

Electronic Supplementary Information

Synthesis and Antiplasmodial Activity of 6H,13H-Pyrazino[1,2-a;4,5-a']diindole Analogues Substituted with Basic Side Chains

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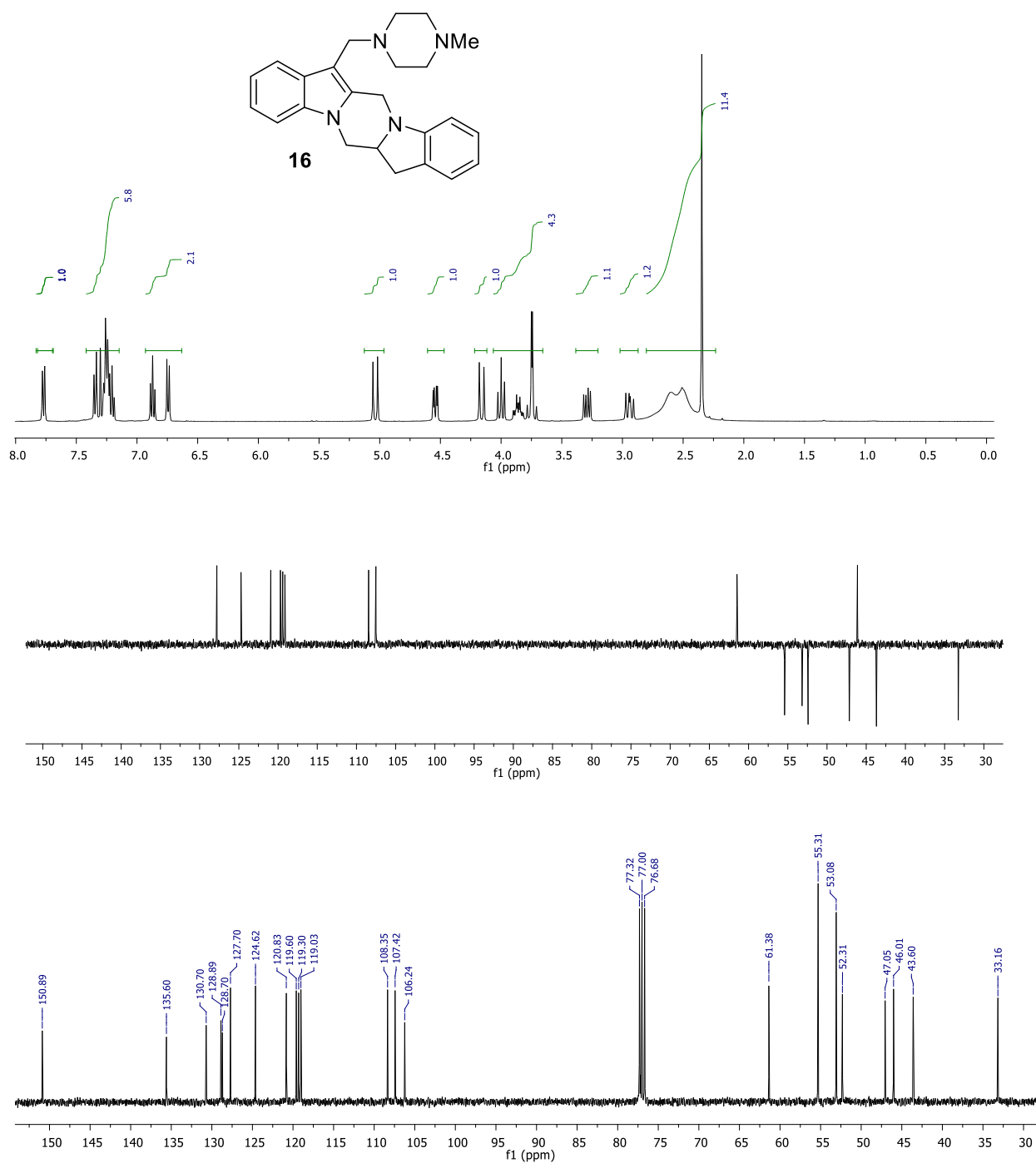
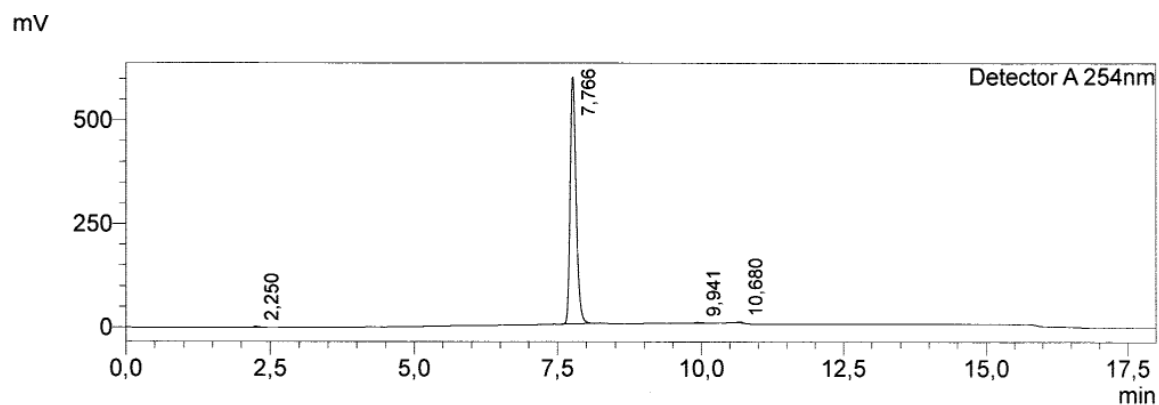
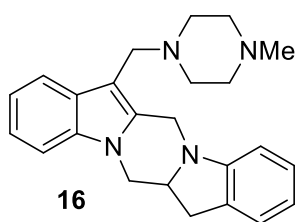


Fig. S1 ^1H (400 MHz), DEPT-135 and ^{13}C (100 MHz)-NMR spectra of compound **16** in CDCl_3



Peak#	Ret. Time	Area	Area%
1	2,250	17592	0,407
2	7,766	4275664	98,848
3	9,941	16540	0,382
4	10,680	15676	0,362
Total		4325472	100,000

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 MassPeaks:536
 Spectrum Mode:Averaged 8,120-8,127(4873-4877) Base Peak:273,05(1143596)
 BG Mode:Calc Segment 1 - Event 1

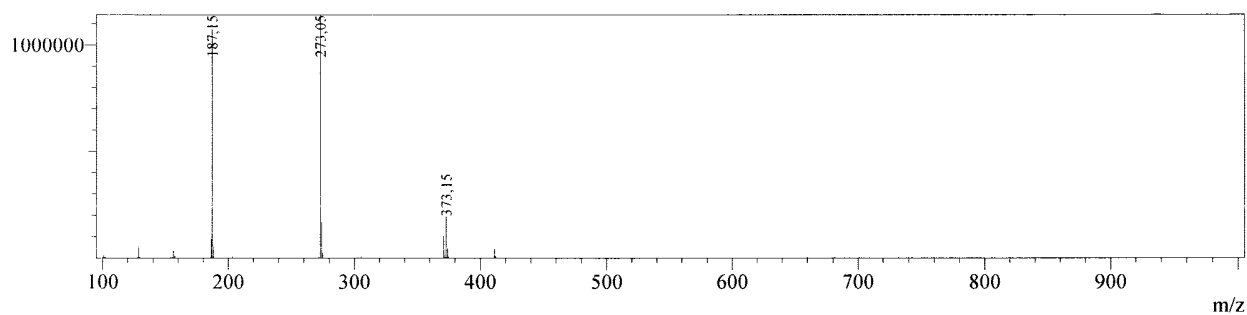


Fig. S2 LCMS data of compound **16**.

