molecules

MDPI

Communication

Synthesis and Cyclooxygenase Inhibition of Sulfonamide-Substituted (Dihydro)Pyrrolo[3,2,1-*hi*]indoles and Their Potential Prodrugs

Supporting Information

Markus Laube [1,*], Cemena Gassner [1], Torsten Kniess [1] and Jens Pietzsch [1,2,*]

[1] Department of Radiopharmaceutical and Chemical Biology, Institute of Radiopharmaceutical Cancer Research, Helmholtz-Zentrum Dresden-Rossendorf, Bautzner Landstrasse 400, 01328 Dresden, Germany; m.laube@hzdr.de (M.L.); c.gassner@hzdr.de (C.G.); t.kniess@hzdr.de (T.K.); j.pietzsch@hzdr.de (J.P.)

[2] Faculty of Chemistry and Food Chemistry, School of Science, Technische Universität Dresden, Mommsenstrasse 4, 01062 Dresden, Germany; j.pietzsch@hzdr.de (J.P.)

* Correspondence: m.laube@hzdr.de (M.L.); j.pietzsch@hzdr.de (J.P.); Tel.: +49-351-260-2810 (M.L.); Tel.: +49-351-260-2622 (J.P.)

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Copies of NMR and HRMS data

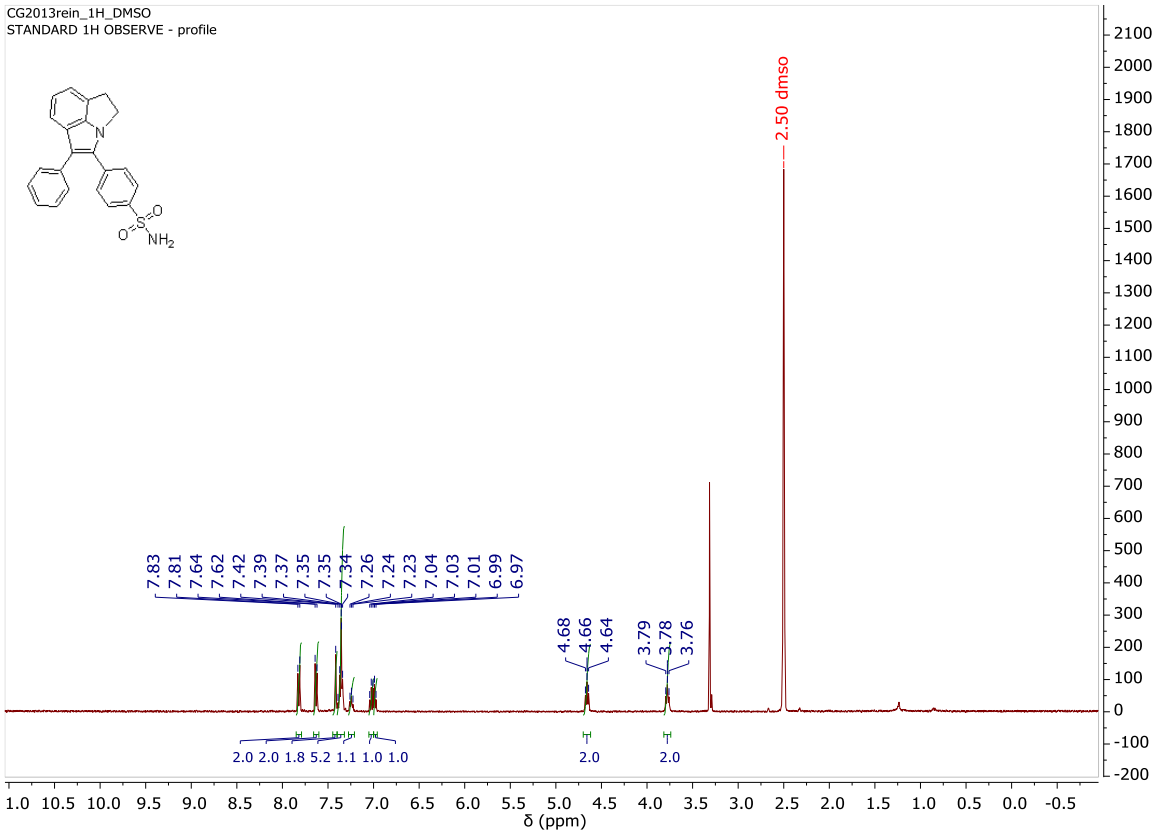


Figure S1. ^{1}H NMR spectrum of compound **1a** in DMSO-d_6

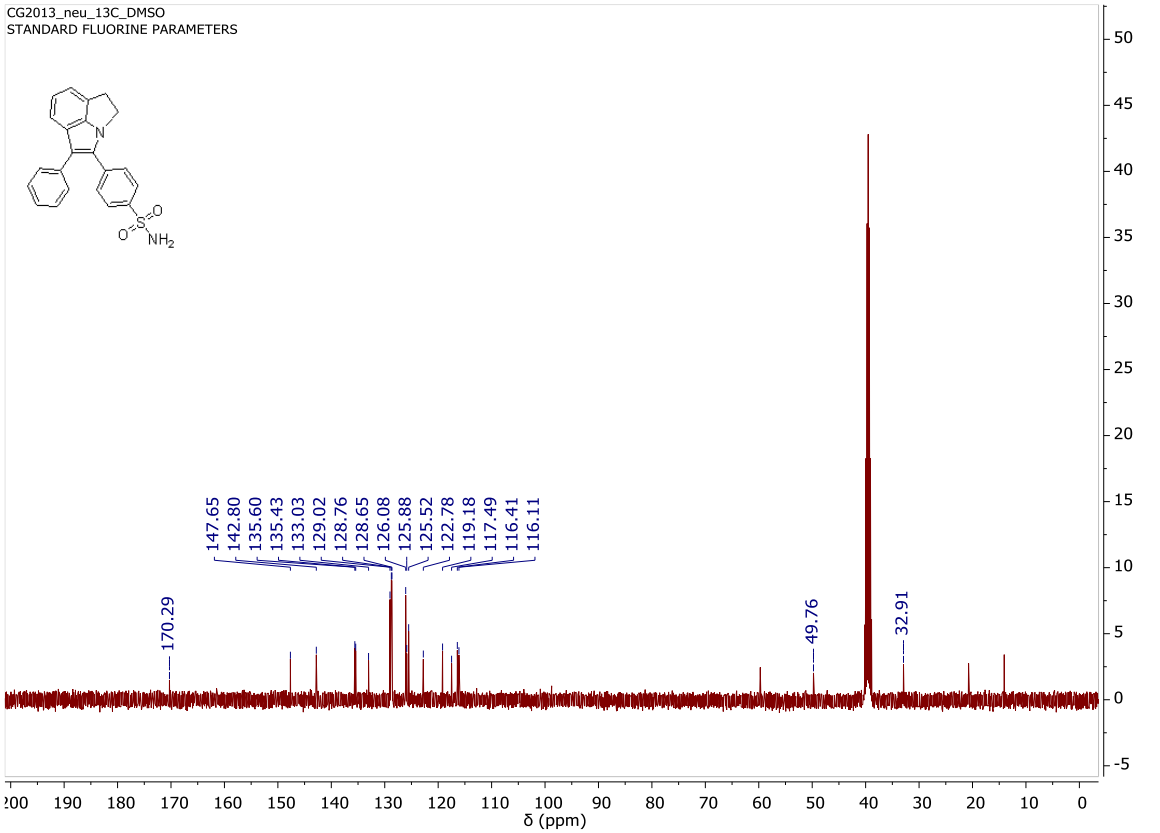
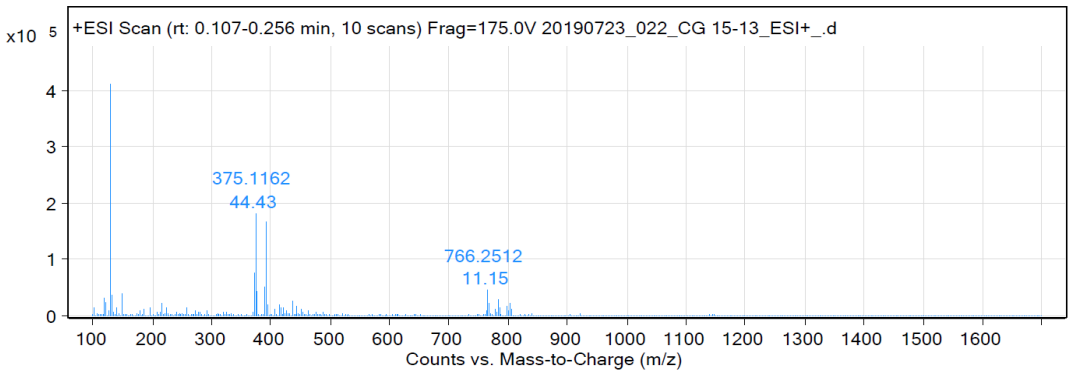


Figure S2. ^{13}C NMR spectrum of compound **1a** in DMSO-d_6



Peak List

m/z	z	Abund
130.1591	1	412724.19
131.1625	1	36210.37
149.0234		40093.52
371.3158	1	76414.01
375.1162	1	183374.05
376.1195	1	44520
388.3421	1	51474.57
391.2844	1	169154.28
392.2877	1	45174.34
766.2512	1	46024.07

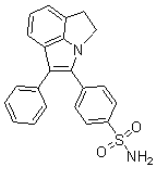


Figure S3. HRMS spectrum of compound **1a**

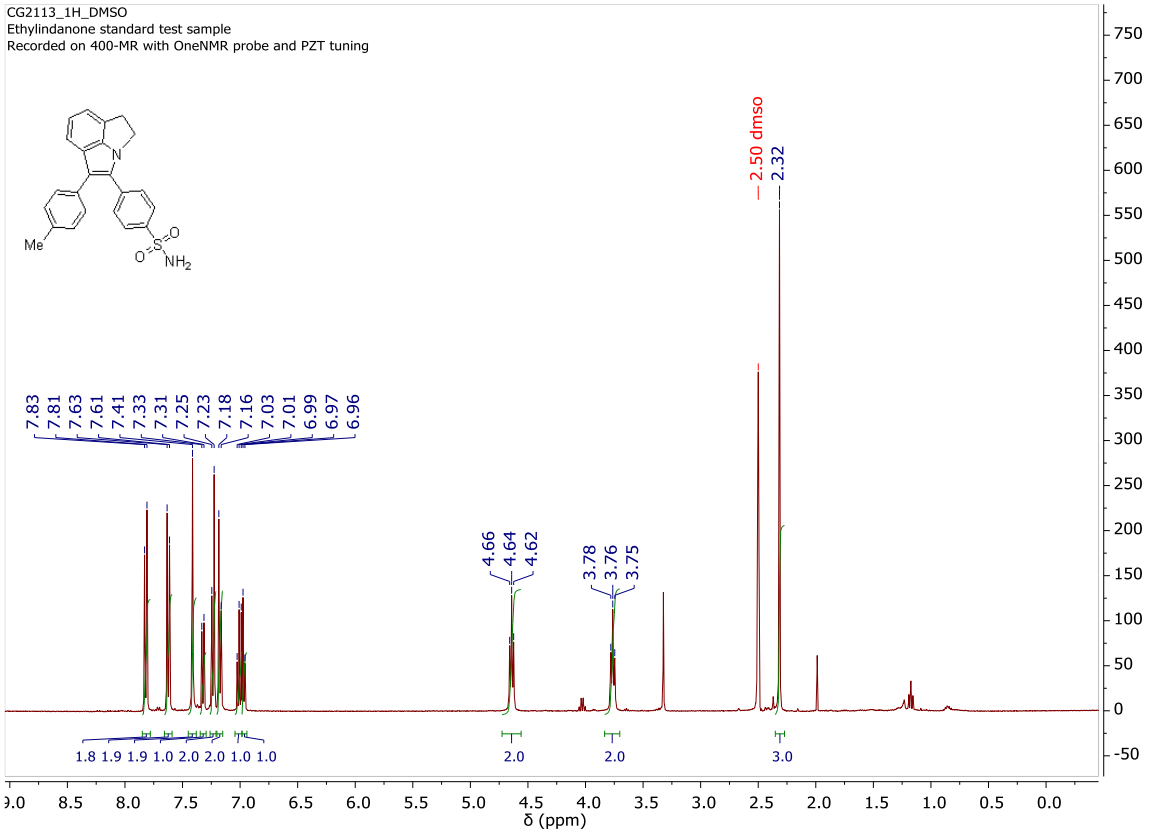


Figure S4. ^{1}H NMR spectrum of compound **1b** in DMSO-d_6

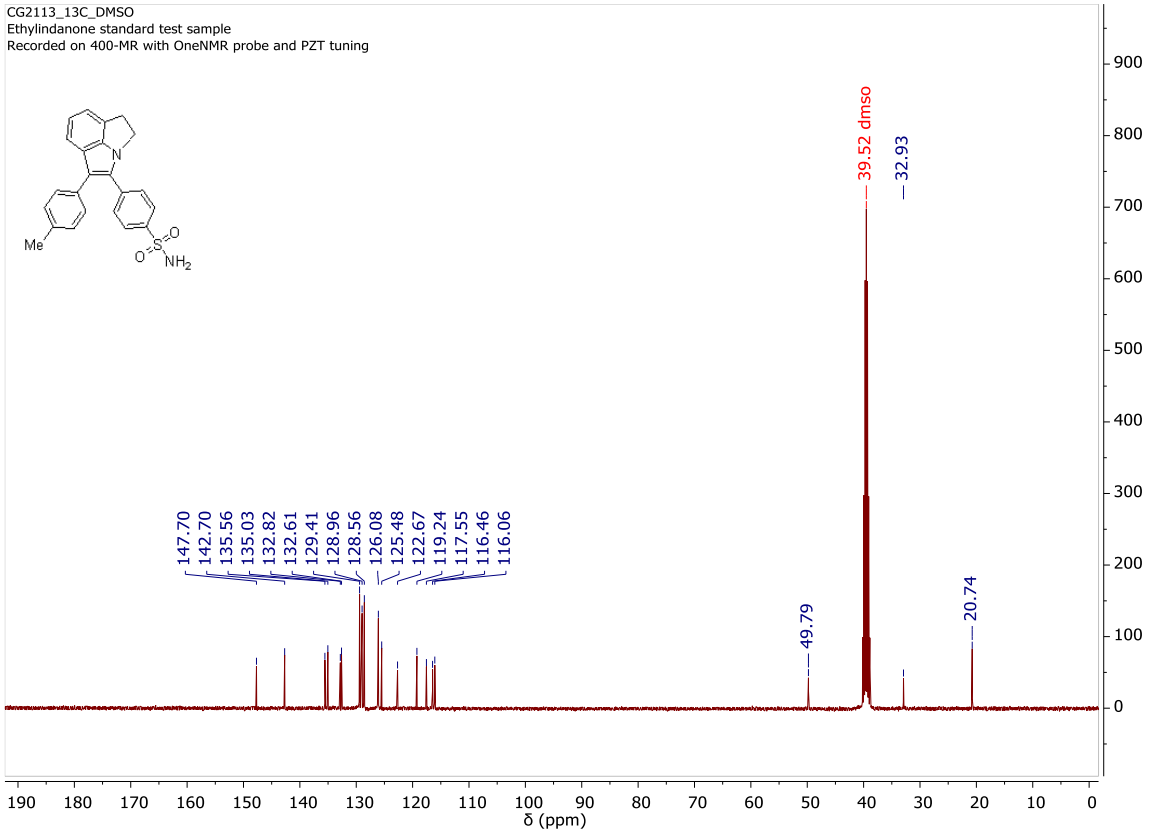
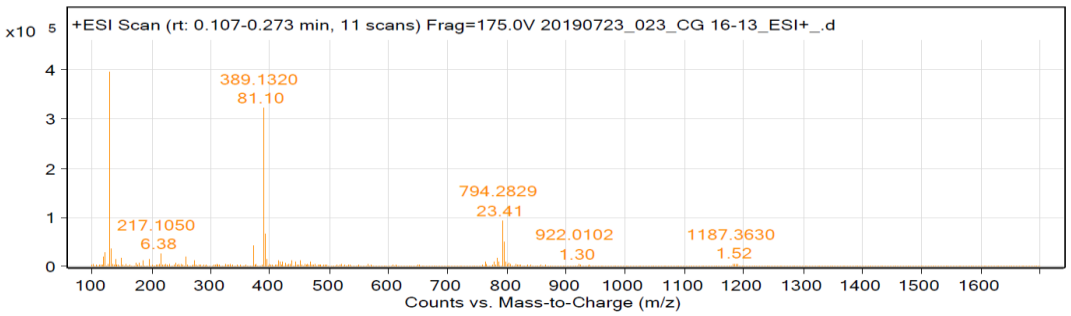


Figure S5. ^{13}C NMR spectrum of compound **1b** in DMSO-d_6



Peak List

m/z	z	Abund
121.0509		28535.96
130.1592	1	396068.91
131.1626	1	36811.17
217.105		25287.13
371.316	1	43780.61
389.132	1	321212.09
390.1352	1	81011.3
391.2845	1	67414.38
794.2829	1	92729.88
795.286	1	49416.65

