A specific dispiropiperazine derivative that arrests cell cycle, induces apoptosis, necrosis and DNA damage

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Supplementary Information

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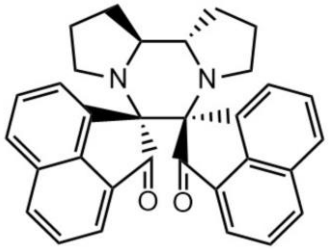
1. Characterization of SPOPP-3 (1) and SPOPP-5 (2).

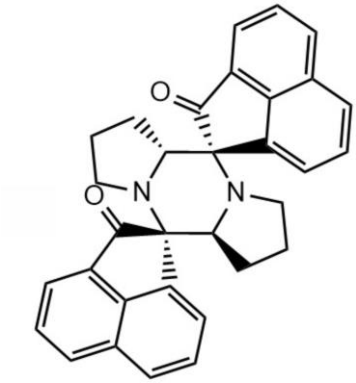
Spiro[2',3]-bis(acenaphthene-1'-one)perhydrodipyrrolo-[1,2-a:1,2-d]-pyrazine (SPOPP-3, **1**) and Spiro[2',5]-bis(acenaphthene-1'-one)perhydrodipyrrolo-[1,2-a:1,2-d]-pyrazine (SPOPP-5, **2**) were synthesized as described in the Materials and Methods section.

SPOPP-3 (1)



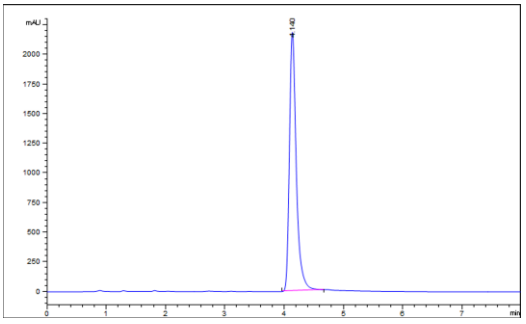
Orange powder; R_f = 0.33 (1 Ethyl acetate: 9 hexanes, ran twice); **LRESI-MS** $[M+H]^+$ m/z of 471 **^{1}H-NMR ($CDCl_3$, 600 MHz)** δ = 7.67 (app d, J = 8.1 Hz, 2H), 7.65 (app d, J = 7.0 Hz, 2H), 7.47 (app d, J = 7. 1 Hz, 2H), 7.43 (app t, J = 7.6 Hz, 2H), 7.39 (d, J = 8.2 Hz, 2H), 7.18 (app t, J = 7.7 Hz, 2H), 3.91-3.86 (m, 2H), 2.60 (td, J = 8.6, 2.9 Hz, 2H), 2.17-2.13 (m, 2H), 2.0 1-1.95 (m, 2H), 1.82- 1.75 ((m, 2H), 1.73-1.67 (m, 2H), 1.64-1.57 ppm (m, 4H); **^{13}C-NMR ($CDCl_3$, 125 MHz)** δ = 207.3, 141.4, 136.9, 134.1, 130.8, 130.2, 127.9, 127.7, 124.8, 123.3, 119.4, 72.3, 60.5, 47.6, 27.9, 21.3 ppm.
This is a known compound and our data is consistent with the published data of the compound.[1]

SPOPP-5 (2)

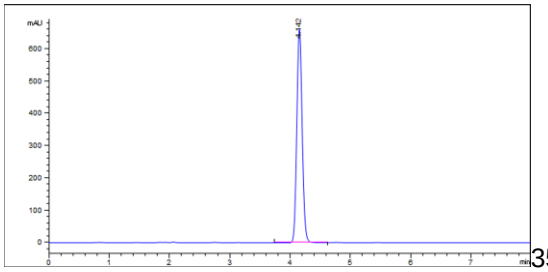


$C_{32}H_{26}N_2O_2$: Yellow powder, R = 0.53 (1 ethyl acetate: 9 hexanes, resolved twice on the same TLC); **LRESI-MS** $[M+H]^+$ m/z of 471. **^{1}H-NMR ($CDCl_3$, 400 MHz)** δ = 8.16-8.13 (m, 4H), 7.97-7.86 (m, 4H), 7.75 (m, 4H), 4.88 (dd, J = 8.4, 5.7 Hz, 2H), 2.58-2.36 (m, 4H), 1.62-1.30 (m, 6H), 0.66-0.49 ppm (m, 2H**). ^{13}C-NMR ($CDCl_3$, 100 MHz)** δ = 208.4, 141.5, 140.4, 131.8, 131.3, 129.9, 128.3, 127.6, 124.0, 121.2, 120.2, 74.6, 60.3, 45.7, 24.4, 24.4 ppm.

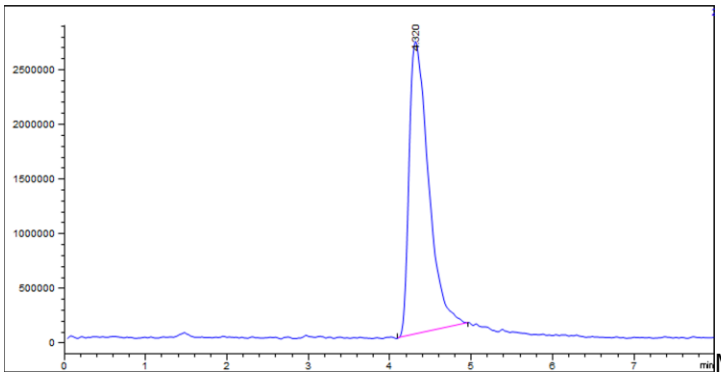
2. Supplementary Figures.



265 nm



354 nm



MSD2 100-1000 m/z

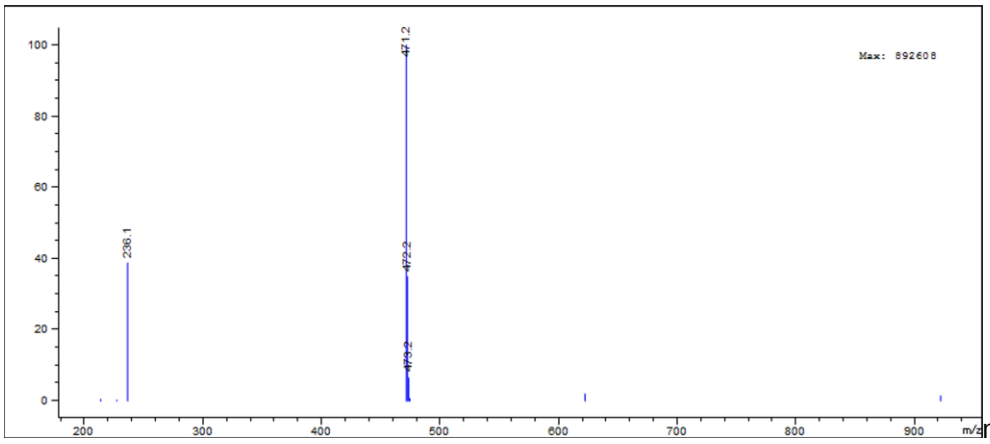


Figure S1: HPLC-chromatogram (265 and 354 nm), and MS-spectra of SPOPP-3 (**1**). The ESIMS spectrum exhibited a $[M + H]^+$ peak at *m/z* = 471.2.

