CHEMMEDCHEM
Chemistry & Drug Discovery

Supporting Information

Radiosynthesis of (*R*,*S*)-[^{18}F]GE387: A Potential PET Radiotracer for Imaging Translocator Protein 18 kDa (TSPO) with Low Binding Sensitivity to the Human Gene Polymorphism rs6971

Luxi Qiao[+],[a] Emily Fisher[+],[a] Lindsay McMurray,[a] Selena Milicevic Sephton,*[a] Matthew Hird,[a] Nisha Kuzhuppilly-Ramakrishnan,[a] David J. Williamson,[a] Xiouyun Zhou,[a] Eryn Werry,[b] Michael Kassiou,[b] Saijinder Luthra,[c] William Trigg,[c] and Franklin I. Aigbirhio*[a]

cmdc_201900023_sm_miscellaneous_information.pdf

Supporting information: CONTENTS

FXF_N schematic	**S2**
NMR Spectra	**S3**
HPLC Data	**S20**

F_XFN schematic

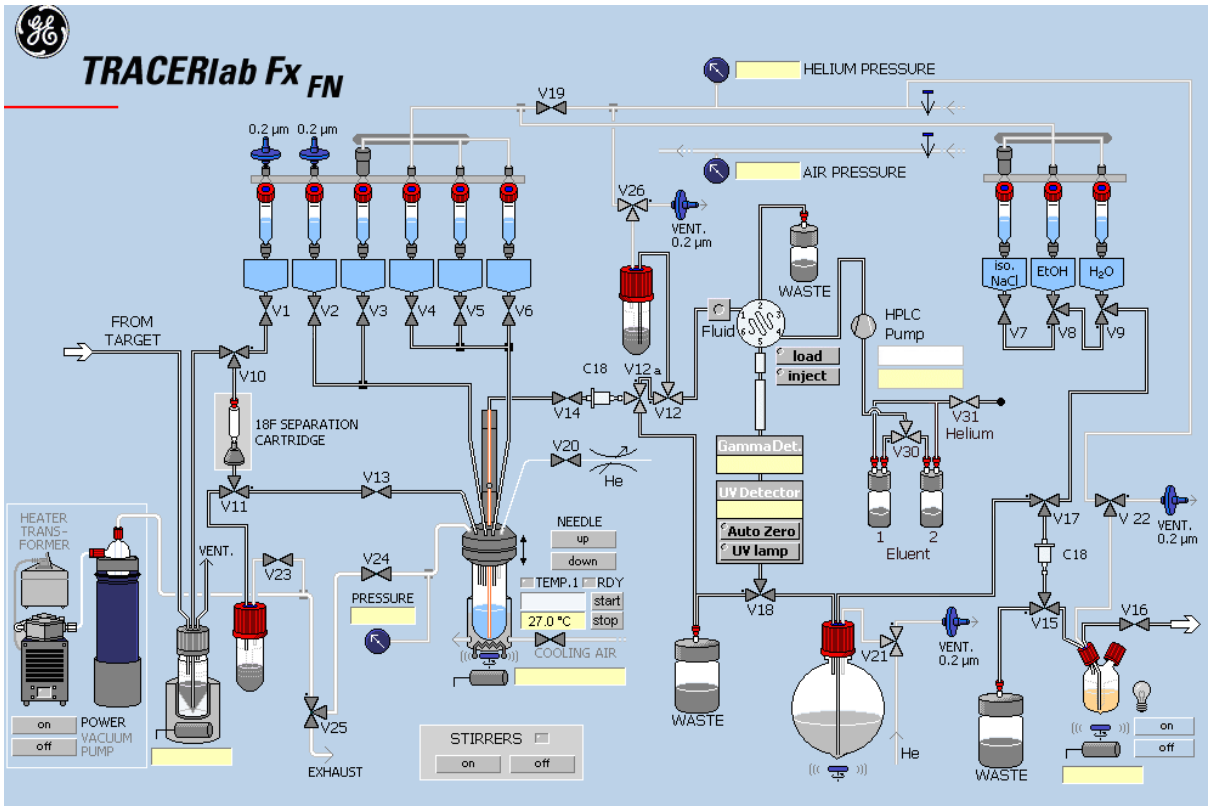


Figure S1: Schematic representation of F_XFN TRACERLab module

Supporting information: NMR Data

^{1}H NMR spectra were recorded in Fourier transform mode at the field strength specified using standard 5 mm diameter tubes. Chemical shifts in ppm is quoted relative to residual solvent signals calibrated as follows: **$CDCl_3$ δ_H** ($CHCl_3$) = 7.26 ppm; **δ_C** ($CHCl_3$) = 77.2 ppm. Unless otherwise stated spectra were collected at ambient temperature.

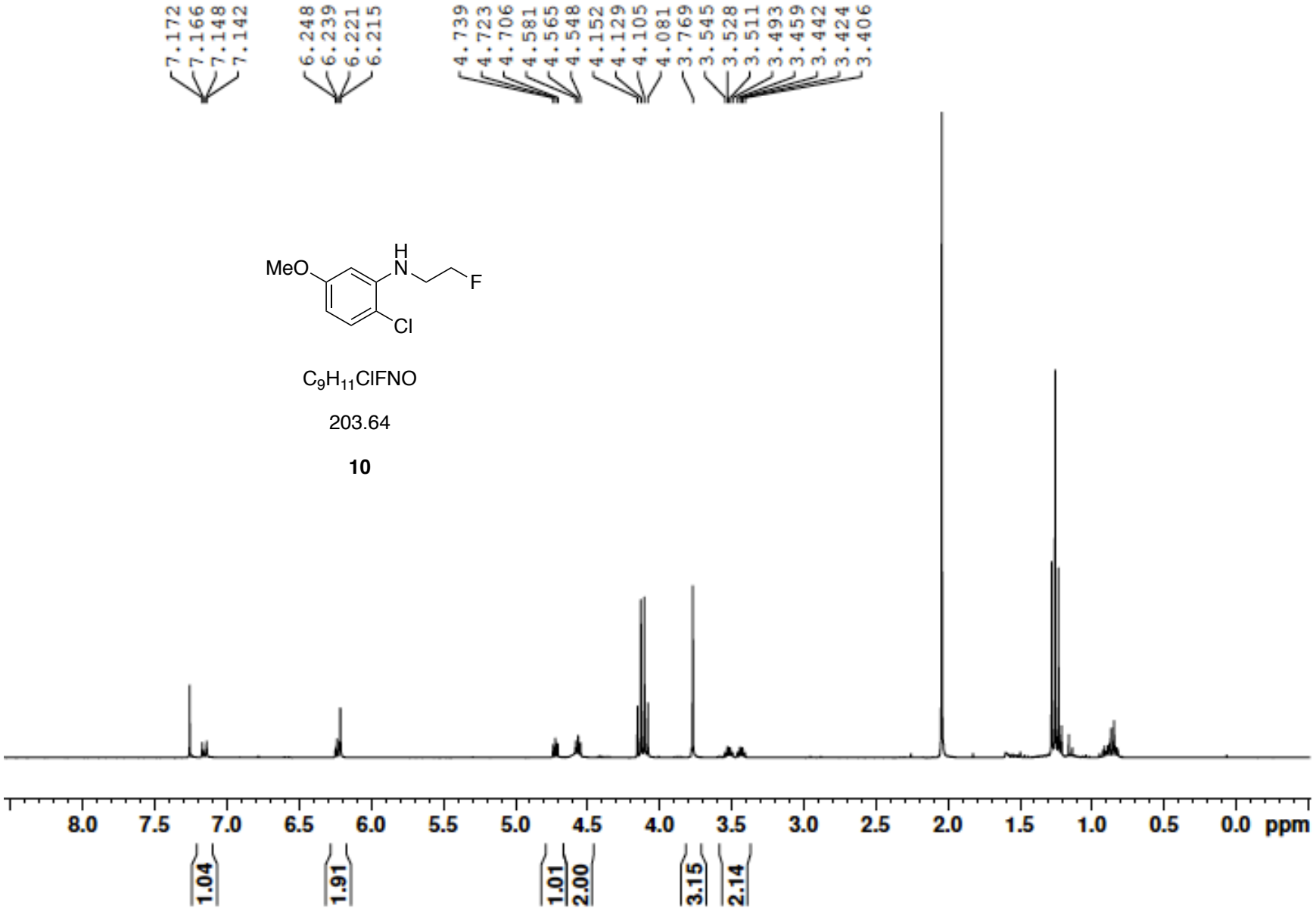
Compound	^{1}H/^{13}C NMR	Page
10	300 MHz, $CDCl_3$	S4
13	300 MHz, $CDCl_3$	S5
6	300/75 MHz, $CDCl_3$	S6/7
18	300 MHz, $CDCl_3$	S8
20	300 MHz, $CDCl_3$	S9
21	300 MHz, $CDCl_3$	S10

Compound	^{1}H/^{13}C NMR	Page
25	300/75 MHz, $CDCl_3$	S11/12
26	300 MHz, $CDCl_3$	S13
27	300 MHz, $CDCl_3$	S14
29	300 MHz, $CDCl_3$	S15/16
30	300 MHz, $CDCl_3$	S17/18

SFC data for chiral separation of **6** **S20/21**

Semi-prep HPLC data for [^{18}F]**6** **S22/23**

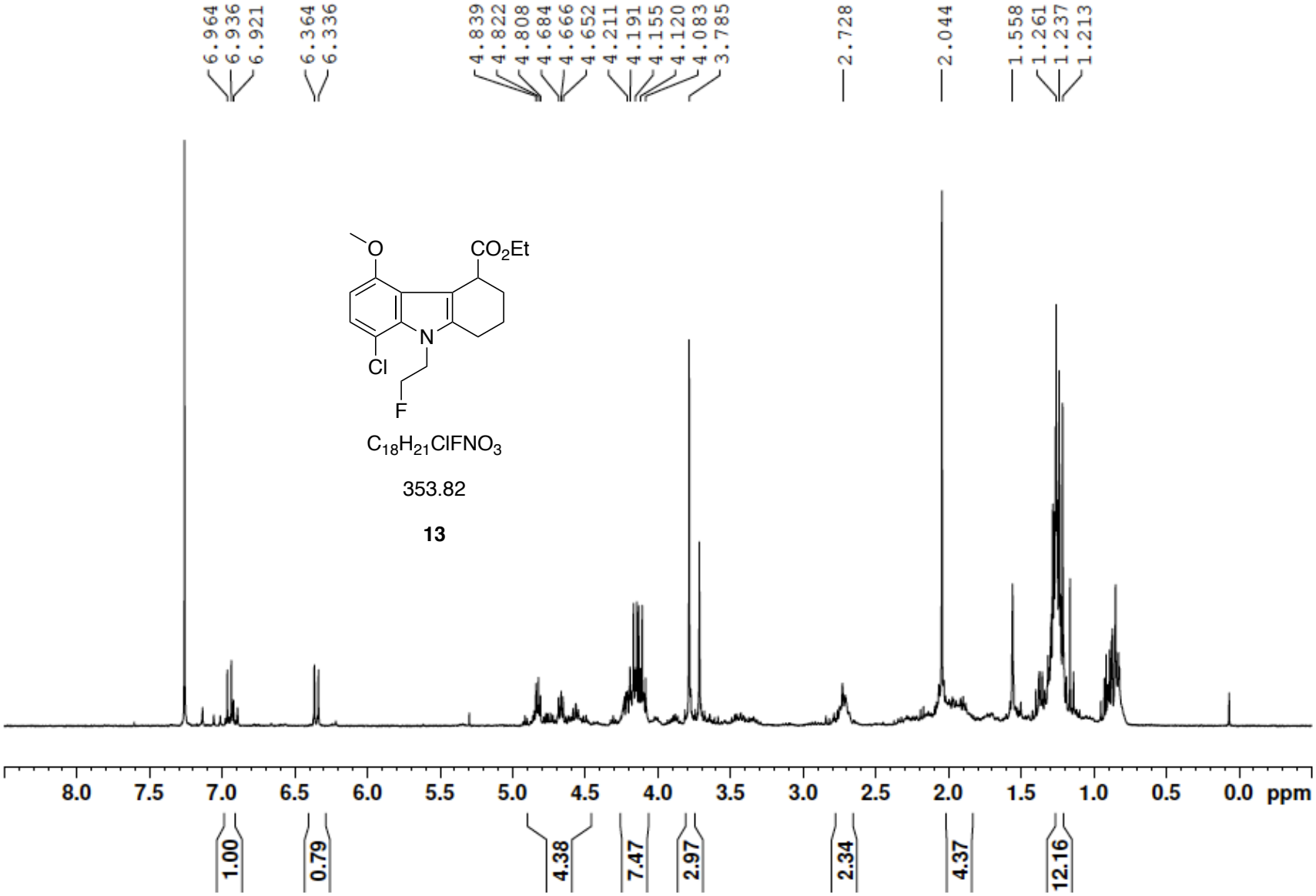
Chiral HPLC data for [^{18}F]**6** **S24/25**

