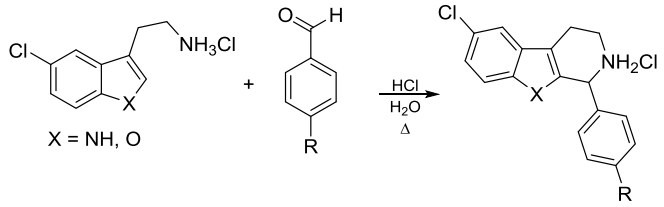
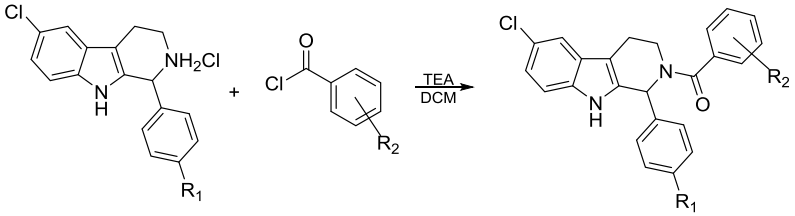
EXPERIMENTAL:

General procedure for the synthesis of the scaffolds:



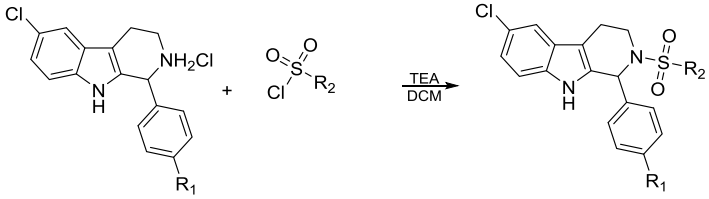
A flask was charged with 5-chlorotryptamine hydrochloride (5 g, 0.0649 mol), 0.5 M hydrochloric acid (130 mL), and the substituted benzaldehyde (1.5 eq). The mixture was refluxed for 14 hr, cooled to room temperature, and vacuum filtered. The solid was resuspended in acetic acid (100 mL), stirred for 1 hr, and vacuum filtered. The solid was resuspended in ethyl acetate (100 mL), stirred for 1 hr, and vacuum filtered to obtain the pure scaffold as a solid.

General procedure for the synthesis of the amide derivatives:



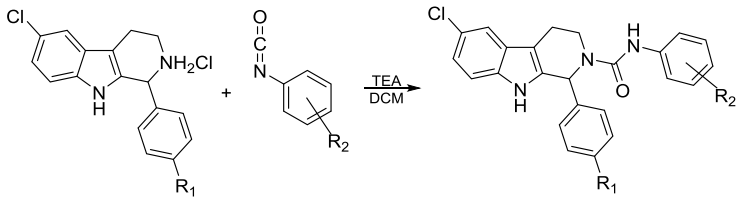
A flask was charged with the scaffold (250 mg), dichloromethane (40 mL), and triethylamine (3 eq) and stirred for 30 min. To the stirring solution was added the acid chloride (1.1 eq) and stirred for an additional 12 hours. The solution was then concentrated under reduced pressure. The resulting oil was dissolved in ethyl acetate (100 mL), washed with 10% HCl (100 mL), saturated sodium bicarbonate (100 mL), and brine (100 mL). The solution was dried with sodium sulfate and concentrated under reduced pressure. The resulting residue was purified via column chromatography, dissolved in a minimal amount of ethyl acetate and triturated with hexanes to afford the pure amide as a solid.

General procedure for the synthesis of the sulfonamide derivatives:



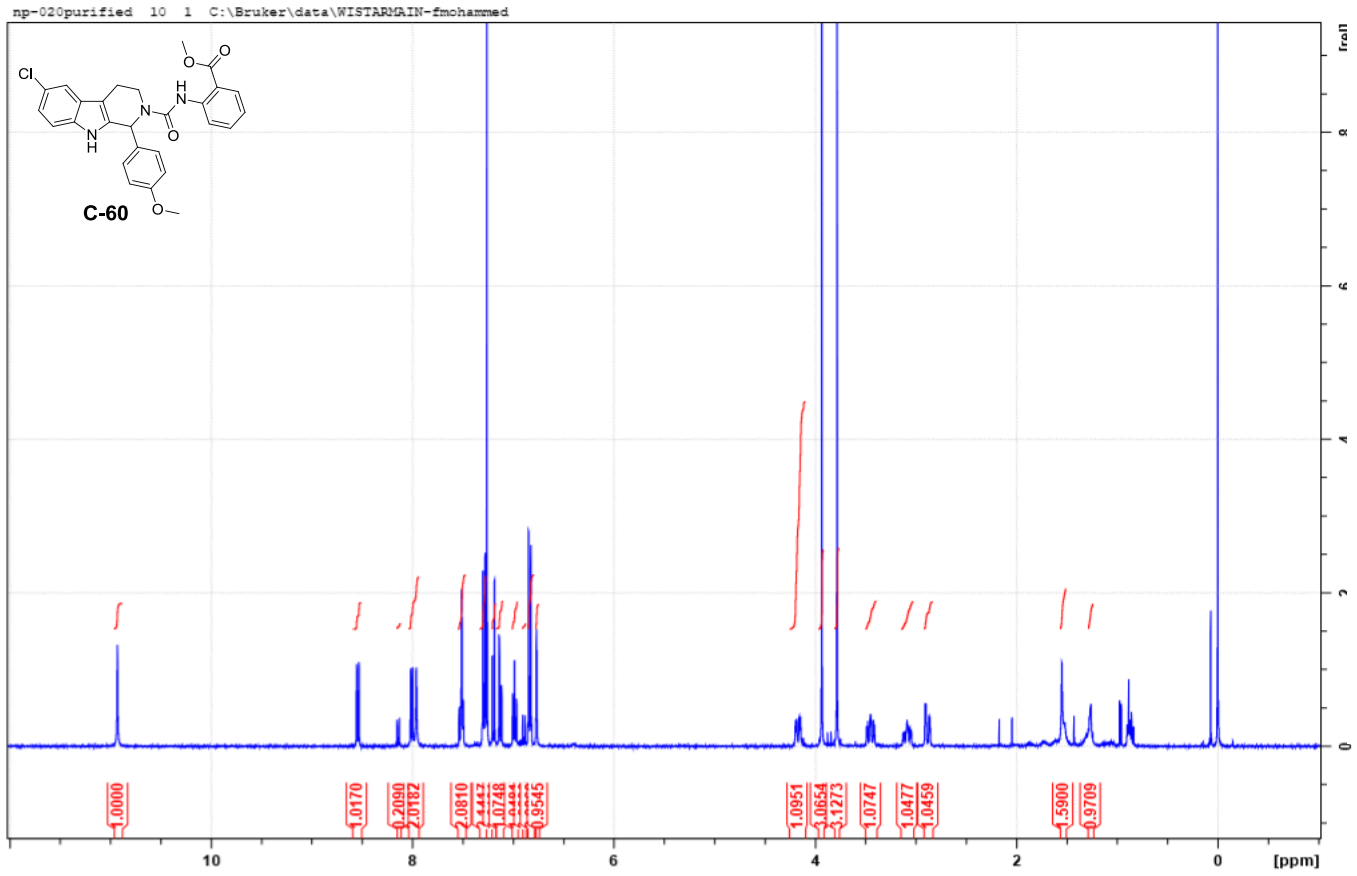
A flask was charged with the scaffold (250 mg), dichloromethane (40 mL), and triethylamine (3 eq) and stirred for 30 min. To the stirring solution was added the sulfonyl chloride (1.1 eq) and stirred for an additional 12 hours. The solution was then concentrated under reduced pressure. The resulting oil was dissolved in ethyl acetate (100 mL), washed with 10% HCl (100 mL), saturated sodium bicarbonate (100 mL), and brine (100 mL). The solution was dried with sodium sulfate and concentrated under reduced pressure. The resulting residue was purified via column chromatography, dissolved in a minimal amount of ethyl acetate and triturated with hexanes to afford the pure sulfonamide as a solid.

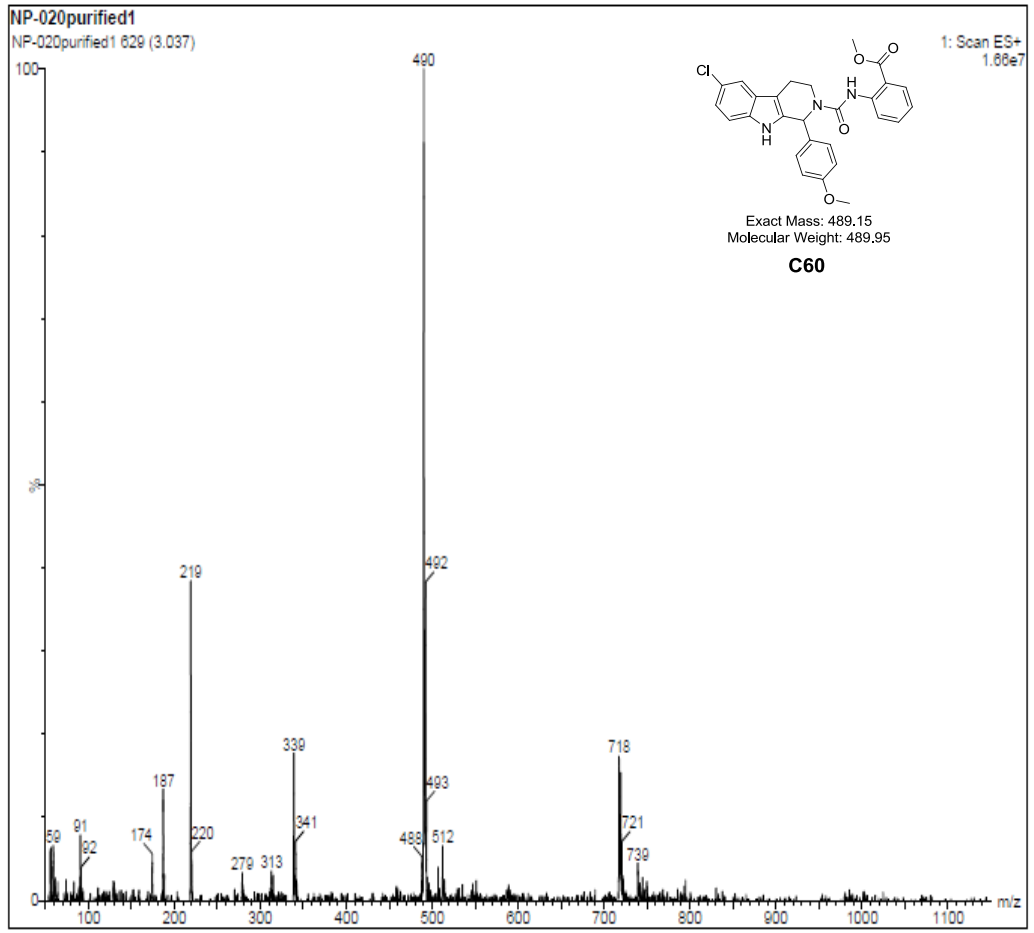
General procedure for the synthesis of the urea derivatives:

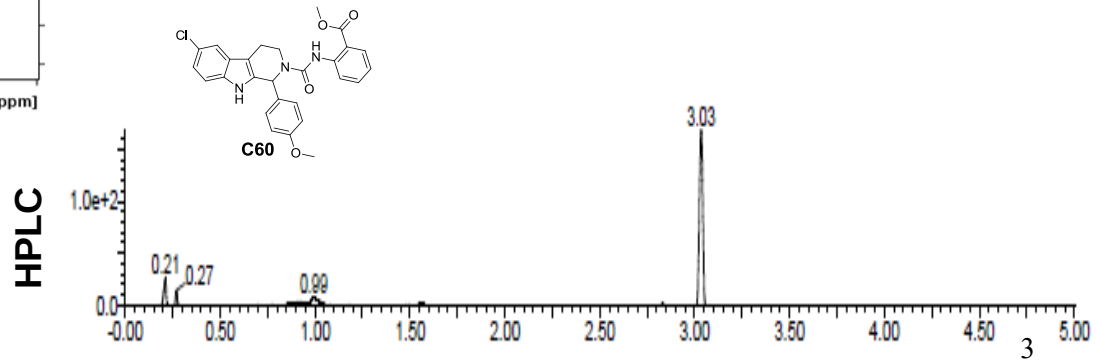


A flask was charged with the scaffold (250 mg), dichloromethane (40 mL), and triethylamine (3 eq) and stirred for 30 min. To the stirring solution was added the substituted phenylisocyanate (1.1 eq) and stirred for an additional 12 hours. The solution was then concentrated under reduced pressure. The resulting oil was dissolved in ethyl acetate (100 mL), washed with 10% HCl (100 mL), saturated sodium bicarbonate (100 mL), and brine (100 mL). The solution was dried with sodium sulfate and concentrated under reduced pressure. The resulting residue was purified via column chromatography, dissolved in a minimal amount of ethyl acetate and triturated with hexanes to afford the pure urea as a solid.

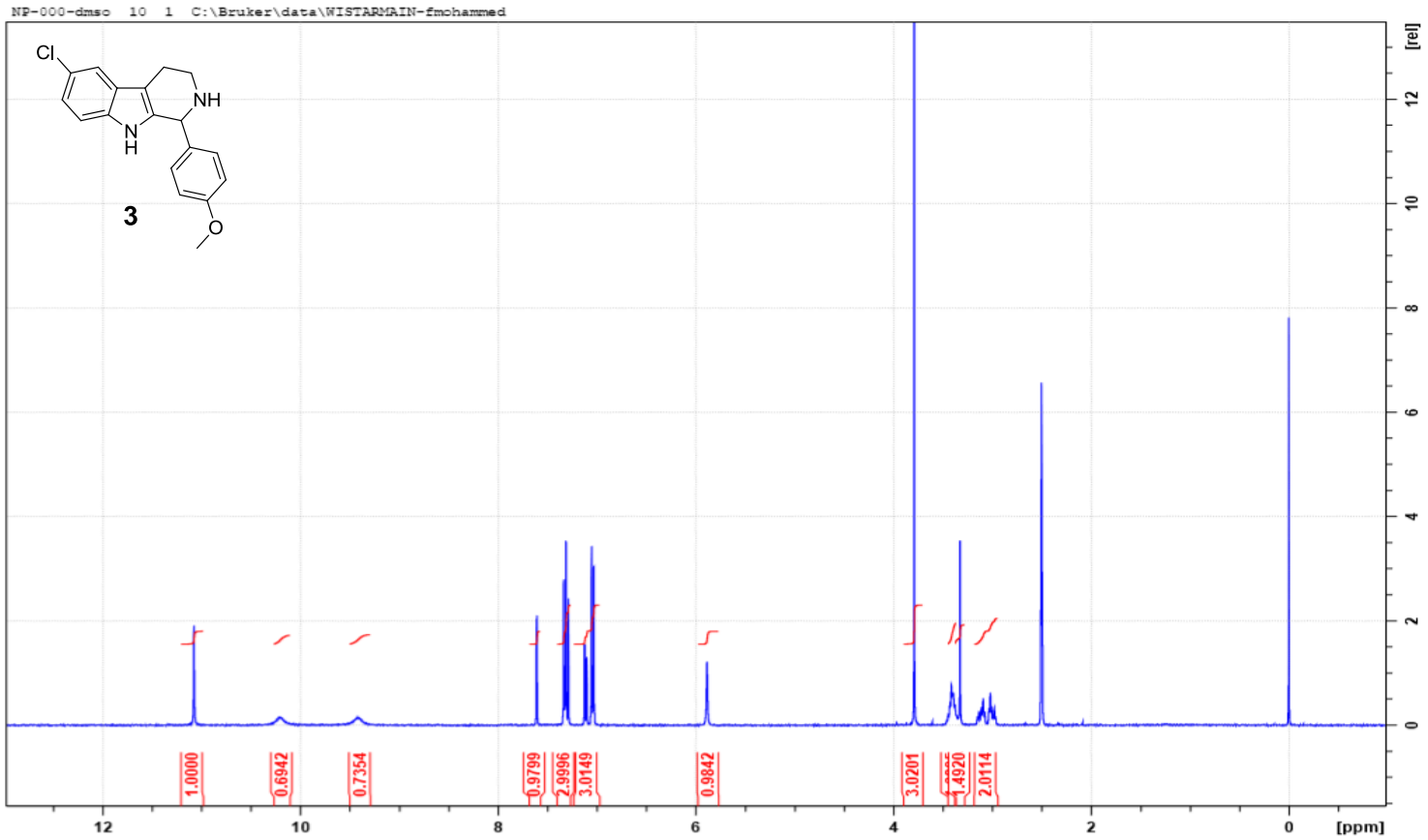
C60

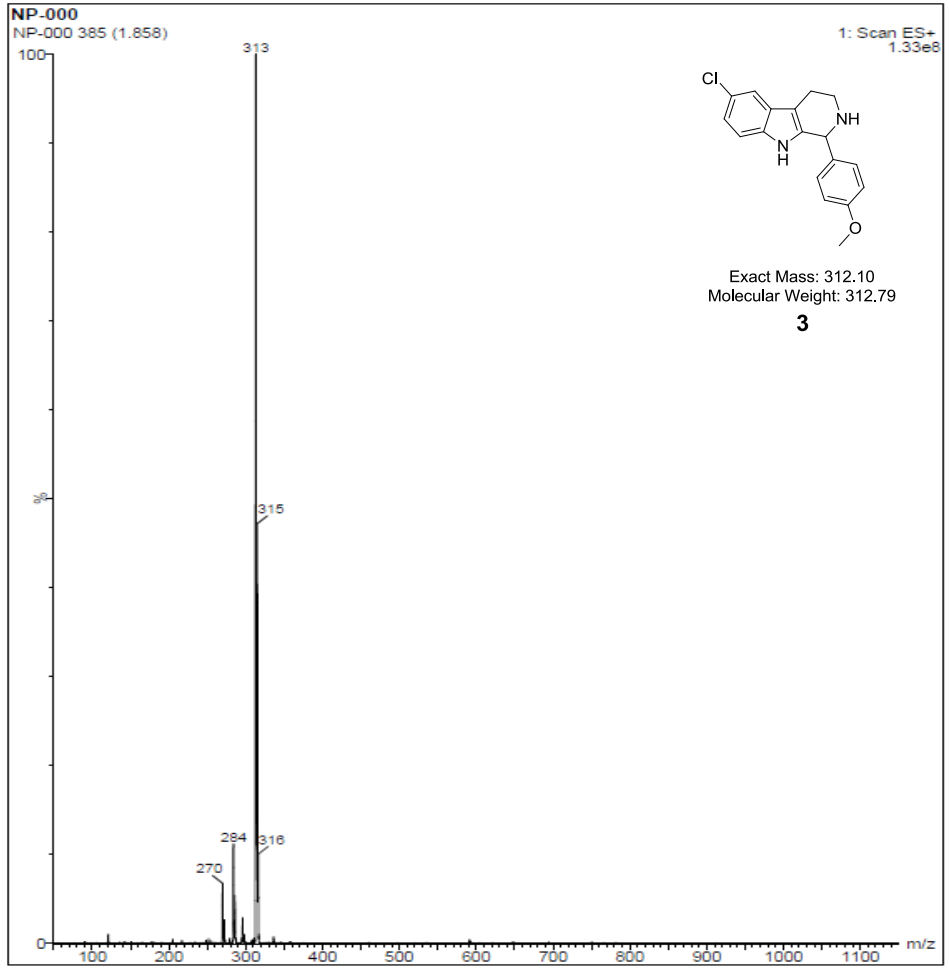

np-020purified 10 1 C:\Bruker\data\WISTARMAIN-fmohammed
C-60
1.0000
1.0170
2.2090
2.0182
2.0810
1.0748
0.9545
1.0951
1.0654
3.1273
1.0747
1.0477
1.0459
1.5900
0.9709
10
8
6
4
2
0
[ppm]

