H)-one 10*{14}*. The general procedure afforded **10*{14}*** (32.4 mg, 0.104 mmol, 52% yield) as a viscous orange oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.85 (t, *J* = 7.2 Hz, 3 H), 1.08 (dt, *J* = 3.6, 12.8 Hz, 1 H), 1.21-1.73 (complex, 9 H), 1.88-2.15 (complex, 6 H), 2.26 (m, 1 H), 2.33 (dd, *J* = 3.6, 13.2 Hz, 1 H), 2.82 (td, *J* = 2.8, 12.0 Hz, 1 H), 3.24 (d, *J* = 14.0 Hz, 1 H), 4.12 (d, *J* = 14.0 Hz, 1 H), 7.25 (dd, *J* = 4.8, 7.6 Hz, 1 H), 7.65 (td, *J* = 2.0, 7.6 Hz, 1 H), 8.49 (dd, *J* = 1.6, 4.8 Hz, 1 H), 8.53 (d, *J* = 2.0 Hz, 1 H),; ^{13}C NMR (100 MHz, $CDCl_3$) δ u: 17.9, 24.5, 30.6, 31.4, 33.0, 48.7, 53.0, 54.7, 135.0, 210.6; d: 11.2, 41.4, 44.6, 50.9, 56.1, 65.3, 123.2, 136.4, 148.2, 150.2; IR (neat) 3400, 2932, 2859, 2792, 1709 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{20}H_{29}N_2O$ ($[M+H]^+$), 313.2280, found 313.2294.

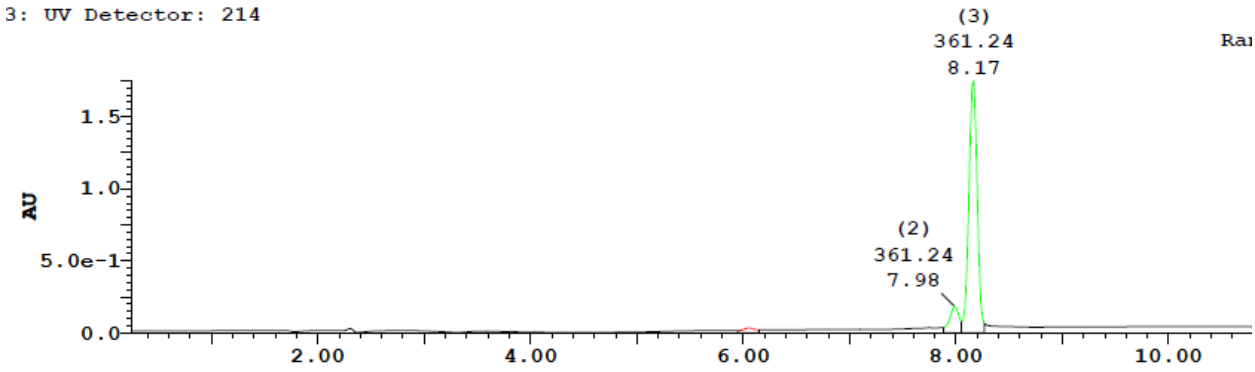




6-Ethyl-1-(naphthalen-2-ylmethyl)decahydro-1H-benzo[de]quinolin-5(3a1H)-one 10*{15}*.

The general procedure afforded **10*{15}*** (21.0 mg, 0.058 mmol, 29% yield) as a viscous orange oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.86 (t, *J* = 7.2 Hz, 3 H), 1.09 (m, 1 H), 1.28-1.60 (complex, 8 H), 1.68 (m, 1 H), 1.90-2.16 (complex, 6 H), 2.32 (dd, *J* = 3.6, 12.8 Hz, 1 H), 2.37 (m, 1 H), 2.89 (td, *J* = 3.2, 11.6 Hz, 1 H), 3.34 (d, *J* = 13.2 Hz, 1 H), 4.31 (d, *J* = 13.6 Hz, 1 H), 7.44-7.48 (m, 3 H), 7.72 (s, 1 H), 7.78-7.83 (m, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ u: 18.0, 24.6, 30.5, 31.5, 33.1, 48.8, 53.0, 57.6, 132.6, 133.3, 137.1, 210.8; d: 11.2, 41.6, 44.8, 50.9, 56.2, 65.6, 125.5, 125.9, 127.3, 127.4, 127.6 (× 2), 127.8; 3397, 2930, 2858, 2793, 1710 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{25}H_{32}NO$ ($[M+H]^+$), 362.2484, found 362.2486.

ID CMC-34-066-U File KF070808L17b Date 10-Jul-2008 Time 10:08:44 Description MDF008635



Peak Number	Time	AreaAbs	Area %Total	Height	Mass Found
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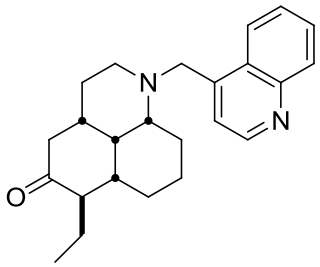
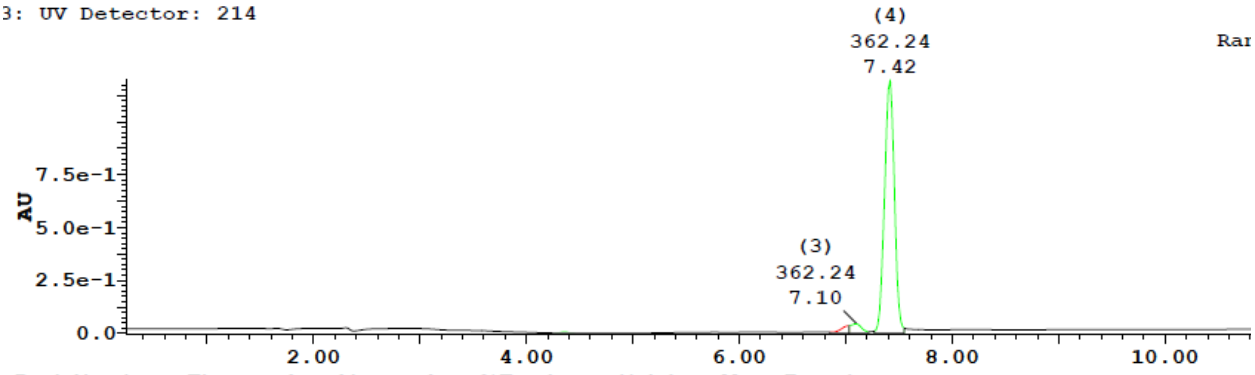
2	7.98	11516	7.17	139550	361.24
3	8.17	147797	92.06	1694618	361.24



6-Ethyl-1-(quinolin-4-ylmethyl)decahydro-1H-benzo[de]quinolin-5(3a1H)-one 10*{16}*. The general procedure afforded **10*{16}*** (34.7 mg, 0.096 mmol, 48% yield) as a viscous orange oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.87 (t, *J* = 8.0 Hz, 3 H), 1.28-1.72 (complex, 8 H), 1.83-2.28 (complex, 8 H), 2.34 (dd, *J* = 4.0, 12.0 Hz, 1 H), 2.77 (td, *J* = 3.2, 11.6 Hz, 1 H), 3.47 (d, *J* = 15.2 Hz, 1 H), 3.74 (t, *J* = 6.8 Hz, 1 H), 4.65 (d, *J* = 14.4 Hz, 1 H), 7.53 (d, *J* = 4.0 Hz, 1 H), 7.55 (ddd, *J* = 1.2, 7.2, 8.0 Hz, 1 H), 7.71 (ddd, *J* = 1.2, 7.2, 8.4 Hz, 1 H), 8.12 (dd, *J* = 0.8, 8.4 Hz, 1 H), 8.28 (dd, *J* = 0.4, 8.0 Hz, 1 H), 8.85 (d, *J* = 4.4 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ u: 17.9, 24.6, 30.5, 31.4, 33.2, 48.7, 53.8, 54.8, 127.4, 146.2, 148.2, 210.7; d: 11.2, 41.5, 44.7, 51.0, 56.2, 66.6, 121.1, 123.8, 126.1, 129.0, 150.1; IR (neat) 3399, 2937, 2859, 2796, 1709 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{24}H_{31}N_2O$ ($[M+H]^+$), 363.2436, found 363.2424.

ID CMC-34-066-V File KF070808L18 Date 08-Jul-2008 Time 12:12:40 Description MDF008570



Peak Number	Time	AreaAbs	Area %Total	Height	Mass Found
1	4.35	439	0.34	5765	362.24
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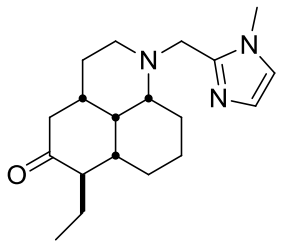
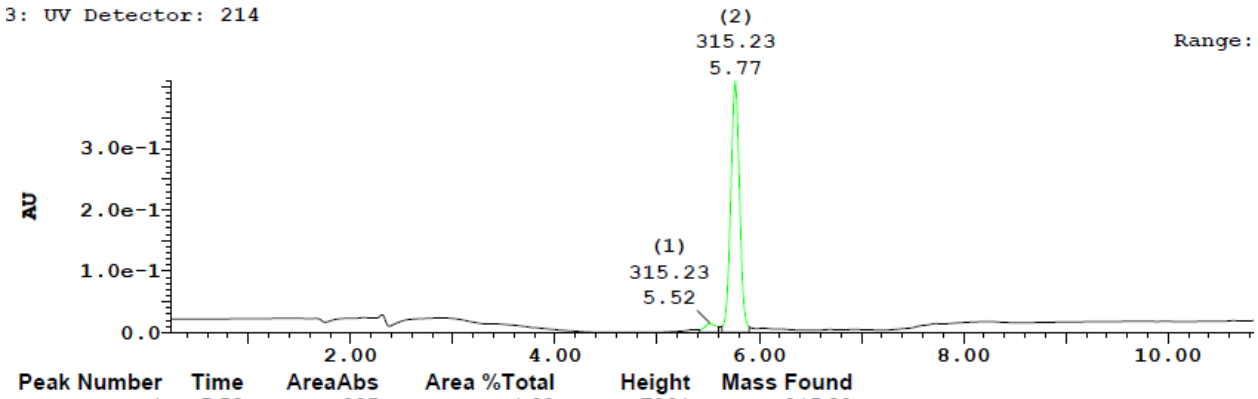


6-ethyl-1-((1-methyl-1H-imidazol-2-yl)methyl)decahydro-1H-benzo[de]quinolin-5(3a1H)-one 10*{17}*. The general procedure afforded **10*{17}*** (26.1 mg, 0.083 mmol, 41% yield) as a viscous orange oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.85 (t, *J* = 7.6 Hz, 3 H), 1.05 (dt, *J* = 3.2, 13.2 Hz, 1 H), 1.16-1.28 (m, 2 H), 1.30-1.39 (m, 3 H), 1.47-1.59 (m, 3 H), 1.68 (m, 1 H), 1.87-2.18 (complex, 6 H), 2.32 (dd, *J* = 4.0, 12.8 Hz, 1 H), 2.33 (m, 1 H), 2.70 (td, *J* = 2.8, 11.6 Hz, 1 H), 3.34 (d, *J* = 13.6 Hz, 1 H), 3.72 (s, 3 H), 4.17 (d, *J* = 13.6 Hz, 1 H), 6.83 (d, *J* = 1.2 Hz, 1 H), 6.92 (d, *J* = 1.2 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ u: 17.9, 24.5, 30.1, 31.4, 33.1, 48.7, 49.7, 52.8, 145.6, 210.6; d: 11.1, 33.0, 41.4, 44.5, 50.8, 56.1, 65.6, 121.4, 127.0; IR (neat) 3392, 2938, 2860, 1707 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{19}H_{30}N_3O$ ($[M+H]^+$), 316.2389, found 316.2376.

ID CMC-34-066-W File KF070808L19 Date 08-Jul-2008 Time 12:24:56 Description MDF008574



Peak Number	Time	AreaAbs	Area %Total	Height	Mass Found
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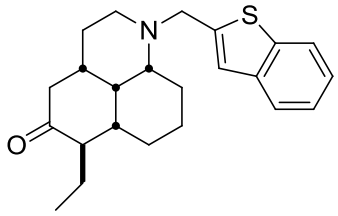
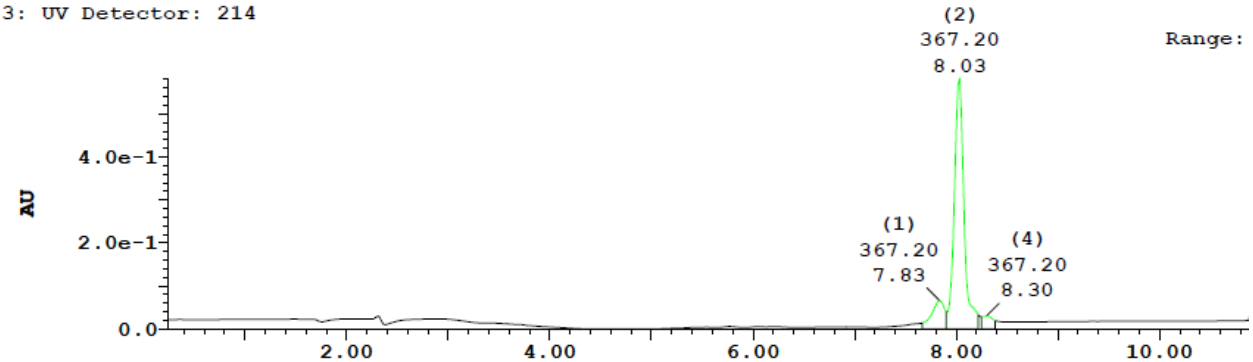


1-(Benzo[b]thiophen-2-ylmethyl)-6-ethyldecahydro-1H-benzo[de]quinolin-5(3a1H)-one 10*{18}*. The general procedure afforded **10*{18}*** (25.9 mg, 0.070 mmol, 35% yield) as a viscous yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.84 (t, *J* = 7.2 Hz, 3 H), 1.03-1.12 (m, 1 H), 1.25-1.70 (complex, 9 H), 1.84-2.16 (complex, 5 H), 2.24-2.36 (m, 3 H), 2.99 (td, *J* = 3.2, 11.6 Hz, 1 H), 3.88 (d, *J* = 14.8 Hz, 1 H), 4.21 (dd, *J* = 0.8, 15.2 Hz, 1 H), 7.11 (d, *J* = 0.8 Hz, 1 H), 7.28-7.34 (m, 2 H), 7.69 (dd, *J* = 1.6, 7.2 Hz, 1 H), 7.78 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ u: 18.0, 24.5, 30.4, 31.4, 33.3, 48.8, 52.3, 53.0, 137.6, 139.7, 143.0, 210.7; d: 11.2, 41.4, 44.6, 51.0, 56.2, 64.1, 122.2, 122.4, 123.0, 123.8, 124.1; IR (neat) 3400, 2932, 2858, 2795, 1709 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{30}NOS$ ($[M+H]^+$), 368.2048, found 368.2034.

ID CMC-34-066-X File KF070808L20 Date 08-Jul-2008 Time 12:37:18 Description MDF008579



Peak Number	Time	AreaAbs	Area %Total	Height	Mass Found
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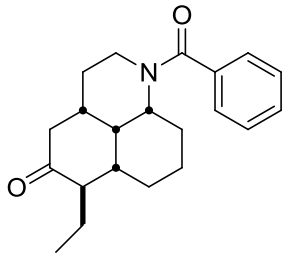
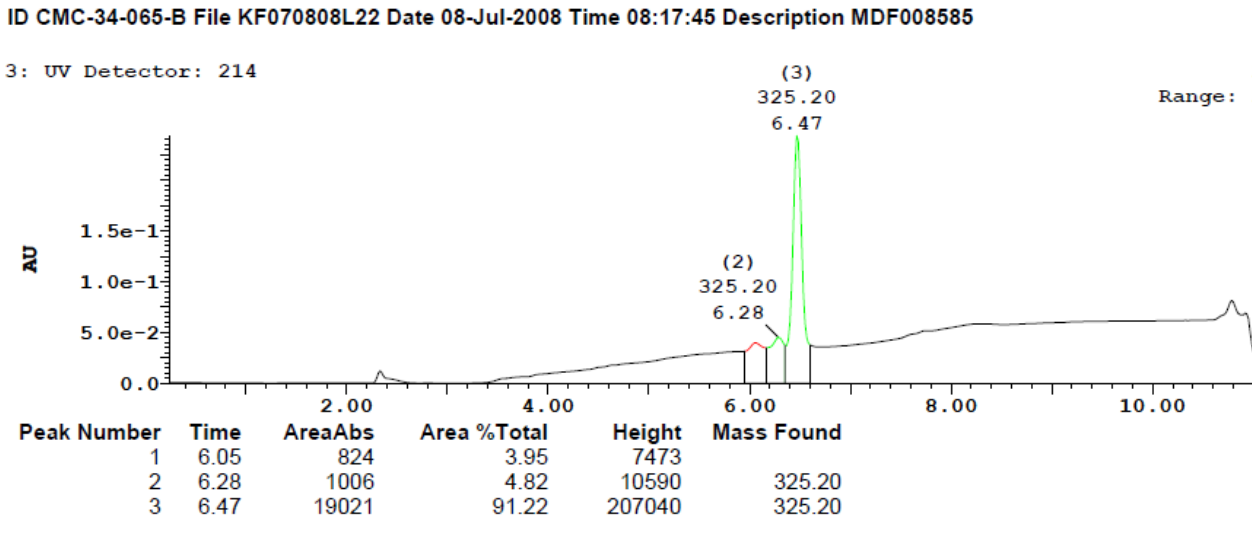
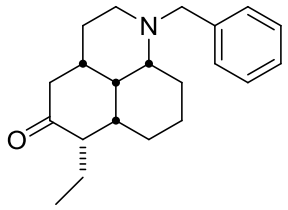
4	8.30	417	0.67	5402	367.20

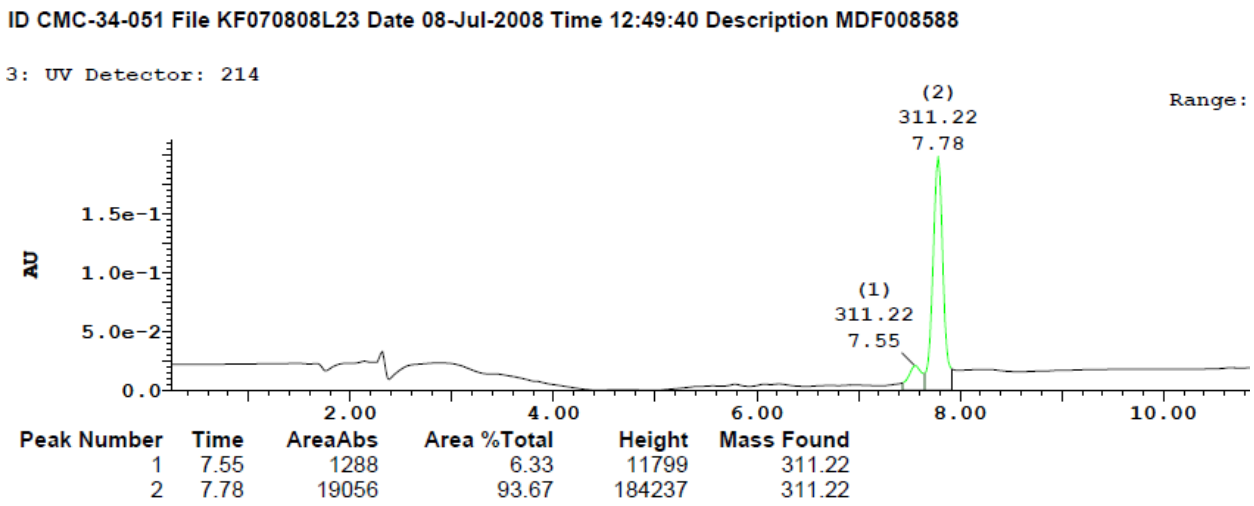


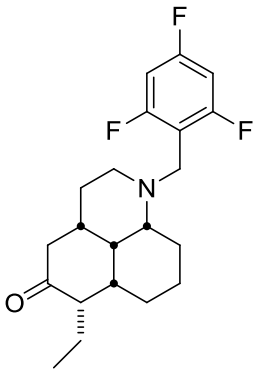
1-Benzoyl-6-ethyldecahydro-1H-benzo[de]quinolin-5(3a1H)-one 11*{19}*. The tricyclic amine (46 mg, 0.21 mmol), triethyl amine (63 mg, 0.62 mmol, 3.0 equiv.) and benzoyl chloride (58 mg, 0.42 mmol, 2.0 equiv.) were dissolved in THF (2.0 mL) then stirred at rt 16 h. The reaction mixture was diluted with 0.5 N HCL (3 mL) and extracted with EtOAc (2 × 3 mL). The combined organics were dried (Na_2SO_4), concentrated and the residue purified by silica chromatography to yield the amide **11*{19}*** (36 mg, 0.111 mmol, 53% yield) as a light orange oil. R_f = 0.58 (1:1 acetone:CH_2Cl_2); ^{1}H NMR δ 0.87 (t, *J* = 7.2 Hz, 3 H), 1.10 (m, 2 H), 1.10-1.84 (complex, 11 H), 1.88-2.18 (complex, 3 H), 2.29 (m, 4 H), 2.47 (dd, *J* = 4.4 Hz, 1 H), 3.40-3.57 (m, 2 H), 7.40 (m, 5 H); ^{13}C NMR δ d 11.3, 37.0, 45.7, 46.5, 56.0, 60.2, 126.9 (×2), 128.4 (×2), 129.5; u 17.9, 24.7, 29.7, 31.4, 32.1, 43.1, 49.0, 137.2, 171.7, 209.9; IR (neat) 2928, 2858, 1706, 1623 cm^{-1}; HRMS calcd for $C_{21}H_{28}NO_2$ [M + H] 326.2120, obsd 326.2109.





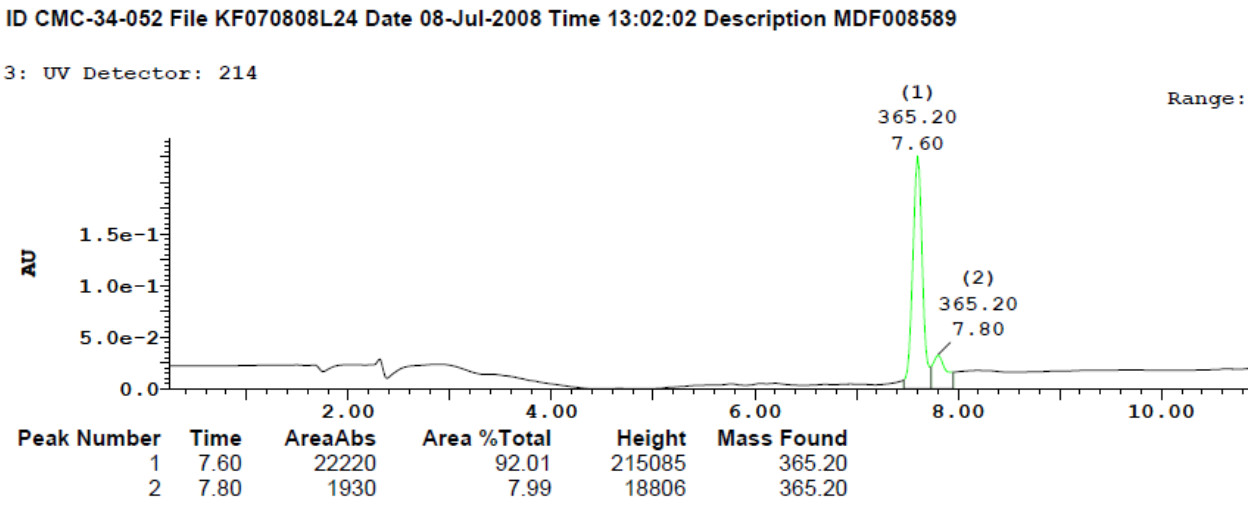
1-Benzyl-6-ethyldecahydro-1H-benzo[de]quinolin-5(3a1H)-one 10*{20}*. The general procedure (adjusted for the new quantity of starting amine (47 mg, 0.21 mmol) and omitting the K_2CO_3 epimerization step) afforded **10{20}** (21 mg, 0.067 mmol, 32% yield) as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.81 (t, *J* = 7.6 Hz, 3 H), 1.19 (m, 1 H), 1.30-1.50 (complex, 6 H), 1.55 (m, 2 H), 1.68 (m, 2 H), 1.88 (m, 2 H), 2.03 (dt, *J* = 3.2, 12.0 Hz, 1 H), 2.13 (m, 1 H), 2.19-2.30 (m, 3 H), 2.86 (td, *J* = 3.6, 11.2 Hz, 1 H), 3.17 (d, *J* = 13.2 Hz, 1 H), 4.12 (d, *J* = 13.2 Hz, 1 H), 7.21-7.33 (complex, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ u: 19.7, 24.8, 29.3, 30.4, 33.1, 44.6, 53.2, 57.4, 139.4, 214.2; d: 11.8, 42.5, 44.2, 44.9, 57.3, 66.3, 126.7, 128.1 (× 2), 129.0 (× 2); IR (neat) 2929, 2860, 1709, 1665 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{21}H_{30}NO$ ($[M+H]^+$), 312.2327, found 312.2316.

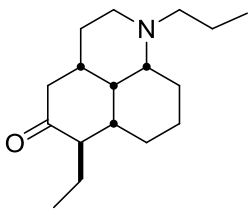




6-Ethyl-1-(2,4,6-trifluorobenzyl)decahydro-1H-benzo[de]quinolin-5(3a1H)-one 10{21}. The general procedure (adjusted for the new quantity of starting amine (59 mg, 0.268 mmol) and omitting the K_2CO_3 epimerization step) afforded **10{21}** (50 mg, 0.137 mmol, 51% yield) as a viscous light orange oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.79 (t, *J* = 7.6 Hz, 3 H), 1.25 (m, 1 H), 1.32-1.56 (complex, 7 H), 1.59-1.72 (m, 2 H), 1.85-1.94 (m, 2 H), 2.11 (m, 2 H), 2.18-2.29 (m, 2 H), 2.40 (dd, *J* = 3.2, 12.0 Hz, 2 H), 2.87 (d, *J* = 11.6 Hz, 1 H), 3.31 (d, *J* = 12.8 Hz, 1 H), 4.08 (d, *J* = 13.2 Hz, 1 H), 6.66 (q, *J* = 8.8, 7.6 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ u: 19.6, 24.7,

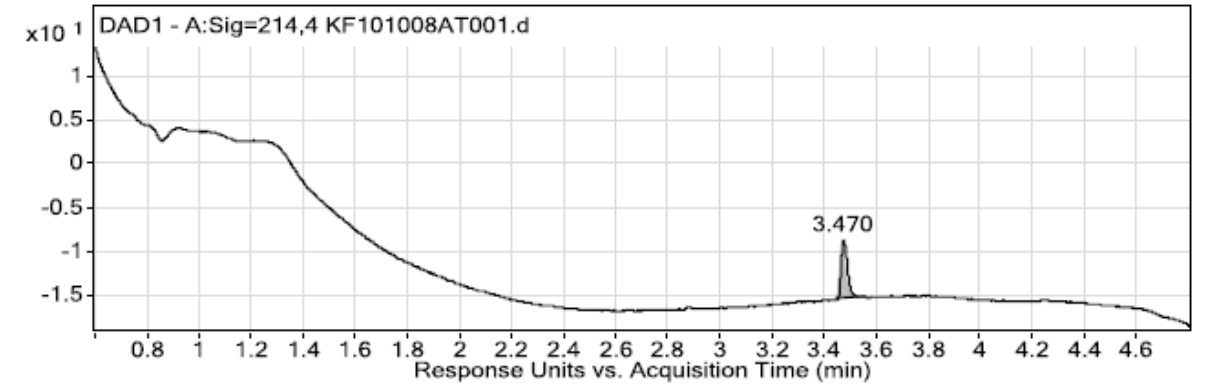
29.2, 32.6, 43.3, 44.4, 52.2, 52.3, 214.2; d: 11.7, 42.2, 44.2, 44.6, 57.2, 66.1, 100.1 (m, 2 C); HRMS (ESI) *m/z* calcd for $C_{21}H_{27}F_3NO$ ($[M+H]^+$), 366.2045, found 366.2019.





6-Ethyl-1-propyldecahydro-1H-benzo[de]quinolin-5(3a1H)-one 10{22}. The general procedure (adjusted for the altered quantity of starting amine (30.6 mg, 0.138 mmol)) afforded **10{22}** (12.4 mg, 0.047 mmol, 34% yield) as a viscous yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83 (t, *J* = 7.2 Hz, 3 H), 0.84 (t, *J* = 7.2 Hz, 3 H), 1.03 (m, 1 H), 1.10-1.34 (complex, 4 H), 1.39-1.56 (complex, 5 H), 1.60-1.67 (m, 2 H), 1.84-1.94 (m, 3 H), 2.01 (m, 1 H), 2.11 (m, 1 H), 2.31 (m, 2 H), 2.47 (m, 1 H), 2.65 (m, 1 H), 2.94 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ u: 17.4, 17.9, 24.6, 29.9, 31.3, 33.3, 48.8, 52.5, 55.1, 210.8; d: 11.1, 12.0, 41.5, 44.7, 50.8, 56.1, 63.9; IR

(neat) 2960, 2933, 2869, 1709 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{17}H_{30}NO$ ($[M+H]^+$), 264.2327, found 264.2327.



User Chromatogram Peak List

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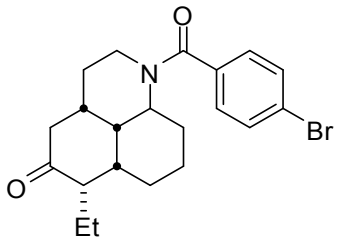
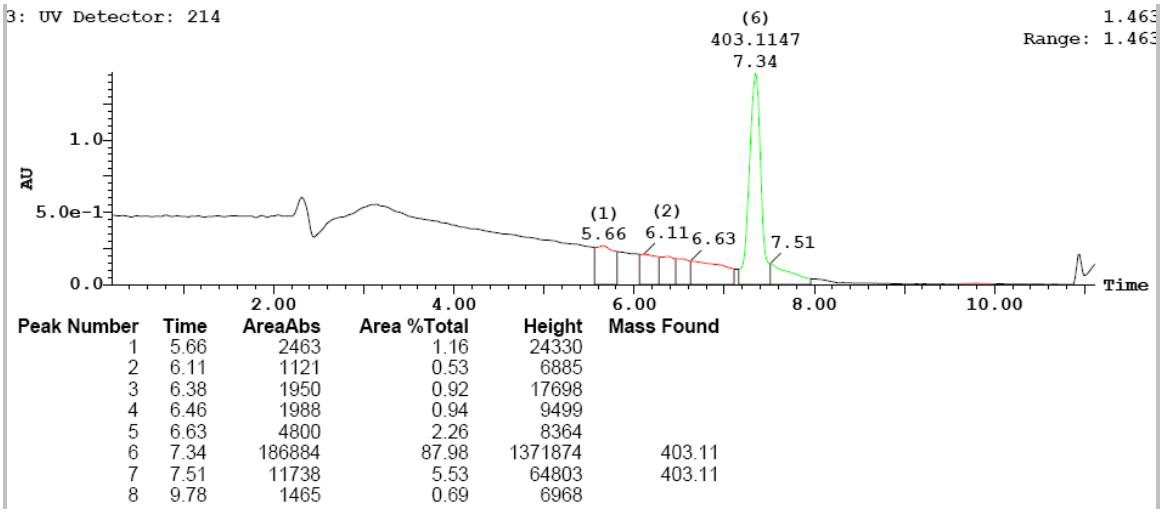


1-(4-Bromobenzoyl)-6-ethyldecahydro-1H-benzo[de]quinolin-5(3a1H)-one 11{23}. The tricyclic amine (32 mg, 0.15 mmol) and *p*-bromobenzoyl chloride were dissolved in CH_2Cl_2 (1.0 mL) and pyridine (0.5 mL) and stirred at rt 16 h. The reaction mixture was concentrated and the residue purified by silica chromatography to yield the amide **11{23}** (37 mg, 0.092 mmol, 61% yield) as a light orange oil. R_f = 0.63 (1:1 acetone:CH_2Cl_2); ^{1}H NMR δ 0.84 (t, *J* = 7.3 Hz, 3 H), 1.26 (m, 2 H), 1.47 (m, 2 H), 1.55-1.77 (complex, 4 H), 1.80-1.92 (m, 4 H), 2.21-2.29 (m, 4 H), 3.34 (m, 2 H), 3.57 (m, 1 H), 7.30 (d, *J* = 8.6 Hz, 2 H), 7.54 (d, *J* = 8.3 Hz, 2 H); ^{13}C NMR δ d

11.7, 38.8, 40.7, 45.0, 56.8, 62.1, 128.7, 131.7; u 19.6, 25.0, 29.1, 29.6, 32.4, 44.6, 44.9, 123.9, 136.1, 170.9, 212.8; IR (neat) 2930, 2858, 1707, 1629 cm^{-1}; HRMS calcd for $C_{21}H_{27}BrNO_2$ [M + H] 404.1225, obsd 404.1230.



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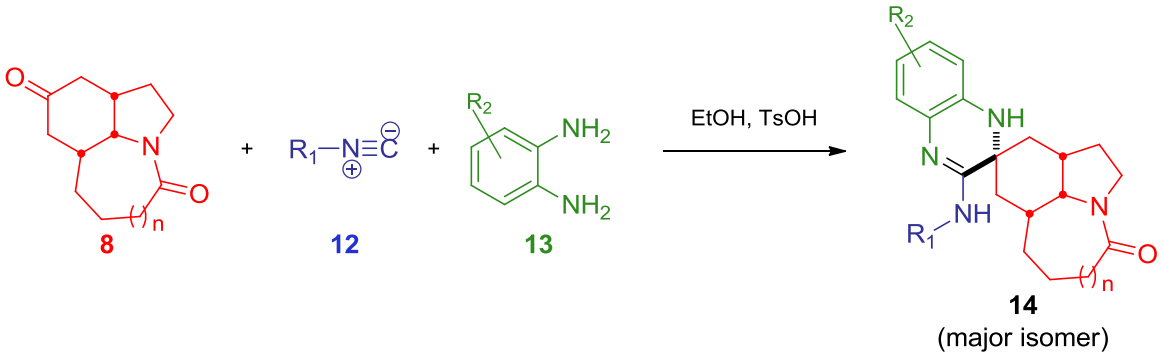
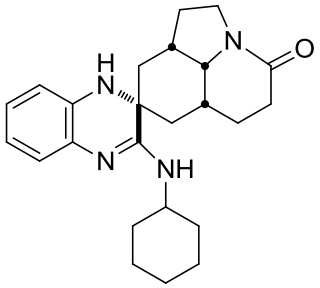
4	6.46	1988	0.94	9499	
5	6.63	4800	2.26	8364	
6	7.34	186884	87.98	1371874	403.11
7	7.51	11738	5.53	64803	403.11
8	9.78	1465	0.69	6968	



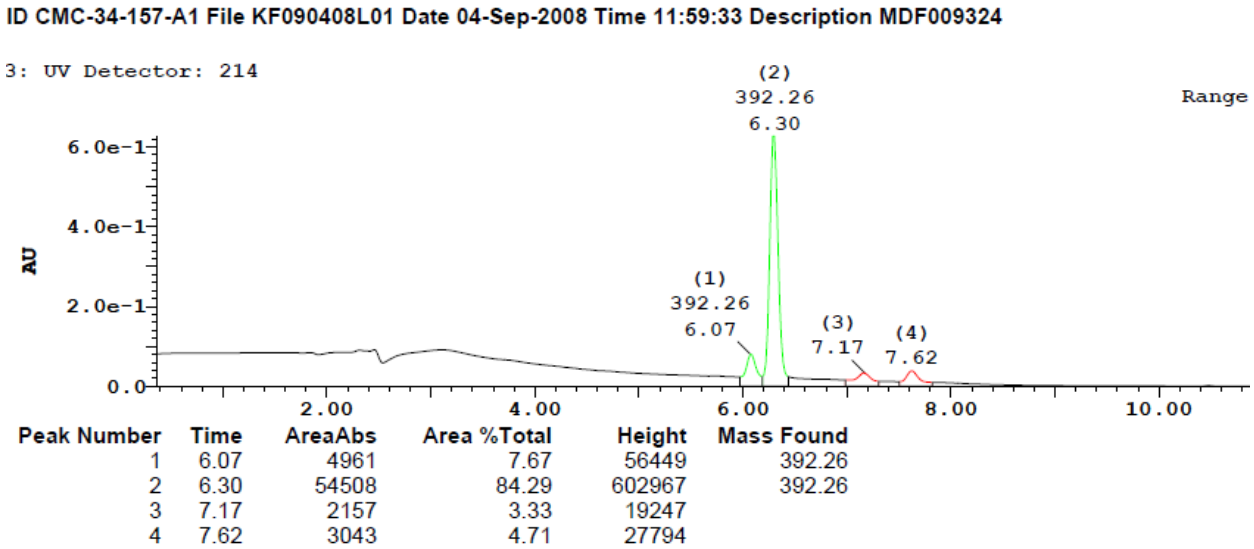
General procedure A for the parallel synthesis of spiroheterocycles 14: The reactions were performed in the 24-position Bohdan MiniBlock XT solution phase synthesis platform. Each tube of the MiniBlock platform was charged with a magnetic stirring bar, ketoamide **8a** (70 mg, 0.23 mmol), diamine fragment **13** (0.28 mmol, 1.2 equiv.) and *p*-toluenesulfonic acid (6 mg, 0.023 mmol, 0.1 equiv.). A solution of isonitrile **12** (0.28 mmol, 1.2 equiv.) in EtOH (2.0 mL)

was added via syringe through the septum and the reactions were stirred for 14 h at rt. Water (7 mL) was added to precipitate the products and the entire contents of each reaction tube was transferred to a fritted reaction tube in a second Miniblock platform. The collected precipitate was washed with NaOH (0.5 N, 2 mL) and water (3 mL) then dissolved in CH_2Cl_2. The organic soluble material was collected, the solvent removed in vacuo and the residue purified by mass-directed, reverse-phase HPLC purification.

General procedure B for the parallel synthesis of spiroheterocycles 14: The reactions were performed in the 24-position Bohdan MiniBlock XT solution phase synthesis platform. Each tube of the MiniBlock platform was charged with a magnetic stirring bar, ketoamide **8b** (70 mg, 0.34 mmol), diamine fragment **13** (0.41 mmol, 1.2 equiv.) and *p*-toluenesulfonic acid (6 mg, 0.034 mmol, 0.1 equiv.). A solution of isonitrile **12** (0.41 mmol, 1.2 equiv.) in EtOH (2.0 mL) was added via syringe through the septum and the reactions were stirred for 14 h at rt. Water (7 mL) was added to precipitate the products. The contents of each reaction tube was transferred to a fritted reaction tube in a second Miniblock platform. The collected precipitate was washed with NaOH (0.5 N, 2 mL) and water (3 mL) then dissolved in CH_2Cl_2. The organic soluble material was collected, the solvent removed in vacuo and the residue purified by mass-directed, reverse-phase HPLC purification.



3'-(Cyclohexylamino)-1,2,5,6,6a,7,9,9a-octahydro-1'H-spiro[pyrrolo[3,2,1-ij]quinoline-8,2'-quinoxalin]-4(31H)-one 14*{1}*. General procedure A afforded the spiroheterocycle **14*{1}*** (26 mg, 0.066 mmol, 29% yield) as a tan solid. IR (neat) 3301, 2924, 2845, 1607, 1575 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{24}H_{33}N_4O$ ($[M+H]^+$) 393.2654, found 393.2654.



Peak Number	Time	AreaAbs	Area %Total	Height	Mass Found
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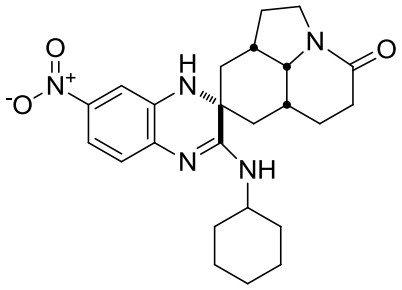
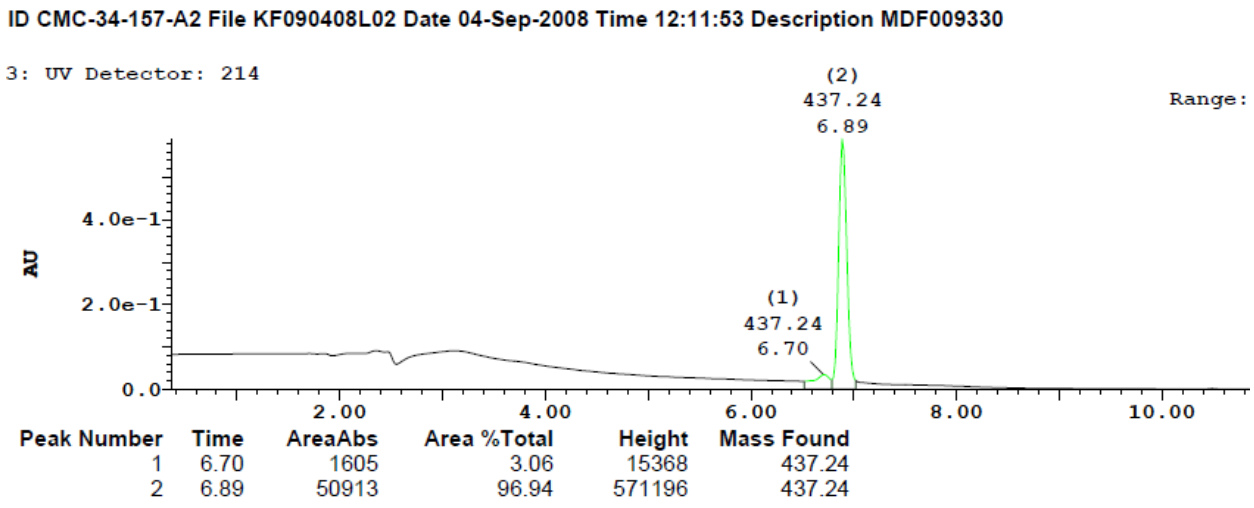
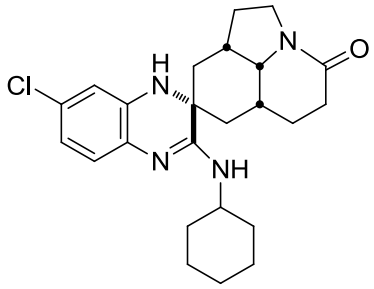
4	7.62	3043	4.71	27794	



3'-(Cyclohexylamino)-7'-nitro-1,2,5,6,6a,7,9,9a-octahydro-1'H-spiro[pyrrolo[3,2,1-ij]quinoline-8,2'-quinoxalin]-4(31H)-one 14*{2}*. General procedure A afforded the spiroheterocycle **14*{2}*** (27 mg, 0.062 mmol, 27% yield) as a reddish-brown solid. MP > 260 ºC; ^{1}H NMR (400 MHz, CD_3OD) δ 1.09 (m, 1 H), 1.25-1.49 (m, 3 H), 1.67-1.83 (complex, 4 H), 1.95-2.09 (complex, 4 H), 2.26 (m, 3 H), 2.62 (m, 1 H), 3.31 (quin, *J* = 2.0 Hz, 2 H), 3.52 (m, 2 H), 3.71-3.76 (complex, 4 H), 4.06 (m, 1 H), 7.03 (d, *J* = 8.4 Hz, 1 H), 7.50 (d, *J* = 2.4 Hz, 1 H),

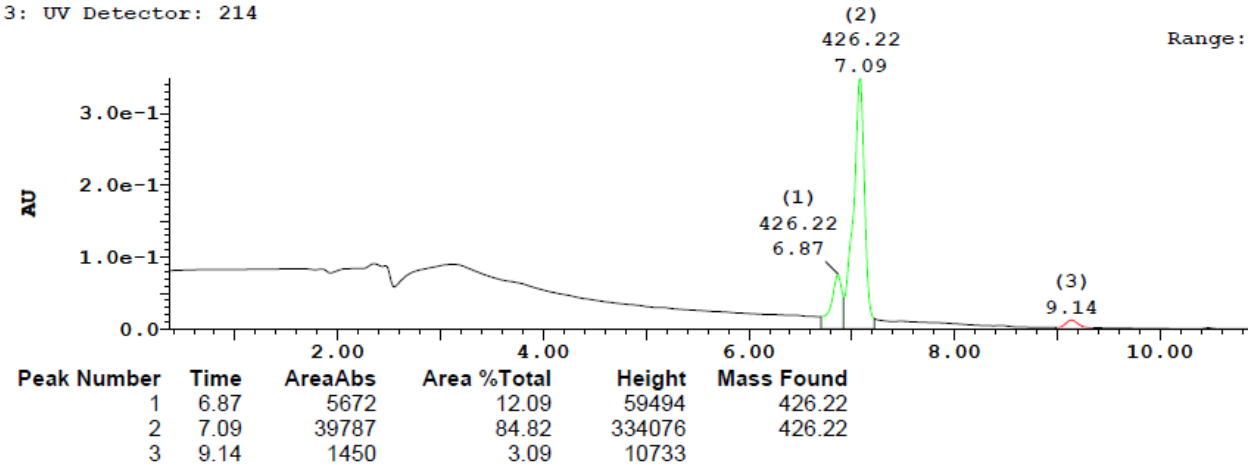
7.62 (dd, J = 2.8, 8.8 Hz, 1 H; ^{13}C NMR (100 MHz, $CDCl_3$) δ u: 26.2, 26.3, 26.5, 26.7, 27.4, 29.2, 32.6, 33.5, 33.6, 34.1, 44.1, 53.8, 68.9, 137.2, 143.4, 155.3, 171.5; d: 30.5, 38.6, 51.3, 60.3, 109.6, 116.3, 122.4; IR (neat) 3448, 3339, 3257, 2923, 2847, 1615, 1521, 1498, 1480 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{24}H_{32}N_5O_3$ ($[M+H]^+$) 438.2505, found 438.2510.





