# Fluorinated azole anticancer drugs: Synthesis, elaborated structure elucidation and docking studies

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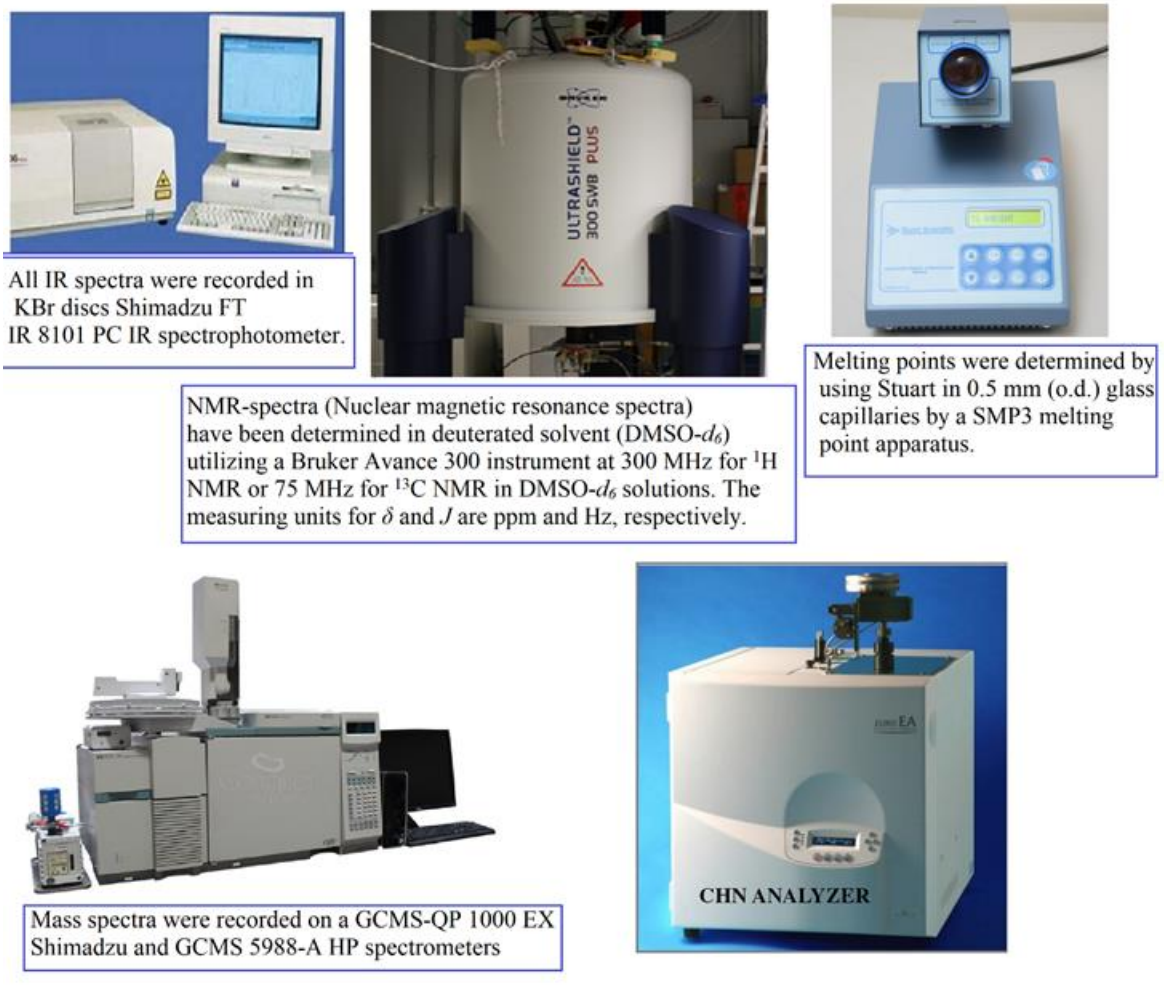
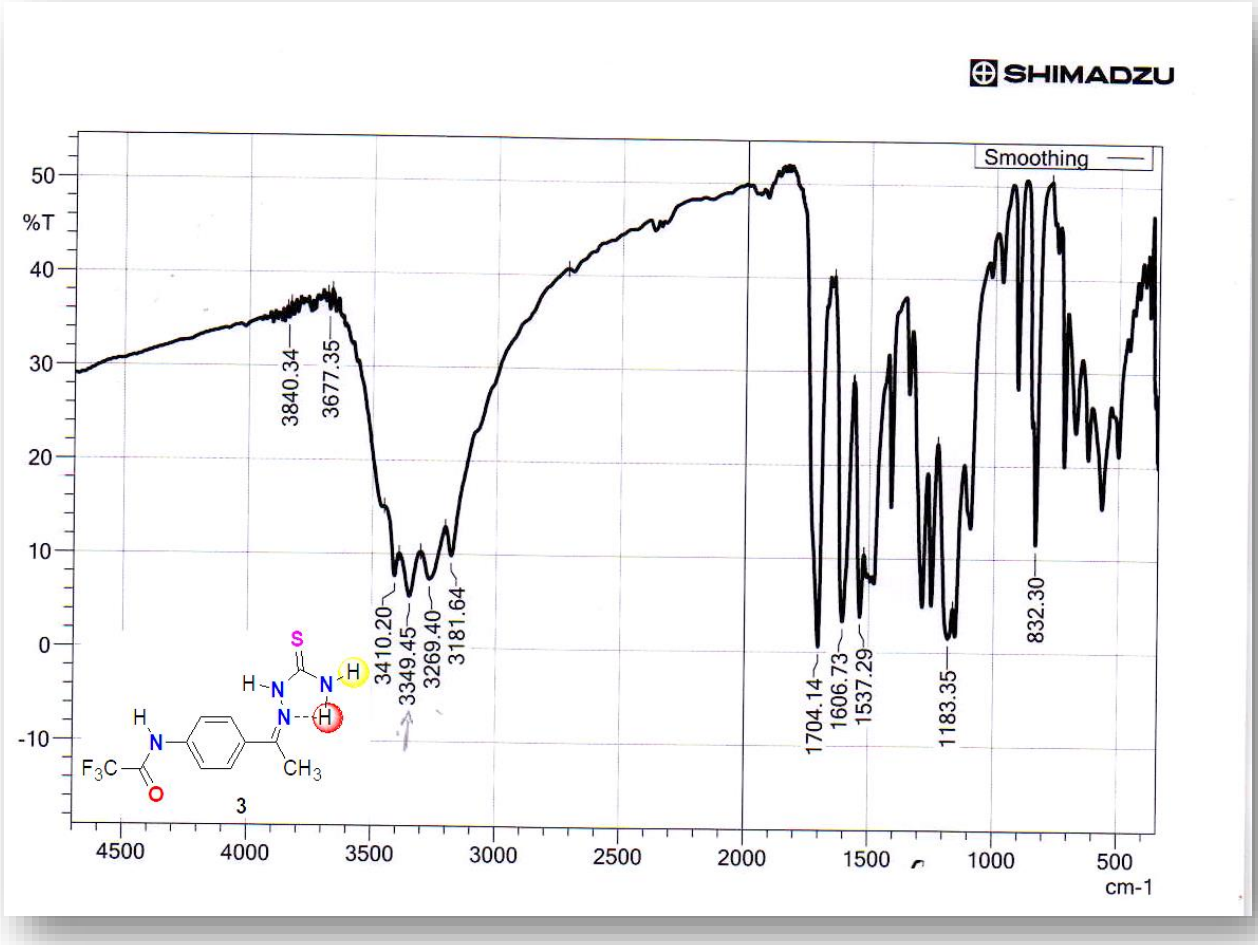
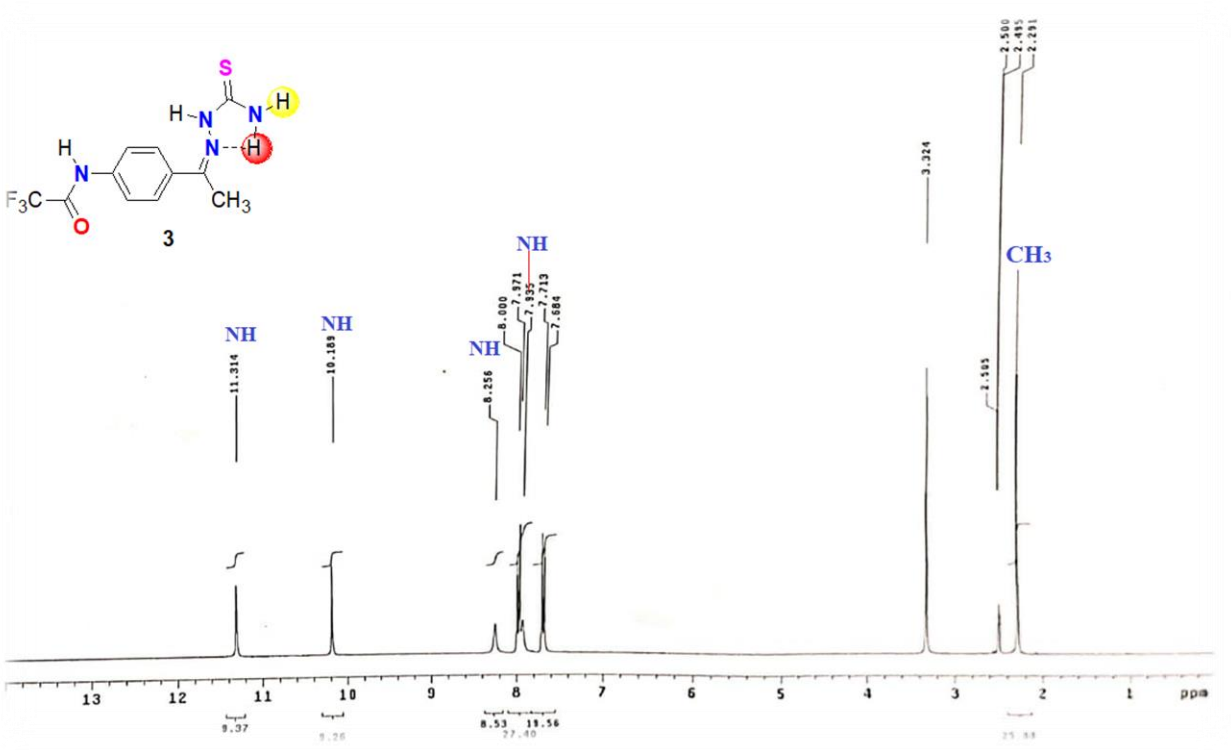
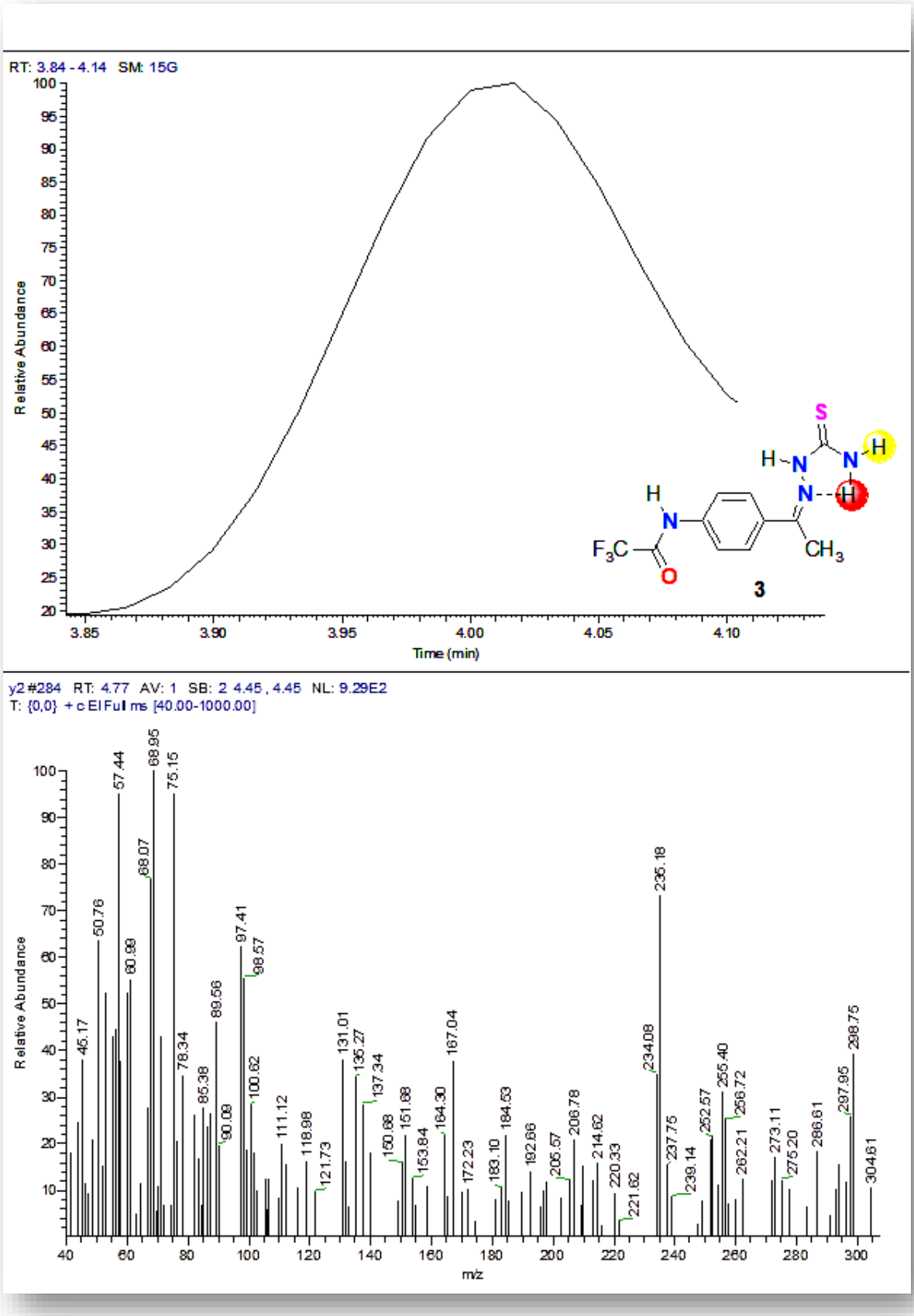
* Correspondence: thoraya-f@hotmail.com; thoraya-f@cu.edu.eg

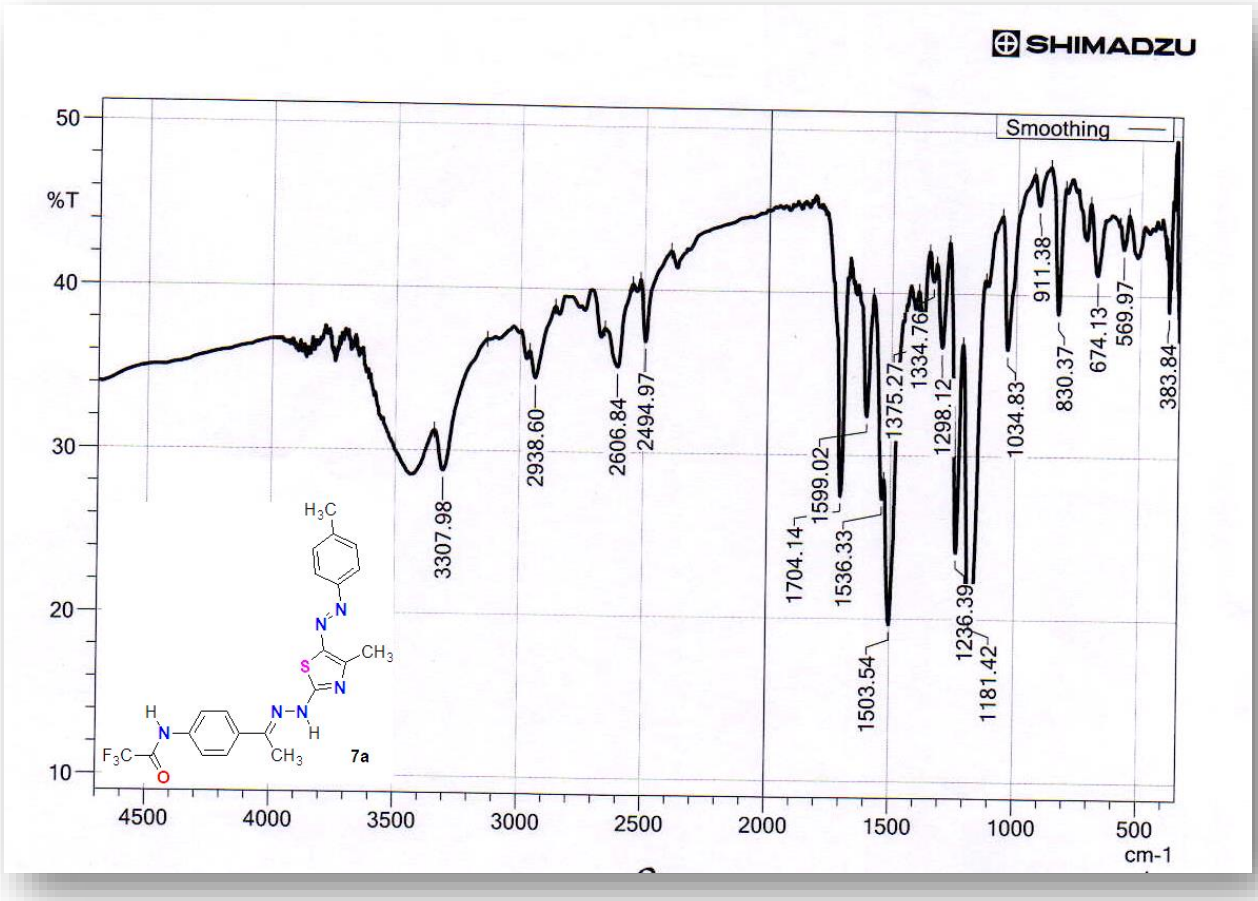


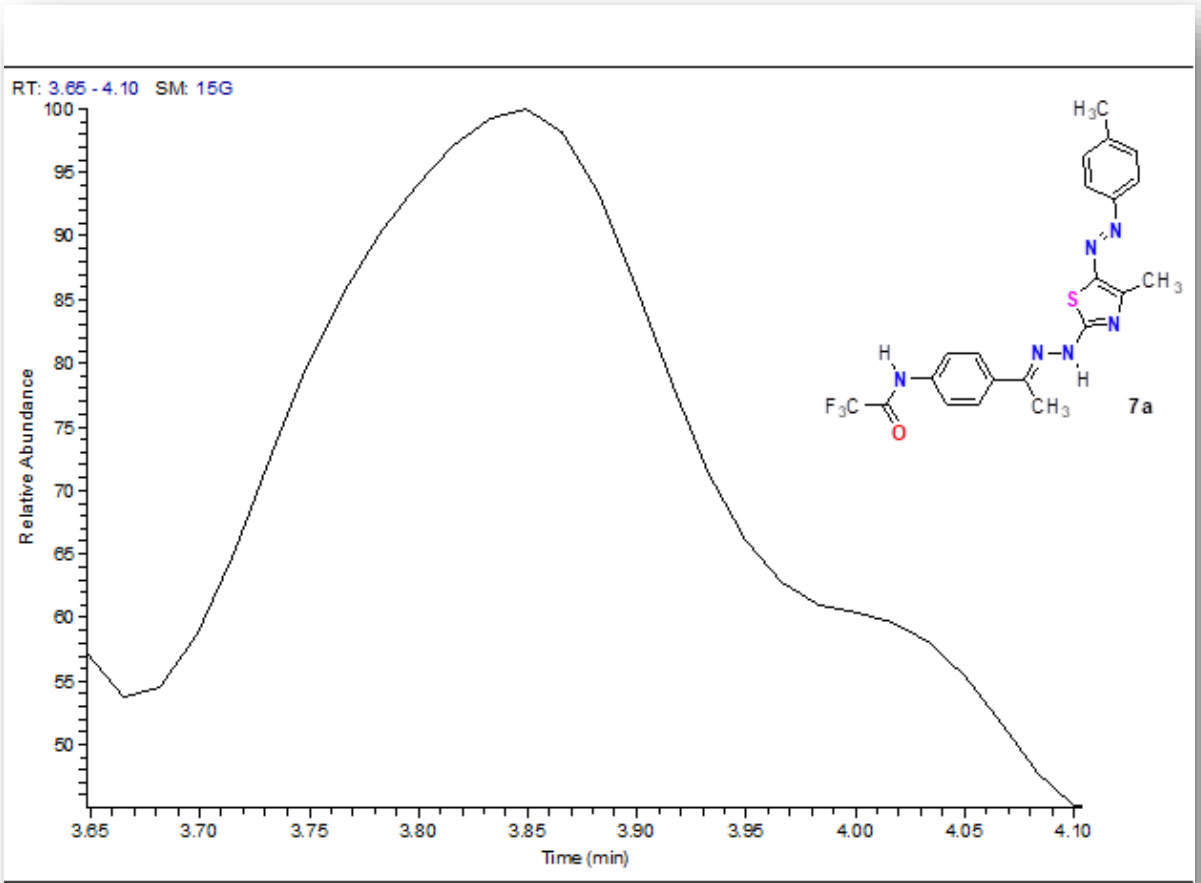

**S1**. The pictures and characterization of all device which have been utilized to record the spectra for derivatives **3**, **7**, **11** and **13**