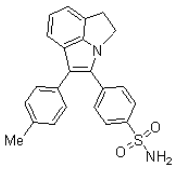


Figure S6. HRMS spectrum of compound **1b**

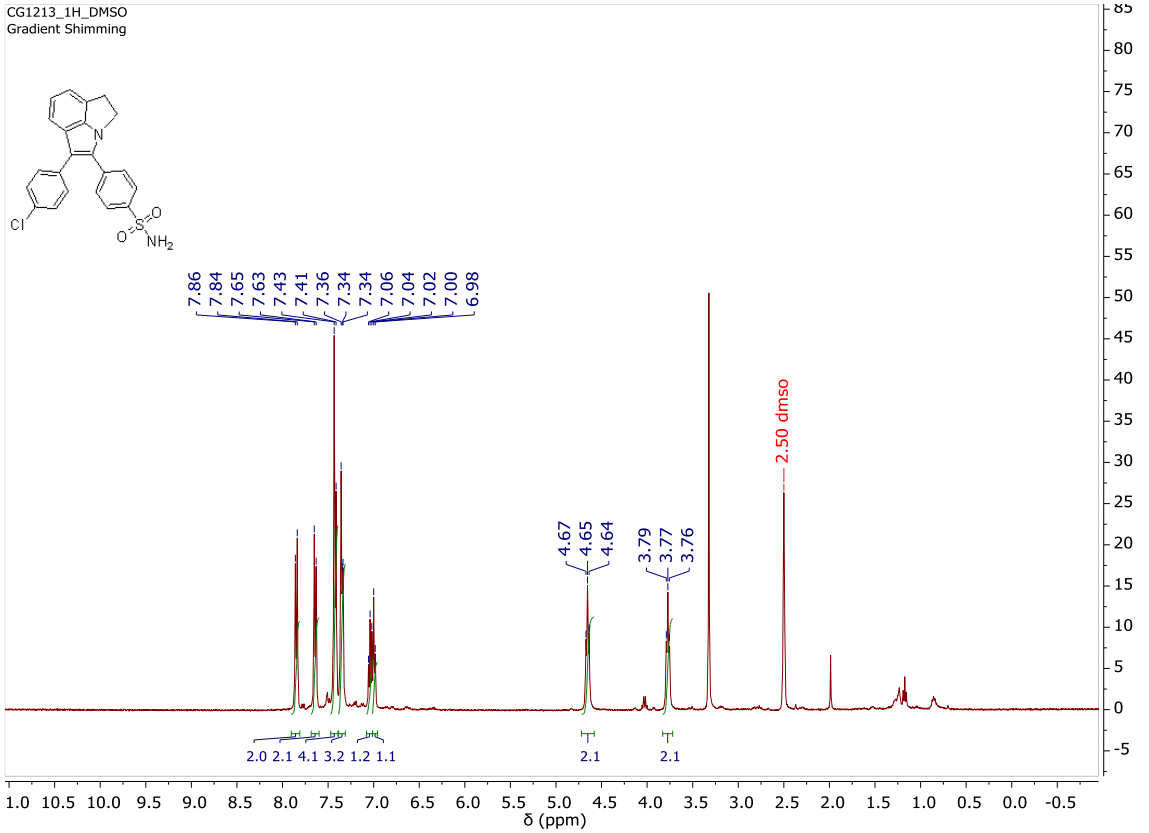


Figure S7. ^{1}H NMR spectrum of compound **1c** in DMSO-d_6

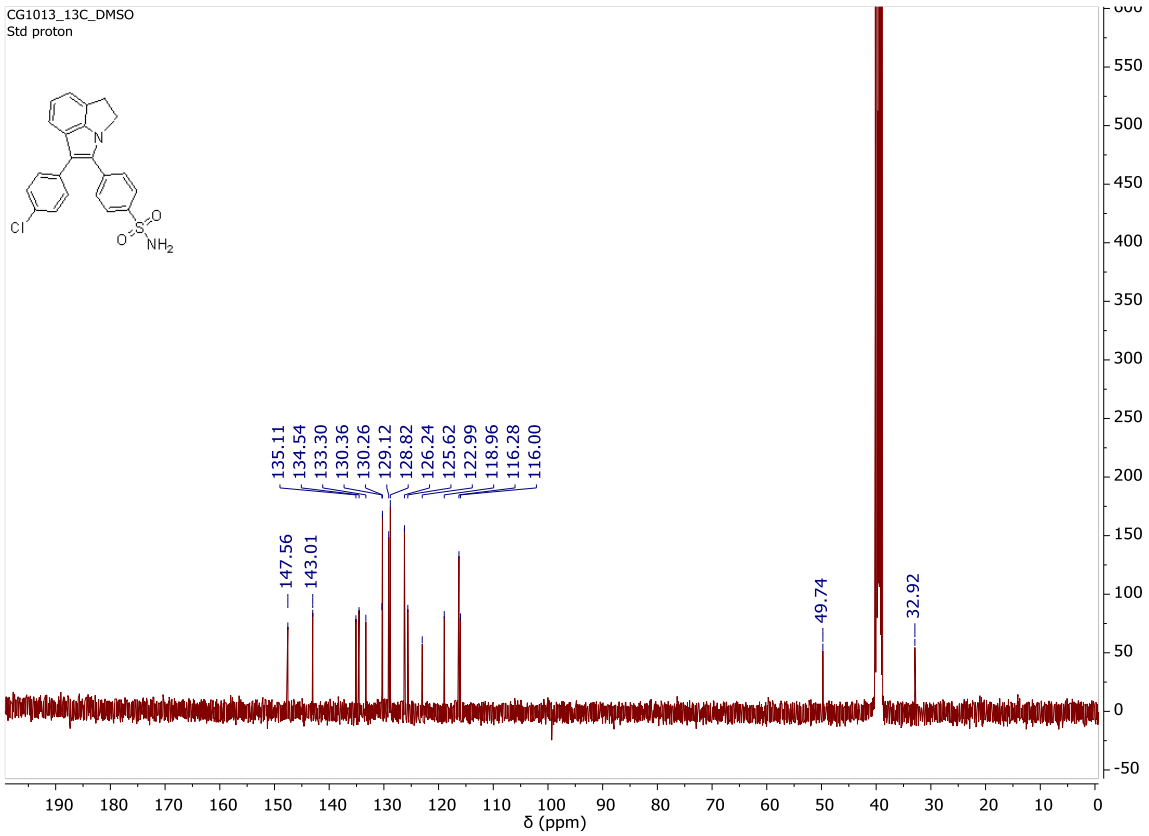
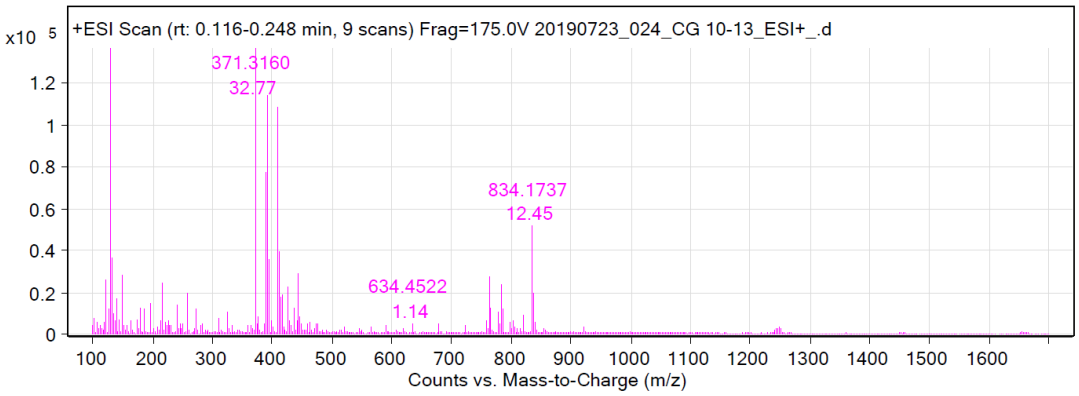


Figure S8. ^{13}C NMR spectrum of compound **1c** in DMSO-d_6



Peak List

m/z	z	Abund
130.1592	1	415979.47
131.1625	1	36817.71
371.316	1	136307.16
388.3424	1	77054.45
391.2845	1	113723.22
393.2975	1	36120.84
409.0773	1	108032.32
411.0745	1	39170.84
834.1737	1	51780
836.1723	1	42403.77

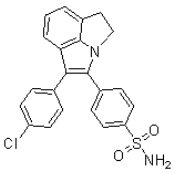


Figure S9. HRMS spectrum of compound **1c**

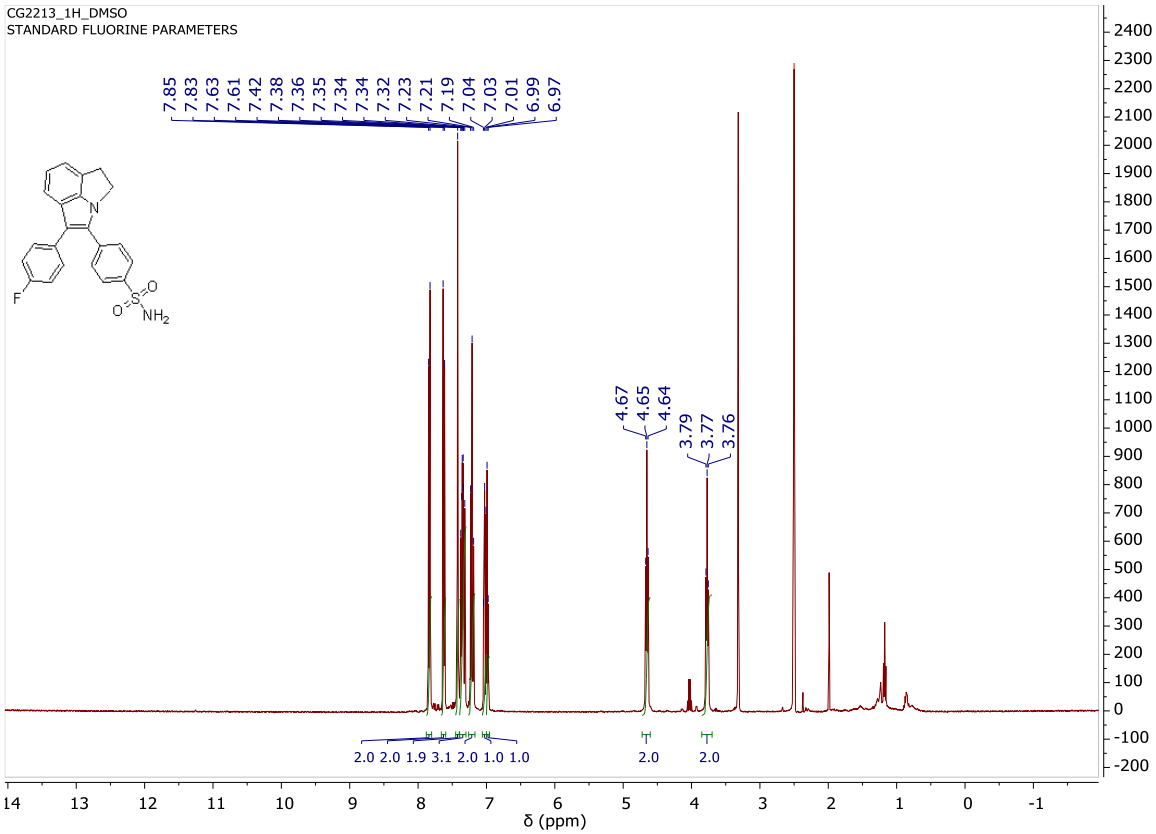


Figure S10. ^{1}H NMR spectrum of compound **1d** in DMSO-d_6

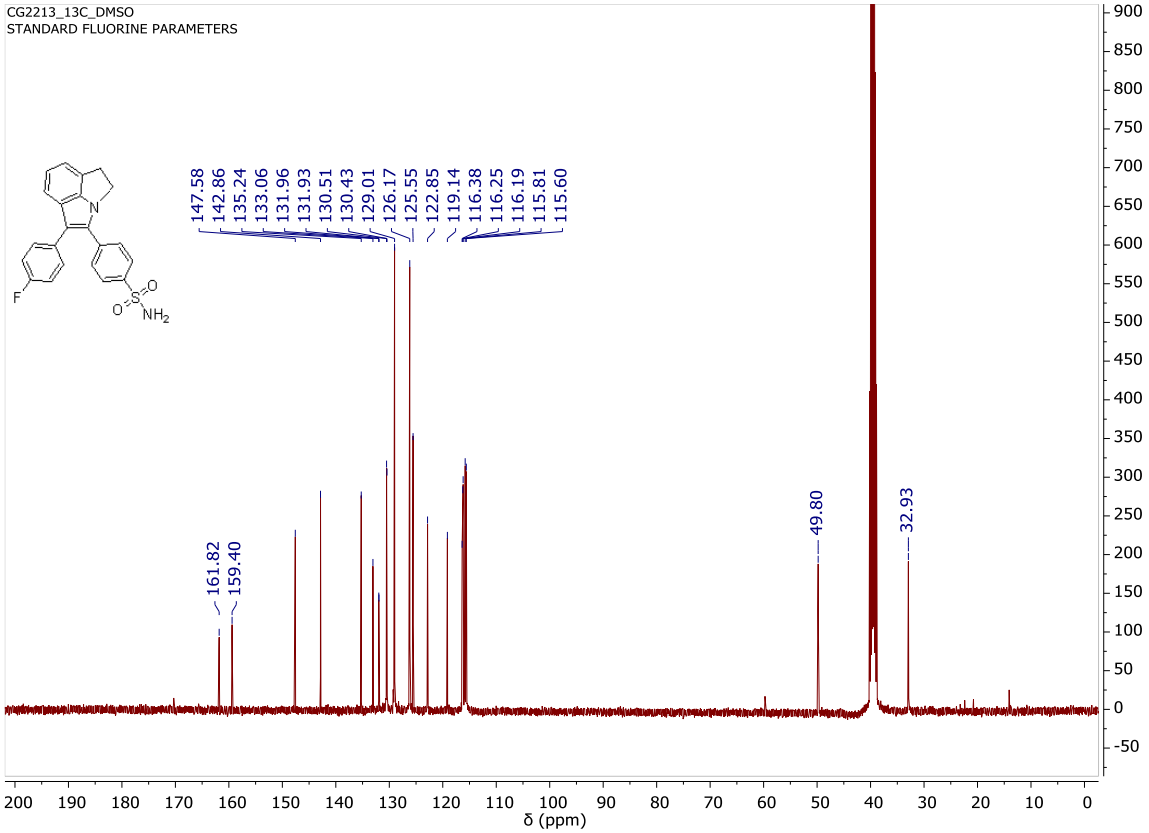


Figure S11. ^{13}C NMR spectrum of compound **1d** in DMSO-d_6

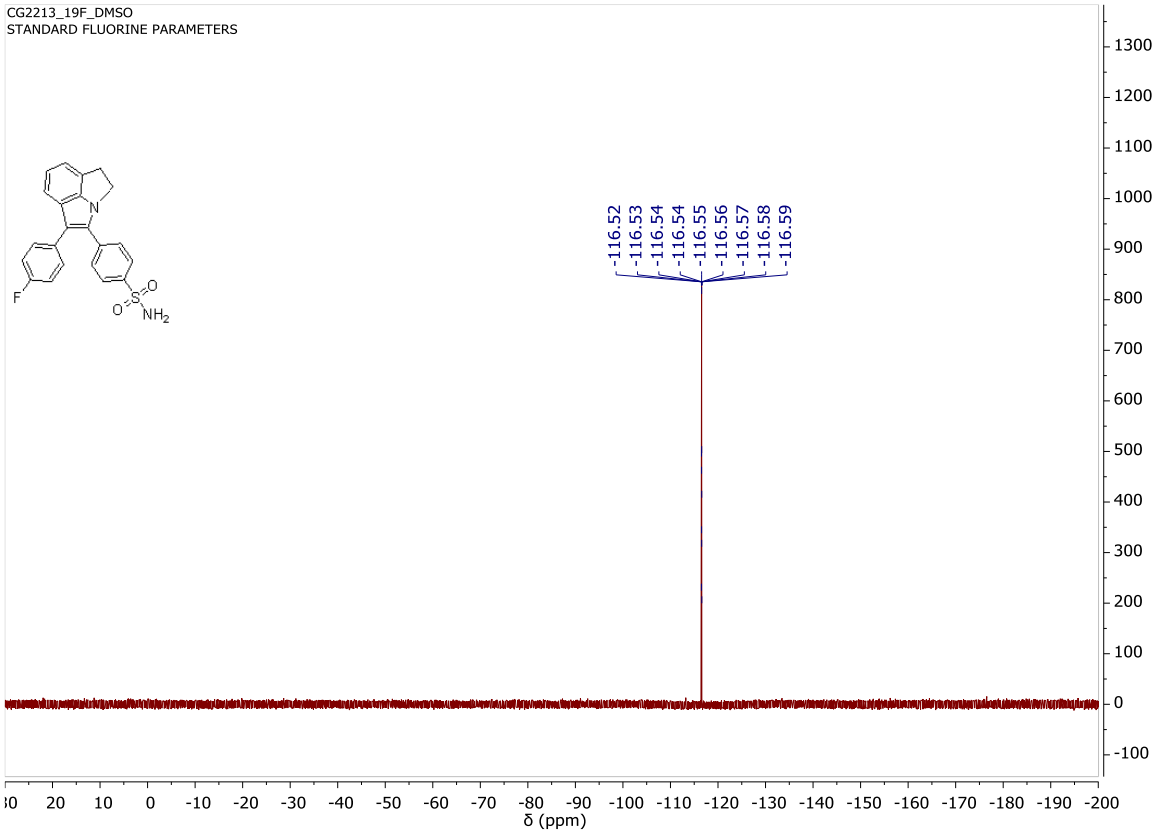
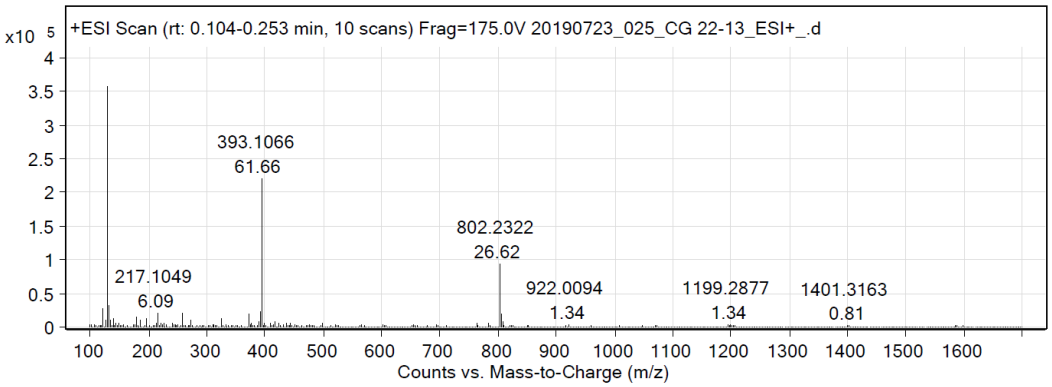


Figure S12. ^{19}F NMR spectrum of compound **1d** in DMSO-d_6



Peak List

m/z	z	Abund
121.0509		26966.77
130.1591	1	357419.66
131.1624	1	31763.78
217.1049		21763
391.2841	1	22836.37
392.0988		21993.41
393.1066	1	220392.3
394.1097	1	53514.43
802.2322	1	95149.47
803.2352	1	46947.27

