

Supplementary Material for:

Derivatives of the β -crinane Amaryllidaceae Alkaloid Haemanthamine as Multi-Target Directed Ligands for Alzheimer's Disease

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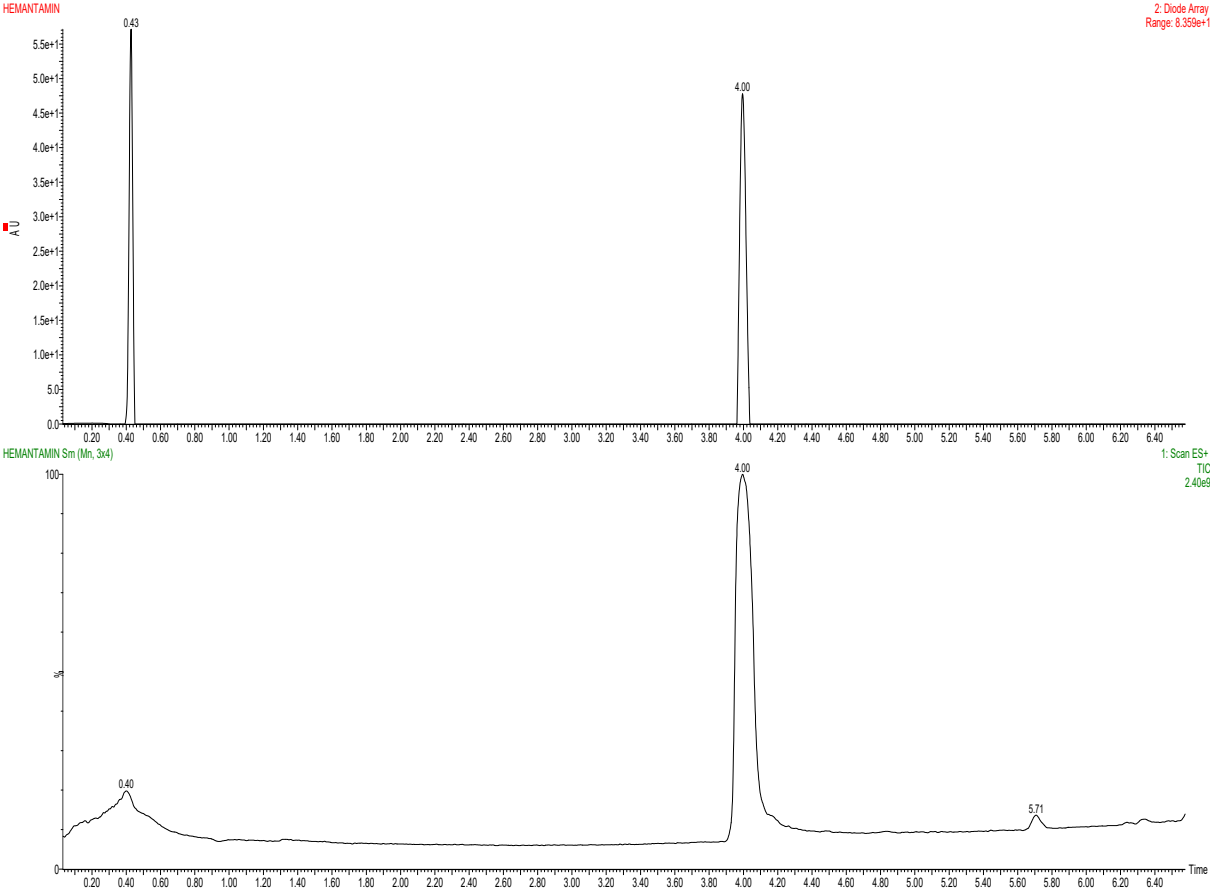
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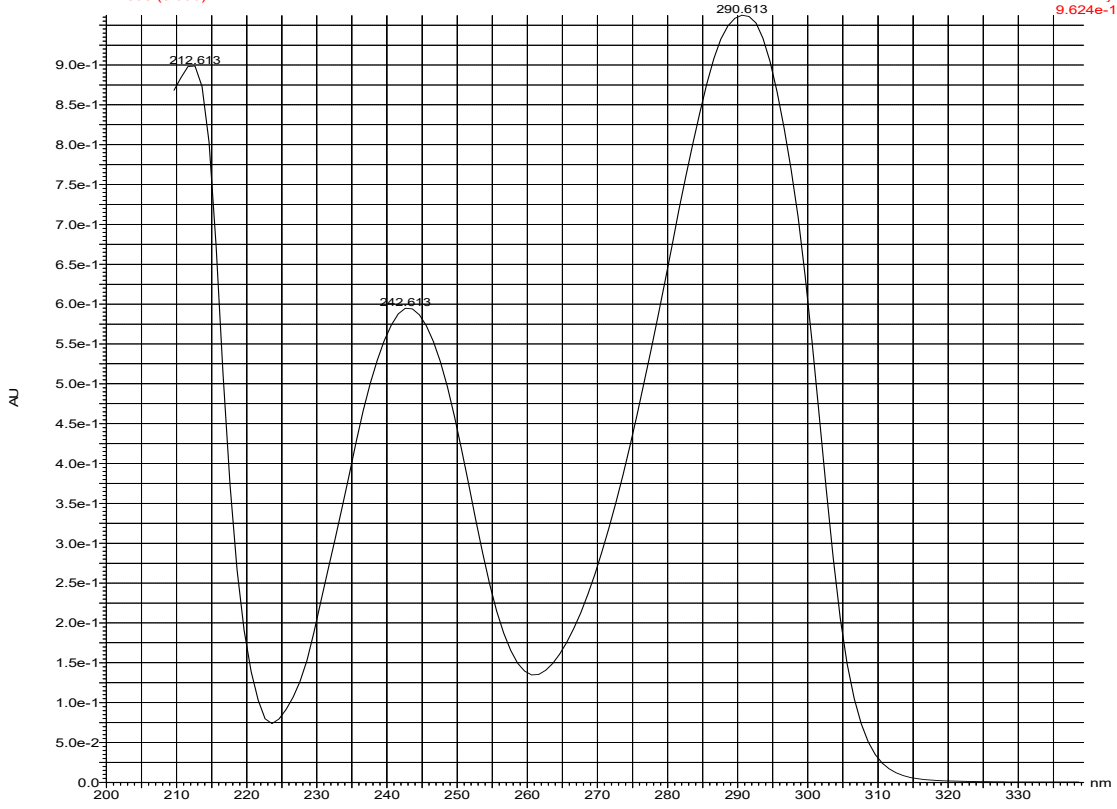
Analytical spectra of haemanthamine:

HPLC (UV/VIS)



HEMANTAMIN 2395 (3.990)

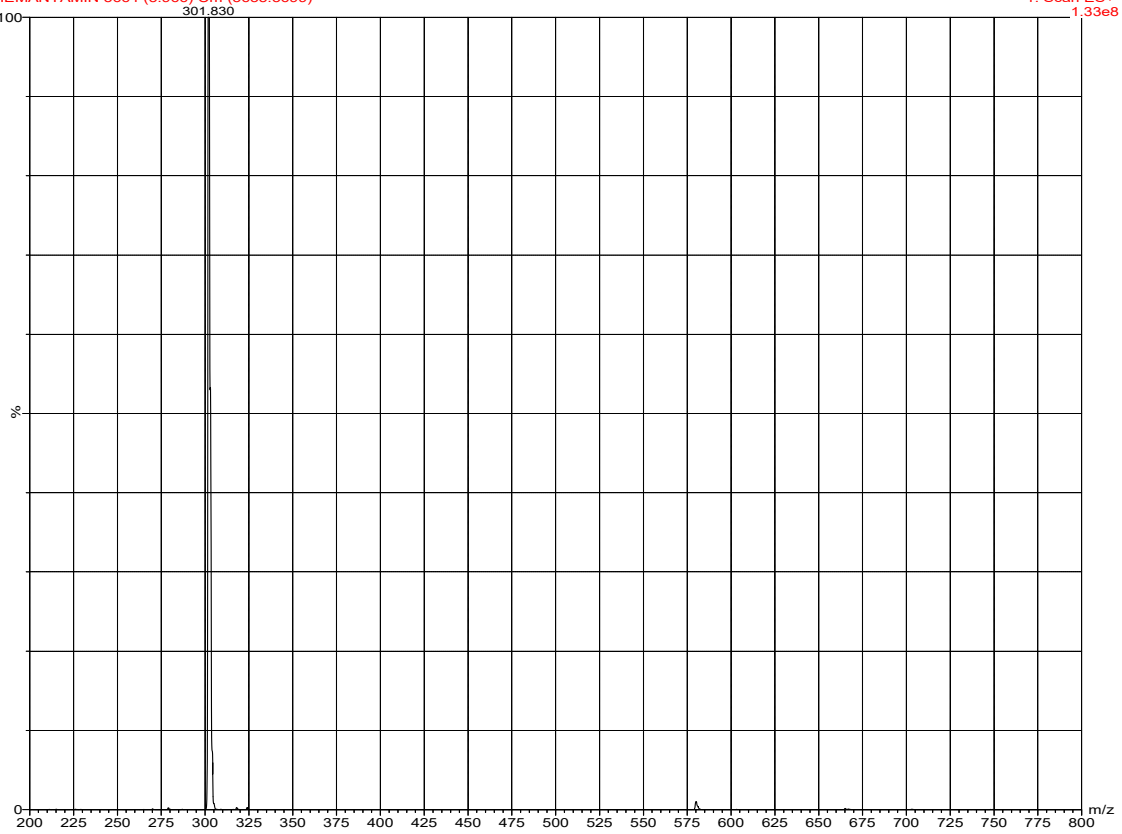
2: Diode Array
9.624e-1



HPLC/MS

HEMANTAMIN 3664 (3.966) Cm (3635:3699)

1: Scan ES+
1.33e8

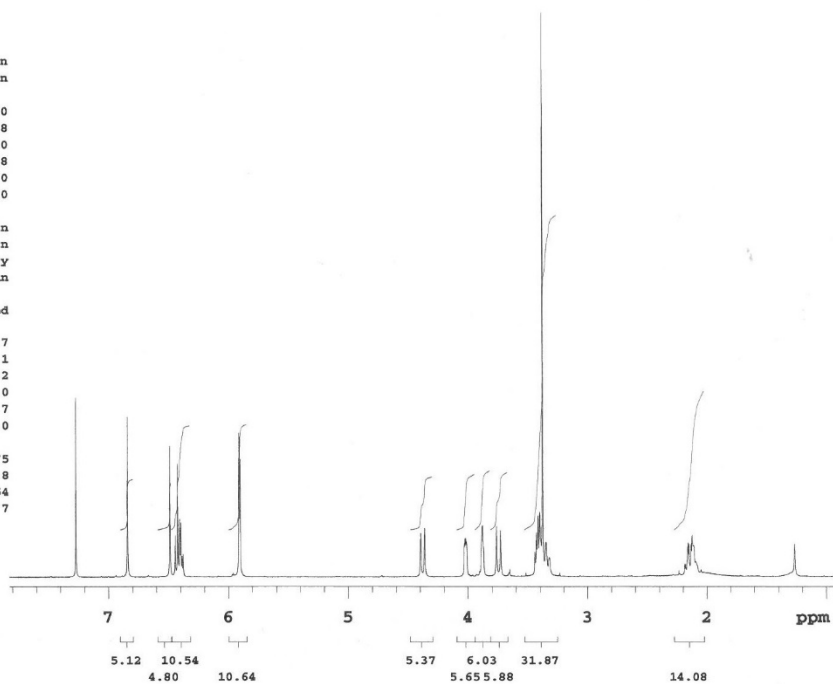


¹H-NMR

H.F.1.3

exp701 PROTON

SAMPLE		PRESATURATION	
date	Mar 14 2019	satmode	n
solvent	cdcl3	wet	n
file	exp	SPECIAL	
ACQUISITION		temp	25.0
sw	8012.8	gain	48
at	2.045	spin	20
np	32768	hst	0.008
fb	4000	pw90	8.800
bs	32	alfa	10.000
d1	1.000	FLAGS	
nt	8	il	n
ct	8	in	n
TRANSMITTER		dp	Y
tn	H1	hs	nn
sfrq		499.866	PROCESSING
tof	499.9	fn	not used
tpwr	60	DISPLAY	
pw	4.400	sp	452.7
DECOUPLER		wp	3459.1
dn	C13	rfl	1007.2
dof	0	rfp	0
dm	nnn	rp	-131.7
decwave W40_OneNMR-		lp	0
_W018		PLOT	
dpwr	37	wc	175
dmf	32258	sc	8
		vs	54
		th	7
		ai	cdc ph

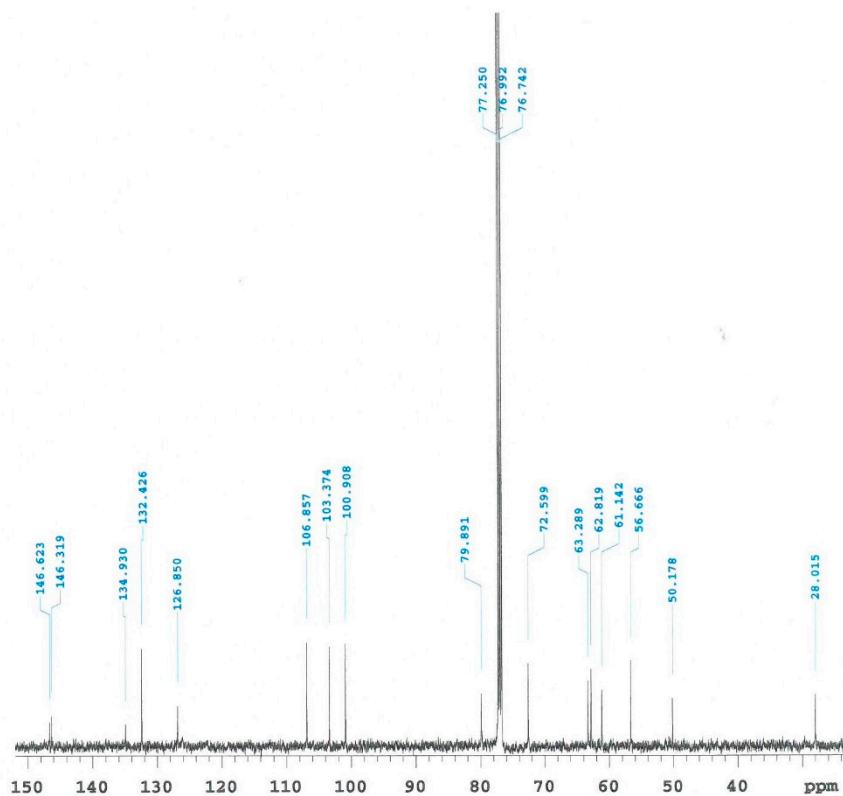


¹³C-NMR

H.F.1.3

exp701 CARBON

SAMPLE		PRESATURATION	
date	Mar 14 2019	satmode	n
solvent	cdcl3	wet	n
file	exp	SPECIAL	
ACQUISITION		temp	25.0
sw	31250.0	gain	30
at	1.049	spin	20
np	65536	hst	0.008
fb	17000	pw90	11.300
bs	1	alfa	10.000
d1	1.000	FLAGS	
nt	2500	il	n
ct	837	in	n
TRANSMITTER		dp	Y
tn	C13	hs	nn
sfrq		125.705	PROCESSING
tof	1913.9	lb	2.50
tpwr	55	fn	not used
pw	5.650	DISPLAY	
DECOUPLER		sp	2923.3
dn	H1	wp	16169.5
dof	0	rfl	11479.4
dm	yyy	rfp	9678.2
decwave		w	-125.3
dpwr	40	lp	0
dmf	10870	PLOT	
		wc	175
		sc	0
		vs	199
		th	2
		nm	cdc ph



