# Supporting Information

# Molecular Networking Reveals Serpentinine-related Bisindole Alkaloids from *Picralima nitida*, a Previously Well-Investigated Species

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**Figure S1.** Molecular network: "molecular family" A

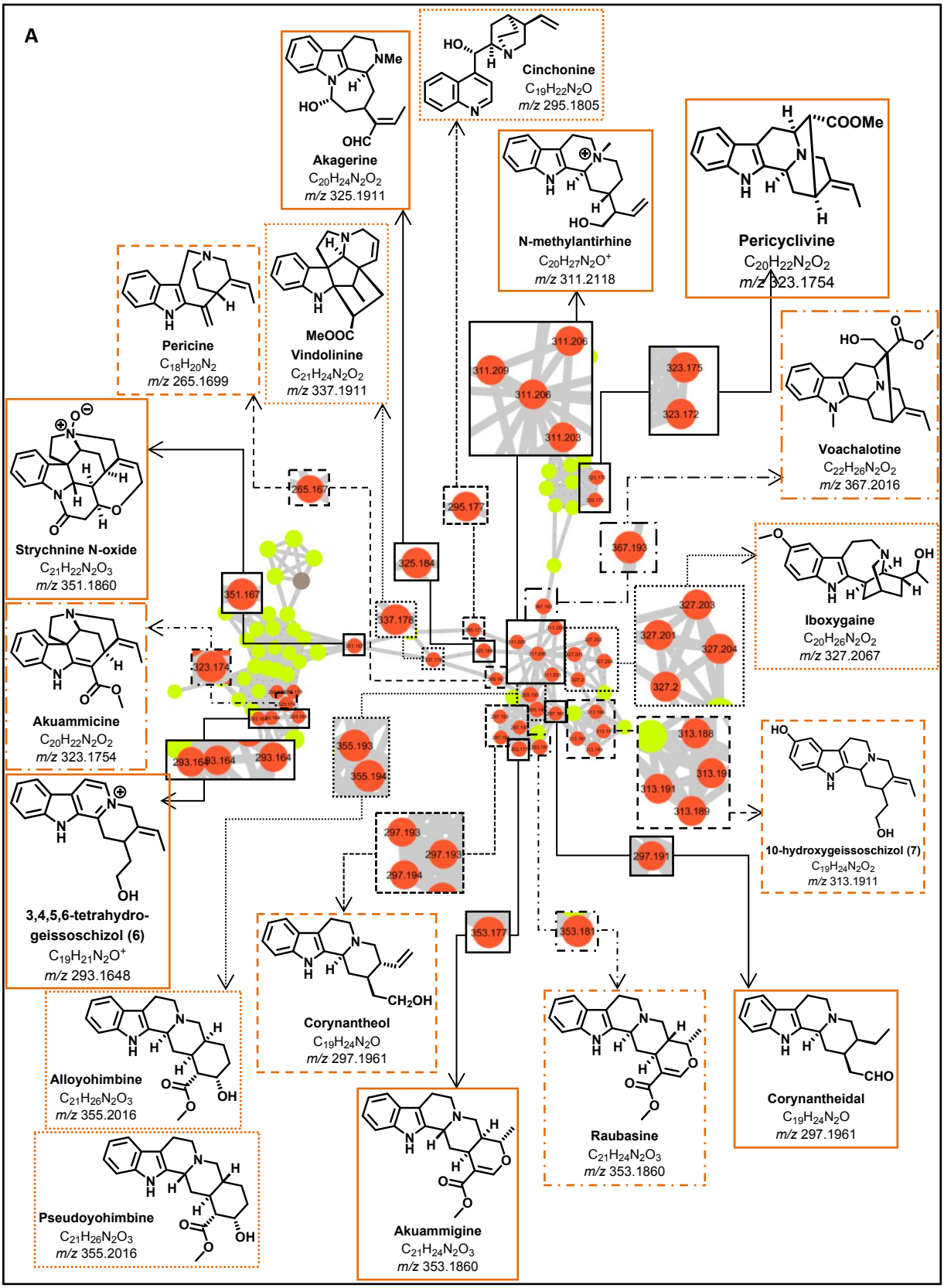



**Figure S1.** "Molecular family" **A** of the full molecular network of the EtOH extract and fractions from the aerial parts of *Picralima nitida*, with the dereplicated compounds (the stereochemistry depicted in this figure derives from that of the standards)

**Table S2.** Dereplicated Compounds Against the MIADB-GNPS

| Compounds | Score (cosine) | ΔRT[1] (min) | MSI identification level[2] |
|---|---|---|---|
| 10-hydroxy-geissoschizol | 0.91 | 0.43 | 1 |
| 3,4,5,6-tetradehydro-geissoschizol | 0.93 | 0.88 | 1 |
| akagerine | 0.79 | 1.57 | 1 |
| akuammicine | 0.69 | 2.57 | 2 |
| akuammigine | 0.95 | 0.41 | 1 |
| alloyohimbine | 0.86 | 1.41 | 1 |
| cinchonine | 0.75 | /[3] | 2 |
| corynantheidal | 0.91 | 1.02 | 1 |
| corynantheol | 0.93 | 2.69 | 2 |
| iboxygaine | 0.67 | 1.15 | 1 |
| *N*-methyl antirhine | 0.85 | 5.95 | 2 |
| pericine | 0.88 | 5.78 | 2 |
| pericyclivine | 0.74 | 0.05 | 1 |
| pseudoyohimbine | 0.83 | 5.26 | 2 |
| strictosamide | 0.91 | 4.55 | 2 |
| strychnine-*N*-oxide | 0.61 | /[3] | 2 |
| raubasine | 0.88 | 3.48 | 2 |
| vindolinine | 0.65 | 4.99 | 2 |
| voachalotine | 0.73 | 5.77 | 2 |

[1] Retention times of the monoterpene indole alkaloids contained in the MIADB are accessible from MetaboLights under the identifier:MTBLS142. Delta RTs can be calculated since both acquisitions were realized under the same chromatographic conditions.

[2] E. L. Schymanski, J. Jeon, R. Gulde, K. Fenner, M. Ruff, H. P. Singer and J. Hollender, Environ. Sci. Technol., **2014**, *48*, 2097–2098.

[3] The retention times were not available since these compounds do not belong to the MIADB

**Figure S3.** Molecular network: molecular families A and B

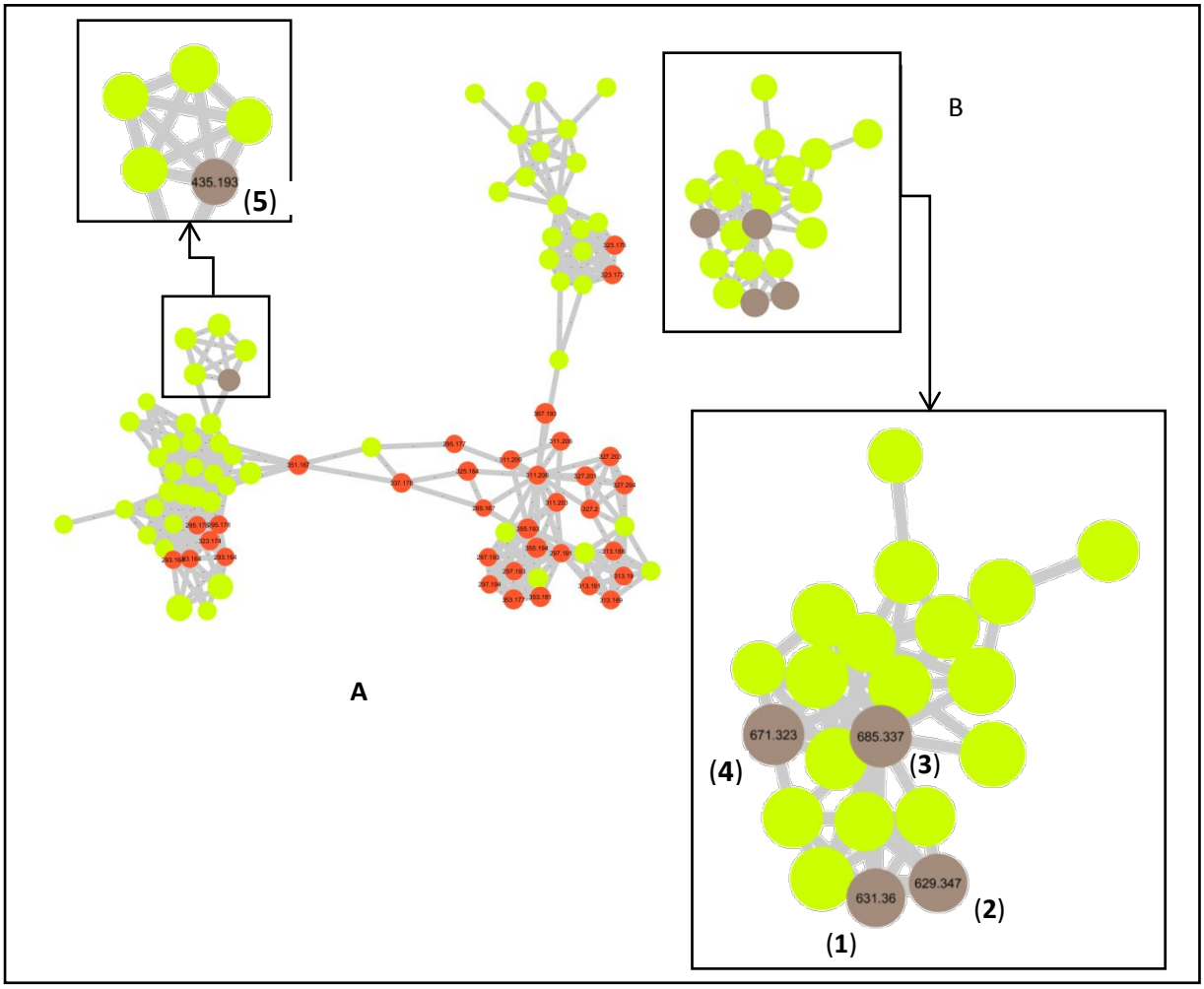



**Figure S3.** Molecular families **A** and **B** of the full molecular network of the ethanolic extract and fractions from the aerial parts of *Picralima nitida*.

**Table S4.** HRMS-based dereplication – Selected compounds

**Table S4:** Dereplication of the selected compounds against DNP and Reaxys® databases

| compounds | species | measured *m/z* | exact *m/z* | hits | molecular formula |
|---|---|---|---|---|---|
| **1** | $[M^+]$ | 631.3628 | 631.3643 | 13 hits - Not described in *P. nitida* | $C_{40}H_{47}N_4O_3^+$ |
| **2** | $[M^+]$ | 629.3477 | 629.3486 | 9 hits - Not described in *P. nitida* | $C_{40}H_{45}N_4O_3^+$ |
| **3** | $[M^+]$ | 685.3410 | 685.3384 | 2 hits - serpentinine and 3-oxovoafrine B | $C_{42}H_{45}N_4O_5^+$ |
| **4** | $[M^+]$ | 671.3247 | 671.3228 | No hits | $C_{41}H_{43}N_4O_5^+$ |

| | | | | | |
|---|---|---|---|---|---|
| **5** | $[M^+]$ | 435.1923 | 435.1914 | No hits | $C_{25}H_{27}N_2O_5^+$ |

**Figure S5.** Comparison between the experimental ECD spectra of 1 and 2

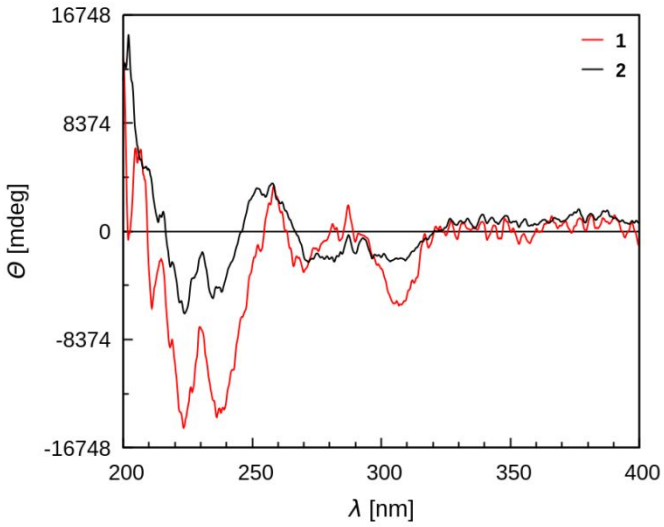



**Figure S5.** Comparison between the experimental ECD spectra of compounds **1** (red) and **2** (black), in methanol

**Figure S6.** Comparison between the experimental ECD spectra of 3 and 4

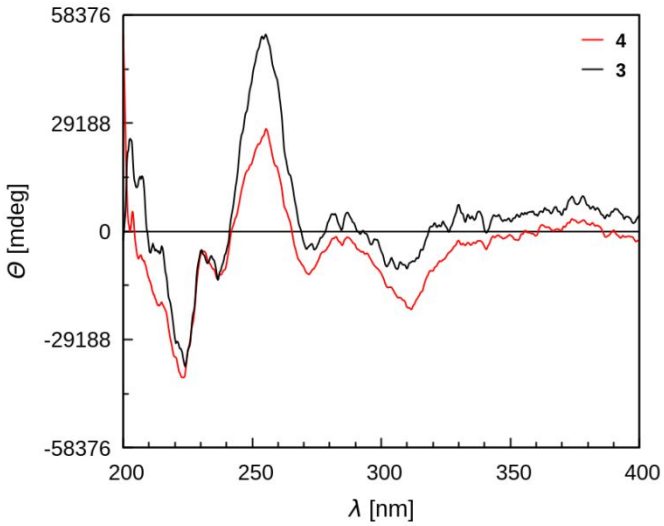
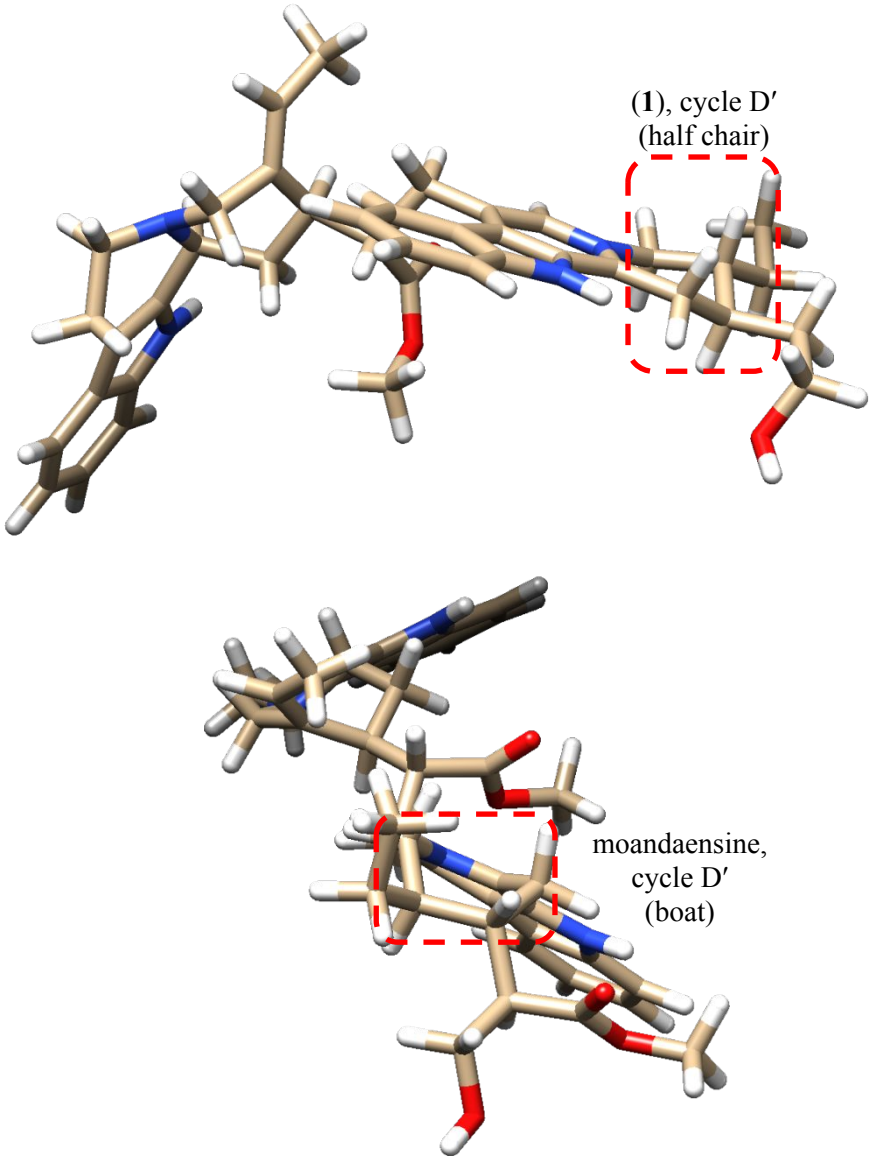



**Figure S6.** Comparison between the experimental ECD spectra of compounds **3** (black) and **4** (red), in methanol

**Figure S7.** Comparison of 3D models of **1** and moandaensine




## S8. Computational methods

Conformations of compound **1**, **3** and **5** were fully optimized *in vacuo* and without constraint using DFT[1,2] with the hybrid Becke-3-parameter-Lee–Yang–Parr[3,4] exchange– correlation functional and the 6-31G* basis,[5] as implemented in the Gaussian 16 revB.01 software package.[6] Upon geometrical optimization convergence, a frequency calculation within the harmonic approximation was conducted at the same level of theory and local minima were characterized by the absence of imaginary frequency. TDDFT at the same level of theory was

then employed to predict energies as well as rotational strengths of the first 60 electronic transitions of the lowest energy conformer. The UCSF Chimera v1.11[7] software package was used for the depiction of the most stable conformer of compounds **1**, **3** and **5**. ECD spectrum envelope was then calculated using SpecDis v1.71[8] (with different sigma/gamma values) and rendered using Gnuplot v5.2.[9]

**Coordinates of the lowest energy conformer of 1 found at the B3LYP/6-31G* level**

Electronic energy (B3LYP): -1997.04808272 Ha.

Lowest frequency: 9.0584 $cm^{-1}$.

Free enthalpy: -1996.31721 Ha.