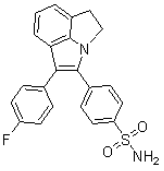


Figure S13. HRMS spectrum of compound **1d**

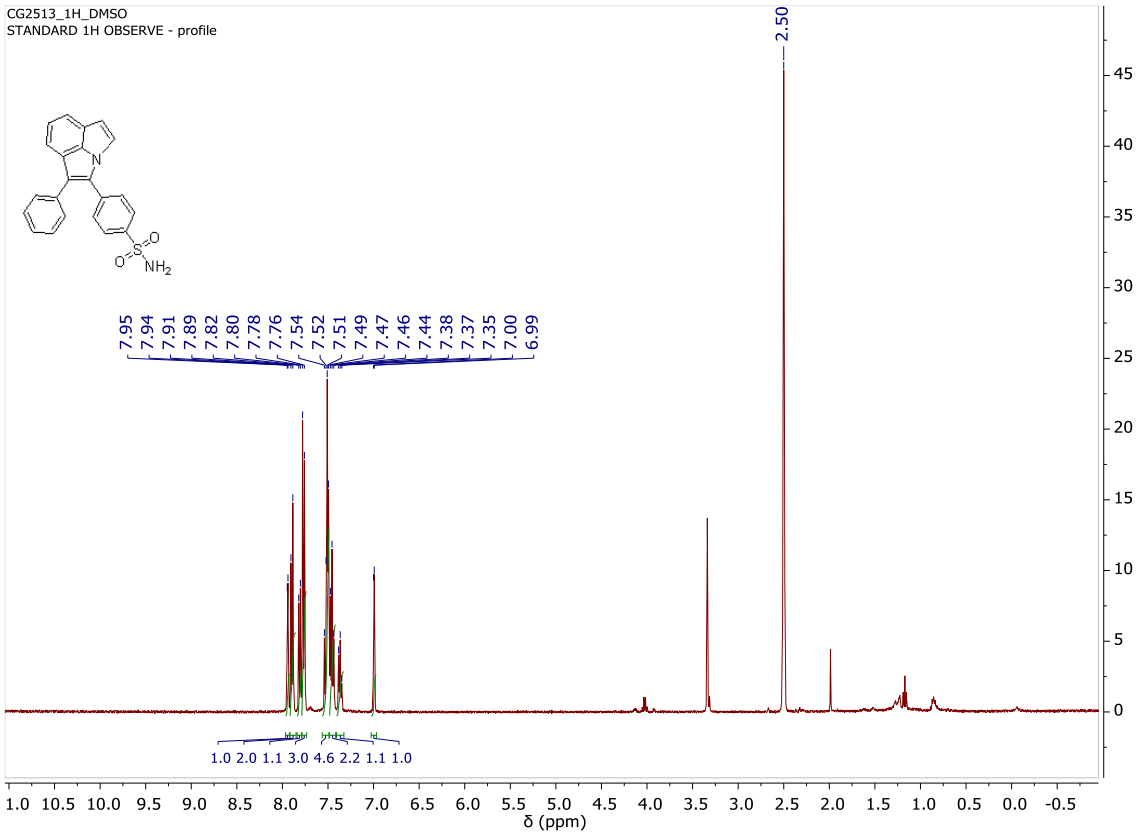


Figure S14. ^{1}H NMR spectrum of compound **2a** in DMSO-d_6

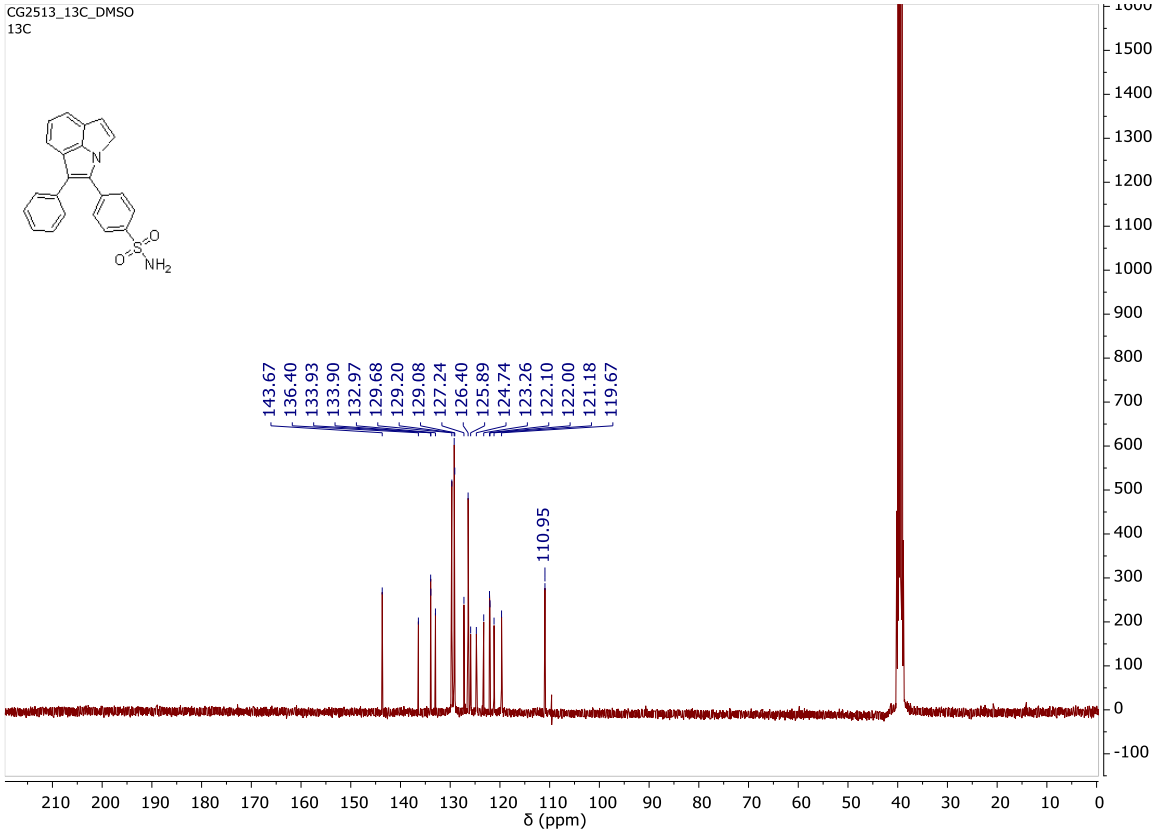
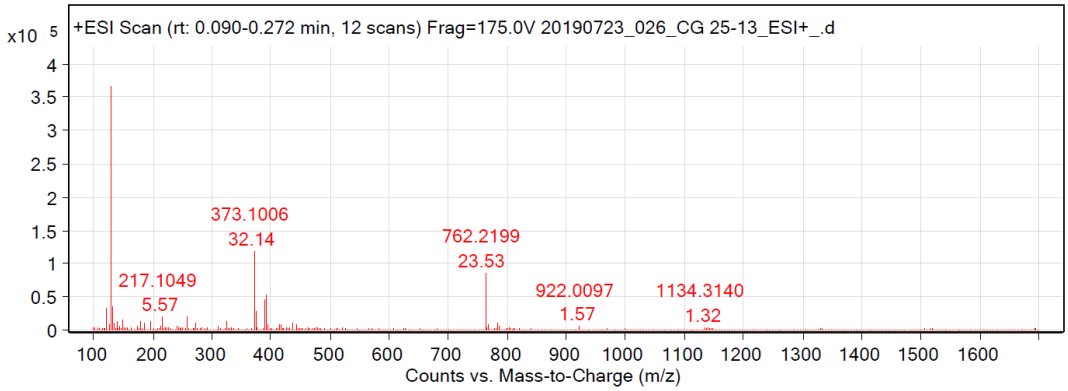


Figure S15. ^{13}C NMR spectrum of compound **2a** in DMSO-d_6



Peak List

m/z	z	Abund
121.0509		32618.89
130.1591	1	366586.25
131.1625	1	34552.07
371.3158	1	32308.4
373.1006	1	117810.12
374.1037	1	29382.16
390.1271	1	46245.35
391.2844	1	52596.21
762.2199	1	86261.83
763.223	1	42440.09

Figure S16. HRMS spectrum of compound **2a**

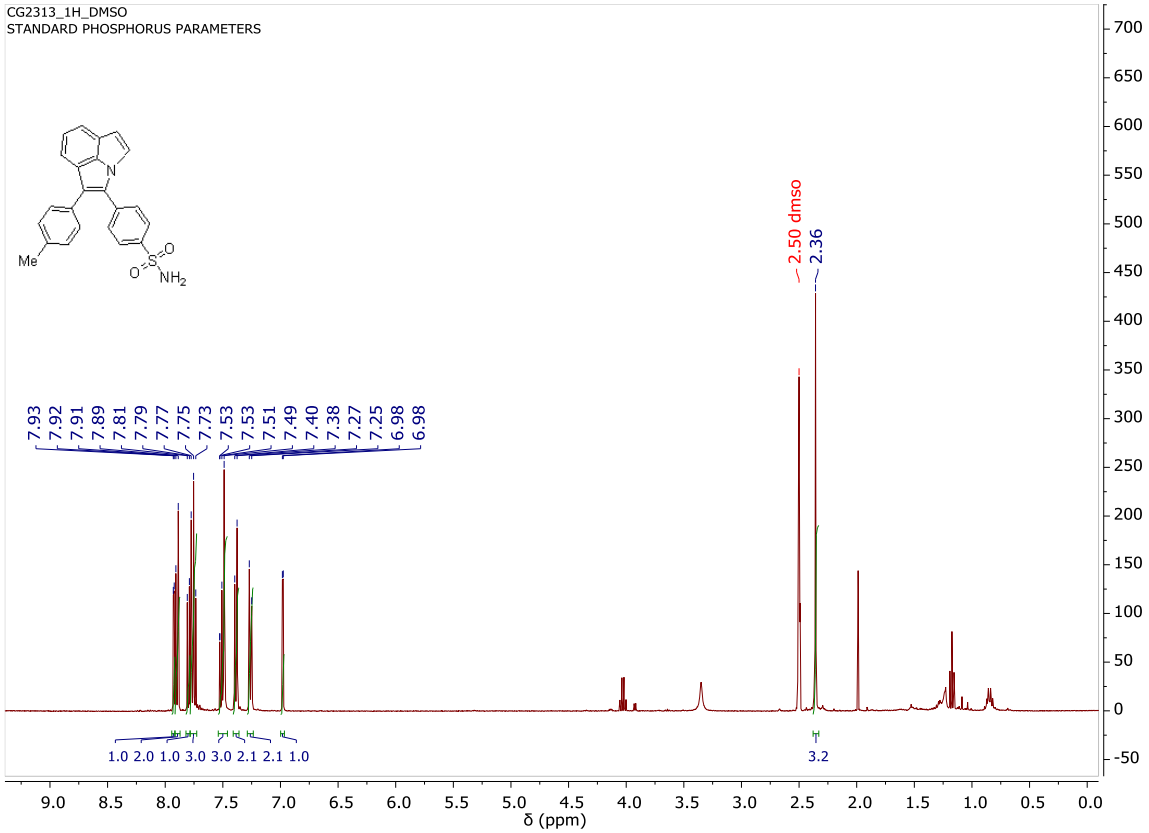


Figure S17. ^{1}H NMR spectrum of compound **2b** in DMSO-d_6

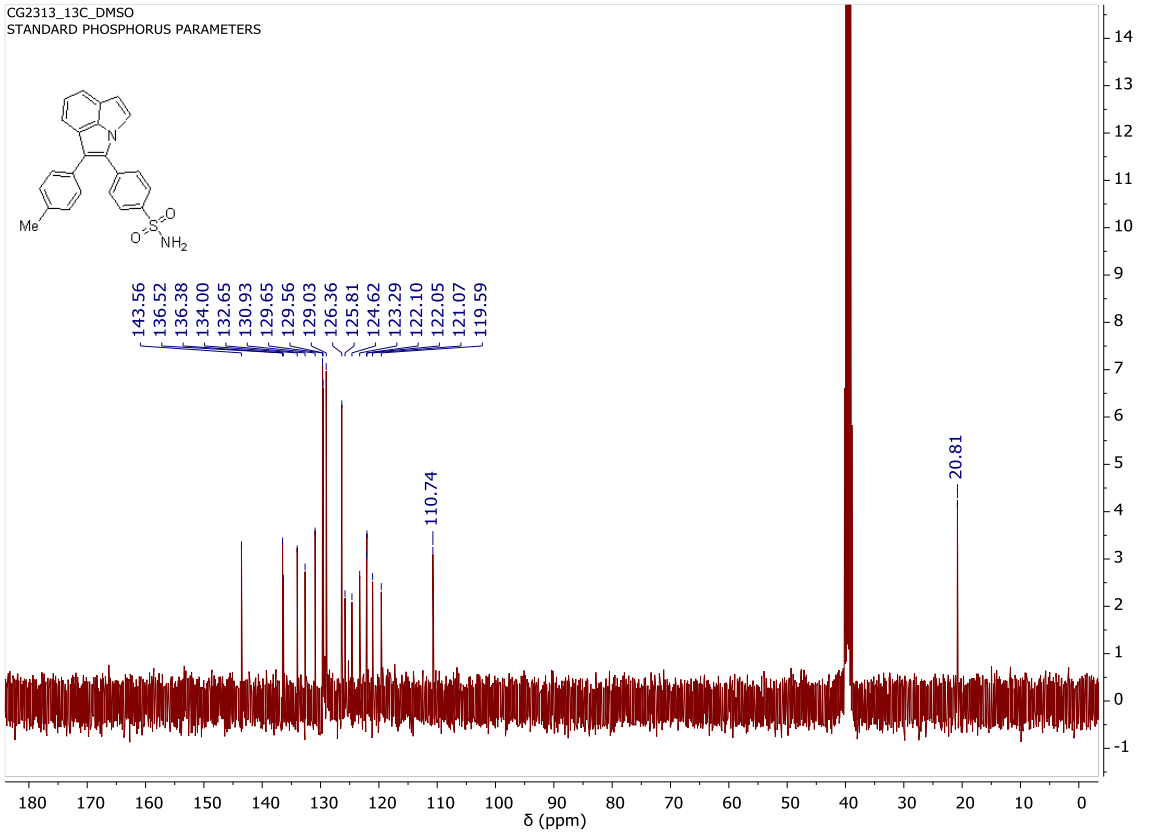
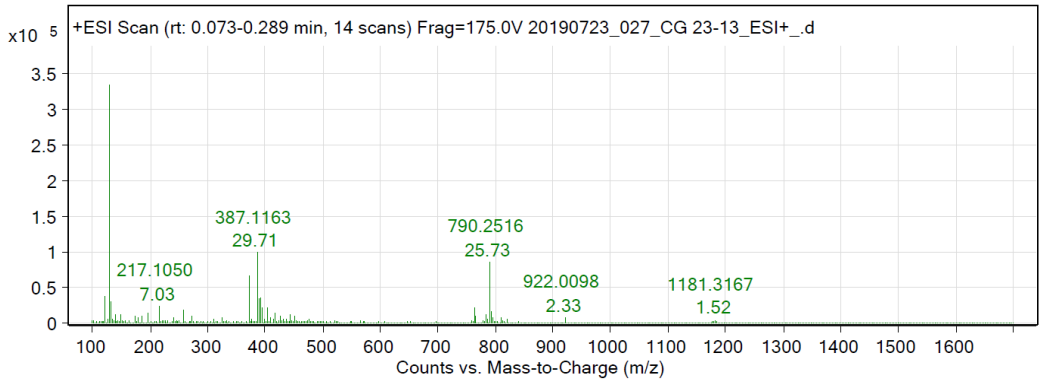


Figure S18. ^{13}C NMR spectrum of compound **2b** in DMSO-d_6



Peak List

m/z	z	Abund
121.0509		38264.94
130.1591	1	334447.66
131.1625	1	30977.04
371.3158	1	65639.97
387.1163	1	99357.01
388.1195	1	24373.81
388.3423	1	34945.52
391.2845	1	35373.11
790.2516	1	86056.86
791.2546	1	44931.02

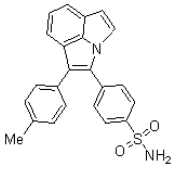


Figure S19. HRMS spectrum of compound **2b**

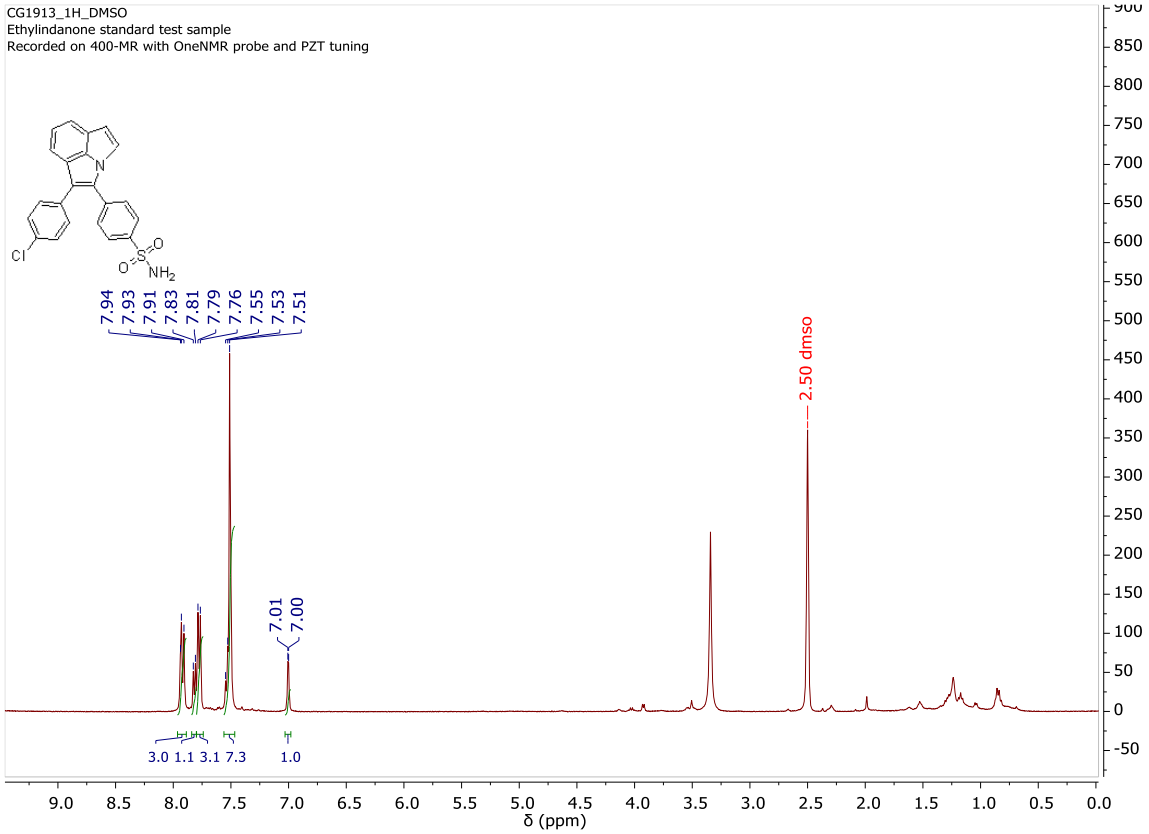


Figure S20. ^{1}H NMR spectrum of compound **2c** in DMSO-d_6

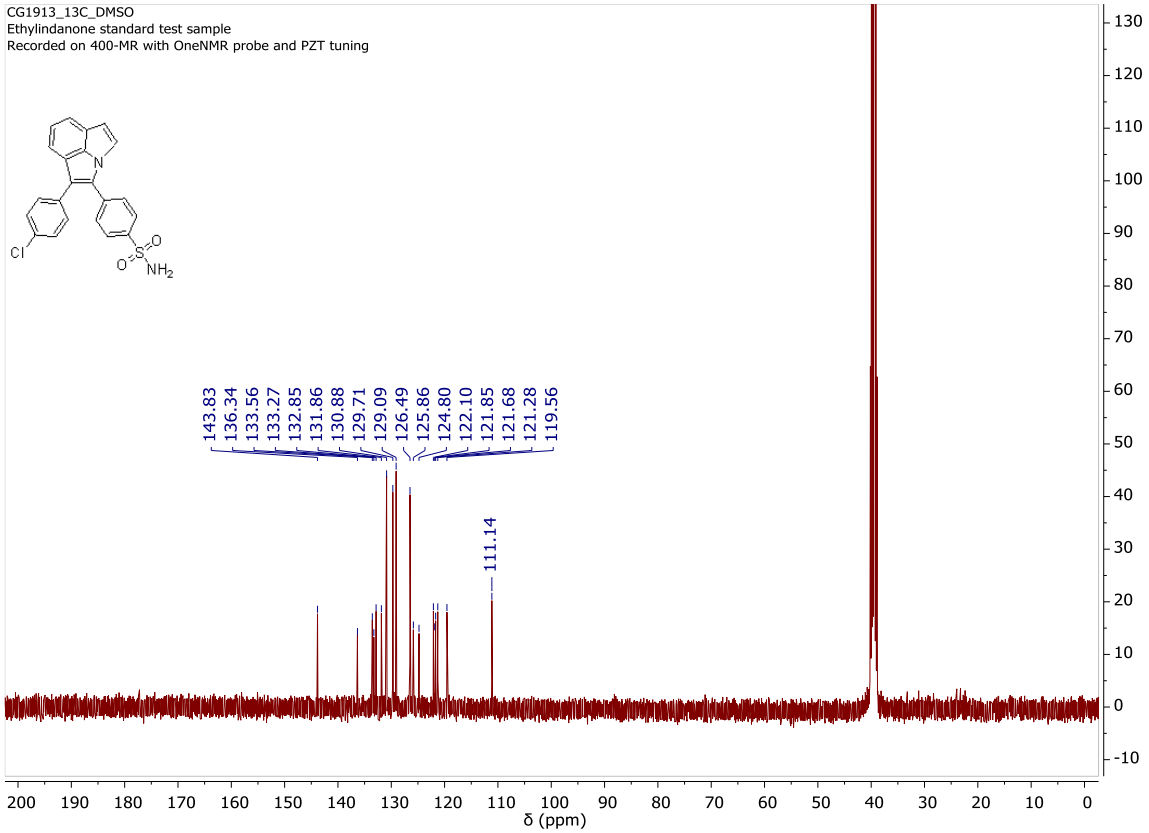
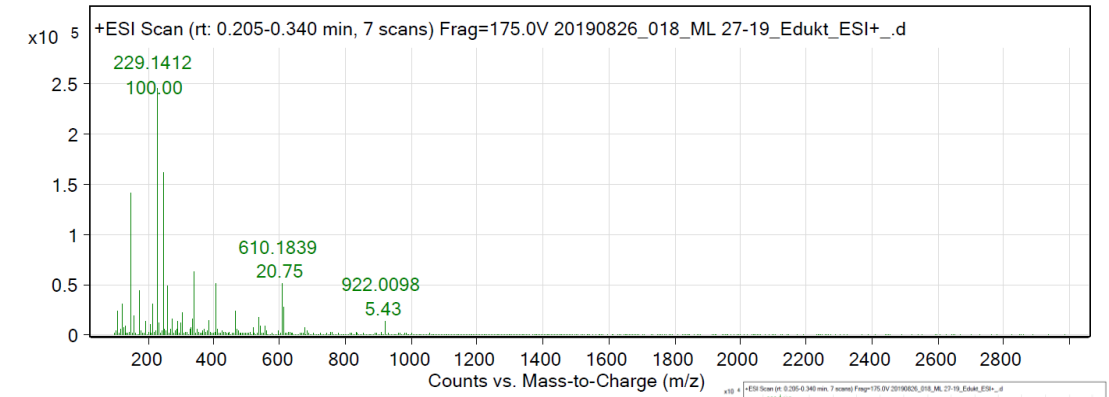
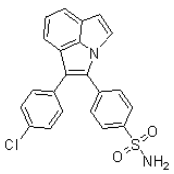


