

Spirochromone-chalcone conjugates as antitubercular agents: synthesis, bio evaluation and molecular modeling studies.

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Supplementary Data

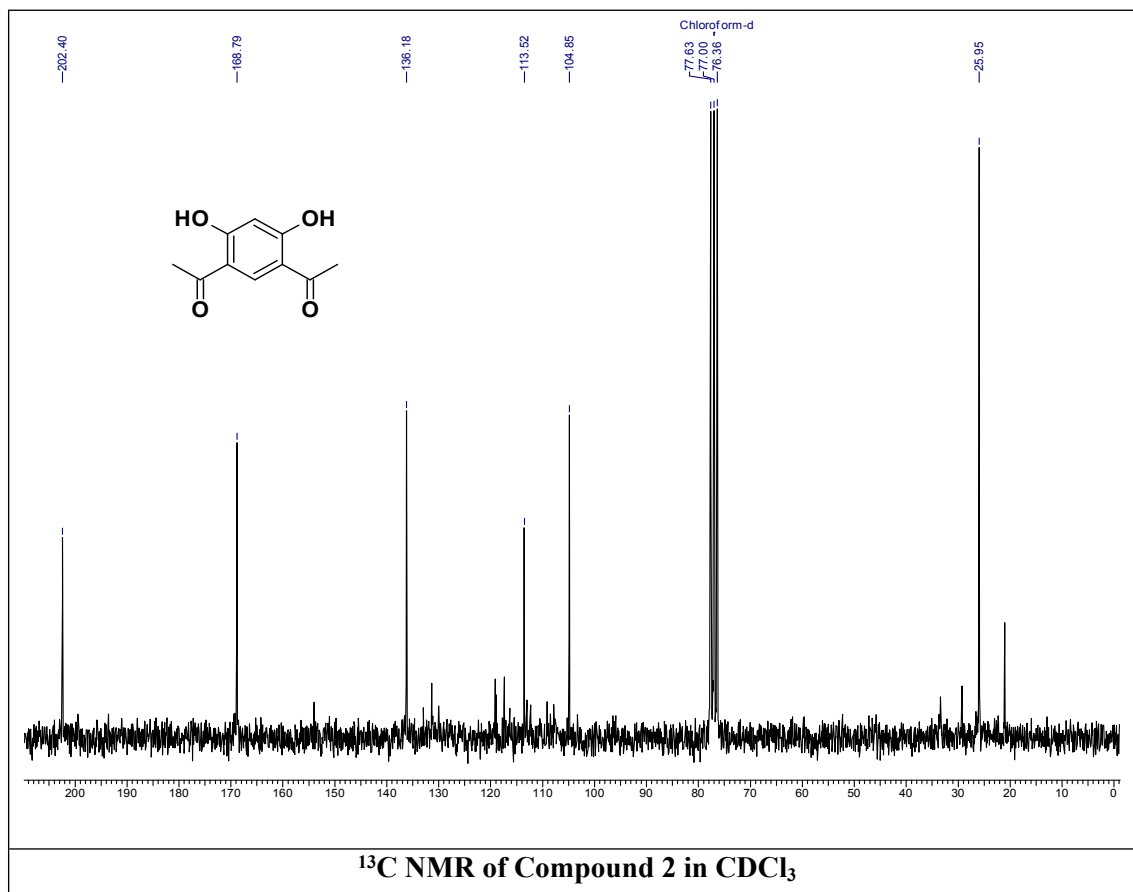
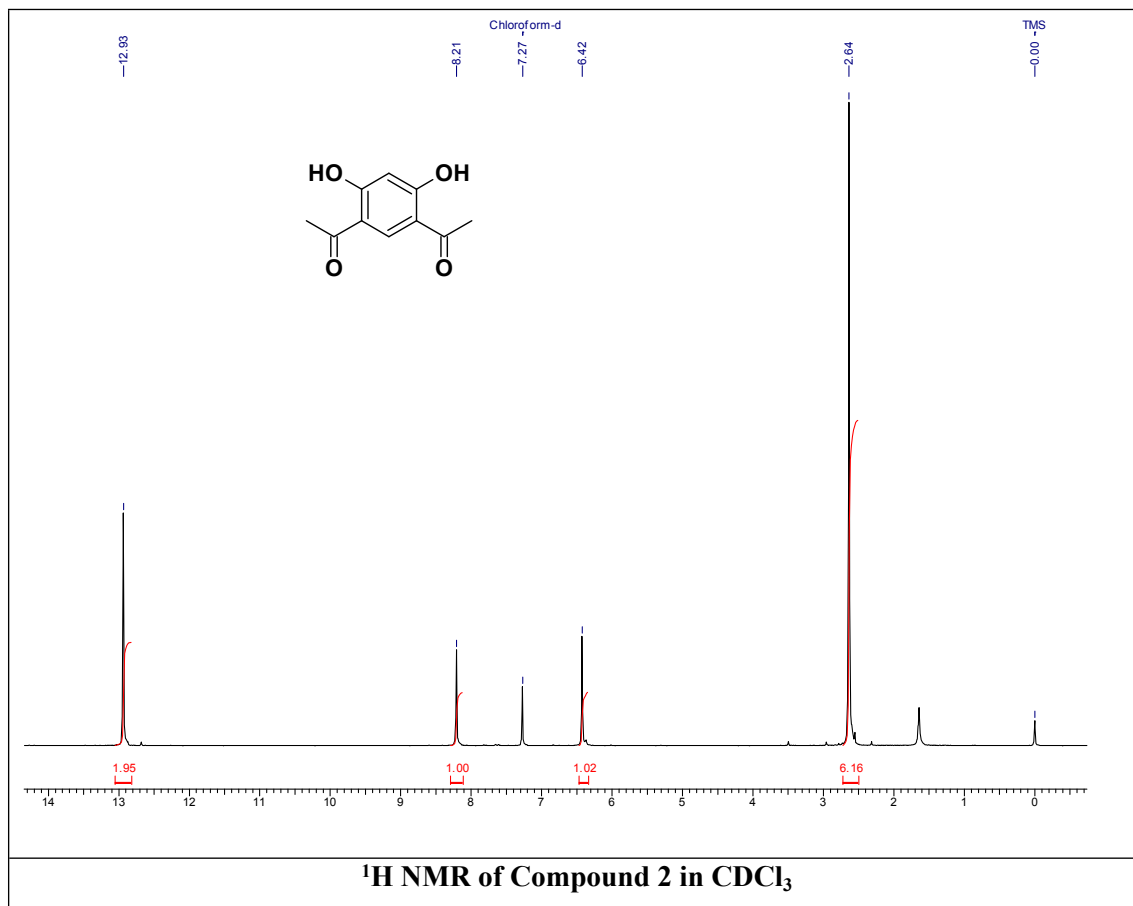
Single crystal X-ray data of compound 4f: (CCDC 1045946)

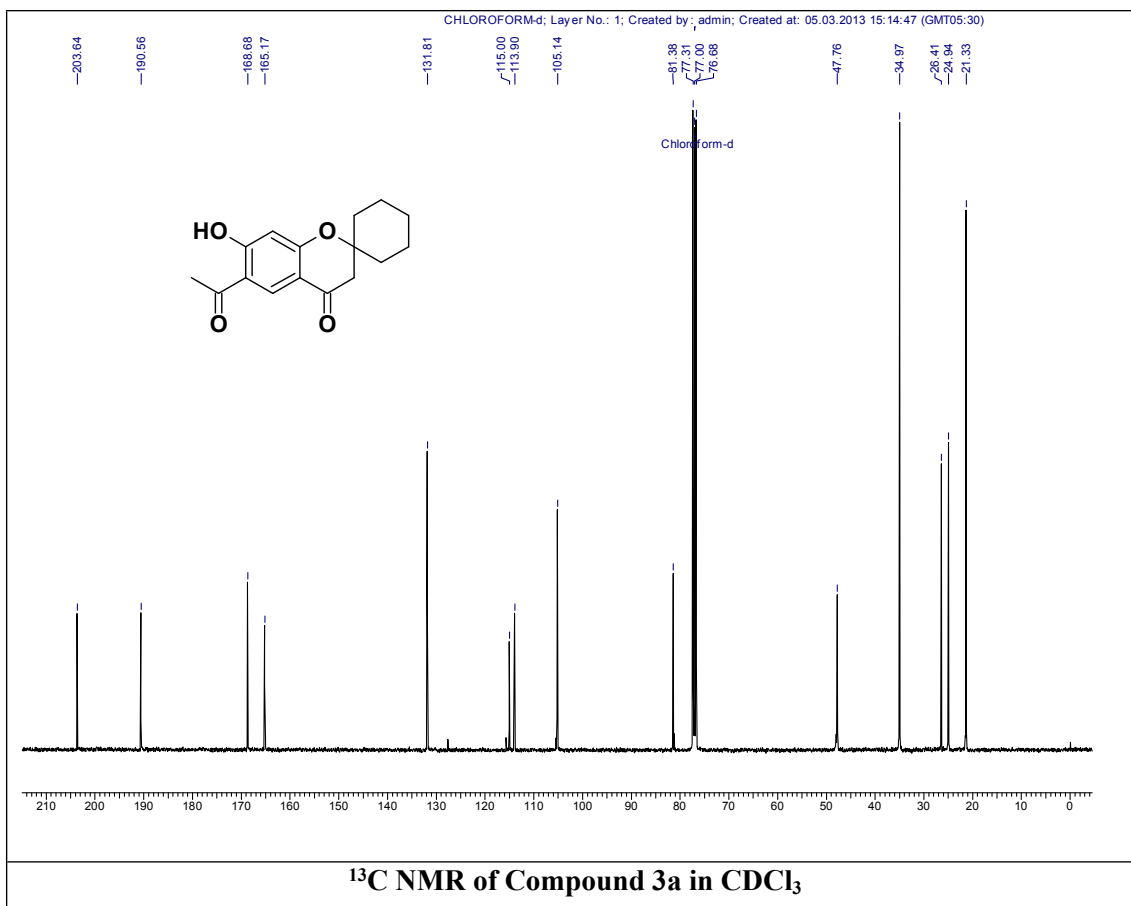
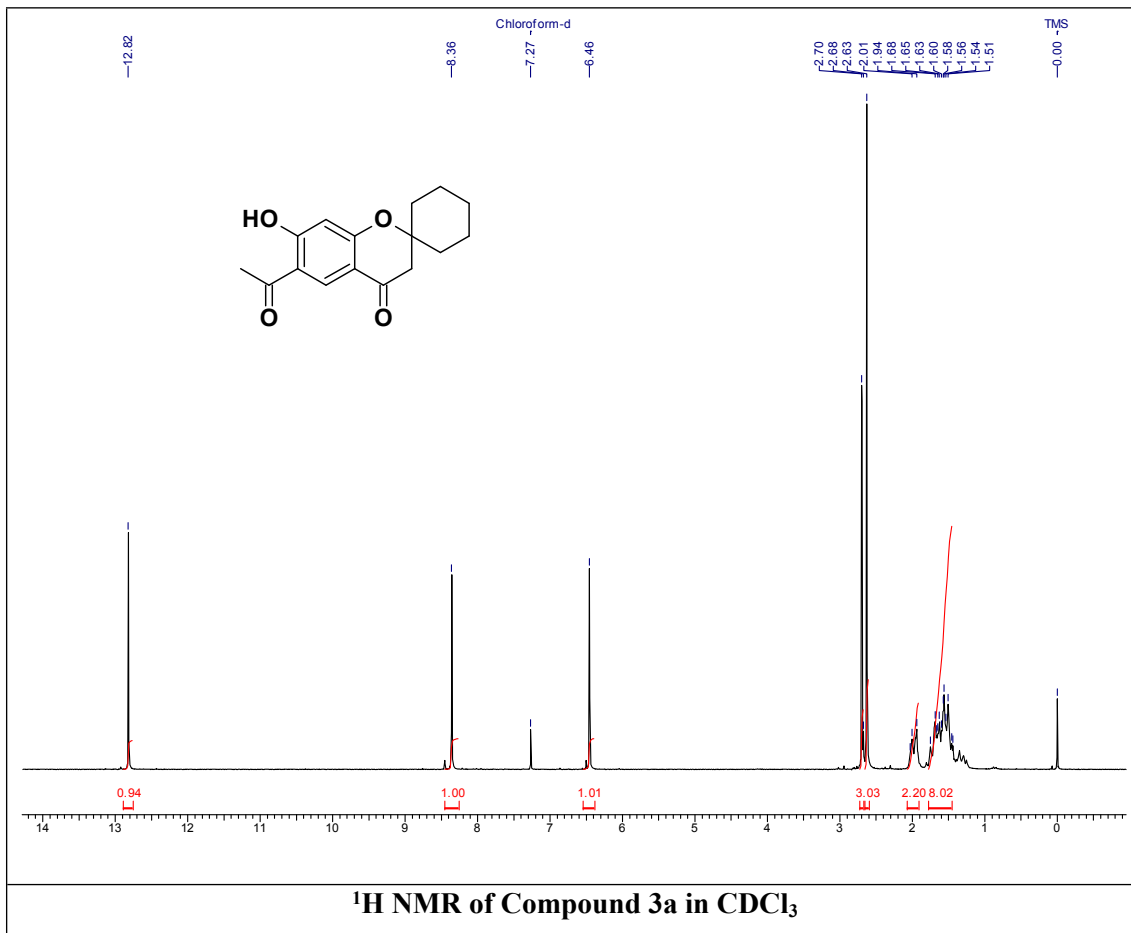
X-ray intensity data measurements of compound **4f** was carried out on a Bruker SMART APEX II CCD diffractometer with graphite-monochromatized (MoK α = 0.71073 Å) radiation at 296 (2) K. The X-ray generator was operated at 50 kV and 30 mA. A preliminary set of cell constants and an orientation matrix were calculated from 277 reflections harvested from three sets of 36 frames. Data were collected with ω scan width of 0.5° at eight different settings of φ and 2θ with a frame time of 10 sec keeping the sample-to-detector distance fixed at 5.00 cm. The X-ray data collection was monitored by APEX2 program (Bruker, 2006).¹ Crystal data of **4f**. C₂₄H₂₄NO₅, M=392.43, colorless plate, 0.54 x 0.42 x 0.21 mm³, monoclinic, space group *P*2₁/*C*, *a* = 7.9447(10), *b* = 19.588(2), *c* = 12.7483(14) Å, β = 97.927(5)°, *V* = 1964.9(4) Å³, *Z* = 4, *T* = 296(2) K, $2\theta_{\max}$ =56.66°, *D*_{calc} (g cm⁻³) = 1.327, *F*(000) = 832, μ (mm⁻¹) = 0.092, 18612 reflections collected, 4865 unique reflections (*R*_{int}=0.0510), 3453 observed (*I* > 2 σ (*I*)) reflections, multi-scan absorption correction, *T*_{min} = 0.952, *T*_{max} = 0.981, 265 refined parameters, *S* = 1.041, *R*1=0.0443, *wR*2=0.1077 (all data *R* = 0.0680, *wR*2 = 0.1211), maximum and minimum residual electron densities; $\Delta\rho_{\max}$ = 0.26, $\Delta\rho_{\min}$ = -0.17 (eÅ⁻³). All the data were corrected for Lorentzian, polarization and absorption effects using SAINT and SADABS programs (Bruker, 2006). SHELX-97 was used for structure solution and full matrix least-squares refinement on *F*².² Hydrogen atoms were placed in geometrically idealized position and constrained to ride on their parent atoms.

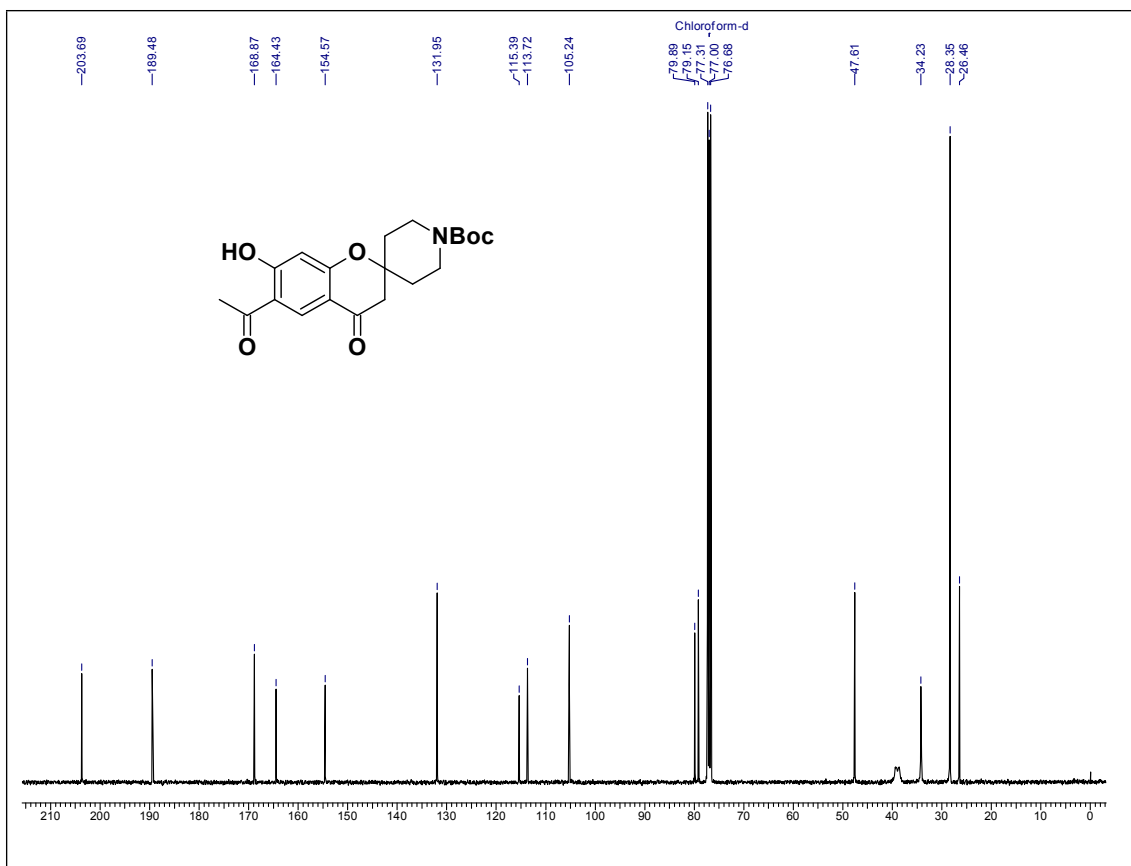
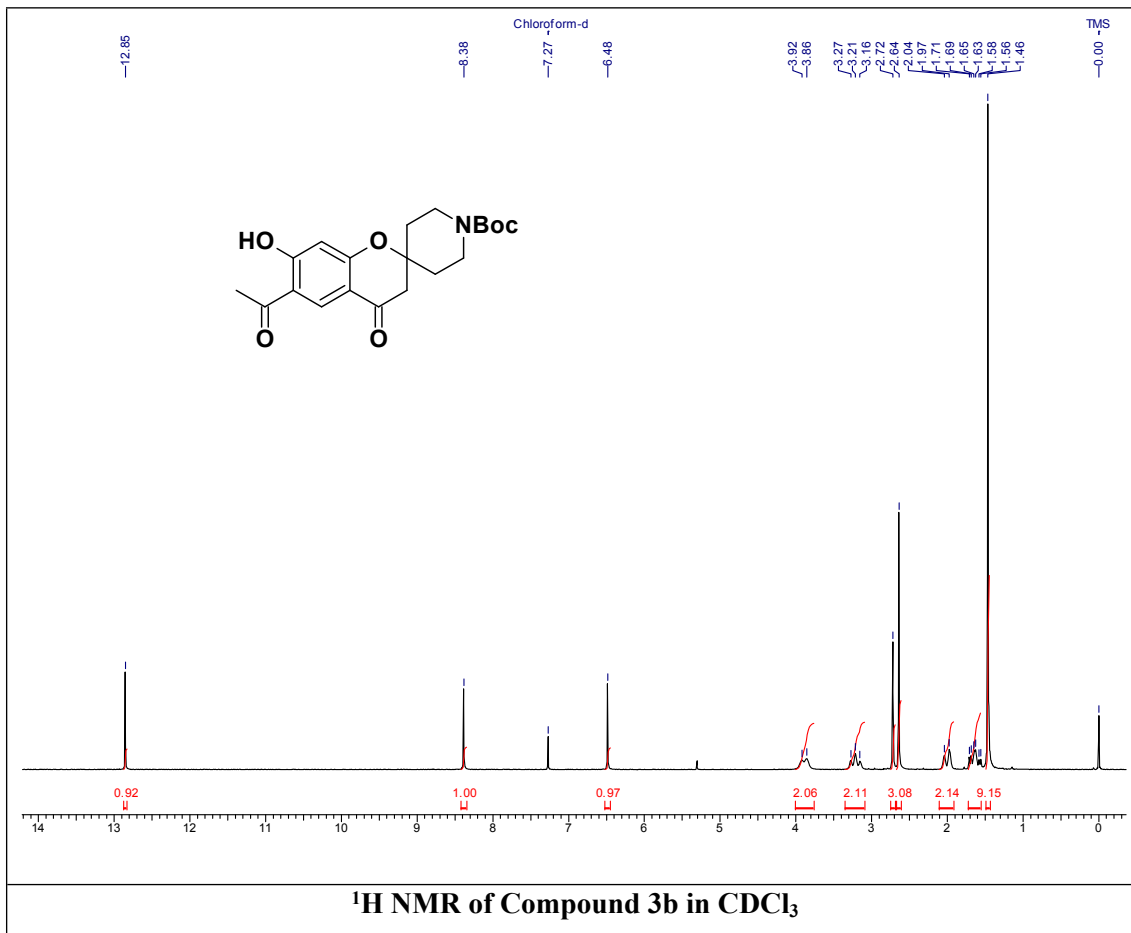
References

- (1) Bruker (2006). *APEX2*, *SAINT* and *SADABS*. Bruker AXS Inc., Madison, Wisconsin, USA.
- (2) G. M. Sheldrick, *Acta Crystallogr.*, 2008, **A64**, 112.

