

Supplementary Materials: Design, Synthesis and Biological Evaluation of Novel Benzofuran Derivatives Bearing *N*-Aryl Piperazine Moiety

Yulu Ma, Xi Zheng, Hui Gao, Chunping Wan, Gaoxiong Rao and Zewei Mao

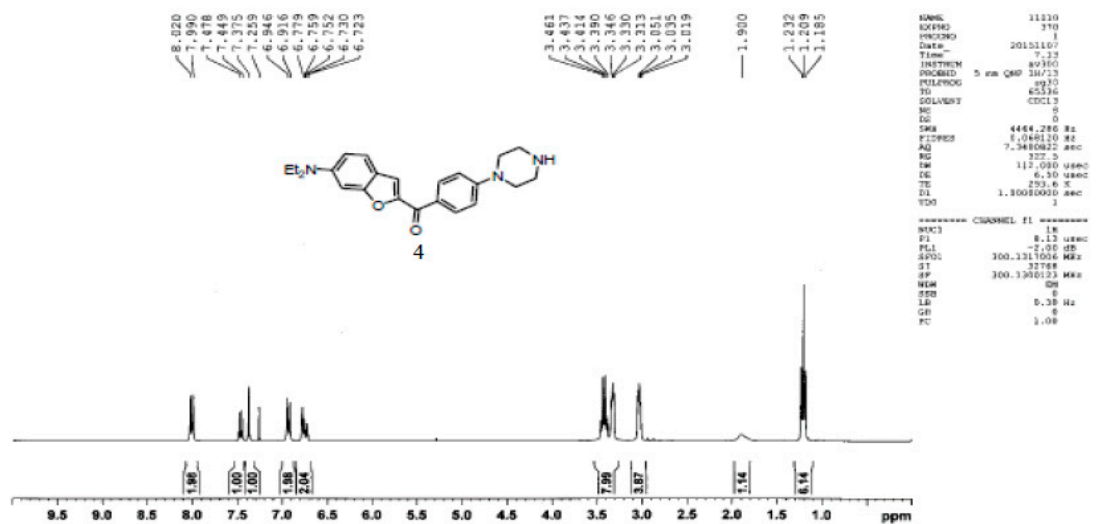


Figure S1. ¹H-NMR spectrum of compound 4.

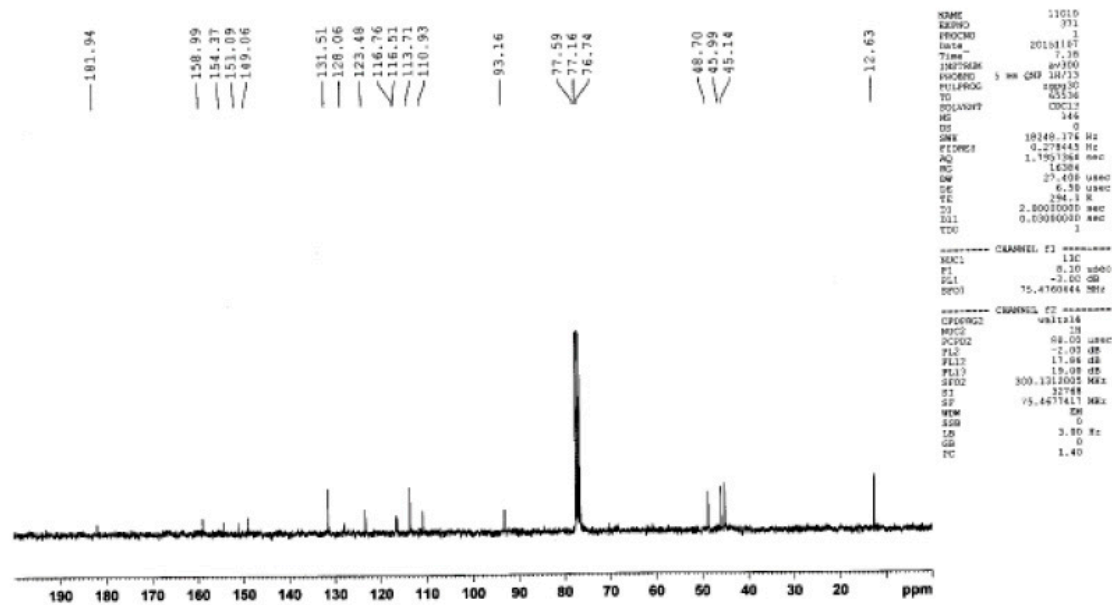
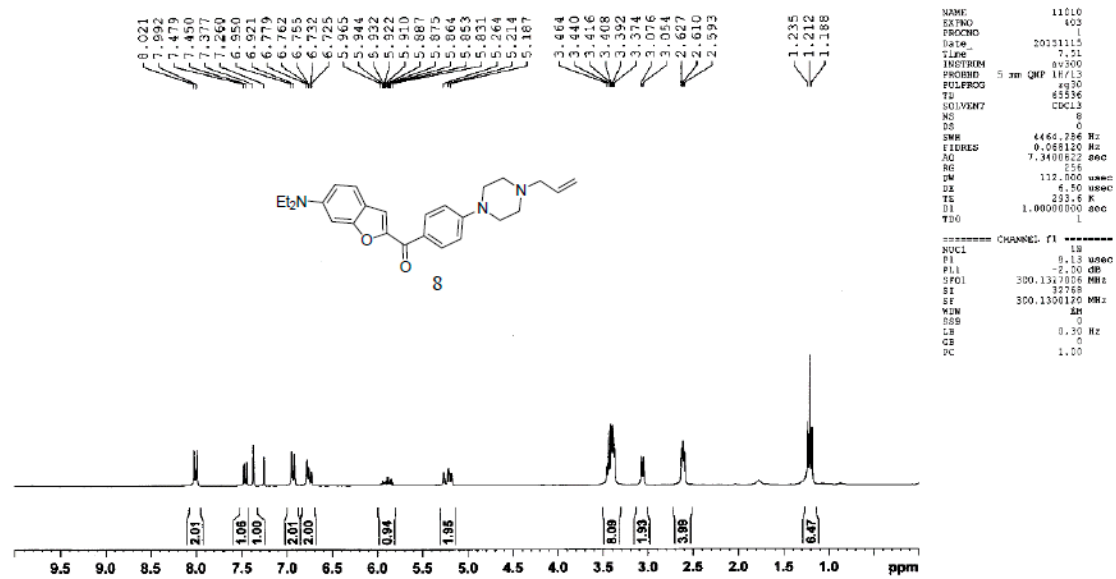
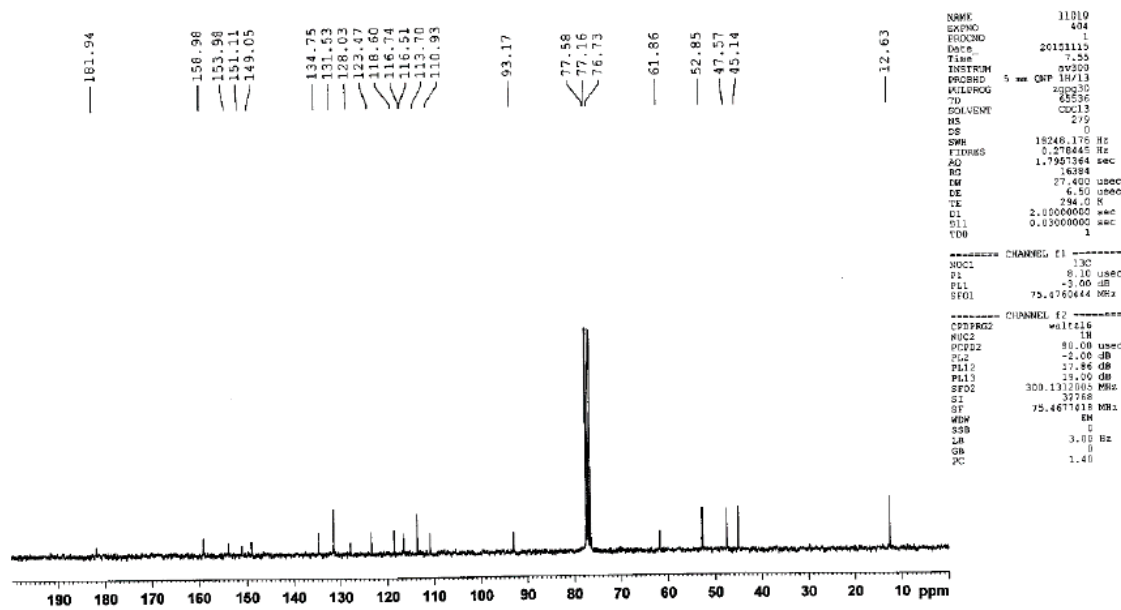
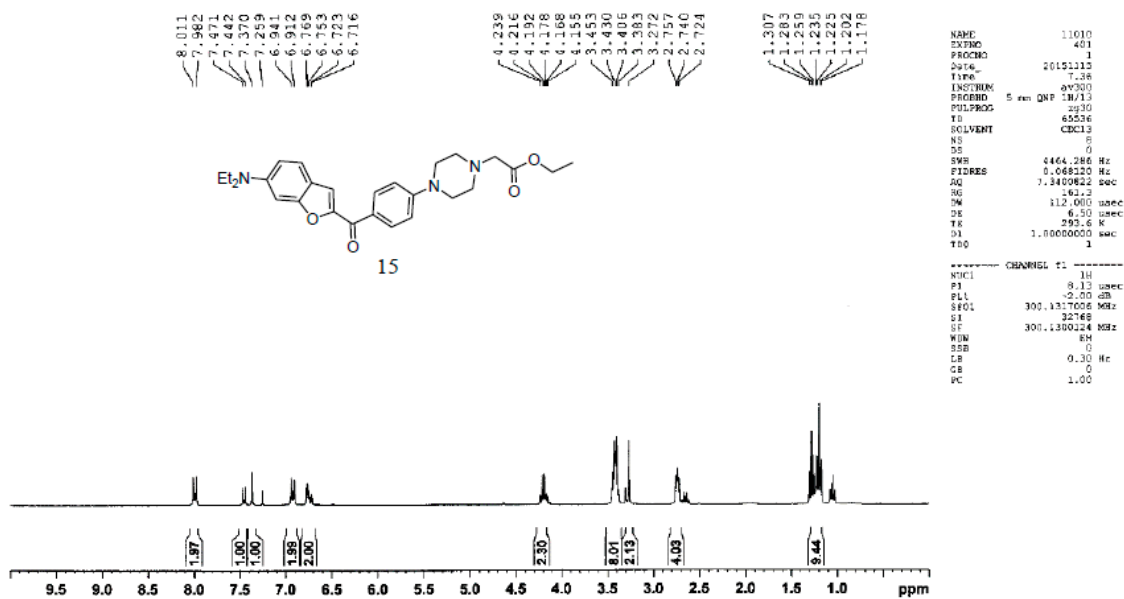
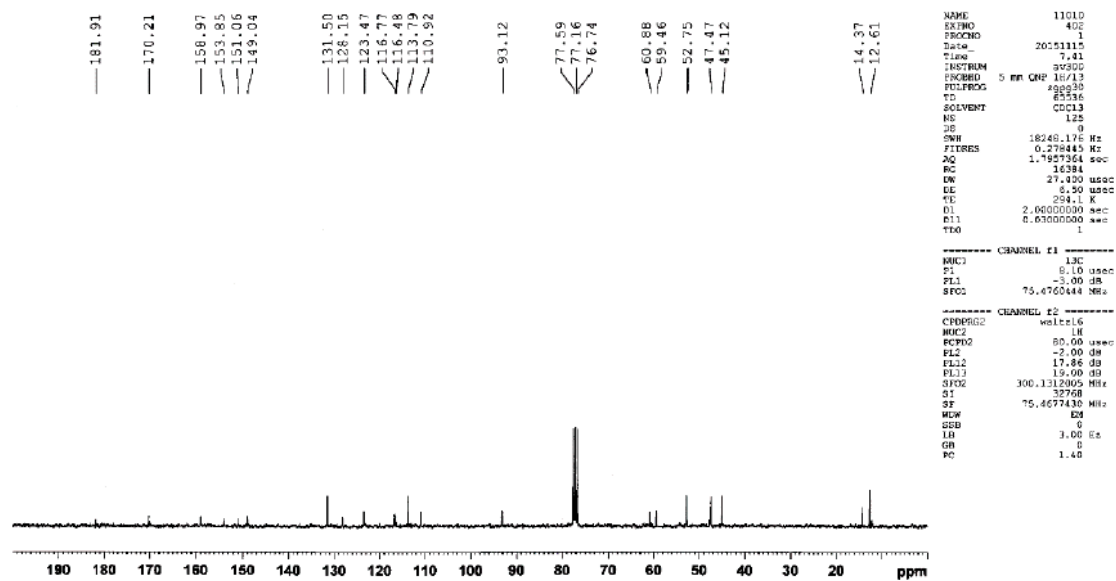


Figure S2. ¹³C-NMR spectrum of compound 4.

Figure S3. ¹H-NMR spectrum of compound 8.Figure S4. ¹³C-NMR spectrum of compound 8.

Figure S5. ¹H-NMR spectrum of compound 15.Figure S6. ¹³C-NMR spectrum of compound 15.

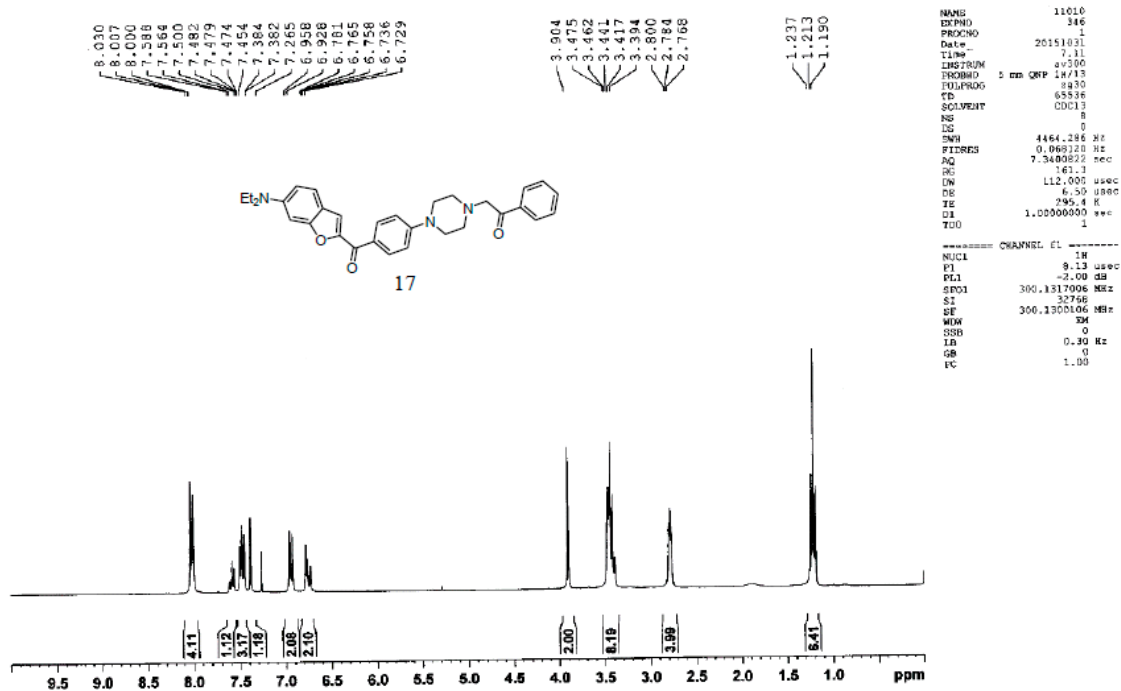


Figure S7. ¹H-NMR spectrum of compound 17.

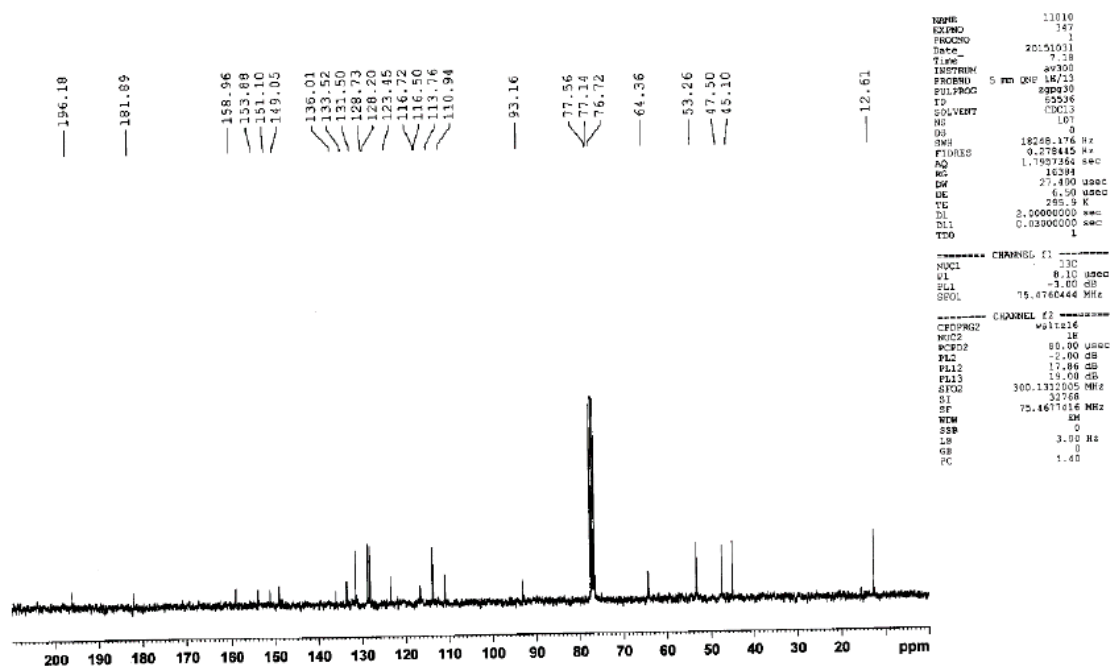


Figure S8. ¹³C-NMR spectrum of compound 17.