Atomic coordinates:

| | | | | |
|---|---|---|---|---|
| 1 | C | 7.790196 | 1.279433 | 2.416231 |
| 2 | C | 8.370060 | 2.507594 | 2.709519 |
| 3 | C | 8.100666 | 3.645833 | 1.923094 |
| 4 | C | 7.245048 | 3.580286 | 0.828358 |
| 5 | C | 6.662630 | 2.343479 | 0.537660 |
| 6 | C | 6.921965 | 1.180094 | 1.315717 |
| 7 | N | 5.783038 | 1.982025 | -0.469090 |
| 8 | C | 6.172308 | 0.104956 | 0.719029 |
| 9 | C | 5.506699 | 0.627114 | -0.360372 |
| 10 | C | 6.109214 | -1.362133 | 1.022502 |
| 11 | C | 4.545134 | -0.109424 | -1.251153 |
| 12 | N | 4.624176 | -1.564798 | -1.012691 |
| 13 | C | 5.795626 | -2.081596 | -0.305316 |
| 14 | C | 3.114145 | 0.417284 | -0.977606 |
| 15 | C | 1.992257 | -0.338900 | -1.734528 |
| 16 | C | 2.385070 | -1.802820 | -1.867058 |
| 17 | C | 3.355991 | -2.252759 | -0.792438 |
| 18 | C | 2.087901 | -2.608376 | -2.900109 |
| 19 | C | 1.323204 | -2.291771 | -4.155064 |
| 20 | C | 0.630792 | -0.149324 | -0.976908 |
| 21 | C | -0.558349 | -0.758178 | -1.766000 |
| 22 | C | 0.346781 | 1.349890 | -0.816378 |
| 23 | O | 0.091609 | 2.036714 | -1.783715 |
| 24 | O | 0.350309 | 1.937816 | 0.399575 |
| 25 | C | 0.558189 | 1.220632 | 1.624892 |
| 26 | C | -1.890233 | -0.613758 | -1.067901 |
| 27 | C | -2.381609 | -1.522061 | -0.106487 |
| 28 | C | -3.656022 | -1.260827 | 0.476432 |
| 29 | C | -4.430030 | -0.147420 | 0.155830 |
| 30 | N | -3.907332 | 0.695454 | -0.770570 |
| 31 | C | -2.693359 | 0.474473 | -1.359833 |
| 32 | N | -3.953182 | -2.267029 | 1.364945 |

| | | | | |
|---|---|---|---|---|
| 33 | C | -2.910479 | -3.181002 | 1.387119 |
| 34 | C | -1.903092 | -2.750182 | 0.479450 |
| 35 | C | -0.736276 | -3.527162 | 0.333334 |
| 36 | C | -0.612001 | -4.688963 | 1.079425 |
| 37 | C | -1.626313 | -5.094685 | 1.971828 |
| 38 | C | -2.787034 | -4.350723 | 2.140720 |
| 39 | C | -5.782252 | 0.092691 | 0.771419 |
| 40 | C | -6.338408 | 1.515325 | 0.592082 |
| 41 | C | -6.109784 | 1.958557 | -0.869420 |
| 42 | C | -4.606662 | 1.961969 | -1.151615 |
| 43 | C | -6.699301 | 3.346552 | -1.202328 |
| 44 | C | -6.476733 | 3.816576 | -2.646441 |
| 45 | C | -7.811438 | 1.599666 | 1.040235 |
| 46 | C | -8.087796 | 0.992540 | 2.416464 |
| 47 | O | -7.110002 | 1.489605 | 3.326211 |
| 48 | H | 4.788937 | 0.103316 | -2.309175 |
| 49 | H | 1.865091 | 0.110970 | -2.725533 |
| 50 | H | -7.406739 | 1.304074 | 4.229902 |
| 51 | H | 5.500401 | 2.579252 | -1.231155 |
| 52 | H | -4.798717 | -2.340323 | 1.910559 |
| 53 | H | 8.006172 | 0.407709 | 3.028714 |
| 54 | H | 9.043950 | 2.595432 | 3.557082 |
| 55 | H | 8.570717 | 4.592238 | 2.175078 |
| 56 | H | 7.040442 | 4.459111 | 0.222252 |
| 57 | H | 5.347170 | -1.600016 | 1.780325 |
| 58 | H | 7.065969 | -1.725237 | 1.420587 |
| 59 | H | 5.636454 | -3.153502 | -0.146366 |
| 60 | H | 6.673188 | -1.981327 | -0.958616 |
| 61 | H | 2.955148 | 0.336672 | 0.103986 |
| 62 | H | 3.071080 | 1.484835 | -1.218814 |
| 63 | H | 3.537472 | -3.329320 | -0.878637 |
| 64 | H | 2.923562 | -2.088632 | 0.218766 |
| 65 | H | 2.496872 | -3.619203 | -2.866777 |
| 66 | H | 1.929623 | -2.550386 | -5.032254 |
| 67 | H | 1.047958 | -1.237188 | -4.240251 |
| 68 | H | 0.403876 | -2.888549 | -4.231202 |
| 69 | H | 0.709904 | -0.647238 | -0.005773 |
| 70 | H | -0.352600 | -1.812833 | -1.958566 |
| 71 | H | -0.608350 | -0.251925 | -2.733285 |
| 72 | H | 1.556988 | 0.779587 | 1.672990 |
| 73 | H | 0.462545 | 1.970412 | 2.411098 |
| 74 | H | -0.201375 | 0.445411 | 1.770155 |
| 75 | H | -2.374605 | 1.231103 | -2.065562 |
| 76 | H | 0.055625 | -3.232271 | -0.347072 |
| 77 | H | 0.279569 | -5.299184 | 0.977202 |
| 78 | H | -1.497094 | -6.010068 | 2.541322 |
| 79 | H | -3.564539 | -4.666930 | 2.829318 |
| 80 | H | -5.717633 | -0.131777 | 1.842547 |
| 81 | H | -6.482633 | -0.637607 | 0.335369 |
| 82 | H | -5.761260 | 2.181489 | 1.246848 |
| 83 | H | -6.583415 | 1.219427 | -1.535138 |
| 84 | H | -4.117203 | 2.771576 | -0.597146 |

| | | | | |
|---|---|---|---|---|
| 85 | H | -4.404176 | 2.110059 | -2.212858 |
| 86 | H | -6.290595 | 4.088496 | -0.501617 |
| 87 | H | -7.776874 | 3.310510 | -1.014871 |
| 88 | H | -6.830279 | 3.070448 | -3.368527 |
| 89 | H | -7.032315 | 4.741030 | -2.831300 |
| 90 | H | -5.424416 | 4.028600 | -2.866047 |
| 91 | H | -8.106988 | 2.652712 | 1.066994 |
| 92 | H | -8.461104 | 1.100556 | 0.307026 |
| 93 | H | -8.053444 | -0.108628 | 2.368778 |
| 94 | H | -9.104818 | 1.267203 | 2.728608 |

**Coordinates of the lowest energy conformer of 3 found at the B3LYP/6-31G* level**

Electronic energy (B3LYP): -2222.52864472 Ha.

Lowest frequency: 7.9883 $cm^{-1}$.

Free enthalpy: -2221.801413 Ha.

Atomic coordinates:

| | | | | |
|---|---|---|---|---|
| 1 | C | -5.515717 | 0.713951 | -3.866587 |
| 2 | C | -5.718905 | 0.651657 | -2.359976 |
| 3 | H | -5.615427 | -0.387324 | -2.015353 |
| 4 | O | -7.101757 | 1.026215 | -2.136292 |
| 5 | C | -7.473610 | 1.370078 | -0.889850 |
| 6 | C | -6.639198 | 1.560073 | 0.153814 |
| 7 | C | -7.122198 | 1.863510 | 1.512062 |
| 8 | O | -8.454359 | 2.045489 | 1.584456 |
| 9 | C | -8.977461 | 2.332949 | 2.896043 |
| 10 | O | -6.374973 | 1.929664 | 2.476813 |
| 11 | C | -5.144515 | 1.466907 | -0.034147 |
| 12 | H | -4.678317 | 2.308733 | 0.492121 |
| 13 | C | -4.579175 | 0.166324 | 0.578579 |
| 14 | C | -3.241722 | -0.282613 | 0.055041 |
| 15 | C | -2.523335 | -1.309666 | 0.659973 |
| 16 | N | -2.856408 | -2.010152 | 1.794085 |
| 17 | C | -1.876867 | -2.957258 | 2.049357 |
| 18 | C | -1.806451 | -3.881686 | 3.094289 |
| 19 | C | -0.712194 | -4.736583 | 3.111935 |
| 20 | C | 0.287383 | -4.676549 | 2.118309 |
| 21 | C | 0.217305 | -3.754706 | 1.085231 |
| 22 | C | -0.879356 | -2.870922 | 1.038419 |
| 23 | C | -1.290764 | -1.813826 | 0.147789 |
| 24 | C | -0.776784 | -1.239173 | -1.034533 |
| 25 | C | 0.521175 | -1.653175 | -1.688830 |
| 26 | C | 1.766597 | -0.892966 | -1.167257 |

| | | | | |
|---|---|---|---|---|
| 27 | H | 1.843093 | -0.946078 | -0.079709 |
| 28 | C | 1.652069 | 0.579282 | -1.544344 |
| 29 | O | 2.188385 | 1.369937 | -0.606088 |
| 30 | C | 2.238423 | 2.782134 | -0.896673 |
| 31 | O | 1.147475 | 0.994689 | -2.573712 |
| 32 | C | 3.063875 | -1.540130 | -1.784430 |
| 33 | C | 3.402695 | -2.847138 | -1.092186 |
| 34 | C | 3.947033 | -2.681305 | 0.328260 |
| 35 | C | 3.329188 | -4.067278 | -1.646818 |
| 36 | C | 2.855879 | -4.458928 | -3.018950 |
| 37 | H | 2.837137 | -1.721763 | -2.839739 |
| 38 | C | 4.332758 | -0.649342 | -1.749797 |
| 39 | C | 5.076623 | -0.678169 | -0.377647 |
| 40 | N | 4.198483 | -1.278309 | 0.640644 |
| 41 | C | 4.668394 | -1.083923 | 2.017196 |
| 42 | C | 4.621073 | 0.399421 | 2.409594 |
| 43 | C | 5.495335 | 0.684938 | 0.087563 |
| 44 | C | 5.289696 | 1.204467 | 1.336962 |
| 45 | C | 5.824347 | 2.542133 | 1.334235 |
| 46 | C | 5.914237 | 3.567567 | 2.291434 |
| 47 | C | 6.528830 | 4.764459 | 1.942879 |
| 48 | C | 7.058135 | 4.961895 | 0.651816 |
| 49 | C | 6.980706 | 3.968301 | -0.319122 |
| 50 | C | 6.359407 | 2.767525 | 0.034226 |
| 51 | N | 6.126944 | 1.624361 | -0.714111 |
| 52 | C | -1.523046 | -0.222222 | -1.604265 |
| 53 | N | -2.702447 | 0.233217 | -1.081059 |
| 54 | C | -3.309123 | 1.423518 | -1.750660 |
| 55 | C | -4.811480 | 1.582195 | -1.531876 |
| 56 | H | -5.046430 | 2.604419 | -1.856650 |
| 57 | H | -5.548365 | 1.748075 | -4.225659 |
| 58 | H | -6.311367 | 0.154133 | -4.365562 |
| 59 | H | -4.560110 | 0.266579 | -4.157859 |
| 60 | H | -8.548710 | 1.489029 | -0.812696 |
| 61 | H | -8.536249 | 3.251894 | 3.288939 |
| 62 | H | -8.763463 | 1.509323 | 3.581613 |
| 63 | H | -10.052019 | 2.449923 | 2.758630 |
| 64 | H | -5.286981 | -0.658128 | 0.409145 |
| 65 | H | -4.527708 | 0.300366 | 1.664725 |
| 66 | H | -3.667370 | -1.845085 | 2.372018 |
| 67 | H | -2.574951 | -3.932196 | 3.859420 |
| 68 | H | -0.625618 | -5.469076 | 3.908764 |
| 69 | H | 1.124091 | -5.366199 | 2.165904 |
| 70 | H | 0.996335 | -3.724375 | 0.331508 |
| 71 | H | 0.446269 | -1.473310 | -2.765701 |

72 H 0.677864 -2.725944 -1.551733
73 H 1.228495 3.201188 -0.909009
74 H 2.710884 2.955601 -1.865764
75 H 2.831603 3.219100 -0.094723
76 H 4.856893 -3.303866 0.447344
77 H 3.220685 -3.052361 1.064371
78 H 3.681535 -4.904951 -1.040058
79 H 2.502570 -3.614156 -3.616155
80 H 2.039657 -5.190943 -2.956918
81 H 3.664512 -4.948042 -3.577814
82 H 4.083323 0.379920 -2.021098
83 H 5.009442 -1.020608 -2.527601
84 H 5.984581 -1.307629 -0.498530
85 H 5.697363 -1.470290 2.147865
86 H 4.017839 -1.670565 2.675914
87 H 5.120616 0.531965 3.378039
88 H 3.574799 0.708596 2.546428
89 H 5.514875 3.424664 3.292346
90 H 6.608021 5.561694 2.676589
91 H 7.537362 5.906191 0.409689
92 H 7.391254 4.122496 -1.313742
93 H 6.507791 1.450177 -1.631744
94 H -1.174408 0.289985 -2.491624
95 H -3.057343 1.351042 -2.809410
96 H -2.793785 2.301678 -1.347201

**Coordinates of the lowest energy conformer of 5 found at the B3LYP/6-31G* level**

Electronic energy (B3LYP): -1454.38856820 Ha.

Lowest frequency: 16.8398 $cm^{-1}$.

Free enthalpy: -1453.959186 Ha.

Atomic coordinates:

1 C -3.796683 1.956272 -0.766905
2 C -4.183413 3.273151 -0.959801
3 C -3.244142 4.325679 -0.924986
4 C -1.893873 4.091034 -0.698223
5 C -1.503375 2.764295 -0.506515
6 C -2.431430 1.684483 -0.534036
7 N -0.233098 2.257799 -0.272310
8 C -1.665482 0.488281 -0.299870
9 C -0.307545 0.893367 -0.141682
10 C -1.962555 -0.890644 -0.221372

| | | | | |
|---|---|---|---|---|
| 11 | C | 0.735269 | -0.000843 | 0.087407 |
| 12 | N | 0.394771 | -1.315015 | 0.150941 |
| 13 | C | -0.900073 | -1.742236 | 0.005083 |
| 14 | C | 2.166276 | 0.456394 | 0.170015 |
| 15 | C | 3.185765 | -0.591392 | 0.668701 |
| 16 | C | 2.845427 | -2.002369 | 0.158328 |
| 17 | C | 1.403557 | -2.356673 | 0.513485 |
| 18 | C | -3.362231 | -1.433471 | -0.364348 |
| 19 | C | 4.591407 | -0.234353 | 0.250881 |
| 20 | C | 5.210657 | -0.924750 | -0.729434 |
| 21 | O | 4.658830 | -1.911467 | -1.459494 |
| 22 | C | 3.235190 | -2.147745 | -1.325973 |
| 23 | C | -4.222783 | -1.231393 | 0.904170 |
| 24 | C | -5.705075 | -1.217507 | 0.560972 |
| 25 | O | -6.160498 | -0.671653 | -0.425314 |
| 26 | O | -6.437389 | -1.843614 | 1.487726 |
| 27 | C | -7.868142 | -1.827923 | 1.279033 |
| 28 | C | 2.988566 | -3.520421 | -1.934269 |
| 29 | C | 5.231234 | 0.887136 | 0.960934 |
| 30 | O | 6.520048 | 1.076051 | 0.623233 |
| 31 | O | 4.631654 | 1.579926 | 1.769708 |
| 32 | C | 7.187703 | 2.170864 | 1.281728 |
| 33 | H | 3.143503 | -0.596798 | 1.764702 |
| 34 | H | 3.464913 | -2.723508 | 0.707658 |
| 35 | H | -4.539700 | 1.165458 | -0.795365 |
| 36 | H | -5.228759 | 3.500753 | -1.141524 |
| 37 | H | -1.175205 | 4.904253 | -0.672778 |
| 38 | H | 0.605489 | 2.813856 | -0.189491 |
| 39 | H | -1.041040 | -2.813262 | 0.082870 |
| 40 | H | 2.453391 | 0.800994 | -0.834116 |
| 41 | H | 2.238594 | 1.334123 | 0.821670 |
| 42 | H | 1.085517 | -3.283489 | 0.033669 |
| 43 | H | 1.327402 | -2.498649 | 1.596912 |
| 44 | H | -3.321792 | -2.500225 | -0.609737 |
| 45 | H | -3.859491 | -0.939761 | -1.204805 |
| 46 | H | 6.240303 | -0.743274 | -1.017161 |
| 47 | H | 2.730777 | -1.379427 | -1.929511 |
| 48 | H | -4.002598 | -0.257517 | 1.360693 |
| 49 | H | -4.014284 | -1.992199 | 1.660393 |
| 50 | H | -8.116381 | -2.317247 | 0.334690 |
| 51 | H | -8.287609 | -2.375452 | 2.121949 |
| 52 | H | -8.235541 | -0.799424 | 1.261945 |
| 53 | H | 3.451460 | -3.569315 | -2.923544 |
| 54 | H | 1.918348 | -3.714681 | -2.057953 |
| 55 | H | 3.424772 | -4.310364 | -1.313660 |

| | | | | |
|---|---|---|---|---|
| 56 | H | 8.204641 | 2.165213 | 0.890708 |
| 57 | H | 7.189032 | 2.020025 | 2.363674 |
| 58 | H | 6.690260 | 3.115859 | 1.050265 |
| 59 | H | -3.584373 | 5.345211 | -1.079359 |

**Experimental Method**

**S9. Biological Assays**

**Antiplasmodial Evaluation.** The chloroquine-resistant strain FcB1/Colombia of *Plasmodium falciparum* was obtained from the National Museum Natural History collection, Paris, France (n°MNHN-CEU-224-PfFCB1). Parasites were maintained in vitro in human erythrocytes in RPMI 1640 medium supplemented by 8% (v/v) heat-inactivated human serum at 37 °C under an atmosphere of 3% $CO_2$, 6% $O_2$, and 91% $N_2$. Human red blood cells and serum were provided by the Etablissement Français du Sang Ile de France under the C-CPSL-UNT approval n°13/EFS/126. In vitro drug susceptibility was measured by [$^3$H]-hypoxanthine incorporation as described previously.[10] Stock solutions of drugs were prepared in DMSO. Compounds were serially diluted two-fold with 100 µL culture medium in 96-well plates. Asynchronous parasite cultures (100 µL, 1% parasitemia and 1% final hematocrit) were then added to each well and incubated for 24 h at 37 °C prior to the addition of 0.5 µCi of [$^3$H]-hypoxanthine (GE Healthcare; 1 to 5 Ci.mmol/mL) per well. After a further incubation of 24 h, plates were frozen and thawed. Cell lysates were then collected onto glass-

fiber filters and counted in a liquid scintillation spectrometer. The growth inhibition for each drug concentration was determined by comparison of the radioactivity incorporated in the treated culture with that in the control culture maintained on the same plate. The concentration causing 50% growth inhibition ($IC_{50}$) was obtained from the drug concentration-response curve and the results were expressed as mean values ± standard deviations as determined from three independent experiments. Chloroquine diphosphate, used as a positive control, was purchased from Sigma (purity>99%).

**Cell Culture and Proliferation Assay.** The MRC-5 cell line was obtained from the American Type Culture Collection (Rockville, MD, USA) and cultured according to the supplier's instructions. Human MRC-5 cells were grown in DMEM supplemented with 10% fetal calf serum (FCS) and 1% glutamine. The cell line was maintained at 37 °C in a humidified atmosphere containing 5% $CO_2$. Cell growth inhibition was determined by an MTS assay according to the manufacturer's instructions (Promega, Madison, WI, USA). Briefly, the cells were seeded in 96-well plates ($2.5 \times 10^3$ cells/well) containing 200 µL of growth medium. After 24 h of culture, the cells were treated with the test compounds at different final concentrations. After 72 h of

incubation, 40 µL of resazurin was added for 2 h before recording absorbance at 490 nm with a spectrophotometric plate reader. The $IC_{50}$ value corresponded to the concentration of compound inducing a decrease of 50% in absorbance of drug-treated cells compared with untreated cells. Experiments were performed in triplicate. Paclitaxel was used as the reference compound.