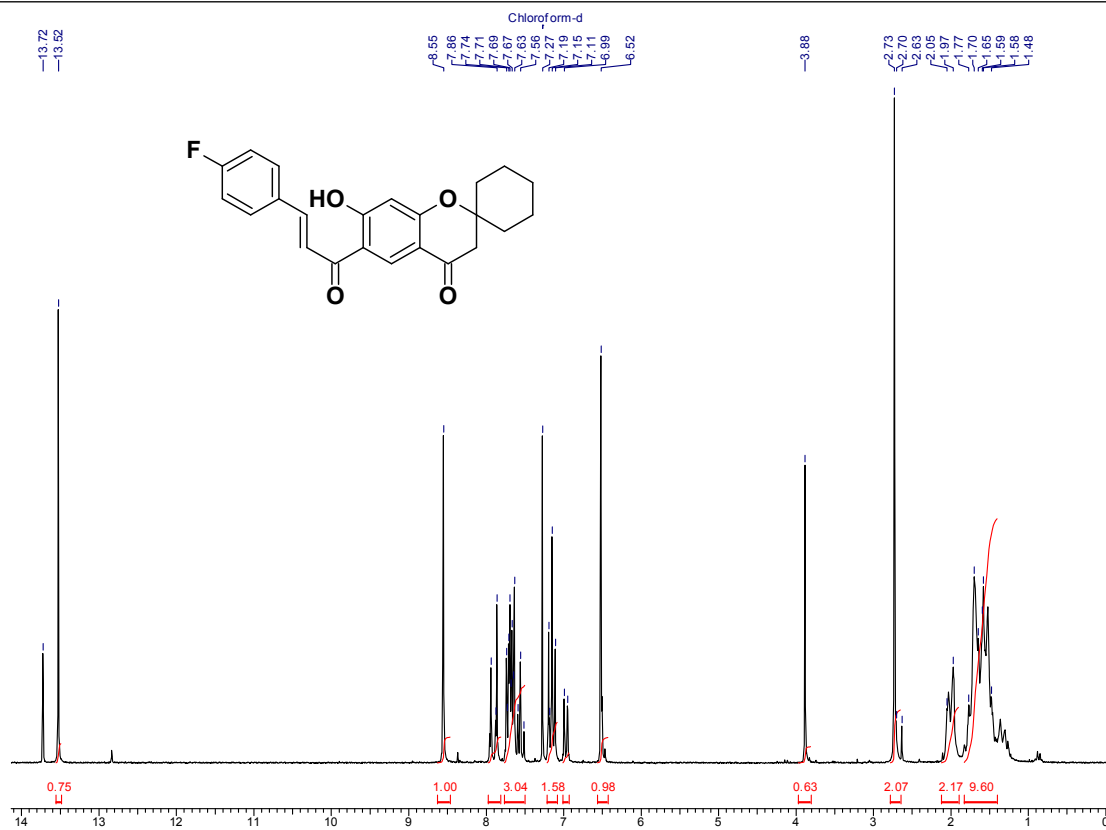
Analytical data



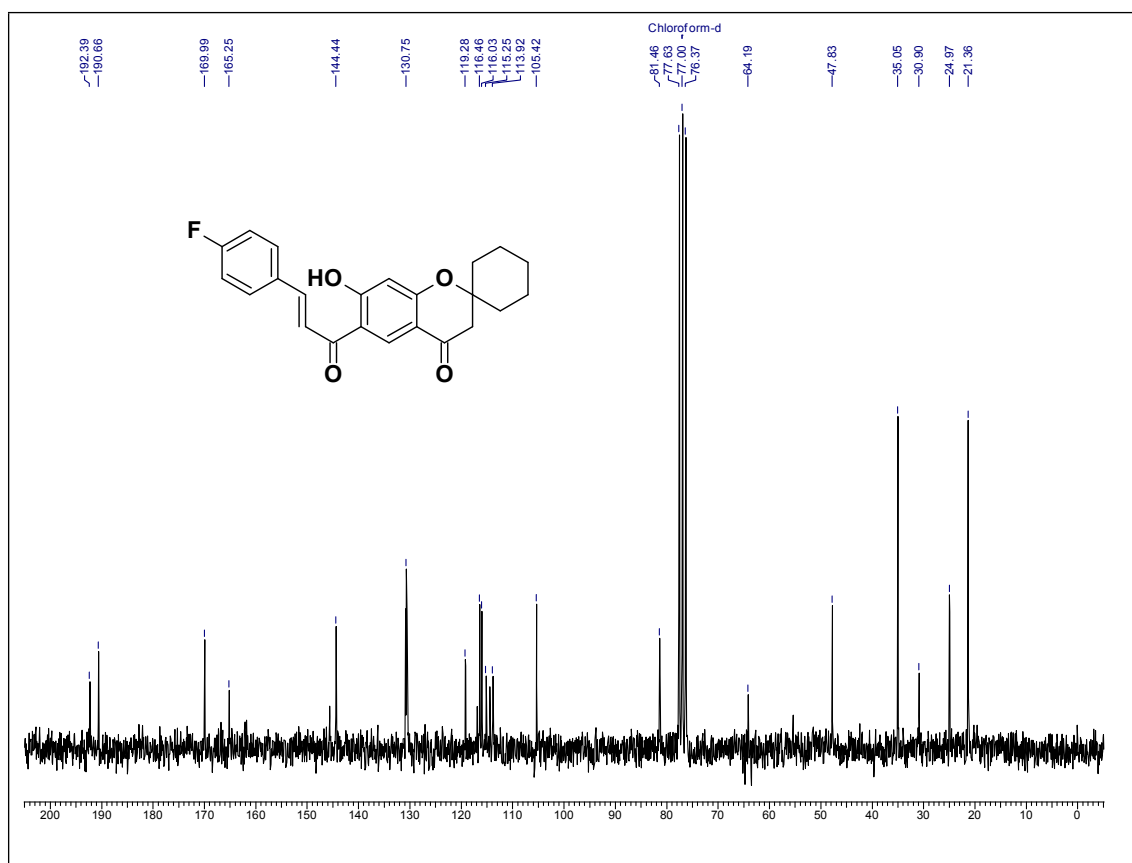




¹³C NMR of Compound 3b in CDCl₃

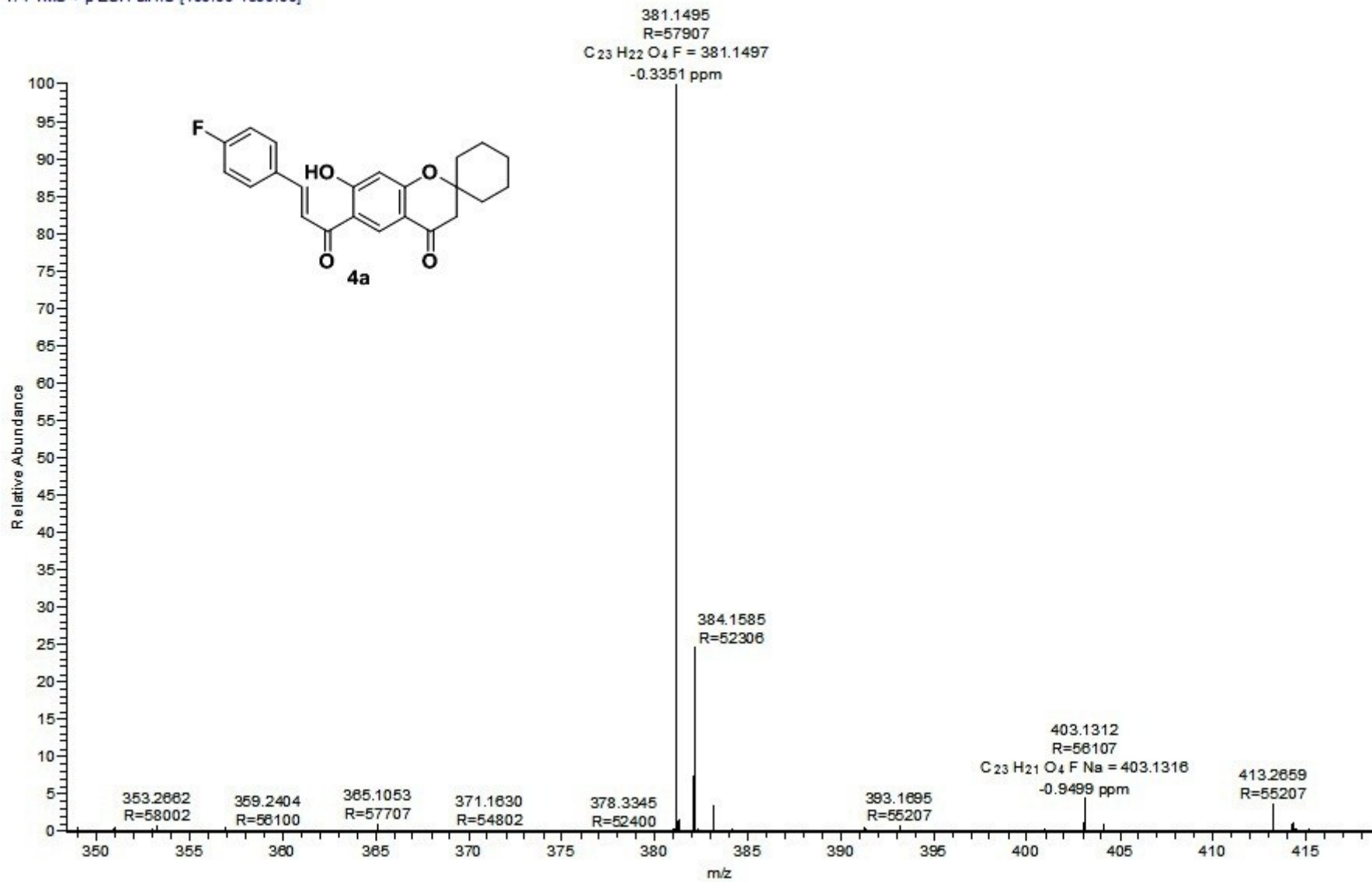


¹H NMR of Compound 4a in CDCl₃

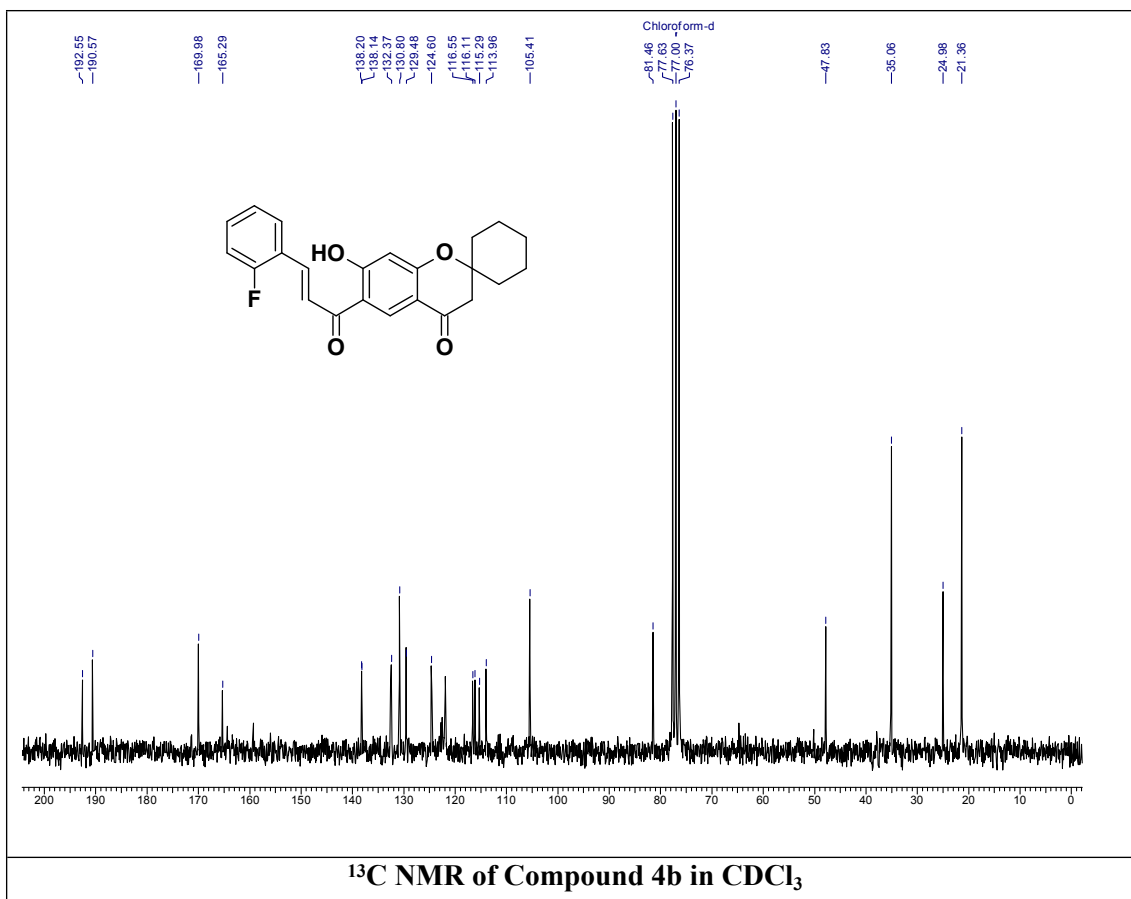
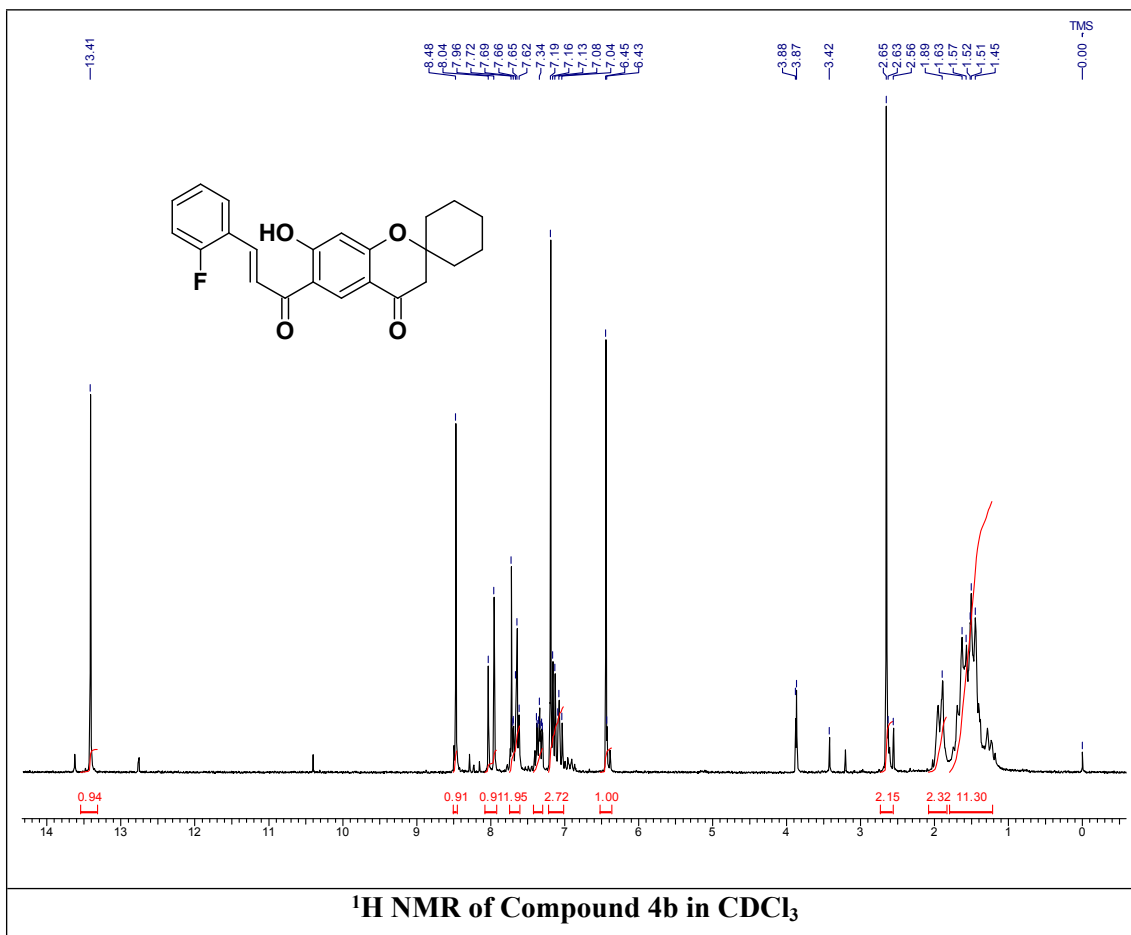