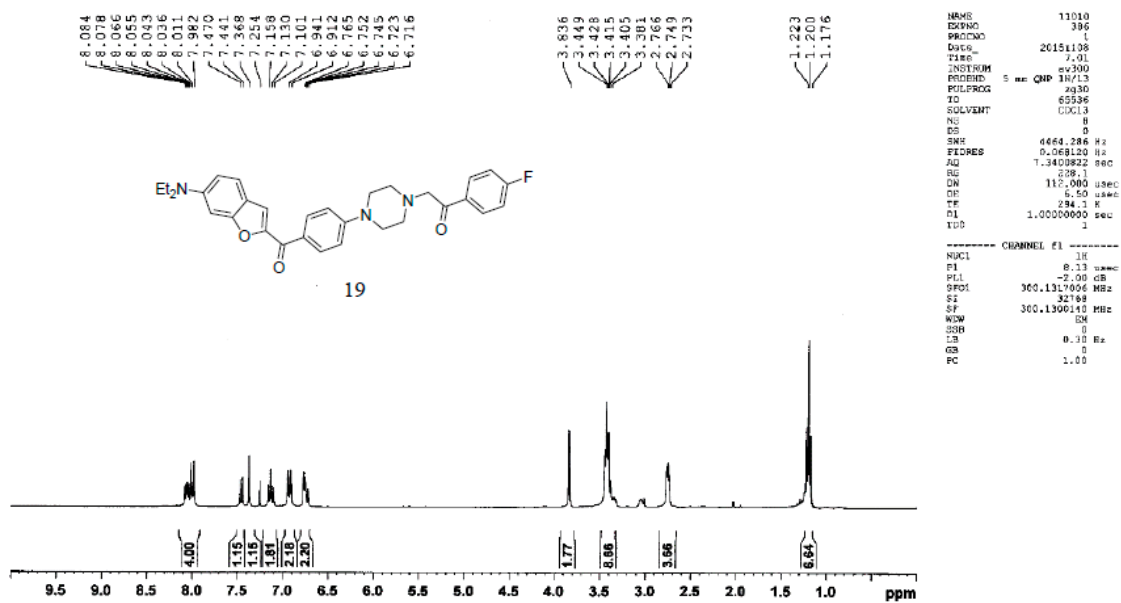


Figure S11. ¹H-NMR spectrum of compound 19.

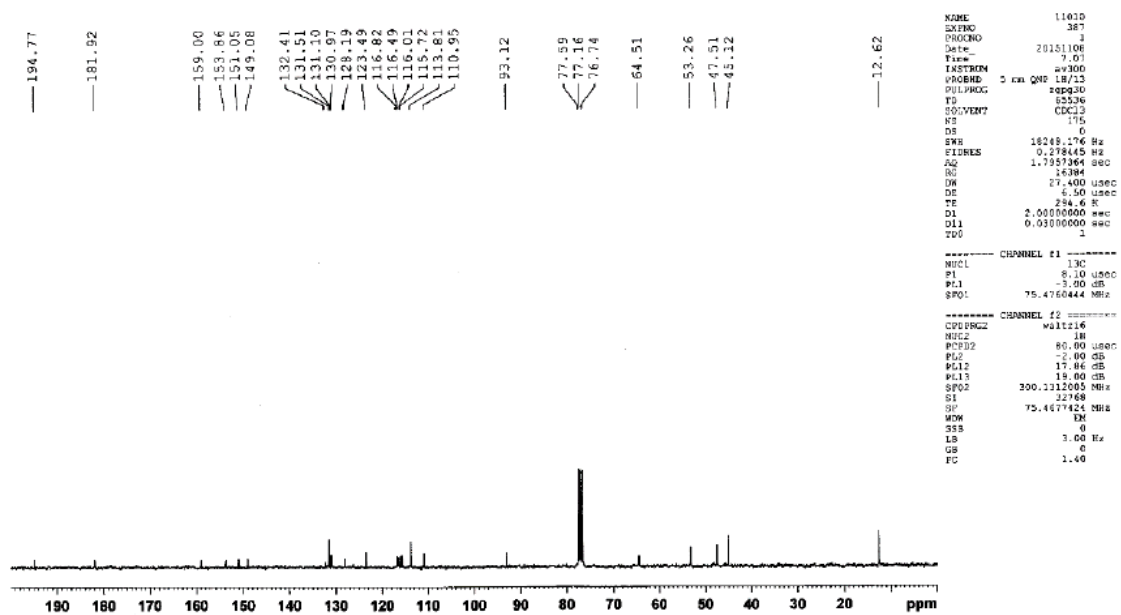


Figure S12. ¹³C-NMR spectrum of compound 19.

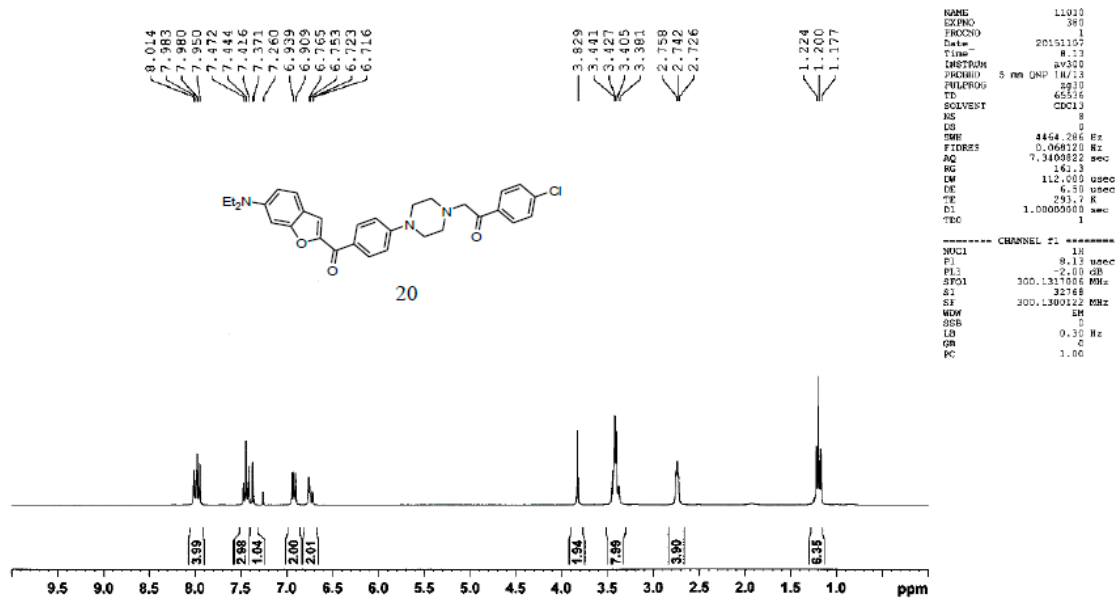


Figure S13. ¹H-NMR spectrum of compound 20.

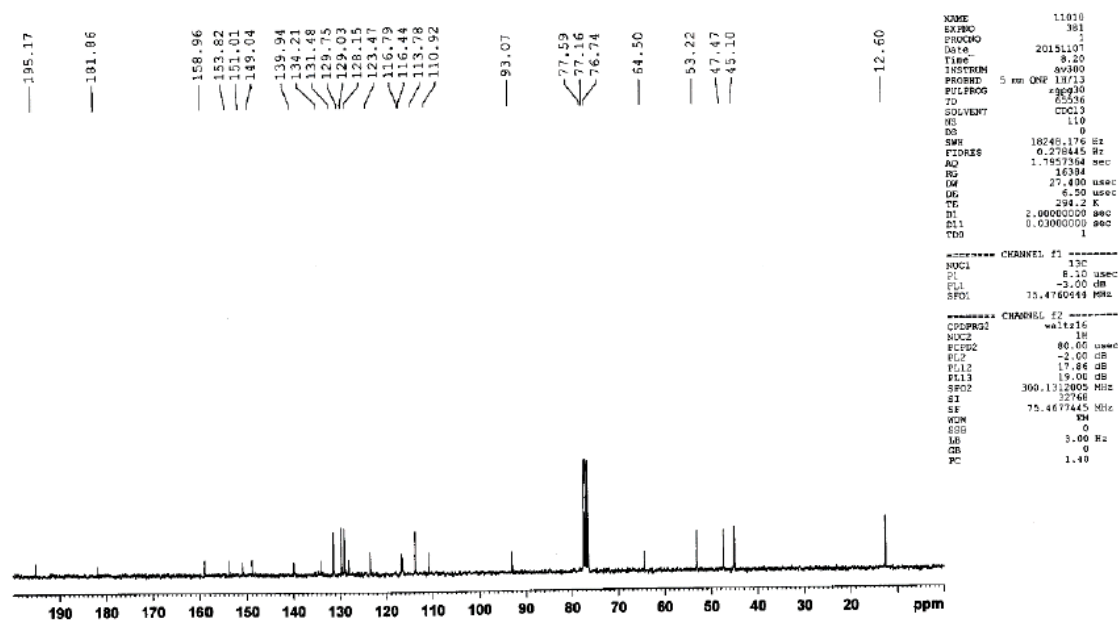


Figure S14. ¹³C-NMR spectrum of compound 20.

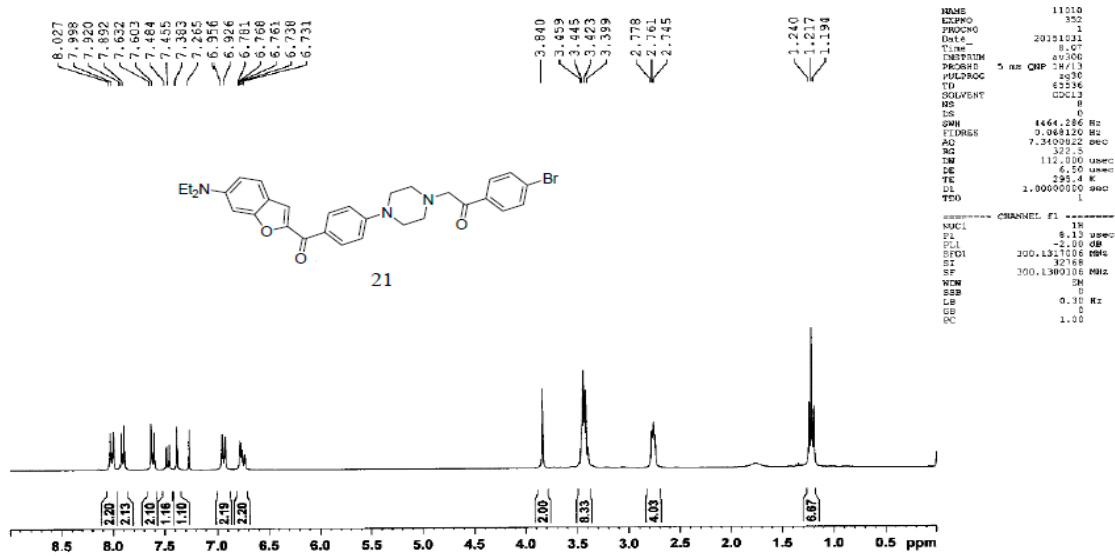


Figure S15. ¹H-NMR spectrum of compound 21.

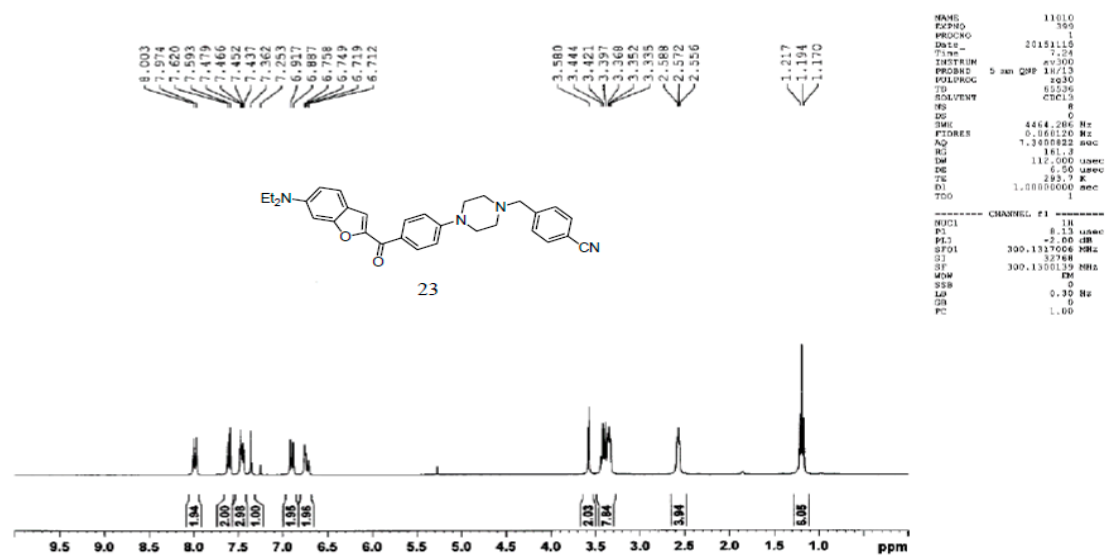


Figure S16. ¹H-NMR spectrum of compound 23.

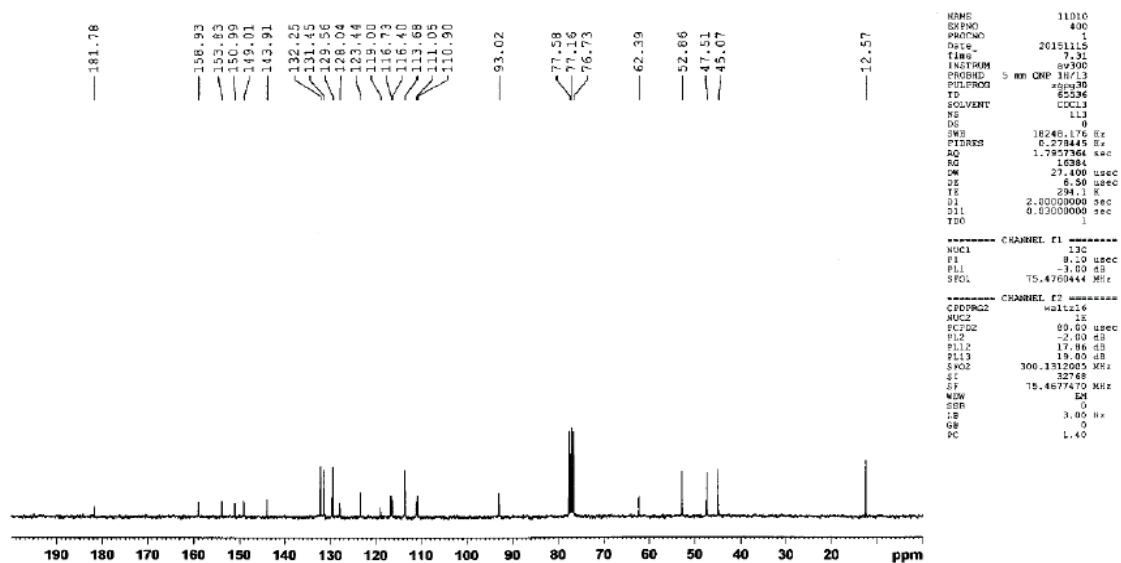


Figure S17. ¹³C-NMR spectrum of compound 23.