7'-Chloro-3'-(cyclohexylamino)-1,2,5,6,6a,7,9,9a-octahydro-1'H-spiro[pyrrolo[3,2,1-ij]quinoline-8,2'-quinoxalin]-4(31H)-one 14*{3}*. General procedure A afforded the spiroheterocycle **14*{3}*** (29 mg, 0.069 mmol, 30% yield) as a tan solid. HRMS (ESI) *m/z* calcd for $C_{24}H_{32}ClN_4O$ ($[M+H]^+$) 427.2265, found 427.2264.

ID CMC-34-157-A3 File KF090408L03 Date 04-Sep-2008 Time 12:24:12 Description MDF009334



Peak Number	Time	AreaAbs	Area %Total	Height	Mass Found
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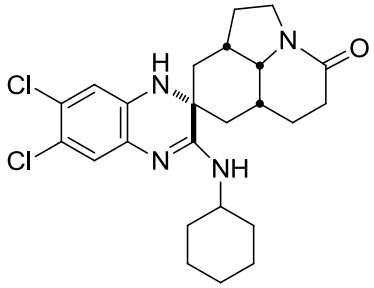
2	7.09	39787	84.82	334076	426.22
3	9.14	1450	3.09	10733	

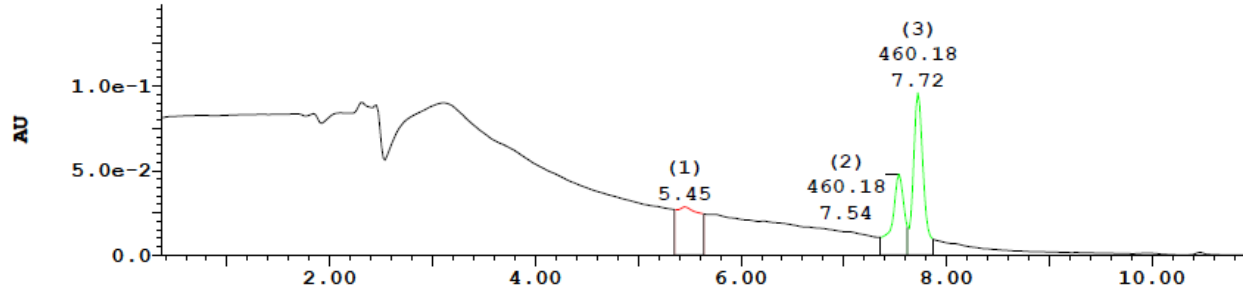


6',7'-Dichloro-3'-(cyclohexylamino)-1,2,5,6,6a,7,9,9a-octahydro-1'H-spiro[pyrrolo[3,2,1-ij]quinoline-8,2'-quinoxalin]-4(31H)-one 14*{4}*. General procedure A afforded the spiroheterocycle **14*{4}*** (7 mg, 0.02 mmol, 7% yield) as a brown solid. HRMS (ESI) *m/z* calcd for $C_{24}H_{31}Cl_2N_4O$ ($[M+H]^+$) 461.1875, found 461.1868.

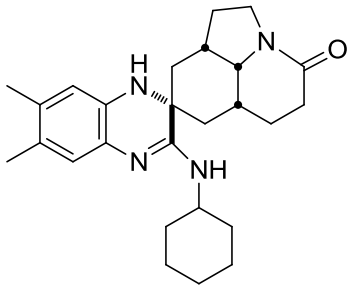
ID CMC-34-157-A4 File KF090408L04 Date 04-Sep-2008 Time 12:36:32 Description MDF009337

3: UV Detector: 214

Range

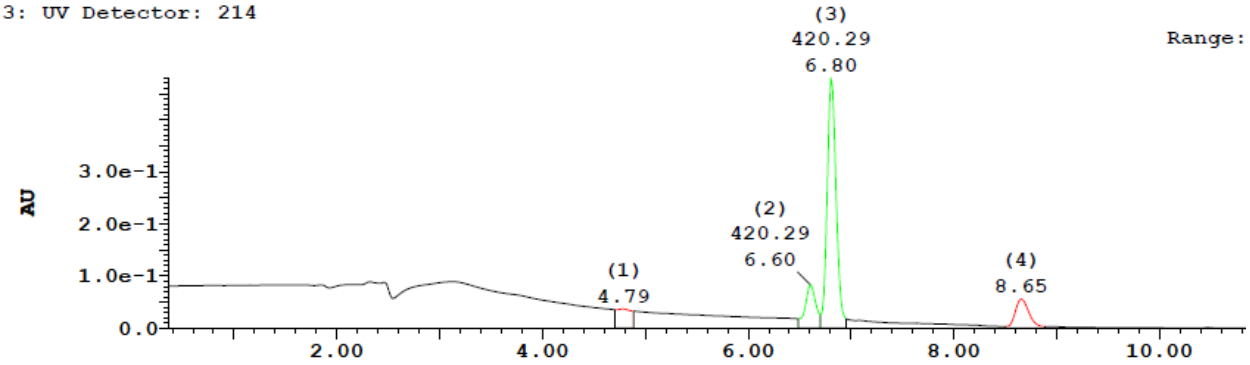


Peak Number	Time	AreaAbs	Area %Total	Height	Mass Found
1	5.45	270	2.16	2535	
2	7.54	3813	30.52	37765	460.18
3	7.72	8411	67.32	86253	460.18

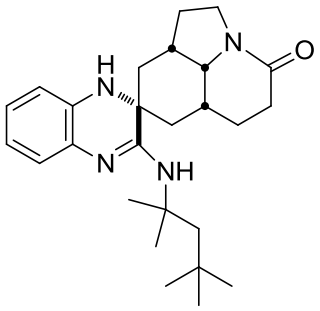


3'-(Cyclohexylamino)-6',7'-dimethyl-1,2,5,6,6a,7,9,9a-octahydro-1'H-spiro[pyrrolo[3,2,1-ij]quinoline-8,2'-quinoxalin]-4(31H)-one 14*{5}*. General procedure A afforded the spiroheterocycle **14*{5}*** (22 mg, 0.052 mmol, 23% yield) as a tan solid. HRMS (ESI) *m/z* calcd for $C_{26}H_{37}N_4O$ ($[M+H]^+$) 421.2967, found 421.2955.

ID CMC-34-157-A5 File KF090408L05 Date 04-Sep-2008 Time 12:48:52 Description MDF009341

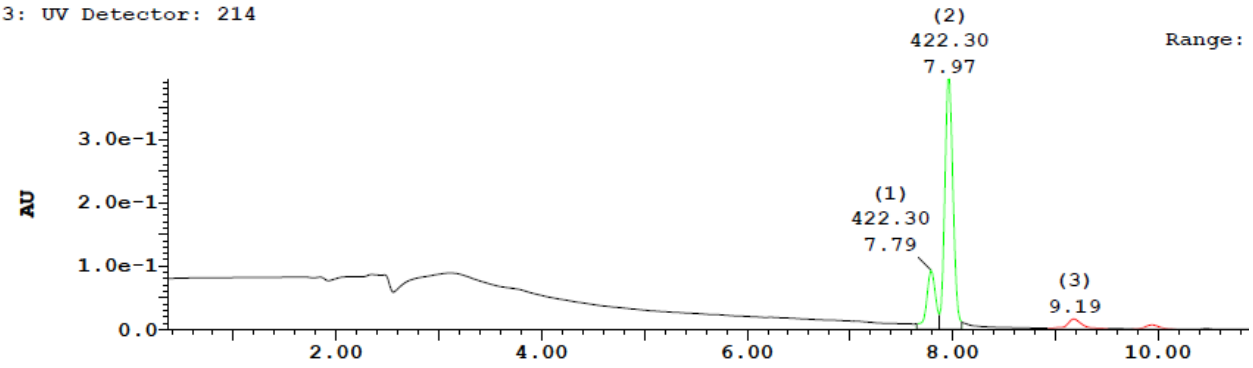


Peak Number	Time	AreaAbs	Area %Total	Height	Mass Found
1	4.79	228	0.39	2848	
2	6.60	6194	10.62	65175	420.29
3	6.80	44286	75.95	462580	420.29
4	8.65	7598	13.03	52708	

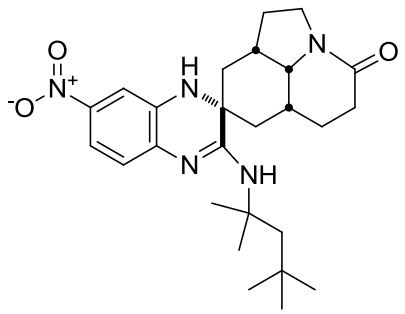


3'-((2,4,4-Trimethylpentan-2-yl)amino)-1,2,5,6,6a,7,9,9a-octahydro-1'H-spiro[pyrrolo[3,2,1-ij]quinoline-8,2'-quinoxalin]-4(31H)-one 14*{6}*. General procedure A afforded the spiroheterocycle **14*{6}*** (42 mg, 0.099 mmol, 43% yield) as a tan solid. HRMS (ESI) *m/z* calcd for $C_{26}H_{39}N_4O$ ($[M+H]^+$) 423.3124, found 423.3115.

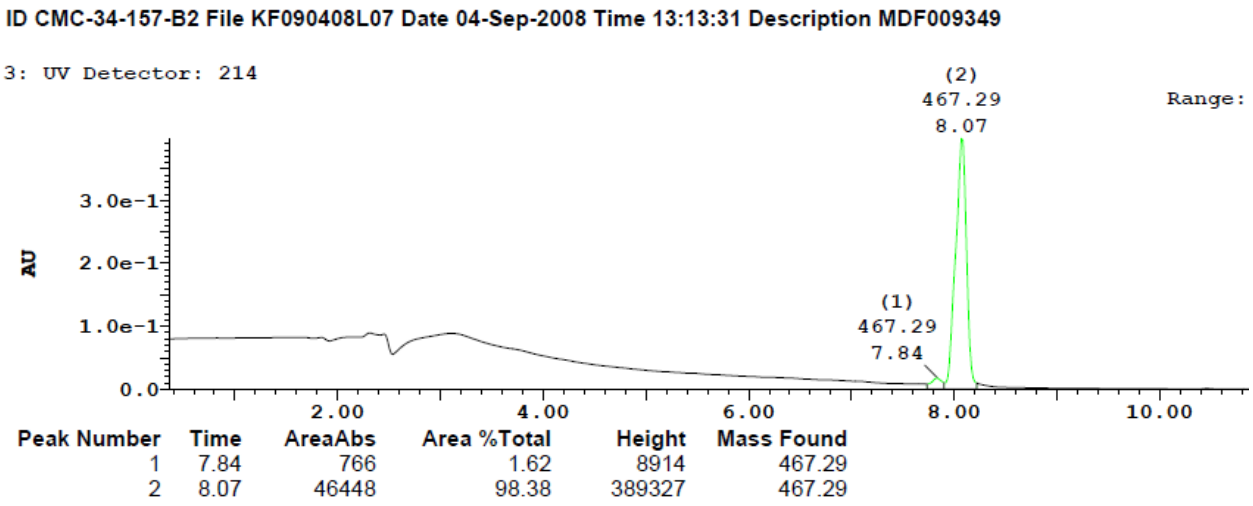
ID CMC-34-157-B1 File KF090408L06 Date 04-Sep-2008 Time 13:01:11 Description MDF009344

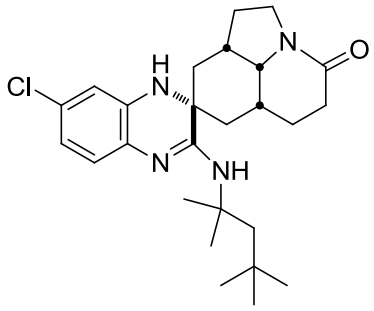


Peak Number	Time	AreaAbs	Area %Total	Height	Mass Found
1	7.79	7356	16.39	83719	422.30
2	7.97	34327	76.48	383801	422.30
3	9.19	2213	4.93	14636	
4	9.94	986	2.20	6467	



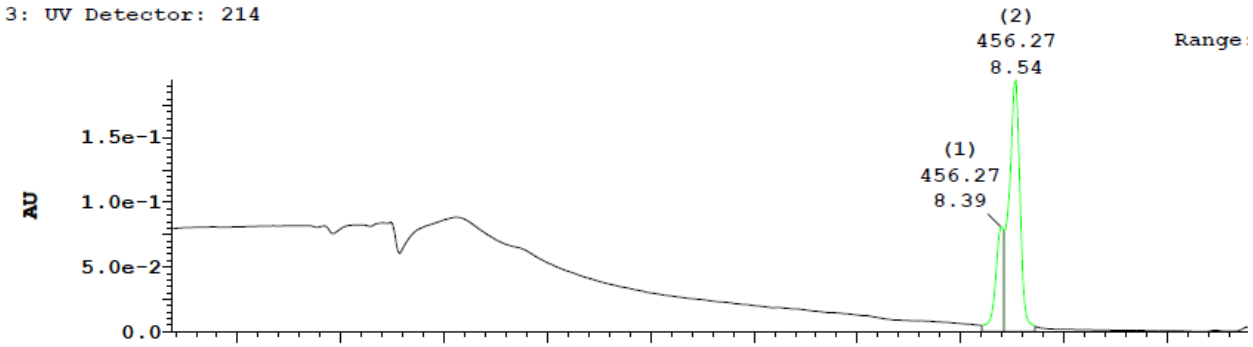
7'-Nitro-3'-((2,4,4-trimethylpentan-2-yl)amino)-1,2,5,6,6a,7,9,9a-octahydro-1'H-spiro[pyrrolo[3,2,1-ij]quinoline-8,2'-quinoxalin]-4(31H)-one 14*{7}*. General procedure A afforded the spiroheterocycle **14*{7}*** (17 mg, 0.036 mmol, 16% yield) as a red solid. HRMS (ESI) *m/z* calcd for $C_{26}H_{38}N_5O_3$ ($[M+H]^+$) 468.2975, found 468.2980.



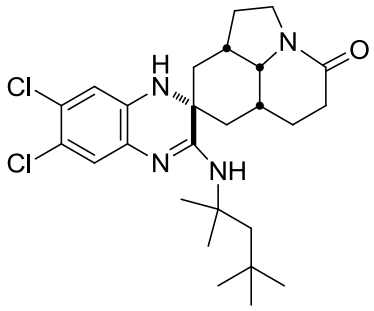


7'-Chloro-3'-((2,4,4-trimethylpentan-2-yl)amino)-1,2,5,6,6a,7,9,9a-octahydro-1'H-spiro[pyrrolo[3,2,1-ij]quinoline-8,2'-quinoxalin]-4(31H)-one 14*{8}*. General procedure A afforded the spiroheterocycle **14*{8}*** (60 mg, 0.13 mmol, 57% yield) as a brown solid. HRMS (ESI) *m/z* calcd for $C_{26}H_{38}ClN_4O$ ($[M+H]^+$) 457.2734, found 457.2730.

ID CMC-34-157-B3 File KF090408L08 Date 04-Sep-2008 Time 13:25:51 Description MDF009352

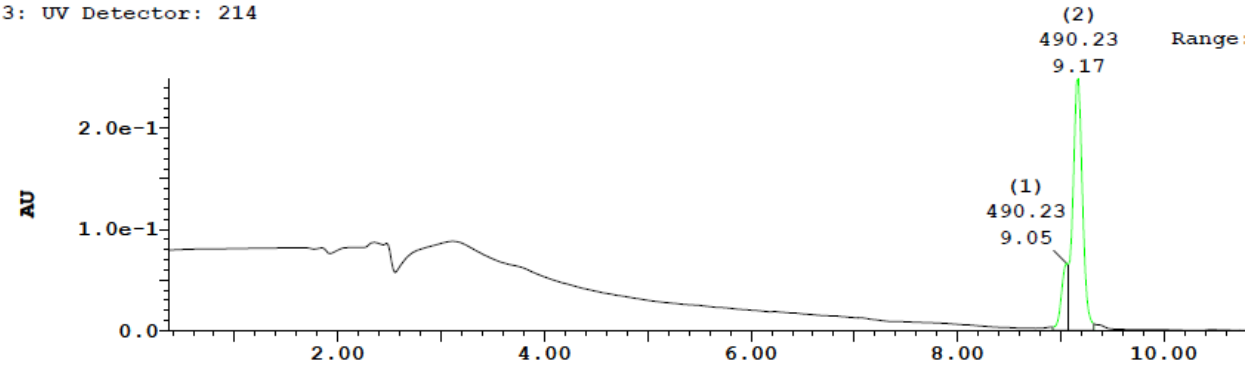


Peak Number	Time	AreaAbs	Area %Total	Height	Mass Found
1	8.39	6287	21.37	76395	456.27
2	8.54	23124	78.63	190205	456.27

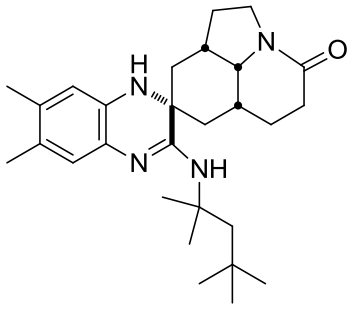


6',7'-Dichloro-3'-((2,4,4-trimethylpentan-2-yl)amino)-1,2,5,6,6a,7,9,9a-octahydro-1'H-spiro[pyrrolo[3,2,1-ij]quinoline-8,2'-quinoxalin]-4(31H)-one 14*{9}*. General procedure A afforded the spiroheterocycle **14*{9}*** (34 mg, 0.070 mmol, 30% yield) as an orange solid. IR (neat) 3483, 3286, 2949, 2874, 1630, 1608, 1580, 1515, 1481 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{26}H_{37}Cl_2N_4O$ ($[M+H]^+$) 491.2344, found 491.2330.

ID CMC-34-157-B4 File KF090408L09 Date 04-Sep-2008 Time 13:38:10 Description MDF009358

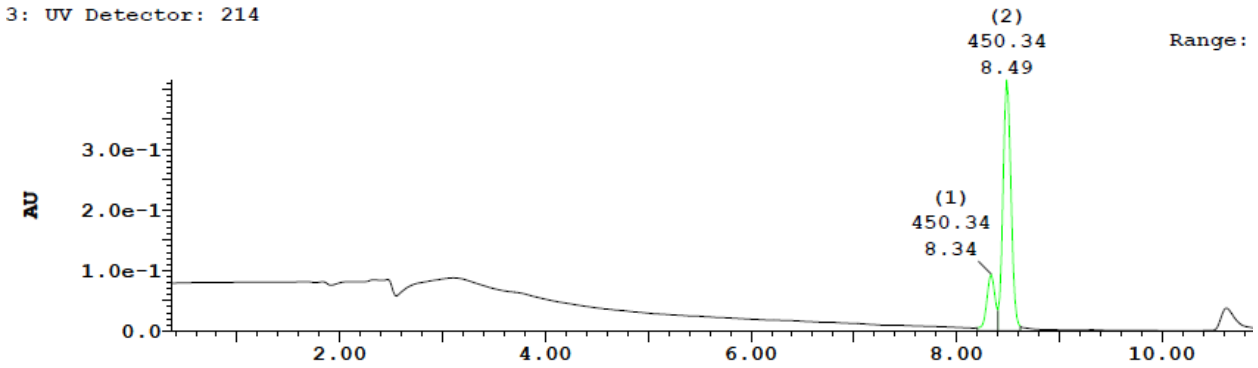


Peak Number	Time	AreaAbs	Area %Total	Height	Mass Found
1	9.05	4081	13.62	61905	490.23
2	9.17	25886	86.38	243821	490.23

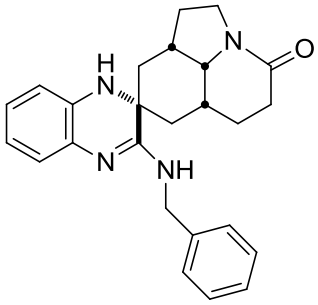


6',7'-Dimethyl-3'-((2,4,4-trimethylpentan-2-yl)amino)-1,2,5,6,6a,7,9,9a-octahydro-1'H-spiro[pyrrolo[3,2,1-ij]quinoline-8,2'-quinoxalin]-4(31H)-one 14*{10}*. General procedure A afforded the spiroheterocycle **14*{10}*** (42 mg, 0.093 mmol, 41% yield) as a tan solid. HRMS (ESI) *m/z* calcd for $C_{28}H_{43}N_4O$ ($[M+H]^+$) 451.3437, found 451.3433.

ID CMC-34-157-B5 File KF090408L10 Date 04-Sep-2008 Time 13:50:30 Description MDF009364

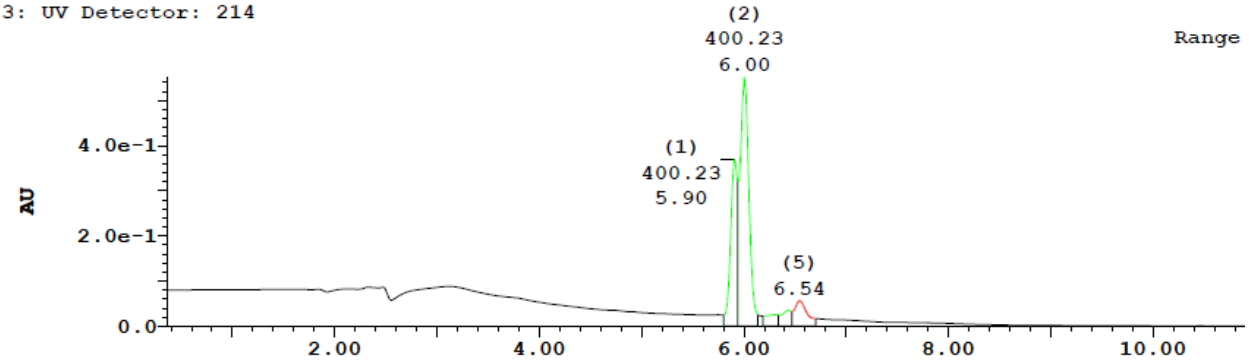


Peak Number	Time	AreaAbs	Area %Total	Height	Mass Found
1	8.34	7710	17.43	87747	450.34
2	8.49	36522	82.57	408443	450.34

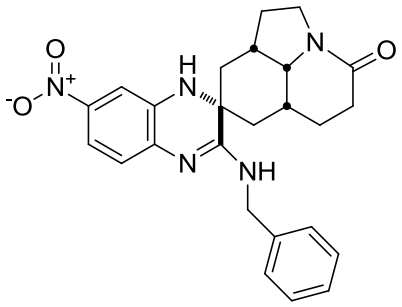


3'-(Benzylamino)-1,2,5,6,6a,7,9,9a-octahydro-1'H-spiro[pyrrolo[3,2,1-ij]quinoline-8,2'-quinoxalin]-4(31H)-one 14*{11}*. General procedure A afforded the spiroheterocycle **14*{11}*** (30 mg, 0.075 mmol, 33% yield) as a tan solid. HRMS (ESI) *m/z* calcd for $C_{25}H_{29}N_4O$ ($[M+H]^+$) 401.2341, found 401.2329.

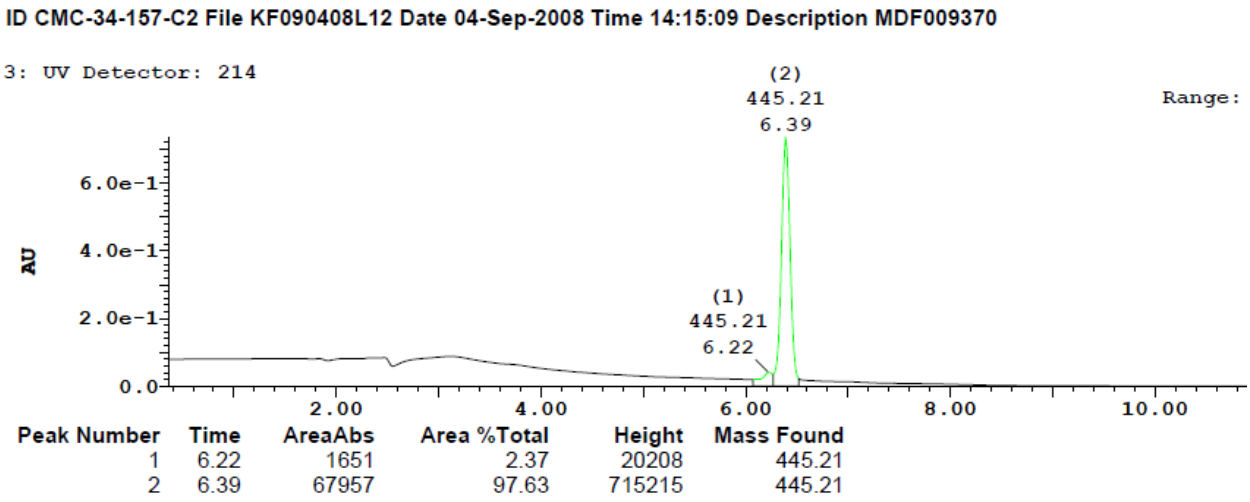
ID CMC-34-157-C1 File KF090408L11 Date 04-Sep-2008 Time 14:02:50 Description MDF009367



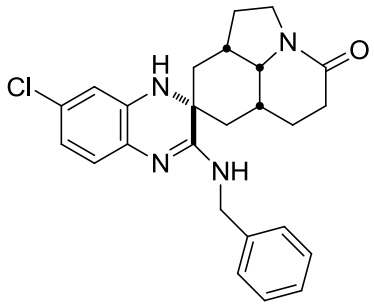
Peak Number	Time	AreaAbs	Area %Total	Height	Mass Found
1	5.90	23326	28.71	343267	400.23
2	6.00	52254	64.31	527038	400.23
3	6.30	340	0.42	4123	400.23
4	6.44	1315	1.62	15299	400.23
5	6.54	4013	4.94	37384	



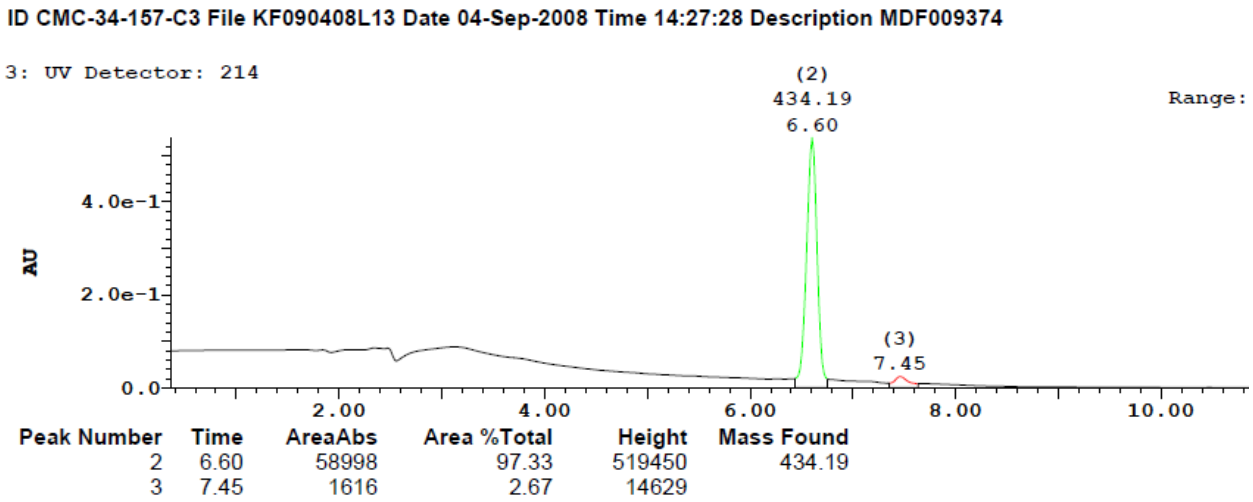
3'-(Benzylamino)-7'-nitro-1,2,5,6,6a,7,9,9a-octahydro-1'H-spiro[pyrrolo[3,2,1-ij]quinoline-8,2'-quinoxalin]-4(31H)-one 14*{12}*. General procedure A afforded the spiroheterocycle **14*{12}*** (53 mg, 0.12 mmol, 51% yield) as a red solid. HRMS (ESI) *m/z* calcd for $C_{25}H_{28}N_5O_3$ ($[M+H]^+$) 446.2192, found 446.2189.

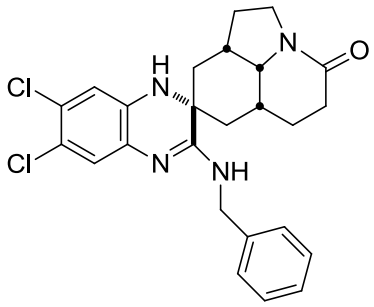


Peak Number	Time	AreaAbs	Area %Total	Height	Mass Found
1	6.22	1651	2.37	20208	445.21
2	6.39	67957	97.63	715215	445.21



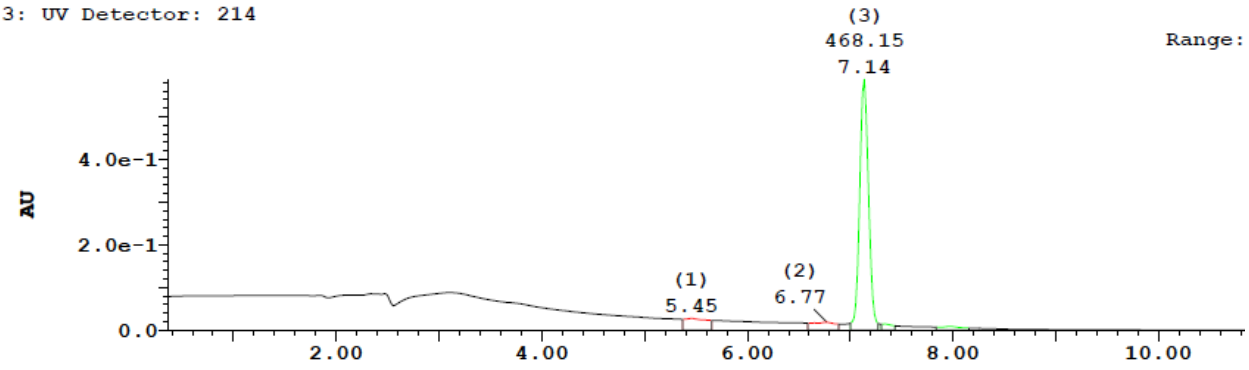
7'-Chloro-1,2,5,6,6a,7,9,9a-octahydro-1'H-spiro[pyrrolo[3,2,1-ij]quinoline-8,2'-quinoxalin]-4(31H)-one 14*{13}*. General procedure A afforded the spiroheterocycle **14*{13}*** (40 mg, 0.092 mmol, 40% yield) as a tan solid. HRMS (ESI) *m/z* calcd for $C_{25}H_{28}ClN_4O$ ($[M+H]^+$) 435.1960, found 435.1960.



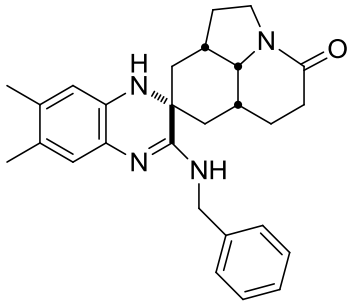


3'-(Benzylamino)-6',7'-dichloro-1,2,5,6,6a,7,9,9a-octahydro-1'H-spiro[pyrrolo[3,2,1-ij]quinoline-8,2'-quinoxalin]-4(31H)-one 14*{14}*. General procedure A afforded the spiroheterocycle **14*{14}*** (34 mg, 0.073 mmol, 32% yield) as a brown solid. HRMS (ESI) *m/z* calcd for $C_{25}H_{27}Cl_2N_4O$ ($[M+H]^+$) 469.1562, found 469.1568.

ID CMC-34-157-C4 File KF090408L14 Date 04-Sep-2008 Time 14:39:48 Description MDF009377

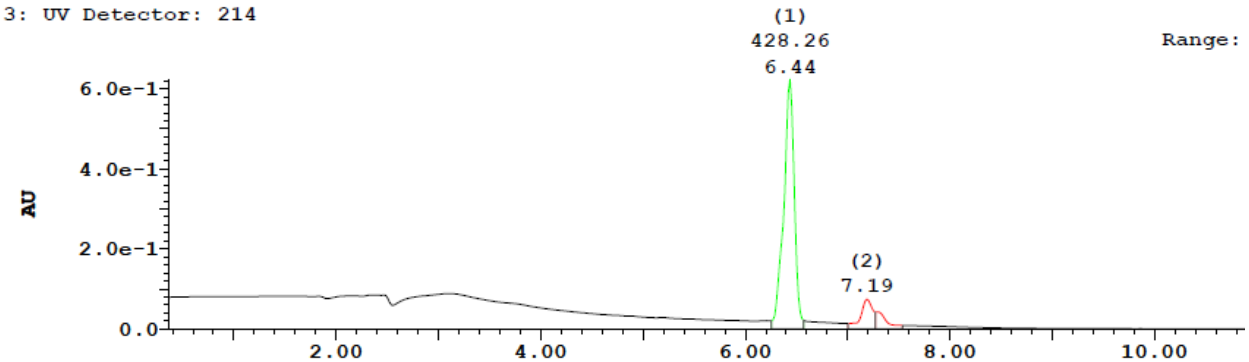


Peak Number	Time	AreaAbs	Area %Total	Height	Mass Found
1	5.45	314	0.56	3014	
2	6.77	445	0.79	3568	
3	7.14	54970	97.91	571200	468.15
4	7.34	106	0.19	1391	468.15
5	7.97	308	0.55	2704	468.15

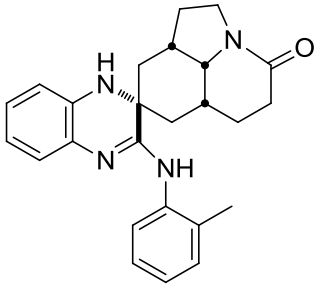


3'-(Benzylamino)-6',7'-dimethyl-1,2,5,6,6a,7,9,9a-octahydro-1'H-spiro[pyrrolo[3,2,1-ij]quinoline-8,2'-quinoxalin]-4(31H)-one 14*{15}*. General procedure A afforded the spiroheterocycle **14*{15}*** (53 mg, 0.12 mmol, 54% yield) as a yellow solid. HRMS (ESI) *m/z* calcd for $C_{27}H_{33}N_4O$ ($[M+H]^+$) 429.2654, found 429.2643.

ID CMC-34-157-C5 File KF090408L15 Date 04-Sep-2008 Time 14:52:08 Description MDF009380

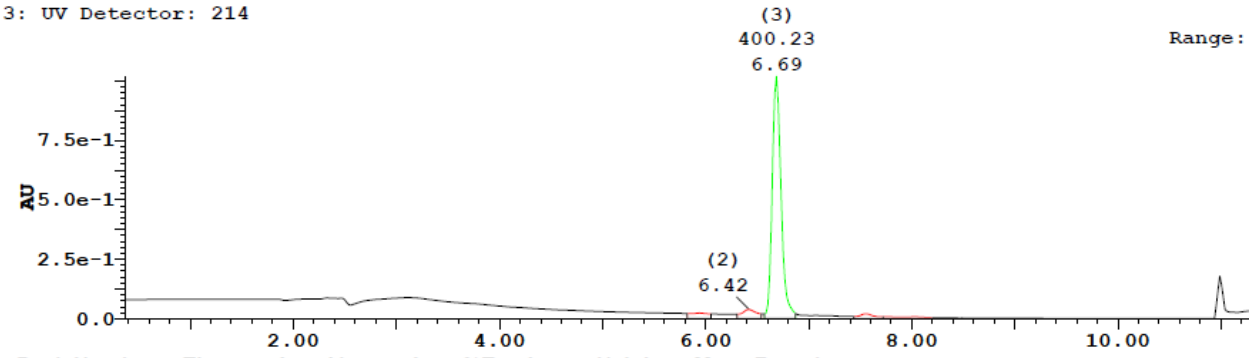


Peak Number	Time	AreaAbs	Area %Total	Height	Mass Found
1	6.44	68129	87.35	603081	428.26
2	7.19	6915	8.87	62997	
3	7.30	2948	3.78	31575	

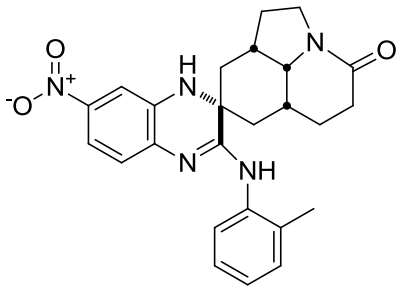


3'-(o-Tolylamino)-1,2,5,6,6a,7,9,9a-octahydro-1'H-spiro[pyrrolo[3,2,1-ij]quinoline-8,2'-quinoxalin]-4(31H)-one 14*{16}*. General procedure A afforded the spiroheterocycle **14*{16}*** (27 mg, 0.067 mmol, 29% yield) as a tan solid. Mp > 260 ºC;); ^{1}H NMR δ 0.91 (t, *J* = 13.2 Hz, 1 H), 1.19 (t, *J* = 13.2 Hz, 1 H), 1.65 (m, 1 H), 1.76 (m, 1 H), 1.96 (m, 2 H), 2.16 (s, 3 H), 2.19 (m, 1 H), 2.36 (m, 2 H), 2.89 (m, 1 H), 3.12 (m, 1 H), 3.51 (t, *J* = 10.4 Hz, 1 H), 3.64 (m, 2 H), 3.76 (m, 1 H), 6.47 (m, 1 H), 6.49 (m, 1 H), 6.69 (m, 2 H), 6.81 (m, 2 H), 7.02 (dt, *J* = 1.2, 7.4 Hz, 1 H), 7.20 (t, *J* = 7.6 Hz, 1 H), 7.24 (br s, 1 H); ^{13}C NMR δ d 18.1, 29.1, 37.0, 59.7, 113.7, 114.9, 119.5, 120.6, 122.4, 123.4, 127.1, 131.1; u 25.5, 27.1, 27.9, 33.0, 35.3, 42.9, 55.2, 126.6, 129.5, 132.3, 146.3, 150.6, 169.0; IR (neat): 3319, 3270, 2942, 2874, 1659, 1601 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{25}H_{29}N_4O$ ($[M+H]^+$) 401.2341, found 401.2334.

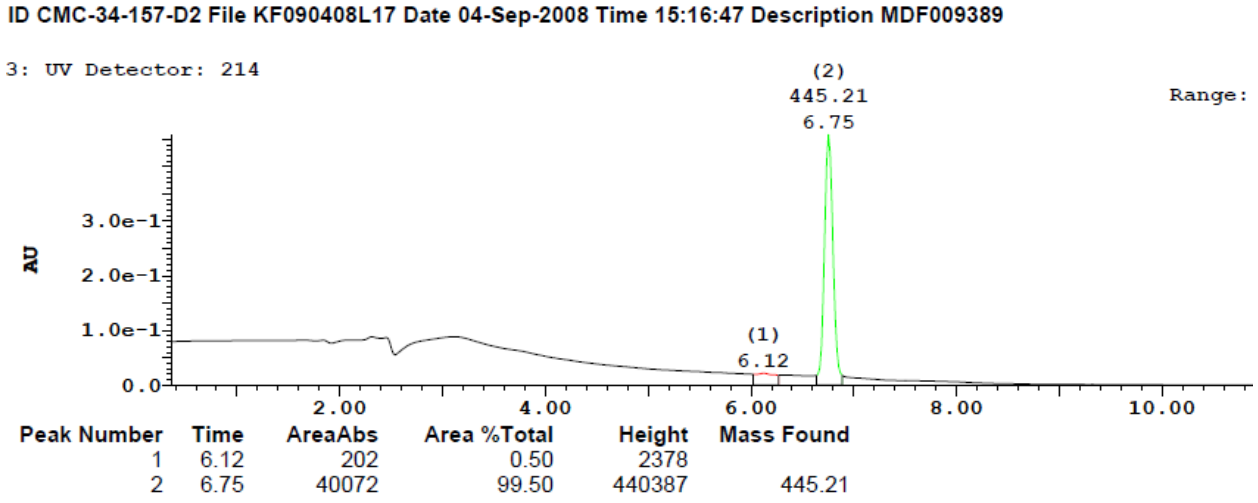
ID CMC-34-157-D1 File KF090408L16 Date 04-Sep-2008 Time 15:04:28 Description MDF009384

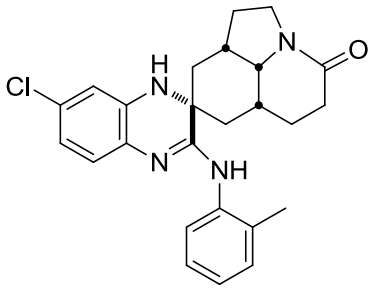


Peak Number	Time	AreaAbs	Area %Total	Height	Mass Found
1	5.94	265	0.27	2966	
2	6.42	1957	1.96	19188	
3	6.69	95769	95.93	998145	400.23
4	7.55	1371	1.37	12318	
5	8.04	467	0.47	2555	



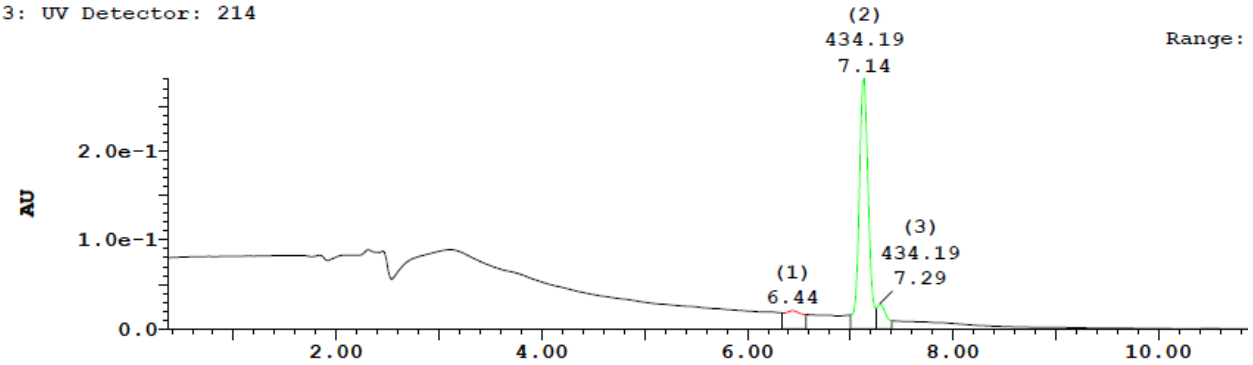
7'-Nitro-3'-(o-tolylamino)-1,2,5,6,6a,7,9,9a-octahydro-1'H-spiro[pyrrolo[3,2,1-ij]quinoline-8,2'-quinoxalin]-4(31H)-one 14*{17}*. General procedure A afforded the spiroheterocycle **14*{17}*** (8 mg, 0.019 mmol, 8% yield) as a red-brown solid. HRMS (ESI) *m/z* calcd for $C_{25}H_{28}N_5O_3$ ($[M+H]^+$) 446.2192, found 446.2187.