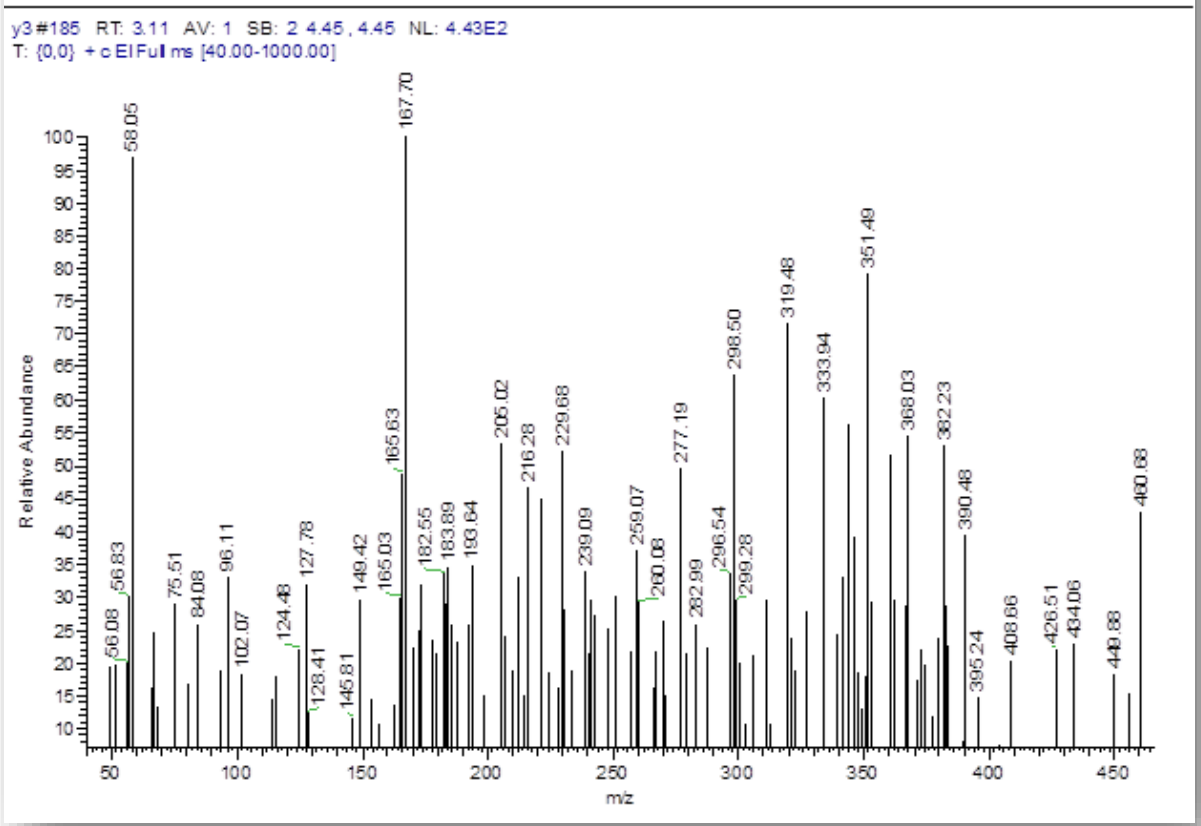

SHIMADZU
Smoothing
%T
50
40
30
20
10
0
-10
3840.34
3677.35
3410.20
3349.45
3269.40
3181.64
1704.14
1606.73
1537.29
1183.35
832.30
4500
4000
3500
3000
2500
2000
1500
1000
500
cm-1
S
H
N
N
H
H
N
N
H
F3C
O
CH3
3

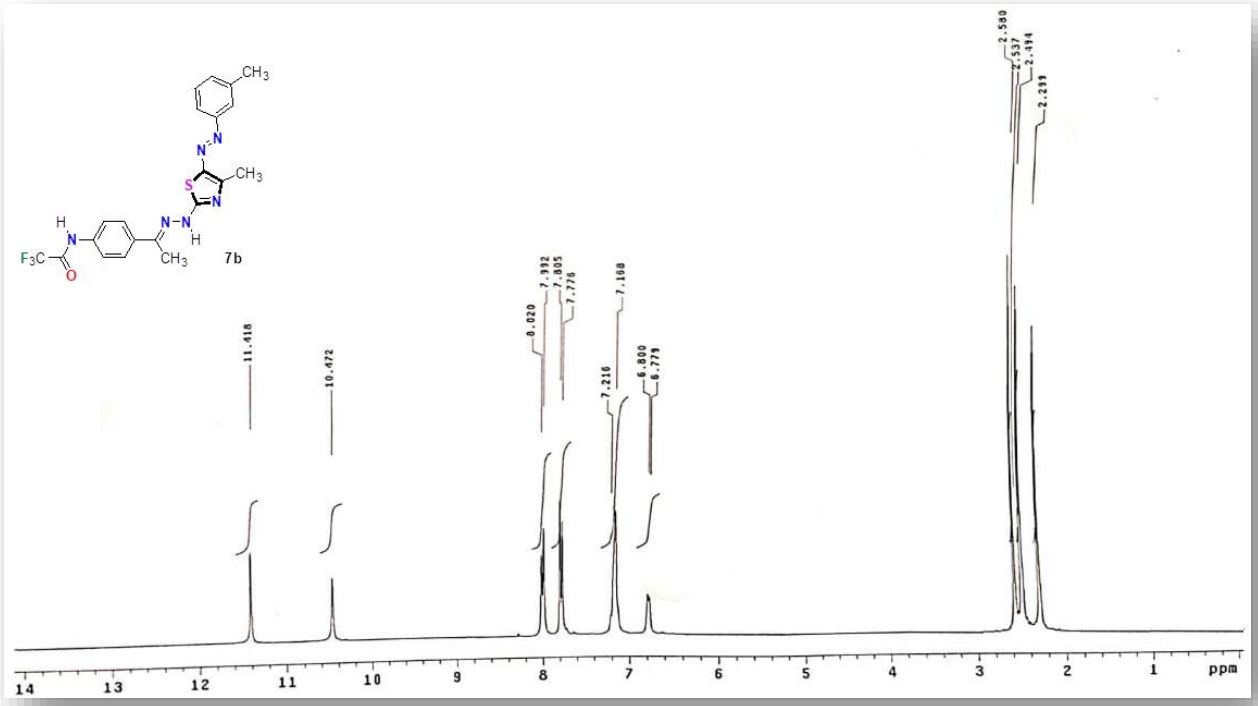

S
H
N
N
H
N
H
H
N
F3C
O
CH3
3
NH
NH
NH
NH
CH3
11.314
10.183
8.256
8.000
7.971
7.955
7.713
7.684
3.324
2.500
2.495
2.291
2.505
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
9.37
8.53
19.56
27.40

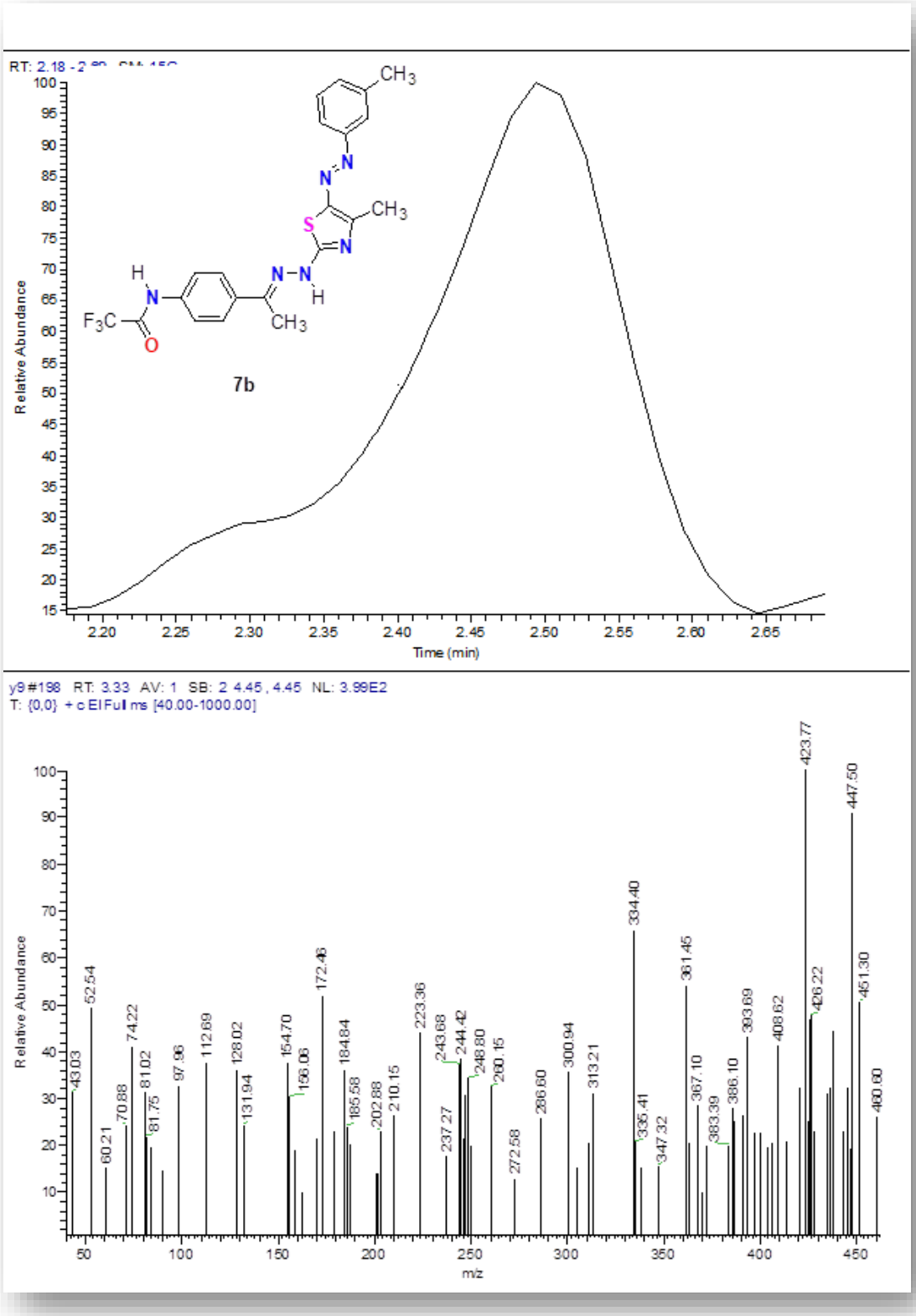

RT: 3.84 - 4.14 SM: 15G
Relative Abundance
Time (min)
3
y2 #284 RT: 4.77 AV: 1 SB: 2 4.45 , 4.45 NL: 9.29E2
T: {0,0} + c EI Full ms [40.00-1000.00]
Relative Abundance
m/z

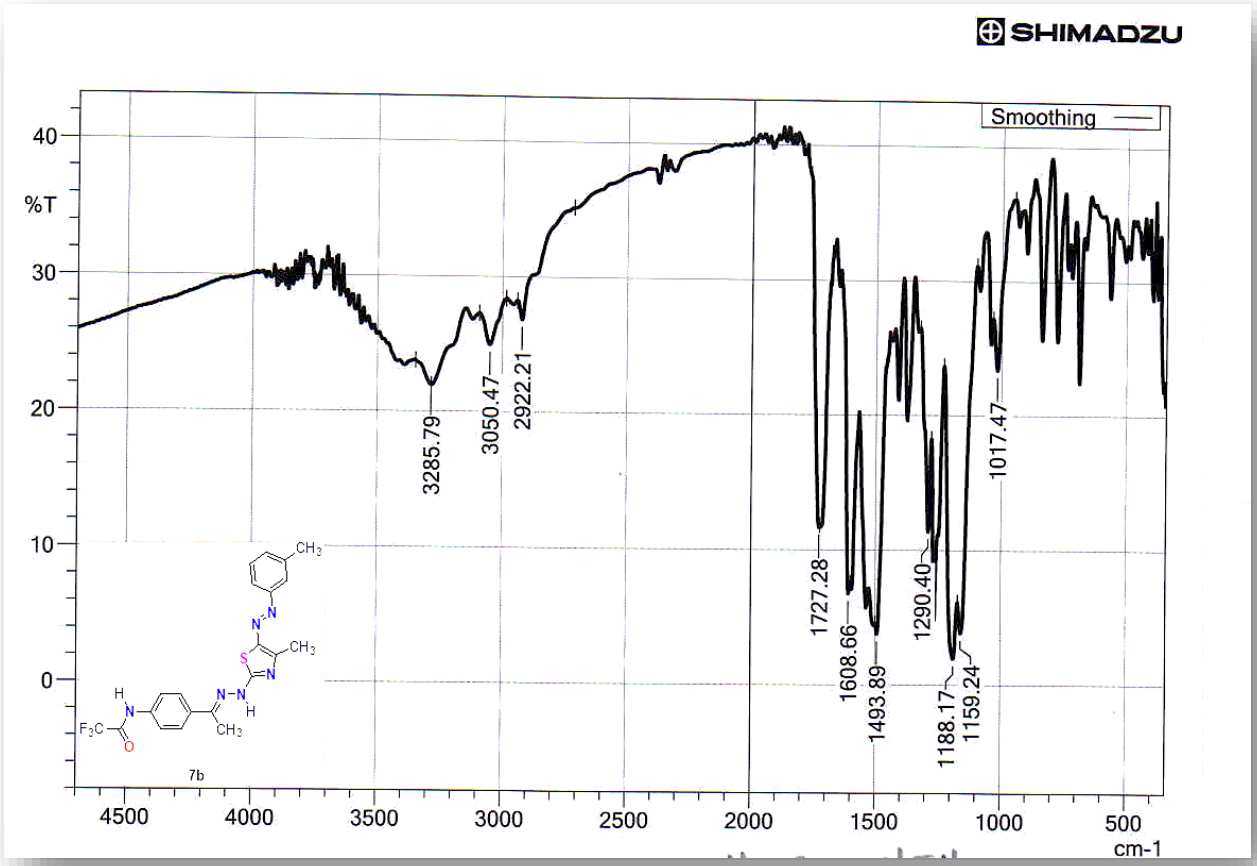

SHIMADZU
Smoothing
%T
50
40
30
20
10
4500
4000
3500
3000
2500
2000
1500
1000
500
cm-1
3307.98
2938.60
2606.84
2494.97
1704.14
1599.02
1536.33
1503.54
1375.27
1334.76
1298.12
1236.39
1181.42
1034.83
911.38
830.37
674.13
569.97
383.84
7a

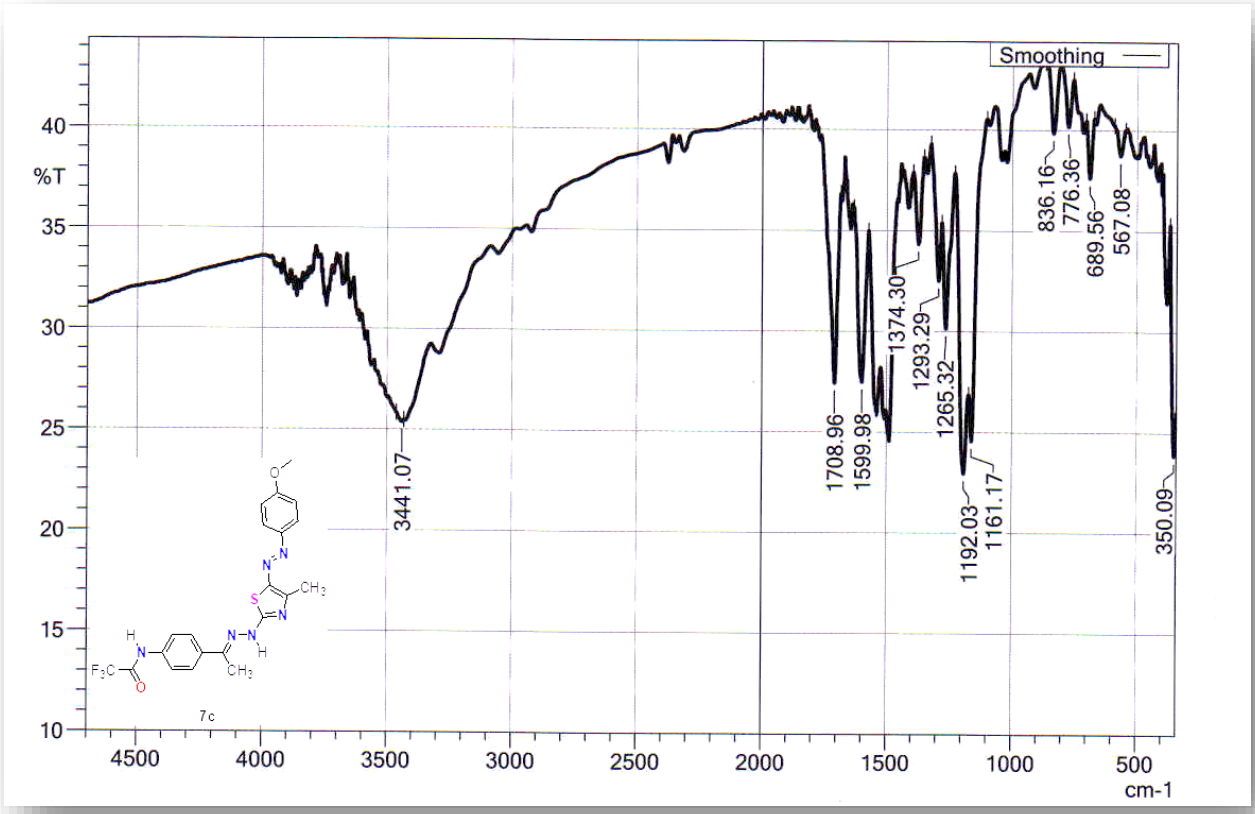

RT: 3.65 - 4.10 SM: 15G
Relative Abundance
Time (min)
7a

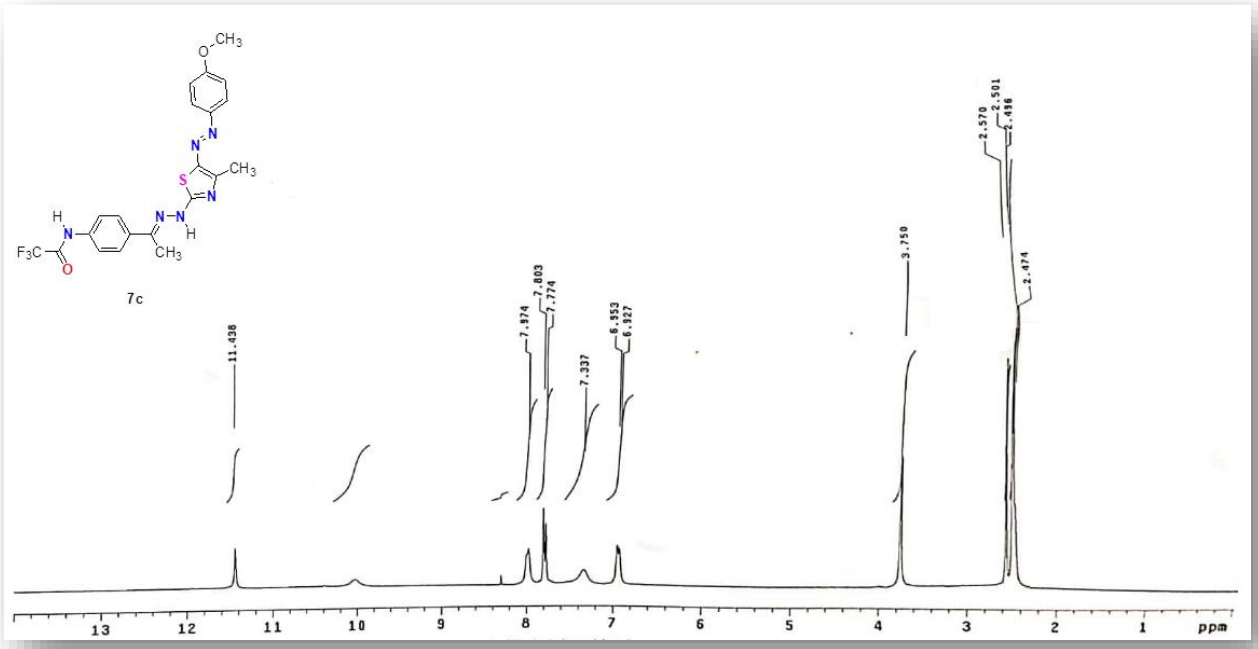

y3#185 RT: 3.11 AV: 1 SB: 2 4.45 , 4.45 NL: 4.43E2
T: {0,0} + c EI Full ms [40.00-1000.00]
Relative Abundance
m/z