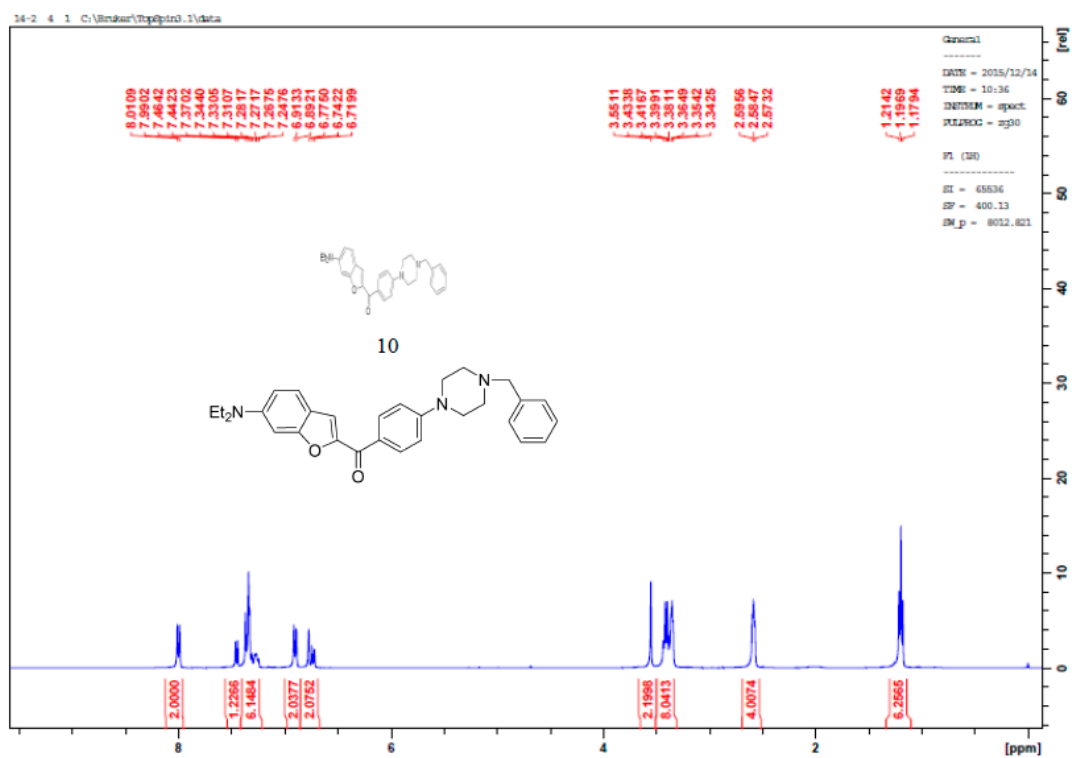
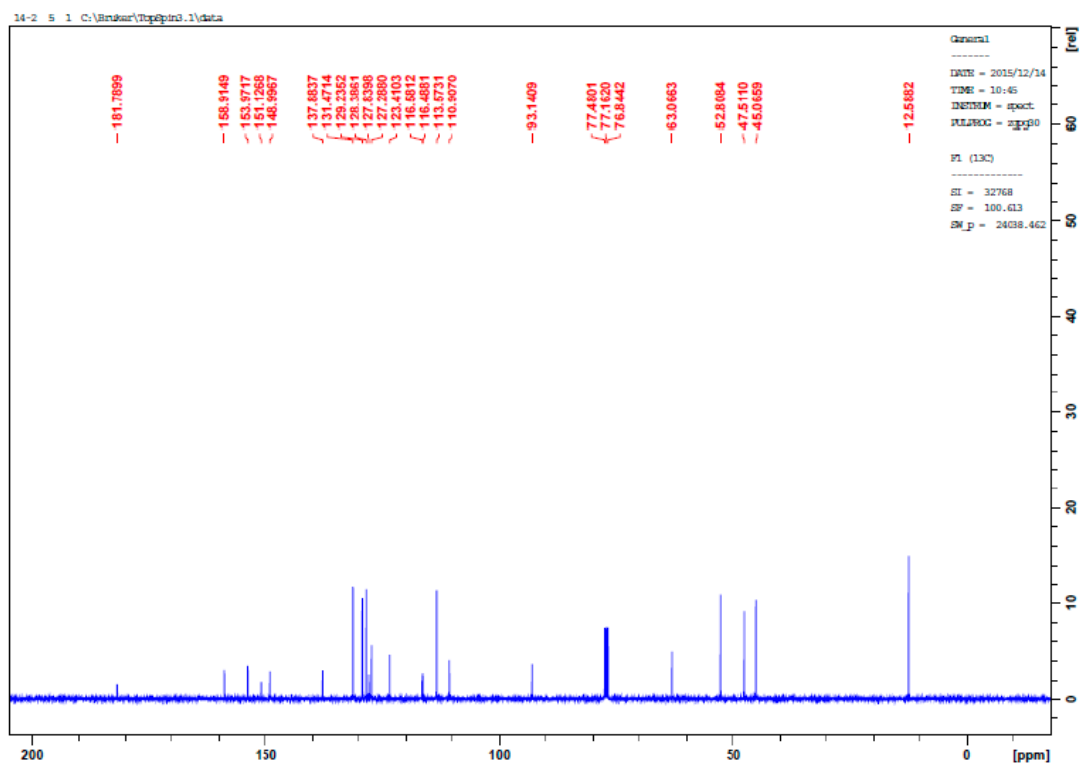
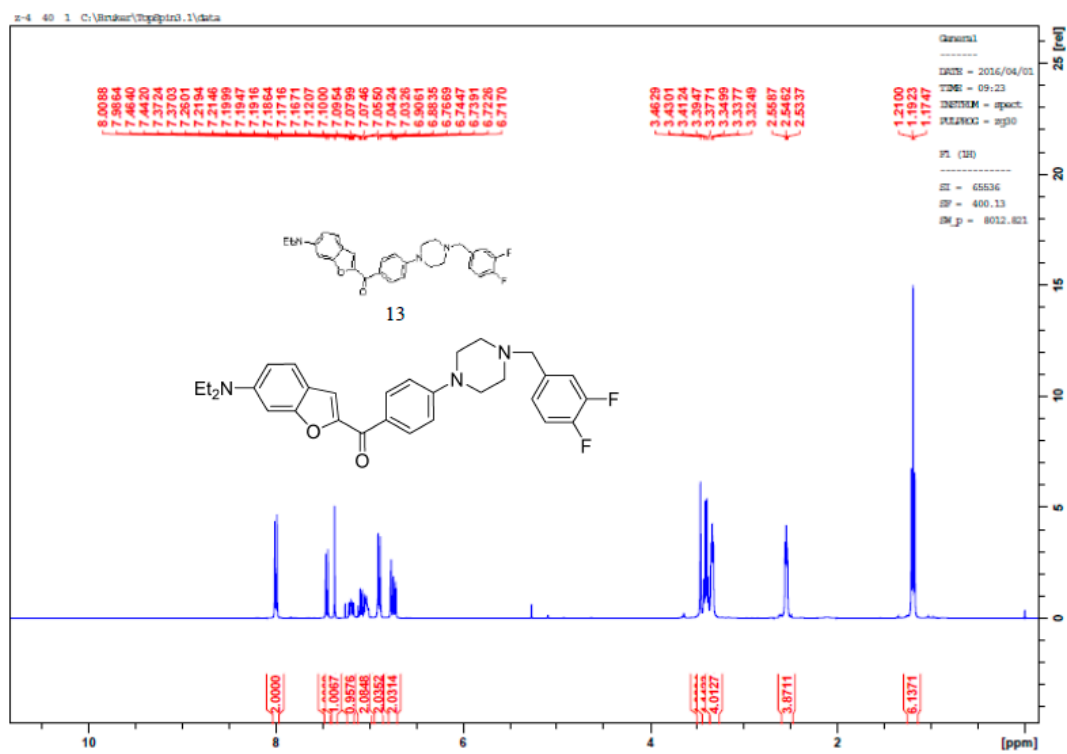
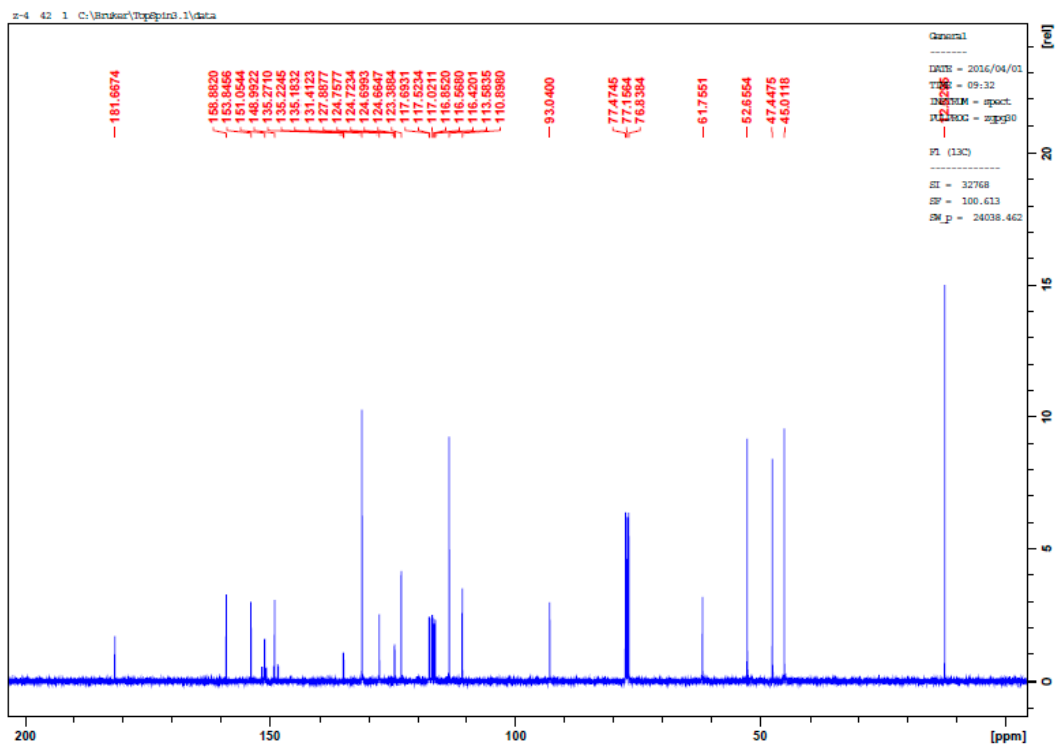
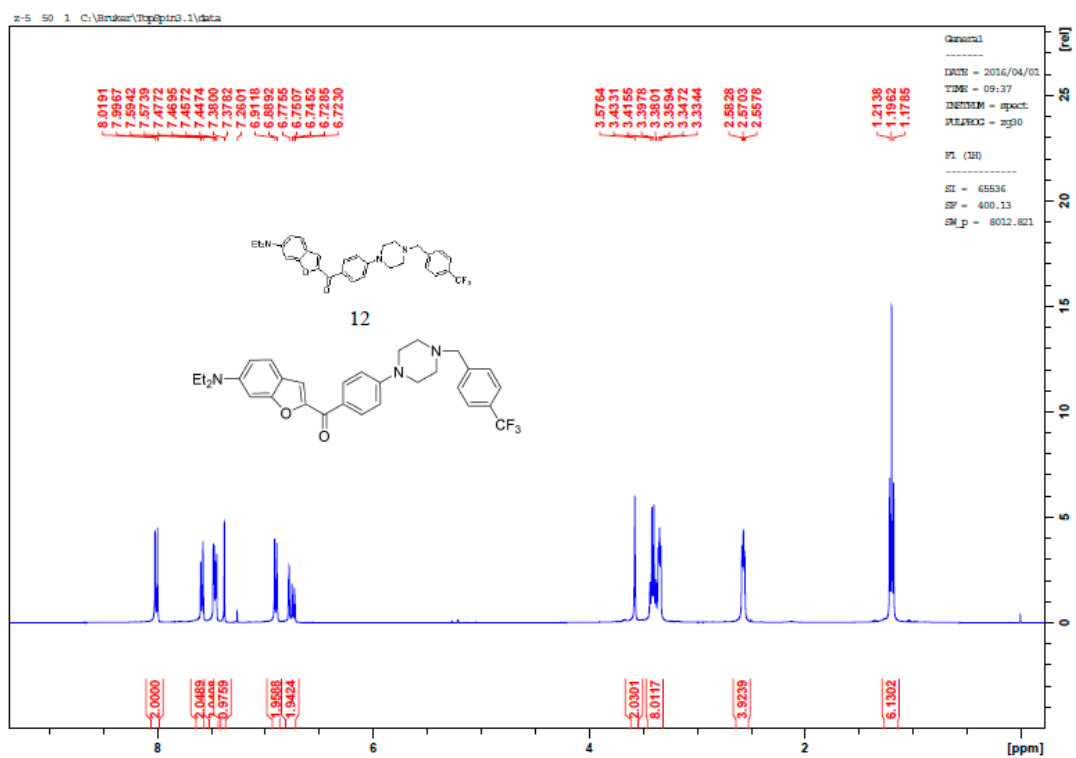
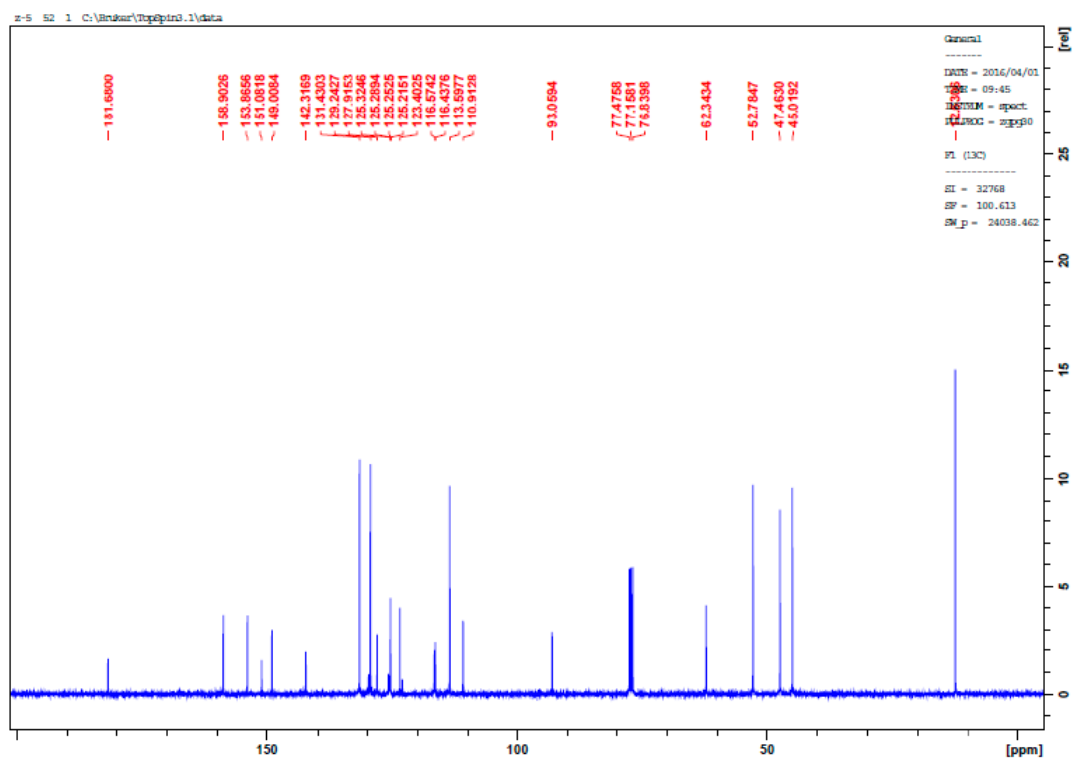
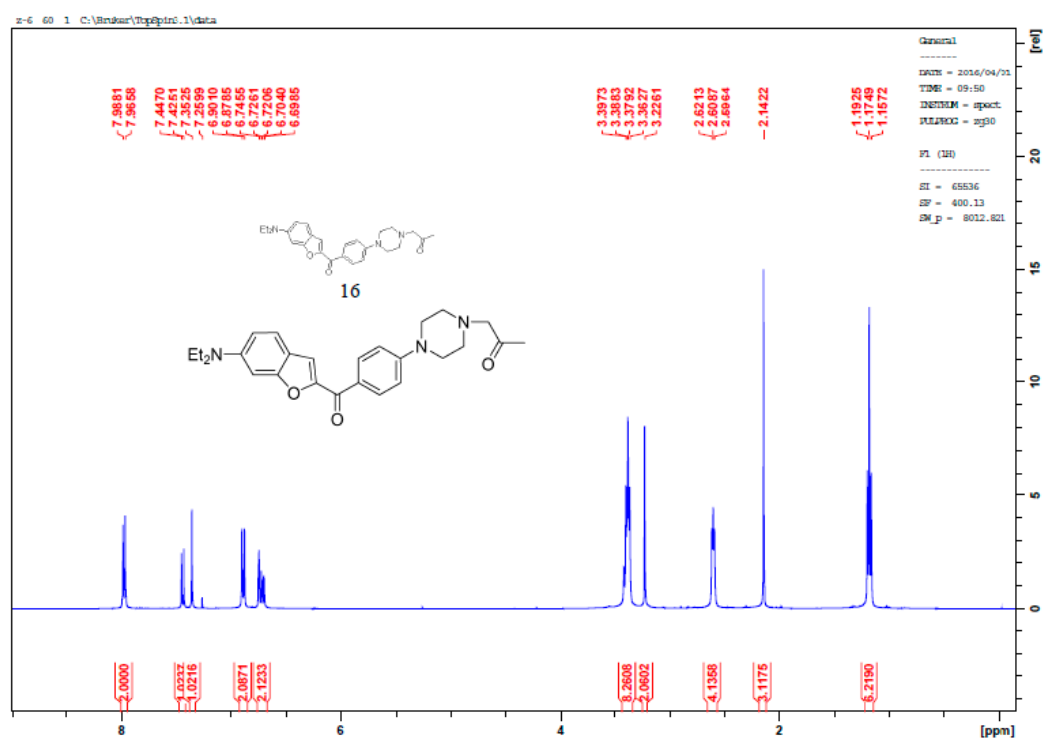
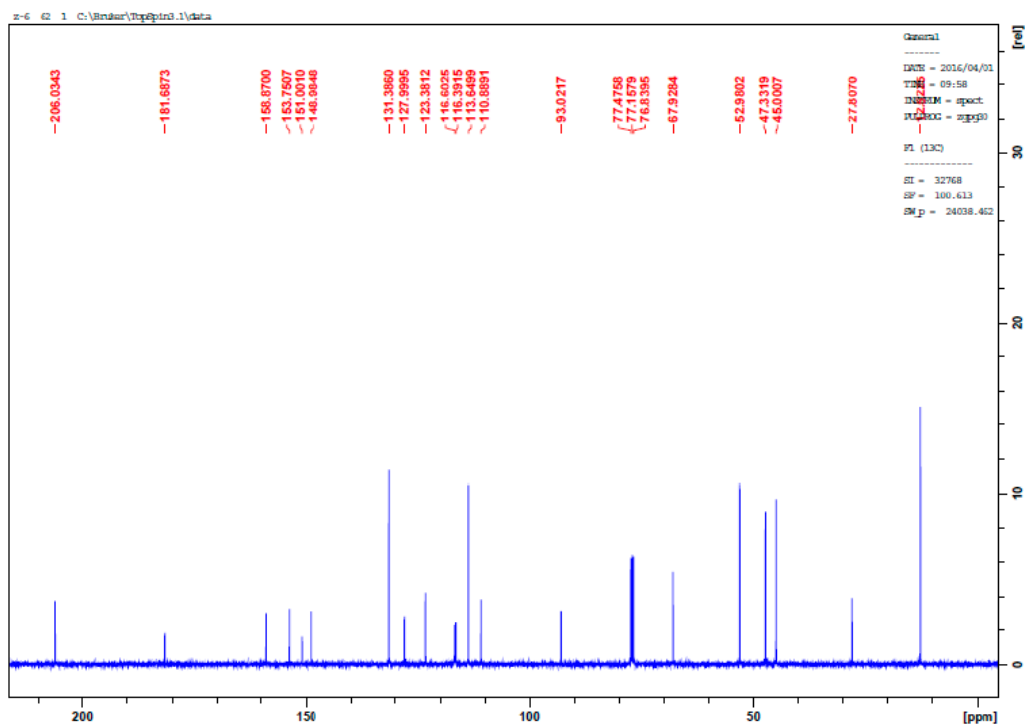
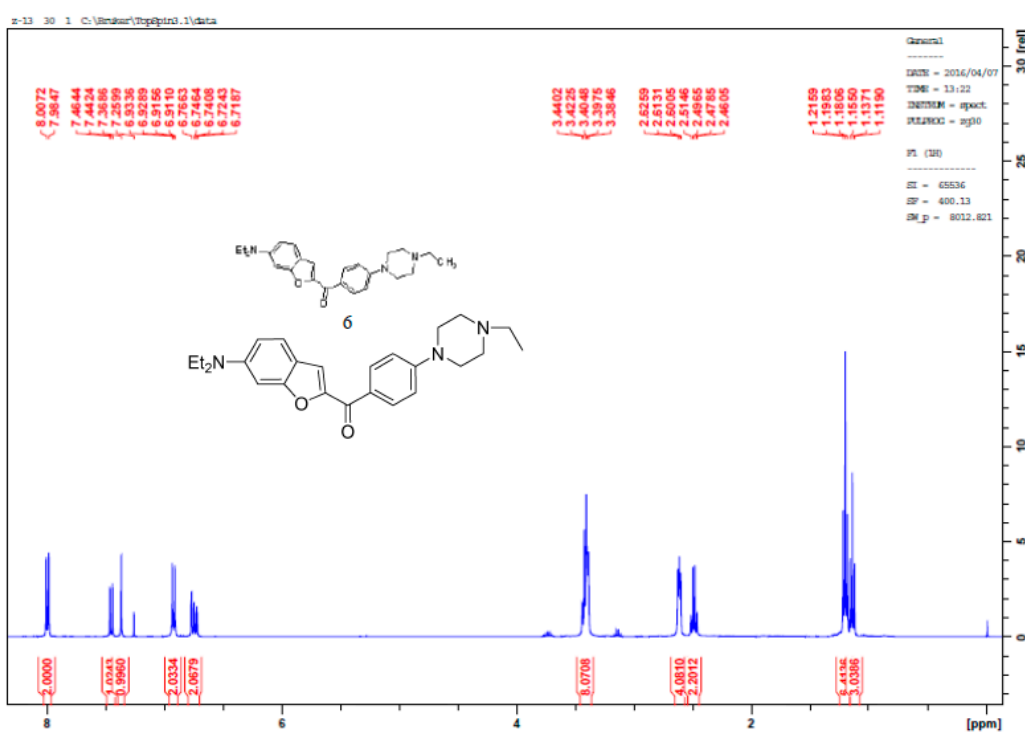


