Supporting Information

Dispirooxindole-β-lactams: Synthesis via Staudinger ketene-imine cycloaddition and biological evaluation

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Spectral data

*1-(4-methoxyphenyl)-2-oxopyrrolidine-3-carboxylic acid (**3a**).*

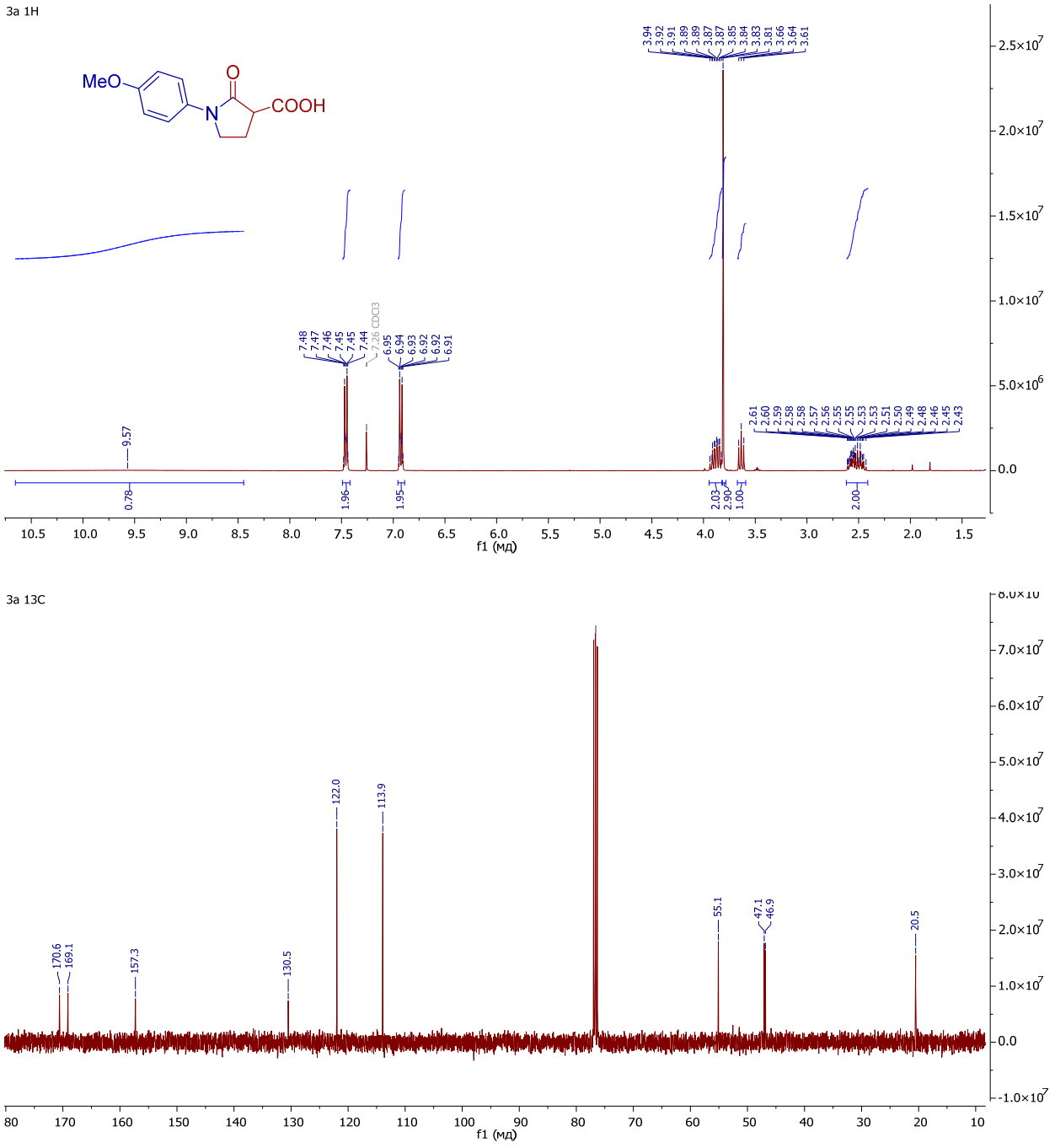


Figure S1

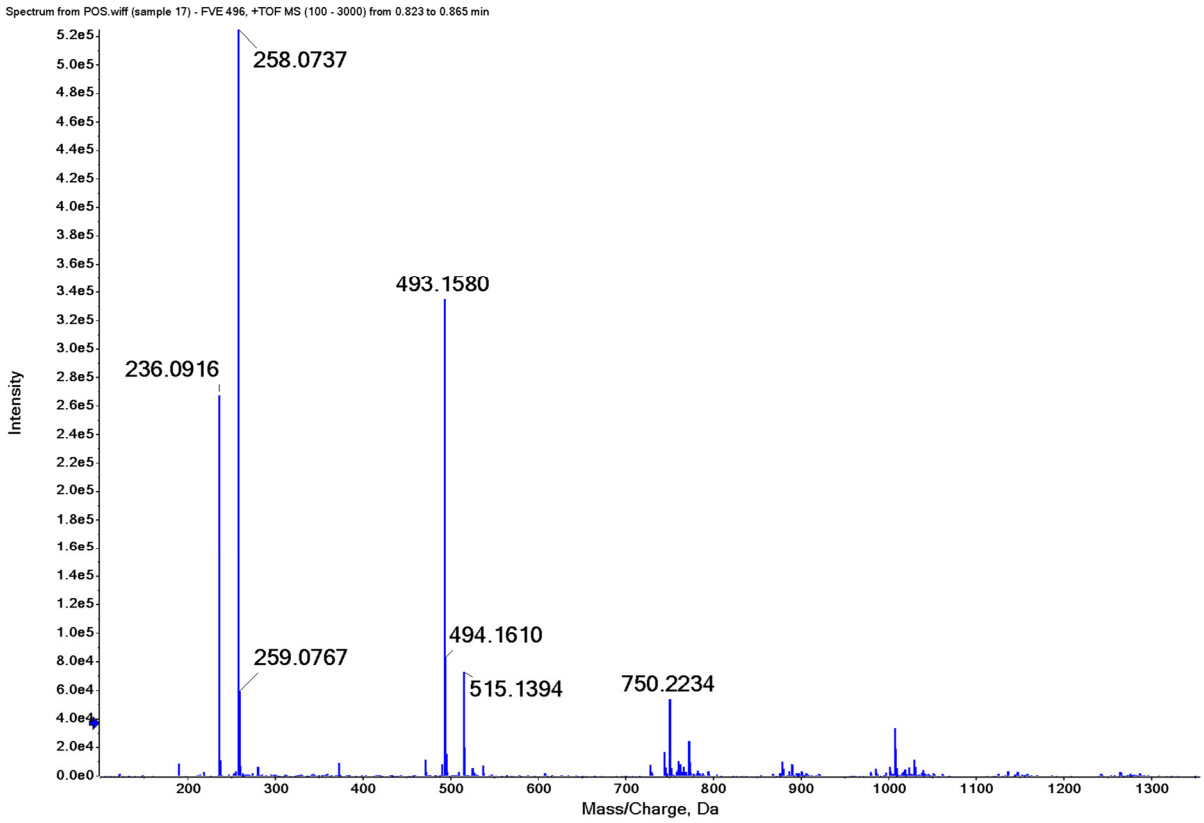

Spectrum from POS.wiff (sample 17) - FVE 496, +TOF MS (100 - 3000) from 0.823 to 0.865 min
Intensity
Mass/Charge, Da
258.0737
493.1580
236.0916
494.1610
259.0767
515.1394
750.2234

Figure S2

*2-oxo-1-(p-tolyl)pyrrolidine-3-carboxylic acid (**3b**)*

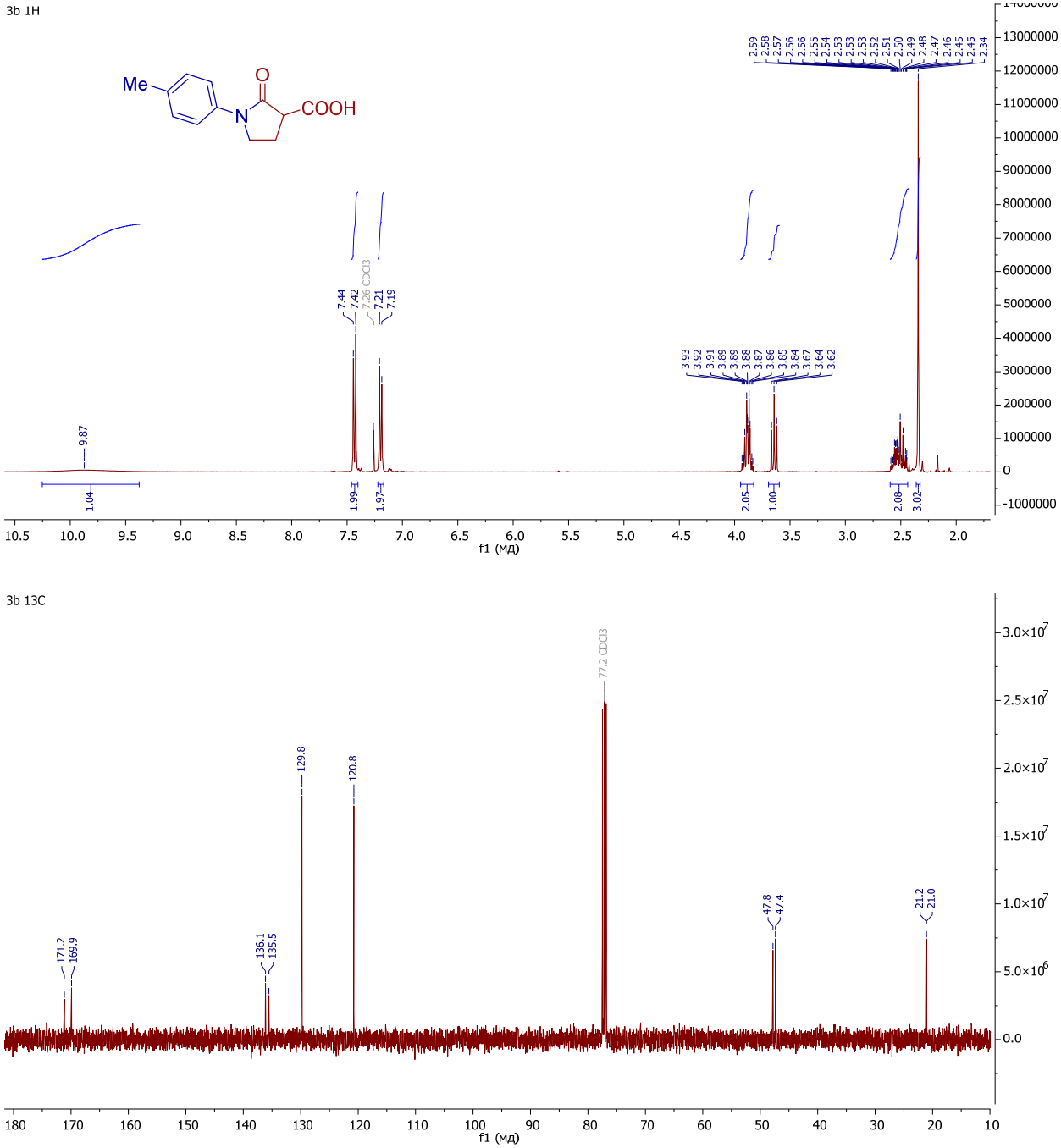


Figure S3

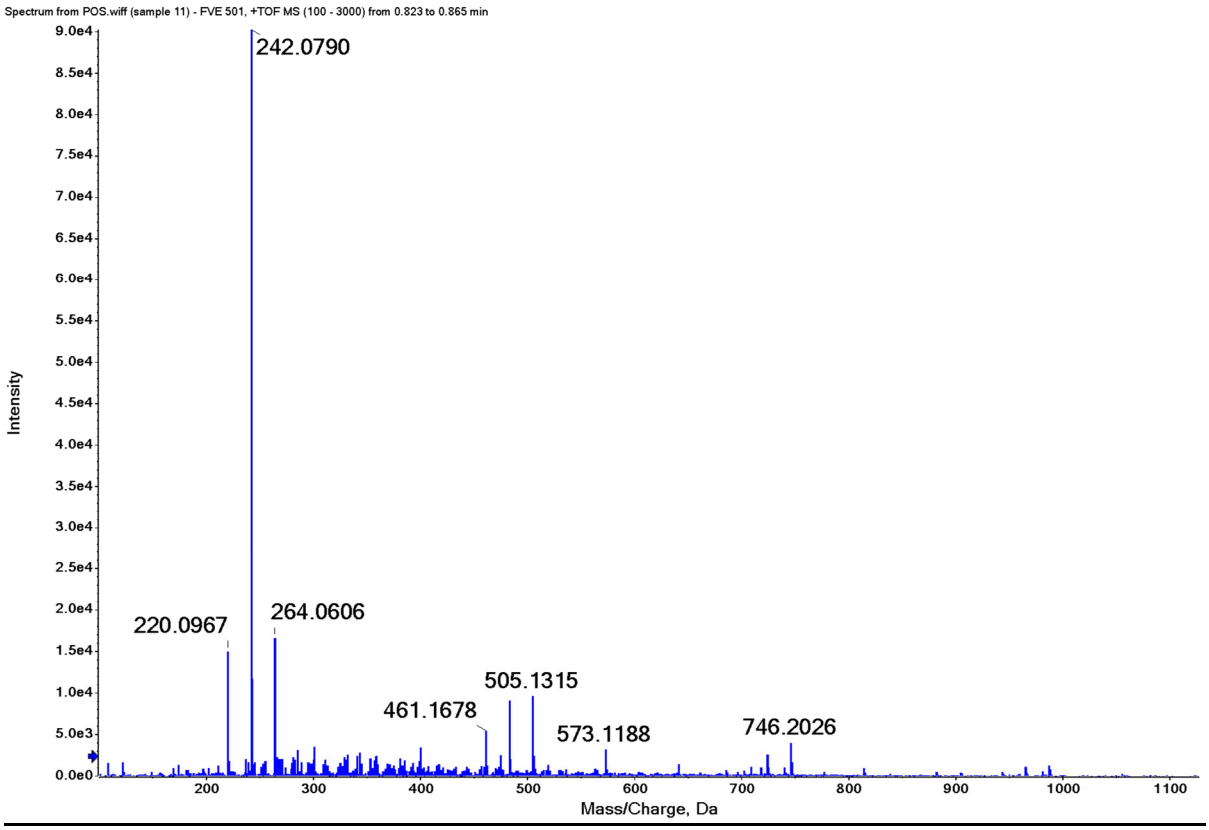

Spectrum from POS.wiff (sample 11) - FVE 501, +TOF MS (100 - 3000) from 0.823 to 0.865 min
Intensity
Mass/Charge, Da
242.0790
220.0967
264.0606
505.1315
461.1678
573.1188
746.2026