7b
11.418
10.472
8.020
7.932
7.895
7.776
7.216
7.168
6.800
6.779
2.580
2.537
2.494
2.293
14
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm

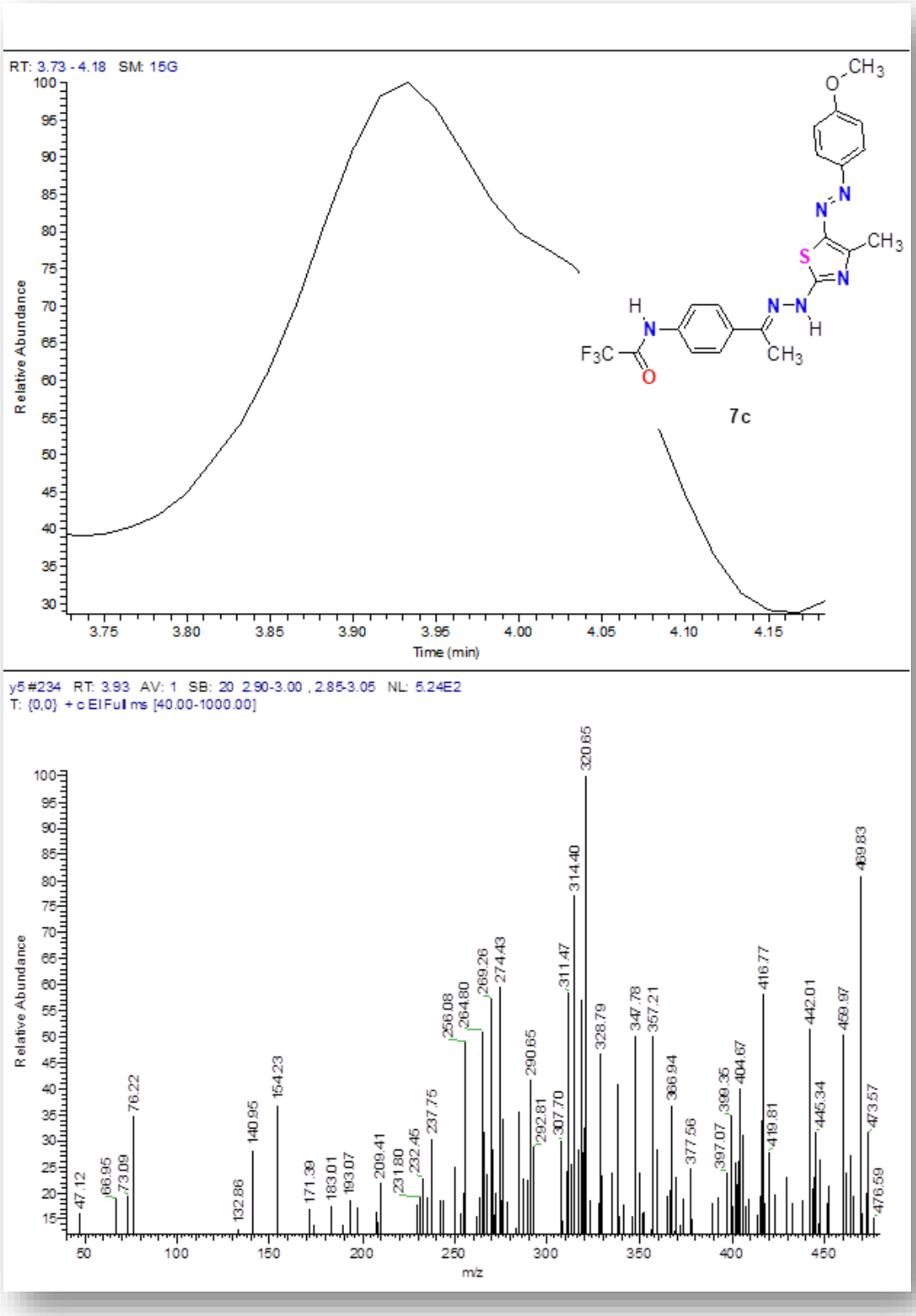

RT: 2.18 - 2.60 SM 15G
Relative Abundance
Time (min)
7b
y9#198 RT: 3.33 AV: 1 SB: 2 4.45 , 4.45 NL: 3.99E2
T: {0,0} + c EI Full ms [40.00-1000.00]
Relative Abundance
m/z
43.03
52.54
60.21
70.88
74.22
81.02
81.75
97.96
112.89
128.02
131.94
154.70
156.06
172.46
184.84
185.58
202.88
210.15
223.36
237.27
243.68
244.42
248.80
260.15
272.58
286.60
300.94
313.21
334.40
335.41
347.32
361.45
367.10
383.39
386.10
393.69
408.62
423.77
426.22
447.50
451.30
460.60

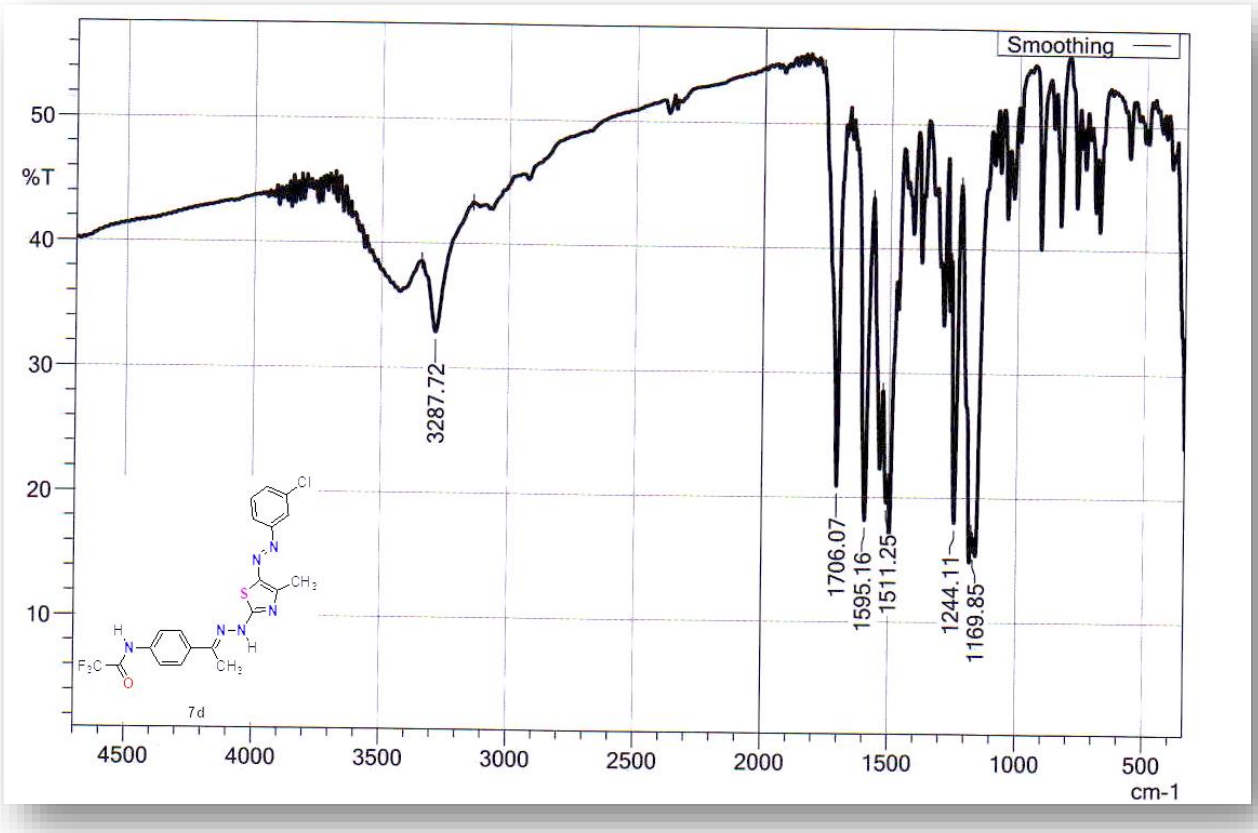

SHIMADZU
Smoothing
%T
40
30
20
10
0
3285.79
3050.47
2922.21
1727.28
1608.66
1493.89
1290.40
1188.17
1159.24
1017.47
4500
4000
3500
3000
2500
2000
1500
1000
500
cm-1
7b

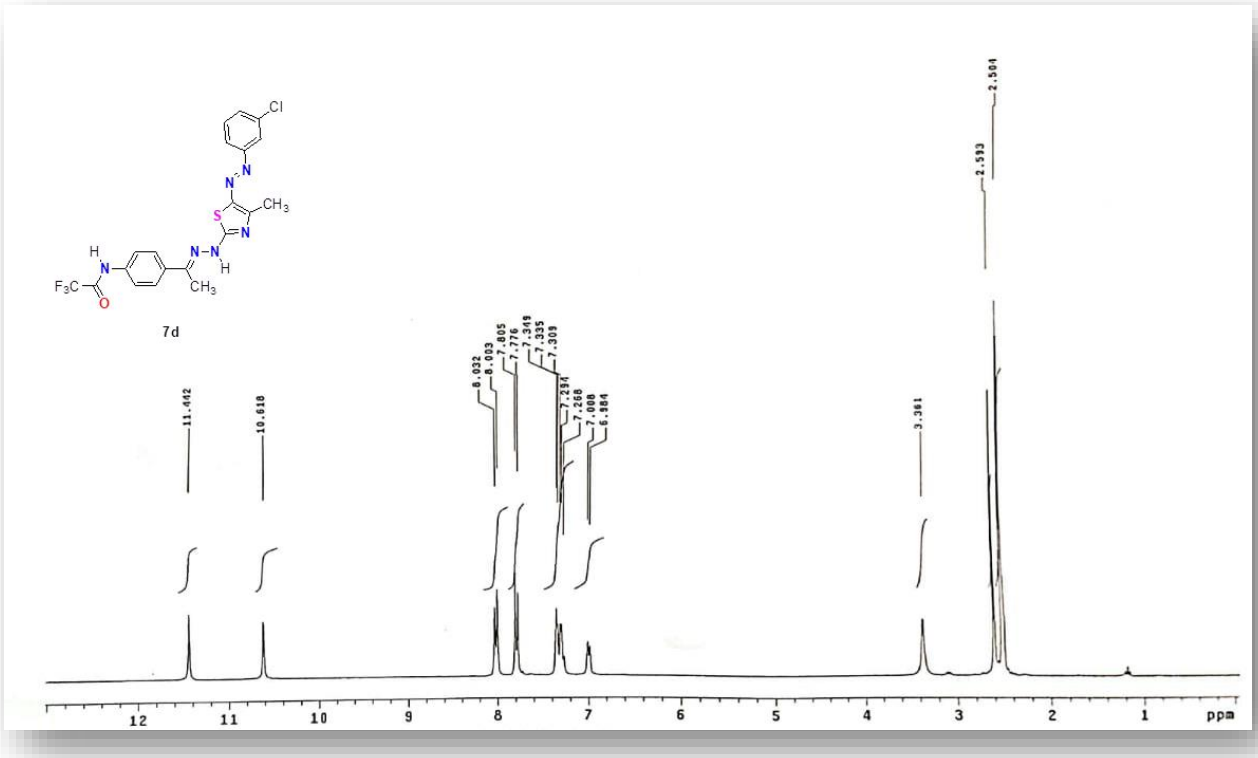

Smoothing
%T
40
35
30
25
20
15
10
4500
4000
3500
3000
2500
2000
1500
1000
500
cm-1
3441.07
1708.96
1599.98
1374.30
1293.29
1265.32
1192.03
1161.17
836.16
776.36
689.56
567.08
350.09
7c

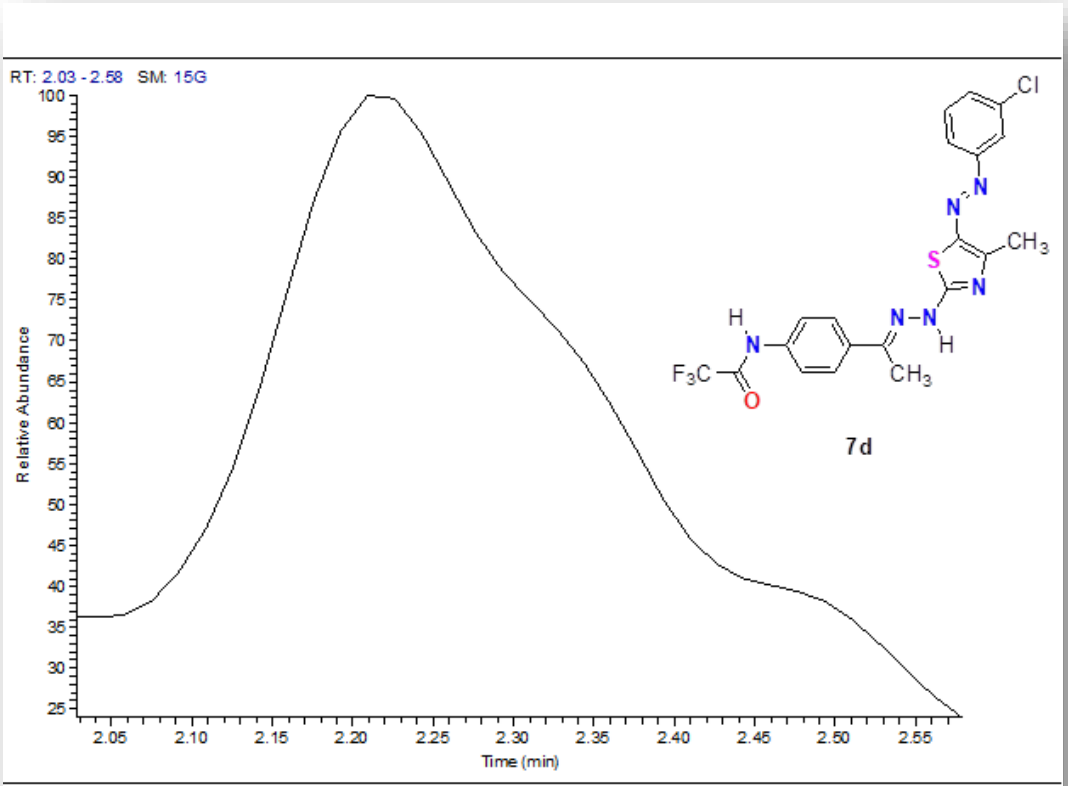

O
CH3
N
N
CH3
S
N
H
N
N–N
H
F3C
O
CH3
11.438
7.974
7.803
7.774
7.337
6.353
6.327
3.750
2.570
2.501
2.436
2.474
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm

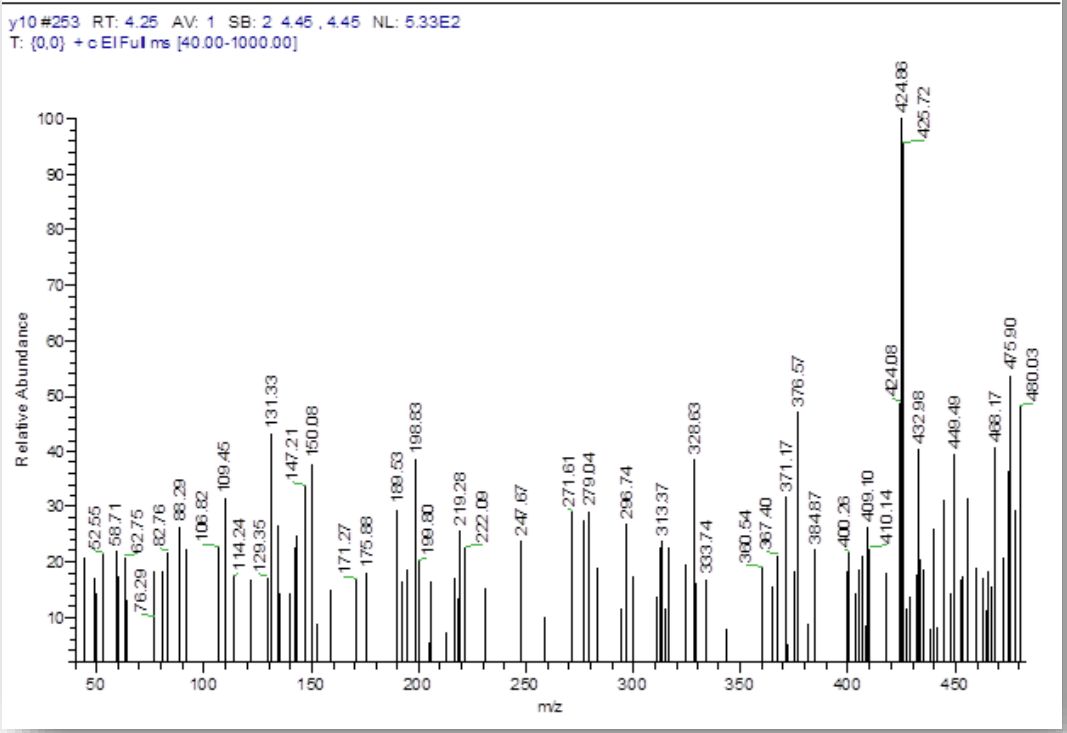
7c

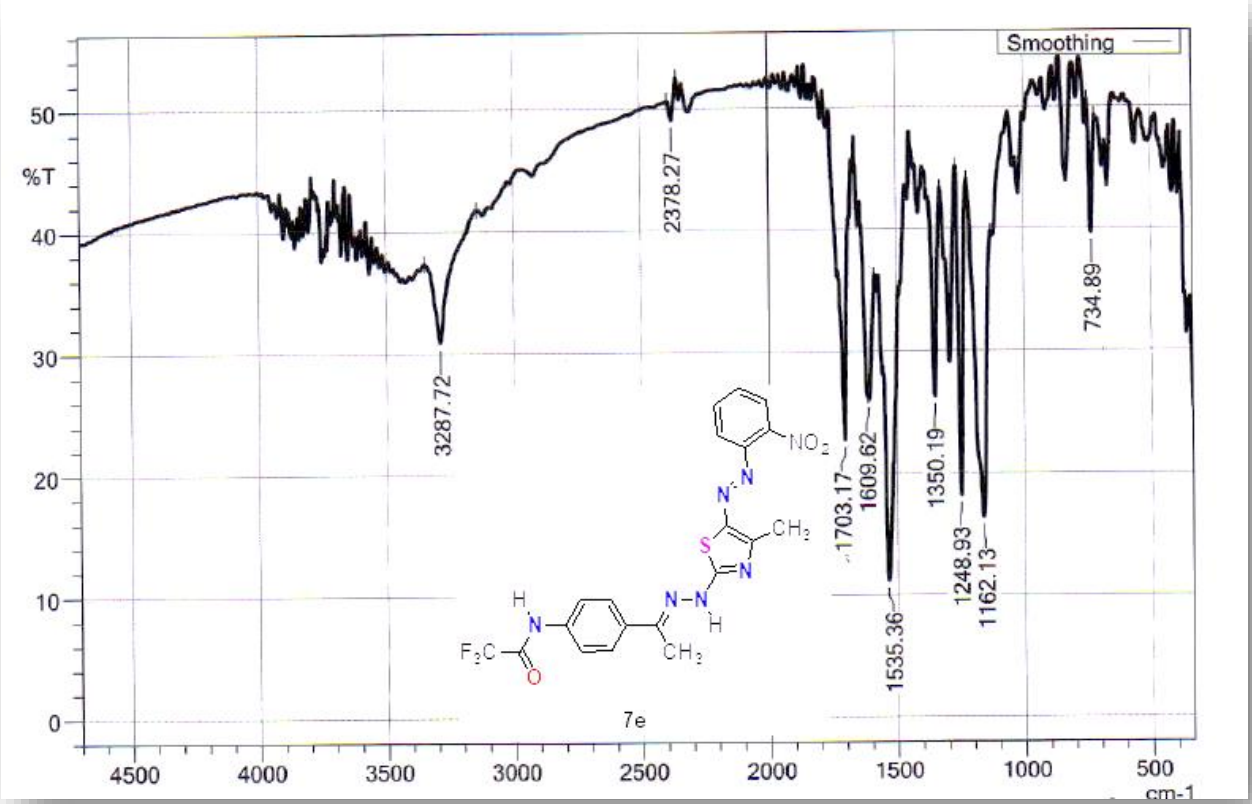

RT: 3.73 - 4.18 SM: 15G
Relative Abundance
Time (min)
7c
y5 #234 RT: 3.93 AV: 1 SB: 20 2.90-3.00 , 2.85-3.05 NL: 5.24E2
T: {0,0} + c EI Full ms [40.00-1000.00]
Relative Abundance
m/z