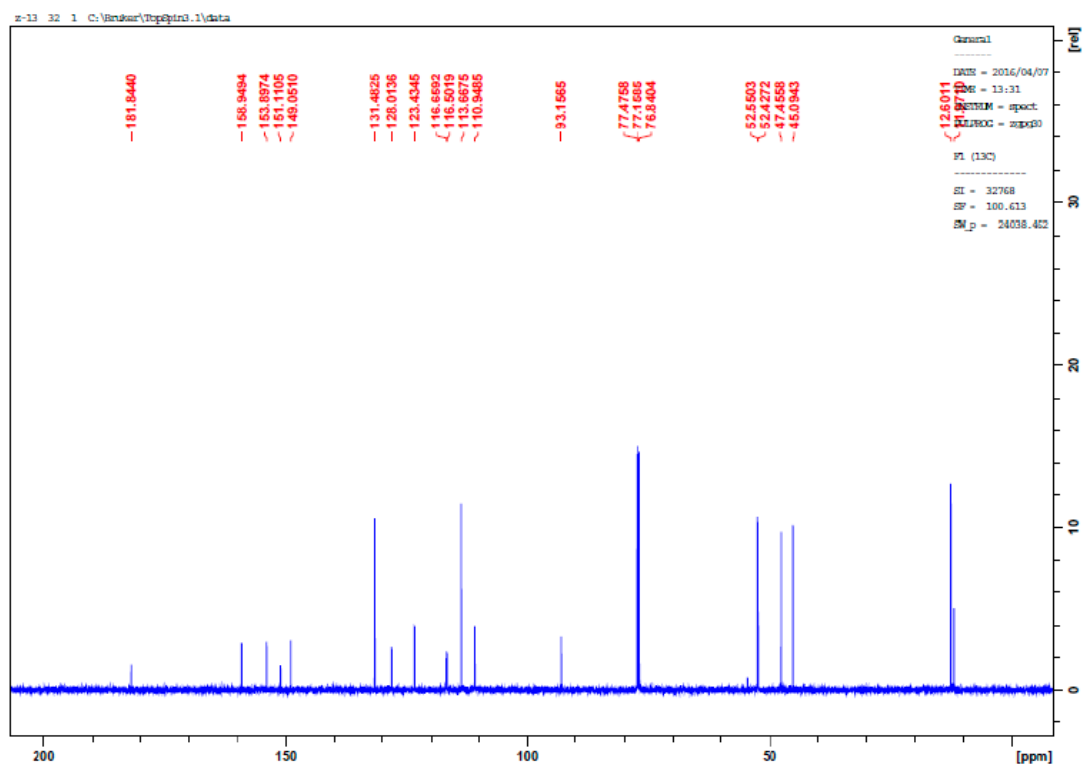
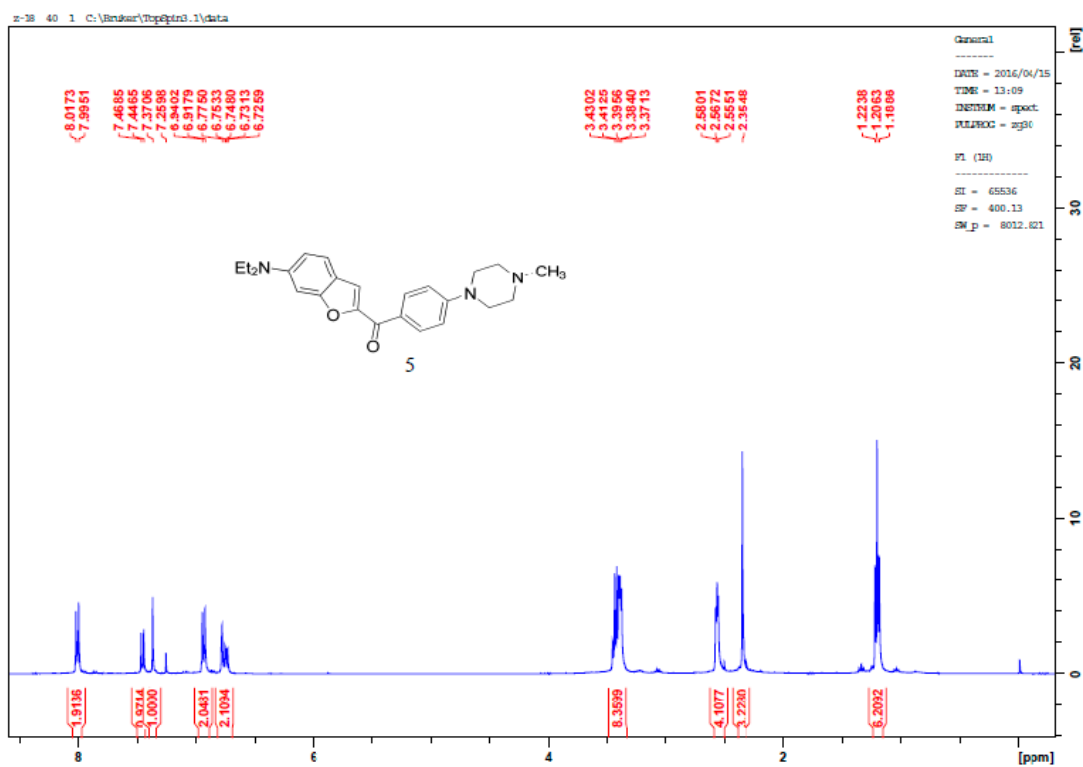
Figure S18. ¹H-NMR spectrum of compound 10.

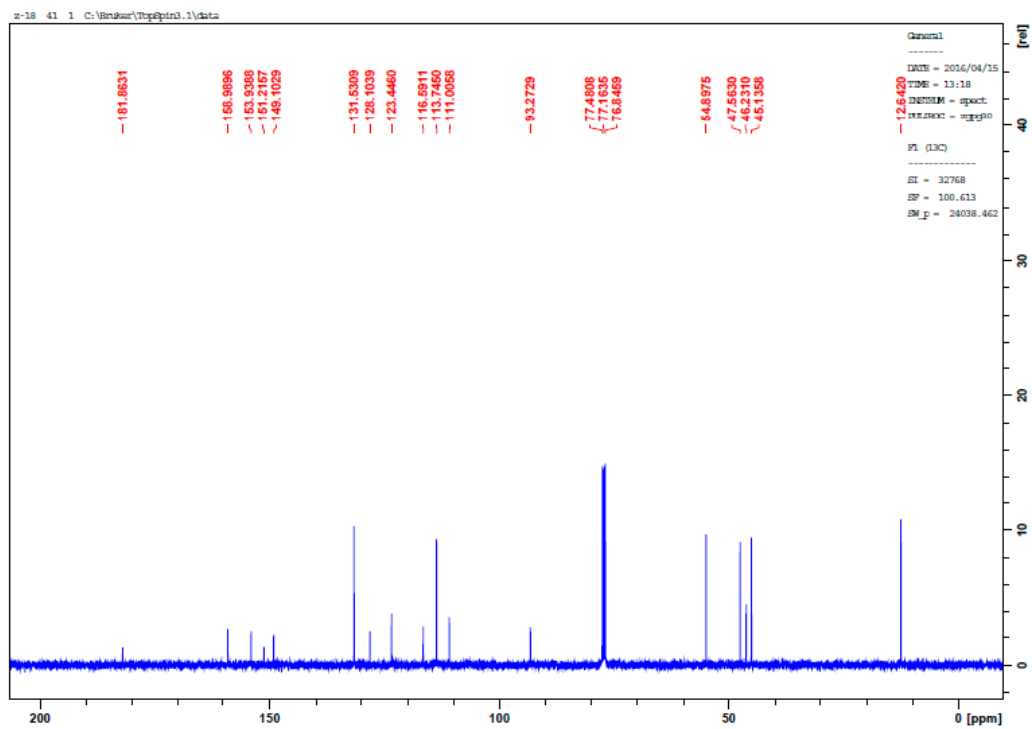
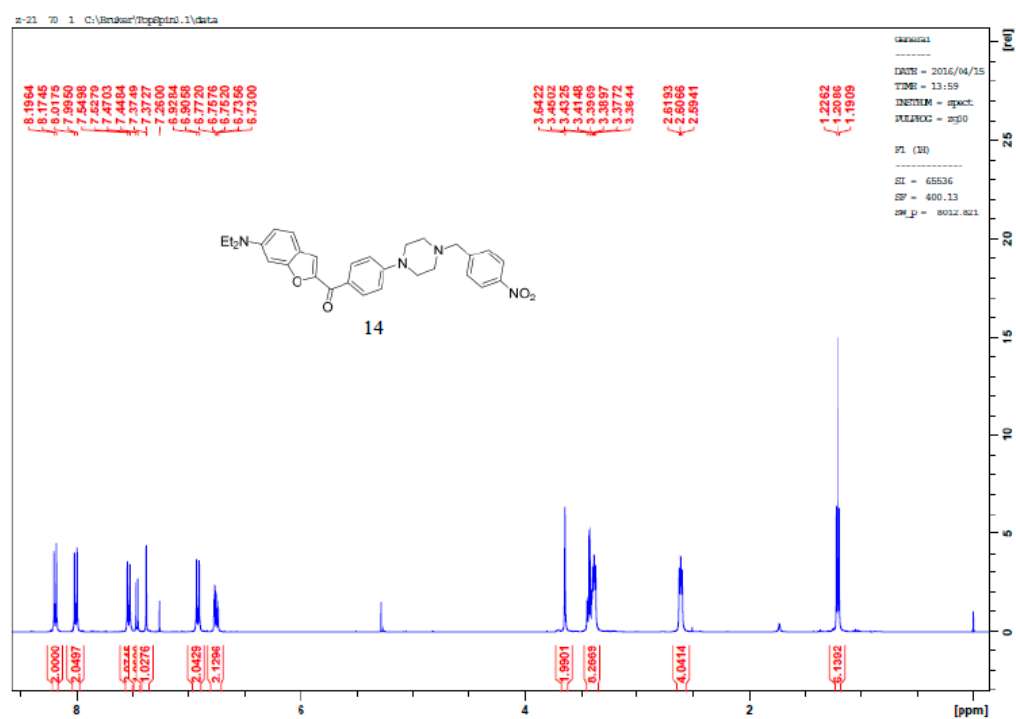
Figure S19. ¹³C-NMR spectrum of compound 10.Figure S20. ¹H-NMR spectrum of compound 13.

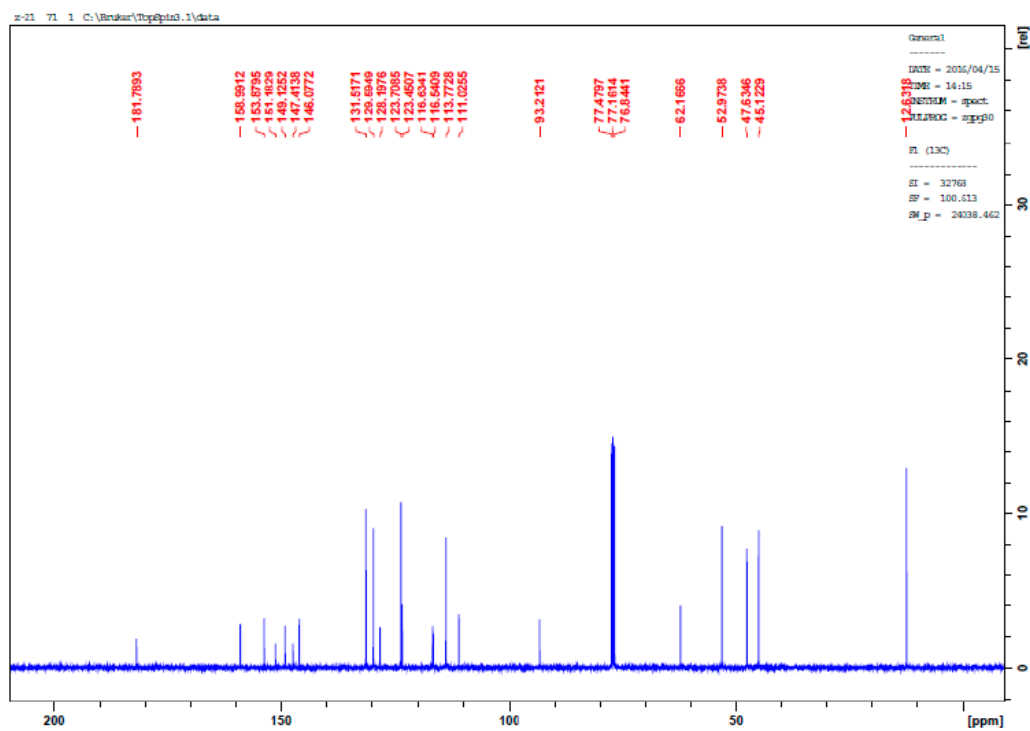
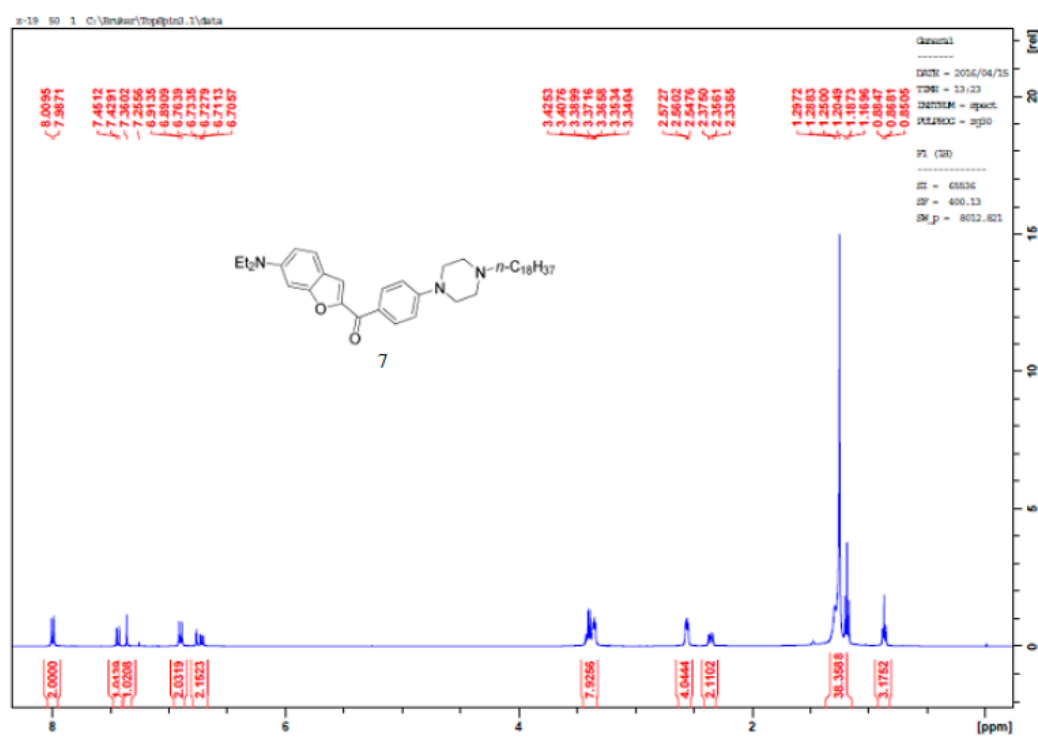
Figure S21. ¹³C-NMR spectrum of compound 13.Figure S22. ¹H-NMR spectrum of compound 12.