Figure S4

*2-oxo-1-(m-tolyl)pyrrolidine-3-carboxylic acid (**3c**)*

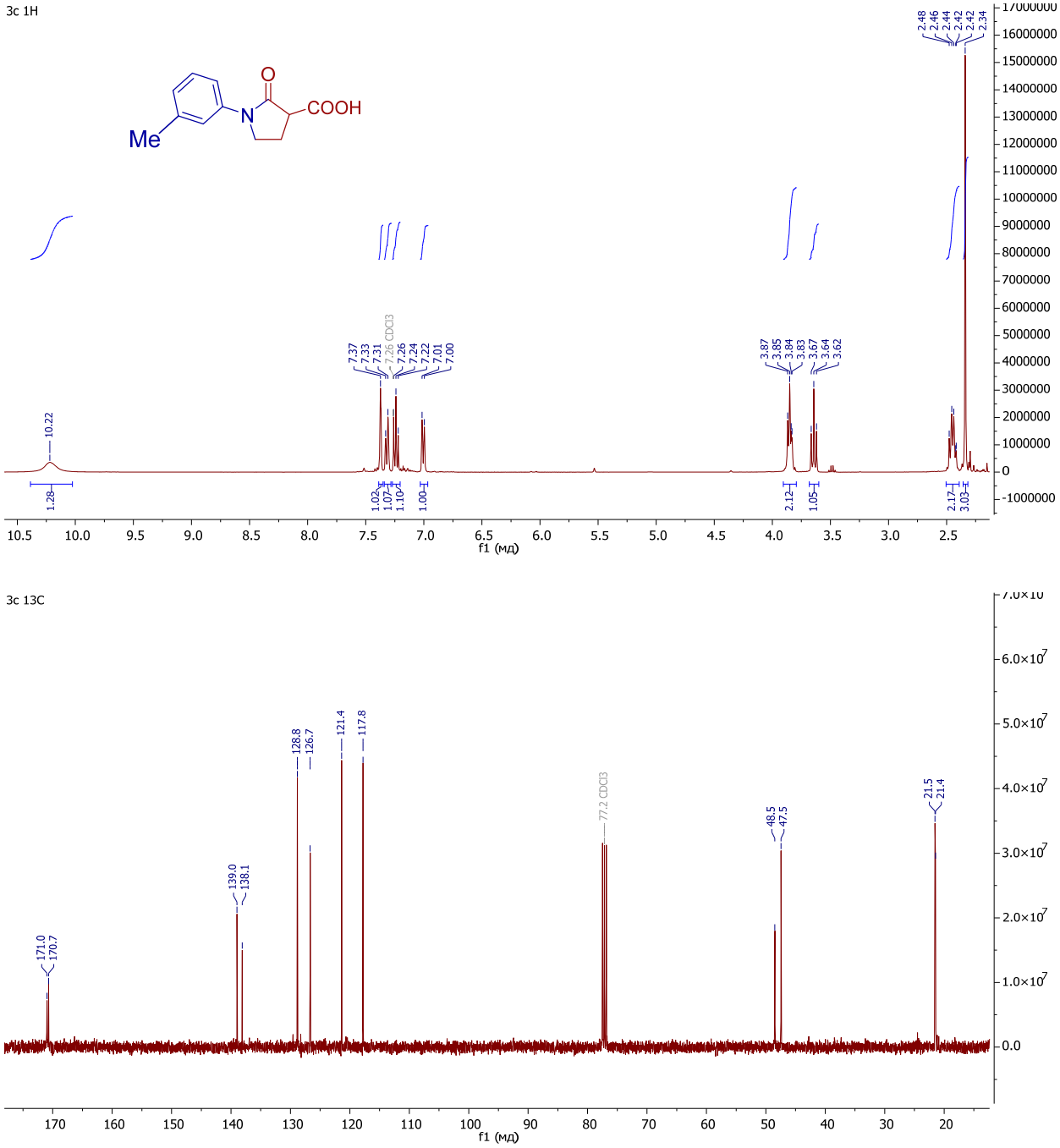


Figure S5

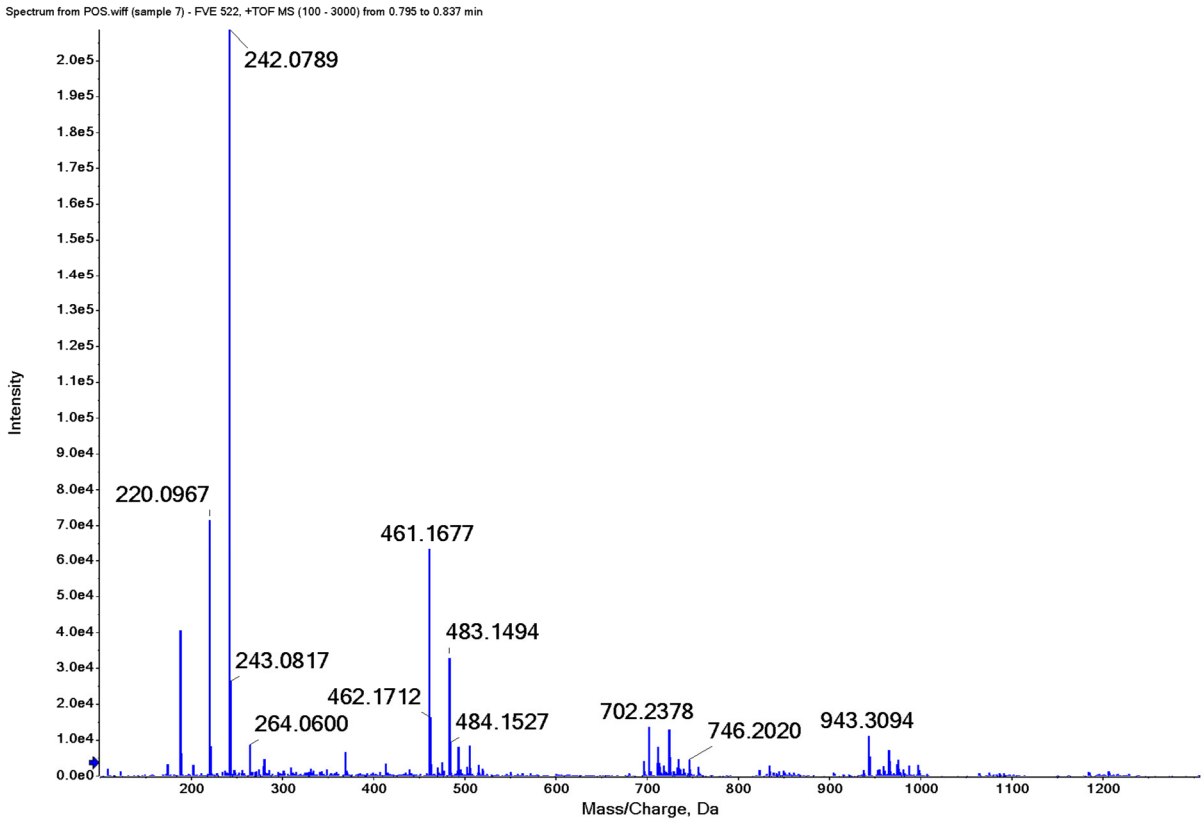

Spectrum from POS.wiff (sample 7) - FVE 522, +TOF MS (100 - 3000) from 0.795 to 0.837 min
Intensity
Mass/Charge, Da
242.0789
220.0967
461.1677
483.1494
243.0817
462.1712
264.0600
484.1527
702.2378
746.2020
943.3094

Figure S6

*1-(4-chlorophenyl)-2-oxopyrrolidine-3-carboxylic acid (**3d**)*

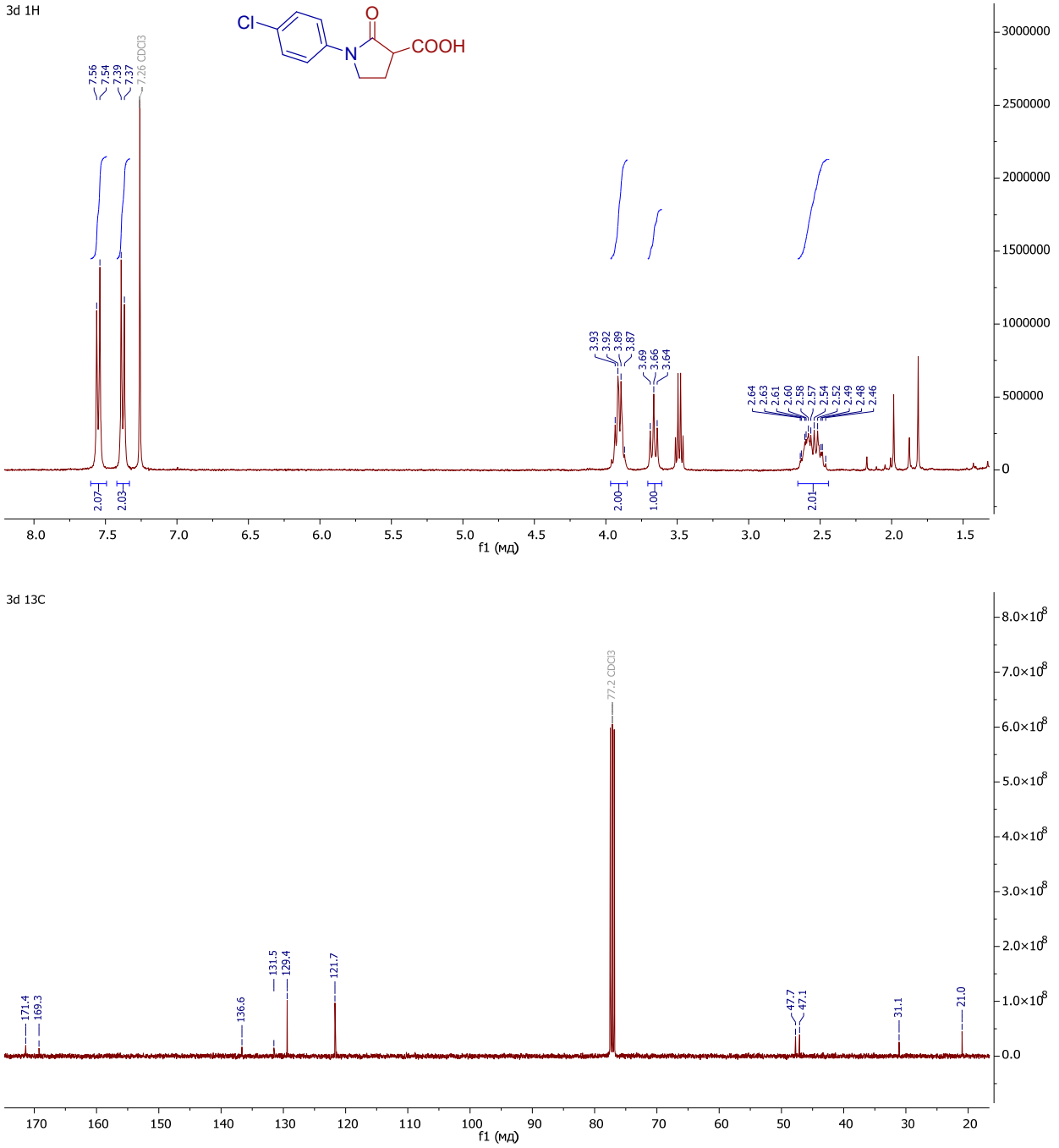


Figure S7

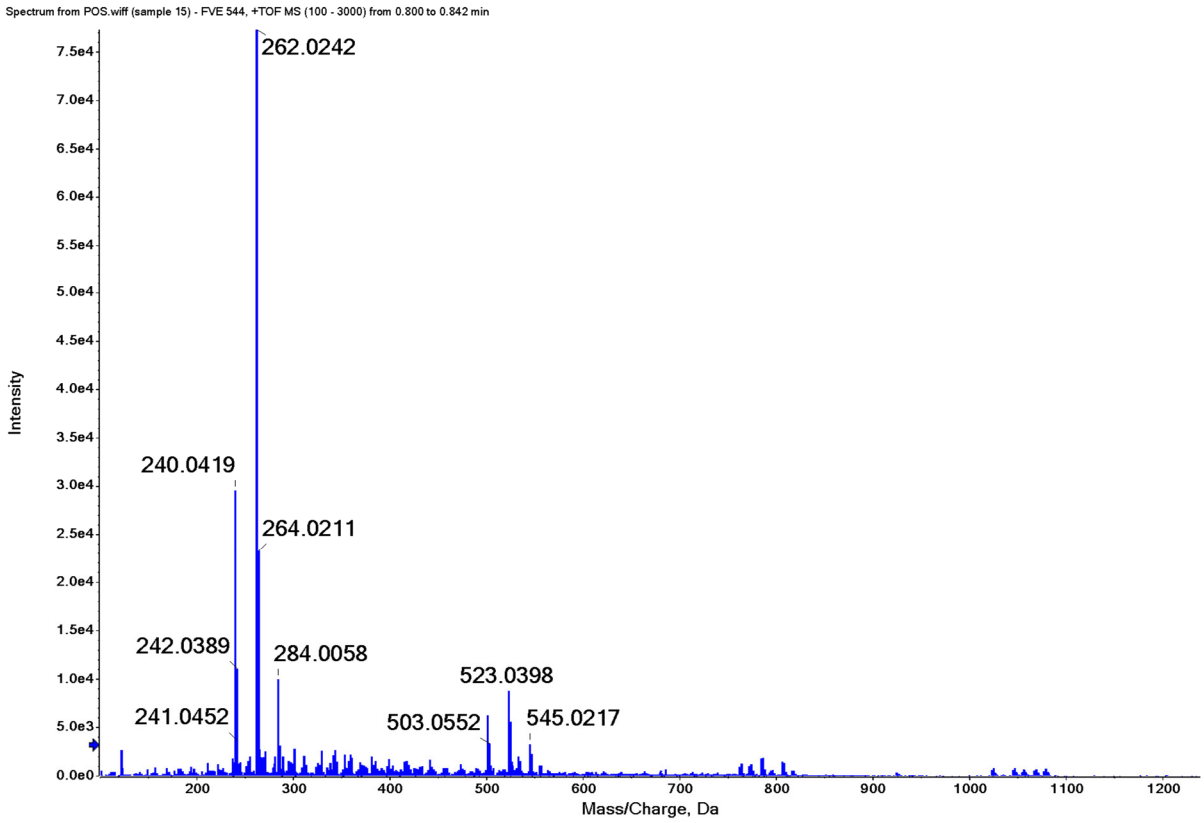

Spectrum from POS.wiff (sample 15) - FVE 544, +TOF MS (100 - 3000) from 0.800 to 0.842 min
Intensity
Mass/Charge, Da
262.0242
240.0419
264.0211
242.0389
284.0058
523.0398
241.0452
503.0552
545.0217

Figure S8

*1-(3-chloro-4-fluorophenyl)-2-oxopyrrolidine-3-carboxylic acid (**3e**)*

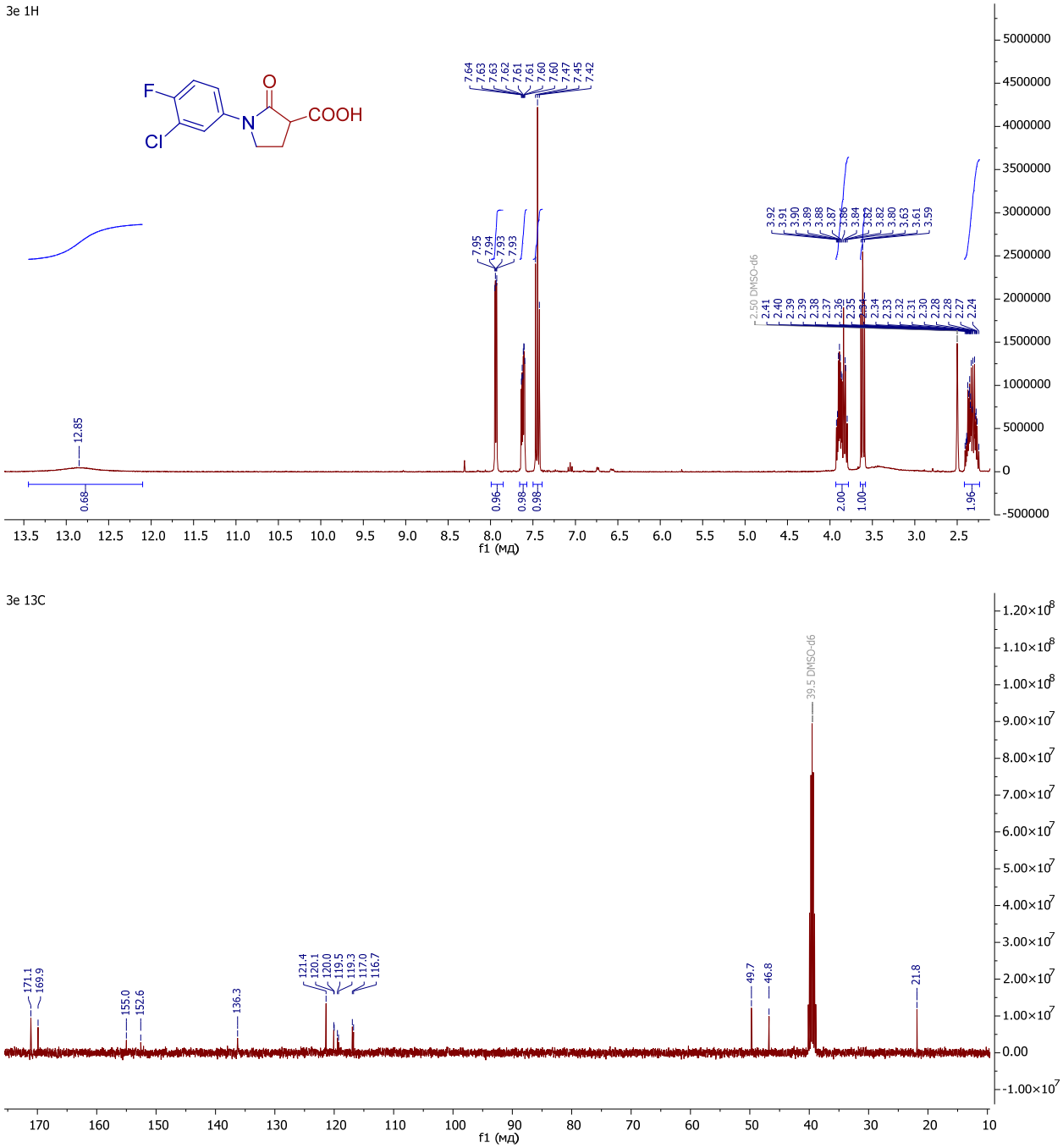


Figure S9

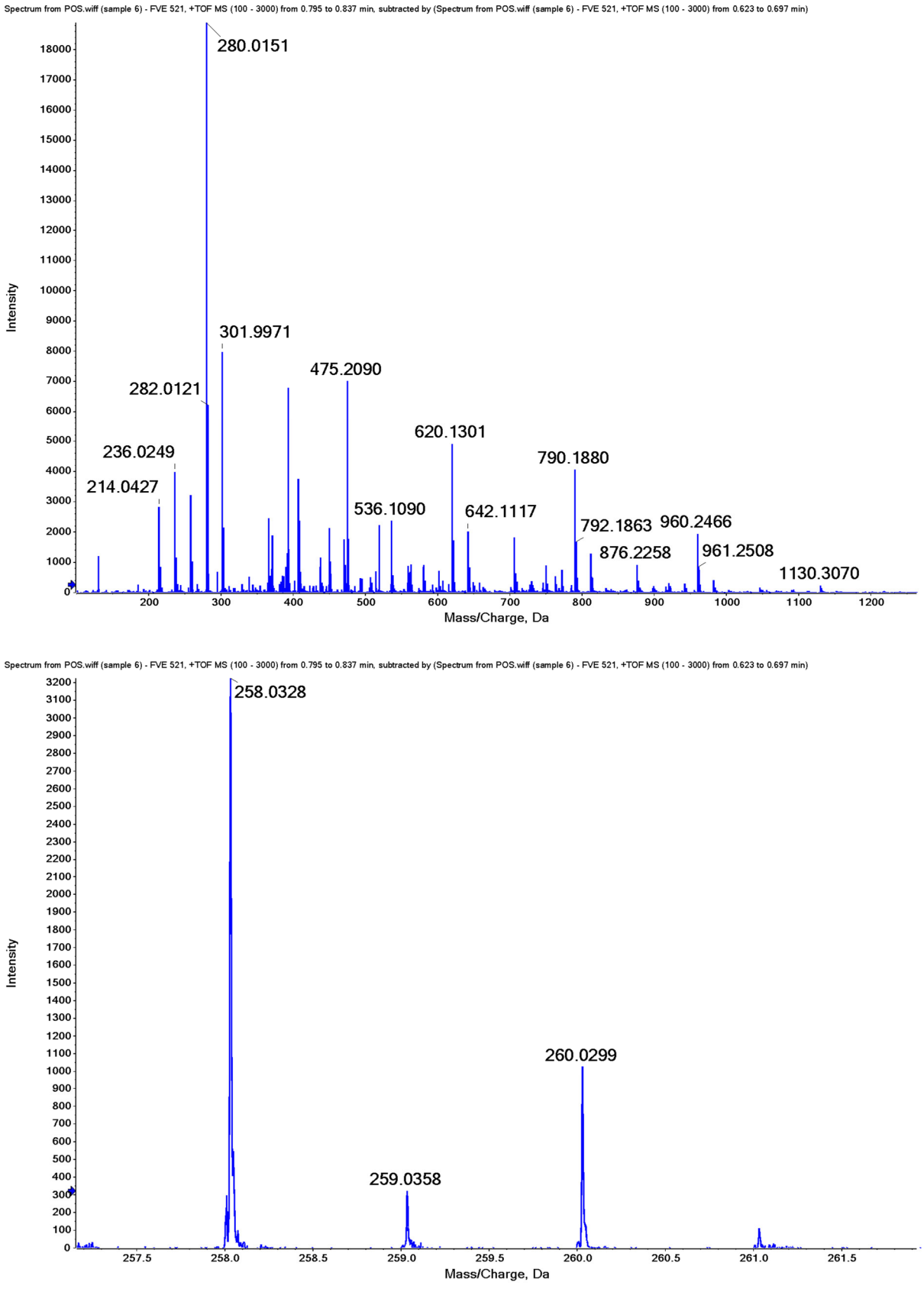

Spectrum from POS.wiff (sample 6) - FVE 521, +TOF MS (100 - 3000) from 0.795 to 0.837 min, subtracted by (Spectrum from POS.wiff (sample 6) - FVE 521, +TOF MS (100 - 3000) from 0.623 to 0.697 min)
Intensity
Mass/Charge, Da
280.0151
301.9971
475.2090
282.0121
620.1301
236.0249
790.1880
214.0427
536.1090
642.1117
792.1863
960.2466
876.2258
961.2508
1130.3070
Spectrum from POS.wiff (sample 6) - FVE 521, +TOF MS (100 - 3000) from 0.795 to 0.837 min, subtracted by (Spectrum from POS.wiff (sample 6) - FVE 521, +TOF MS (100 - 3000) from 0.623 to 0.697 min)
Intensity
Mass/Charge, Da
258.0328
260.0299
259.0358