7'-Chloro-3'-(o-tolylamino)-1,2,5,6,6a,7,9,9a-octahydro-1'H-spiro[pyrrolo[3,2,1-ij]quinoline-8,2'-quinoxalin]-4(31H)-one 14*{18}*. General procedure A afforded the spiroheterocycle **14*{18}*** (6 mg, 0.014 mmol, 6% yield) as a tan solid. Mp > 260 ºC; ^{1}H NMR ($CDCl_3$) δ 0.90 (dt, *J* = 3.6, 12.8 Hz, 1 H), 1.19 (dt, *J* = 3.6, 13.2 Hz, 1 H), 1.65 (m, 1 H), 1.77 (m, 1 H), 1.85 (m, 1 H), 1.95 (m, 1 H), 2.15 (s, 3 H), 2.25-2.44 (m, 2 H), 2.88 (m, 1 H), 3.10 (m, 1 H), 3.51(t, *J* = 10.4 Hz, 1 H), 3.65 (m, 2 H), 6.39 (d, *J* = 8.8 Hz, 1 H), 6.46 (s, 1 H), 6.50 (d, *J* = 2.0 Hz, 1 H), 6.63 (m, 1 H), 6.78 (m, 1 H), 7.03 (t, *J* = 7.2 Hz, 1 H), 7.20 (t, *J* = 7.2 Hz, 1 H), 7.24 (s, 1 H); ^{13}C NMR δ d 18.2, 29.1, 37.0, 40.1, 59.7, 114.5, 114.7, 119.3, 120.5, 123.6, 127.2, 131.3; u 25.5, 27.1, 27.9, 33.1, 35.6, 43.0, 55.3, 129.5, 130.9, 133.5, 145.9, 146.2, 150.2, 169.1; IR 3300, 3268, 2940, 1656, 1596, 1505 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{25}H_{28}ClN_4O$ ($[M+H]^+$) 435.1960, found 435.1948.

ID CMC-34-157-D3 File KF090408L18 Date 04-Sep-2008 Time 15:29:07 Description MDF009393



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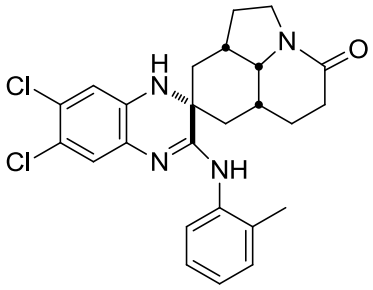
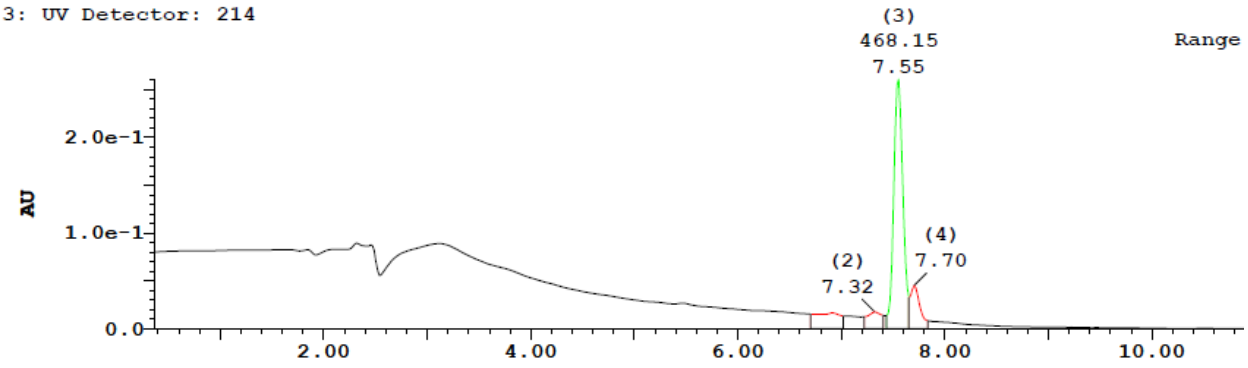
1	6.44	306	1.12	3333	
2	7.14	25654	93.88	267679	434.19
3	7.29	1367	5.00	16726	434.19

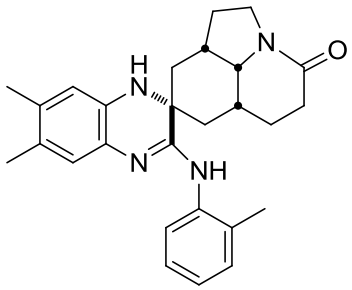


6',7'-Dichloro-3'-(o-tolylamino)-1,2,5,6,6a,7,9,9a-octahydro-1'H-spiro[pyrrolo[3,2,1-ij]quinoline-8,2'-quinoxalin]-4(31H)-one 14*{19}*. General procedure A afforded the spiroheterocycle **14*{19}*** (8 mg, 0.017 mmol, 7% yield) as a brown solid. HRMS (ESI) *m/z* calcd for $C_{25}H_{27}Cl_2N_4O$ ($[M+H]^+$) 469.1562, found 469.1570.

ID CMC-34-157-D4 File KF090408L19 Date 04-Sep-2008 Time 15:41:27 Description MDF009397

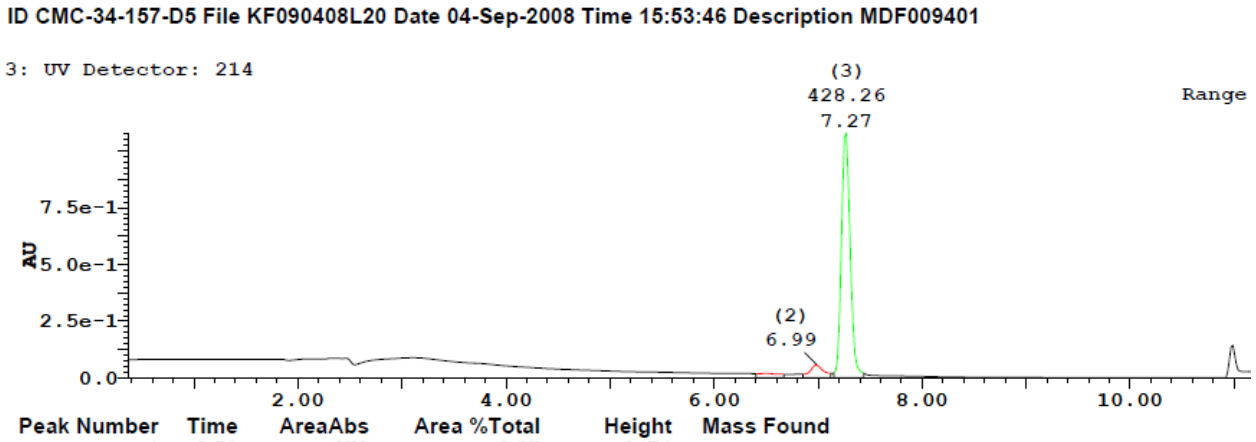


Peak Number	Time	AreaAbs	Area %Total	Height	Mass Found
1	6.92	295	1.05	2690	
2	7.32	369	1.31	4238	
3	7.55	24225	86.28	248995	468.15
4	7.70	3188	11.36	34939	

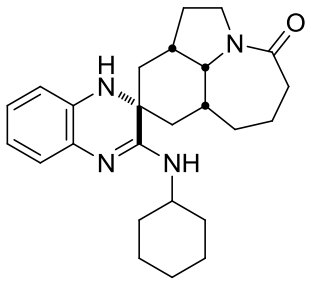


6',7'-Dimethyl-3'-(o-tolylamino)-1,2,5,6,6a,7,9,9a-octahydro-1'H-spiro[pyrrolo[3,2,1-ij]quinoline-8,2'-quinoxalin]-4(31H)-one 14*{20}*. General procedure A afforded the spiroheterocycle **14*{20}*** (34 mg, 0.080 mmol, 35% yield) as a tan solid. Mp > 260 ºC;); ^{1}H NMR δ 0.87 (t, *J* = 12.0 Hz, 1 H), 1.15 (t, *J* = 13.2 Hz, 1 H), 1.64 (dd, *J* = 6.8, 13.2 Hz, 1 H), 1.75 (m, 1 H), 1.90-2.01 (m, 3 H), 2.09 (s, 3 H), 2.14 (s, 3 H), 2.15 (s, 3 H), 2.18 (m, 2 H), 2.32 (m, 2 H), 2.87 (td, *J* = 3.6, 12.8 Hz, 1 H), 3.12 (m, 1 H), 3.50 (m, 1 H), 3.63 (m, 1 H), 6.28 (s, 1 H), 6.38 (s, 1 H), 6.48 (s, 1 H), 6.80 (dd, *J* = 1.2, 7.6 Hz, 1 H), 7.00 (dt, *J* = 1.2, 7.6 Hz, 1 H), 7.18 (dt, *J* = 1.6, 8.0 Hz, 1 H), 7.23 (d, *J* = 7.2 Hz, 1 H); ^{13}C NMR δ d 18.1, 18.9, 19.2, 29.1, 37.0, 59.8, 115.0, 116.3, 120.6, 123.3, 127.0, 131.1; u 25.5, 27.1, 27.9, 32.9, 35.3, 42.9, 55.2,

124.5, 127.6, 129.4, 129.9, 130.3, 146.5, 150.8, 169.1; IR (neat): 3385, 3289, 2935, 2874, 1646, 1620, 1518 cm^{-1};HRMS (ESI) *m/z* calcd for $C_{27}H_{33}N_4O$ ($[M+H]^+$) 429.2654, found 429.2654.

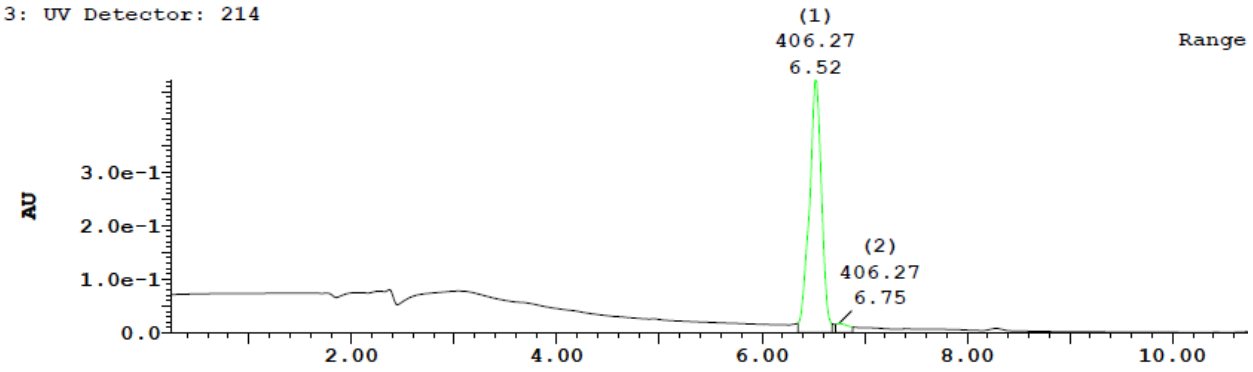


Peak Number	Time	AreaAbs	Area %Total	Height	Mass Found
1	6.50	279	0.27	3174	
2	6.99	4049	3.87	38080	
3	7.27	100288	95.86	1057530	428.26



3'-(Cyclohexylamino)-31,5,6,7,7a,8,10,10a-octahydro-1H,1'H-spiro[azepino[3,2,1-hi]indole-9,2'-quinoxalin]-4(2H)-one 14*{21}*. General procedure B afforded the spiroheterocycle **14*{21}*** (24 mg, 0.06 mmol, 17% yield) as a tan solid. HRMS (ESI) *m/z* calcd for $C_{25}H_{35}N_4O$ ($[M+H]^+$) 407.2811, found 407.2828.

ID CMC-34-076-A1 File KF071008L26 Date 10-Jul-2008 Time 21:48:58 Description MDF008636



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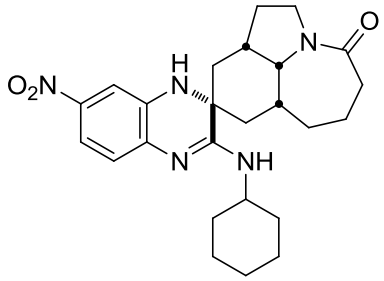
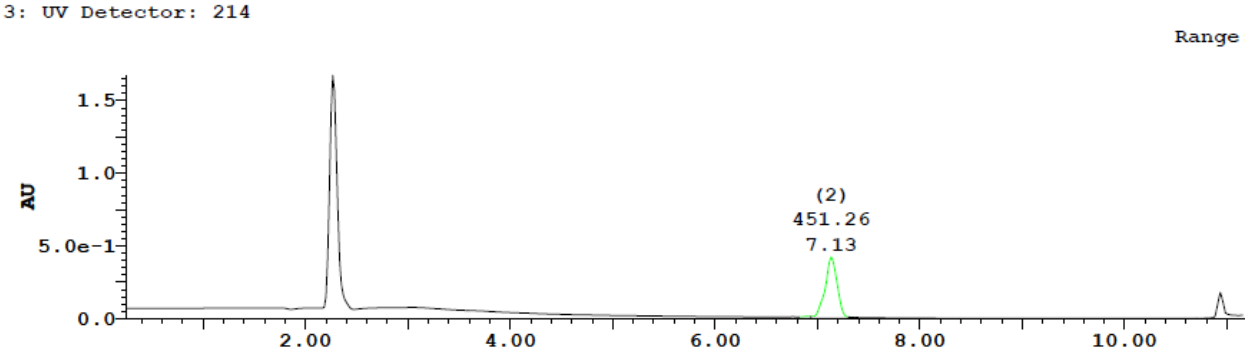
1	6.52	59324	99.63	455758	406.27
2	6.75	220	0.37	1995	406.27

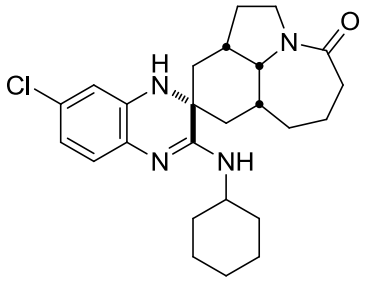


3'-(Cyclohexylamino)-7'-nitro-31,5,6,7,7a,8,10,10a-octahydro-1H,1'H-spiro[azepino[3,2,1-hi]indole-9,2'-quinoxalin]-4(2H)-one 14*{22}*. General procedure B afforded the spiroheterocycle **14*{22}*** (69 mg, 0.15 mmol, 45% yield) as a red solid. HRMS (ESI) *m/z* calcd for $C_{25}H_{34}N_5O_3$ ($[M+H]^+$) 452.2662, found 452.2667.

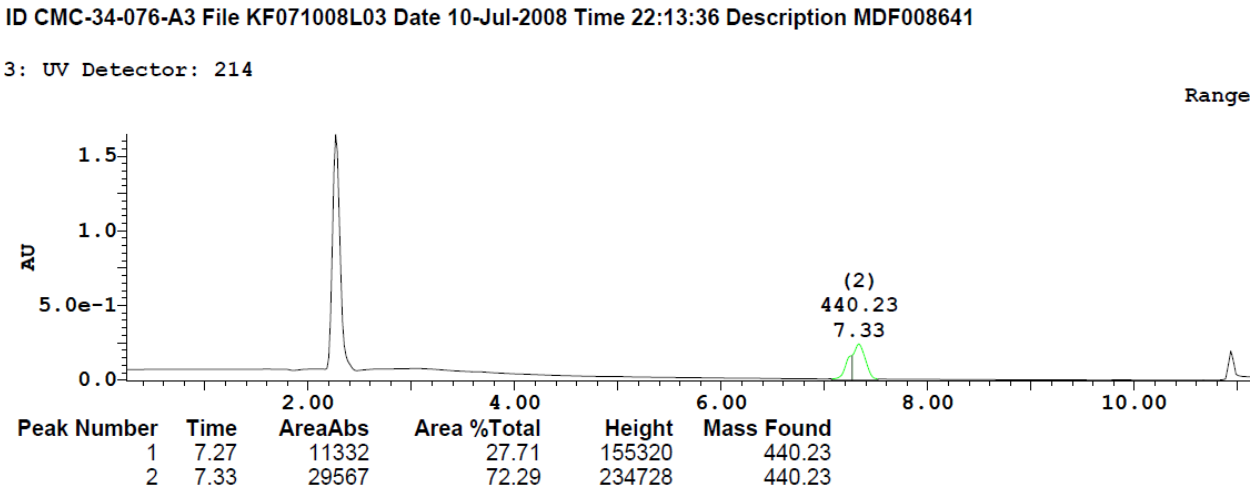
ID CMC-34-076-A2 File KF071008L27 Date 10-Jul-2008 Time 22:01:17 Description MDF008638

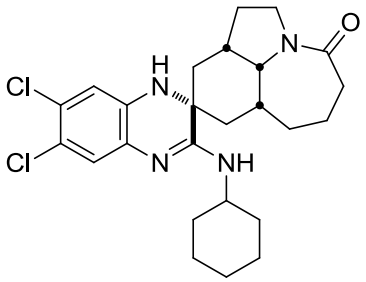


Peak Number	Time	AreaAbs	Area %Total	Height	Mass Found
1	6.90	333	0.60	4572	451.26
2	7.13	54778	99.40	412867	451.26



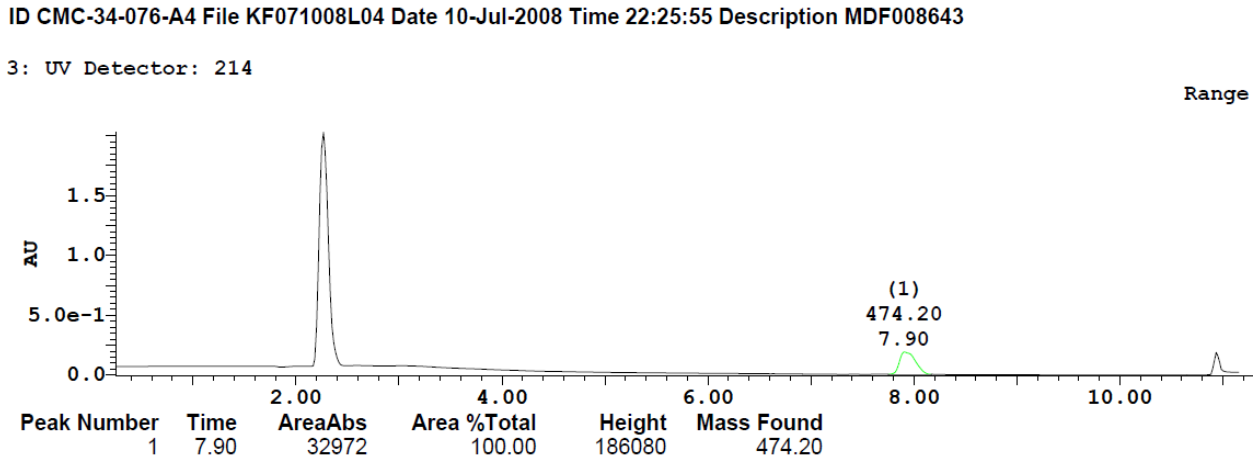
7'-Chloro-3'-(cyclohexylamino)-31,5,6,7,7a,8,10,10a-octahydro-1H,1'H-spiro[azepino[3,2,1-hi]indole-9,2'-quinoxalin]-4(2H)-one 14*{23}*. General procedure B afforded the spiroheterocycle **14*{23}*** (74 mg, 0.17 mmol, 50% yield) as a tan solid. HRMS (ESI) *m/z* calcd for $C_{25}H_{34}ClN_4O$ ($[M+H]^+$) 441.2421, found 441.2435.

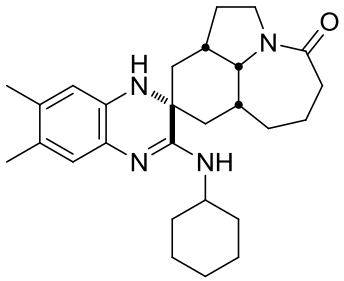




6',7'-Dichloro-3'-(cyclohexylamino)-31,5,6,7,7a,8,10,10a-octahydro-1H,1'H-spiro[azepino[3,2,1-hi]indole-9,2'-quinoxalin]-4(2H)-one 14*{24}*. General procedure B

afforded the spiroheterocycle **14*{24}*** (24 mg, 0.051 mmol, 15% yield) as a tan solid. HRMS (ESI) *m/z* calcd for $C_{25}H_{33}Cl_2N_4O$ ($[M+H]^+$) 475.2031, found 475.2031.



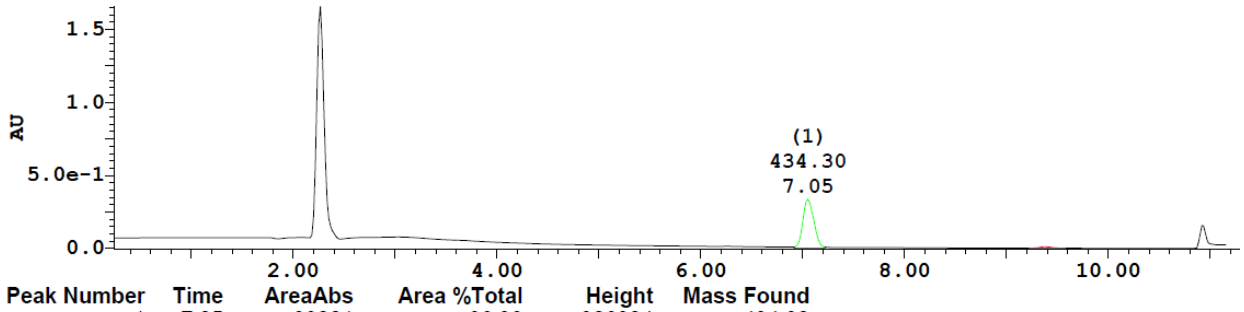


3'-(Cyclohexylamino)-6',7'-dimethyl-31,5,6,7,7a,8,10,10a-octahydro-1H,1'H-spiro[azepino[3,2,1-hi]indole-9,2'-quinoxalin]-4(2H)-one 14*{25}*. General procedure B afforded the spiroheterocycle **14*{25}*** (58 mg, 0.13 mmol, 40% yield) as a tan solid. HRMS (ESI) *m/z* calcd for $C_{27}H_{39}N_4O$ ($[M+H]^+$) 435.3124, found 435.3137.

ID CMC-34-076-A5 File KF071008L05 Date 10-Jul-2008 Time 22:38:14 Description MDF008647

3: UV Detector: 214

Range:



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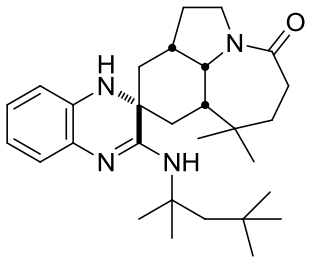
2	9.38	1469	3.61	9711	

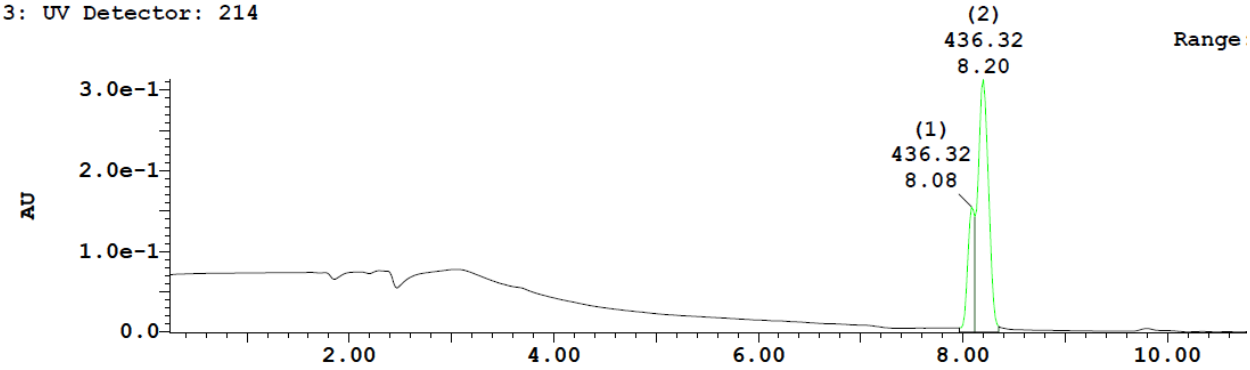


7,7-Dimethyl-3'-((2,4,4-trimethylpentan-2-yl)amino)-31,5,6,7,7a,8,10,10a-octahydro-1H,1'H-spiro[azepino[3,2,1-hi]indole-9,2'-quinoxalin]-4(2H)-one 14*{26}*. General procedure B afforded the spiroheterocycle **14*{26}*** (66 mg, 0.14 mmol, 42% yield) as a tan solid. HRMS (ESI) *m/z* calcd for $C_{27}H_{41}N_4O$ ($[M+H]^+$) 437.3280, found 437.3290.

ID CMC-34-076-B1 File KF071008L06 Date 10-Jul-2008 Time 22:50:34 Description MDF008650

3: UV Detector: 214

Range:



Peak Number	Time	AreaAbs	Area %Total	Height	Mass Found
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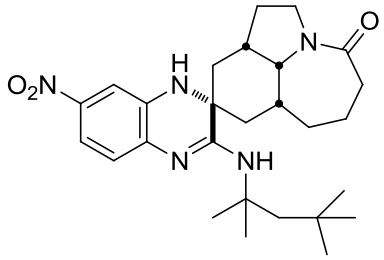
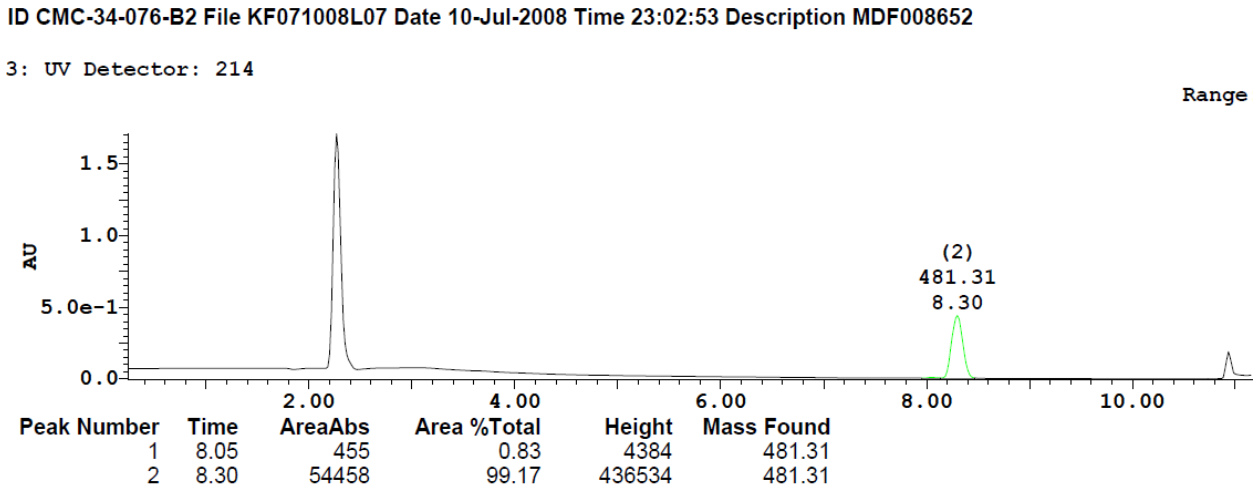
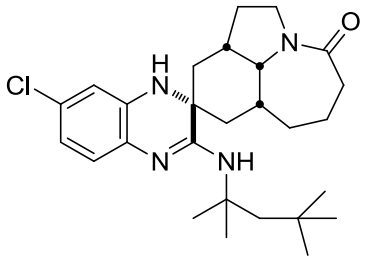
2	8.20	36183	76.90	307087	436.32



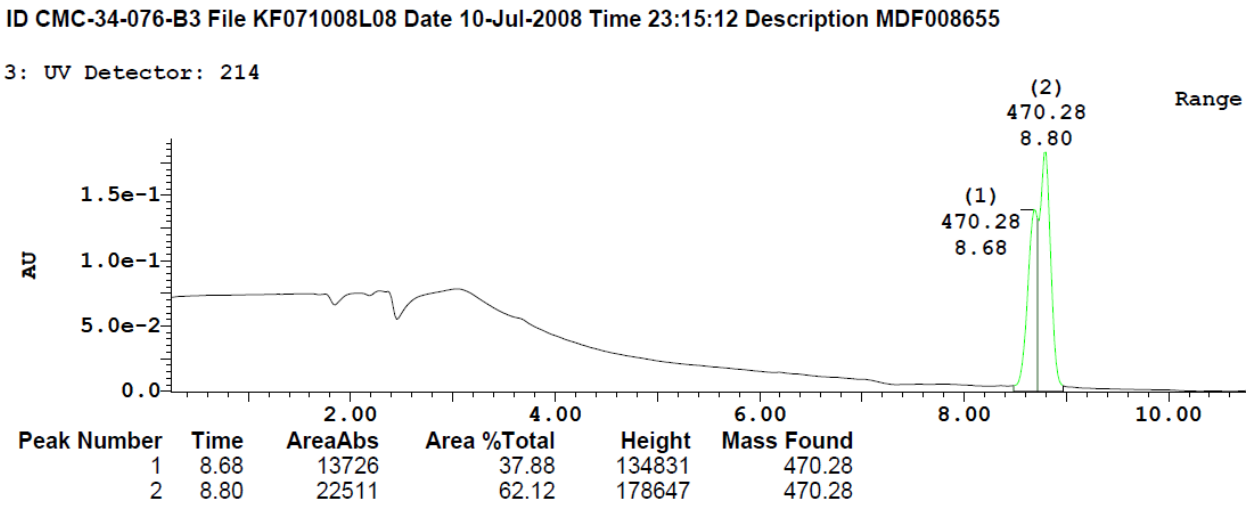
7'-Nitro-3'-((2,4,4-trimethylpentan-2-yl)amino)-31,5,6,7,7a,8,10,10a-octahydro-1H,1'H-spiro[azepino[3,2,1-hi]indole-9,2'-quinoxalin]-4(2H)-one 14*{27}*. General procedure B afforded the spiroheterocycle **14*{27}*** (71 mg, 0.15 mmol, 44% yield) as a red solid. HRMS (ESI) *m/z* calcd for $C_{27}H_{40}N_5O_3$ ($[M+H]^+$) 482.3131, found 482.3124.

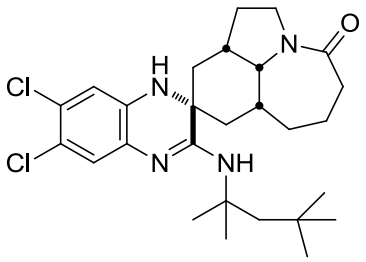




7'-Chloro-3'-((2,4,4-trimethylpentan-2-yl)amino)-31,5,6,7,7a,8,10,10a-octahydro-1H,1'H-spiro[azepino[3,2,1-hi]indole-9,2'-quinoxalin]-4(2H)-one 14*{28}*. General procedure B

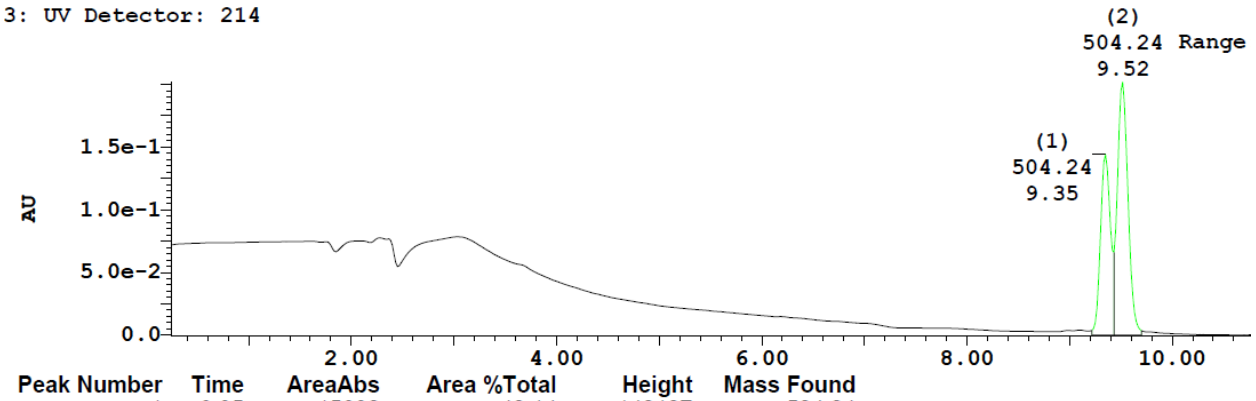
afforded the spiroheterocycle **14*{28}*** (95 mg, 0.20 mmol, 60% yield) as a yellow solid. HRMS (ESI) *m/z* calcd for $C_{27}H_{40}ClN_4O$ ($[M+H]^+$) 471.2891, found 471.2900.





6',7'-Dichloro-3'-((2,4,4-trimethylpentan-2-yl)amino)-31,5,6,7,7a,8,10,10a-octahydro-1H,1'H-spiro[azepino[3,2,1-hi]indole-9,2'-quinoxalin]-4(2H)-one 14*{29}*. General procedure B afforded the spiroheterocycle **14*{29}*** (78 mg, 0.15 mmol, 46% yield) as a light brown solid. HRMS (ESI) *m/z* calcd for $C_{27}H_{39}Cl_2N_4O$ ($[M+H]^+$) 505.2501, found 505.2503.

ID CMC-34-076-B4 File KF071008L09 Date 10-Jul-2008 Time 23:27:32 Description MDF008658



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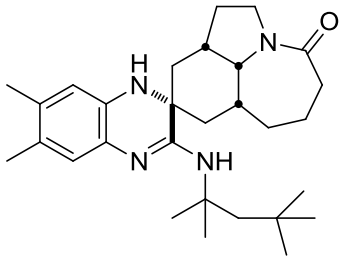
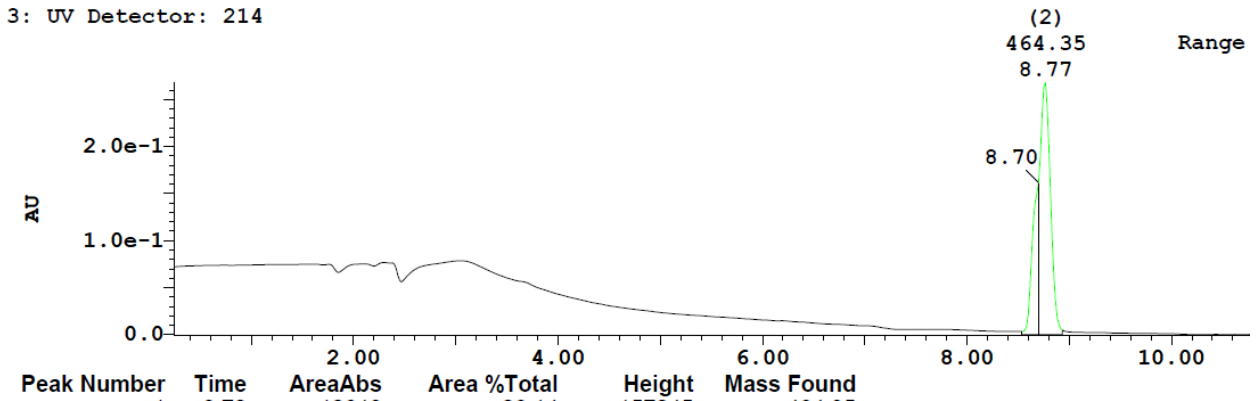
2	9.52	23314	59.86	198150	504.24



6',7'-Dimethyl-3'-((2,4,4-trimethylpentan-2-yl)amino)-31,5,6,7,7a,8,10,10a-octahydro-1H,1'H-spiro[azepino[3,2,1-hi]indole-9,2'-quinoxalin]-4(2H)-one 14*{30}*. General procedure B afforded the spiroheterocycle **14*{30}*** (96 mg, 0.21 mmol, 61% yield) as a tan solid. HRMS (ESI) *m/z* calcd for $C_{29}H_{45}N_4O$ ($[M+H]^+$) 465.3593, found 465.3615.

ID CMC-34-076-B5 File KF071008L10 Date 10-Jul-2008 Time 23:39:51 Description MDF008661



Peak Number	Time	AreaAbs	Area %Total	Height	Mass Found
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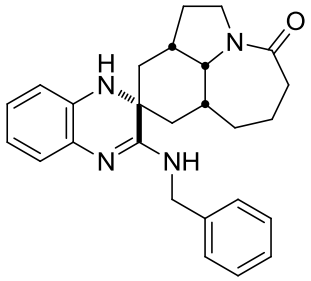
2	8.77	29991	73.86	263671	464.35

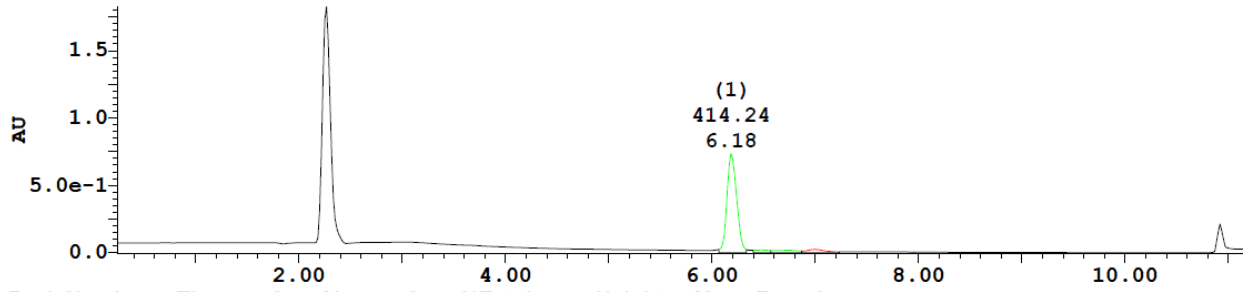


3'-(Benzylamino)-31,5,6,7,7a,8,10,10a-octahydro-1H,1'H-spiro[azepino[3,2,1-hi]indole-9,2'-quinoxalin]-4(2H)-one 14*{31}*. General procedure B afforded the spiroheterocycle **14*{31}*** (56 mg, 0.135 mmol, 40% yield) as a tan solid. HRMS (ESI) *m/z* calcd for $C_{26}H_{31}N_4O$ ($[M+H]^+$) 415.2498, found 415.2512.

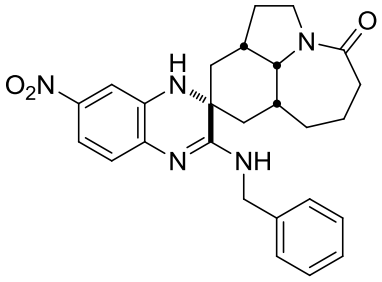
ID CMC-34-076-C1 File KF071008L11 Date 10-Jul-2008 Time 23:52:10 Description MDF008664

3: UV Detector: 214

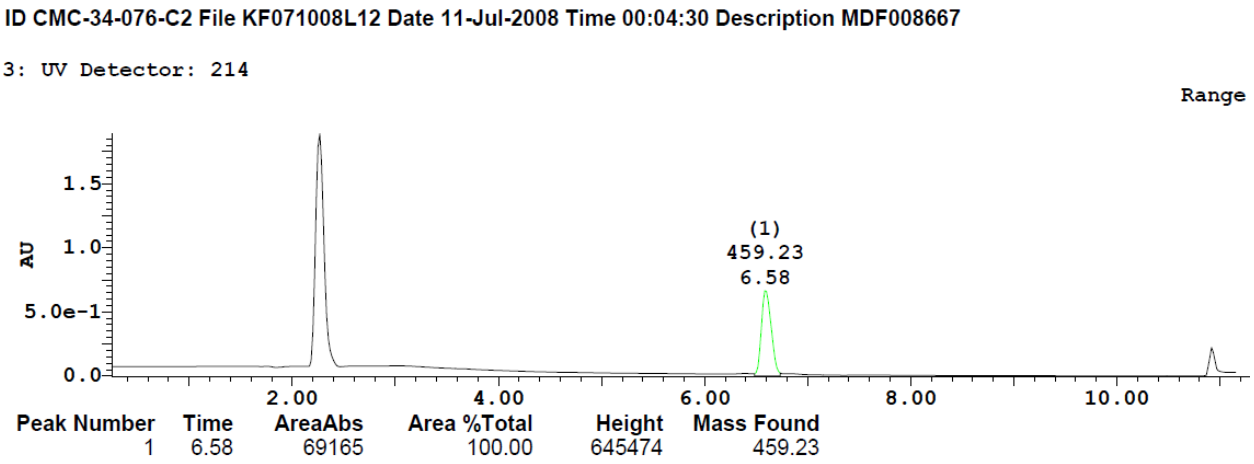
Range

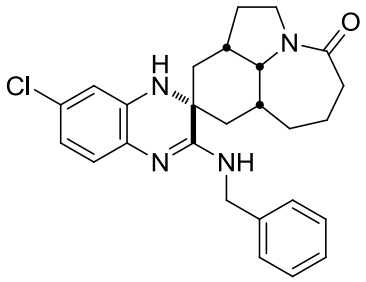


Peak Number	Time	AreaAbs	Area %Total	Height	Mass Found
1	6.18	73915	95.34	711904	414.24
2	6.47	325	0.42	2952	414.24
3	6.73	977	1.26	5414	414.24
4	7.00	2310	2.98	14869	



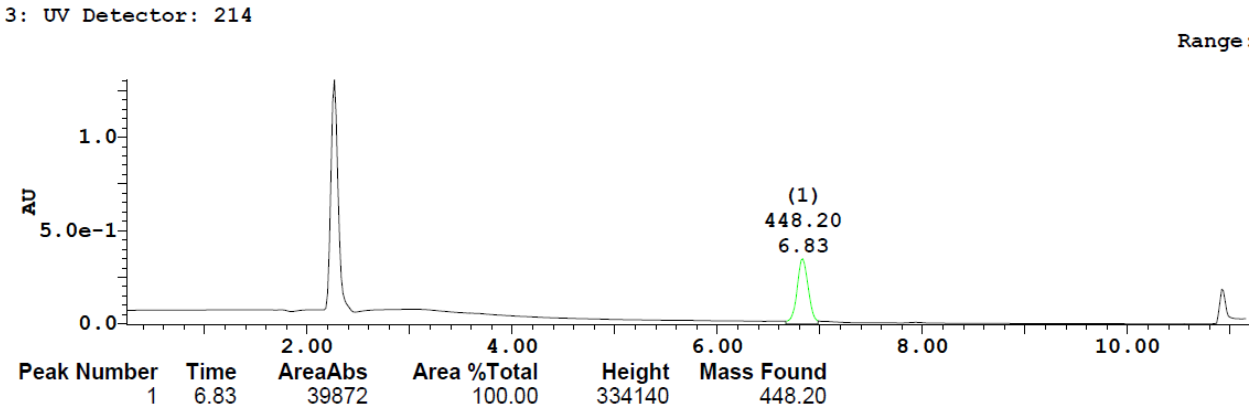
3'-(Benzylamino)-7'-nitro-31,5,6,7,7a,8,10,10a-octahydro-1H,1'H-spiro[azepino[3,2,1-hi]indole-9,2'-quinoxalin]-4(2H)-one 14*{32}*. General procedure B afforded the spiroheterocycle **14*{32}*** (42 mg, 0.092 mmol, 27% yield) as a reddish brown solid. HRMS (ESI) *m/z* calcd for $C_{26}H_{30}N_5O_3$ ($[M+H]^+$) 460.2349, found 460.2378.





