

Supporting Information

Functionalisation of Vitamin B₁₂ Derivatives with a Cobalt β-Phenyl Ligand Boosters Antimetabolite Activity in Bacteria

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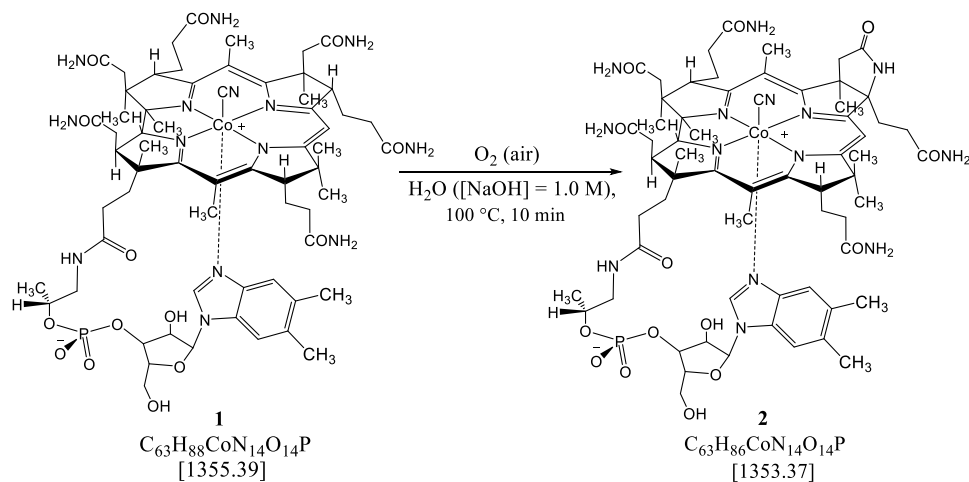
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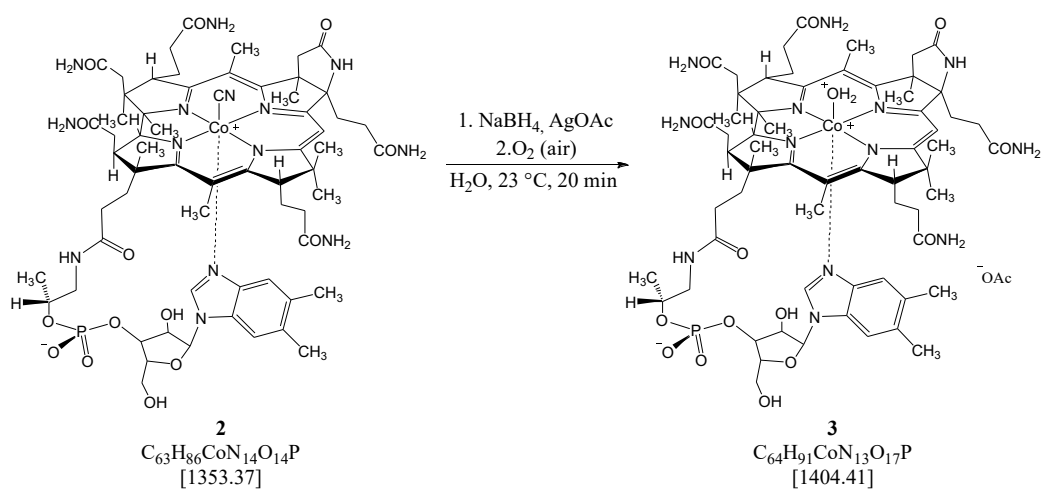
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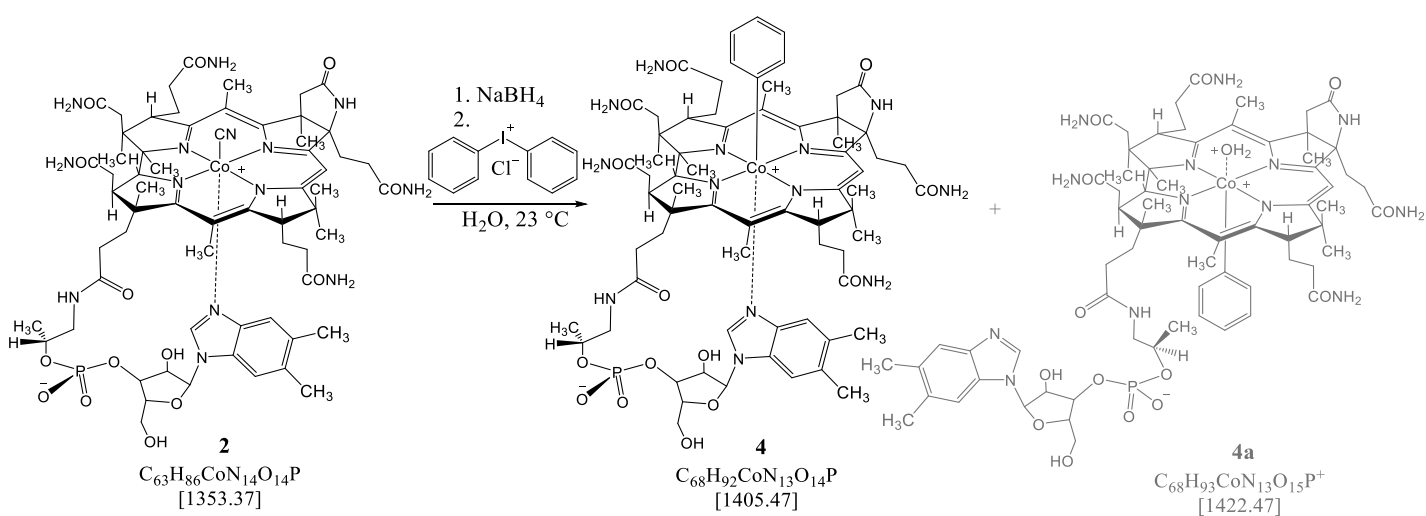
Reaction Schemes.