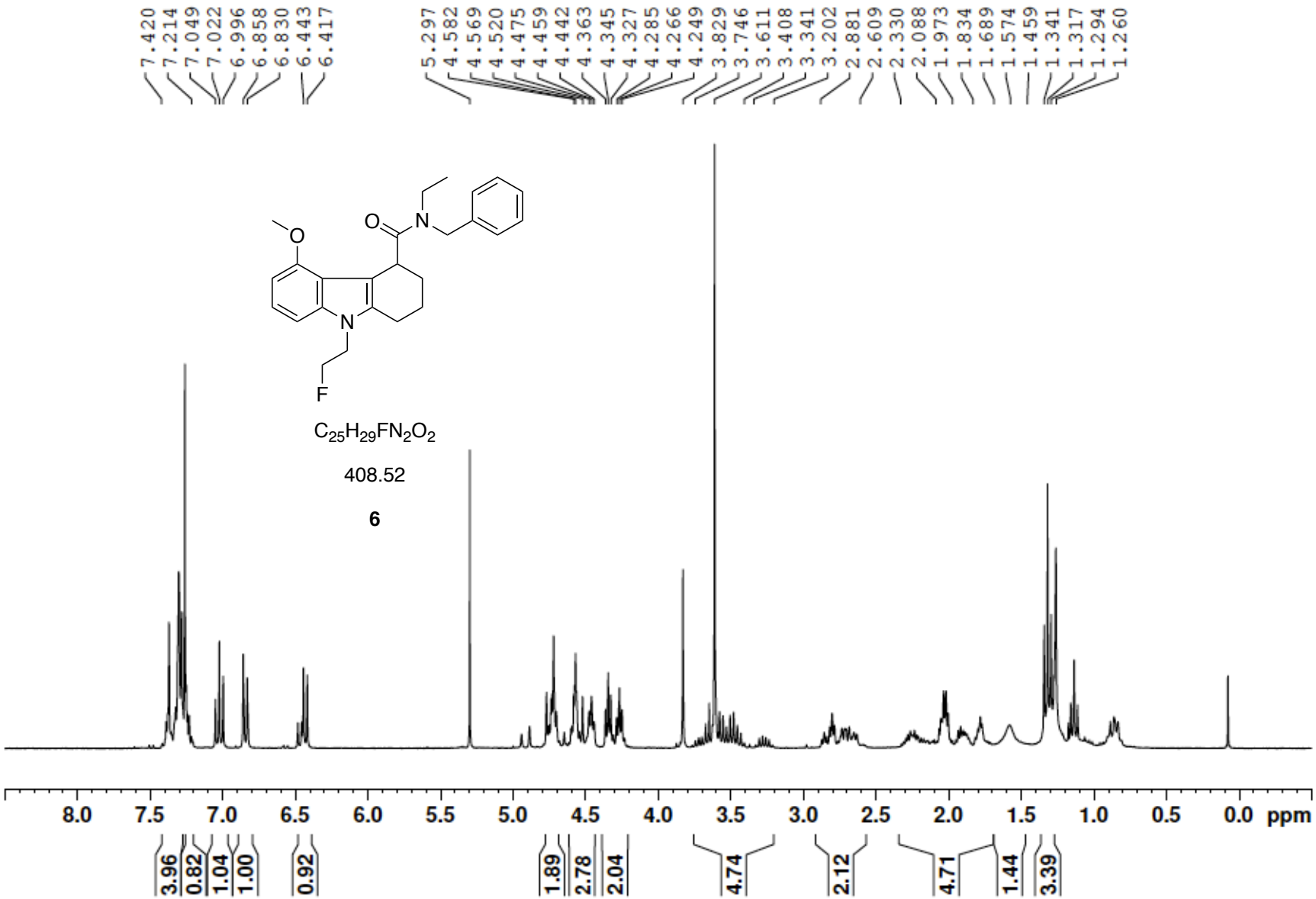


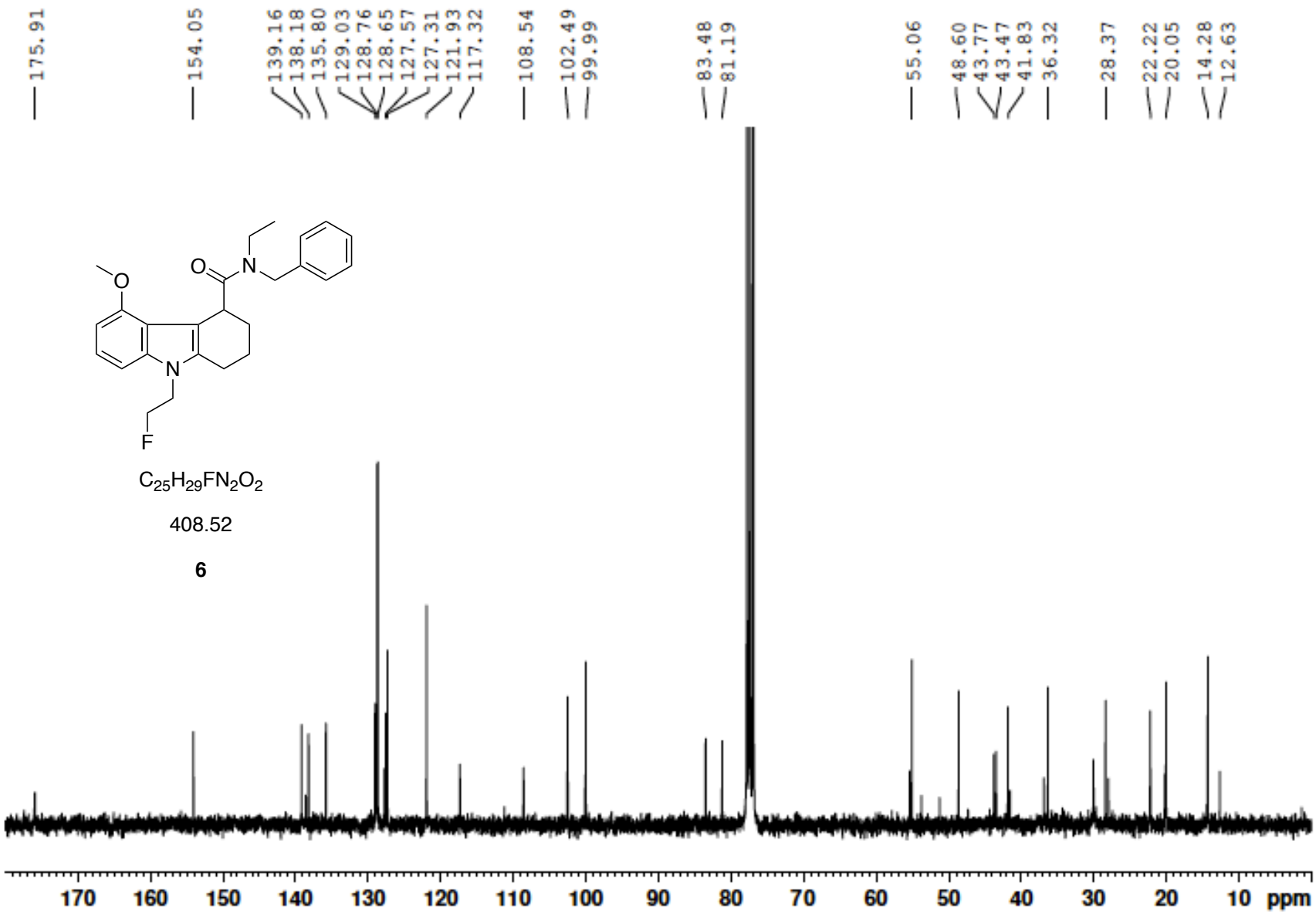
$C_9H_{11}ClFNO$

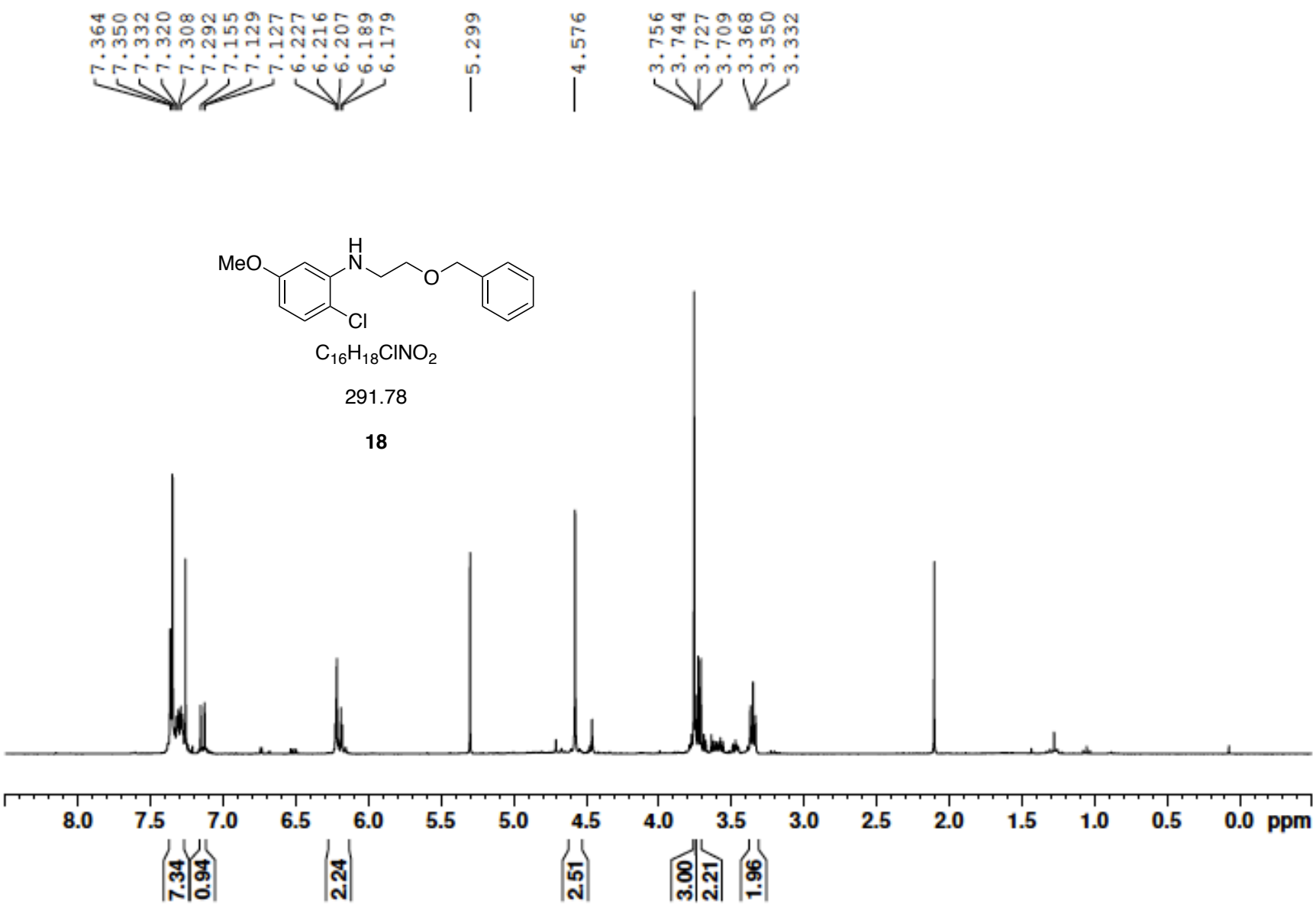
203.64

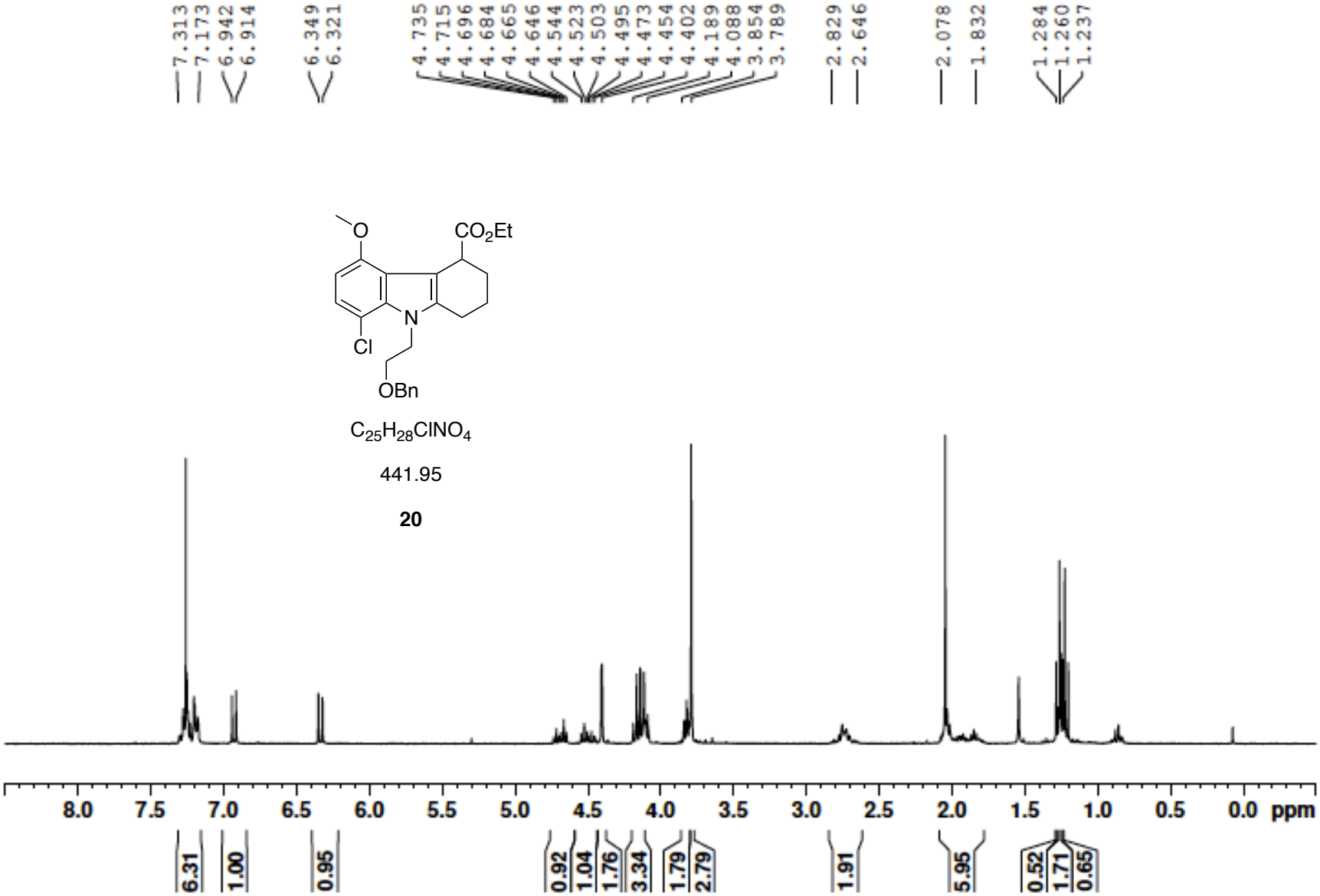
10

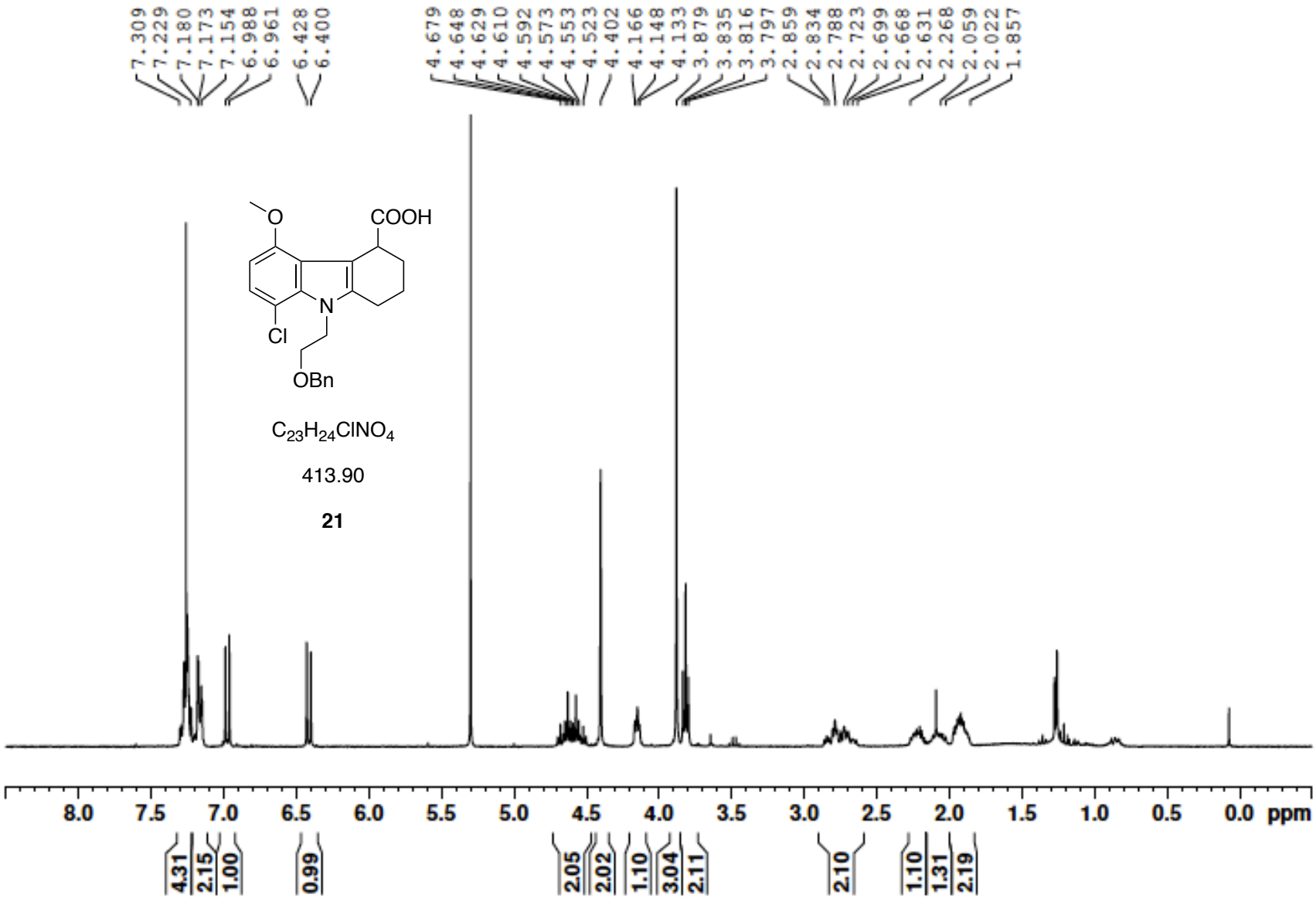

6.964
6.936
6.921
6.364
6.336
4.839
4.822
4.808
4.684
4.666
4.652
4.211
4.191
4.155
4.120
4.083
3.785
2.728
2.044
1.558
1.261
1.237
1.213
O
CO2Et
N
Cl
F
C18H21ClFNO3
353.82
13
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
0.79
4.38
7.47
2.97
2.34
4.37
12.16