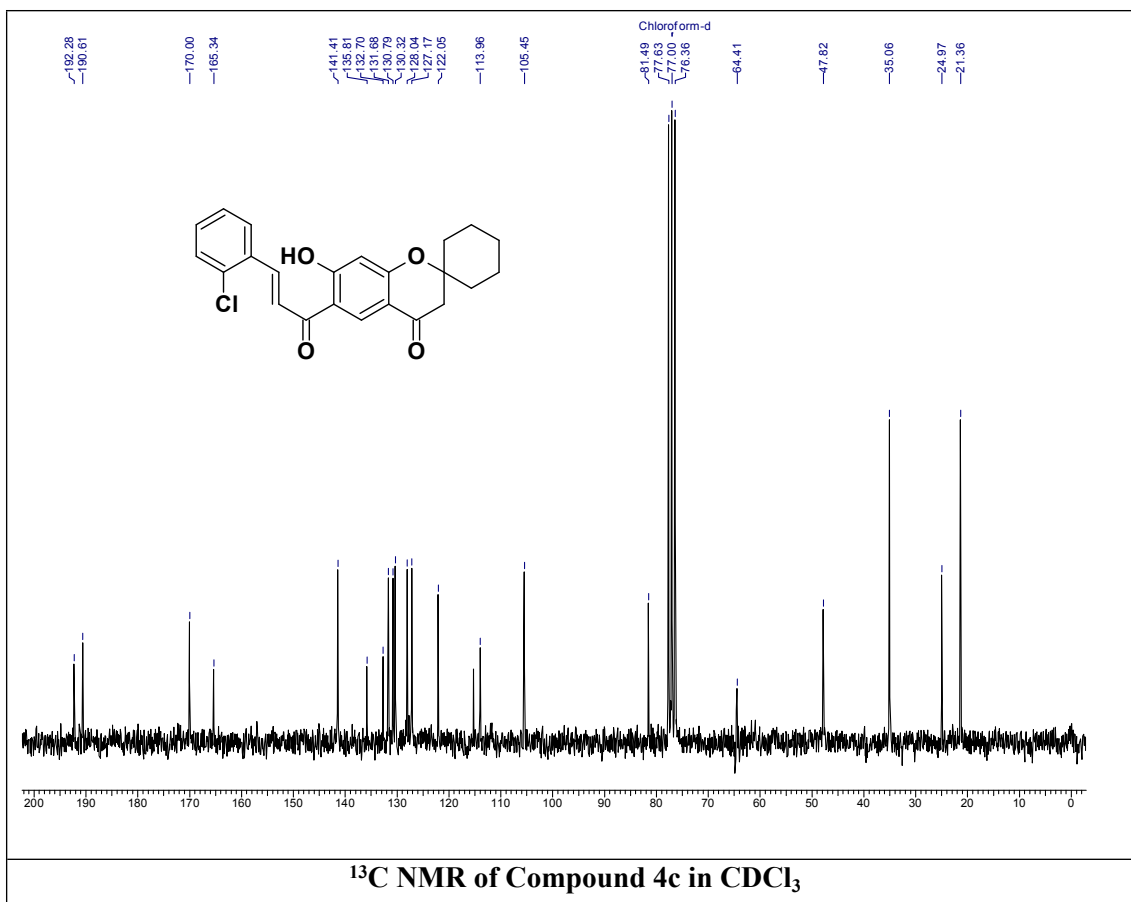
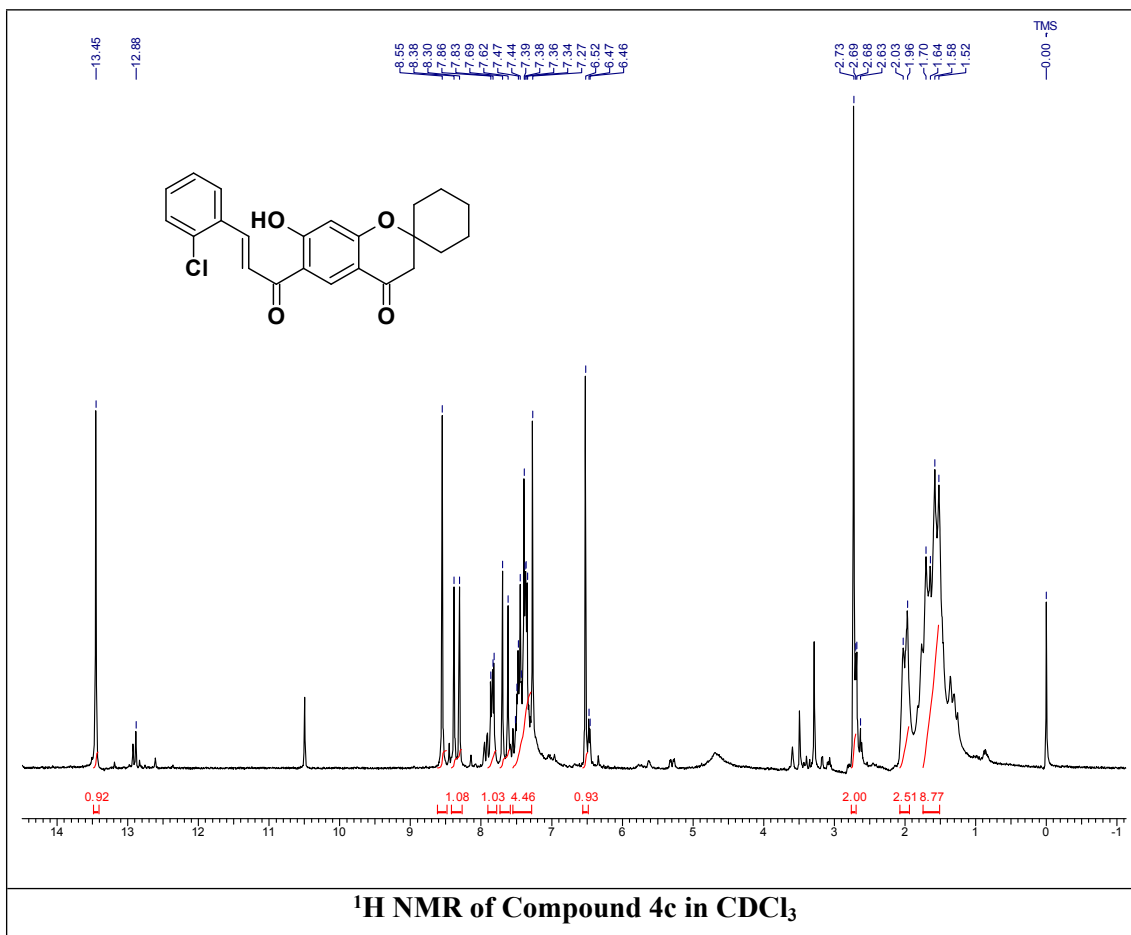
^{13}C NMR of Compound 4a in CDCl_3

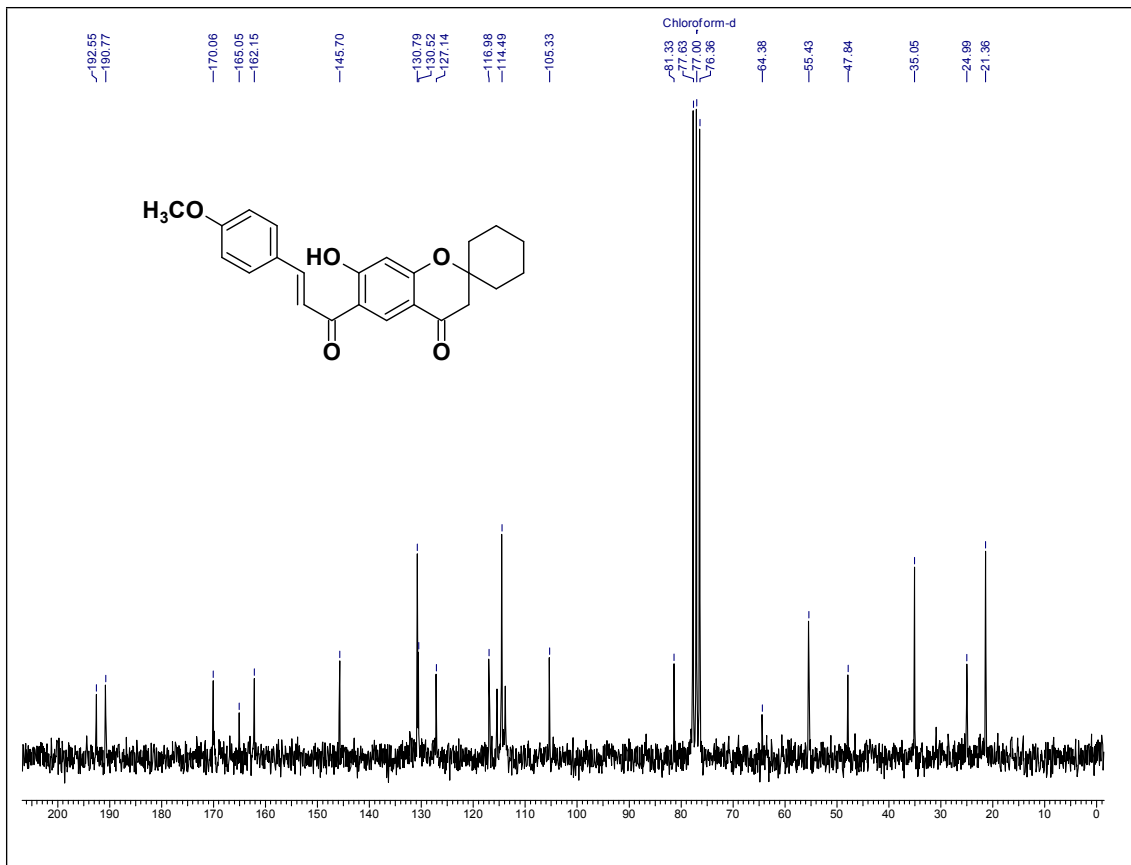
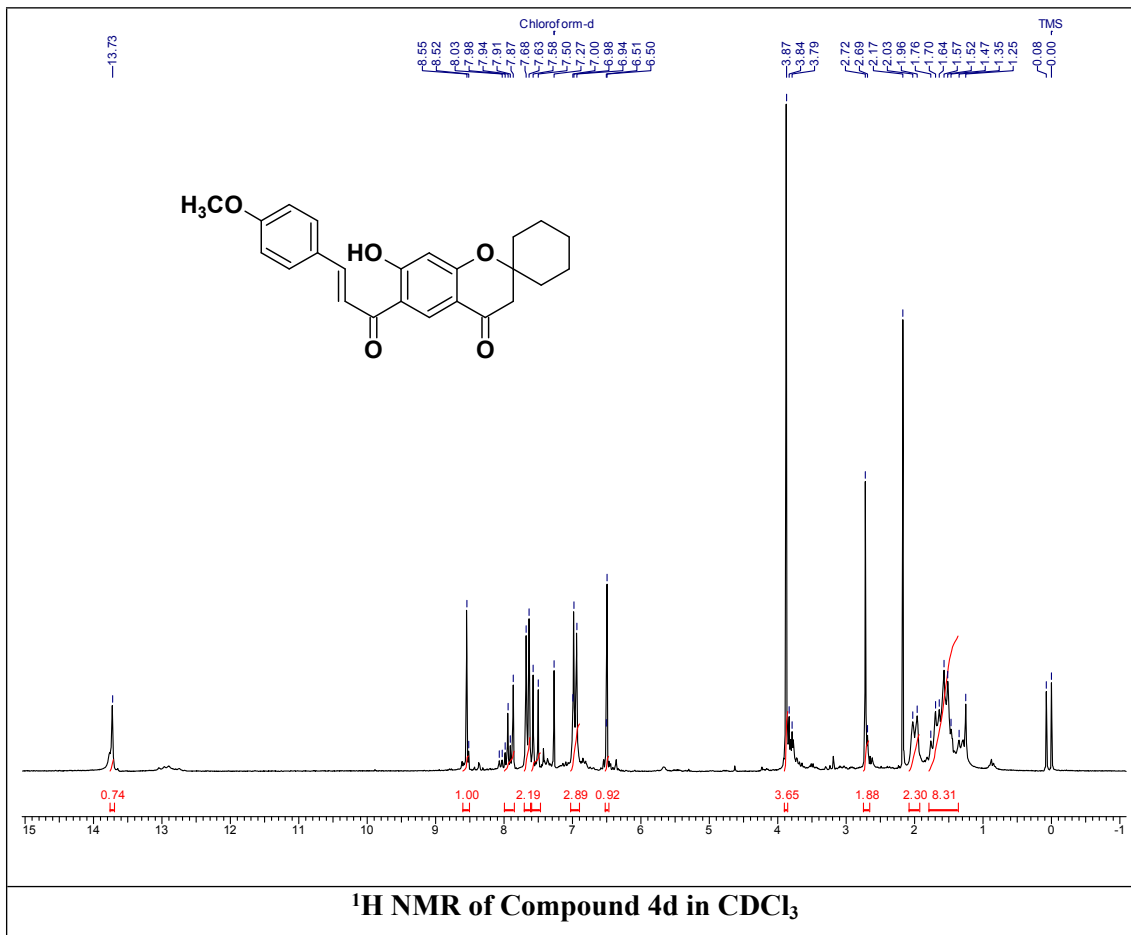
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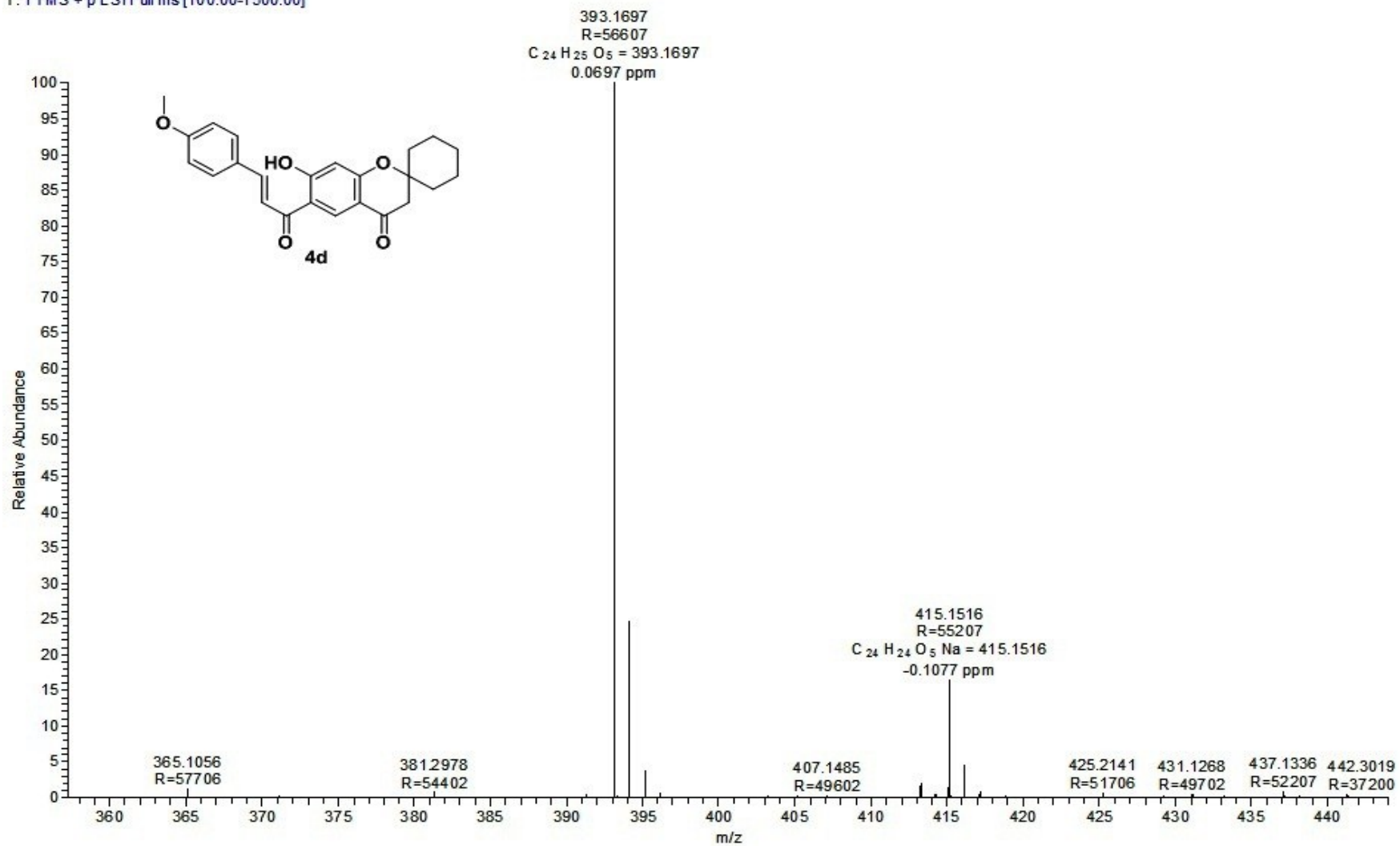




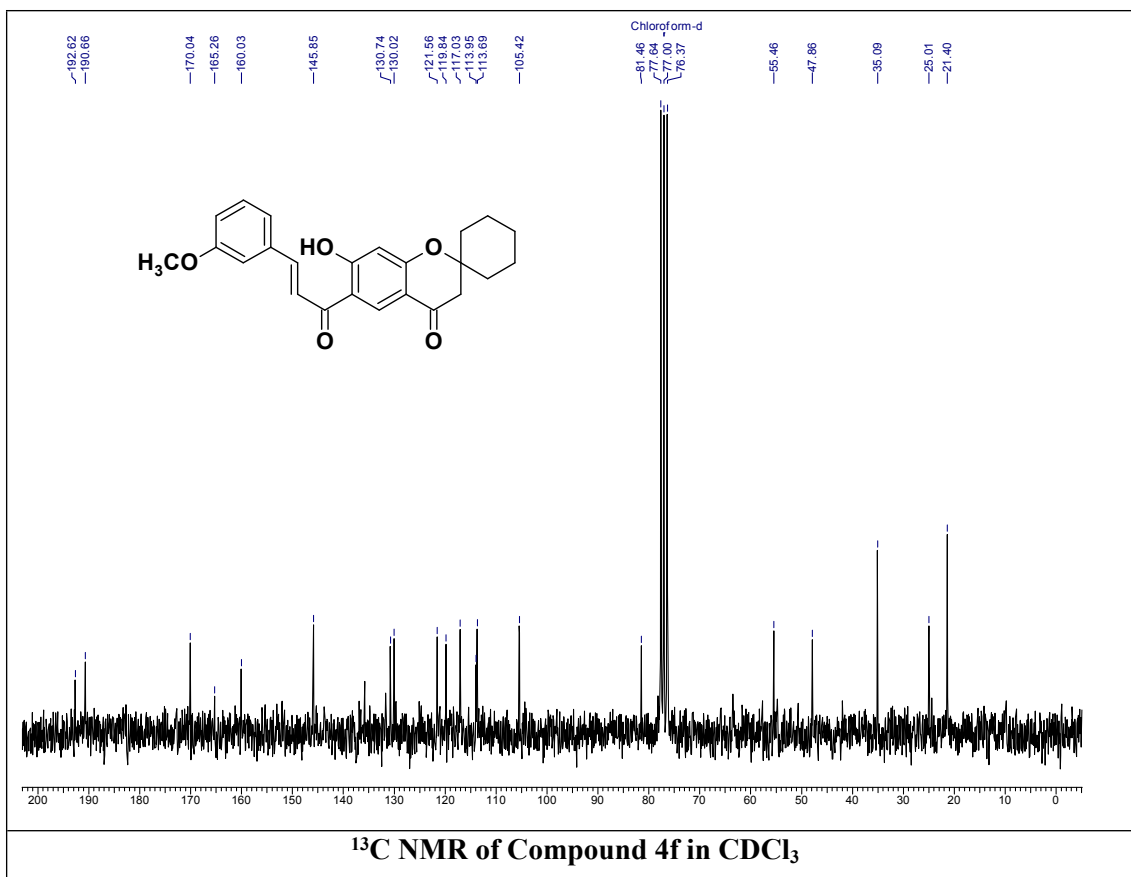
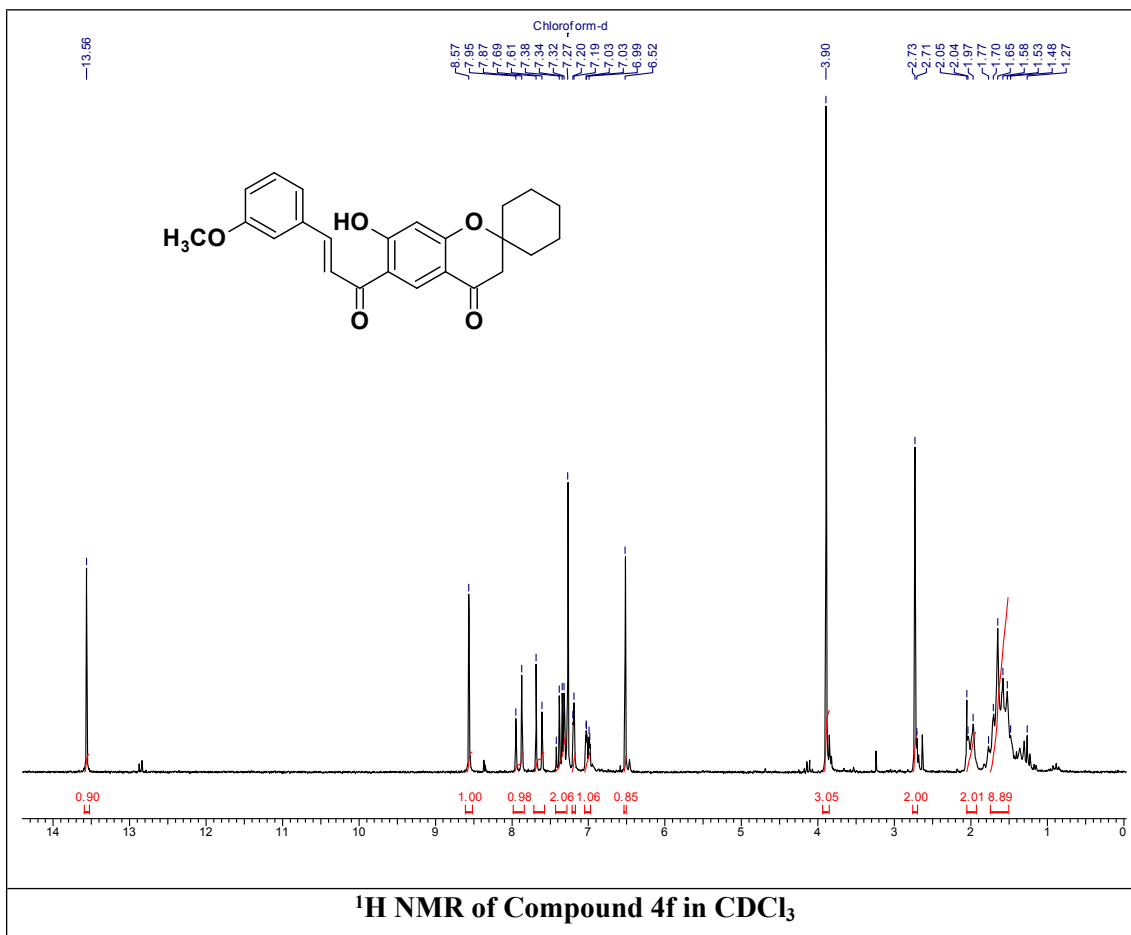