Figure S10

(3S,3′S*)-1′,1′′-bis(4-methoxyphenyl)dispiro[indoline-3,2′-azetidine-3′,3′′-pyrrolidine]-2,2′′,4′-trione (**5a**)*

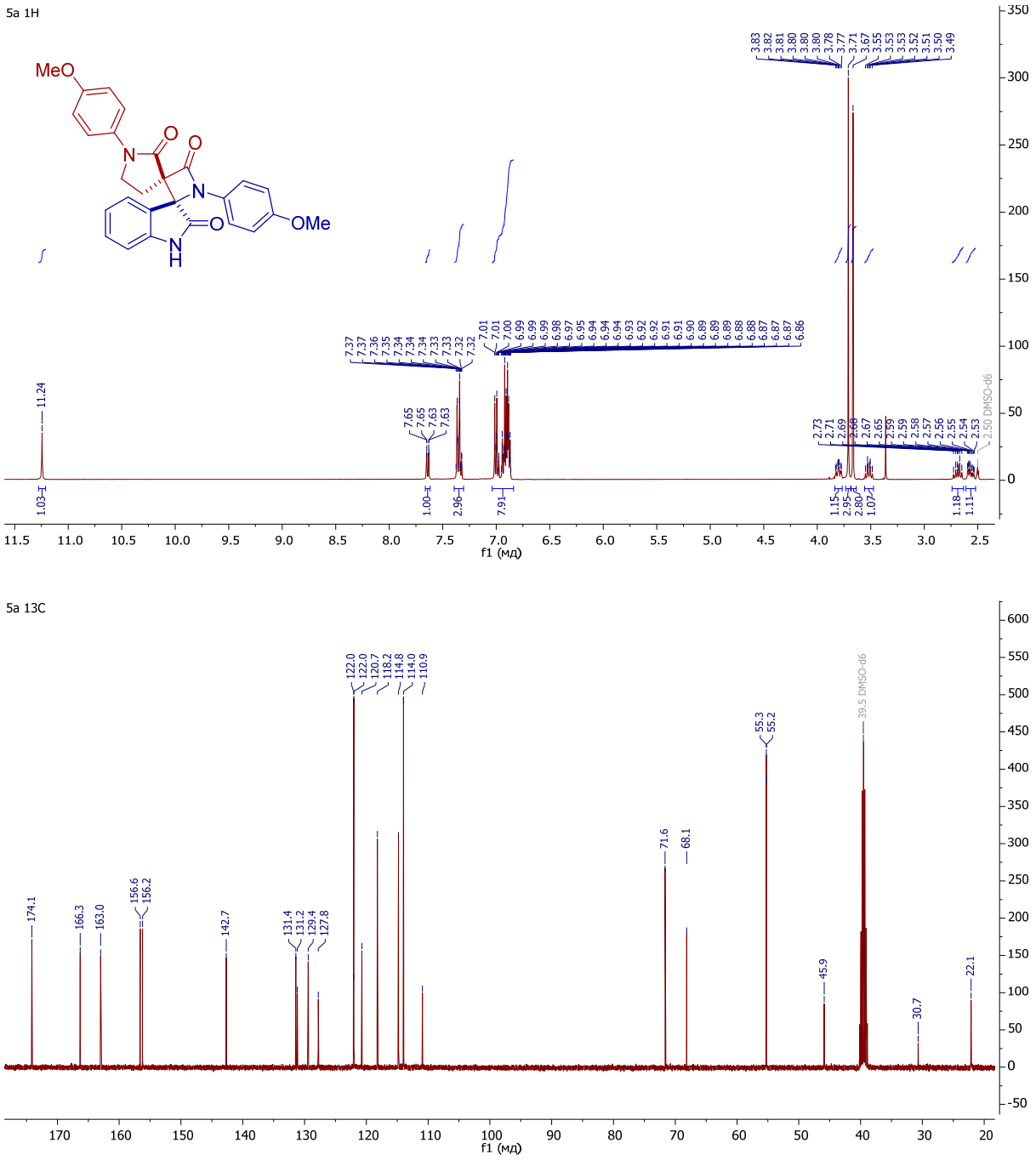
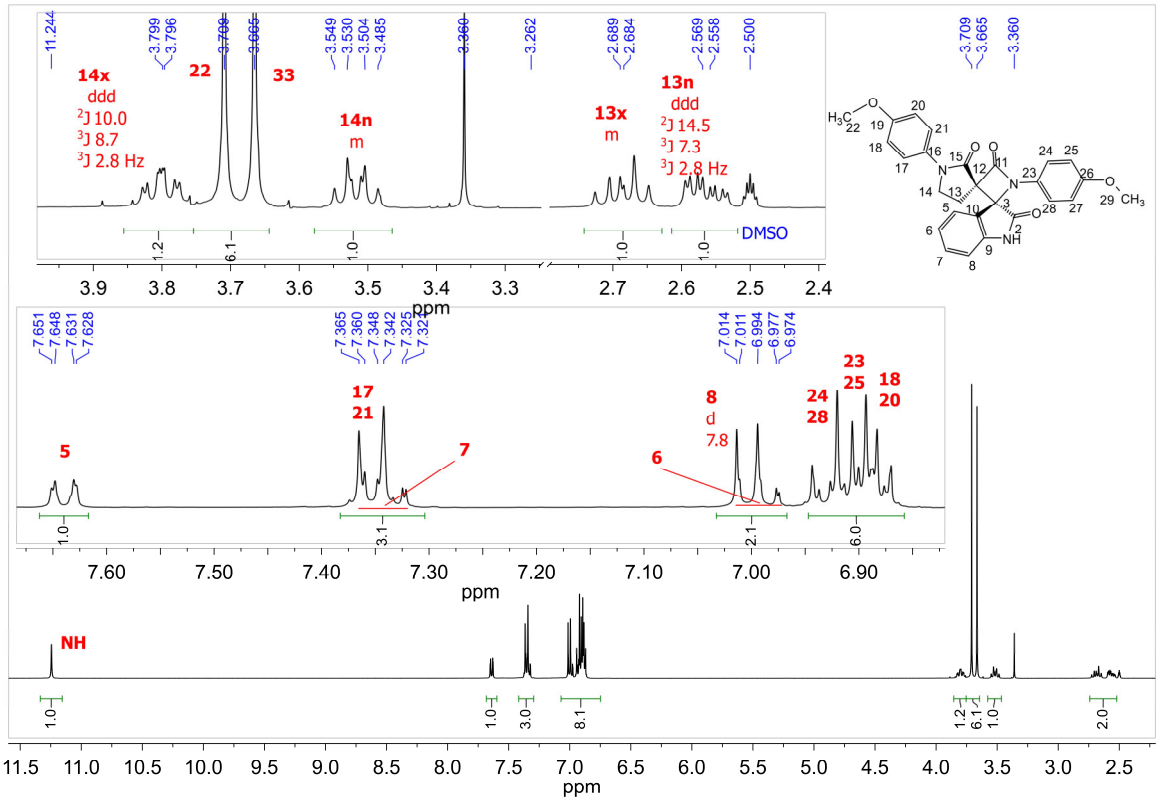


Figure S11


14x
ddd
2J 10.0
3J 8.7
3J 2.8 Hz
22
33
14n
m
13x
m
13n
ddd
2J 14.5
3J 7.3
3J 2.8 Hz
DMSO
ppm
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17
21
7
8
d
7.8
6
24
28
23
25
18
20
NH
ppm

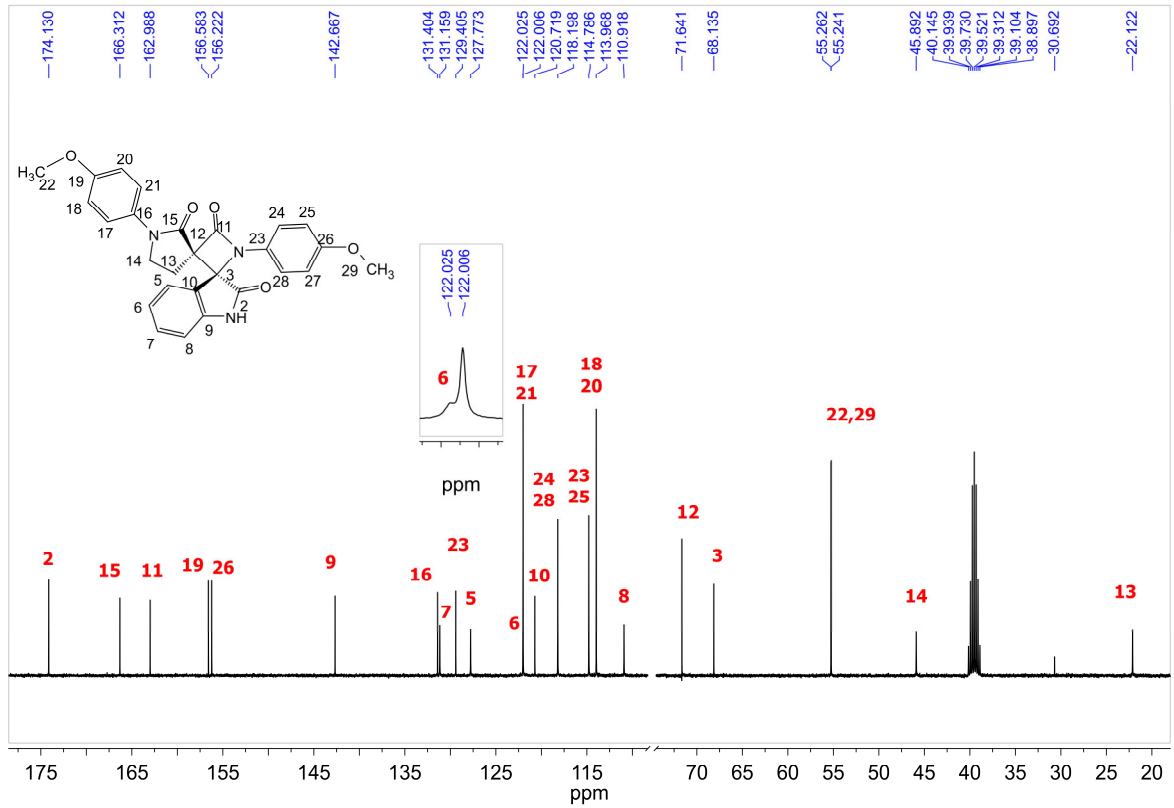

6
ppm
2
15
11
19
26
9
16
23
7
5
6
10
17
21
24
28
23
25
8
12
3
22,29
14
13
ppm

Figure S12

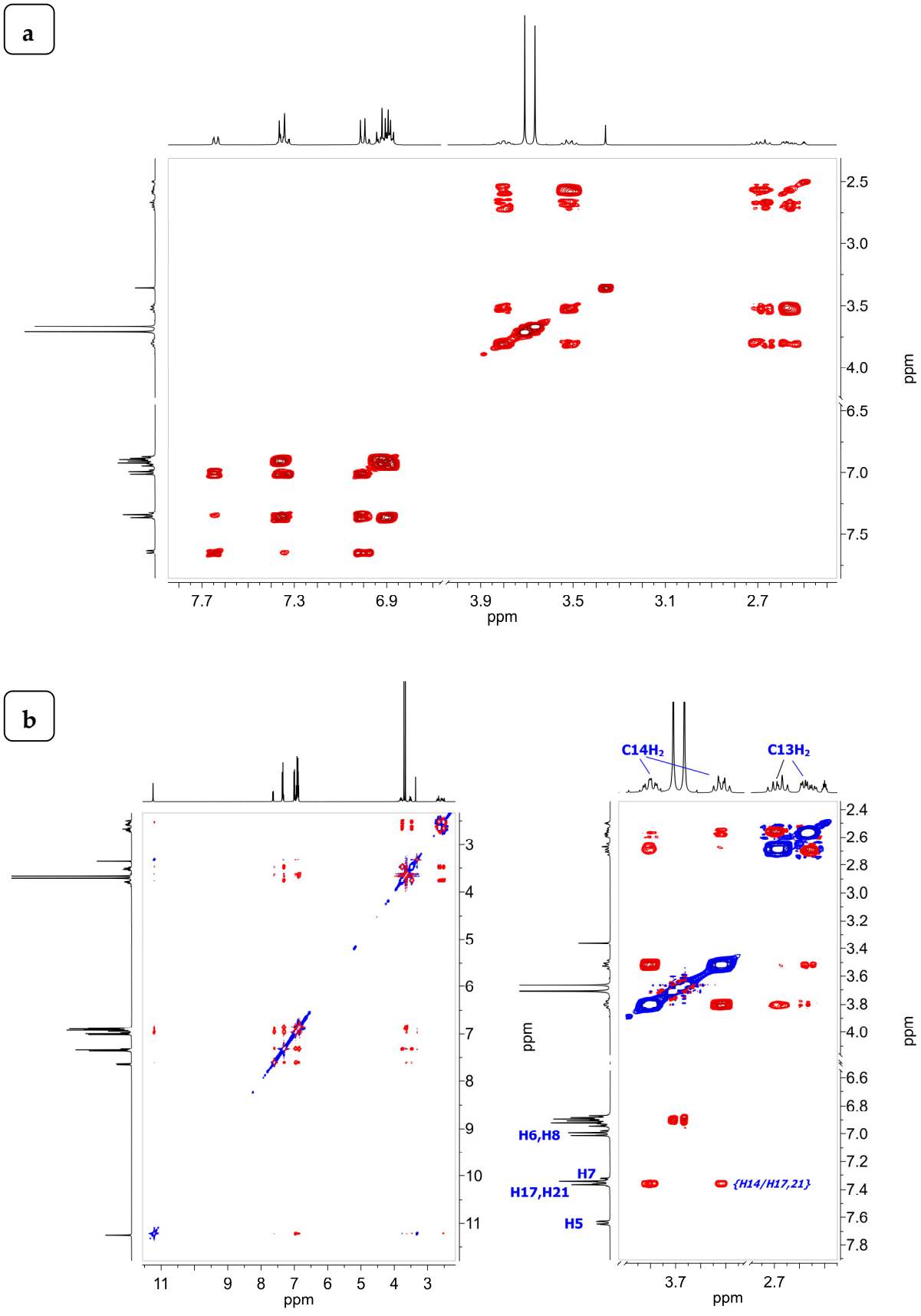


Figure S13: (a) gCOSY; (b)ROESYAD)