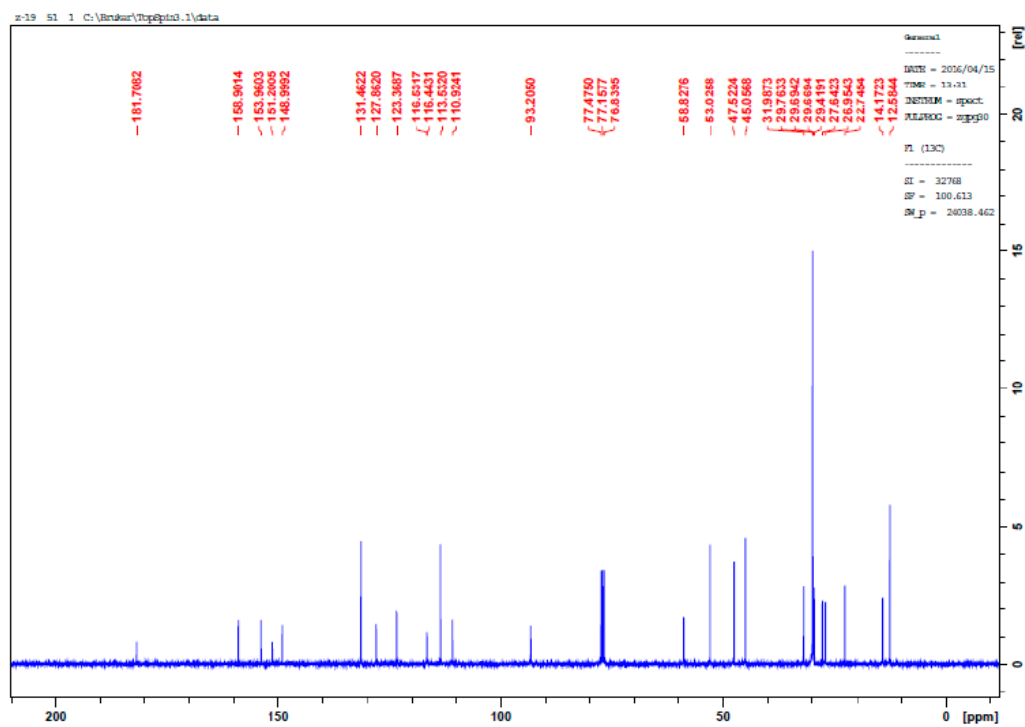
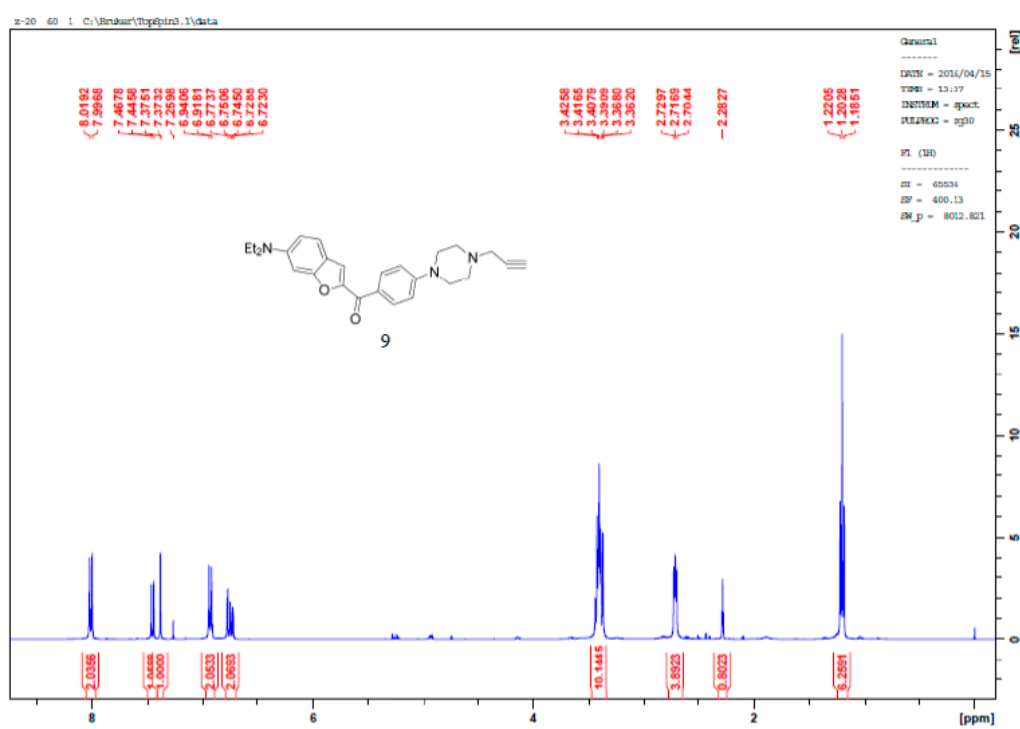
Figure S23. ^{13}C -NMR spectrum of compound 12.Figure S24. ^1H -NMR spectrum of compound 16.

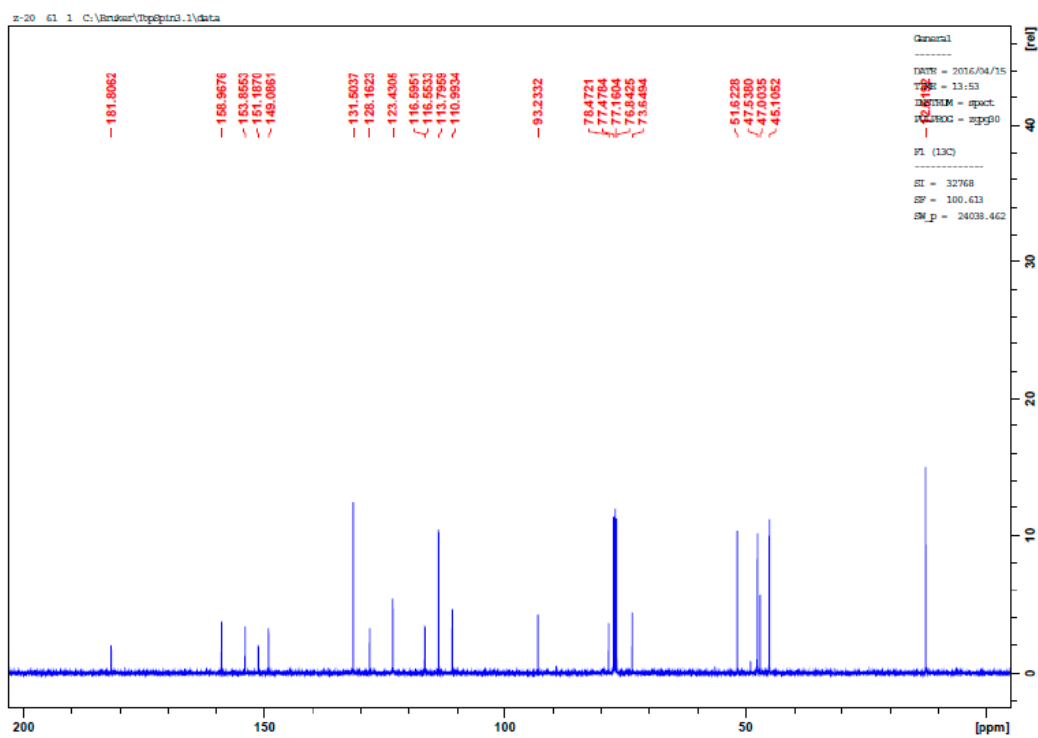
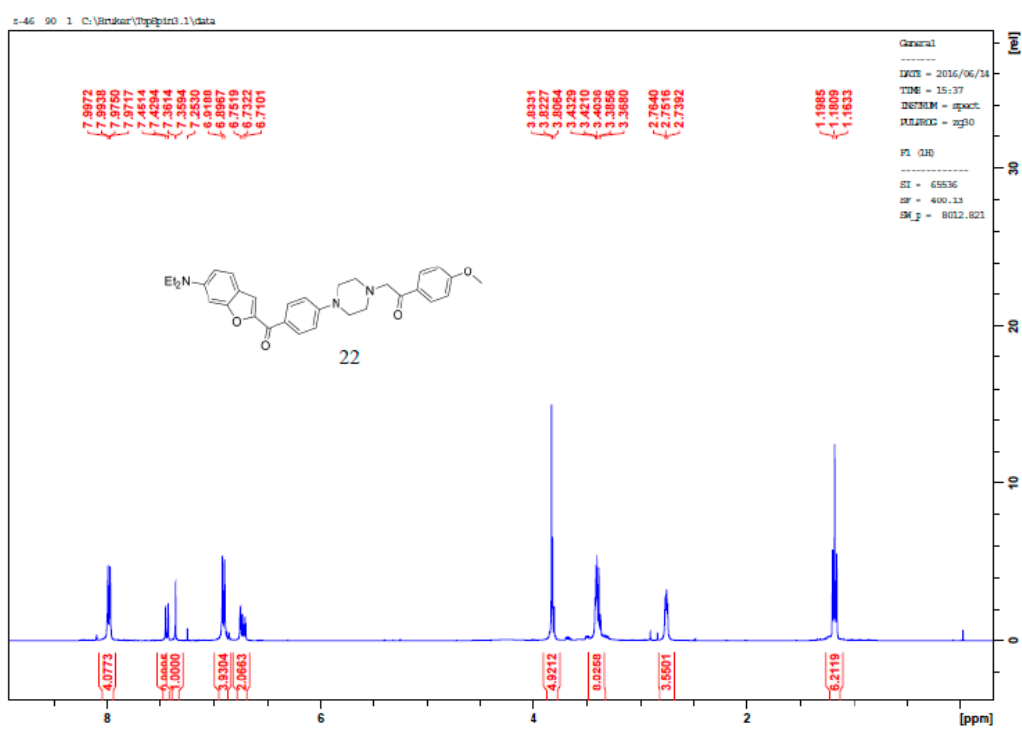
Figure S25. ¹³C-NMR spectrum of compound 16.Figure S26. ¹H-NMR spectrum of compound 6.

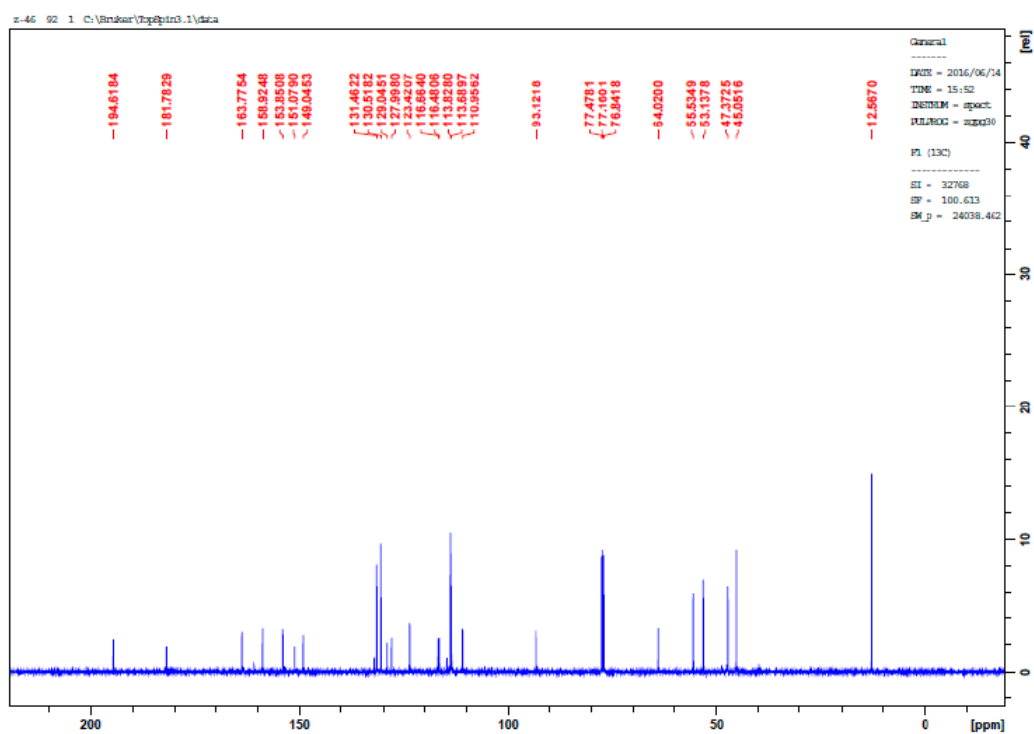
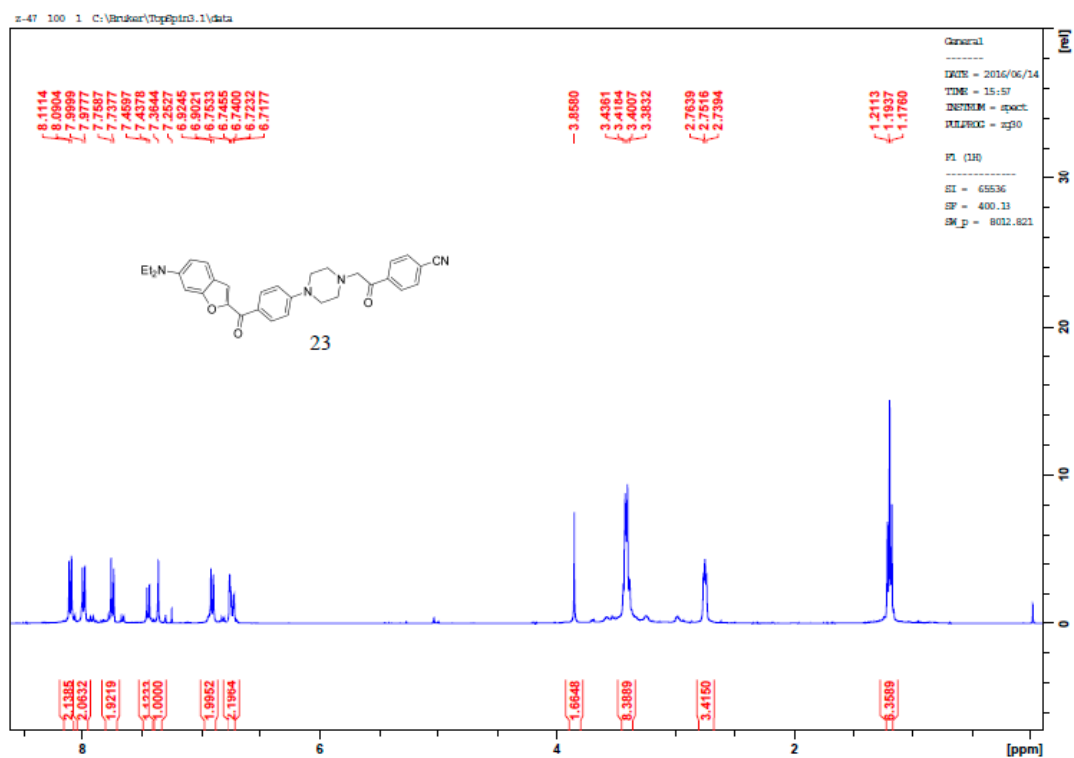
Figure S27. ^{13}C -NMR spectrum of compound 6.Figure S28. ^1H -NMR spectrum of compound 5