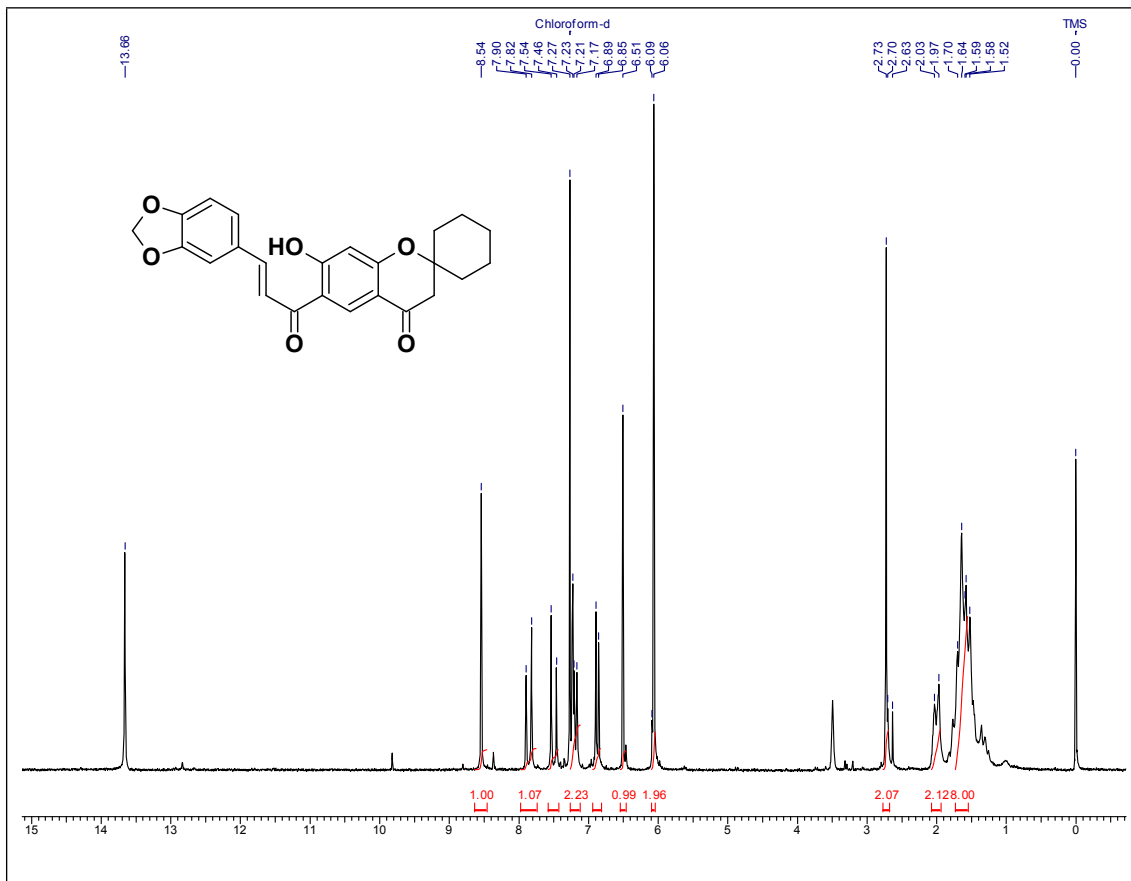
^{13}C NMR of Compound 4d in CDCl_3

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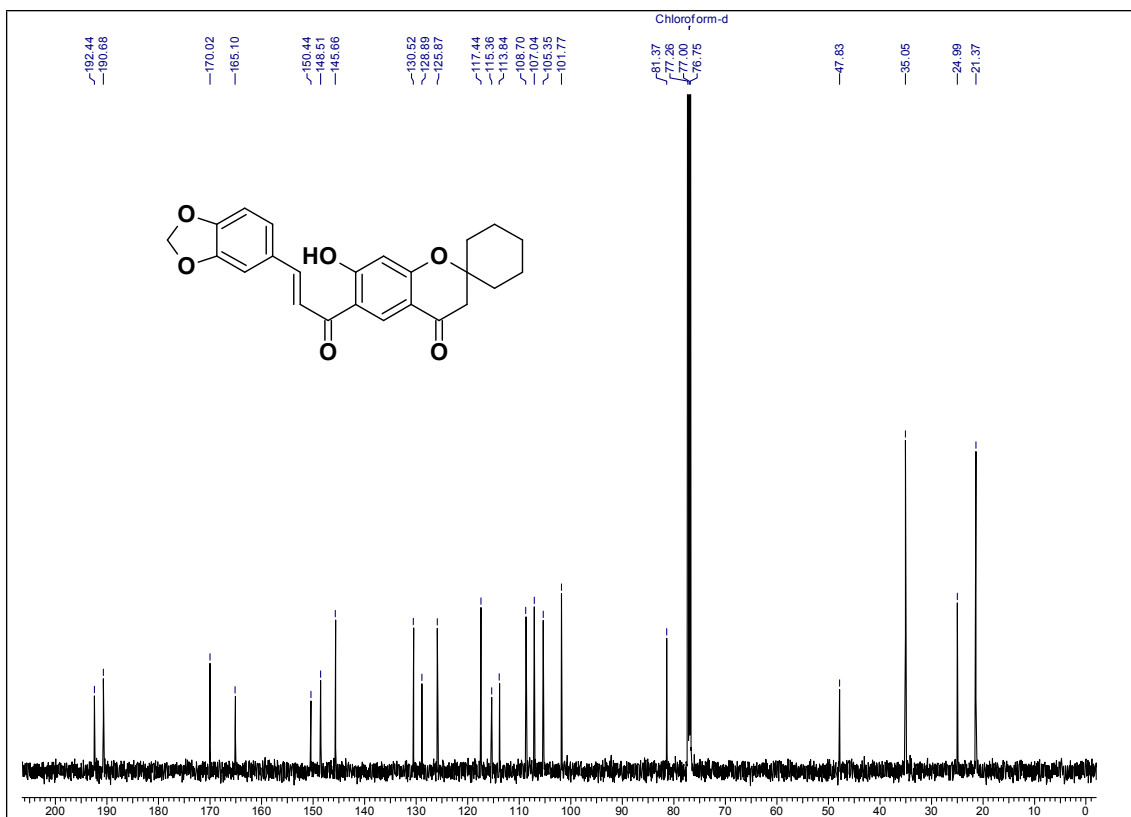


HRMS of Compound 4d



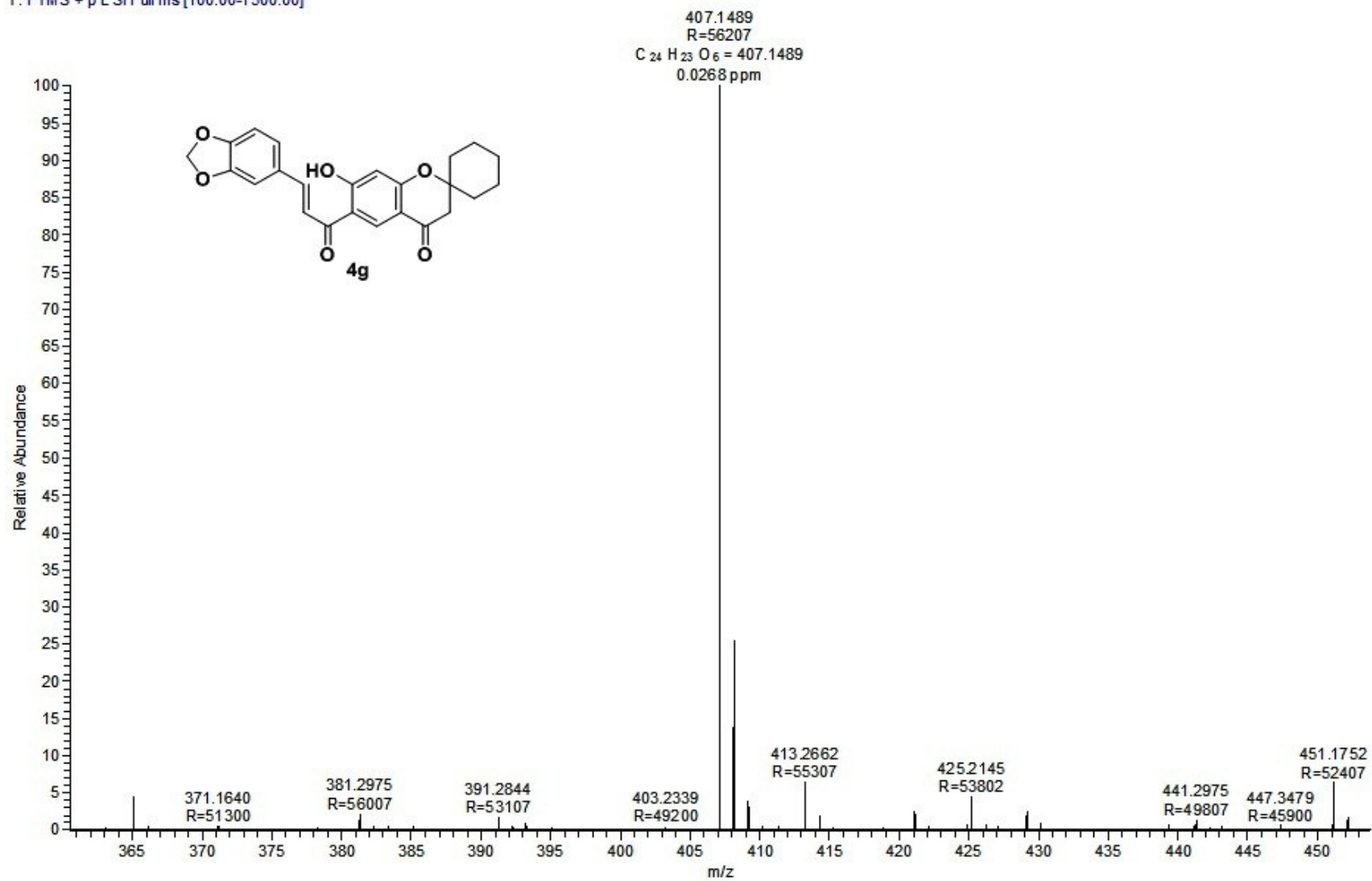


¹H NMR of Compound 4g in CDCl₃

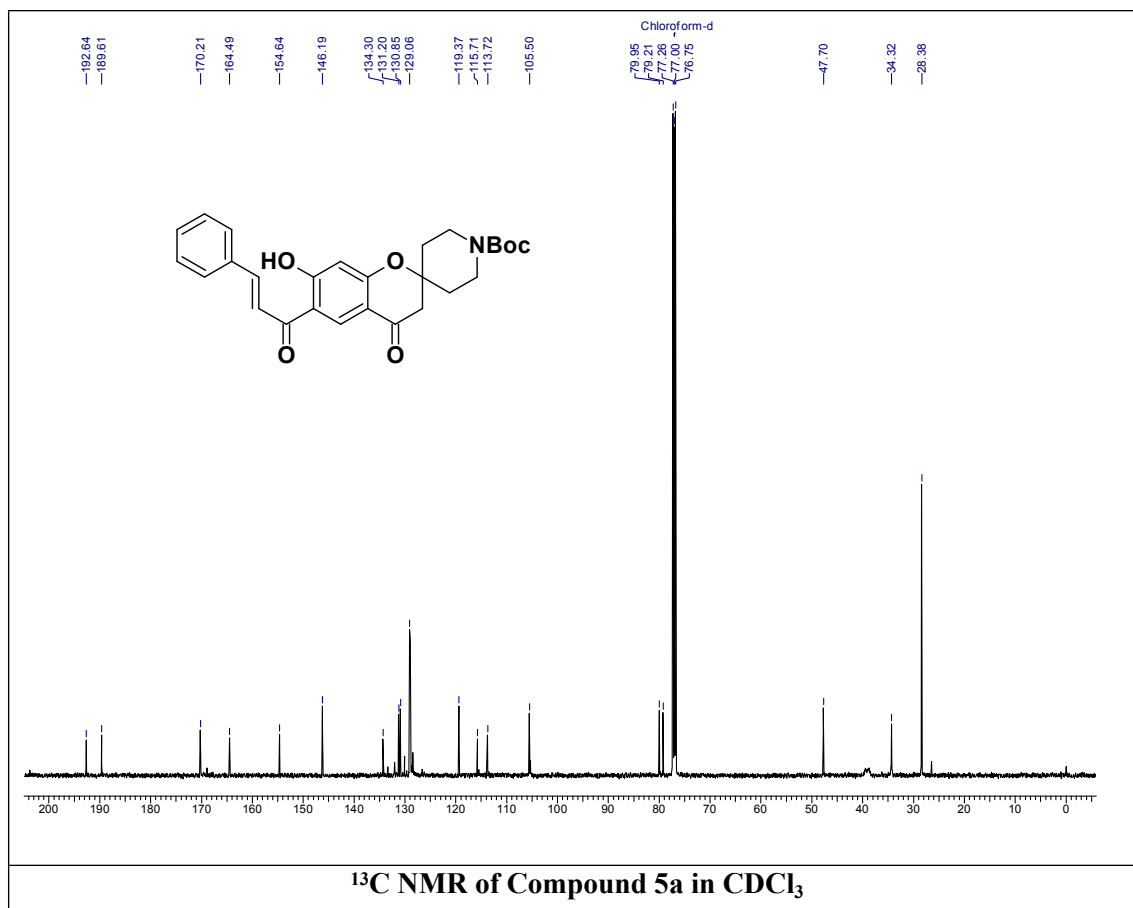
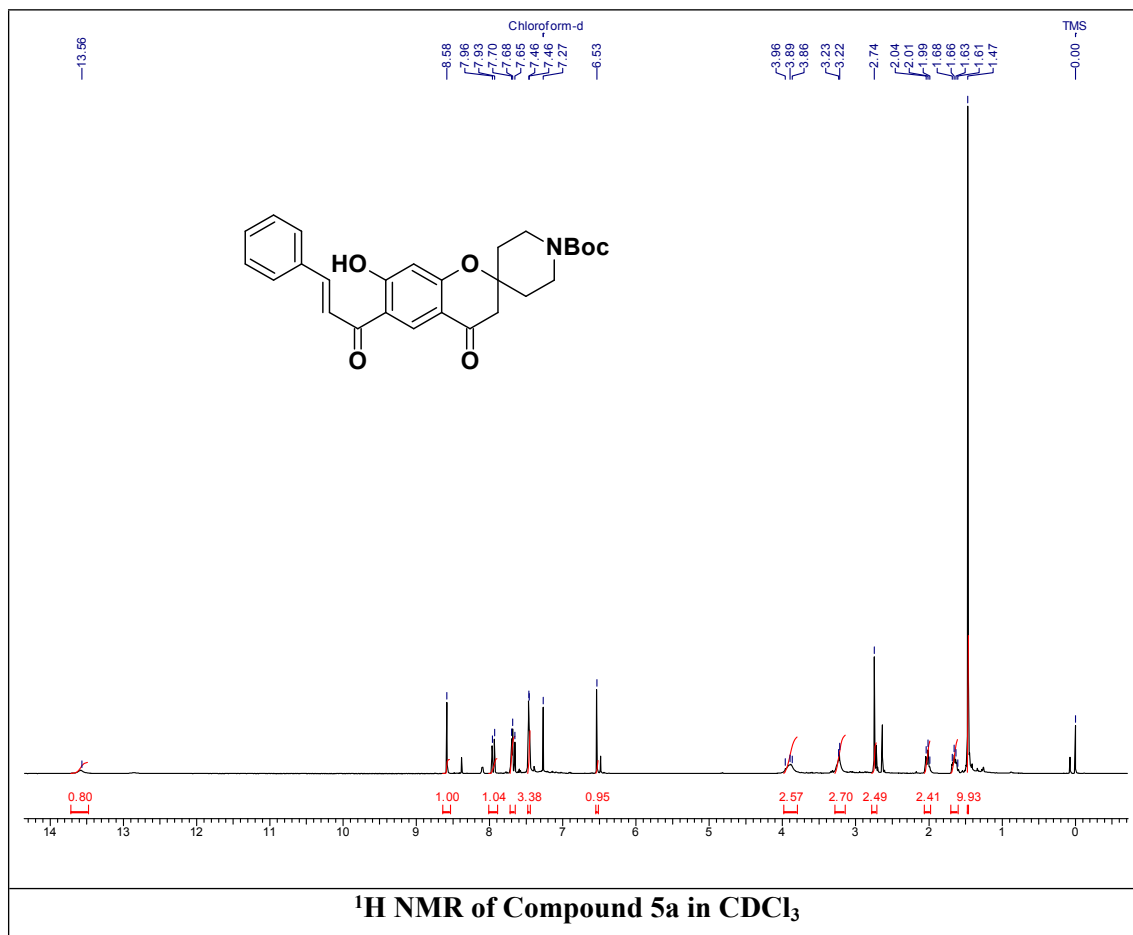