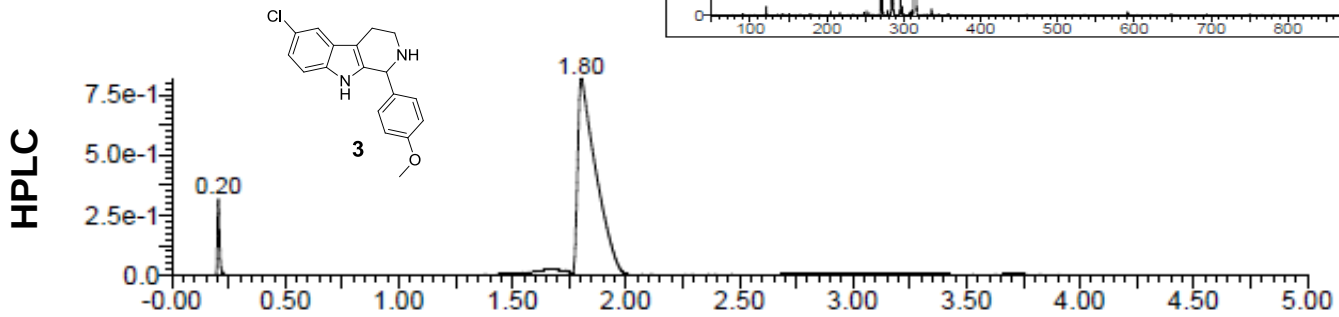

NP-020purified1
NP-020purified1 629 (3.037)
1: Scan ES+
1.66e7
Exact Mass: 489.15
Molecular Weight: 489.95
C60
490
492
219
339
718
187
493
721
739
91
92
174
220
279
313
341
488
512
m/z


C60
HPLC
3.03
1.0e+2
0.21
0.27
0.99
0.0
-0.00
0.50
1.00
1.50
2.00
2.50
3.00
3.50
4.00
4.50
5.00

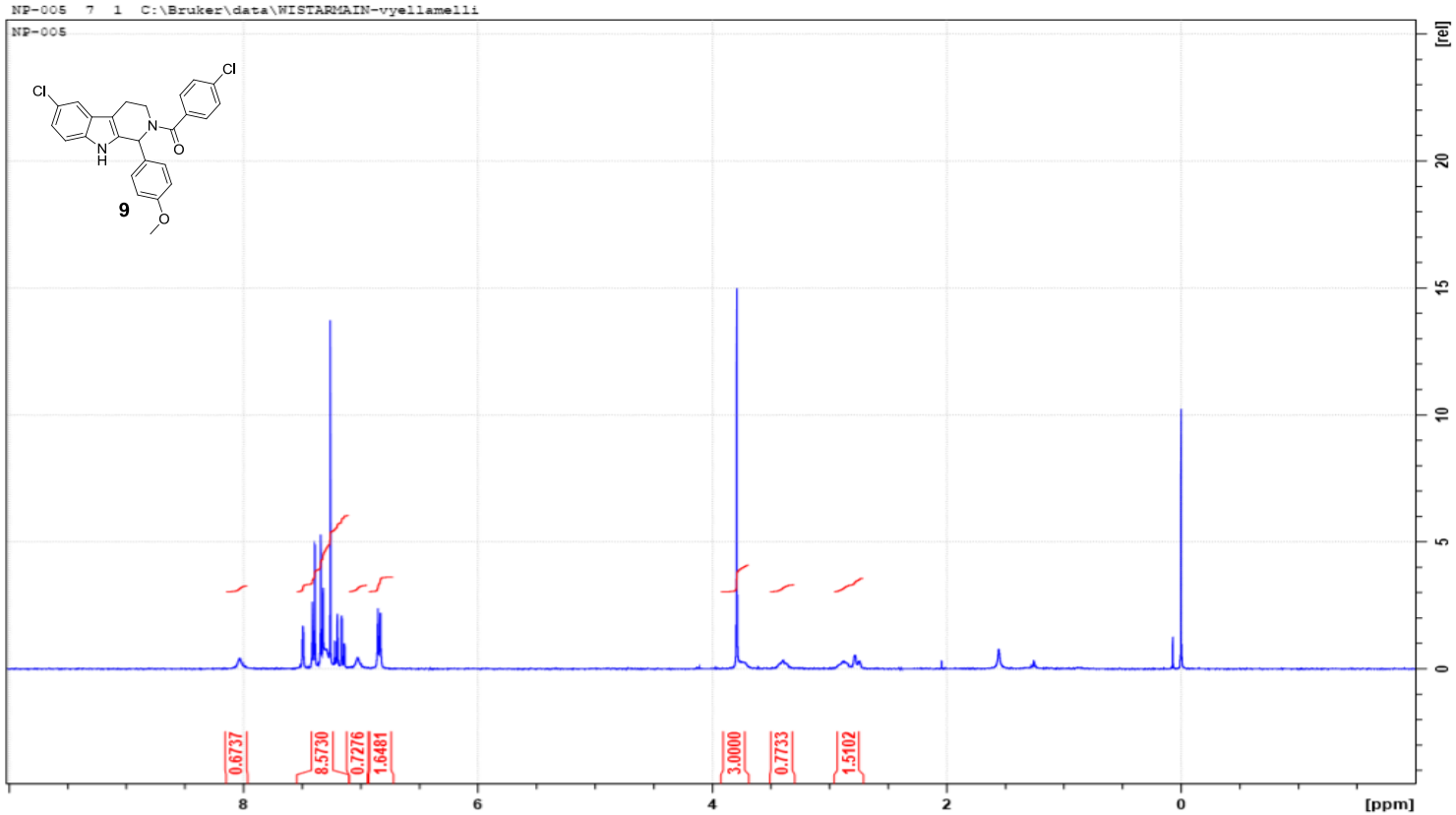
Compound-3

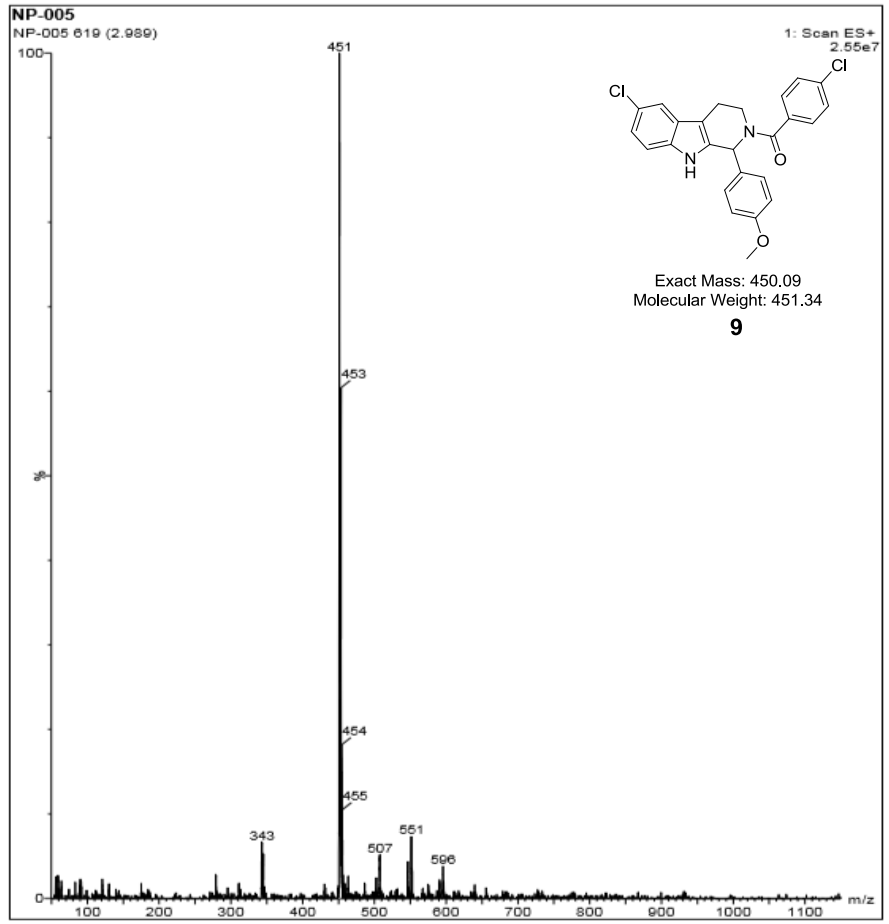

NP-000-dmso 10 1 C:\Bruker\data\WISTARMAIN-fmohammed
Cl
NH
N
H
O
3
[rel]
[ppm]
1.0000
0.6942
0.7354
0.9799
2.9996
3.0149
0.9842
3.0201
1.4920
2.0114


NP-000
NP-000 385 (1.858)
1: Scan ES+
1.33e8
313
315
284
316
270
%
m/z
Cl
NH
N
H
O
Exact Mass: 312.10
Molecular Weight: 312.79
3

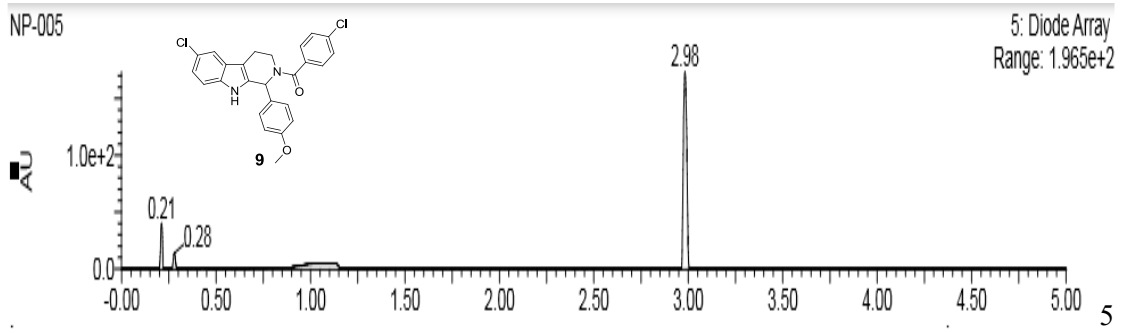

HPLC
Cl
NH
N
H
O
3
1.80
0.20
7.5e-1
5.0e-1
2.5e-1
0.0
-0.00
0.50
1.00
1.50
2.00
2.50
3.00
3.50
4.00
4.50
5.00