3'-(Benzylamino)-7'-chloro-31,5,6,7,7a,8,10,10a-octahydro-1H,1'H-spiro[azepino[3,2,1-hi]indole-9,2'-quinoxalin]-4(2H)-one 14*{33}*. General procedure B afforded the spiroheterocycle **14*{33}*** (84 mg, 0.188 mmol, 55% yield) as a tan solid. HRMS (ESI) *m/z* calcd for $C_{26}H_{30}ClN_4O$ ($[M+H]^+$) 449.2108, found 449.2095.

ID CMC-34-076-C3 File KF071008L13 Date 11-Jul-2008 Time 00:16:49 Description MDF008669



Peak Number	Time	AreaAbs	Area %Total	Height	Mass Found
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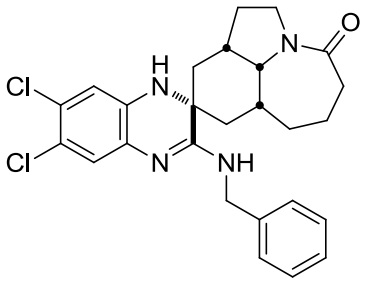
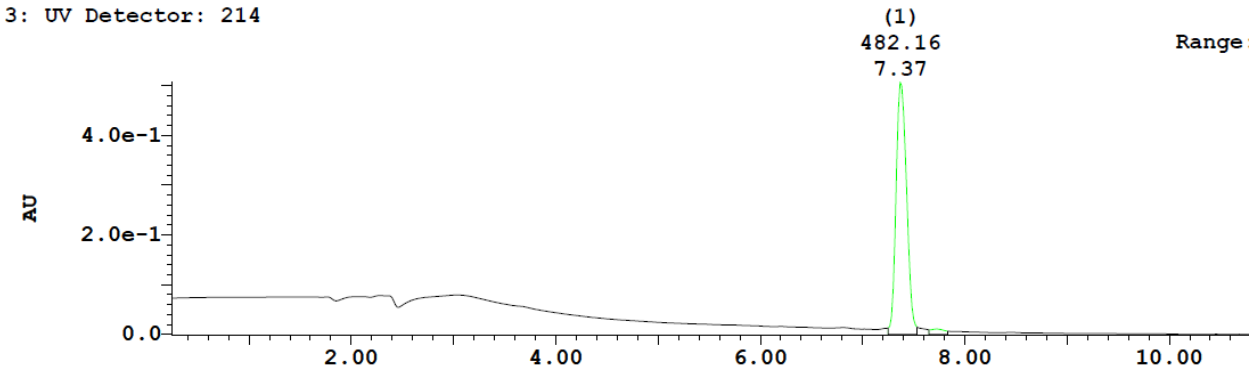


3'-(Benzylamino)-6',7'-dichloro-31,5,6,7,7a,8,10,10a-octahydro-1H,1'H-spiro[azepino[3,2,1-hi]indole-9,2'-quinoxalin]-4(2H)-one 14*{34}*. General procedure B afforded the spiroheterocycle **14*{34}*** (46 mg, 0.096 mmol, 28% yield) as a tan solid. HRMS (ESI) *m/z* calcd for $C_{26}H_{29}Cl_2N_4O$ ($[M+H]^+$) 483.1718, found 483.1729.

ID CMC-34-076-C4 File KF071008L14 Date 11-Jul-2008 Time 00:29:08 Description MDF008671



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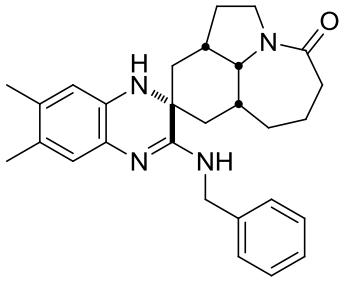
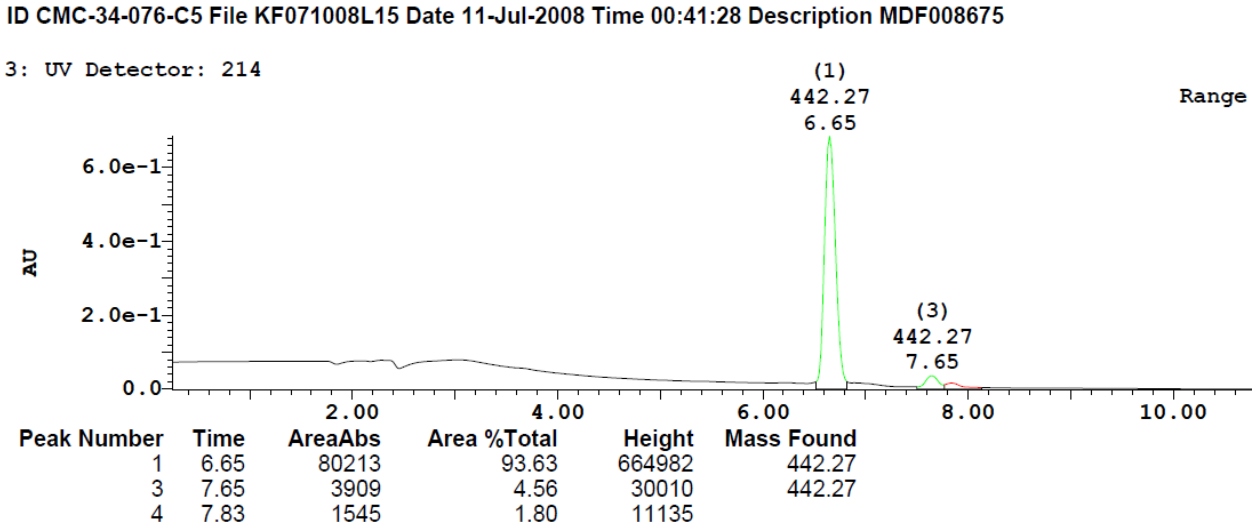


3'-(Benzylamino)-6',7'-dimethyl-31,5,6,7,7a,8,10,10a-octahydro-1H,1'H-spiro[azepino[3,2,1-hi]indole-9,2'-quinoxalin]-4(2H)-one 14*{35}*. General procedure B afforded the spiroheterocycle **14*{35}*** (79 mg, 0.178 mmol, 53% yield) as a tan solid. HRMS (ESI) *m/z* calcd for $C_{28}H_{35}N_4O$ ($[M+H]^+$) 443.2811, found 443.2814.



Peak Number	Time	AreaAbs	Area %Total	Height	Mass Found
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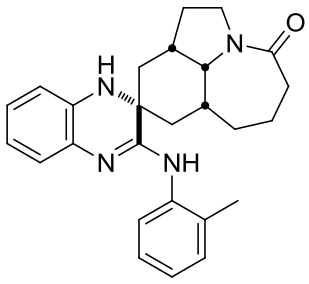
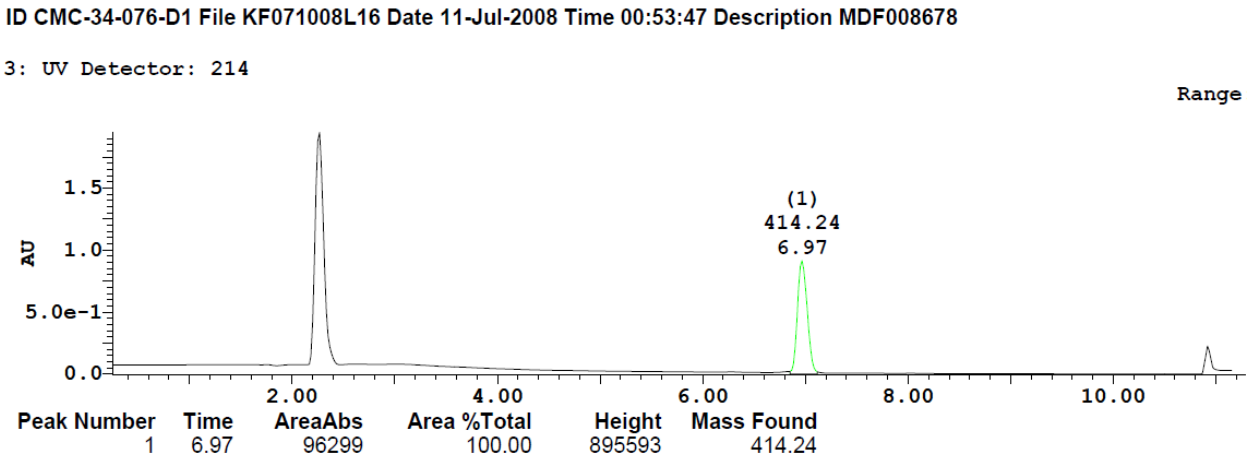
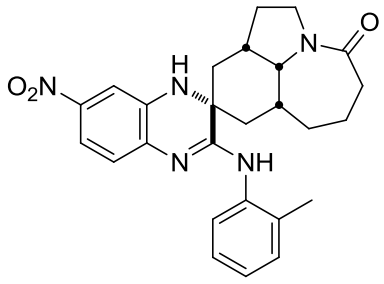
3	7.65	3909	4.56	30010	442.27
4	7.83	1545	1.80	11135	



3'-(o-Tolylamino)-31,5,6,7,7a,8,10,10a-octahydro-1H,1'H-spiro[azepino[3,2,1-hi]indole-9,2'-quinoxalin]-4(2H)-one 14*{36}*. General procedure B afforded the spiroheterocycle **14*{36}*** (34

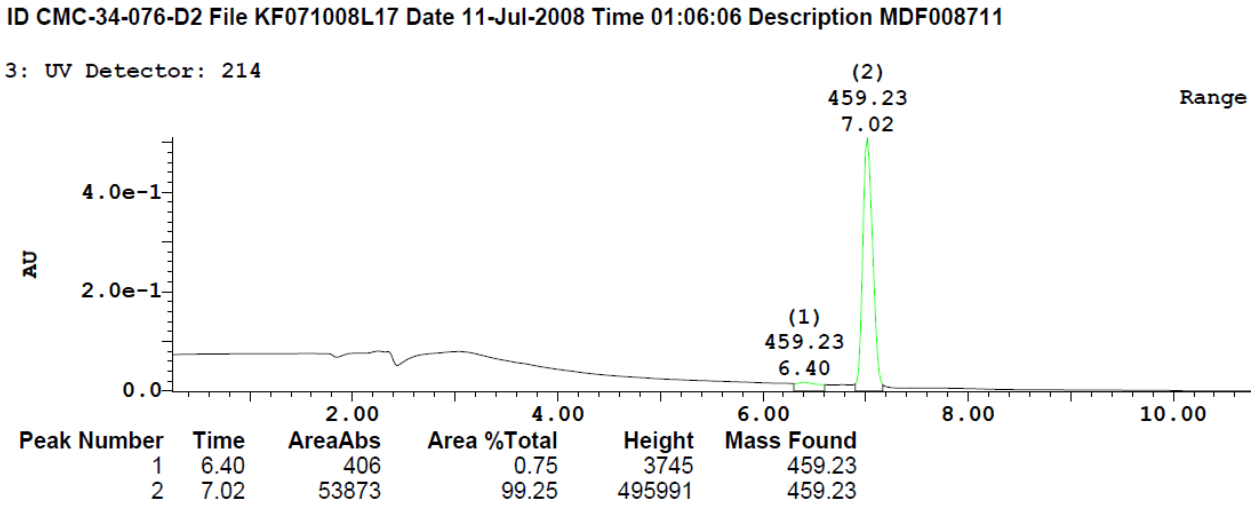
mg, 0.082 mmol, 24% yield) as a tan solid. Mp > 260 ºC; ^{1}H NMR ($CDCl_3$) δ 1.13 (t, *J* = 11.6 Hz, 1 H), 1.43 (t, *J* = 13.6 Hz, 1 H), 1.54-1.63 (complex, 3 H), 1/71-1.88 (complex, 3 H), 2.15 (s, 3 H), 2.31 (m, 1 H), 2.40 (ddd, *J* = 2.0, 6.0, 11.2 Hz, 1 H), 2.66 (m, 1 H), 2.73 (m, 1 H), 3.26 (m, 1 H), 3.58 (m, 2 H), 3.85 (m, 2 H), 6.46 (d, *J* = 7.2 Hz, 1 H), 6.49 (m, 1 H), 6.71 (m, 2 H), 6.82 (m, 2 H), 7.02 (dt, *J* = 1.2, 7.2 Hz, 1 H), 7.22 (m, 2 H); ^{13}C NMR δ d 18.2, 33.5, 40.1, 60.9, 113.8, 114.9, 119.6, 120.7, 122.4, 123.4, 127.1, 131.2; u 18.3, 28.9, 34.2, 35.6, 36.9, 39.4, 47.3, 55.7, 126.6, 129.5, 132.4, 146.4, 151.0, 175.4; IR 3397, 3289, 2928, 1648, 1617, 1609, 1594, 1506 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{26}H_{31}N_4O$ ($[M+H]^+$) 415.2498, found 415.2513.

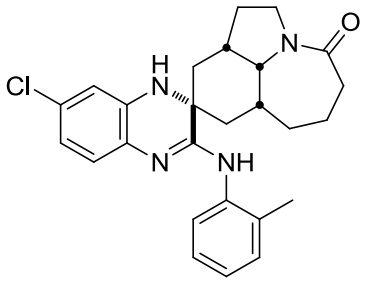




7'-Nitro-3'-(o-tolylamino)-31,5,6,7,7a,8,10,10a-octahydro-1H,1'H-spiro[azepino[3,2,1-hi]indole-9,2'-quinoxalin]-4(2H)-one 14*{37}*. General procedure B afforded the

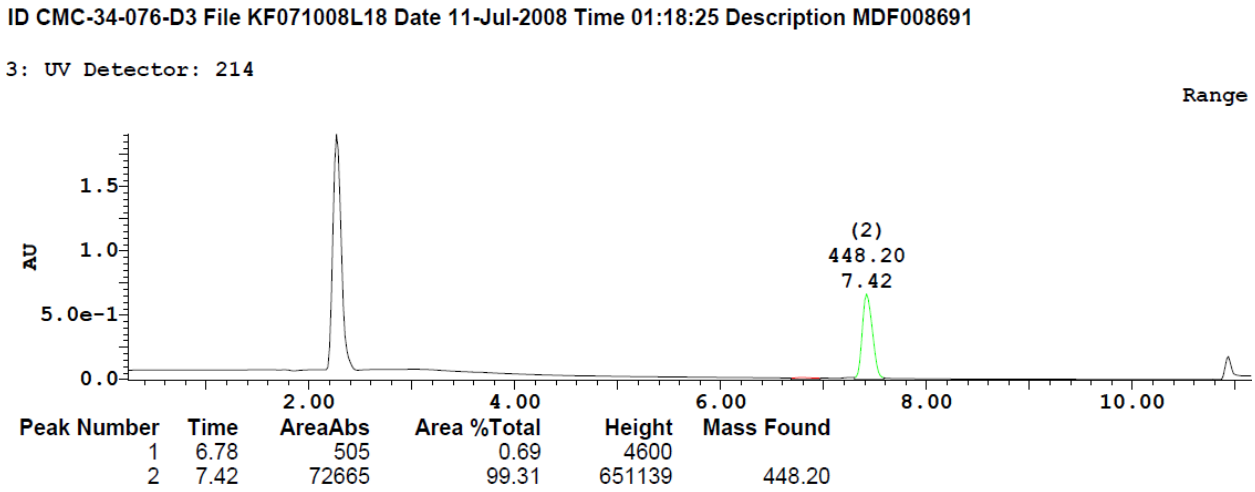
spiroheterocycle **14*{37}*** (9 mg, 0.020 mmol, 6% yield) as a reddish brown solid. HRMS (ESI) *m/z* calcd for $C_{26}H_{30}N_5O_3$ ($[M+H]^+$) 460.2349, found 460.2350.

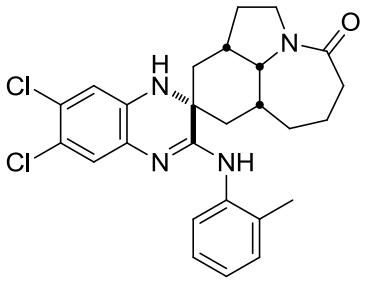




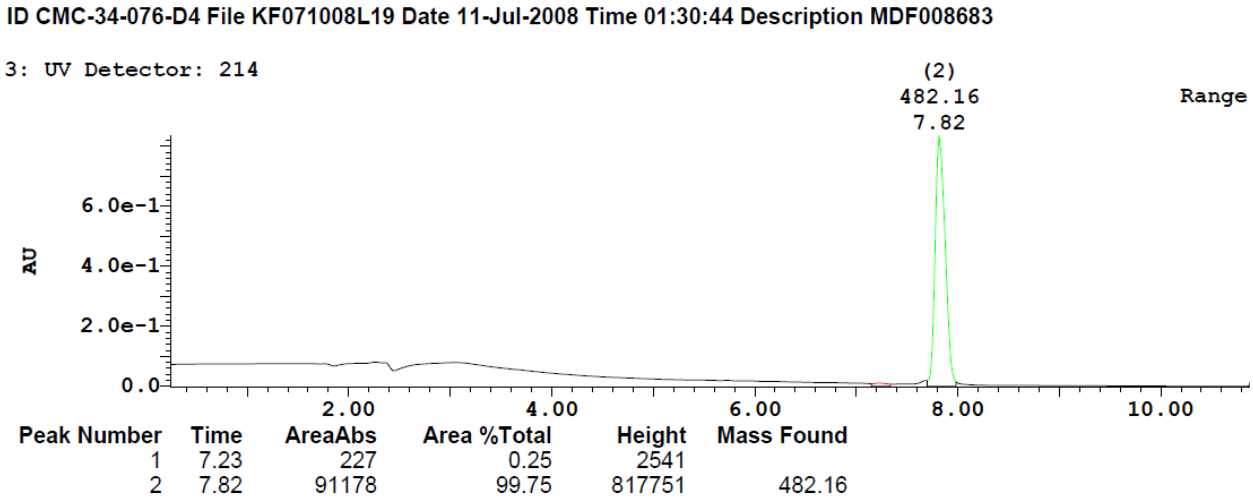
7'-Chloro-3'-(o-tolylamino)-31,5,6,7,7a,8,10,10a-octahydro-1H,1'H-spiro[azepino[3,2,1-hi]indole-9,2'-quinoxalin]-4(2H)-one 14*{38}*. General procedure B afforded the spiroheterocycle **14*{38}*** (37 mg, 0.082 mmol, 24% yield) as a yellow solid. Mp > 260 ºC; ^{1}H NMR ($CDCl_3$) δ 1.13 (t, *J* = 12.8 Hz, 1 H), 1.44 (m, 1 H), 1.53-1.71 (complex, 5 H), 1.75-1.88 (complex, 3 H), 2.14 (s, 3 H), 2.27-2.41 (m, 2 H), 2.64-2.73 (m, 2 H), 3.24 (m, 1 H), 3.57 (dt, *J* = 6.4, 16.0 Hz, 1 H), 3.82 (br s, 1 H), 3.85 (m, 1 H), 3.26 (m, 1 H), 6.49 (m, 1 H), 6.50 (d, *J* = 2.0 Hz, 1 H), 6.61 (d, *J* = 8.0 Hz, 1 H), 6.65 (m, 1 H), 6.78 (m, 1 H), 7.03 (t, *J* = 7.2 Hz, 1 H), 7.22 (m, 1 H); ^{13}C NMR δ d 33.5, 40.1, 41.1, 60.9, 113.8, 115.7, 120.5, 122.0, 123.8, 127.2, 131.3; u 18.4, 28.9, 34.1, 35.6, 36.8, 39.4, 47.4, 55.8, 124.3, 129.3, 131.1, 141.4, 146.1, 154.2, 175.4; IR

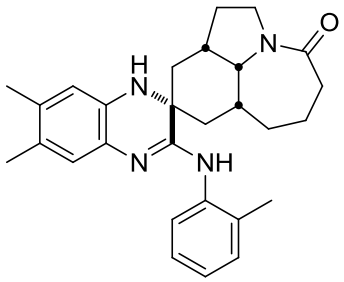
3300, 3268, 2940, 1656, 1596, 1505 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{26}H_{30}ClN_4O$ ($[M+H]^+$) 449.2108, found 449.2116.





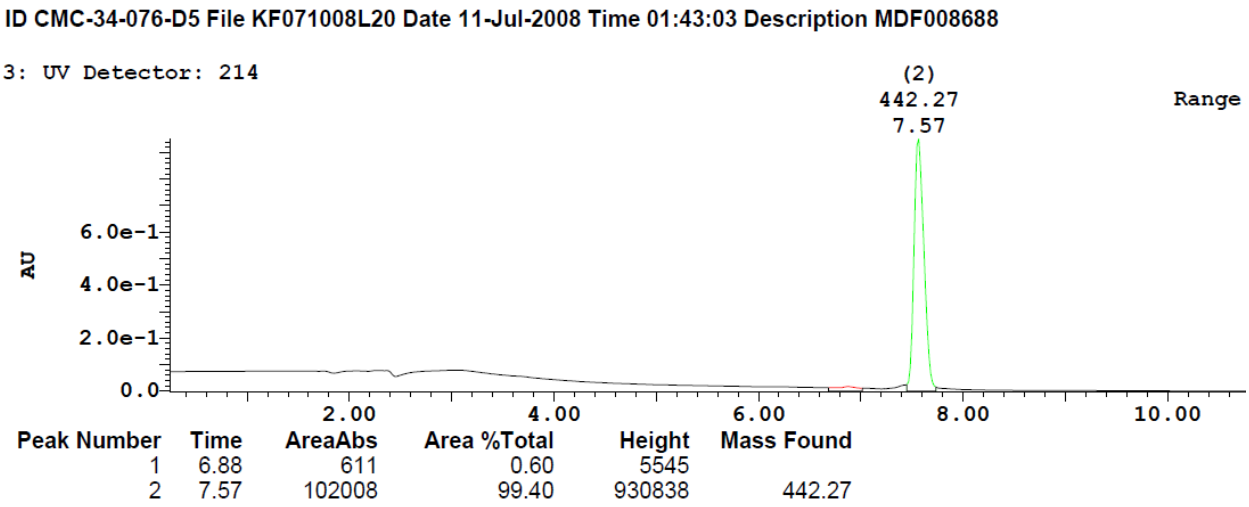
6',7'-Dichloro-3'-(o-tolylamino)-31,5,6,7,7a,8,10,10a-octahydro-1H,1'H-spiro[azepino[3,2,1-hi]indole-9,2'-quinoxalin]-4(2H)-one 14*{39}*. General procedure B afforded the spiroheterocycle **14*{39}*** (23 mg, 0.048 mmol, 14% yield) as a tan solid. HRMS (ESI) *m/z* calcd for $C_{26}H_{29}Cl_2N_4O$ ($[M+H]^+$) 483.1718, found 483.1702.

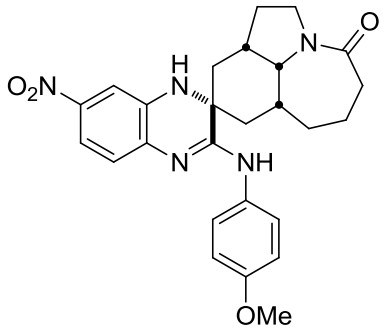




6',7'-Dimethyl-3'-(o-tolylamino)-31,5,6,7,7a,8,10,10a-octahydro-1H,1'H-spiro[azepino[3,2,1-hi]indole-9,2'-quinoxalin]-4(2H)-one 14*{40}*. General procedure B afforded the spiroheterocycle **14*{40}*** (52 mg, 0.118 mmol, 35% yield) as a tan solid. Mp = 243-248 ºC (dec); ^{1}H NMR ($CDCl_3$) δ 1.10 (t, *J* = 12.8 Hz, 1 H), 1.39 (t, *J* = 12.8 Hz, 1 H), 1.51-1.62 (m, 3 H), 1.72-1.82 (complex, 4 H), 2.09 (s, 3 H), 2.14 (s, 3 H), 2.15 (s, 3 H), 2.30 (m, 1 H), 2.38 (ddd, *J* = 2.4, 7.6, 14.0 Hz, 1 H), 2.63 (m, 1 H), 2.68 (m, 1 H), 3.25 (m, 1 H), 3.57 (dt, *J* = 6.4, 12.0 Hz, 1 H), 3.82 (m, 1 H), 3.85 (m, 1 H), 6.29 (s, 1 H), 6.35 (s, 1 H), 6.49 (s, 1 H), 6.80 (dd, *J* = 1.2, 7.6 Hz, 1 H), 7.00 (dt, *J* = 1.2, 7.6 Hz, 1 H), 7.19 (dt, *J* = 1.2, 7.6 Hz, 1 H), 7.23 (d, *J* = 7.2 Hz); ^{13}C NMR δ d 18.2, 18.9, 19.2, 33.5, 40.1, 61.1, 115.1, 116.5, 120.8, 123.4, 127.1, 131.2; u 18.4, 28.9, 34.1, 35.7, 36.9, 39.4, 47.4, 55.8, 124.6, 127.6, 129.5, 130.2, 130.4, 146.7, 151.3,

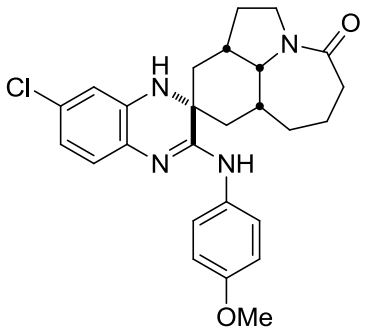
175.4; IR 3311, 2928, 2861, 1644, 1615, 1592, 1516 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{28}H_{35}N_4O$ ($[M+H]^+$) 443.2811, found 443.2798.





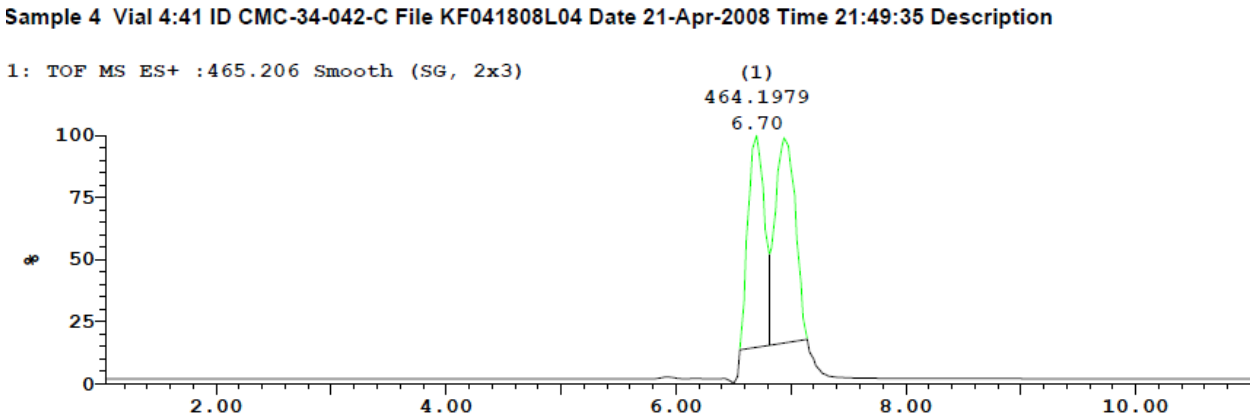
((4-Methoxyphenyl)amino)-7'-nitro-31,5,6,7,7a,8,10,10a-octahydro-1H,1'H-spiro[azepino[3,2,1-hi]indole-9,2'-quinoxalin]-4(2H)-one 14*{41}*. A reaction vial was charged with a magnetic stir bar, ketoamide **8b** (50 mg, 0.24 mmol), diamine fragment **13b** (44 mg, 0.29 mmol, 1.2 equiv.) and *p*-toluenesulfonic acid (5 mg, 0.024 mmol, 0.1 equiv.). A solution of isonitrile **12e** (38 mg, 0.29 mmol, 1.2 equiv.) in EtOH (2.0 mL) was added via syringe through the septum cap and the reaction stirred for 14 h at rt. Water (7 mL) was added to precipitate the products. The reaction mixture was filtered and the collected precipitate was washed with NaOH (0.5 N, 2 mL) and water (3 mL). The crude product was purified by chromatography on silica gel

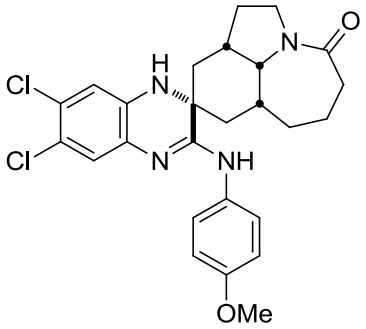
to afford the spiroheterocycle **14*{41}*** (79 mg, 0.166 mmol, 69% yield) as a red-brown solid. Mp > 260 ºC; ^{1}H NMR ($CDCl_3$) δ 1.31 (m, 1 H), 1.47-1.62 (complex, 5 H), 1.75-1.88 (complex, 3 H), 2.35 (m, 2 H), 2.62 (m, 2 H), 3.23 (m, 1 H), 3.56 (m, 1 H), 3.83 (s, 3 H), 3.84 (m, 2 H), 5.20 (s, 1 H), 6.53 (d, *J* = 8.8 Hz, 1 H), 6.84 (m, 2 H), 6.94 (m, 2 H), 7.04 (br s, 1 H), 7.62 (m, 2 H); ^{13}C NMR δ d 33.3, 39.8, 55.5, 60.8, 109.8, 112.8, 115.2 (× 2), 115.6, 122.0 (× 2); u 18.3, 28.8, 34.0, 35.7, 36.0, 47.3, 55.4, 133.1, 140.1, 142.5, 150.8, 156.2, 175.2; IR 3335, 2929, 2855, 1612, 1524, 1502 cm^{-1}; HRMS calcd for $C_{26}H_{30}N_5O_4$ [M + H$^+$] 476.2298, found 476.2292.



((4-Methoxyphenyl)amino)-31,5,6,7,7a,8,10,10a-octahydro-1H,1'H-spiro[azepino[3,2,1-hi]indole-9,2'-quinoxalin]-4(2H)-one 14*{42}*. A reaction vial was charged with a magnetic stir bar, ketoamide **8b** (50 mg, 0.24 mmol), diamine fragment **13c** (41 mg, 0.29 mmol, 1.2 equiv.) and *p*-toluenesulfonic acid (5 mg, 0.024 mmol, 0.1 equiv.). A solution of isonitrile **12e** (38 mg, 0.29 mmol, 1.2 equiv.) in EtOH (2.0 mL) was added via syringe through the septum cap and the reaction stirred for 14 h at rt. Water (7 mL) was added to precipitate the products. The reaction mixture was filtered and the collected precipitate was washed with NaOH (0.5 N, 2 mL) and water (3 mL). The crude product was purified by chromatography on silica gel to afford the spiroheterocycle **14*{42}*** (81 mg, 0.174 mmol, 73% yield) as a pink solid. Mp > 260 ºC; ^{1}H NMR ($CDCl_3$) δ 1.12 (t, *J* = 12.8 Hz, 1 H), 1.41 (t, *J* = 13.2 Hz, 1 H), 1.58 (m, 1 H), 1.64 (m, 2 H), 1.75-1.86 (complex, 3 H), 2.33 (m, 2 H), 2.62 (m, 2 H), 3.22 (m, 1 H), 3.54 (m, 1 H), 3.82 (s, 3

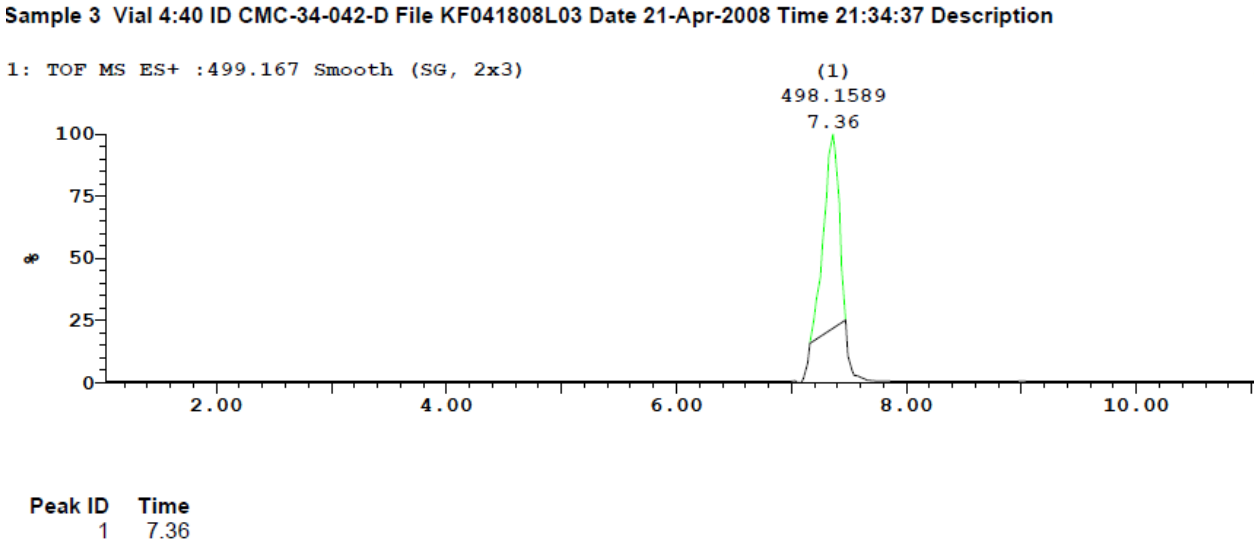
H), 3.87 (m, 3 H), 6.51 (d, J = 2.0 Hz, 1 H), 6.63 (m, 2 H), 6.76 (dd, J = 2.0, 8.4 Hz, 1 H), 6.81 (d, J = 2.0 Hz, 1 H), 6.83 (t, J = 2.4 Hz, 2 H), 6.93 (m, 2 H); ^{13}C NMR δ d 33.4, 40.0, 55.6, 61.0, 113.7, 115.2 (× 2), 115.7, 121.9, 122.2 (× 2); u 18.4, 28.9, 34.1, 35.7, 36.5, 39.4, 47.4, 55.6, 124.2, 127.7, 131.2, 140.7, 151.5, 156.0, 175.4; IR 3287, 2928, 2873, 1604, 1571, 1515 cm^{-1}; HRMS calcd for $C_{26}H_{30}ClN_4O_2$ [M + H$^+$] 465.2057, found 465.2050.

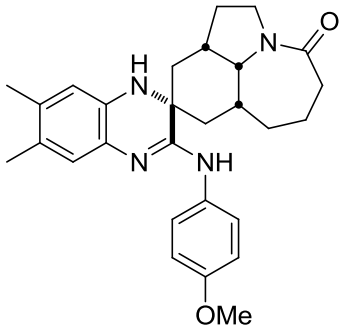




6',7'-Dichloro-3'-((4-methoxyphenyl)amino)-31,5,6,7,7a,8,10,10a-octahydro-1H,1'H-spiro[azepino[3,2,1-hi]indole-9,2'-quinoxalin]-4(2H)-one 14*{43}*. A reaction vial was charged with a magnetic stir bar, ketoamide **8b** (50 mg, 0.24 mmol), diamine fragment **13c** (41 mg, 0.29 mmol, 1.2 equiv.) and *p*-toluenesulfonic acid (5 mg, 0.024 mmol, 0.1 equiv.). A solution of isonitrile **12e** (38 mg, 0.29 mmol, 1.2 equiv.) in EtOH (2.0 mL) was added via syringe through the septum cap and the reaction stirred for 14 h at rt. Water (7 mL) was added to precipitate the

products. The reaction mixture was filtered and the collected precipitate was washed with NaOH (0.5 N, 2 mL) and water (3 mL). The crude product was purified by chromatography on silica gel to afford the spiroheterocycle **14*{43}*** (27 mg, 0.055 mmol, 23% yield) as a light brown solid. Mp > 260 ºC; ^{1}H NMR ($CDCl_3$) δ 1.15 (t, *J* = 13.2 Hz, 1 H), 1.40-1.68 (complex, 4 H), 1.75-1.87 (complex, 4 H), 2.31 (m, 1 H), 2.62 (m, 2 H), 3.22 (m, 1 H), 3.52 (m, 1 H), 3.82 (s, 3 H), 3.84 (m, 2 H), 6.59 (s, 1 H), 6.67 (br s, 1 H), 6.78 (m, 1 H), 6.79 (m, 1 H), 6.82 (m, 1 H), 6.91 (t, *J* = 2.8 Hz, 1 H), 6.94 (m, 1 H); ^{13}C NMR δ d 33.3, 39.8, 55.5, 60.8, 114.7, 115.2 (× 2), 115.7, 122.0 (× 2); u 18.3, 28.8, 34.1, 35.7, 36.2, 39.3, 47.3, 55.6, 121.7, 124.7, 126.4, 132.5, 140.5, 151.1, 156.0, 175.3; IR 3289, 2929, 2877, 1606, 1574, 1515 cm^{-1}; HRMS calcd for $C_{26}H_{29}Cl_2N_4O_2$ [M + H^+] 499.1668, found 499.1664.

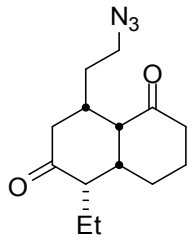




(X-ray)

3'-((4-Methoxyphenyl)amino)-6',7'-dimethyl-31,5,6,7,7a,8,10,10a-octahydro-1H,1'H-spiro[azepino[3,2,1-hi]indole-9,2'-quinoxalin]-4(2H)-one 14*{44}*. A reaction vial was charged with a magnetic stir bar, ketoamide **8b** (50 mg, 0.24 mmol), diamine fragment **13e** (39 mg, 0.29 mmol, 1.2 equiv.) and *p*-toluenesulfonic acid (5 mg, 0.024 mmol, 0.1 equiv.). A solution of isonitrile **12e** (38 mg, 0.29 mmol, 1.2 equiv.) in EtOH (2.0 mL) was added via syringe through the septum cap and the reaction stirred for 14 h at rt. Water (7 mL) was added to precipitate the products. The reaction mixture was filtered and the collected precipitate was washed with NaOH (0.5 N, 2 mL) and water (3 mL). The crude product was purified by chromatography on silica gel to afford the spiroheterocycle **14*{44}*** (78 mg, 0.170 mmol, 71% yield) as a light brown solid. TLC R_f = 0.54 (50% acetone in CH_2Cl_2); mp > 260 ºC; ^{1}H NMR ($CDCl_3$) δ 1.08 (t, *J* = 11.6 Hz, 1 H), 1.36 (m, 1 H), 1.55 (m, 2 H), 1.70-1.82 (m, 3 H), 2.09 (s, 3 H), 2.14 (s, 3 H), 2.32 (m, 2 H), 2.62 (m, 2 H), 3.23(m, 1 H), 3.50 (m, 1 H), 3.56 (m, 1 H), 3.81 (s, 3 H), 3.83 (m, 1 H), 5.30 (s, 1 H), 6.29 (s, 1 H), 6.49 (m, 2 H), 6.82 (d, *J* = 8.8 Hz, 1 H), 6.92 (d, *J* = 8.8 Hz, 2 H); ^{13}C NMR δ d 18.9, 19.2, 33.4, 39.9, 55.5, 61.0, 115.0, 115.1 (× 2), 116.4, 122.3 (× 2); u 18.3, 28.8, 34.0, 35.7, 36.5, 39.3, 47.3, 55.6, 124.5, 127.5, 130.0, 130.2, 141.3, 152.3, 155.7, 175.3; IR 3294, 2927, 2857, 1640, 1611, 1500 cm^{-1}; HRMS calcd for $C_{28}H_{35}N_4O_2$ [M + H$^+$] 459.2760, found 459.2728.