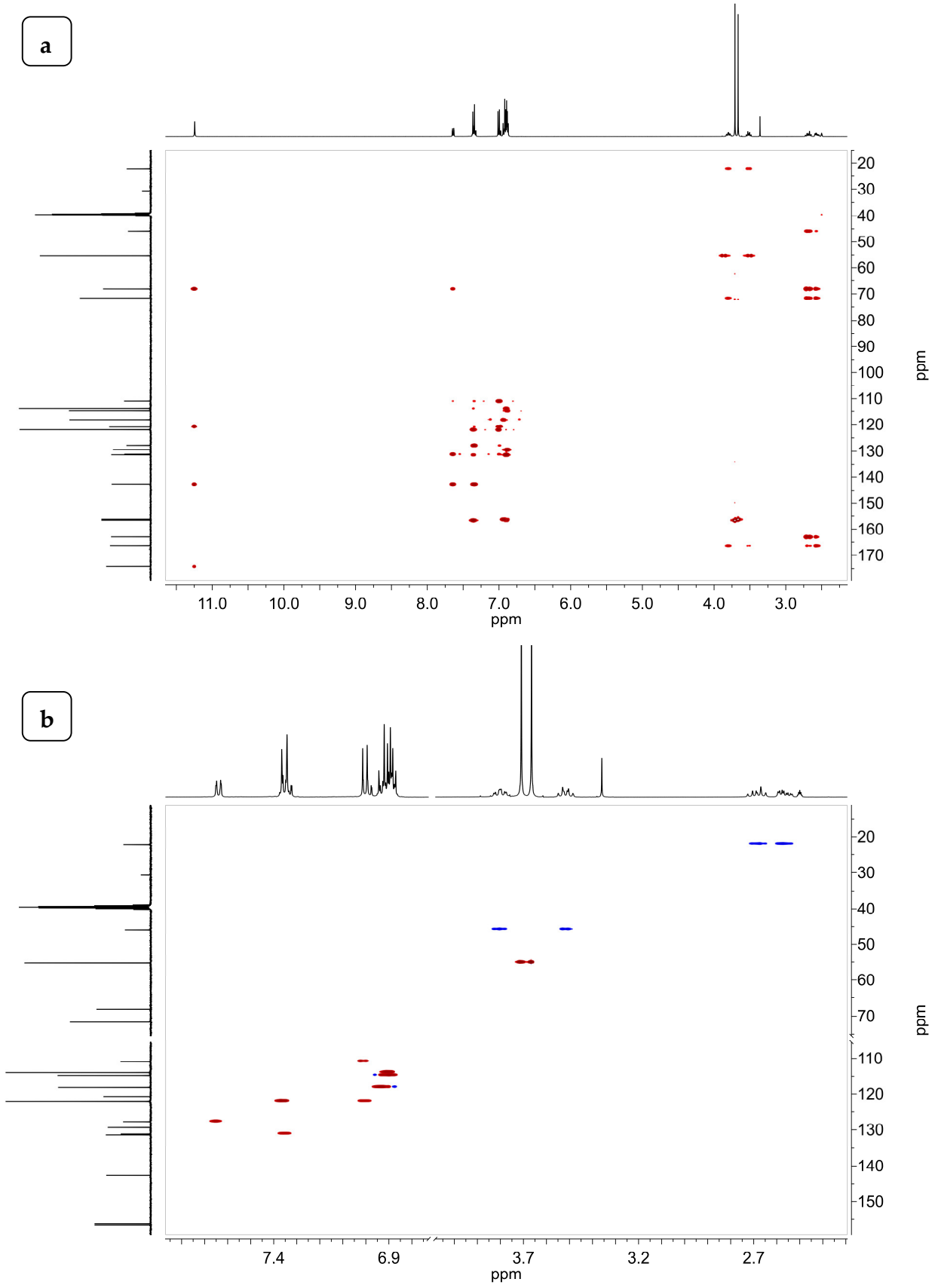


Figure S14: (a) gHSQCAD; (b)gHMBCAD

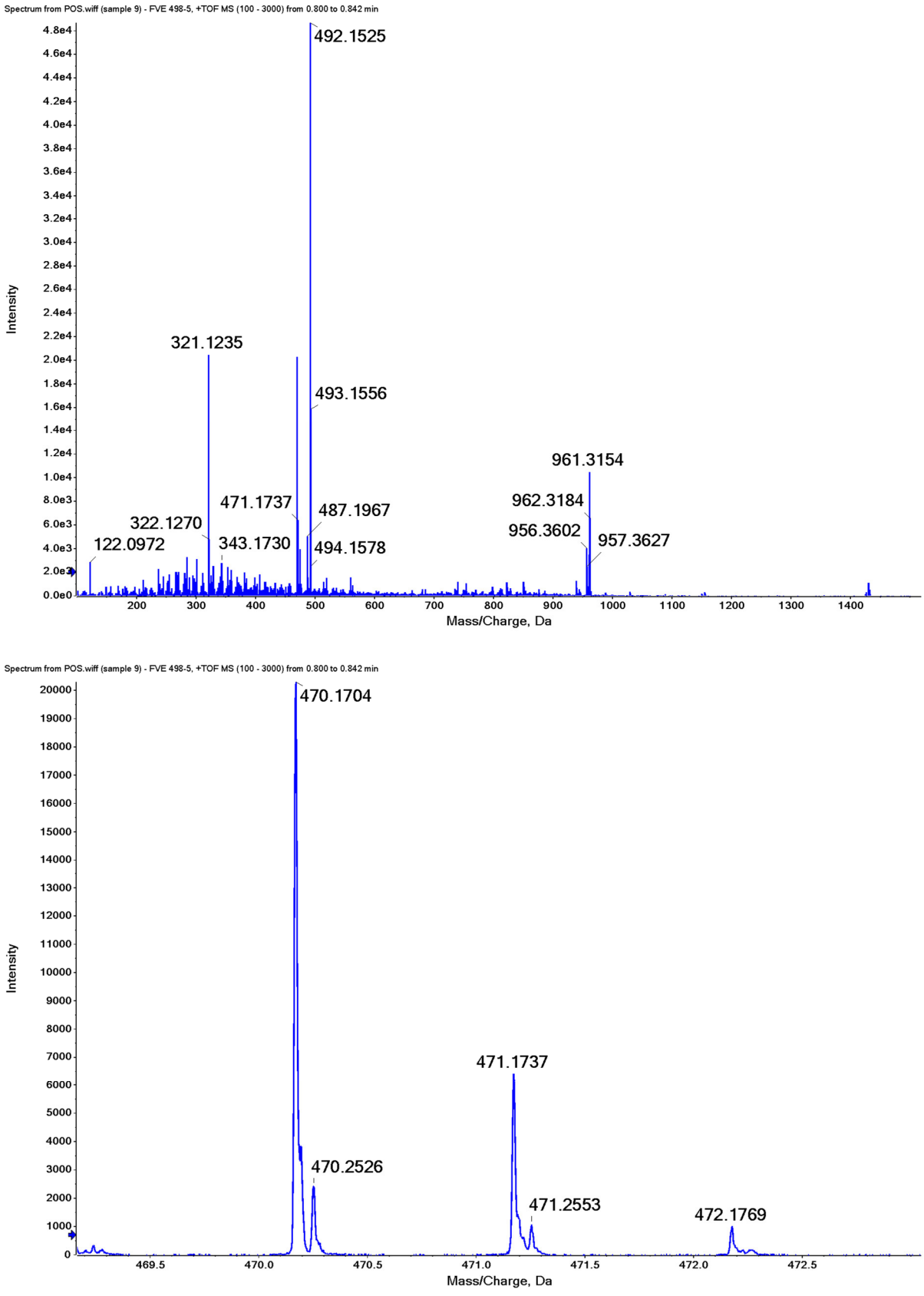

Spectrum from POS.wiff (sample 9) - FVE 498-5, +TOF MS (100 - 3000) from 0.800 to 0.842 min
Intensity
Mass/Charge, Da
492.1525
321.1235
493.1556
961.3154
471.1737
487.1967
962.3184
322.1270
956.3602
957.3627
122.0972
343.1730
494.1578
Spectrum from POS.wiff (sample 9) - FVE 498-5, +TOF MS (100 - 3000) from 0.800 to 0.842 min
Intensity
Mass/Charge, Da
470.1704
471.1737
470.2526
471.2553
472.1769

Figure S15

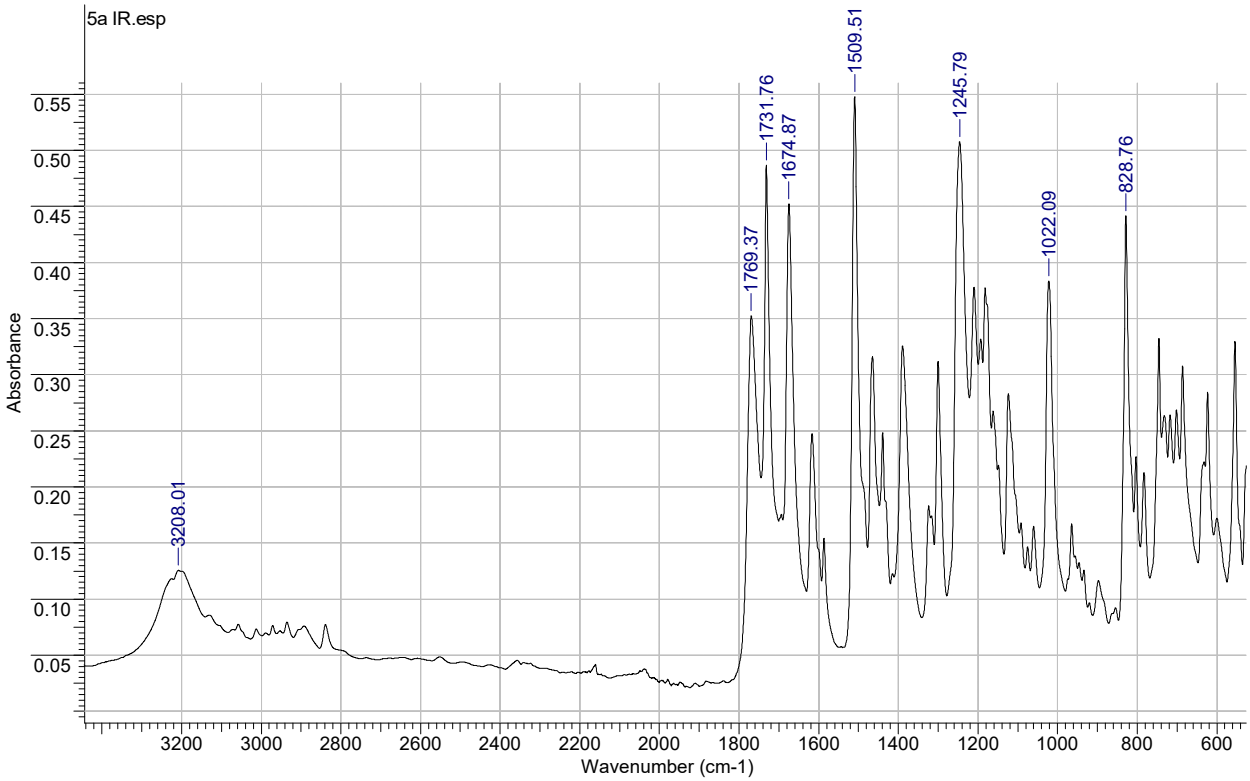

5a IR.esp
Absorbance
Wavenumber (cm-1)
3208.01
1769.37
1731.76
1674.87
1509.51
1245.79
1022.09
828.76

Figure S16

*(3S,3′S)-1′,1′′-bis(4-methoxyphenyl)-1-tosyldispiro[indoline-3,2′-azetidine-3′,3′′-pyrrolidine]-2,2′′,4′-trione (**6**)*

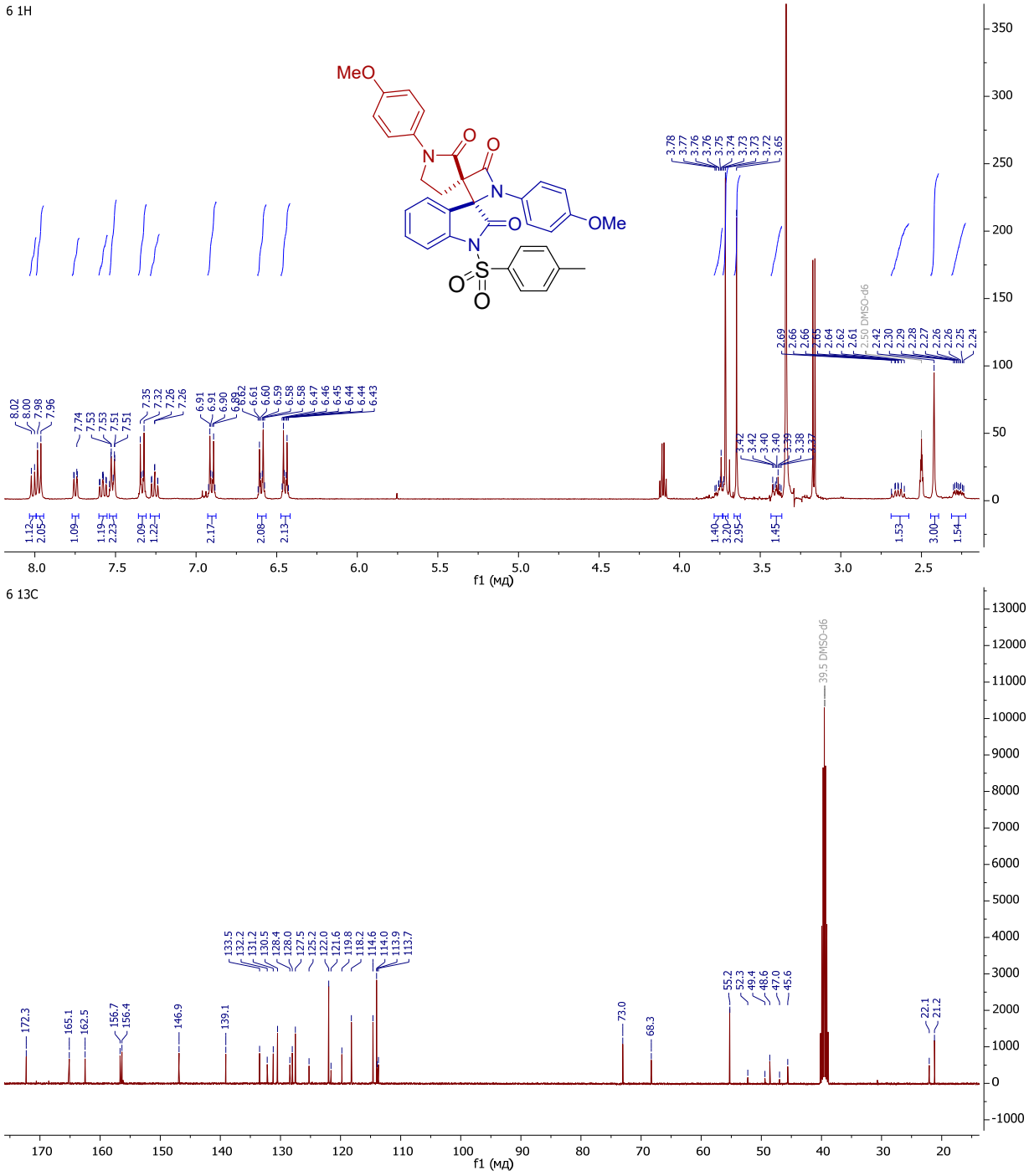


Figure S17

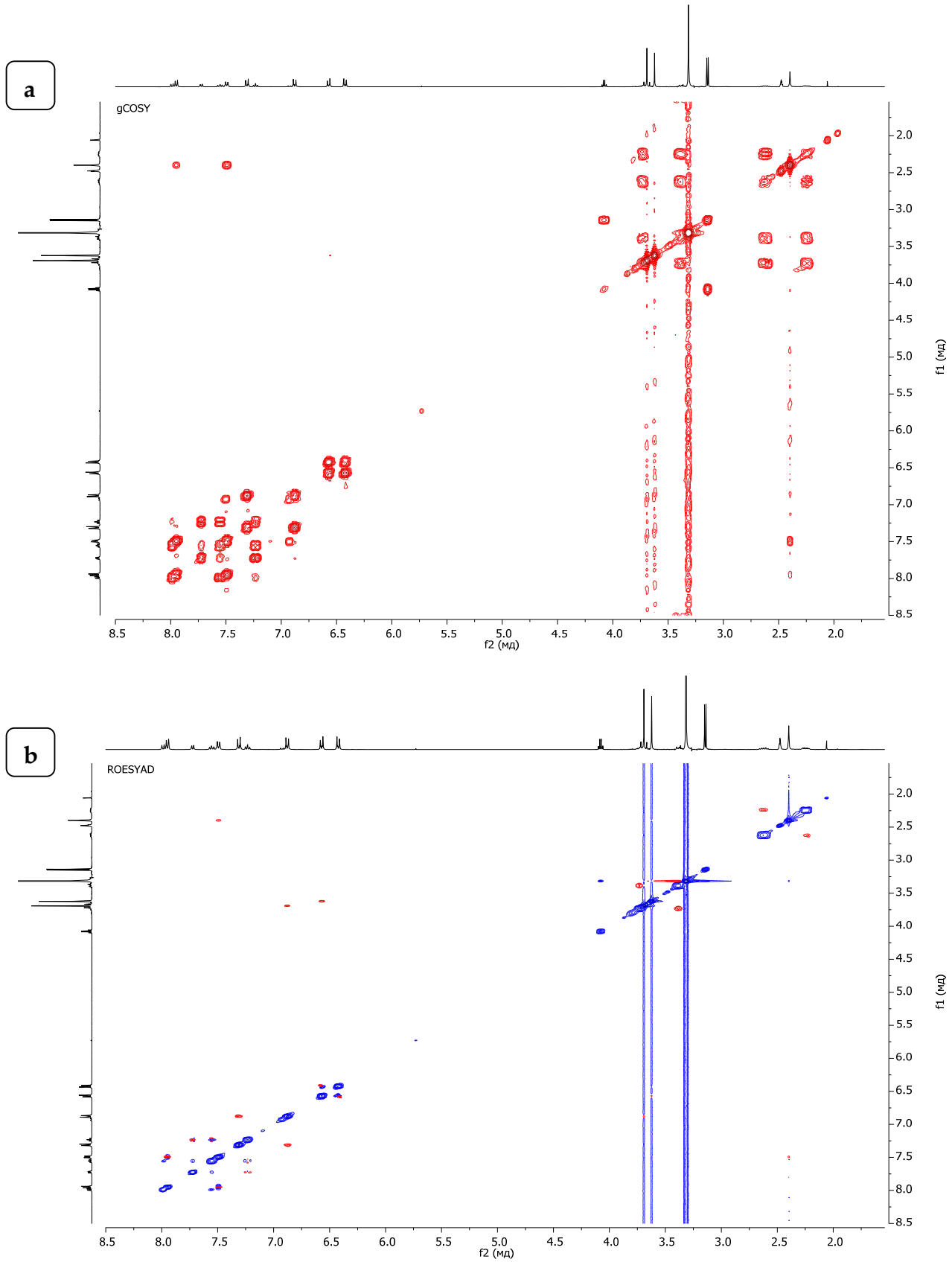


Figure S18: (a) gCOSY; (b)ROESYAD)