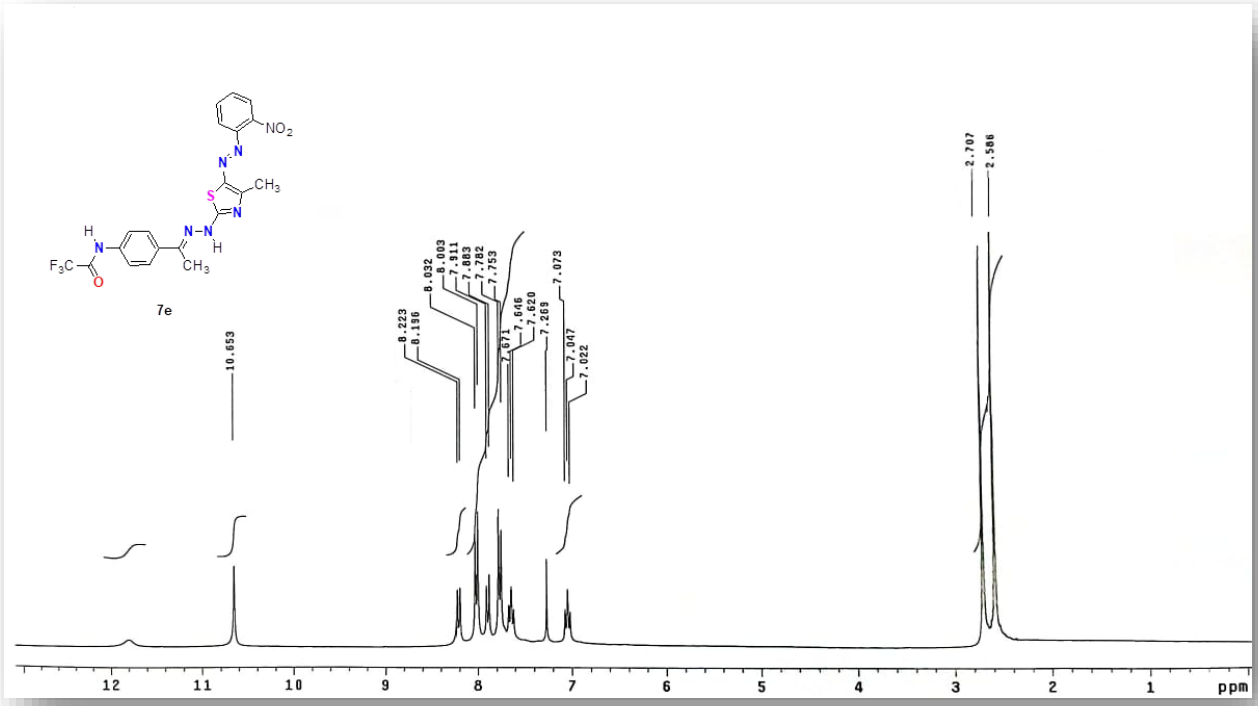

Smoothing
%T
50
40
30
20
10
3287.72
1706.07
1595.16
1511.25
1244.11
1169.85
4500
4000
3500
3000
2500
2000
1500
1000
500
cm-1
7d

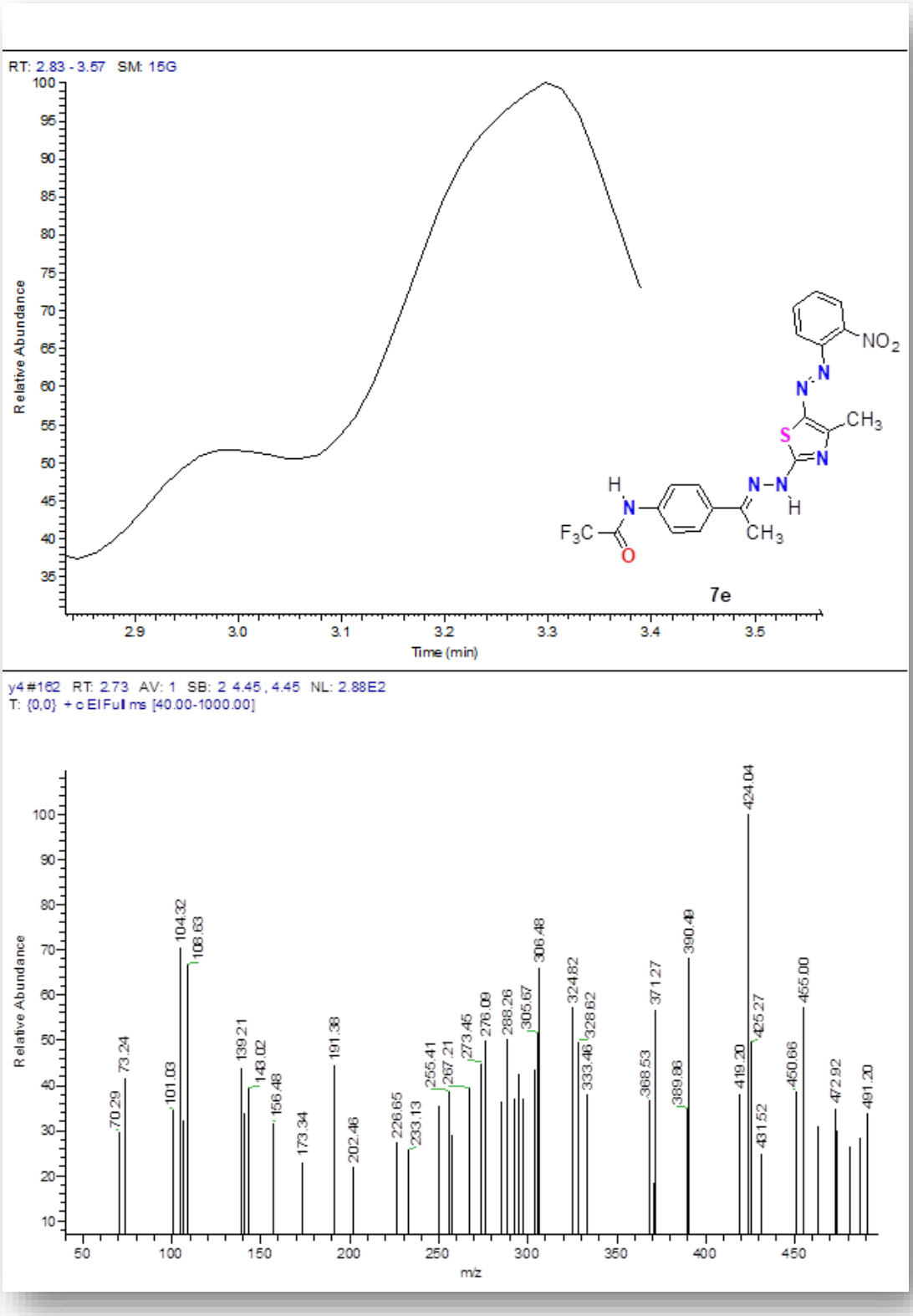

7d
11.442
10.618
8.032
8.003
7.805
7.776
7.349
7.335
7.309
7.294
7.268
7.000
6.984
3.361
2.593
2.564
12
11
10
9
8
7
6
5
4
3
2
1
ppm

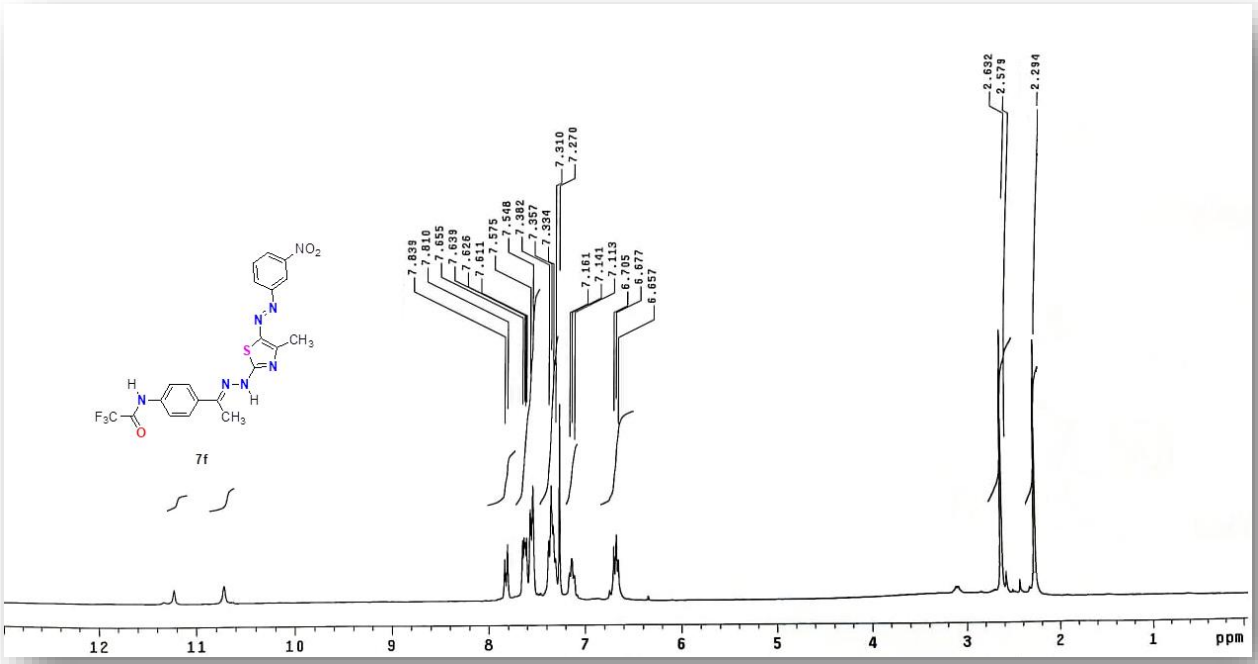

RT: 2.03 - 2.58 SM: 15G
Relative Abundance
Time (min)
Cl
N
N
CH3
S
N
H
N
N–N
H
F3C
O
CH3
7d

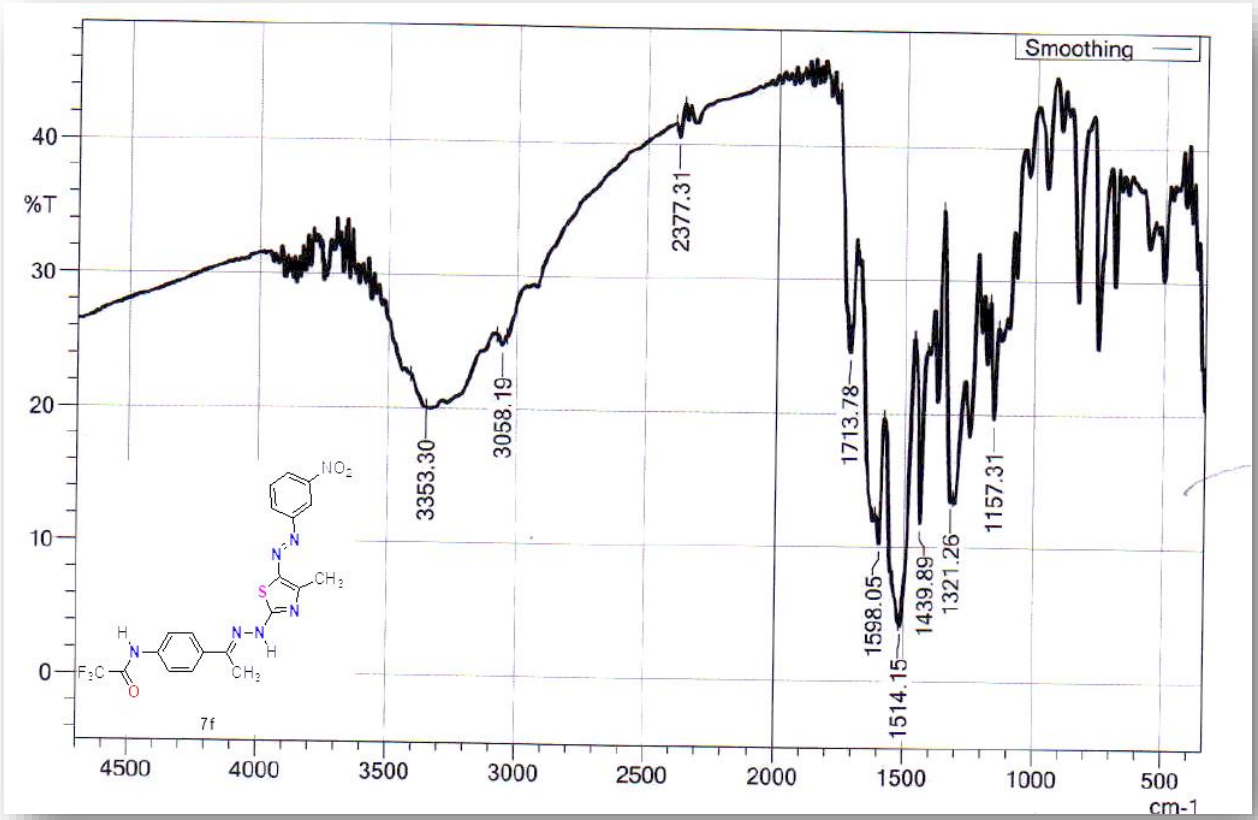

y10 #253 RT: 4.25 AV: 1 SB: 2 4.45 , 4.45 NL: 5.33E2
T: {0,0} + c EI Full ms [40.00-1000.00]
Relative Abundance
m/z


Smoothing
%T
50
40
30
20
10
0
3287.72
2378.27
1703.17
1609.62
1535.36
1350.19
1248.93
1162.13
734.89
4500
4000
3500
3000
2500
2000
1500
1000
500
cm-1
7e


7e
10.653
8.223
8.196
8.032
8.003
7.911
7.803
7.782
7.753
7.671
7.646
7.620
7.269
7.073
7.047
7.022
2.707
2.586
12
11
10
9
8
7
6
5
4
3
2
1
ppm


RT: 2.83 - 3.57 SM: 15G
Relative Abundance
Time (min)
7e
y4#162 RT: 2.73 AV: 1 SB: 2 4.45 , 4.45 NL: 2.88E2
T: {0,0} + c EI Full ms [40.00-1000.00]
Relative Abundance
m/z


7.833
7.810
7.655
7.639
7.626
7.611
7.575
7.548
7.382
7.357
7.334
7.310
7.270
7.161
7.141
7.113
6.705
6.677
6.657
2.632
2.579
2.294
7f
12
11
10
9
8
7
6
5
4
3
2
1
ppm