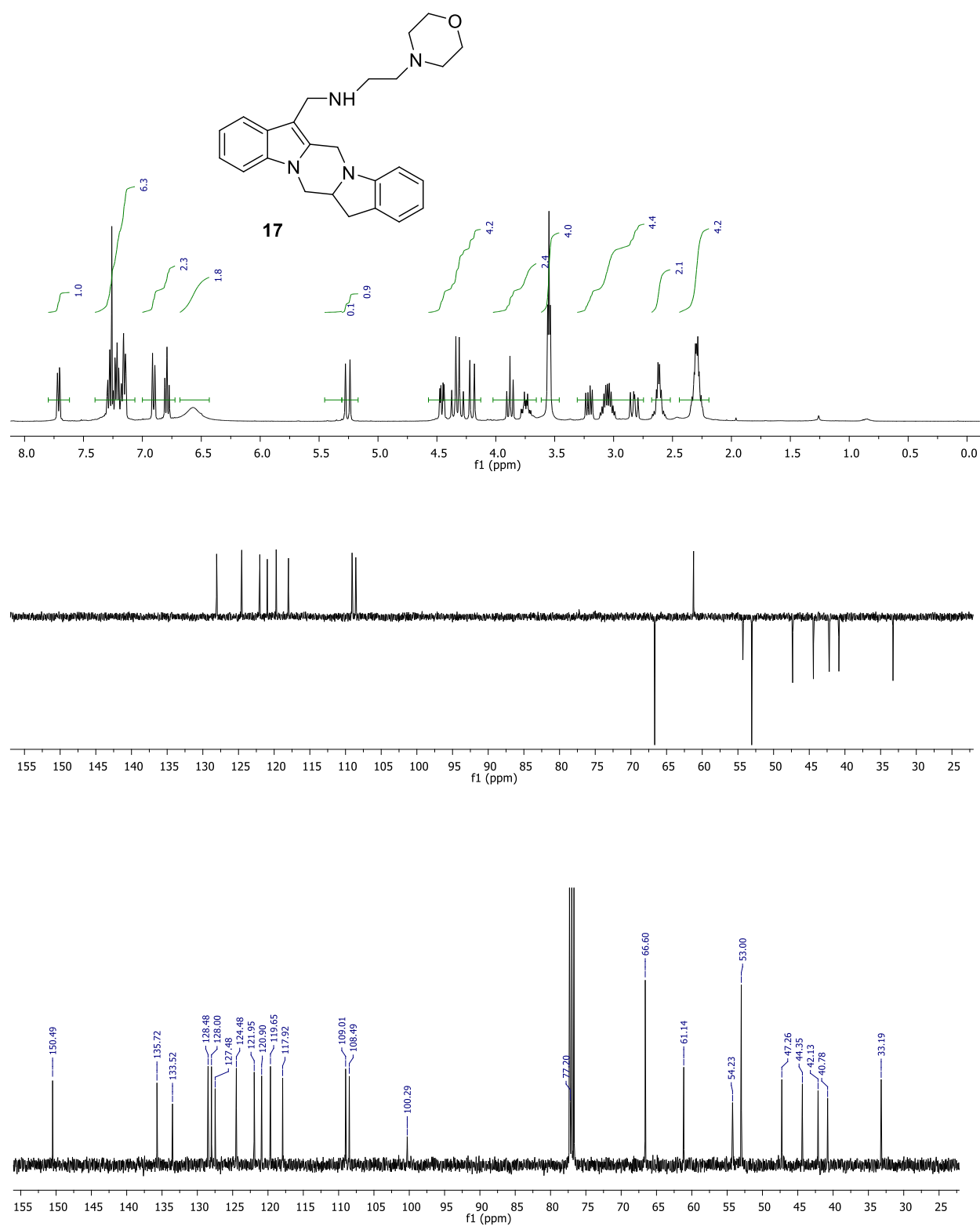
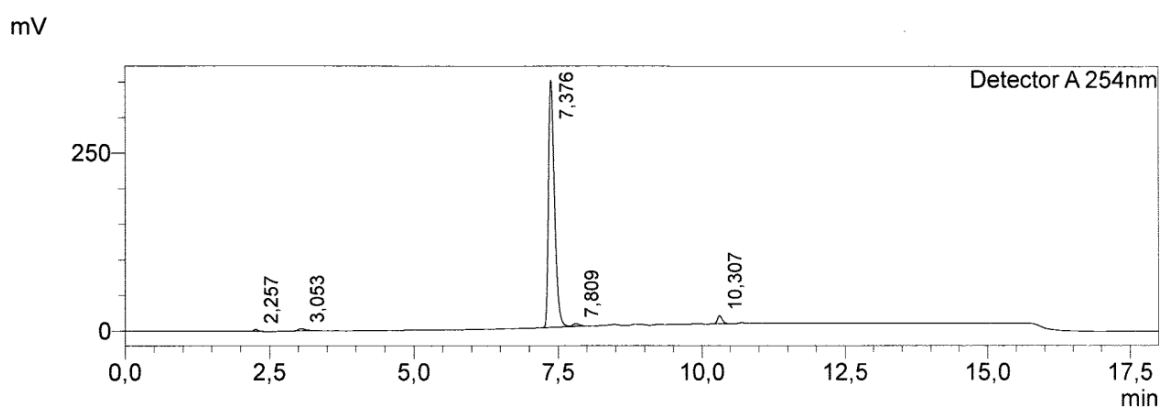
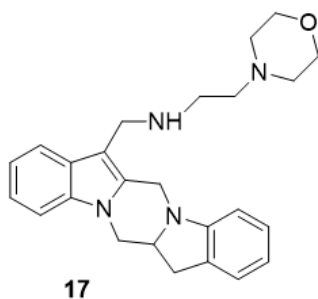


Fig. S3 ^1H (400 MHz), DEPT-135 and ^{13}C (100 MHz)-NMR spectra of compound **17** in CDCl_3



Peak#	Ret. Time	Area	Area%
1	2,257	16629	0,627
2	3,053	28663	1,081
3	7,376	2507674	94,593
4	7,809	32043	1,209
5	10,307	66004	2,490
Total		2651013	100,000

Line#:2 R.Time:---(Scan#;----)
 MassPeaks:484
 Spectrum Mode:Averaged 7.773-7.780(4665-4669) Base Peak:273.05(441952)
 BG Mode:Calc Segment 1 - Event 1

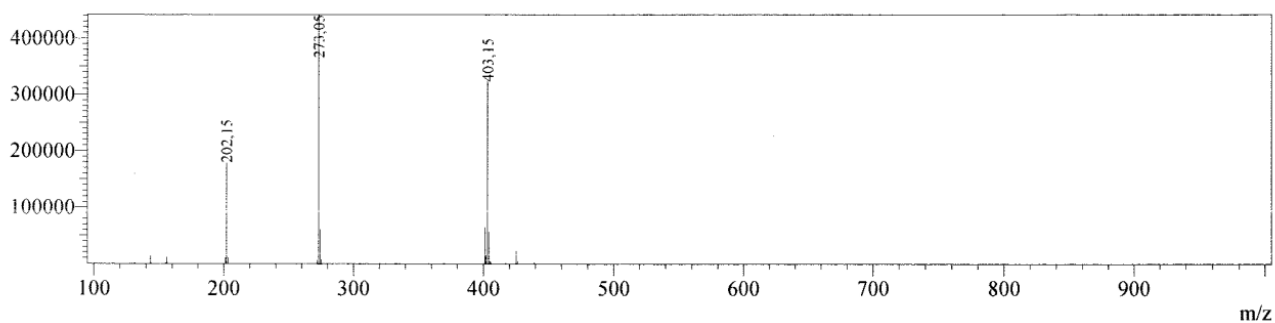


Fig. S4 LCMS data of compound **17**.