Figure S21. ^{13}C NMR spectrum of compound **2c** in DMSO-d_6



Peak List

m/z	z	Abund
121.0509		30939.54
149.0234	1	141272.8
177.0547	1	44773.76
217.1048		31618.14
229.1412	1	246345.47
245.0786	1	162709.48
261.1311	1	49169.85
338.3418	1	63847.57
407.0613	1	51024.46
610.1839	1	51125.37



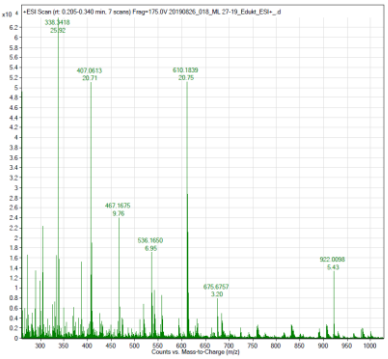


Figure S22. HRMS spectrum of compound **2c**

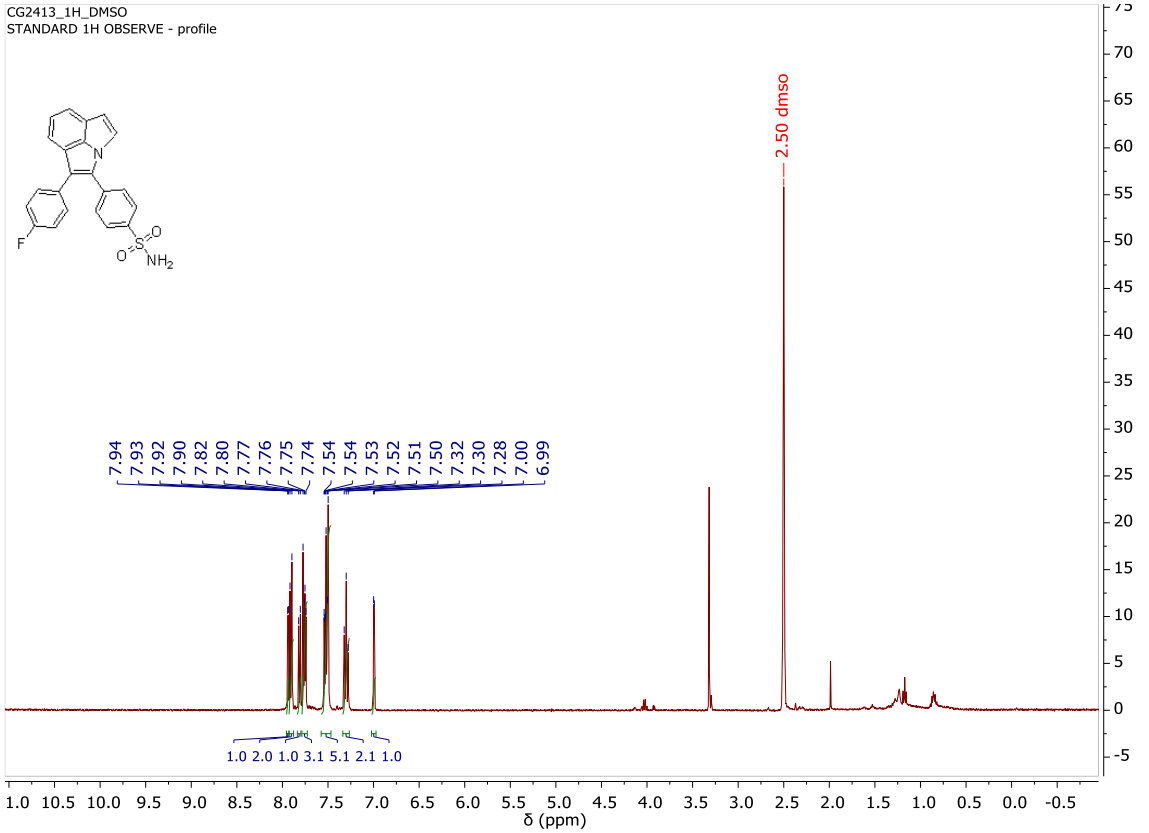


Figure S23. ^{1}H NMR spectrum of compound **2d** in DMSO-d_6

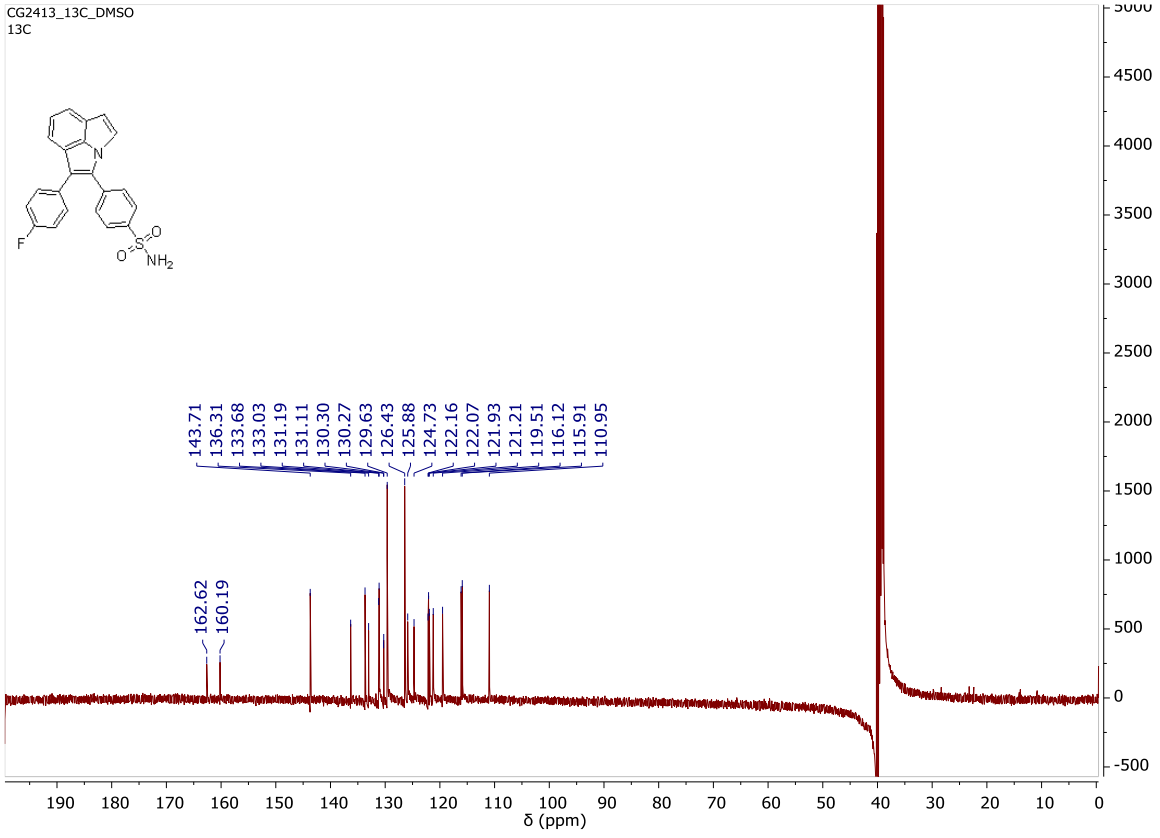


Figure S24. ^{13}C NMR spectrum of compound **2d** in DMSO-d_6

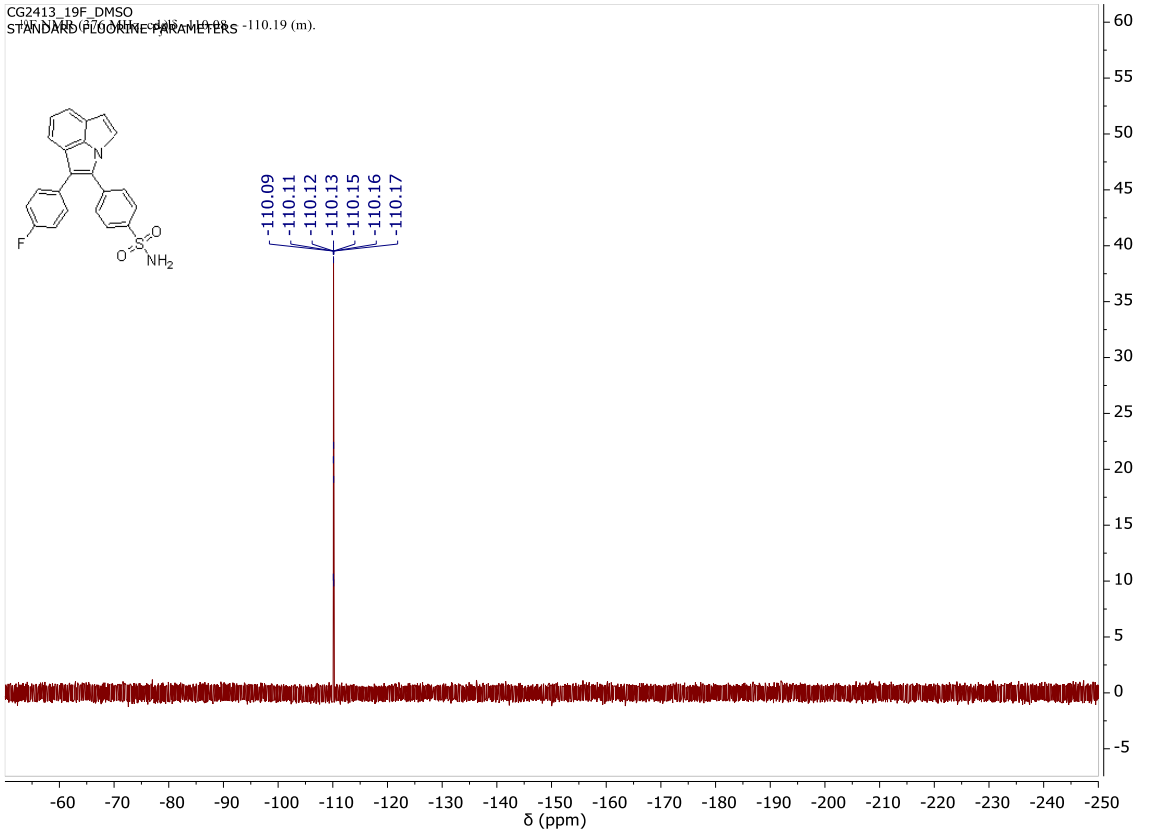
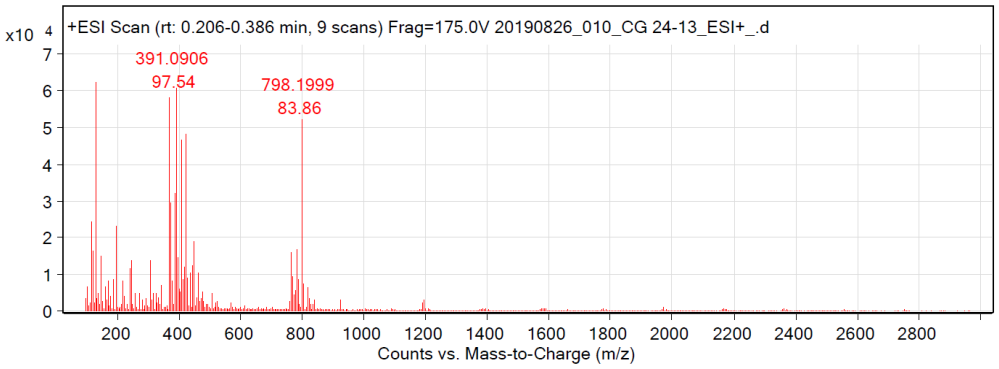


Figure S25. ^{19}F NMR spectrum of compound **2d** in DMSO-*d*$_6$



Peak List

m/z	z	Abund
130.159	1	62308.33
371.3151	1	58025.08
376.259	1	29556.12
388.3415	1	32174.27
391.0906	1	60777.33
391.2837	1	52361.62
393.2876	1	53565.48
408.117	1	46610.83
421.3167	1	48193.05
798.1999	1	52254.48