Analytical spectra of prepared derivatives:

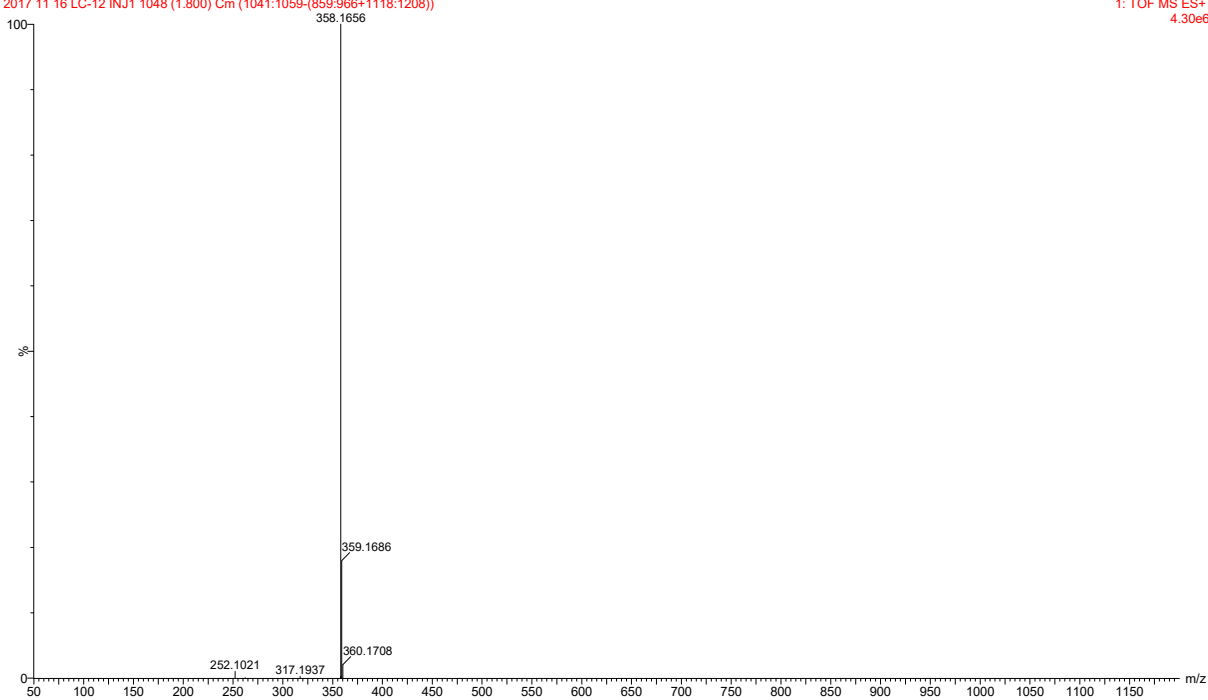
11-O-Propionylhaemanthamine (1b)

ESI-HRMS

358.1654

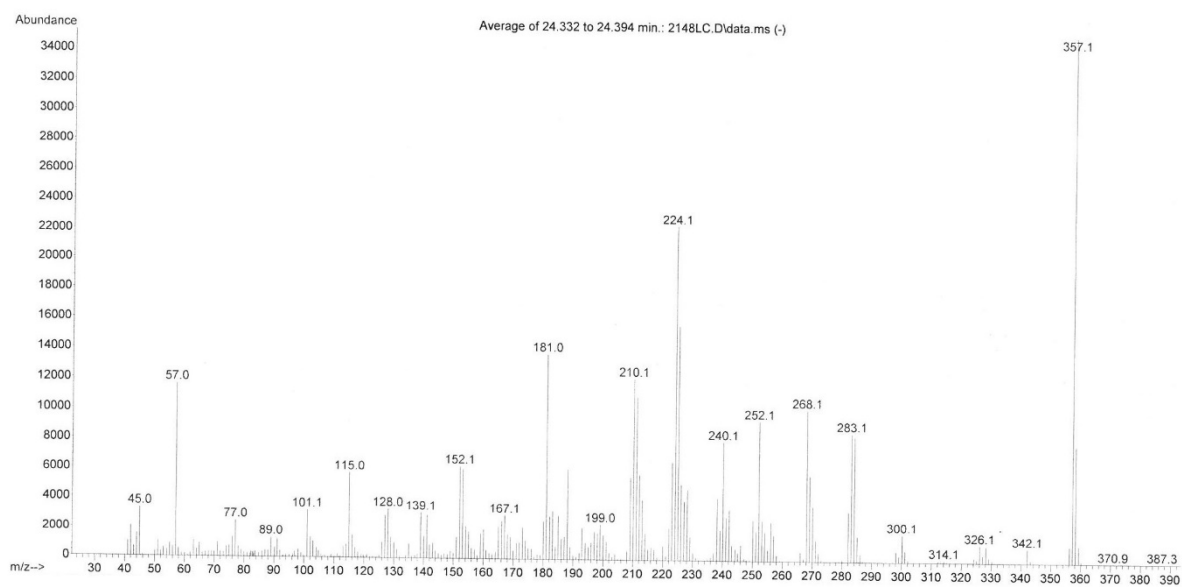
2017 11 16 LC-12 INJ1 1048 (1.800) Cm (1041:1059-(859:966+1118:1208))

1: TOF MS ES+
4.30e6



EI-MS

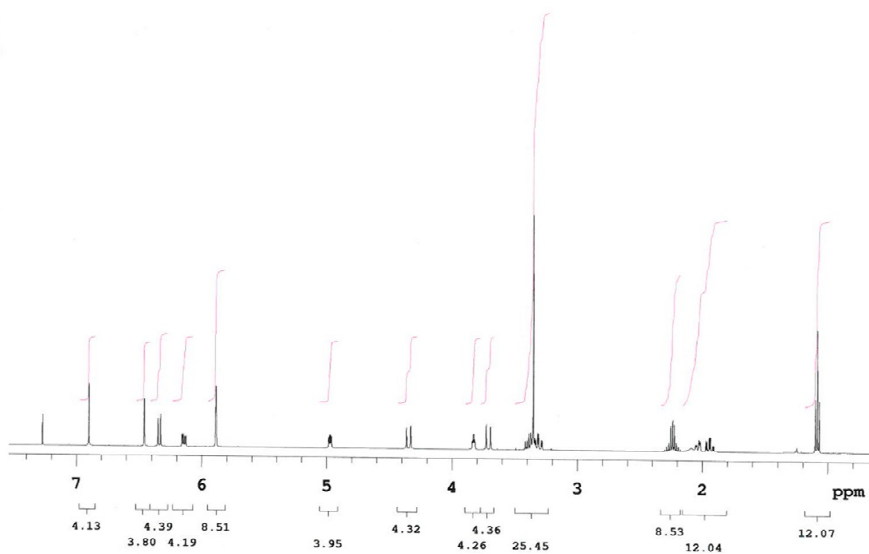
File :C:\msdchem\1\data\SNAP\2148LC.D
Operator :
Acquired : 21 Apr 2015 15:55 using AcqMethod LUCKA_7.M
Instrument : GCMS
Sample Name: LC-12
Misc Info :
Vial Number: 14



¹H-NMR

exp109 PROTON

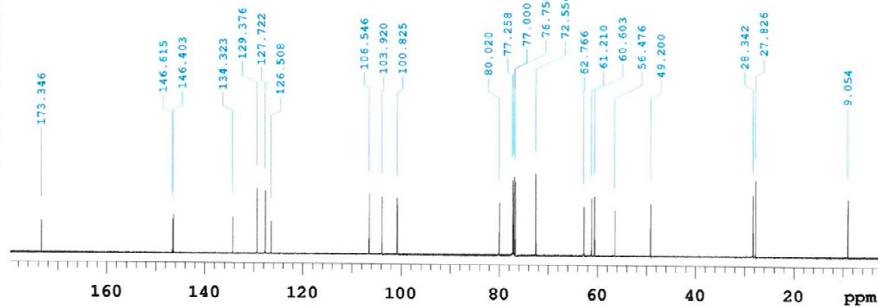
```
SAMPLE      PRESATURATION
date Aug 4 2015 satmode n
solvent cdcl3 wet n
file /home/vnmr1/v- SPECIAL
nmrsys/data/Lucie/- temp 25.0
Obmeny/LC-12/LC-12- gain 30
.H.fid spin not used
ACQUISITION het 0.008
sw 8012.8 pw90 9.100
at 2.045 alfa 10.000
np 32768 FLAGS
fb 4000 il n
bs 32 in n
dl 1.000 dp y
nt 8 hs nn
ct 8 PROCESSING
TRANSMITTER fn not used
tn H1 DISPLAY
sfrq 499.866 sp 326.5
tof 499.9 wp 3441.5
tpwr 60 rfl 1007.2
pw 4.550 rfp 0
DECOUPLER rp -163.2
dn C13 lp 0
dof 0 PLOT
dm nnn wc 190
decwave W40_OneNMR~ sc 8
_W018 vs 14
dpwr 37 th 7
dmf 32258 ai cdc ph
```



¹³C-NMR

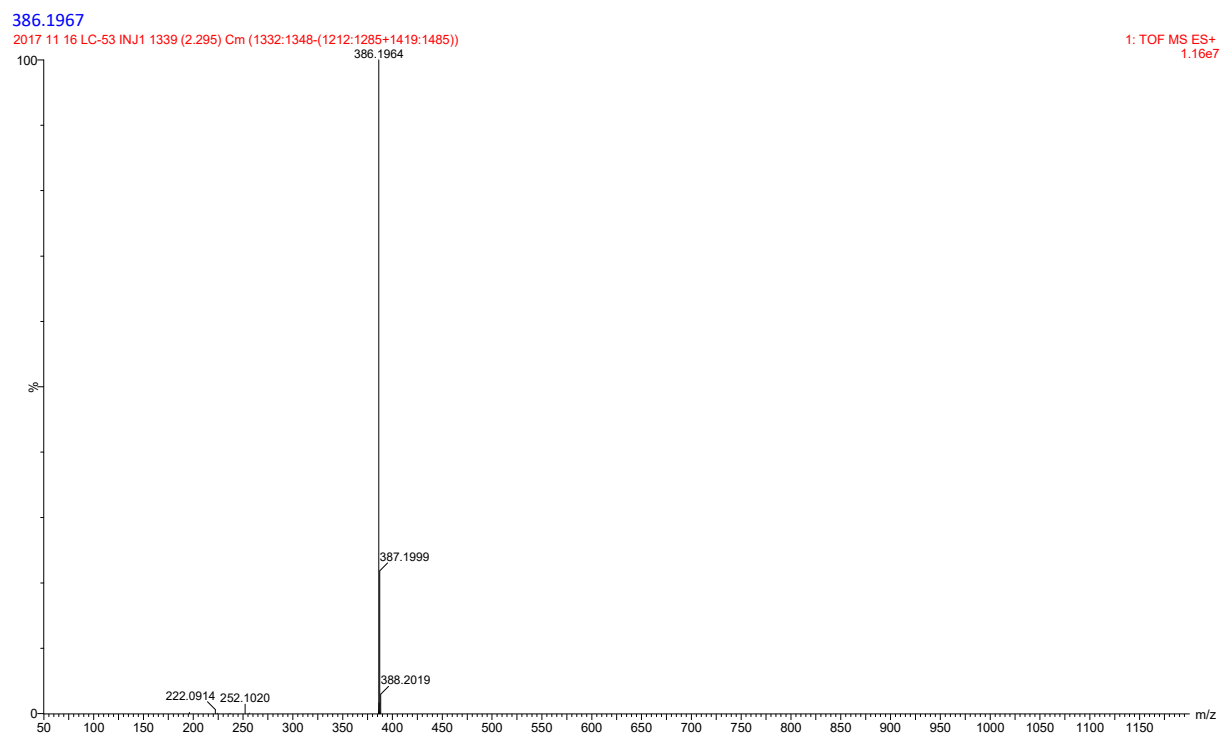
exp109 CARBON

```
SAMPLE      PRESATURATION
date Aug 4 2015 satmode n
solvent cdcl3 wet n
file /home/vnmr1/v- SPECIAL
nmrsys/data/Lucie/- temp 25.0
Obmeny/LC-12/LC-12- gain 30
.C.fid spin not used
ACQUISITION het 0.008
sw 31250.0 pw90 11.300
at 1.049 alfa 10.000
np 65536 FLAGS
fb 17000 il n
bs 1 in n
dl 1.000 dp y
nt 1500 hs nn
ct 790 PROCESSING
TRANSMITTER lb 0.50
tn C13 fn not used
sfrq 125.705 DISPLAY
tof 1913.9 sp 218.7
tpwr 55 wp 22357.9
pw 5.650 rfl 11482.2
DECOUPLER rfp 9678.2
dn H1 rp 49.3
dof 0 lp 0
dm YYY PLOT
decwave w wc 190
dpwr 41 sc 8
dmf 12346 vs 17
th 4
nm cdc ph
```