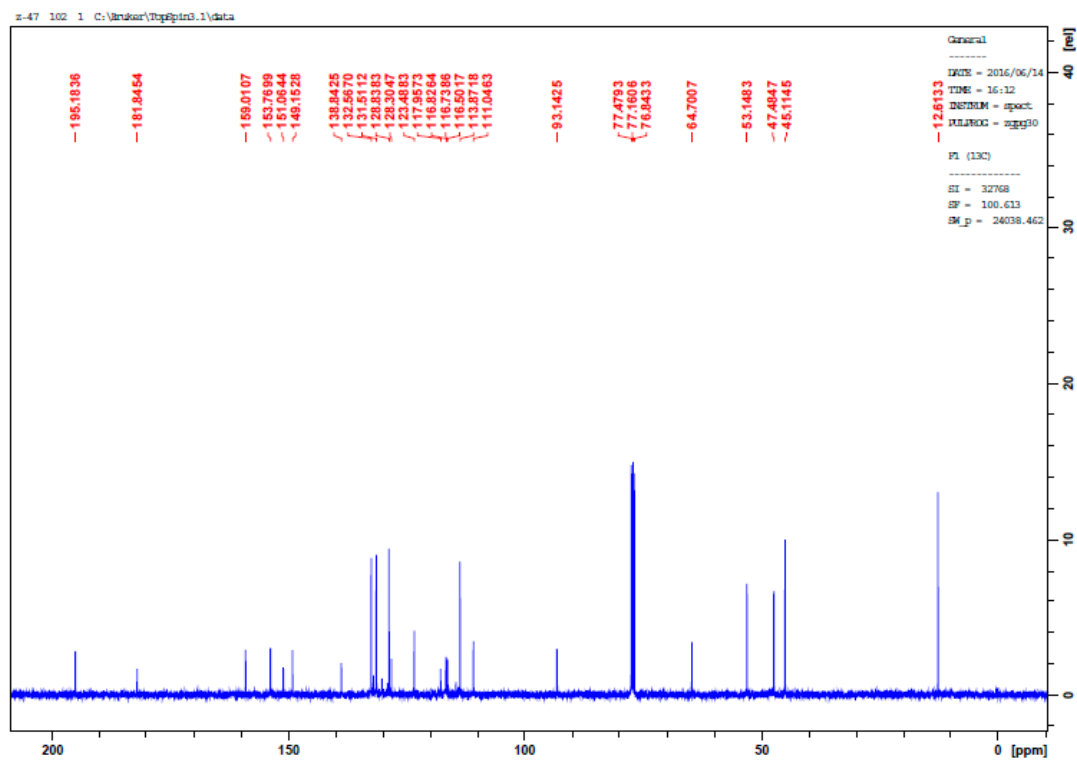
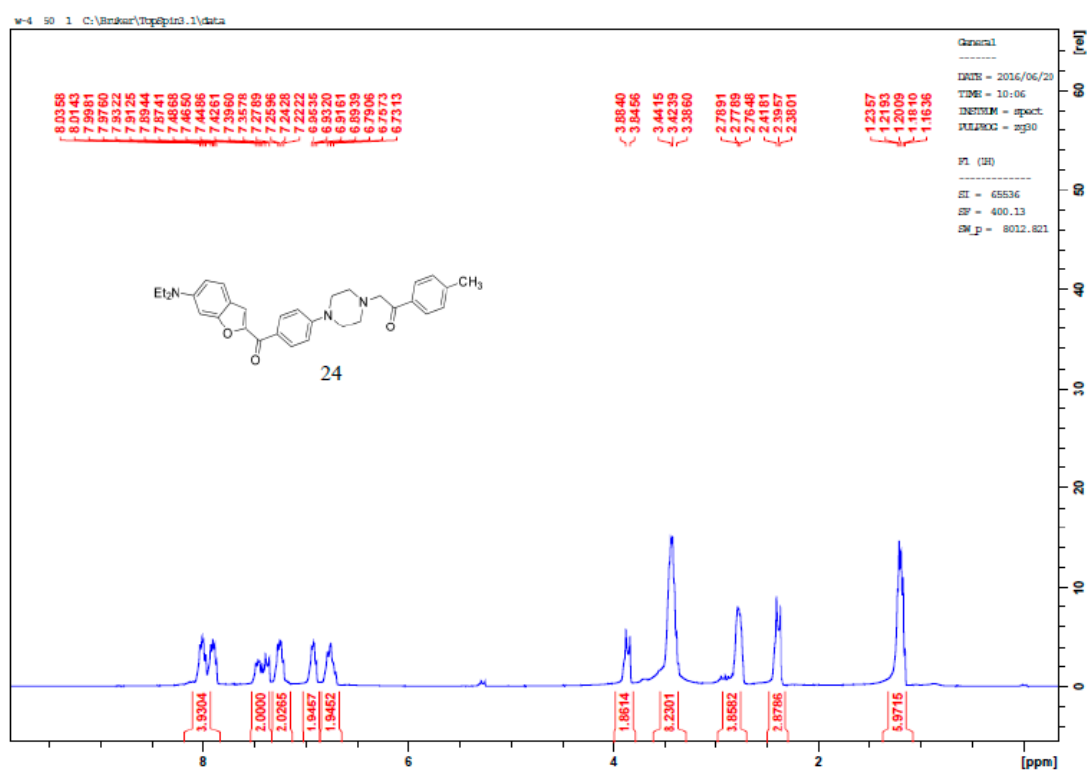
Figure S29. ^{13}C -NMR spectrum of compound 5.Figure S30. ^1H -NMR spectrum of compound 14.

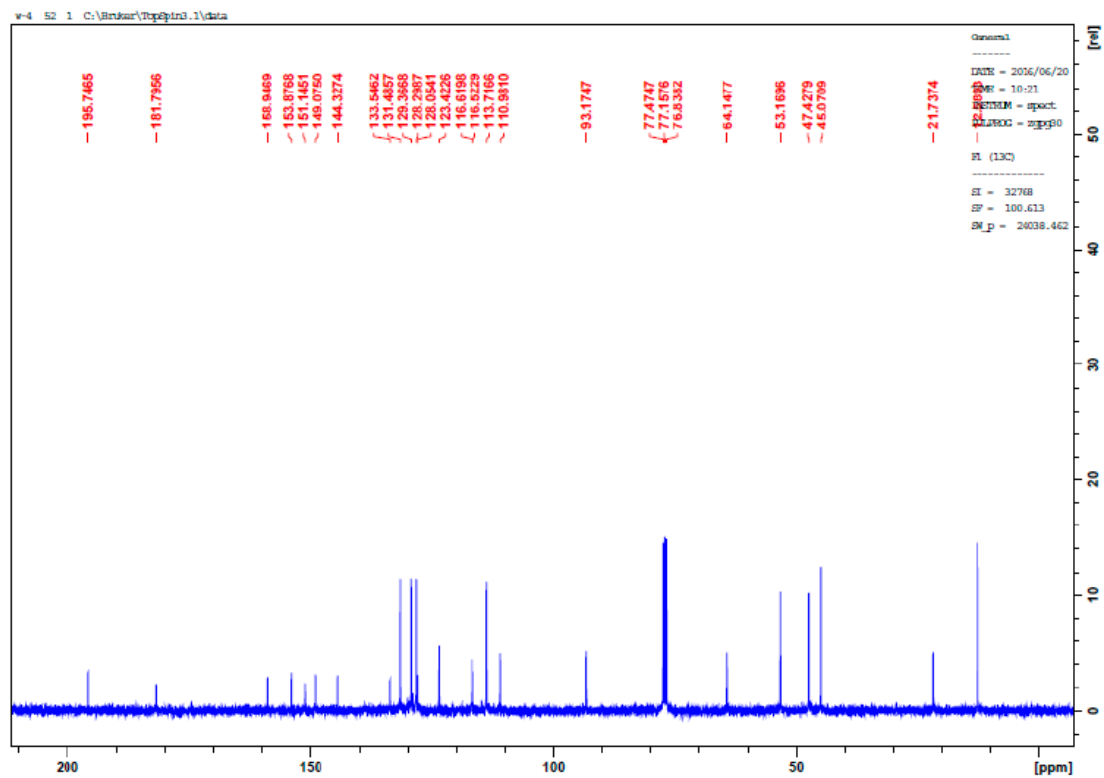
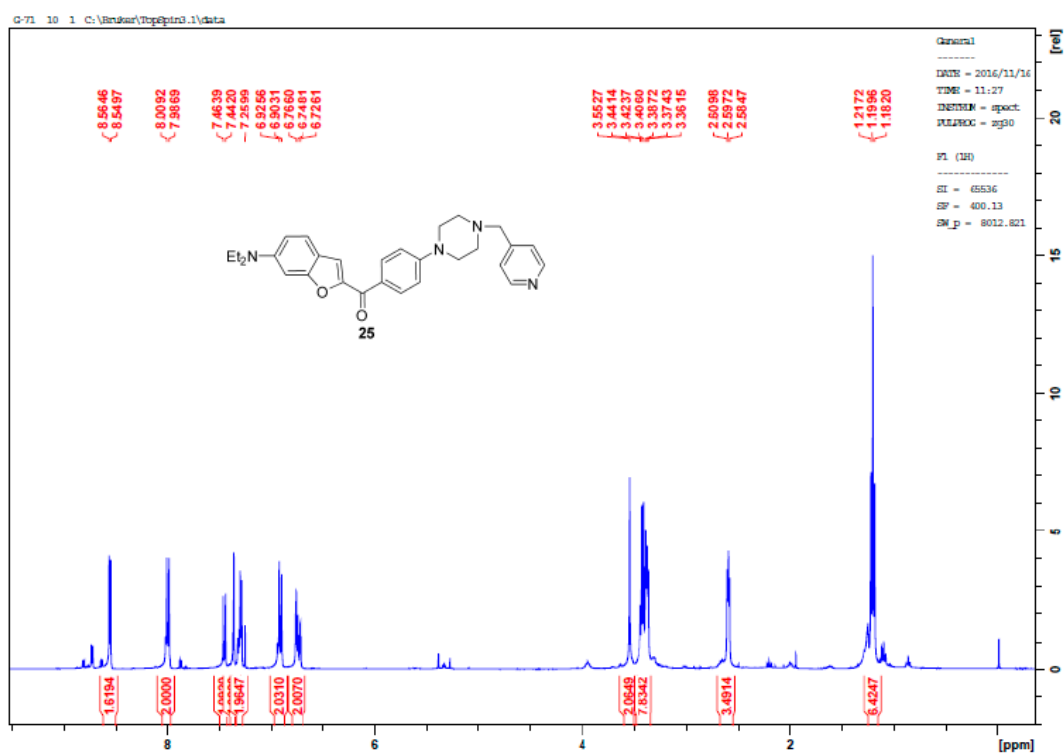
Figure S31. ^{13}C -NMR spectrum of compound 14.Figure S32. ^1H -NMR spectrum of compound 7.

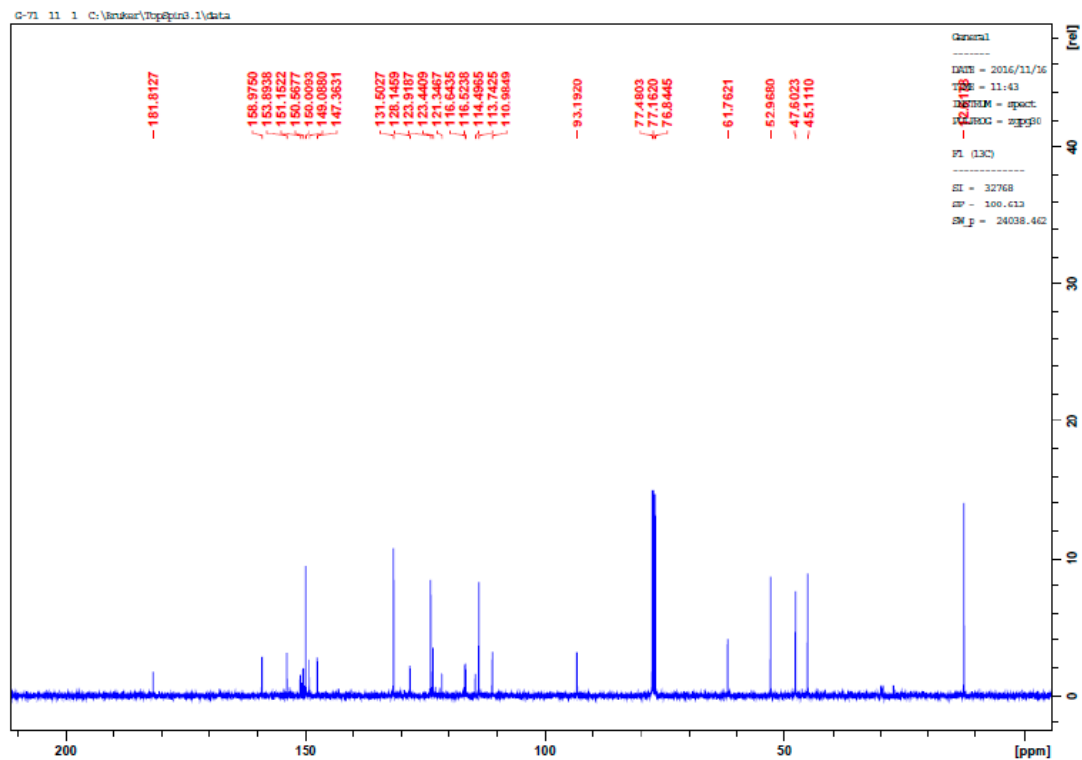
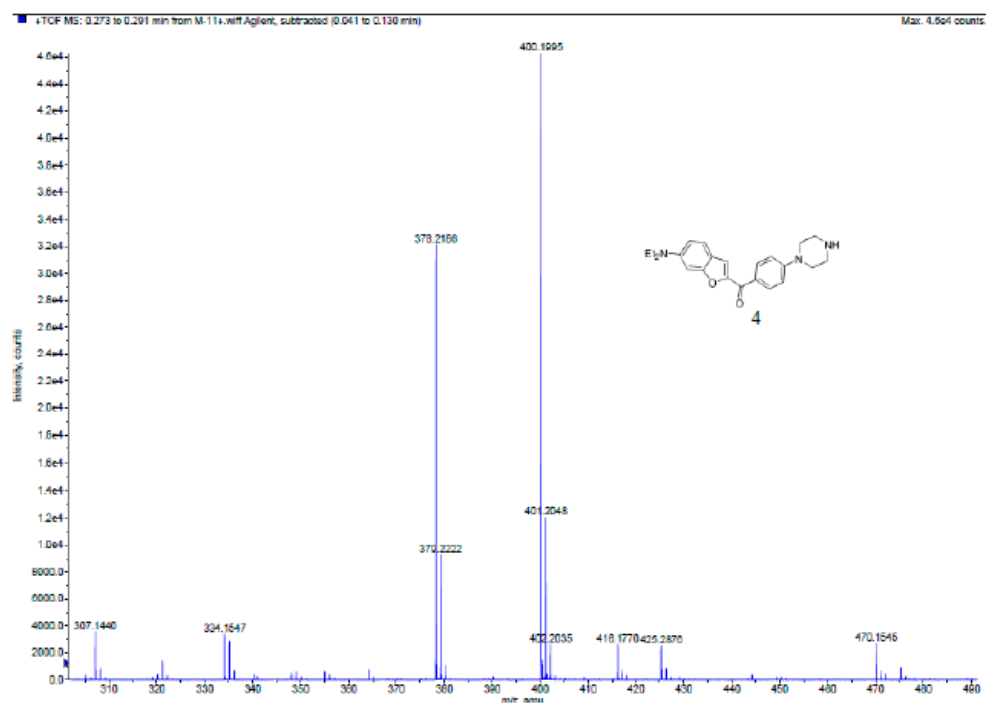
Figure S33. ¹³C-NMR spectrum of compound 7.Figure S34. ¹H-NMR spectrum of compound 9.

Figure S35. ^{13}C -NMR spectrum of compound 9.Figure S36. ^1H -NMR spectrum of compound 22.

Figure S37. ¹³C-NMR spectrum of compound 22.Figure S38. ¹H-NMR spectrum of compound 23.

Figure S39. ^{13}C -NMR spectrum of compound 23.Figure S40. ^1H -NMR spectrum of compound 24.

Figure S41. ¹³C-NMR spectrum of compound 24.Figure S42. ¹H-NMR spectrum of compound 25.

Figure S43. ^{13}C -NMR spectrum of compound 25.

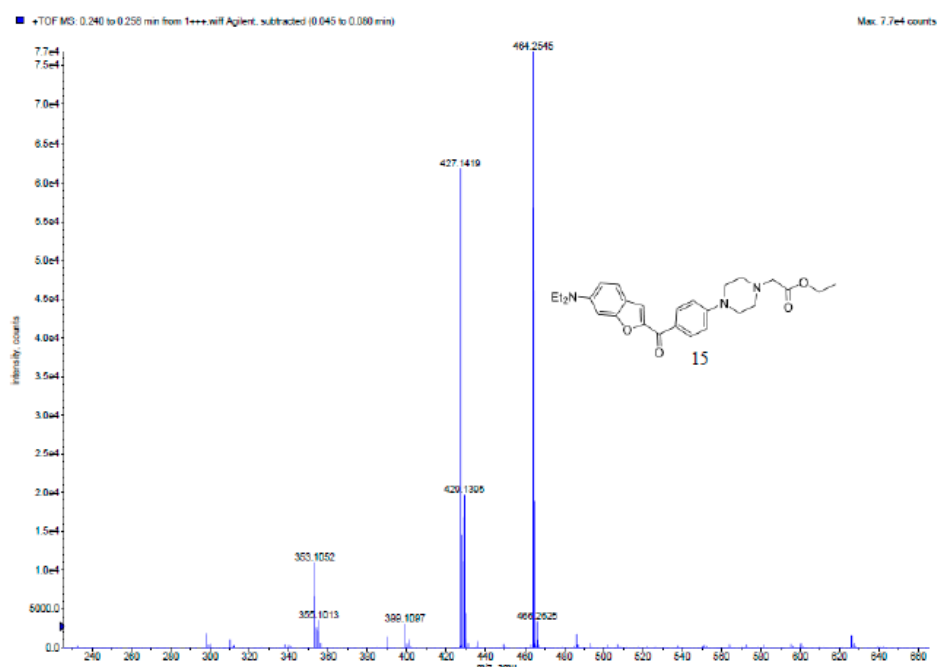
Elemental composition calculator

Target m/z: +400.1995 amu
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 Result type: Elemental
 Max num of results: 100
 Min DSE: -0.5000 Max DSE: +50.0000
 Electron state: OddAndEven
 Num of charges: 1
 Add water: N/A
 Add proton: N/A
 File Name: M-11+.v11ff

	Element	Min Number	Max Number
1	C	0	23
2	F	0	0
3	N	0	27
4	O	0	0
5	S	0	3
6	Na	0	1
7	Cl	0	0
8	Br	0	0
9	S	0	0

	Formula	Calculated m/z (amu)	mDa Error	PPM Error	DSE
1	C23 H27 N3 O2 Na	400.1995	-0.0485	-0.1211	11.5

Figure S44. HRMS spectrum of compound 4.