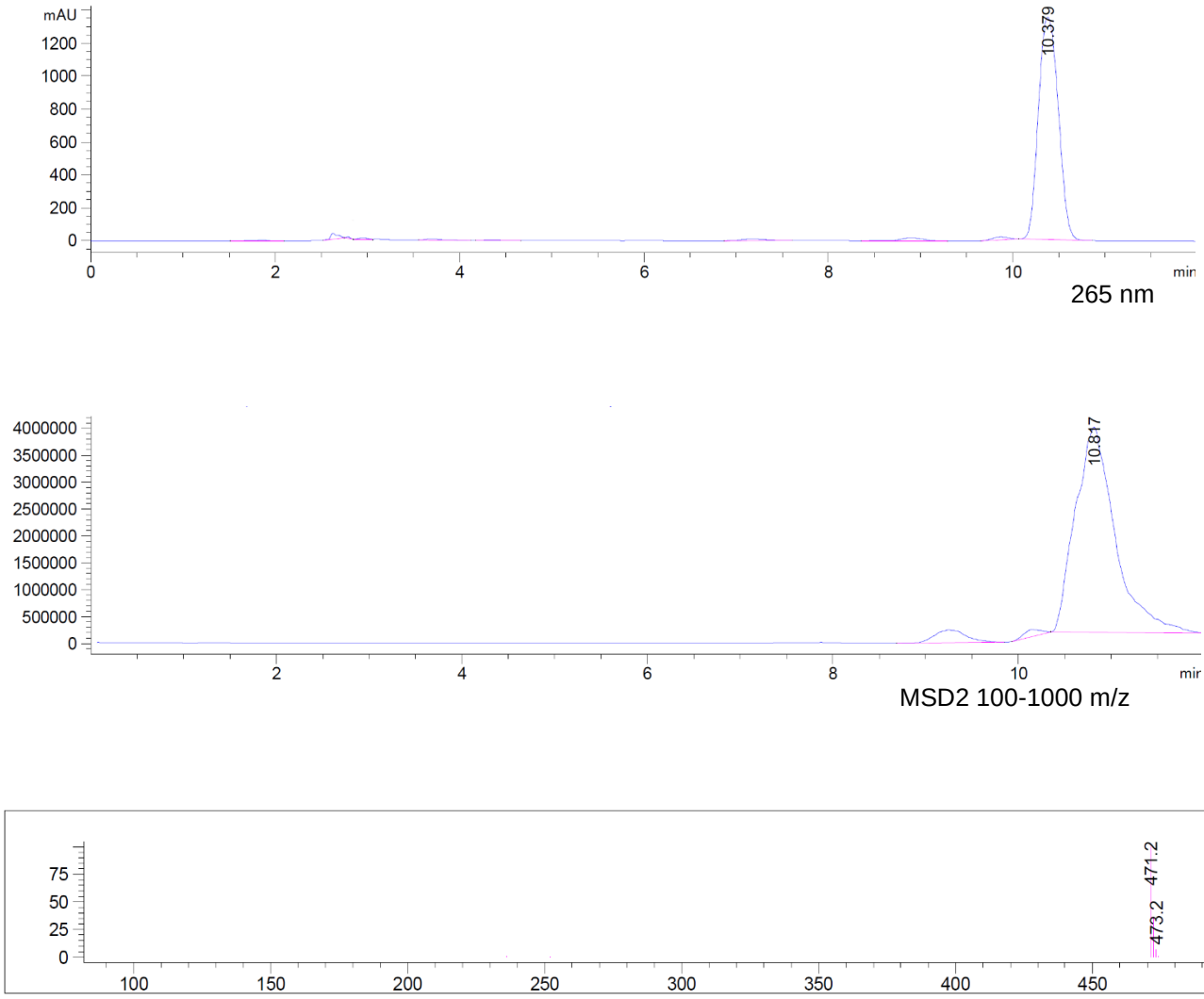


Figure S2: HPLC-chromatogram (265 nm), and MS-spectra of SPOPP-5 (**2**). The ESIMS spectrum exhibited a $[M + H]^+$ peak at *m/z* = 471.2.