CMC-6-235_001000fid



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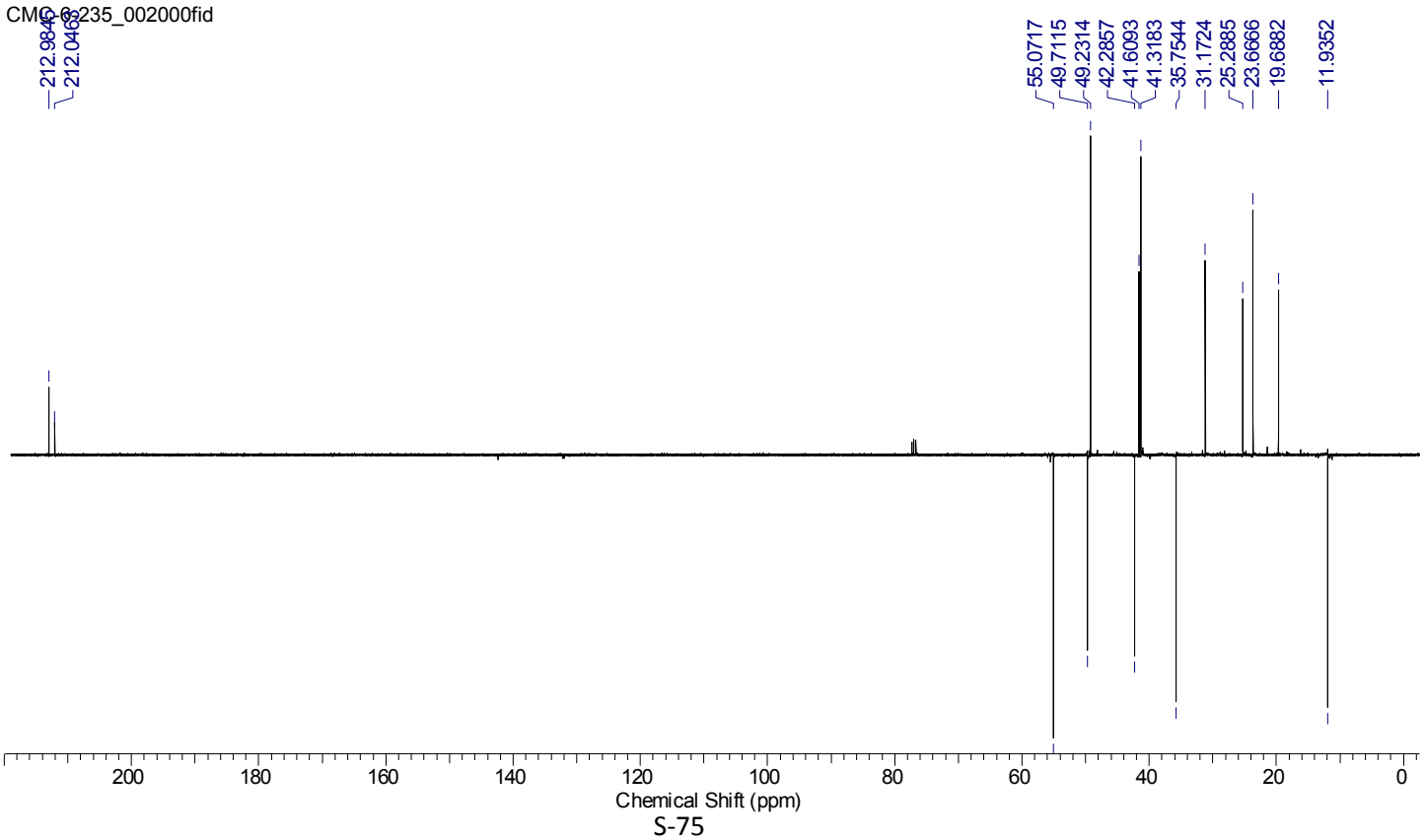

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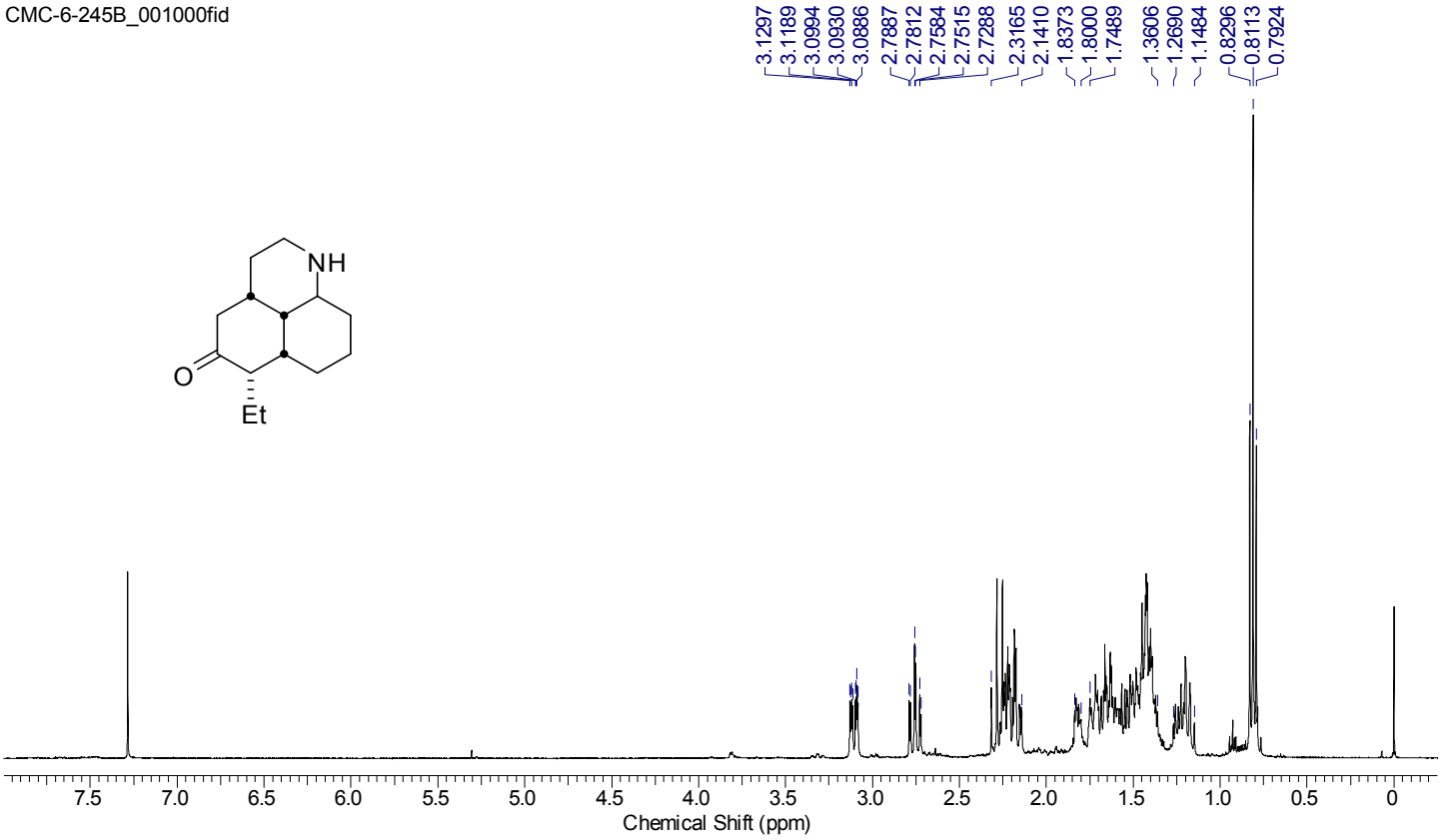

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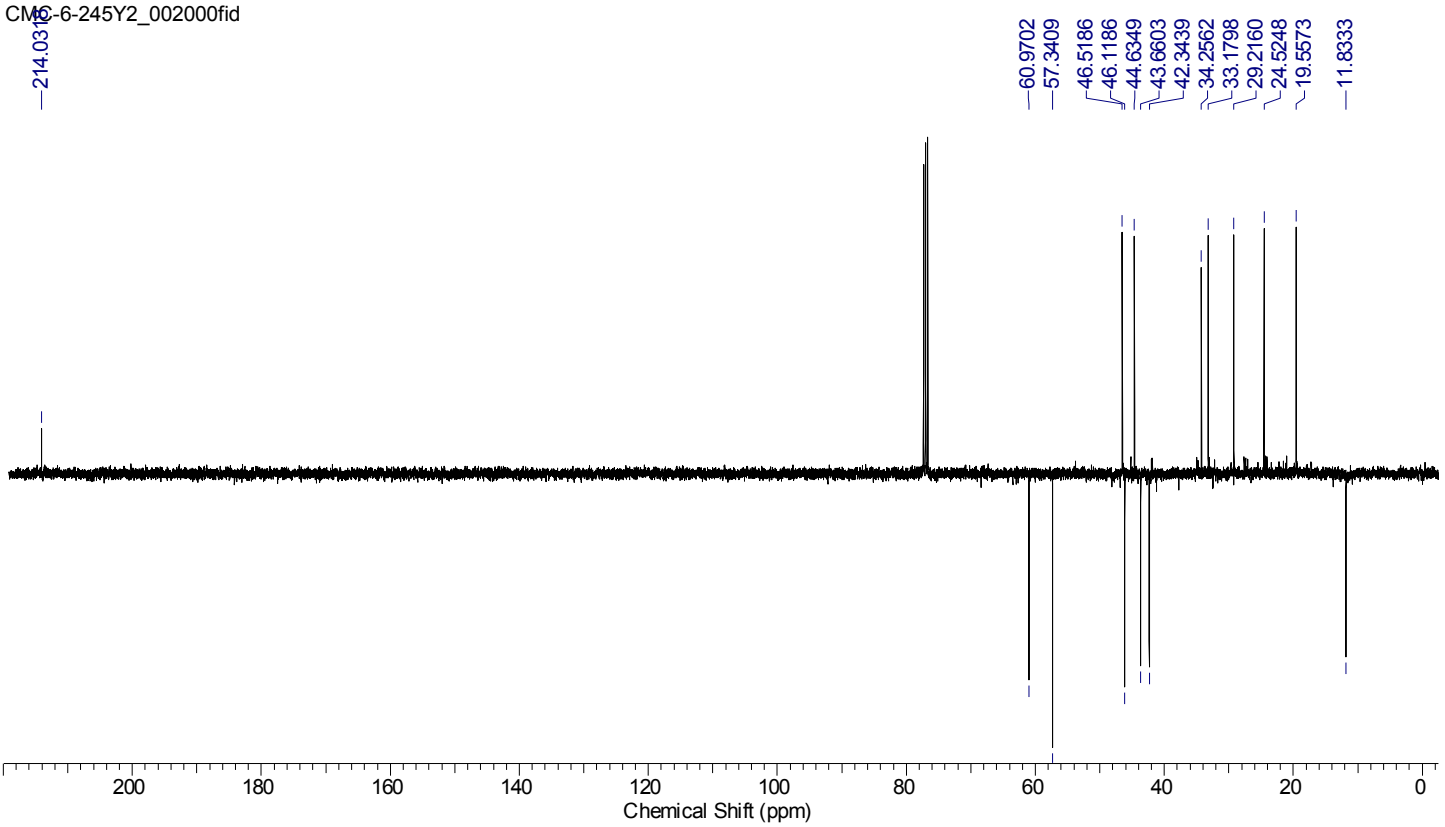

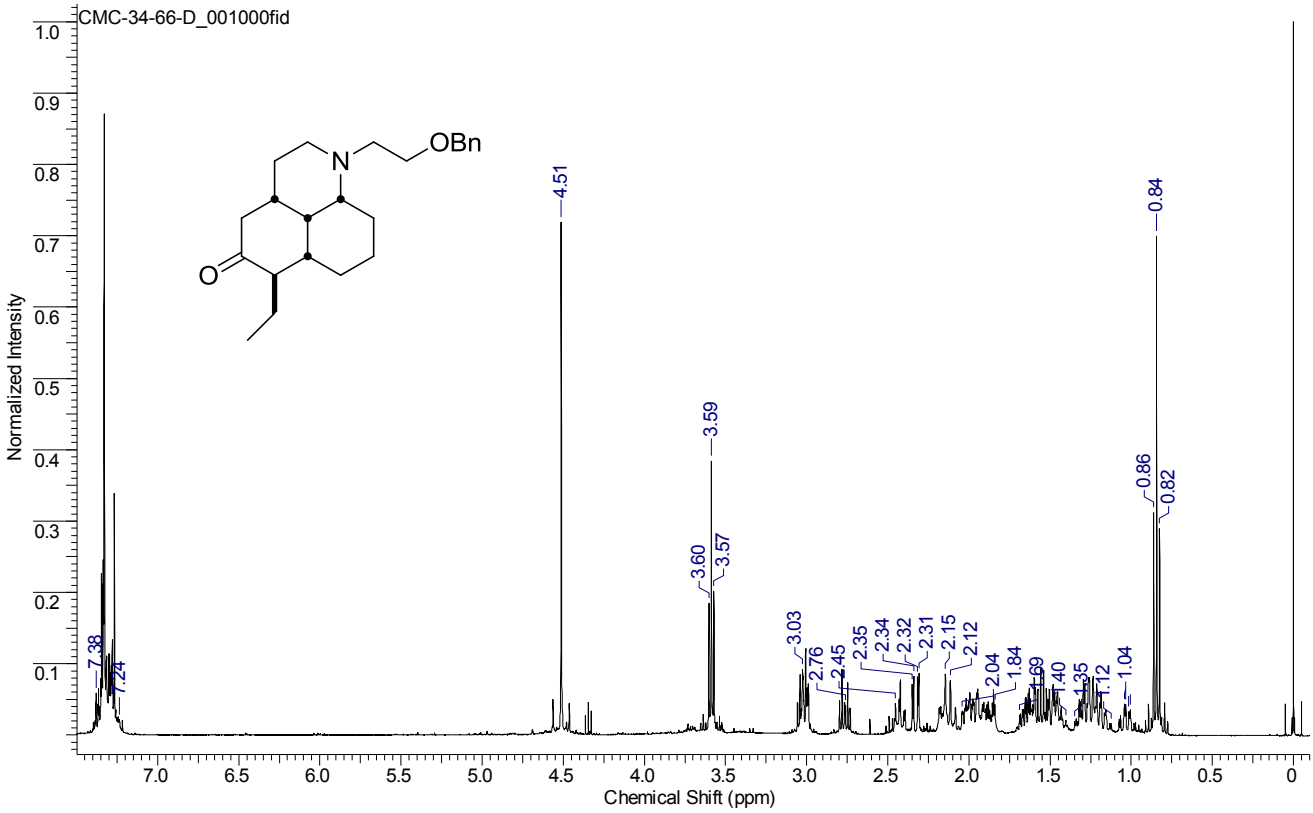
CMC-34-66-D_001000fid
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N
O
Normalized Intensity
Chemical Shift (ppm)
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7.24
4.51
3.59
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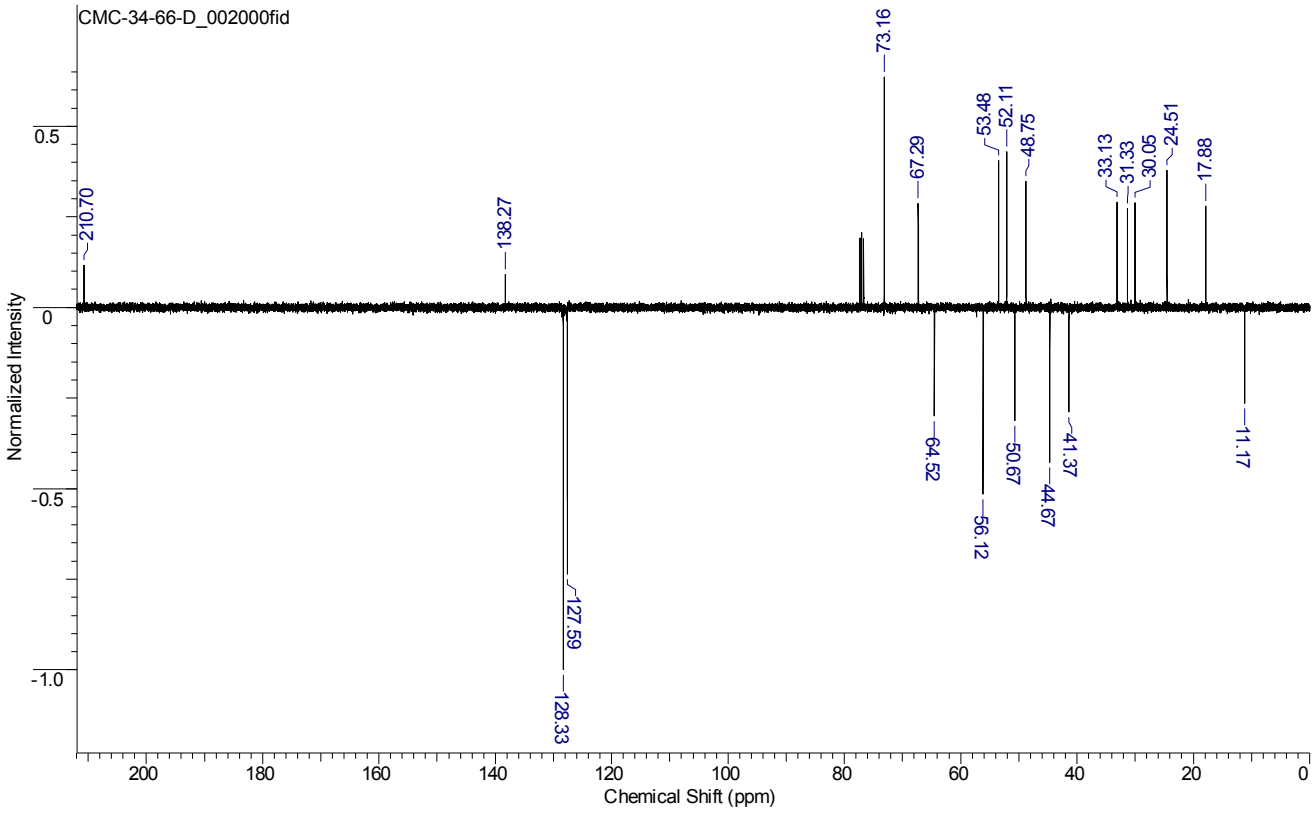
3.03
2.76
2.45
2.35
2.34
2.32
2.31
2.15
2.12
2.04
1.84
1.69
1.40
1.35
1.12
1.04
0.86
0.84
0.82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Normalized Intensity
Chemical Shift (ppm)
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73.16
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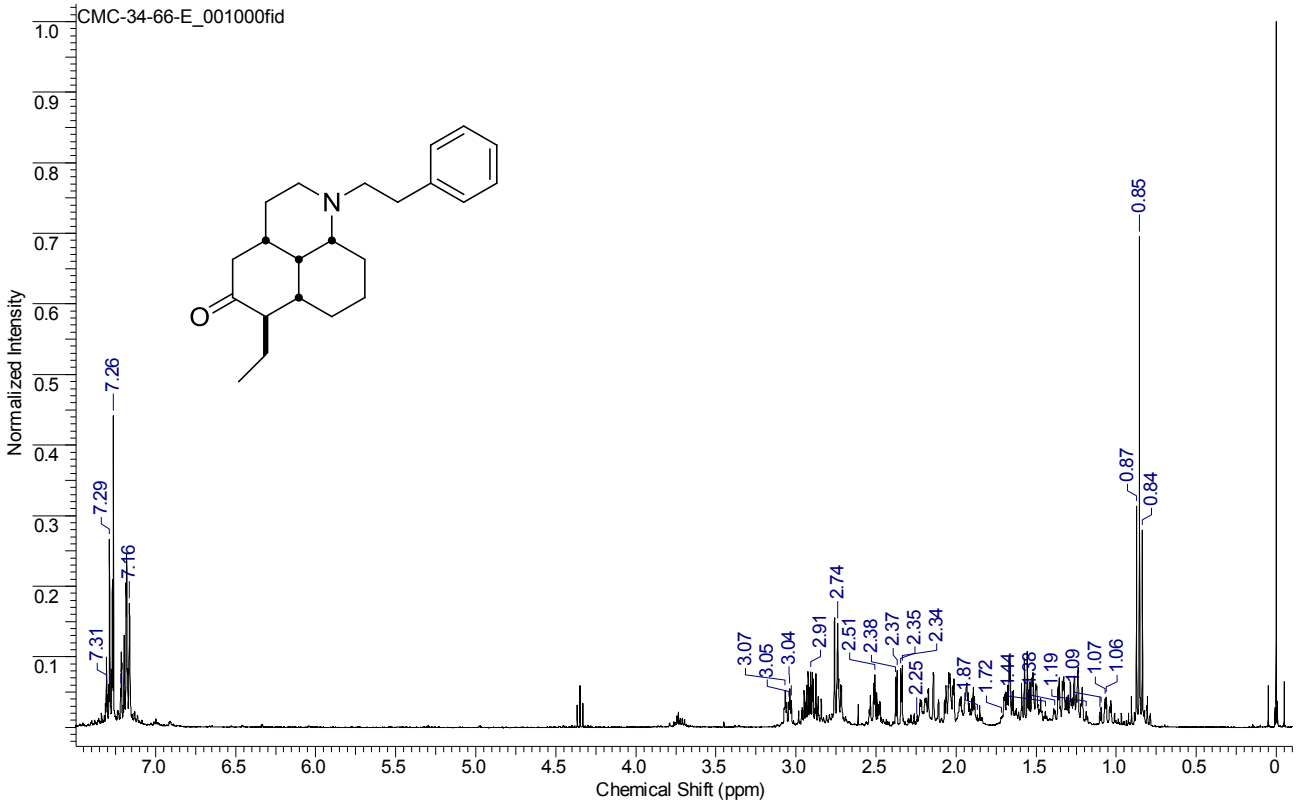
64.52
56.12
53.48
52.11
50.67
48.75
44.67
41.37
33.13
31.33
30.05
24.51
17.88
11.17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Normalized Intensity
Chemical Shift (ppm)
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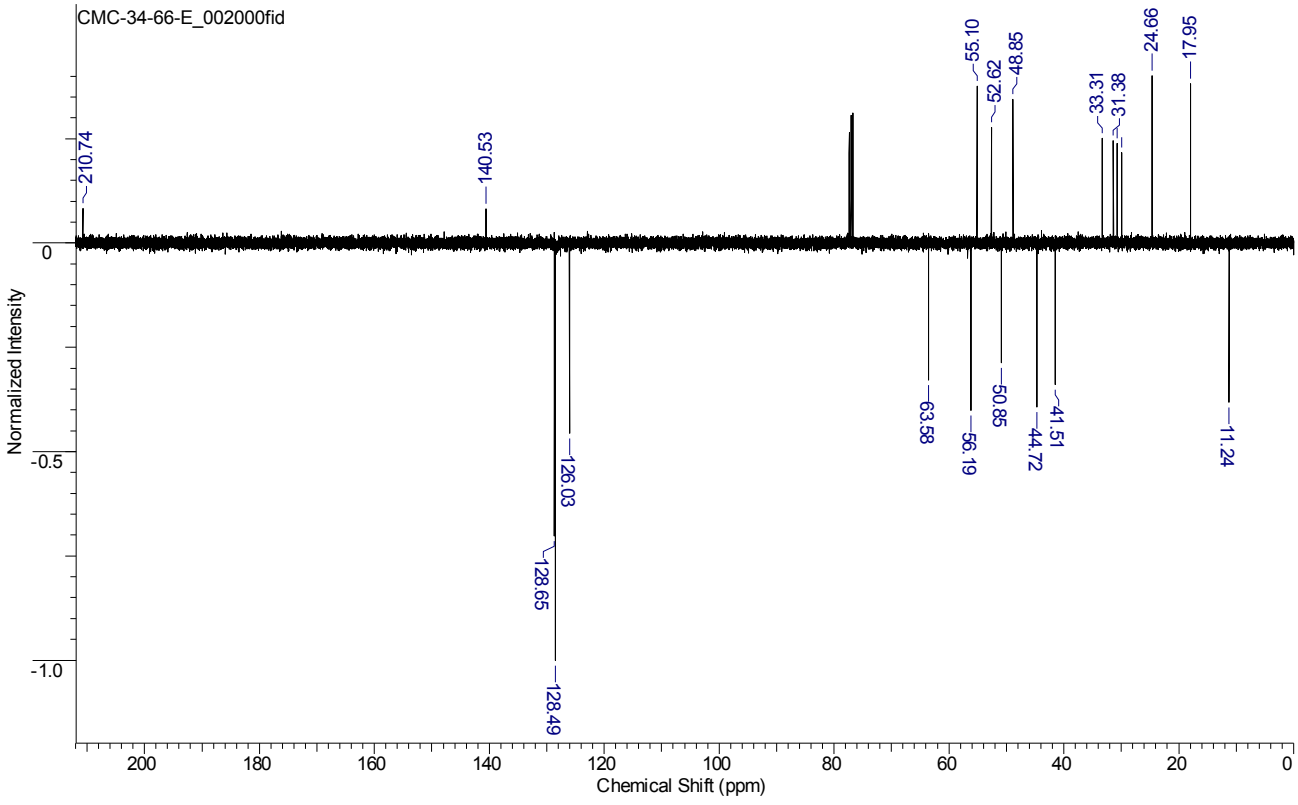
0.87
0.84
2.74
2.91
2.51
2.38
2.37
2.35
2.34
2.25
3.07
3.05
3.04
1.87
1.72
1.07
1.06
O
N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Normalized Intensity
Chemical Shift (ppm)
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128.65
126.03
63.58
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44.72
41.51
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52.62
48.85
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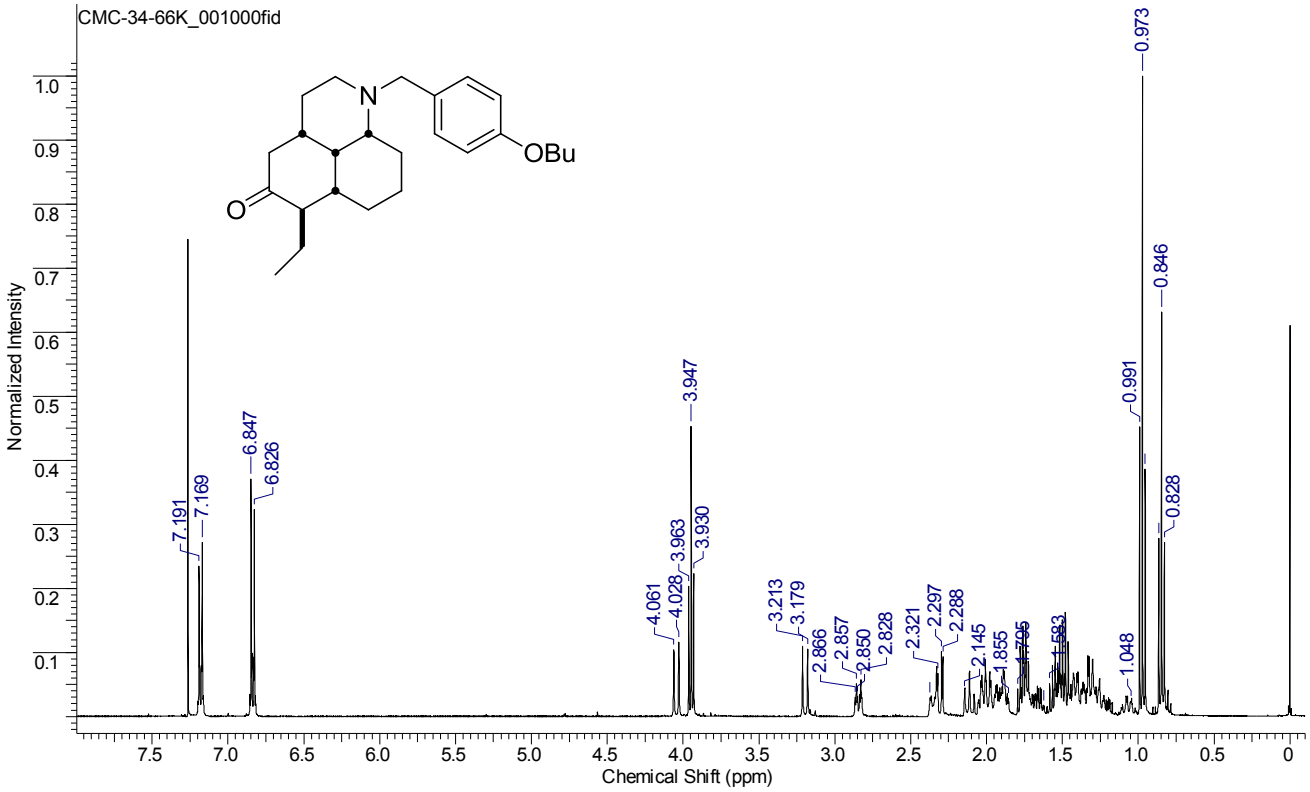
31.38
24.66
17.95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OBu
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6.826
7.191
7.169
3.963
3.930
4.061
4.028
3.213
3.179
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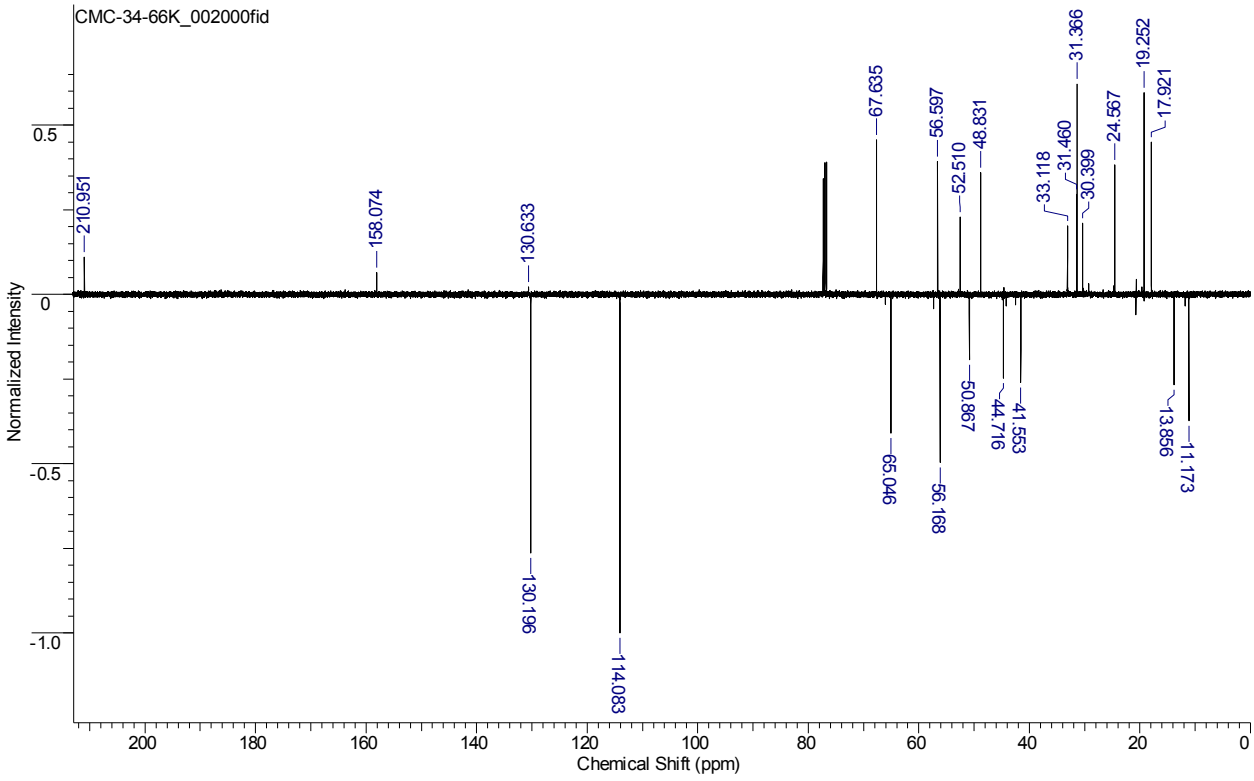
1.583
1.048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Chemical Shift (ppm)
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33.118
31.460
31.366
30.399
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130.196
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65.046
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50.867
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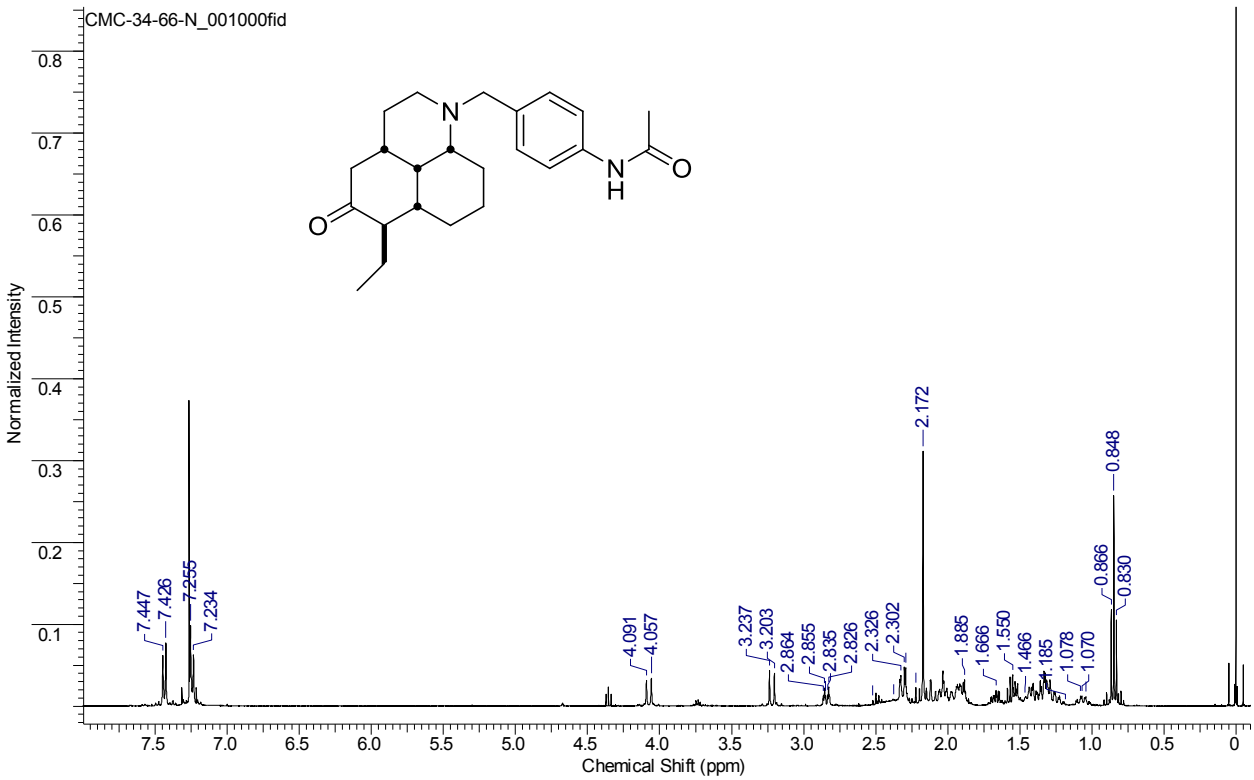
41.553
13.856
11.173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Normalized Intensity
Chemical Shift (ppm)
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4.057
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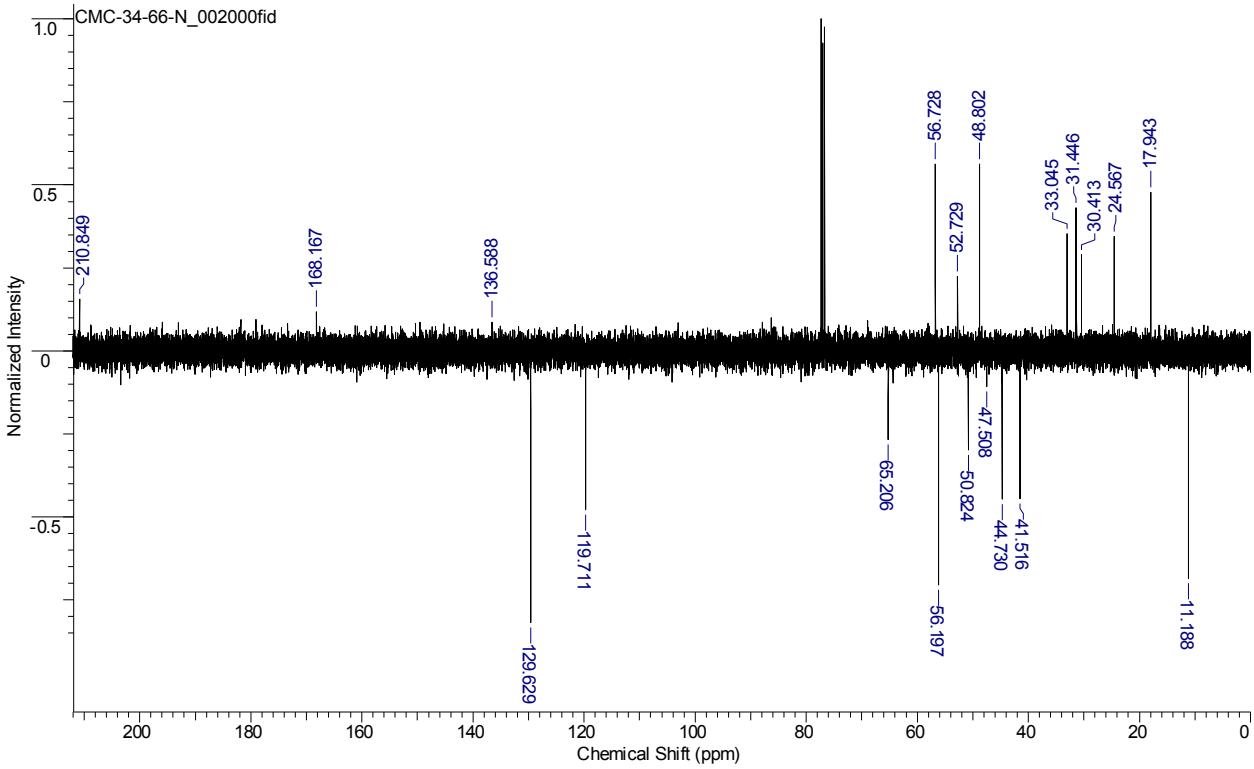
3.203
2.864
2.855
2.835
2.826
2.326
2.302
2.172
1.885
1.666
1.550
1.466
1.185
1.078
1.070
0.866
0.848
0.830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Chemical Shift (ppm)
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56.728
55.197
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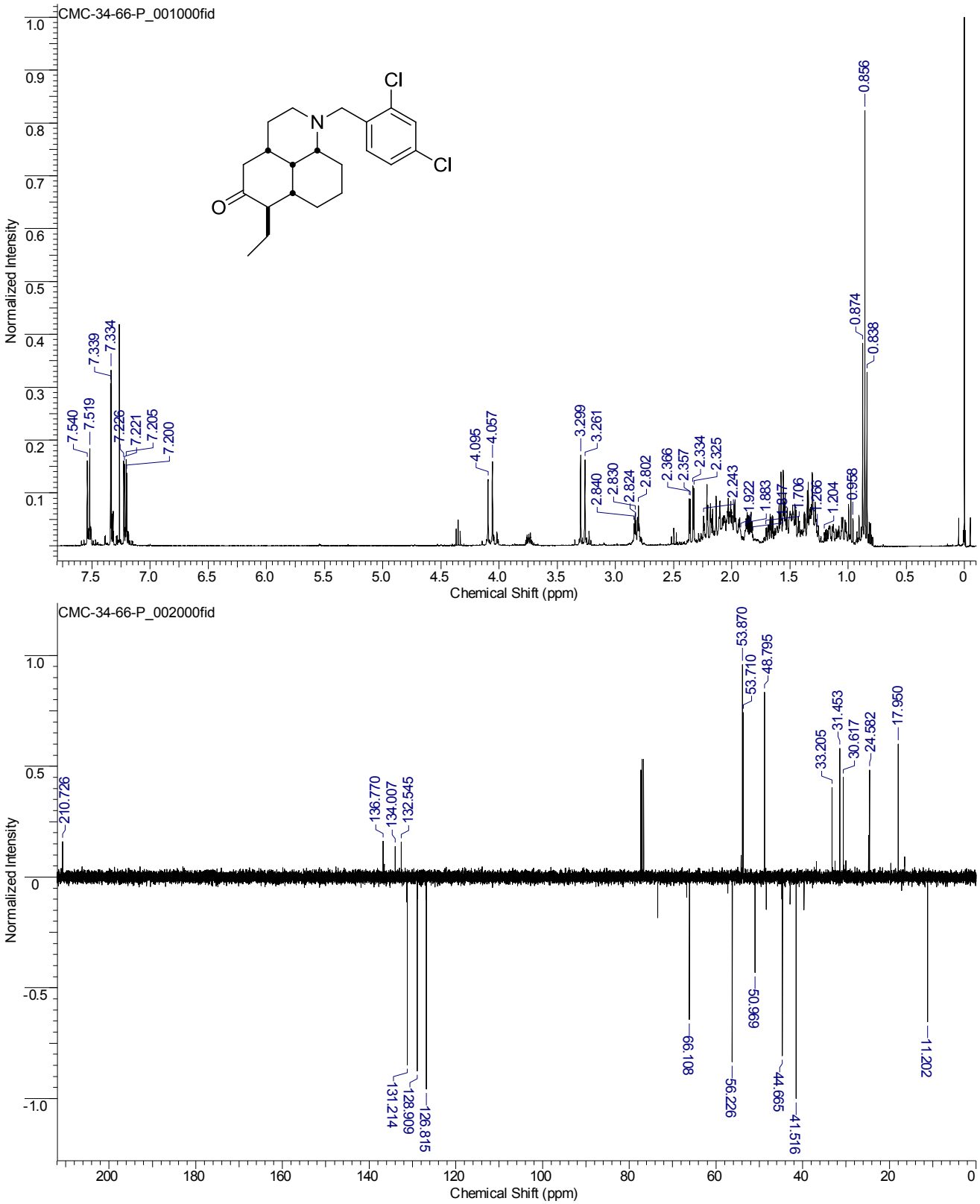
41.516
33.045
31.446
30.413
24.567
17.943
11.188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Normalized Intensity
Chemical Shift (ppm)
Cl
Cl
N
O
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7.519
7.339
7.334
7.226
7.221
7.205
7.200
4.095
4.057
3.299
3.261
2.840
2.830
2.824
2.802
2.366
2.357
2.334
2.325
2.243
1.922
1.883
1.706
1.266
1.204
0.958
CMC-34-66-P_002000fid
Normalized Intensity
Chemical Shift (ppm)
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136.770
134.007
132.545
131.214
128.969
126.815
80.199
60.969
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53.710
48.795
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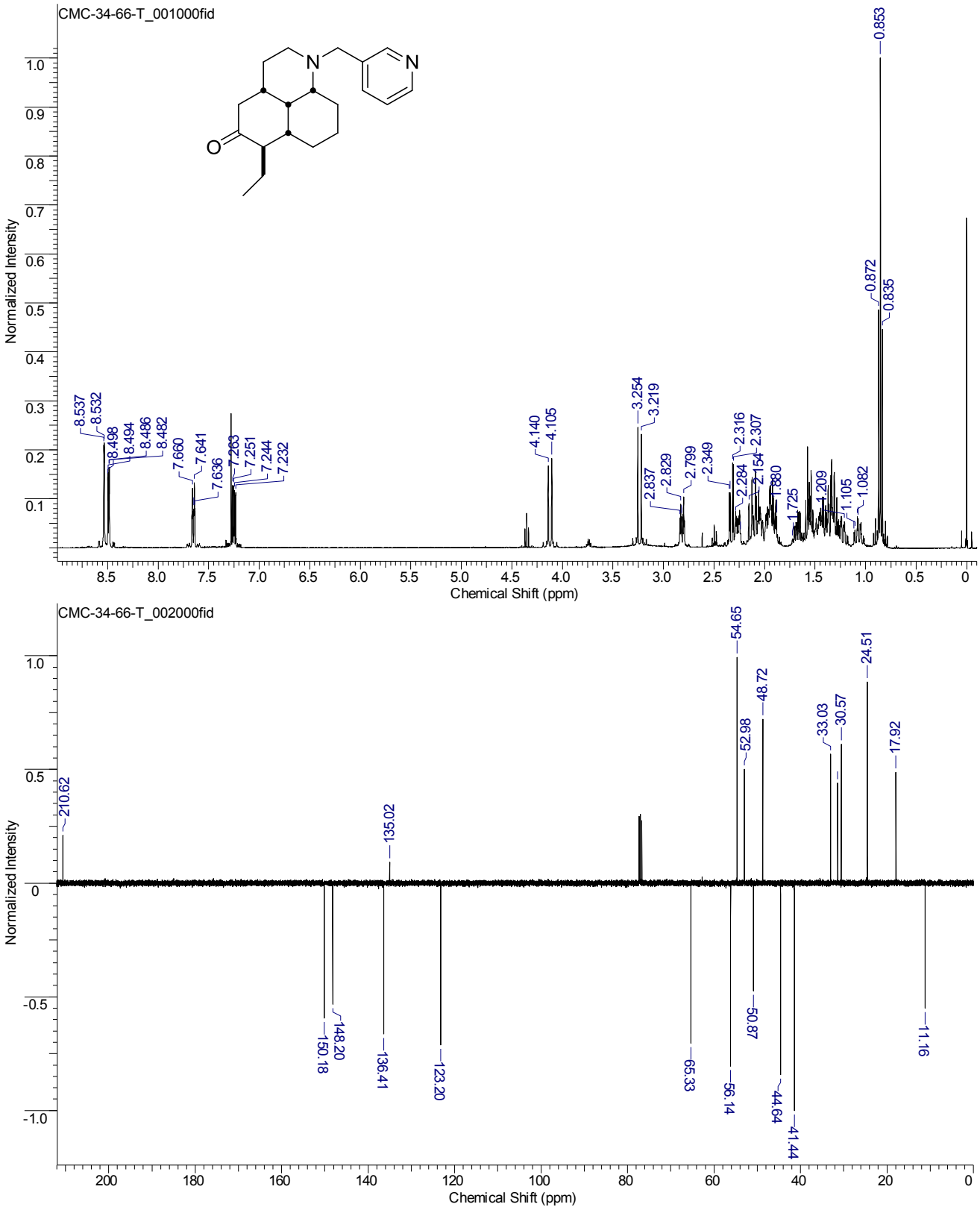
17.960
11.202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Normalized Intensity
Chemical Shift (ppm)
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8.486
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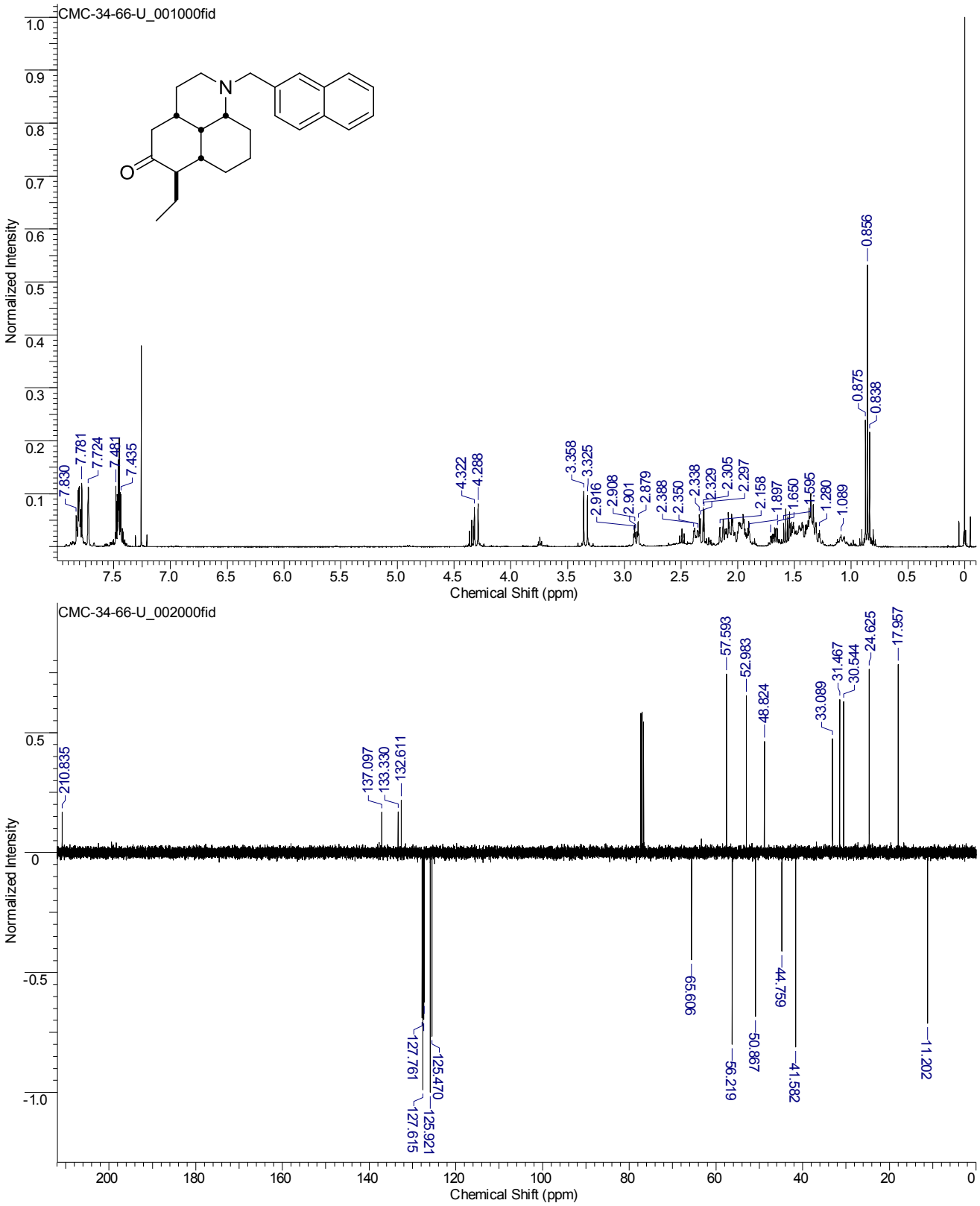
7.660
7.641
7.636
7.263
7.251
7.244
7.232
4.140
4.105
3.254
3.219
2.837
2.829
2.799
2.349
2.316
2.307
2.284
2.154
1.880
1.725
1.209
1.105
1.082
0.872
0.835
0.853
CMC-34-66-T_002000fid
Normalized Intensity
Chemical Shift (ppm)
210.62
150.18
148.20
136.41
135.02
123.20
65.33
56.14
54.65
52.98
50.87
48.72
44.64
41.44
33.03
30.57
24.51
17.92
11.16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Normalized Intensity
Chemical Shift (ppm)
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4.288
3.358
3.325
2.916
2.908
2.901
2.879
2.388
2.350
2.338
2.329
2.305
2.297
2.158
1.897
1.650
1.595
1.280
1.089
0.875
0.838
0.856
CMC-34-66-U_002000fid
Normalized Intensity
Chemical Shift (ppm)
210.835
137.097
133.330
132.611
127.761
127.615
125.470
125.921
66.606
57.593
56.219
52.983
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48.824
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31.467
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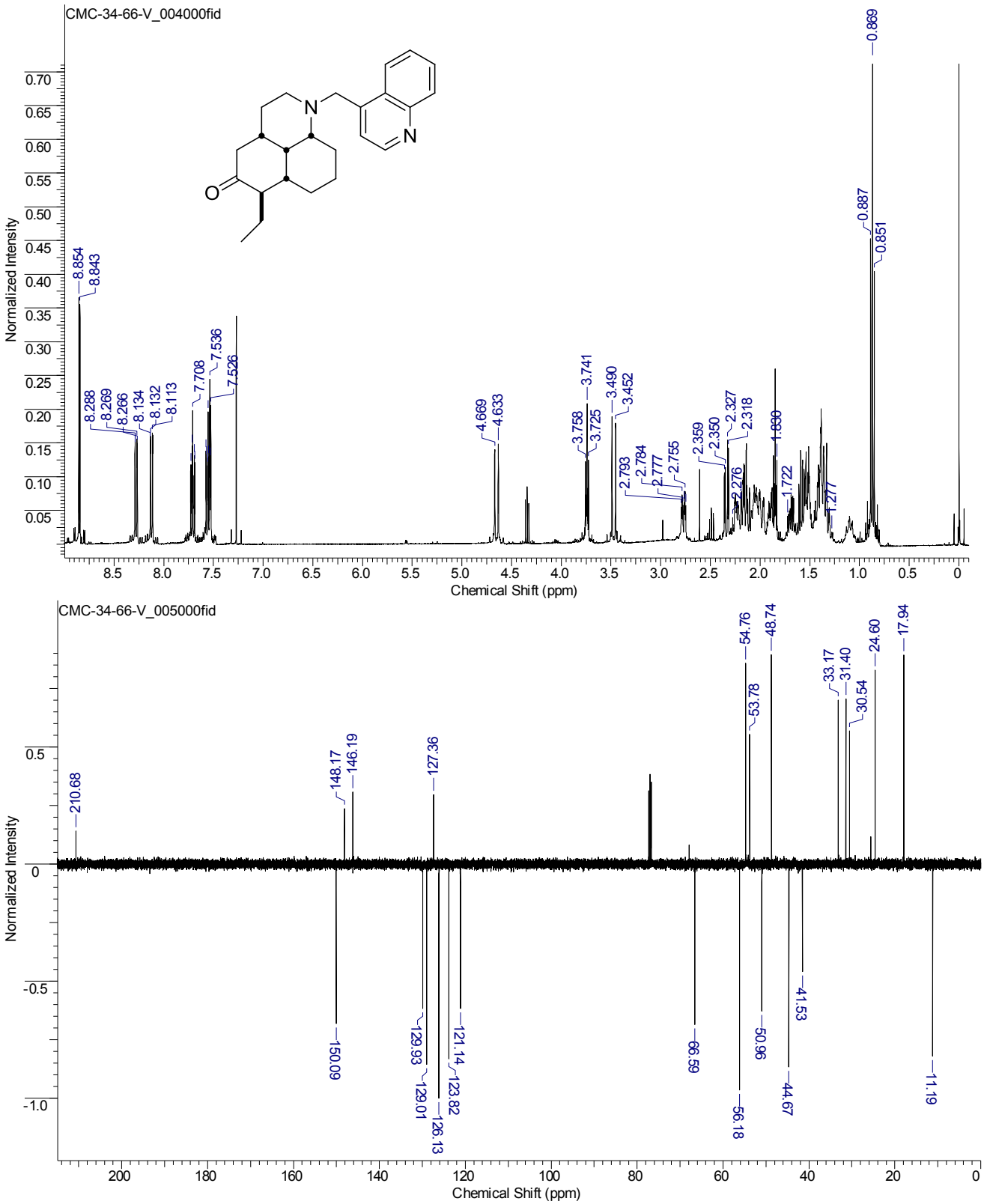
11.202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Chemical Shift (ppm)
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7.708
7.536
7.526
4.669
4.633
3.758
3.741
3.725
3.490
3.452
2.793
2.784
2.777
2.755
2.359
2.350
2.327
2.318
2.276
1.830
1.722
1.277
0.887
0.869
0.851
CMC-34-66-V_005000fid
Normalized Intensity
Chemical Shift (ppm)
210.68
148.17
146.19
127.36
150.09
129.93
129.01
126.13
121.14
123.82
66.59
54.76
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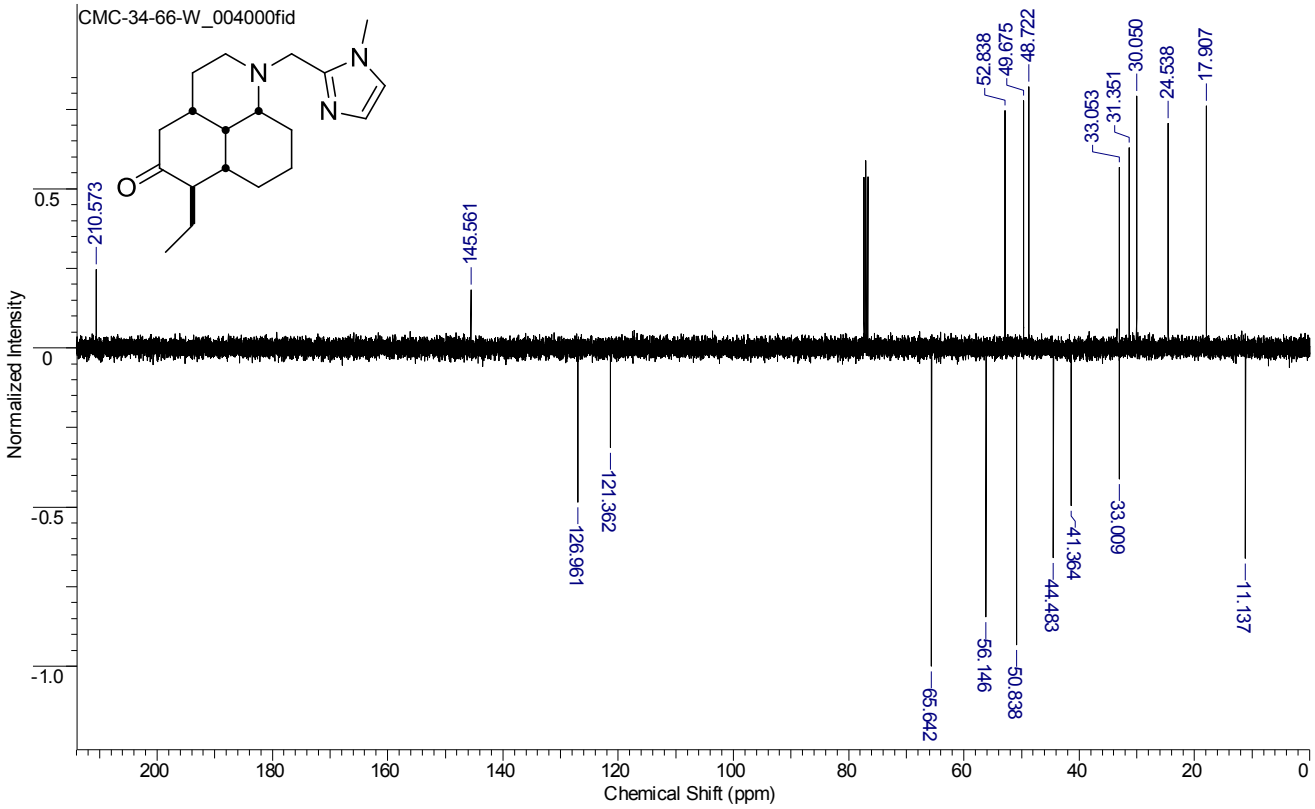
30.54
24.60
41.53
44.67
17.94
11.19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Normalized Intensity
Chemical Shift (ppm)
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50.838
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49.675
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33.053
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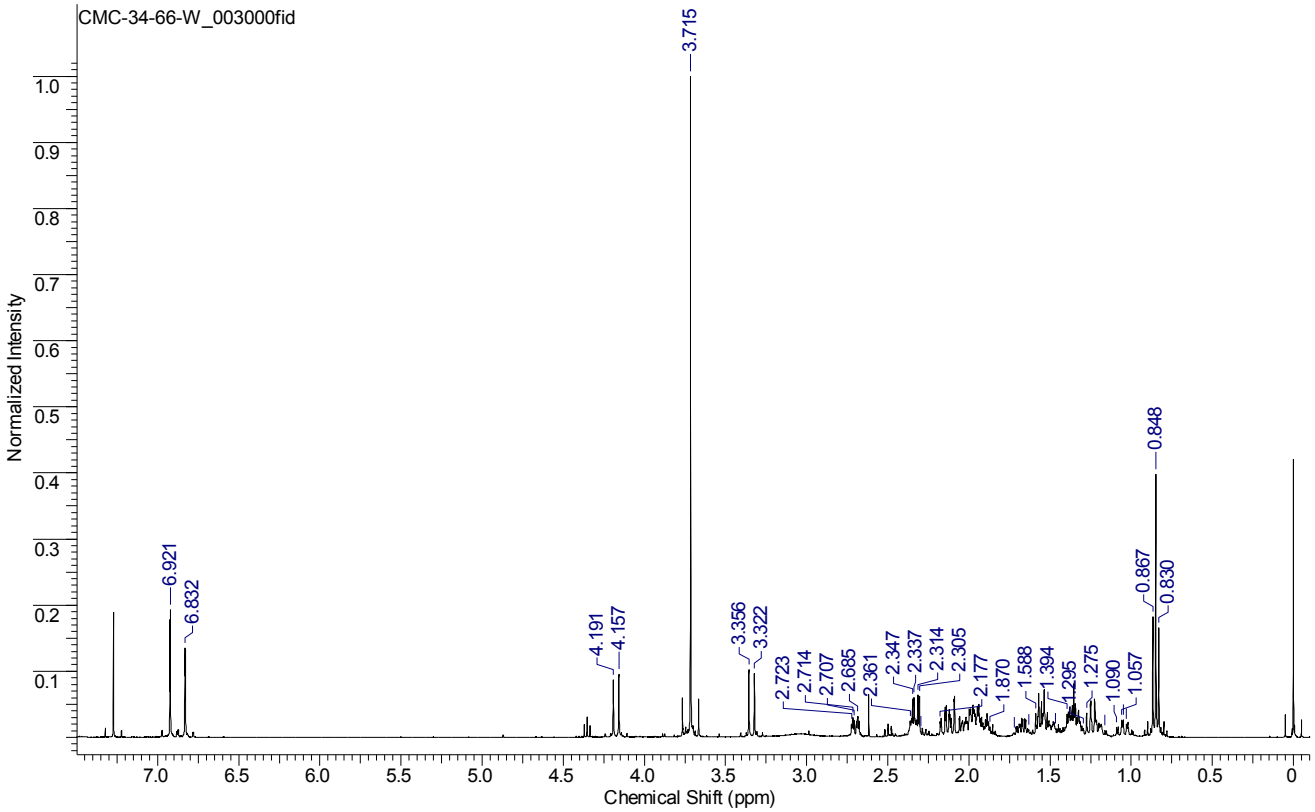
24.538
17.907