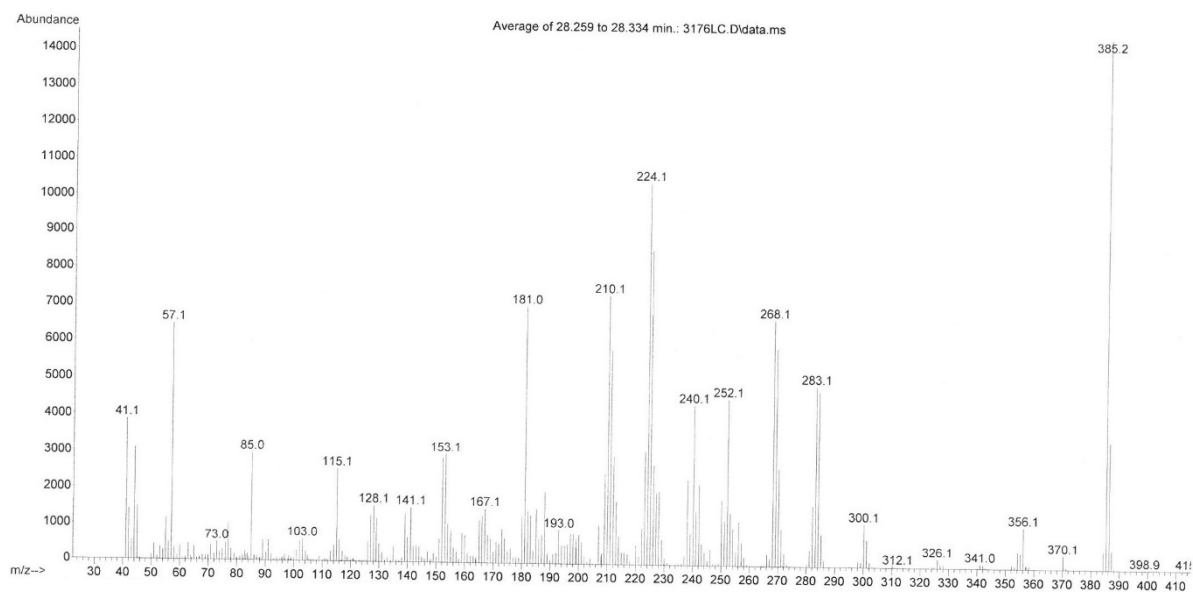
11-O-Pentanoylhaemanthamine (1d)

ESI-HRMS



EI-MS

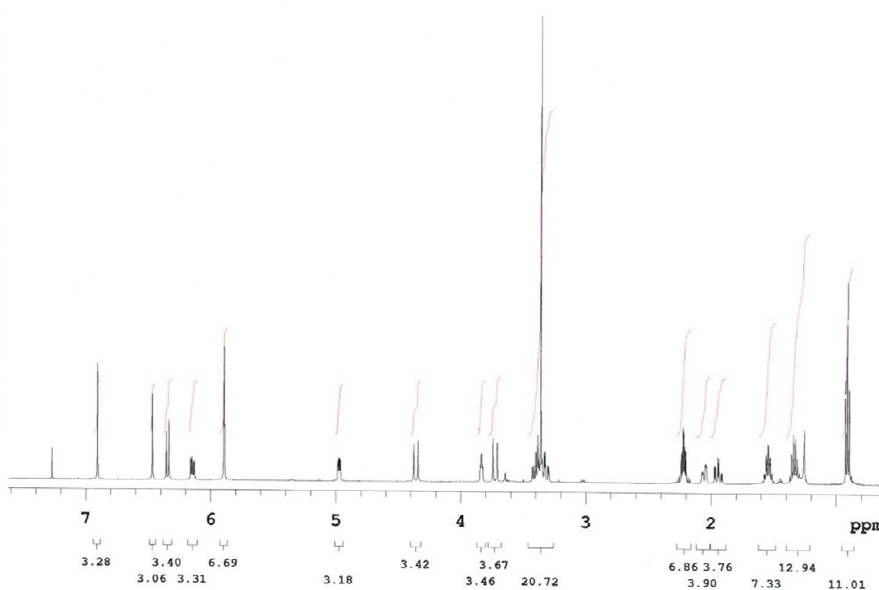
File : C:\msdchem\1\data\SNAP\3176LC.D
Operator :
Acquired : 24 Oct 2016 14:47 using AcqMethod LUCKA_7.M
Instrument : GCMS
Sample Name : LC-53
Misc Info :
Vial Number : 8



¹H-NMR

expl00 PROTON

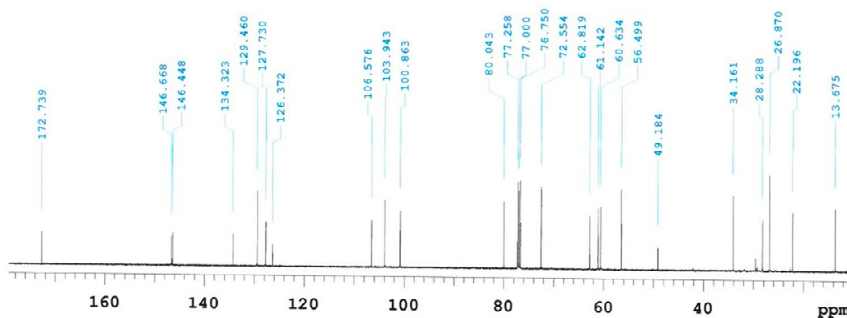
```
SAMPLE      PRESATURATION
date Apr 4 2017 satmode n
solvent cdcl3 wet n
file exp SPECIAL
ACQUISITION temp 25.0
sw 8012.8 gain 28
at 2.045 spin 20
np 32768 hat 0.008
fb 4000 pw90 9.100
bs 32 alfa 10.000
d1 1.000 FLAGS
nt 8 il n
ct 8 in n
TRANSMITTER dp y
tn H1 hs nn
sfrq 499.866 PROCESSING
tof 499.8 fn not used
tpwr 60 DISPLAY
pw 4.550 sp 284.3
DECOUPLER wp 3523.2
dn C13 rfl 1007.3
dof 0 rfp 0
dm nnn rp -160.2
decwave W40_OneNMR lp 0
          _W018 PLOT
dpwr 37 wc 190
dmf 32258 sc 8
vs 48
th 7
ai cdc ph
```



¹³C-NMR

expl00 CARBON

```
SAMPLE      PRESATURATION
date Apr 4 2017 satmode n
solvent cdcl3 wet n
file exp SPECIAL
ACQUISITION temp 25.0
sw 31250.0 gain 30
at 1.049 spin 20
np 65536 hat 0.008
fb 17000 pw90 11.300
bs 1 alfa 10.000
d1 1.000 FLAGS
nt 1500 il n
ct 750 in n
TRANSMITTER dp y
tn C13 hs nn
sfrq 125.705 PROCESSING
tof 1913.9 lb 0.50
tpwr 55 fn not used
pw 5.650 DISPLAY
DECOUPLER sp 1180.9
dn H1 wp 21351.8
dof 0 rfl 11480.3
dm yyy rfp 9678.2
decwave w rp -177.7
dpwr 40 lp 0
dmf 11173 PLOT
wc 190
sc 0
vs 21
th 3
nm odc ph
```



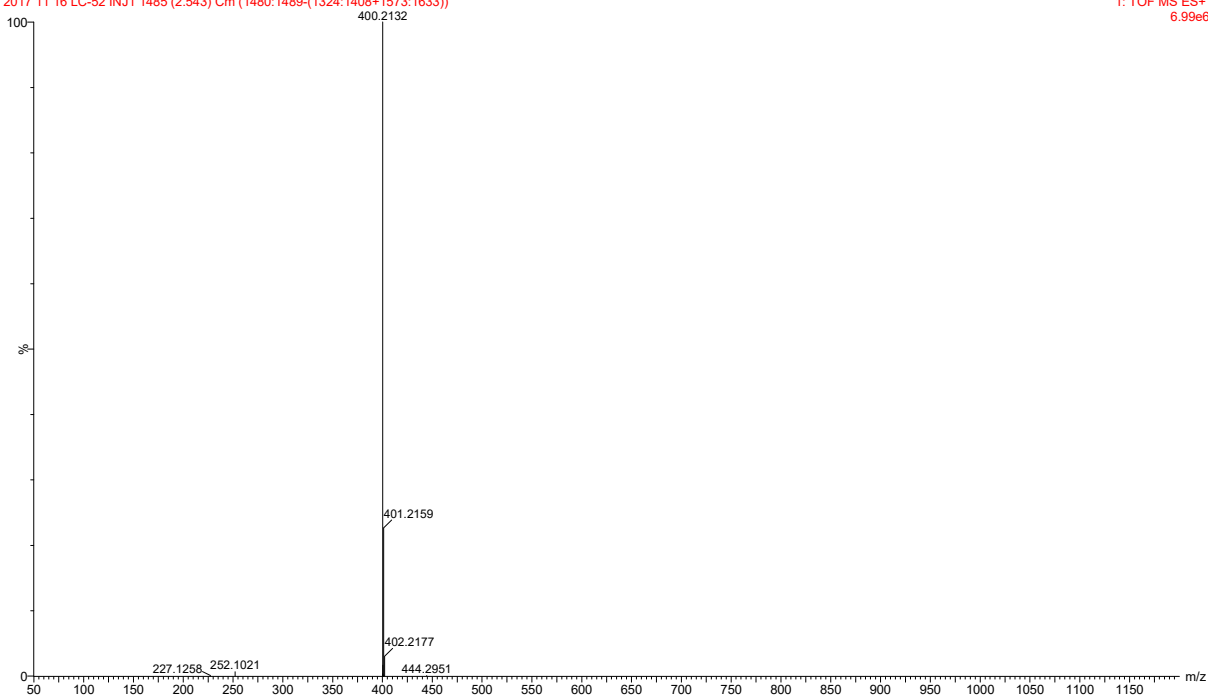
11-O-Hexanoylhaemanthamine (1e)

ESI-HRMS

400.2124

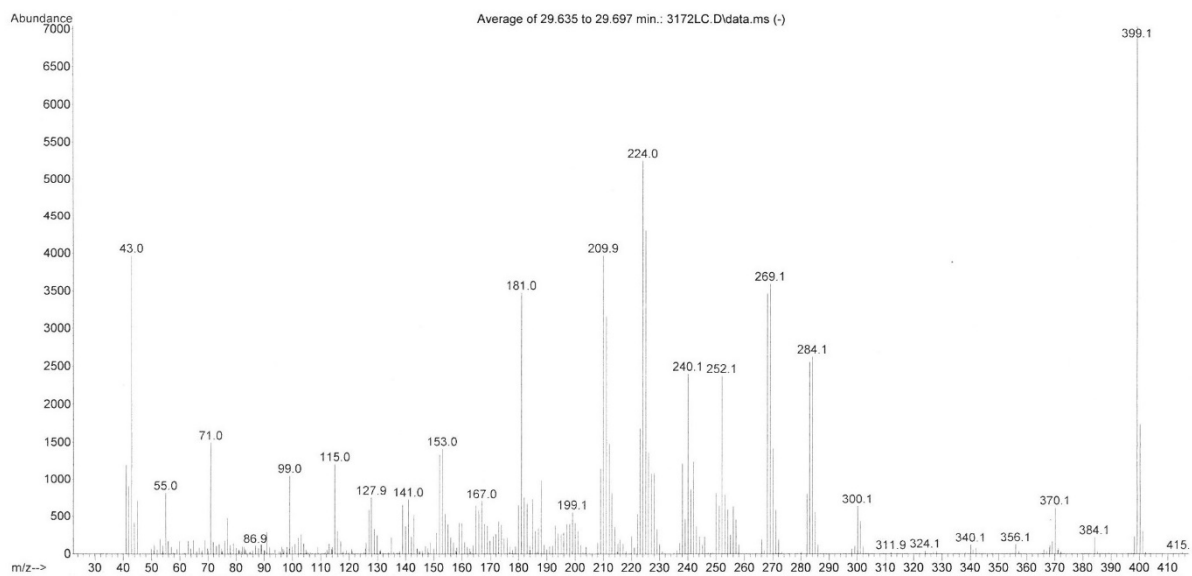
2017 11 16 LC-52 INJ1 1485 (2.543) Cm (1480:1489-(1324:1408+1573:1633))

1: TOF MS ES+
6.99e6



EI-MS

File : C:\msdchem\1\data\SNAP\3172LC.D
Operator :
Acquired : 18 Oct 2016 13:31 using AcqMethod LUCKA_7.M
Instrument : GCMS
Sample Name : LC-52
Misc Info :
Vial Number : 5

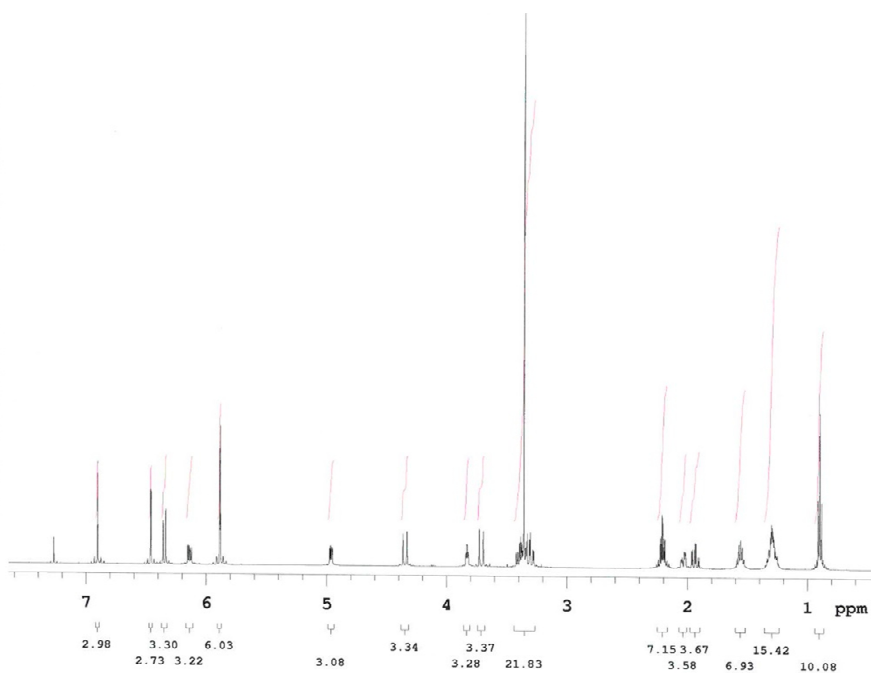


¹H-NMR

exp8 PROTON

```
SAMPLE      PRESATURATION
date Mar 21 2017 satmode n
solvent cdcl3 wet n
file /home/vnmr1/v~ SPECIAL
nmrsys/data/Lucie/~ temp 25.0
Obmeny/LC-52_H_fid gain 28
ACQUISITION spin 20
sw 8012.8 hst 0.008
at 2.045 pw90 9.100
np 32768 alfa 10.000
fb 4000
bs 32 il n
dl 1.000 in n
nt 8 dp y
ct 8 hs nn

TRANSMITTER PROCESSING
tn H1 fn not used
sfrq 499.866 DISPLAY
tof 499.9 sp 223.3
tpwr 60 wp 3600.0
pw 4.550 rfl 1007.2
DECOUPLER rfp 0
dn C13 rp 161.8
dof 0 lp 0
dm nnn PLOT
decwave W40_OneNMR- wc 190
_M018 sc 8
dpwr 37 vs 34
dmf 32258 th 7
ai cdc ph
```