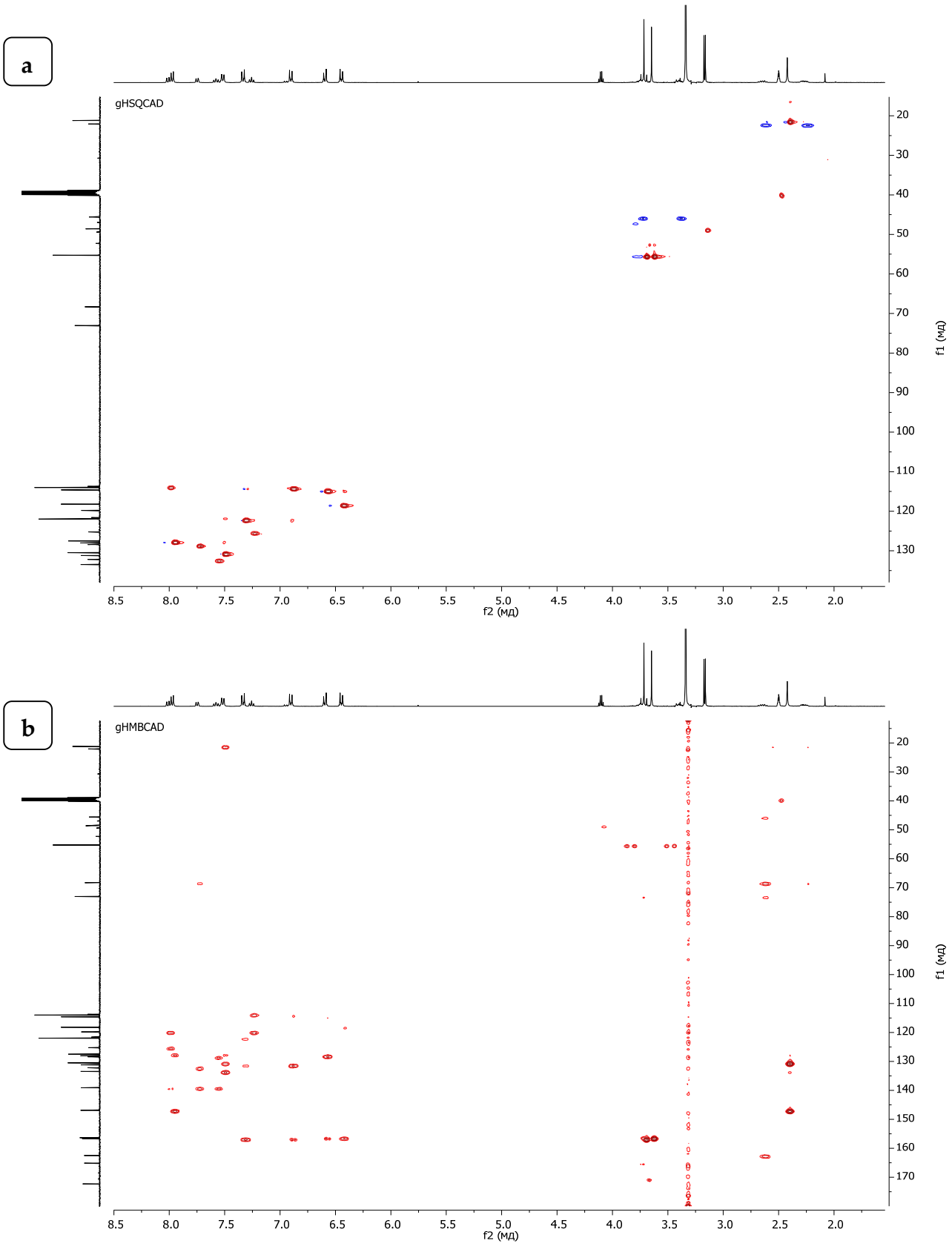


Figure S19: (a) gHSQCAD; (b)gHMBCAD

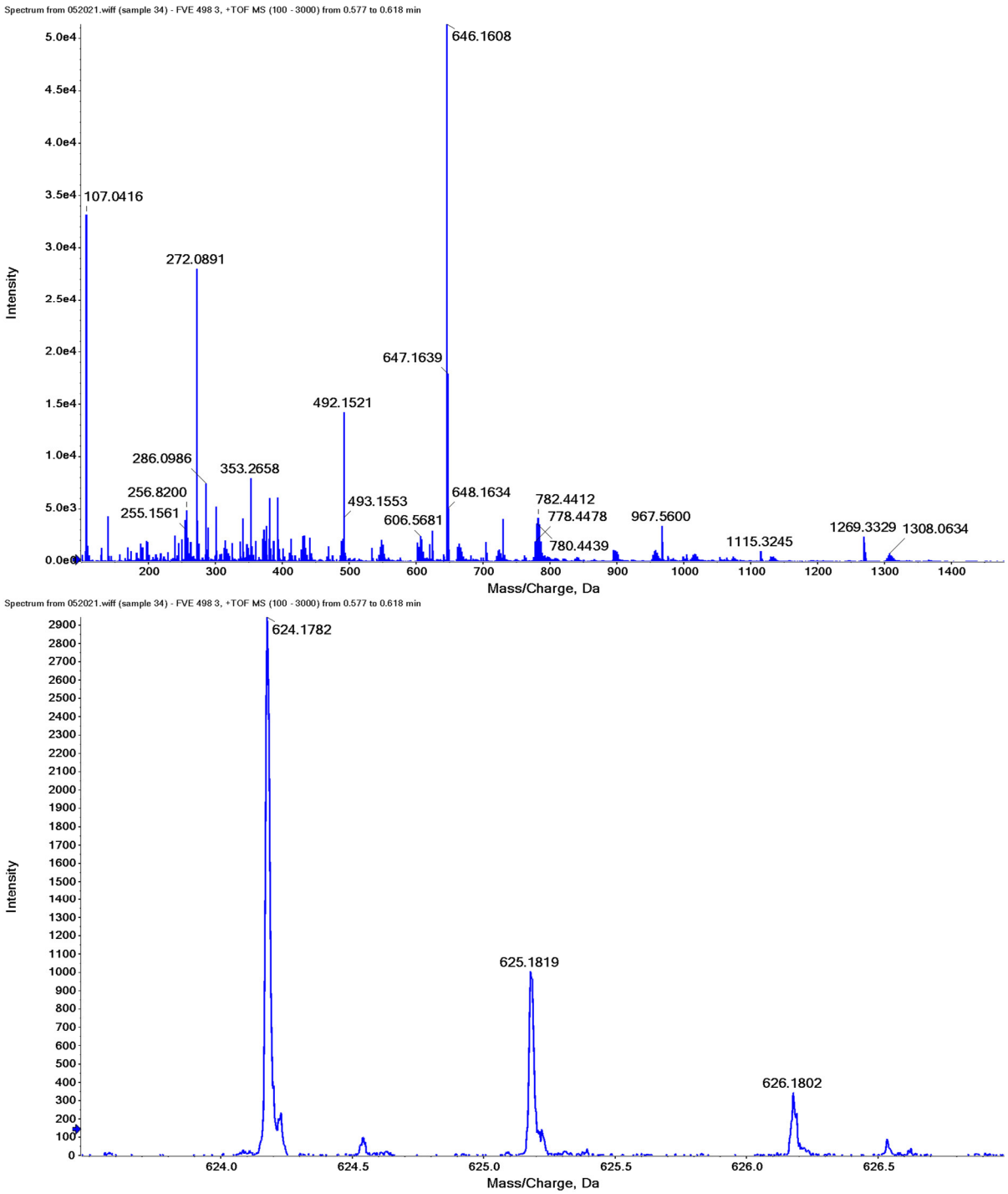

Spectrum from 052021.wiff (sample 34) - FVE 498 3, +TOF MS (100 - 3000) from 0.577 to 0.618 min
Intensity
Mass/Charge, Da
646.1608
107.0416
272.0891
647.1639
492.1521
286.0986
353.2658
256.8200
255.1561
493.1553
606.5681
648.1634
782.4412
778.4478
780.4439
967.5600
1115.3245
1269.3329
1308.0634
Spectrum from 052021.wiff (sample 34) - FVE 498 3, +TOF MS (100 - 3000) from 0.577 to 0.618 min
Intensity
Mass/Charge, Da
624.1782
625.1819
626.1802

Figure S20

*N,1-bis(4-methoxyphenyl)-2-oxopyrrolidine-3-carboxamide (**7**)*

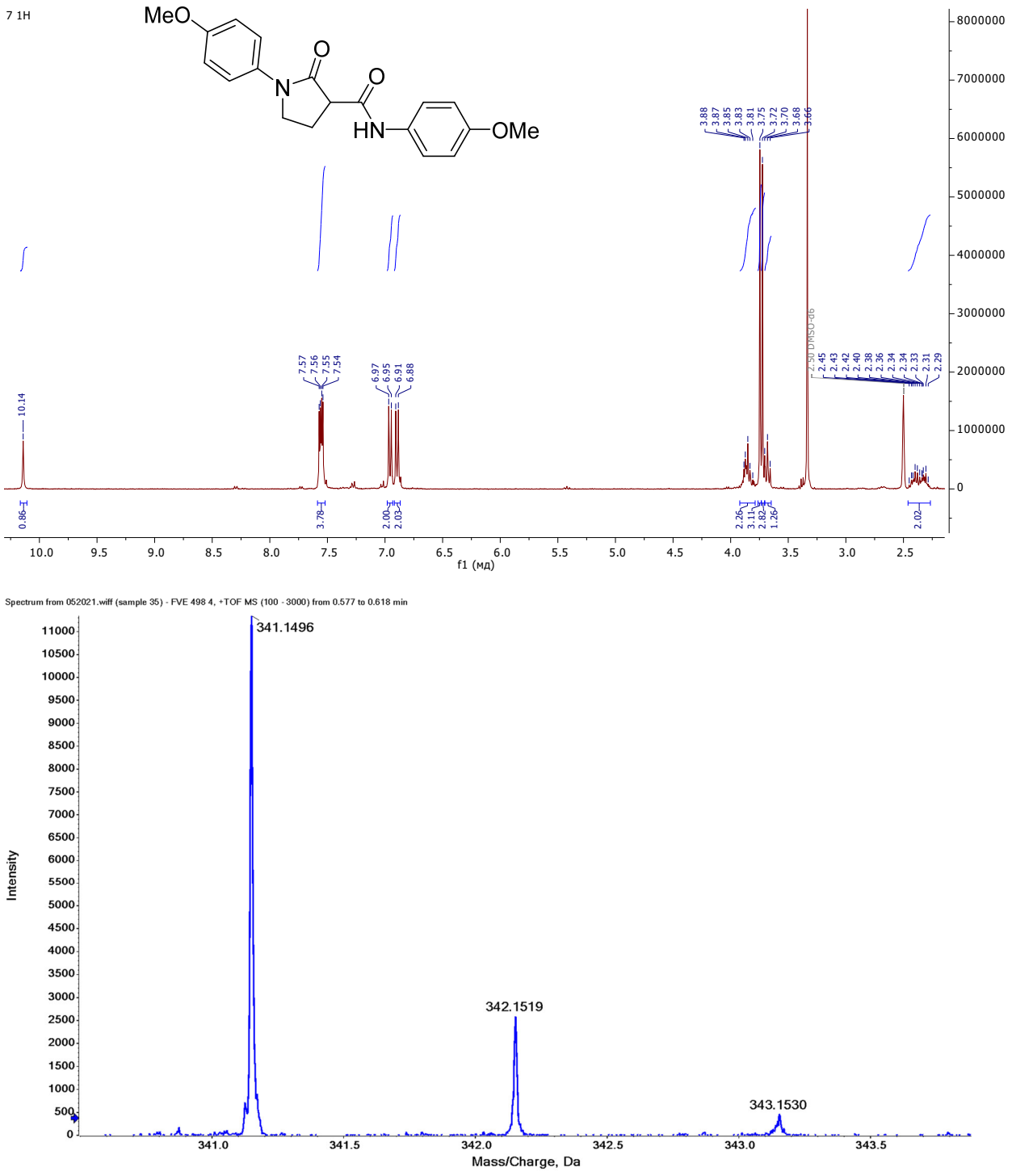


Figure S21

*(3S,3′S)-1′-(4-methoxyphenyl)-1′′-(p-tolyl)dispiro[indoline-3,2′-azetidine-3′,3′′-pyrrolidine]-2,2′′,4′-trione (**5b**)*

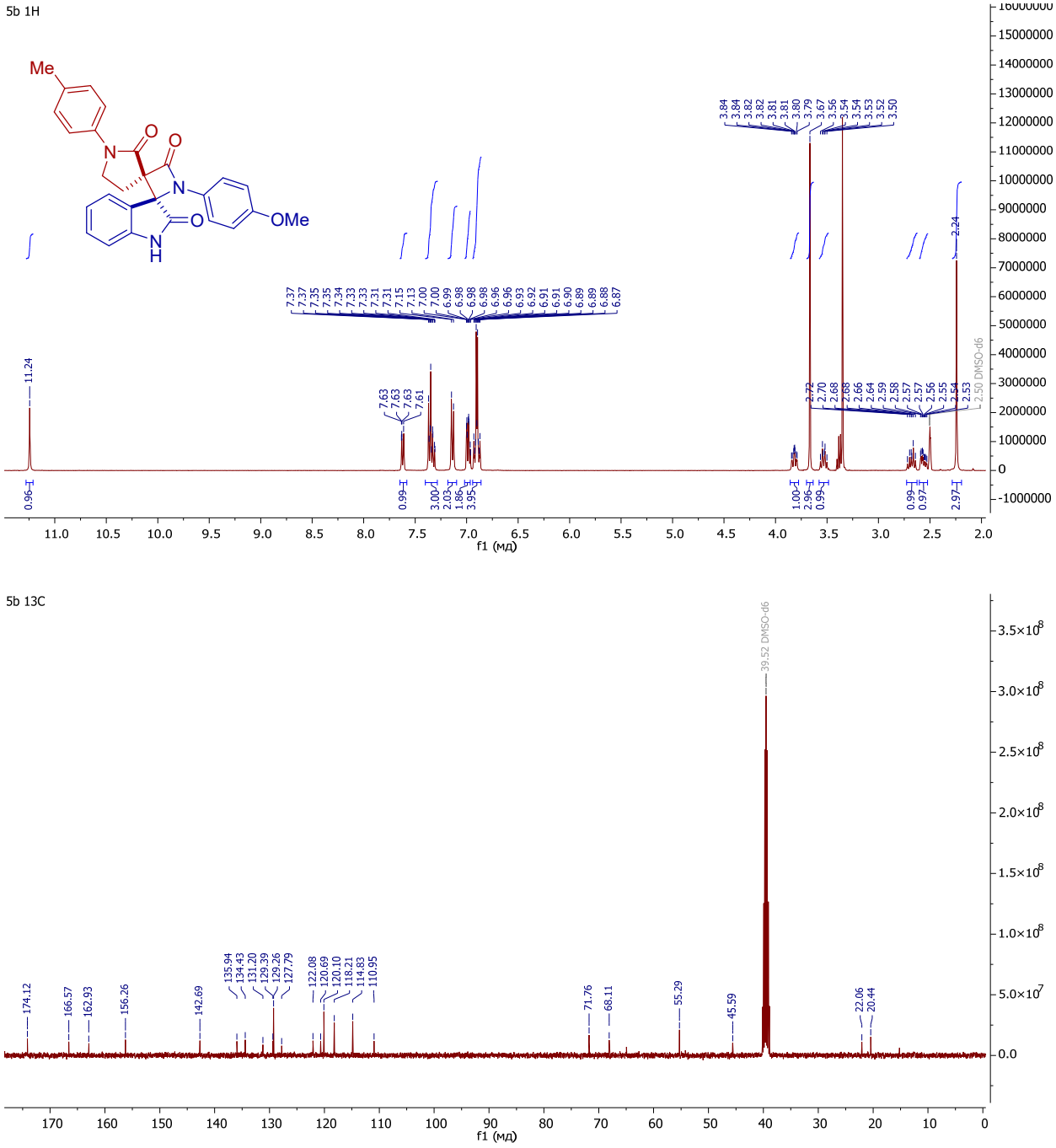


Figure S22

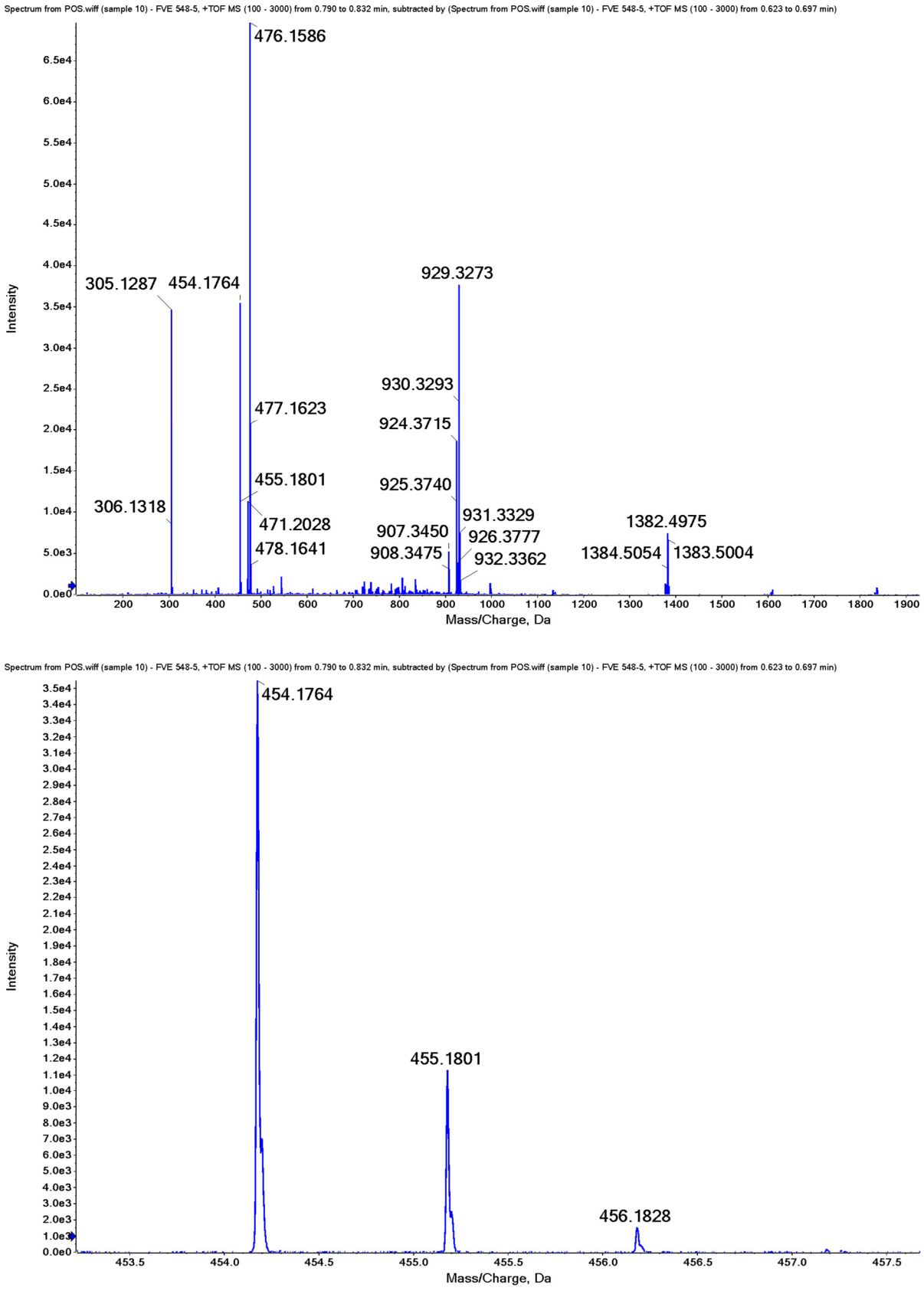

Spectrum from POS.wiff (sample 10) - FVE 548-5, +TOF MS (100 - 3000) from 0.790 to 0.832 min, subtracted by (Spectrum from POS.wiff (sample 10) - FVE 548-5, +TOF MS (100 - 3000) from 0.623 to 0.697 min)
476.1586
305.1287
454.1764
929.3273
930.3293
477.1623
924.3715
455.1801
925.3740
306.1318
931.3329
471.2028
907.3450
926.3777
1382.4975
478.1641
908.3475
932.3362
1384.5054
1383.5004
Intensity
Mass/Charge, Da
Spectrum from POS.wiff (sample 10) - FVE 548-5, +TOF MS (100 - 3000) from 0.790 to 0.832 min, subtracted by (Spectrum from POS.wiff (sample 10) - FVE 548-5, +TOF MS (100 - 3000) from 0.623 to 0.697 min)
454.1764
455.1801
456.1828
Intensity
Mass/Charge, Da