**Figure S10.** $^{1}$H NMR Spectrum (500 MHz, DMSO-$d_6$) of moandaensine B (**1**)

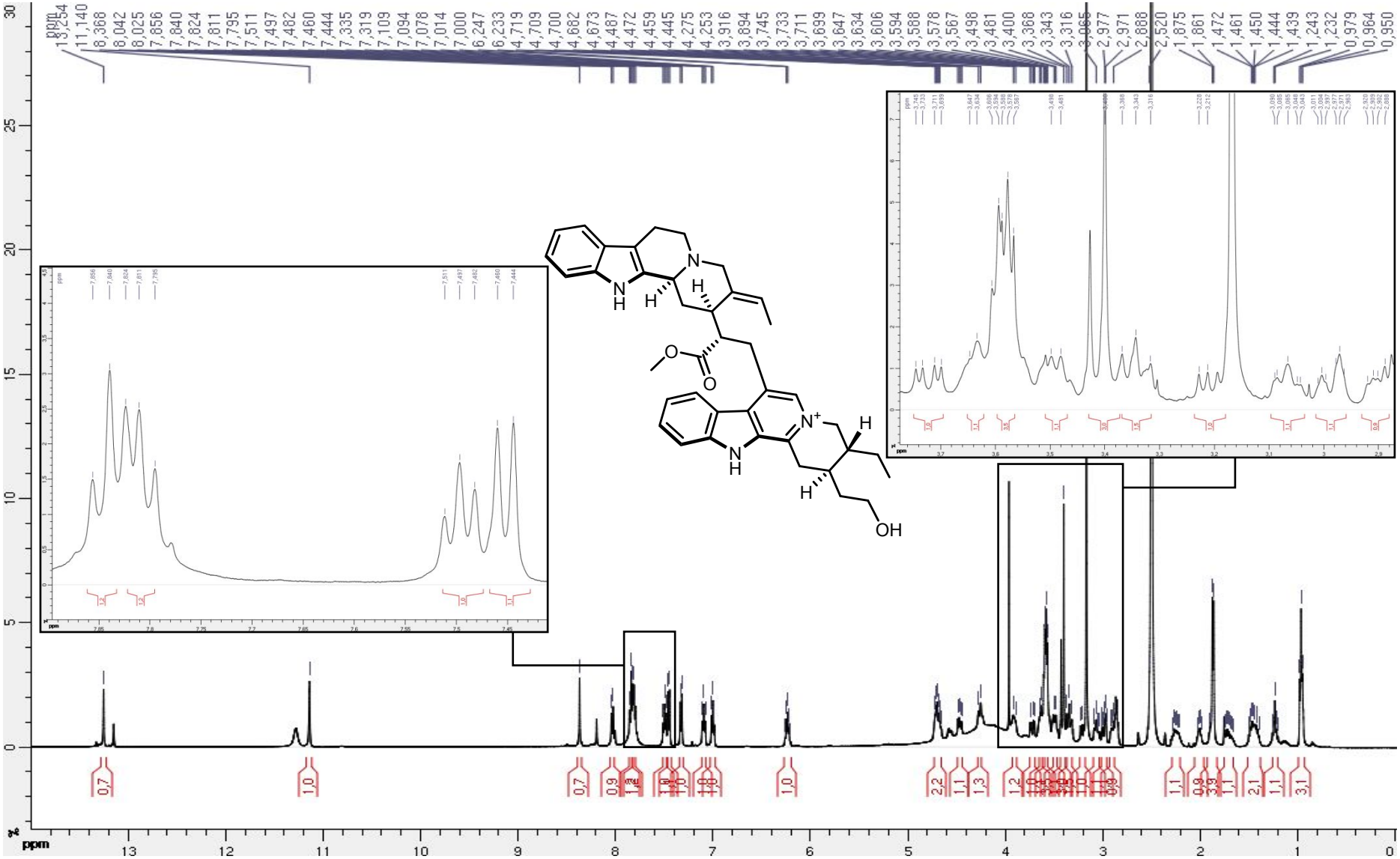


**Figure S11.** $^{13}$C NMR Spectrum (125 MHz, DMSO-$d_6$) of moandaensine B (**1**)

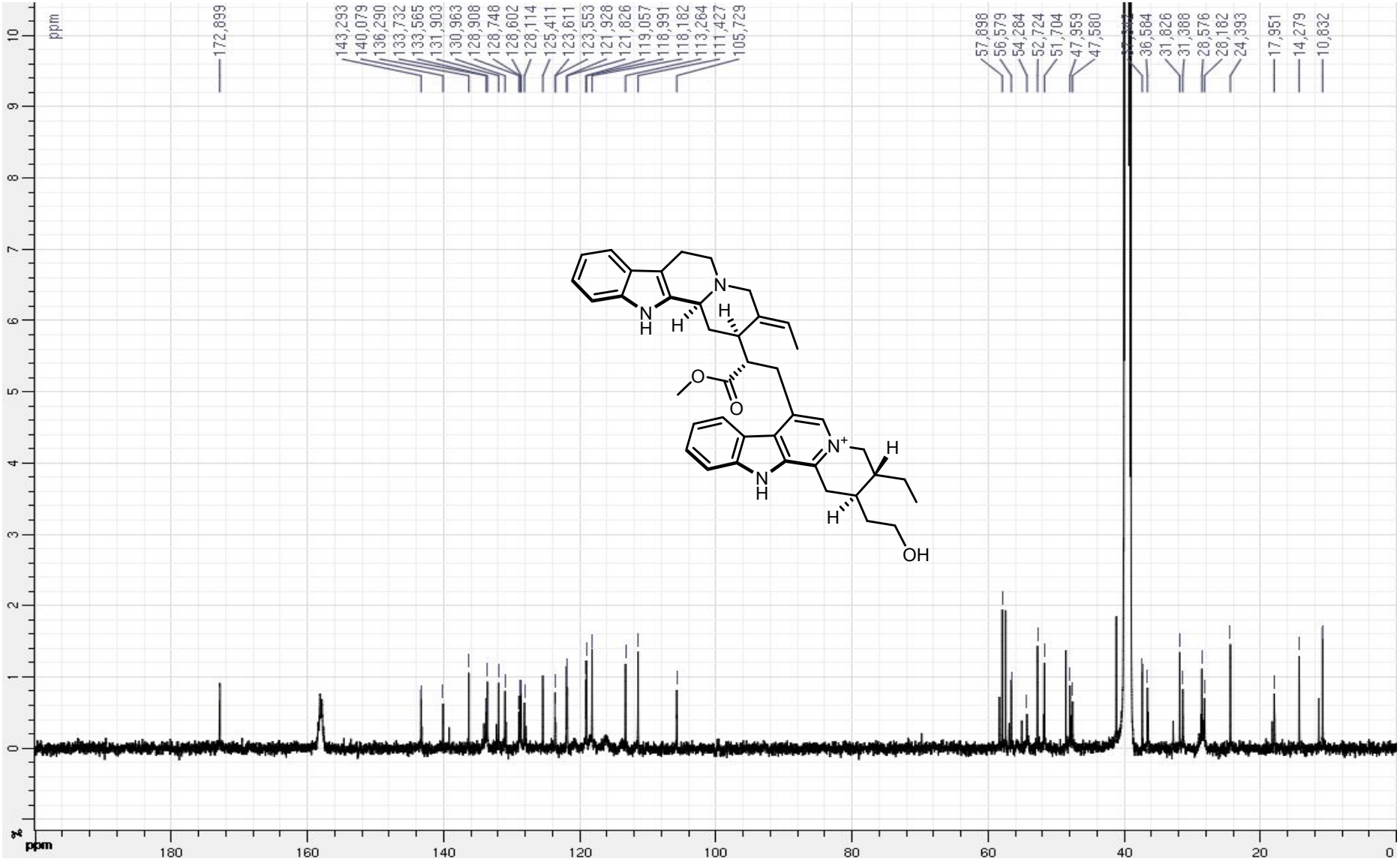


**Figure S12.** COSY spectrum (500 MHz, DMSO-$d_6$) of moandaensine B (**1**)

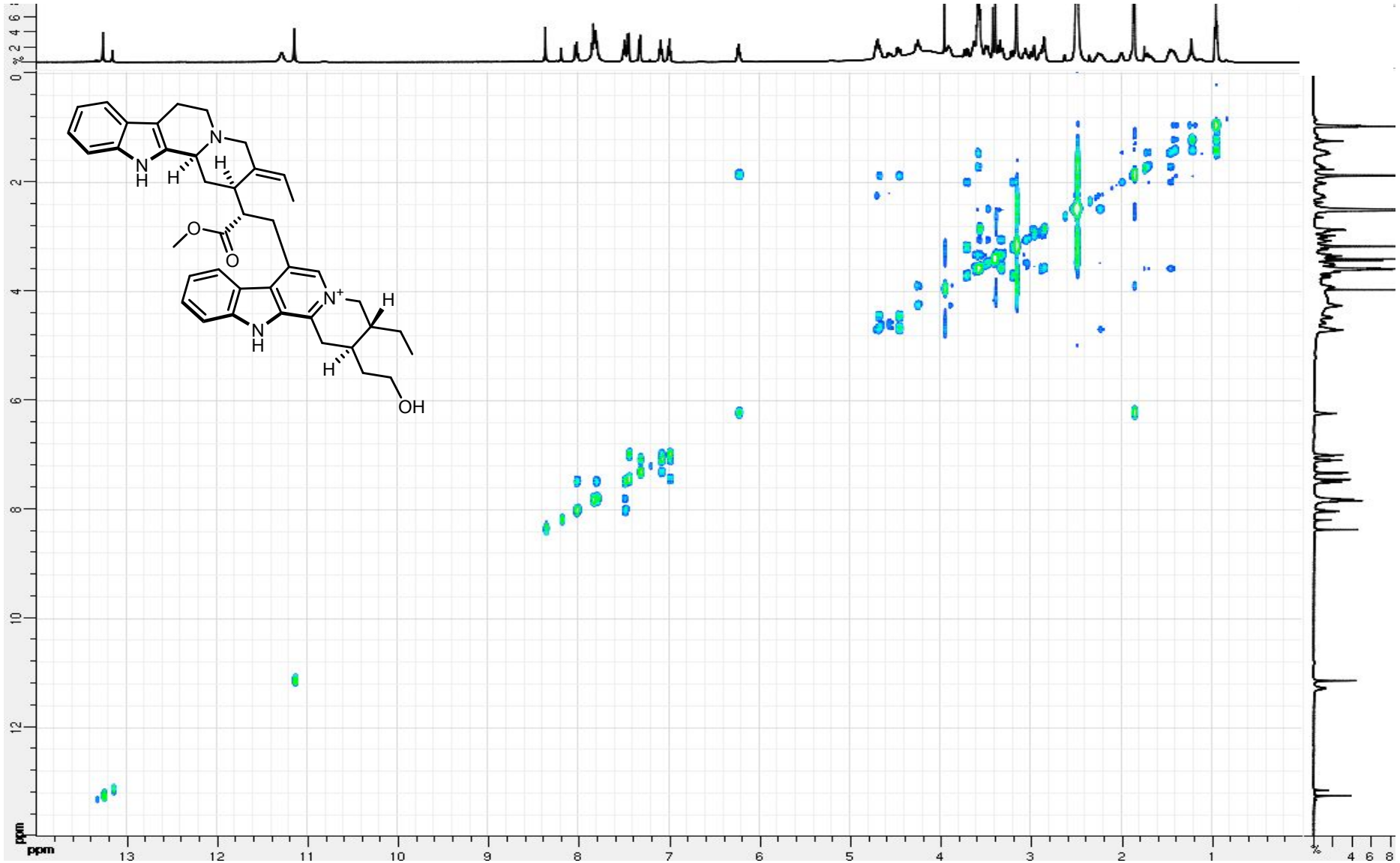


**Figure S13.** HSQC spectrum (500 MHz, DMSO-$d_6$) of moandaensine B (**1**)

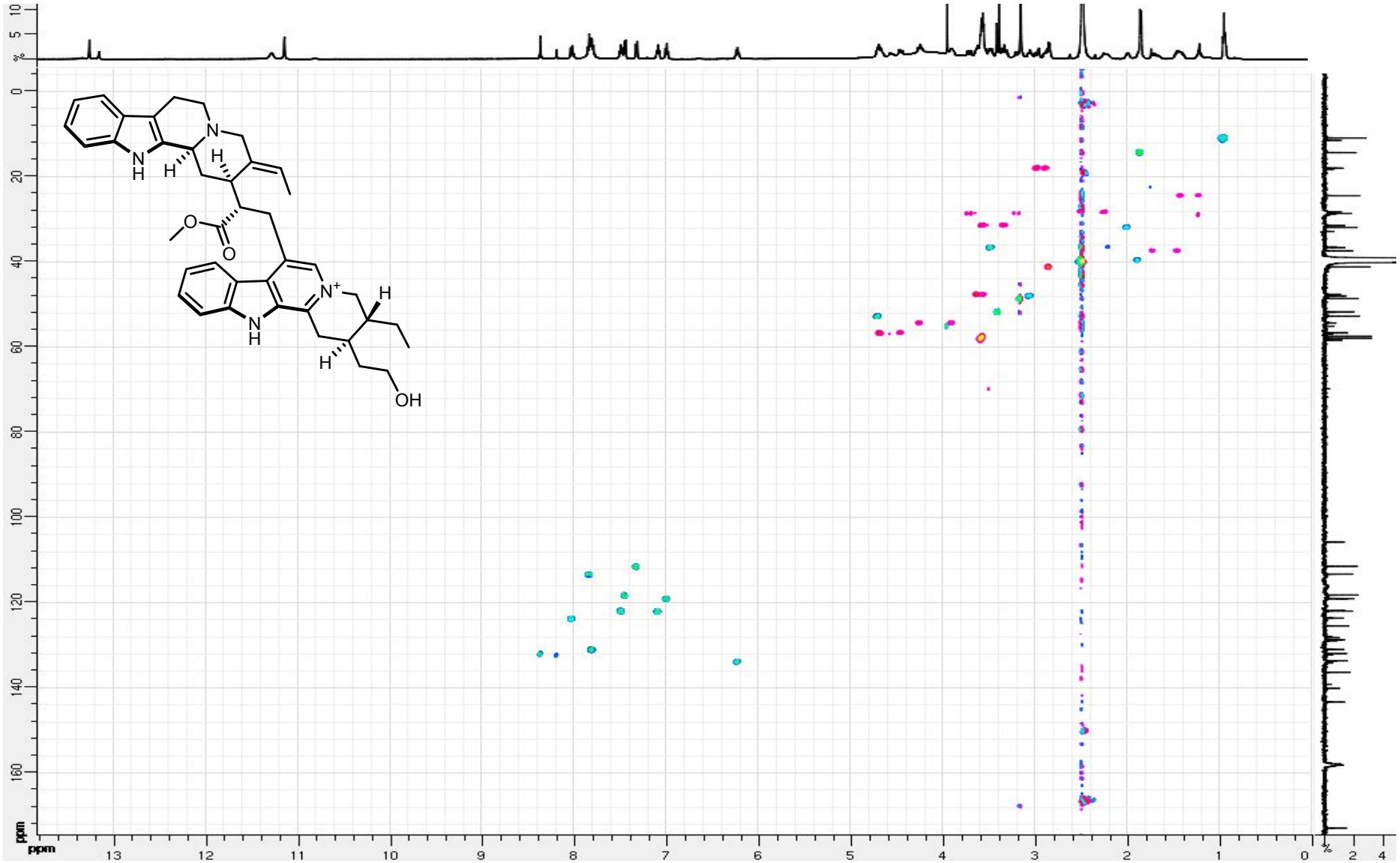


**Figure S14.** HMBC spectrum (500 MHz, DMSO-$d_6$) of moandaensine B (**1**)

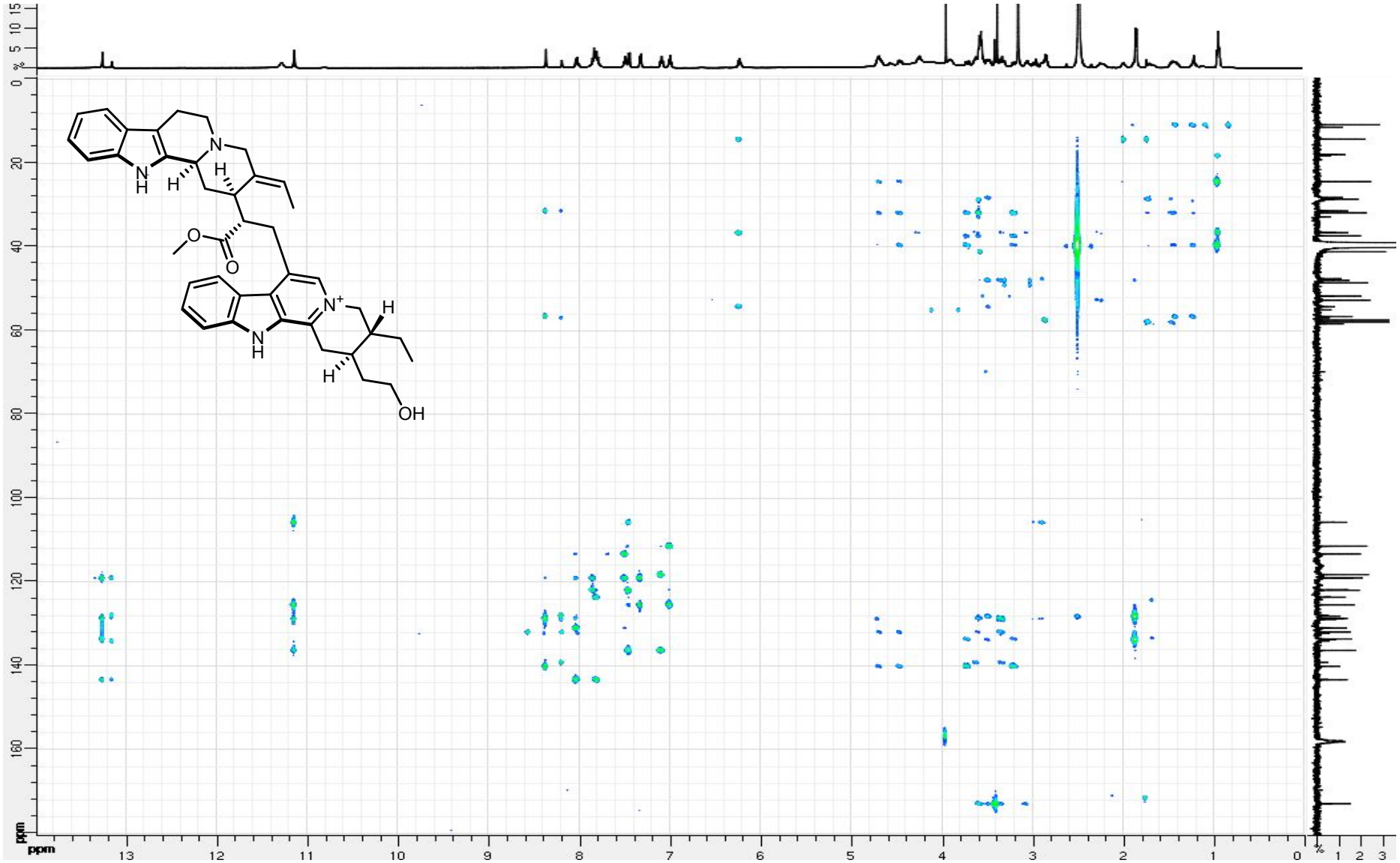


**Figure S15.** ROESY spectrum (500 MHz, DMSO-$d_6$) of moandaensine B (**1**)

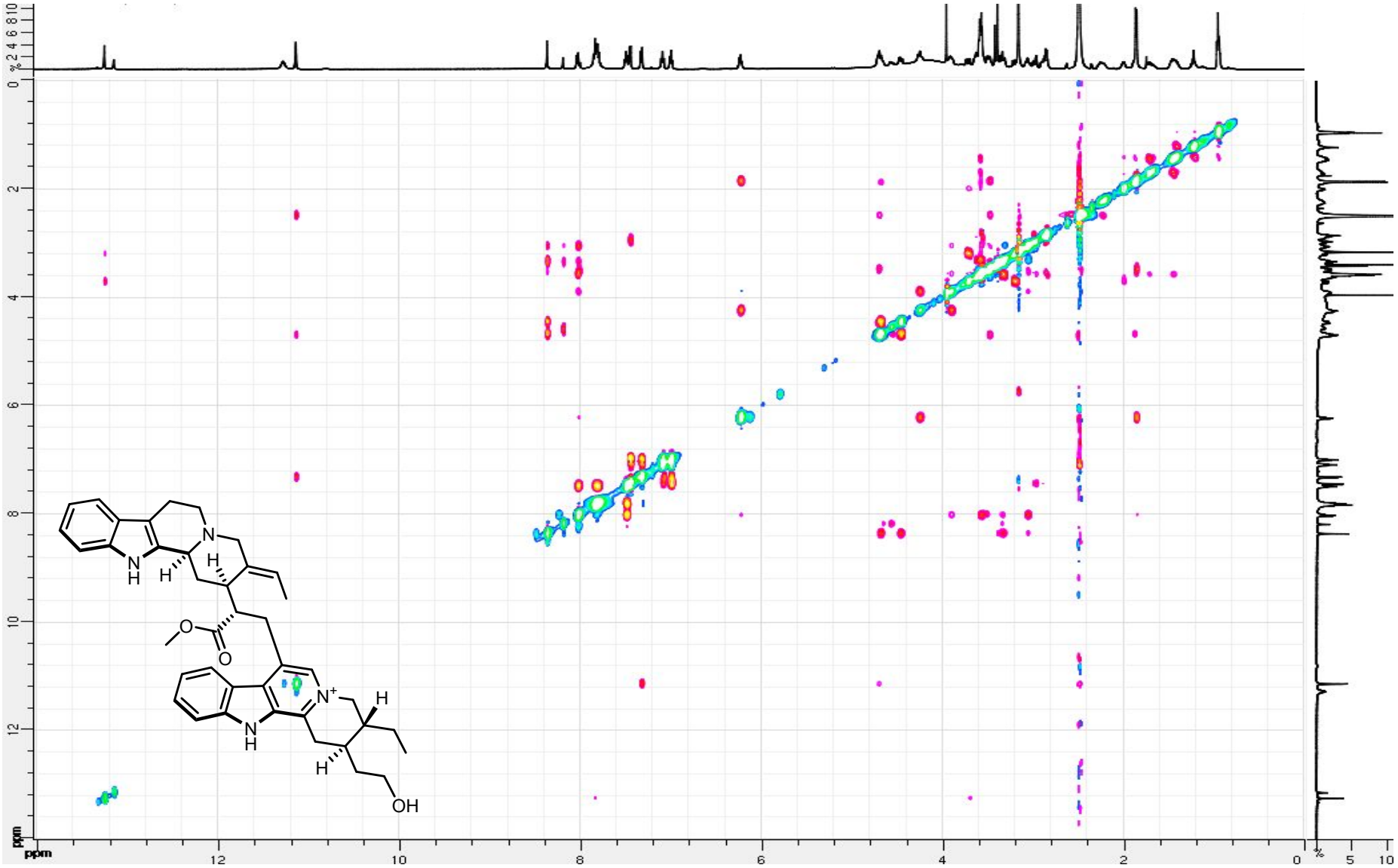