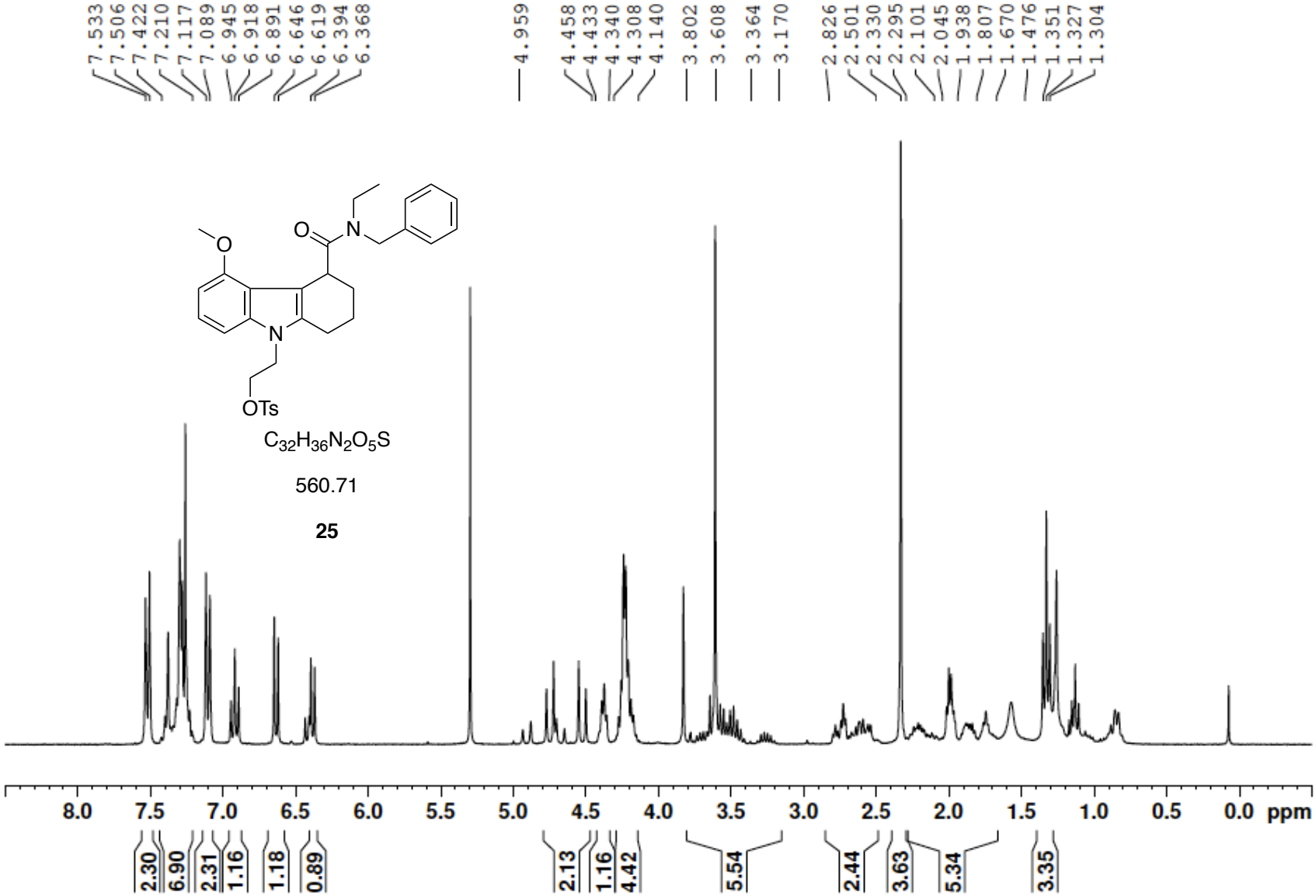

7.420
7.214
7.049
7.022
6.996
6.858
6.830
6.443
6.417
5.297
4.582
4.569
4.520
4.475
4.459
4.442
4.363
4.345
4.327
4.285
4.266
4.249
3.829
3.746
3.611
3.408
3.341
3.202
2.881
2.609
2.330
2.088
1.973
1.834
1.689
1.574
1.459
1.341
1.317
1.294
1.260
O
N
O
N
F
C25H29FN2O2
408.52
6
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
3.96
0.82
1.04
1.00
0.92
1.89
2.78
2.04
4.74
2.12
4.71
1.44
3.39

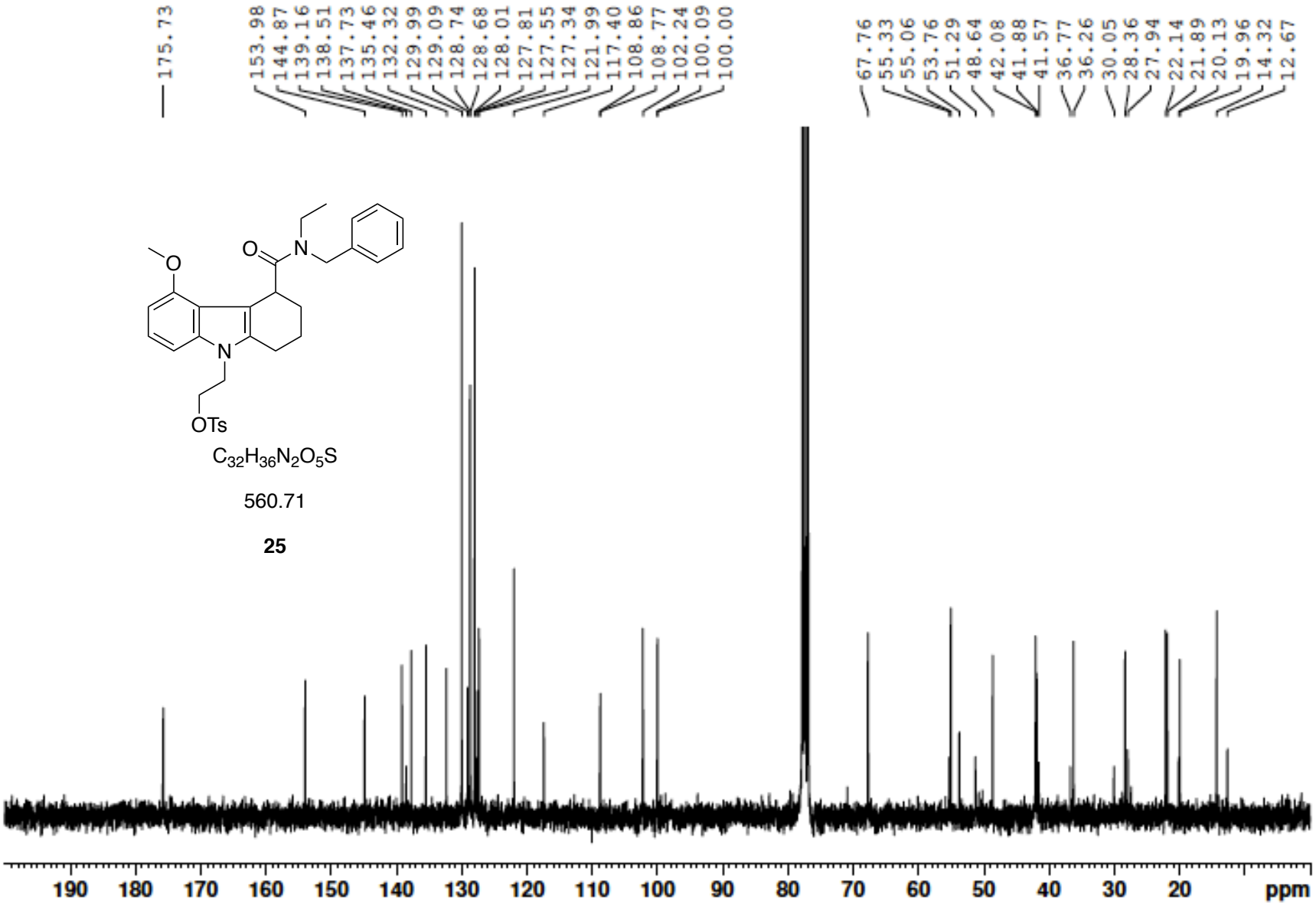

175.91
154.05
139.16
138.18
135.80
129.03
128.76
128.65
127.57
127.31
121.93
117.32
108.54
102.49
99.99
83.48
81.19
55.06
48.60
43.77
43.47
41.83
36.32
28.37
22.22
20.05
14.28
12.63
O
O
N
N
F
C25H29FN2O2
408.52
6
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


7.364
7.350
7.332
7.320
7.308
7.292
7.155
7.129
7.127
6.227
6.216
6.207
6.189
6.179
5.299
4.576
3.756
3.744
3.727
3.709
3.368
3.350
3.332
MeO
H
N
O
Cl
C16H18ClNO2
291.78
18
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
7.34
0.94
2.24
2.51
3.00
2.21
1.96


7.313
7.173
6.942
6.914
6.349
6.321
4.735
4.715
4.696
4.684
4.665
4.646
4.544
4.523
4.503
4.495
4.473
4.454
4.402
4.189
4.088
3.854
3.789
2.829
2.646
2.078
1.832
1.284
1.260
1.237
O
CO2Et
N
Cl
OBn
C25H28ClNO4
441.95
20
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
6.31
1.00
0.95
0.92
1.04
1.76
3.34
1.79
2.79
1.91
5.95
0.52
1.71
0.65


7.309
7.229
7.180
7.173
7.154
6.988
6.961
6.428
6.400
4.679
4.648
4.629
4.610
4.592
4.573
4.553
4.523
4.402
4.166
4.148
4.133
3.879
3.835
3.816
3.797
2.859
2.834
2.788
2.723
2.699
2.668
2.631
2.268
2.059
2.022
1.857
O
COOH
N
Cl
OBn
C23H24ClNO4
413.90
21
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
4.31
2.15
1.00
0.99
2.05
2.02
1.10
3.04
2.11
2.10
1.10
1.31
2.19