Compound-9

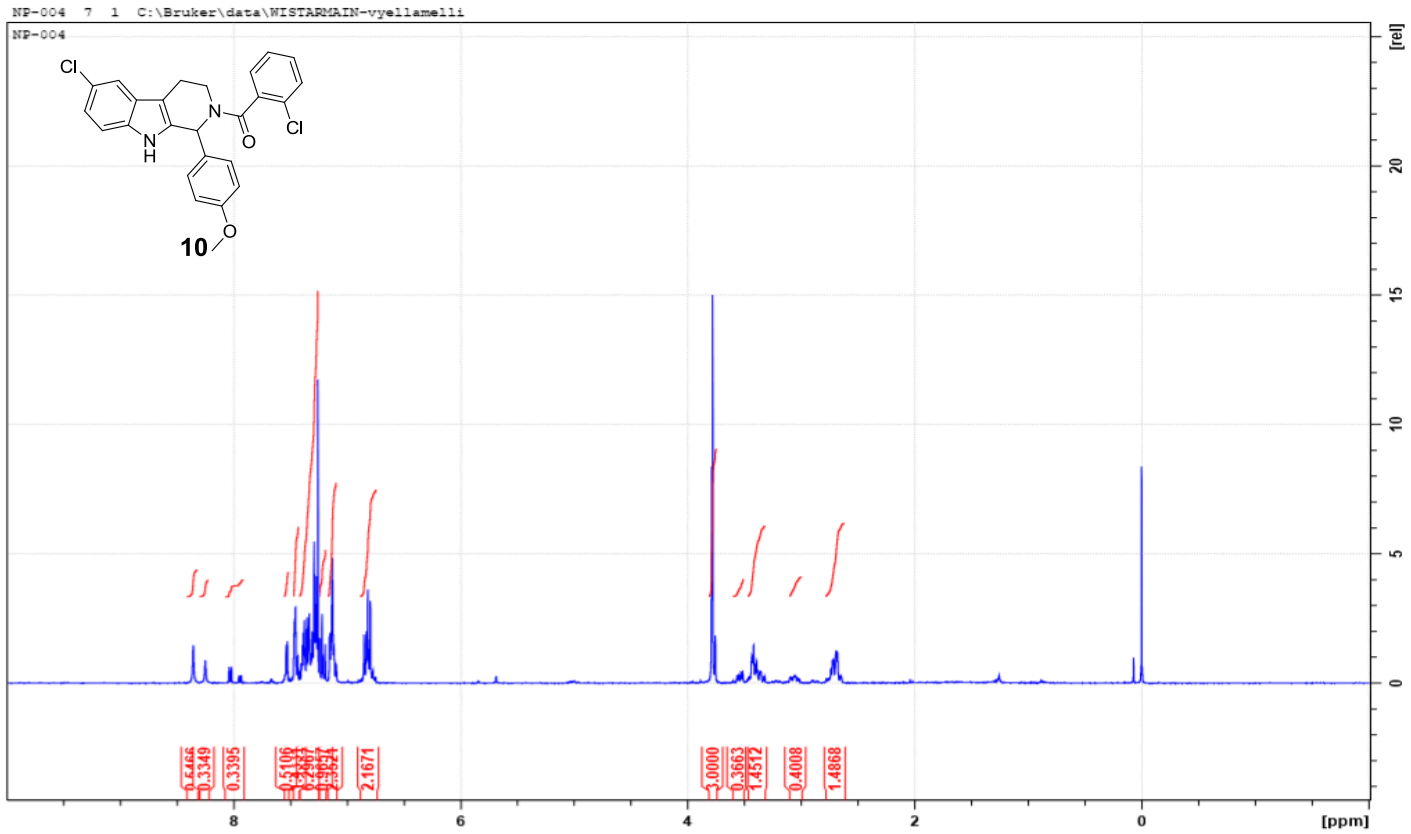


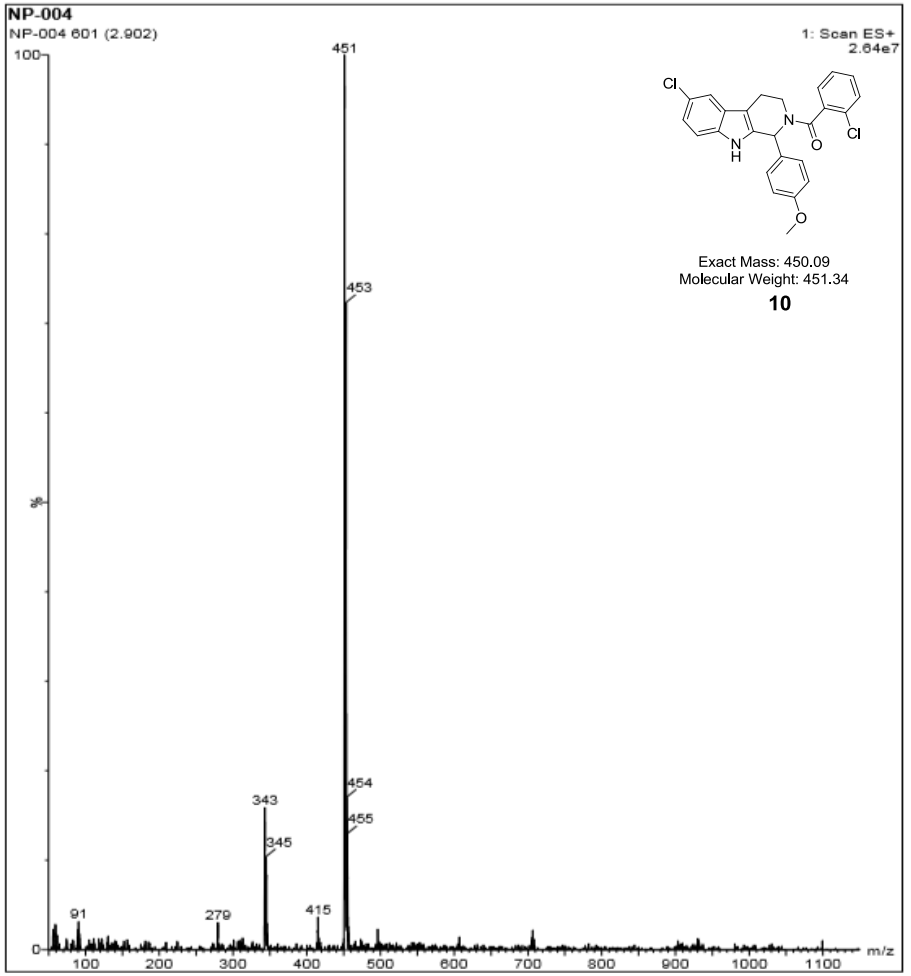


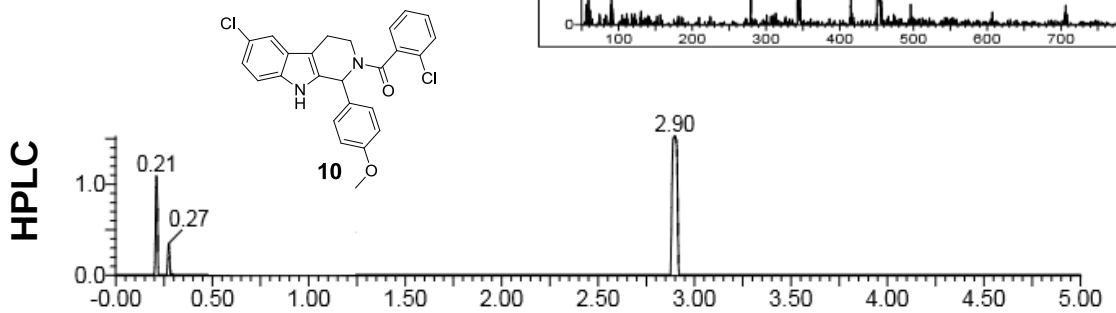
HPLC



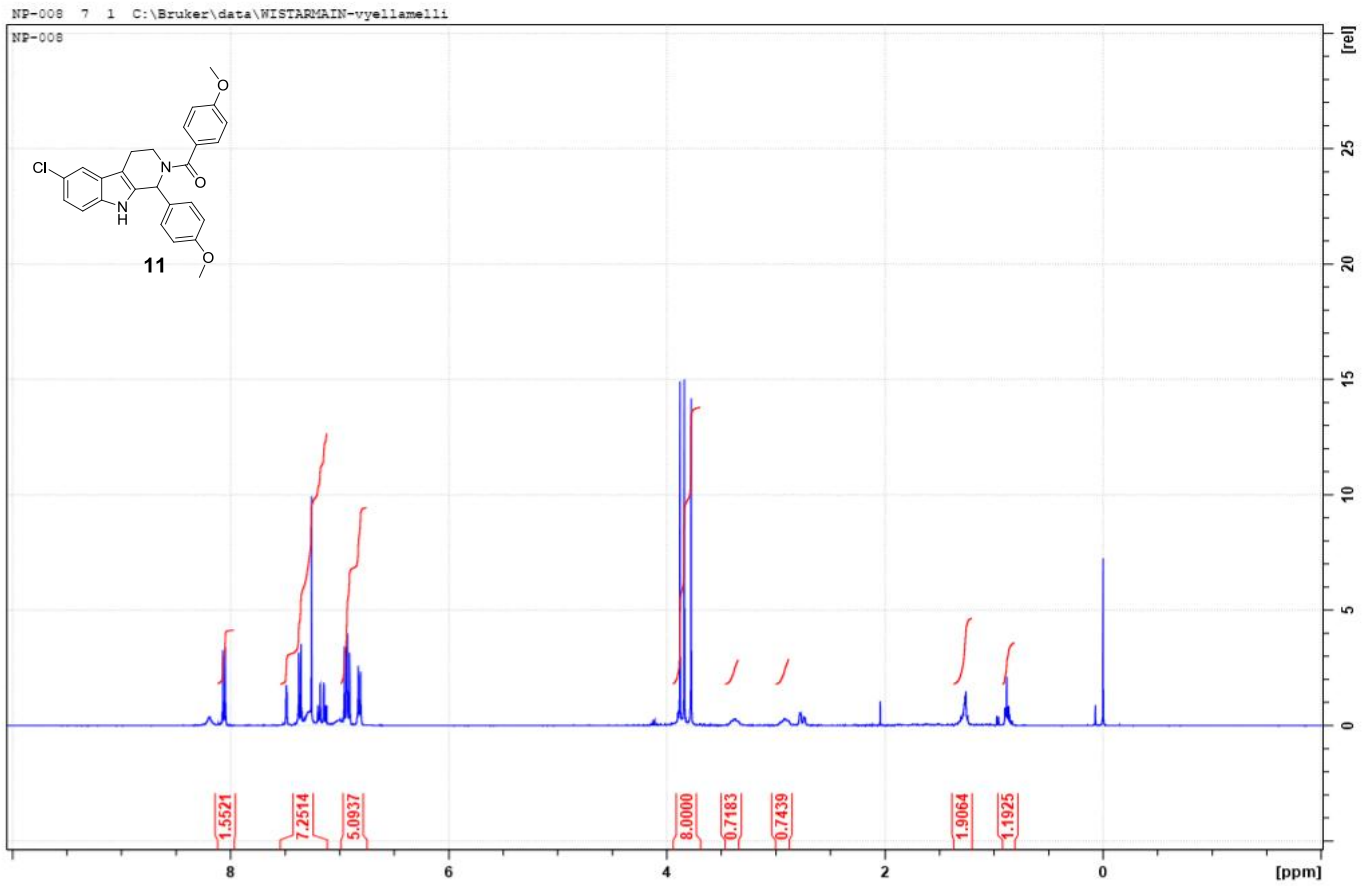
Compound-10

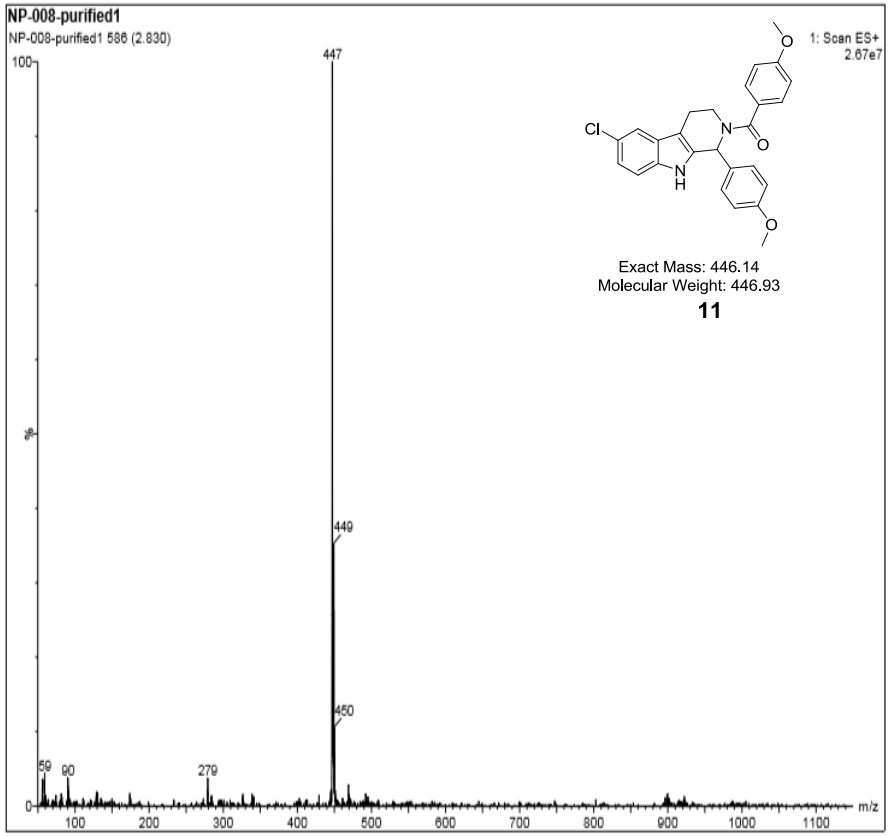

NP-004 7 1 C:\Bruker\data\WISTARMAIN-vyellamelli
NP-004
Cl
N
H
O
Cl
O
10
[rel]
[ppm]
0.3349
0.3395
2.1671
5.0000
0.3663
1.4512
0.4008
1.4868


NP-004
NP-004 601 (2.902)
1: Scan ES+
2.64e7
Exact Mass: 450.09
Molecular Weight: 451.34
10
451
453
454
455
343
345
91
279
415
m/z