**Figure S16.** $^{1}$H NMR spectrum (500 MHz, DMSO-$d_6$) of moandaensine C (**2**)

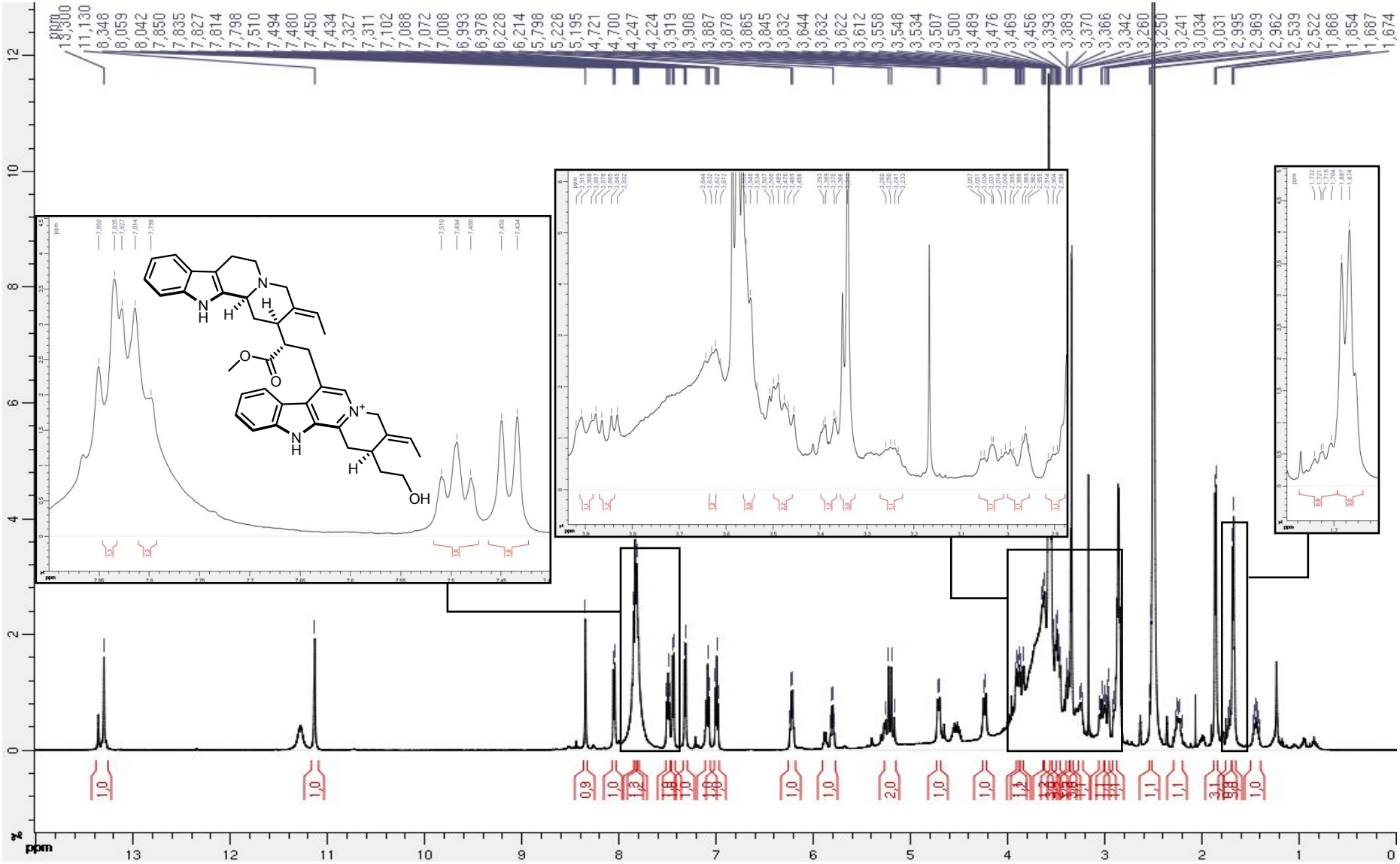


**Figure S17.** $^{13}$C NMR spectrum (125 MHz, DMSO-$d_6$) of moandaensine C (**2**)

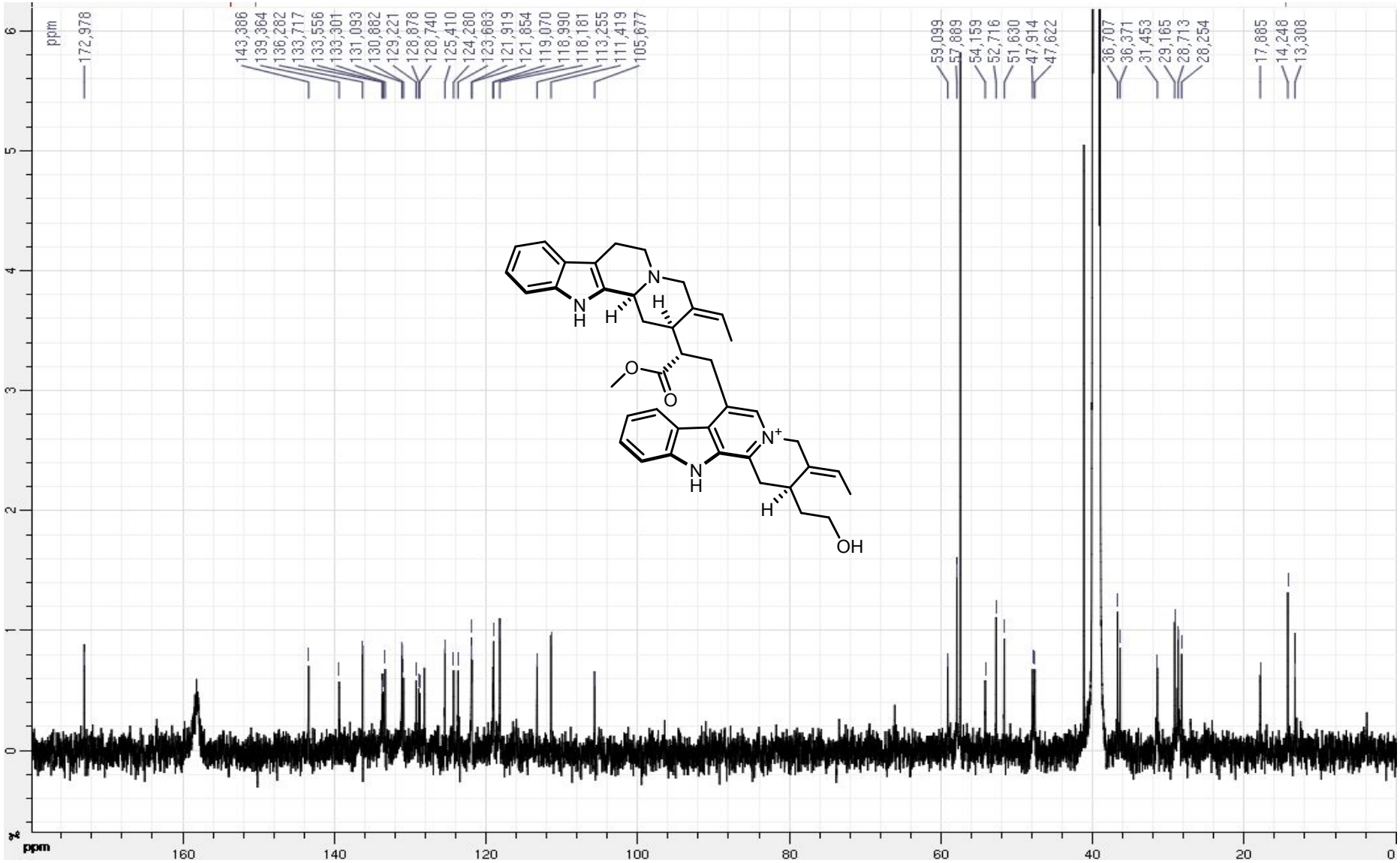


**Figure S18.** COSY spectrum (500 MHz, DMSO-$d_6$) of moandaensine C (**2**)

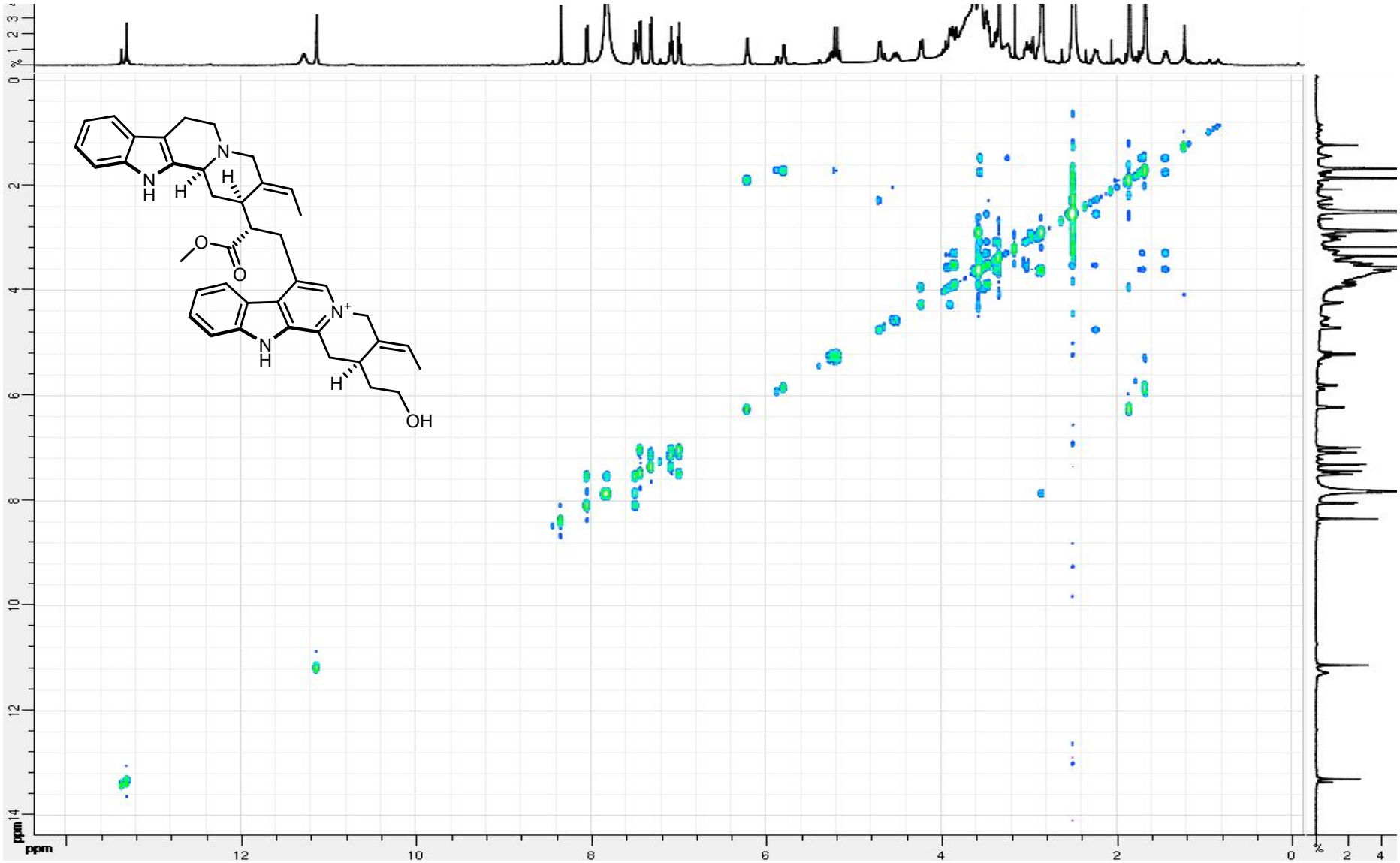


**Figure S19.** HSQC spectrum (500 MHz, DMSO-$d_6$) of moandaensine C (**2**)

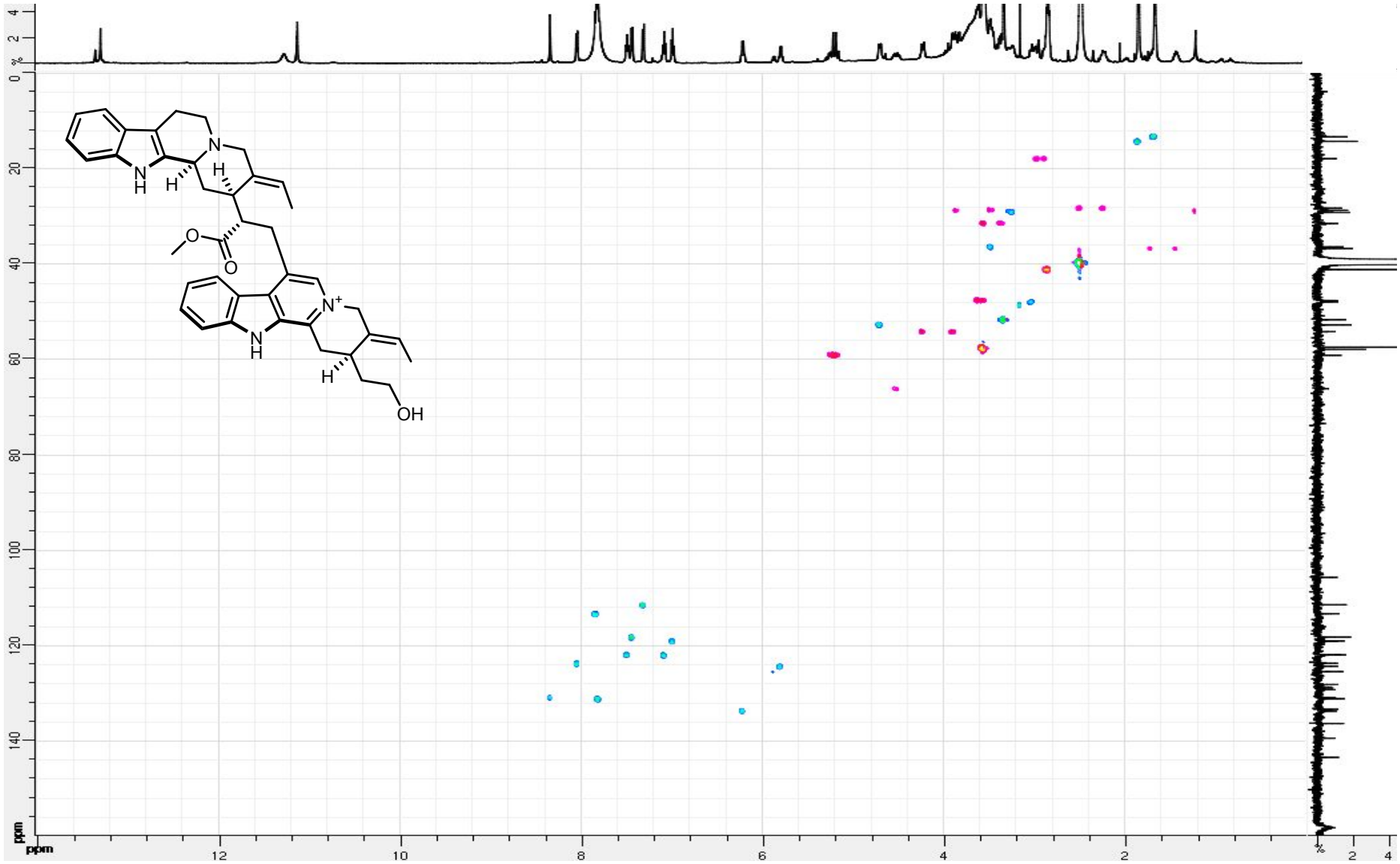


**Figure S20.** HMBC spectrum (500 MHz, DMSO-$d_6$) of moandaensine C (**2**)

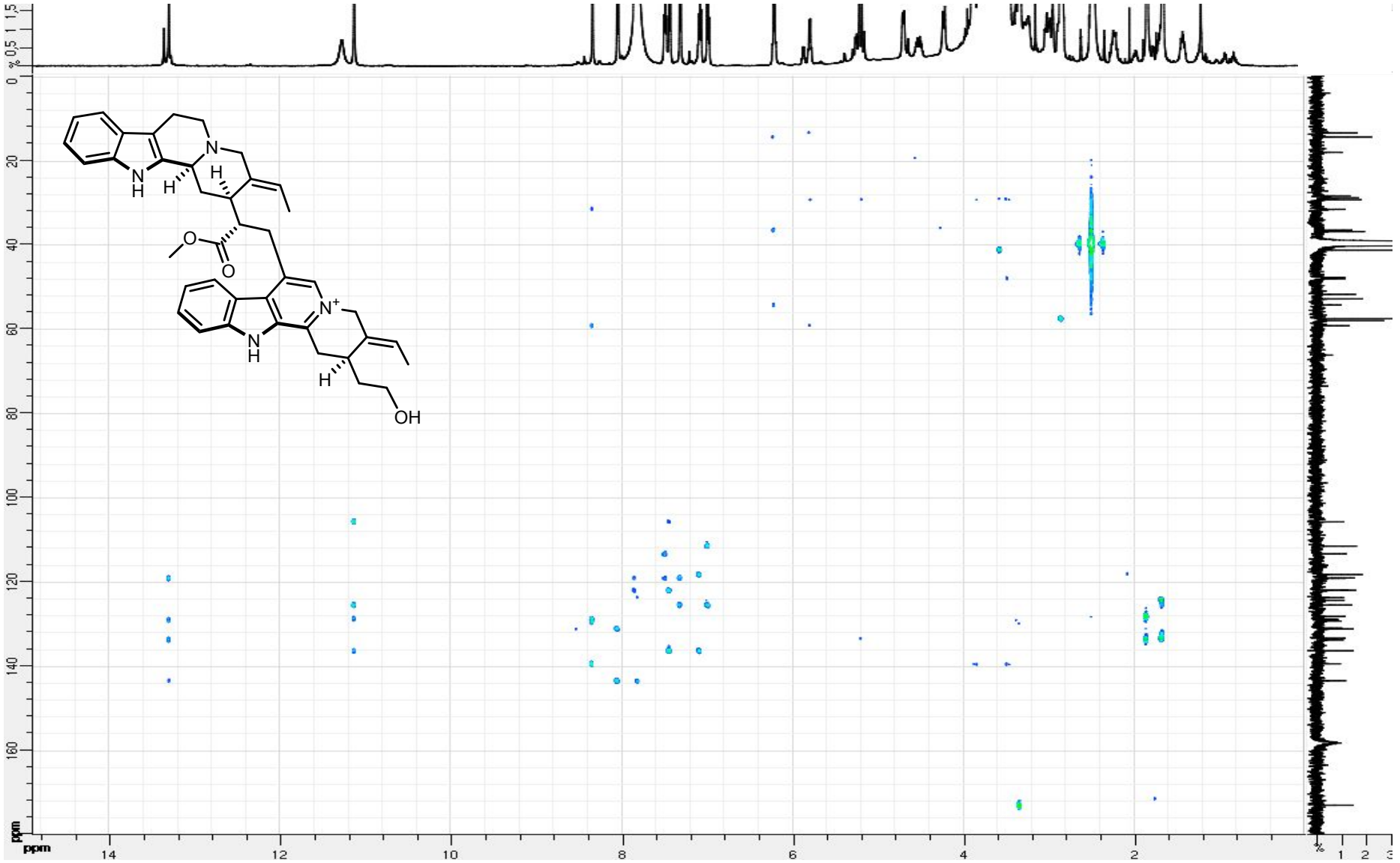


**Figure S21.** ROESY spectrum (500 MHz, DMSO-$d_6$) of moandaensine C (**2**)

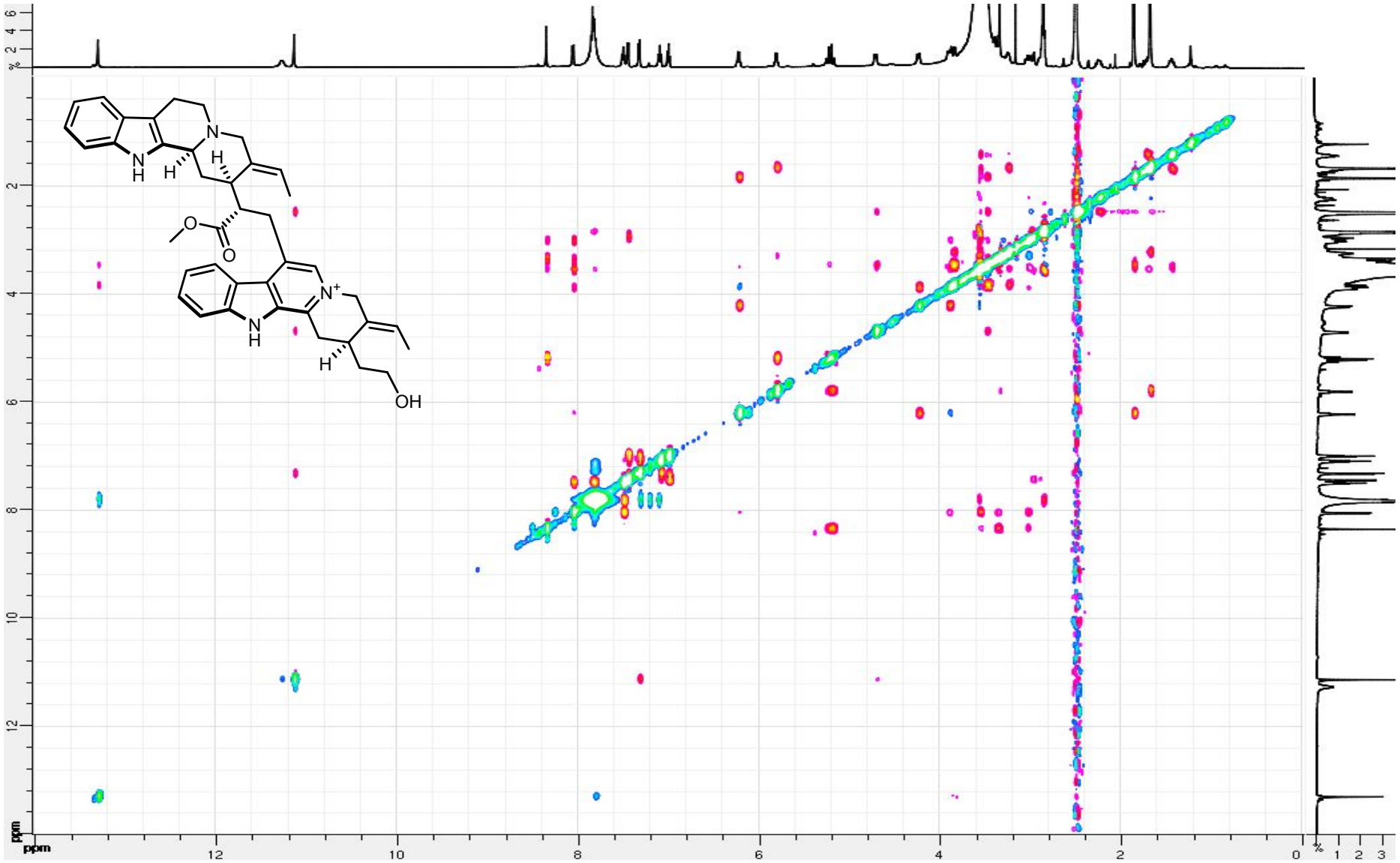