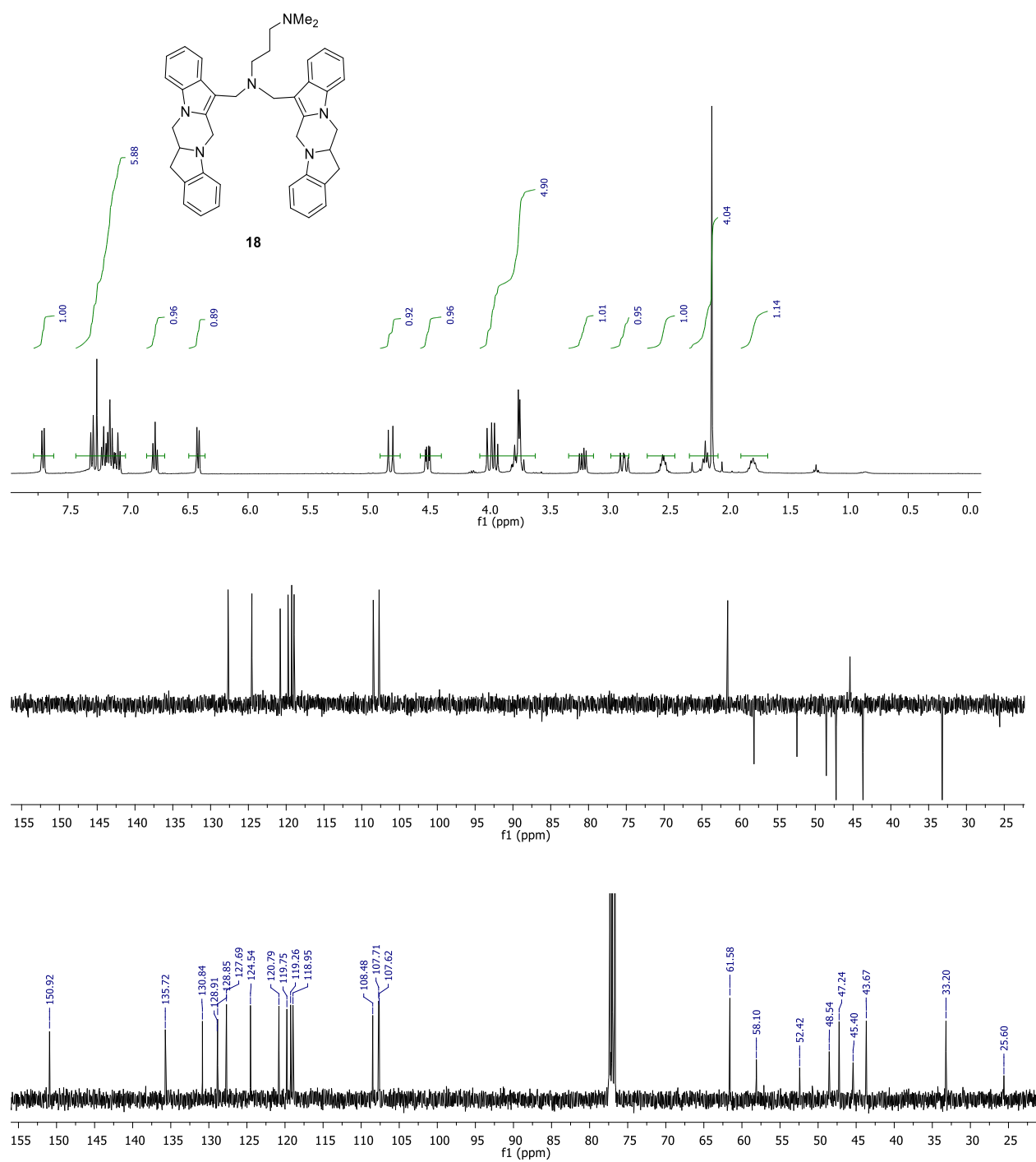
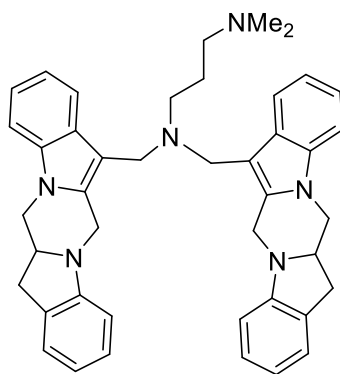
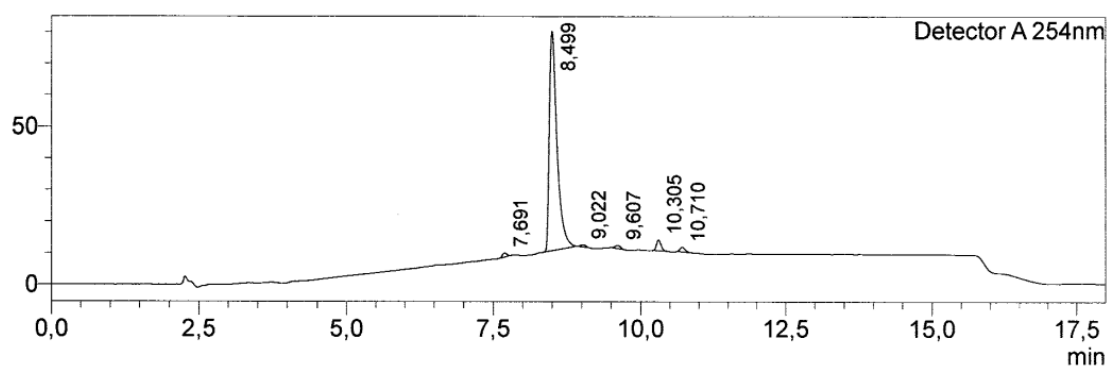


Fig. S5 ¹H (400 MHz), DEPT-135 and ¹³C (100 MHz)-NMR spectra of compound **18** in CDCl₃



18

mv



Peak#	Ret. Time	Area	Area%
1	7,691	6893	1,017
2	8,499	631480	93,148
3	9,022	4618	0,681
4	9,607	6716	0,991
5	10,305	18865	2,783
6	10,710	9359	1,380
Total		677930	100,000

Line#:3 R.Time:----(Scan#:----)
 MassPeaks:392
 Spectrum Mode:Averaged 8,900-8,907(5341-5345) Base Peak:273,05(216185)
 BG Mode:Calc Segment 1 - Event 1