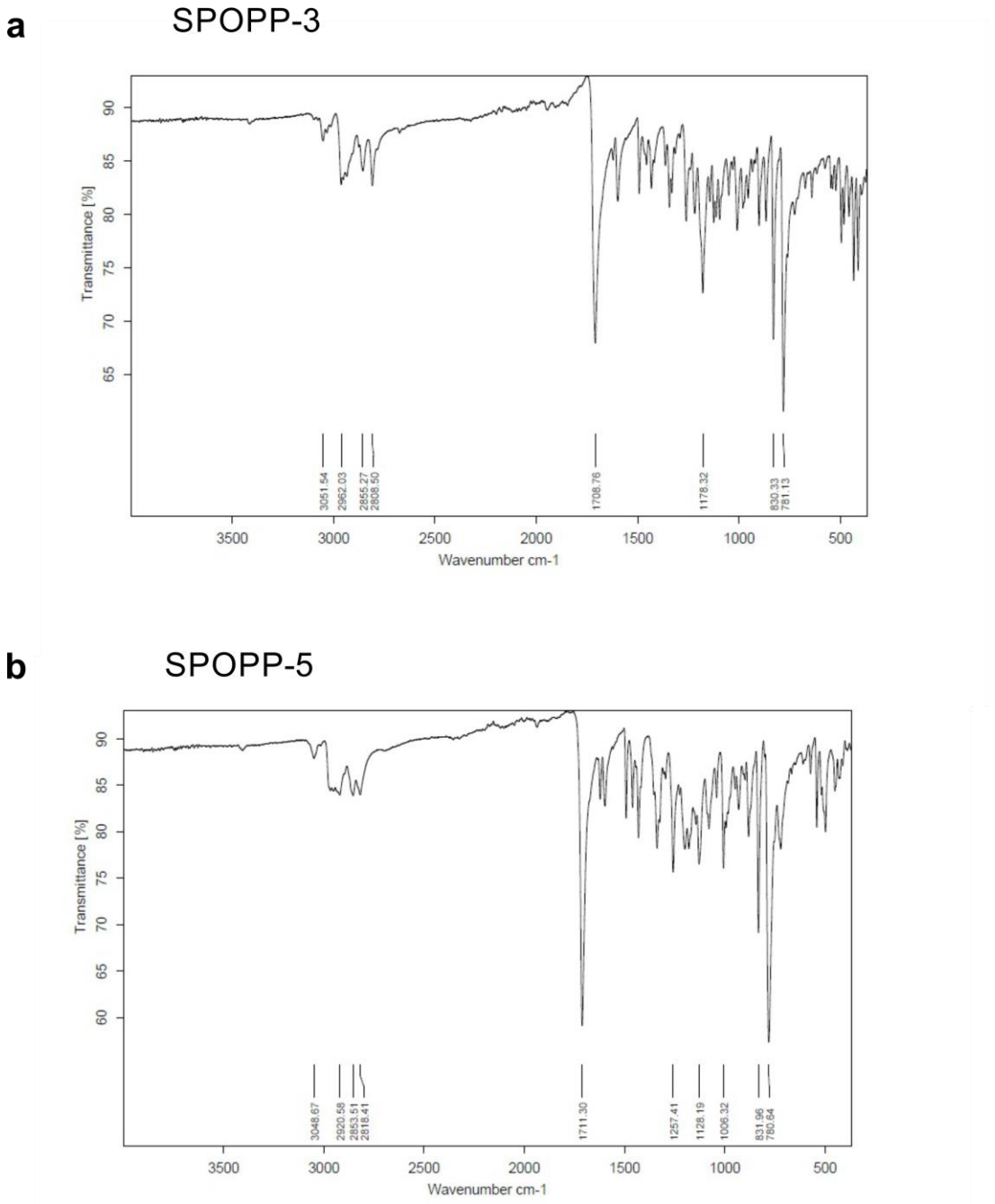


Figure S3: FTIR spectrum of (A) SPOPP-3 (**1**) and (B) SPOPP-5 (**2**). For SPOPP-3 (**1**), the C-H stretch can be seen between 2808.50 to 3051.54 cm^{-1}. The typical C=O absorption is also noted at 1708.76 cm^{-1}. Similarly, SPOPP-5 (**2**) has the notable C-H stretch from 2818.41 to 3048.67 cm^{-1} and the C=O absorption is at 1711.30 cm^{-1}. The difference in the two molecules are also evidenced by the absorption intensity differences in the fingerprint region. The peak at 1178.32 cm^{-1} for SPOPP-3 (**1**) is the notable differentiating absorption peak.

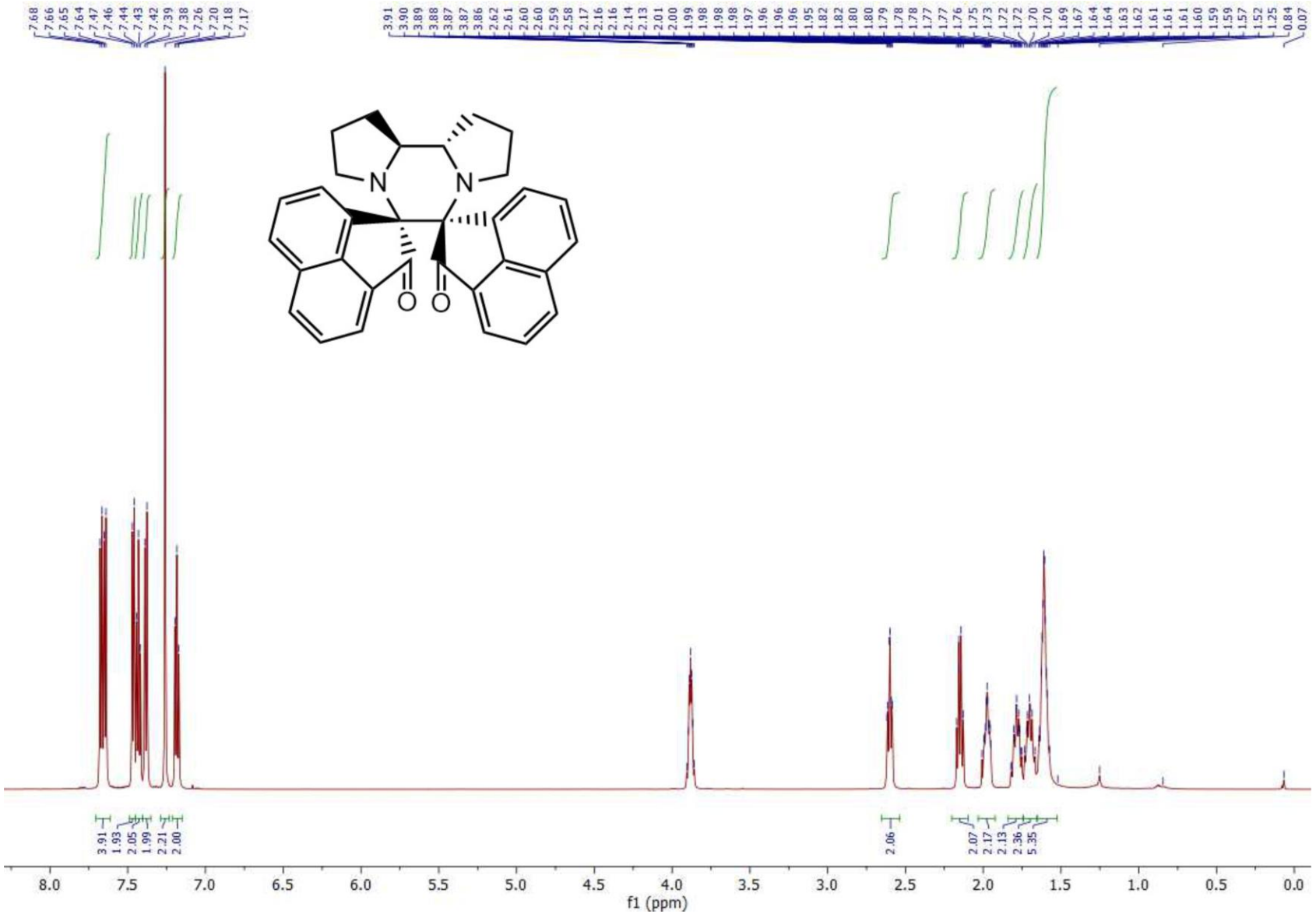


Figure S4: ^{1}H-NMR spectrum of SPOPP-3 (**1**) ($CDCl_3$ with 0.3% TMS, 600 MHz).