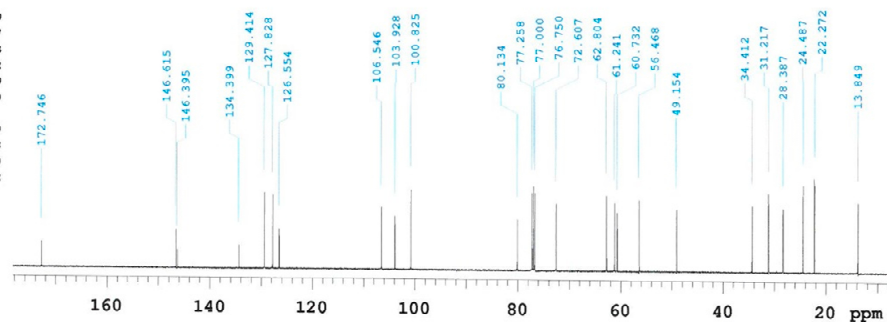


¹³C-NMR

exp8 CARBON

```
SAMPLE      PRESATURATION
date Mar 21 2017 satmode n
solvent cdcl3 wet n
file /home/vnmr1/v~ SPECIAL
nmrsys/data/Lucie/~ temp 25.0
Obmeny/LC-52_C_fid gain 30
ACQUISITION spin 20
sw 31250.0 hst 0.008
at 1.049 pw90 11.300
np 65536 alfa 10.000
fb 17000
bs 1 il n
dl 1.000 in n
nt 1000 dp y
ct 703 hs nn

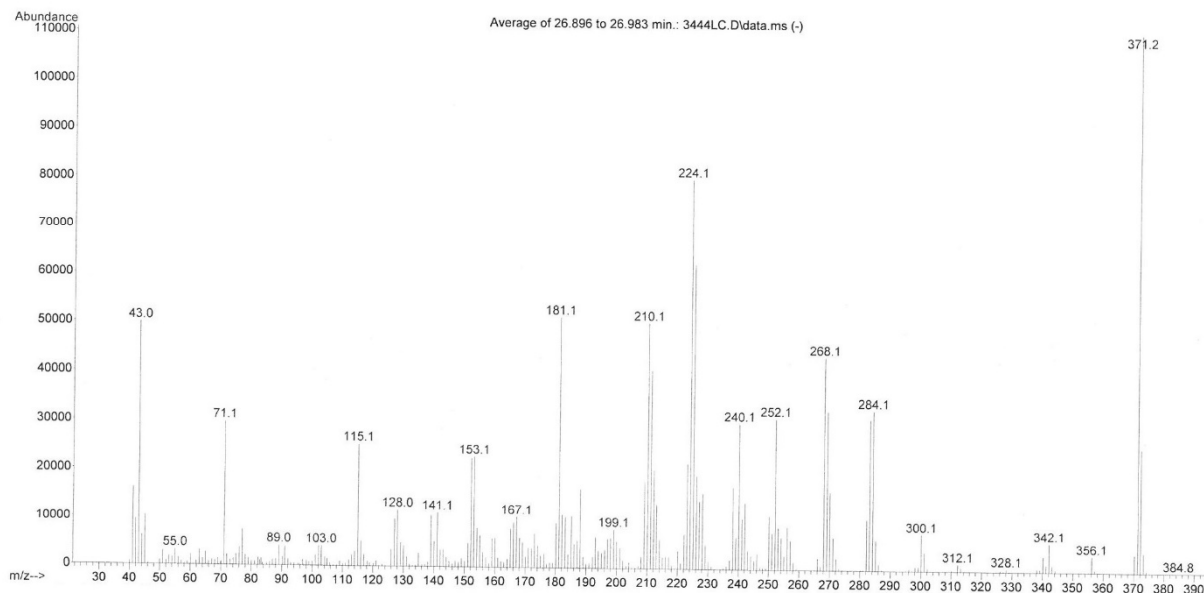
TRANSMITTER PROCESSING
tn C13 lb 0.50
sfrq 125.705 fn not used
tof 1913.9 DISPLAY
tpwr 55 sp 955.9
pw 5.650 wp 21457.7
DECOUPLER rfl 11481.3
dn H1 rfp 9678.2
dof 0 rp 133.9
dm vvy lp 0
decwave w PLOT
dpwr 40 wc 190
dmf 11173 sc 8
vs 20
th 2
nm odc ph
```



11-O-Butanoylhaemanthamine (1f)

EI-MS

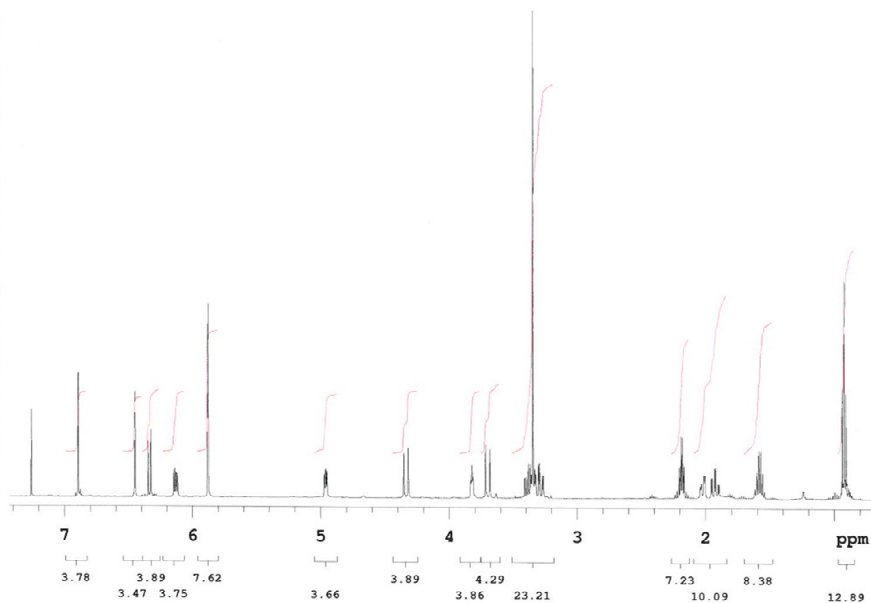
File :C:\msdchem\1\data\SNAP\3444LC.D
Operator : Lucka
Acquired : 24 Mar 2017 13:19 using AcqMethod LUCKA_7.M
Instrument : GCMS
Sample Name: JM-1
Misc Info :
Vial Number: 8



¹H-NMR

exp9 PROTON

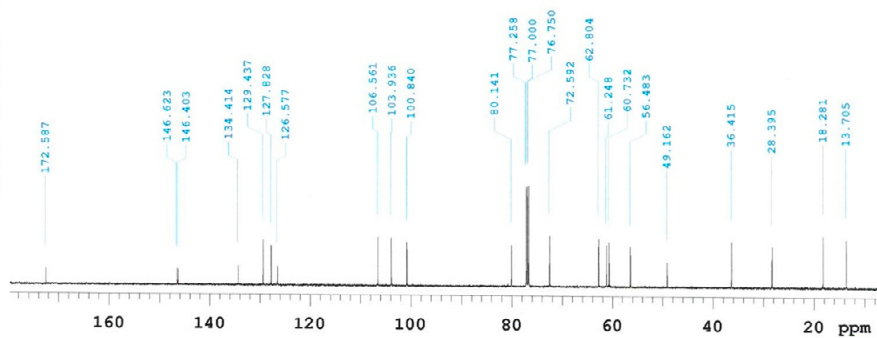
```
SAMPLE      PRESATURATION
date Nov 10 2015 satmode n
solvent cdcl3 wet n
file /home/vnmr1/v- SPECIAL
nmrsys/data/Zalohy- temp 25.0
/Hrabalek-160825/N- gain 30
emecek_Jan/Botanic- spin not used
a/JM-1_H_fid hat 0.008
ACQUISITION pw90 9.100
sw 8012.8 alfa 10.000
at 2.045
np 32768 il
fb 4000 in
bs 32 dp
dl 1.000 hs
nt 8
ct 8 fn not used
PROCESSING
TRANSMITTER DISPLAY
tn H1 sp 340.5
sfrq 499.866 wf 3372.1
tof 499.9 rfl 4642.7
tpwr 60 rfp 3629.0
pw 4.550 rp 1.8
DECOUPLER lp 0
dn C13
dof 0 wc 190
dm nnn sc 8
decwave W40_OneNMR- vs 59
_W018 th 7
dpwr 37 ai cdc ph
dmf 32258
```



¹³C-NMR

exp9 CARBON

SAMPLE		PRESATURATION	
date	Nov 10 2015	satmode	n
solvent	cdcl3	wet	n
file	/home/vnmr1/v-	SPECIAL	
nmrsys/data/Zalchy-		temp	25.0
/Hrabalek-160825/N-		gain	30
emecek_Jan/Botank-		spin	not used
a/JM-1.C.fid		hst	0.008
ACQUISITION		pw90	11.300
sw	31250.0	alfa	10.000
at	1.049	ELAGS	
np	65536	il	n
fb	17000	in	n
bs	1	dp	y
d1	1.000	hs	nn
nt	1000	PROCESSING	
ct	345	lb	1.00
TRANSMITTER		fn	not used
tn	C13	DISPLAY	
sfrq	125.705	sp	934.9
tof	1913.9	wp	21648.4
tpwr	55	rfl	11480.3
pw	5.650	rfl	9678.2
DECOUPLER		rp	-183.6
dn	H1	lp	0
dof	0	PLOT	
dm	yyy	wc	190
decwave	w	sc	8
dpwr	41	vs	22
dmf	12346	th	2
	nm	cdc	ph



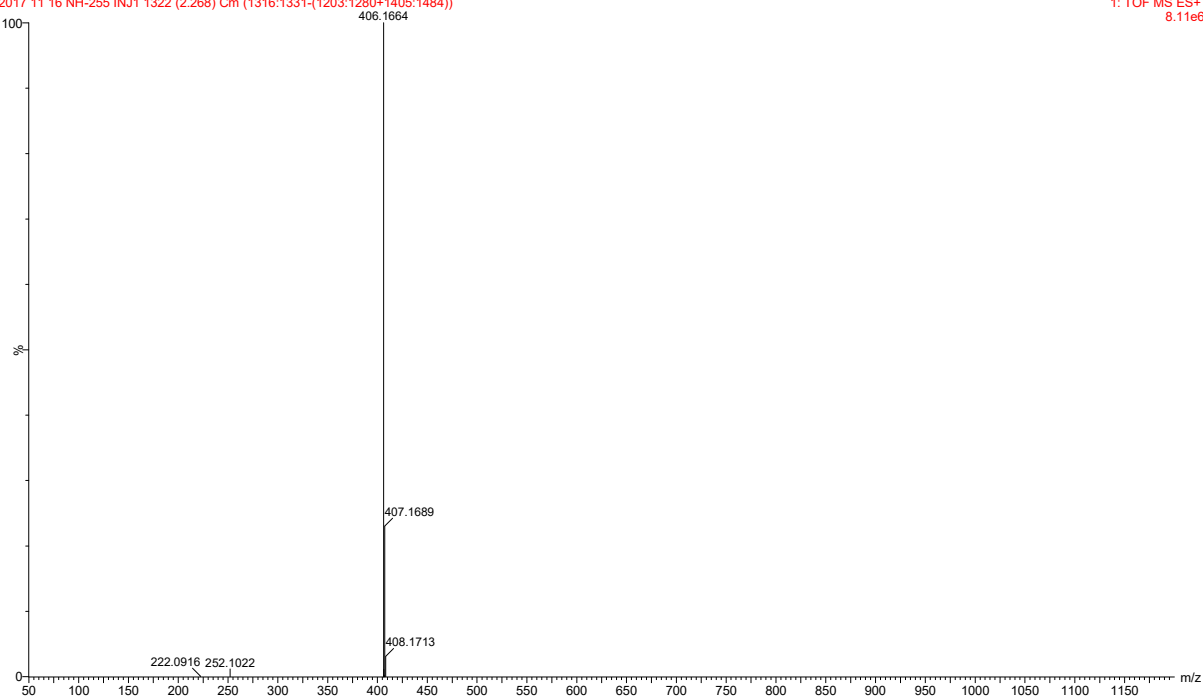
11-O-Benzoylhaemanthamine (1g)