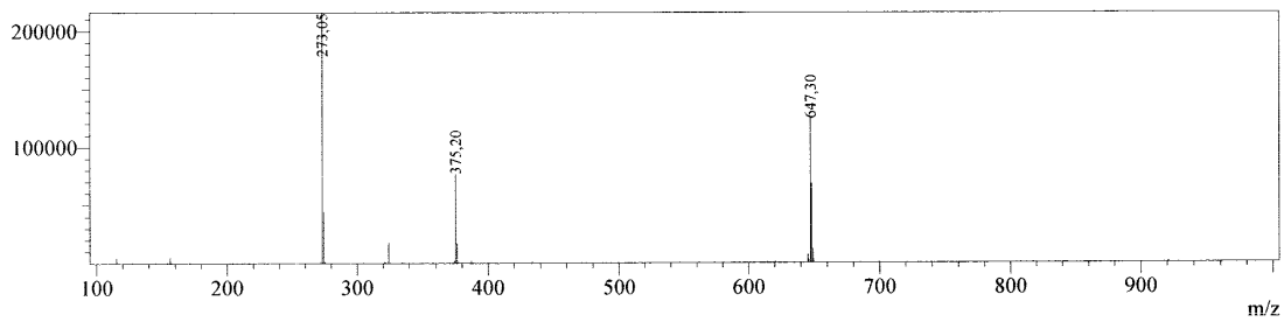


Fig. S6 LCMS data of compound 18

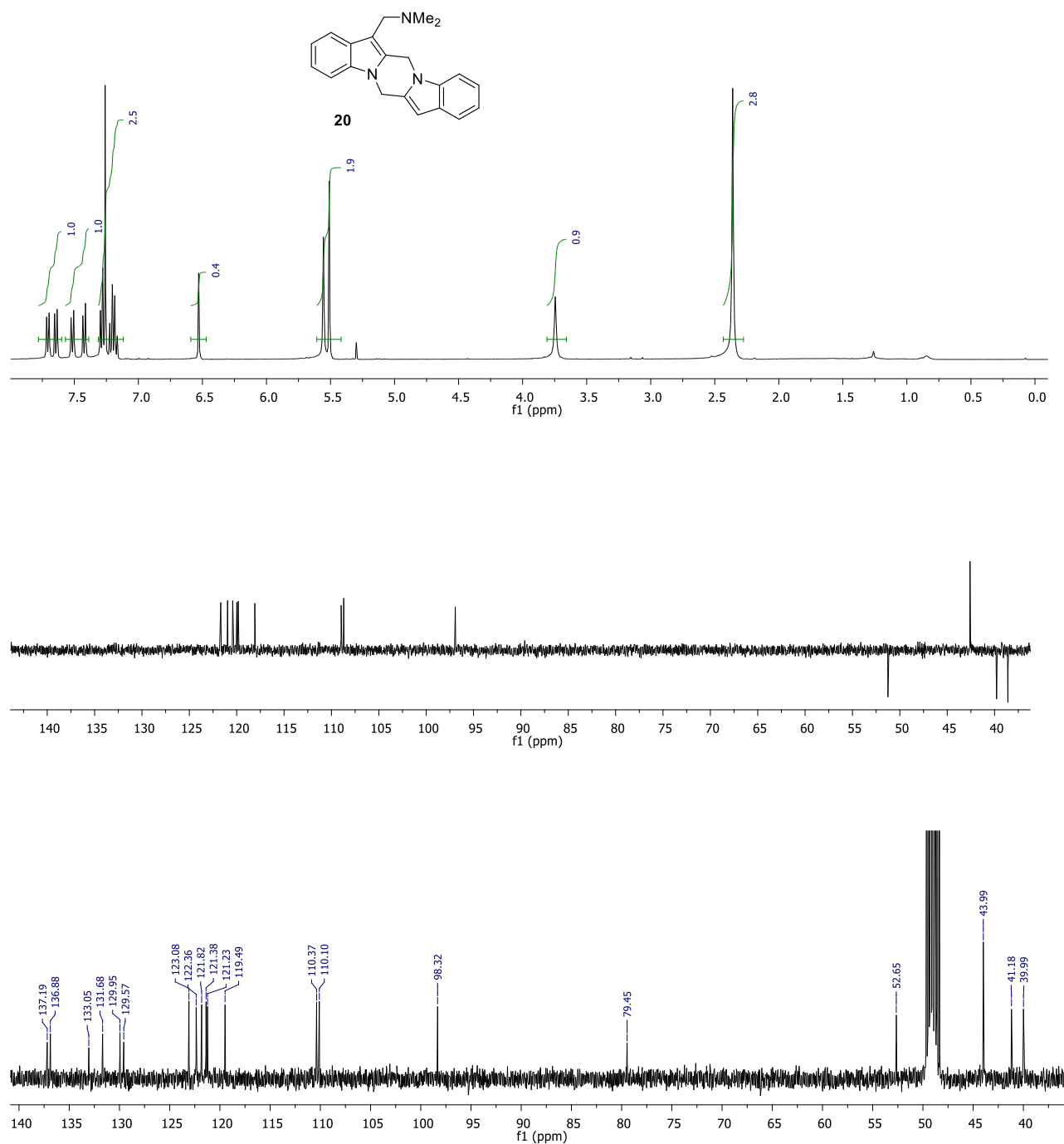
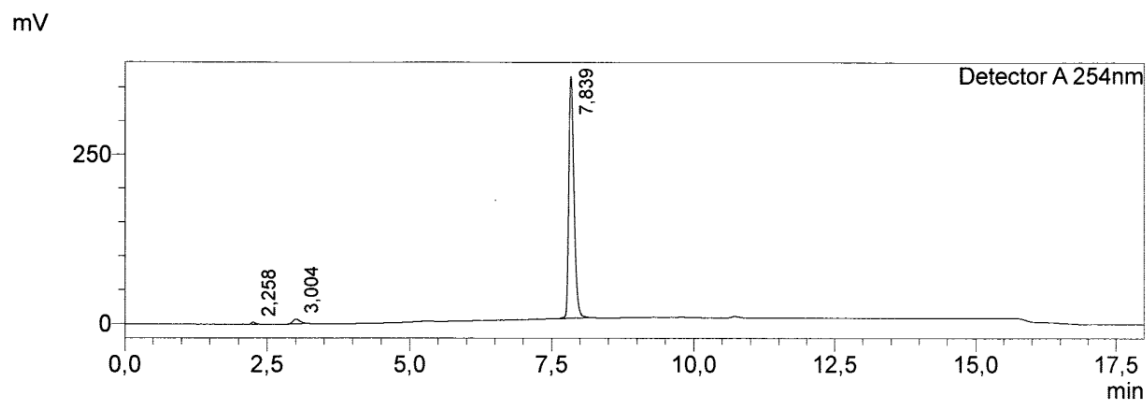
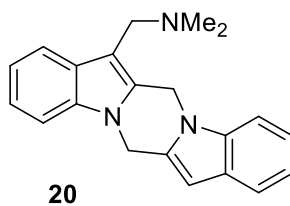


Fig. S7 ^1H (400 MHz, CDCl_3), DEPT-135 ($\text{MeOH-}d_4$) and ^{13}C (100 MHz, $\text{MeOH-}d_4$)-NMR spectra of compound **20**



Peak#	Ret. Time	Area	Area%
1	2,258	15022	0,628
2	3,004	64363	2,689
3	7,839	2313920	96,683
Total		2393304	100,000

Line#:1 R.Time:----(Scan#:----)
 MassPeaks:422
 Spectrum Mode:Averaged 8,220-8,227(4933-4937) Base Peak:273.05(1339325)
 BG Mode:Calc Segment 1 - Event 1

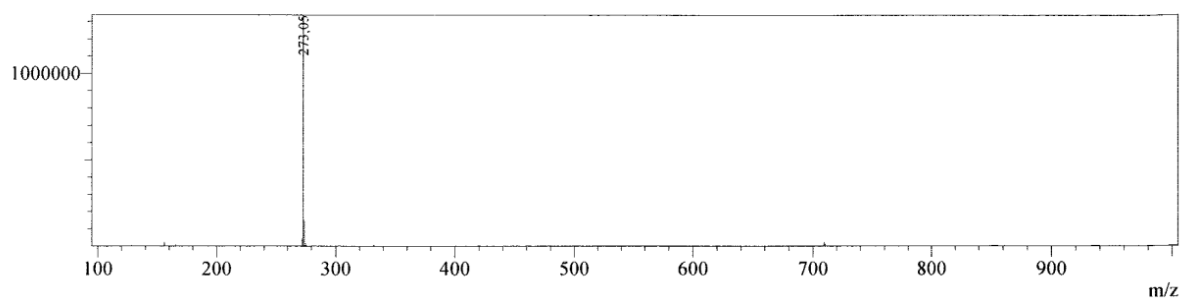


Fig. S8 LCMS data of compound **20**

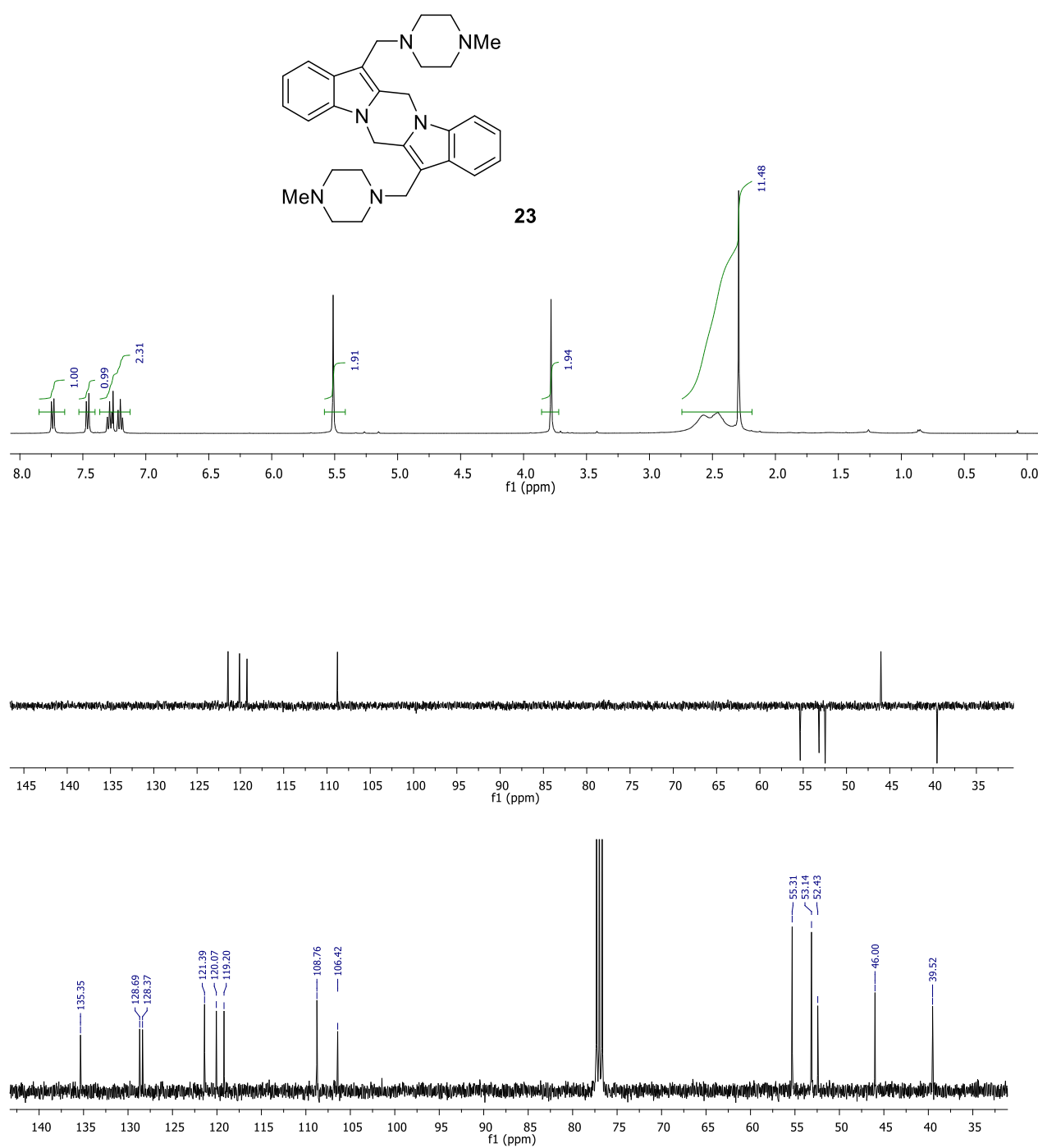
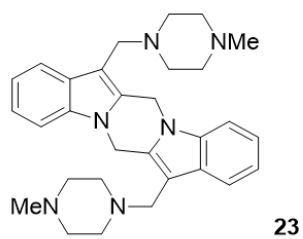
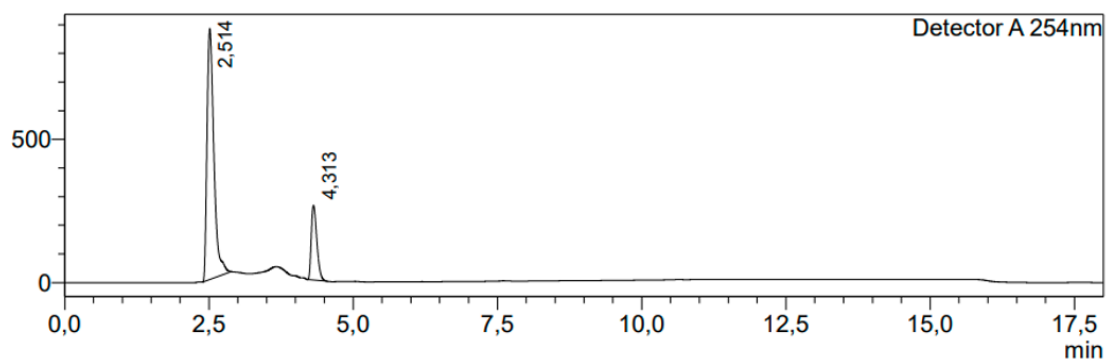