**Figure S22.** $^{1}$H NMR spectrum (600 MHz, DMSO-$d_6$) of 20′-*epi*-serpentinine (**3**)

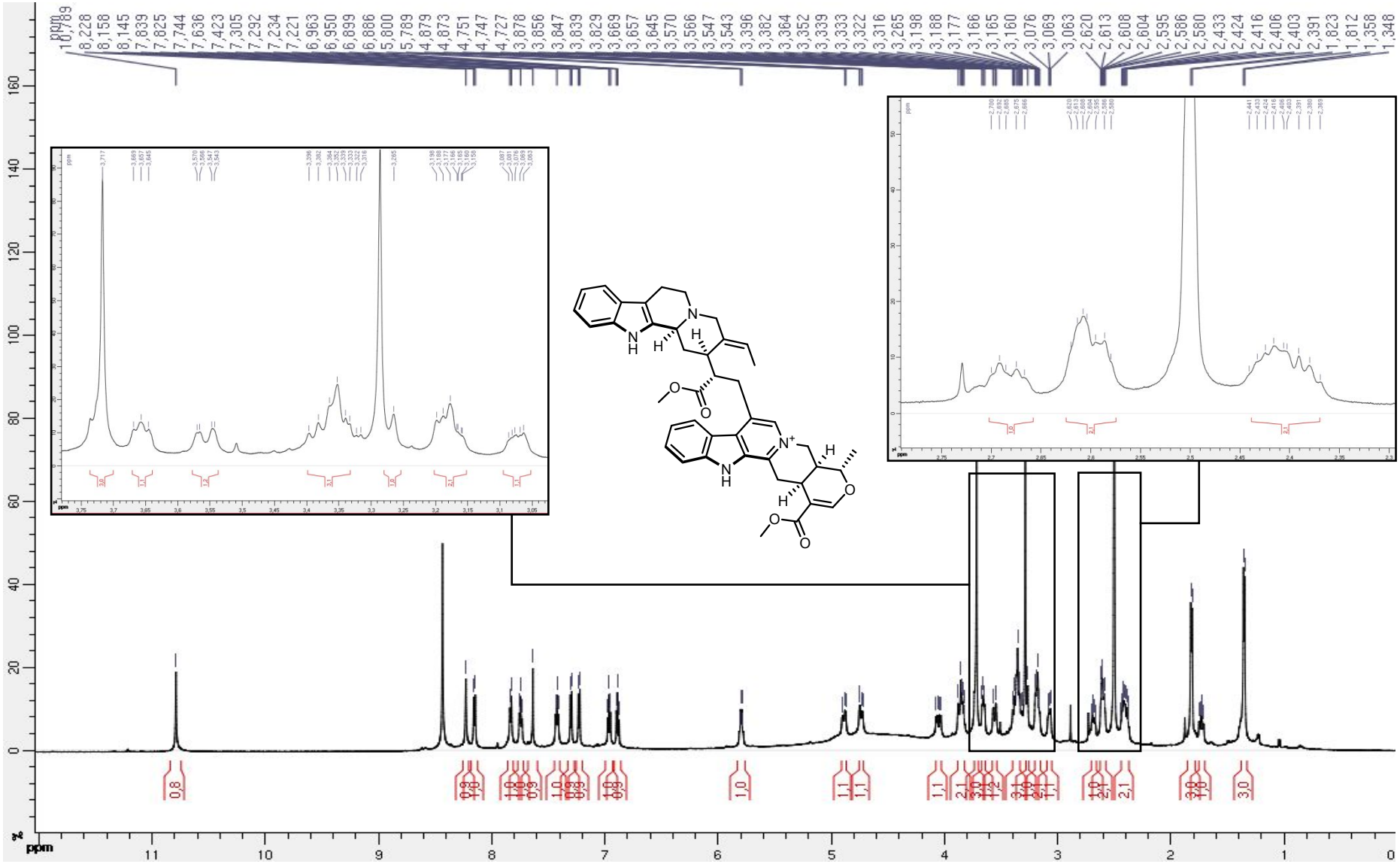


**Figure S23.** $^{13}$C NMR spectrum (150 MHz, DMSO-$d_6$) of 20′-*epi*-serpentinine (**3**)

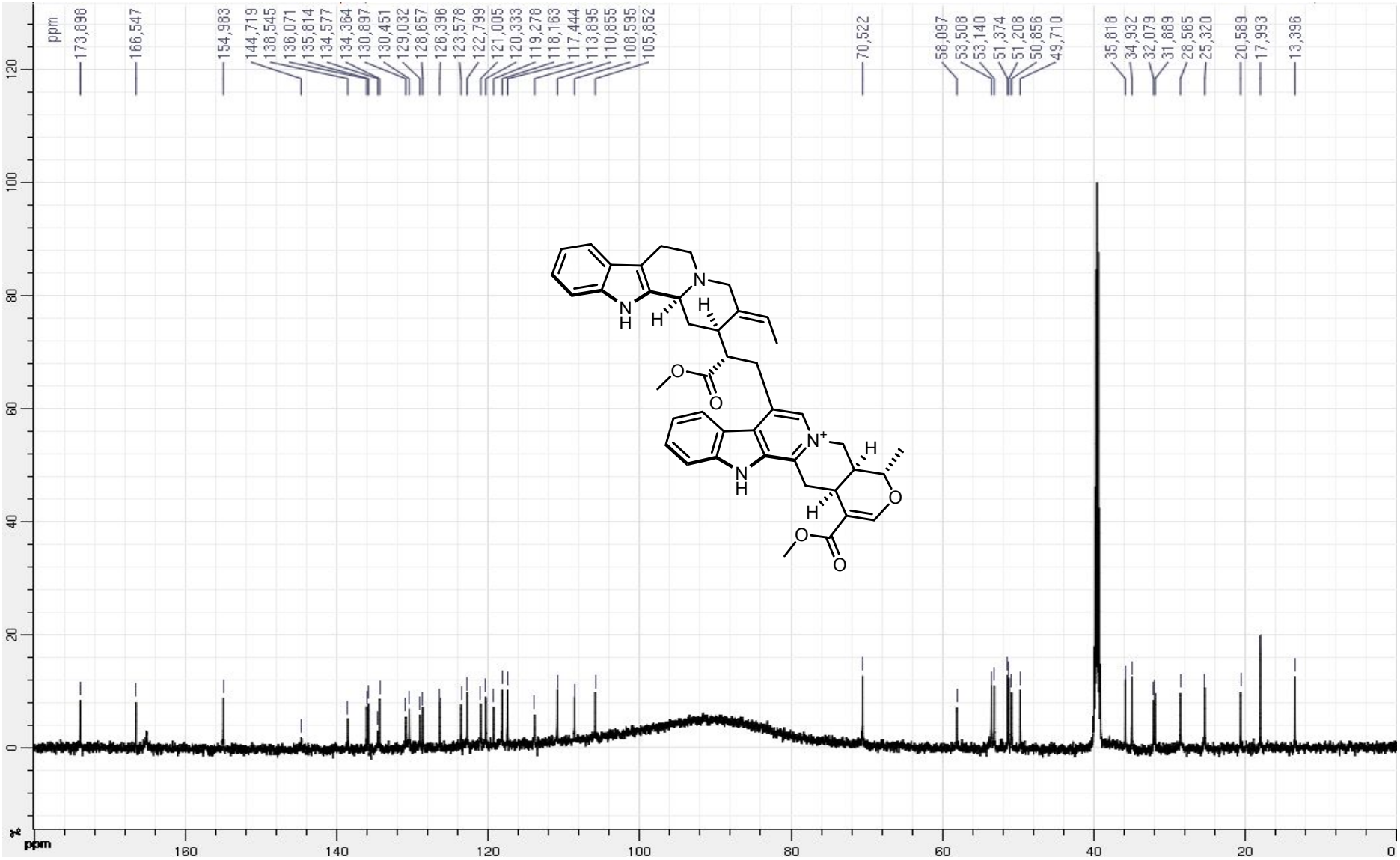


**Figure S24.** COSY spectrum (600 MHz, DMSO-$d_6$) of 20′-*epi*-serpentinine (**3**)

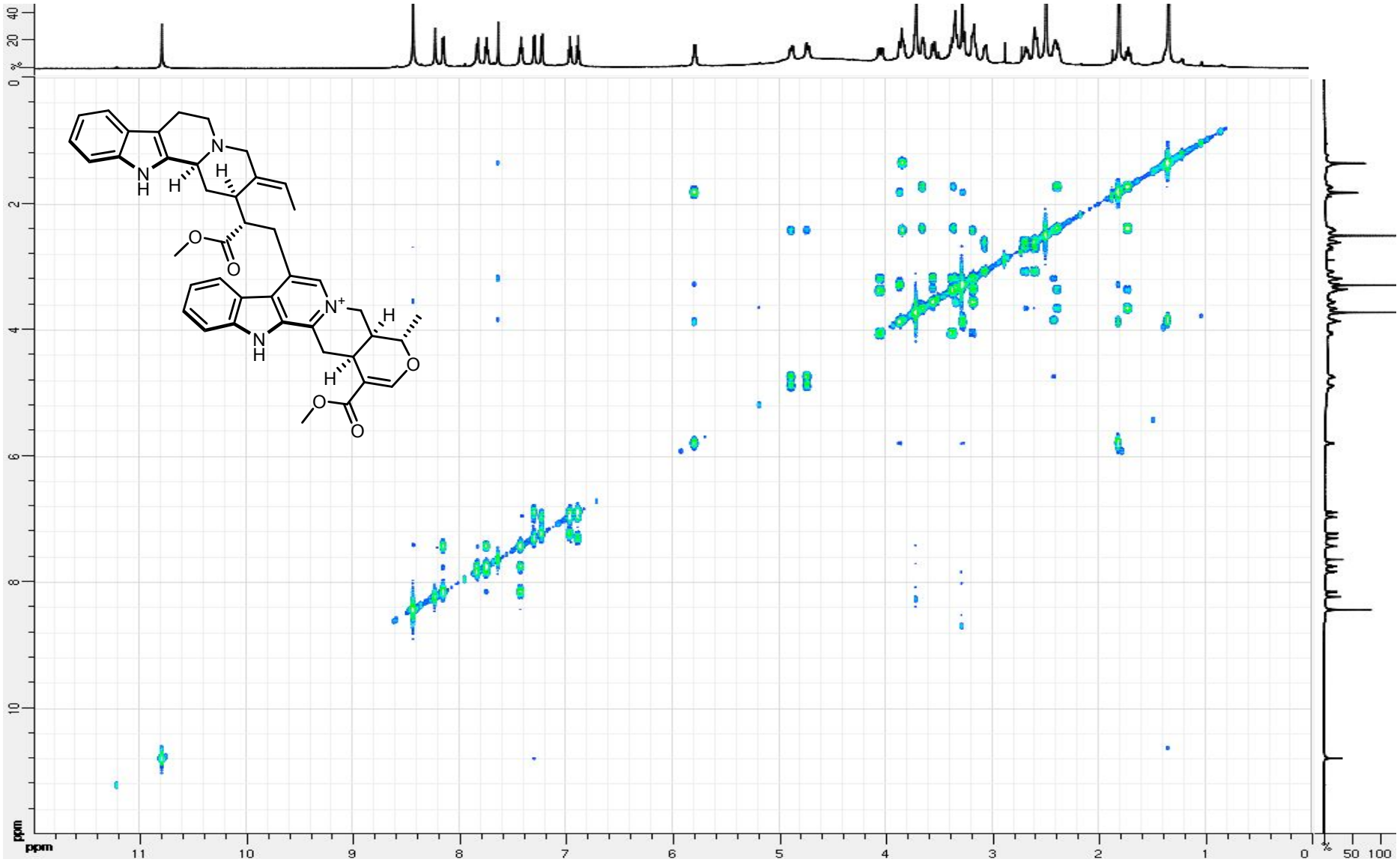


**Figure S25.** HSQC spectrum (600 MHz, DMSO-$d_6$) of 20′-*epi*-serpentinine (**3**)

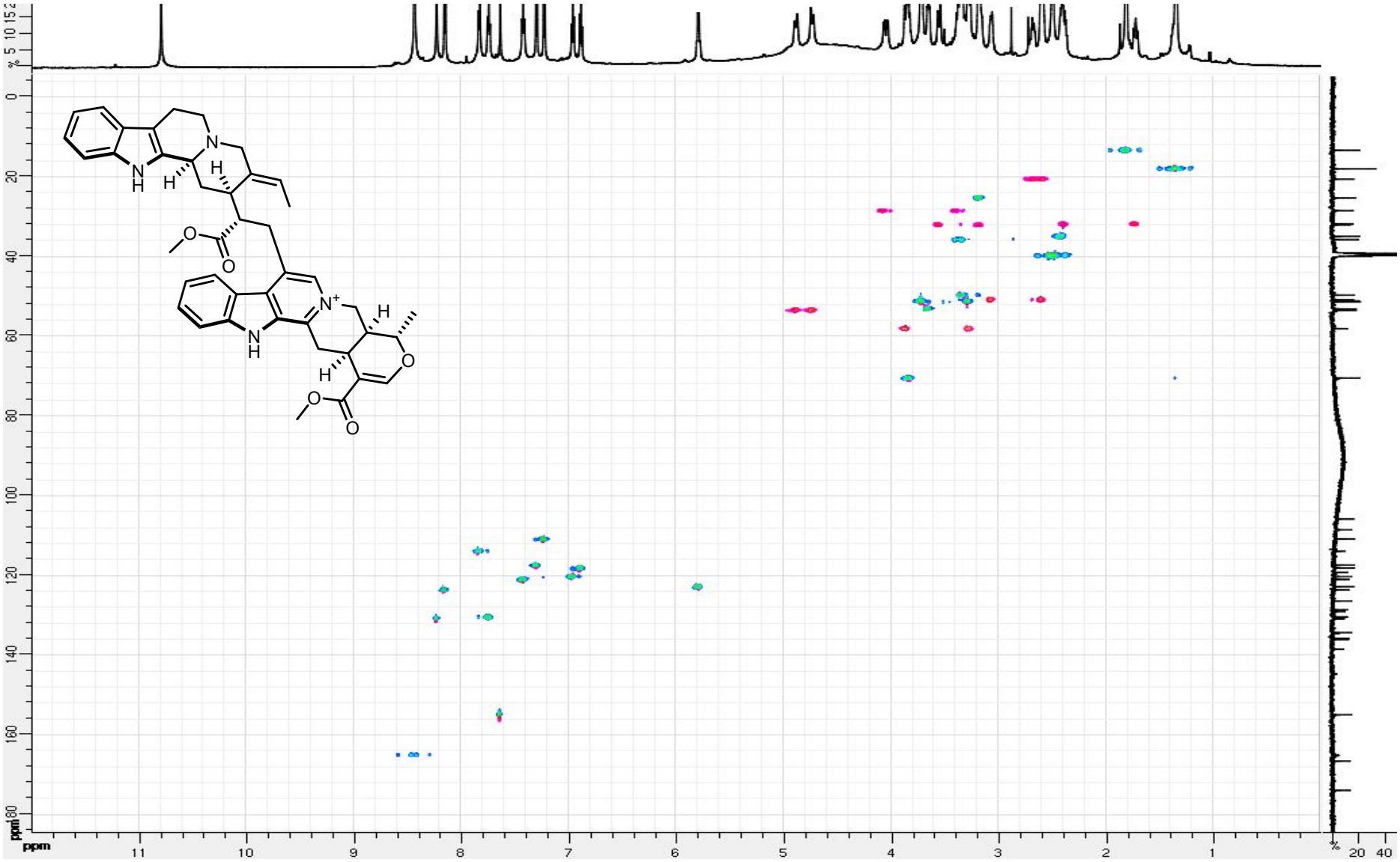


**Figure S26.** HMBC spectrum (600 MHz, DMSO-$d_6$) of 20′-*epi*-serpentinine (**3**)

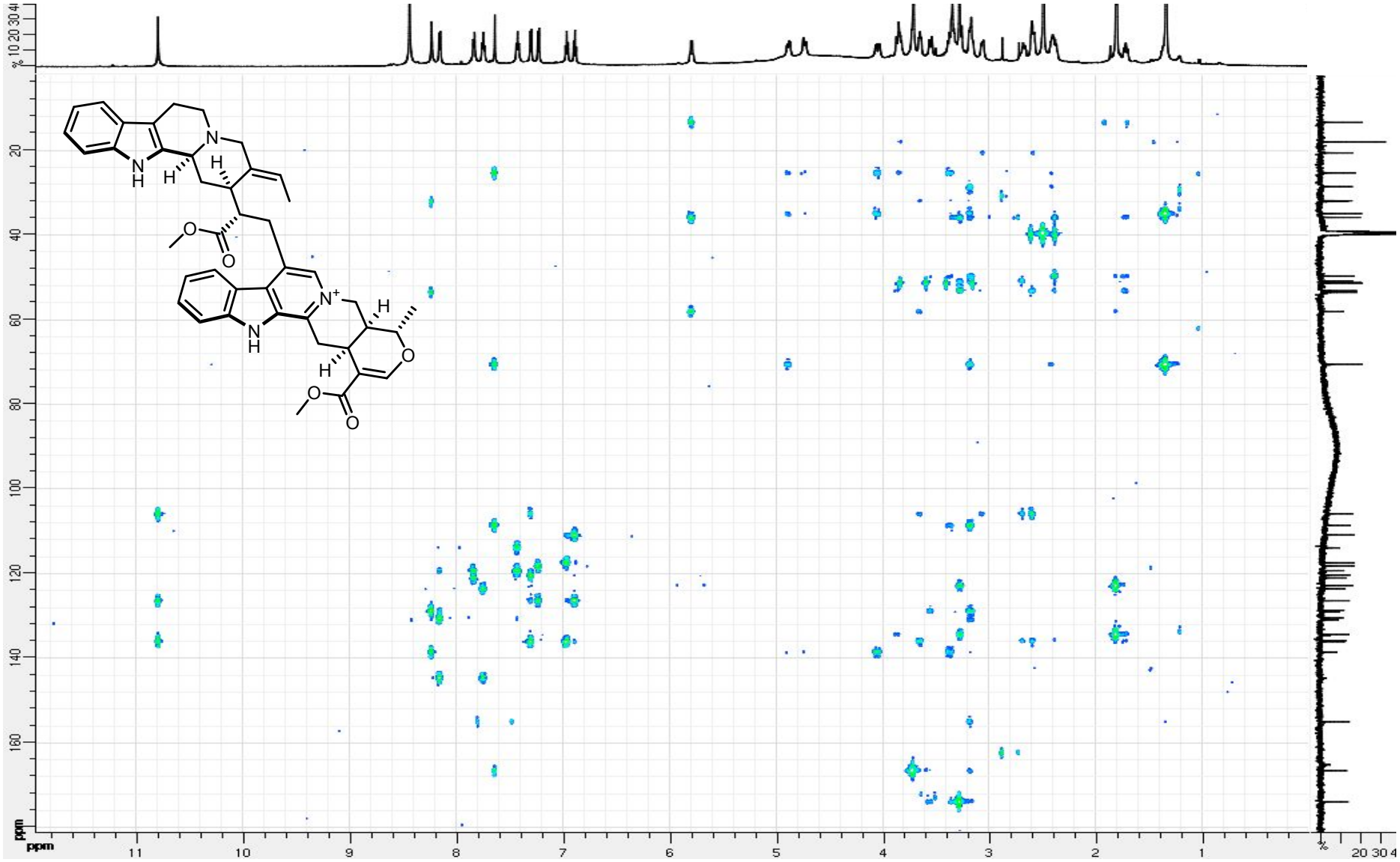


**Figure S27.** ROESY spectrum (600 MHz, DMSO-$d_6$) of 20′-*epi*-serpentinine (**3**)

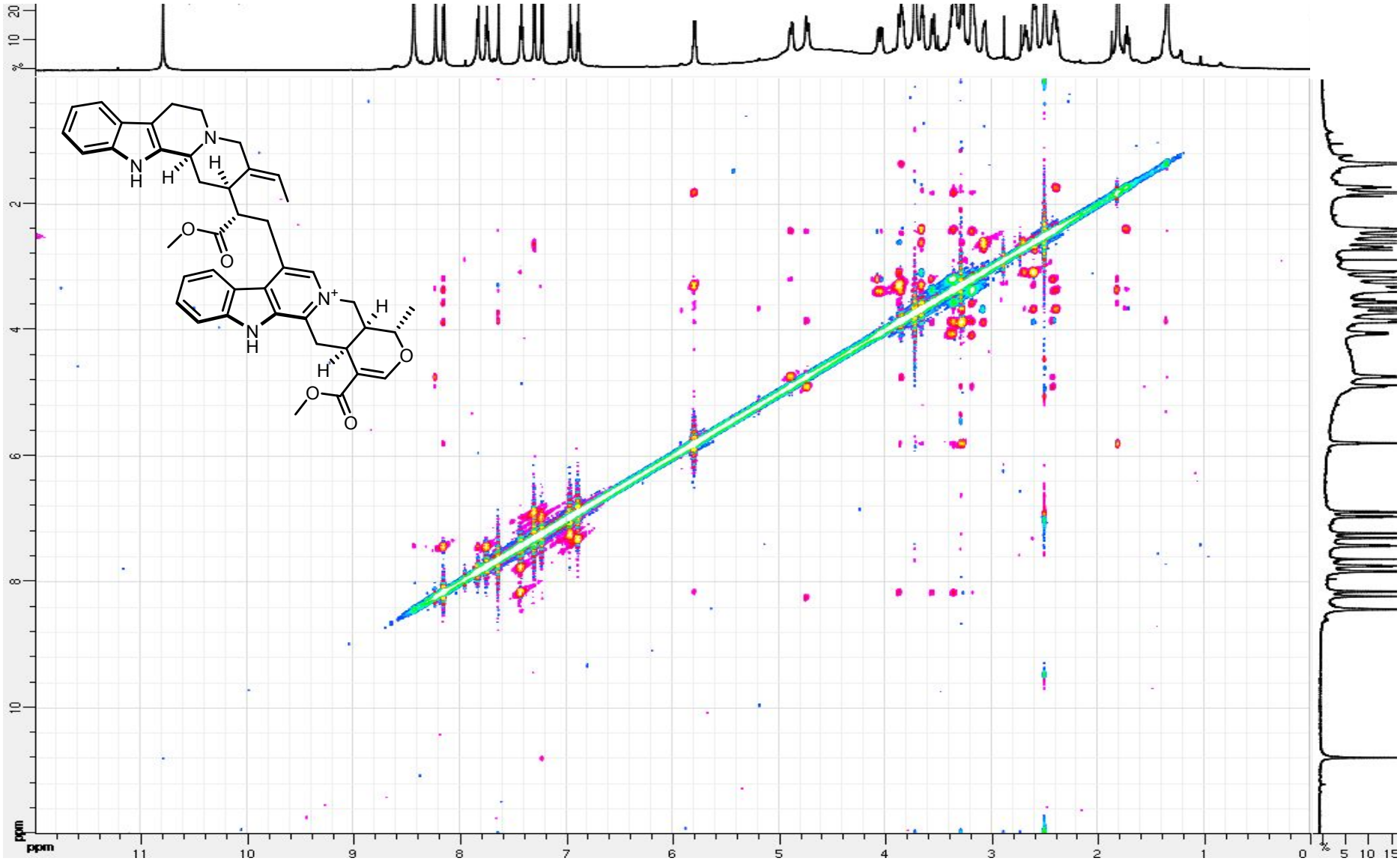