Elemental composition calculator

Target m/z: +464.2545 amu
 Tolerance: +100.0000 ppm
 Result type: Elemental
 Max num of results: 100
 Min DSE: -0.5000 Max DSE: +50.0000
 Electron state: Even
 Num of charges: 1
 Add water: N/A
 Add proton: N/A
 File Name: 1+++ v11ff

	Element	Min Number	Max Number
1	N	0	0
2	C	0	27
3	F	0	0
4	H	0	34
5	Cl	0	0
6	N	0	0
7	Na	0	1
8	O	0	4
9	S	0	0

	Formula	Calculated m/z (amu)	mDa Error	PPM Error	DSE
1	C27 H24 N2 O4	464.2543	0.1104	0.2352	12.5

Figure S45. HRMS spectrum of compound 15.

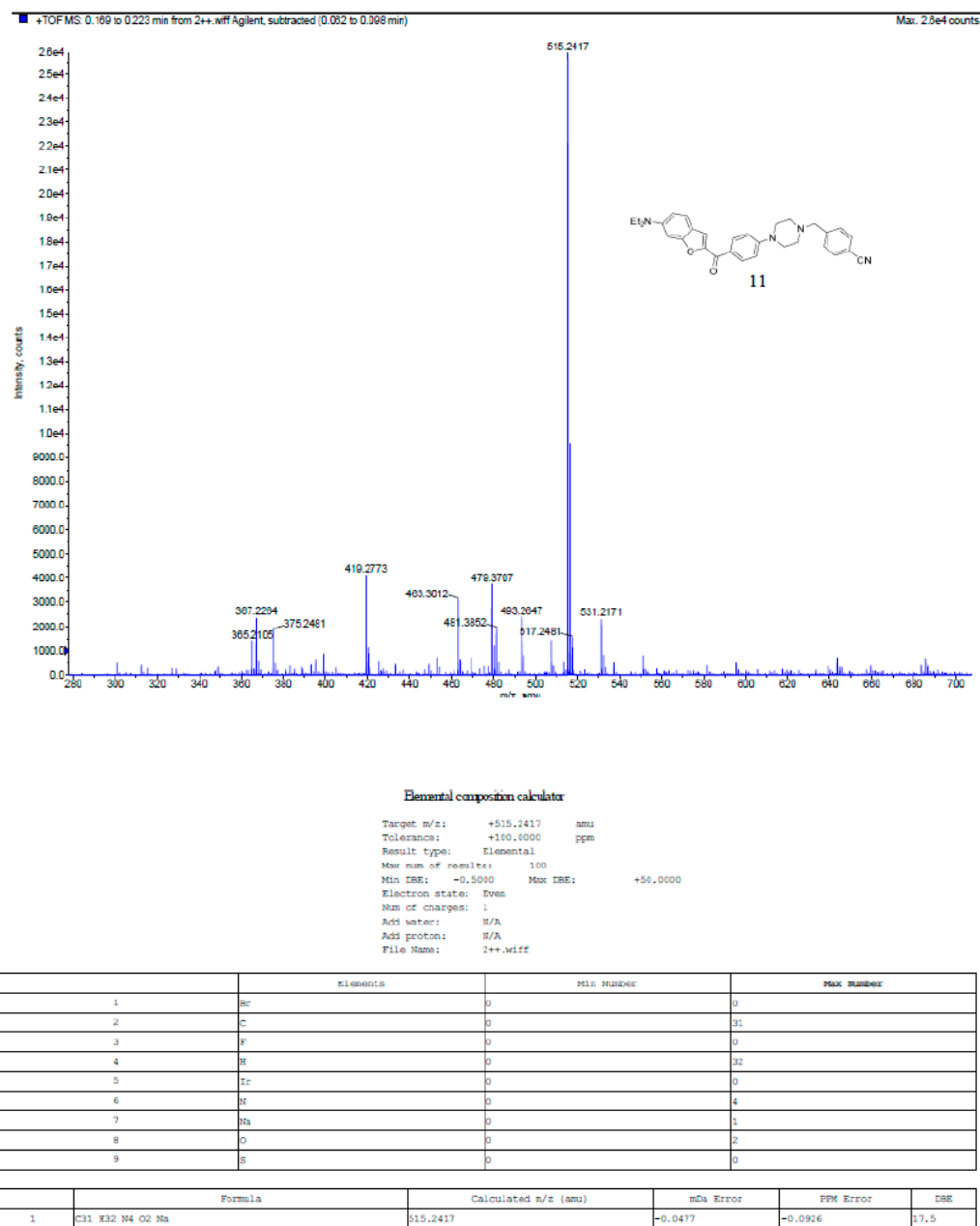


Figure S46. HRMS spectrum of compound 11.

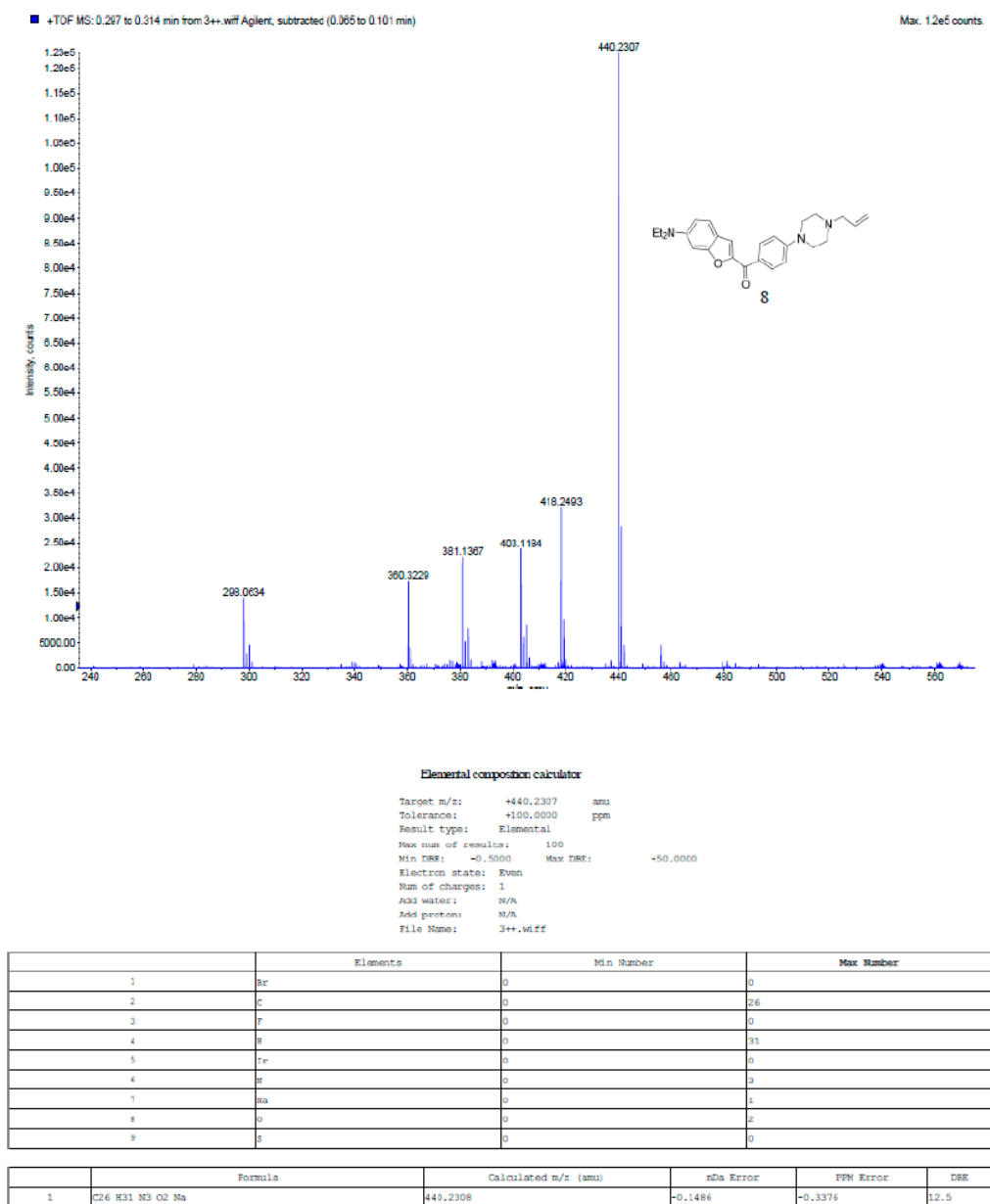


Figure S47. HRMS spectrum of compound 8.

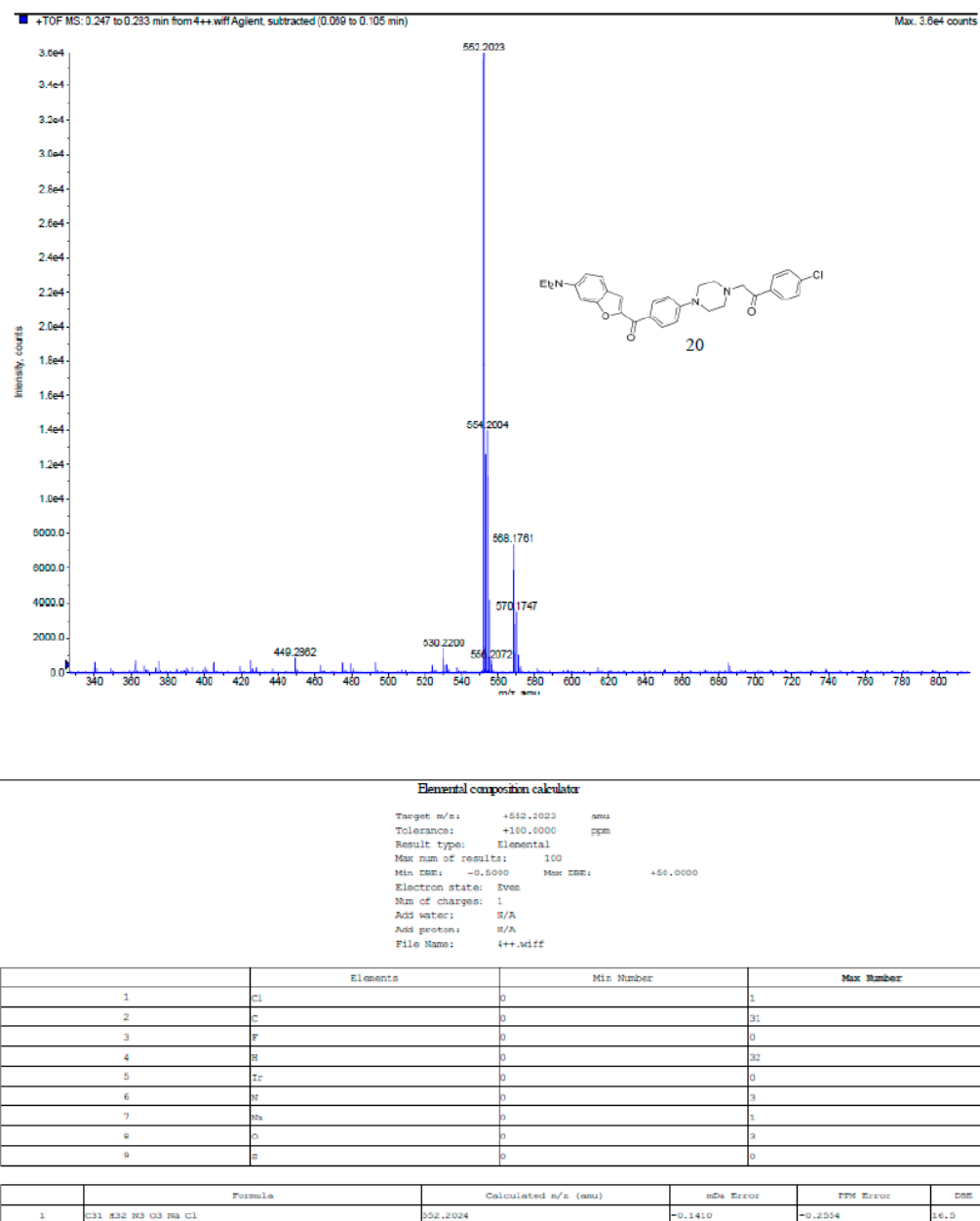
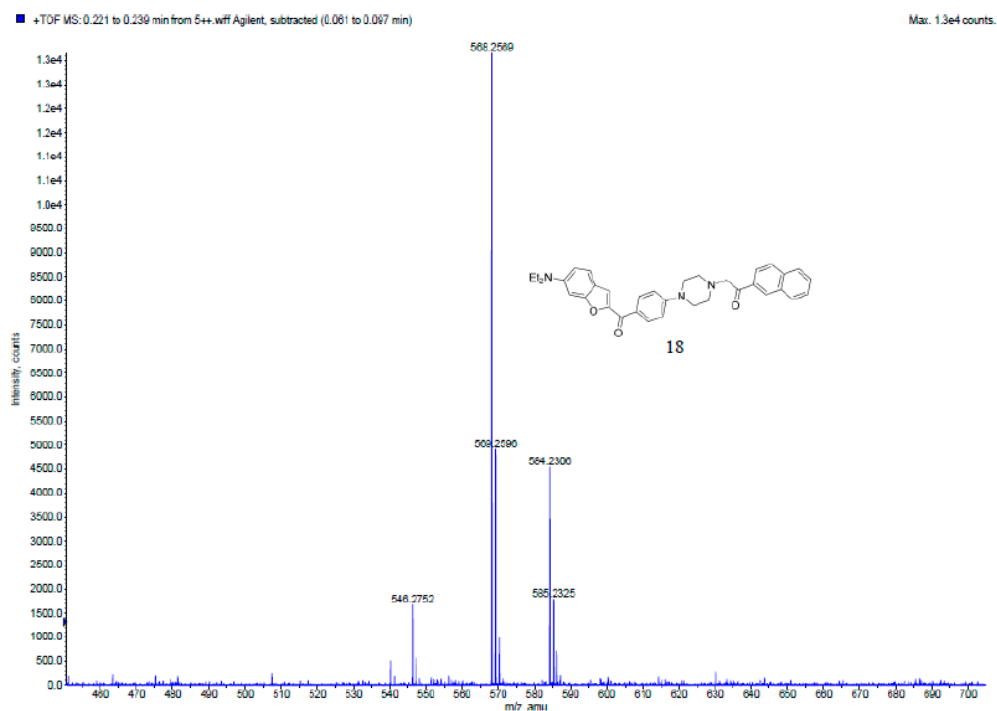


Figure S48. HRMS spectrum of compound 20.



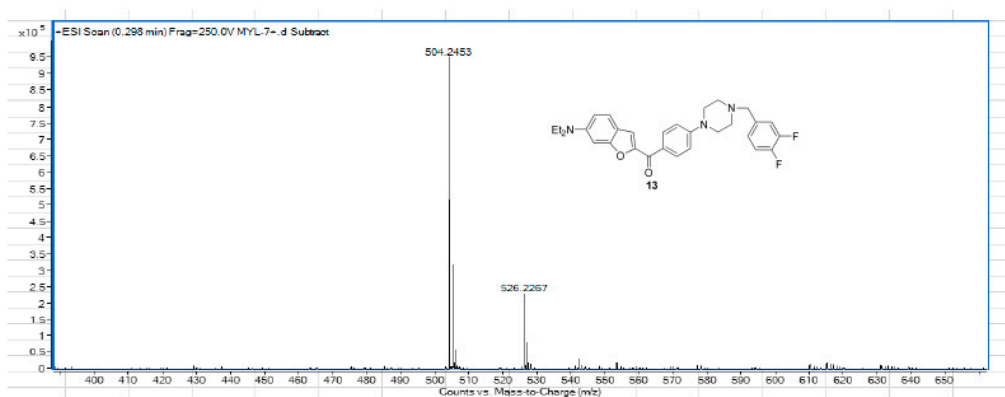
Elemental composition calculator

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 Tolerance: +10.0000 ppm
 Result type: Elemental
 Max num of results: 100
 Min dB: -0.5000 Max dB: +10.0000
 Electron state: Even
 Min of charges: 1
 Add water: N/A
 Add proton: N/A
 File Name: 5++.wiff

	Elements	Min Number	Max Number
1	Cl	0	1
2	C	0	35
3	F	0	0
4	H	0	35
5	Ir	0	0
6	N	0	3
7	Na	0	1
8	O	0	3
9	S	0	2

	Formula	Calculated m/z (amu)	mDa Error	PPM Error	DBE
1	C ₂₆ H ₃₁ N ₃ O ₃ Na	568.2570	-0.1434	-0.2574	14.5

Figure S49. HRMS spectrum of compound 18.

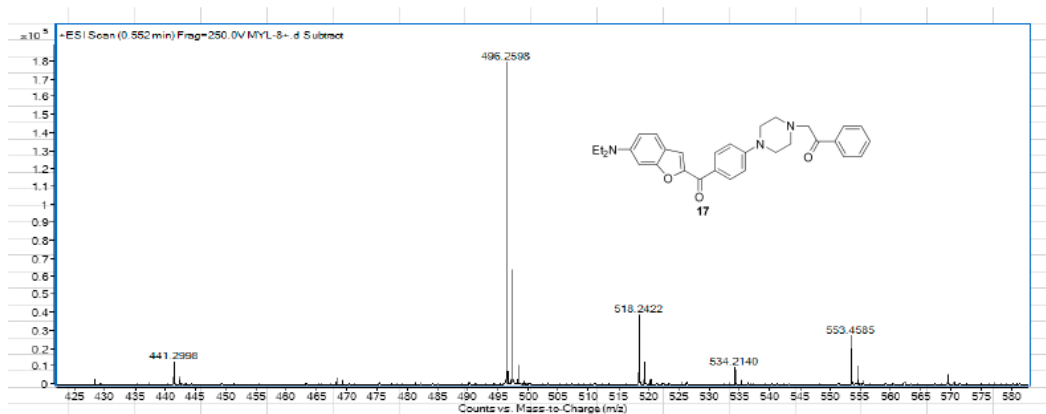


MS Formula Results: + Scan (0.298 min) Sub (MYL-7+.d)

m/z	Ion	Formula	Abundance
504.2453	(M+H) ⁺	C30 H32 F2 N3 O2	952181.8

Best	Formula (M)	Ion Formula	Score	Cross Score	Calc m/z	Diff (ppm)	Mass Match	Abund Match	Spacing Match
✓	C30 H31 F2 N3	C30 H32 F2 N3 O2	99.19		504.2457	0.92	99.07	99.91	98.55

Figure S50. HRMS spectrum of compound 13.