Figure S23

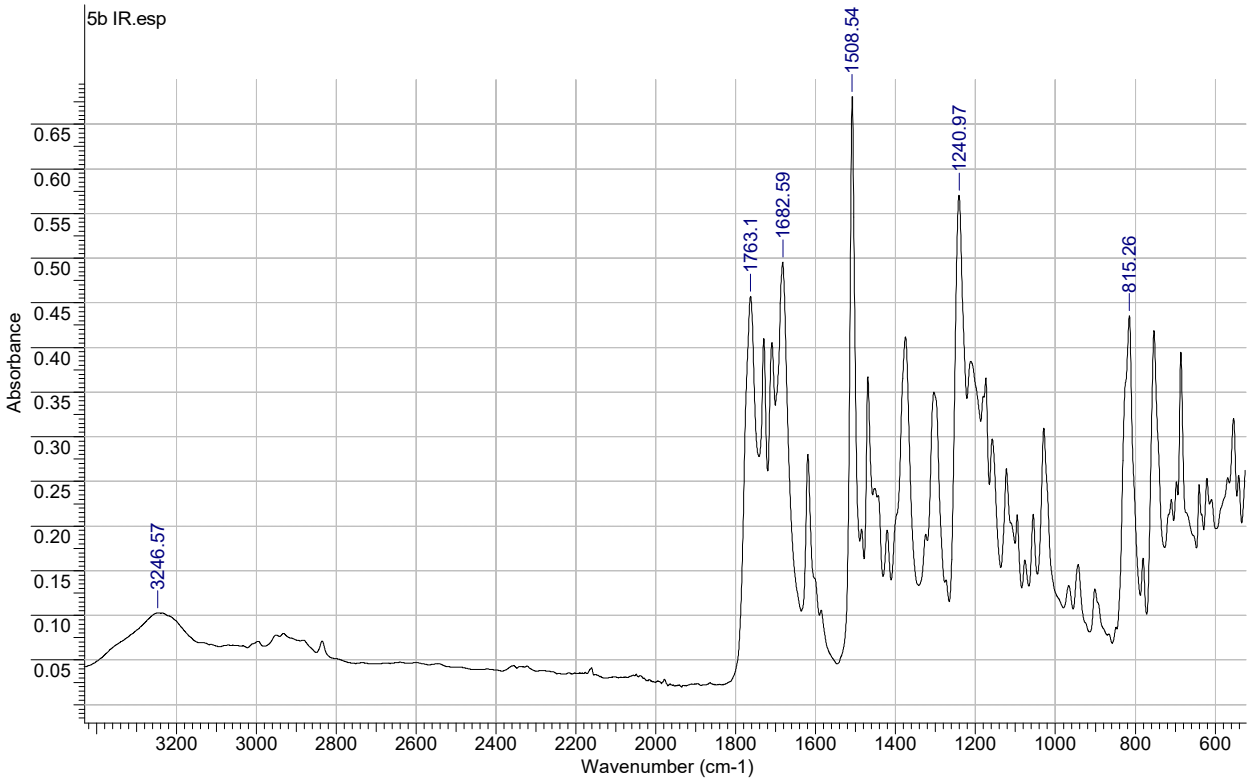

5b IR.esp
Absorbance
Wavenumber (cm-1)
3246.57
1763.1
1682.59
1508.54
1240.97
815.26

Figure S24

*(3S,3′S)-1′′-(4-chlorophenyl)-1′-(4-methoxyphenyl)dispiro[indoline-3,2′-azetidine-3′,3′′-pyrrolidine]-2,2′′,4′-trione (**5c**)*

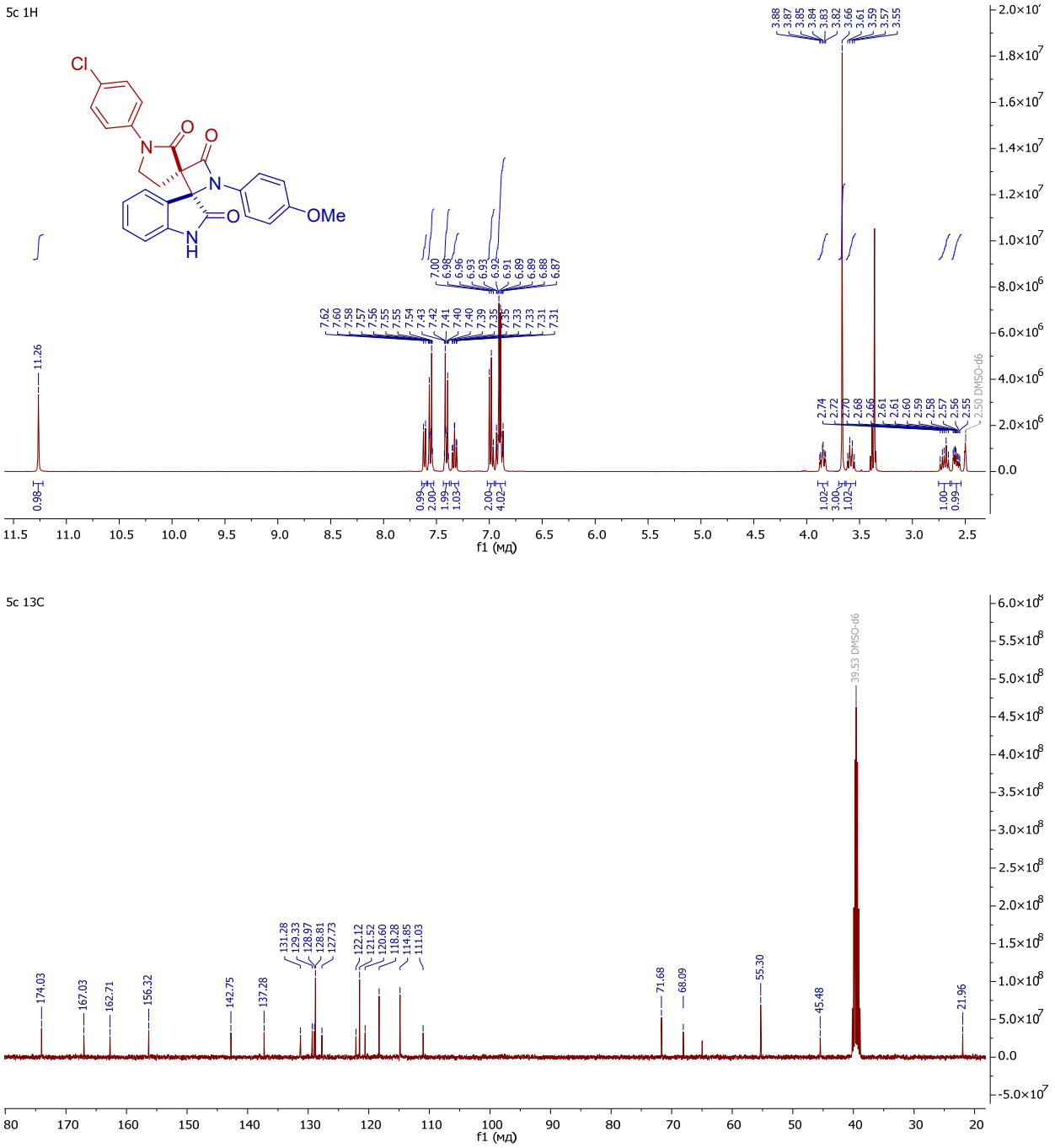


Figure S25

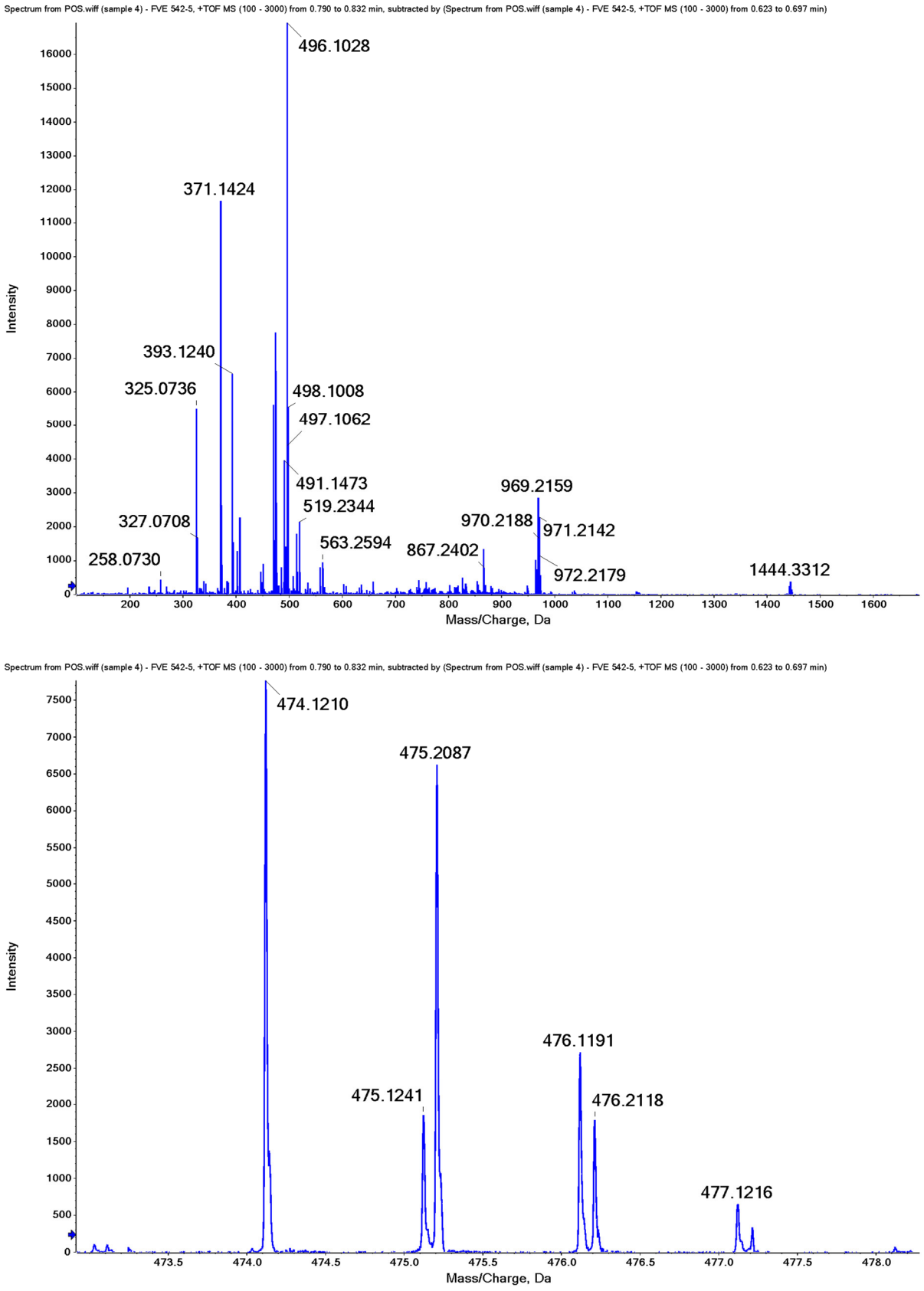

Spectrum from POS.wiff (sample 4) - FVE 542-5, +TOF MS (100 - 3000) from 0.790 to 0.832 min, subtracted by (Spectrum from POS.wiff (sample 4) - FVE 542-5, +TOF MS (100 - 3000) from 0.623 to 0.697 min)
Intensity
Mass/Charge, Da
496.1028
371.1424
393.1240
325.0736
498.1008
497.1062
491.1473
519.2344
327.0708
563.2594
258.0730
867.2402
969.2159
970.2188
971.2142
972.2179
1444.3312
Spectrum from POS.wiff (sample 4) - FVE 542-5, +TOF MS (100 - 3000) from 0.790 to 0.832 min, subtracted by (Spectrum from POS.wiff (sample 4) - FVE 542-5, +TOF MS (100 - 3000) from 0.623 to 0.697 min)
Intensity
Mass/Charge, Da
474.1210
475.2087
476.1191
475.1241
476.2118
477.1216

Figure S26

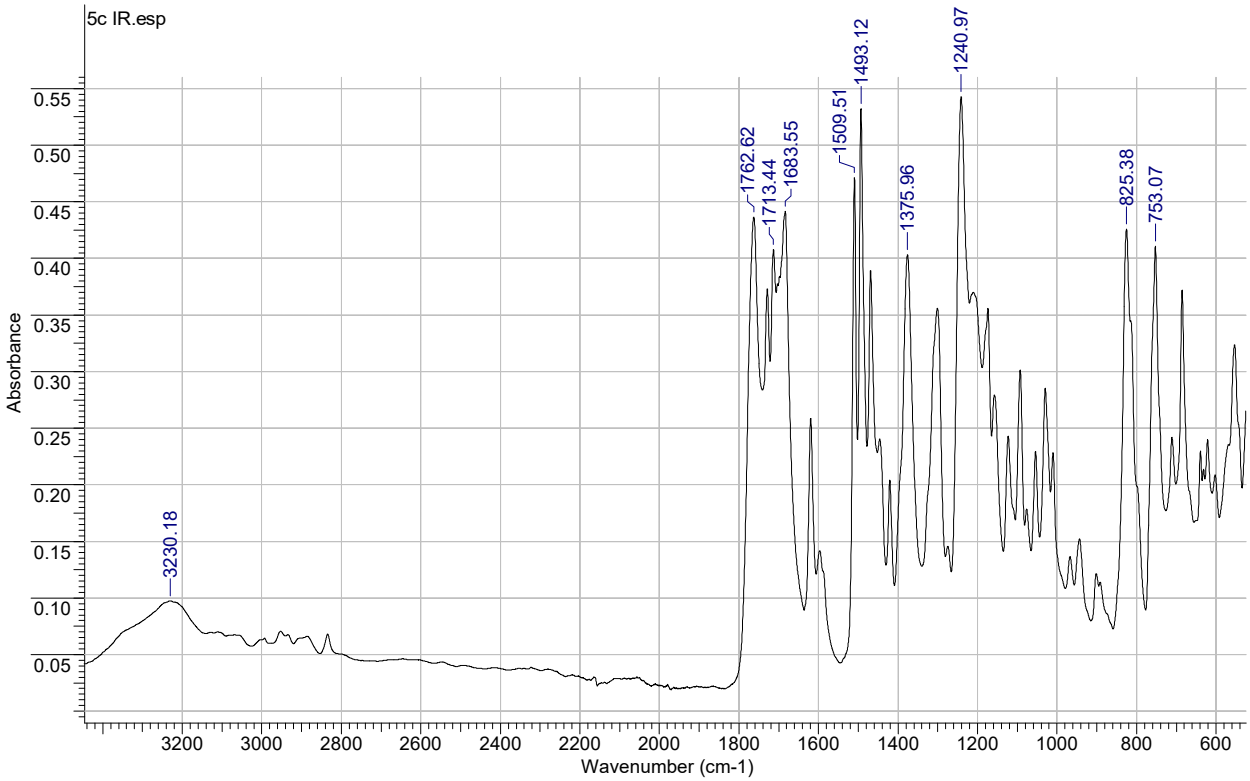

5c IR.esp
Absorbance
Wavenumber (cm-1)
3230.18
1762.62
1713.44
1683.55
1509.51
1493.12
1375.96
1240.97
825.38
753.07

Figure S27

*(3S,3′S)-1′,1′′-di-m-tolyldispiro[indoline-3,2′-azetidine-3′,3′′-pyrrolidine]-2,2′′,4′-trione (**5d**)*