ESI-HRMS

406.1654

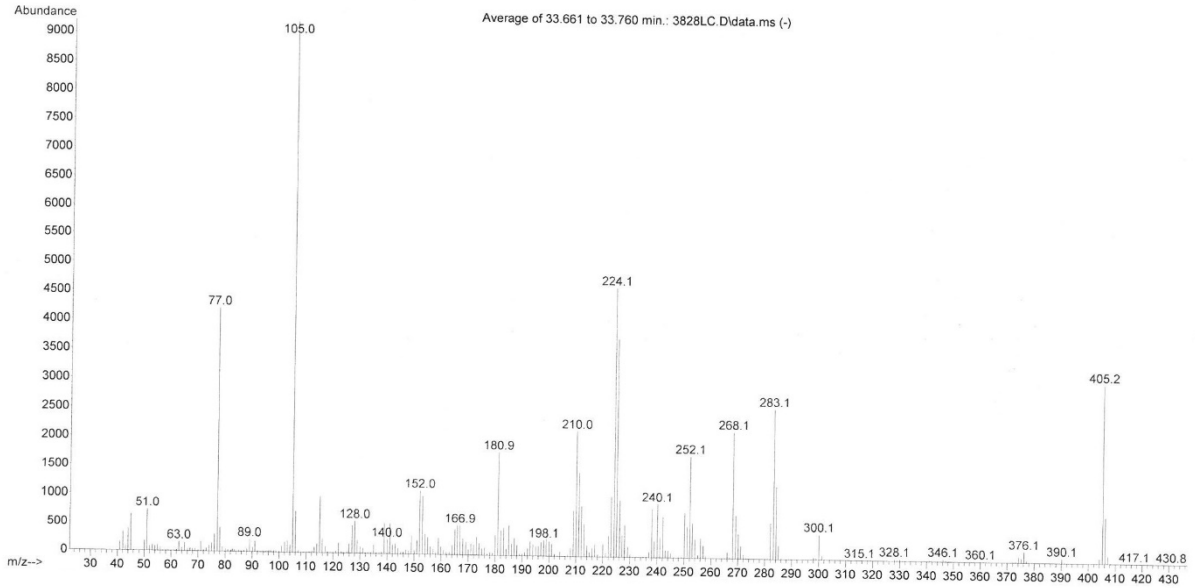
2017 11 16 NH-255 INJ1 1322 (2.268) Cm (1316:1331-(1203:1280+1405:1484))

1: TOF MS ES+
8.1166



EI-MS

File : C:\msdchem\1\data\SNAP\3828LC.D
Operator : Lucka
Acquired : 17 Jan 2018 10:14 using AcqMethod LUCKA_7.M
Instrument : GCMS
Sample Name: LC-118
Misc Info :
Vial Number: 13



¹H-NMR

exp39 PROTON

SAMPLE		PRESATURATION	
date	Jan 23 2018	satmode	n
solvent	cdcl3	wet	n
file	/home/vmr1/v-nmr/sys/data/Lucie/-	SPECIAL	temp 25.0
Obmeny/LC-118_Ha.f-	gain	24	
	id	spin	20

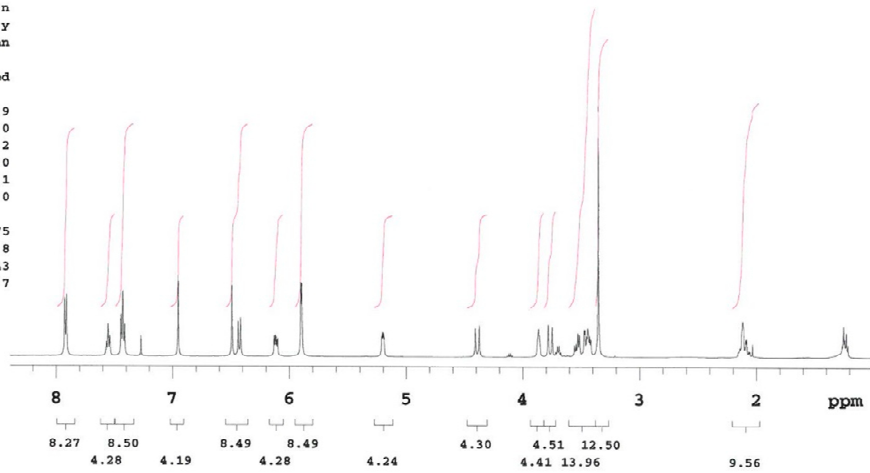
ACQUISITION			
sw	8012.8	hst	0.008
at	2.045	pw90	8.700
np	32768	alfa	10.000

FLAGS			
fb	4000	il	n
bs	32	in	n
d1	1.000	dp	y
nt	8	hs	nn
ct	8		

TRANSMITTER		PROCESSING	
tn	H1	fn	not used

DISPLAY			
sfrq	499.866	sp	507.9
tof	499.9	wp	3689.0
tpwr	60	rf1	1007.2
pw	4.350	rpf	0

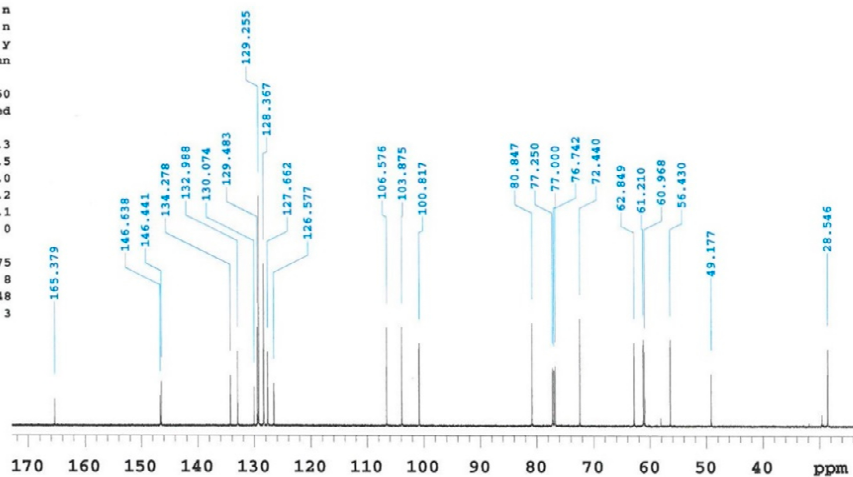
DECOUPLER		PLOT	
dn	C13	lp	0
dof	0		
dm	nnn	wc	175
decwave	W40_OneNMR-	sc	8
	_W018	vs	43
dpwr	37	th	7
dmf	32258	ai	cdc ph



¹³C-NMR

exp39 CARBON

SAMPLE		PRESATURATION	
date	Jan 23 2018	satmode	n
solvent	cdcl3	wet	n
file	/home/vmml/v-nmr/sys/data/lacie/-	SPECIAL	
Olmeny/LC-118_Ca.f-	gain	25.0	
id	spin	30	
20			
ACQUISITION		FLAGS	
sw	31250.0	hst	0.008
at	1.049	pw90	11.300
np	65536	alfa	10.000
fb	17000	il	n
bs	1	in	n
dl	1.000	dp	y
nt	1000	hs	nn
ct	565		
TRANSMITTER		PROCESSING	
tn	C13	lb	0.50
sfrq	125.705	fn	not used
tof	1913.9	sp	2964.3
pwpr	55	wp	18764.5
tpw	5.650	rfl	11488.0
DECOUPLER		rfp	
dn	H1	rp	-168.1
dof	0	lp	0
dm	yyy		
PLOT			
decwave	w	wc	175
dpwr	40	sc	8
dmf	11050	vs	48
		th	3
		nm	cdc ph



11-O-(3-chlorobenzoyl)haemanthamine (1h)

ESI-HRMS

440.1265

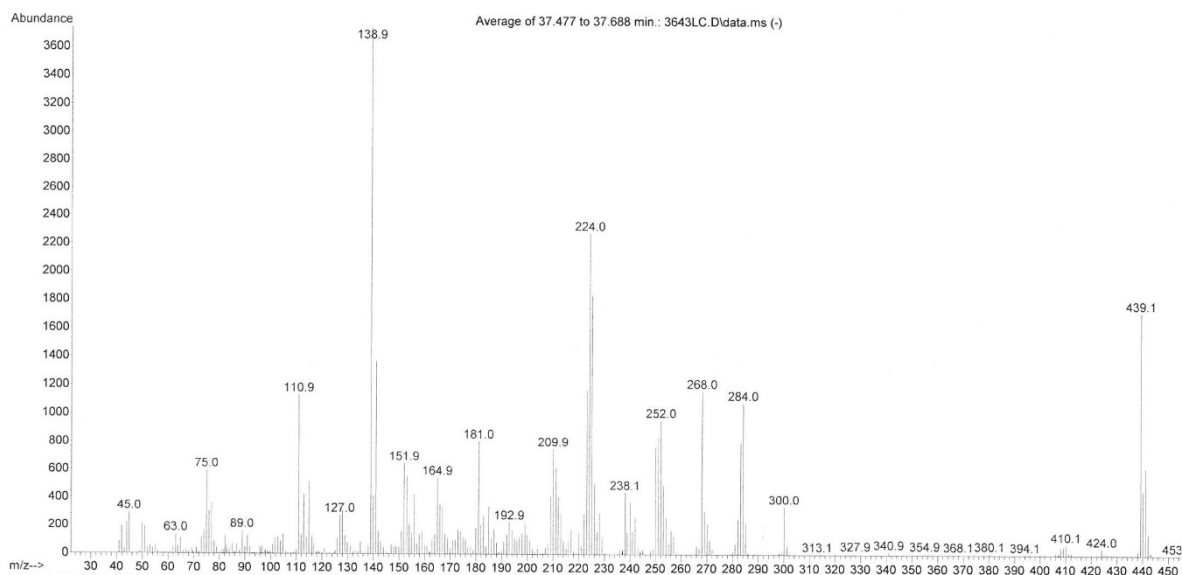
2017 11 16 NH-257 INJ1 1486 (2.548) Cm (1481:1497-(1290:1426+1565:1644))

1: TOF MS ES+
5.07e6



EI-MS

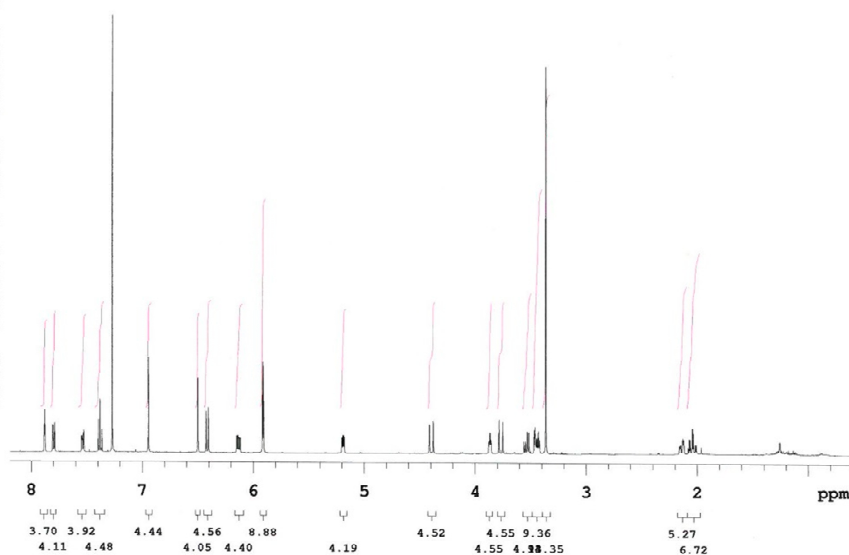
File :C:\msdchem\1\data\SNAP\3643LC.D
Operator :
Acquired : 19 Oct 2017 13:55 using AcqMethod LUCKA_7.M
Instrument : GCMS
Sample Name: LC-91
Misc Info :
Vial Number: 12



¹H-NMR

exp109 PROTON

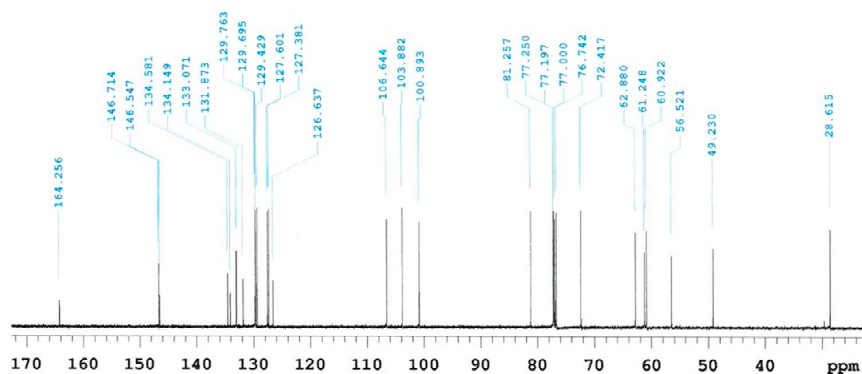
SAMPLE		PRESATURATION	
date	Mar 2 2016	satmode	n
solvent	cdcl3	wet	n
file	/home/vrmr1/v-	SPECIAL	
nmrsys/data/Zalohy-	temp	25.0	
/2016/Hrabalek-160-	gain	30	
825/Nemocek Jan/Bo-	spin	not used	
tanika/HN-257-B2_H-	ht	0.008	
	fid	pw90	9.100
	acq	aifa	10.000
ACQUISITION			
sw	8012.8	FLAGS	
at	2.045	il	n
np	32768	in	n
fb	4000	dp	y
bs	32	hs	nn
d1	1.000	PROCESSING	
nt	8	fn	not used
ct	8	DISPLAY	
TRANSMITTER			
tn	H1	wp	3808.8
sfrq	499.866	rfl	1007.2
tof	499.9	rfp	0
tpwr	60	rp	30.5
pw	4.550	lp	0
DECOUPLER			
dn	C13	wc	190
dof	0	sc	8
dm	nnn	vs	24
decwave	W40_OneNMR-	th	7
	_W018	ai	cdc
dpwr	37	ph	
dmf	32258		



¹³C-NMR

exp109 CARBON

```
SAMPLE          PRESATURATION
date   Mar 2 2016  satmode      n
solvent cdcl3      wet         n
file /home/vnmr1/v- SPECIAL
nmrsys/data/Zalohy- temp      25.0
/2016/Hrabalok-160- gain      30
825/Namecek-Jan/Bo- spin      not used
tanika/RN-257-B2_C- hst       0.008
.fid pw90         11.300
ACQUISITION     alfa         10.000
sw 31250.0      FLAGS
at 1.049       il          n
np 65536       in          n
fb 17000       dp          y
bs 1           hs          nn
dl 1.000      PROCESSING
nt 1000       lb          0.50
ct 430       fn          not used
TRANSMITTER     DISPLAY
tn C13        sp         2805.1
sfrq 125.705  wp         18899.0
tof 1913.9   rfl         11482.2
tpwr 55      rfp         9678.2
pw 5.650    rp          18.7
DECOUPLER      lp          0
dn H1        H1         PLOT
dof 0        wc         190
dm yyy       sc          8
decwave w     vs         29
dprc 41     th          3
dmf 12346   nm         cdc ph
```