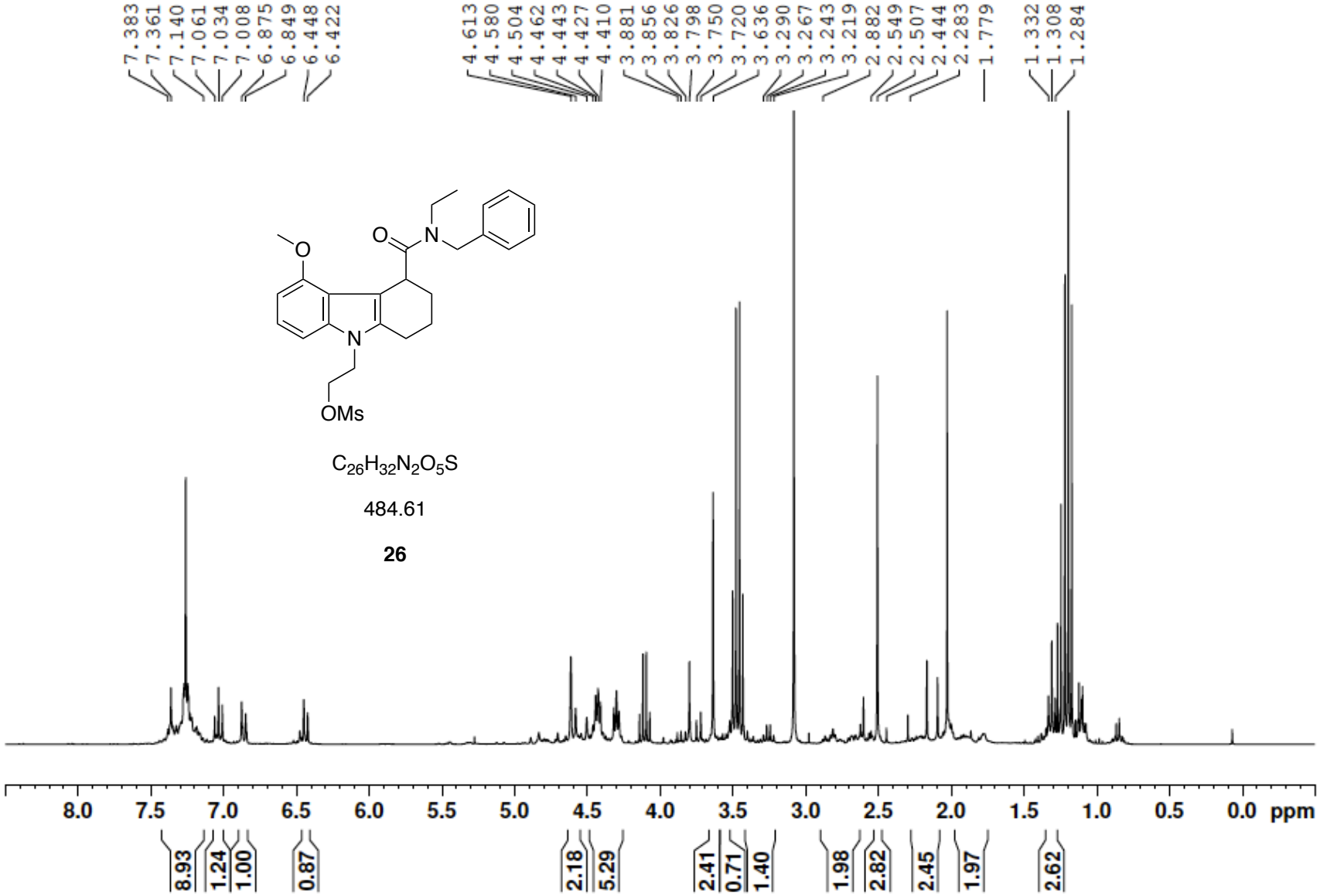

7.533
7.506
7.422
7.210
7.117
7.089
6.945
6.918
6.891
6.646
6.619
6.394
6.368
4.959
4.458
4.433
4.340
4.308
4.140
3.802
3.608
3.364
3.170
2.826
2.501
2.330
2.295
2.101
2.045
1.938
1.807
1.670
1.476
1.351
1.327
1.304
O
O
N
N
OTs
$C_{32}H_{36}N_2O_5S$
560.71
25
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
2.30
6.90
2.31
1.16
1.18
0.89
2.13
1.16
4.42
5.54
2.44
3.63
5.34
3.35