**Figure S28.** $^{1}$H NMR spectrum (500 MHz, DMSO-$d_6$) of 16-demethoxy-20′-*epi*-serpentinine (**4**)

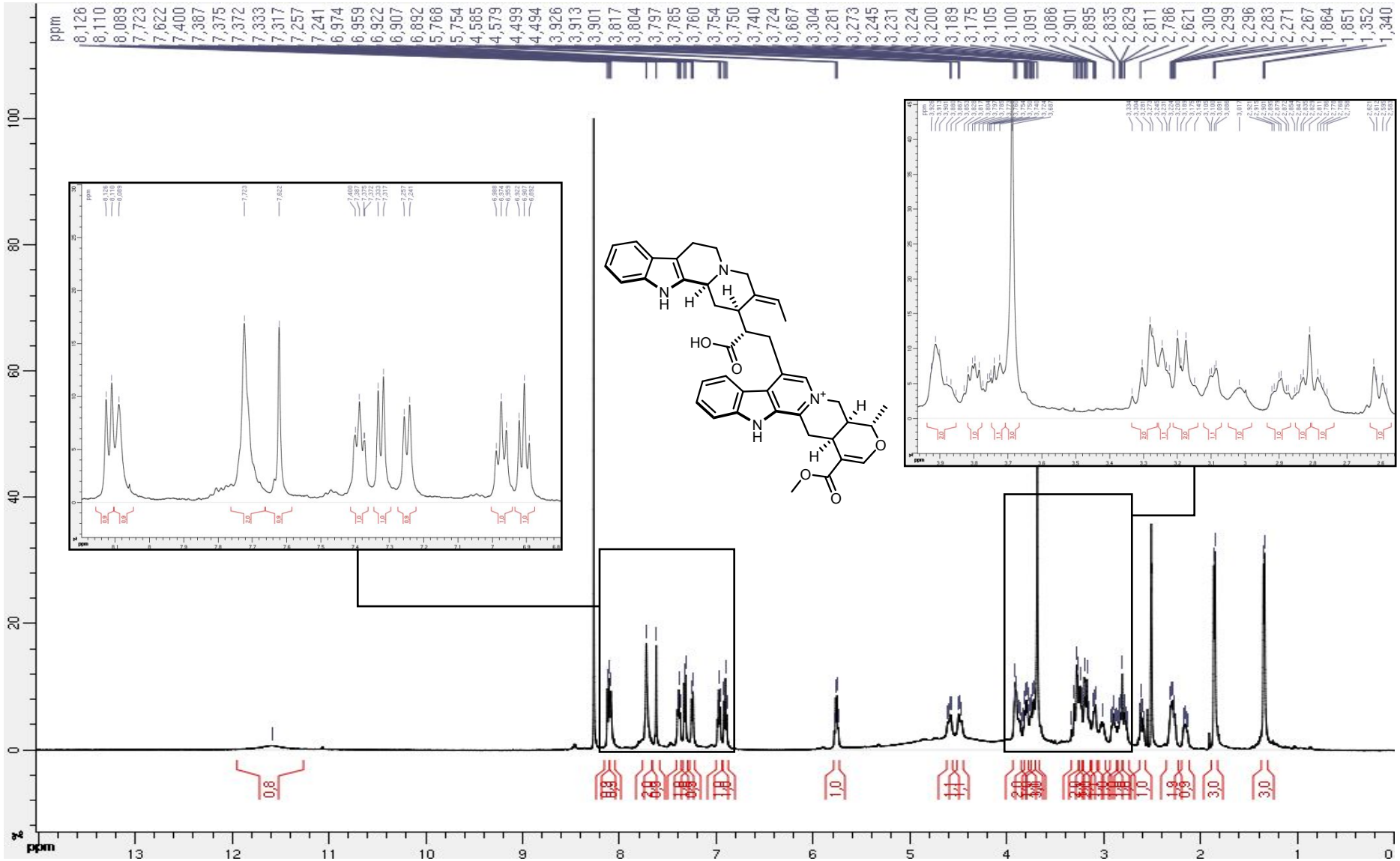


**Figure S29.** $^{13}$C NMR spectrum (125 MHz, DMSO-$d_6$) of 16-demethoxy-20′-*epi*-serpentinine (**4**)

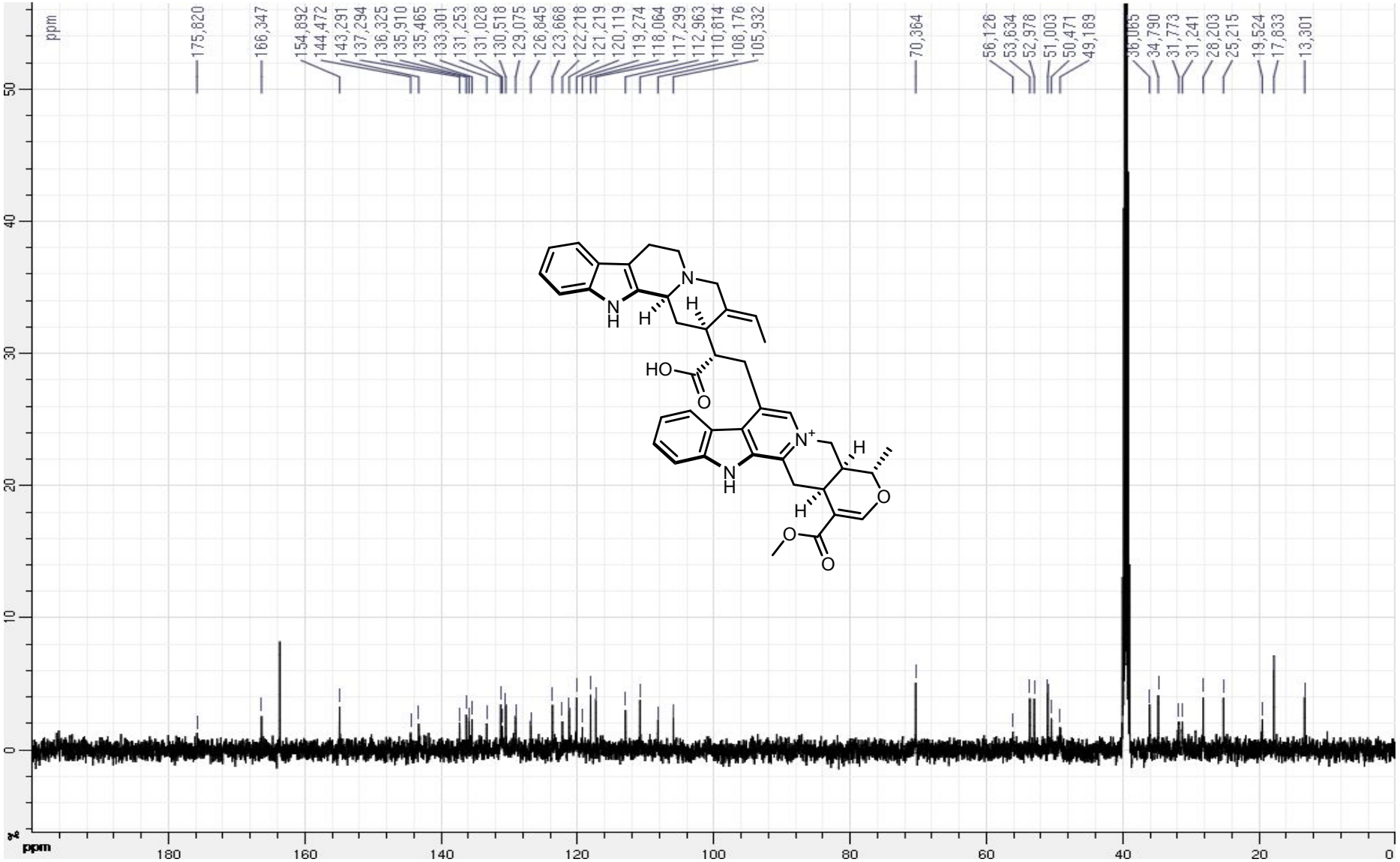


**Figure S30.** COSY spectrum (500 MHz, DMSO-$d_6$) of 16-demethoxy-20′-*epi*-serpentinine (**4**)

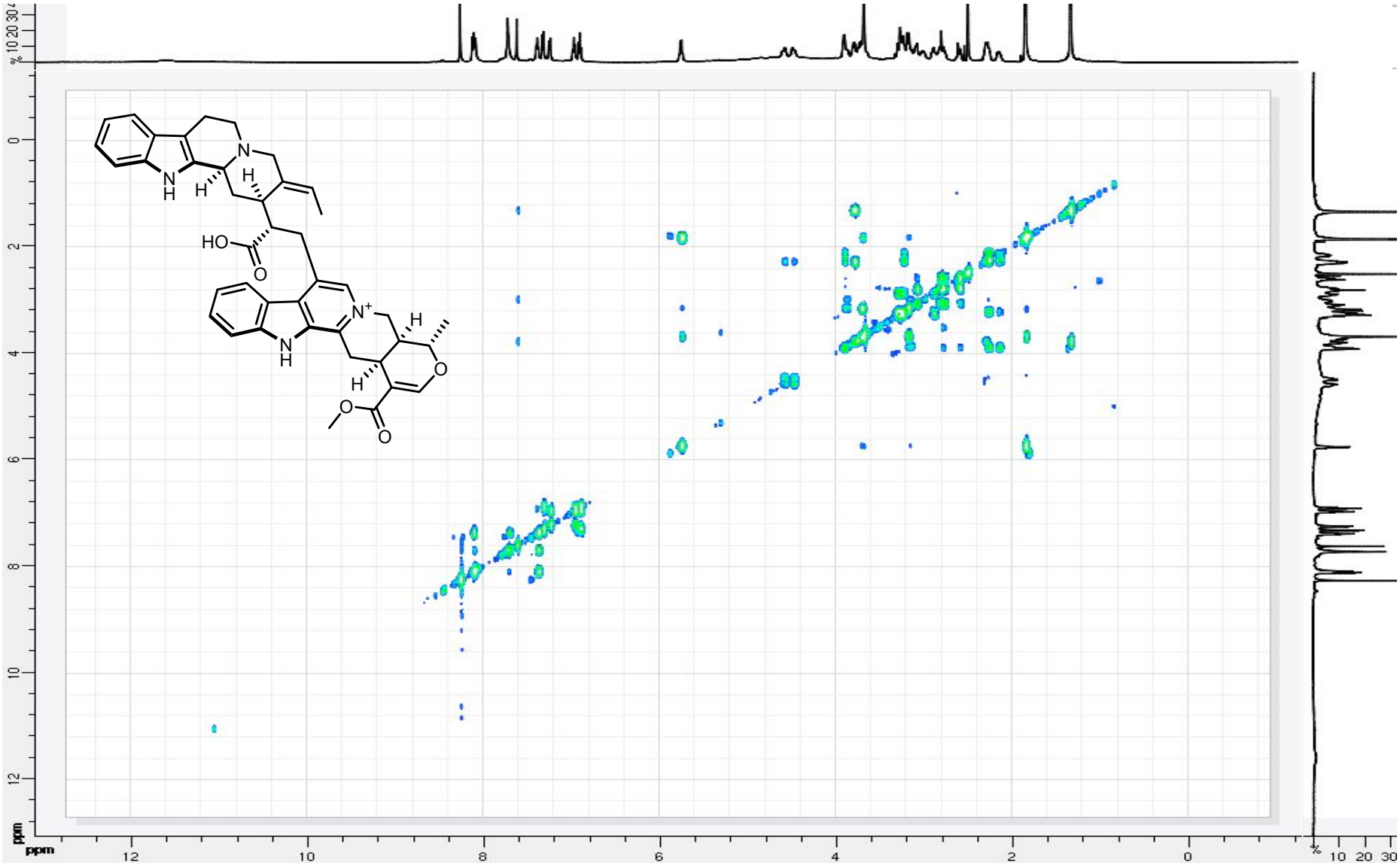


**Figure S31.** HSQC spectrum (500 MHz, DMSO-$d_6$) of 16-demethoxy-20′-*epi*-serpentinine (**4**)

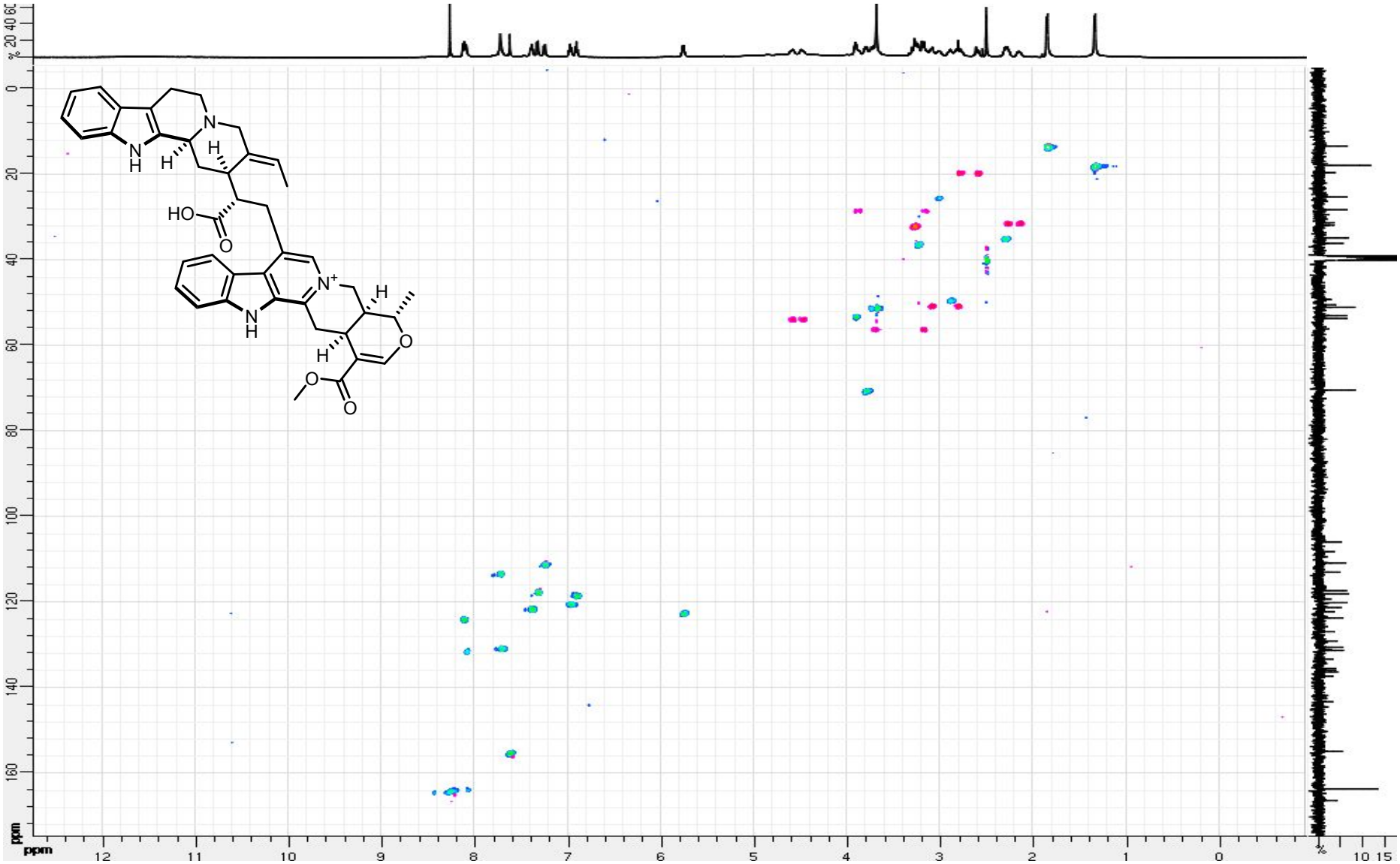


**Figure S32.** HMBC spectrum (500 MHz, DMSO-$d_6$) of 16-demethoxy-20′-*epi*-serpentinine (**4**)

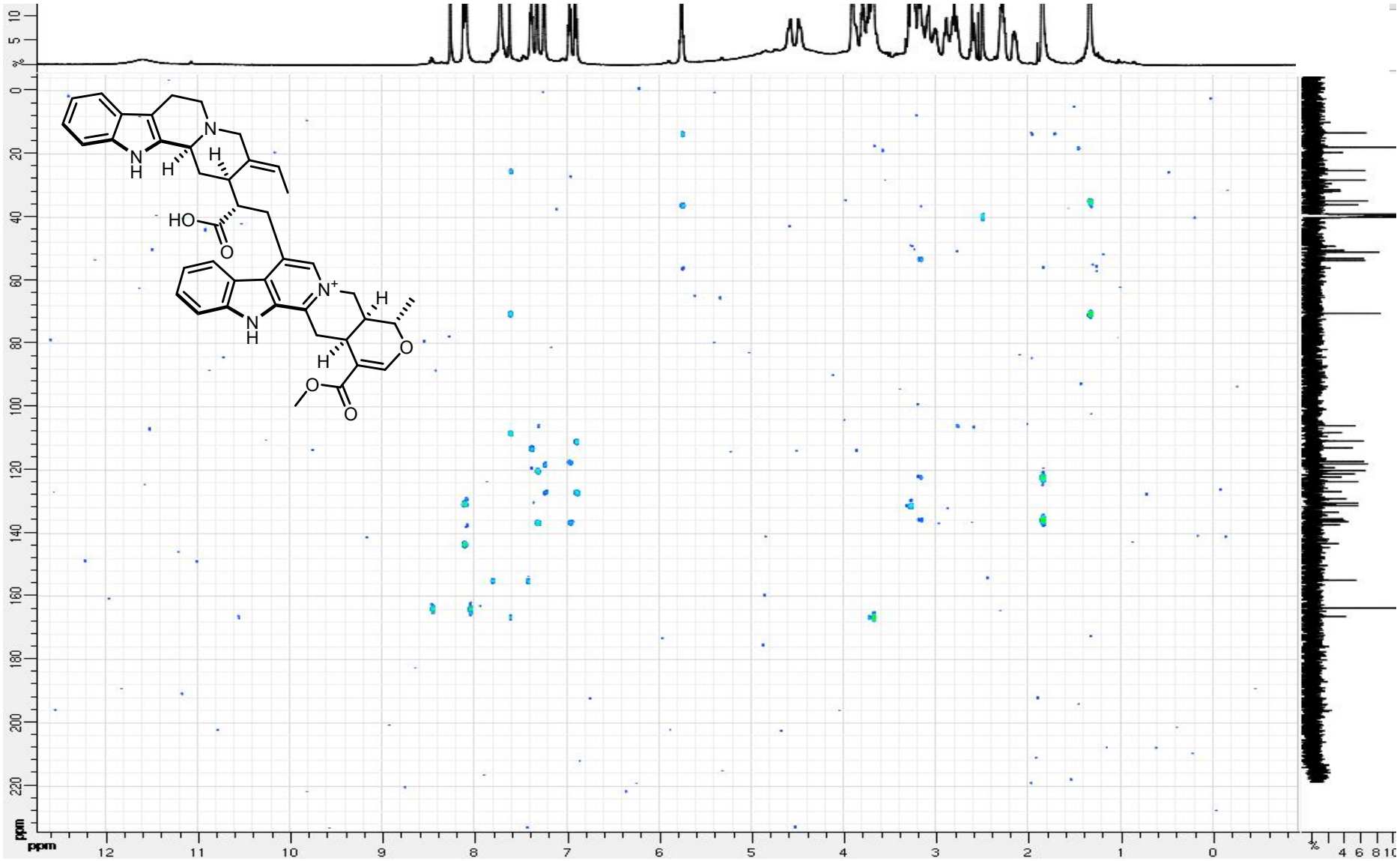