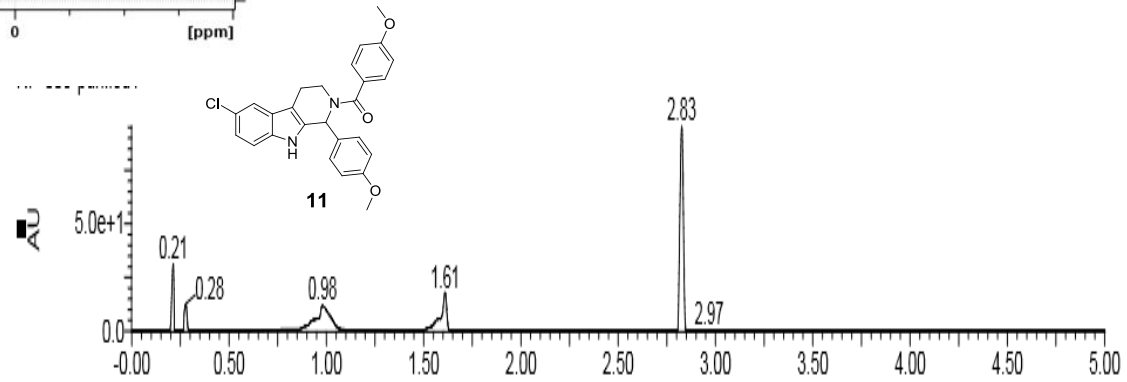

HPLC
Cl
N
H
O
Cl
O
10
0.21
0.27
2.90

Compound-11

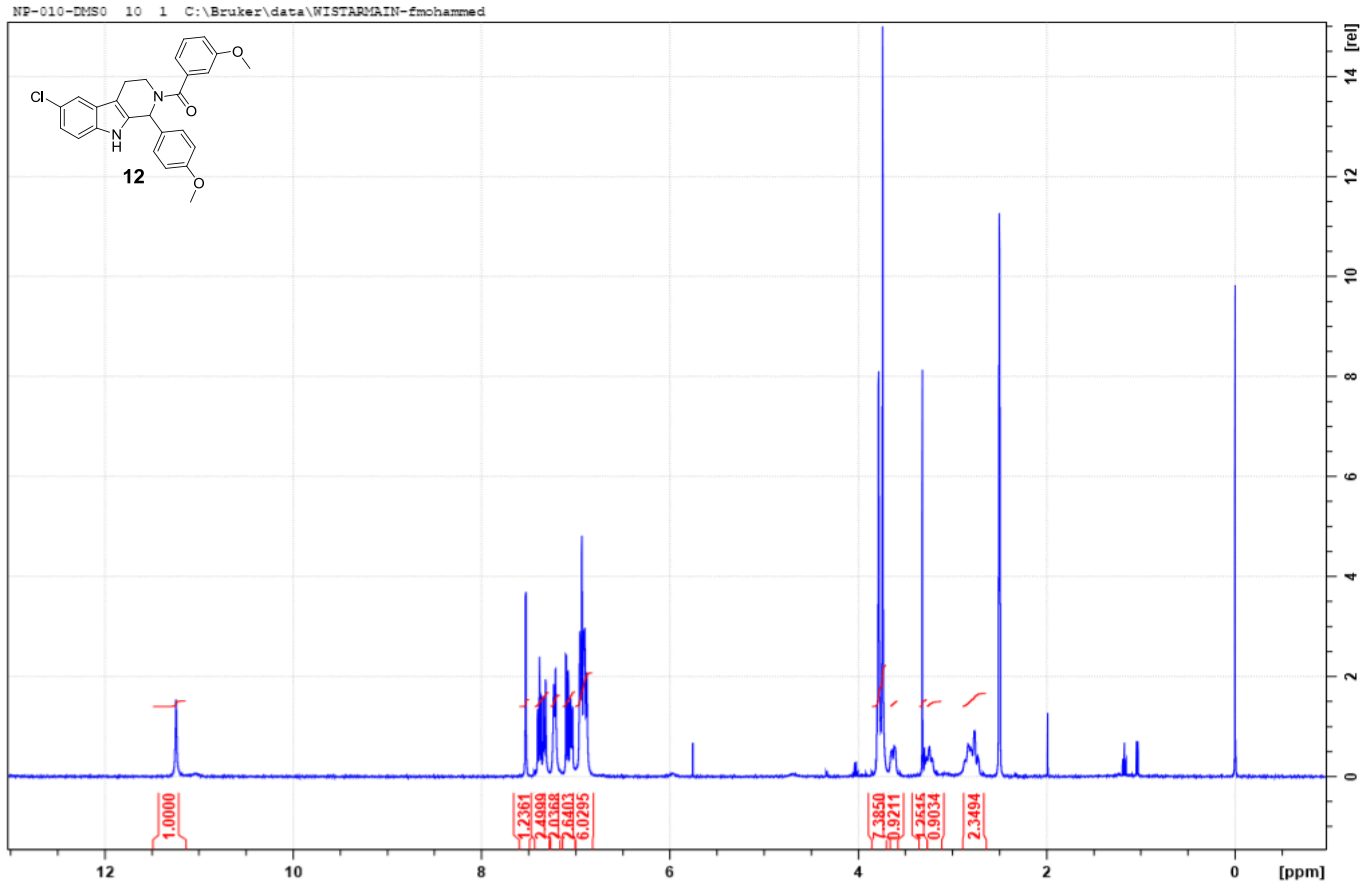


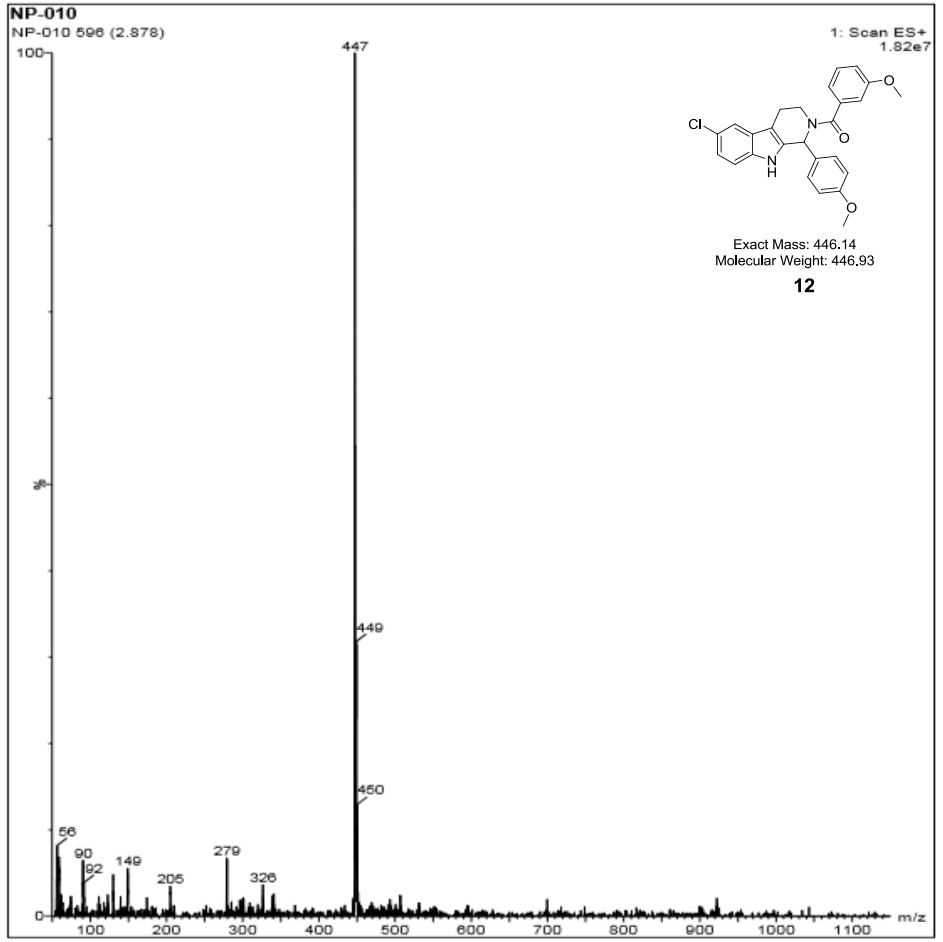


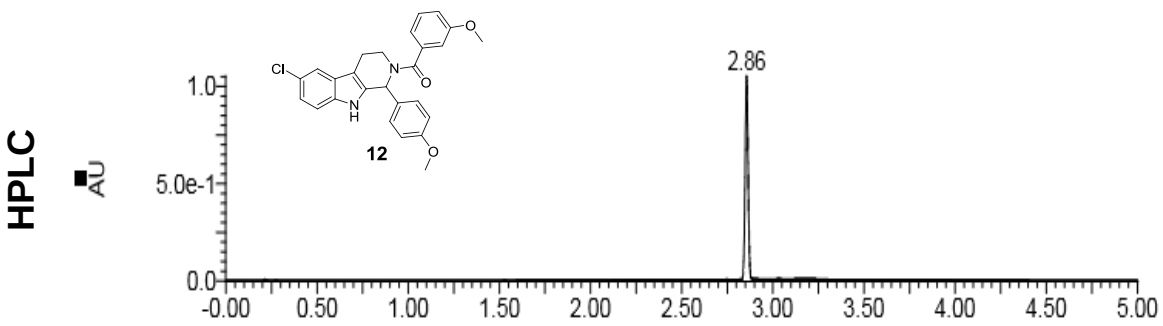
HPLC



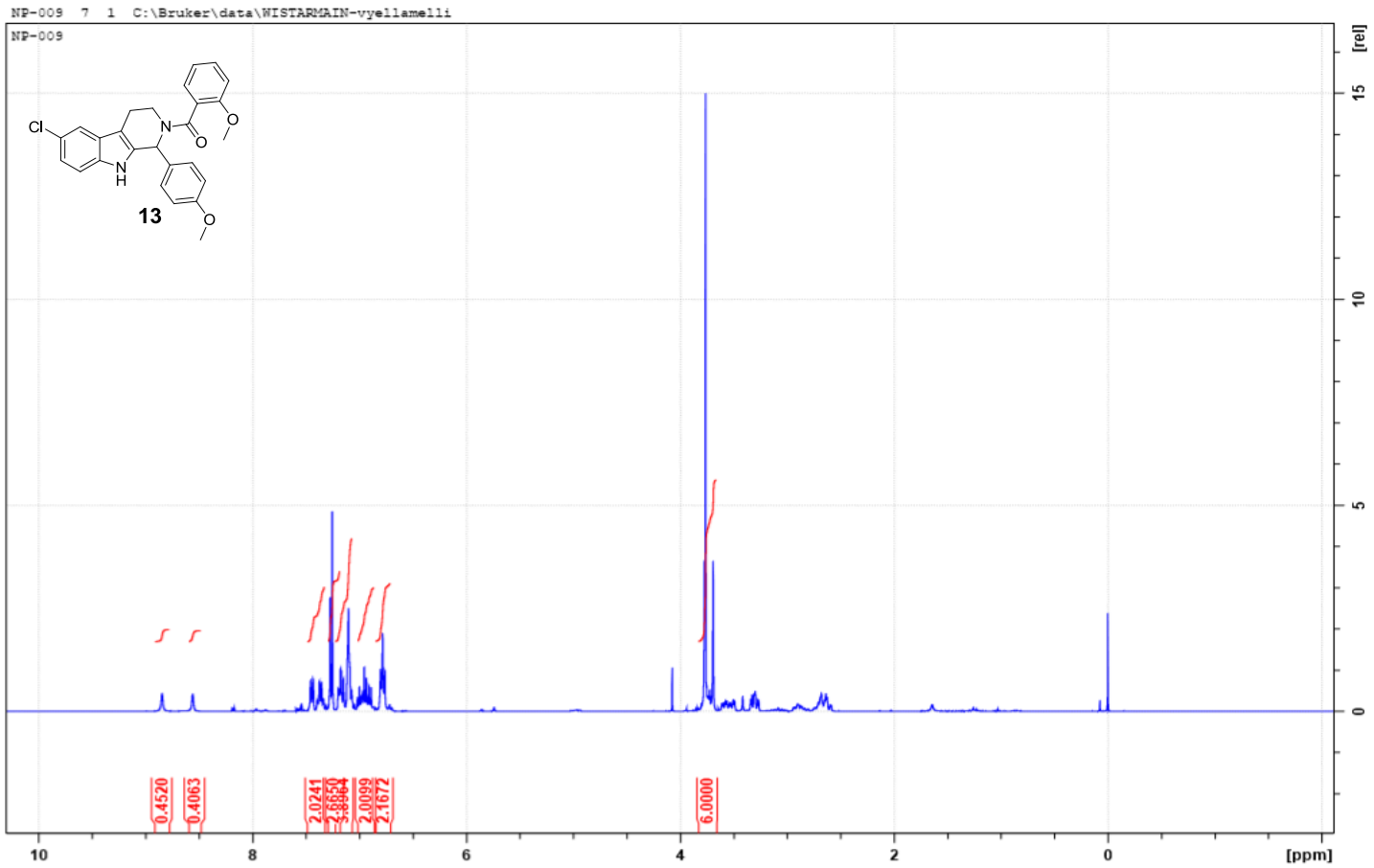
Compound-12

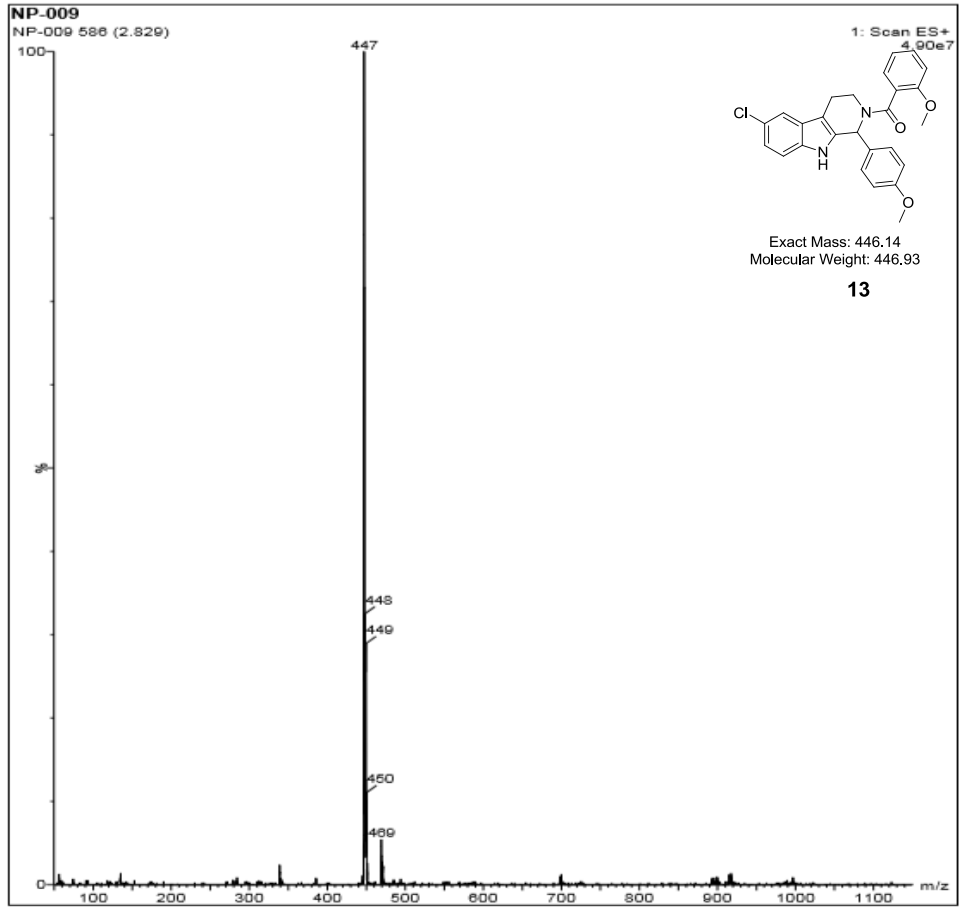

NP-010-DMS0 10 1 C:\Bruker\data\WISTARMAIN-fmohammed
12
[rel]
[ppm]
1.0000
1.2361
2.4909
2.0368
2.6402
6.0295
7.3850
0.9211
0.9645
0.9034
2.3494

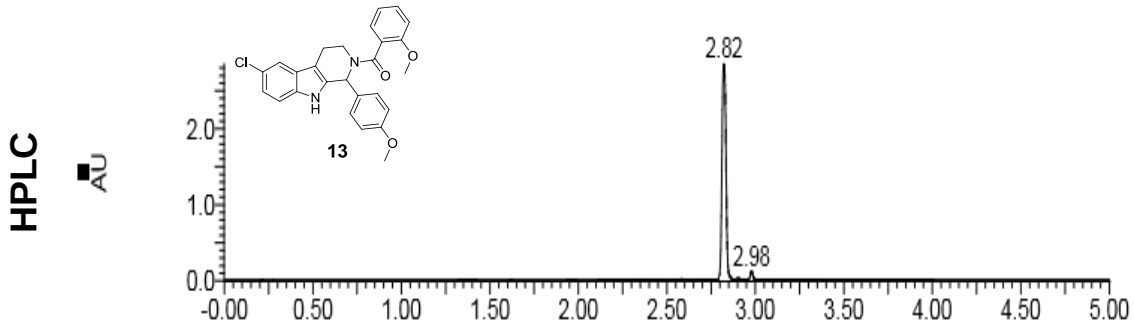

NP-010
NP-010 596 (2.878)
1: Scan ES+
1.82e7
Exact Mass: 446.14
Molecular Weight: 446.93
12
m/z


HPLC
AU
12
2.86

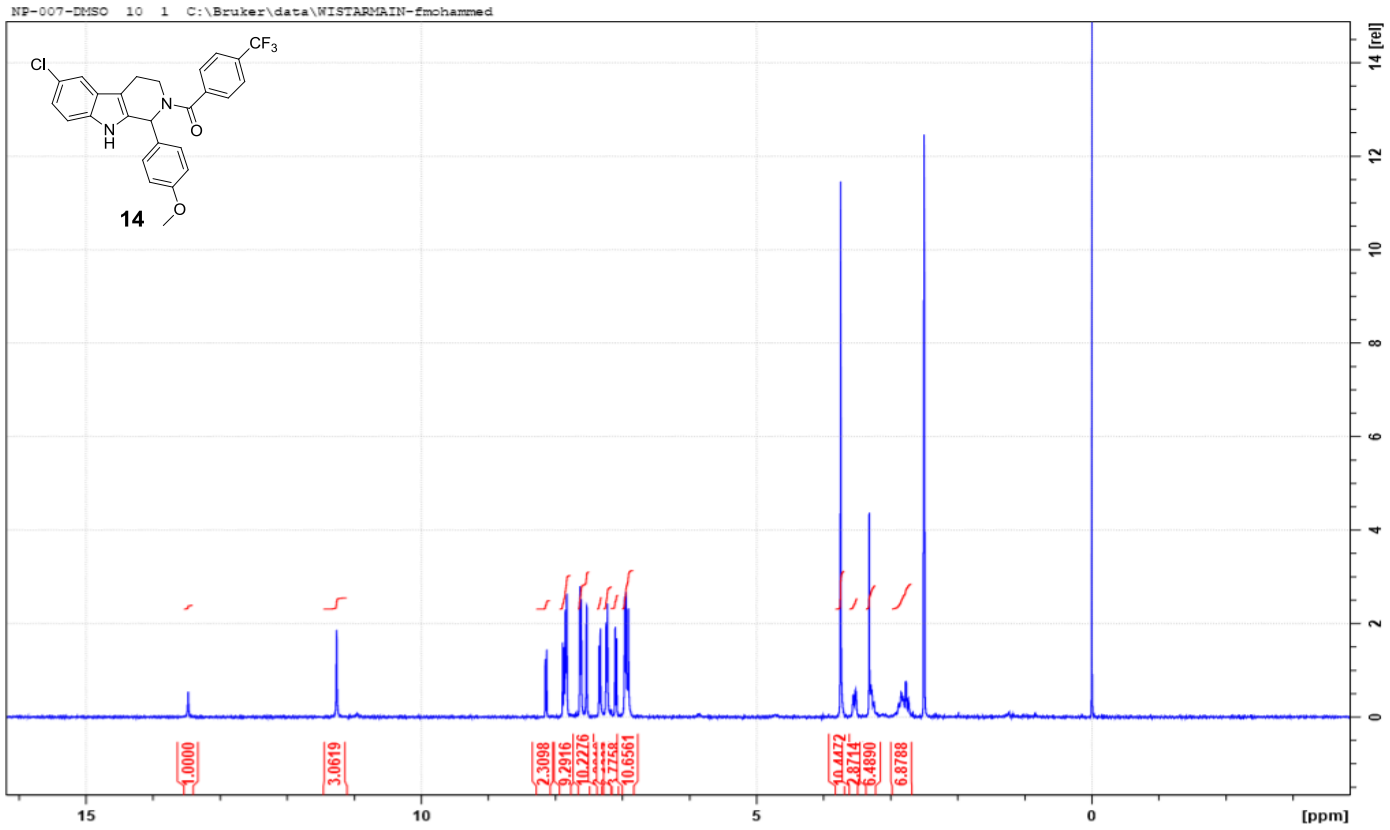
Compound-13

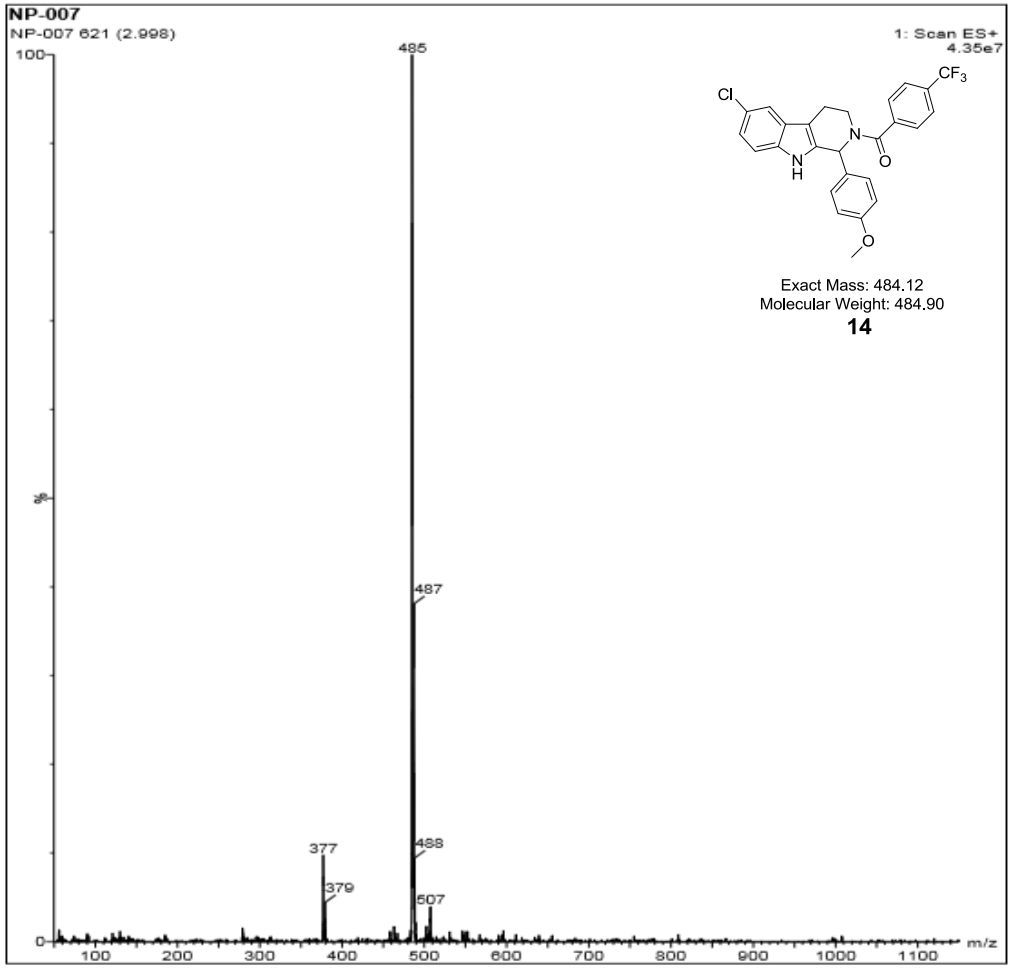

NP-009 7 1 C:\Bruker\data\WISTARMAIN-vyellamelli
NP-009
13
0.4520
0.4063
2.0241
2.0099
2.1672
6.0000
[rel]
[ppm]

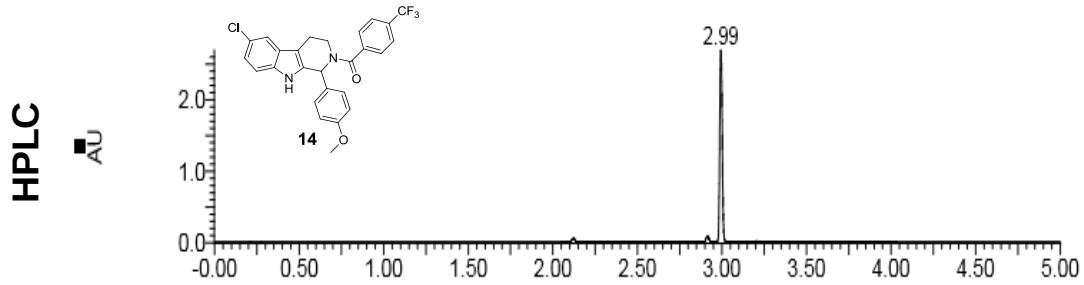

NP-009
NP-009 586 (2.829)
1: Scan ES+
4.90e7
447
448
449
450
469
%
m/z
Exact Mass: 446.14
Molecular Weight: 446.93
13