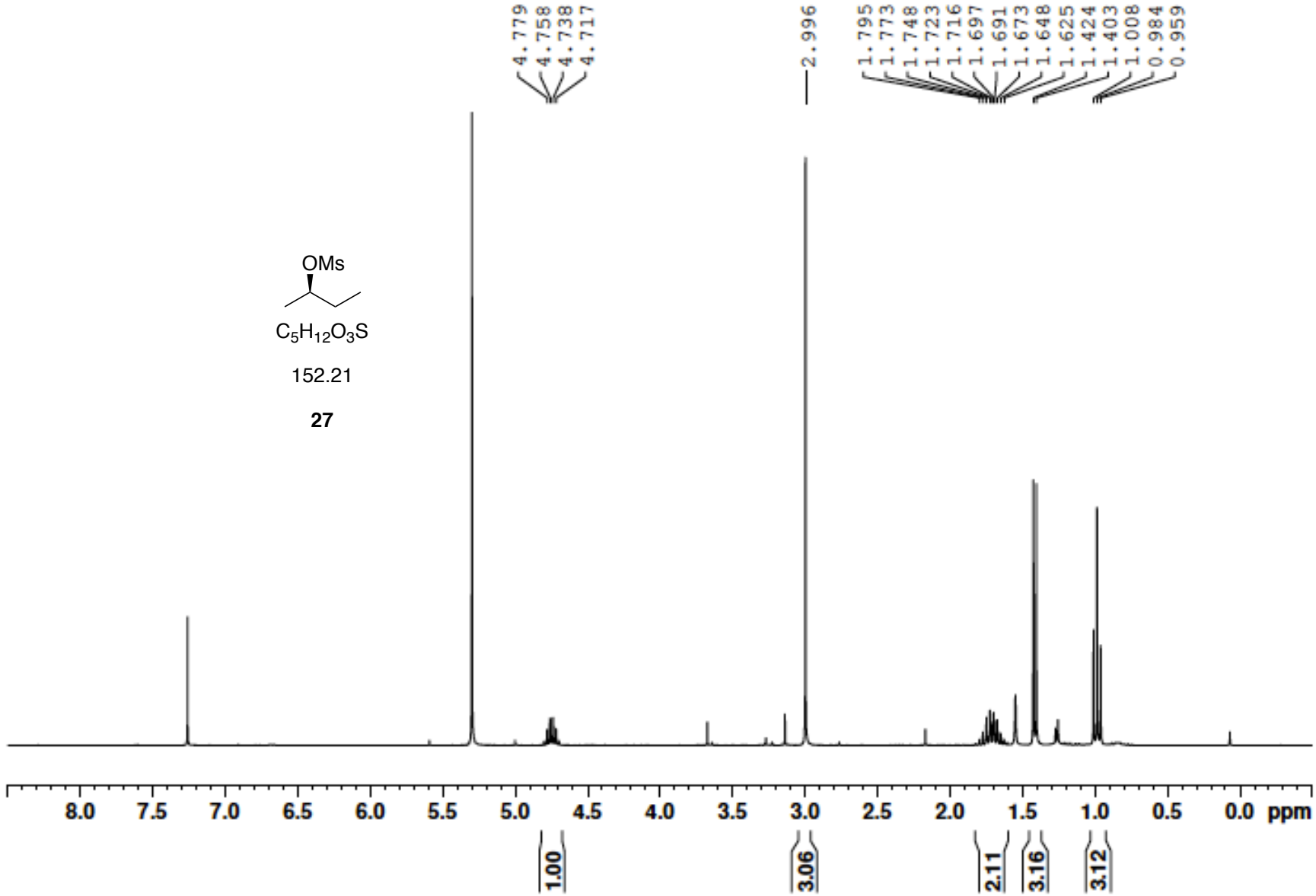


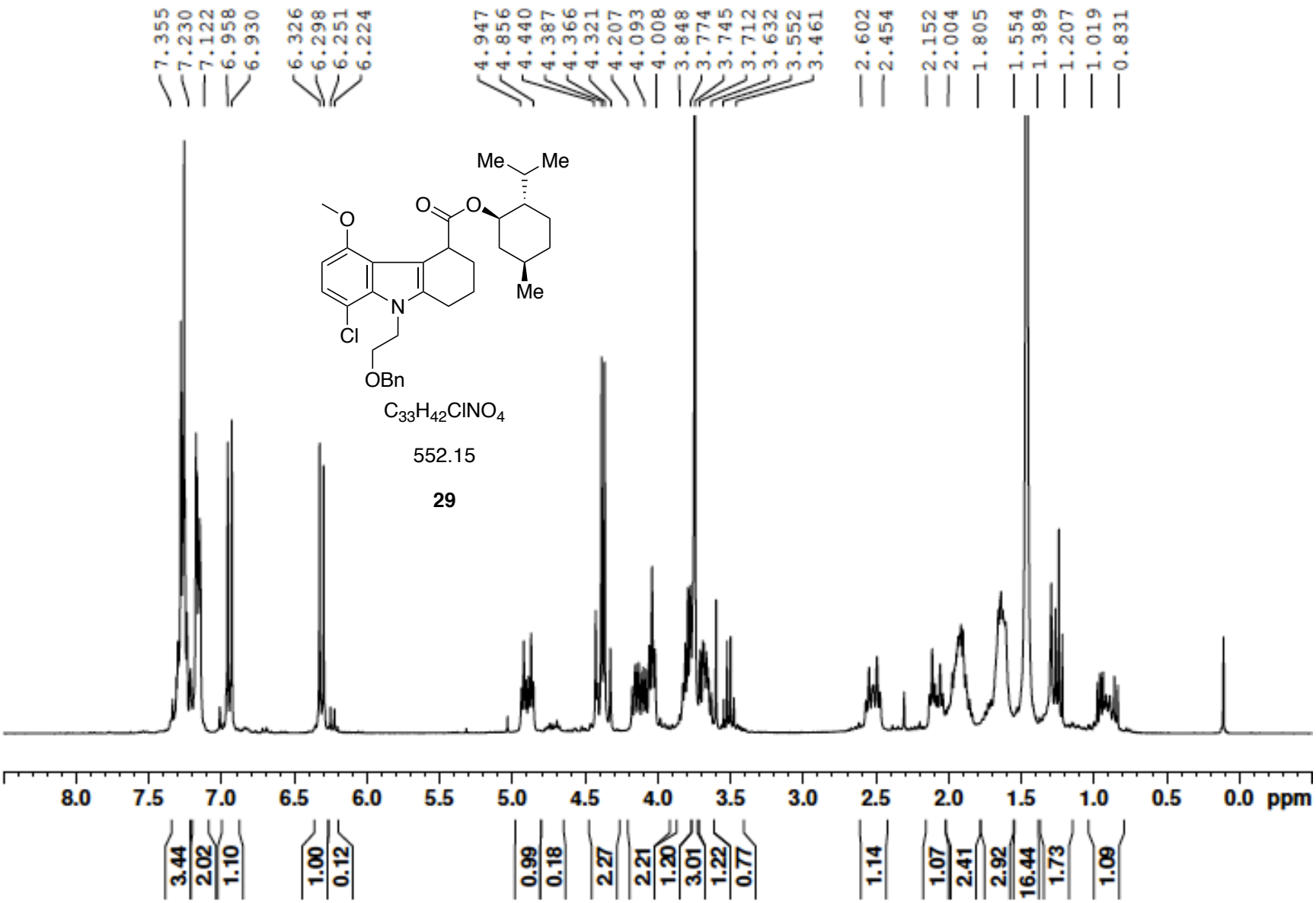
$C_{32}H_{36}N_2O_5S$

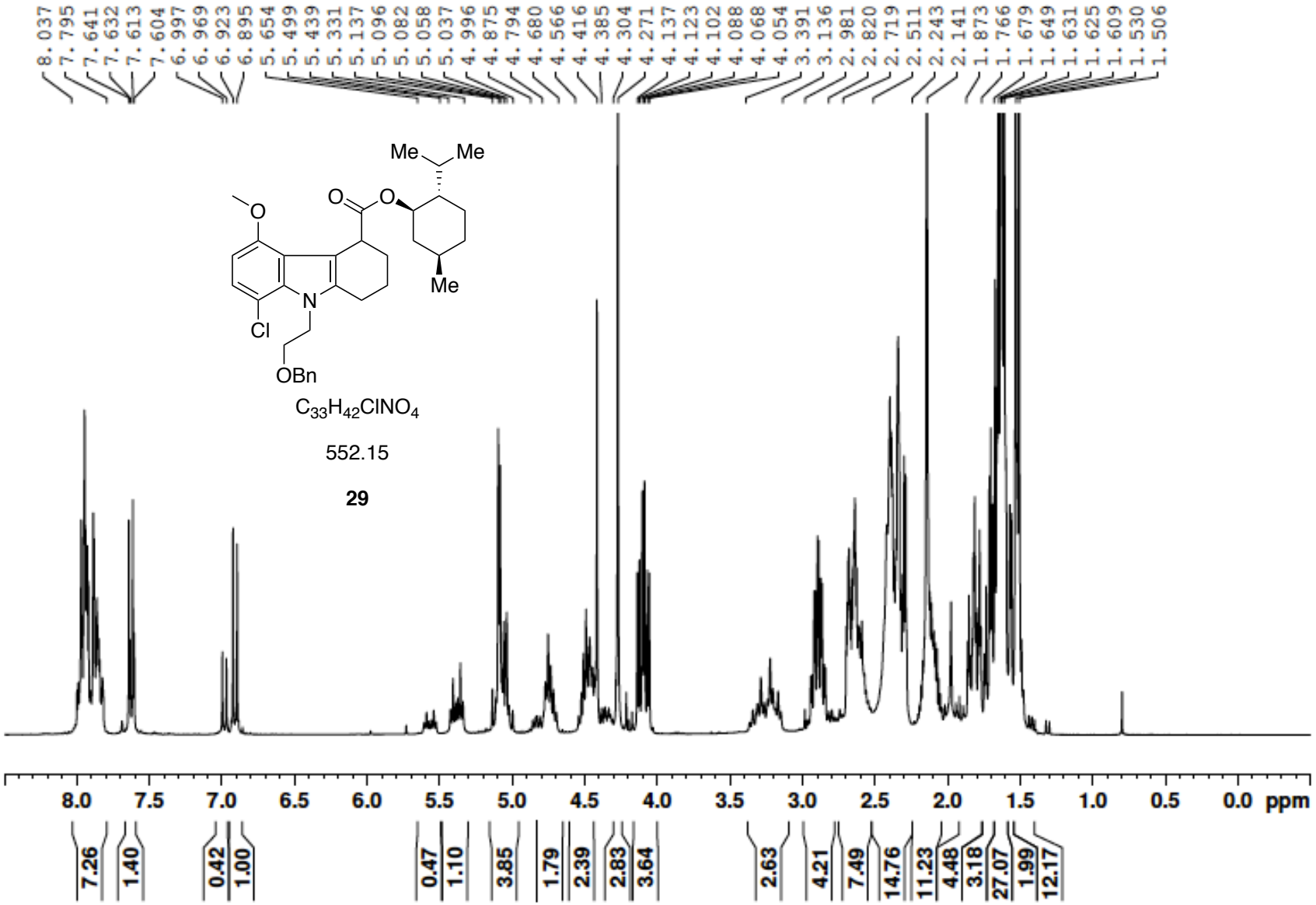
560.71

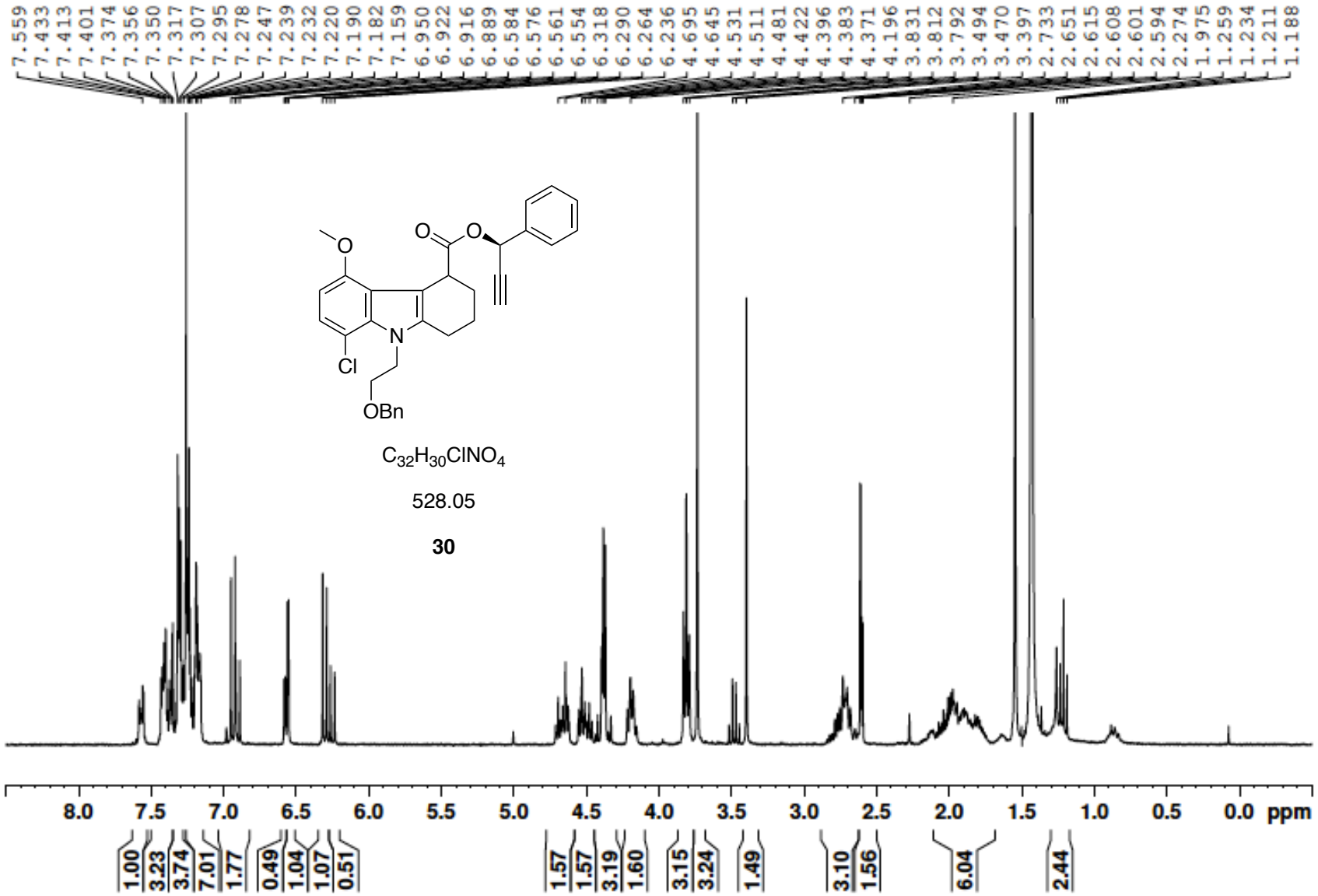
25

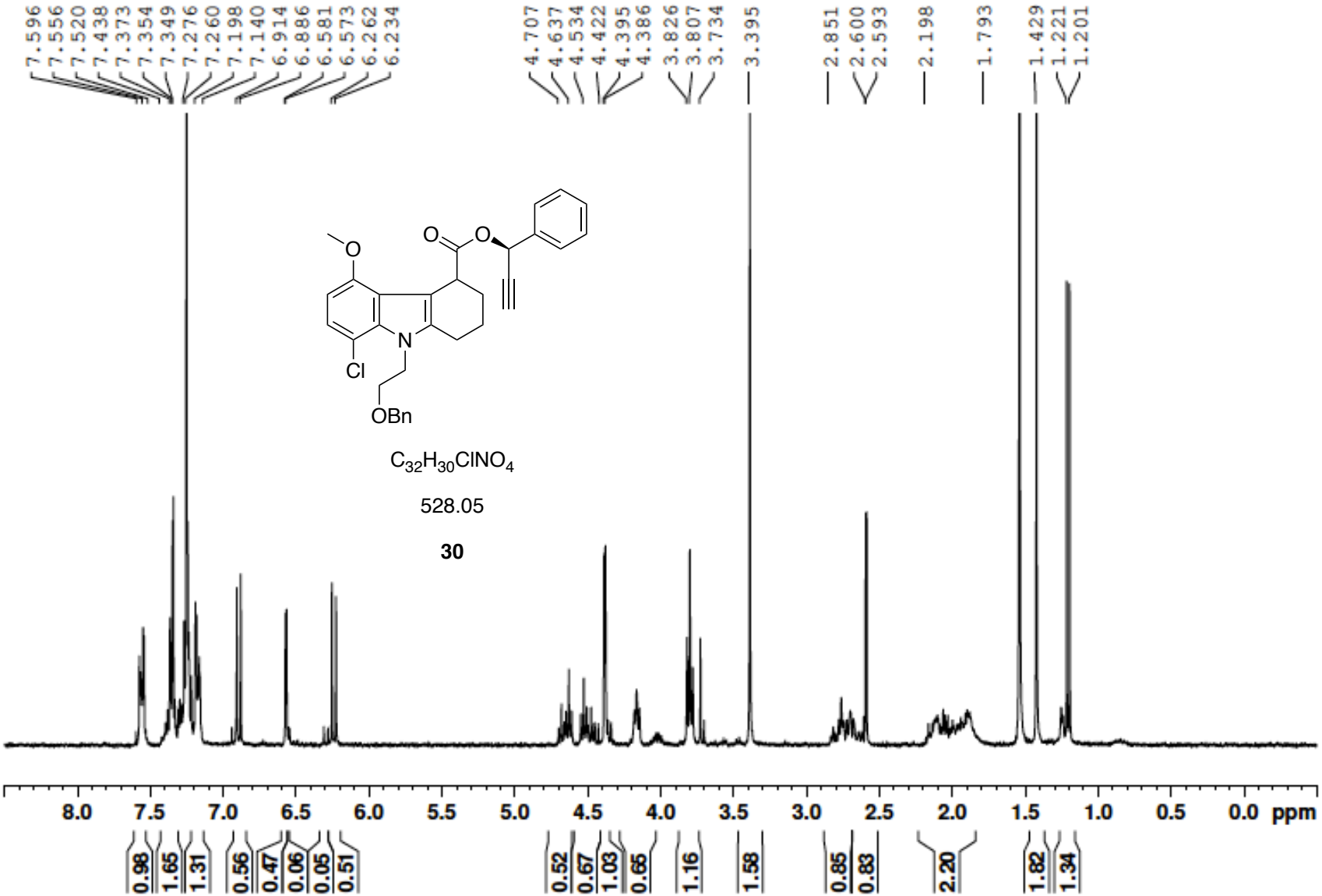

7.383
7.361
7.140
7.061
7.034
7.008
6.875
6.849
6.448
6.422
4.613
4.580
4.504
4.462
4.443
4.427
4.410
3.881
3.856
3.826
3.798
3.750
3.720
3.636
3.290
3.267
3.243
3.219
2.882
2.549
2.507
2.444
2.283
1.779
1.332
1.308
1.284
O
N
O
N
OMs
C26H32N2O5S
484.61
26
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
8.93
1.24
1.00
0.87
2.18
5.29
2.41
0.71
1.40
1.98
2.82
2.45
1.97
2.62


4.779
4.758
4.738
4.717
2.996
1.795
1.773
1.748
1.723
1.716
1.697
1.691
1.673
1.648
1.625
1.424
1.403
1.008
0.984
0.959
OMs
C5H12O3S
152.21
27
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
3.06
2.11
3.16
3.12


7.355
7.230
7.122
6.958
6.930
6.326
6.298
6.251
6.224
4.947
4.856
4.440
4.387
4.366
4.321
4.207
4.093
4.008
3.848
3.774
3.745
3.712
3.632
3.552
3.461
2.602
2.454
2.152
2.004
1.805
1.554
1.389
1.207
1.019
0.831
Me
Me
O
O
O
Me
N
Cl
OBn
C33H42ClNO4
552.15
29
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
3.44
2.02
1.10
1.00
0.12
0.99
0.18
2.27
2.21
1.20
3.01
1.22
0.77
1.14
1.07
2.41
2.92
16.44
1.73
1.09