CMC-34-66-W_003000fid
Normalized Intensity
Chemical Shift (ppm)
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4.191
4.157
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3.322
2.723
2.714
2.707
2.685
2.361
2.347
2.337
2.314
2.305
2.177
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1.394
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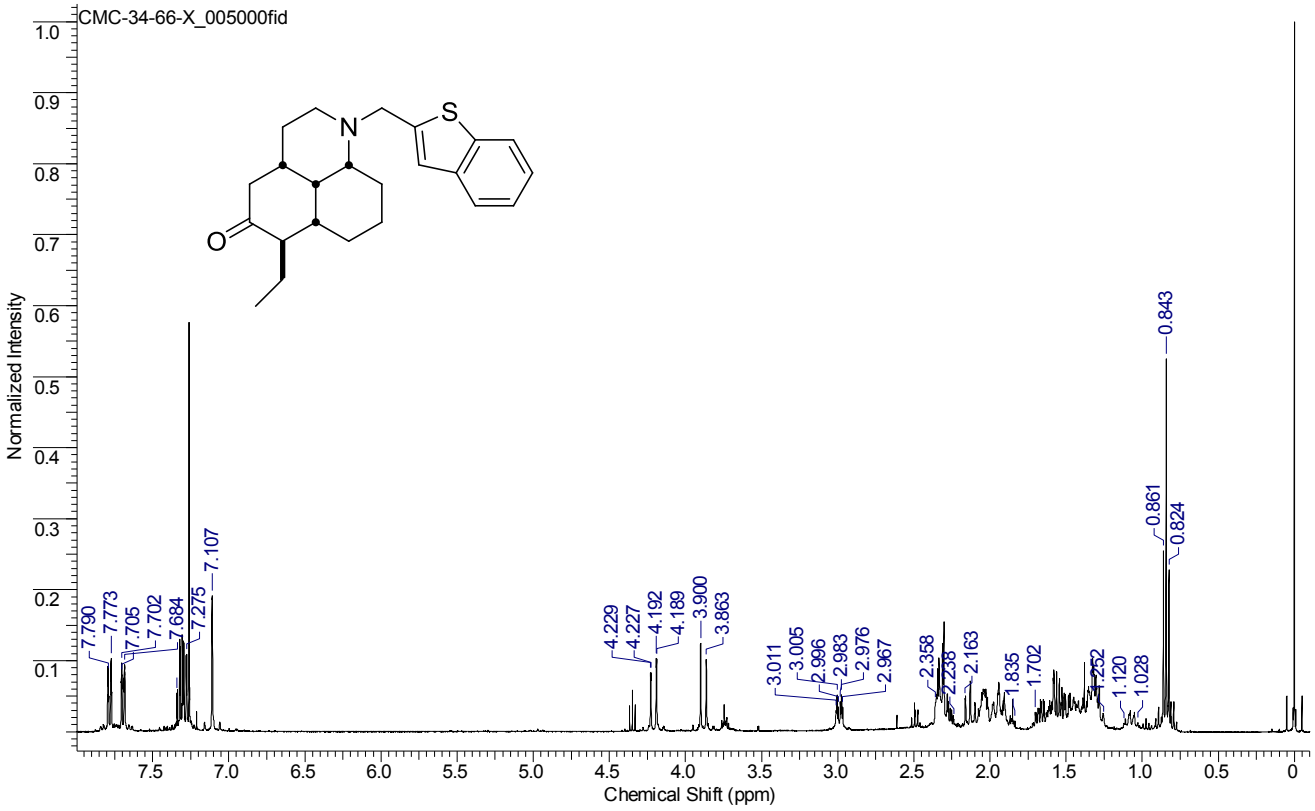
0.848
0.830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Normalized Intensity
Chemical Shift (ppm)
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4.192
4.189
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3.011
3.005
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2.983
2.976
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0.824
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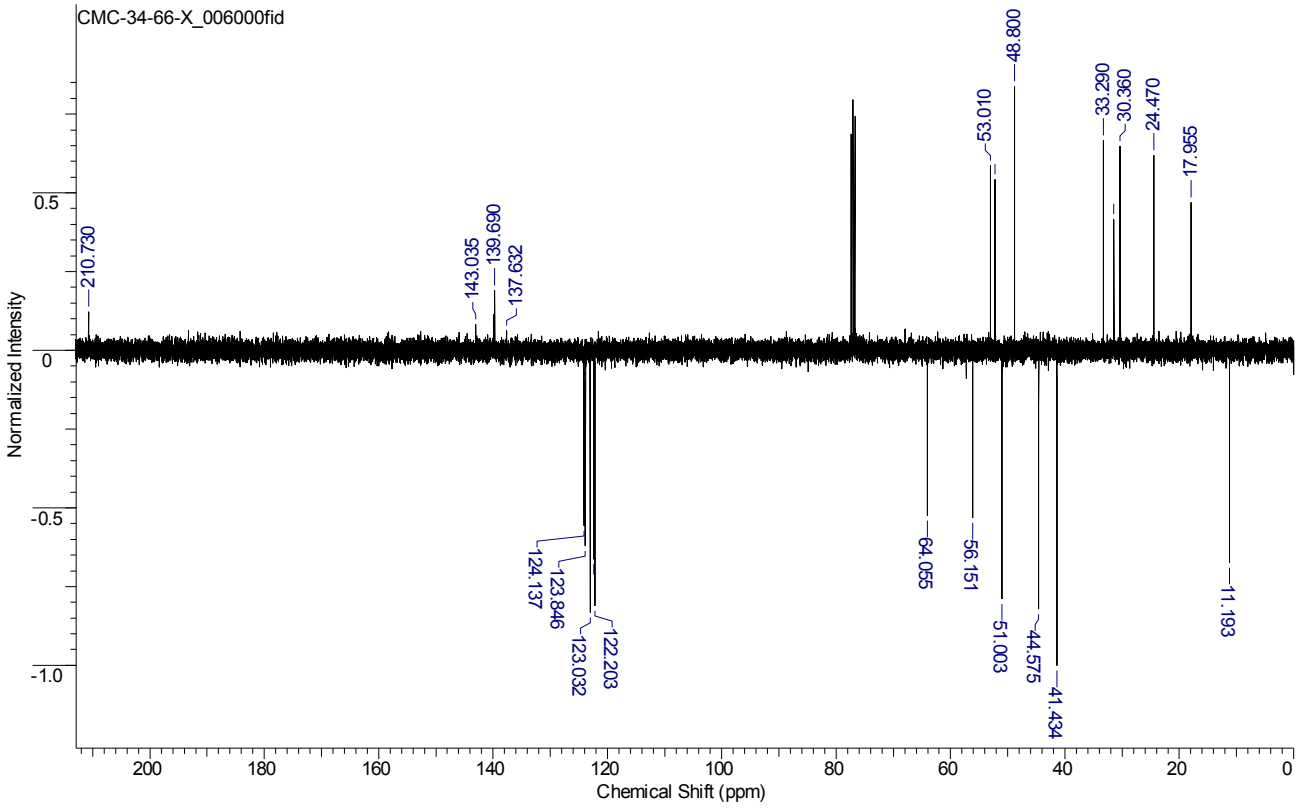
CMC-34-66-X_006000fid
Normalized Intensity
Chemical Shift (ppm)
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123.032
122.203
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51.003
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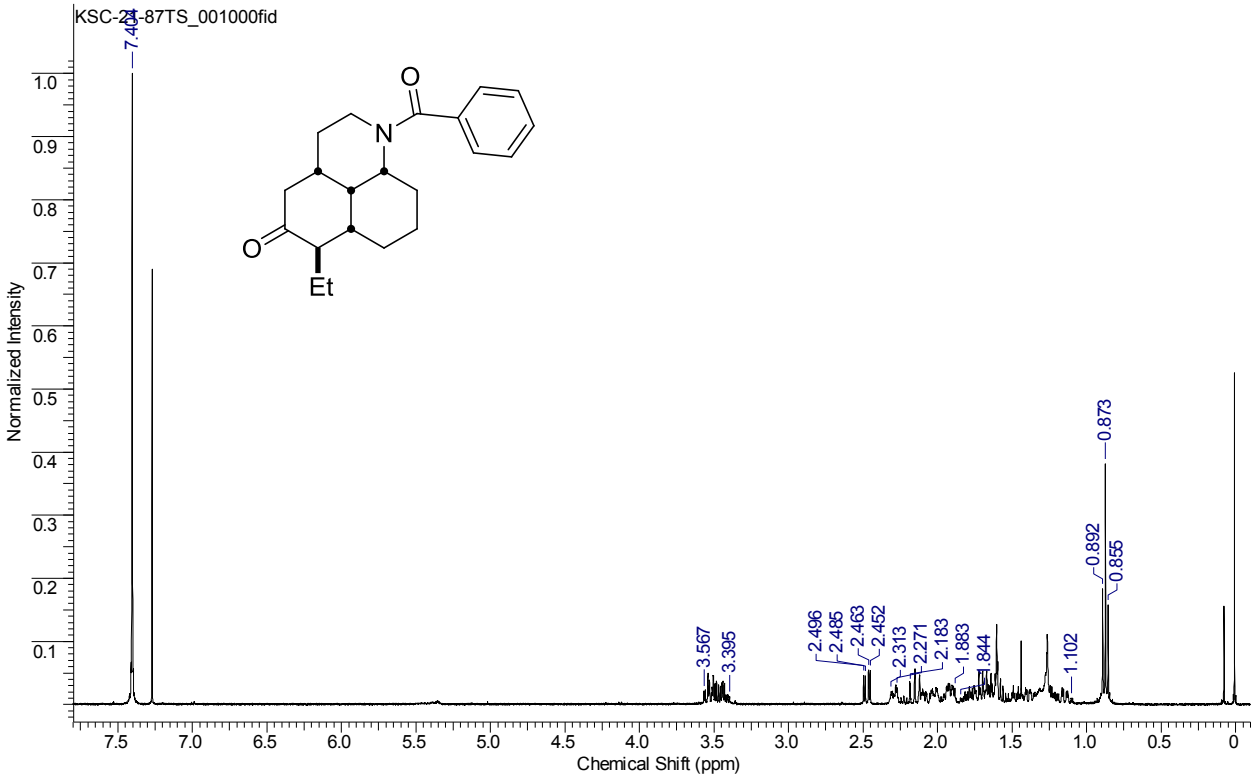
33.290
30.360
24.470
17.955
11.193


KSC-21-87TS_001000fid
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O
N
O
Et
Normalized Intensity
Chemical Shift (ppm)
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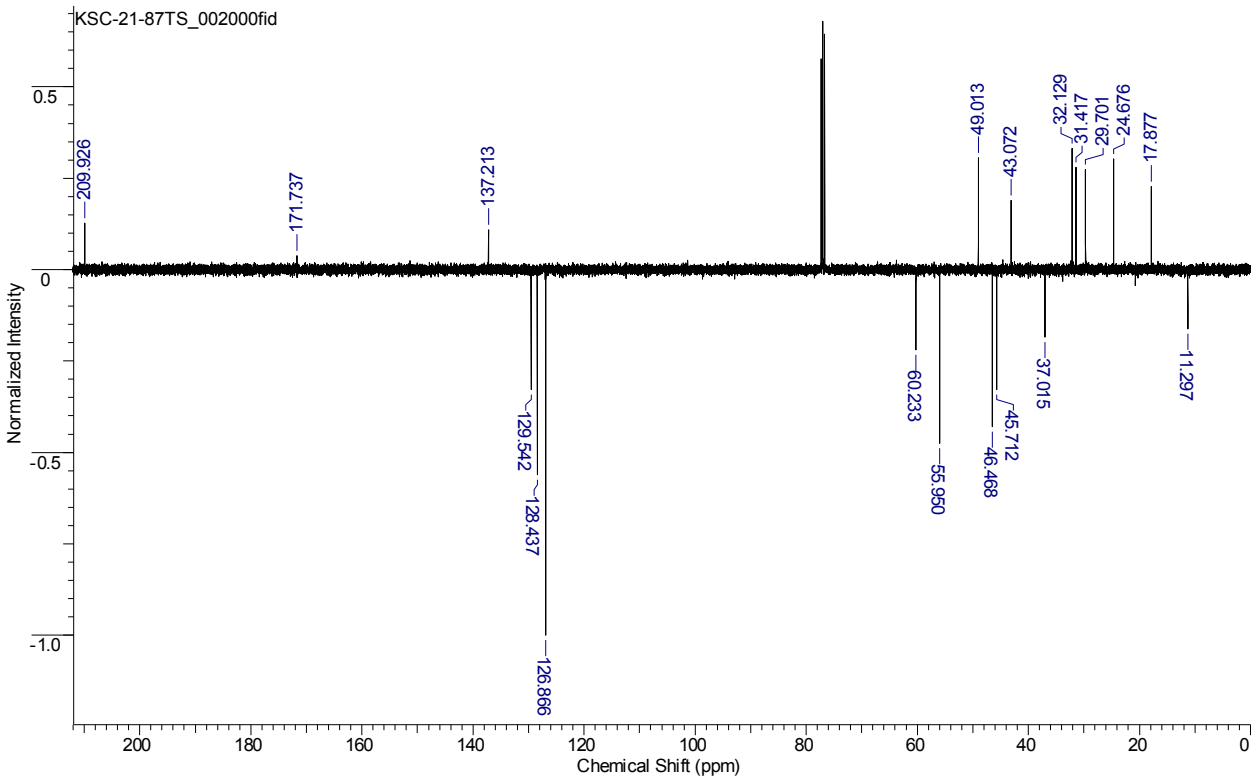
0.855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Normalized Intensity
Chemical Shift (ppm)
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60.233
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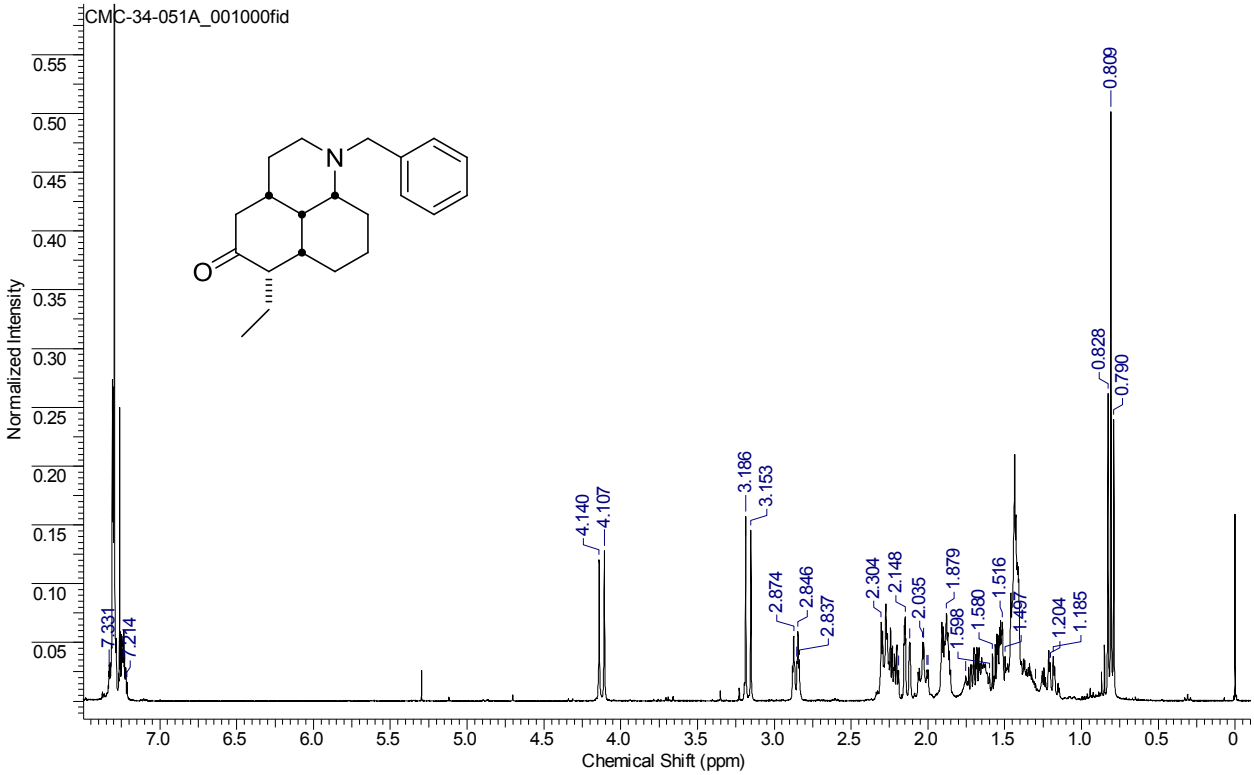
31.417
29.701
24.676
17.877
11.297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Normalized Intensity
Chemical Shift (ppm)
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4.107
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3.153
2.874
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2.148
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1.580
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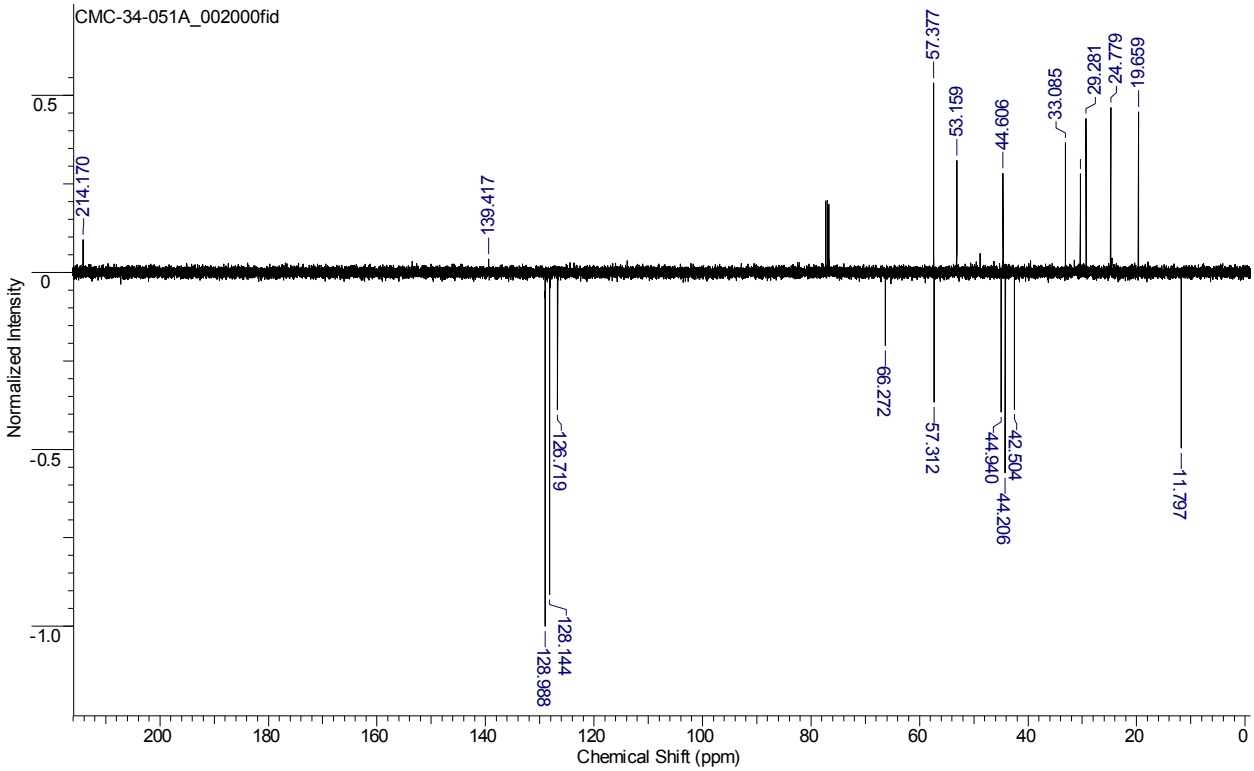
1.497
1.204
1.185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Normalized Intensity
Chemical Shift (ppm)
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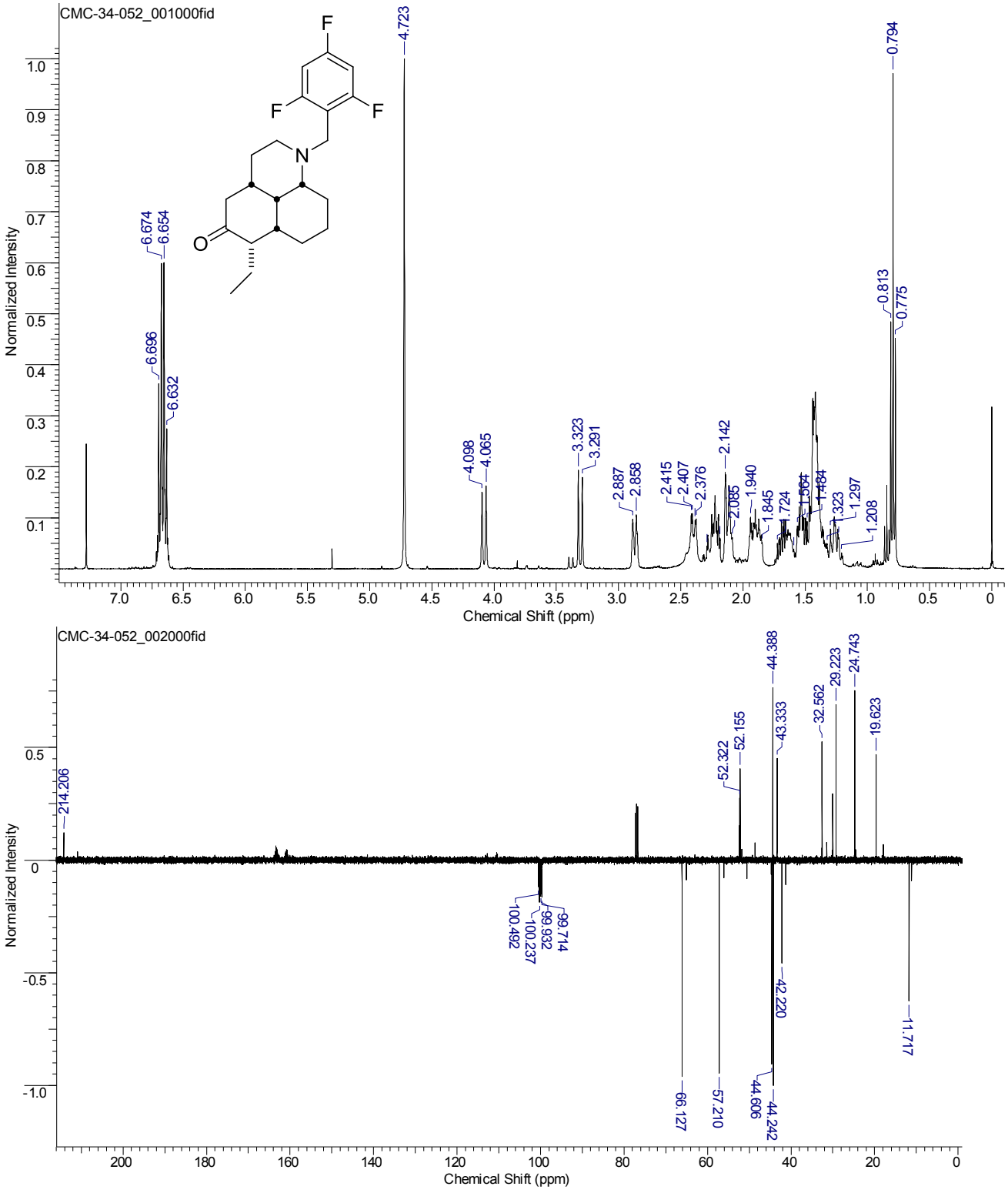
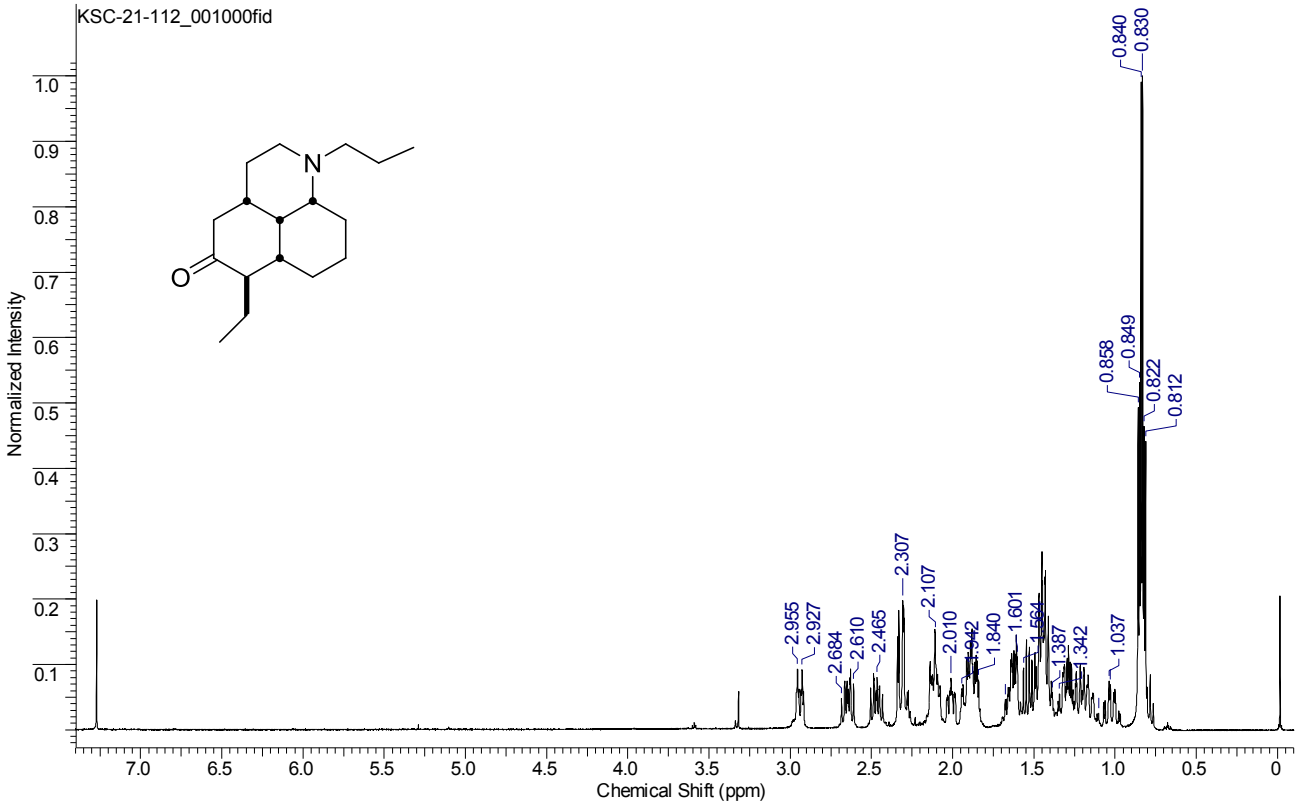
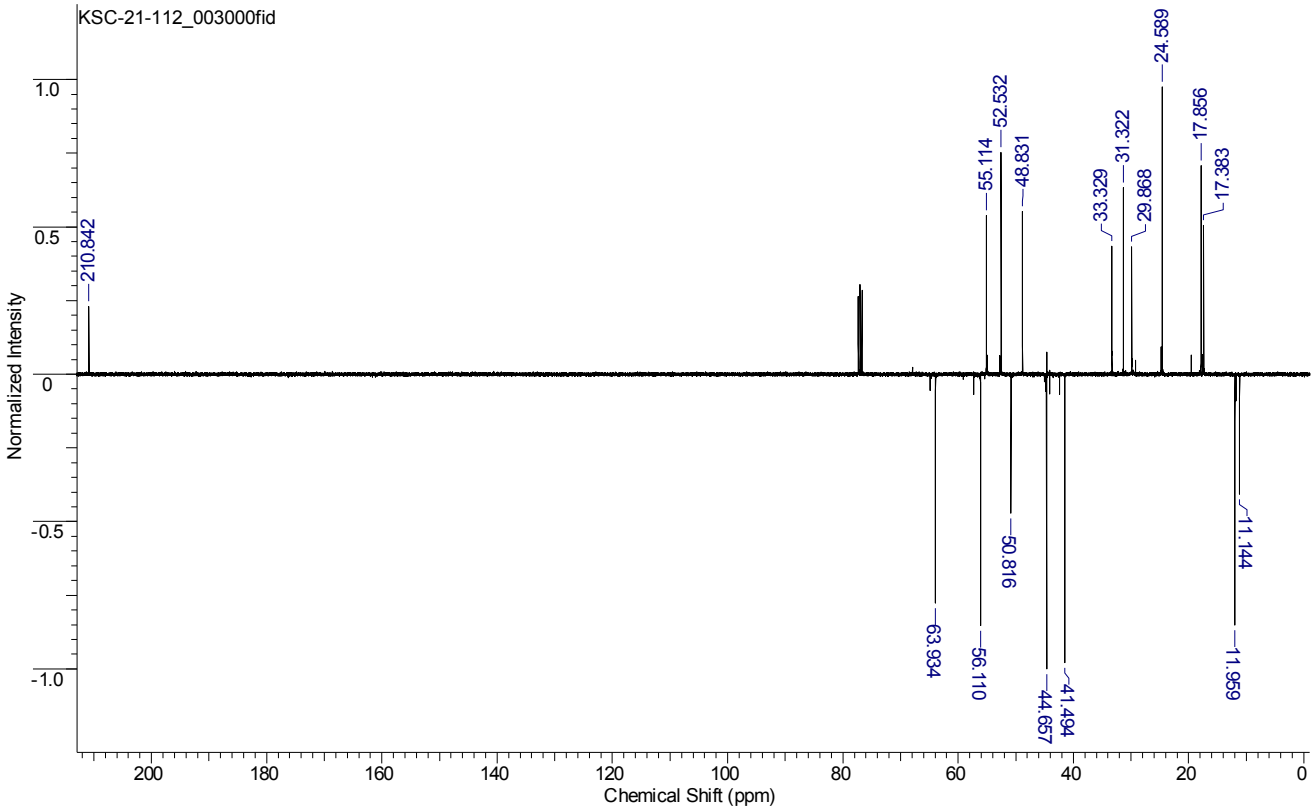
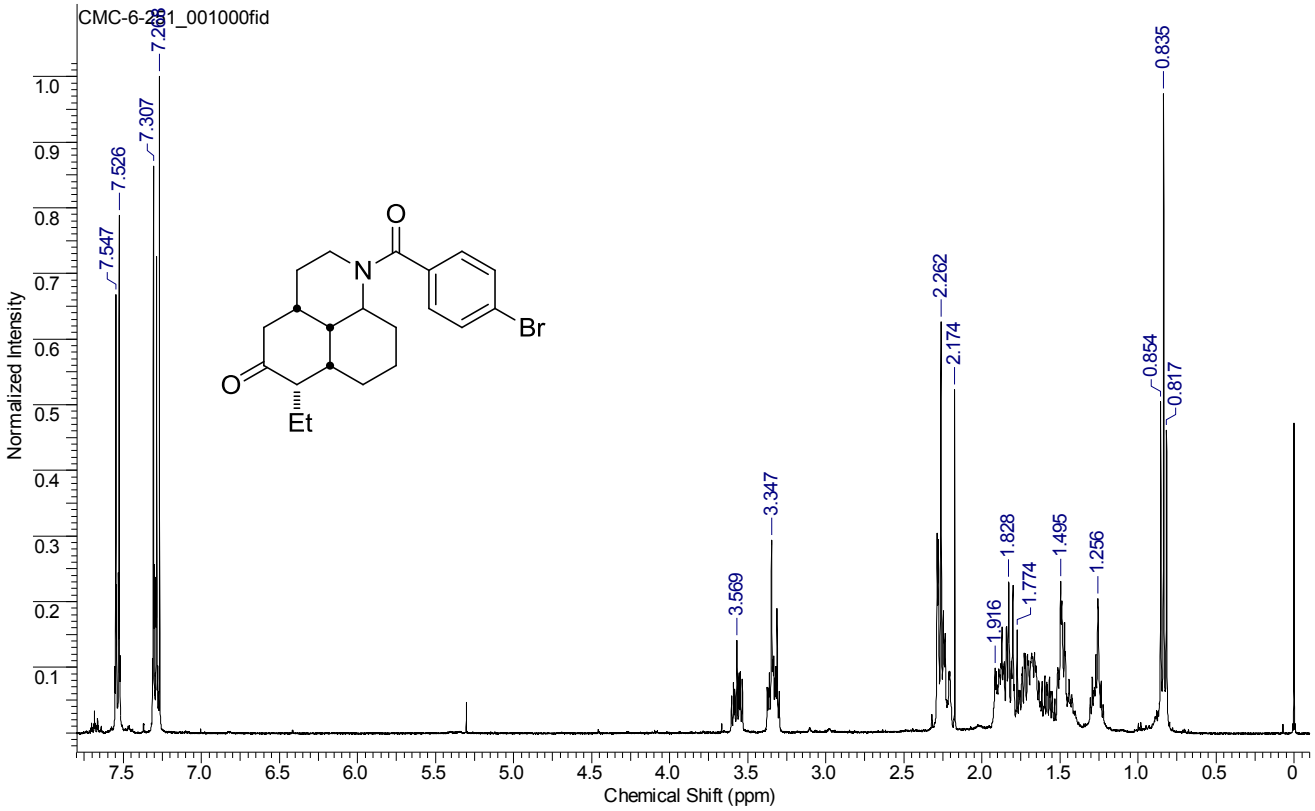
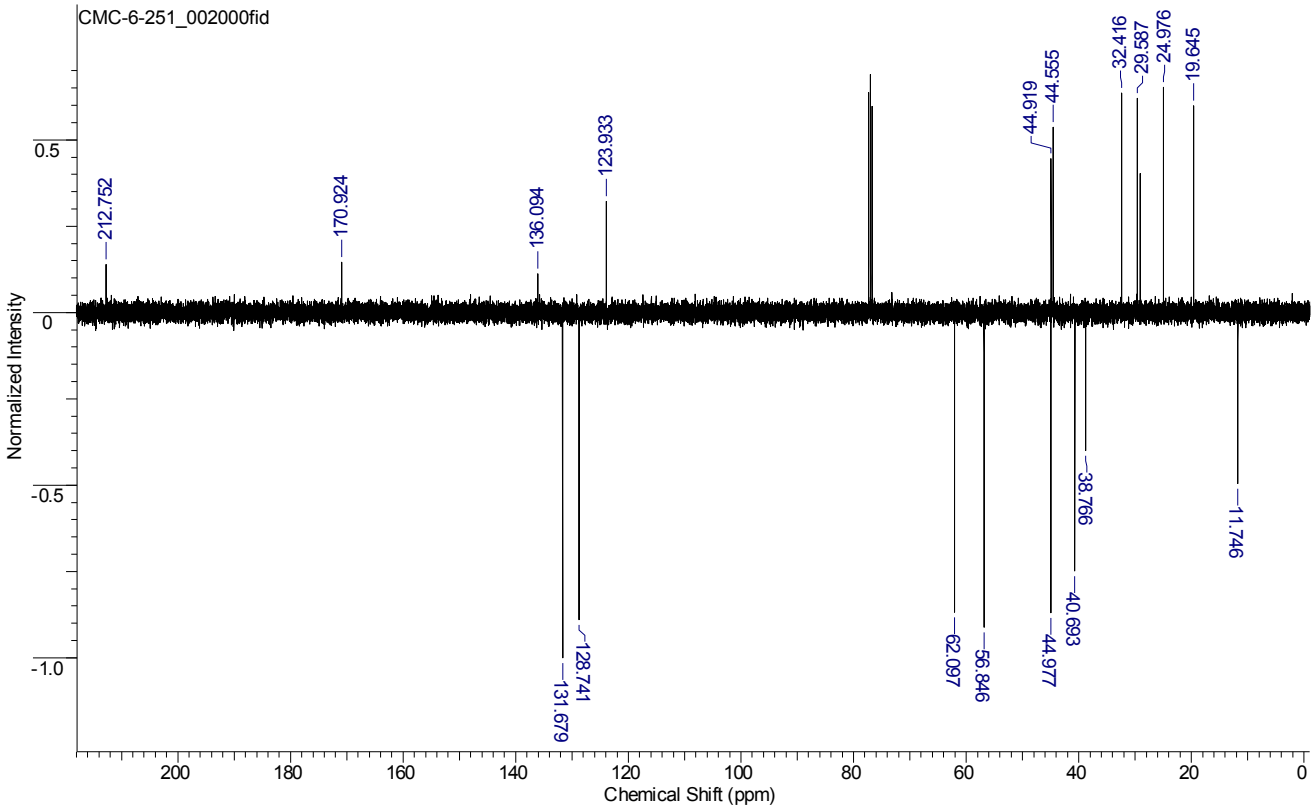
42.504
11.797
128.719
128.144
128.988