HPLC
AU
13
2.82
2.98

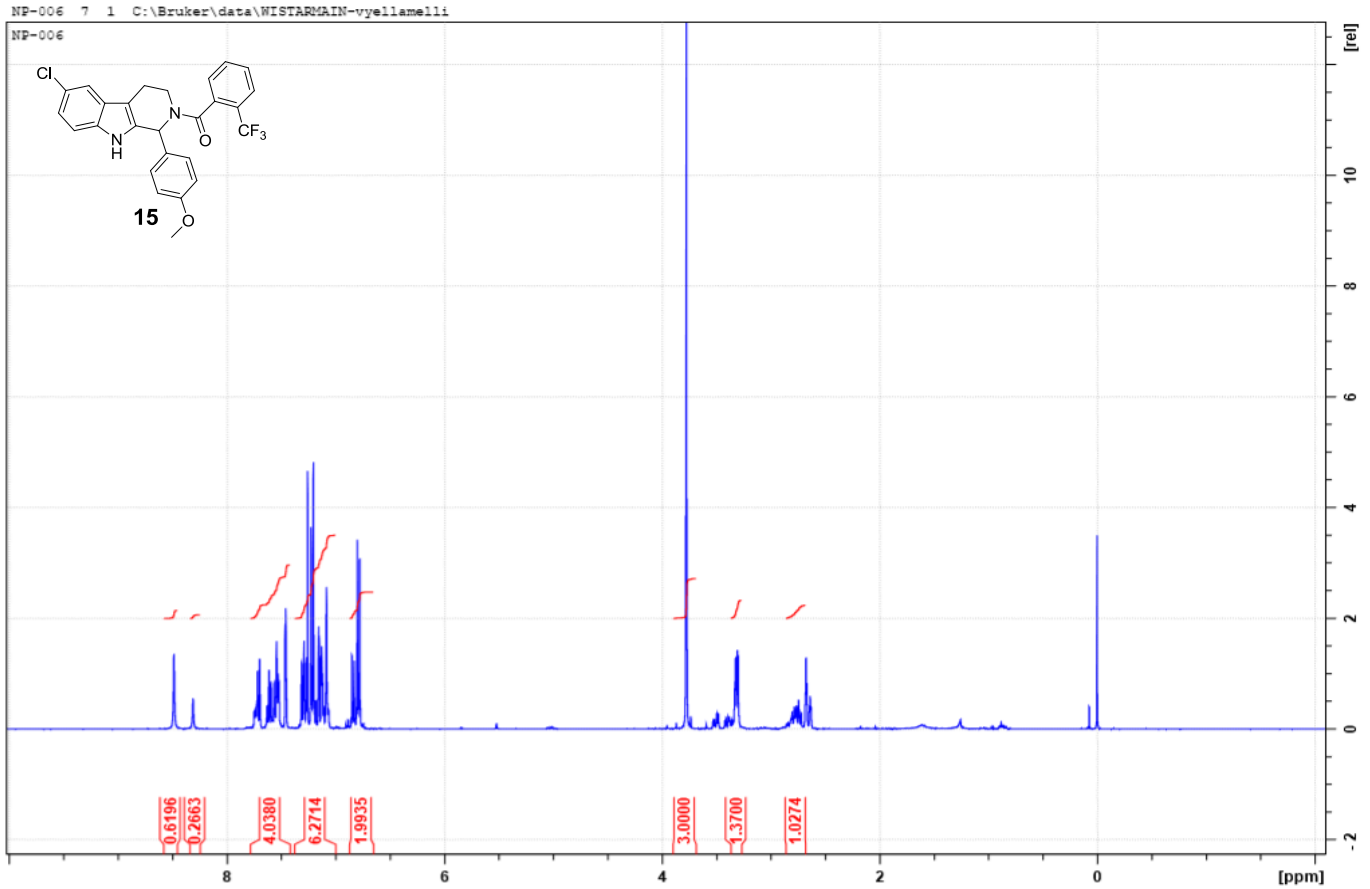
Compound-14

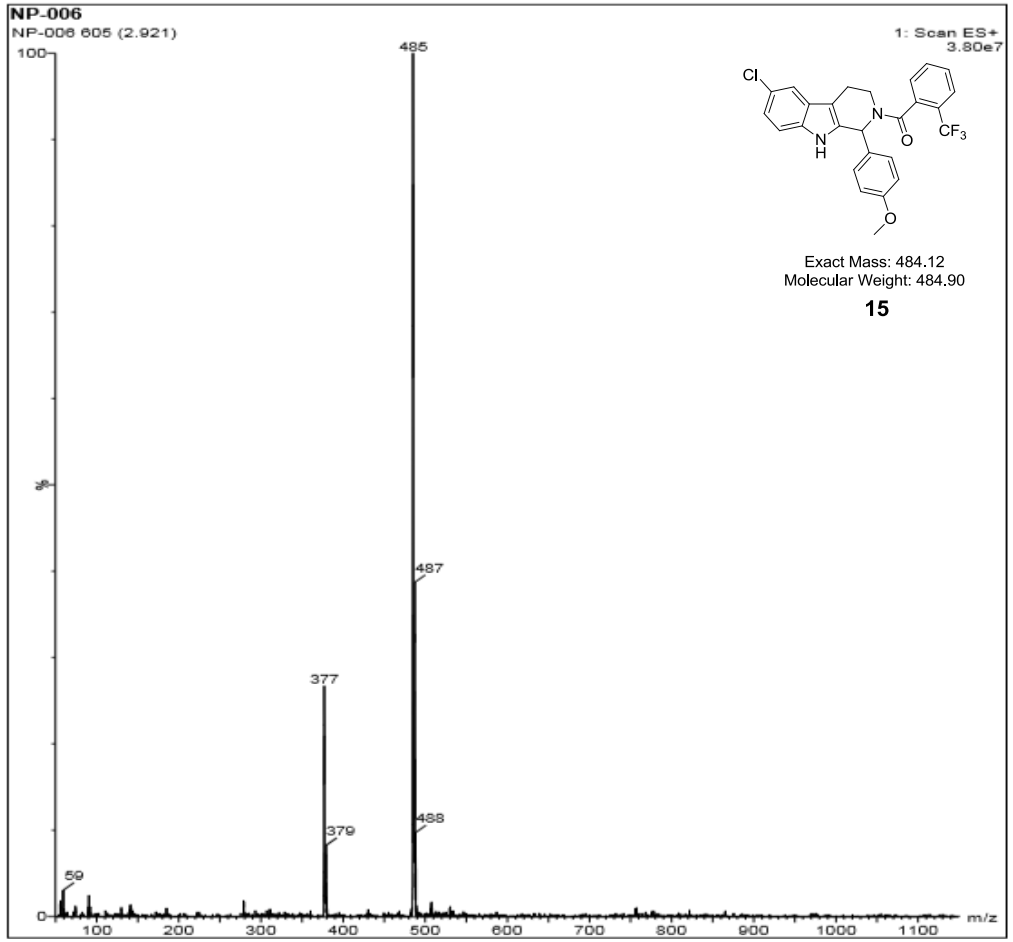

NP-007-DMSO 10 1 C:\Bruker\data\WISTARMAIN-fmohammed
14
[ppm]
14 [rel]

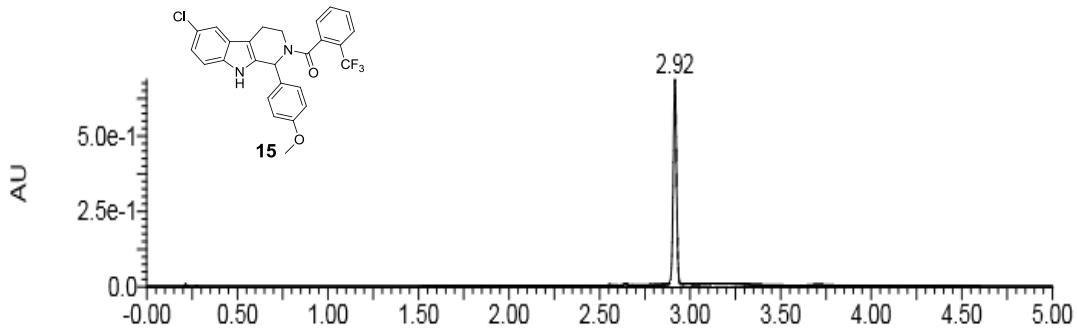

NP-007
NP-007 621 (2.998)
1: Scan ES+
4.35e7
485
487
488
377
379
507
m/z
Exact Mass: 484.12
Molecular Weight: 484.90
14


HPLC
AU
14
2.99

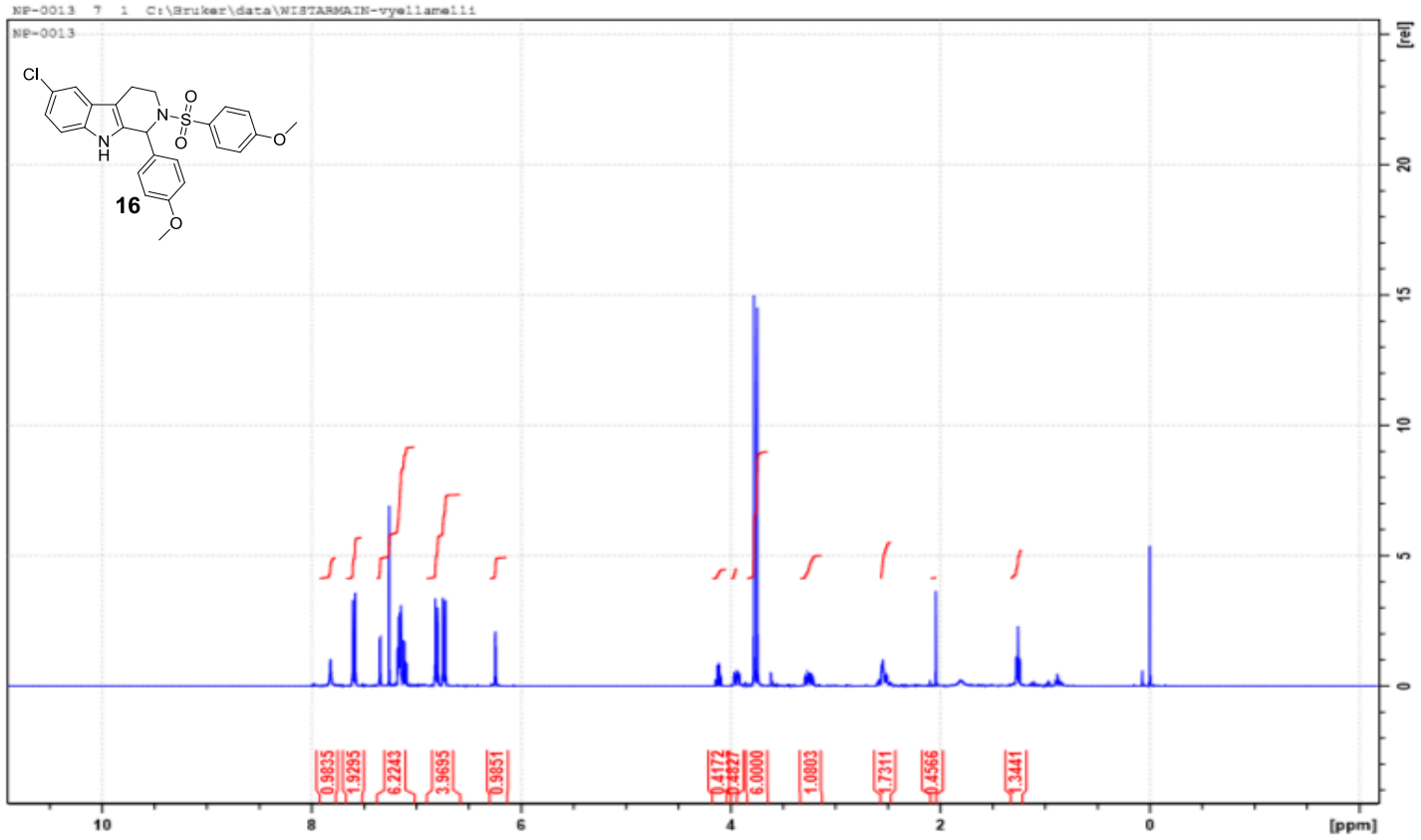
Compound-15

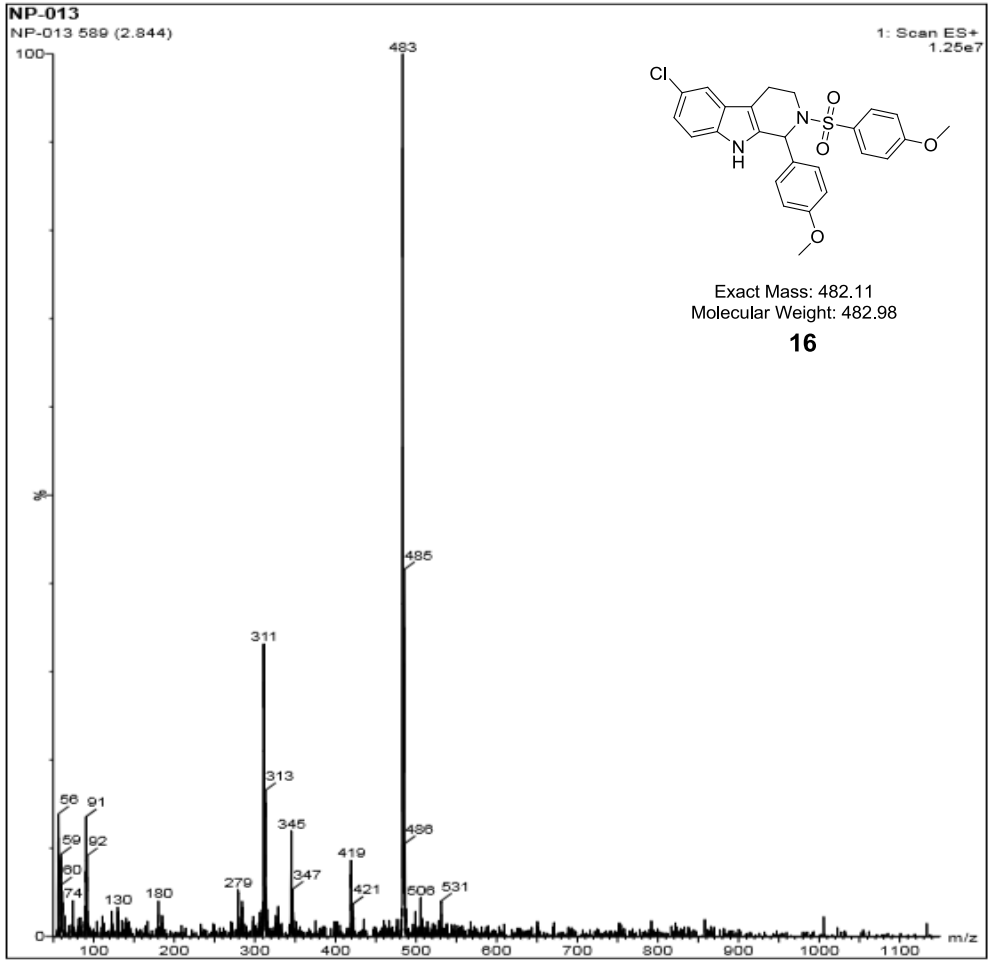

NP-006 7 1 C:\Bruker\data\WISTARMAIN-vyellamelli
NP-006
15
0.6196
0.2663
4.0380
6.2714
1.9935
3.0000
1.3700
1.0274
[rel]
[ppm]

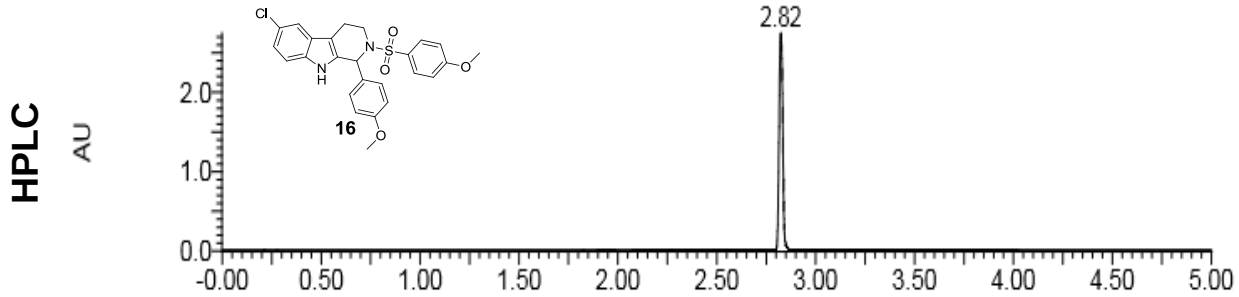

NP-006
NP-006 605 (2.921)
1: Scan ES+
3.80e7
485
487
377
379
488
59
%
m/z
Exact Mass: 484.12
Molecular Weight: 484.90
15