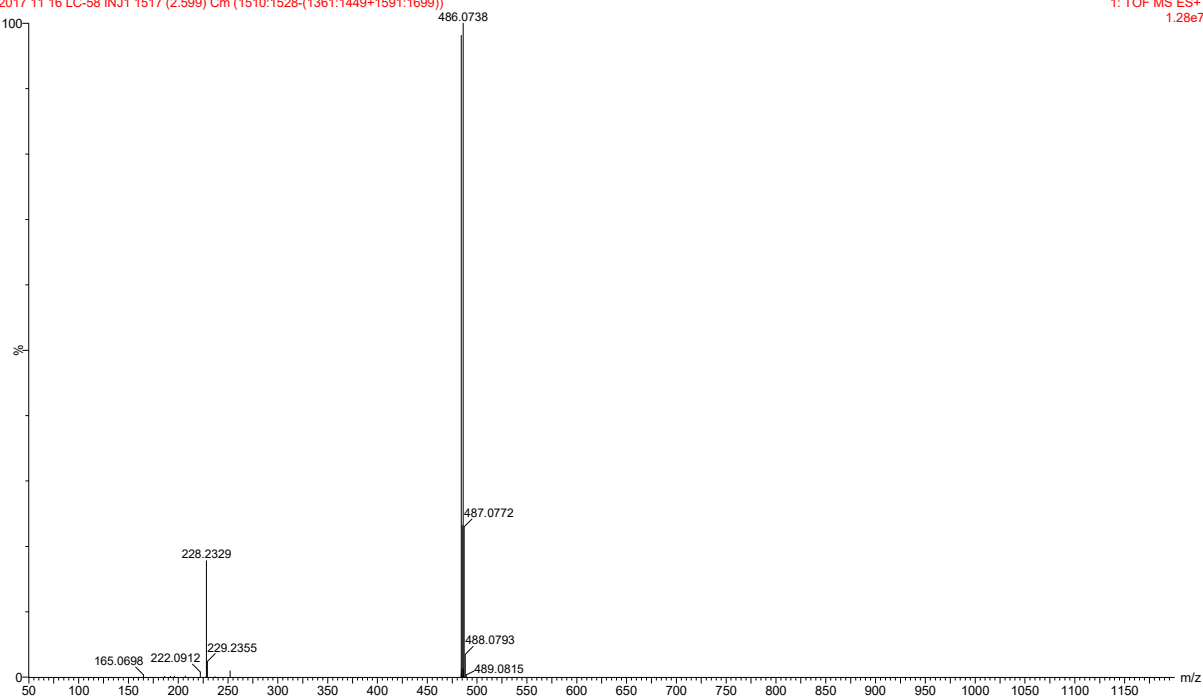
11-O-(3-bromobenzoyl)haemanthamine (1i)

ESI-HRMS

484.0760

2017 11 16 LC-58 INJ1 1517 (2.599) Cm (1510:1528-(1361:1449+1591:1699))

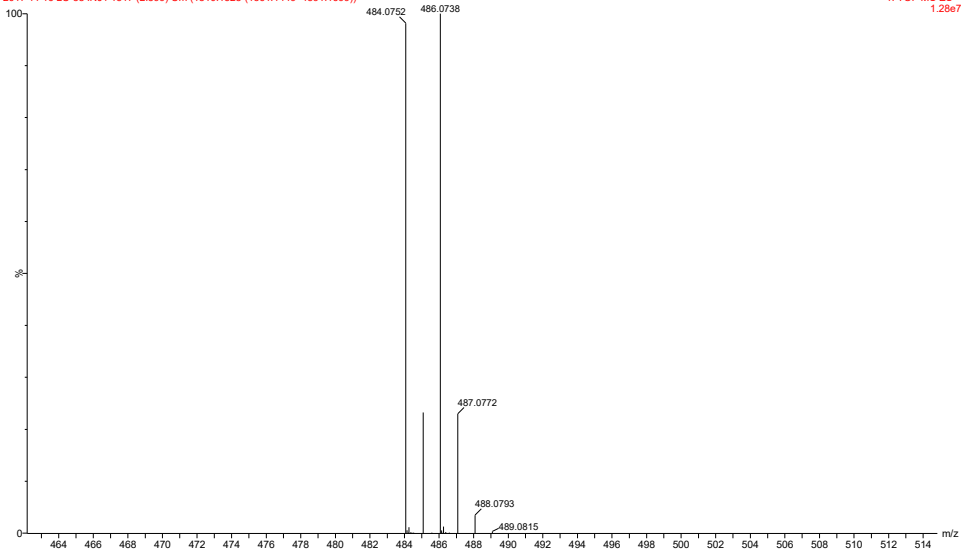
1: TOF MS ES+
1.28e7



484.0760

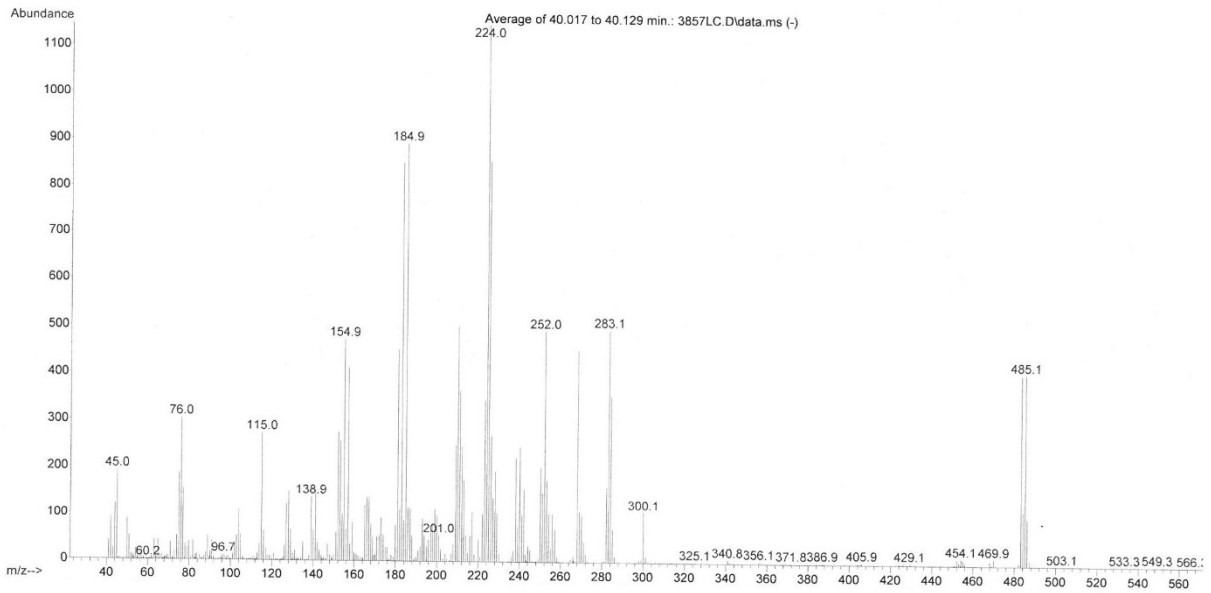
2017 11 16 LC-58 INJ1 1517 (2.599) Cm (1510:1528-(1361:1449+1591:1699))

1: TOF MS ES+
1.2867



EI-MS

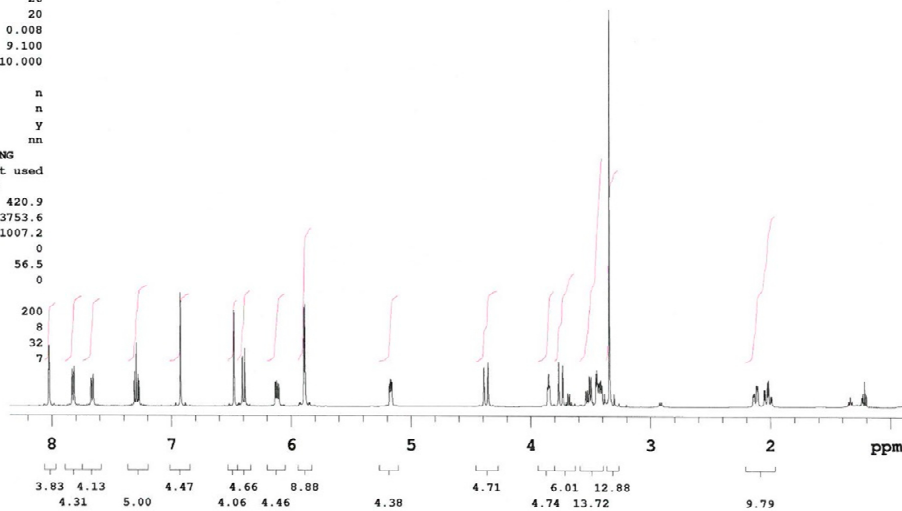
File :C:\msdchem\1\data\SNAP\3857LC.D
Operator : Lucka
Acquired : 25 Jan 2018 15:19 using AcqMethod LUCKA_7.M
Instrument : GCMS
Sample Name: LC-58
Misc Info :
Vial Number: 7



¹H-NMR

expl08 PROTON

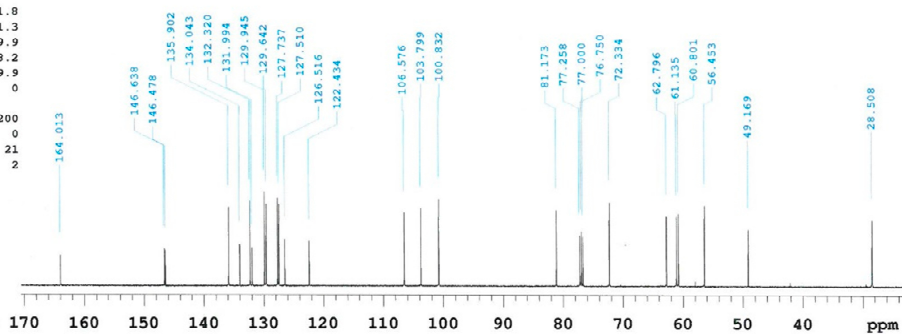
SAMPLE		PRESATURATION	
date	Apr 24 2017	satmode	n
solvent	cdcl3	wet	n
file	exp	SPECIAL	
ACQUISITION		temp	
sw	8012.8	gain	26
at	2.045	spin	20
np	32768	hst	0.008
fb	4000	pw90	9.100
bs	32	alfa	10.000
dl	1.000	FLAGS	
nt	8	il	n
ct	8	in	n
TRANSMITTER		dp	
tn	H1	hs	nn
sfrq	499.866	PROCESSING	
tof	499.9	fn	not used
tpwr	60	DISPLAY	
pw	4.550	sp	420.9
DECOUPLER		wp	3753.6
dn	C13	zfl	1007.2
dof	0	rfl	0
dm	nnn	rp	56.5
decwave	W40_OneNMR~_W018	lp	0
PLOT		wc	200
dpwr	37	sc	8
dmf	32258	vs	32
		th	7
		ai	cdc ph



¹³C-NMR

expl09 CARBON

SAMPLE		PRESATURATION	
date	Apr 24 2017	satmode	n
solvent	cdcl3	wet	n
file	exp	SPECIAL	
ACQUISITION		temp	
sw	31250.0	gain	30
at	1.049	spin	20
np	65536	hst	0.008
fb	17000	pw90	11.300
bs	1	alfa	10.000
dl	1.000	FLAGS	
nt	1000	il	n
ct	275	in	n
TRANSMITTER		dp	
tn	C13	hs	nn
sfrq	125.705	PROCESSING	
tof	1913.9	lb	1.00
tpwr	55	fn	not used
pw	5.650	DISPLAY	
DECOUPLER		sp	2891.8
dn	H1	wp	18541.3
dof	0	rfl	11489.9
dm	yyy	rfl	9678.2
decwave	w	rp	139.9
dpwr	40	lp	0
dmf	11173	PLOT	
		wc	200
		sc	0
		vs	21
		th	2
		nm	cdc ph



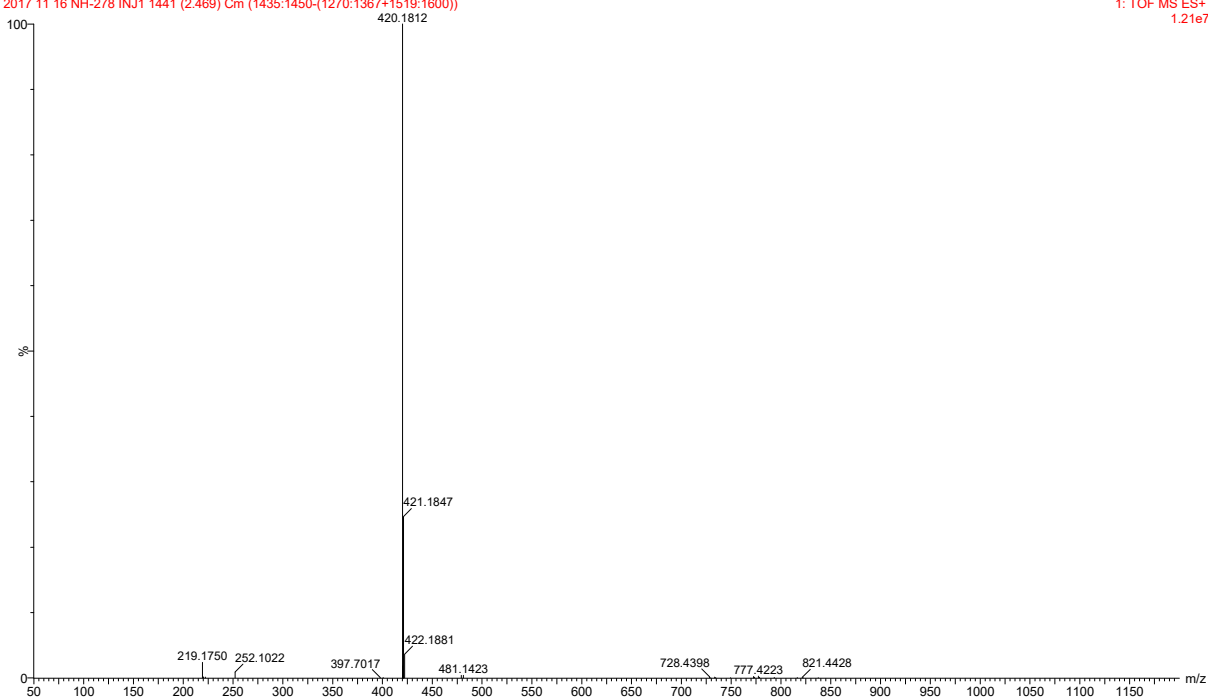
11-O-(2-methylbenzoyl)haemanthamine (1j)