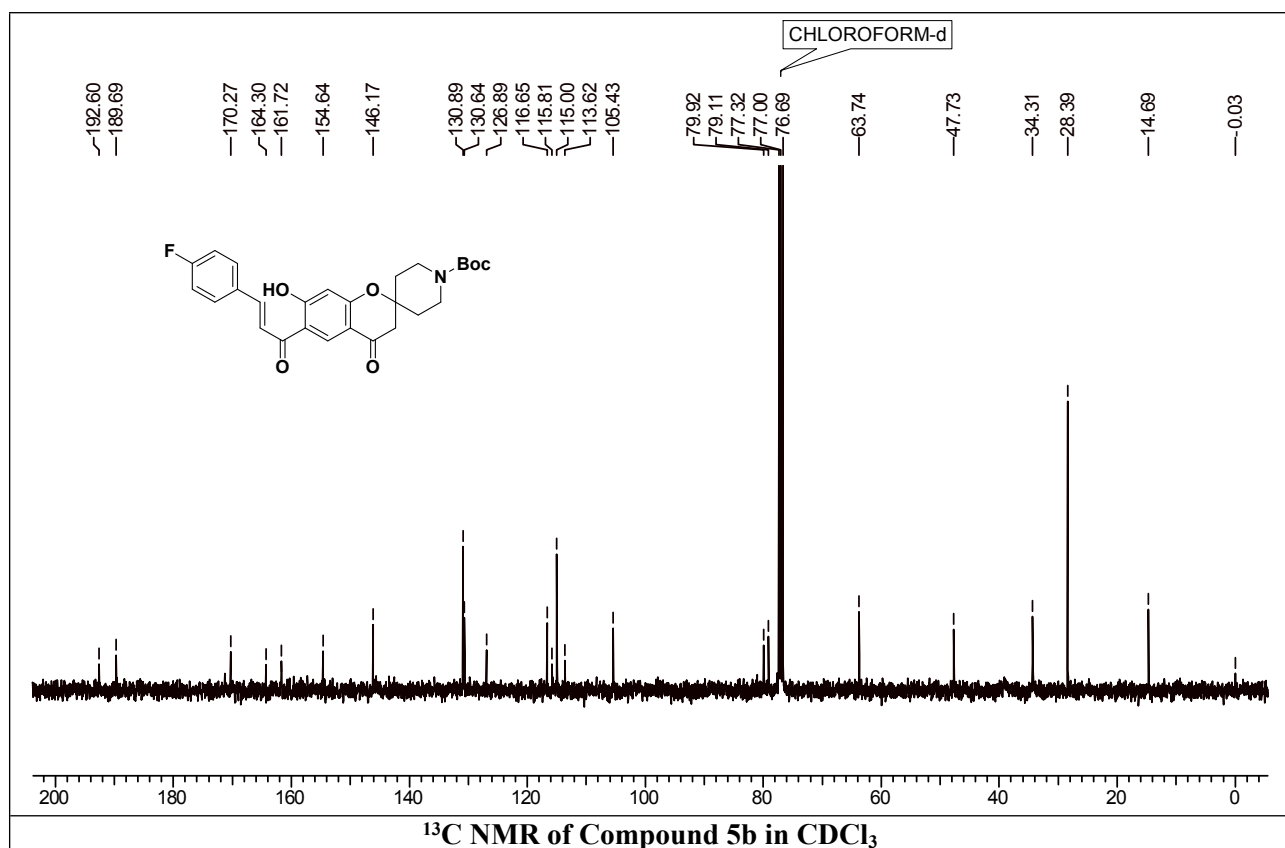
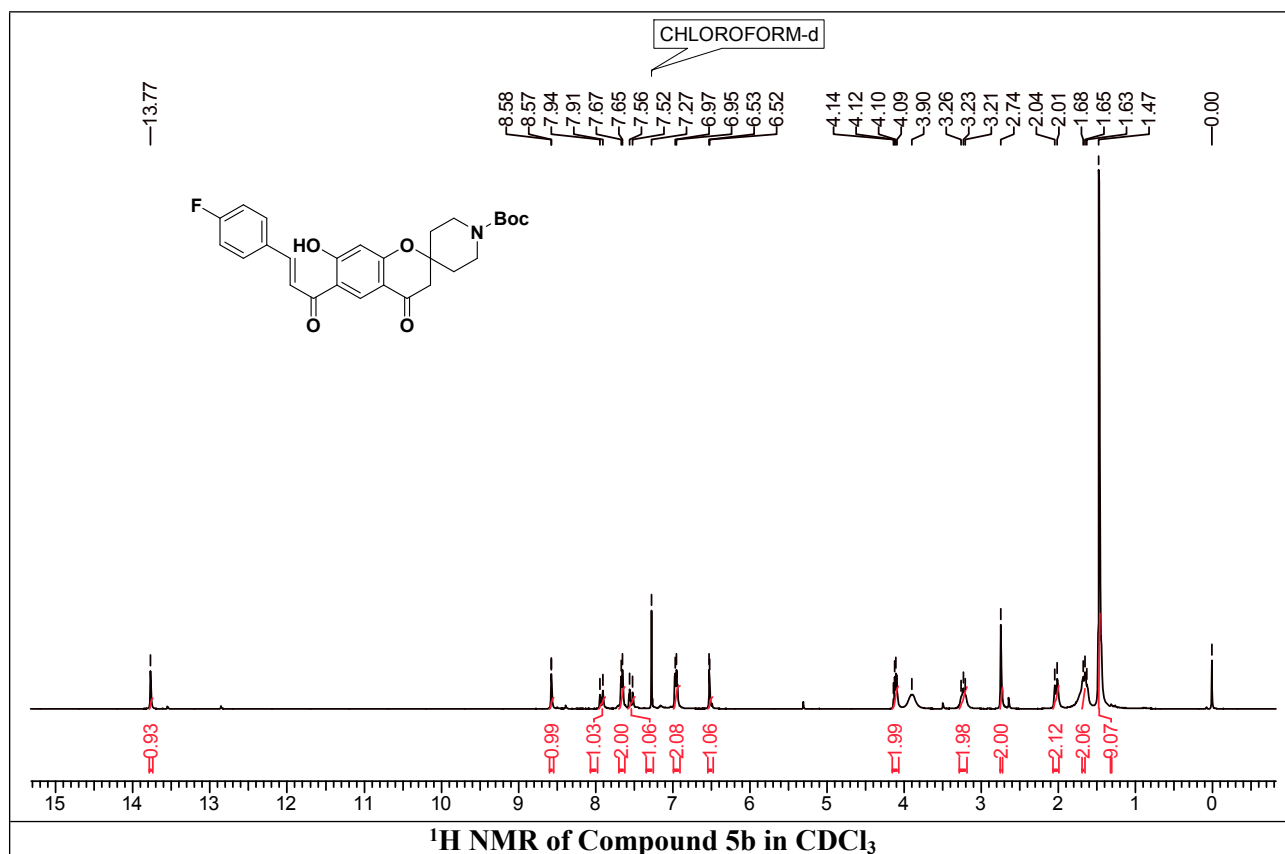
¹³C NMR of Compound 4g in CDCl₃

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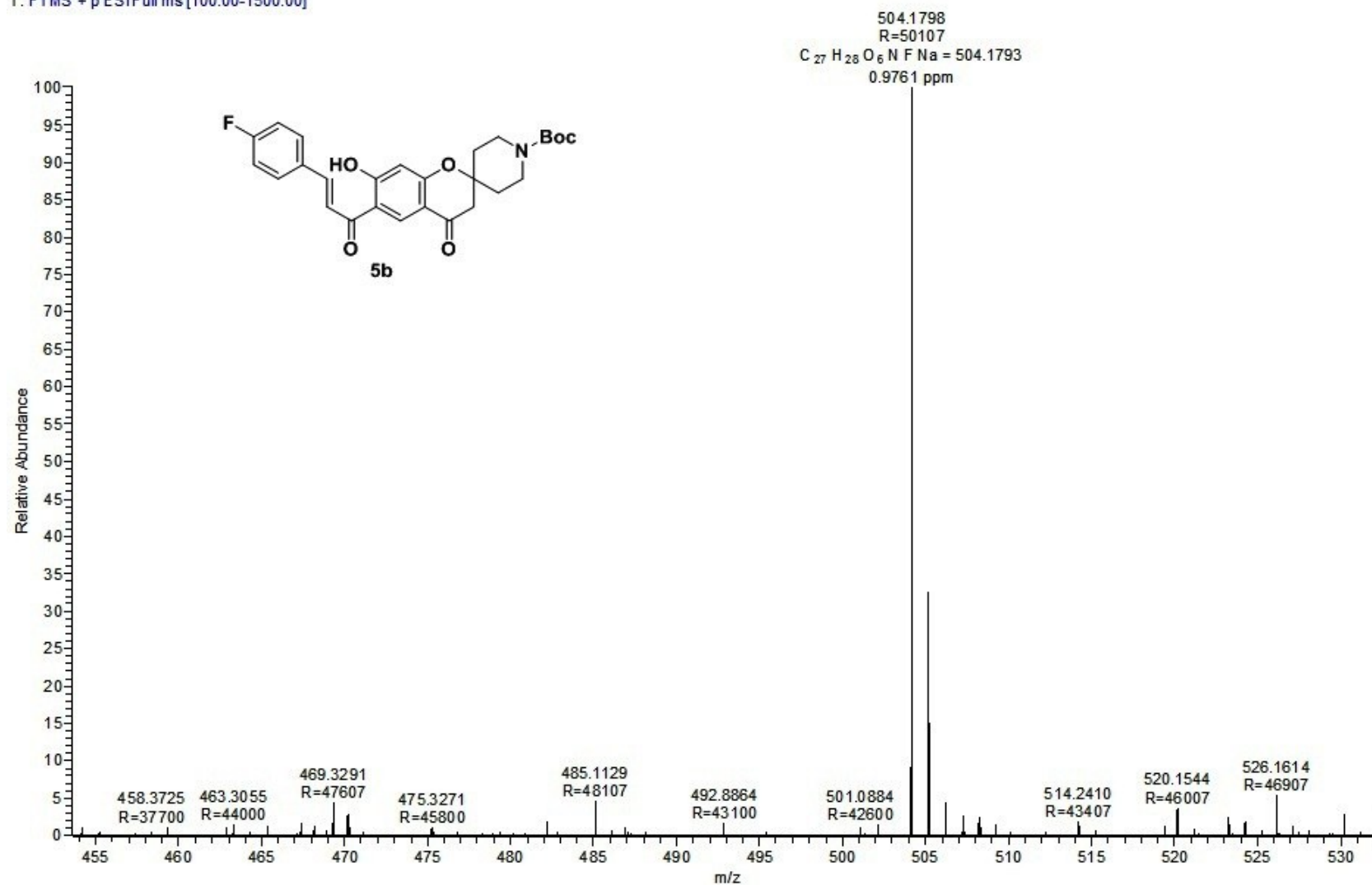


HRMS of Compound 4g

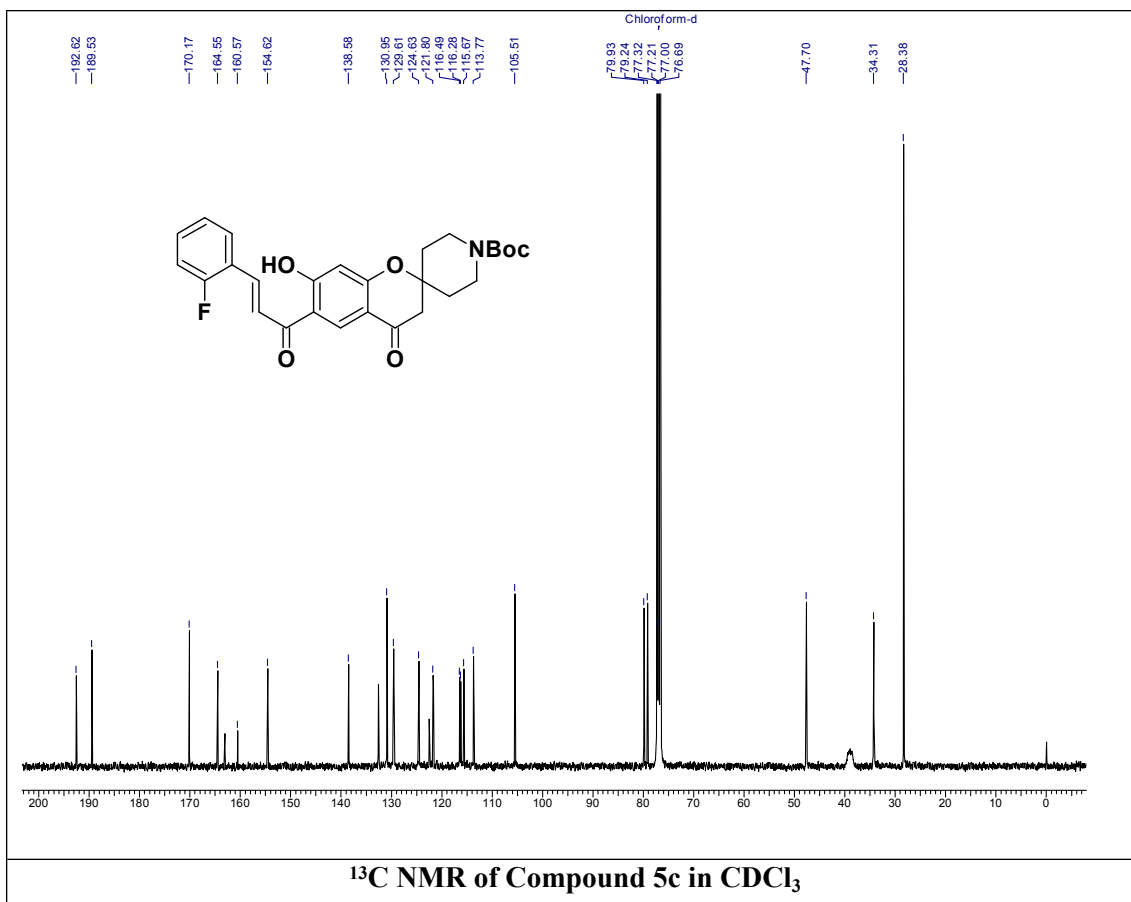
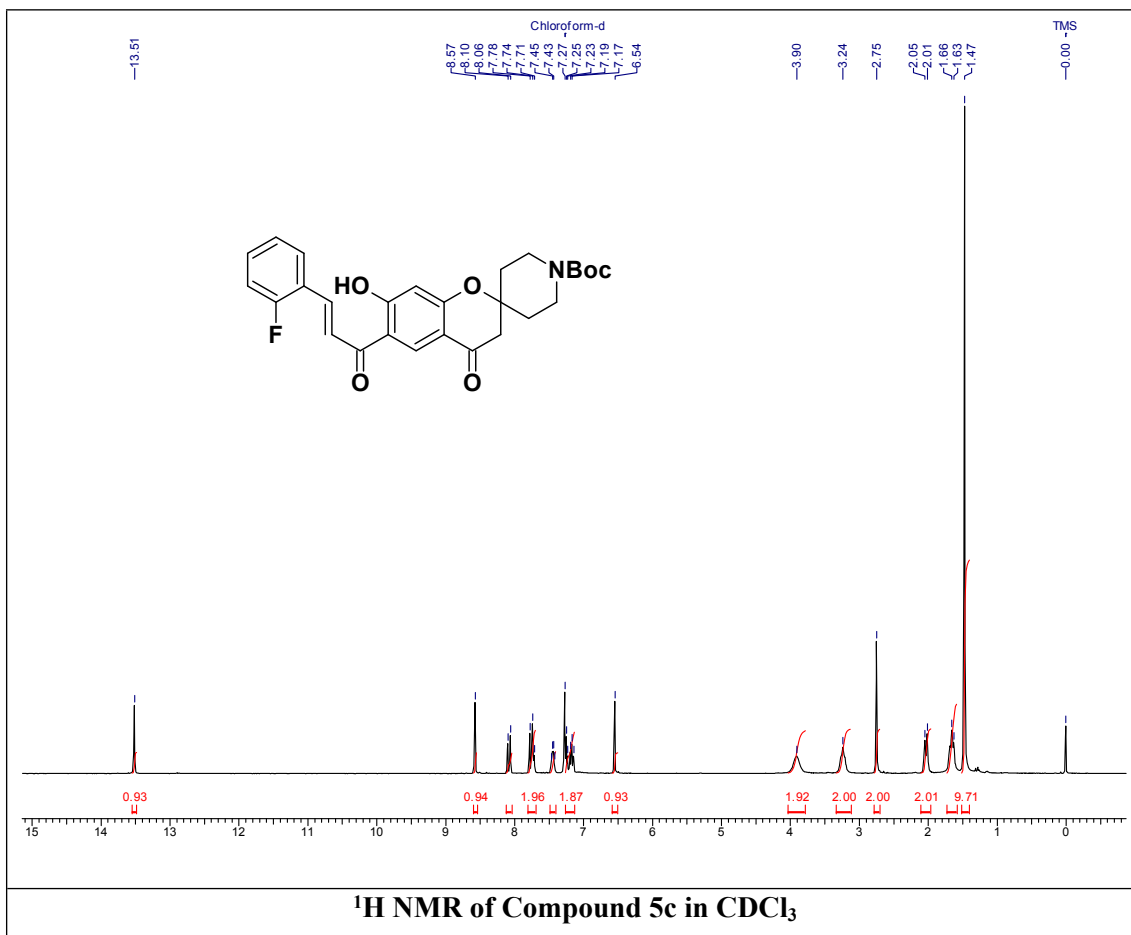