Figure S26. HRMS spectrum of compound **2d**

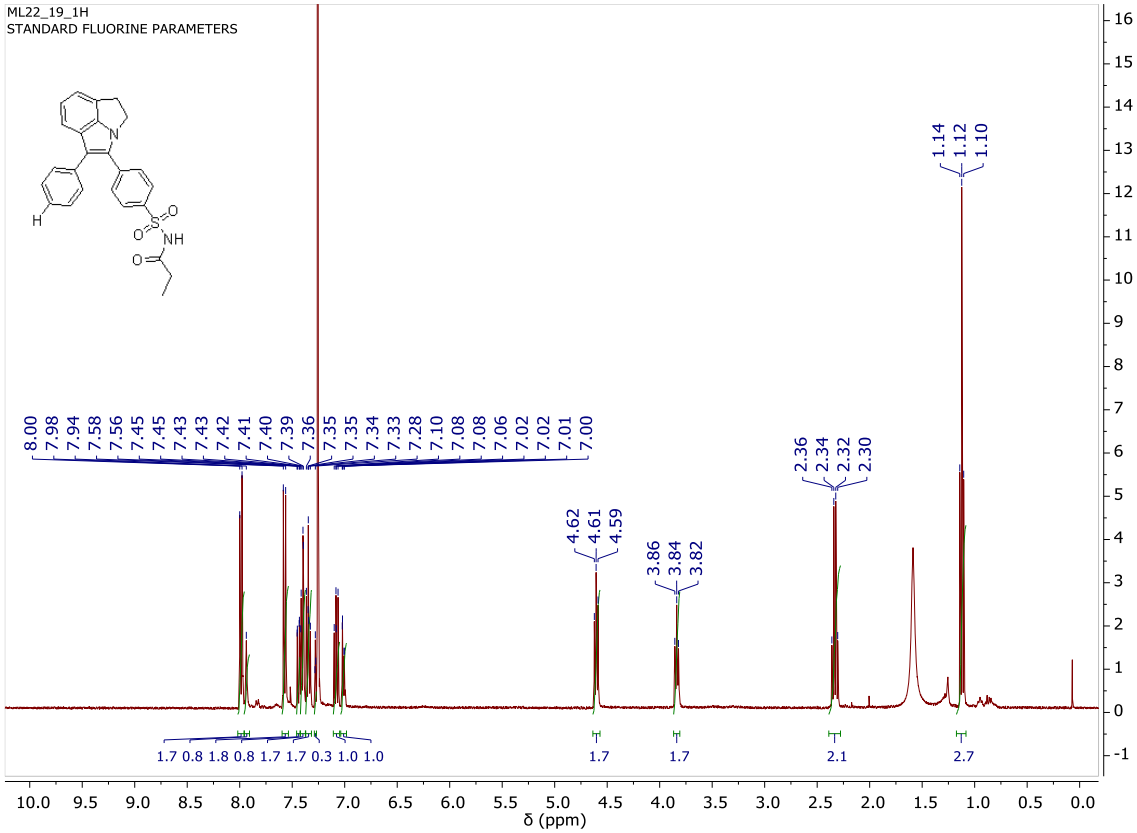


Figure S27. ^{1}H NMR spectrum of compound **3a** in $CDCl_3$

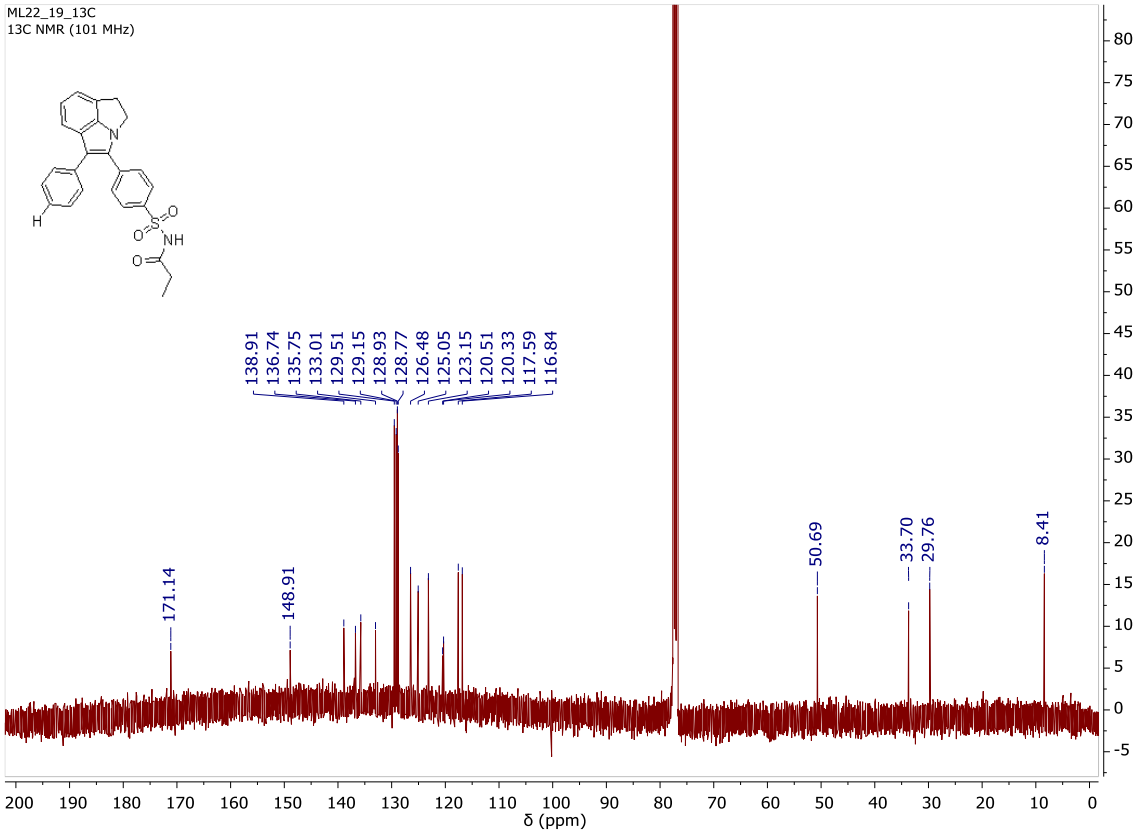
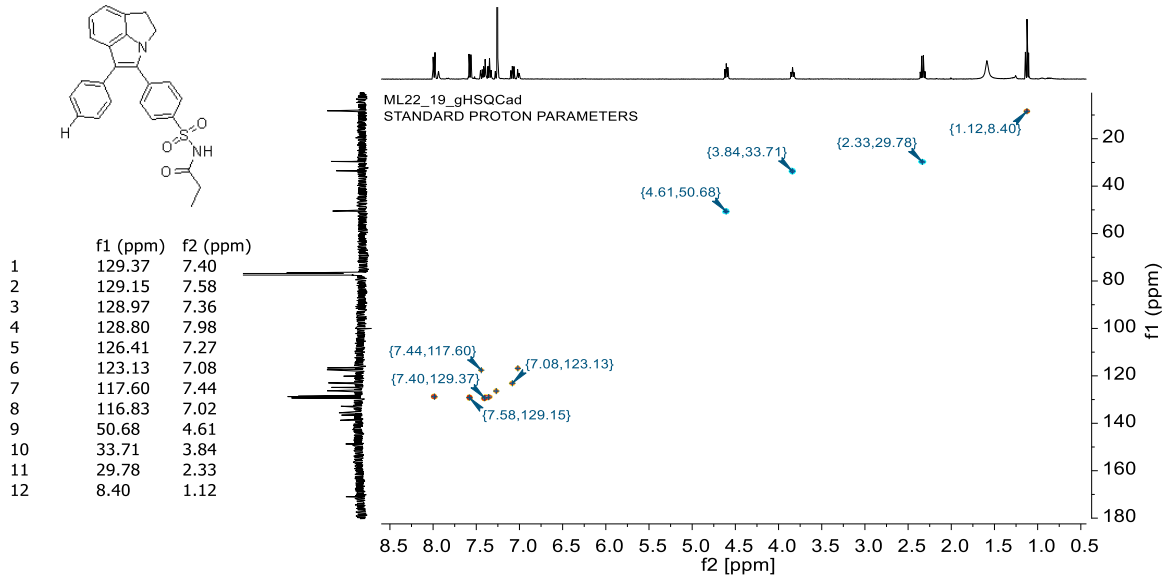
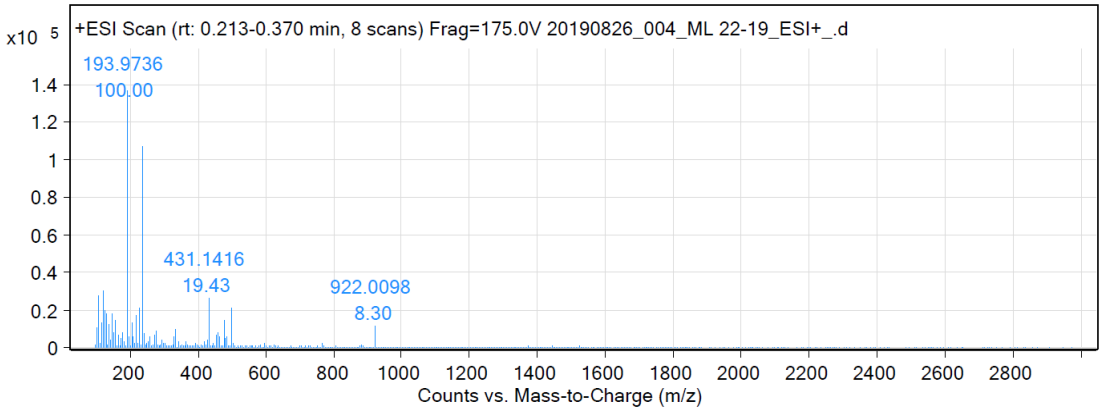


Figure S28. ^{13}C NMR spectrum of compound **3a** in $CDCl_3$



	f1 (ppm)	f2 (ppm)
1	129.37	7.40
2	129.15	7.58
3	128.97	7.36
4	128.80	7.98
5	126.41	7.27
6	123.13	7.08
7	117.60	7.44
8	116.83	7.02
9	50.68	4.61
10	33.71	3.84
11	29.78	2.33
12	8.40	1.12

Figure S29. HSQC spectrum of compound **3a** in $CDCl_3$



Peak List

m/z	z	Abund
106.0044		27924.8
121.0509		30735.99
125.9862		19984.91
130.159		18119.27
147.0308		17996.67
193.9736	1	136905.94
229.1408	1	21039.79
235.0002	1	107047.13
431.1416	1	26596.59
500.9322	1	21391.08

Figure S30. HRMS spectrum of compound **3a**

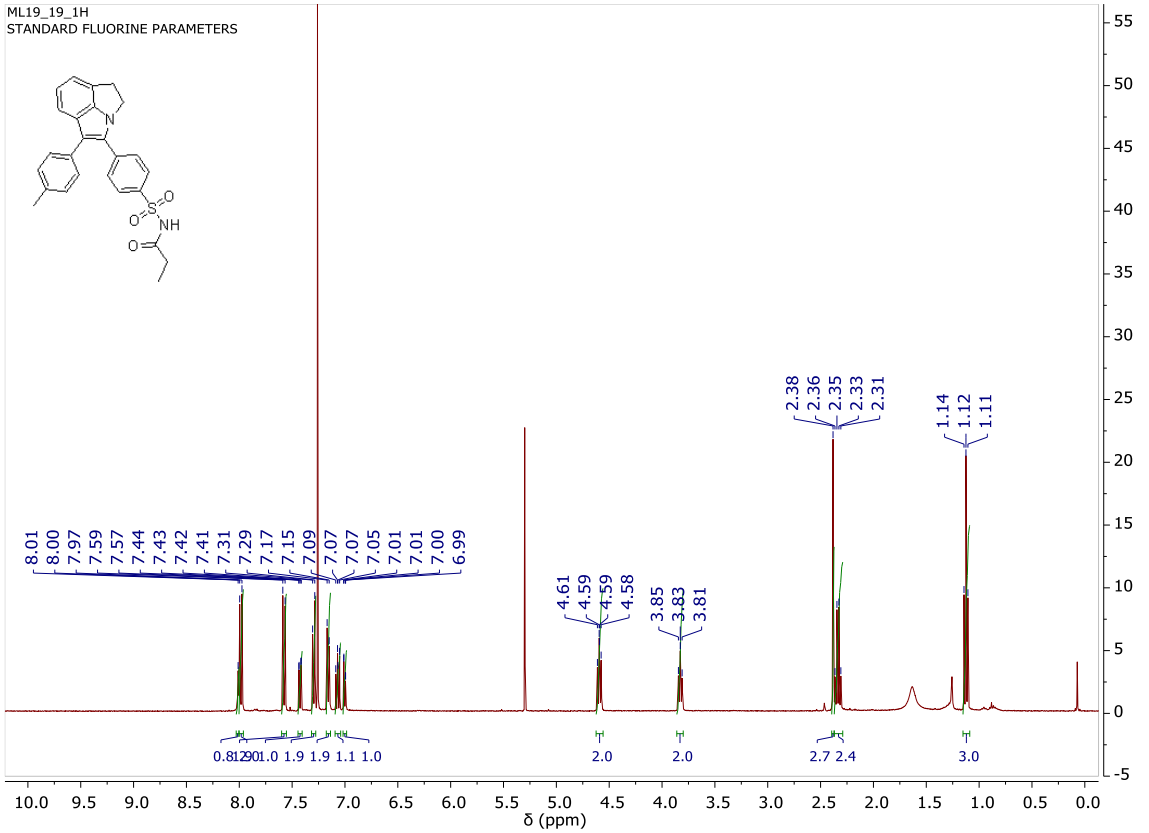


Figure S31. ^{1}H NMR spectrum of compound **3b** in $CDCl_3$

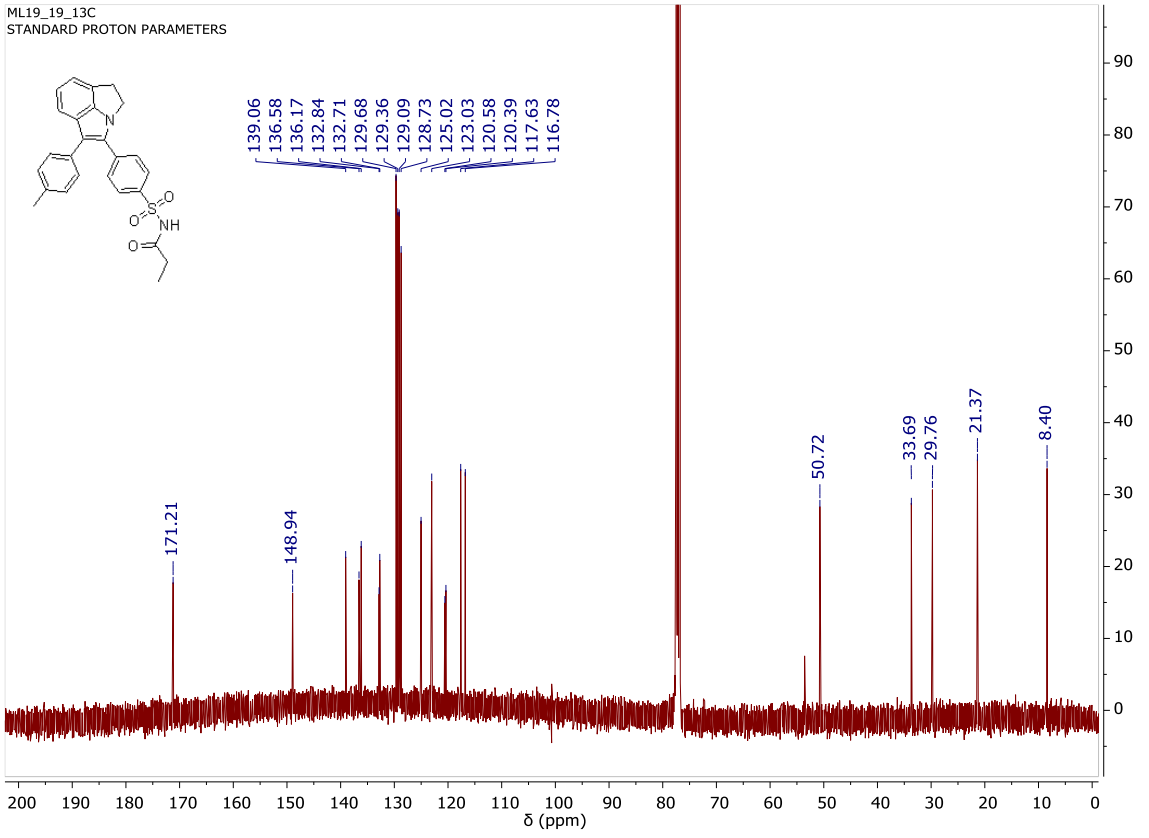
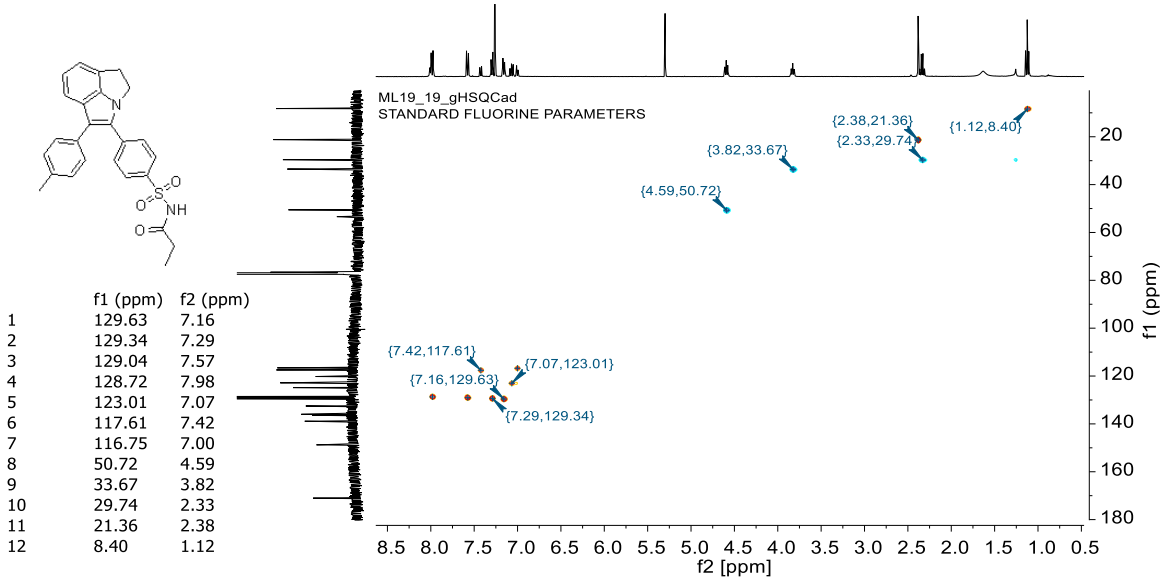
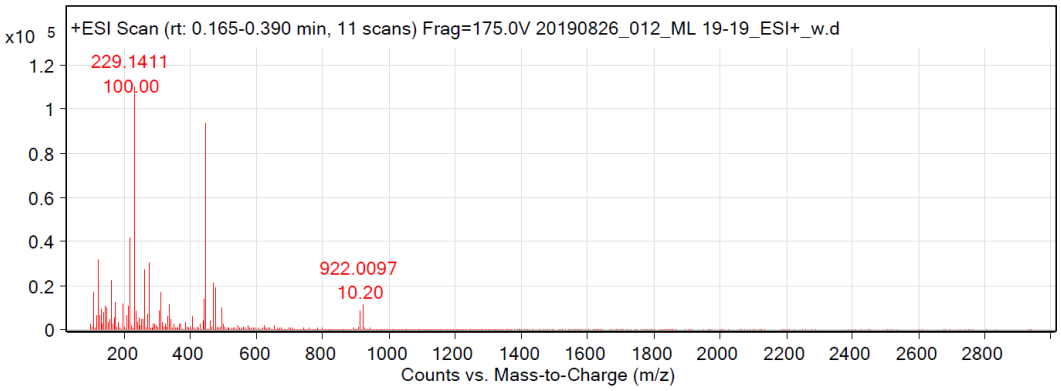


Figure S32. ^{13}C NMR spectrum of compound **3b** in $CDCl_3$



	f1 (ppm)	f2 (ppm)
1	129.63	7.16
2	129.34	7.29
3	129.04	7.57
4	128.72	7.98
5	123.01	7.07
6	117.61	7.42
7	116.75	7.00
8	50.72	4.59
9	33.67	3.82
10	29.74	2.33
11	21.36	2.38
12	8.40	1.12

Figure S33. HSQC spectrum of compound **3b** in $CDCl_3$



Peak List

m/z	z	Abund
121.0509	1	31624.99
158.964		22749.56
217.1047	1	41589.95
229.1411	1	110270.3
261.131	1	27135.38
273.1673	1	30355.43
445.1576	1	93525.45
446.1606	1	27179.08
467.1395	1	21082.94
477.1475	1	19456.43