15
2.92
AU
5.0e-1
2.5e-1
0.0

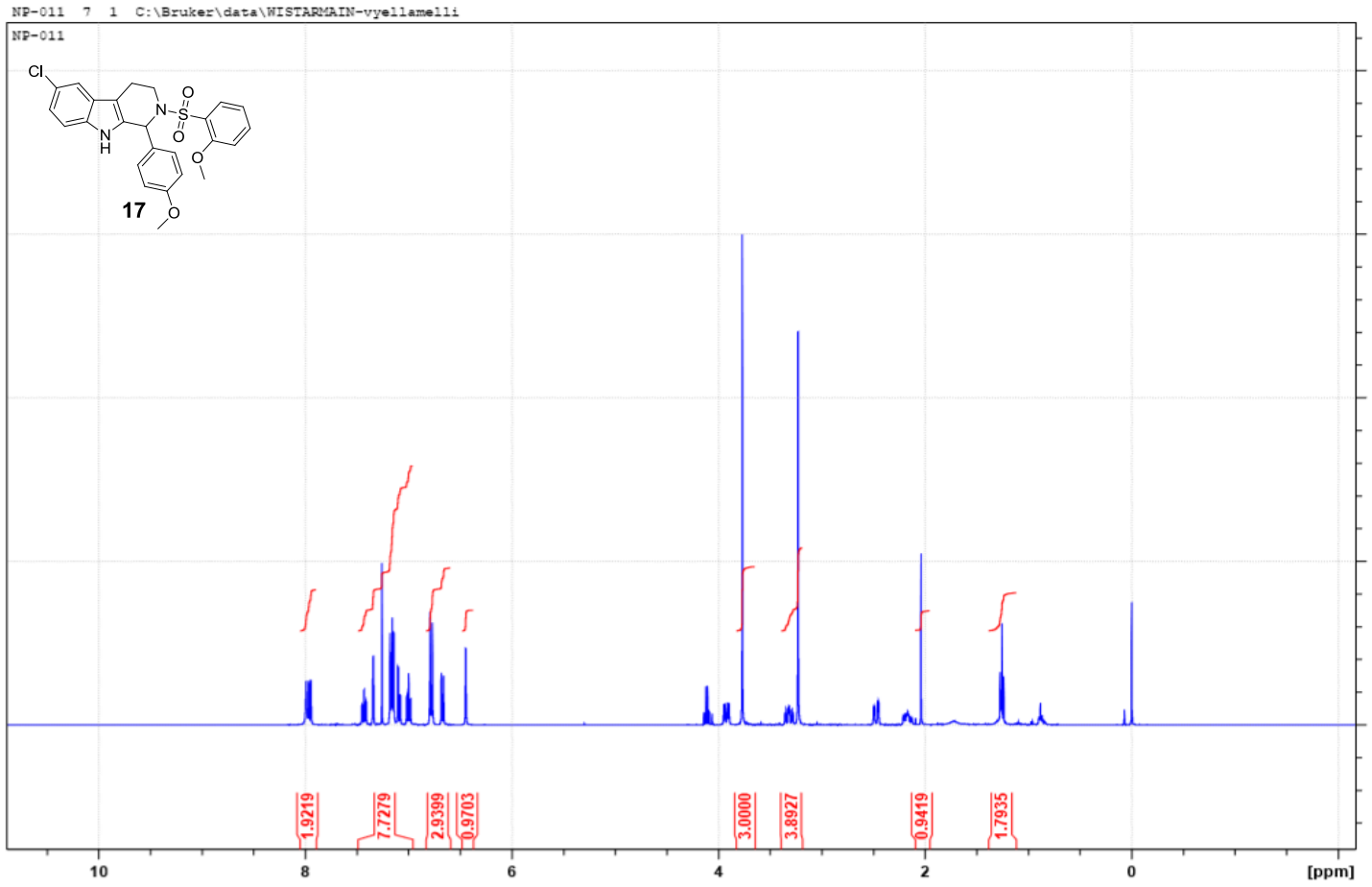
Compound-16

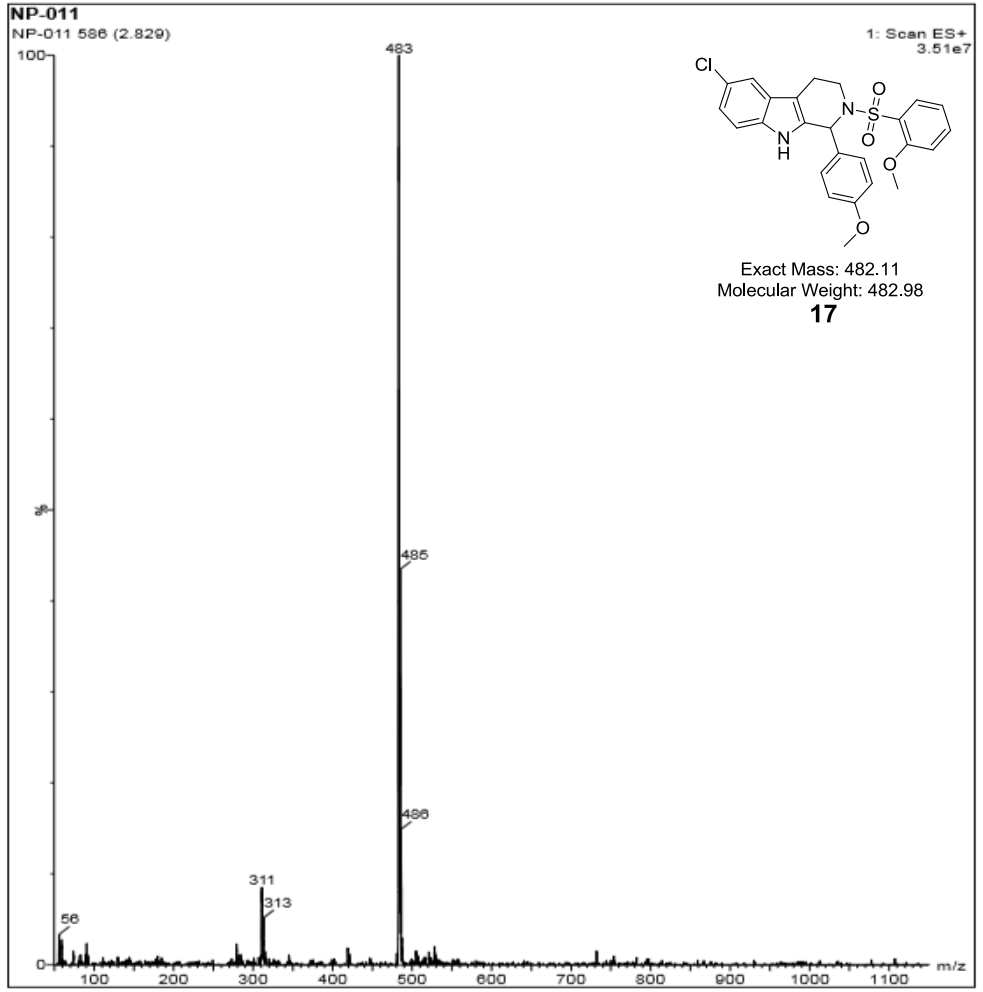

NP-0013
16
[rel]
[ppm]


NP-013
NP-013 589 (2.844)
1: Scan ES+
1.25e7
16
Exact Mass: 482.11
Molecular Weight: 482.98
m/z