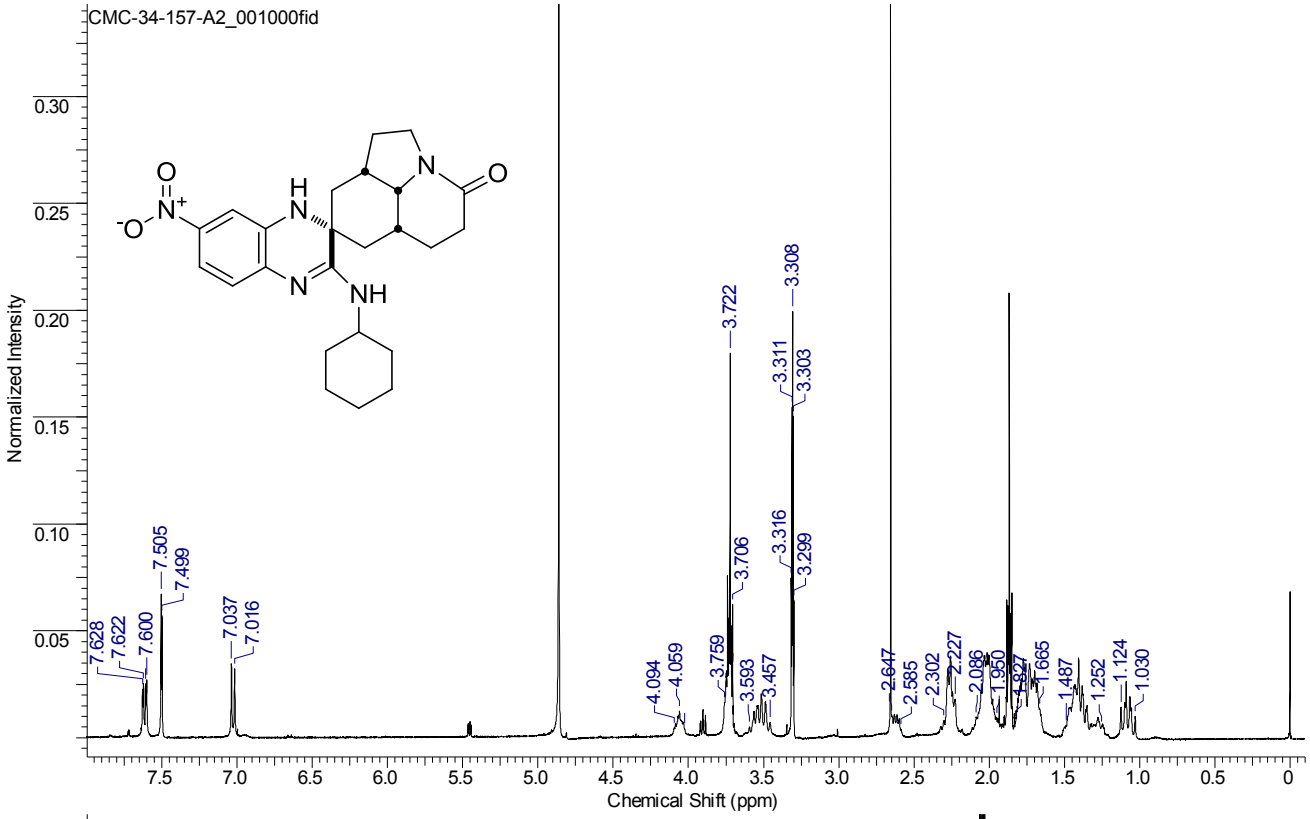

CMC-34-052_001000fid
Normalized Intensity
Chemical Shift (ppm)
6.674
6.654
6.696
6.632
4.723
4.098
4.065
3.323
3.291
2.887
2.858
2.415
2.407
2.376
2.142
2.085
1.940
1.845
1.724
1.564
1.484
1.323
1.297
1.208
0.813
0.794
0.775
F
F
F
N
O
CMC-34-052_002000fid
Normalized Intensity
Chemical Shift (ppm)
214.206
100.492
100.237
99.932
99.714
66.127
57.210
52.322
52.155
44.388
43.333
42.220
44.606
44.242
32.562
29.223
24.743
19.623
11.717

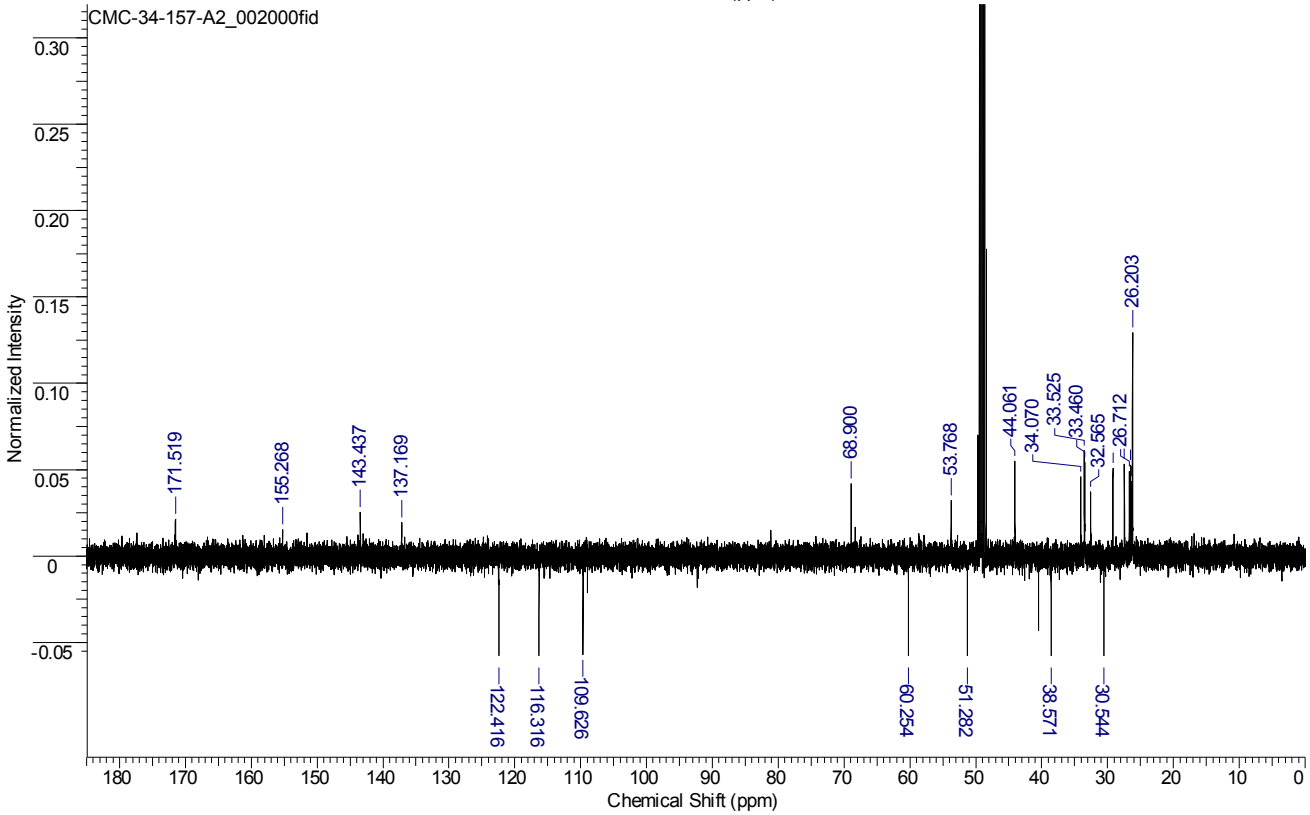

KSC-21-112_001000fid
Normalized Intensity
Chemical Shift (ppm)
0.840
0.830
0.858
0.849
0.822
0.812
2.955
2.927
2.684
2.610
2.465
2.307
2.107
2.010
1.840
1.601
1.037
1.387
1.342
N
O

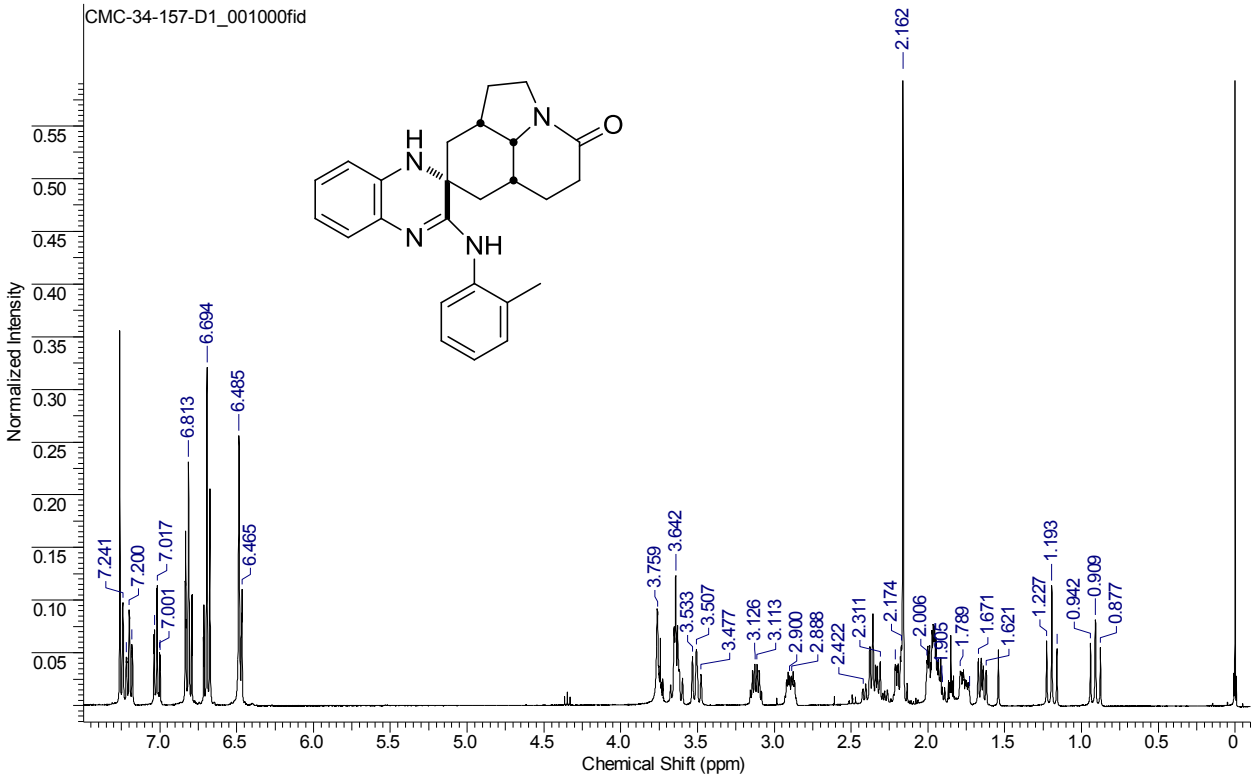

KSC-21-112_003000fid
Normalized Intensity
Chemical Shift (ppm)
210.842
63.334
55.110
55.114
52.532
50.816
48.831
44.657
41.494
33.329
31.322
29.868
24.589
17.856
17.383
11.144
11.959

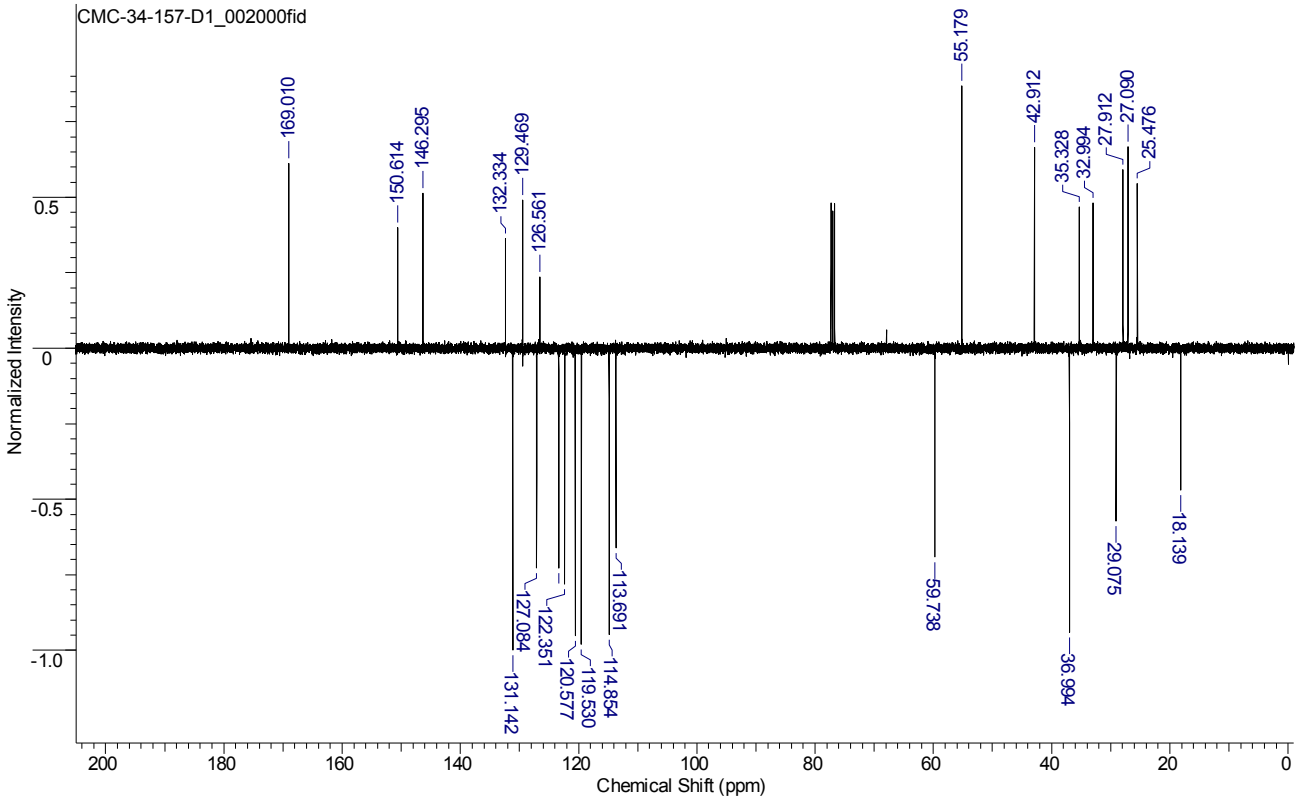

CMC-6-251_001000fid
Normalized Intensity
Chemical Shift (ppm)
7.547
7.526
7.307
7.261
3.569
3.347
2.262
2.174
1.916
1.828
1.774
1.495
1.256
0.854
0.835
0.817
O
N
Br
O
Et

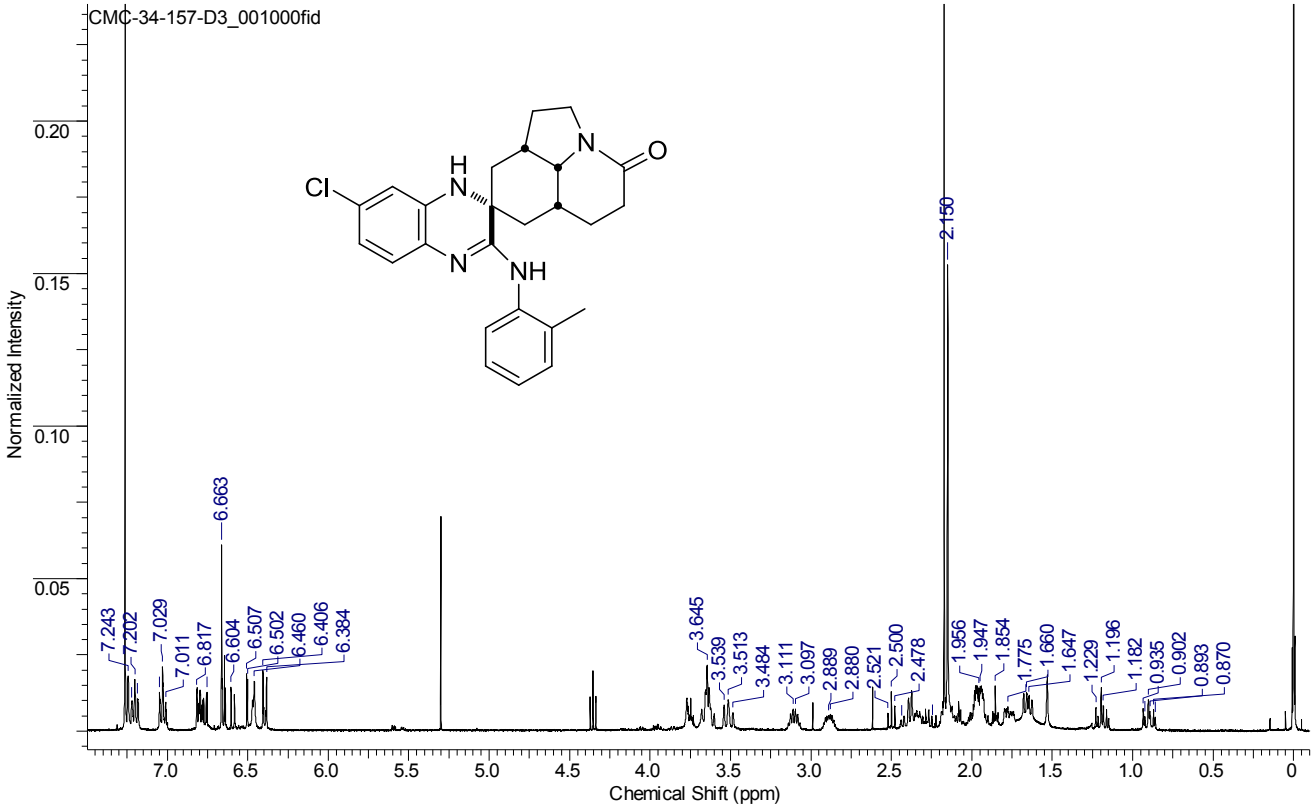

CMC-6-251_002000fid
Normalized Intensity
Chemical Shift (ppm)
212.752
170.924
136.094
123.933
131.679
128.741
62.097
56.846
44.977
44.919
44.555
40.693
38.766
32.416
29.587
24.976
19.645
11.746

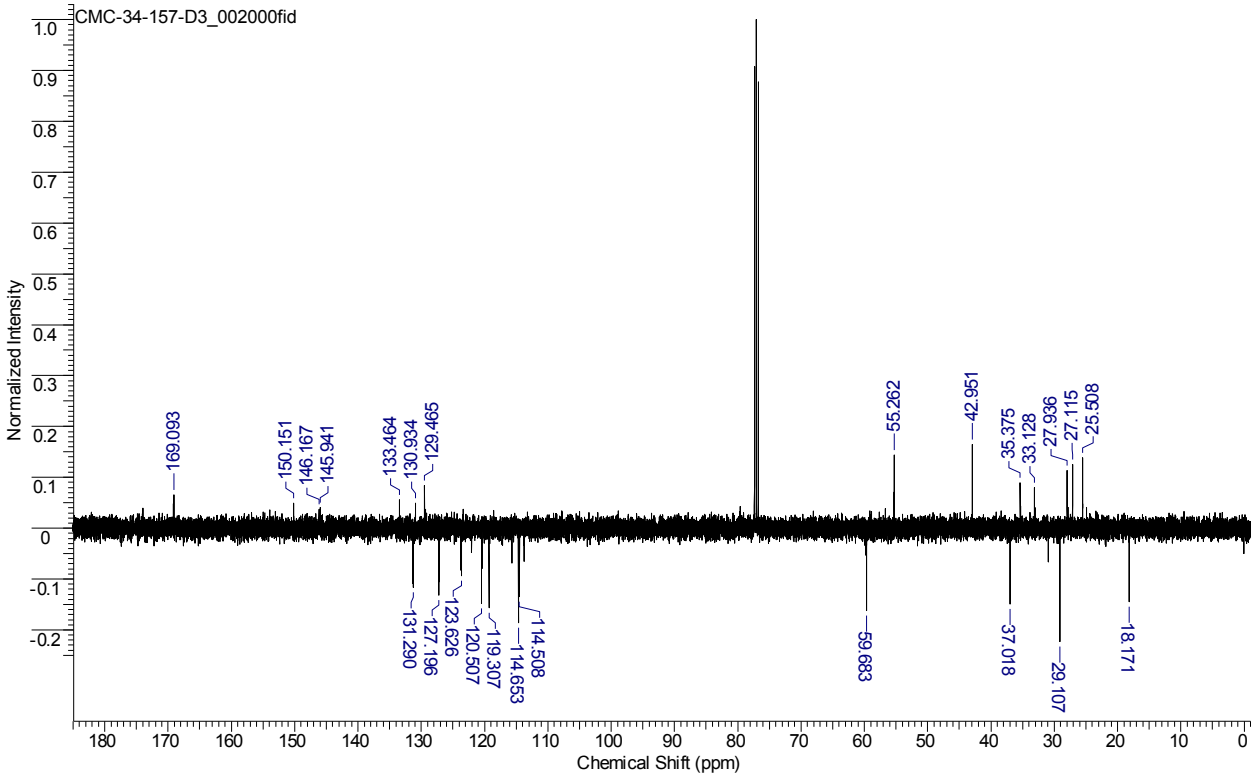

CMC-34-157-A2_001000fid
Normalized Intensity
Chemical Shift (ppm)
7.628
7.622
7.600
7.505
7.499
7.037
7.016
4.094
4.059
3.759
3.722
3.706
3.593
3.457
3.316
3.308
3.311
3.303
3.299
2.647
2.585
2.302
2.227
1.665
1.487
1.252
1.124
1.030

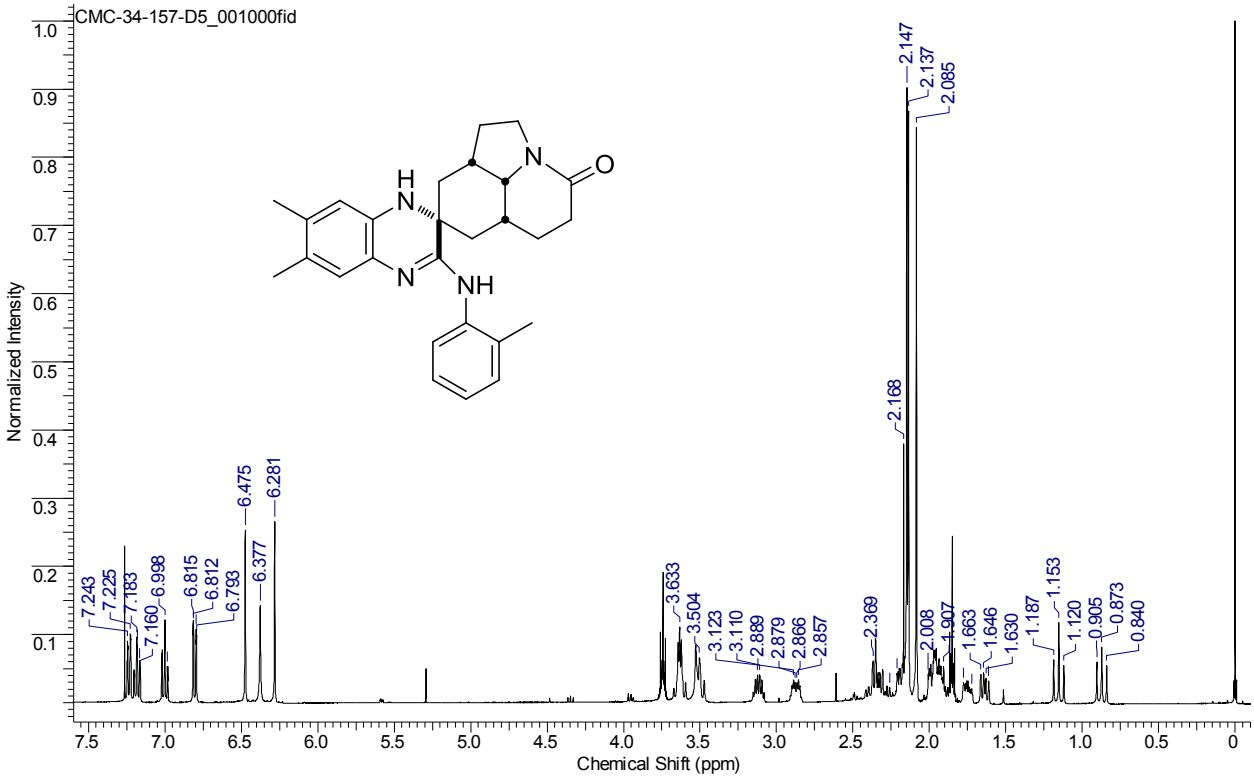

CMC-34-157-A2_002000fid
Normalized Intensity
Chemical Shift (ppm)
171.519
155.268
143.437
137.169
122.416
116.316
109.626
68.900
60.254
53.768
51.282
44.061
34.070
33.525
33.460
32.565
26.712
26.203
38.571
30.544

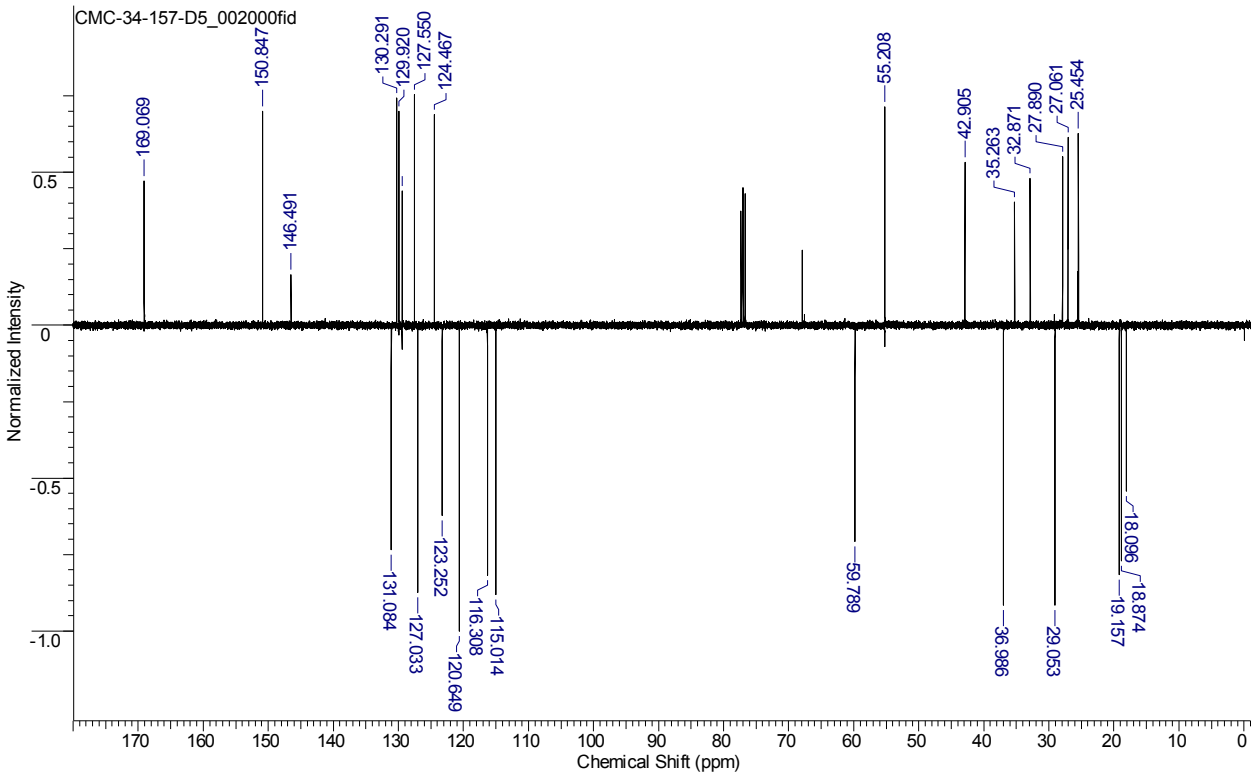

CMC-34-157-D1_001000fid
Normalized Intensity
Chemical Shift (ppm)
7.241
7.200
7.017
7.001
6.813
6.694
6.485
6.465
3.759
3.642
3.533
3.507
3.477
3.126
3.113
2.900
2.888
2.422
2.311
2.174
2.162
2.006
1.789
1.671
1.621
1.227
1.193
0.942
0.909
0.877
H
N
N
O
N
NH

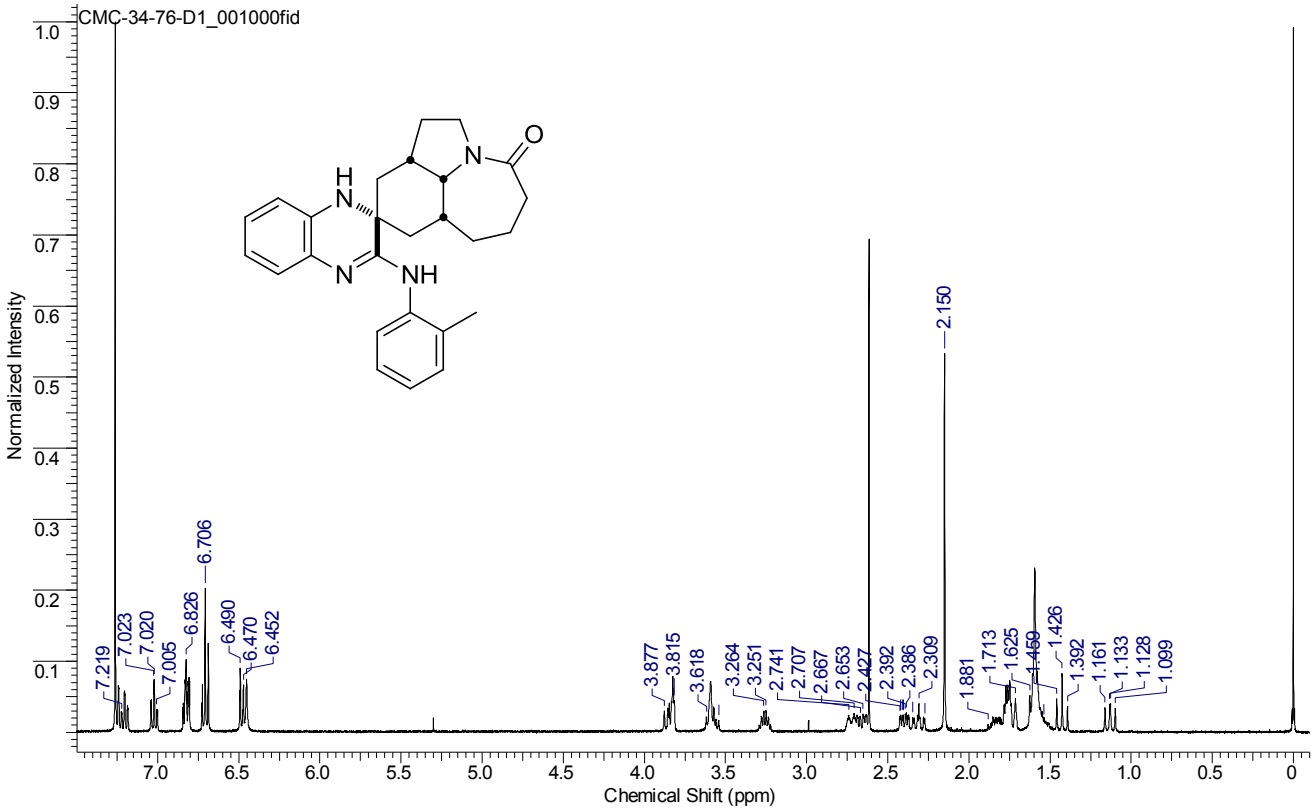

CMC-34-157-D1_002000fid
Normalized Intensity
Chemical Shift (ppm)
169.010
150.614
146.295
132.334
129.469
126.561
131.142
127.084
122.351
120.577
119.530
114.854
113.691
59.738
55.179
42.912
36.994
35.328
32.994
29.075
27.912
27.090
25.476
18.139

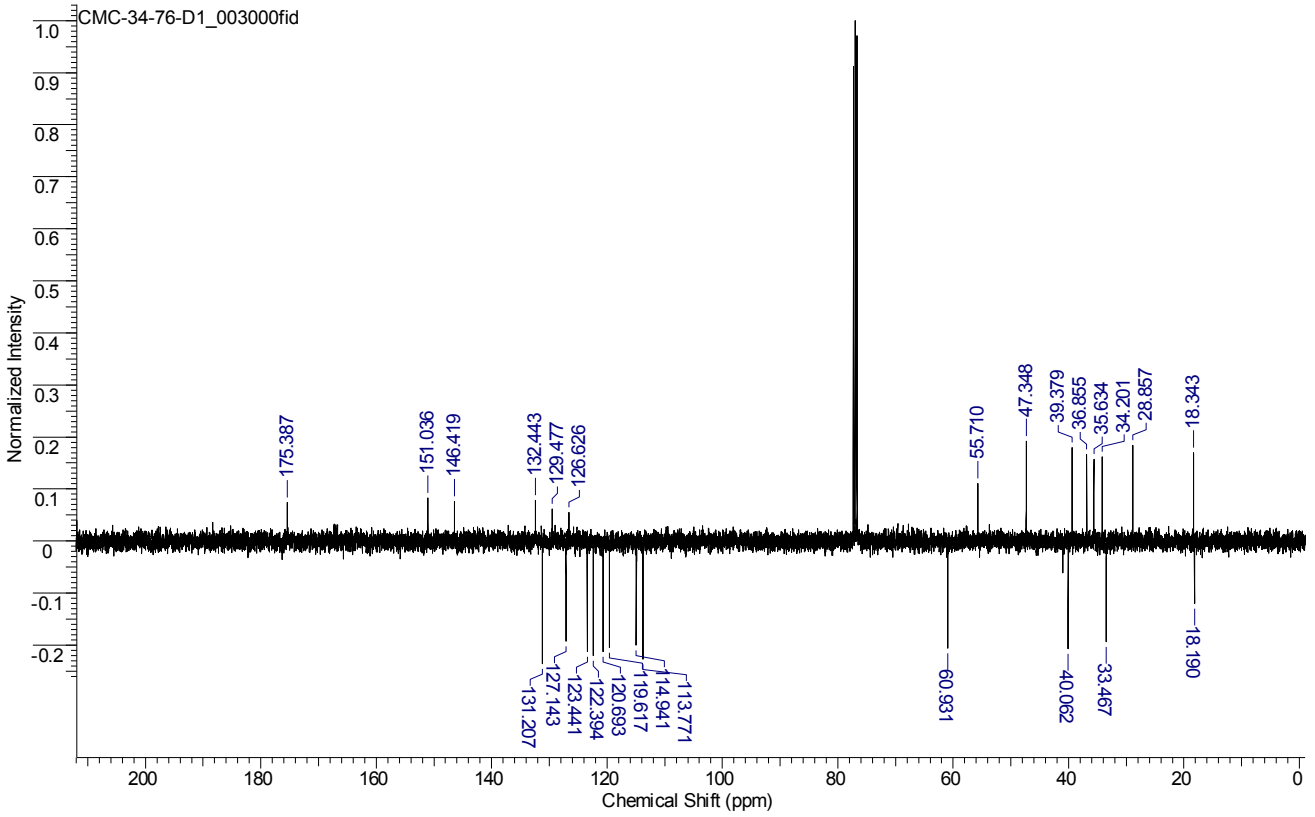

CMC-34-157-D3_001000fid
Normalized Intensity
Chemical Shift (ppm)
7.243
7.202
7.029
7.011
6.817
6.663
6.604
6.507
6.502
6.460
6.406
6.384
3.645
3.539
3.513
3.484
3.111
3.097
2.889
2.880
2.521
2.500
2.478
2.150
1.956
1.947
1.854
1.775
1.660
1.647
1.229
1.196
1.182
0.935
0.902
0.893
0.870