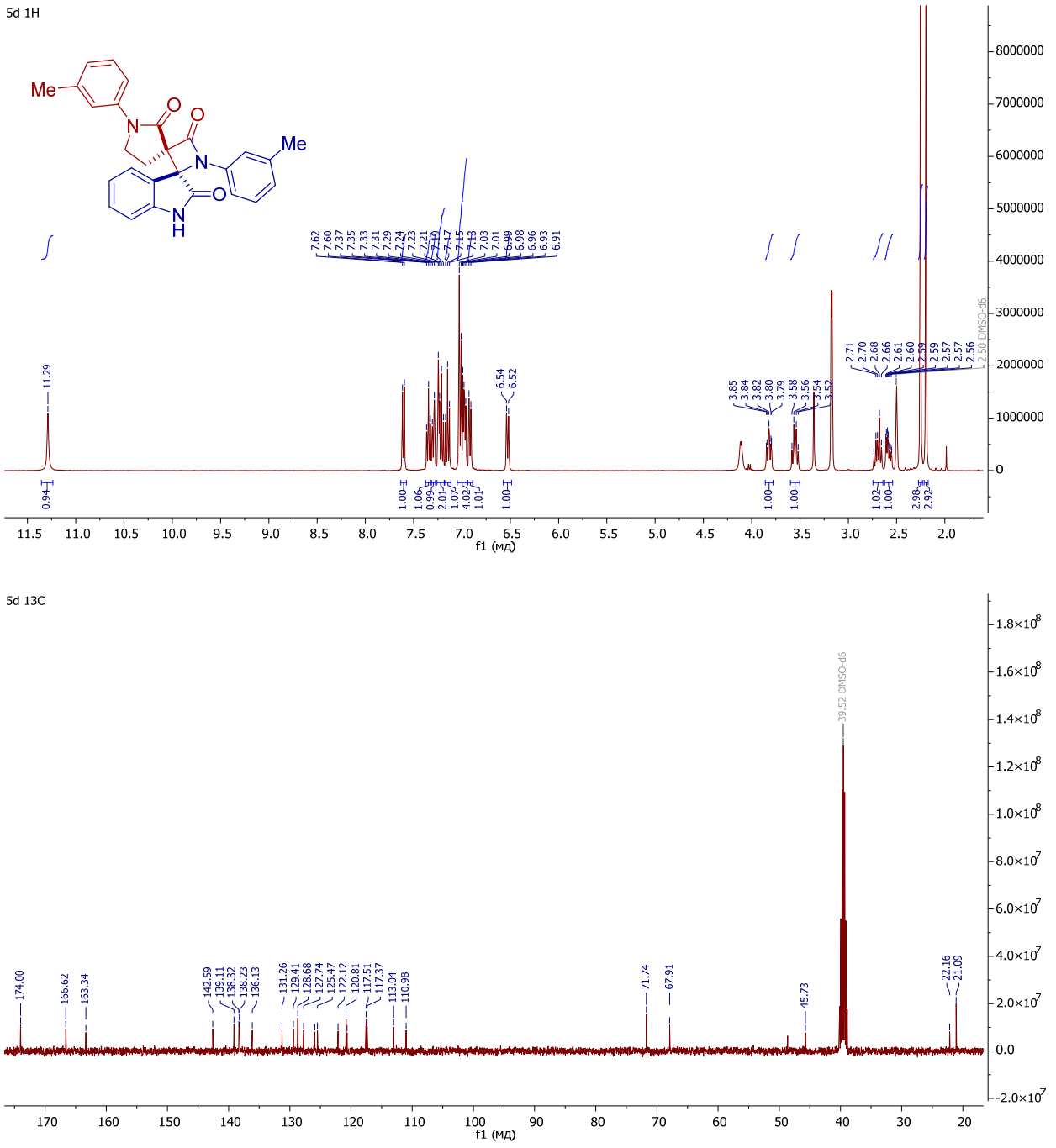


Figure S28

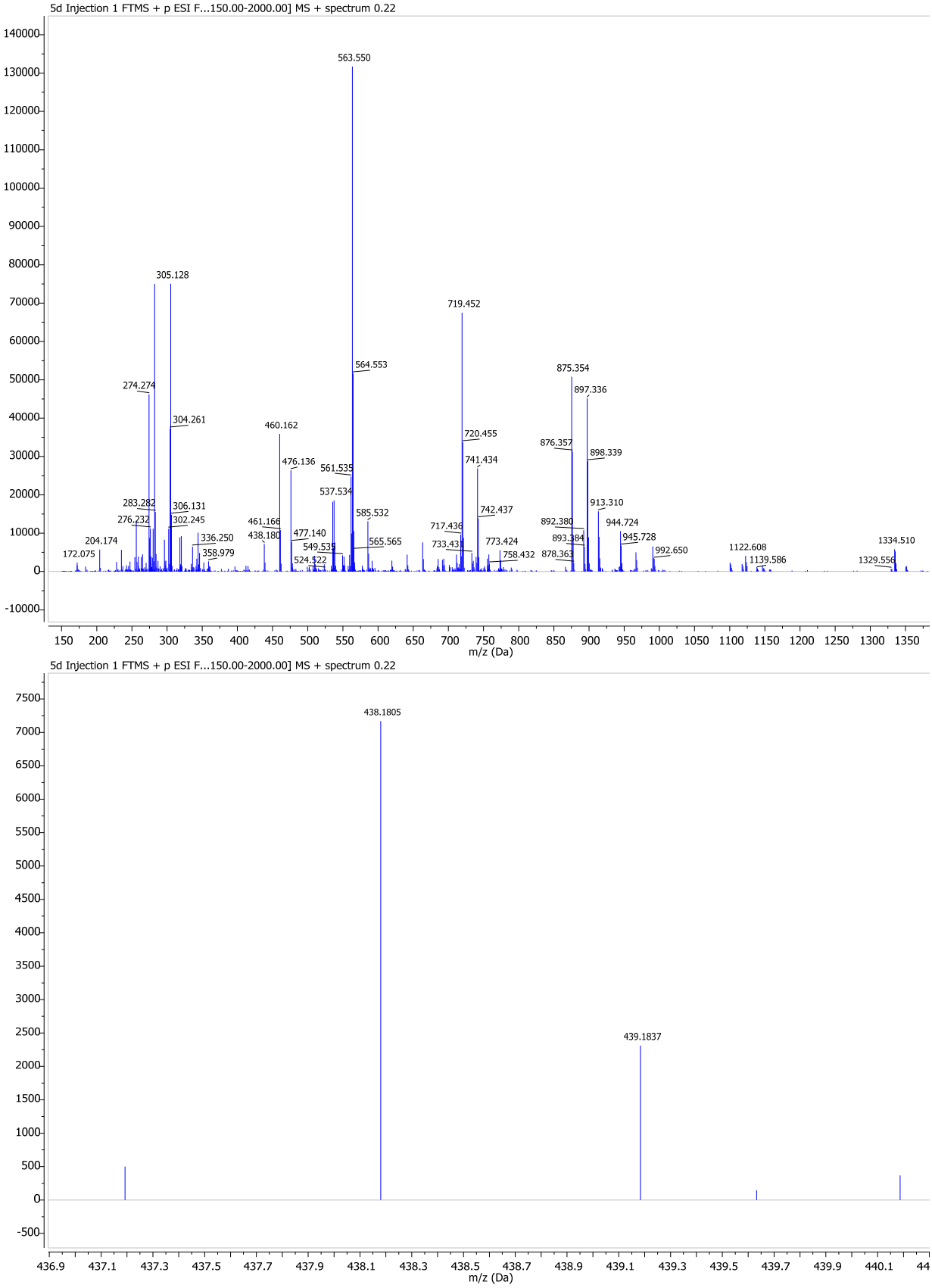

5d Injection 1 FTMS + p ESI F...150.00-2000.00] MS + spectrum 0.22
563.550
305.128
719.452
564.553
875.354
897.336
274.274
304.261
460.162
720.455
876.357
898.339
476.136
741.434
561.535
537.534
913.310
283.282
306.131
585.532
742.437
276.232
302.245
461.166
717.436
892.380
944.724
204.174
336.250
438.180
477.140
565.565
733.43
773.424
893.384
945.728
172.075
358.979
549.535
758.432
878.363
992.650
1122.608
1334.510
524.522
1139.586
1329.556
m/z (Da)
5d Injection 1 FTMS + p ESI F...150.00-2000.00] MS + spectrum 0.22
438.1805
439.1837
m/z (Da)

Figure S29

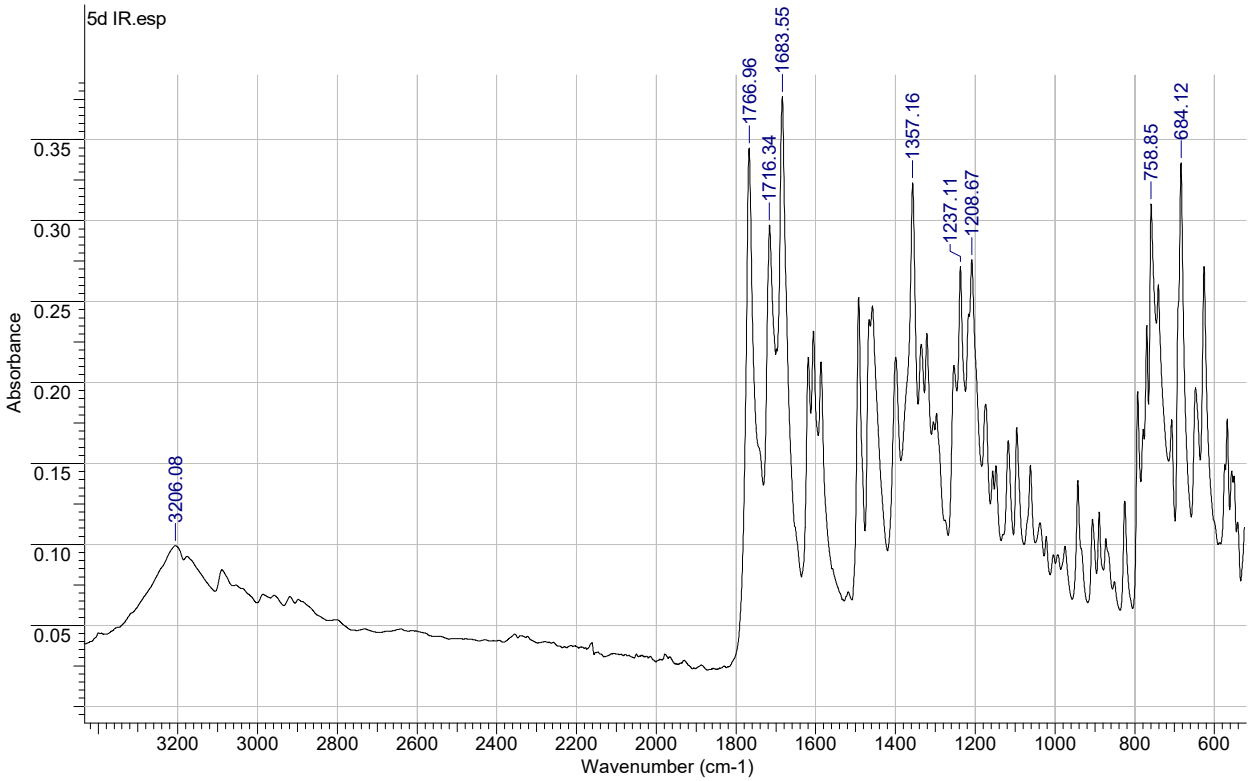

5d IR.esp
Absorbance
0.35
0.30
0.25
0.20
0.15
0.10
0.05
3206.08
1766.96
1716.34
1683.55
1357.16
1237.11
1208.67
758.85
684.12
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
Wavenumber (cm-1)

Figure S30

*(3S,3′S)-1′′-(4-chlorophenyl)-1′-(m-tolyl)dispiro[indoline-3,2′-azetidine-3′,3′′-pyrrolidine]-2,2′′,4′-trione (**5e**)*

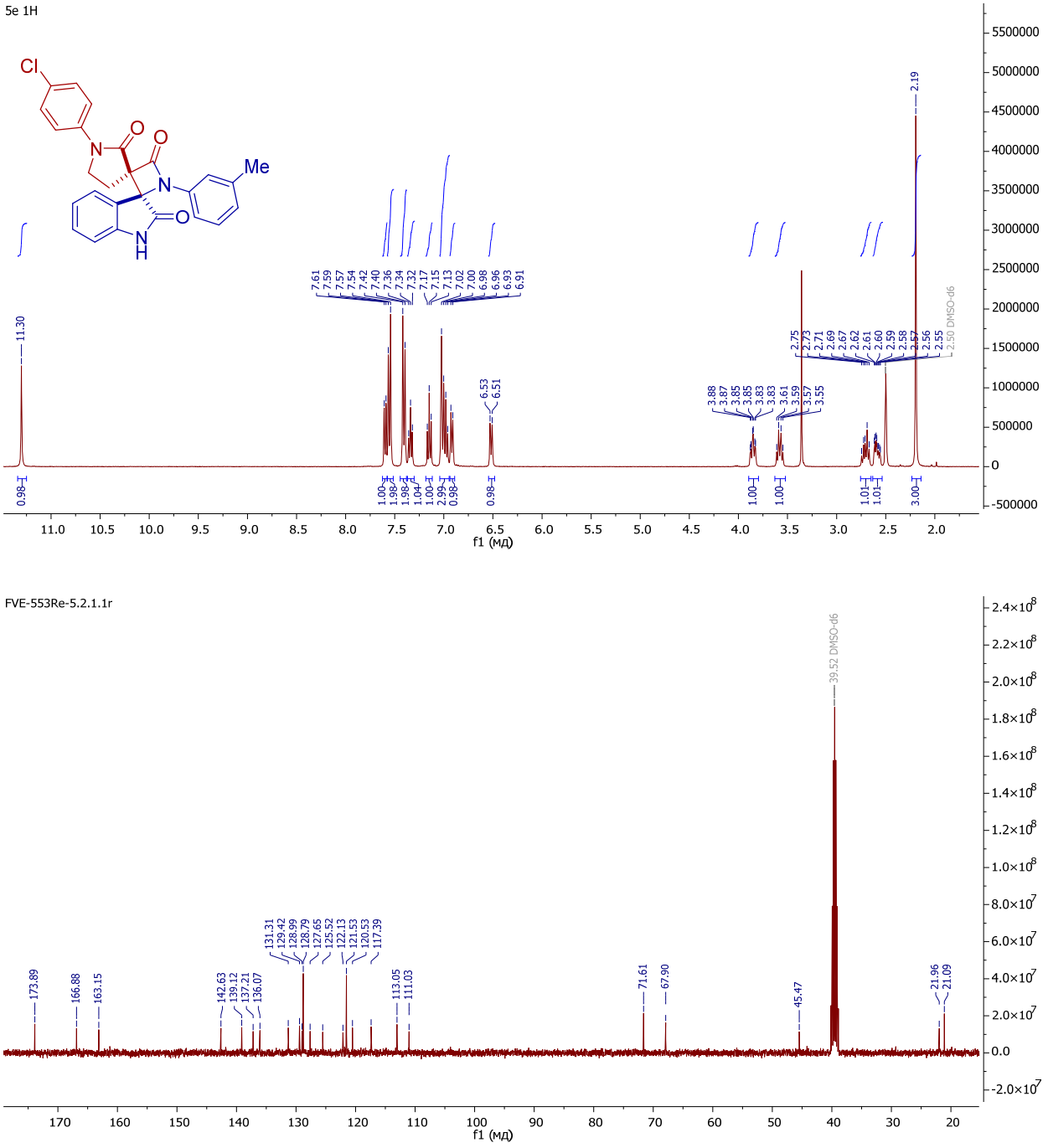


Figure S31

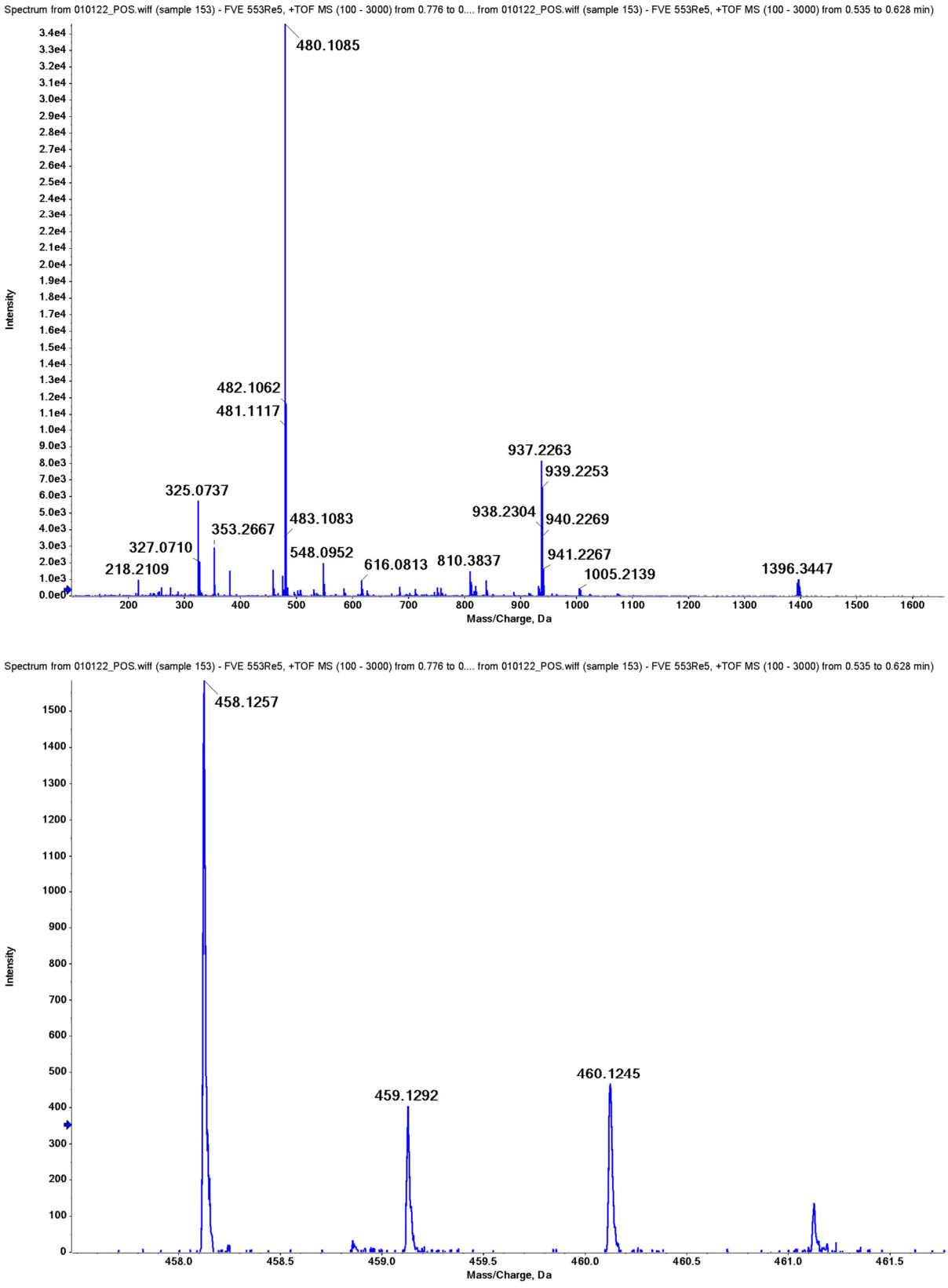

Spectrum from 010122_POS.wiff (sample 153) - FVE 553Re5, +TOF MS (100 - 3000) from 0.776 to 0.... from 010122_POS.wiff (sample 153) - FVE 553Re5, +TOF MS (100 - 3000) from 0.535 to 0.628 min)
Intensity
Mass/Charge, Da
480.1085
482.1062
481.1117
937.2263
939.2253
325.0737
938.2304
940.2269
353.2667
483.1083
327.0710
548.0952
941.2267
218.2109
616.0813
810.3837
1005.2139
1396.3447
458.1257
459.1292
460.1245

Figure S32

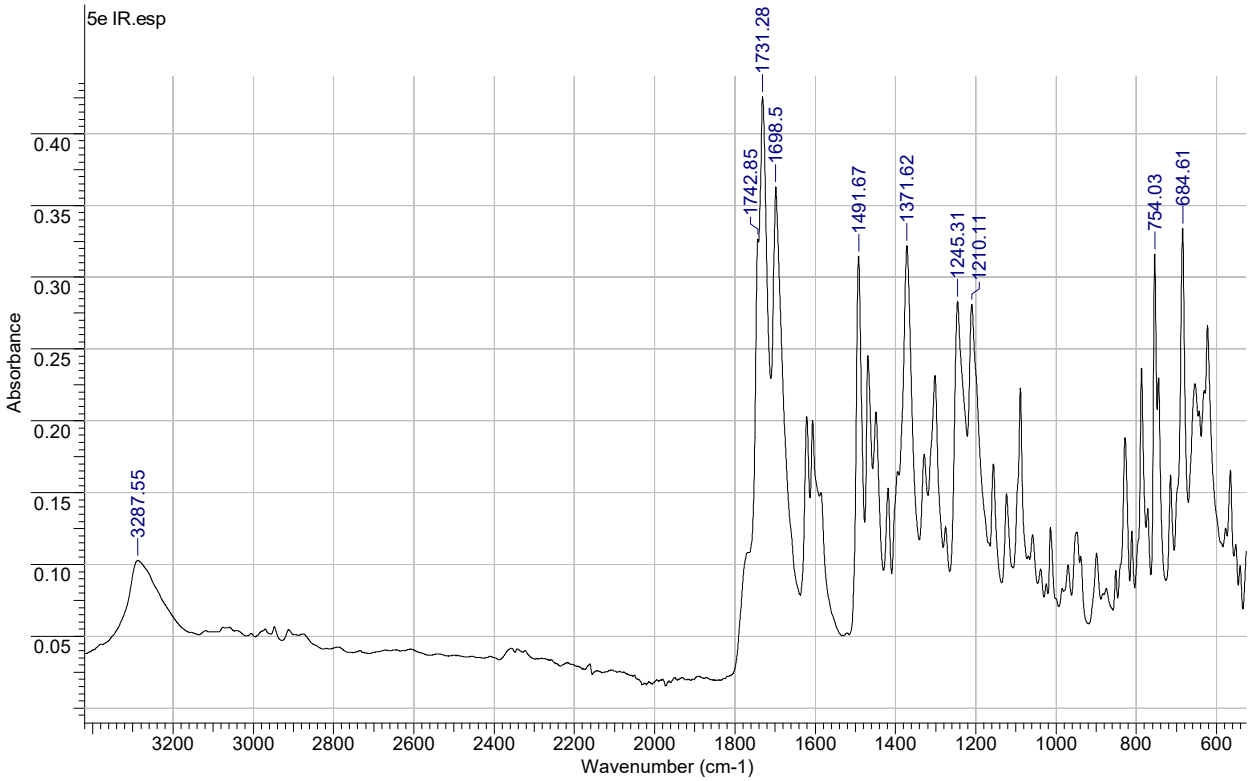

5e IR.esp
Absorbance
Wavenumber (cm-1)
3287.55
1742.85
1731.28
1698.5
1491.67
1371.62
1245.31
1210.11
754.03
684.61