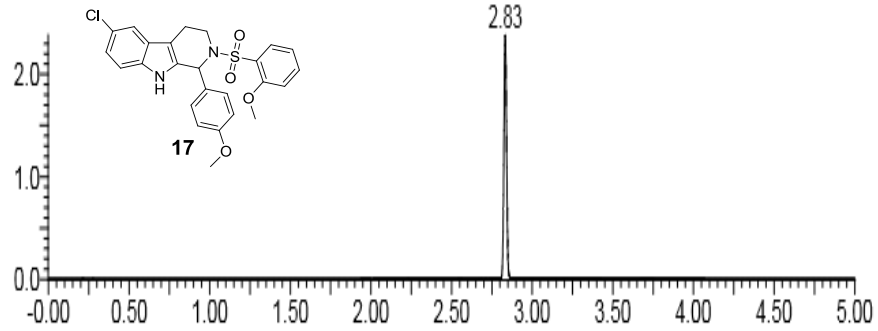

HPLC
AU
16
2.82

Compound-17

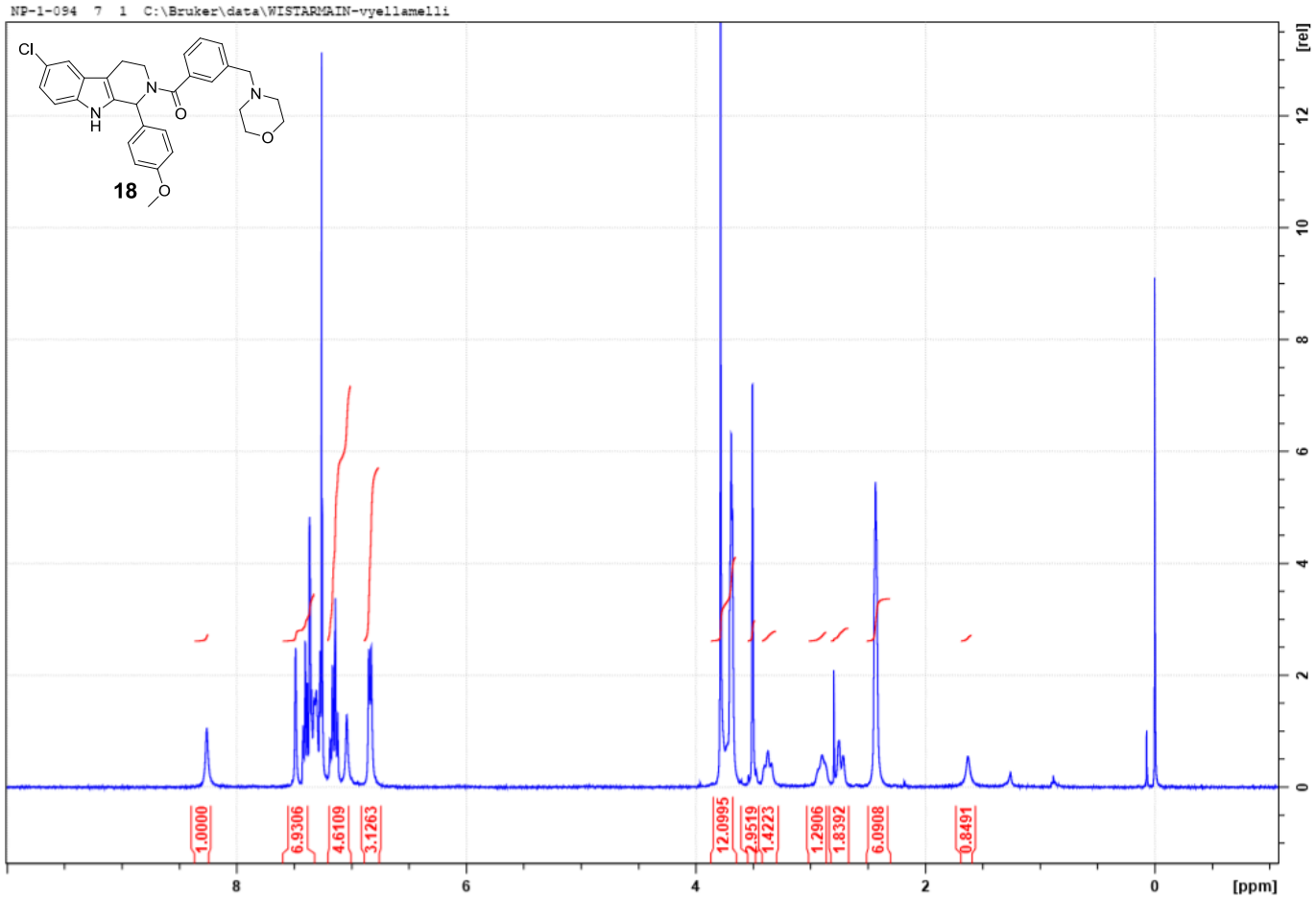


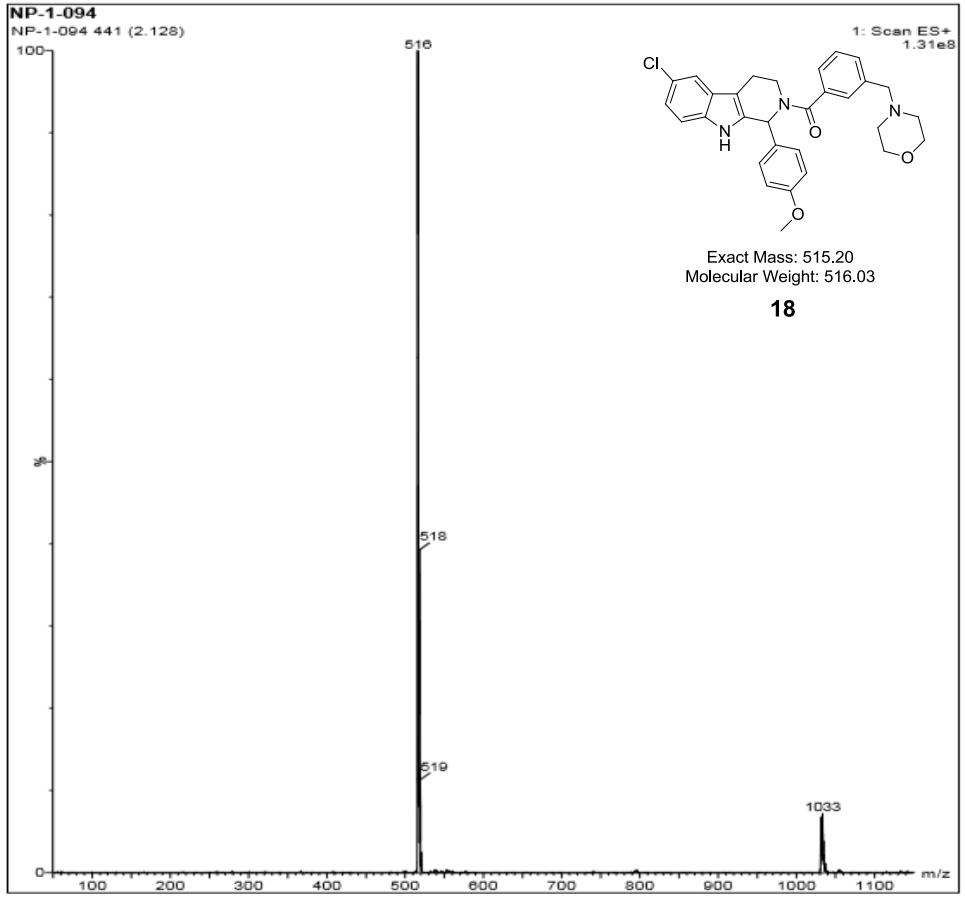


HPLC

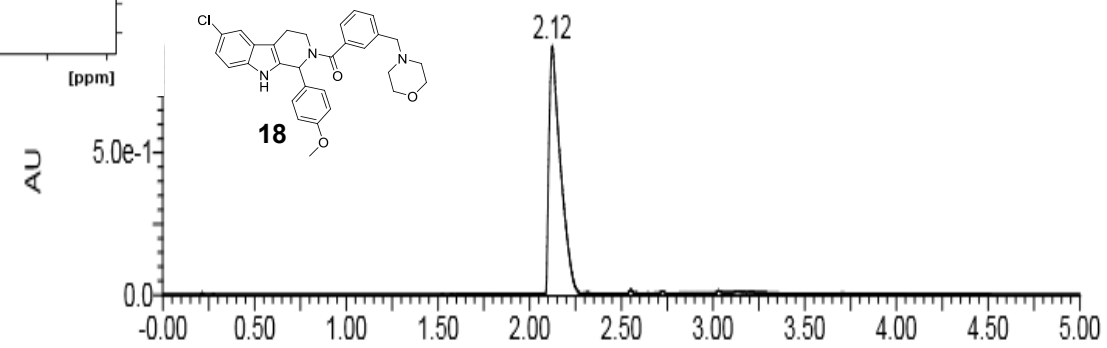


Compound-18

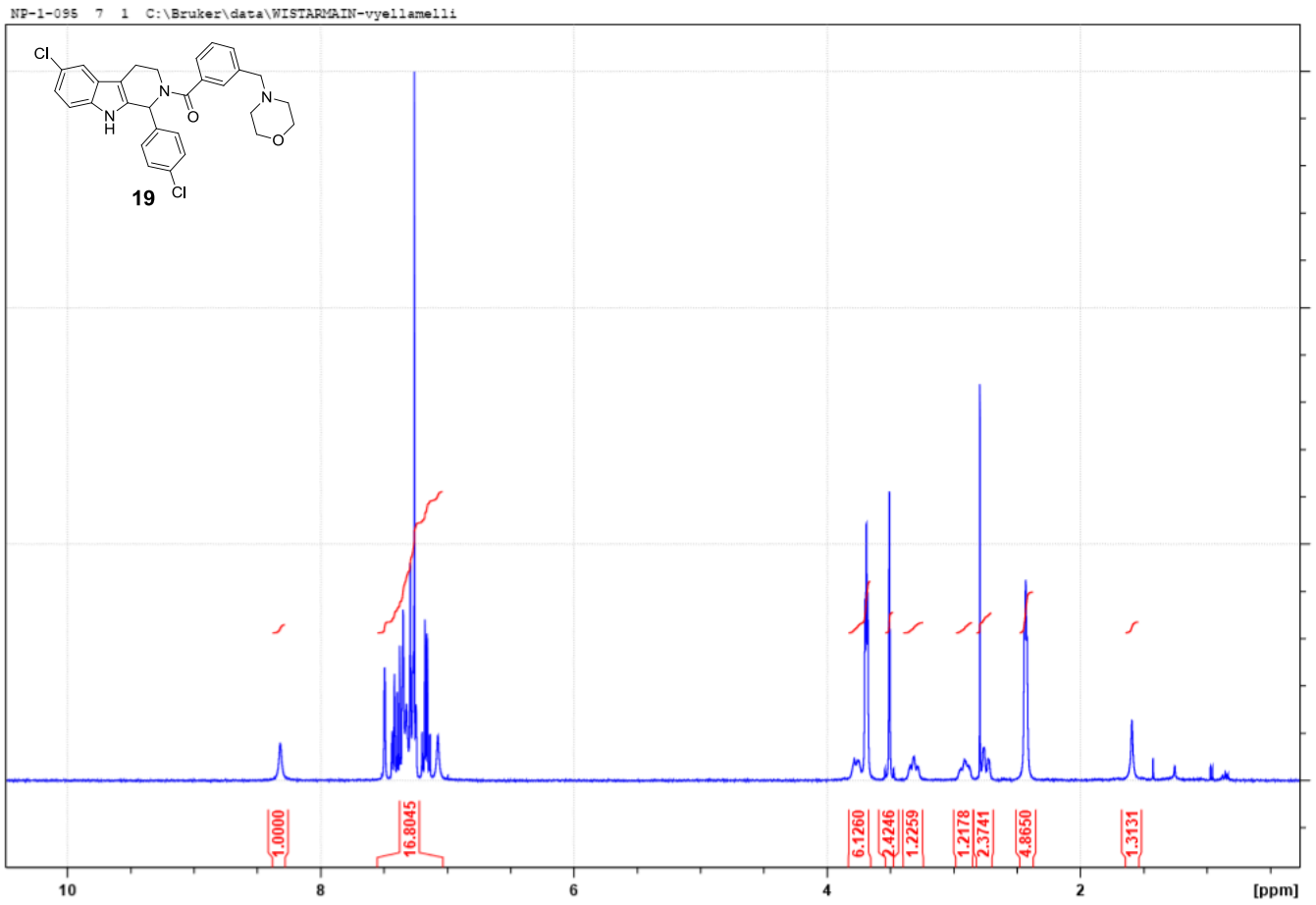


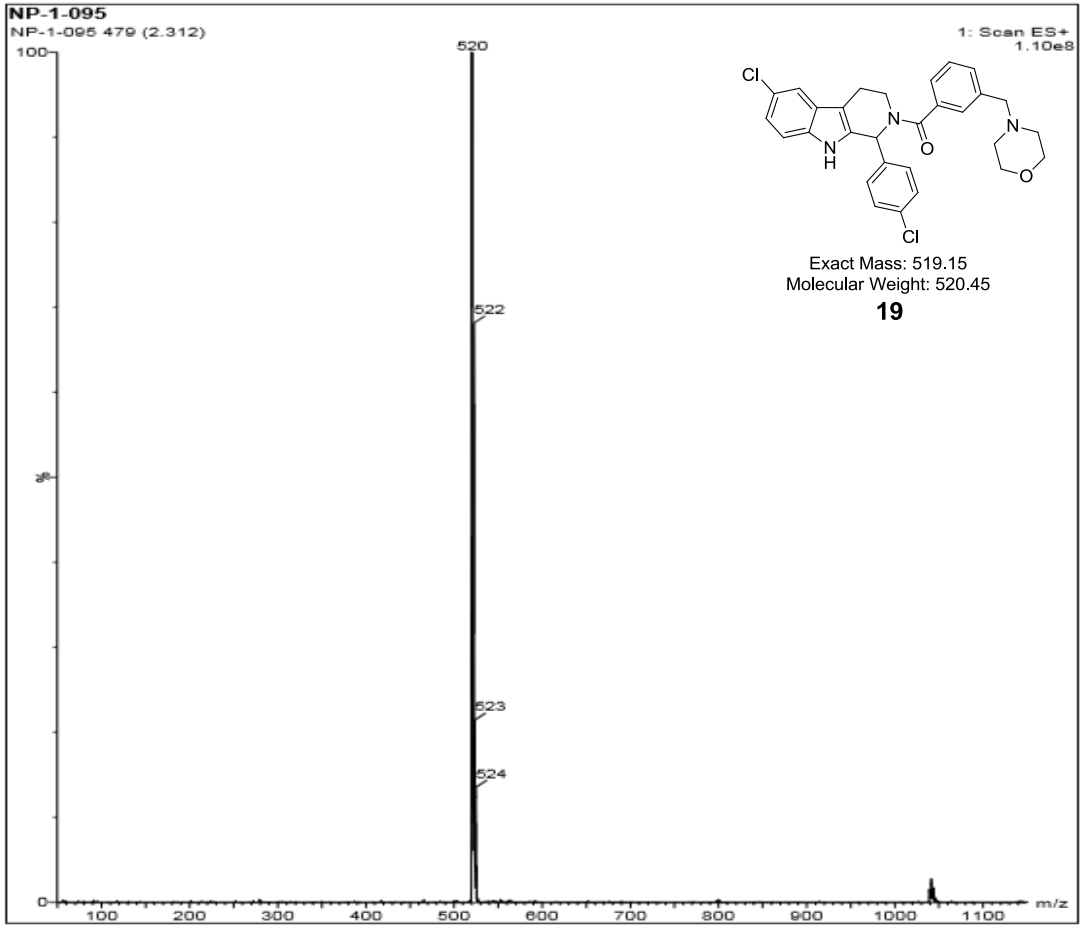


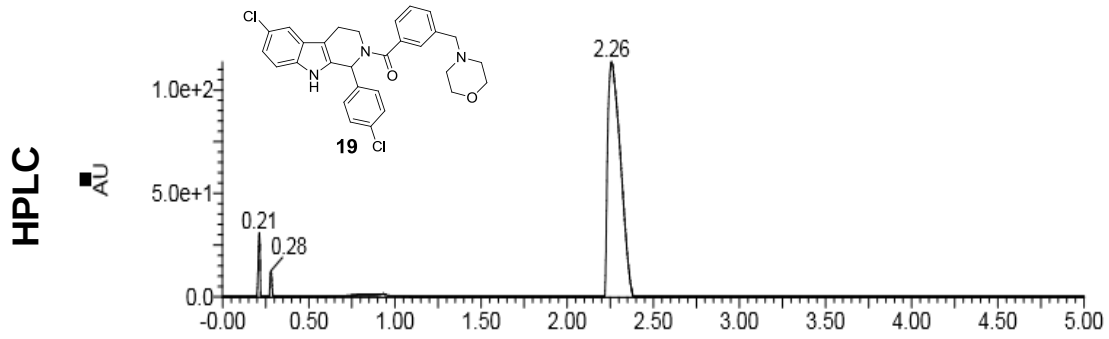
HPLC



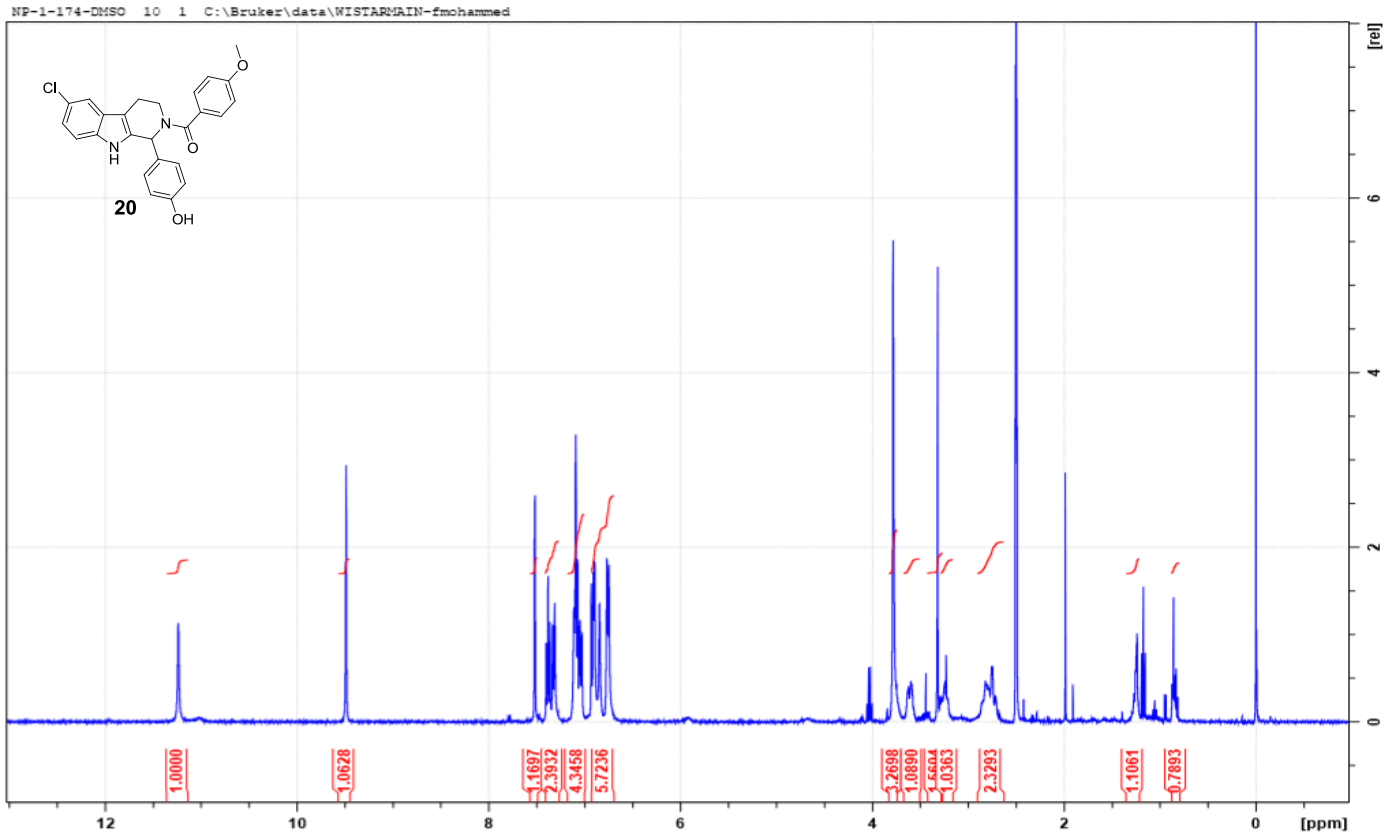
Compound-19

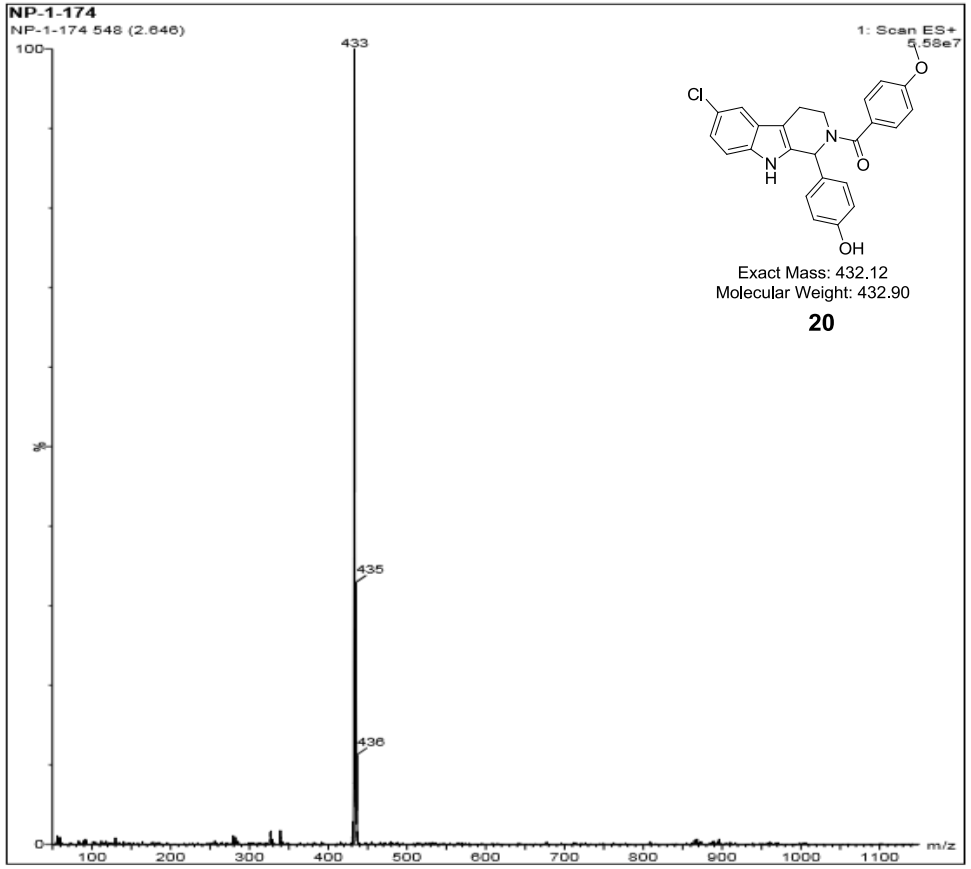

NP-1-095 7 1 C:\Bruker\data\WISTARMAIN-vyellamelli
19
15 [rel]
10
5
0
1.0000
16.8045
6.1260
2.4246
1.2259
1.2178
2.3741
4.8650
1.3131
10
8
6
4
2
[ppm]

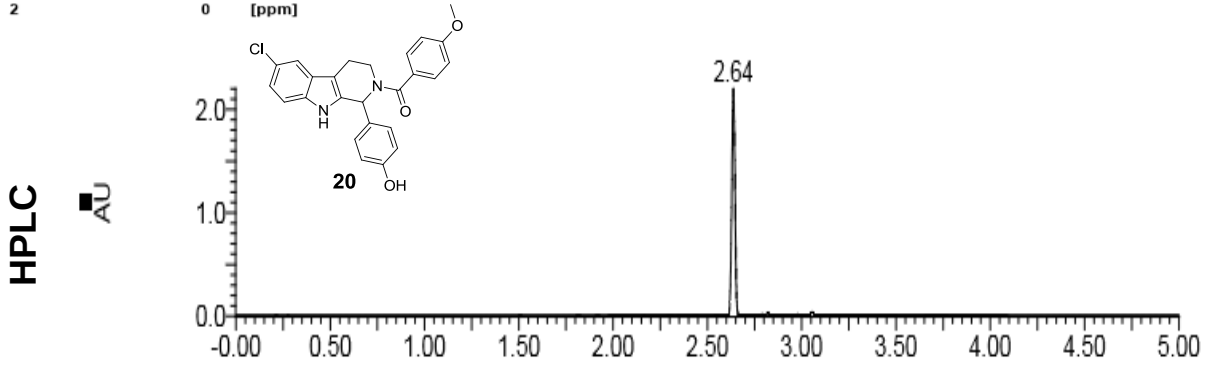

NP-1-095
NP-1-095 479 (2.312)
1: Scan ES+
1.10e8
100
%
0
520
522
523
524
100
200
300
400
500
600
700
800
900
1000
1100
m/z
Exact Mass: 519.15
Molecular Weight: 520.45
19


HPLC
AU
19
1.0e+2
5.0e+1
0.0
0.21
0.28
2.26
-0.00
0.50
1.00
1.50
2.00
2.50
3.00
3.50
4.00
4.50
5.00