**Figure S33.** ROESY spectrum (500 MHz, DMSO-$d_6$) of 16-demethoxy-20′-*epi*-serpentinine (**4**)

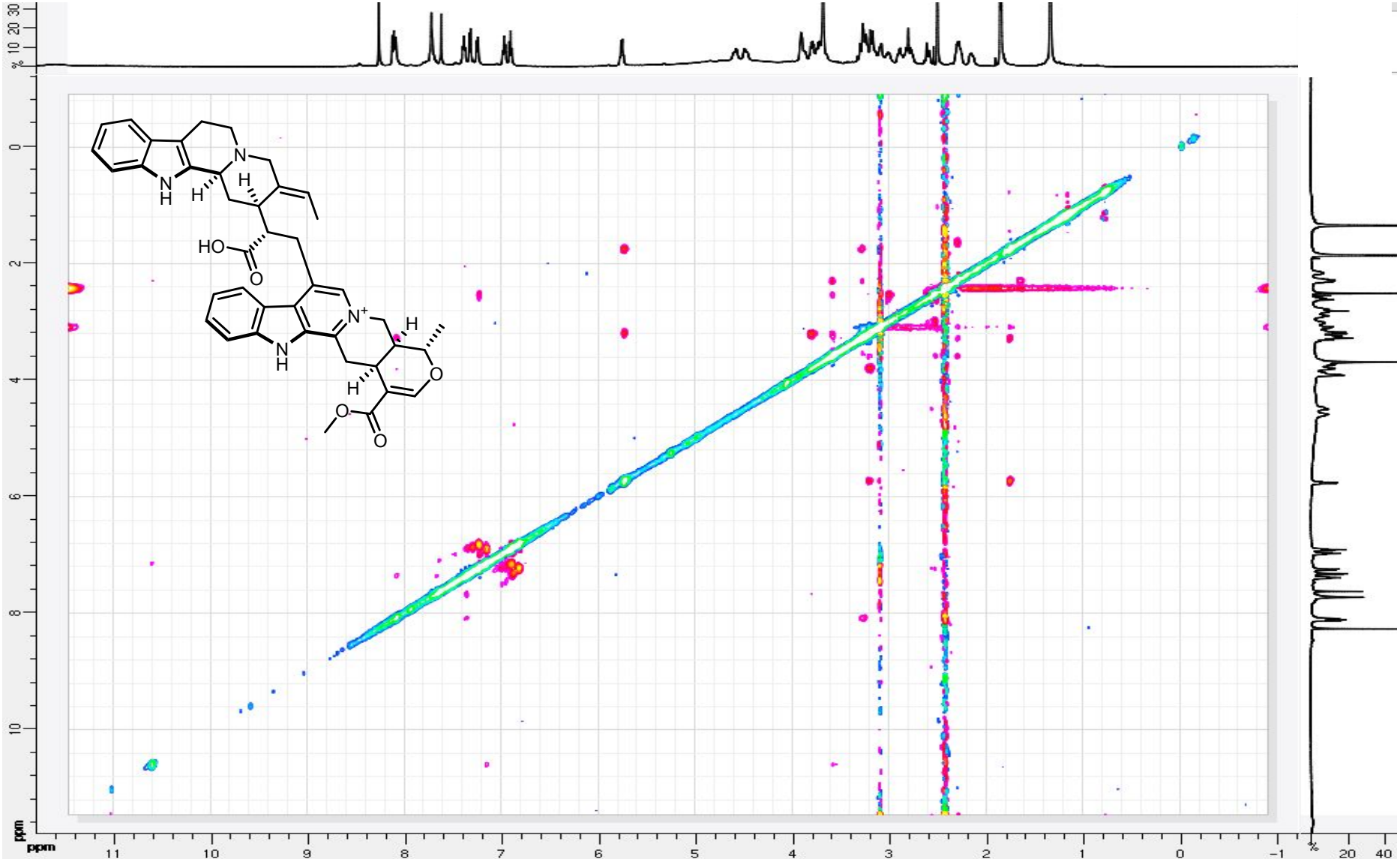


**Figure S34.** $^{1}$H NMR spectrum (400 MHz, DMSO-$d_6$) of alstonine 6-methylpropionate (**5**)

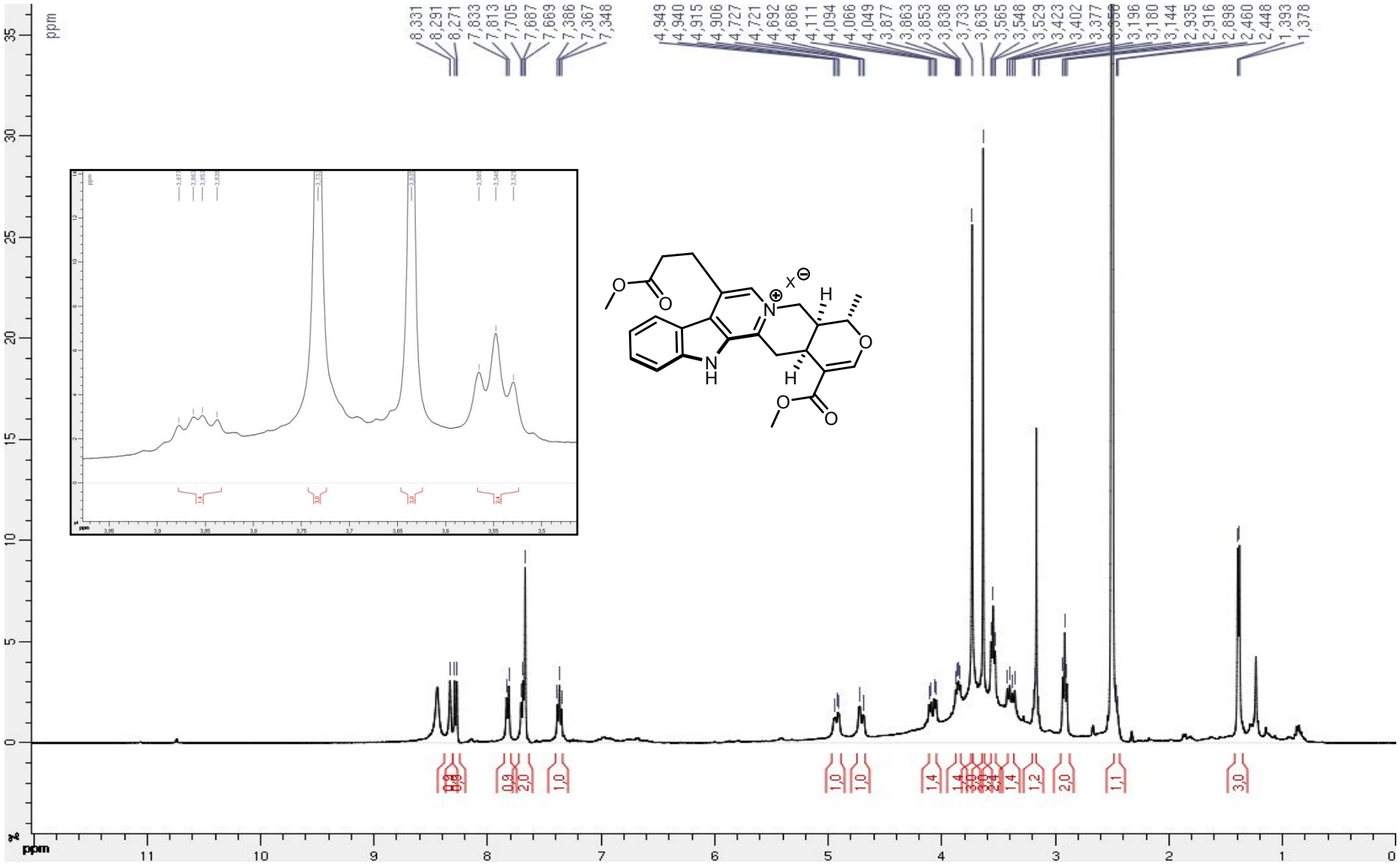


**Figure S35.** $^{13}$C NMR spectrum (100 MHz, DMSO-$d_6$) of alstonine 6-methylpropionate (**5**)

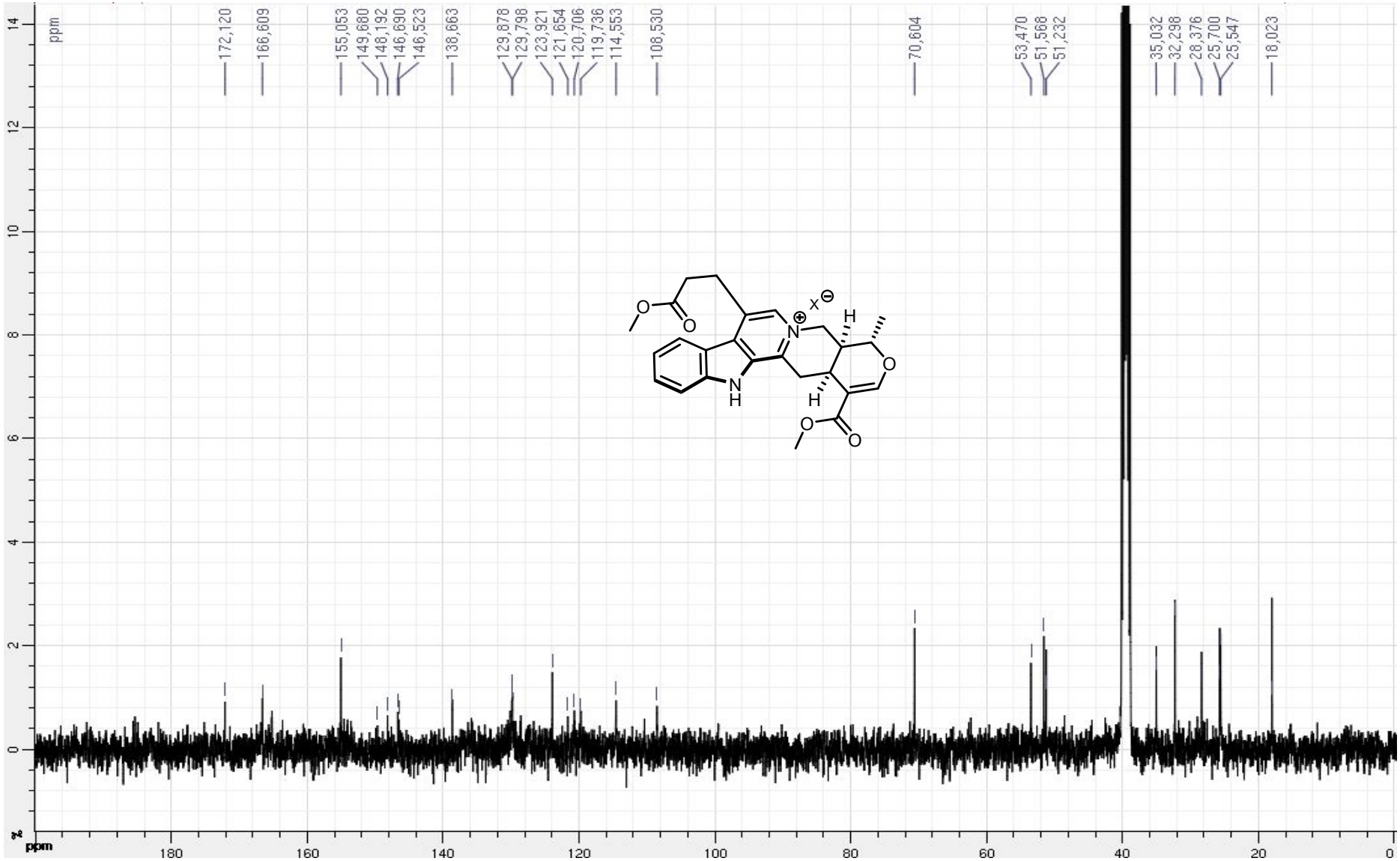


**Figure S36.** COSY spectrum (400 MHz, DMSO-$d_6$) of alstonine 6-methylpropionate (**5**)

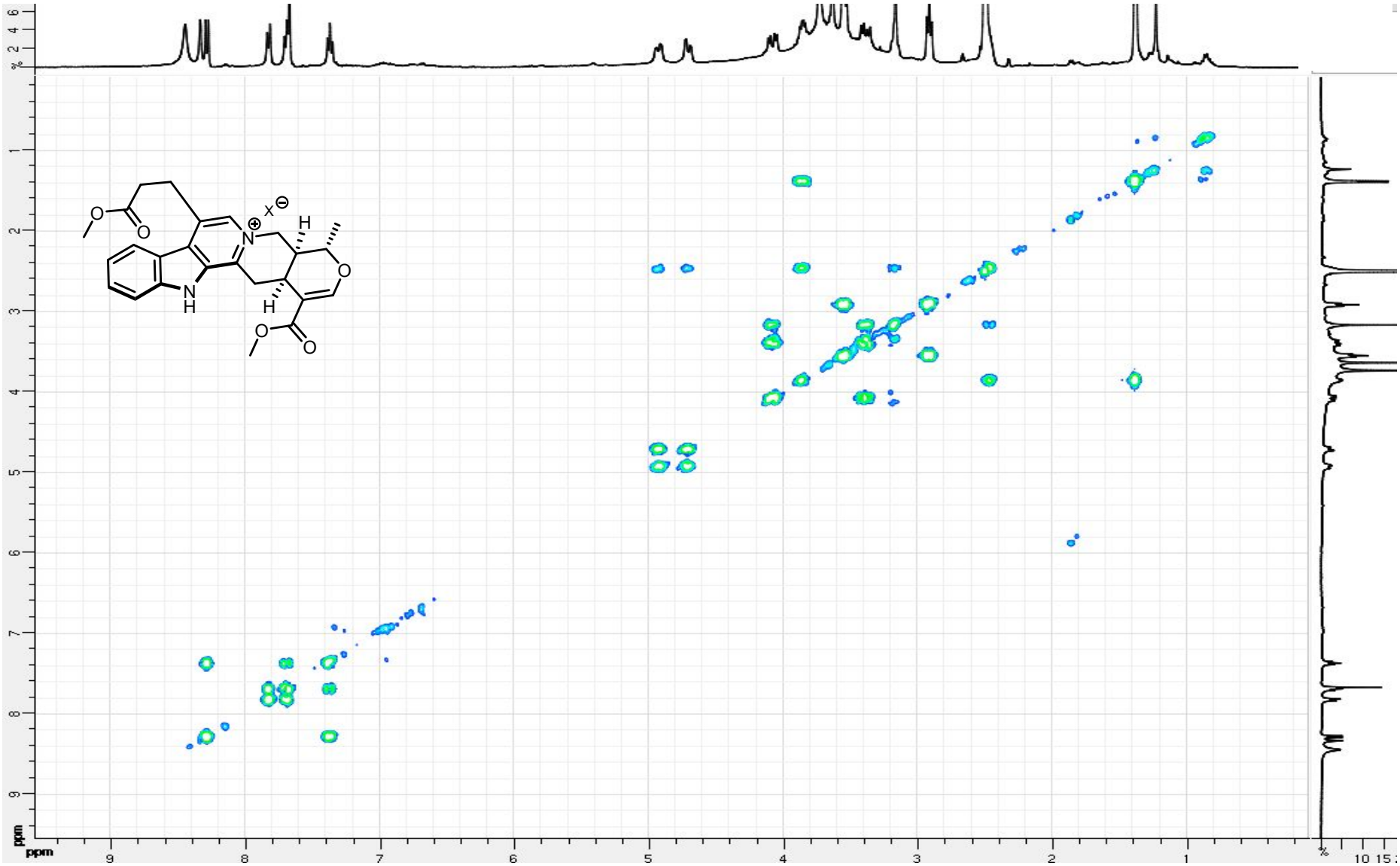


**Figure S37.** HSQC spectrum (400 MHz, DMSO-$d_6$) of alstonine 6-methylpropionate (**5**)

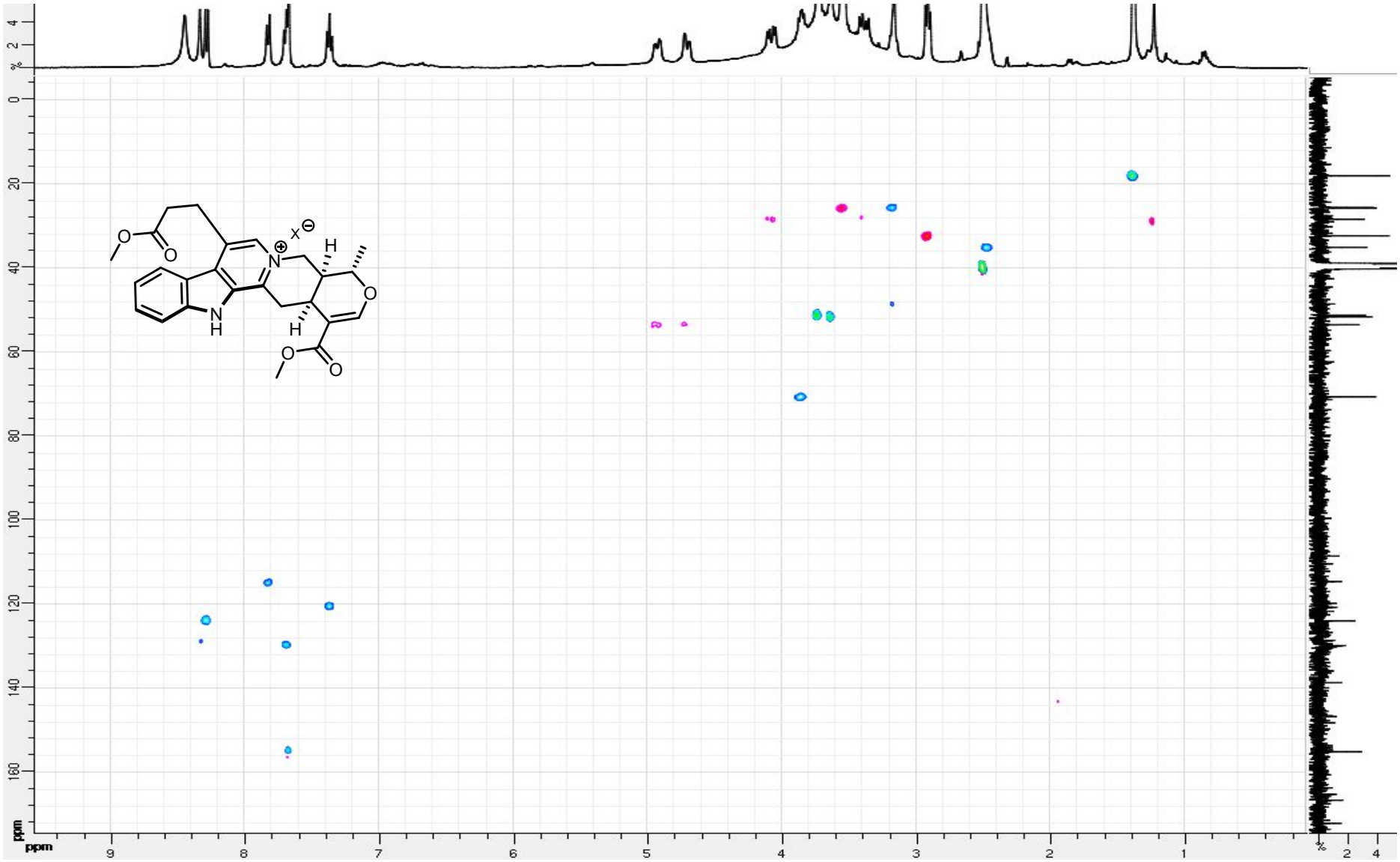