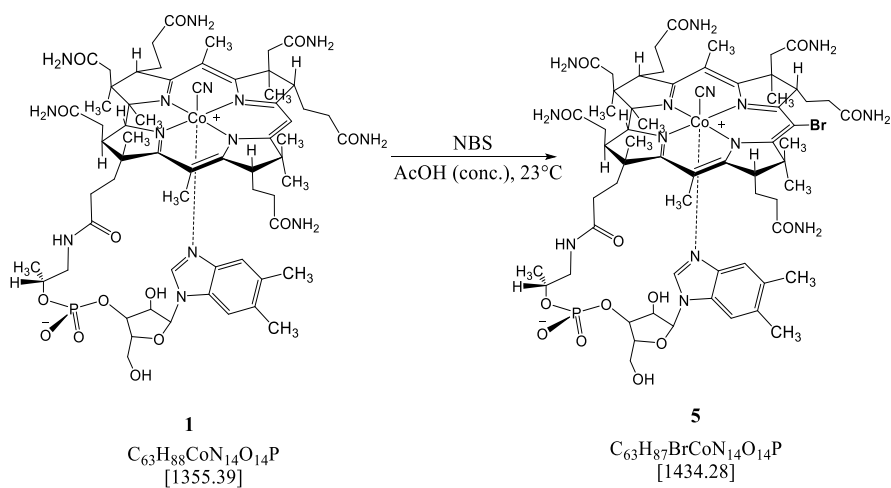
Scheme S1. Synthesis of Co_β -cyanocobalamin-*c*,8-lactam (**2**).