Smoothing
%T
40
30
20
10
0
3353.30
3058.19
2377.31
1713.78
1598.05
1514.15
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7f
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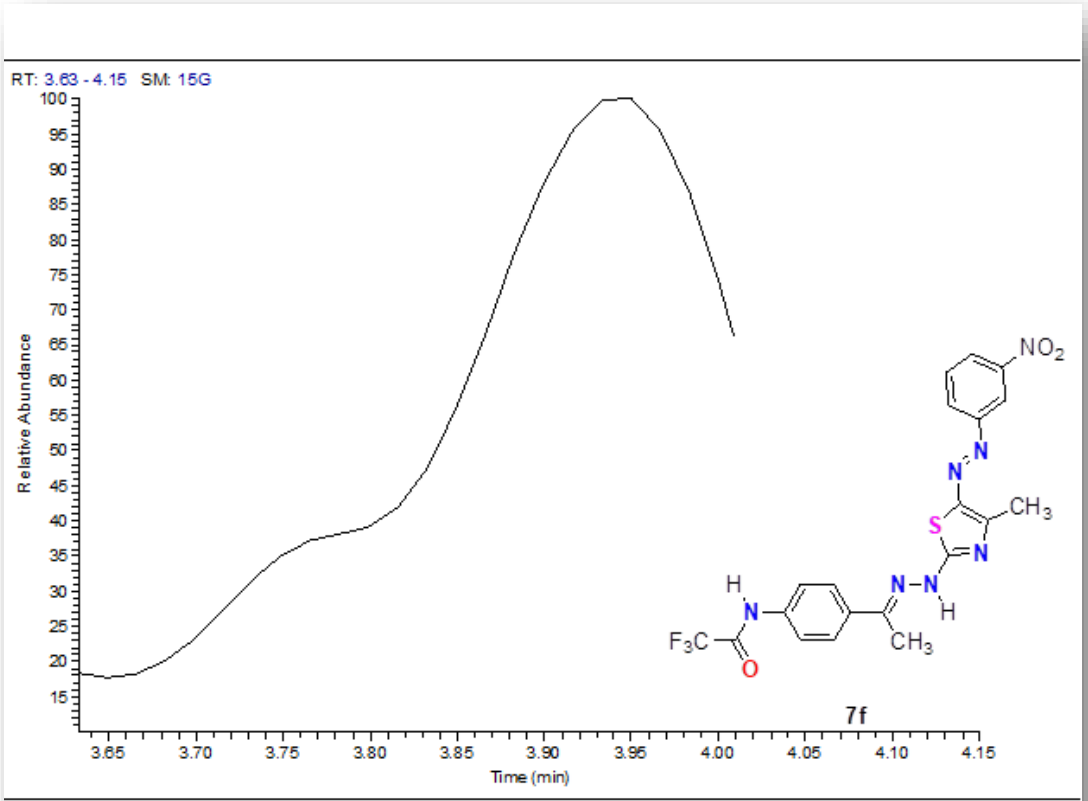
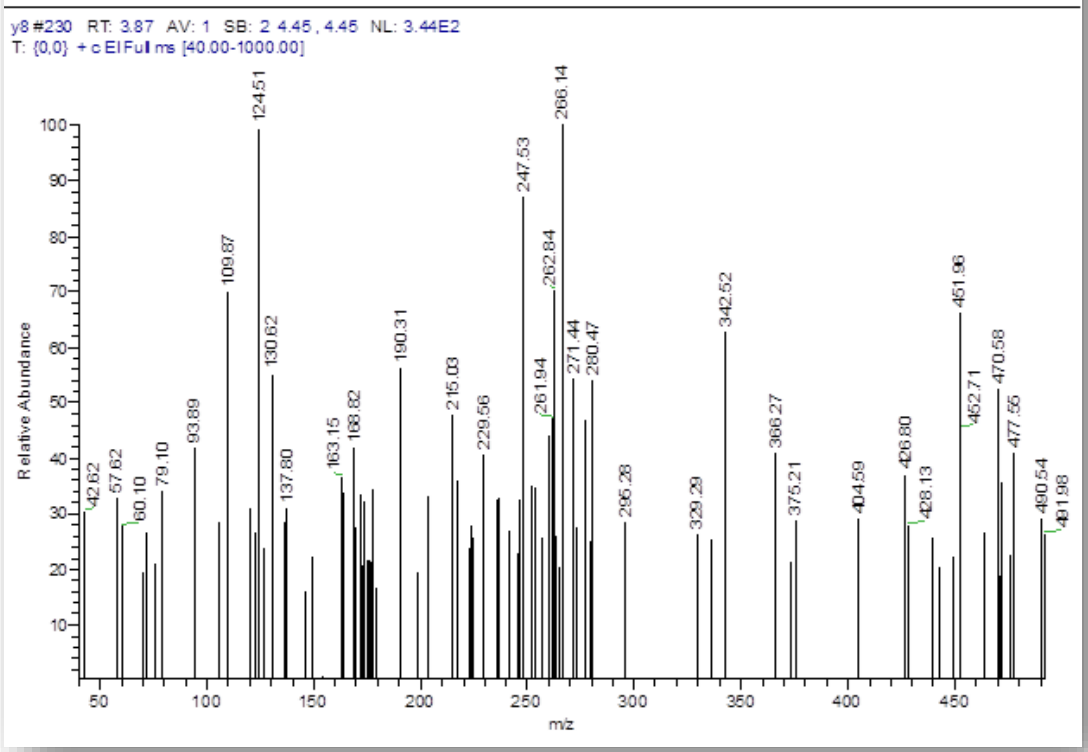
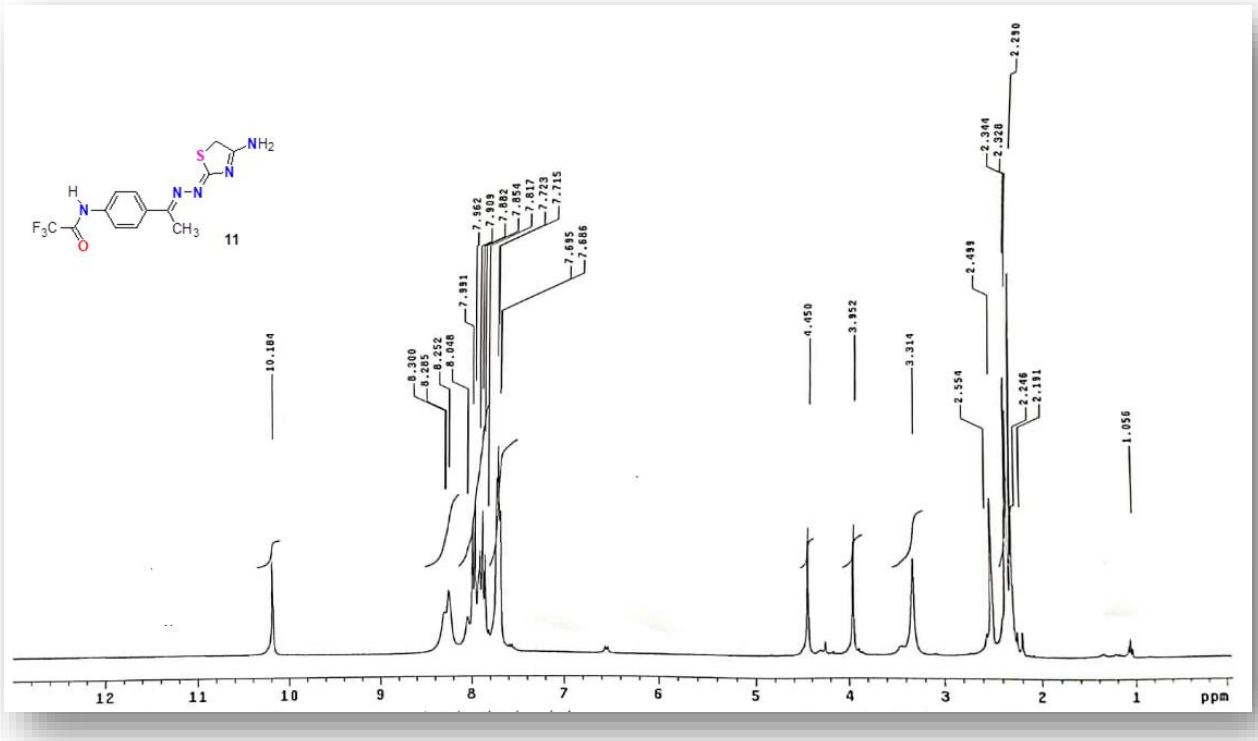
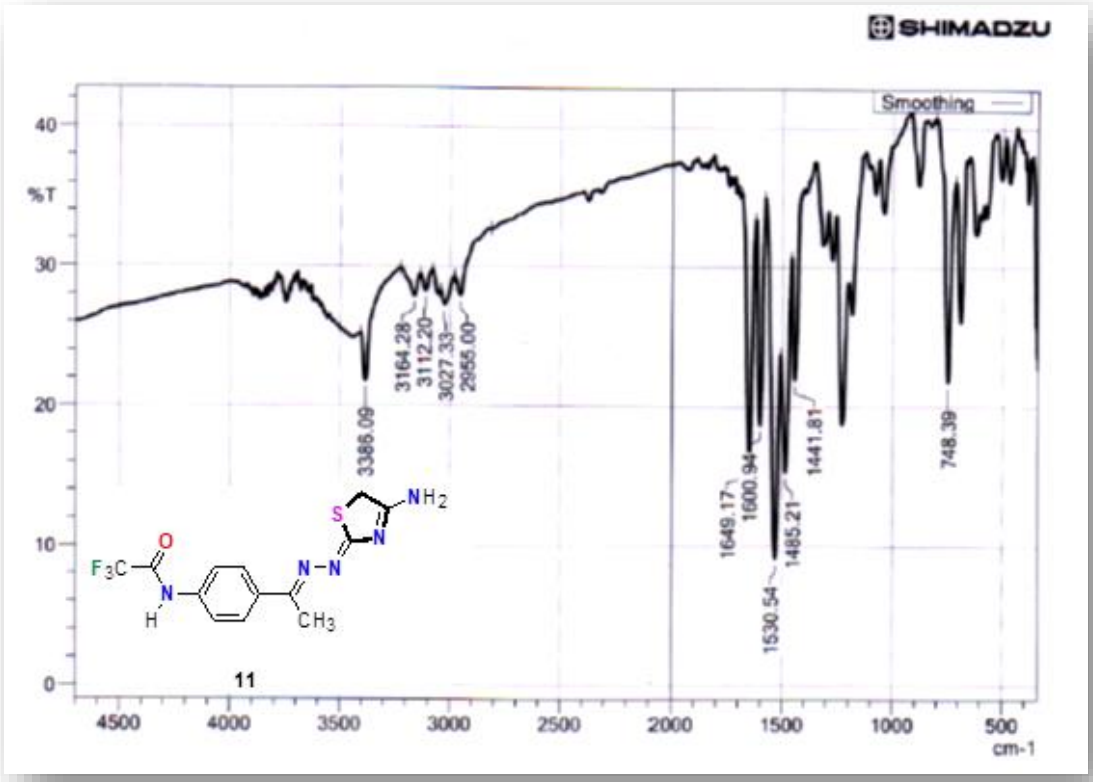
4000
3500
3000
2500
2000
1500
1000
500
cm-1


RT: 3.63 - 4.15 SM: 15G
Relative Abundance
Time (min)
7f


y8 #230 RT: 3.87 AV: 1 SB: 2 4.45 , 4.45 NL: 3.44E2
T: {0,0} + c EI Full ms [40.00-1000.00]
Relative Abundance
m/z


11
10.184
8.300
8.285
8.252
8.048
7.891
7.862
7.809
7.882
7.854
7.817
7.723
7.715
7.695
7.686
4.450
3.952
3.314
2.554
2.499
2.344
2.328
2.290
2.246
2.191
1.056
12
11
10
9
8
7
6
5
4
3
2
1
ppm


SHIMADZU
Smoothing
%T
40
30
20
10
0
3386.09
3164.28
3112.20
3027.33
2955.00
1649.17
1600.94
1530.54
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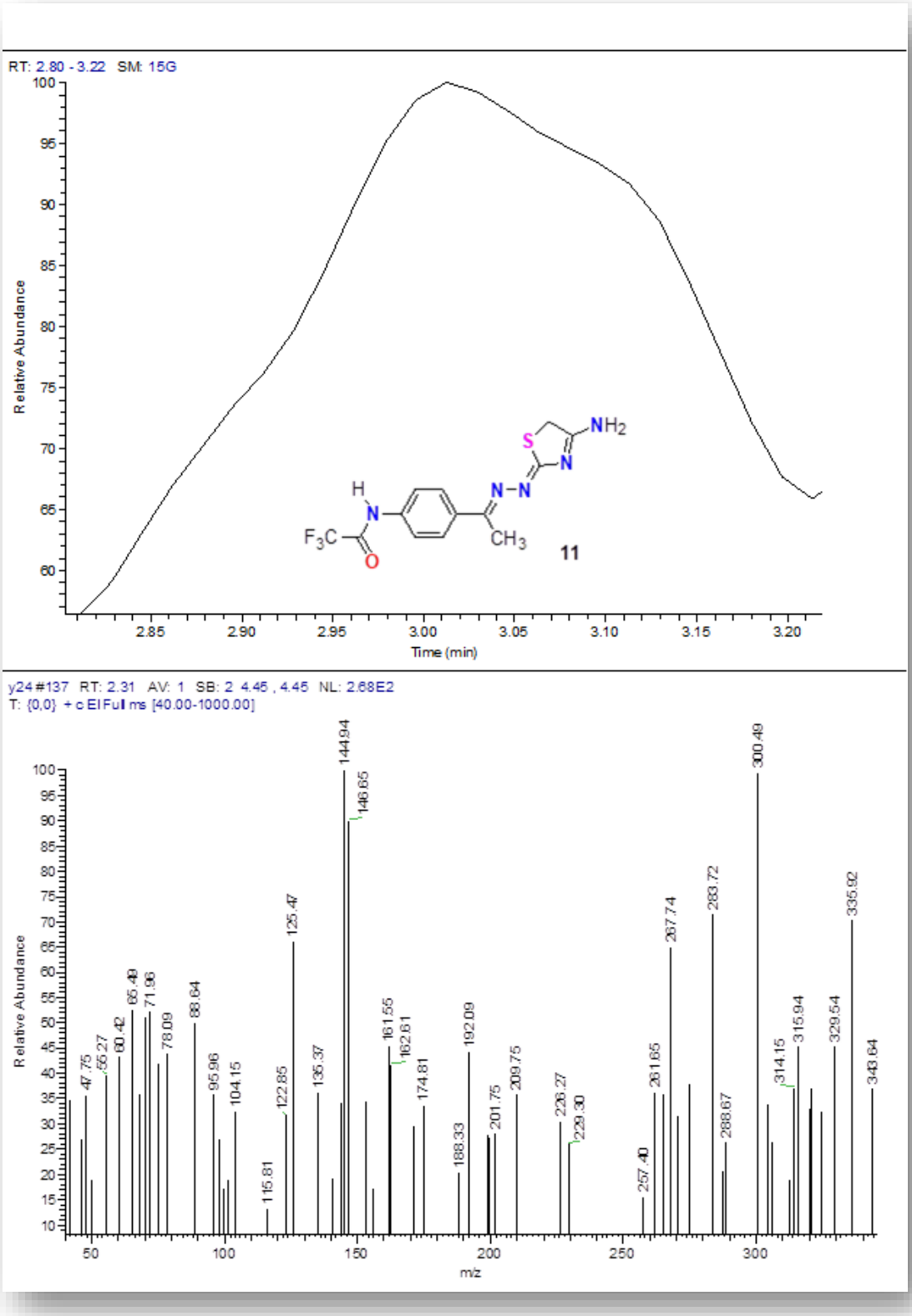
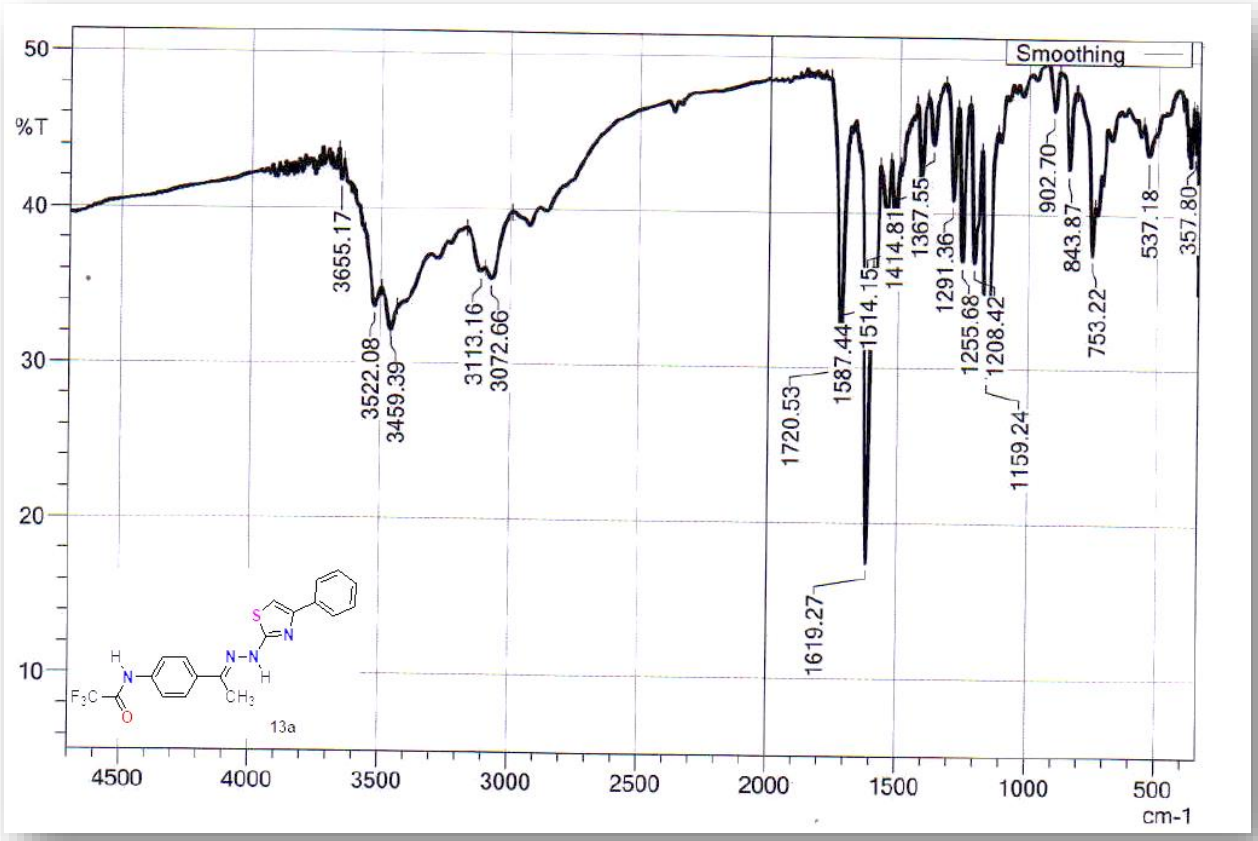
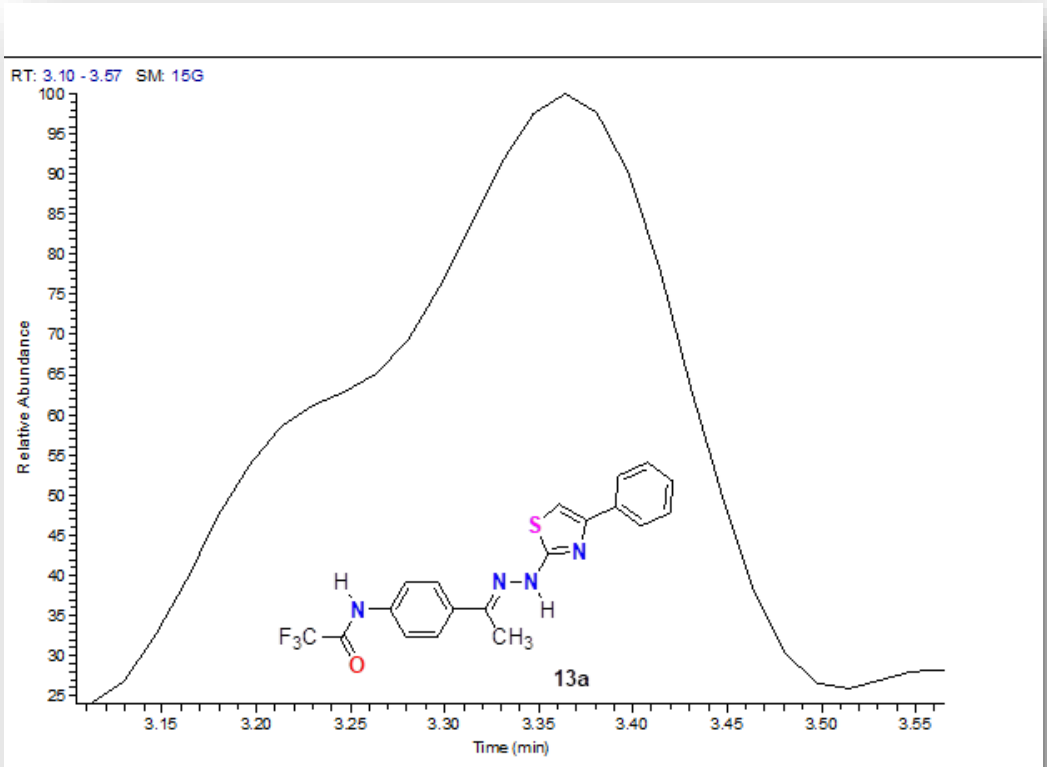
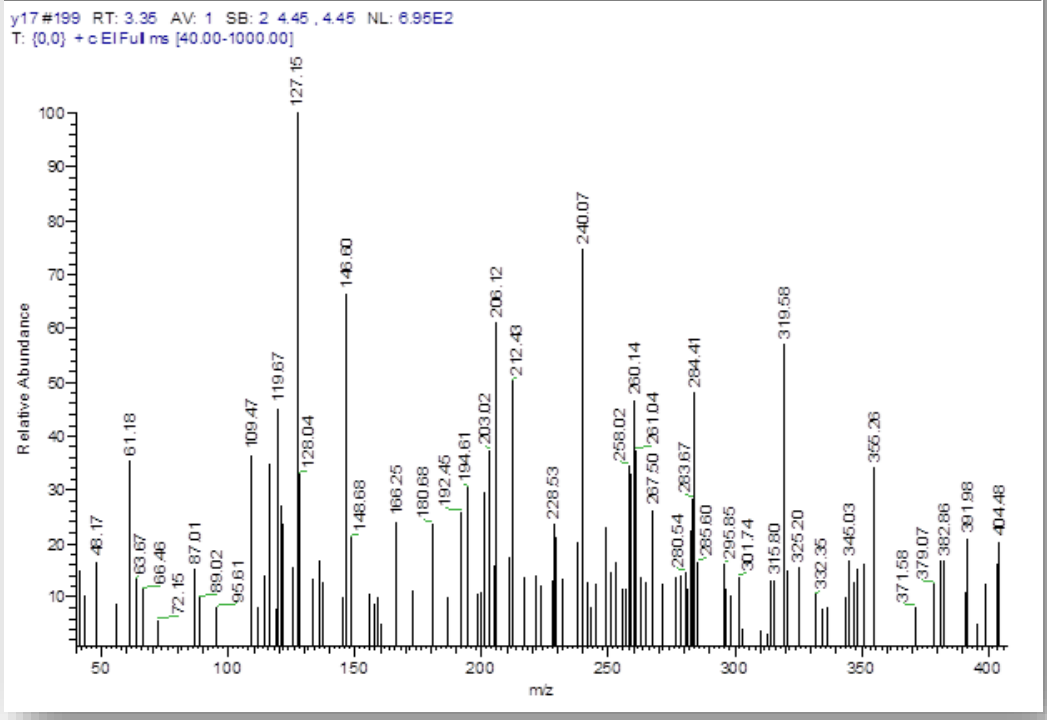
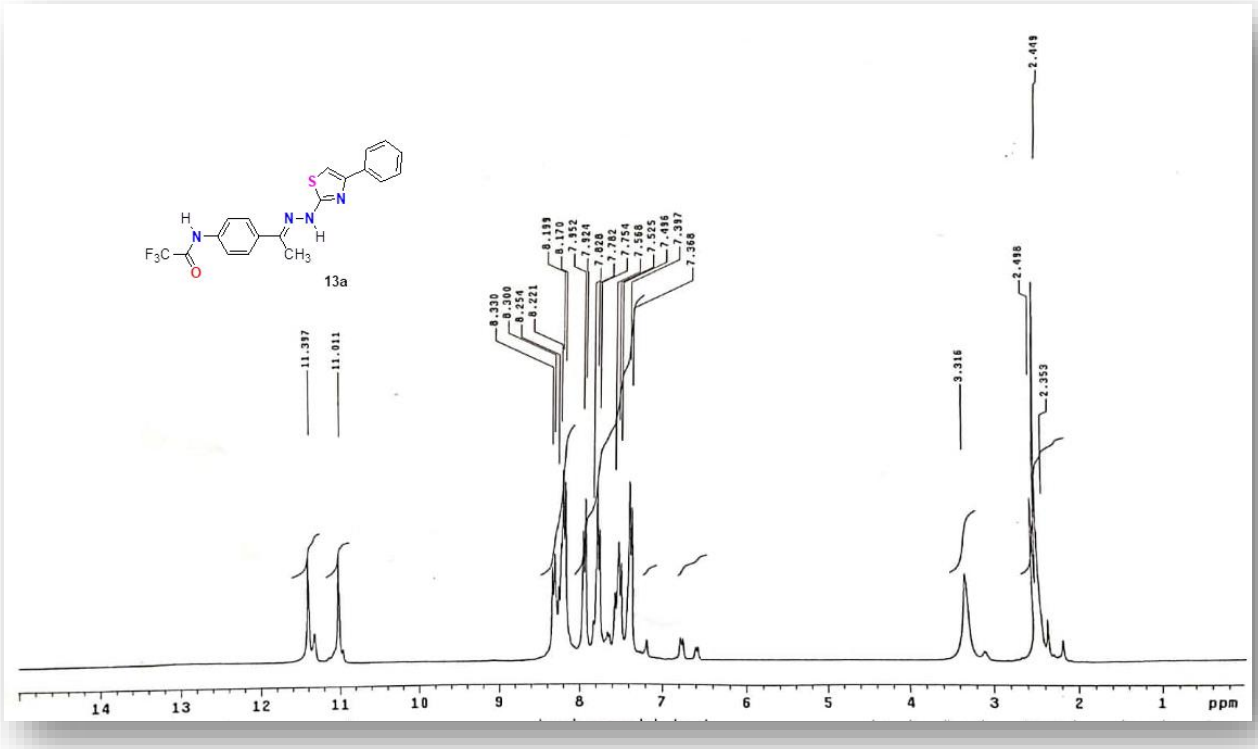
1441.81
748.39
4500
4000
3500
3000
2500
2000
1500
1000
500
cm-1
11