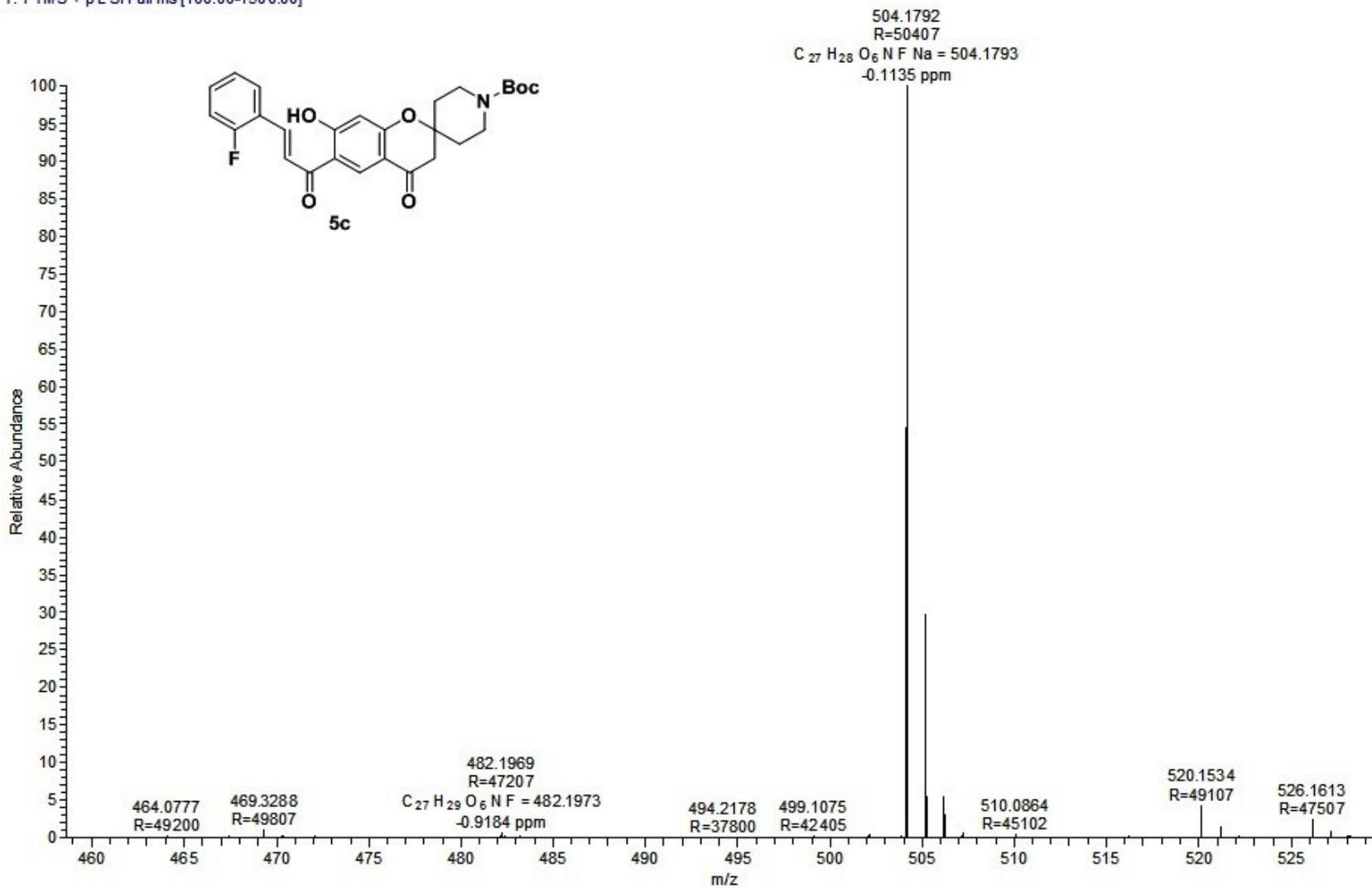
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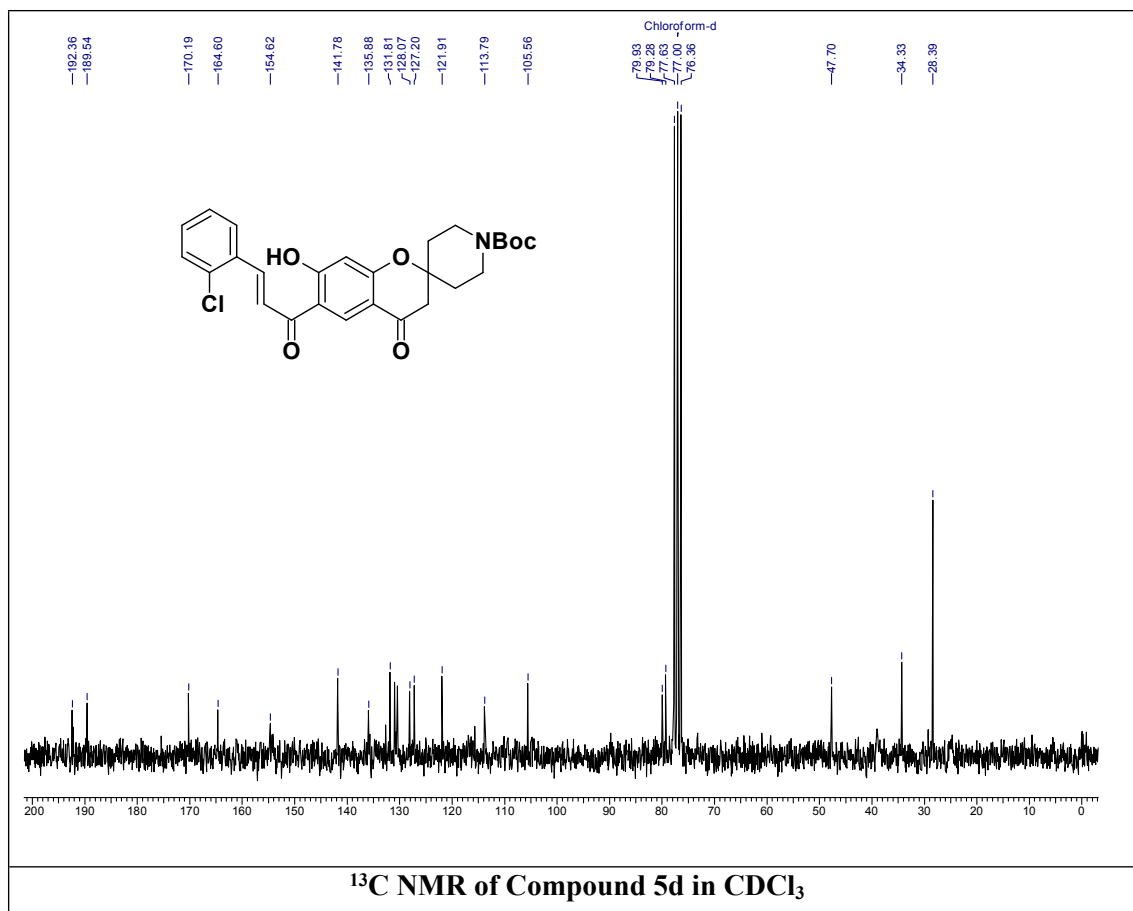
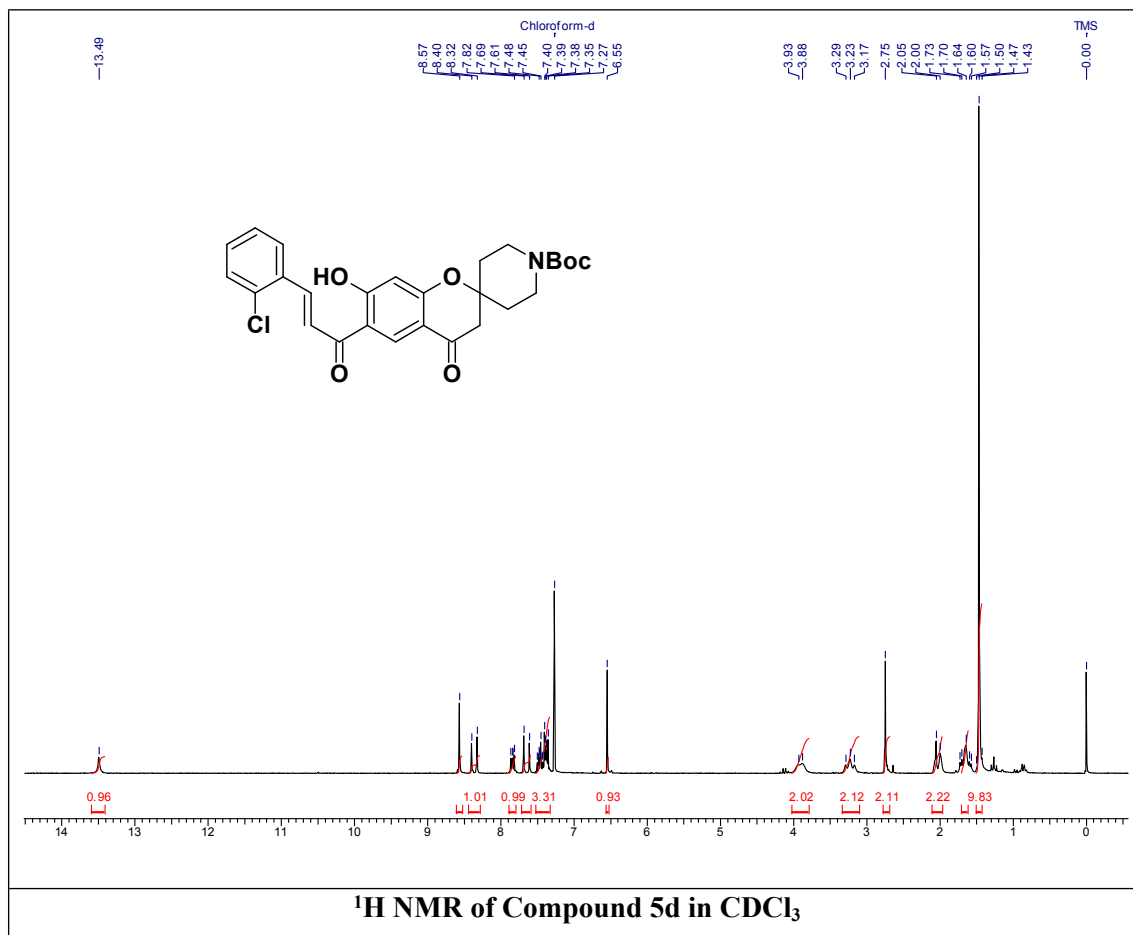
HRMS of Compound 5b

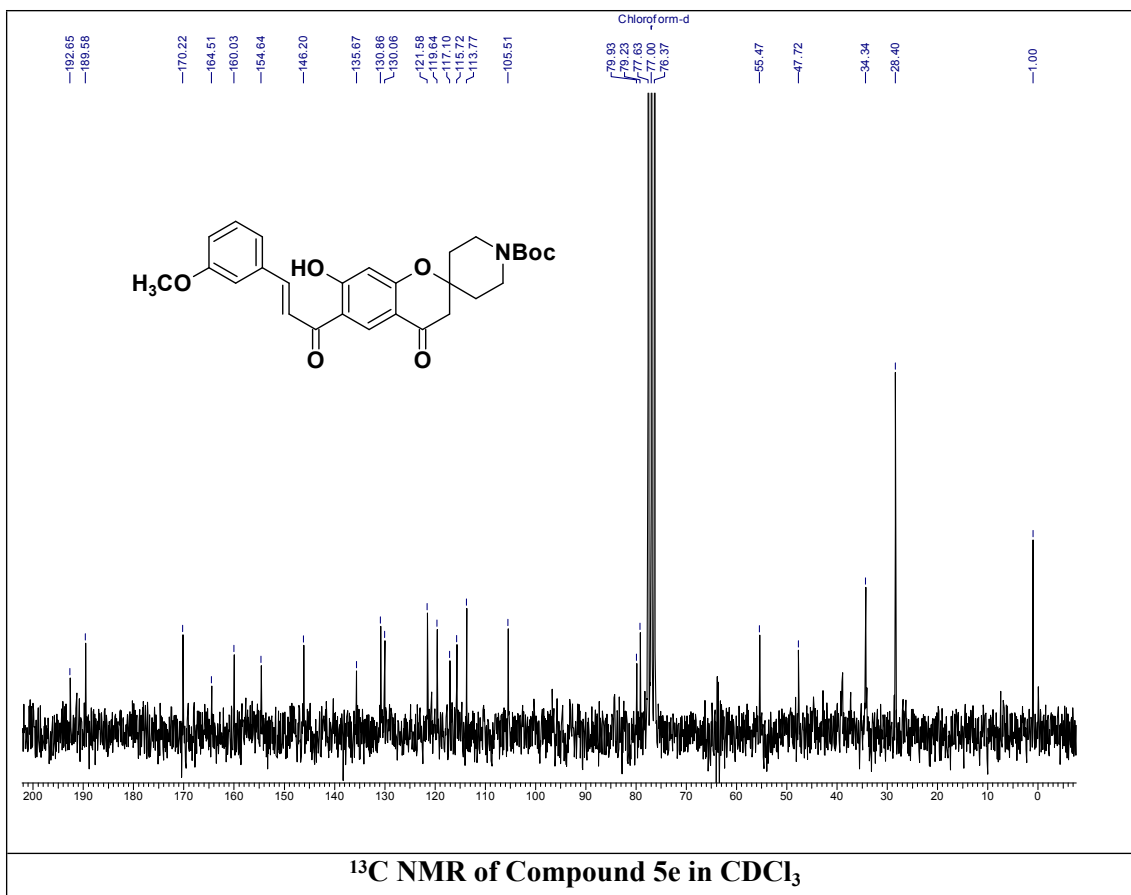
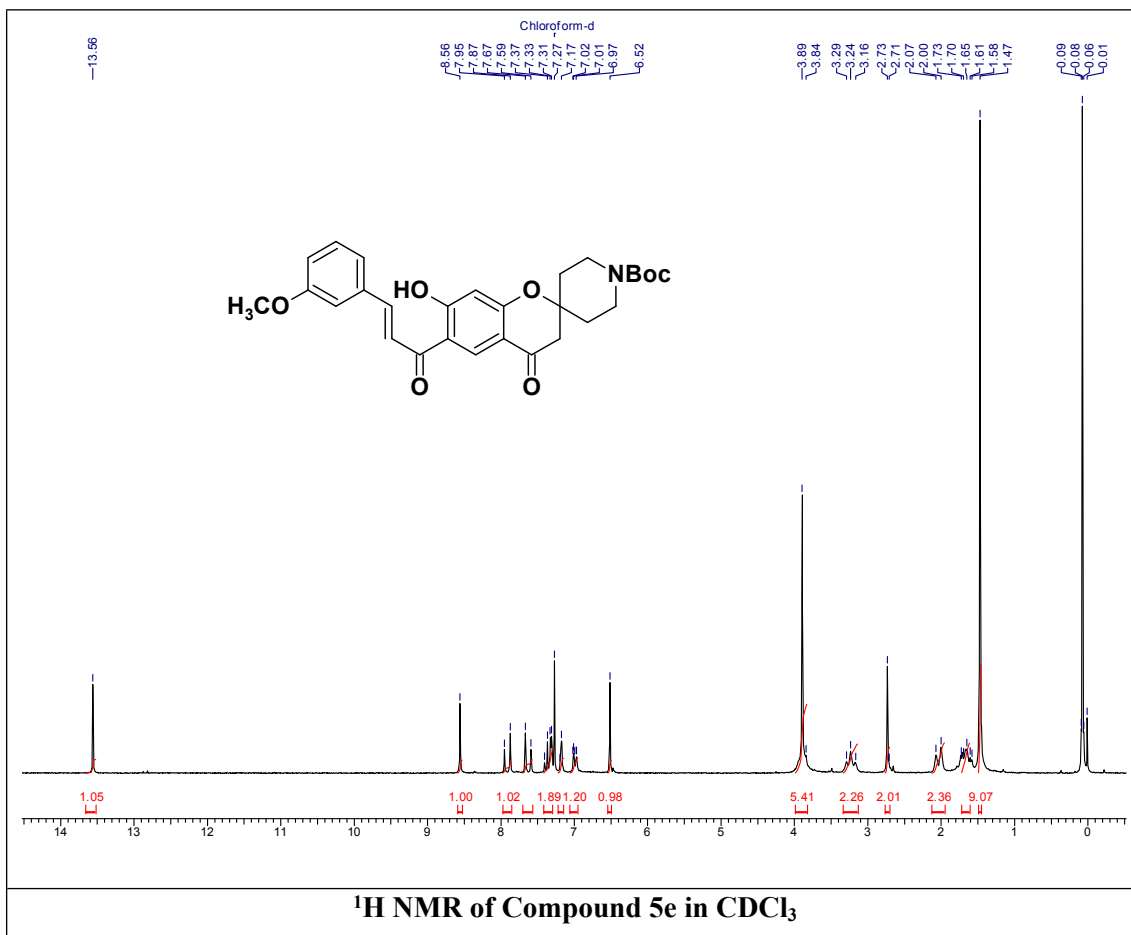


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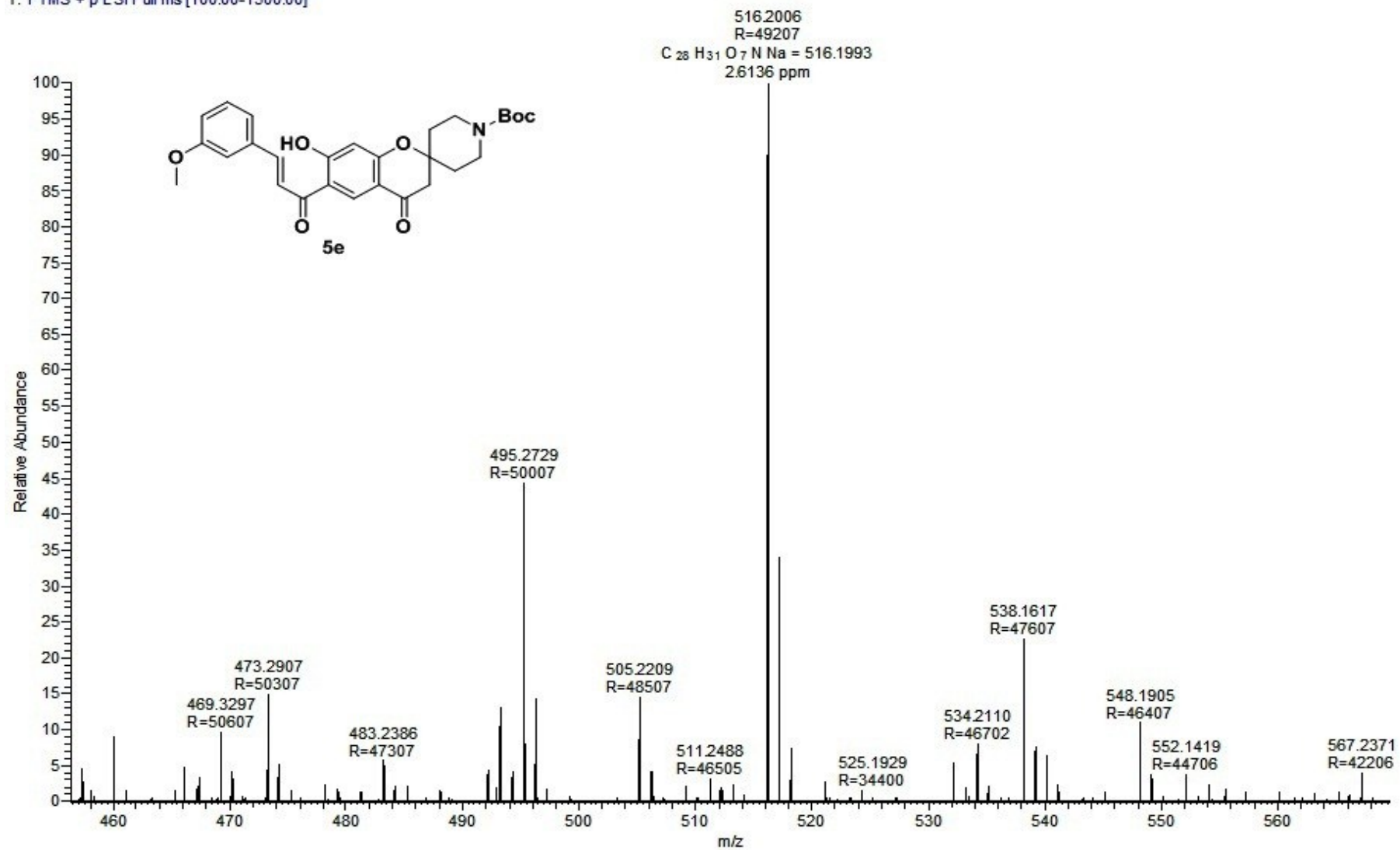


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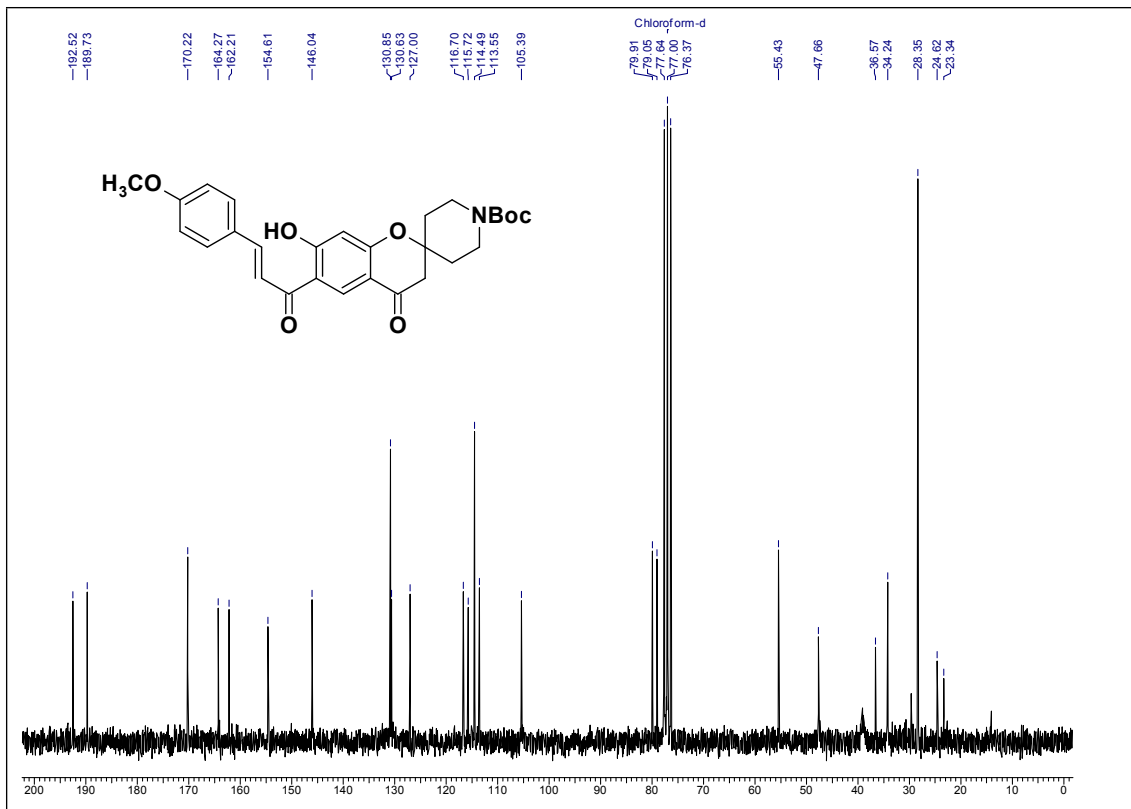
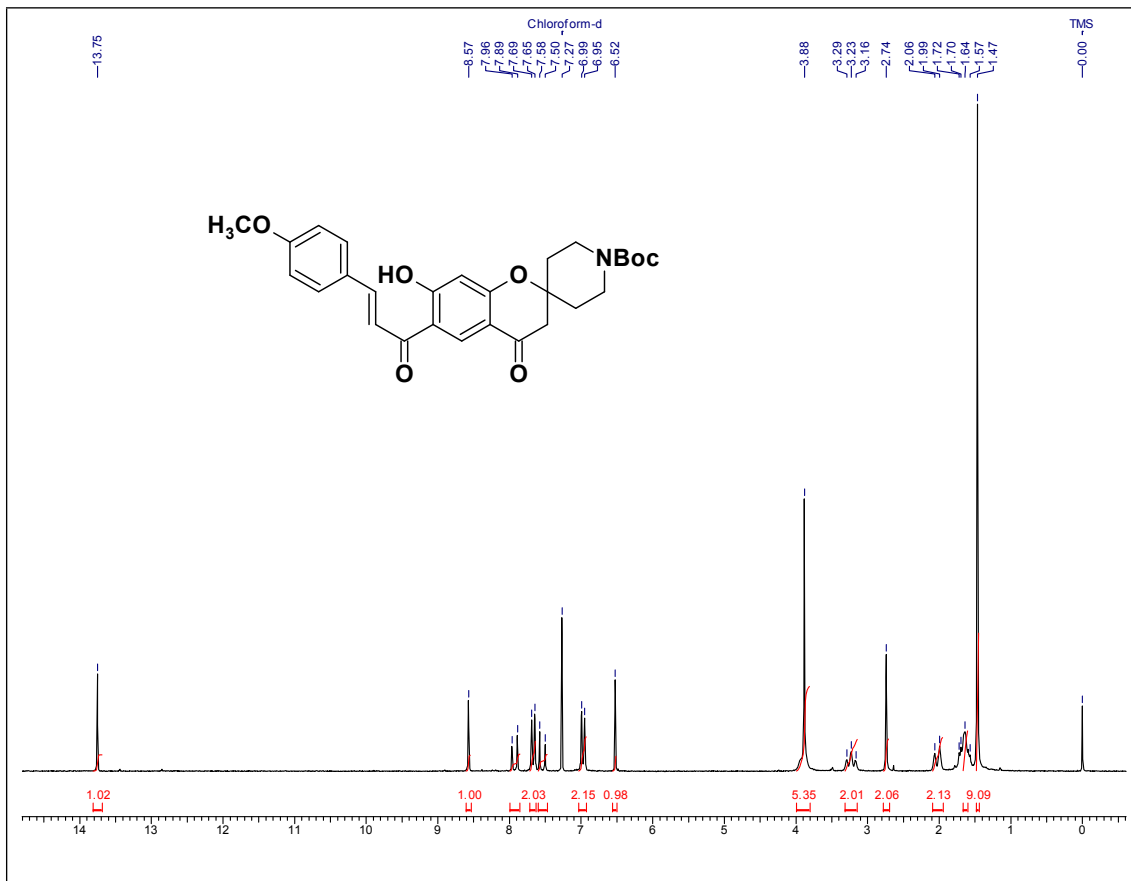