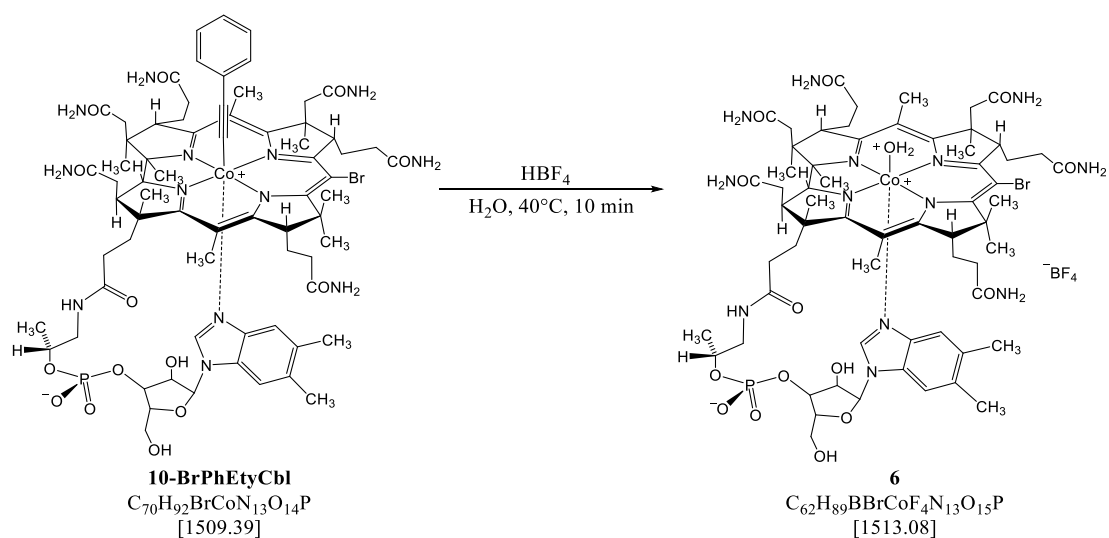
Scheme S2. Synthesis of Co_β -aquacobalamin-*c*,8-lactam acetate (**3**)



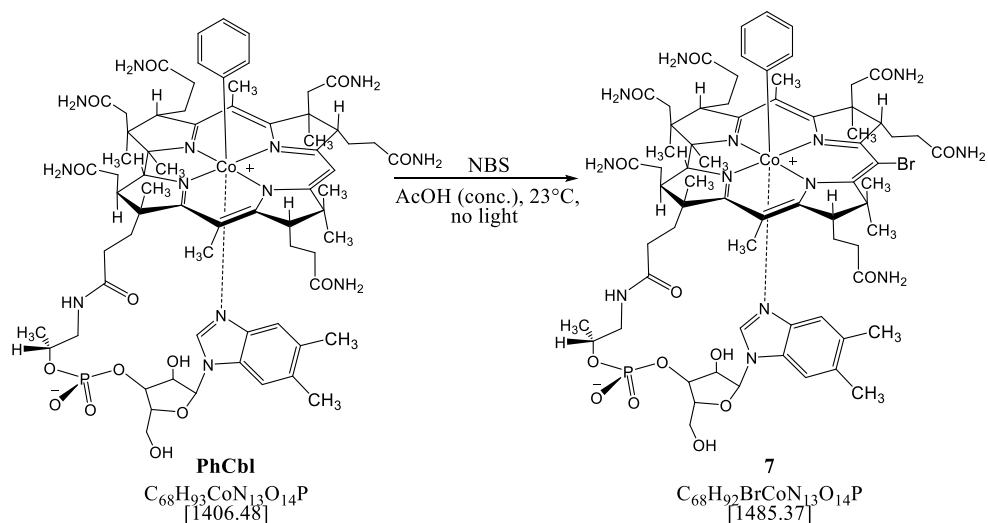
Scheme S3. Synthesis of Co_β -phenylcobalamin-*c*,8-lactam (**4**) and its side product Co_α -phenylcobalamin-*c*,8-lactam (**4a**, not characterized).



Scheme S4. Synthesis of 10-bromo-Co β -cyanocobalamin (**5**).



Scheme S5. Synthesis of 10-bromo-Co β -aquacobalamin tetrafluoroborate (**6**) from intermediate 10-Bromo-Co β -phenylethynylcobalamin (reported in ref^[S41]).



Scheme S6. Synthesis of 10-bromo-Co β -phenylcobalamin (**7**) from Co β -phenylcobalamin (reported in ref^[S33]).

Atom Numbering.