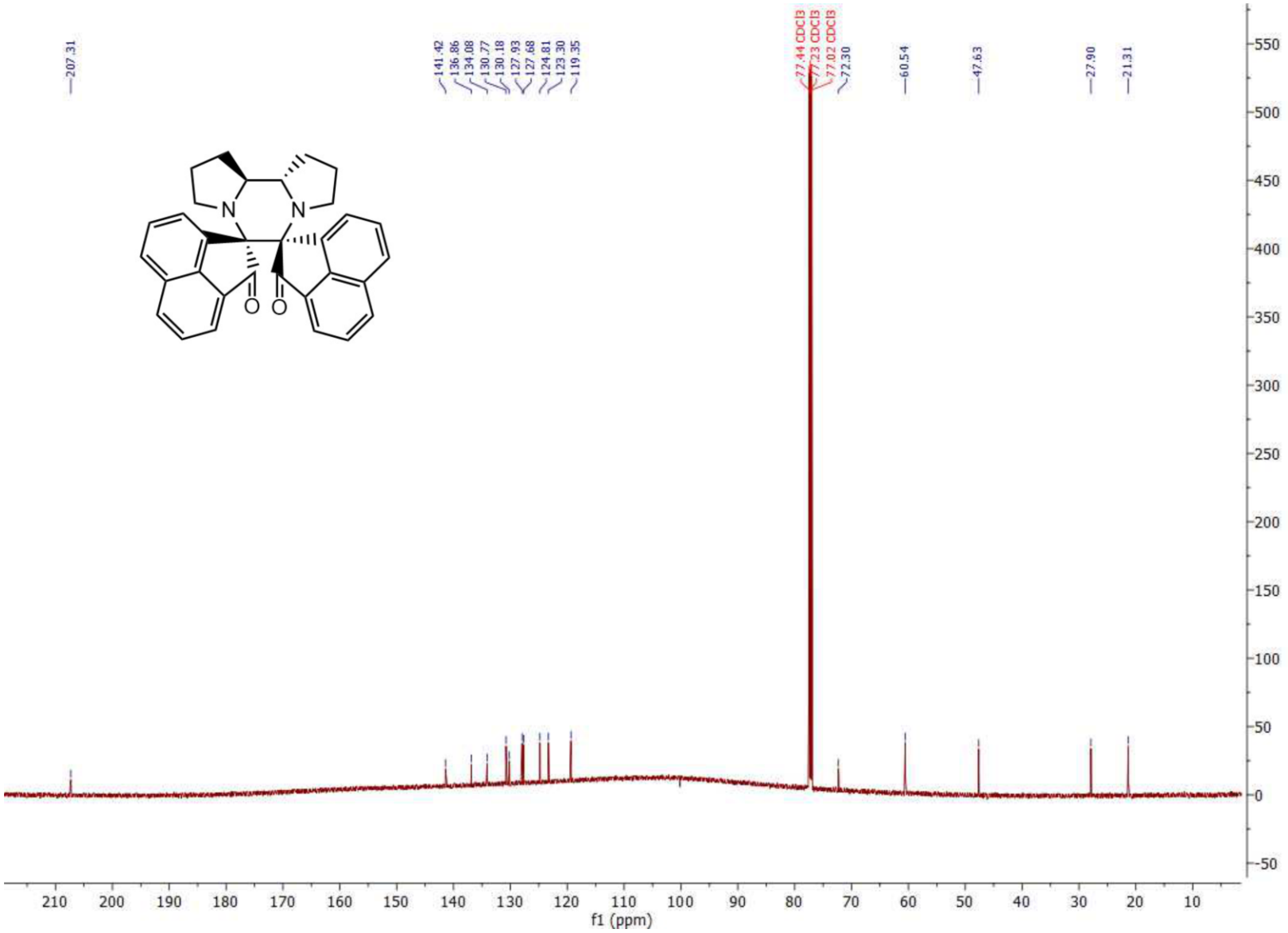


Figure S5: ^{13}C-NMR spectrum of SPOPP-3 (**1**) ($CDCl_3$ with 0.3% TMS, 600 MHz).