ESI-HRMS

420.1733

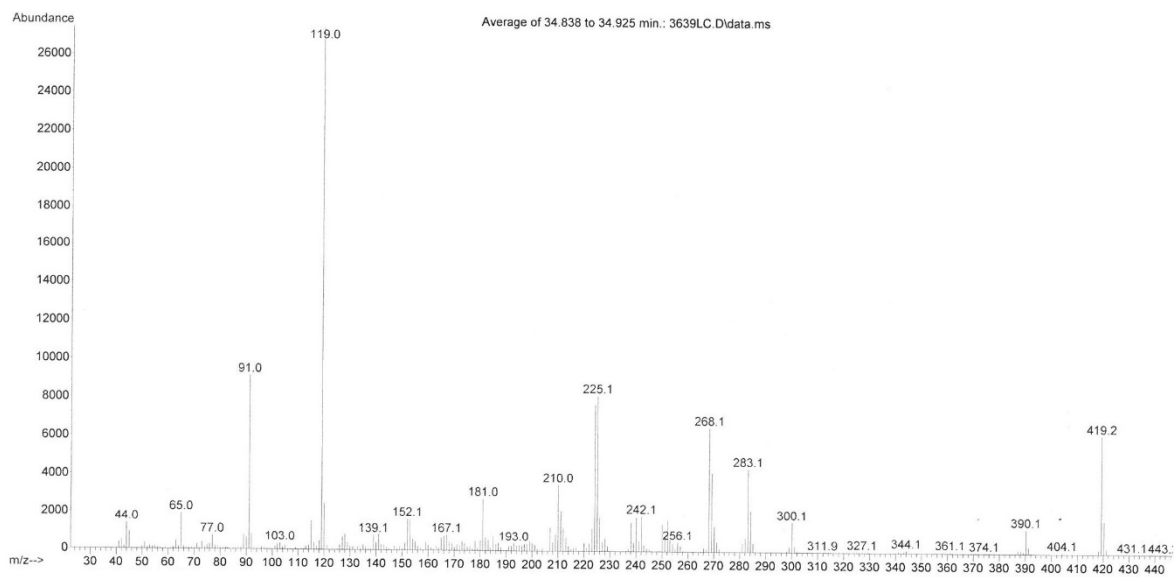
2017 11 16 NH-278 INJ1 1441 (2.469) Cm (1435:1450-(1270:1367+1519:1600))

1: TOF MS ES+
1.21e7



EI-MS

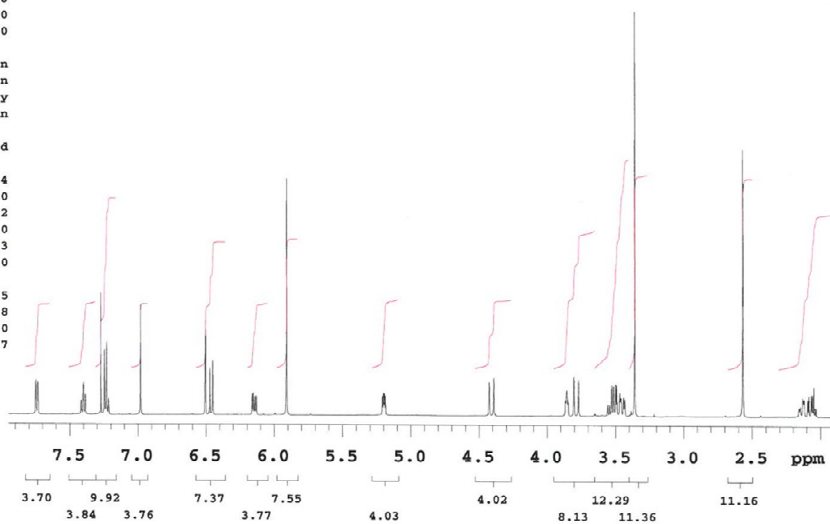
File :C:\msdchem\1\data\SNAP\3639LC.D
Operator :
Acquired : 17 Oct 2017 9:58 using AcqMethod LUCKA_7.M
Instrument : GCMS
Sample Name: LC-90
Misc Info :
Vial Number: 9



¹H-NMR

exp50 PROTON

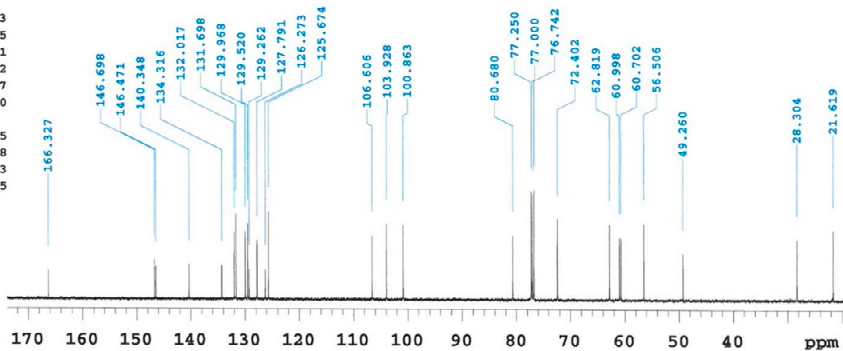
```
SAMPLE      PRESATURATION
date Jun 27 2016 satmode n
solvent cdcl3 wet n
file /home/vnmr1/v- SPECIAL
nmrsys/data/Zalchy- temp 25.0
/2016/Hrabalek-160- gain 28
825/Nemecek_Jan/Bo- spin 20
tanika/HN-278A_H.f- hst 0.008
id pw90 9.100
ACQUISITION alfa 10.000
sw 8012.8 FLAGS
at 2.045 il n
np 32768 in n
fb 4000 dp y
bs 32 hs nn
d1 1.000 PROCESSING
nt 8 fn not used
ct 8 DISPLAY
TRANSMITTER sp 956.4
tn H1 vp 3017.0
sfrq 499.866 rfl 1007.2
tof 499.9 rfp 0
tpwr 60 rp -111.3
pw 4.550 lp 0
DECOUPLER PLOT
dn C13 wc 175
dof 0 sc 8
dm nnn vs 30
decwave W40_OneNMR- th 7
_w018 ai cdc ph
dpwr 37
dmf 32258
```



¹³C-NMR

exp50 CARBON

```
SAMPLE      PRESATURATION
date Jun 27 2016 satmode n
solvent cdcl3 wet n
file /home/vnmr1/v- SPECIAL
nmrsys/data/Zalchy- temp 25.0
/2016/Hrabalek-160- gain 30
825/Nemecek_Jan/Bo- spin 20
tanika/HN-278A_C.f- hst 0.008
id pw90 11.300
ACQUISITION alfa 10.000
sw 31250.0 FLAGS
at 1.049 il n
np 65536 in n
fb 17000 dp y
bs 1 hs nn
d1 1.000 PROCESSING
nt 1000 lb 1.00
ct 186 fn not used
TRANSMITTER DISPLAY
tn C13 sp 2408.3
sfrq 125.705 wp 19443.5
tof 1913.9 rfl 11486.1
tpwr 55 rfp 9678.2
pw 5.650 rp -58.7
DECOUPLER lp 0
dn H1 PLOT
dof 0 wc 175
dm yyy sc 8
decwave w vs 23
dpwr 41 th 5
dmf 12346 nm cdc ph
```



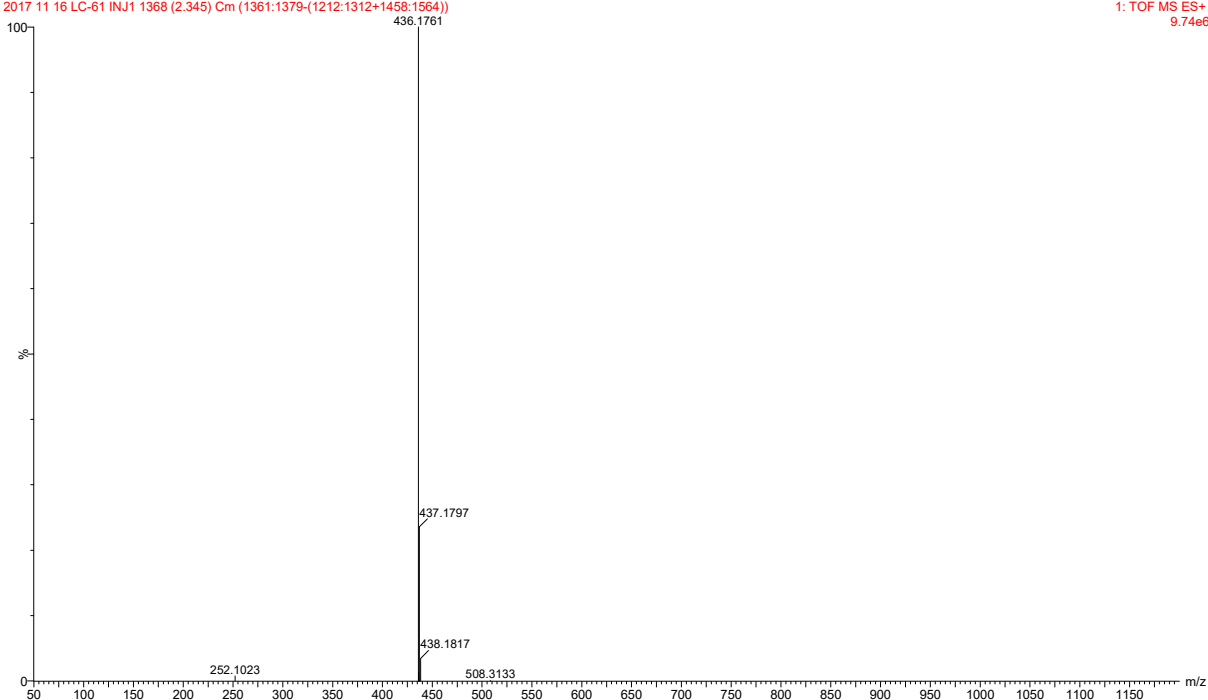
11-O-(3-methoxybenzoyl)haemanthamine (1k)

ESI-HRMS

436.1760

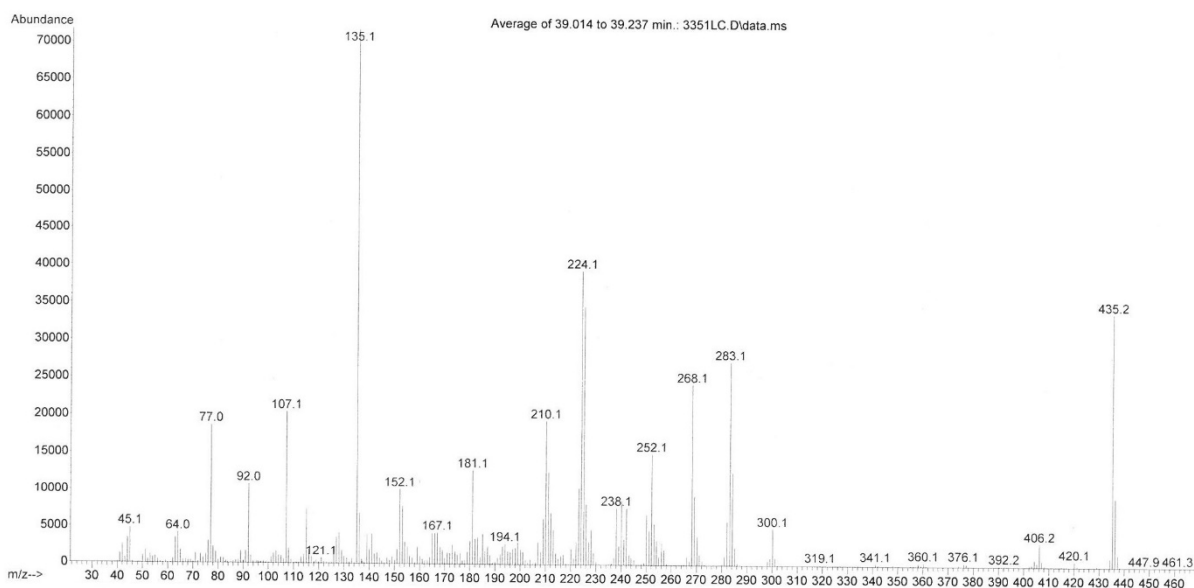
2017 11 16 LC-61 INJ1 1368 (2.345) Cm (1361:1379-(1212:1312+1458:1564))

1: TOF MS ES+
9.74e6



EI-MS

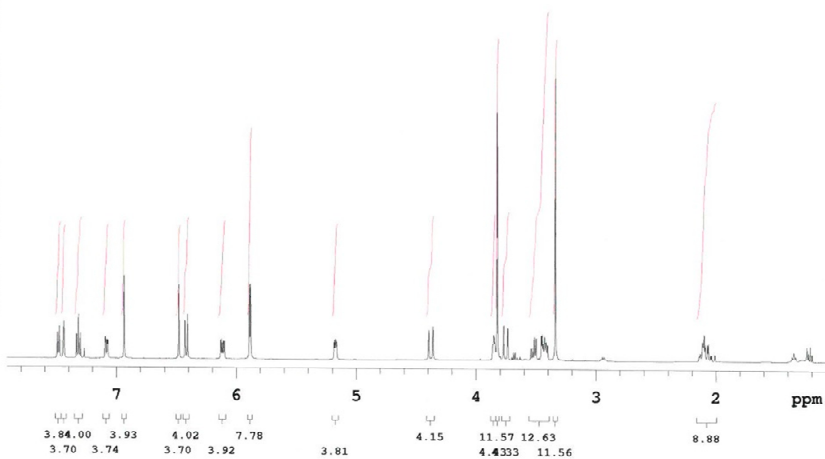
File :C:\msdchem\1\data\SNAP\3351LC.D
Operator : Lucka
Acquired : 19 Jan 2017 17:22 using AcqMethod LUCKA_7.M
Instrument : GCMS
Sample Name: LC-61
Misc Info :
Vial Number: 6