Fig. S9 ^1H (400 MHz), DEPT-135 and ^{13}C (100 MHz)-NMR spectra of compound **23** in CDCl_3



mV



Peak#	Ret. Time	Area	Area%
1	2,514	7281676	80,454
2	4,313	1769080	19,546
Total		9050756	100,000

MassPeaks:444
Spectrum Mode:Averaged 2,710-2,717(1627-1631) Base Peak:193,00(3317063)
BG Mode:Calc Segment 1 - Event 1

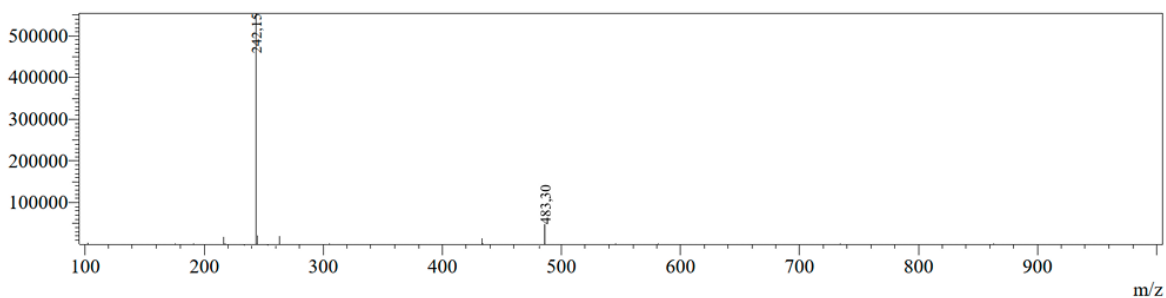


Fig. S10 LCMS data of compound **23**

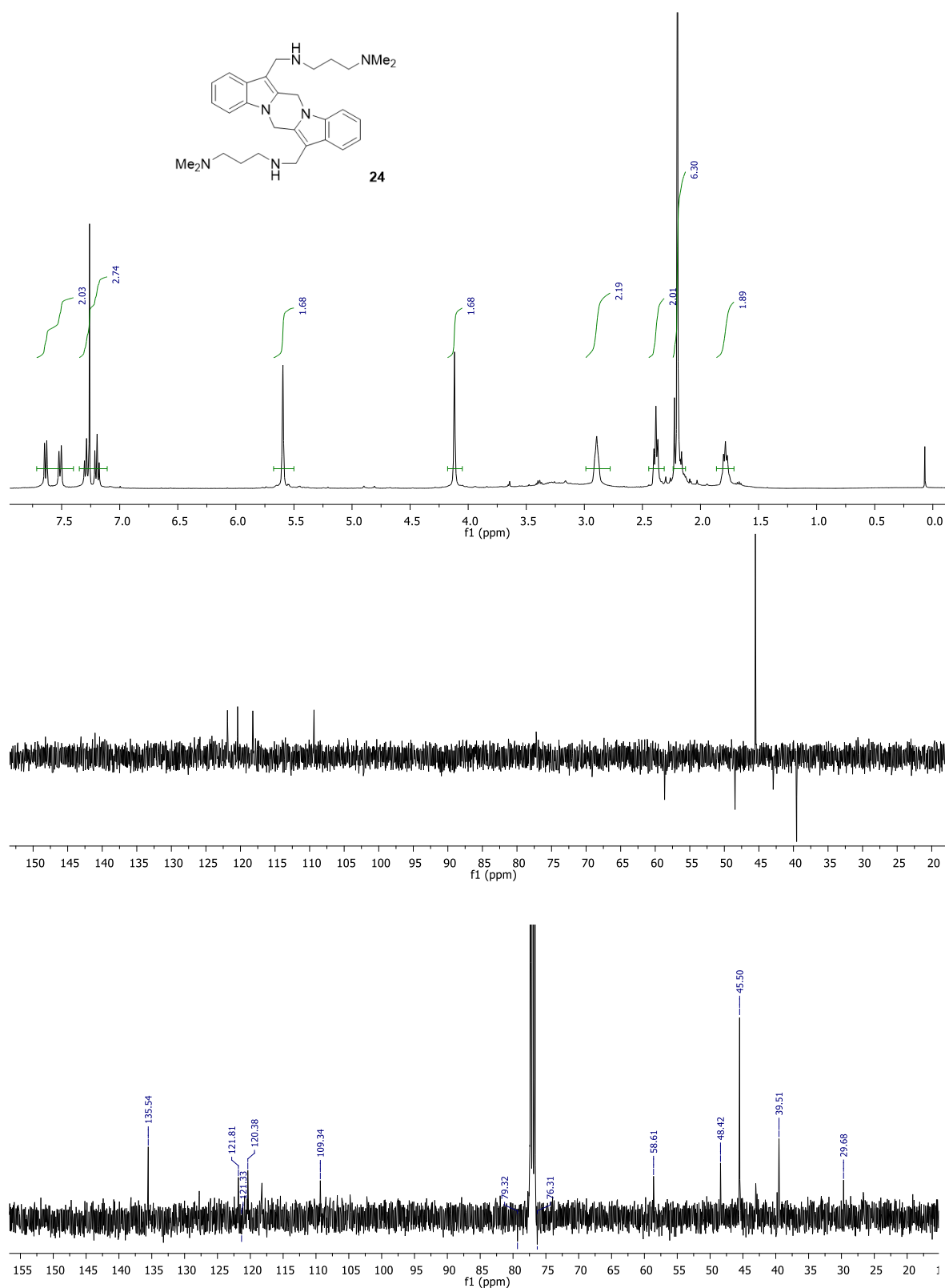
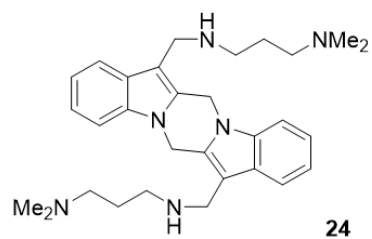
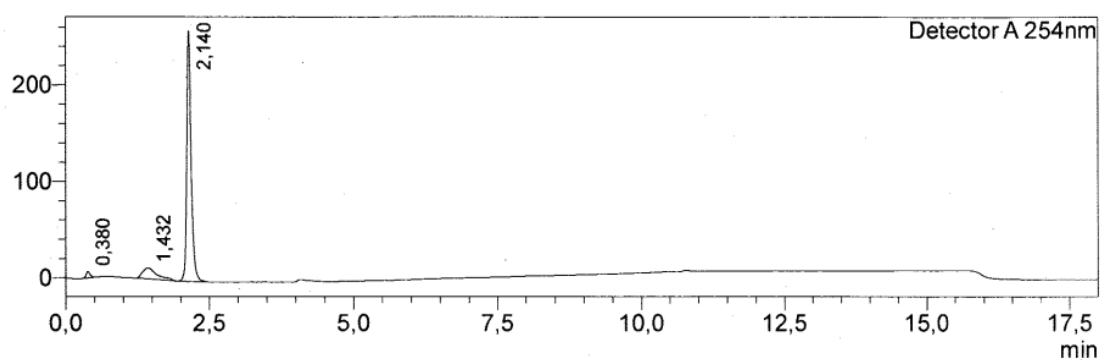