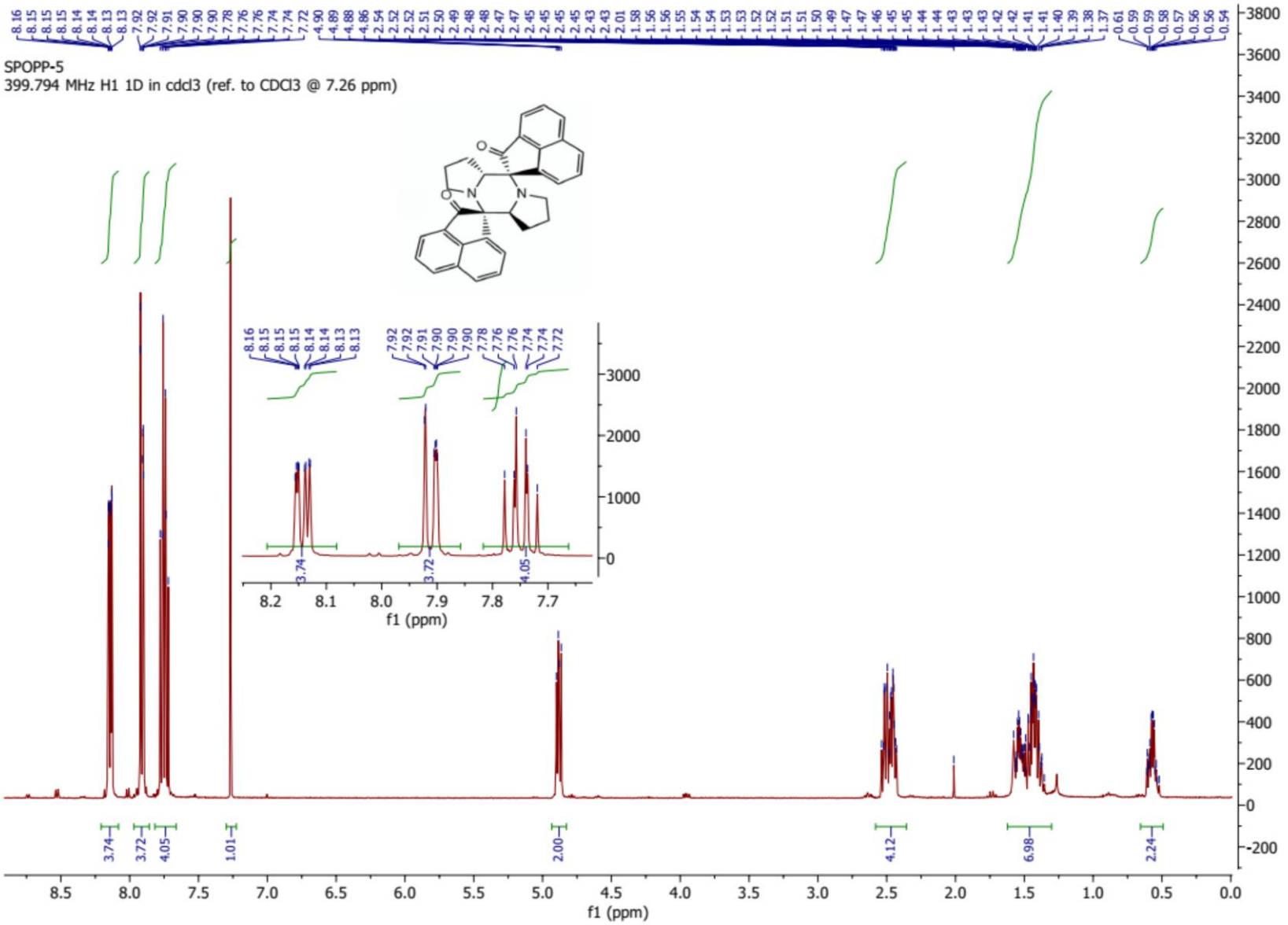


Figure S6: ^{1}H-NMR spectrum of SPOPP-5 (**2**) ($CDCl_3$ with 0.3% TMS, 400 MHz)

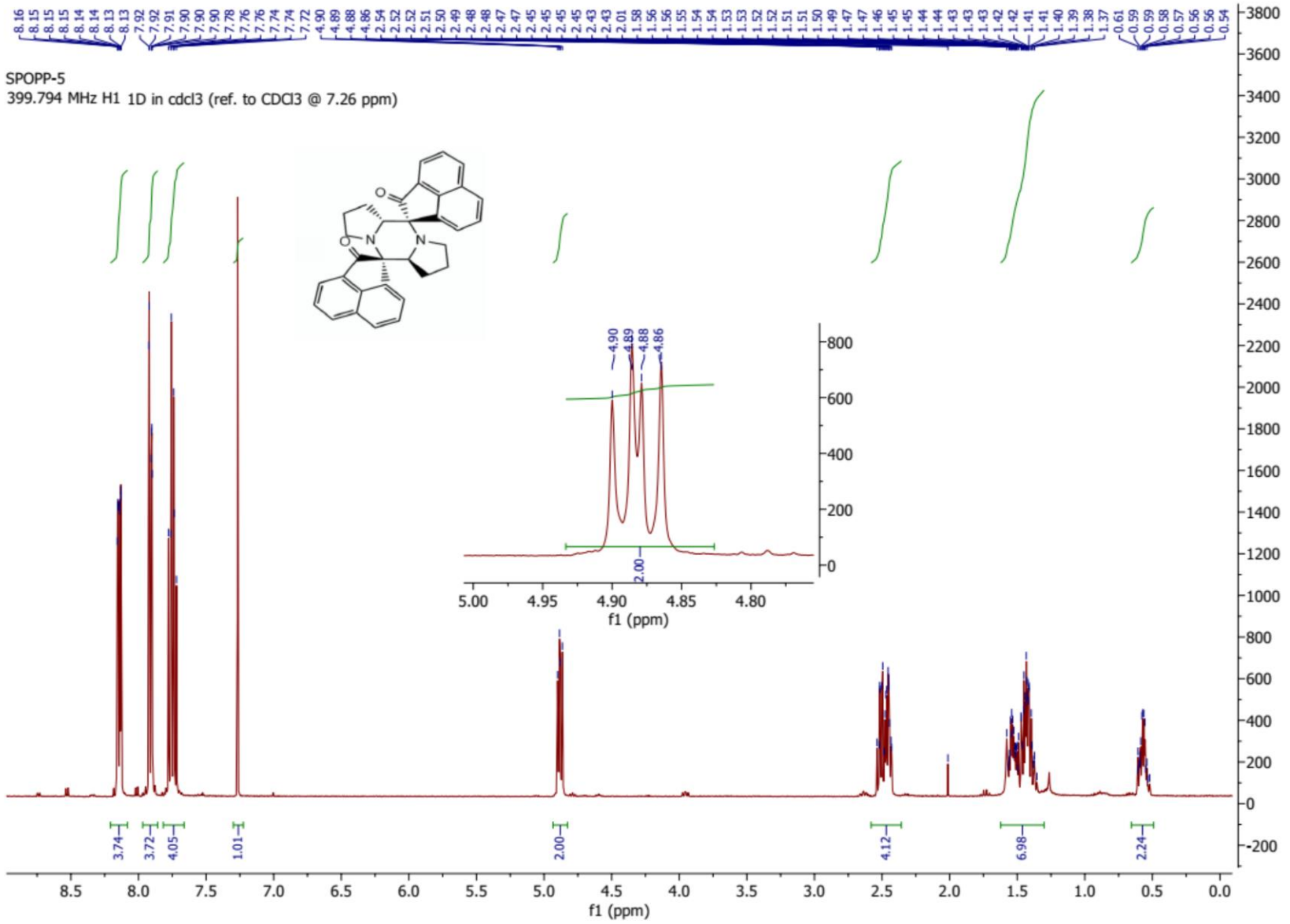


Figure S7: ^{1}H-NMR spectrum of SPOPP-5 (**2**) ($CDCl_3$ with 0.3% TMS, 400 MHz)