8.037
7.795
7.641
7.632
7.613
7.604
6.997
6.969
6.923
6.895
5.654
5.499
5.439
5.331
5.137
5.096
5.082
5.058
5.037
4.996
4.875
4.794
4.680
4.566
4.416
4.385
4.304
4.271
4.137
4.123
4.102
4.088
4.068
4.054
3.391
3.136
2.981
2.820
2.719
2.511
2.243
2.141
1.873
1.766
1.679
1.649
1.631
1.625
1.609
1.530
1.506
Me
Me
O
O
O
Me
N
Cl
OBn
C33H42ClNO4
552.15
29
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
7.26
1.40
0.42
1.00
0.47
1.10
3.85
1.79
2.39
2.83
3.64
2.63
4.21
7.49
14.76
11.23
4.48
3.18
27.07
1.99
12.17


7.559
7.433
7.413
7.401
7.374
7.356
7.350
7.317
7.307
7.295
7.278
7.247
7.239
7.232
7.220
7.190
7.182
7.159
6.950
6.922
6.916
6.889
6.584
6.576
6.561
6.554
6.318
6.290
6.264
6.236
4.695
4.645
4.531
4.511
4.481
4.422
4.396
4.383
4.371
4.196
3.831
3.812
3.792
3.494
3.470
3.397
2.733
2.651
2.615
2.608
2.601
2.594
2.274
1.975
1.259
1.234
1.211
1.188
O
O
O
N
Cl
OBn
$C_{32}H_{30}ClNO_4$
528.05
30
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
3.23
3.74
7.01
1.77
0.49
1.04
1.07
0.51
1.57
1.57
3.19
1.60
3.15
3.24
1.49
3.10
1.56
6.04
2.44


7.596
7.556
7.520
7.438
7.373
7.354
7.349
7.276
7.260
7.198
7.140
6.914
6.886
6.581
6.573
6.262
6.234
4.707
4.637
4.534
4.422
4.395
4.386
3.826
3.807
3.734
3.395
2.851
2.600
2.593
2.198
1.793
1.429
1.221
1.201
O
O
O
N
Cl
OBn
$C_{32}H_{30}ClNO_4$
528.05
30
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
0.98
1.65
1.31
0.56
0.47
0.06
0.05
0.51
0.52
0.67
1.03
0.65
1.16
1.58
0.85
0.83
2.20
1.82
1.34

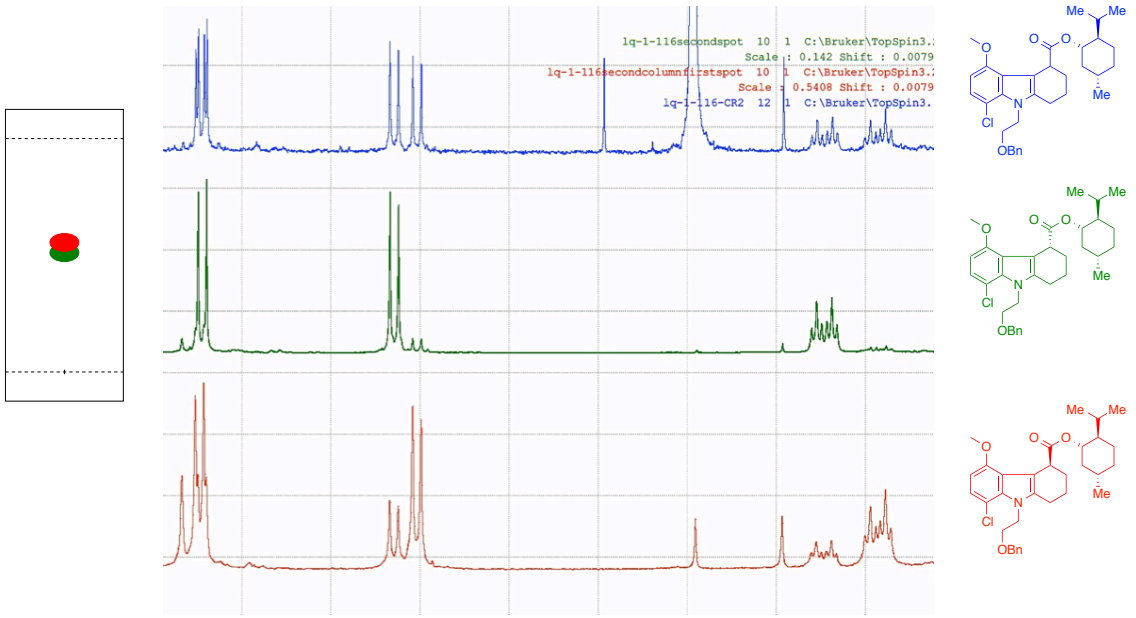
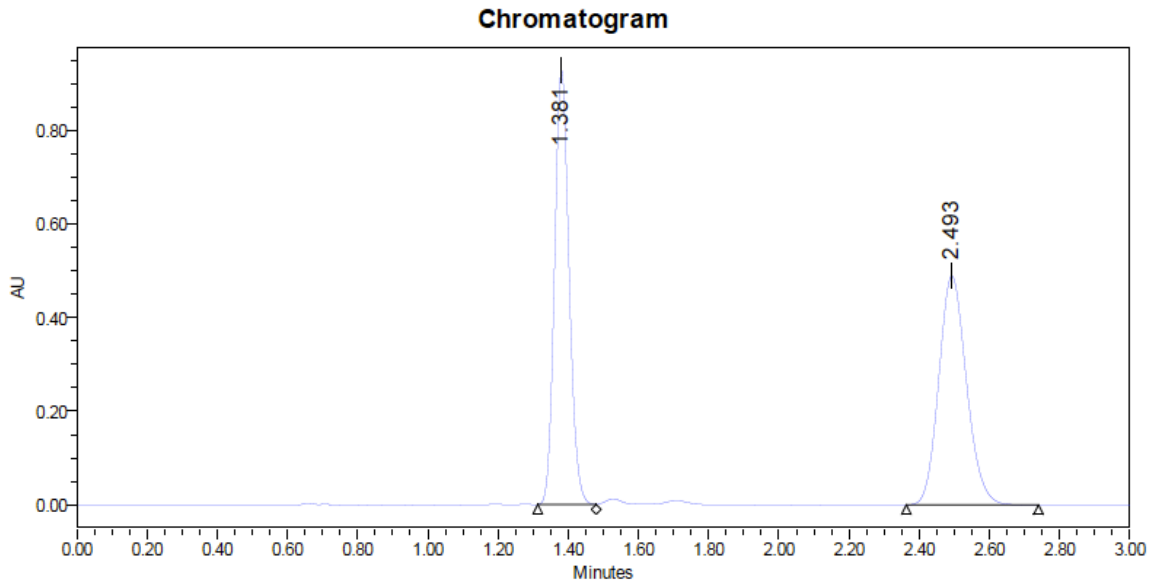


Figure S2: TLC and ^{1}H NMR evidence of the diastereomeric mixture of ester **29** (absolute stereochemistry of the diastereomers was not determined).

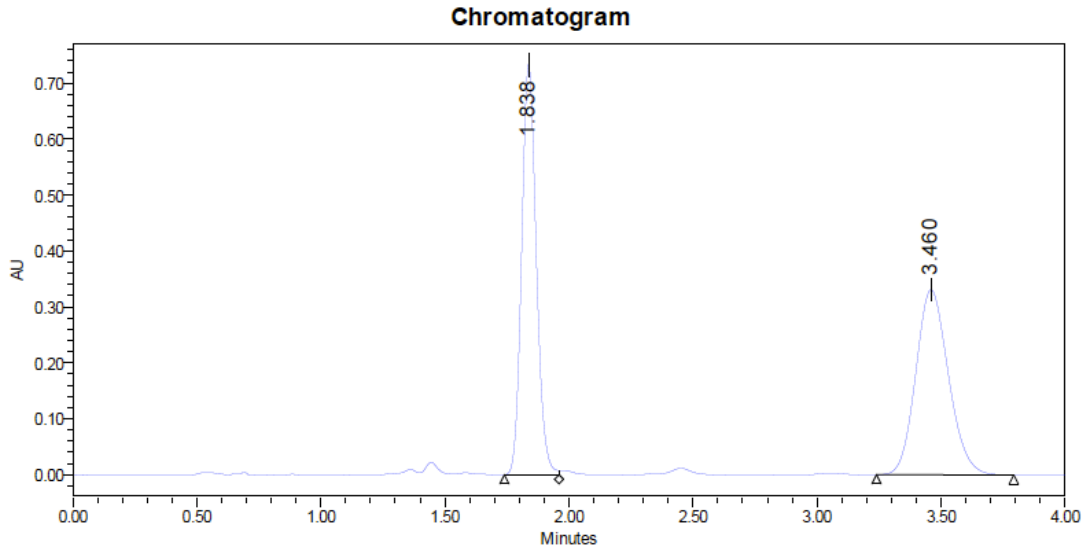
Chiral separation by SFC – Chromatogram of **6** (GE387)



Peak Results

	Retention Time (min)	Area (µV*sec)	% Area
1	1.38	2668428	49.9
2	2.49	2682310	50.1

Chiral separation by SFC – Chromatogram of **25** (GE387 radiolabelling precursor)

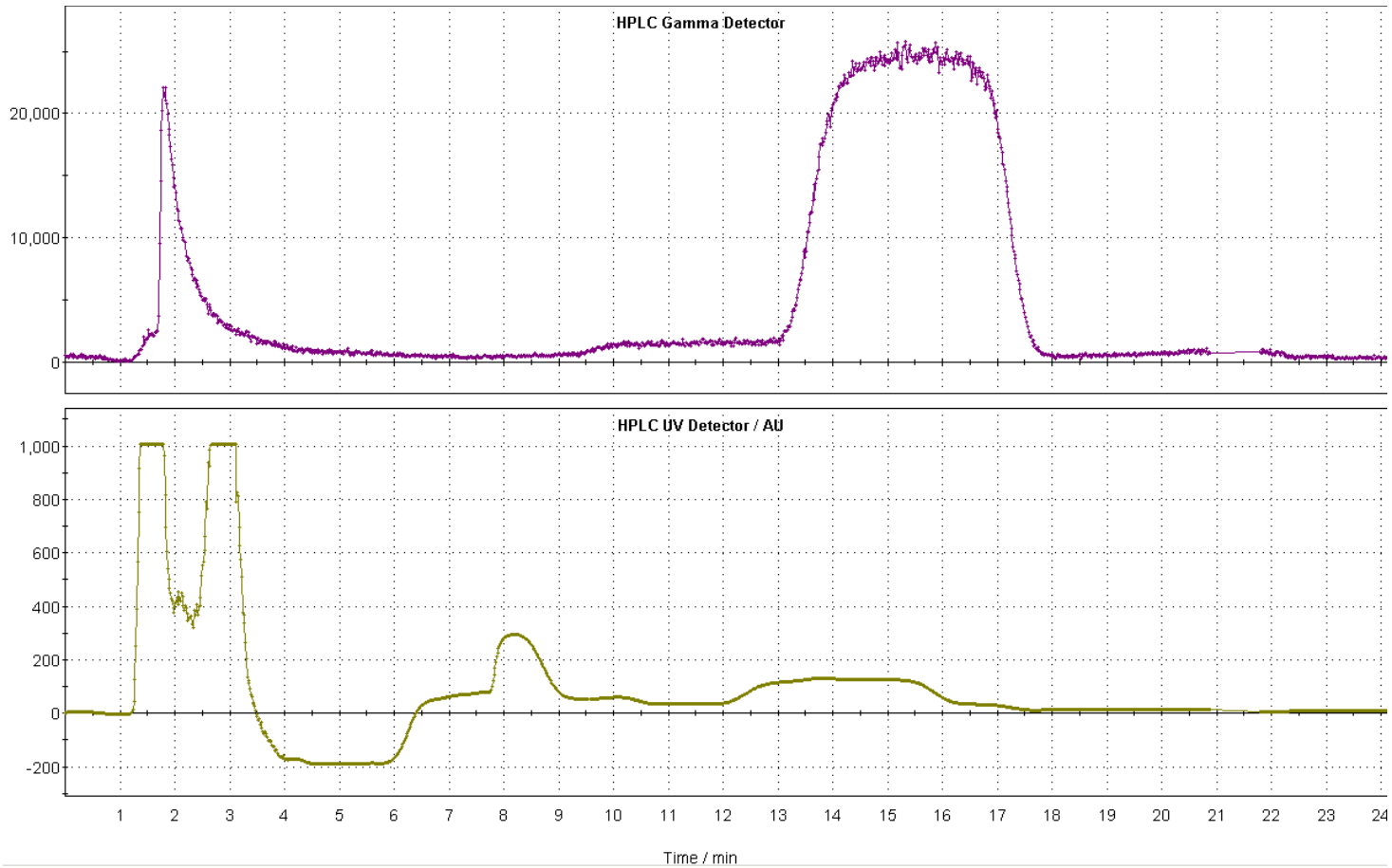


Peak Results

	Retention Time (min)	Area (µV*sec)	% Area
1	1.84	3009365	49.8
2	3.46	3030606	50.2