Figure S34. HRMS spectrum of compound **3b**

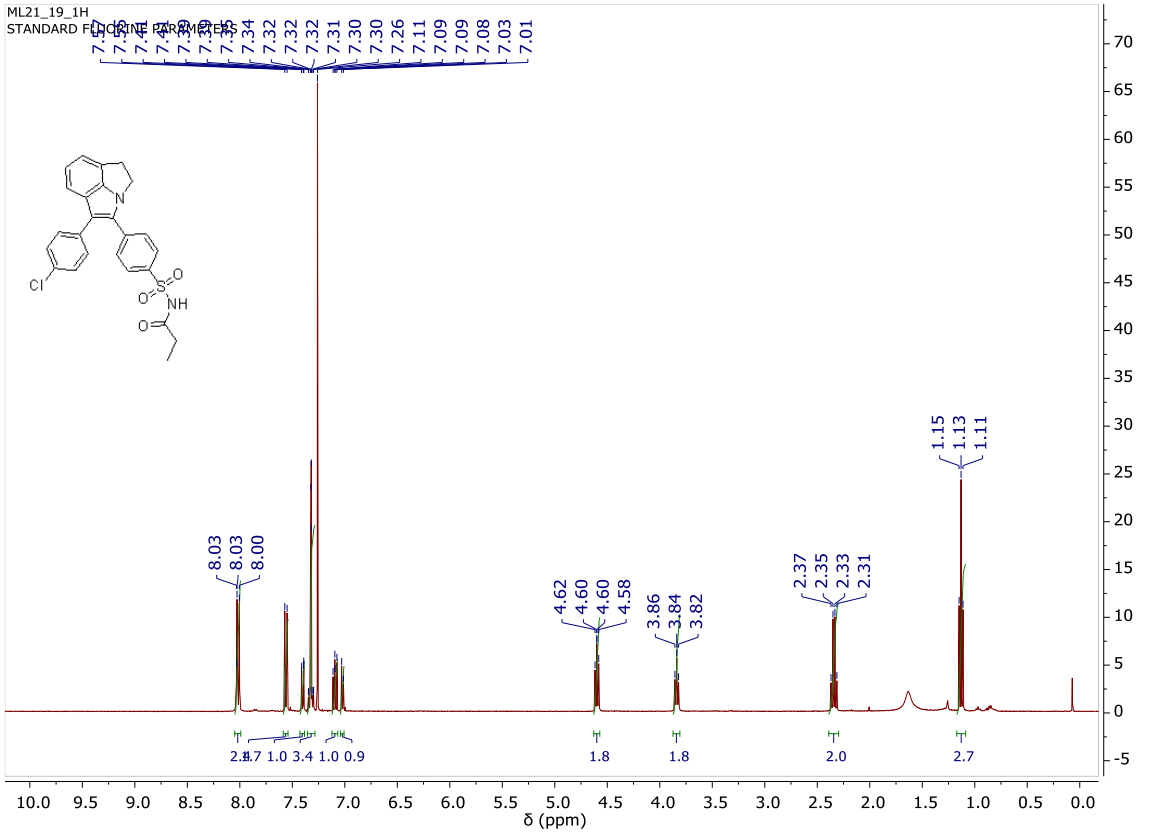


Figure S35. ^{1}H NMR spectrum of compound **3c** in $CDCl_3$

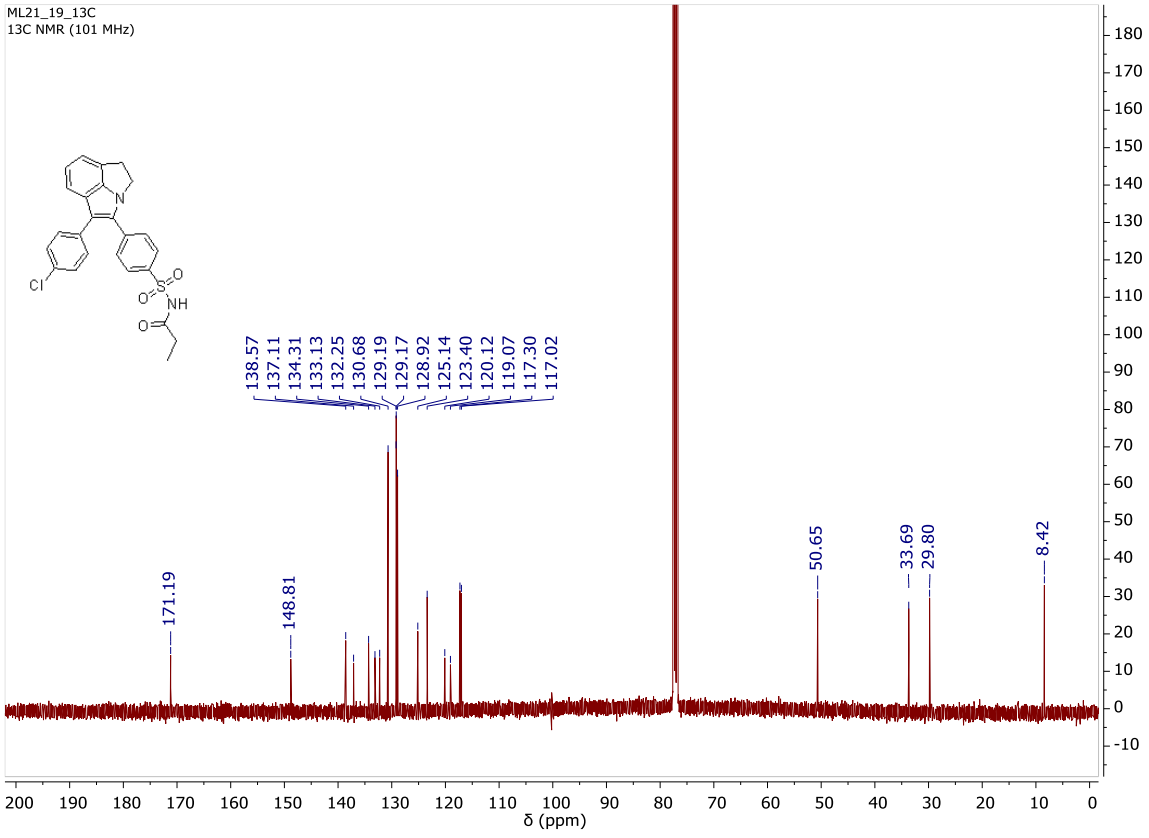
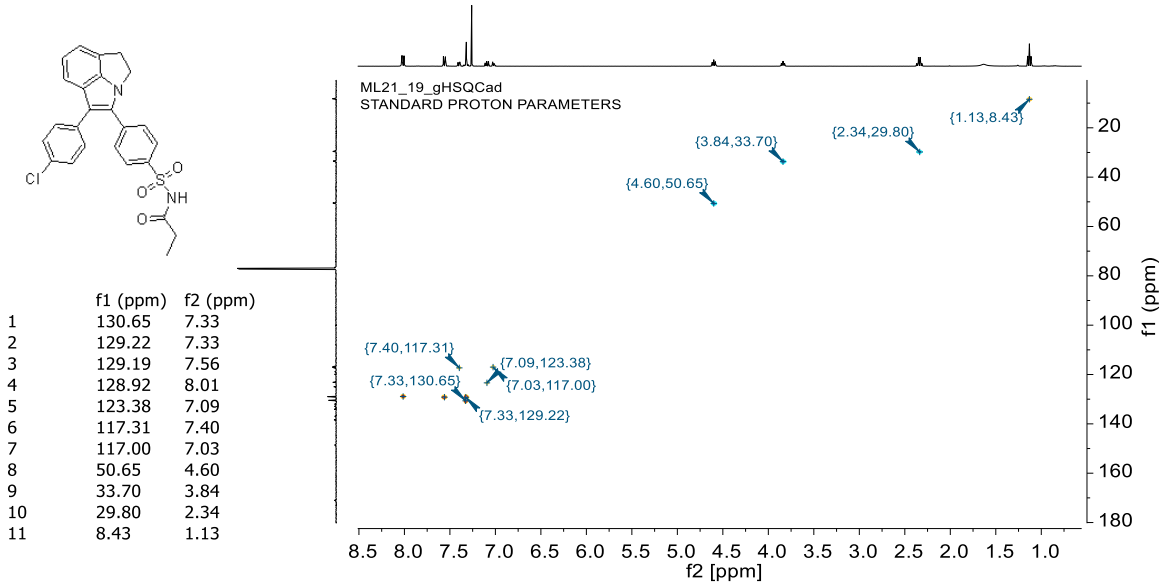
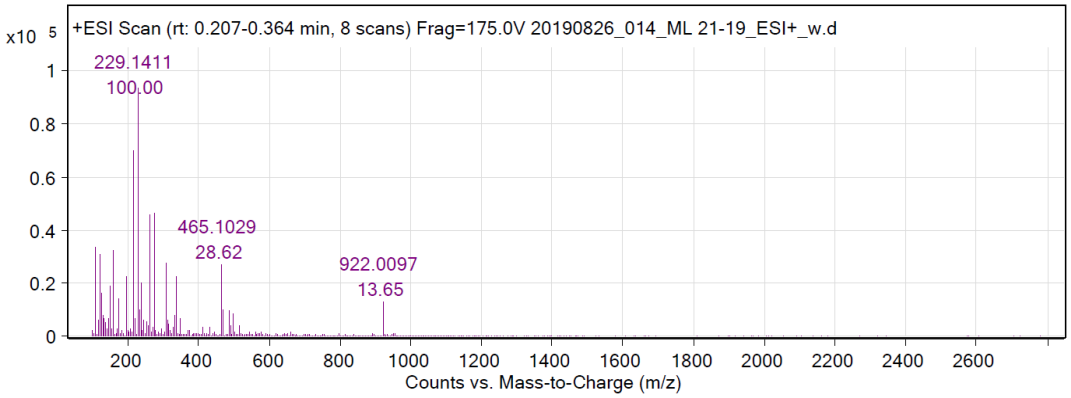


Figure S36. ^{13}C NMR spectrum of compound **3c** in $CDCl_3$



	f1 (ppm)	f2 (ppm)
1	130.65	7.33
2	129.22	7.33
3	129.19	7.56
4	128.92	8.01
5	123.38	7.09
6	117.31	7.40
7	117.00	7.03
8	50.65	4.60
9	33.70	3.84
10	29.80	2.34
11	8.43	1.13

Figure S37. HSQC spectrum of compound **3c** in $CDCl_3$



Peak List

m/z	z	Abund
106.0044		33744.67
121.0509		30595.82
158.964		32376.59
217.1047	1	70016.06
229.1411	1	93579.58
261.131	1	45712.89
273.1672	1	46580.42
305.1571	1	27645.86
335.0042	1	22481
465.1029	1	26784.51

Figure S38. HRMS spectrum of compound **3c**

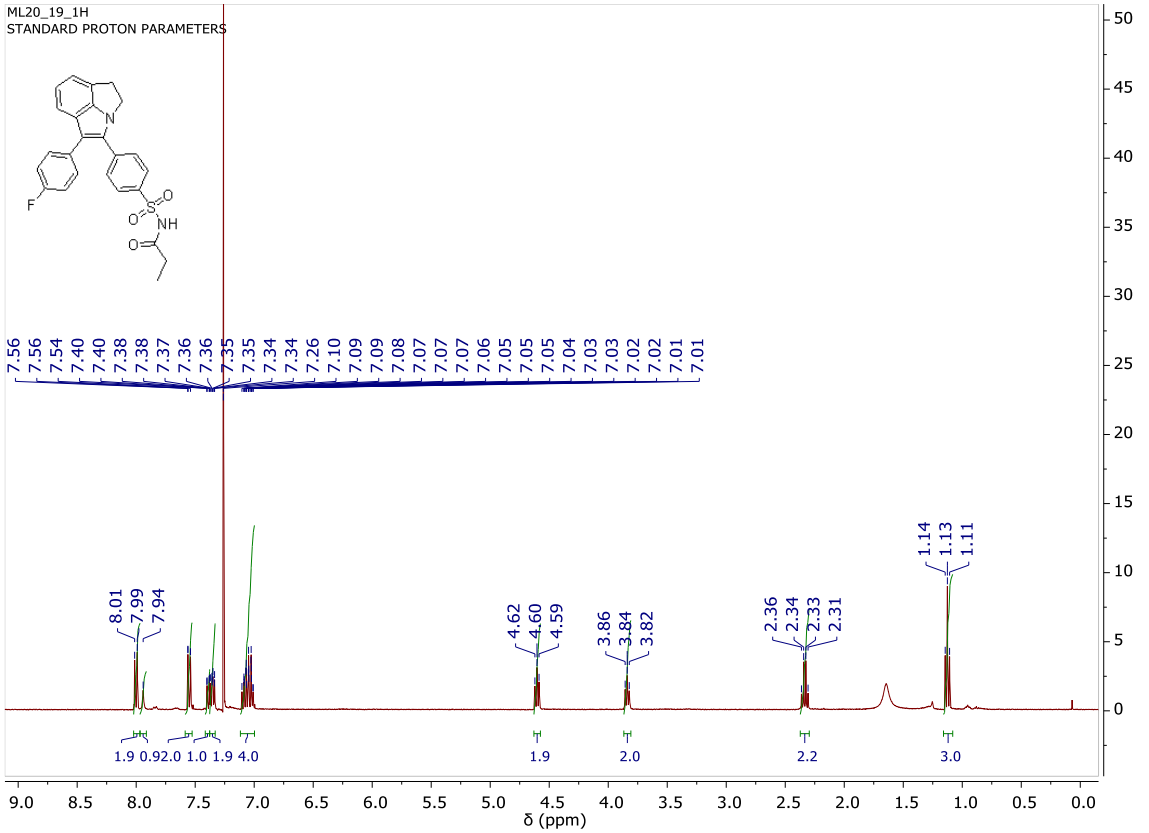


Figure S39. ^{1}H NMR spectrum of compound **3d** in $CDCl_3$

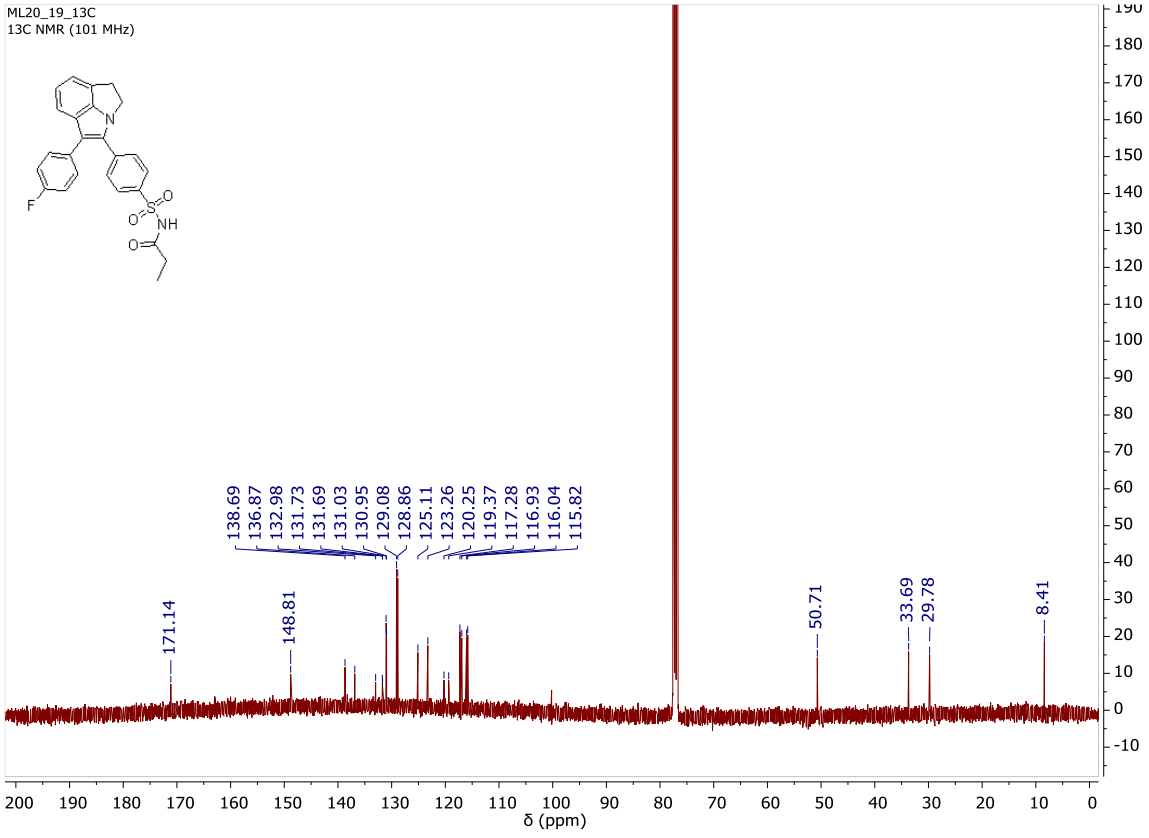
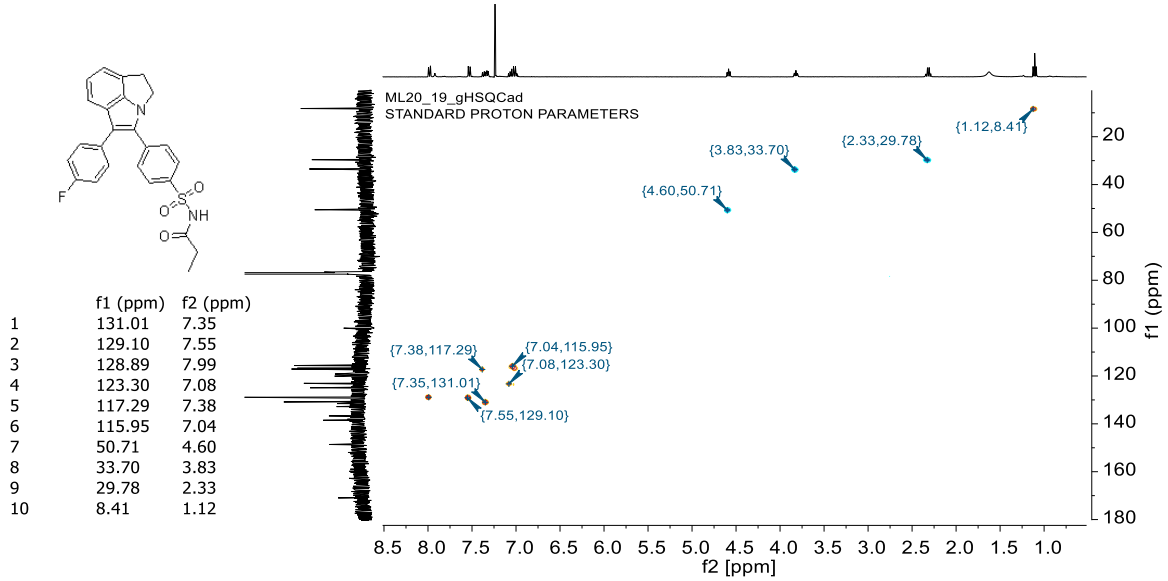


Figure S40. ^{13}C NMR spectrum of compound **3d** in $CDCl_3$



	f1 (ppm)	f2 (ppm)
1	131.01	7.35
2	129.10	7.55
3	128.89	7.99
4	123.30	7.08
5	117.29	7.38
6	115.95	7.04
7	50.71	4.60
8	33.70	3.83
9	29.78	2.33
10	8.41	1.12

Figure S41. HSQC spectrum of compound **3d** in $CDCl_3$

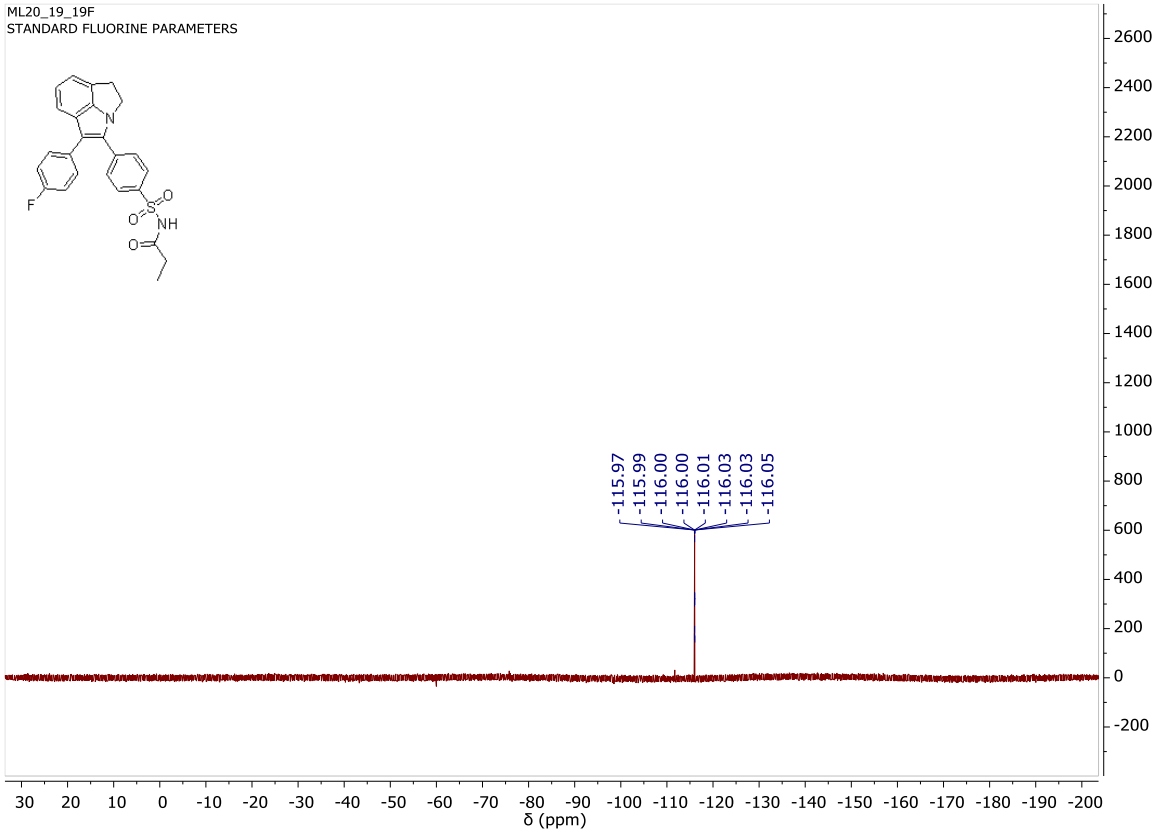
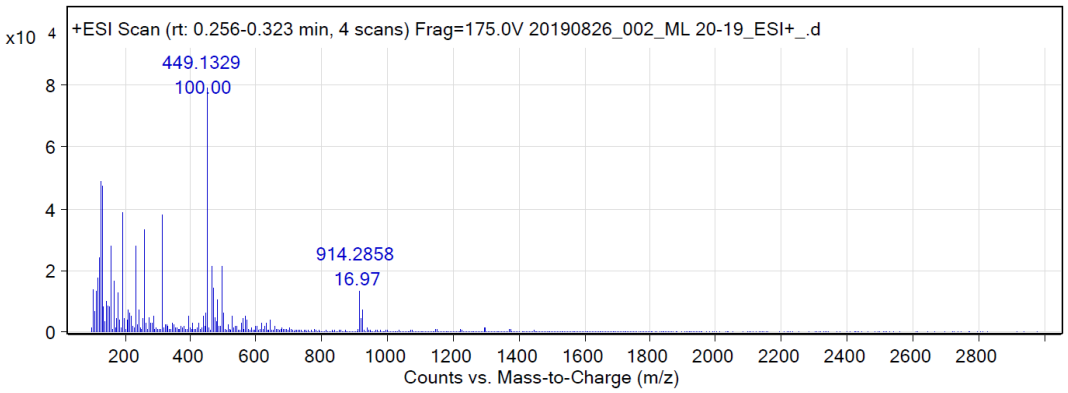