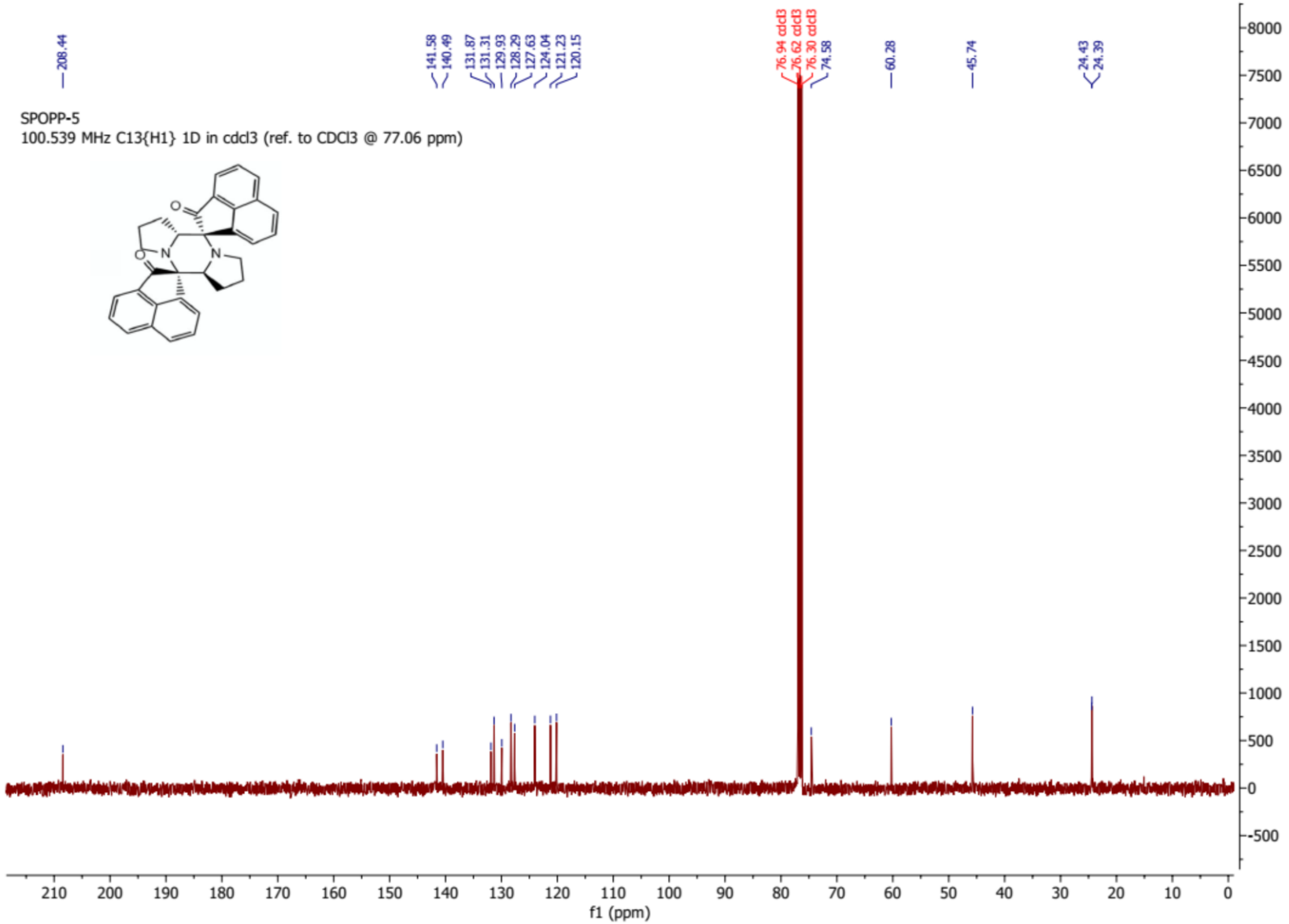


Figure S8: ^{13}C-NMR spectrum of SPOPP-5 (**2**) ($CDCl_3$ with 0.3% TMS, 100 MHz)