**Figure S38.** HMBC spectrum (400 MHz, DMSO-$d_6$) of alstonine 6-methylpropionate (**5**)

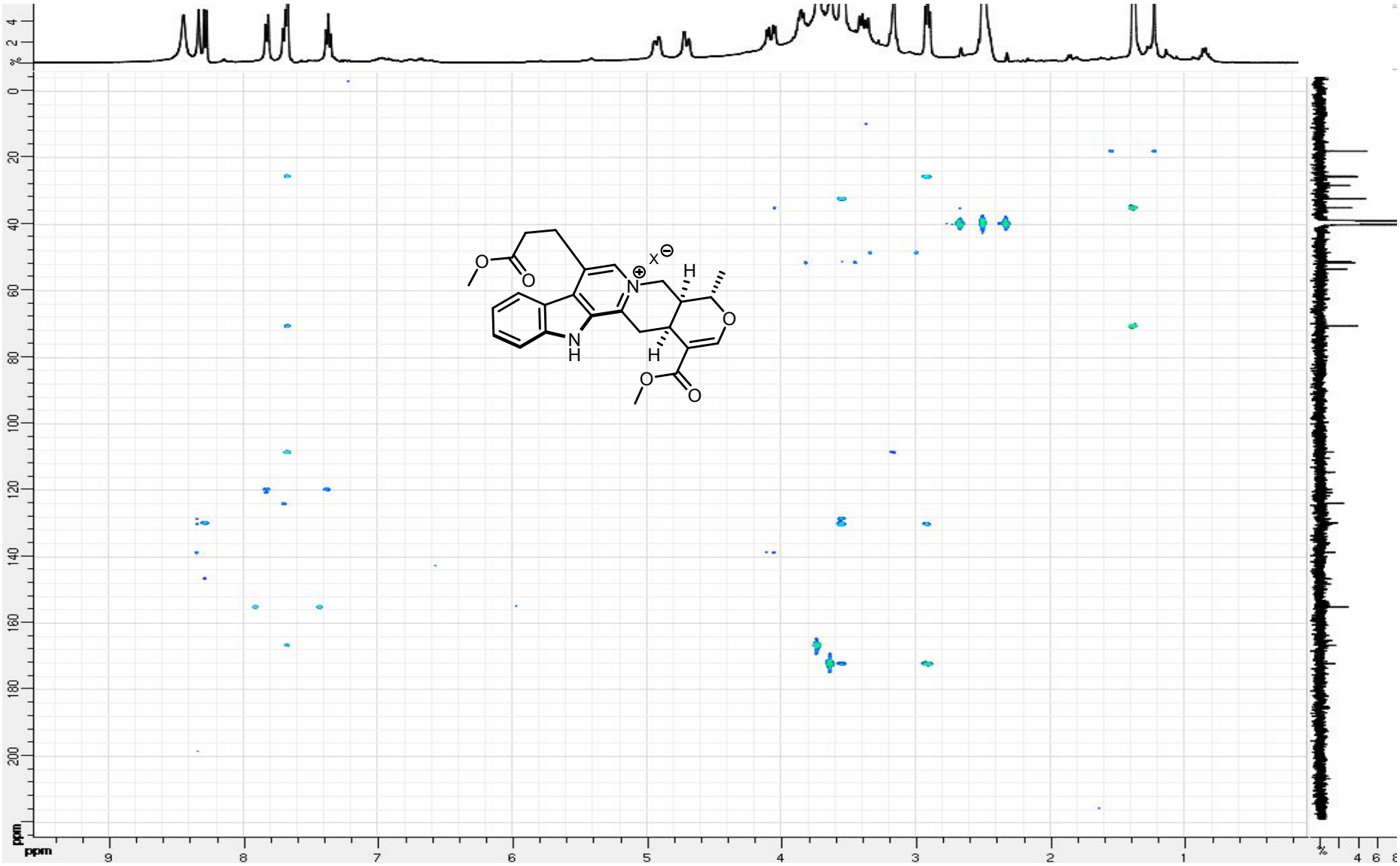


**Figure S39.** NOESY spectrum (400 MHz, DMSO-$d_6$) of alstonine 6-methylpropionate (**5**)

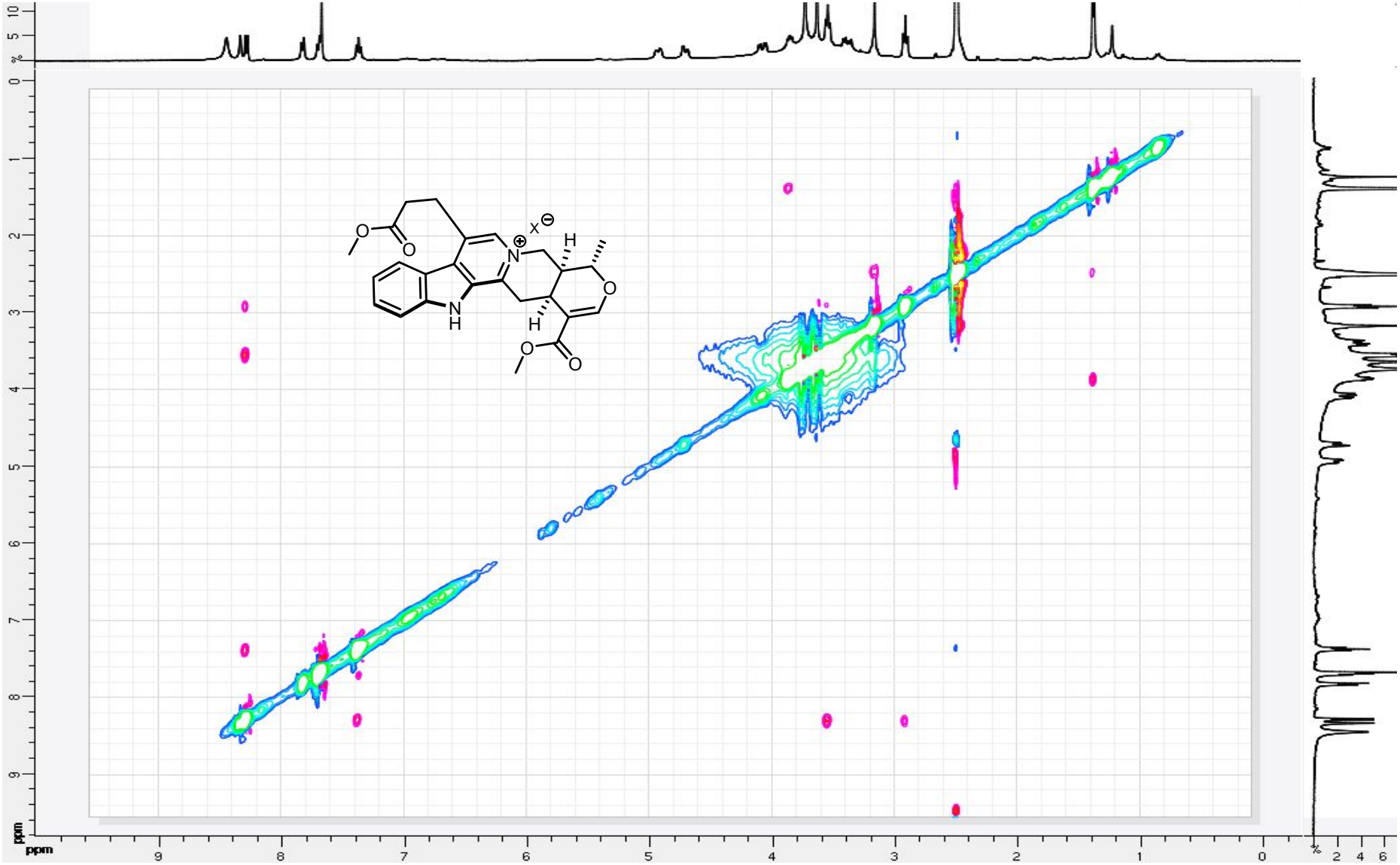


**Figure S40.** ECD and UV spectra of **1**

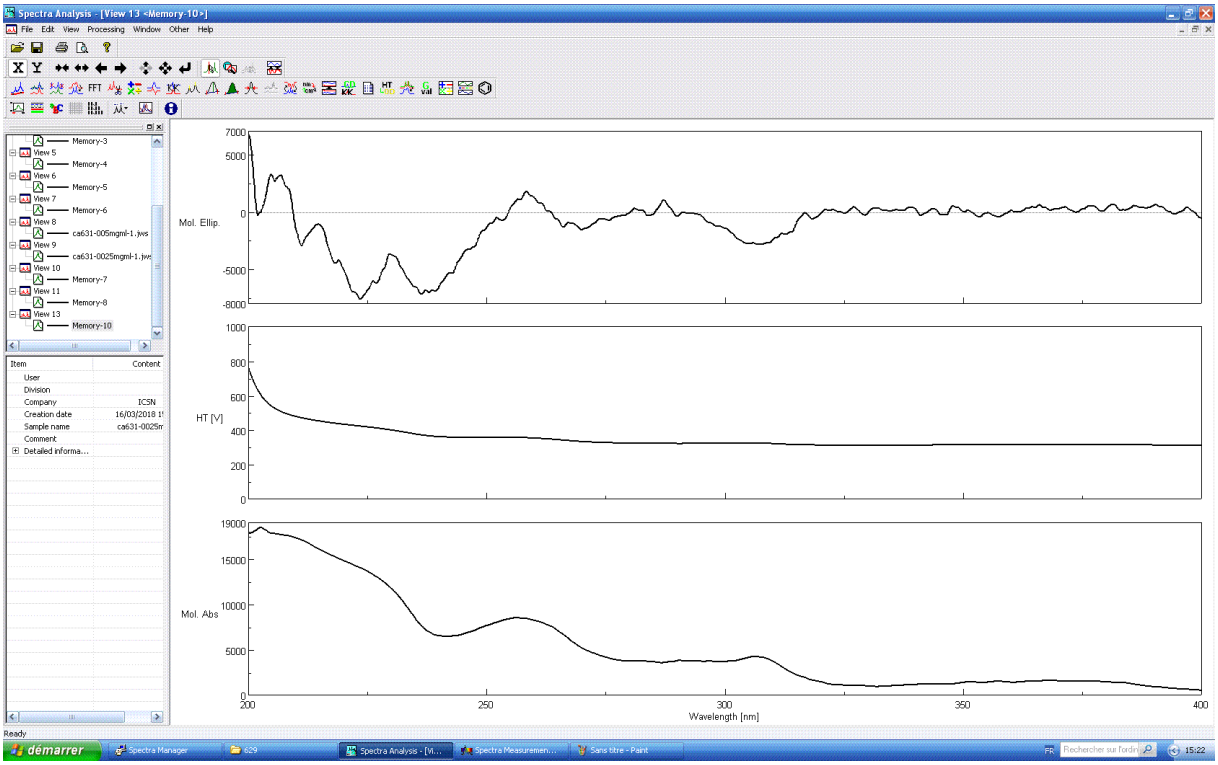


**Figure S40.** ECD and UV spectra of **2**

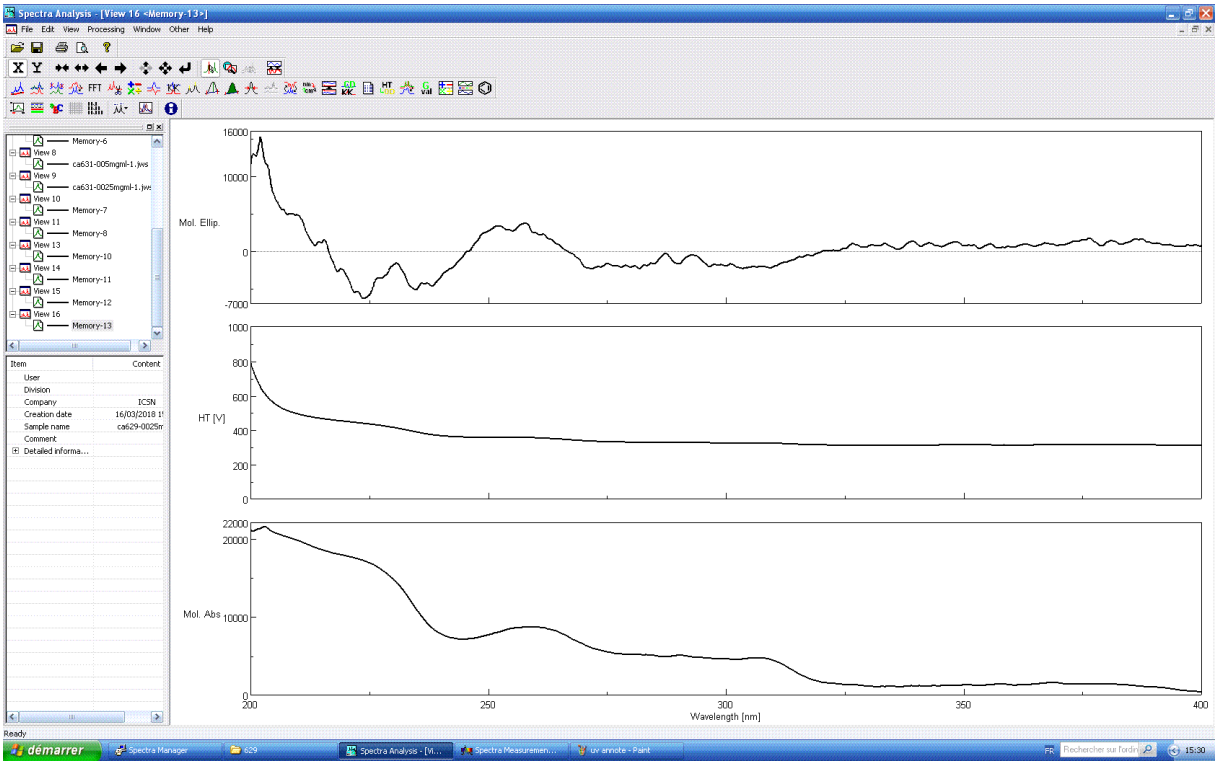


**Figure S40.** ECD and UV spectra of **3**

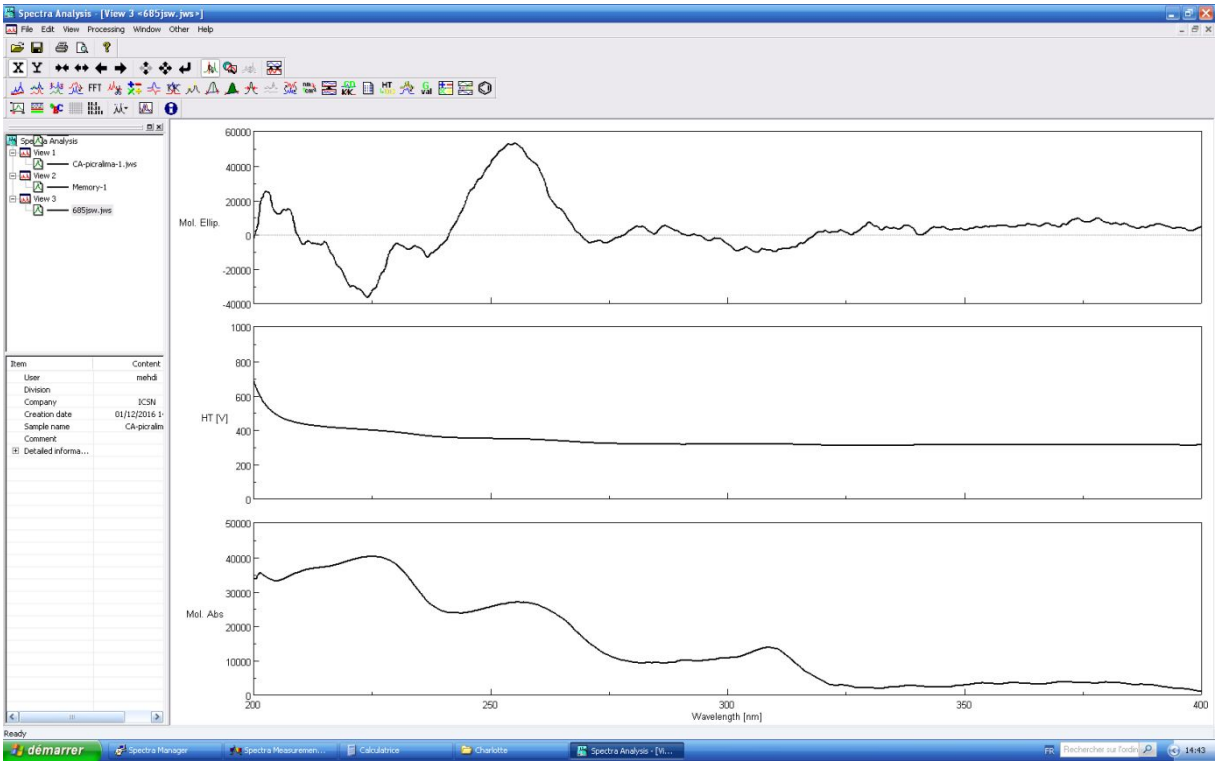


**Figure S40.** ECD and UV spectra of **4**

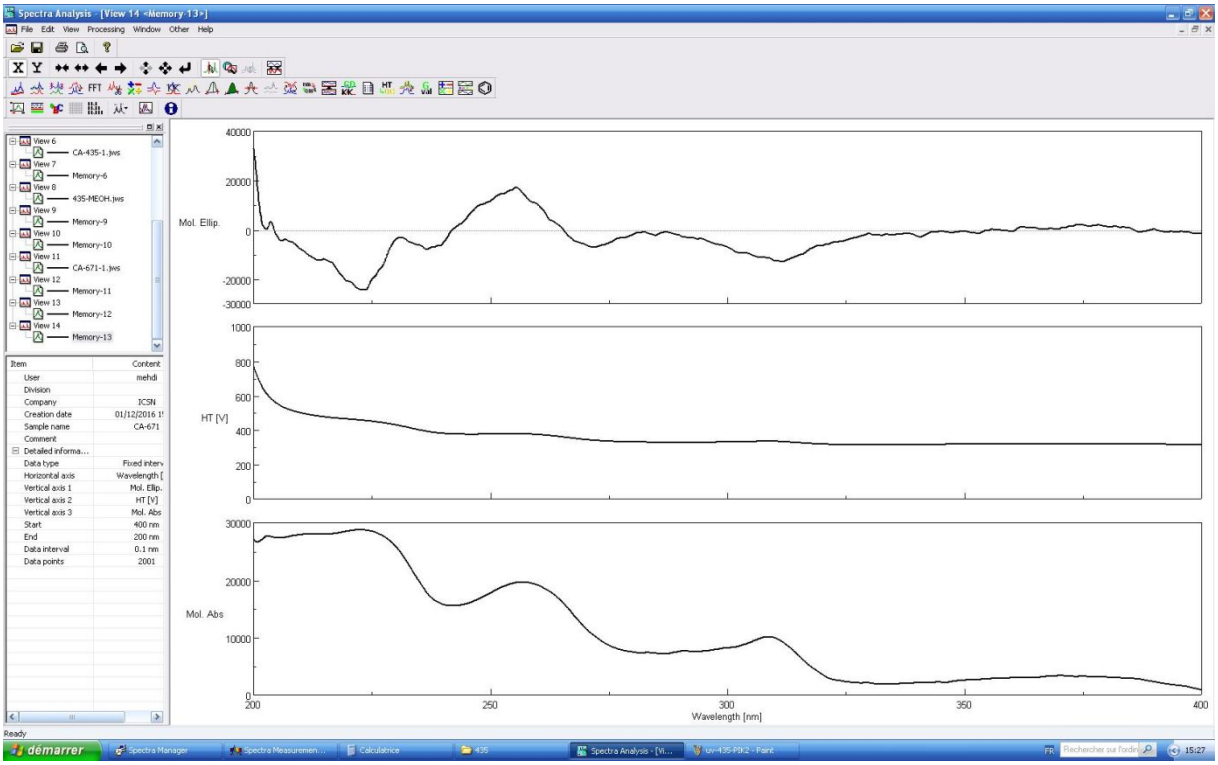
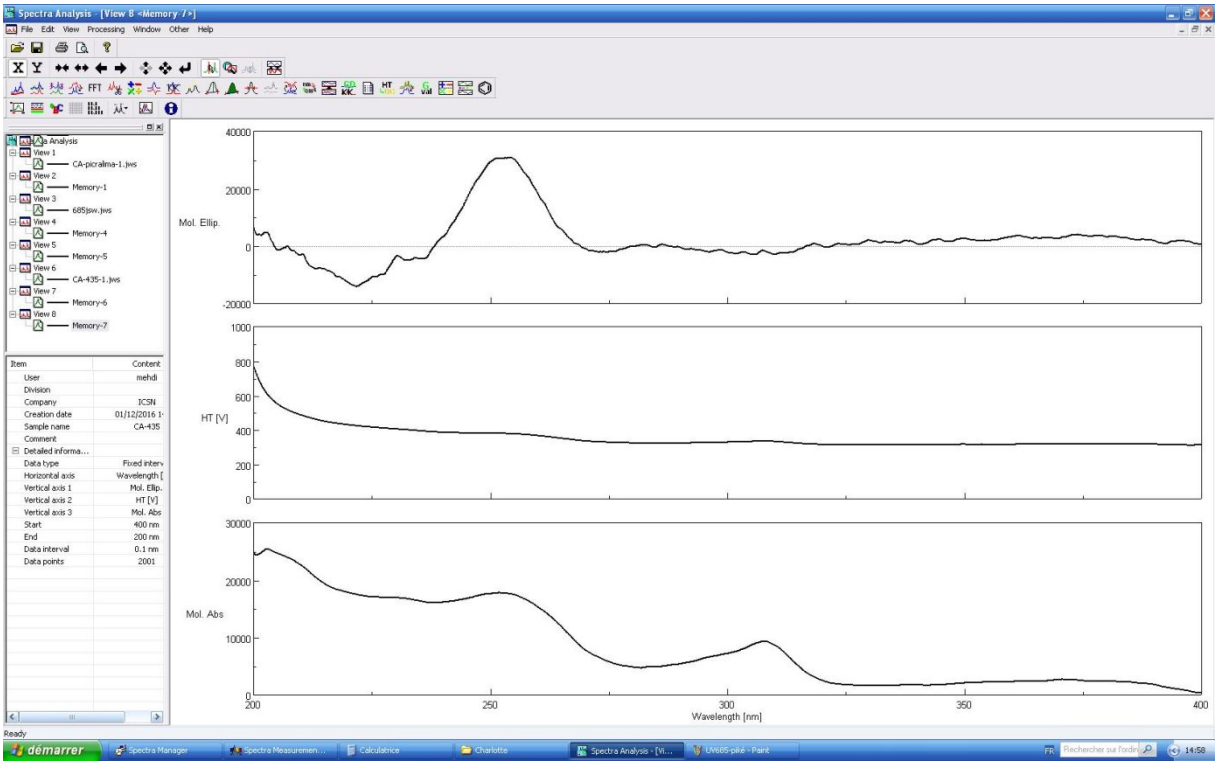


**Figure S40.** ECD and UV spectra of **5**



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