Fig. S11 ¹H (400 MHz), DEPT-135 and ¹³C (100 MHz)-NMR spectra of compound **24** in CDCl₃



mV



Peak#	Ret. Time	Area	Area%
1	0,380	31328	1,894
2	1,432	205443	12,421
3	2,140	1417187	85,685
Total		1653958	100,000

MassPeaks:689

Spectrum Mode:Averaged 2,387-2,393(1433-1437) Base Peak:244,10(10714402)

BG Mode:Calc Segment 1 - Event 1

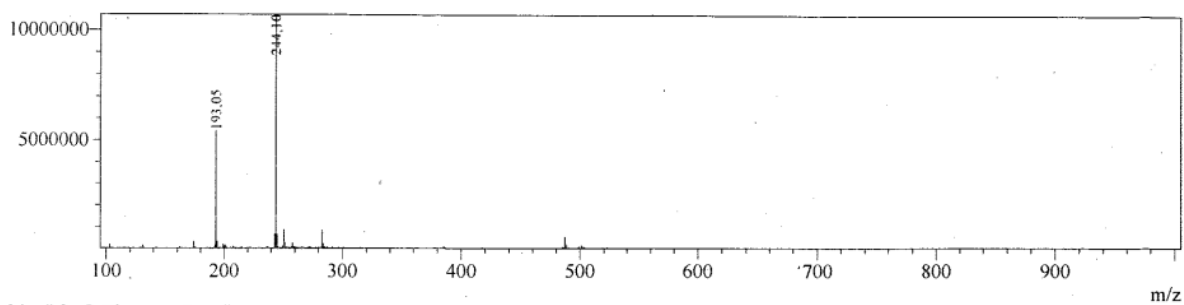


Fig. S12 LCMS data of compound **24**

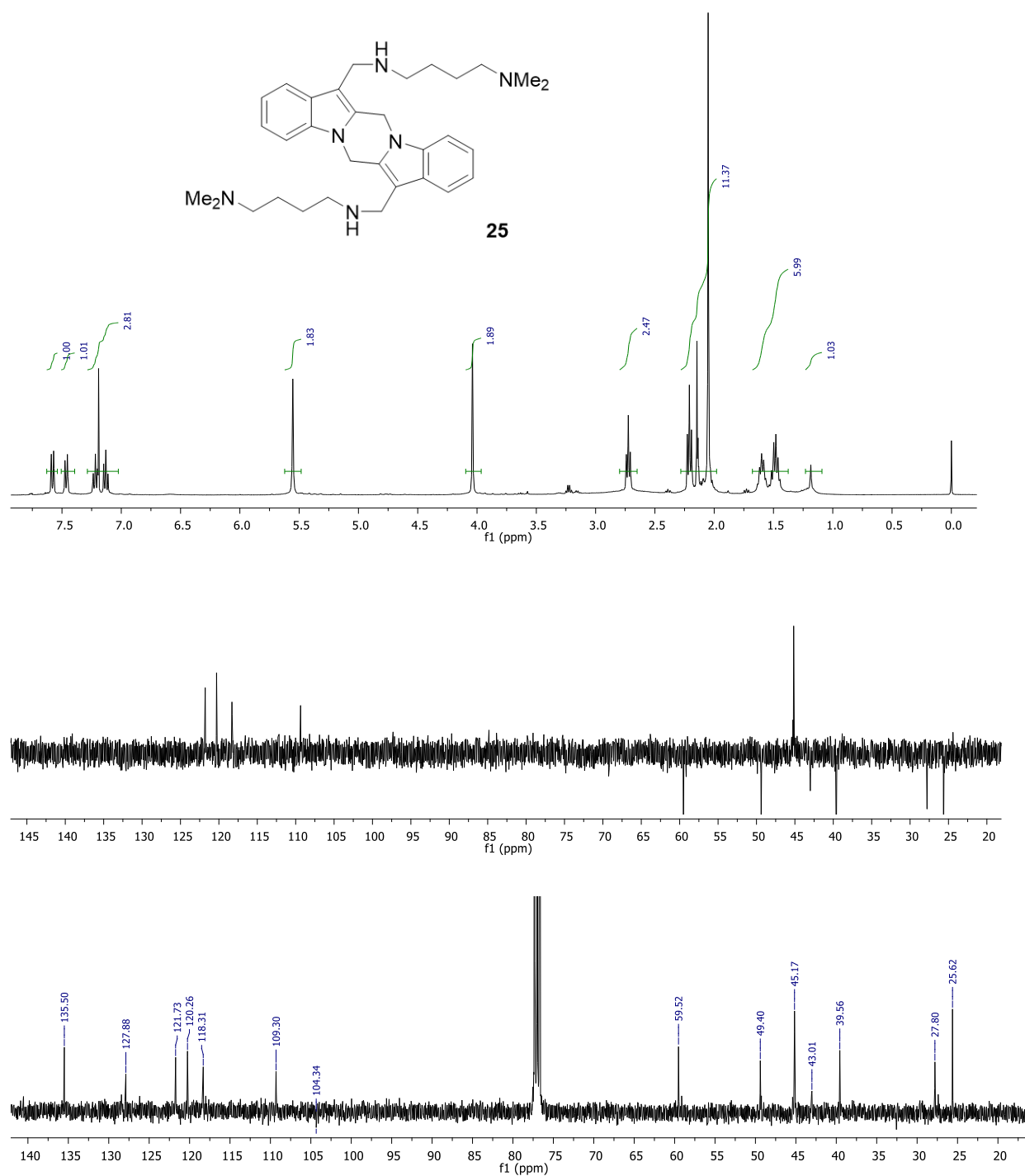
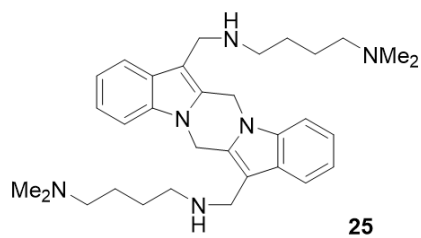
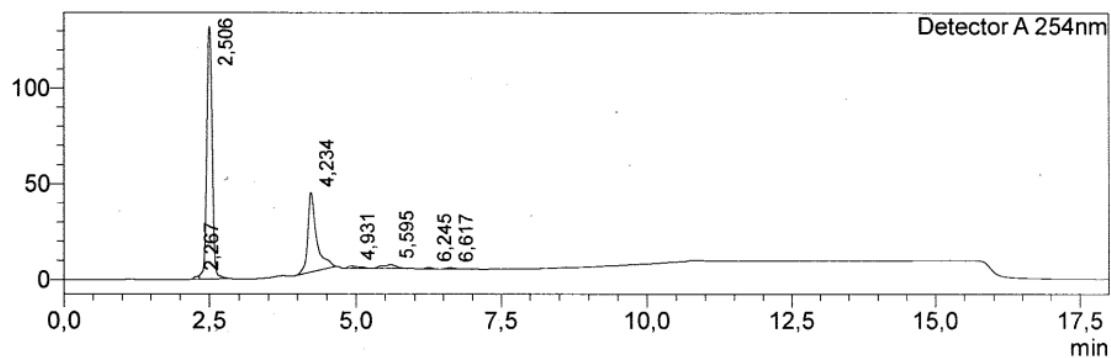


Fig. S13 ^1H (400 MHz), DEPT-135 and ^{13}C (100 MHz)-NMR spectra of compound **25** in CDCl_3



mV



Peak#	Ret. Time	Area	Area%
1	2,267	9406	0,691
2	2,506	848181	62,339
3	4,234	439067	32,270
4	4,931	18083	1,329
5	5,595	34679	2,549
6	6,245	6182	0,454
7	6,617	4999	0,367
Total		1360597	100,000

Line# 2 R Time:----(Scan#----)
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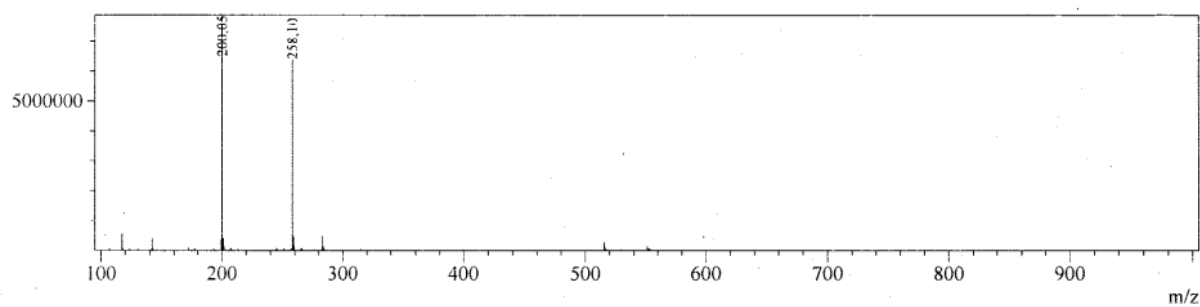