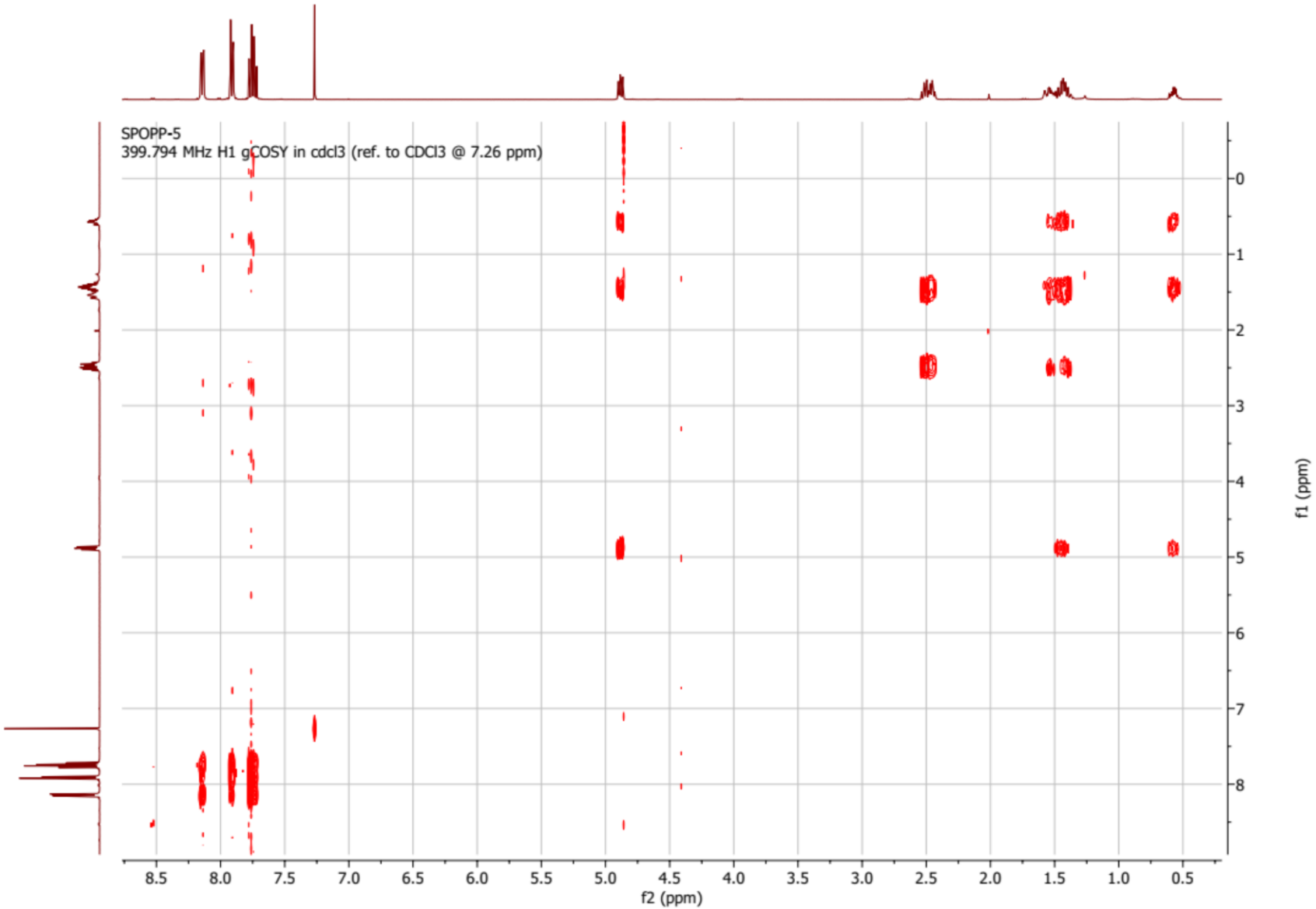


Figure S9: COSY spectrum of SPOPP-5 (**2**) ($CDCl_3$ with 0.3% TMS, 400 MHz)**.**

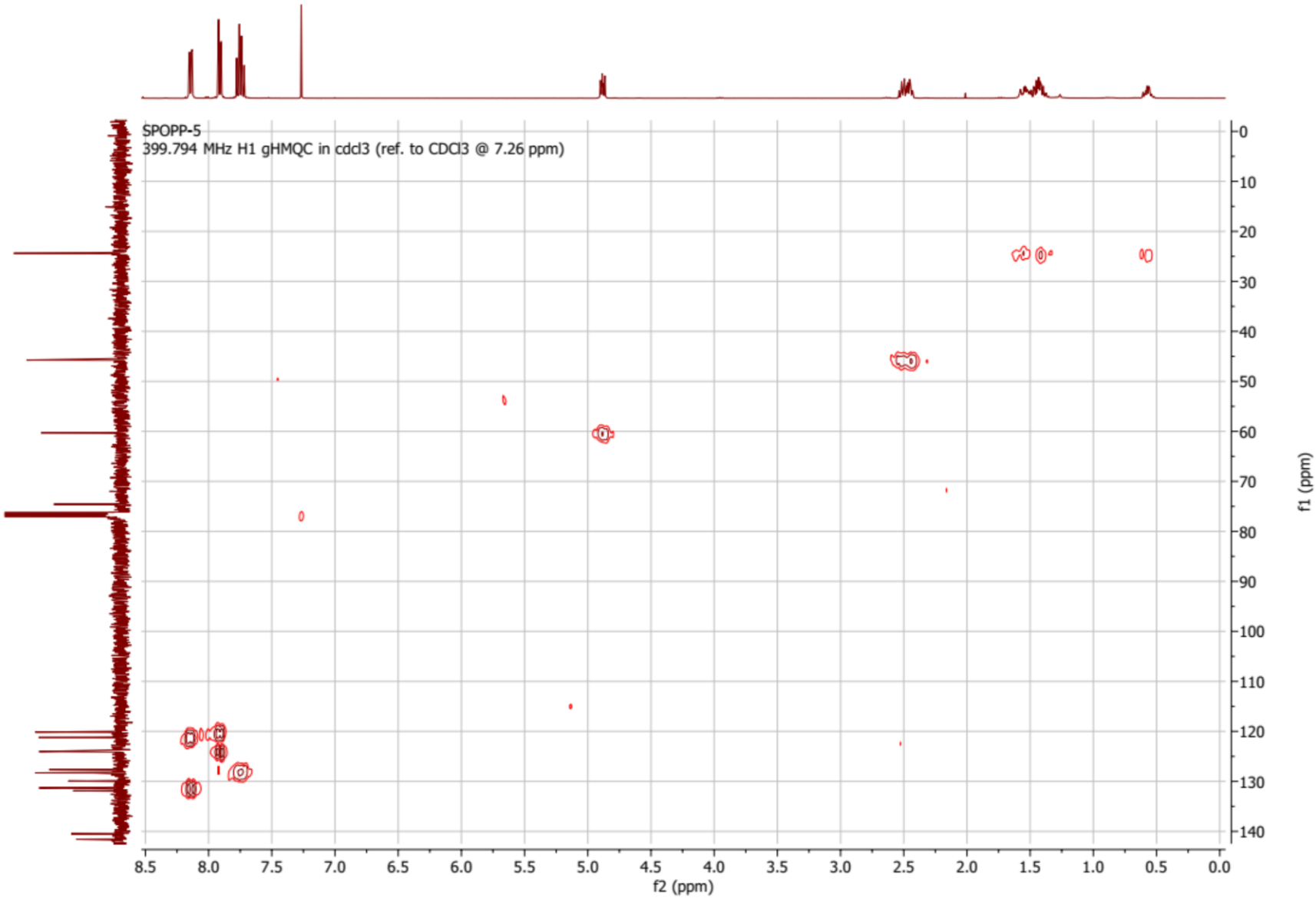


Figure S10: HMQC spectrum of SPOPP-5 (**2**) ($CDCl_3$ with 0.3% TMS, 400 MHz)**.**