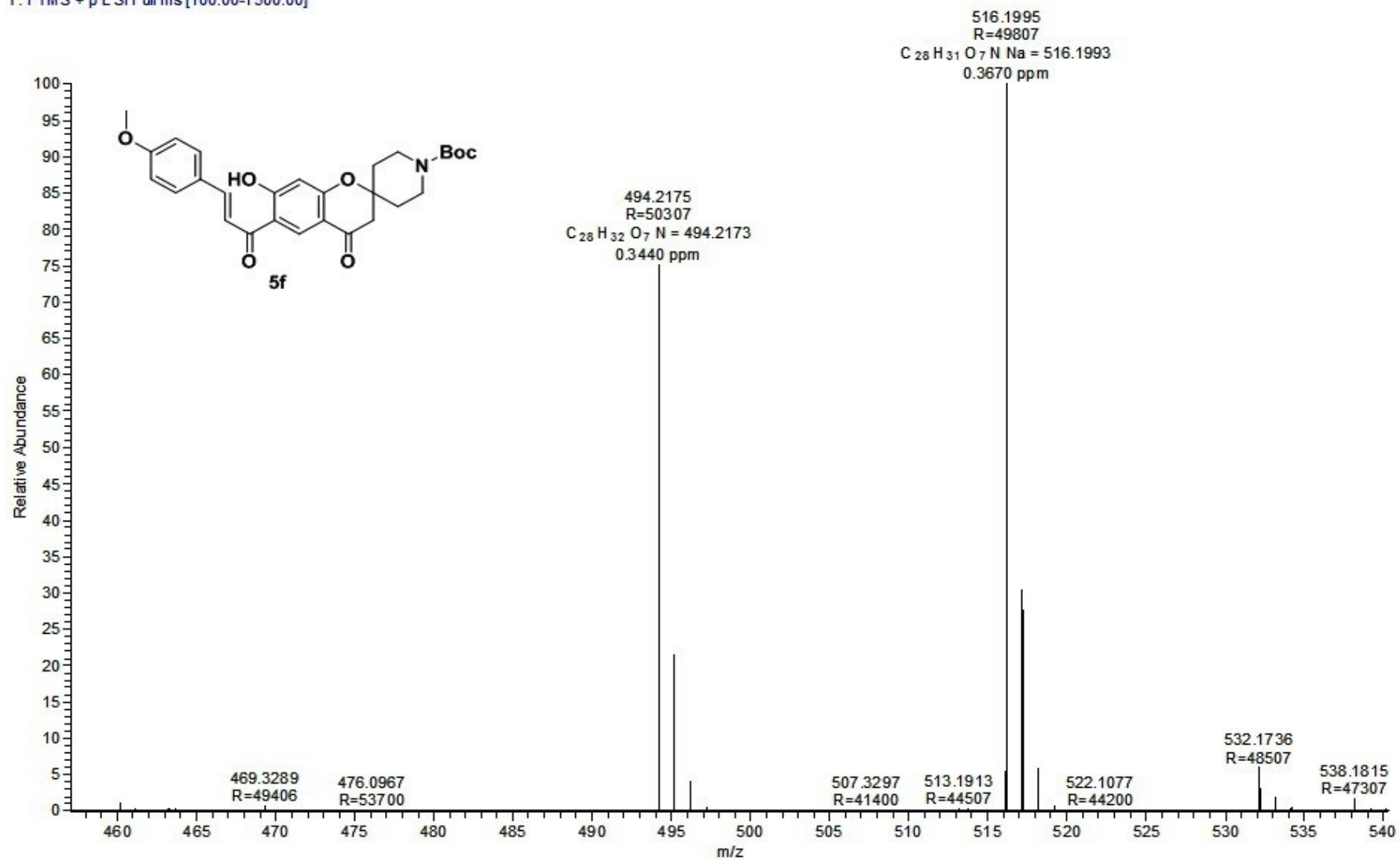
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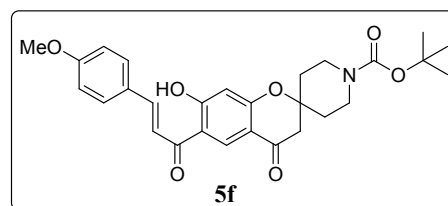
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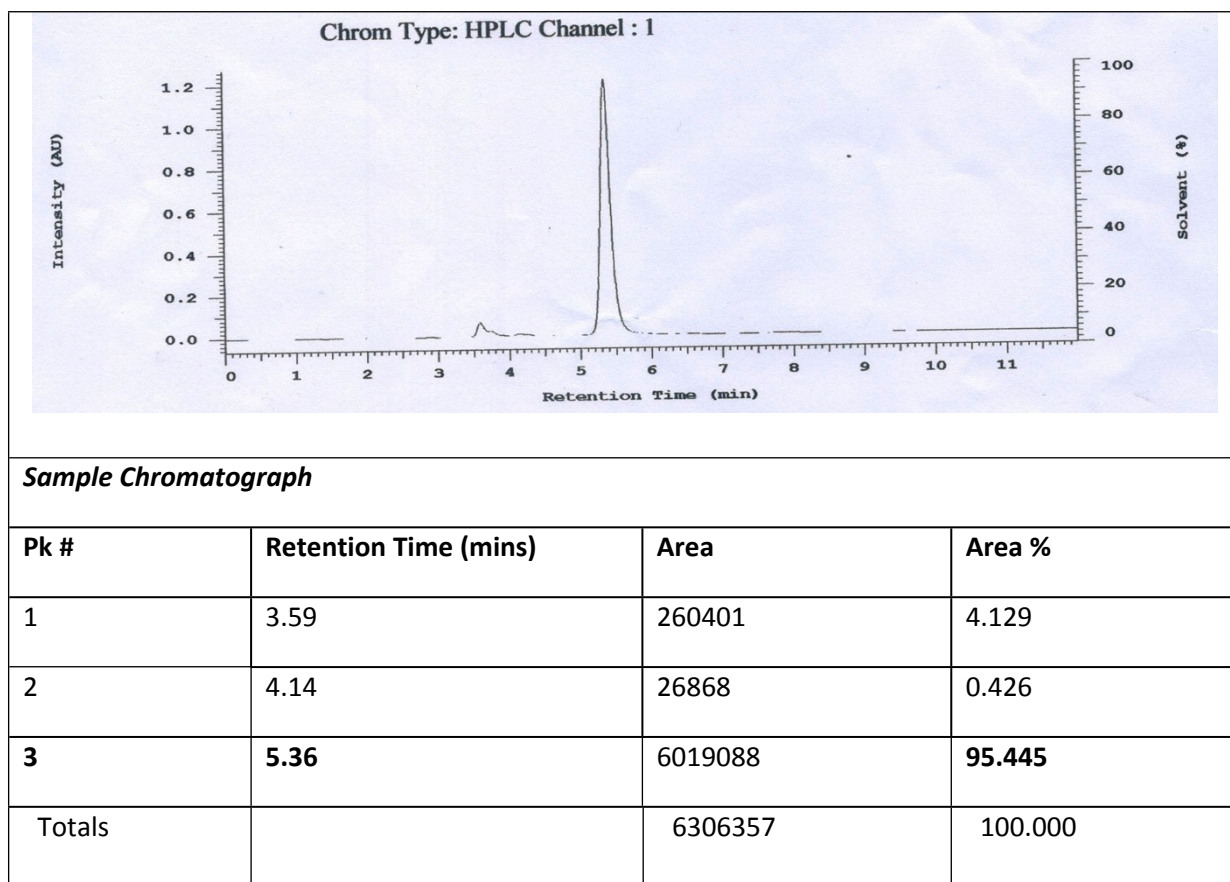
HRMS of Compound 5f

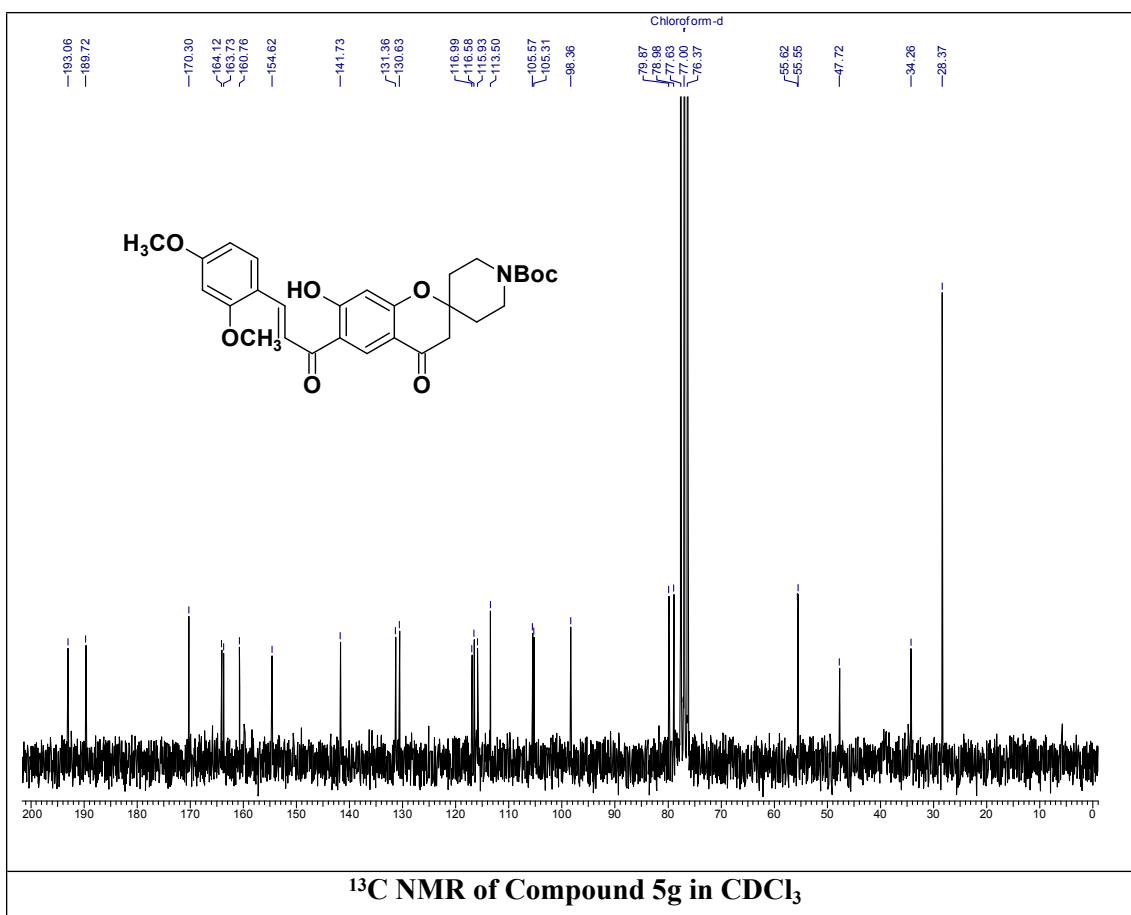
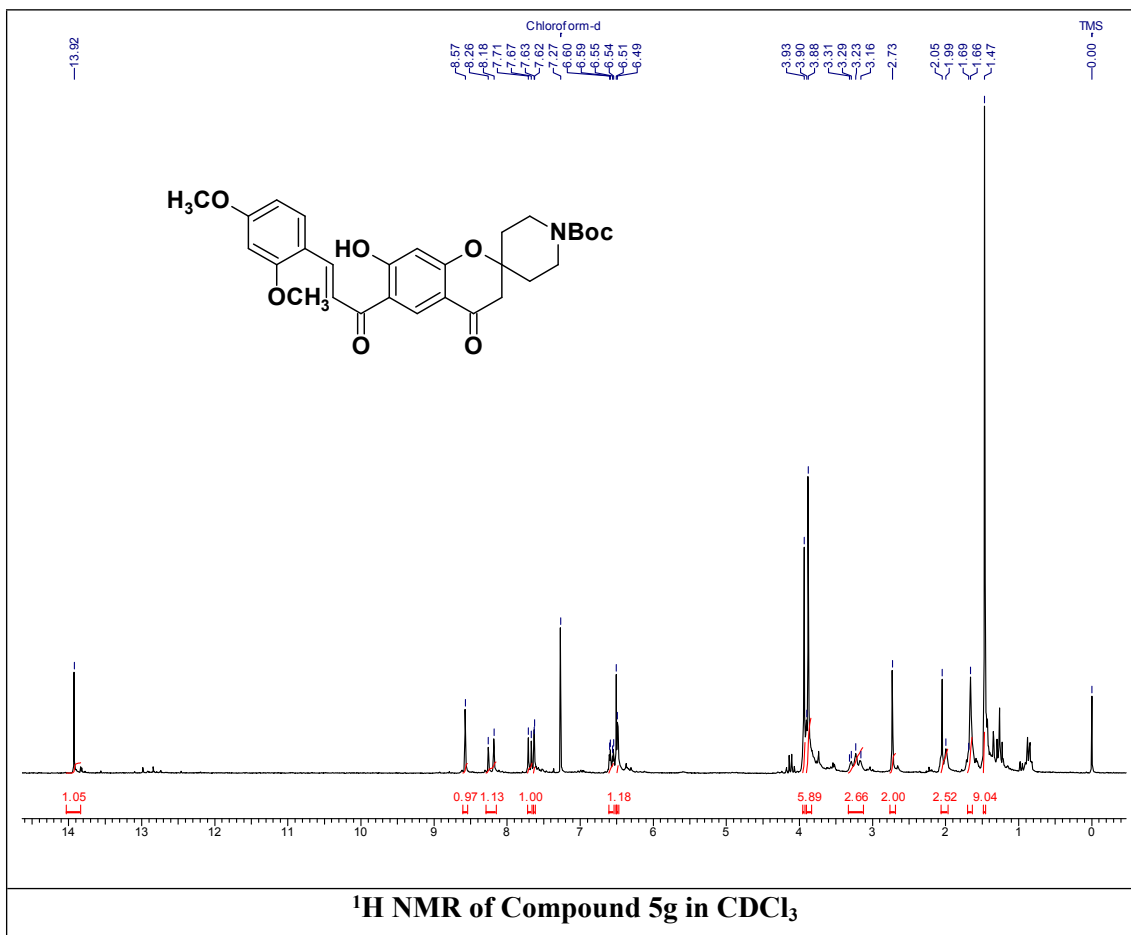
HPLC purity of Compound 5f

Conditions: Grace Smart RP-18 (250 X 4.6 mm) column;
eluent: MeOH:H₂O (90:10); flow rate: 1 mL/min; detector
254 nm.