Fig. S14 LCMS data of compound **25**

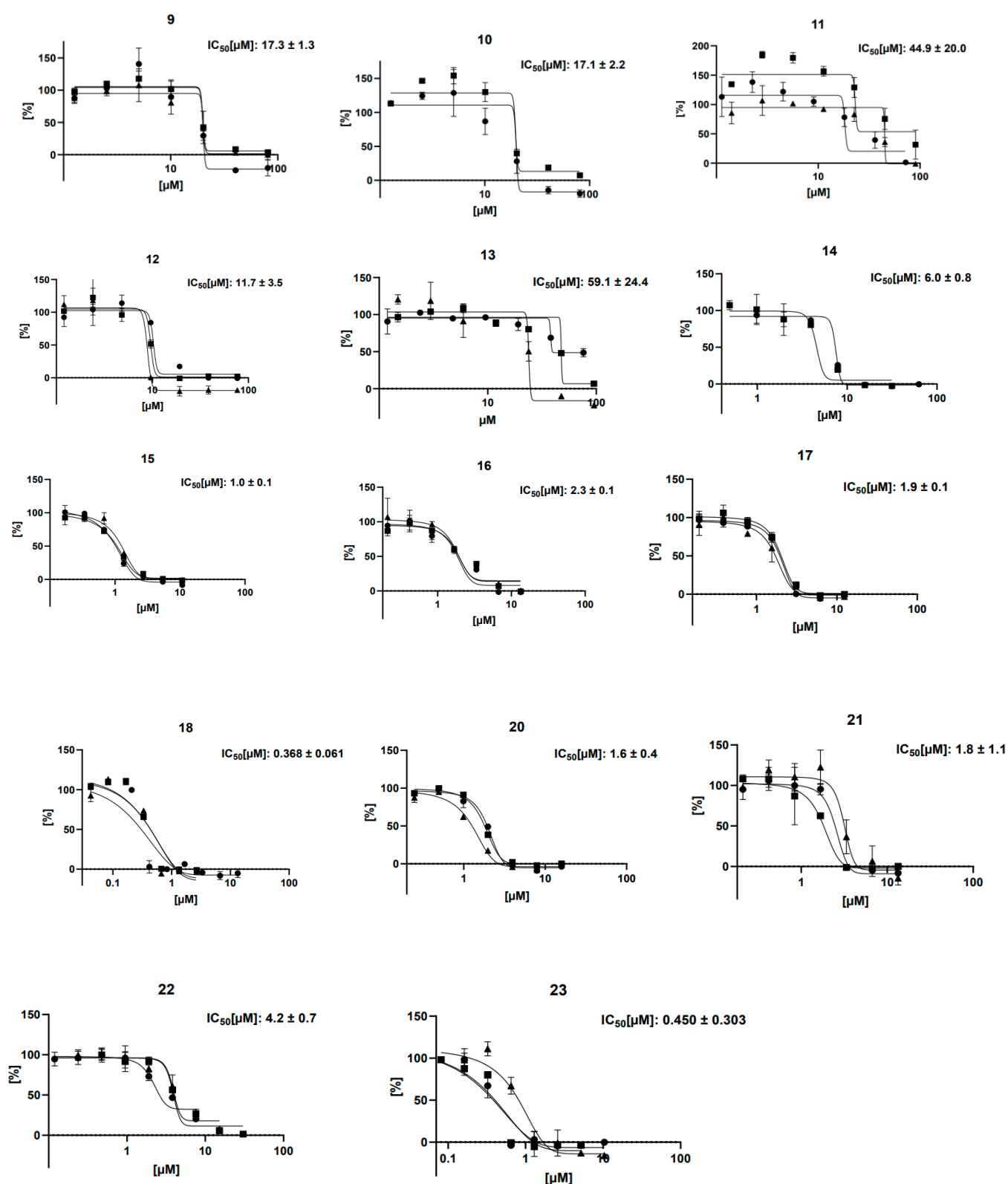


Fig. S15 Dose-response curves for the $[^3\text{H}]$ hypoxanthine incorporation assay for compounds 9-18 and 20-23.

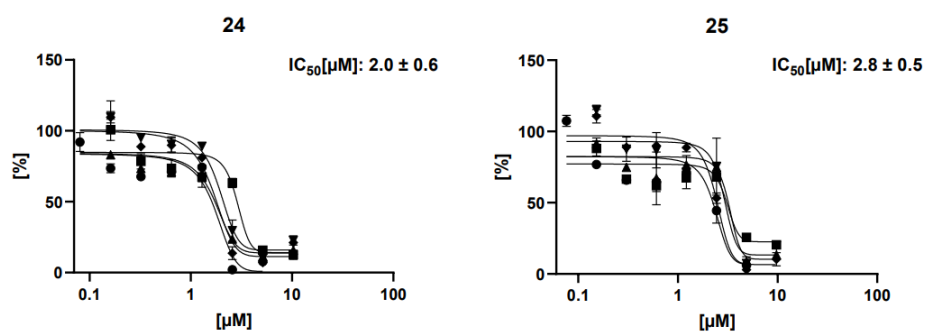


Fig. S16 Dose-response curves for the SYBR® Green assay for compounds **24** and **25**.

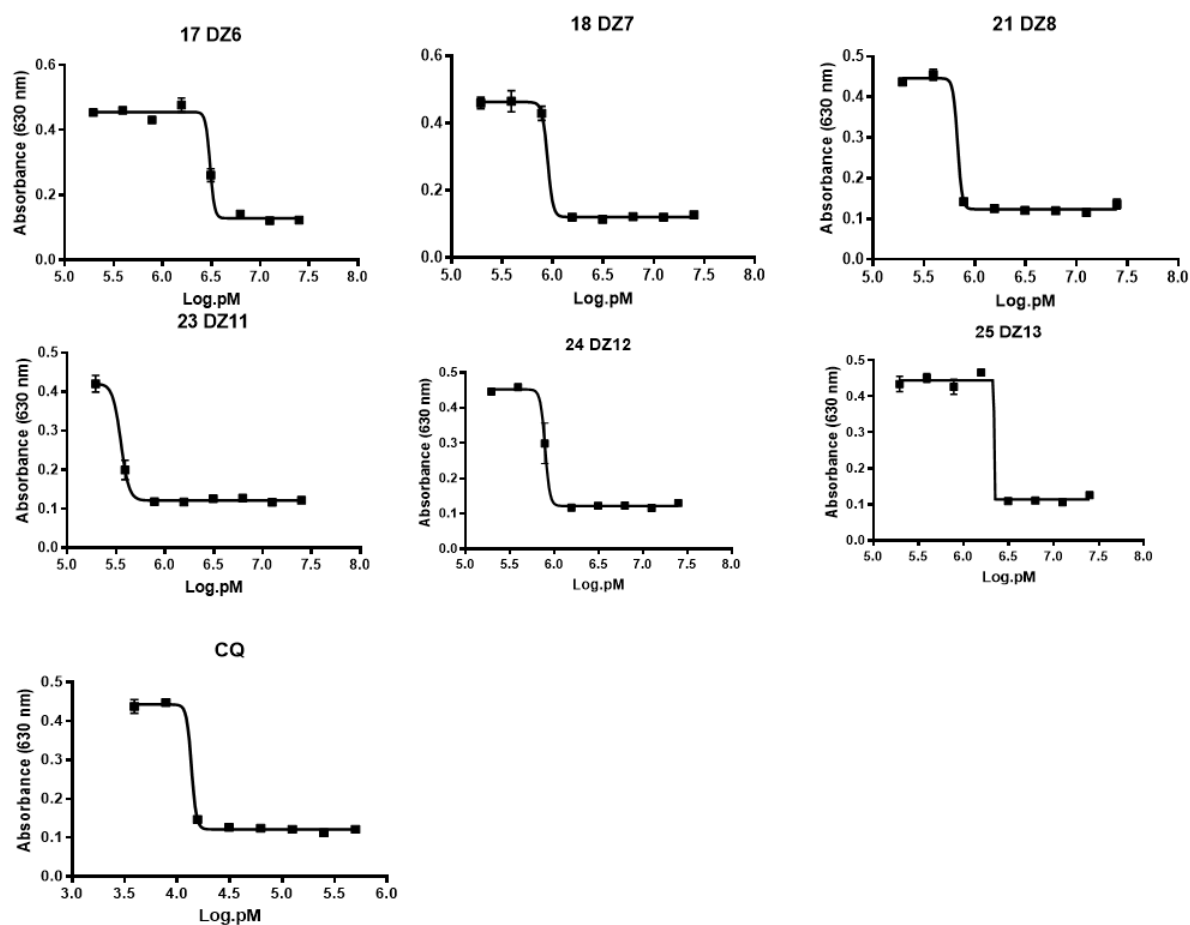


Fig. S17 Dose-response curves for the Malstat assay on *Plasmodium falciparum* 3D7 strain for compounds **17**, **18**, **21**, **23-25** and chloroquine, CQ (the graphs represent one out of three experiments).