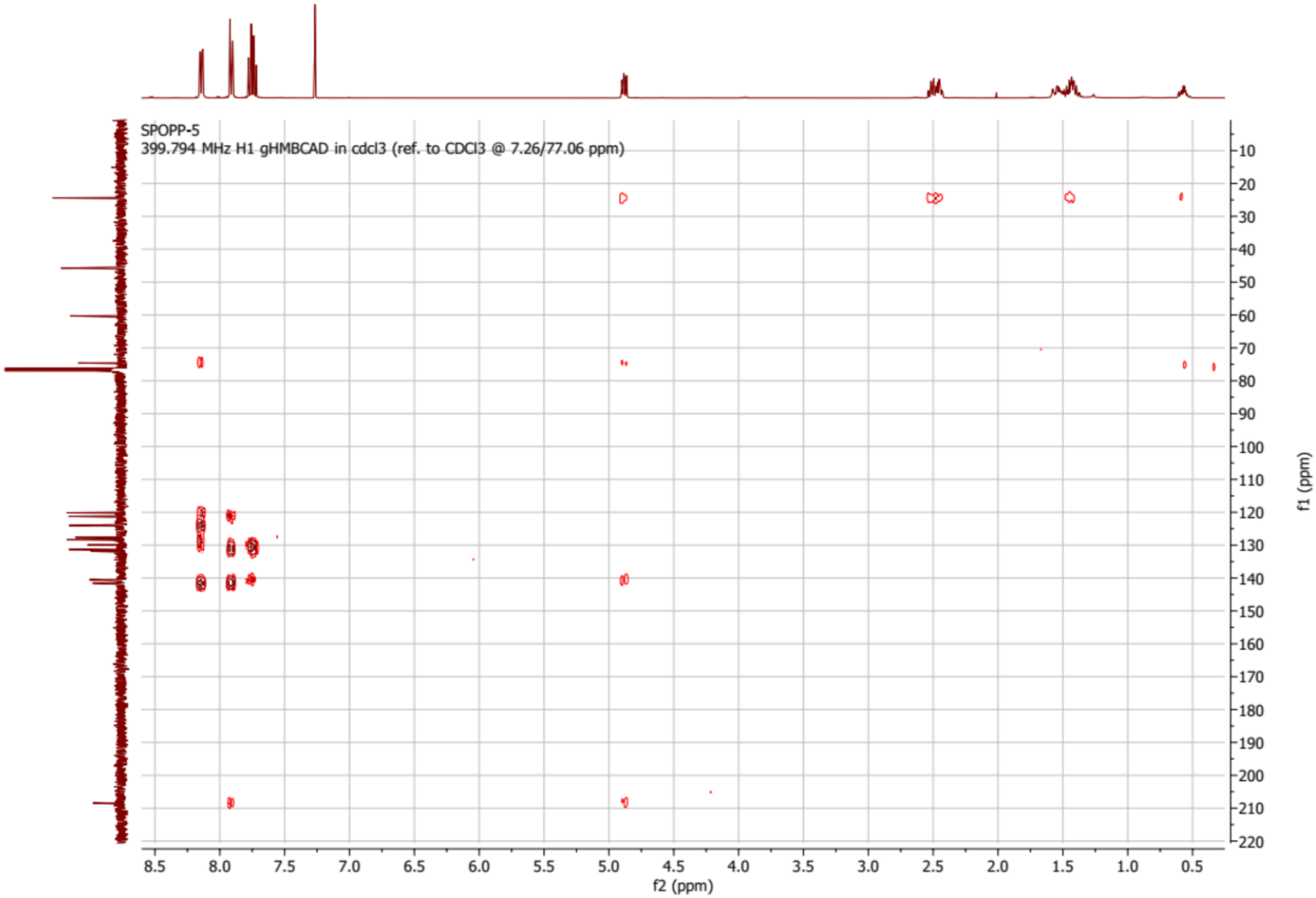


Figure S11: HMBC spectrum of SPOPP-5 (**2**) ($CDCl_3$ with 0.3% TMS, 400 MHz)**.**

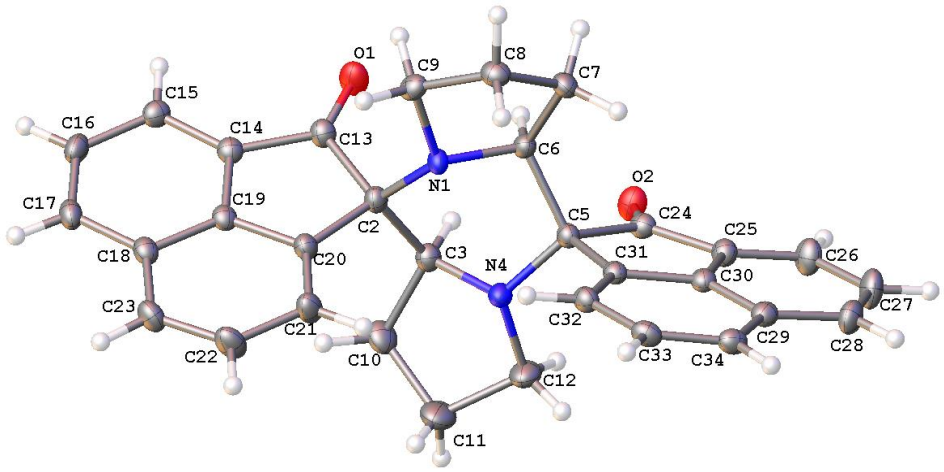


Figure S12: X-ray ORTEP drawing of SPOPP-5 (**2**).

Crystal Data. $C_{32}H_{26}N_2O_2$, M_r = 470.55, monoclinic, $P2_1/c$ (No. 14), a = 11.7680(4) Å, b = 13.4613(4) Å, c = 15.0138(5) Å, β = 97.045(2)˚, $\alpha = \gamma$ = 90˚, V = 2360.42(13) Å^3, T = 90(2) K, Z = 4, Z' = 1, μ(CuK_α) = 0.652, 29690 reflections measured, 4166 unique (R_{int} = 0.0472) which were used in all calculations. The final wR_2 was 0.0957 (all data) and R_1 was 0.0367 (I > 2(I)).
X-ray crystallographic data of SPOPP-5 (**2**) (CIF)

Compound	**SPOPP-5**
Formula	$C_{32}H_{26}N_2O_2$
$D_{calc.}$/ g cm^{-3}	1.324
μ/mm^{-1}	0.652
Formula Weight	470.55
Colour	orange
Shape	irregular
Size/mm^3	0.22×0.20×0.11
T/K	90(2)
Crystal System	monoclinic
Space Group	$P2_1/c$
a/Å	11.7680(4)
b/Å	13.4613(4)
c/Å	15.0138(5)
α/˚	90
β/˚	97.045(2)
γ/˚	90
V/Å^3	2360.42(13)
Z	4
Z'	1
Wavelength/Å	1.54178
Radiation type	CuK_α
Θ_{min}/˚	3.785
Θ_{max}/˚	66.711
Measured Refl's.	29690
Ind't Refl's	4166
Refl's with I > 2(I)	3660
R_{int}	0.0472
Parameters	325
Restraints	0
Largest Peak	0.204
Deepest Hole	-0.208
GooF	1.036
wR_2 (all data)	0.0957
wR_2	0.0917
R_1 (all data)	0.0422
R_1	0.0367

3. References

1. S. Haddad, S. Boudriga, F. Porzio, A. Soldera, M. Askri, M. Knorr, Y. Rousselin, M. M. Kubicki, C. Golz and C. J. Strohmann, *J. Org. Chem.,* 2015, **80,** 9064-9075.