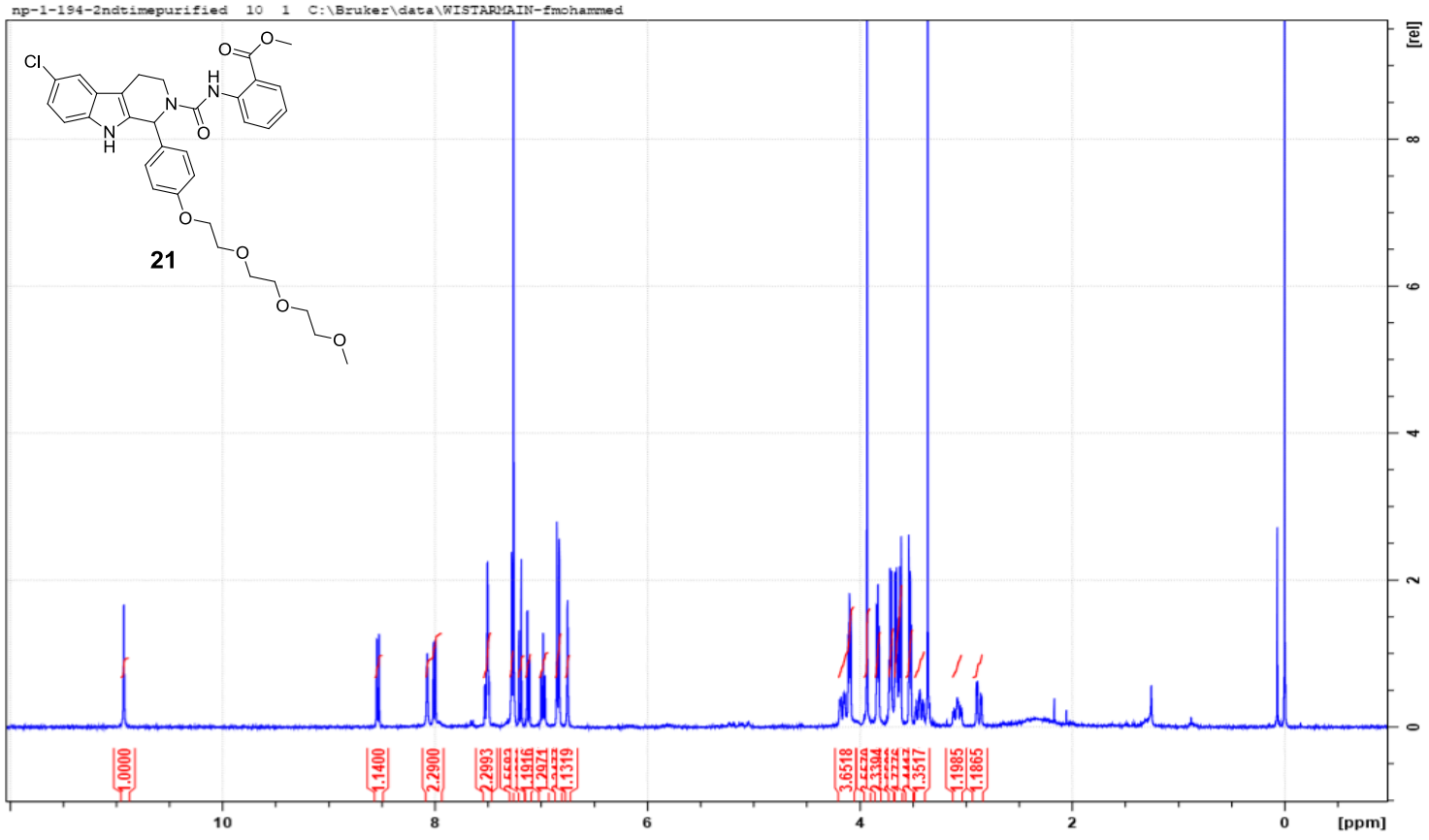
Compound-20

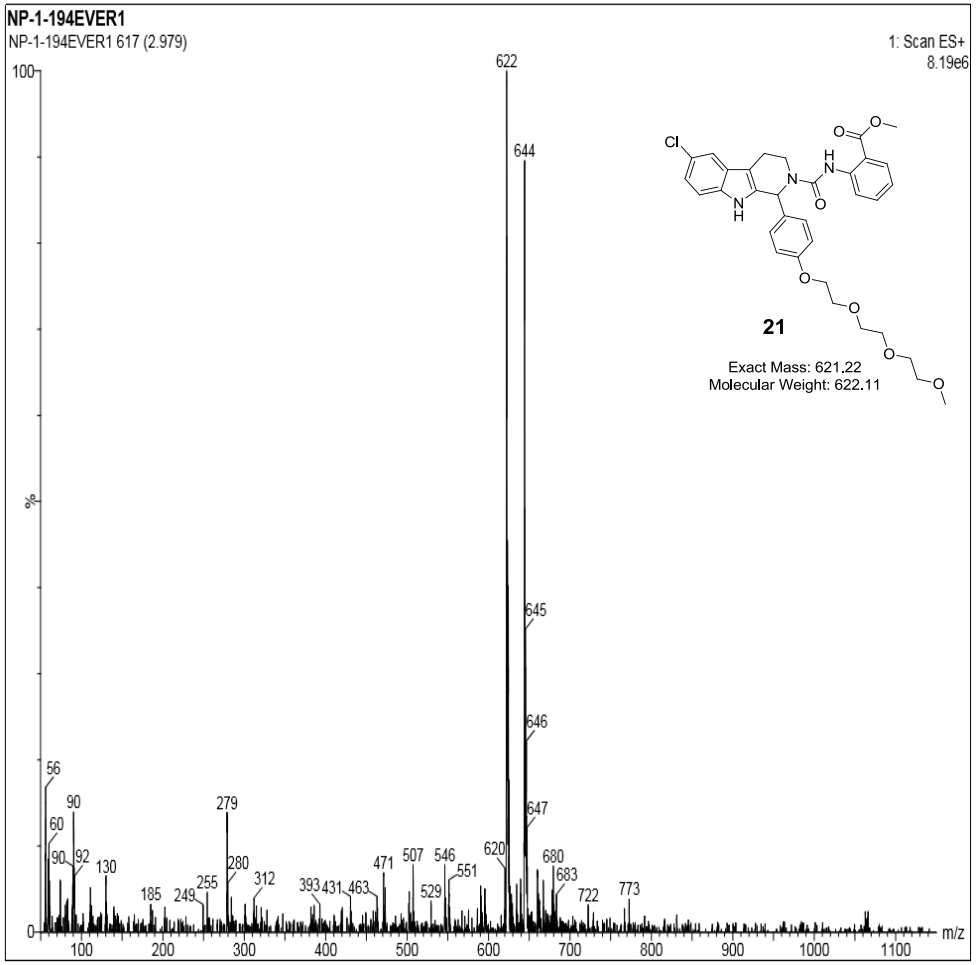

NP-1-174-DMSO 10 1 C:\Bruker\data\WISTARMAIN-fmohammed
20
OH
[rel]
[ppm]
1.0000
1.0628
1.1697
2.3932
4.3458
5.7236
3.2698
1.0890
1.5604
1.0363
2.3293
1.1061
0.7893

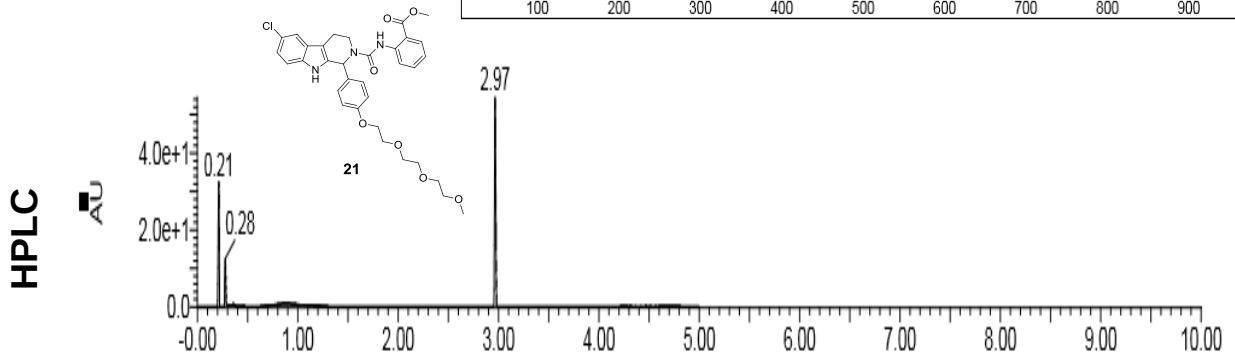

NP-1-174
NP-1-174 548 (2.646)
1: Scan ES+
5.58e7
433
435
436
%
m/z
Exact Mass: 432.12
Molecular Weight: 432.90
20


HPLC
AU
20
OH
2.64

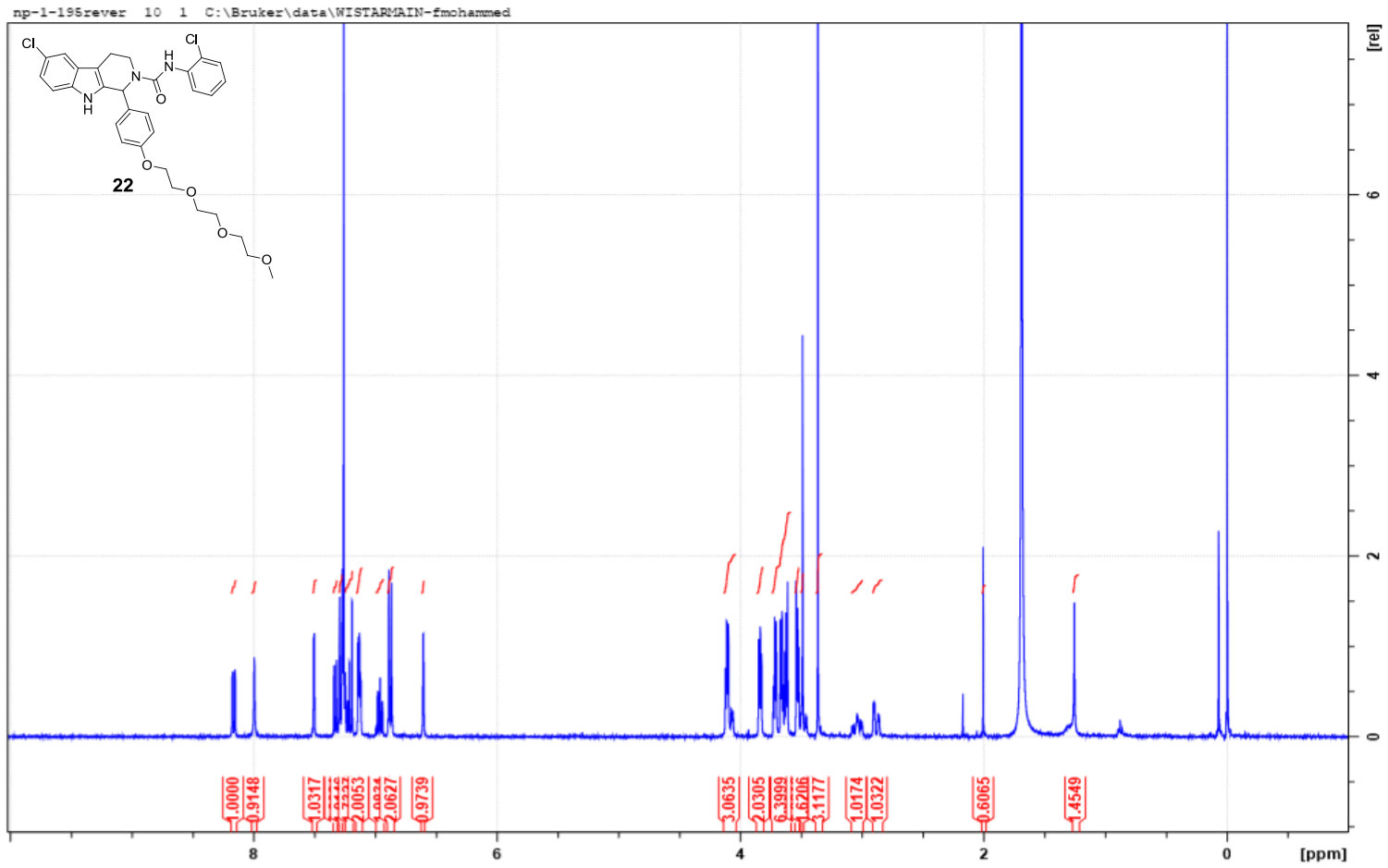
Compound-21

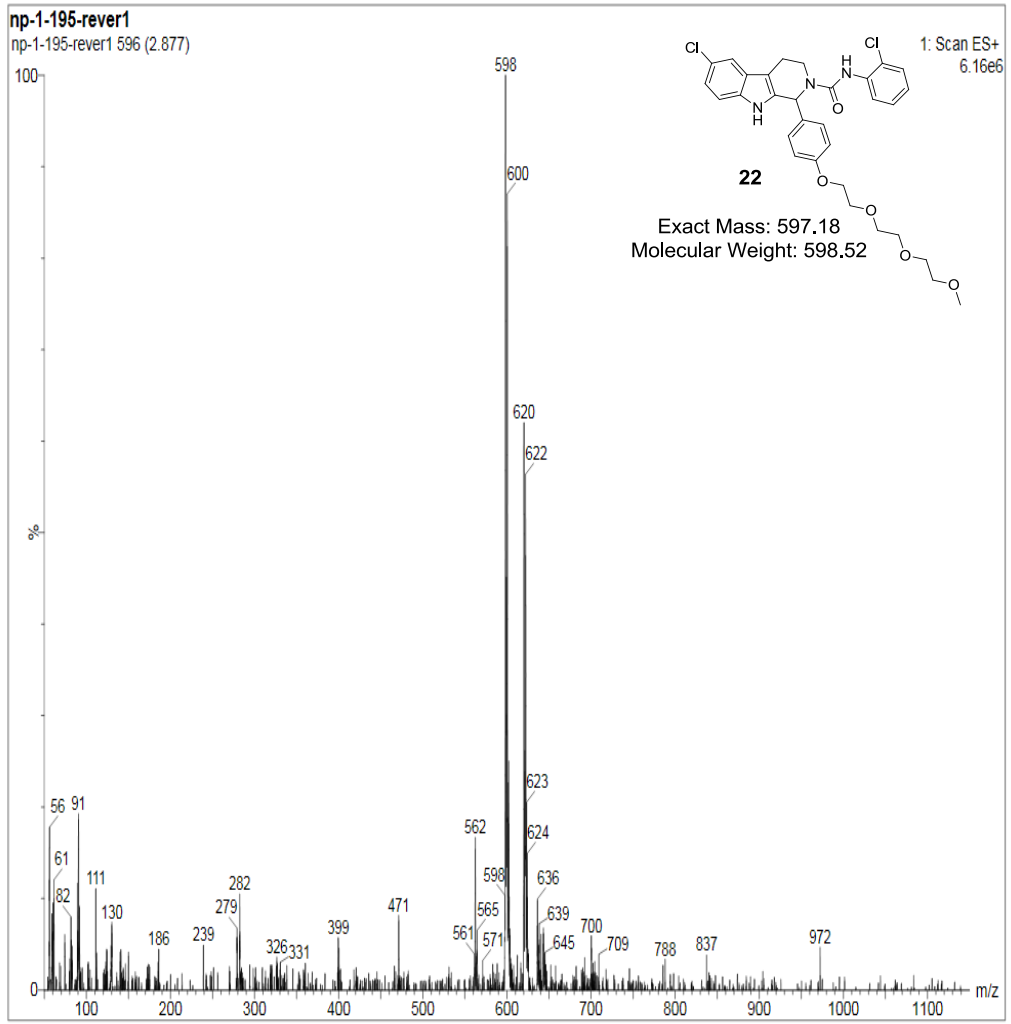

np-1-194-2ndtimepurified 10 1 C:\Bruker\data\WISTARMAIN-fmohammed
21
[rel]
[ppm]
1.0000
1.1400
2.2900
2.2993
1.1916
1.2021
1.1319
3.6518
1.3517
1.1985
1.1865

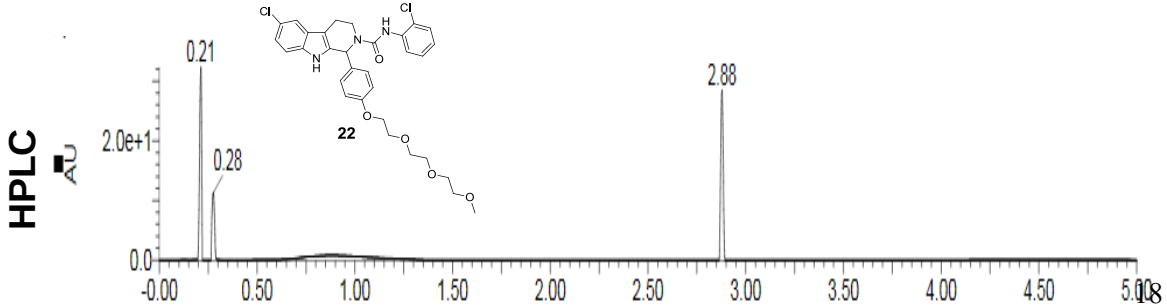

NP-1-194EVER1
NP-1-194EVER1 617 (2.979)
1: Scan ES+
8.19e6
21
Exact Mass: 621.22
Molecular Weight: 622.11
m/z


HPLC
AU
21
2.97
0.21
0.28

Compound-22


np-1-195rever 10 1 C:\Bruker\data\WISTARMAIN-fmohammed
22
[rel]
[ppm]


np-1-195-rever1
np-1-195-rever1 596 (2.877)
1: Scan ES+
6.16e6
22
Exact Mass: 597.18
Molecular Weight: 598.52
m/z


HPLC
AU
22
0.21
0.28
2.88

SNU719 xenograft testing: 1x107 SNU719 gastric carcinoma cells were injected subcutaneously into the left and right flanks of NSG (*NOD/LtSz-scid/IL2Rγ^{null}*) mice (Jackson Labs) mice. 28 days post-injection animals were injected once per day with control vehicle (DMSO/Kollipher), PBS, C60 or C60 analogues (30 mg/kg in Expt 1 and 60 mg/kg in Expt 2) or injected once with the positive control lytic inducing chemotherapy agent, gemcitabine (60 mg/kg). Animals were euthanized and tumor masses were collected after 4 days of treatment. Tumor masses were homogenized and immunoblot analysis was performed to detect the lytic EBV protein, BZLF1 (Z) and β-actin (loading control).

AGS-Akata xenograft testing: NSG (*NOD/LtSz-scid/IL2Rγ^{null}*) mice (Jackson Labs) were injected with 1X10^7 AGS-Akata cells. The cells were resuspended in 100 µL PBS and 100 µL Matrigel (Corning, catalog number: 254248). Cells were injected subcutaneously into both flanks of the mouse and tumors developed about 6 weeks (42 days). Mice were treated daily for 3 days with either vehicle (PBS with 5% DMSO and 5% Kolliphor), Gemcitabine (60 mg/kg) or C60 analogues (25 mg/kg or 50 mg/kg). Animals were euthanized after treatment and tumors were flash frozen upon collection to be used for western blot analysis. Frozen tumors were turned into tumor powder using the cell crusher system (Cell crusher) and then turned into cell lysates by resuspending in SUMO buffer. Lysates were run in a 10% SDS-PAGE gel as previously described and immunoblot analysis was performed.[15]

Antibodies against Z (EBV immediate early lytic protein, Santa Cruz Biotech., sc-53904, clone BZ1), BMRF1 (EBV early lytic protein, Millipore Sigma, MAB8186), EBNA1 (EBV latency protein, Santa Cruz Biotech., sc-57719, clone 0211), and Actin (Sigma Aldrich, A5441) were used in the immunoblot analysis.