Figure S42. ^{19}F NMR spectrum of compound **3d** in $CDCl_3$



Peak List

m/z	z	Abund
121.0509		24270.76
125.9863		48989.84
130.159	1	47452.37
158.0029		28017.24
193.9736		39126.17
235.0004		28141.35
258.0929	1	33404.07
312.1186	1	37871.18
449.1329	1	79288.77
497.1177	1	21572.33

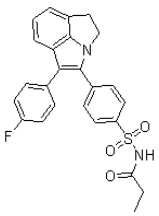


Figure S43. HRMS spectrum of compound **3d**

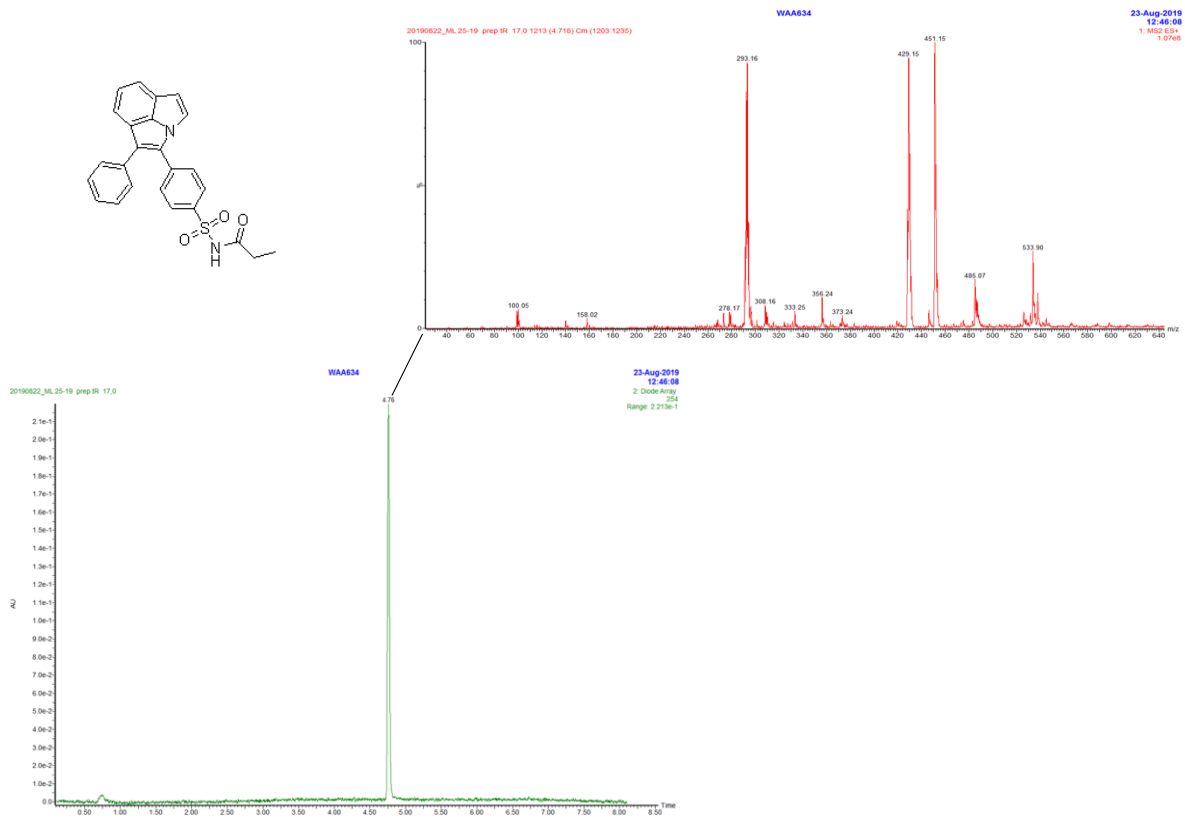
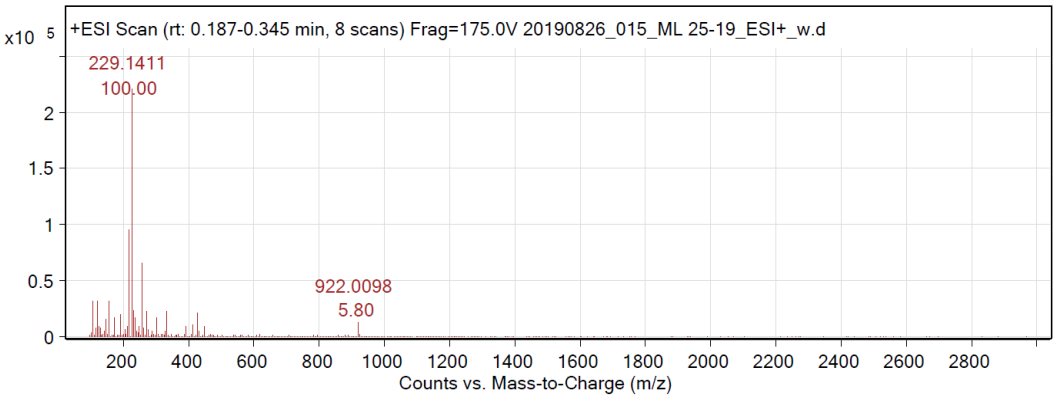
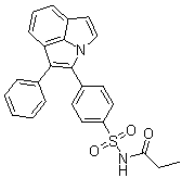


Figure S44. UPLC-MS chromatogram and spectrum of compound **4a**



Peak List

m/z	z	Abund
106.0044		31731.66
121.0509	1	32320.74
158.964		31221.07
217.1047	1	95616.11
229.1411	1	220864.17
230.1444	1	23971.44
261.131	1	66121.91
273.1671	1	22571.94
335.0041	1	22657.35
429.1262	1	20862.11



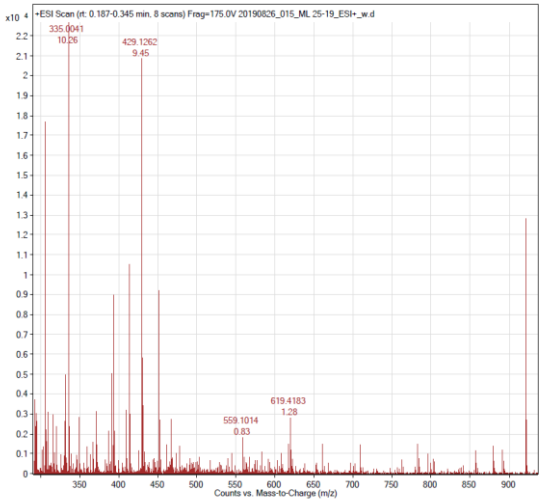


Figure S45. HRMS spectrum of compound **4a**

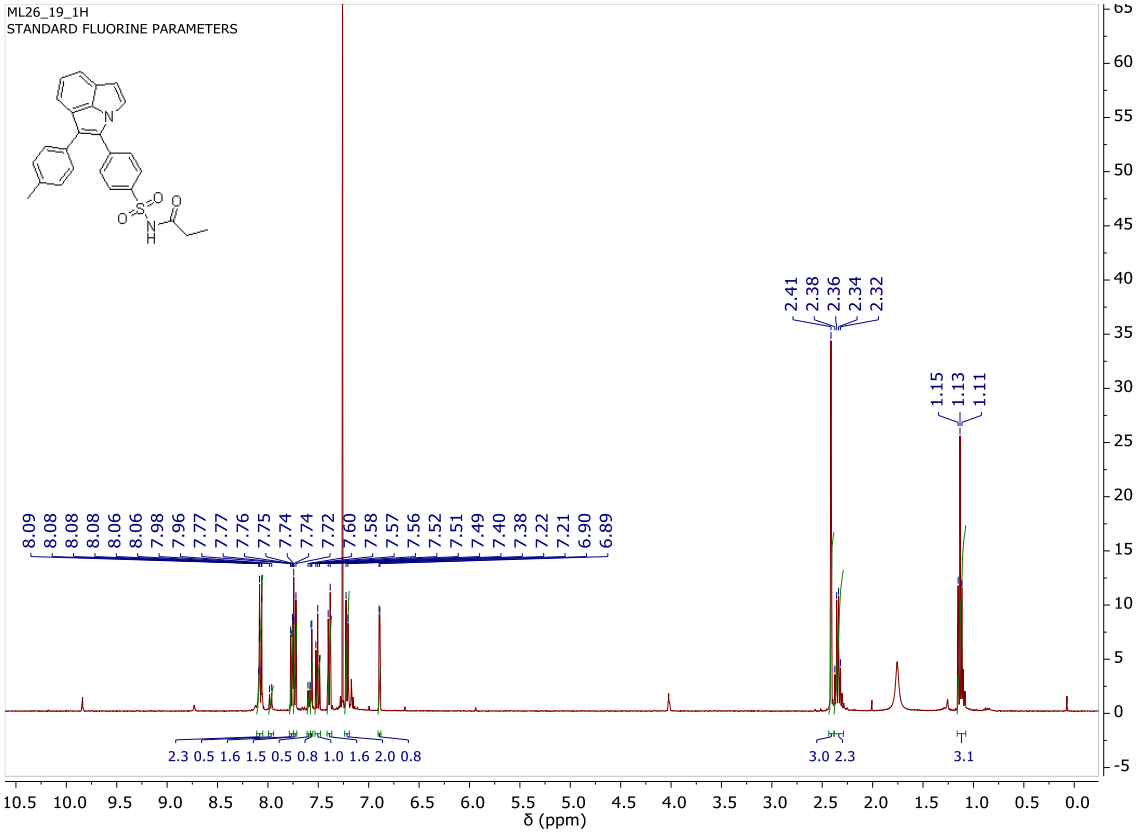
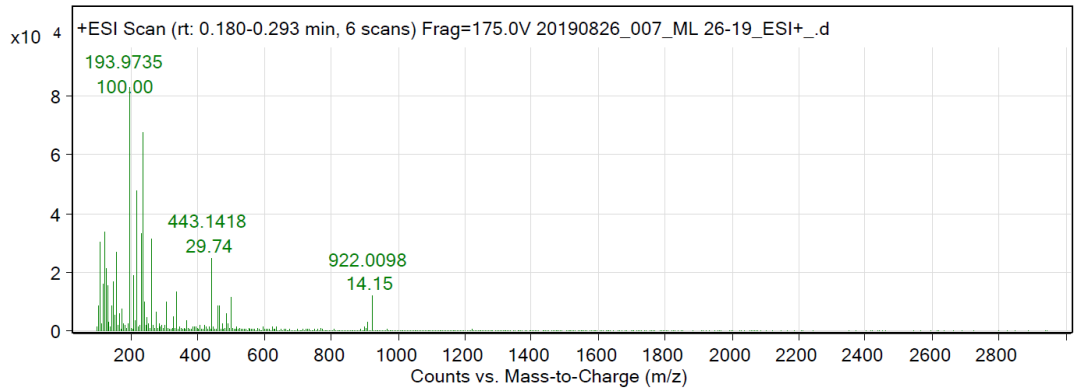


Figure S46. ^{1}H NMR spectrum of compound **4b** in $CDCl_3$



Peak List

m/z	z	Abund
106.0043		30195.72
121.0509	1	33797.78
125.9862		21587.03
158.0028		27033.29
193.9735	1	83212.66
217.1046	1	47688.3
229.1409	1	33173.68
235.0003	1	67918.05
261.1309	1	31159.07
443.1418	1	24750.84

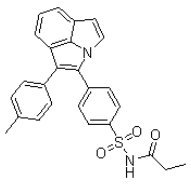


Figure S47. HRMS spectrum of compound **4b**

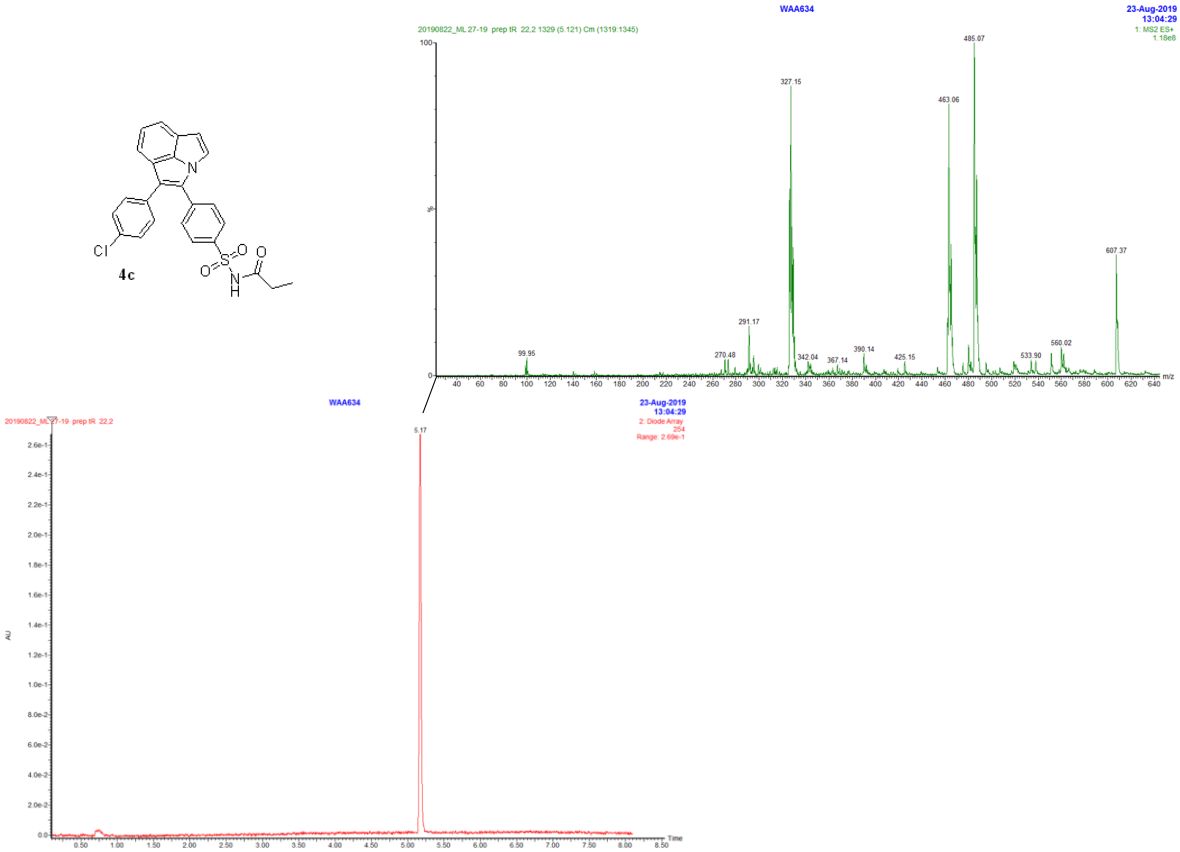
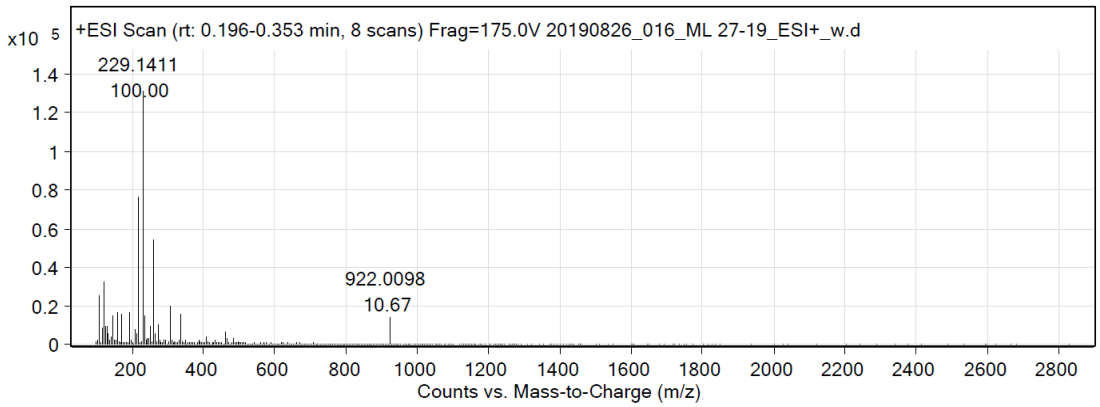
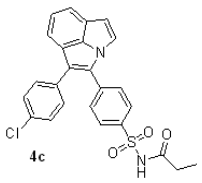


Figure S48. UPLC-MS chromatogram and spectrum of compound **4c**



Peak List

m/z	z	Abund
106.0044		25123.54
121.0509	1	32327.33
158.9638		16616.79
173.0783		15839.42
193.9735		16413.49
217.1047	1	76198.04
229.1411	1	131354.94
261.1309	1	54065.89
305.1571	1	20059.2
335.004	1	15615.05