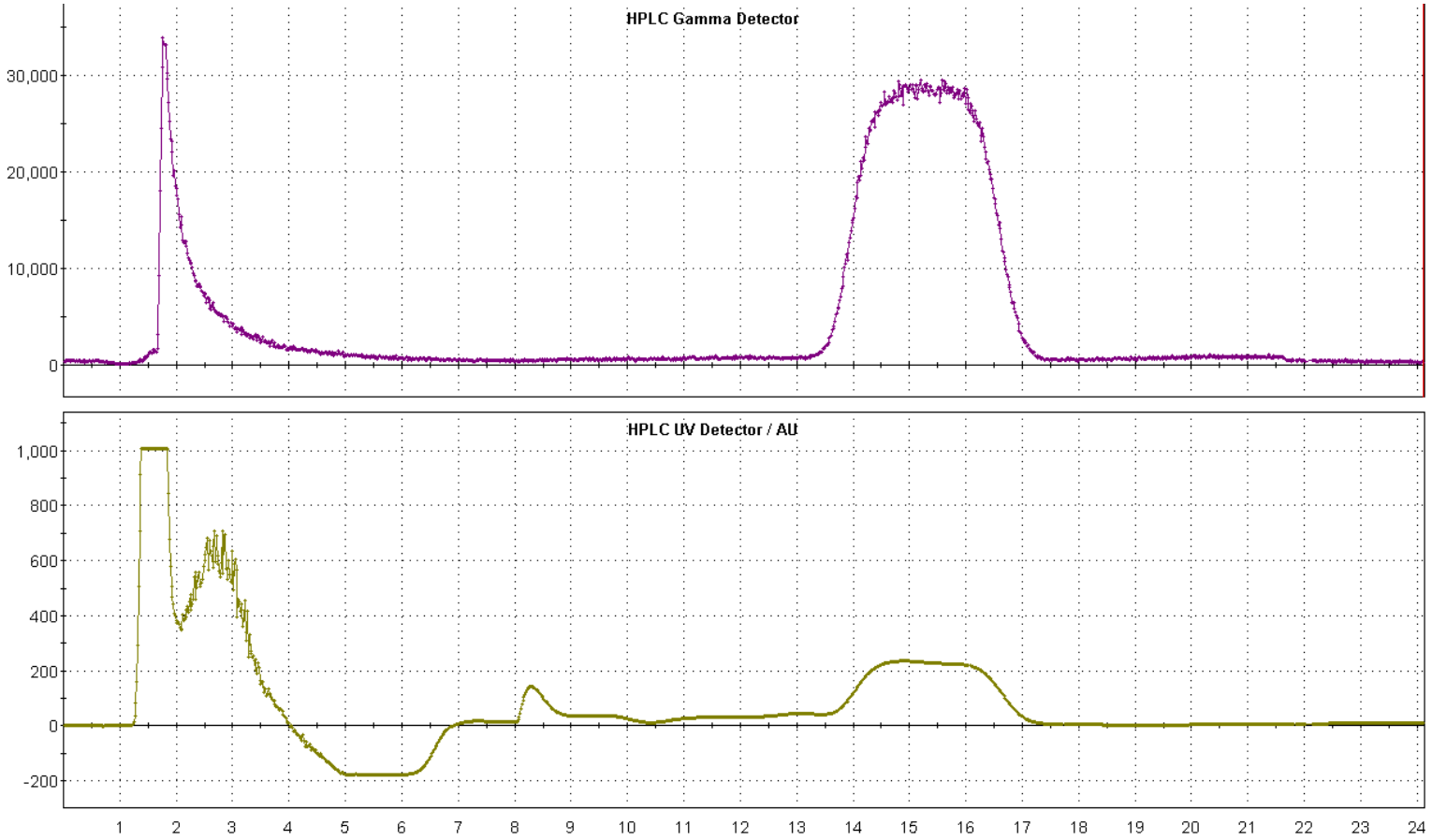
Gamma and UV chromatograms respectively of semi-preparative purification of a) (*S*)-[^{18}F]**6** and b) (*R*)-[^{18}F]**6**

a)



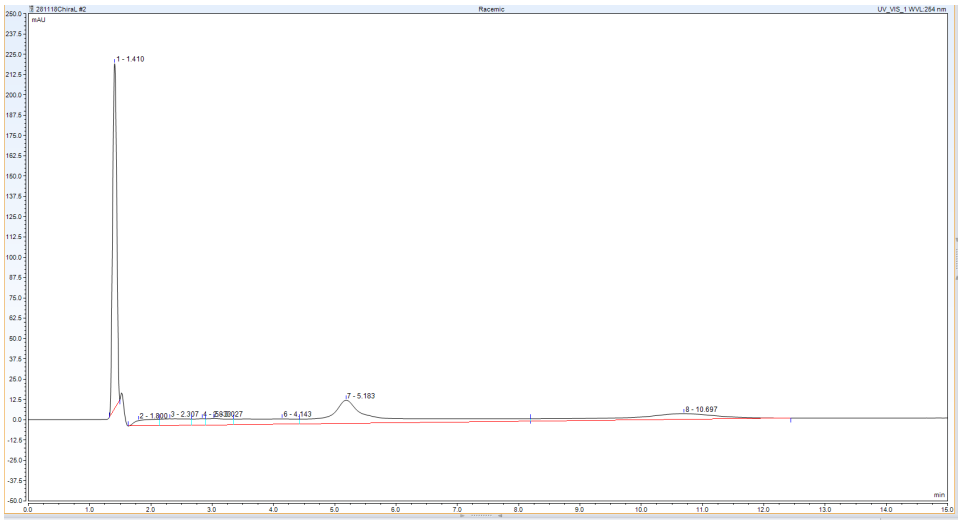
Gamma and UV chromatograms respectively of semi-preparative purification of a) (*S*)-[^{18}F]**6** and b) (*R*)-[^{18}F]**6**

b)



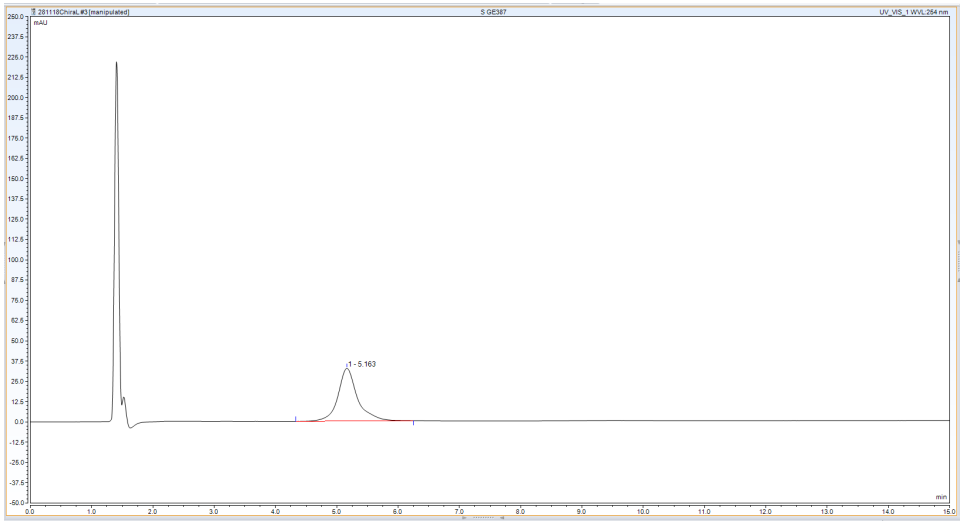
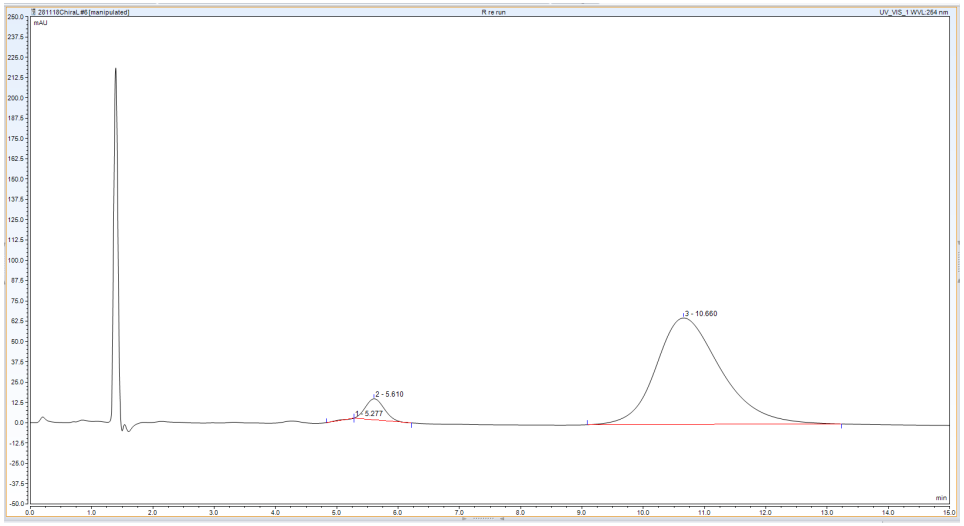
Chiral HPLC separation of a) (*S*, *R*)-**6**; b) (*S*)-**6** and c) (*R*)-**6** using Whelk-O1 (*S*, *S*) Kromasil 5 μm, 2.1x150 mm column, eluting with 40% MeOH in ^{i}PrOH at 0.3 mL/min.

a)



Chiral HPLC separation of a) (*S*, *R*)-**6**; b) (*S*)-**6** and c) (*R*)-**6** using Whelk-O1 (*S*, *S*) Kromasil 5 μm, 2.1x150 mm column, eluting with 40% MeOH in ^{i}PrOH at 0.3 mL/min.

b)



c)