Purity: 95.4 %

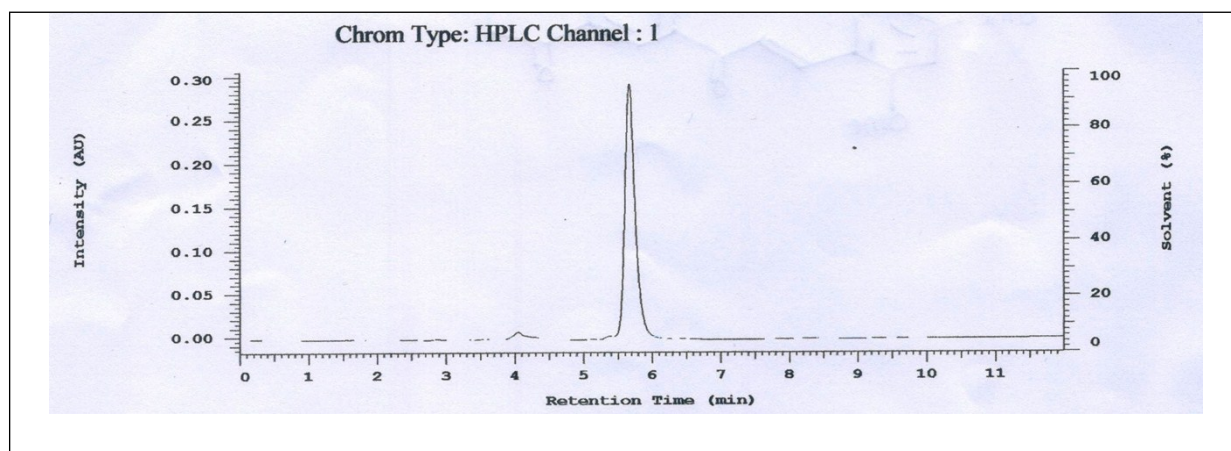
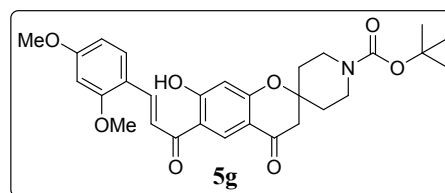




HPLC purity of Compound 5g

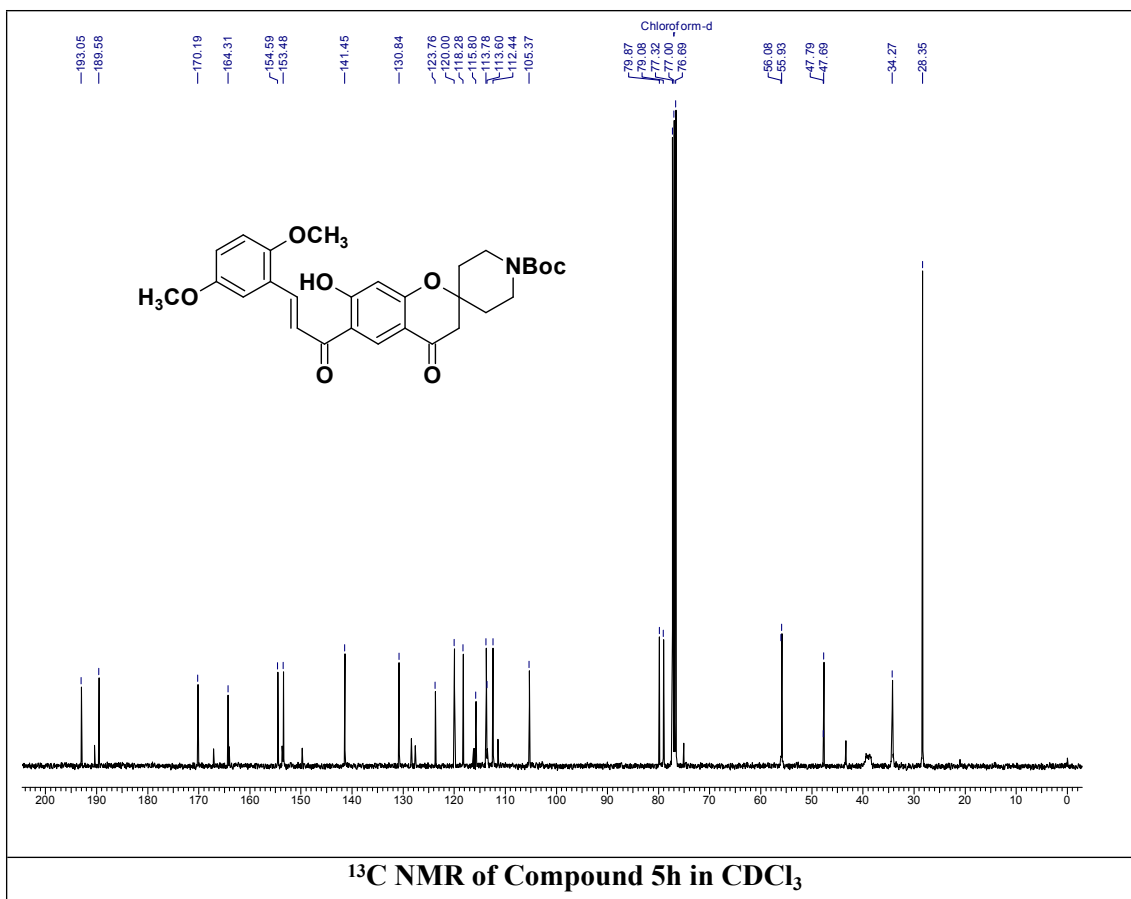
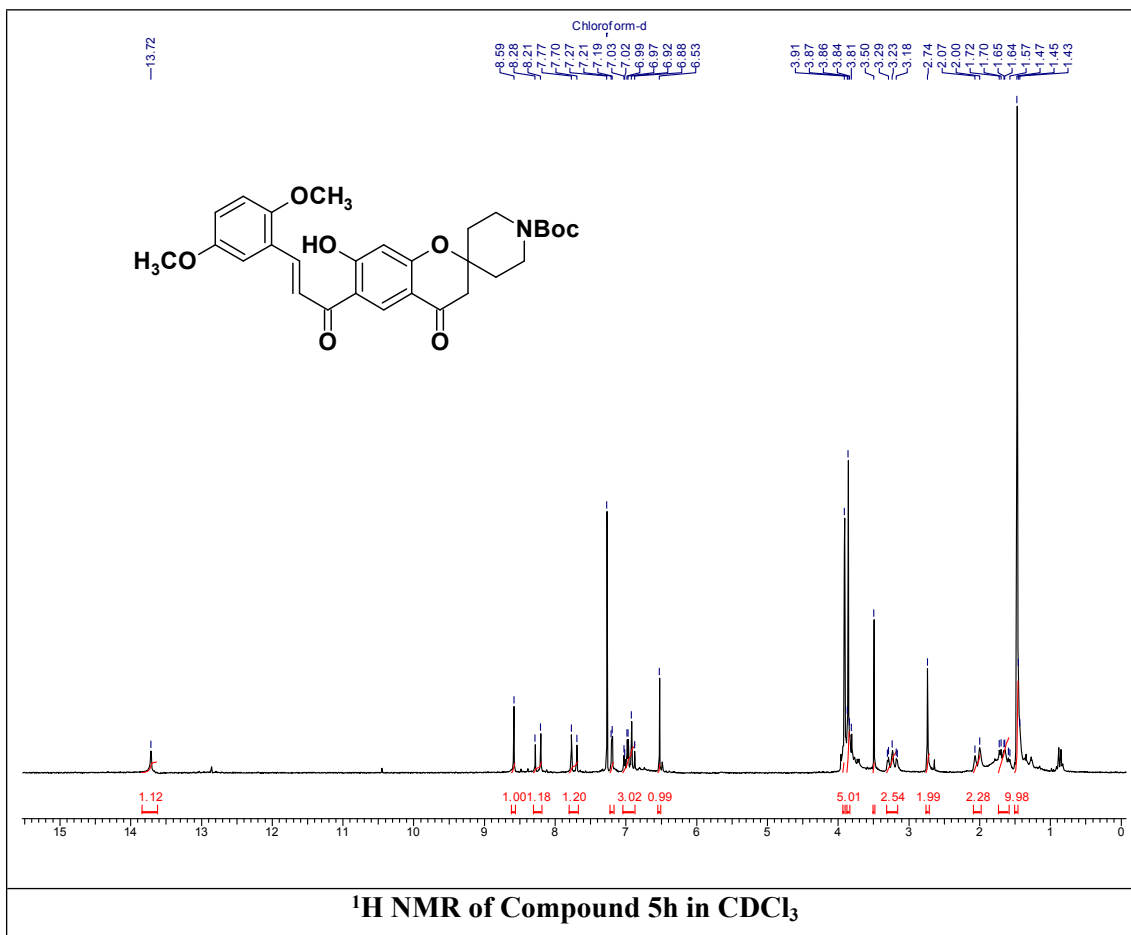
Conditions: Grace Smart RP-18 (250 X 4.6 mm) column; eluent: MeOH:H₂O (90:10); flow rate: 1 mL/min; detector 254 nm.

Purity: 99 %



Sample Chromatograph

Pk #	Retention Time (mins)	Area	Area %
1	4.05	12909	0.844
2	5.67	1516690	99.156
Totals		1529599	100.000



SAR studies

Table S1: Electronic descriptors employed for correlation studies in GP.

Entry	AM1_HOMO	AM1_LUMO	PM3_HOMO	PM3_LUMO	MNDO_HOMO	MNDO_LUMO
1	-9.4004498	-1.09475	-9.4795599	-1.17154	-9.3516397	-0.78029001
2	-9.3777103	-0.89129001	-9.3791599	-0.99450999	-9.3366003	-0.71710998
3	-9.4397097	-0.80559999	-9.4141598	-0.87725002	-9.3687696	-0.70893002
4	-8.7639599	-0.64767998	-8.88239	-0.64622998	-9.2380104	-0.65597999
5	-8.8987398	-0.70765001	-9.14433	-0.52806997	-8.9541798	-0.57546997
6	-9.0514898	-0.67987001	-9.1579905	-0.67756999	-9.2597103	-0.62260002
7	-8.8529701	-0.75334001	-8.97649	-0.69361001	-8.94069	-0.67491001
8	-9.4781399	-0.95204997	-9.5657597	-0.89903003	-9.3961897	-0.69998002
9	-9.4634399	-1.1199	-9.6143198	-1.14518	-9.4680996	-0.76512998
10	-9.5252399	-1.10922	-9.5693703	-1.1987799	-9.4319201	-0.73268002
11	-9.5628004	-1.03737	-9.5262804	-0.99789	-9.4316301	-0.73553997
12	-9.0907297	-0.74800003	-9.18186	-0.68338001	-9.21418	-0.69173998
13	-8.7935896	-0.73268998	-8.94485	-0.68347001	-9.2528095	-0.73294997
14	-8.9224596	-0.78347999	-9.1386299	-0.61229002	-8.9632902	-0.67711002
15	-8.84021	-0.78132999	-8.96099	-0.74167001	-9.1269398	-0.70254999

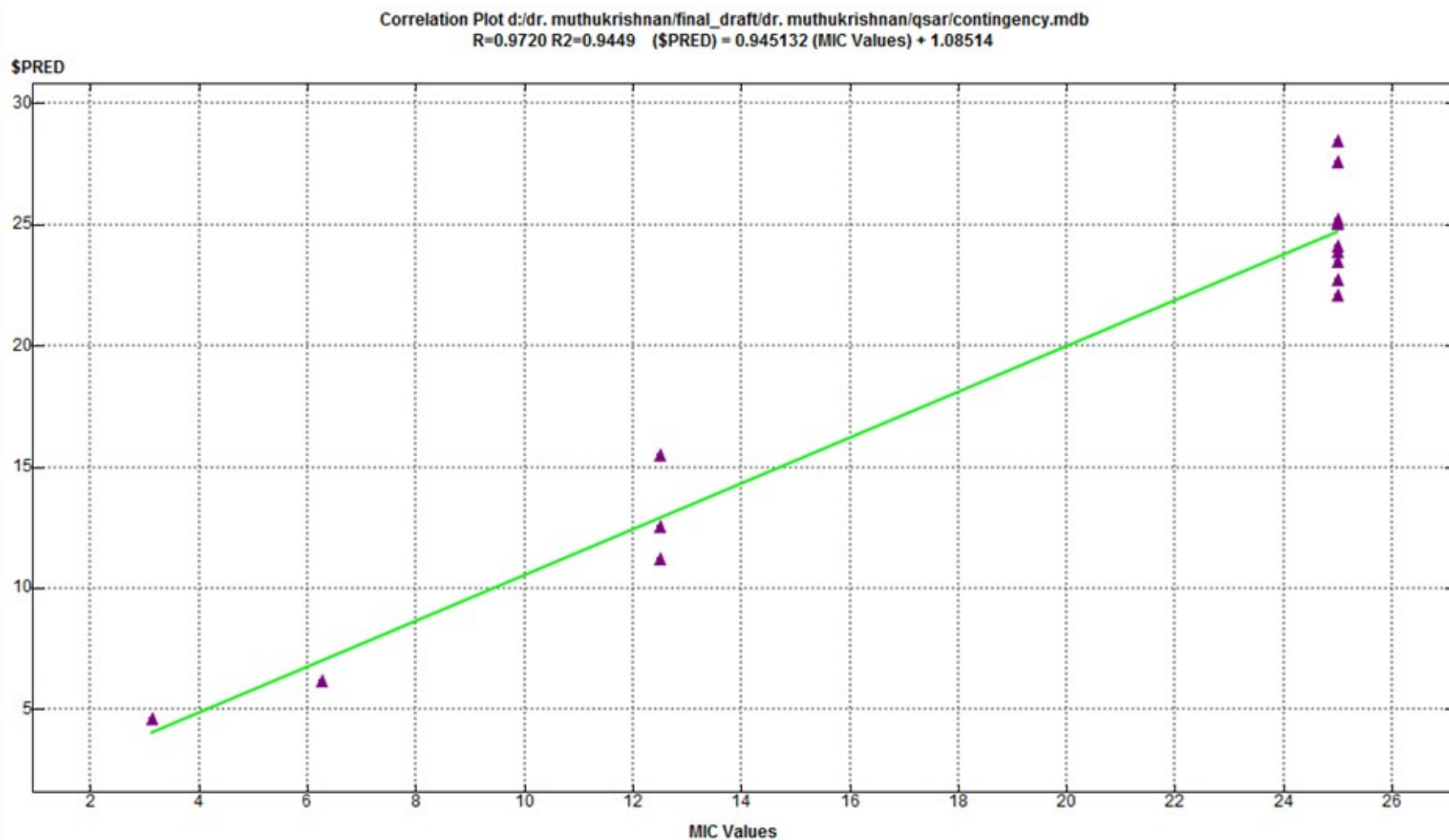


Figure-S1: Correlation plot of 2D Electronic Descriptor QSAR Predicted Data with Experimental MIC Values

Correlation Plot d:/dr. muthukrishnan/final_draft/dr. muthukrishnan/qsar/mtbfinal.mdb
R=0.9355 R²=0.8751 (\$PRED) = 0.875069 (MIC values(ug/mL)) + 2.47264

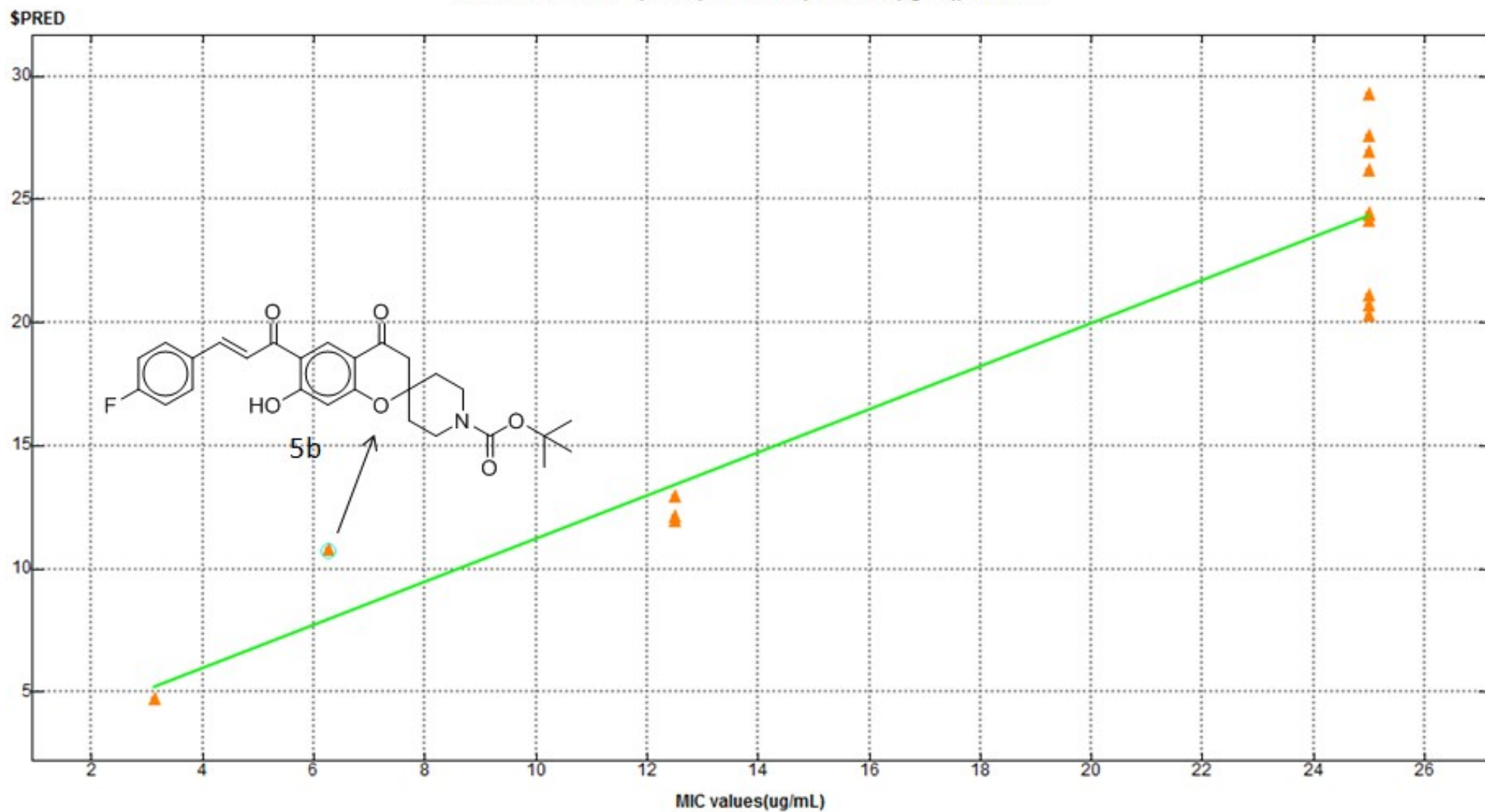


Figure-S2: Correlation plot of 3D Electronic Descriptor QSAR based Predicted Data with Experimental MIC Values

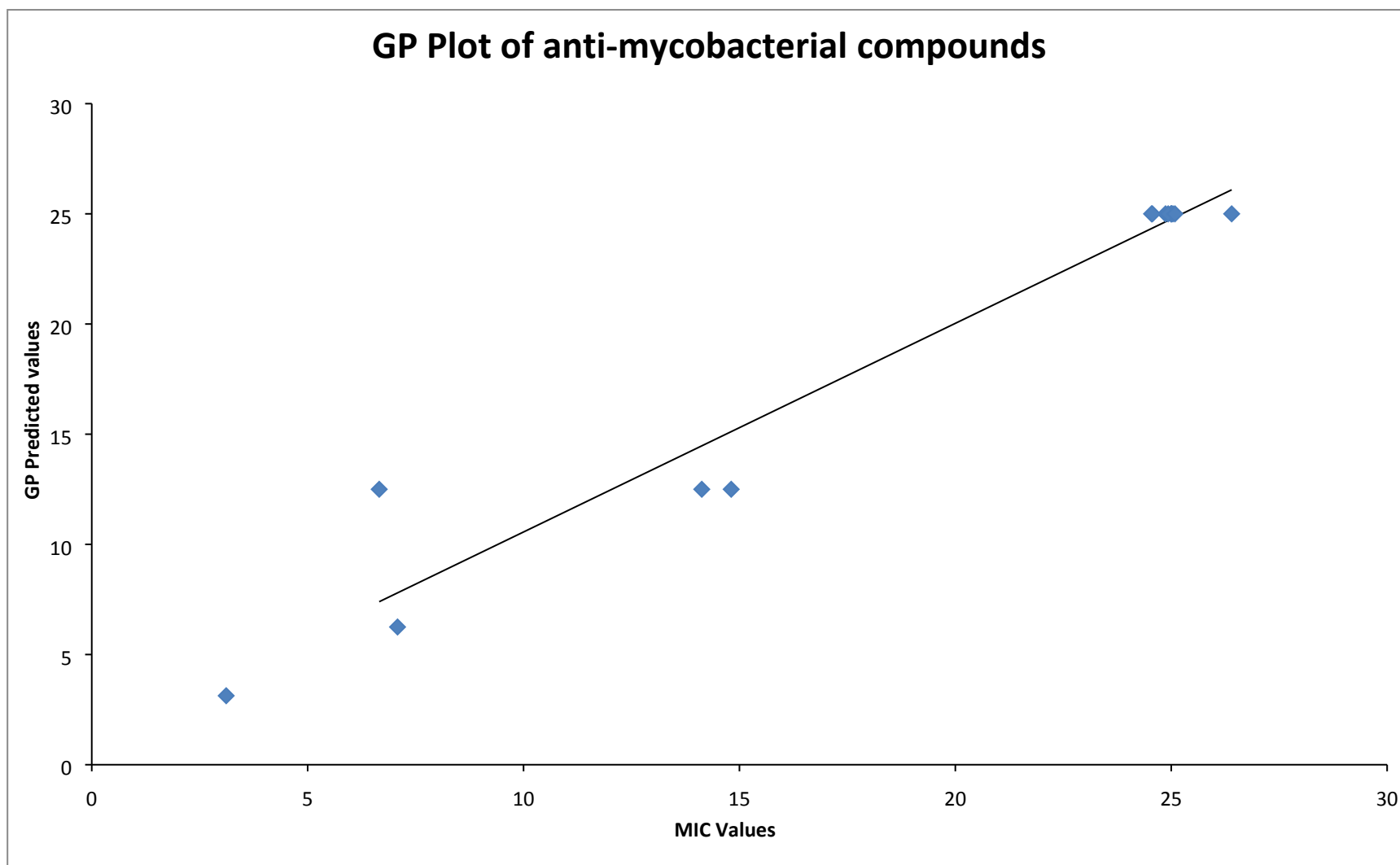


Figure S3: Parity plot of experimental MIC values with predicted values by GP approach