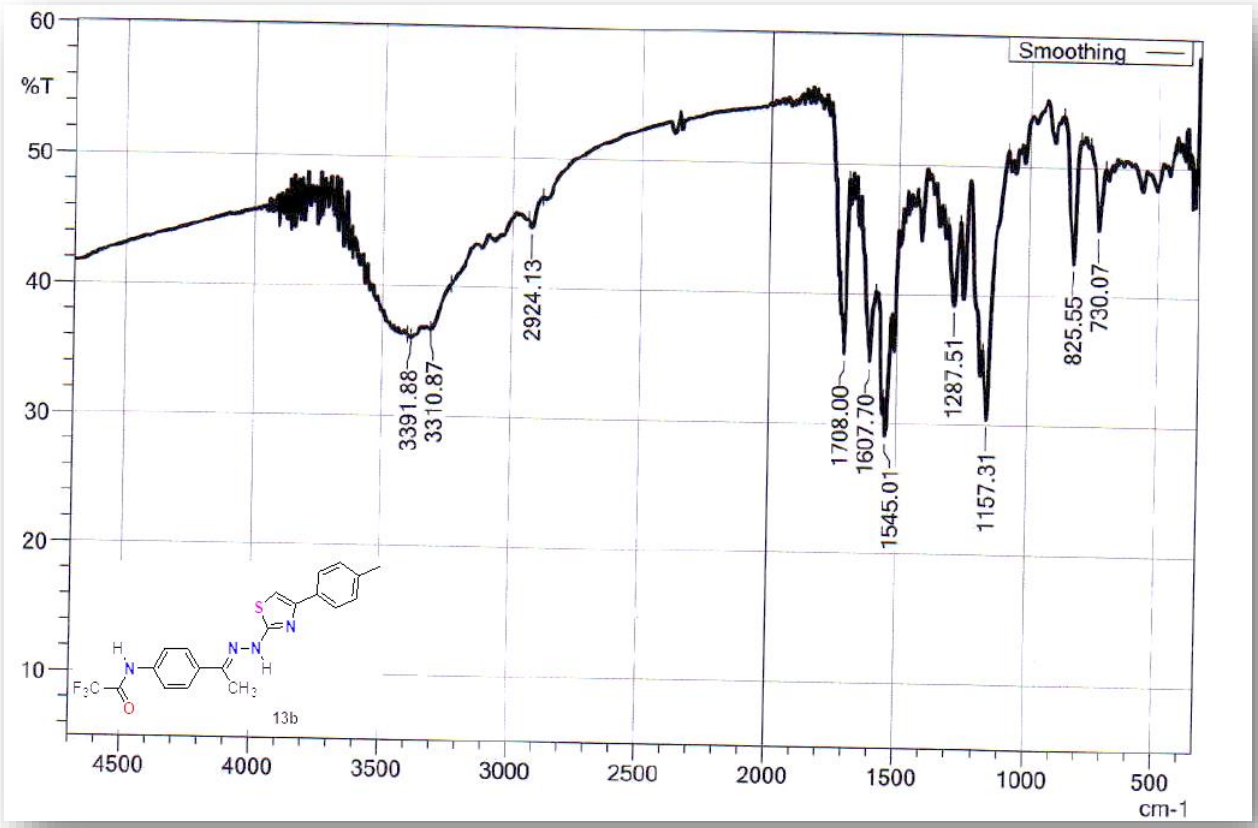

RT: 2.80 - 3.22 SM: 15G
Relative Abundance
Time (min)
11
y24#137 RT: 2.31 AV: 1 SB: 2 4.45 , 4.45 NL: 2.68E2
T: {0,0} + c EI Full ms [40.00-1000.00]
Relative Abundance
m/z

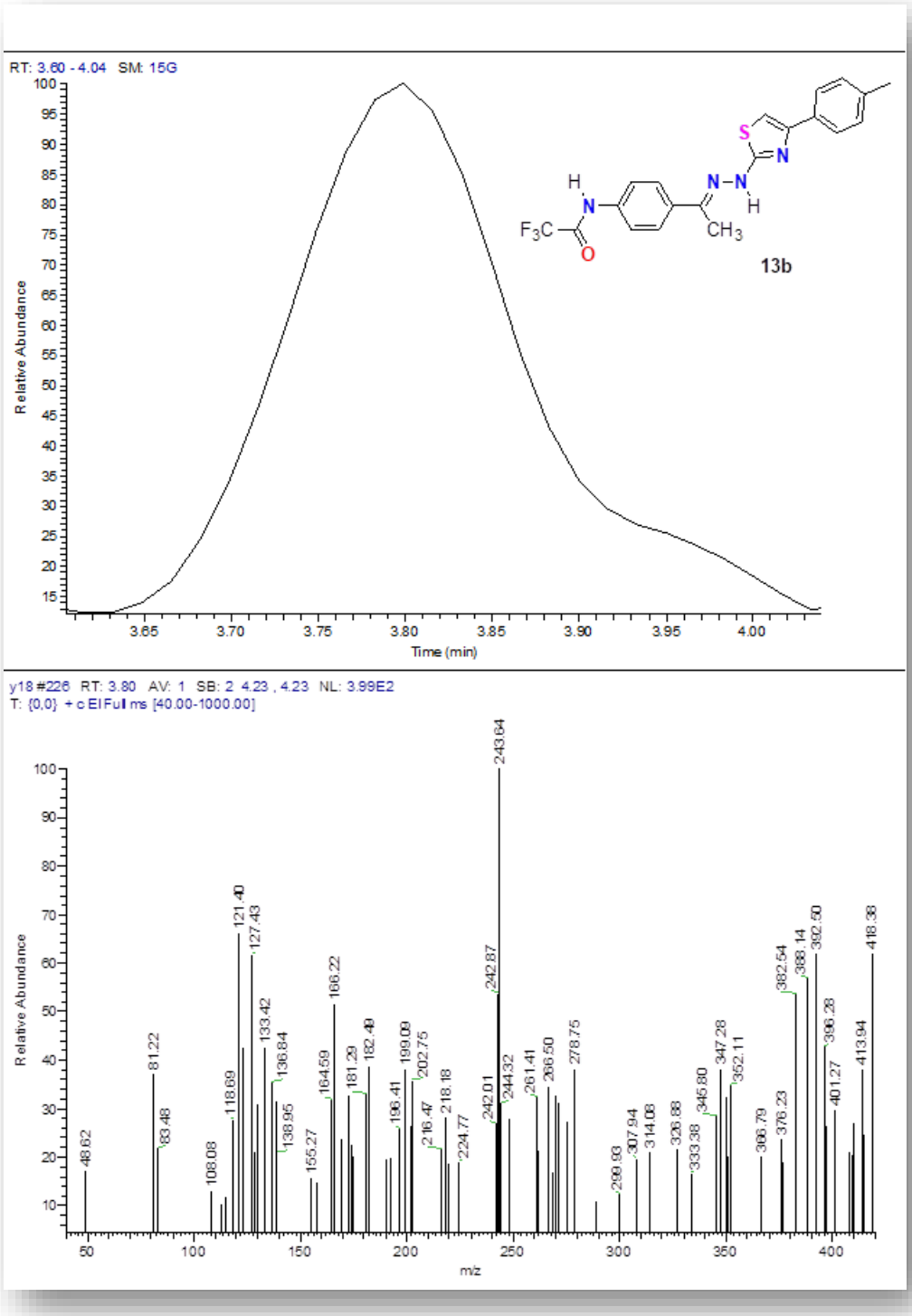

Smoothing
%T
50
40
30
20
10
3655.17
3522.08
3459.39
3113.16
3072.66
1720.53
1619.27
1587.44
1514.15
1414.81
1367.55
1291.36
1255.68
1208.42
1159.24
902.70
843.87
753.22
537.18
357.80
4500
4000
3500
3000
2500
2000
1500
1000
500
cm-1
13a

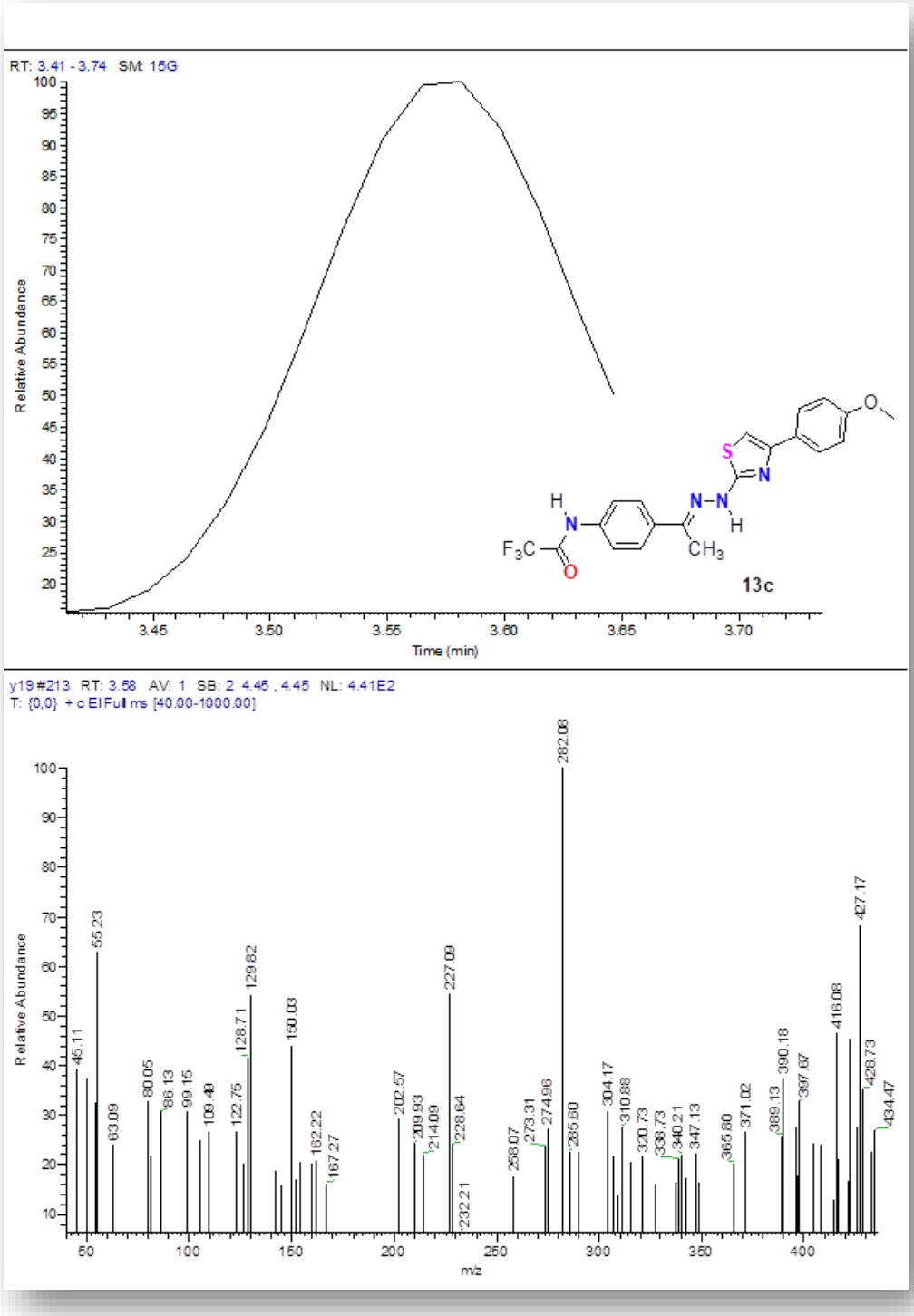

RT: 3.10 - 3.57 SM: 15G
Relative Abundance
Time (min)
13a

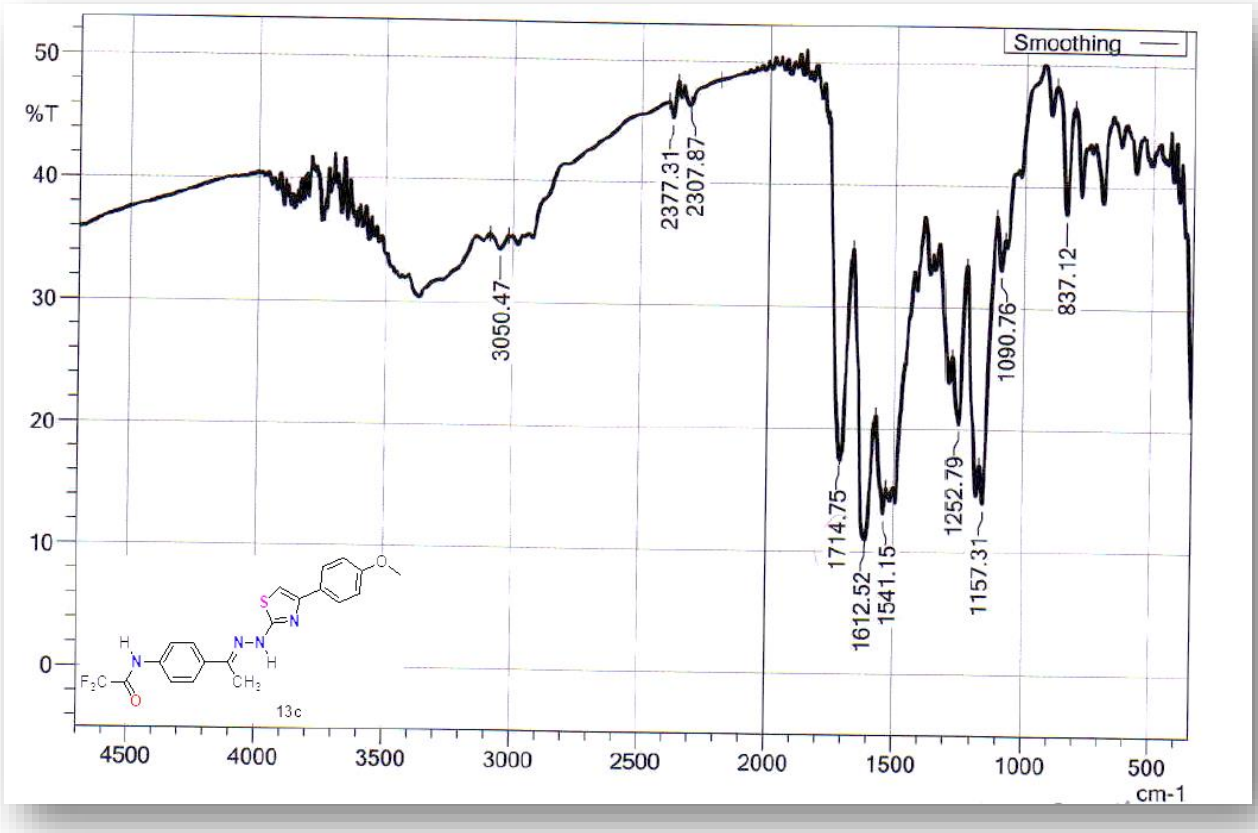

y17#199 RT: 3.35 AV: 1 SB: 2 4.45 , 4.45 NL: 6.95E2
T: {0,0} + c EI Full ms [40.00-1000.00]
Relative Abundance
m/z

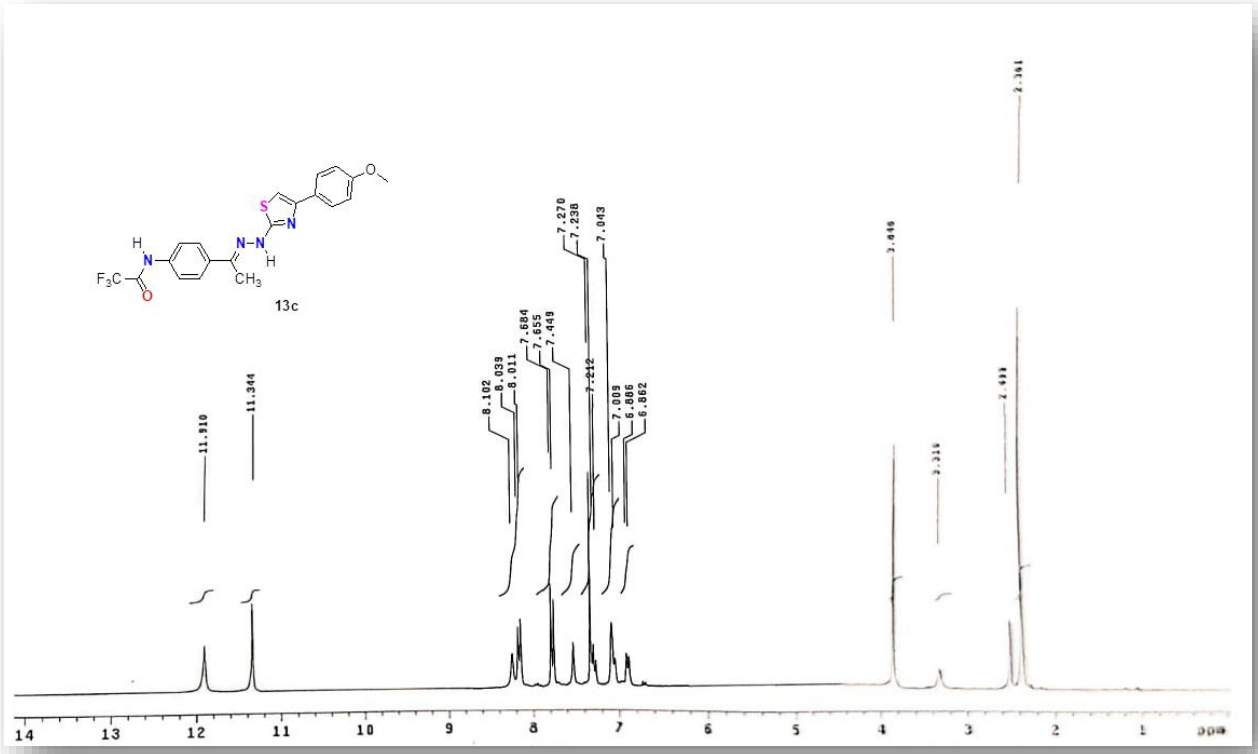

13a
11.397
11.011
8.330
8.300
8.254
8.221
8.199
8.170
7.952
7.924
7.828
7.782
7.754
7.568
7.525
7.496
7.397
7.368
9.316
2.498
2.449
2.353
14
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm

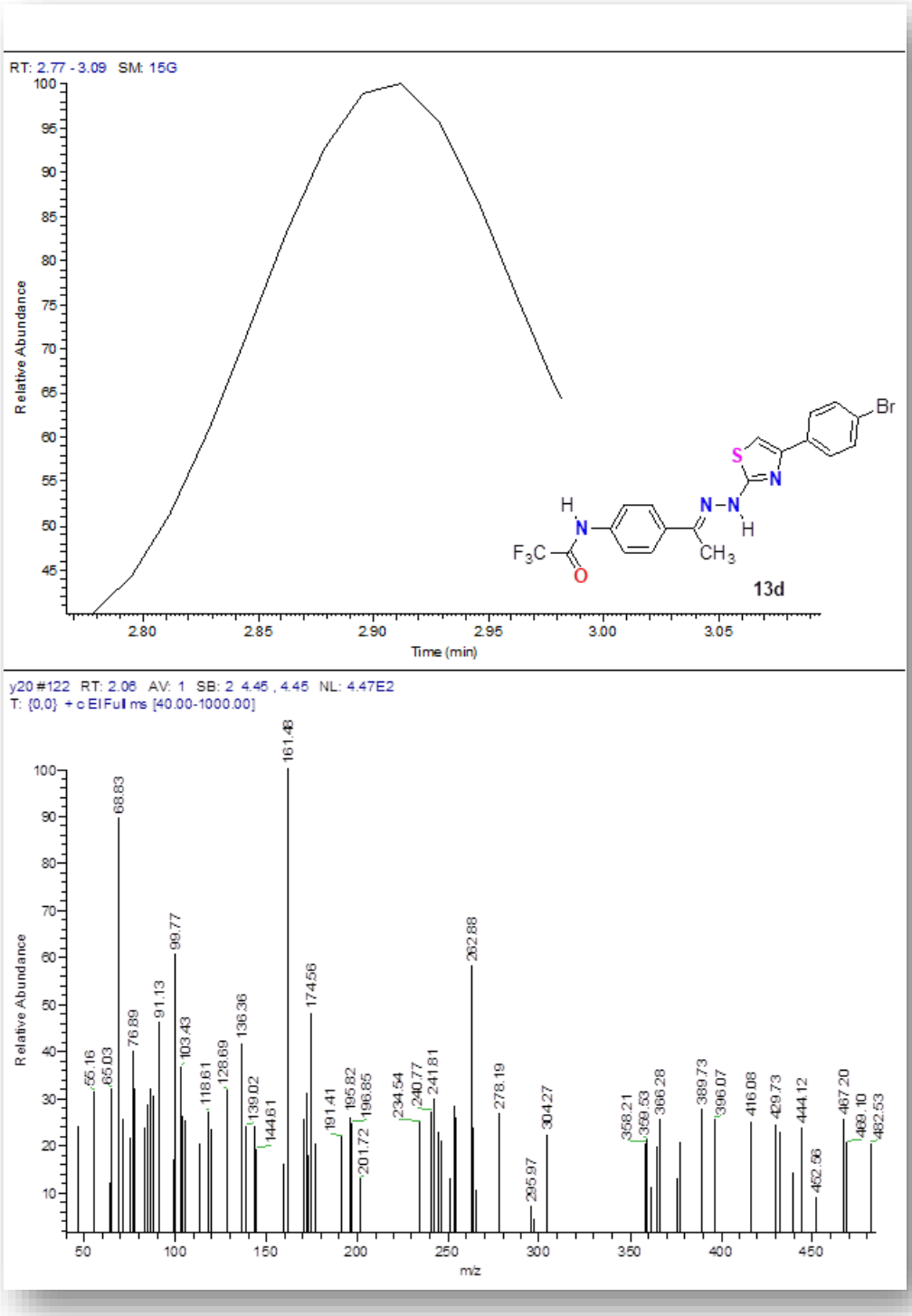

Smoothing
%T
60
50
40
30
20
10
3391.88
3310.87
2924.13
1708.00
1607.70
1545.01
1287.51
1157.31
825.55
730.07
4500
4000
3500
3000
2500
2000
1500
1000
500
cm-1
13b

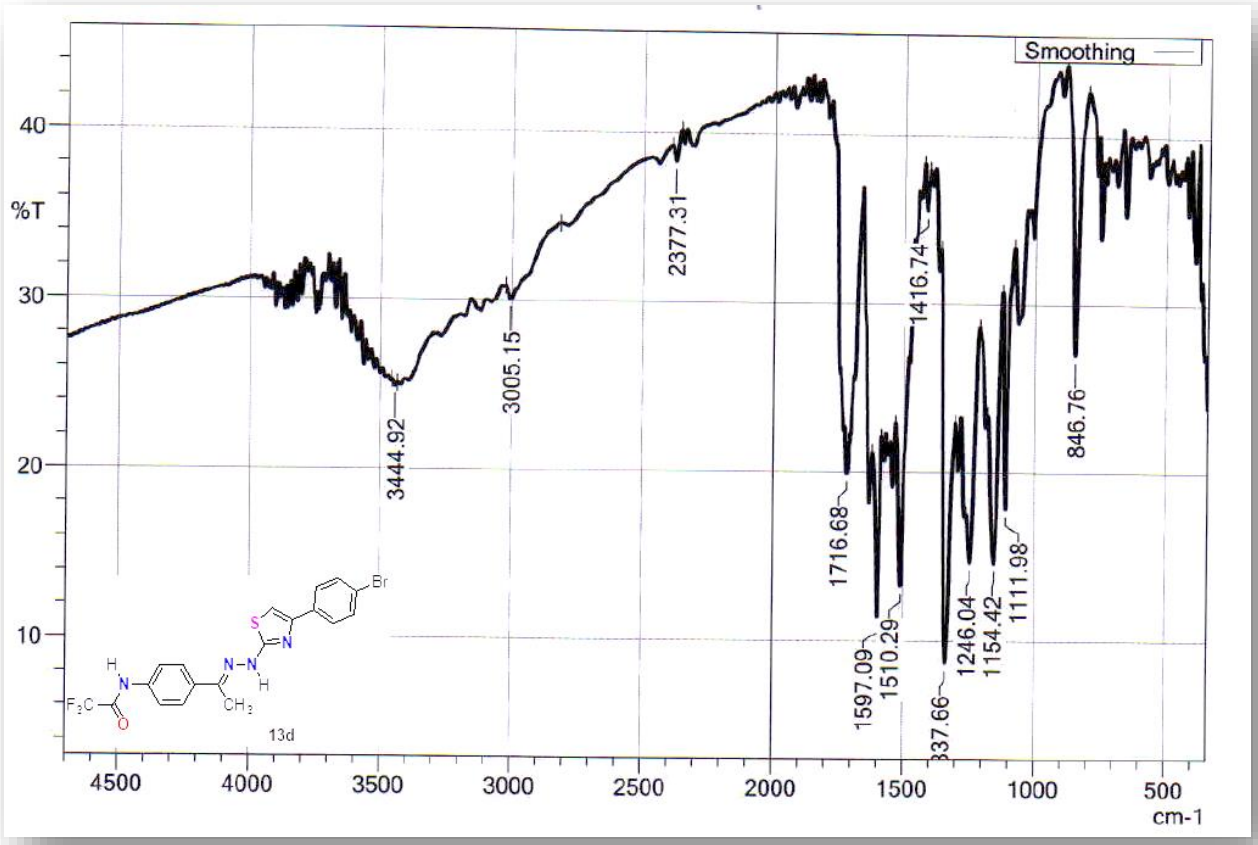

RT: 3.60 - 4.04 SM: 15G
Relative Abundance
Time (min)
13b
y18 #226 RT: 3.80 AV: 1 SB: 2 4.23 , 4.23 NL: 3.99E2
T: {0,0} + c EI Full ms [40.00-1000.00]
Relative Abundance
m/z
48.62
81.22
83.48
108.08
118.69
121.40
127.43
133.42
136.84
138.95
155.27
164.59
166.22
181.29
182.49
196.41
199.09
202.75
216.47
218.18
224.77
242.01
242.87
243.64
244.32
261.41
266.50
278.75
299.93
307.94
314.08
326.88
333.38
345.80
347.28
352.11
366.79
376.23
382.54
388.14
392.50
396.28
401.27
413.94
418.38

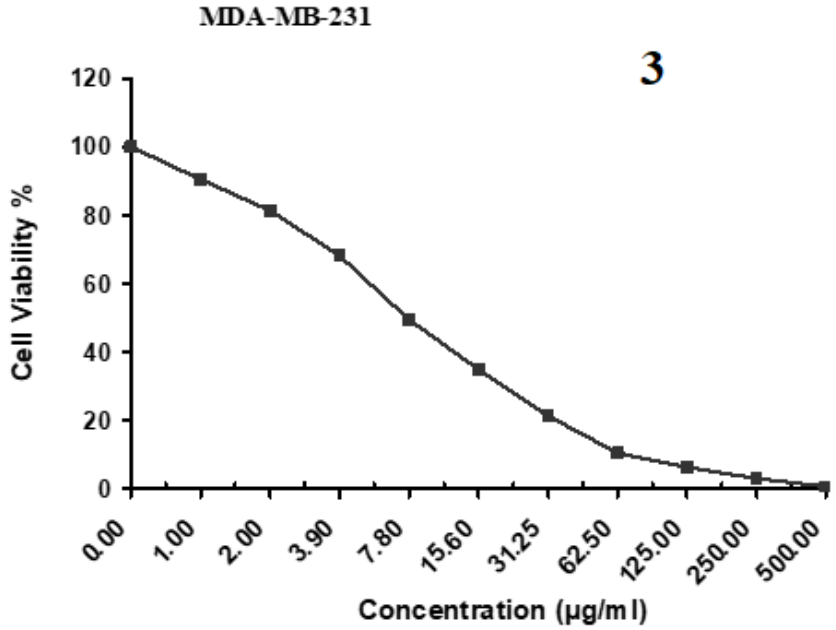

RT: 3.41 - 3.74 SM: 15G
Relative Abundance
Time (min)
13c
y19#213 RT: 3.58 AV: 1 SB: 2 4.45 , 4.45 NL: 4.41E2
T: {0,0} + c EIFull ms [40.00-1000.00]
Relative Abundance
m/z


Smoothing
%T
50
40
30
20
10
0
4500
4000
3500
3000
2500
2000
1500
1000
500
cm-1
3050.47
2377.31
2307.87
1714.75
1612.52
1541.15
1252.79
1157.31
1090.76
837.12
13c


13c
11.910
11.344
8.102
8.039
8.011
7.884
7.655
7.449
7.270
7.238
7.212
7.043
7.009
6.886
6.862
3.446
2.361
14
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm


RT: 2.77 - 3.09 SM: 15G
Relative Abundance
Time (min)
13d
y20 #122 RT: 2.06 AV: 1 SB: 2 4.45 , 4.45 NL: 4.47E2
T: {0,0} + c EI Full ms [40.00-1000.00]
Relative Abundance
m/z

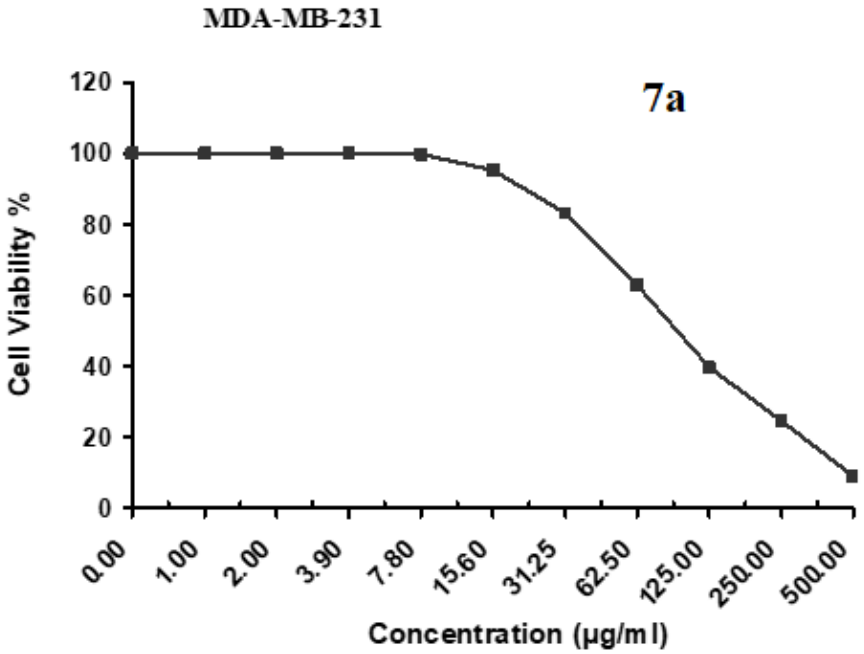

Smoothing
%T
40
30
20
10
3444.92
3005.15
2377.31
1716.68
1597.09
1510.29
1416.74
1337.66
1246.04
1154.42
1111.98
846.76
4500
4000
3500
3000
2500
2000
1500
1000
500
cm-1
Br
S
N
N-N
H
H
N
F3C
O
CH3
13d




| Sample conc. (µg/ml) | Viability % | Inhibitory % | S.D. (±) |
|---|---|---|---|
| 500 | 0.78 | 99.22 | 0.44 |
| 250 | 3.09 | 96.91 | 0.75 |
| 125 | 6.38 | 93.62 | 0.96 |
| 62.5 | 10.53 | 89.47 | 0.81 |
| 31.25 | 21.34 | 78.66 | 1.28 |
| 15.6 | 34.92 | 65.08 | 2.46 |
| 7.8 | 49.53 | 50.47 | 3.91 |
| 3.9 | 68.14 | 31.86 | 2.84 |
| 2 | 81.36 | 18.64 | 2.92 |
| 1 | 90.45 | 9.55 | 1.73 |
| 0 | 100 | 0 | |

## ***Comment*:**

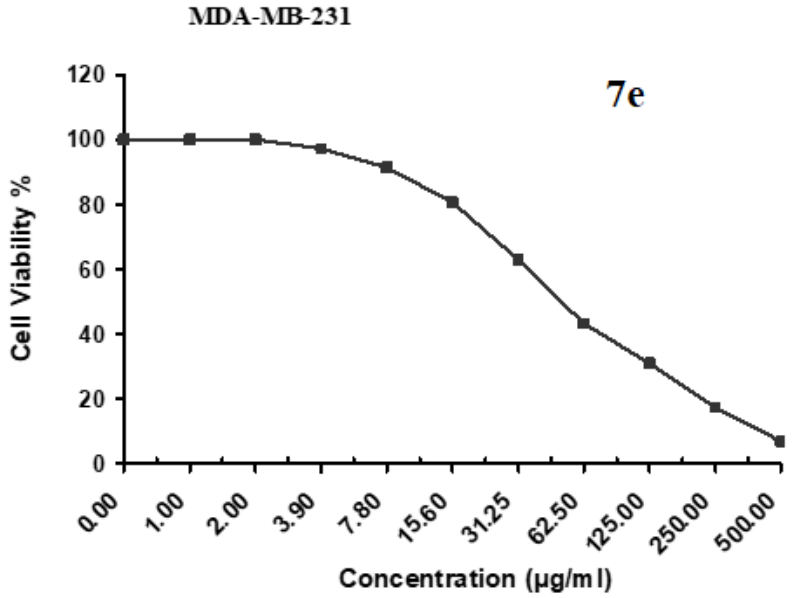
***Inhibitory activity against breast carcinoma cells was detected under these experimental conditions with $IC_{50}$ = 7.7 ± 0.41 µg/ml.***




| Sample conc. (µg/ml) | Viability % | Inhibitory % | S.D. (±) |
|---|---|---|---|
| 500 | 8.95 | 91.05 | 0.99 |
| 250 | 24.67 | 75.33 | 1.75 |
| 125 | 39.70 | 60.3 | 2.84 |
| 62.5 | 62.81 | 37.19 | 3.17 |
| 31.25 | 83.14 | 16.86 | 1.78 |
| 15.6 | 95.22 | 4.78 | 0.64 |
| 7.8 | 99.73 | 0.27 | 0.25 |
| 3.9 | 100 | 0 | |
| 2 | 100 | 0 | |
| 1 | 100 | 0 | |
| 0 | 100 | 0 | |

***Comment*:**

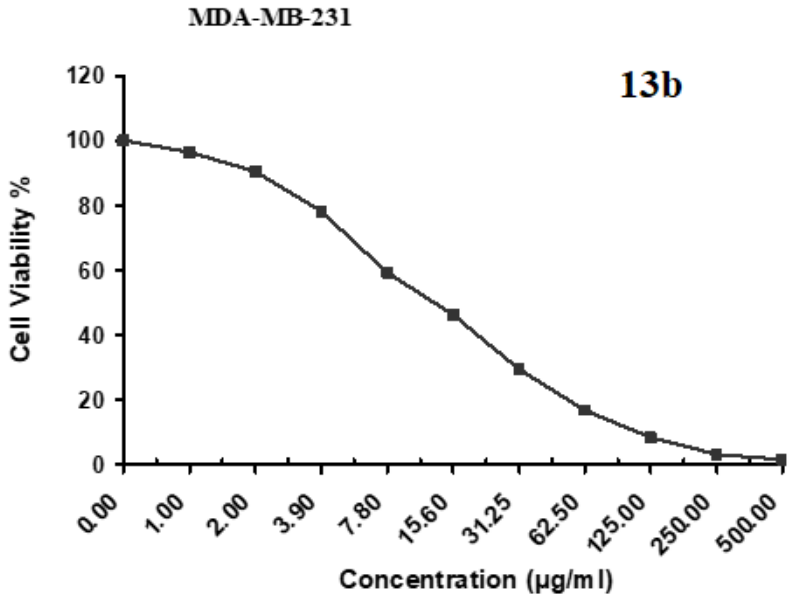
***Inhibitory activity against breast carcinoma cells was detected under these experimental conditions with $IC_{50}$ = 97.1 ± 4.9 µg/ml.***




| Sample conc. (µg/ml) | Viability % | Inhibitory % | S.D. (±) |
|---|---|---|---|
| 500 | 6.93 | 93.07 | 0.45 |
| 250 | 17.40 | 82.6 | 0.64 |
| 125 | 30.98 | 69.02 | 2.32 |
| 62.5 | 43.26 | 56.74 | 1.98 |
| 31.25 | 62.96 | 37.04 | 3.28 |
| 15.6 | 80.67 | 19.33 | 1.73 |
| 7.8 | 91.34 | 8.66 | 1.29 |
| 3.9 | 97.15 | 2.85 | 0.73 |
| 2 | 100 | 0 | |
| 1 | 100 | 0 | |
| 0 | 100 | 0 | |

## ***Comment***:

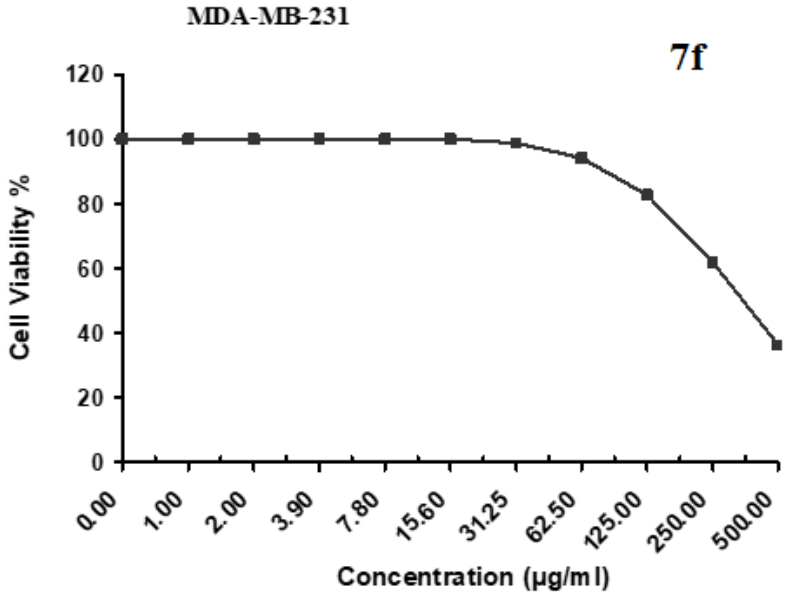
***Inhibitory activity against breast carcinoma cells was detected under these experimental conditions with $IC_{50}$ = 51.8 ± 3.4 µg/ml.***




| Sample conc. (µg/ml) | Viability % | Inhibitory % | S.D. (±) |
|---|---|---|---|
| 500 | 1.63 | 98.37 | 0.29 |
| 250 | 3.27 | 96.73 | 0.15 |
| 125 | 8.45 | 91.55 | 0.81 |
| 62.5 | 16.83 | 83.17 | 0.97 |
| 31.25 | 29.46 | 70.54 | 1.43 |
| 15.6 | 46.31 | 53.69 | 2.87 |
| 7.8 | 59.28 | 40.72 | 1.86 |
| 3.9 | 78.15 | 21.85 | 1.34 |
| 2 | 90.42 | 9.58 | 1.06 |
| 1 | 96.39 | 3.61 | 0.75 |
| 0 | 100 | 0 | |