¹H-NMR

exp8 PROTON

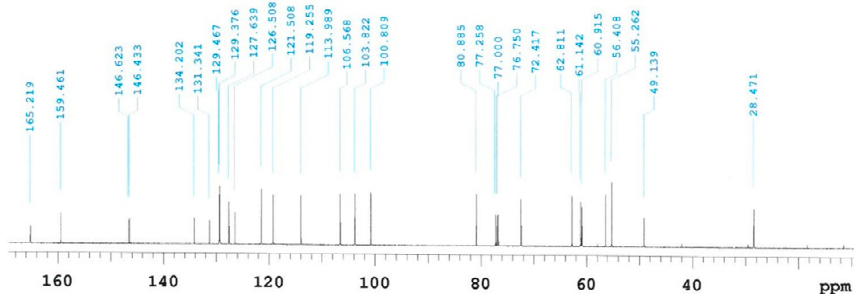
```
SAMPLE      PRESATURATION
date Mar 24 2017 satmode n
solvent cdcl3 wet n
file exp SPECIAL
ACQUISITION temp 25.0
sw 8012.8 gain 22
at 2.045 spin 20
np 32768 hst 0.008
fb 4000 pw90 9.100
bs 32 alfa 10.000
dl 1.000 FLAGS
nt 8 il n
ct 8 in n
TRANSMITTER dp y
tn H1 hs nn
sfrq 499.866 PROCESSING
tof 499.9 fn not used
tpwr 60 DISPLAY
pw 4.550 sp 529.9
DECOUPLER wp 3426.9
dn C13 rfl 1007.2
dof 0 rfp 0
dn nnn rp 163.2
decwave W40_OneNMR~ lp 0
_W018 PLOT
dpwr 37 wc 190
dmf 32258 sc 8
ve 33
th 7
ai cdc ph
```



¹³C-NMR

exp7 CARBON

```
SAMPLE      PRESATURATION
date Mar 24 2017 satmode n
solvent cdcl3 wet n
file exp SPECIAL
ACQUISITION temp 25.0
sw 31250.0 gain 30
at 1.049 spin 20
np 65536 hst 0.008
fb 17000 pw90 11.300
bs 1 alfa 10.000
dl 1.000 FLAGS
nt 1000 il n
ct 620 in n
TRANSMITTER dp y
tn C13 hs nn
sfrq 125.705 PROCESSING
tof 1913.9 lb 1.00
tpwr 55 fn not used
pw 5.650 DISPLAY
DECOUPLER sp 1105.6
dn H1 wp 20169.3
dof 0 rfl 11489.9
dn yyy rfp 9678.2
decwave w rp 135.4
dpwr 40 lp 0
dmf 11173 PLOT
wc 190
sc 0
vs 14
th 2
nm cdc ph
```



11-O-(4-nitrobenzoyl)haemanthamine (1m)

ESI-HRMS

451.1505

2017 11 16 JB-1 INJ3 1373 (2.352) Cm (1363:1384-(1164:1274+1460:1555))

1: TOF MS ES+
1.49e7



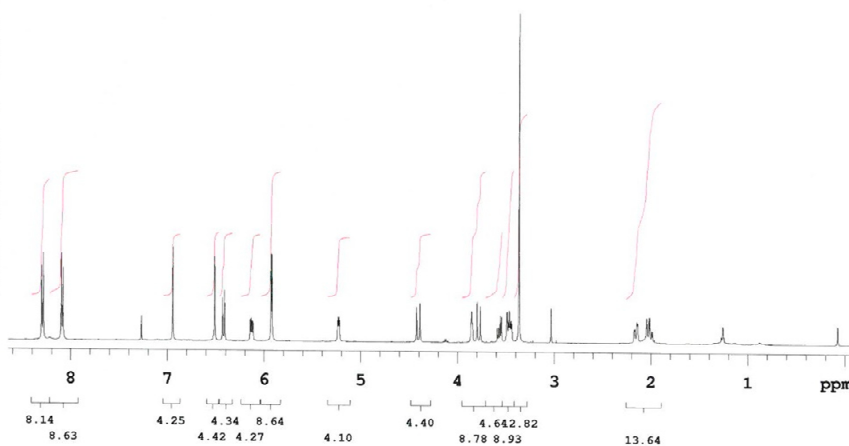
EI-MS

No ionization under EI-MS conditions

¹H-NMR

exp51 PROTON

SAMPLE		PRESATURATION	
date	Nov 13 2015	satmode	n
solvent	cdcl3	wet	n
file	/home/vnmr1/v-	SPECIAL	
nmrays/data/Zalohy-	temp	25.0	
/2016/Hrabalek-160-	gain	30	
825/Nemecek_Jan/Bo-	spin	not used	
tanika/JB-1_H.fid	hst	0.008	
ACQUISITION		pw90	9.100
sw	8012.8	alfa	10.000
at	2.045	FLAGS	
np	32768	il	n
fb	4000	in	n
bs	32	dp	y
dl	1.000	hs	nn
nt	8	PROCESSING	
ct	8	fn	not used
TRANSMITTER		DISPLAY	
tn	H1	sp	-72.1
sfrq	499.866	wp	4394.7
tof	499.9	rfl	1007.2
tpwr	60	rfp	0
pw	4.550	rp	3.4
DECOUPLER		lp	0
dn	C13	PLOT	
dof	0	wc	190
dm	nn	sc	8
decwave	W40_OneNMR-	vs	73
	_W018	th	7
dpwr	37	ai	cdc ph
daf	32258		



¹³C-NMR

exp51 CARBON

```
SAMPLE          PRESATURATION
date Nov 13 2015 satmode n
solvent cdcl3   wet      n
file /home/vnmr1/vnmrsys/data/Zalchy-
/2016/Hrabalek-160-
825/Memecek_Jan/Bo-
tanika/JB-1_C.fid hst     0.008
ACQUISITION    pw90     11.300
sw 31250.0      alfa     10.000
at 1.049
np 65536        il       n
fb 17000        in       n
be 1            dp       y
dl 1.000        hs       nn
nt 1000
ct 380          lb       1.00
TRANSMITTER    fn       not used
tn C13
sfrq 125.705    sp       2923.3
tof 1913.9      wp       18513.7
tpwr 55         rfl      11480.3
pw 5.650        rfp      9678.2
DECOUPLER     rp       177.0
dn H1           lp       0
dof 0
dm          yyy      wc       190
decwave w       sc       8
dpwr 41        vs       30
dmf 12346     th       2
nm cdc ph
```

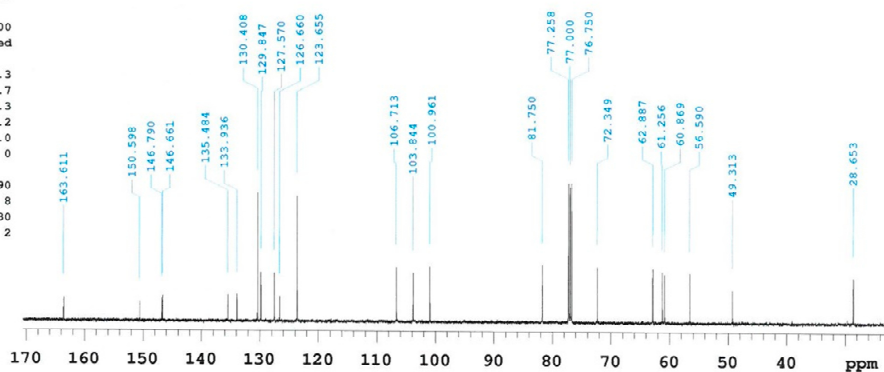


Table S1. Permeability (Pe 10^{-6} cm s^{-1}) in the PAMPA-BBB assay for 10 commercial drugs (used in the experiment validation) and compounds **1g**, **1j** and **1m** with their predictive penetration in the CNS.^a

Compound	Bibl. ^b	Pe (10^{-6} cm s^{-1}) ^c	Prediction
Atenolol	0,8	0,3 \pm 0,3	
Caffeine	1,3	0,1 \pm 0,1	
Desipramine	12	7,7 \pm 0,4	
Enoxacin	0,9	0,6 \pm 0,5	
Hydrocortisone	1,9	0,8 \pm 0,2	
Ofloxacin	0,8	0,3 \pm 0,1	
Piroxicam	2,5	0,9 \pm 0,2	
Promazine	8,8	8,6 \pm 0,5	
Testosterone	17	13,6 \pm 0,3	
Verapamil	16	15,5 \pm 0,8	
18g		8,4 \pm 0,2	CNS +
18j		5,8 \pm 0,9	CNS +
18m		7,1 \pm 0,3	CNS +

^aPBS:EtOH (70:30) was used as solvent. ^bReference Di et al. ^cData are the mean \pm SD of 2 independent experiments.

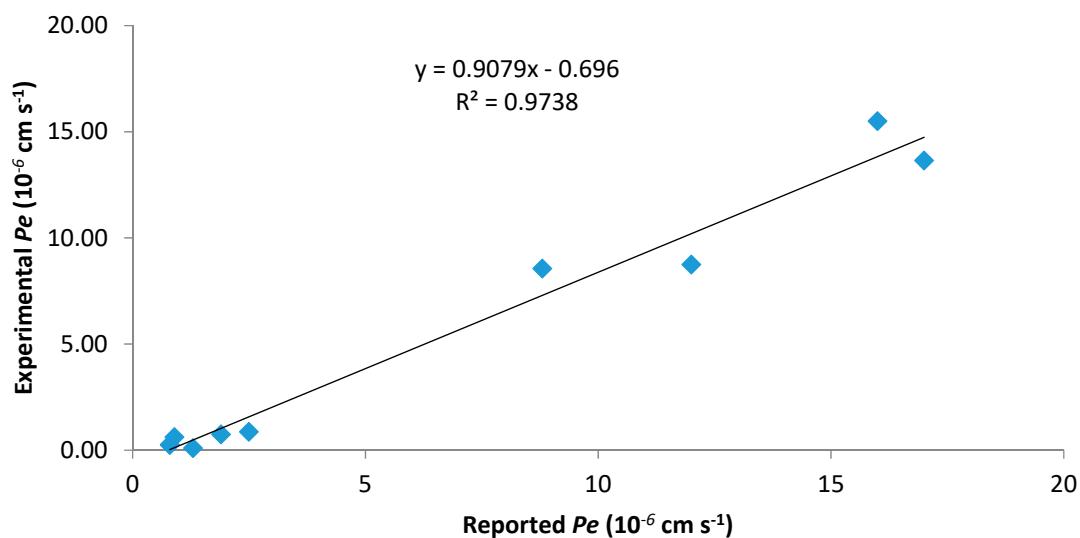


Figure S1. Linear correlation between experimental and reported permeability of commercial drugs using the PAMPA-BBB assay.

Table S2. Cell proliferation of haemanthamine derivatives (**1a – 1m**; c = 10 μ M) for 10 human cell lines.

	1	1a	1b	1c	1d	1e	1f	1g	1	1i	1j	1k	1m	DOX
Jurkat	13 \pm 3	100 \pm 13	104 \pm 3	110 \pm 3	92 \pm 1	100 \pm 7	90 \pm 12	83 \pm 11	69 \pm 6	133 \pm 10	95 \pm 11	83 \pm 1	69 \pm 7	0 \pm 3
MOLT-4	1 \pm 1	106 \pm 9	97 \pm 8	99 \pm 8	96 \pm 1	97 \pm 3	101 \pm 18	110 \pm 19	135 \pm 22	115 \pm 15	91 \pm 3	94 \pm 18	76 \pm 12	0 \pm 1
A549	30 \pm 6	95 \pm 9	84 \pm 3	84 \pm 3	99 \pm 7	105 \pm 9	106 \pm 12	98 \pm 2	75 \pm 25	122 \pm 5	96 \pm 8	102 \pm 5	74 \pm 6	66 \pm 16
HT-29	37 \pm 6	97 \pm 10	79 \pm 15	82 \pm 17	94 \pm 4	100 \pm 3	101 \pm 3	110 \pm 17	97 \pm 23	120 \pm 4	98 \pm 6	93 \pm 3	73 \pm 2	77 \pm 12
PANC-1	37 \pm 3	114 \pm 4	70 \pm 13	85 \pm 13	88 \pm 3	96 \pm 4	99 \pm 6	100 \pm 10	118 \pm 9	108 \pm 2	95 \pm 6	88 \pm 5	71 \pm 7	59 \pm 9
A2780	30 \pm 5	107 \pm 17	104 \pm 3	123 \pm 9	99 \pm 2	106 \pm 5	104 \pm 8	120 \pm 10	122 \pm 24	162 \pm 9	129 \pm 11	108 \pm 7	86 \pm 4	5 \pm 1
HeLa	16 \pm 2	83 \pm 6	69 \pm 11	74 \pm 8	93 \pm 6	98 \pm 3	88 \pm 3	98 \pm 2	72 \pm 4	93 \pm 5	104 \pm 4	84 \pm 12	71 \pm 1	7 \pm 10
MCF-7	11 \pm 1	97 \pm 19	85 \pm 7	103 \pm 7	93 \pm 5	95 \pm 4	96 \pm 13	108 \pm 10	90 \pm 11	105 \pm 4	112 \pm 3	100 \pm 2	62 \pm 10	41 \pm 7
SAOS-2	28 \pm 3	88 \pm 6	96 \pm 16	85 \pm 15	88 \pm 6	96 \pm 8	104 \pm 7	104 \pm 9	135 \pm 6	97 \pm 10	97 \pm 17	89 \pm 15	69 \pm 4	73 \pm 8
MRC-5	30 \pm 2	113 \pm 12	102 \pm 13	95 \pm 7	89 \pm 3	96 \pm 4	87 \pm 14	101 \pm 5	100 \pm 5	105 \pm 3	112 \pm 9	92 \pm 1	61 \pm 8	40 \pm 4

Values represent cell proliferation after haemanthamine analogue treatment and are expressed as percent of proliferation of untreated control cells. Each value is a mean of three independent experiments. Doxorubicin was used as a reference drug.