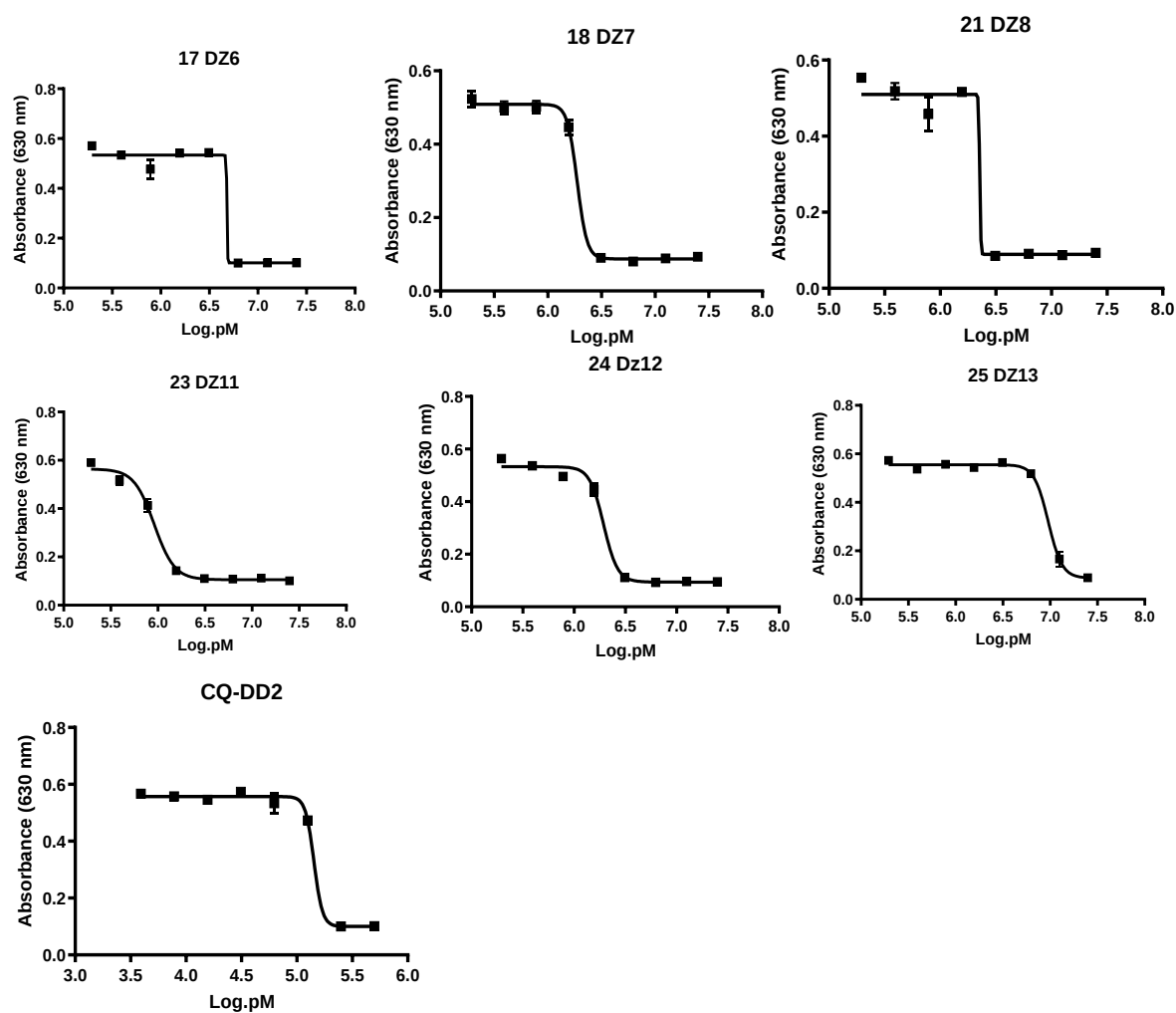


Fig. S18 Dose-response curves for the Malstat assay on *Plasmodium falciparum* DD2 strain for compounds **17**, **18**, **21**, **23**-**25** and chloroquine, CQ (the graphs represent one out of three experiments).

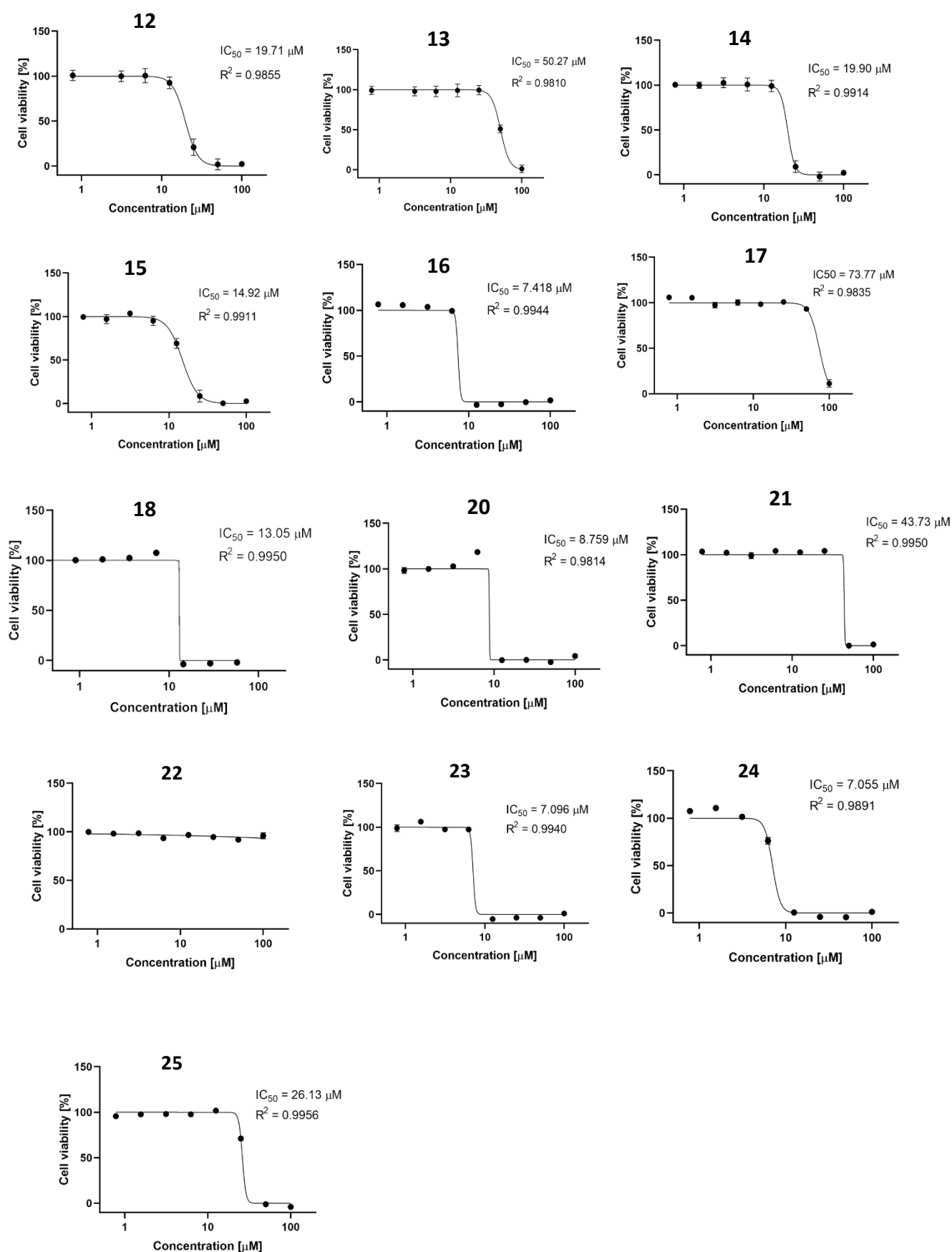


Fig. S19 Dose-response curves from the cytotoxicity assay (the graphs represent one out of three experiments).