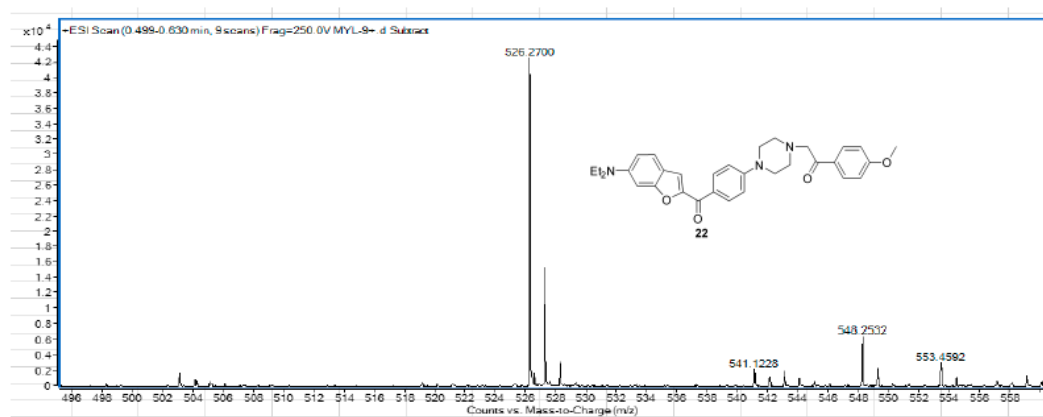


MS Formula Results: + Scan (0.552 min) Sub (MYL-8+.d)

m/z	Ion	Formula	Abundance
496.2598	(M+H) ⁺	C31 H34 N3 O3	182076.2

Best	Formula (M)	Ion Formula	Score	Cross Score	Calc m/z	Diff (ppm)	Mass Match	Abund Match	Spacing Match
✓	C31 H33 N3 O3	C31 H34 N3 O3	98.98		496.2595	-0.78	99.36	99.49	97.62

Figure S51. HRMS spectrum of compound 17.

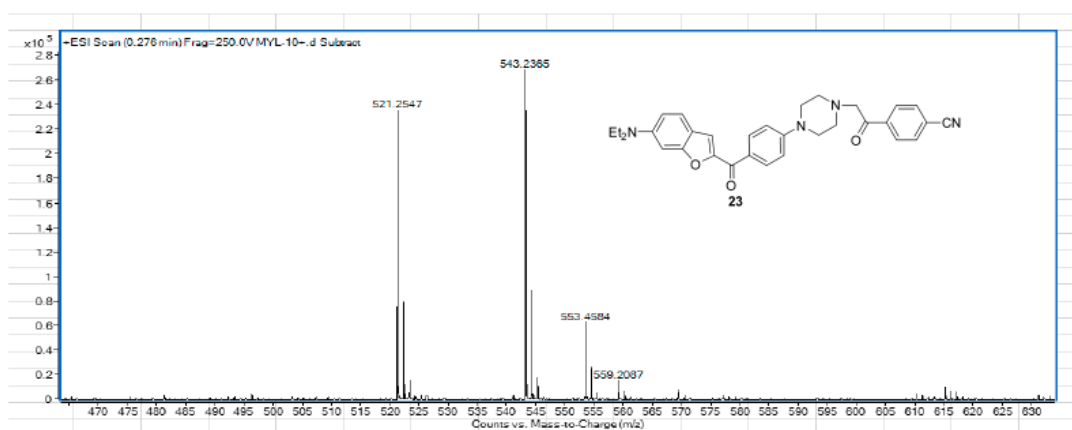


MS Formula Results: + Scan (0.499-0.630 min) Sub (MYL-9+.d)

m/z	Ion	Formula	Abundance
526.27	(M+H) ⁺	C32 H36 N3 O4	42866.6

Best	Formula (M)	Ion Formula	Score	Cross Score	Calc. m/z	Diff. (ppm)	Mass Match	Abund. Match	Spacing Match
<input checked="" type="checkbox"/>	C32 H35 N3 O4	C32 H36 N3 O4	98.74		526.27	-0.04	100	99.82	94.92

Figure S52. HRMS spectrum of compound 22.



MS Formula Results: + Scan (0.276 min) Sub (MYL-10+.d)

m/z	Ion	Formula	Abundance
521.2547	(M+H) ⁺	C32 H33 N4 O3	235941.4

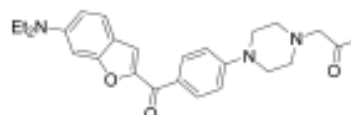
Best	Formula (M)	Ion Formula	Score	Cross Score	Calc. m/z	Diff. (ppm)	Mass Match	Abund. Match	Spacing Match
<input checked="" type="checkbox"/>	C32 H32 N4 O3	C32 H33 N4 O3	99.08		521.2547	0.15	99.97	98.08	98.48

Figure S53. HRMS spectrum of compound 23.

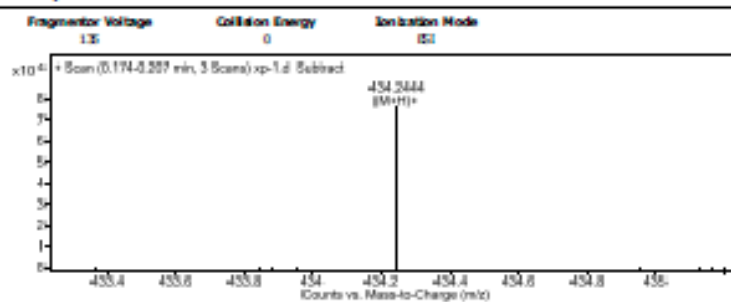
Qualitative Analysis Report

Data Filename	xp-1.d	Sample Name	xp-1
Sample Type	Sample	Position	P1-07
Instrument Name	Instrument1	User Name	
Acq Method	SBL.m	Acquired Time	5/3/2016 3:15:08PM
IRM Calibration Status	Success	DA Method	ES1+.m
Comment			

Sample Group Info.
 Acquisition SW 6200 series TOF/5500 series
 Version Q-TOF 8.05.01 (85125.2)



User 3 spectra



Peak List

m/z	z	Abund	Formula	Ion
217.0264	2	8952.2		
218.1264	2	2990.61		
434.2444	1	76264.91	C ₂₆ H ₃₁ N ₃ O ₃	(M+H) ⁺
436.2475	1	21341.15	C ₂₆ H ₃₁ N ₃ O ₃	(M+H) ⁺
436.2495	1	3163.94	C ₂₆ H ₃₁ N ₃ O ₃	(M+H) ⁺
456.2261	1	11120.98		
457.2292	1	2948.91		
472.1999	1	2430.06		

Formula Calculator Element Limits

Element	Min	Max
C	3	60
H	0	120
O	0	30
N	0	10

Formula Calculator Results

Formula	Calculated Mass	Calculated Mz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C ₂₆ H ₃₁ N ₃ O ₃	433.2365	434.2438	434.2444	-0.6	-1.3	13.0000

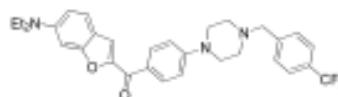
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Figure S54. HRMS spectrum of compound 16.

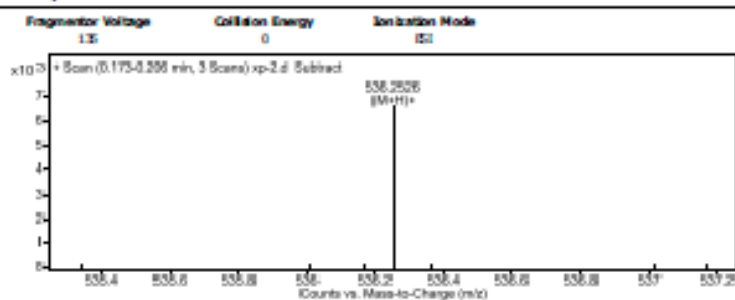
Qualitative Analysis Report

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IRM Calibration Status	Success	DA Method	ESI+.m

Sample Group: Info.
 Acquisition SW: 6200 series TOF/6500 series
 Version: Q-TOF 8.05.01 (85125.2)



User 3 spectra



Peak List

m/z	Z	Abund	Formula	Ion
121.0500	1	8854.64		
277.1775		1434.44		
536.2526	1	8588.54	C31 H32 F3 N3 O2	(M+H)+
537.254	1	2069.8	C31 H32 F3 N3 O2	(M+H)+
558.235	1	1422.66		
574.209	1	1774.92		
607.4705	1	1835.52		
622.0098		4675.40		

Formula Calculator Element Limits

Element	Min	Max
C		60
H		120
O		30
N		10
F		10

Formula Calculator Results

Formula	Calculated Mass	Calculated Mz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C31 H32 F3 N3 O2	535.2447	536.2519	536.2526	-0.3	-0.5	16.0000

--- End Of Report ---

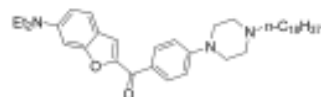
Figure S55. HRMS spectrum of compound 12.

Qualitative Analysis Report

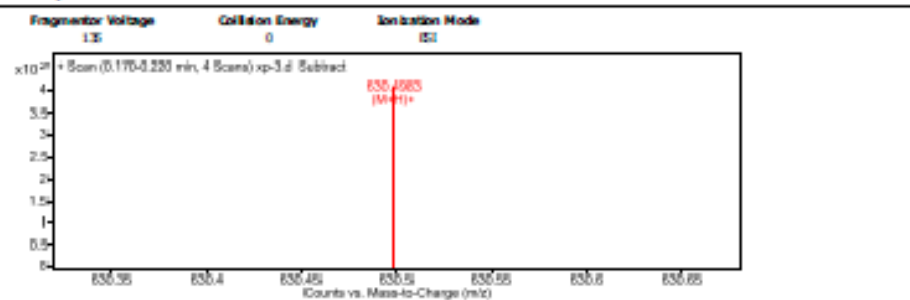
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Sample Type	Sample	Position	P1-09
Instrument Name	Instrument 1	User Name	
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IRM Calibration Status	Success	DA Method	ES1+.m
Comment			

Sample Group
Acquisition SW 6200 series TOF/6500 series
Version Q-TOF 8.05.01 (85125.2)

Info.



User Spectra



Peak List

m/z	z	Abund.
274.2747	1	2374.47
318.3003	1	1604.12
358.3685	1	2149.94
399.2565	1	1377.72
391.1634	1	1476.04
424.2822	1	1844.82
536.2526	1	2189.1
607.4688		1698.78

Formula Calculator Element Limits

Element	Min	Max
C	3	60
H	0	120
O	0	30
N	0	10

Formula Calculator Results

Formula	Calculated Mass	Calculated Mz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C41 H63 N3 O2	630.49920	630.4993	630.4983	-0.7	-1.1	12.0000

--- End Of Report ---

Figure S56. HRMS spectrum of compound 7.

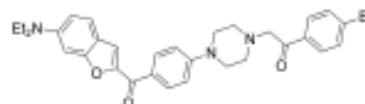
Qualitative Analysis Report

Data Filename	xp-4.d	Sample Name	xp-4
Sample Type	Sample	Position	P1-C1
Instrument Name	Instrument11	User Name	
Acq Method	SBL.m	Acquired Time	5/3/2016 3:19:11 PM
IRM Calibration Status	Success	DA Method	ES14.m

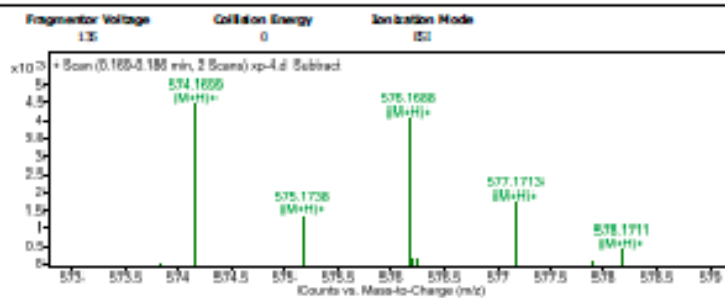
Comment

Sample Group
Acquisition SW 6200 series TOP/6500 series
Version Q-TOF B.05.01 (B5125.2)

Info



User Spectra



Peak List

m/z	z	Abund	Formula	Ion
294.2066		1246.78		
574.1699	1	4464.83	C31 H32 Br N3 O3	(M+H) ⁺
575.1738	1	1313.03	C31 H32 Br N3 O3	(M+H) ⁺
576.1688	1	4028.82	C31 H32 Br N3 O3	(M+H) ⁺
577.1713	1	1702.03	C31 H32 Br N3 O3	(M+H) ⁺
607.8572	1	1181.44		
614.1236		1438.36		
622.2098		1438.96		

Formula Calculator Element Limits

Element	Min	Max
C	3	60
H	0	120
O	0	30
N	0	10
Br	0	5

Formula Calculator Results

Formula	Calculated Mass	Calculated Δ m/z	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C31 H32 Br N3 O3	573.1627	574.1700	574.1699	-0.1	-0.1	17.0000

--- End of Report ---

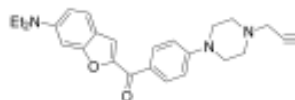
Figure S57. HRMS spectrum of compound 21.

Qualitative Analysis Report

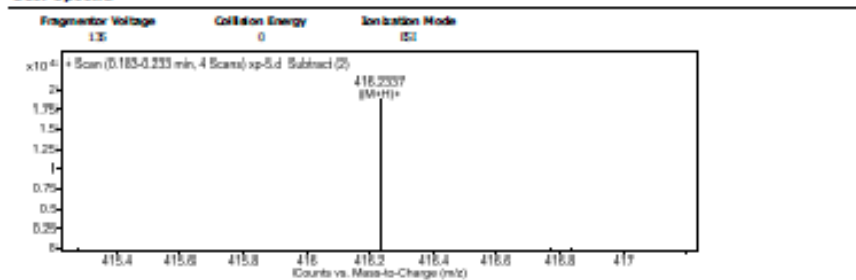
Data Filename	xp-5.d	Sample Name	xp-5
Sample Type	Sample	Position	P1-C2
Instrument Name	Instrument1	User Name	
Acq. Method	S2BL.m	Acquired Time	5/3/2016 3:20:33 PM
IRM Calibration Status	Success	DA Method	ES1+.m

Sample Group
 Acquisition SW 6200 series TOF/6500 series
 Version Q-TOF 8.05.01 (85125.2)

Info



User Spectra



Peak List

m/z	z	Abund.	Formula	Ion
359.257	1	1.795.73		
407.1378	1	1684.78		
416.2337	1	18712.71	C ₂₆ H ₂₉ N ₃ O ₂	(M+H) ⁺
417.2373	1	5685.55	C ₂₆ H ₂₉ N ₃ O ₂	(M+H) ⁺
438.2156	1	3498.21		
454.1889	1	3801.03		
454.2494	1	6063.16		
455.2515	1	2248.17		

Formula Calculator Element Limits

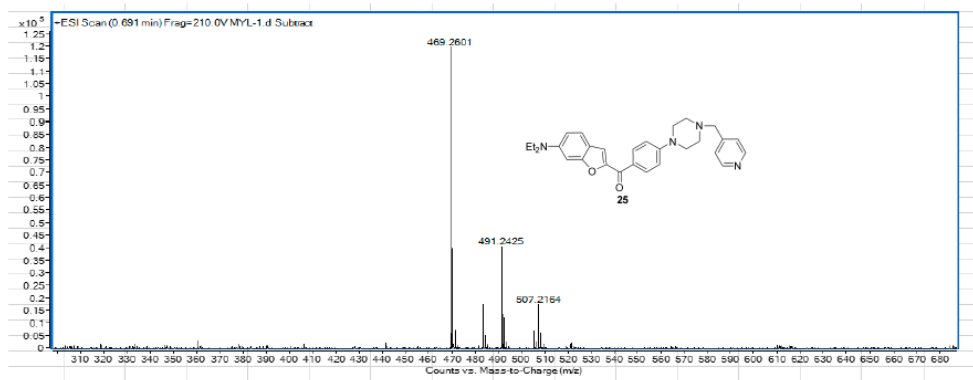
Element	Min	Max
C	3	60
H	0	120
O	0	30
N	0	10

Formula Calculator Results

Formula	Calculated Mass	Calculated Mz	Mz	Diff. (mDa)	DM (ppm)	DBE
C ₂₆ H ₂₉ N ₃ O ₂	415.2240	416.2333	416.2337	-0.5	-1.2	14.0000

--- End Of Report ---

Figure S58. HRMS spectrum of compound 9.



MS Formula Results: + Scan (0.691 min) Sub (MYL-1.d)

m/z	Ion	Formula	Abundance
469.2601	(M+H) ⁺	C29 H33 N4 O2	121334.3

Best	Formula (M)	Ion Formula	Score	Cross Score	Calc m/z	Diff (ppm)	Mass Match	Abund Match	Spacing Match
<input checked="" type="checkbox"/>	C29 H32 N4 O2	C29 H33 N4 O2	99.14		469.2598	-0.7	99.5	99.37	98.14

Figure S59. HRMS spectrum of compound 25.