Figure S33

*(3S,3′S)-1′′-(3-chloro-4-fluorophenyl)-1′-(m-tolyl)dispiro[indoline-3,2′-azetidine-3′,3′′-pyrrolidine]-2,2′′,4′-trione (**5f**)*

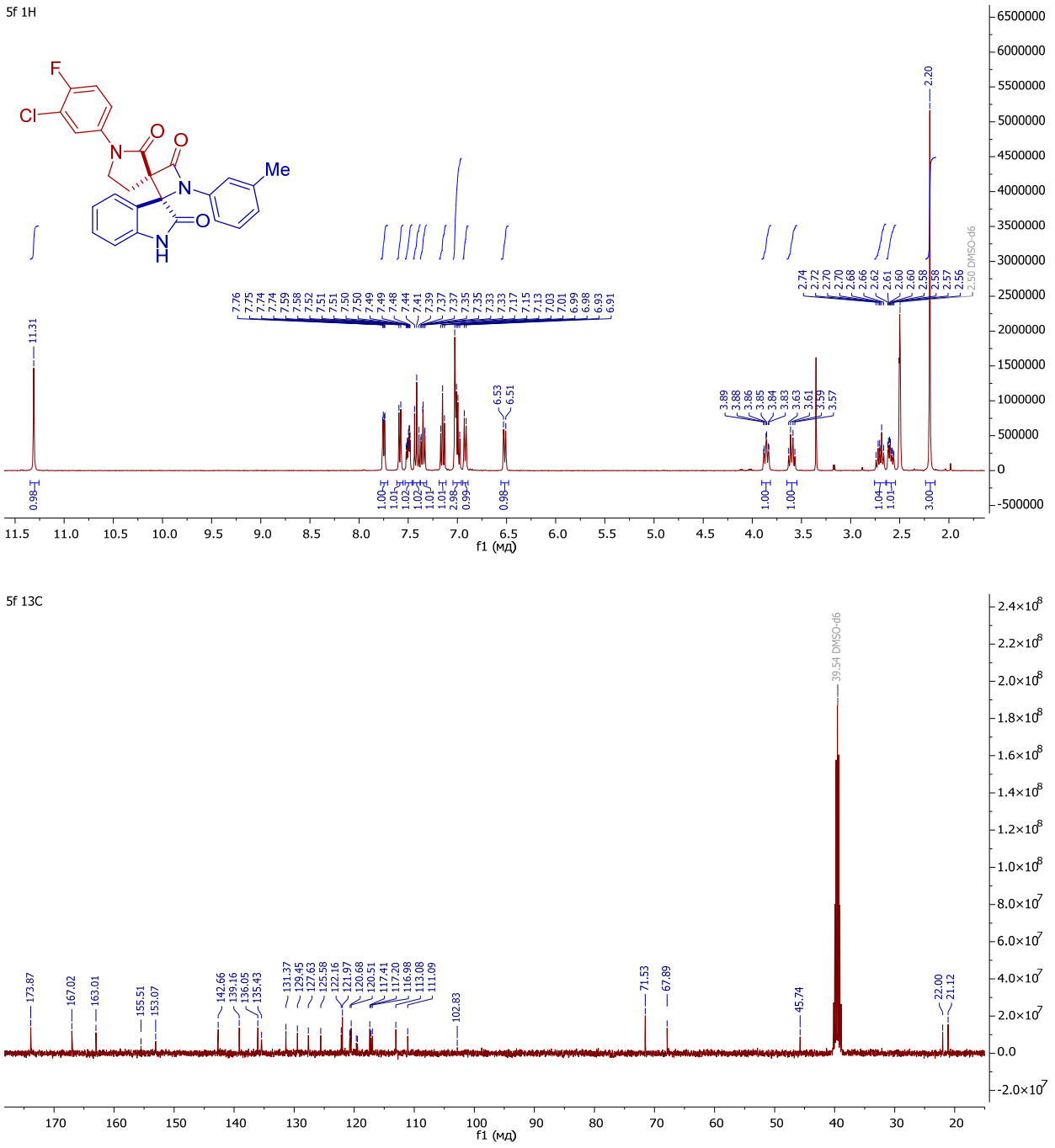


Figure S34

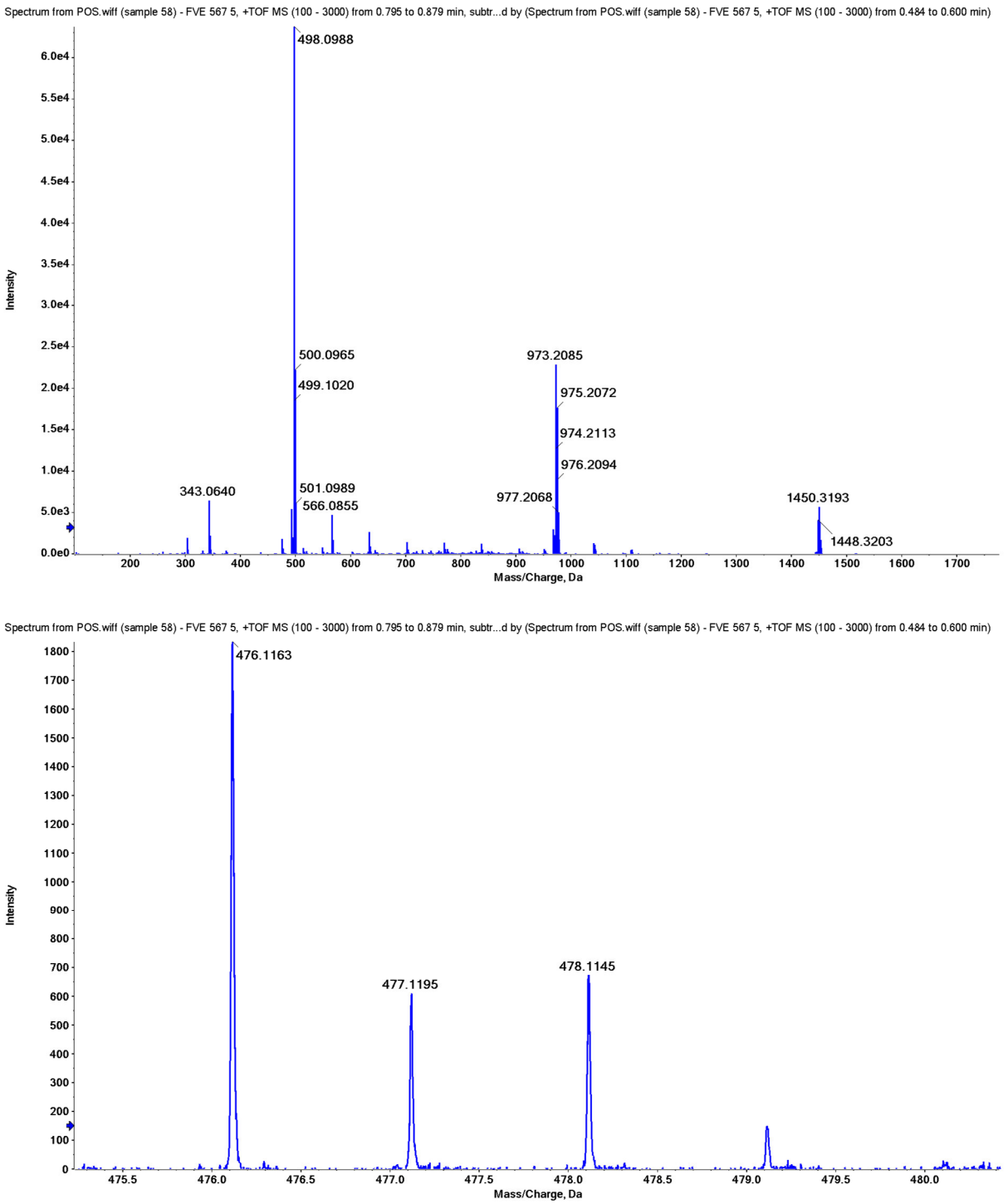

Spectrum from POS.wiff (sample 58) - FVE 567 5, +TOF MS (100 - 3000) from 0.795 to 0.879 min, subtr...d by (Spectrum from POS.wiff (sample 58) - FVE 567 5, +TOF MS (100 - 3000) from 0.484 to 0.600 min)
Intensity
Mass/Charge, Da
498.0988
500.0965
499.1020
973.2085
975.2072
974.2113
976.2094
343.0640
501.0989
566.0855
977.2068
1450.3193
1448.3203
Spectrum from POS.wiff (sample 58) - FVE 567 5, +TOF MS (100 - 3000) from 0.795 to 0.879 min, subtr...d by (Spectrum from POS.wiff (sample 58) - FVE 567 5, +TOF MS (100 - 3000) from 0.484 to 0.600 min)
Intensity
Mass/Charge, Da
476.1163
477.1195
478.1145

Figure S35

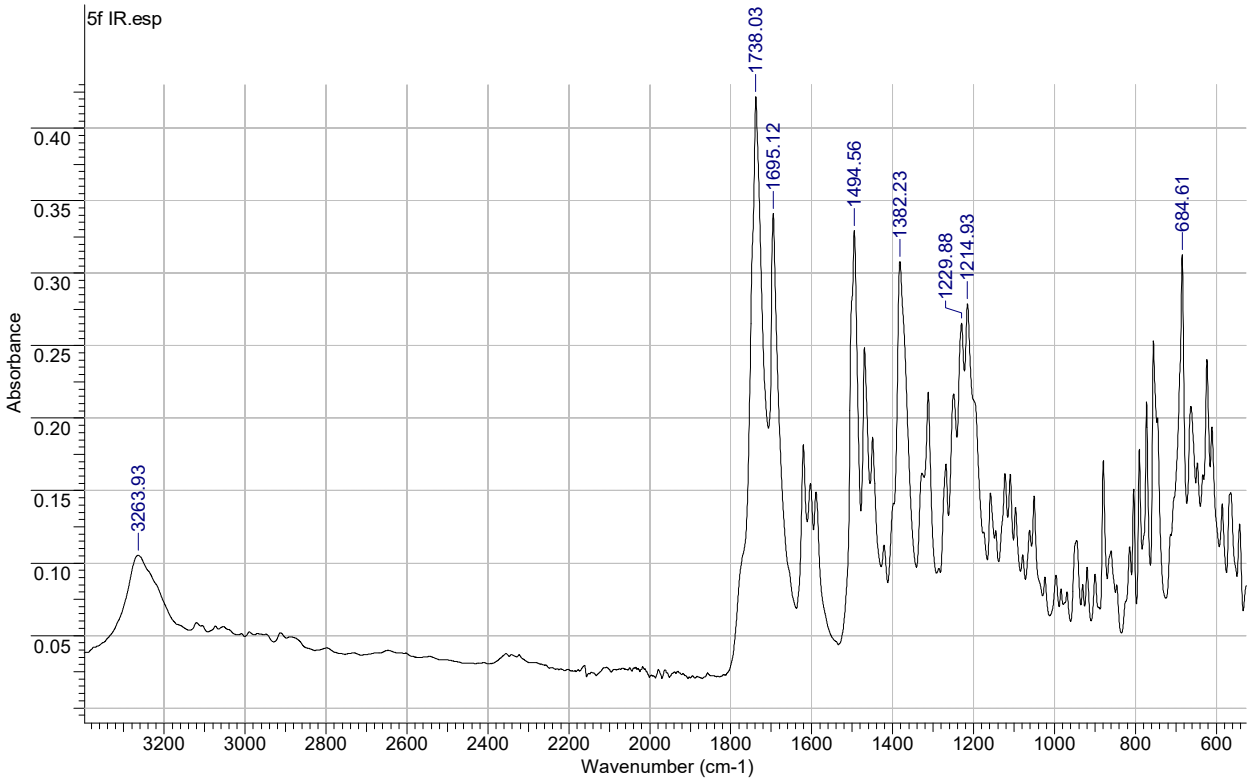
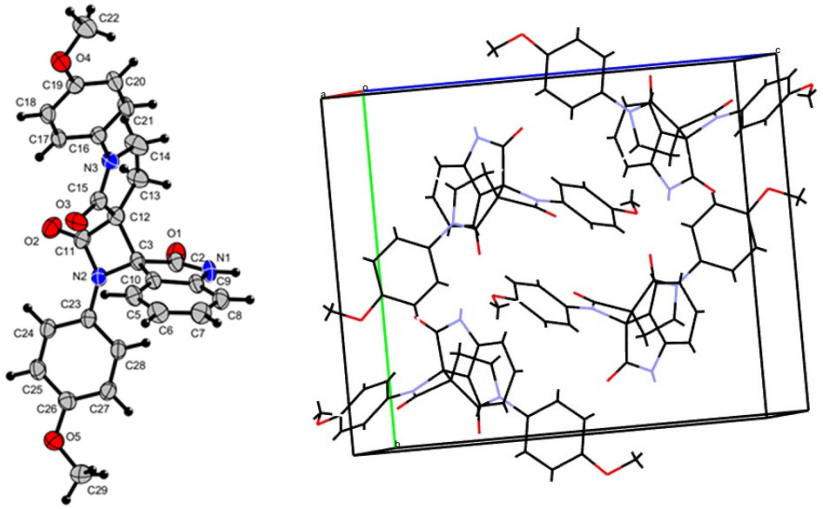

5f IR.esp
1738.03
1695.12
1494.56
1382.23
1229.88
1214.93
684.61
3263.93
Absorbance
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
Wavenumber (cm-1)

Figure S36

X-Ray

5a **(CCDC-2171648)**



6 **(CCDC-2172682)**

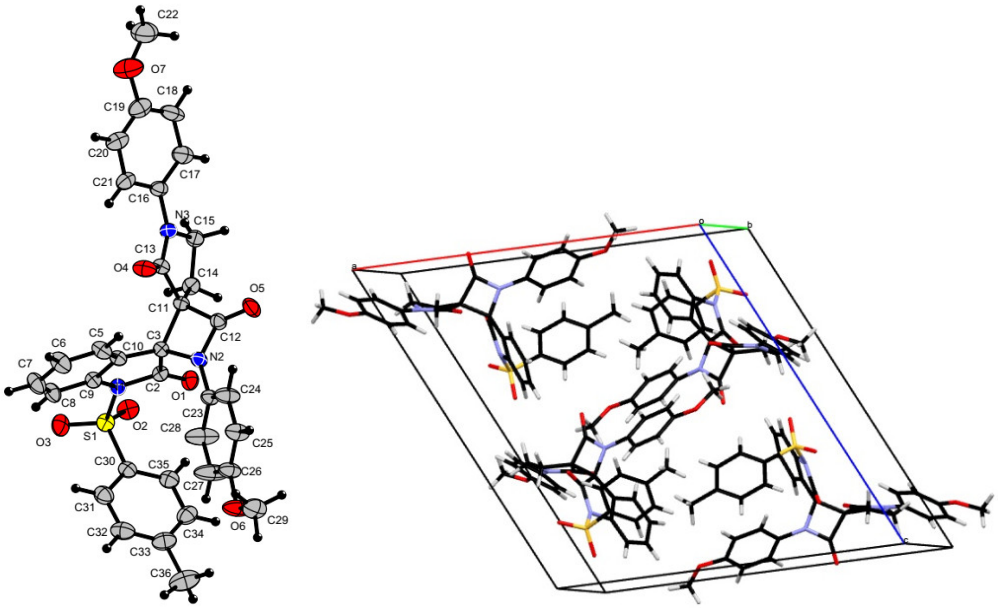


Figure S37

Table S1. Crystal data and structure refinement for compound **5a**.

Identification code	fve 4985	
Empirical formula	C27 H23 N3 O5	
Formula weight	469.48	
Temperature	295(2) K	
Wavelength	1.54186 Å	
Crystal system	Monoclinic	
Space group	P 21/n	
Unit cell dimensions	a = 10.2318(2) Å	α= 90°.
	b = 14.1437(3) Å	β= 102.589(3)°.
	c = 16.3407(4) Å	γ = 90°.
Volume	2307.90(9) $Å^3$	
Z	4	
Density (calculated)	1.351 Mg/m^3	
Absorption coefficient	0.777 mm^{-1}	
F(000)	984	
Theta range for data collection	4.178 to 68.269°.	
Index ranges	-12<=h<=8, -13<=k<=17, -16<=l<=19	
Reflections collected	17339	
Independent reflections	4170 [R(int) = 0.1830]	
Completeness to theta = 67.686°	99.4 %	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4170 / 0 / 322	
Goodness-of-fit on F^2	0.893	
Final R indices [I>2sigma(I)]	R1 = 0.0632, wR2 = 0.1619	
R indices (all data)	R1 = 0.0925, wR2 = 0.1766	
Largest diff. peak and hole	0.308 and -0.311 e. $Å^{-3}$	

Table S2. Crystal data and structure refinement for compound 6.

Identification code	fve498_3	
Empirical formula	C34 H29 N3 O7 S	
Formula weight	623.66	
Temperature	295(2) K	
Wavelength	1.54186 Å	
Crystal system	Monoclinic	
Space group	P 21/c	
Unit cell dimensions	a = 17.7403(4) Å	α= 90°.
	b = 9.93690(10) Å	β= 116.337(2)°.
	c = 18.9331(5) Å	γ = 90°.
Volume	2991.15(12) $Å^3$	
Z	4	
Density (calculated)	1.385 Mg/m^3	
Absorption coefficient	1.430 mm^{-1}	
F(000)	1304	
Theta range for data collection	4.695 to 68.608°.	
Index ranges	-18<=h<=21, -11<=k<=6, -22<=l<=21	
Reflections collected	22548	
Independent reflections	5436 [R(int) = 0.0676]	
Completeness to theta = 67.686°	99.1 %	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5436 / 0 / 410	
Goodness-of-fit on F^2	0.914	
Final R indices [I>2sigma(I)]	R1 = 0.0501, wR2 = 0.1264	
R indices (all data)	R1 = 0.0818, wR2 = 0.1376	
Extinction coefficient	0.0017(2)	
Largest diff. peak and hole	0.902 and -0.287 e. $Å^{-3}$	