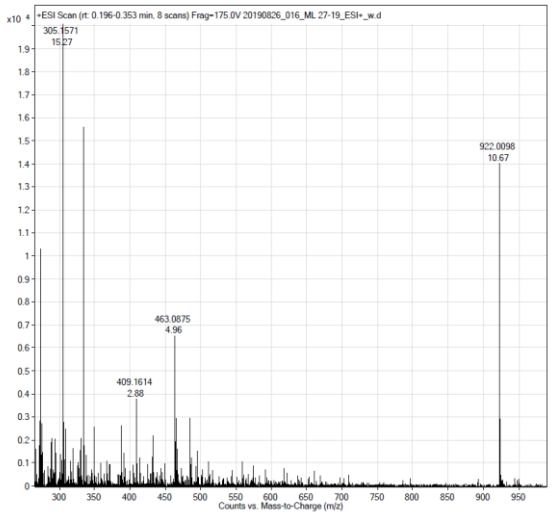


Figure S49. HRMS spectrum of compound **4c**

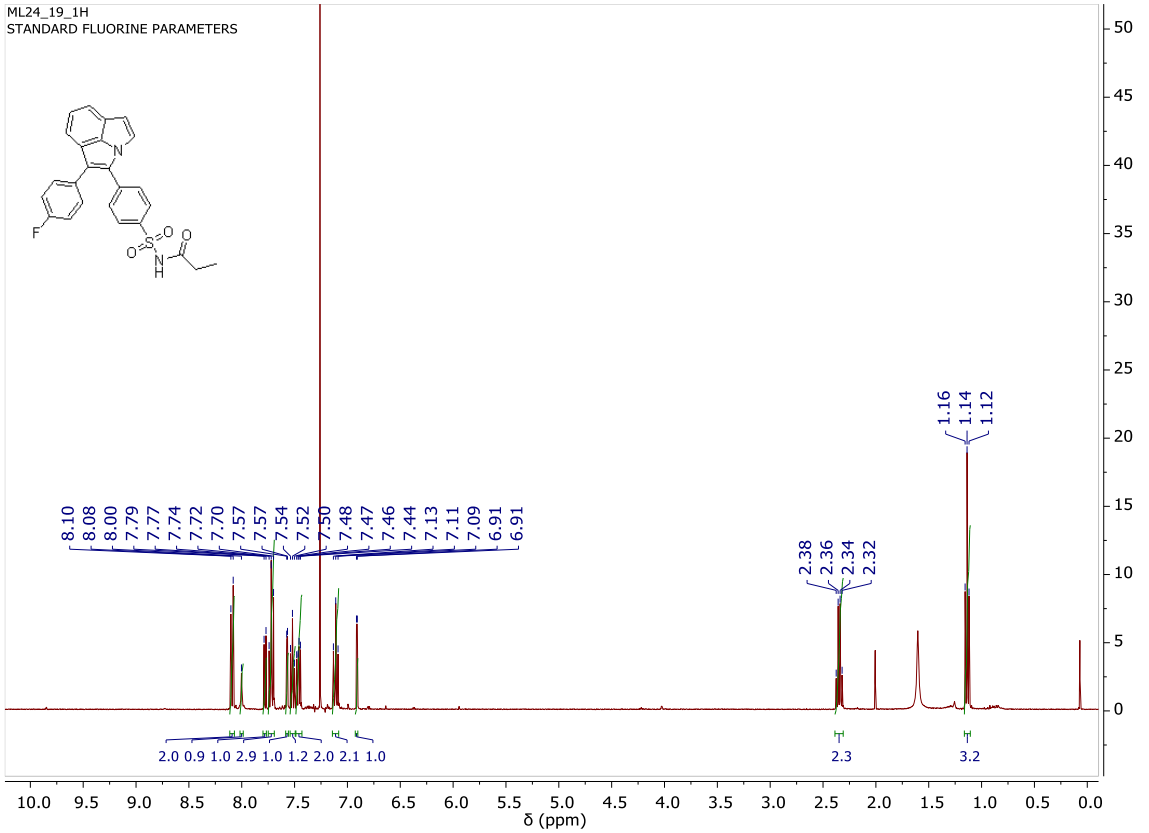


Figure S50. ^{1}H NMR spectrum of compound **4d** in $CDCl_3$

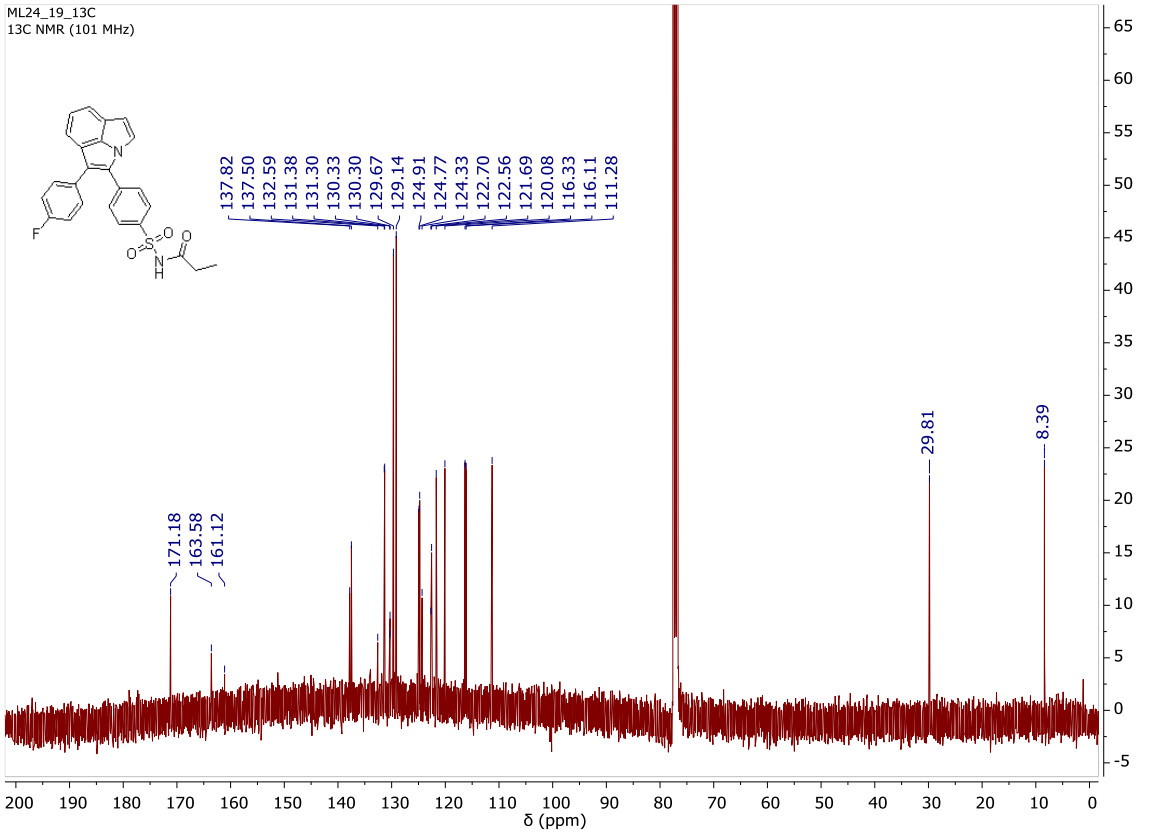


Figure S51. ^{13}C NMR spectrum of compound **4d** in $CDCl_3$

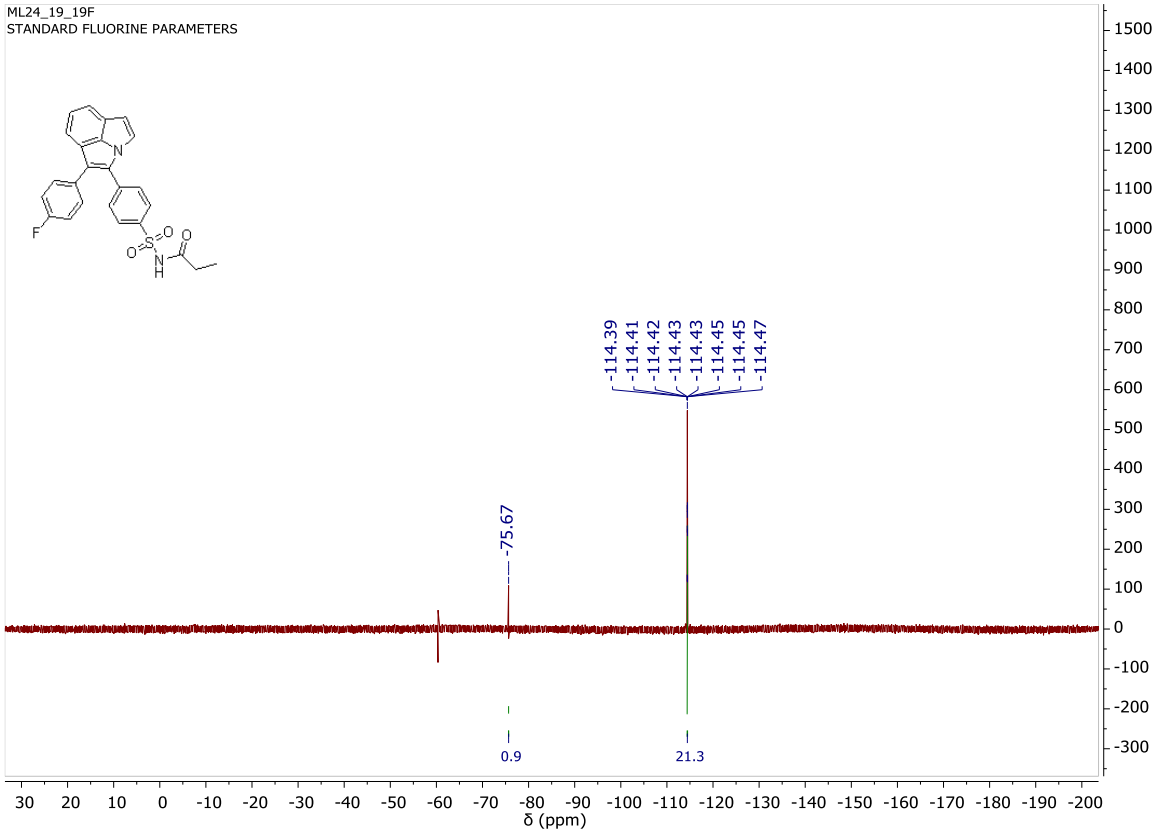
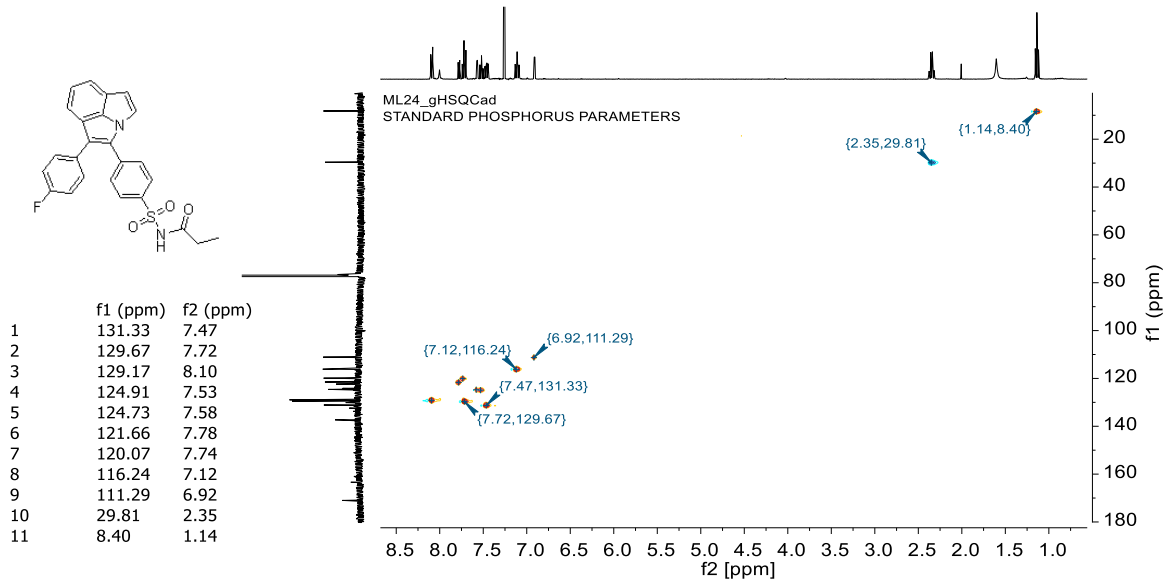
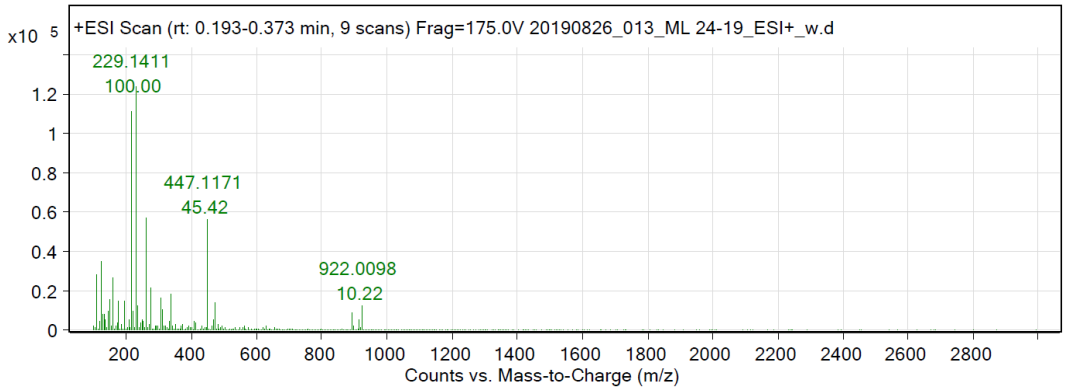


Figure S52. ^{19}F NMR spectrum of compound **4d** in $CDCl_3$



	f1 (ppm)	f2 (ppm)
1	131.33	7.47
2	129.67	7.72
3	129.17	8.10
4	124.91	7.53
5	124.73	7.58
6	121.66	7.78
7	120.07	7.74
8	116.24	7.12
9	111.29	6.92
10	29.81	2.35
11	8.40	1.14

Figure S53. HSQC spectrum of compound **4d** in $CDCl_3$



Peak List

m/z	z	Abund
106.0043		27947.44
121.0509	1	33566.79
123.0916		35098.75
158.9639		27044.28
217.1047	1	111031.84
229.1411	1	123962.66
261.131	1	57119.01
273.1674	1	21577.87
335.0043		18749.91
447.1171	1	56299.96

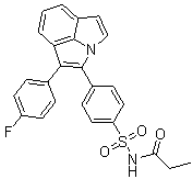


Figure S54. HRMS spectrum of compound **4d**

Optimization of *N*-propionamide formation

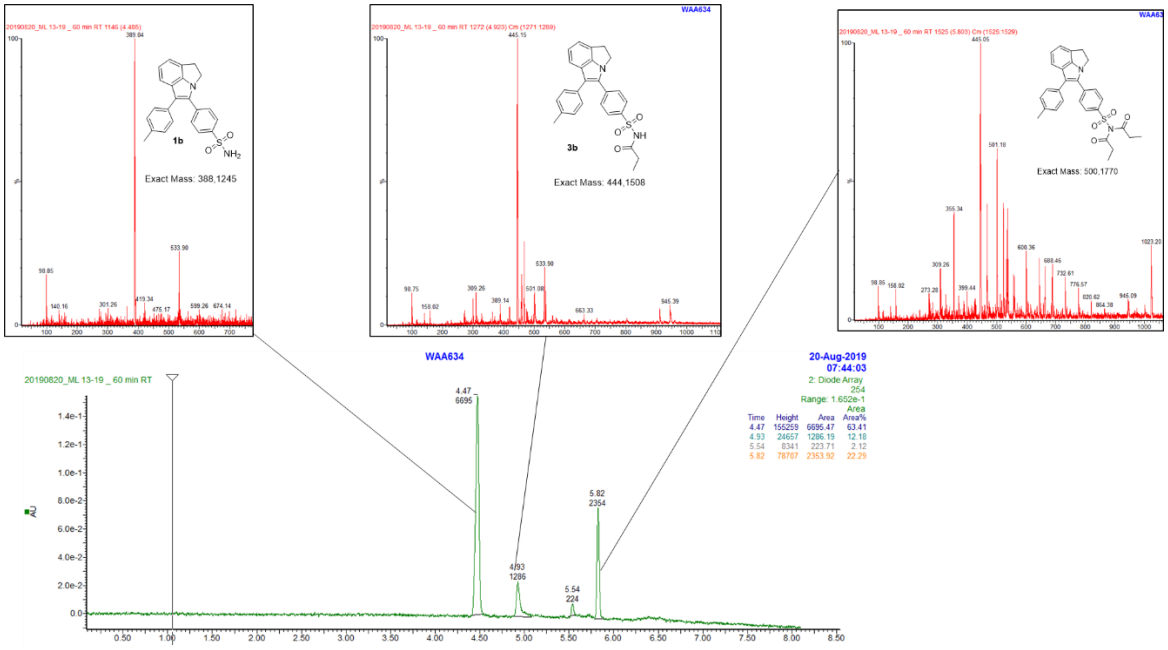


Figure S55. Exemplary UPLC-MS chromatogram resulting from the synthesis of **3b** using triethylamine as base.

The following procedure was used: The (dihydro)pyrrolo[3,2,1-*hi*]indole **1b** (1.39 mg, 3.58 µmol, 1.0 equiv) and triethylamine (0.65 µL, 4.71 µmol, 1.32 equiv) were dissolved in anhydrous DCM (108 µL). Then, propionyl chloride (0.82 µL, 0.87 mg, 9.38 µmol, 2.62 equiv) was added and the solution was stirred at room temperature for 60 min. The analytical HPLC sample was taken, the solvent was removed and the sample redissolved in acetonitrile for further analysis by UPLC-MS.

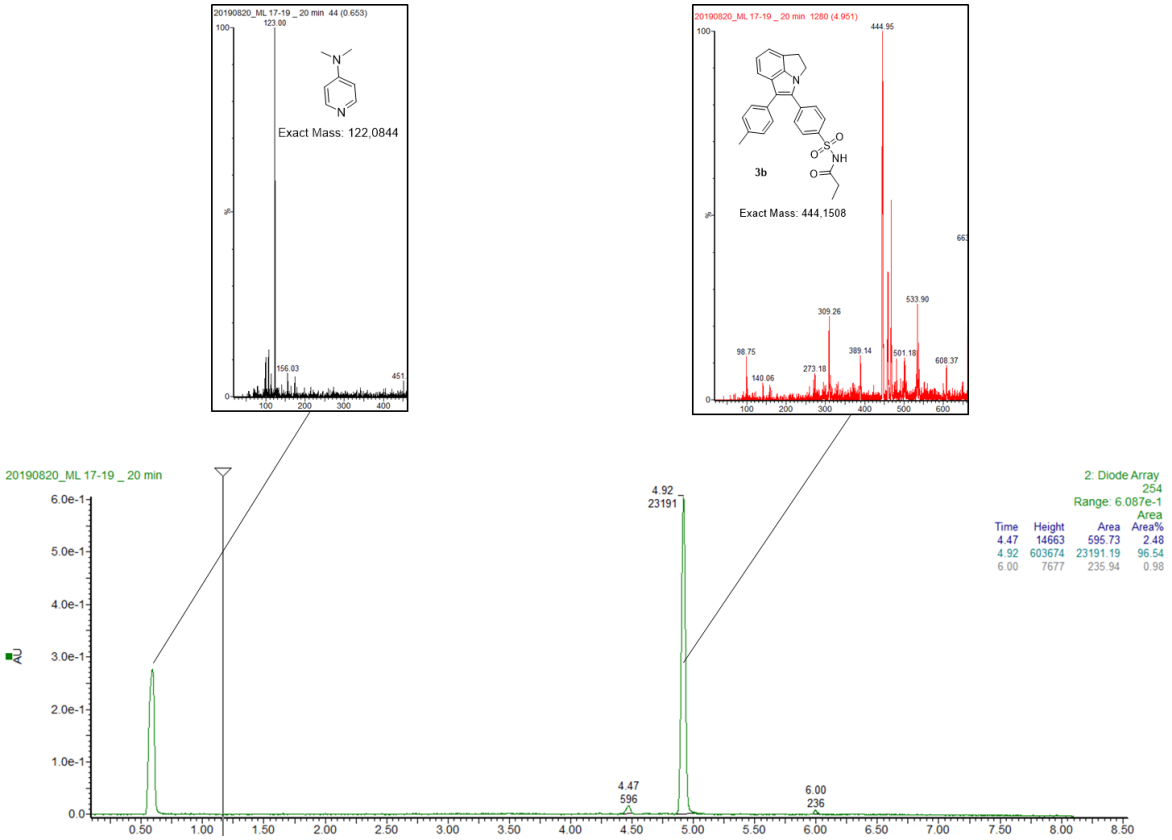


Figure S56. Exemplary UPLC-MS chromatogram resulting from the synthesis of **3b** using 4-dimethylaminopyridine as base.

The following procedure was used: The (dihydro)pyrrolo[3,2,1-*hi*]indole **1b** (1.76 mg, 4.53 µmol, 1.0 equiv) and dimethylaminopyridine (1.38 µL, 11.33 µmol, 2.50 equiv) were dissolved in anhydrous THF (137 µL) and DCM (137 µL). Then, propionyl chloride (0.46 µL, 0.49 mg, 5.94 µmol, 1.31 equiv) was added and the solution was stirred at room temperature for 20 min. The analytical HPLC sample was taken, the solvent was removed and the sample redissolved in acetonitrile for further analysis by UPLC-MS.