## ***Comment*:**

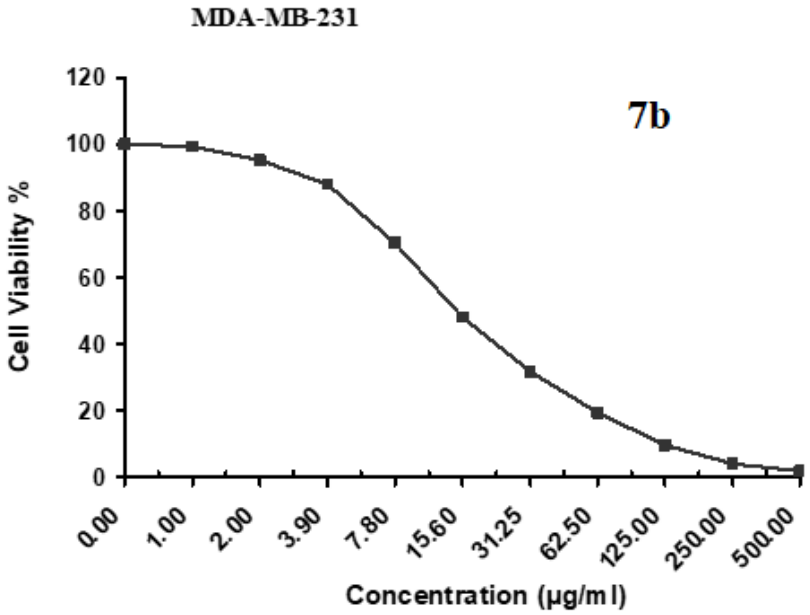
***Inhibitory activity against breast carcinoma cells was detected under these experimental conditions with $IC_{50}$ = 13.4 ± 0.85 µg/ml.***




| Sample conc. (µg/ml) | Viability % | Inhibitory % | S.D. (±) |
|---|---|---|---|
| 500 | 36.28 | 63.72 | 3.14 |
| 250 | 61.92 | 38.08 | 4.26 |
| 125 | 82.64 | 17.36 | 2.82 |
| 62.5 | 94.13 | 5.87 | 1.75 |
| 31.25 | 98.76 | 1.24 | 0.89 |
| 15.6 | 100 | 0 | |
| 7.8 | 100 | 0 | |
| 3.9 | 100 | 0 | |
| 2 | 100 | 0 | |
| 1 | 100 | 0 | |
| 0 | 100 | 0 | |

## ***Comment*:**

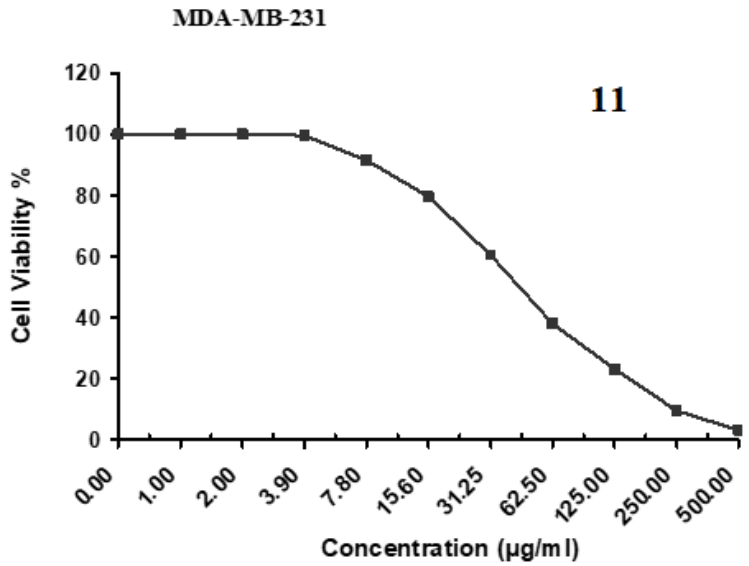
***Inhibitory activity against breast carcinoma cells was detected under these experimental conditions with $IC_{50}$ = 366 ± 21.4 µg/ml.***




| Sample conc. (µg/ml) | Viability % | Inhibitory % | S.D. (±) |
|---|---|---|---|
| 500 | 1.89 | 98.11 | 0.43 |
| 250 | 4.12 | 95.88 | 0.64 |
| 125 | 9.73 | 90.27 | 0.51 |
| 62.5 | 19.45 | 80.55 | 0.89 |
| 31.25 | 31.79 | 68.21 | 1.67 |
| 15.6 | 48.02 | 51.98 | 2.84 |
| 7.8 | 70.34 | 29.66 | 3.19 |
| 3.9 | 87.96 | 12.04 | 2.62 |
| 2 | 95.17 | 4.83 | 0.95 |
| 1 | 99.23 | 0.77 | 0.49 |
| 0 | 100 | 0 | |

## ***Comment*:**

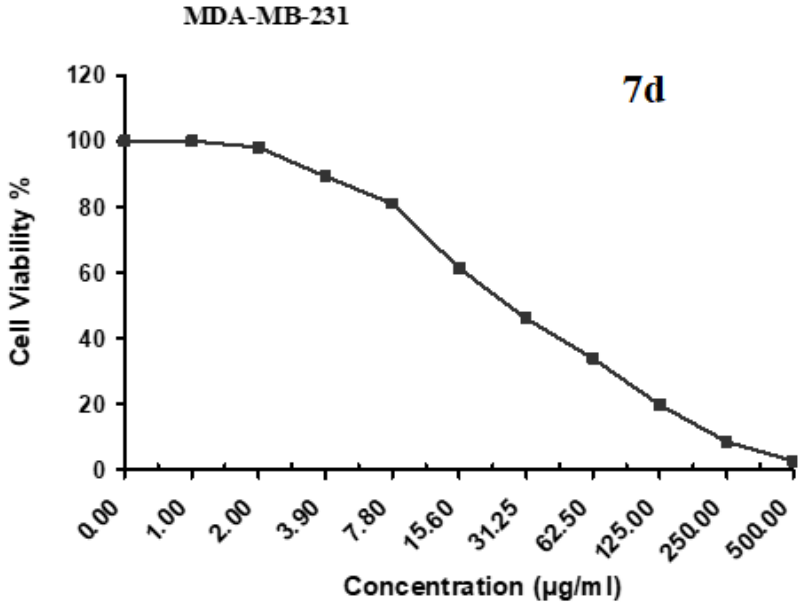
***Inhibitory activity against breast carcinoma cells was detected under these experimental conditions with $IC_{50}$ = 14.9 ± 0.97 µg/ml.***




| Sample conc. (µg/ml) | Viability % | Inhibitory % | S.D. (±) |
|---|---|---|---|
| 500 | 3.18 | 96.82 | 0.29 |
| 250 | 9.54 | 90.46 | 0.72 |
| 125 | 23.19 | 76.81 | 1.37 |
| 62.5 | 38.02 | 61.98 | 2.86 |
| 31.25 | 60.43 | 39.57 | 3.19 |
| 15.6 | 79.56 | 20.44 | 2.08 |
| 7.8 | 91.47 | 8.53 | 1.71 |
| 3.9 | 99.52 | 0.48 | 0.64 |
| 2 | 100 | 0 | |
| 1 | 100 | 0 | |
| 0 | 100 | 0 | |

## ***Comment*:**

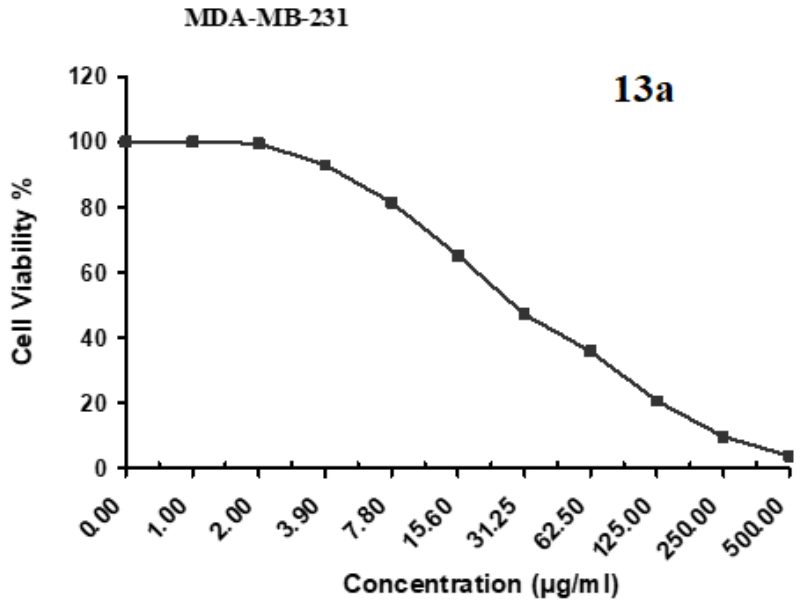
***Inhibitory activity against breast carcinoma cells was detected under these experimental conditions with $IC_{50}$ = 45.8 ± 2.8 µg/ml.***




| Sample conc. (µg/ml) | Viability % | Inhibitory % | S.D. (±) |
|---|---|---|---|
| 500 | 2.74 | 97.26 | 0.34 |
| 250 | 8.65 | 91.35 | 1.03 |
| 125 | 19.76 | 80.24 | 0.68 |
| 62.5 | 33.89 | 66.11 | 1.72 |
| 31.25 | 46.02 | 53.98 | 3.24 |
| 15.6 | 61.37 | 38.63 | 2.89 |
| 7.8 | 80.95 | 19.05 | 1.37 |
| 3.9 | 89.23 | 10.77 | 0.91 |
| 2 | 98.04 | 1.96 | 0.62 |
| 1 | 100 | 0 | |
| 0 | 100 | 0 | |

## ***Comment*:**

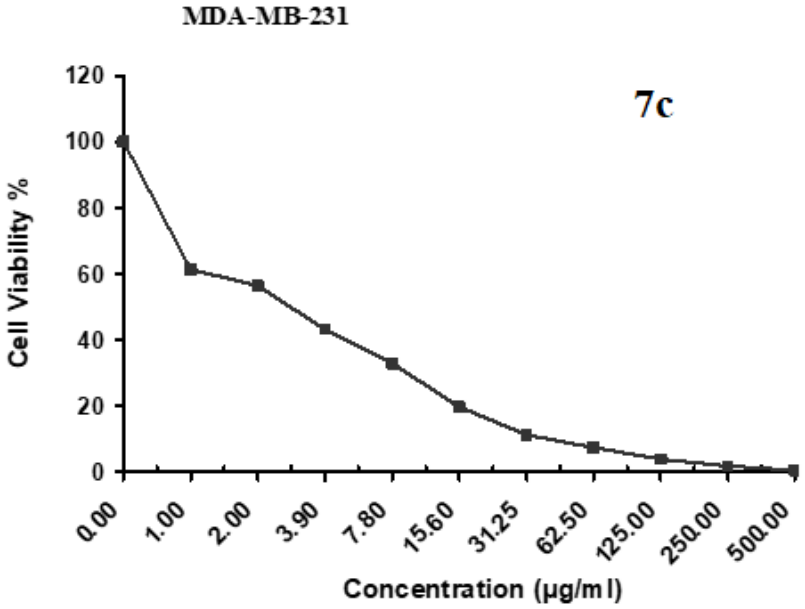
***Inhibitory activity against breast carcinoma cells was detected under these experimental conditions with $IC_{50}$ = 27.2 ± 1.7 µg/ml.***




| Sample conc. (µg/ml) | Viability % | Inhibitory % | S.D. (±) |
|---|---|---|---|
| 500 | 3.86 | 96.14 | 0.28 |
| 250 | 9.73 | 90.27 | 0.69 |
| 125 | 20.65 | 79.35 | 0.53 |
| 62.5 | 35.83 | 64.17 | 1.75 |
| 31.25 | 47.16 | 52.84 | 2.62 |
| 15.6 | 65.29 | 34.71 | 3.13 |
| 7.8 | 81.44 | 18.56 | 0.82 |
| 3.9 | 92.87 | 7.13 | 1.09 |
| 2 | 99.45 | 0.55 | 0.37 |
| 1 | 100 | 0 | |
| 0 | 100 | 0 | |

## ***Comment*:**

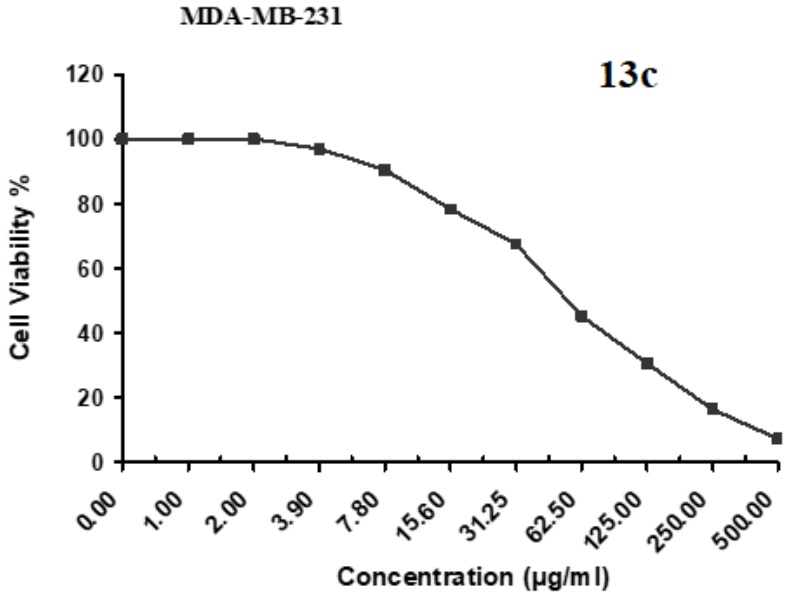
***Inhibitory activity against breast carcinoma cells was detected under these experimental conditions with $IC_{50}$ = 28.8 ± 1.9 µg/ml.***




| Sample conc. (µg/ml) | Viability % | Inhibitory % | S.D. (±) |
|---|---|---|---|
| 500 | 0.59 | 99.41 | 0.17 |
| 250 | 1.87 | 98.13 | 0.61 |
| 125 | 3.95 | 96.05 | 0.53 |
| 62.5 | 7.43 | 92.57 | 0.69 |
| 31.25 | 11.28 | 88.72 | 1.74 |
| 15.6 | 19.76 | 80.24 | 1.08 |
| 7.8 | 32.95 | 67.05 | 1.83 |
| 3.9 | 43.18 | 56.82 | 2.91 |
| 2 | 56.42 | 43.58 | 3.24 |
| 1 | 61.34 | 38.66 | 1.62 |
| 0 | 100 | 0 | |

## ***Comment***:

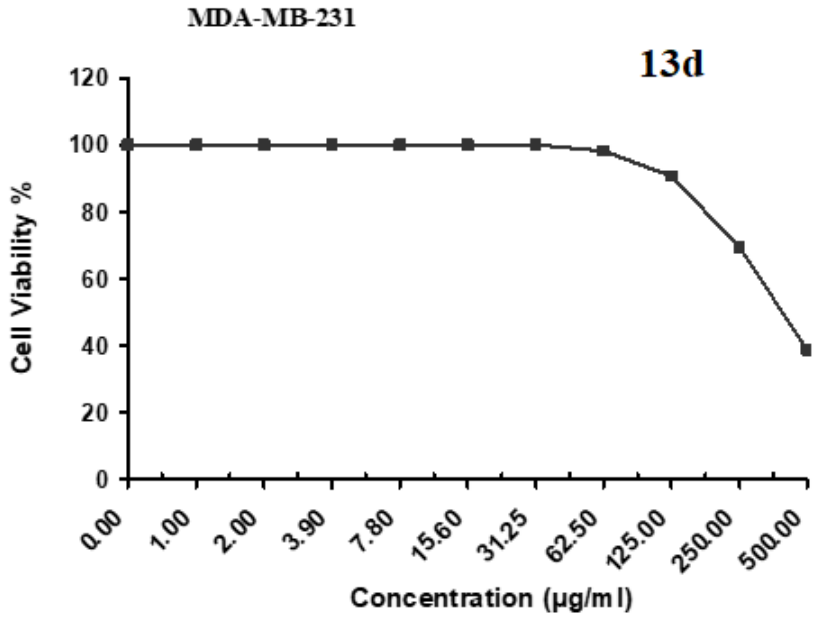
***Inhibitory activity against breast carcinoma cells was detected under these experimental conditions with $IC_{50}$ = 2.97± 0.32 µg/ml.***




| Sample conc. (µg/ml) | Viability % | Inhibitory % | S.D. (±) |
|---|---|---|---|
| 500 | 7.28 | 92.72 | 0.74 |
| 250 | 16.43 | 83.57 | 0.91 |
| 125 | 30.58 | 69.42 | 1.75 |
| 62.5 | 45.26 | 54.74 | 2.83 |
| 31.25 | 67.49 | 32.51 | 2.97 |
| 15.6 | 78.31 | 21.69 | 2.43 |
| 7.8 | 90.48 | 9.52 | 1.74 |
| 3.9 | 97.02 | 2.98 | 0.98 |
| 2 | 100 | 0 | |
| 1 | 100 | 0 | |
| 0 | 100 | 0 | |

## ***Comment*:**

***Inhibitory activity against breast carcinoma cells was detected under these experimental conditions with $IC_{50}$ = 55.8 ± 3.8 µg/ml.***

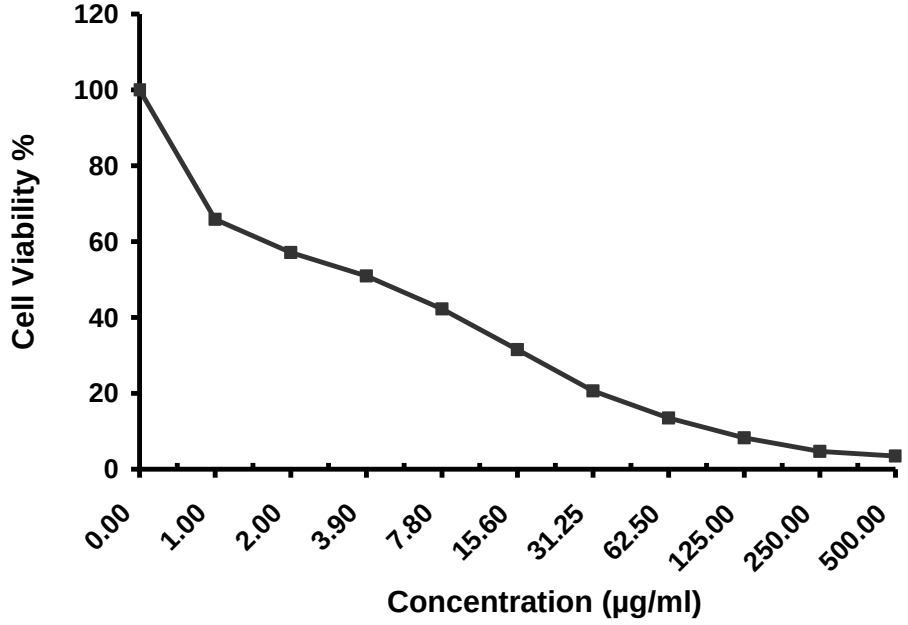



| Sample conc. (µg/ml) | Viability % | Inhibitory % | S.D. (±) |
|---|---|---|---|
| 500 | 38.76 | 61.24 | 3.28 |
| 250 | 69.41 | 30.59 | 2.97 |
| 125 | 90.64 | 9.36 | 2.42 |
| 62.5 | 98.16 | 1.84 | 0.89 |
| 31.25 | 100 | 0 | |
| 15.6 | 100 | 0 | |
| 7.8 | 100 | 0 | |
| 3.9 | 100 | 0 | |
| 2 | 100 | 0 | |
| 1 | 100 | 0 | |
| 0 | 100 | 0 | |

## ***Comment*:**

***Inhibitory activity against breast carcinoma cells was detected under these experimental conditions with $IC_{50}$ = 408 ± 19.8 µg/ml.***

**MDA-MB-231** **Cisplatin**




| Sample conc. (µg/ml) | Viability % | S.D. (±) |
|---|---|---|
| 500 | 3.48 | 0.24 |
| 250 | 4.71 | 0.35 |
| 125 | 8.25 | 0.47 |
| 62.5 | 13.49 | 0.78 |
| 31.25 | 20.62 | 0.54 |
| 15.6 | 31.53 | 0.91 |
| 7.8 | 42.24 | 0.78 |
| 3.9 | 50.96 | 2.36 |
| 2 | 57.13 | 0.75 |
| 1 | 65.86 | 0.42 |
| 0 | 100 | |