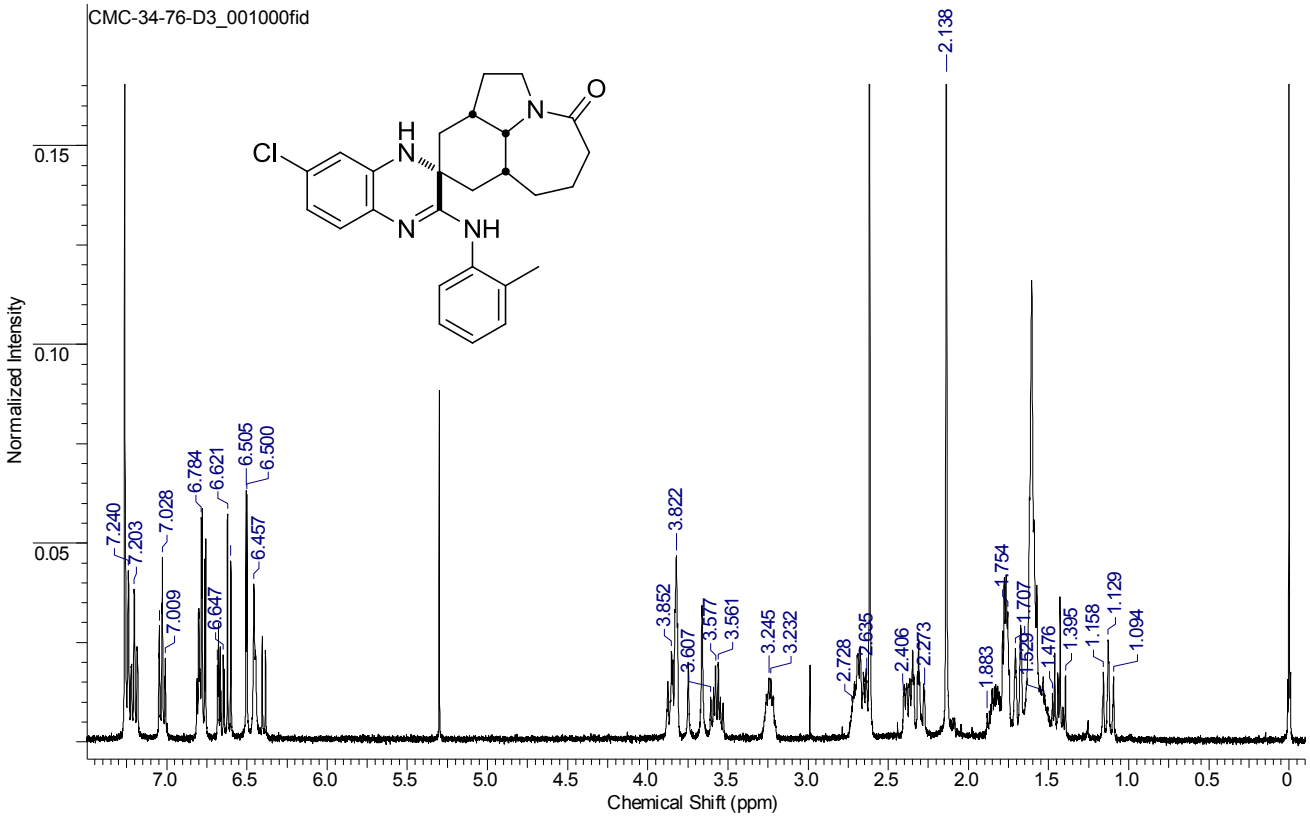

CMC-34-157-D3_002000fid
Normalized Intensity
Chemical Shift (ppm)
169.093
150.151
146.167
145.941
133.464
130.934
129.465
131.290
127.196
123.626
120.507
119.307
114.653
114.508
55.262
69.683
42.951
37.018
35.375
33.128
29.107
27.936
27.115
25.508
18.171

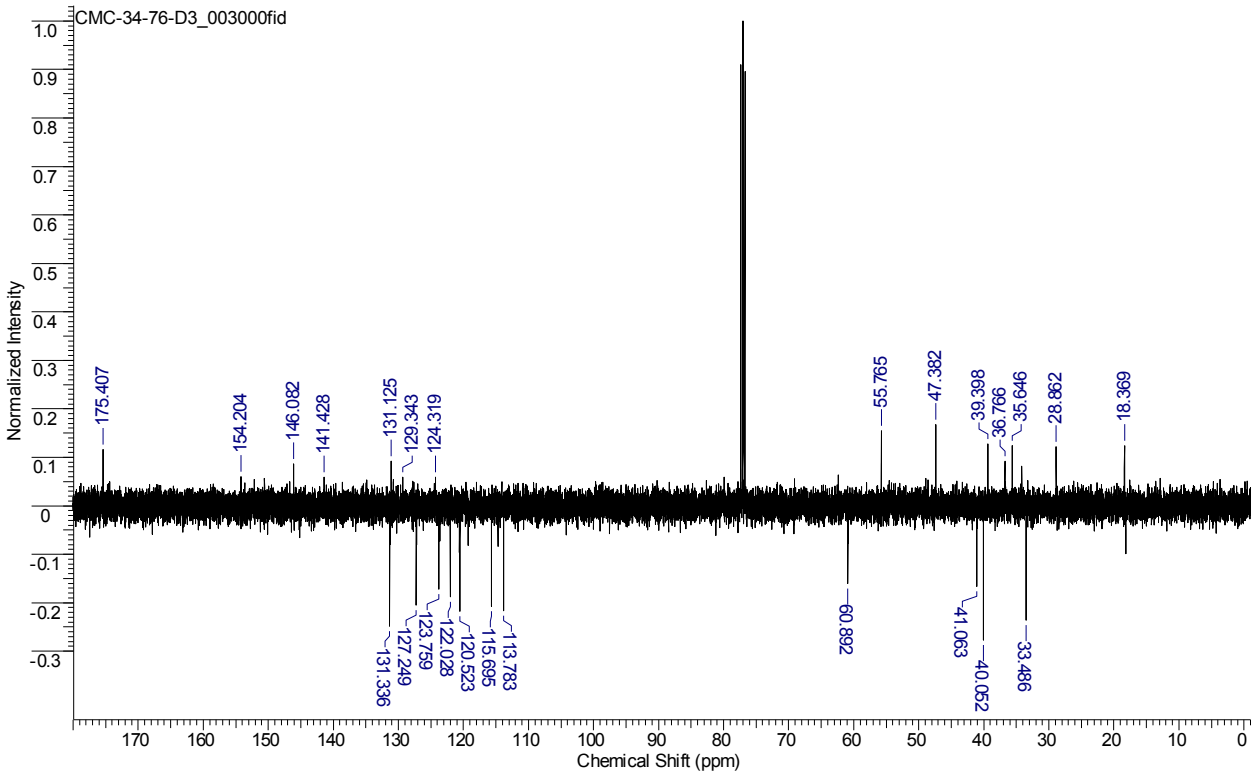

CMC-34-157-D5_001000fid
Normalized Intensity
Chemical Shift (ppm)
7.243
7.225
7.183
7.160
6.998
6.815
6.812
6.793
6.475
6.377
6.281
3.633
3.504
3.123
3.110
2.889
2.879
2.866
2.857
2.369
2.168
2.147
2.137
2.085
2.008
1.907
1.663
1.646
1.630
1.187
1.153
1.120
0.905
0.873
0.840
H
N
N
N
NH
O

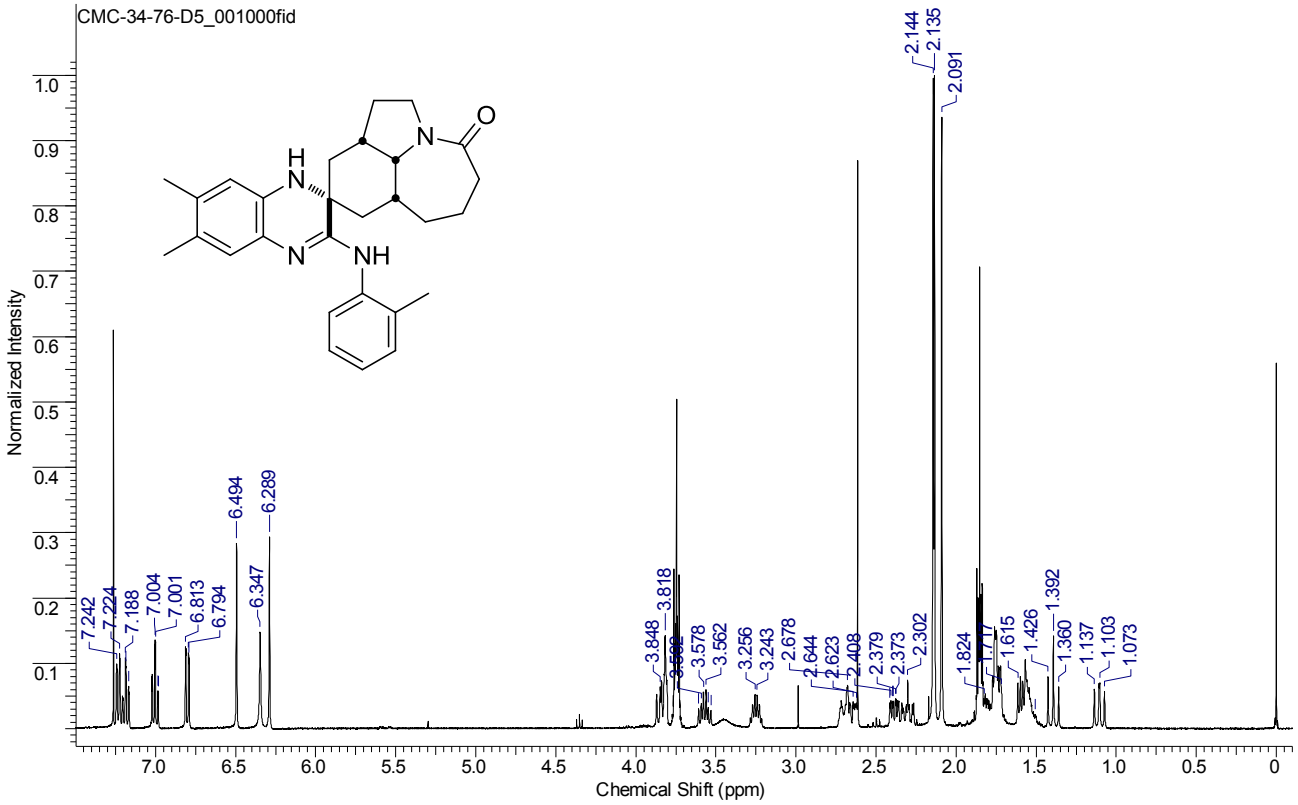

CMC-34-157-D5_002000fid
Normalized Intensity
Chemical Shift (ppm)
169.069
150.847
146.491
130.291
129.920
127.550
124.467
55.208
42.905
35.263
32.871
27.890
27.061
25.454
131.084
127.033
123.252
120.649
116.308
115.014
59.789
36.986
29.053
19.157
18.896
18.874

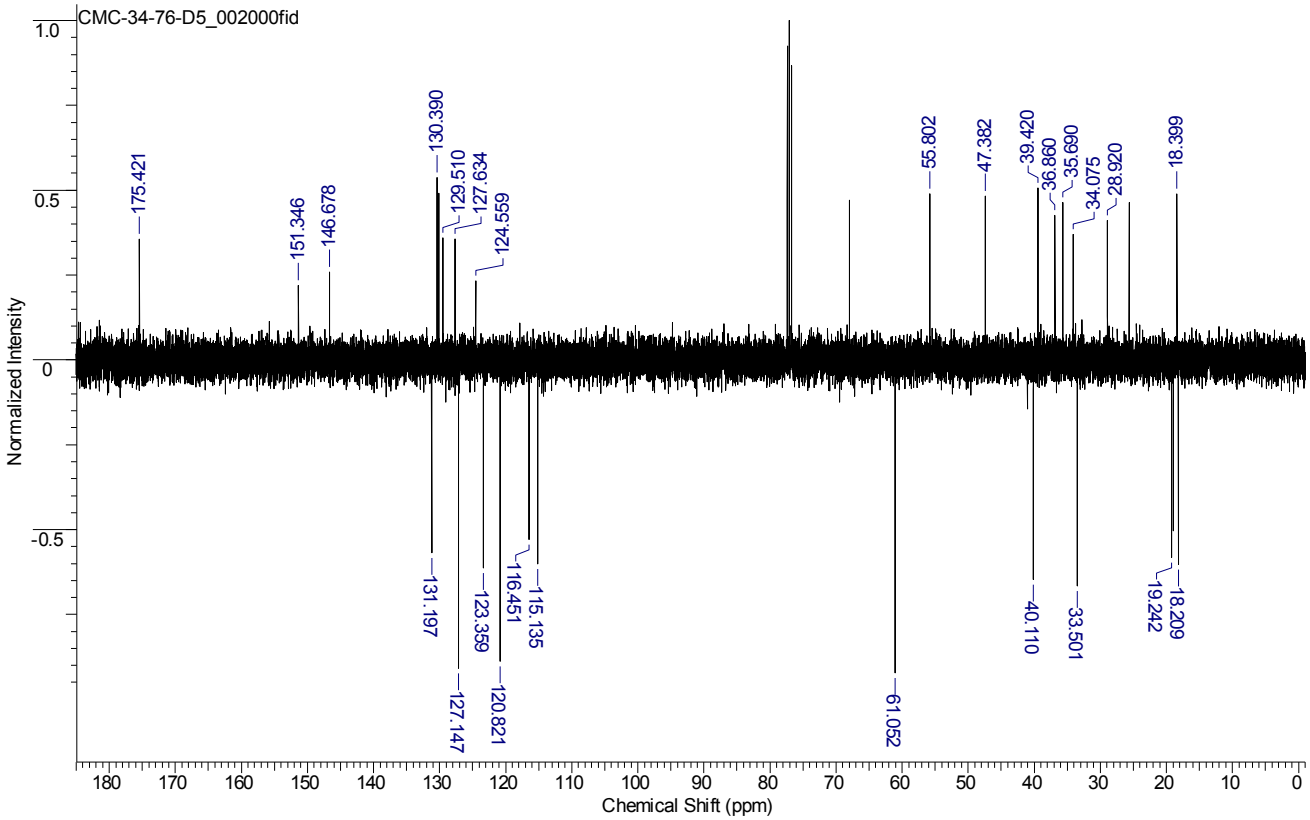

CMC-34-76-D1_001000fid
Normalized Intensity
Chemical Shift (ppm)
7.219
7.023
7.020
7.005
6.826
6.706
6.490
6.470
6.452
3.877
3.815
3.618
3.264
3.251
2.741
2.707
2.667
2.653
2.427
2.392
2.386
2.309
2.150
1.881
1.713
1.625
1.460
1.426
1.392
1.161
1.133
1.128
1.099

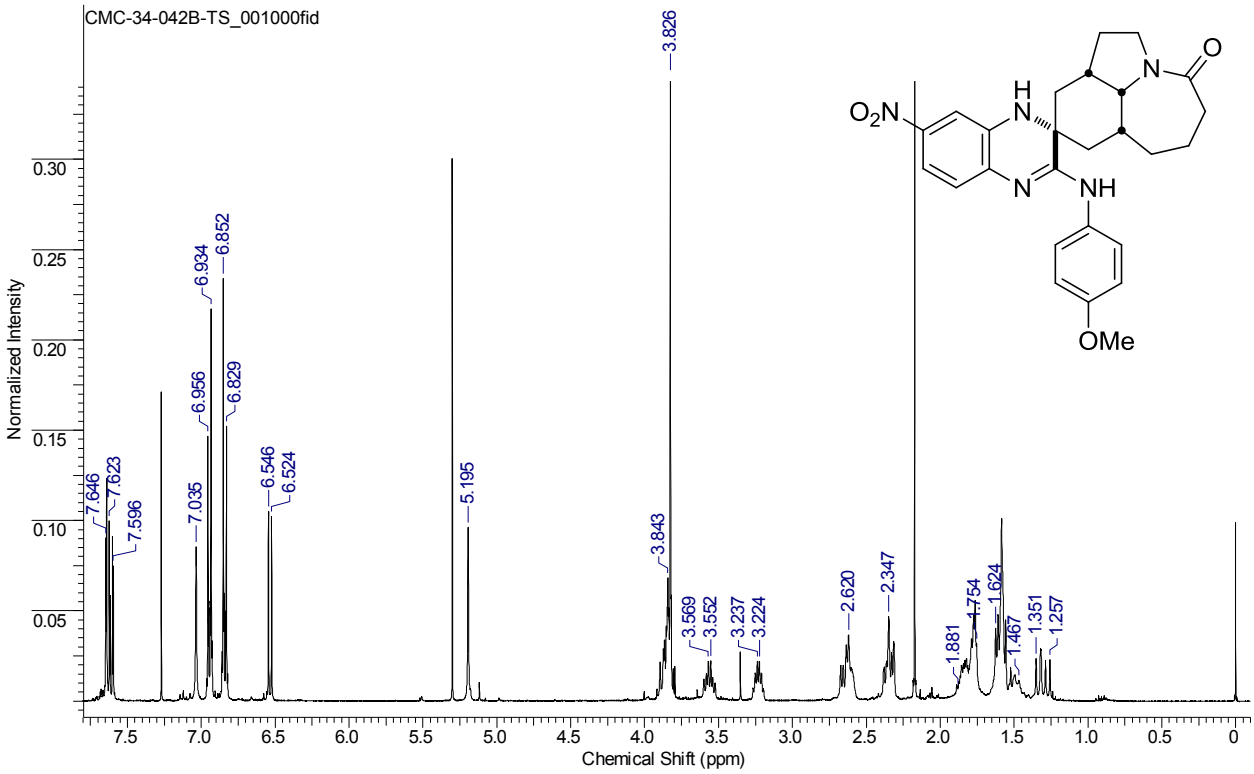

CMC-34-76-D1_003000fid
Normalized Intensity
Chemical Shift (ppm)
175.387
151.036
146.419
132.443
129.477
126.626
131.207
127.143
123.441
122.394
120.693
119.617
114.941
113.771
55.710
47.348
39.379
36.855
35.634
34.201
28.857
18.343
60.931
40.092
33.467
18.190

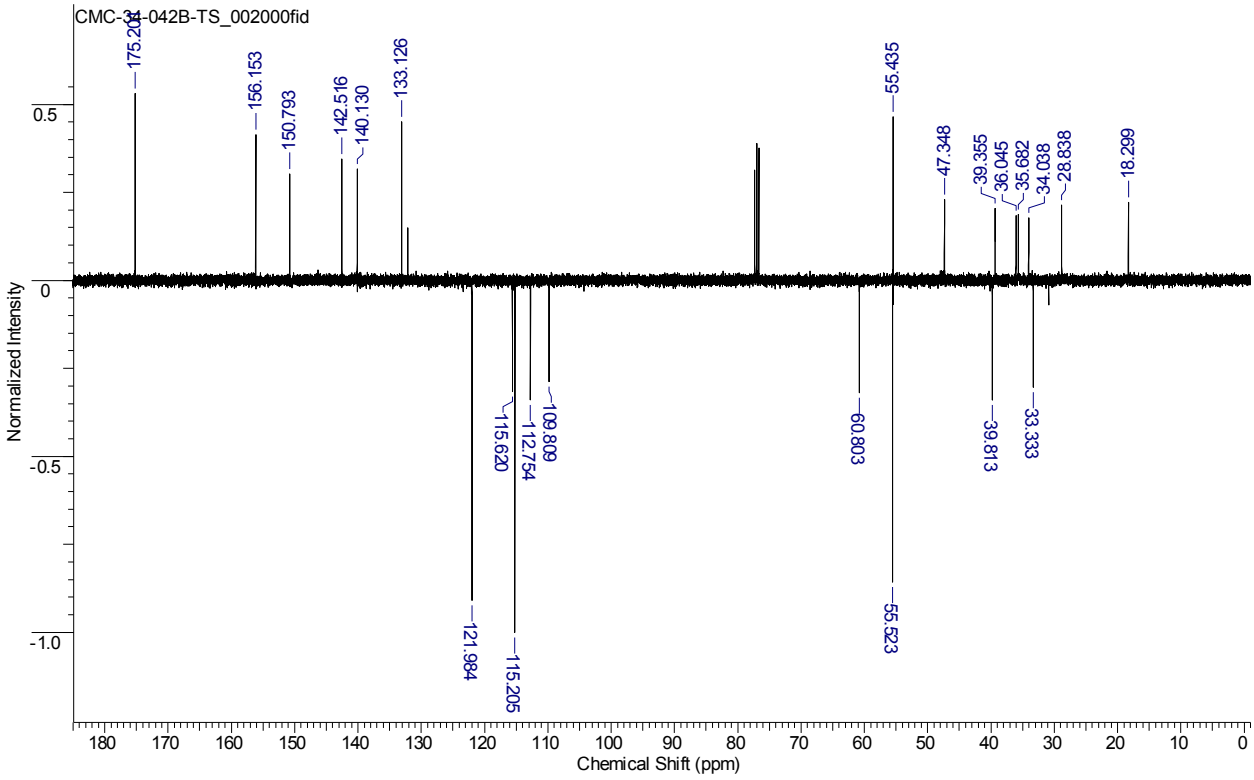

CMC-34-76-D3_001000fid
Normalized Intensity
Chemical Shift (ppm)
7.240
7.203
7.028
7.009
6.784
6.647
6.621
6.505
6.500
6.457
3.852
3.822
3.607
3.577
3.561
3.245
3.232
2.728
2.635
2.406
2.273
2.138
1.883
1.754
1.707
1.529
1.476
1.395
1.158
1.129
1.094

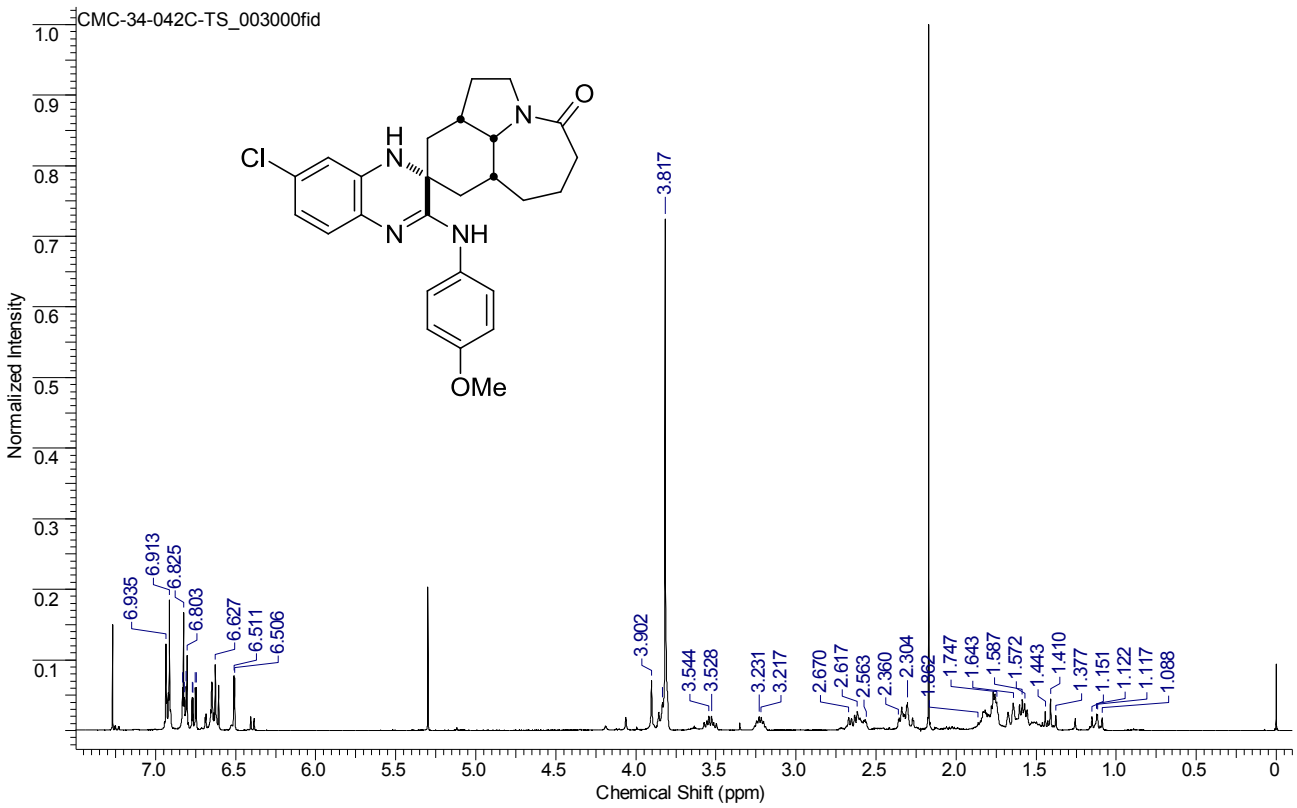

CMC-34-76-D3_003000fid
Normalized Intensity
Chemical Shift (ppm)
175.407
154.204
146.082
141.428
131.125
129.343
124.319
131.336
127.249
123.759
122.028
120.523
115.695
113.783
55.765
47.382
39.398
36.766
35.646
28.862
18.369
60.892
41.063
40.052
33.486

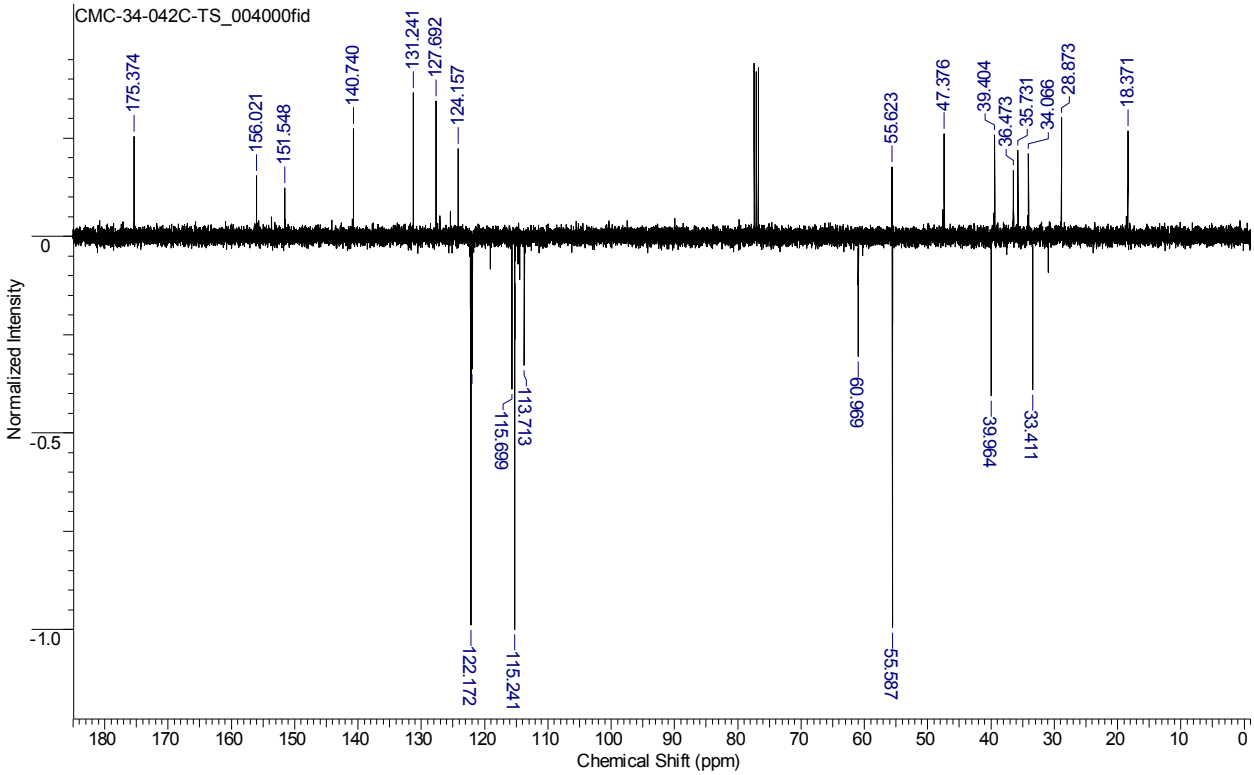

CMC-34-76-D5_001000fid
Normalized Intensity
Chemical Shift (ppm)
7.242
7.224
7.188
7.004
7.001
6.813
6.794
6.494
6.347
6.289
3.848
3.818
3.578
3.562
3.256
3.243
2.678
2.644
2.623
2.408
2.379
2.373
2.302
2.144
2.135
2.091
1.824
1.615
1.426
1.392
1.360
1.137
1.103
1.073

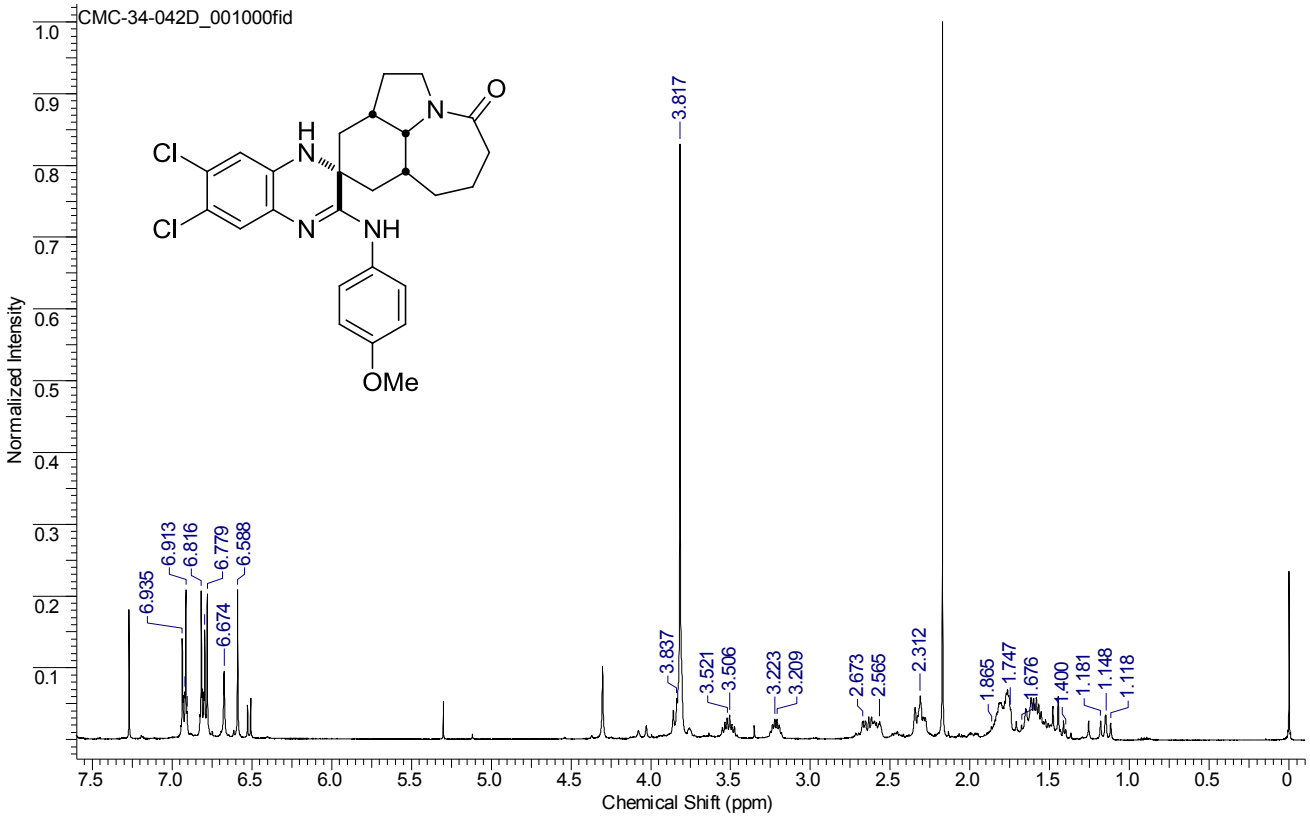

CMC-34-76-D5_002000fid
Normalized Intensity
Chemical Shift (ppm)
175.421
151.346
146.678
130.390
129.510
127.634
124.559
55.802
47.382
39.420
36.860
35.690
34.075
28.920
18.399
131.197
127.147
123.359
120.821
116.451
115.135
61.052
40.110
33.501
19.242
18.209

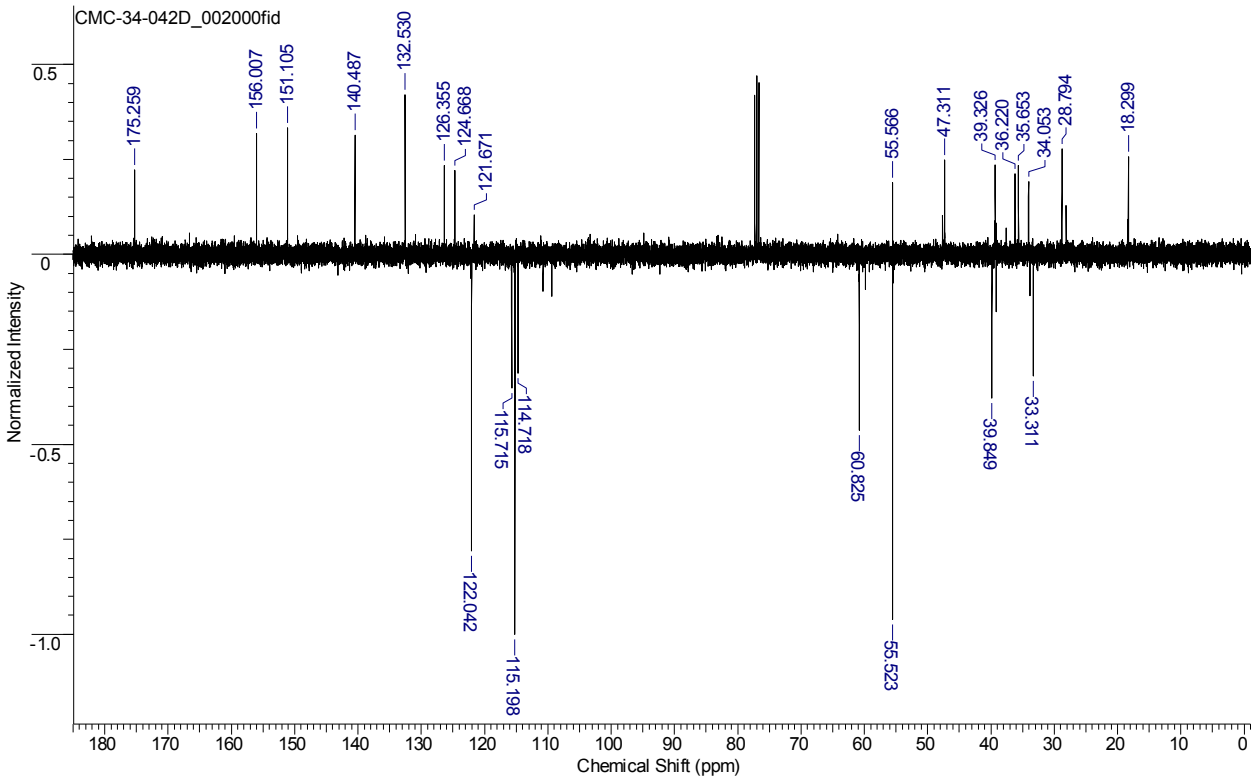

CMC-34-042B-TS_001000fid
Normalized Intensity
Chemical Shift (ppm)
3.826
6.934
6.852
6.956
6.829
6.546
6.524
7.646
7.623
7.596
7.035
5.195
3.843
3.569
3.552
3.237
3.224
2.620
2.347
1.881
1.754
1.624
1.467
1.351
1.257
O2N
H
N
N
NH
N
O
OMe

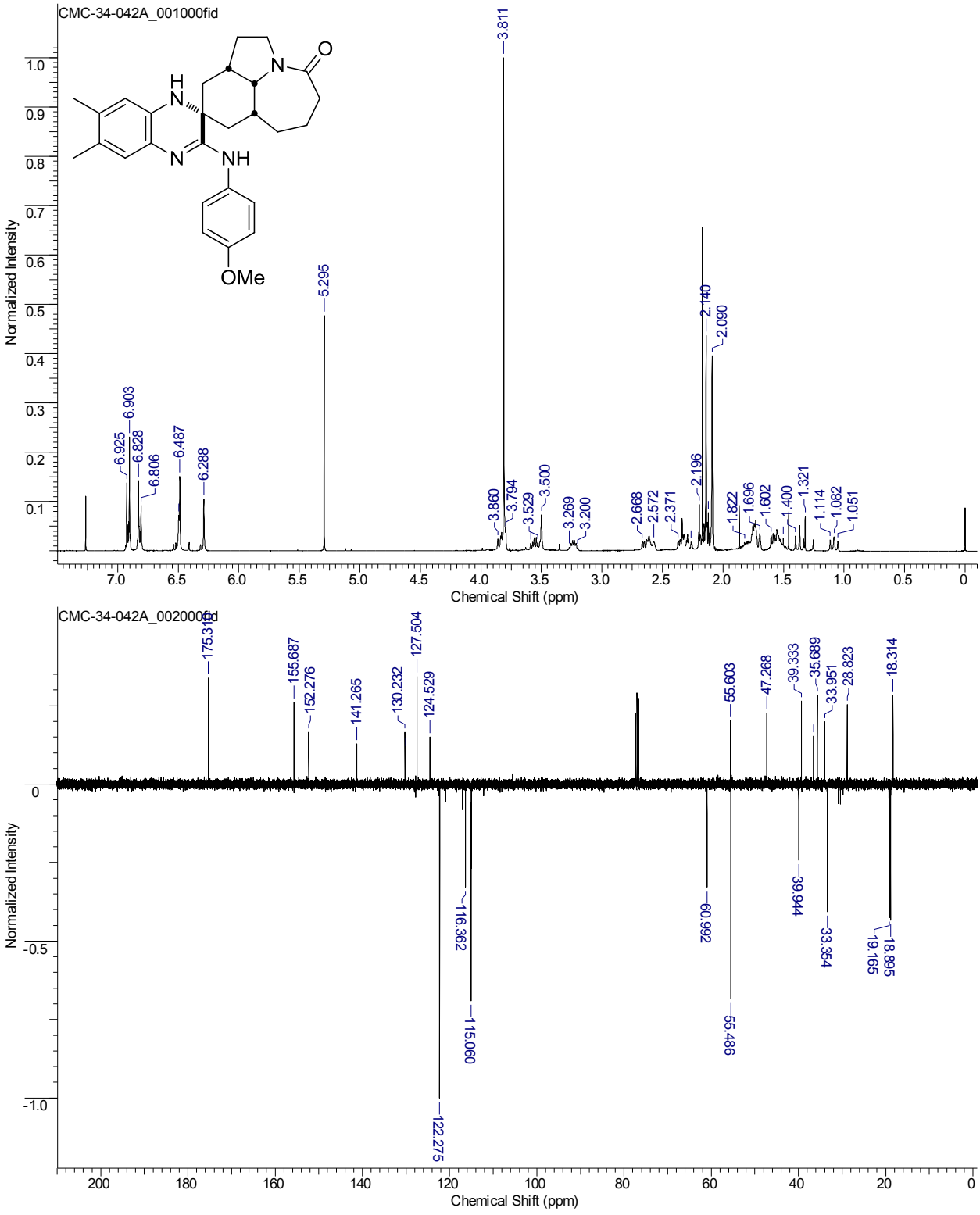

CMC-34-042B-TS_002000fid
Normalized Intensity
Chemical Shift (ppm)
175.204
156.153
150.793
142.516
140.130
133.126
55.435
47.348
39.355
36.045
35.682
34.038
28.838
18.299
121.984
115.620
115.205
112.754
109.809
60.803
39.813
33.333
55.523


CMC-34-042C-TS_003000fid
Cl
H
N
N
N
NH
O
OMe
Normalized Intensity
Chemical Shift (ppm)
6.935
6.913
6.825
6.803
6.627
6.511
6.506
3.902
3.817
3.544
3.528
3.231
3.217
2.670
2.617
2.563
2.360
2.304
1.962
1.747
1.643
1.587
1.572
1.443
1.410
1.377
1.151
1.122
1.117
1.088


CMC-34-042C-TS_004000fid
Normalized Intensity
Chemical Shift (ppm)
175.374
156.021
151.548
140.740
131.241
127.692
124.157
122.172
115.699
113.713
115.241
60.969
55.623
55.587
47.376
39.404
39.364
36.473
35.731
34.066
33.411
28.873
18.371


CMC-34-042D_001000fid
Cl
Cl
H
N
N
N
NH
O
OMe
3.817
6.935
6.913
6.816
6.779
6.588
6.674
3.837
3.521
3.506
3.223
3.209
2.673
2.565
2.312
1.865
1.747
1.676
1.400
1.181
1.148
1.118
Normalized Intensity
Chemical Shift (ppm)


CMC-34-042D_002000fid
175.259
156.007
151.105
140.487
132.530
126.355
124.668
121.671
55.566
47.311
39.326
36.220
35.653
34.053
28.794
18.299
122.042
115.715
114.718
115.198
60.825
55.523
39.849
33.311
Normalized Intensity
Chemical Shift (ppm)


CMC-34-042A_001000fid
Normalized Intensity
Chemical Shift (ppm)
3.811
5.295
6.903
6.925
6.828
6.806
6.487
6.288
3.860
3.794
3.529
3.500
3.269
3.200
2.668
2.572
2.371
2.196
2.140
2.090
1.822
1.696
1.602
1.400
1.321
1.114
1.082
1.051
CMC-34-042A_002000fid
175.314
155.687
152.276
141.265
130.232
127.504
124.529
116.362
115.060
122.275
55.603
55.486
60.992
47.268
39.333
39.944
35.689
33.951
33.364
28.823
18.314
19.165
18.895

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