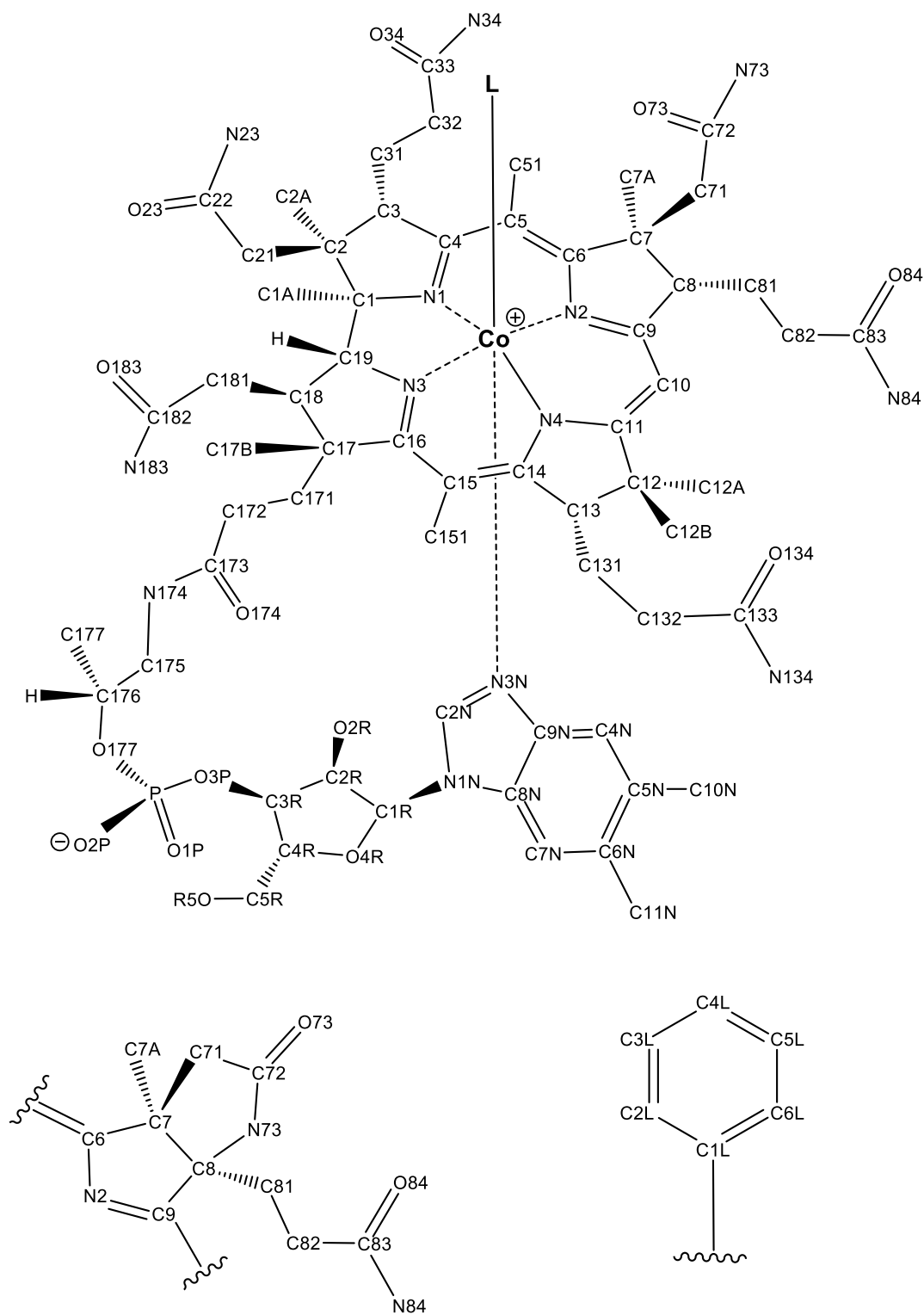


Figure S1. Atom numbering of vitamin B₁₂ (1) and its analogues. *Bottom:* Atom numbering of the c,8-lactam ring in derivatives 2 and 4, as well as nomenclature of the phenyl ligand of β -PhCbl, 4 and 7.

NMR and optical Spectra.

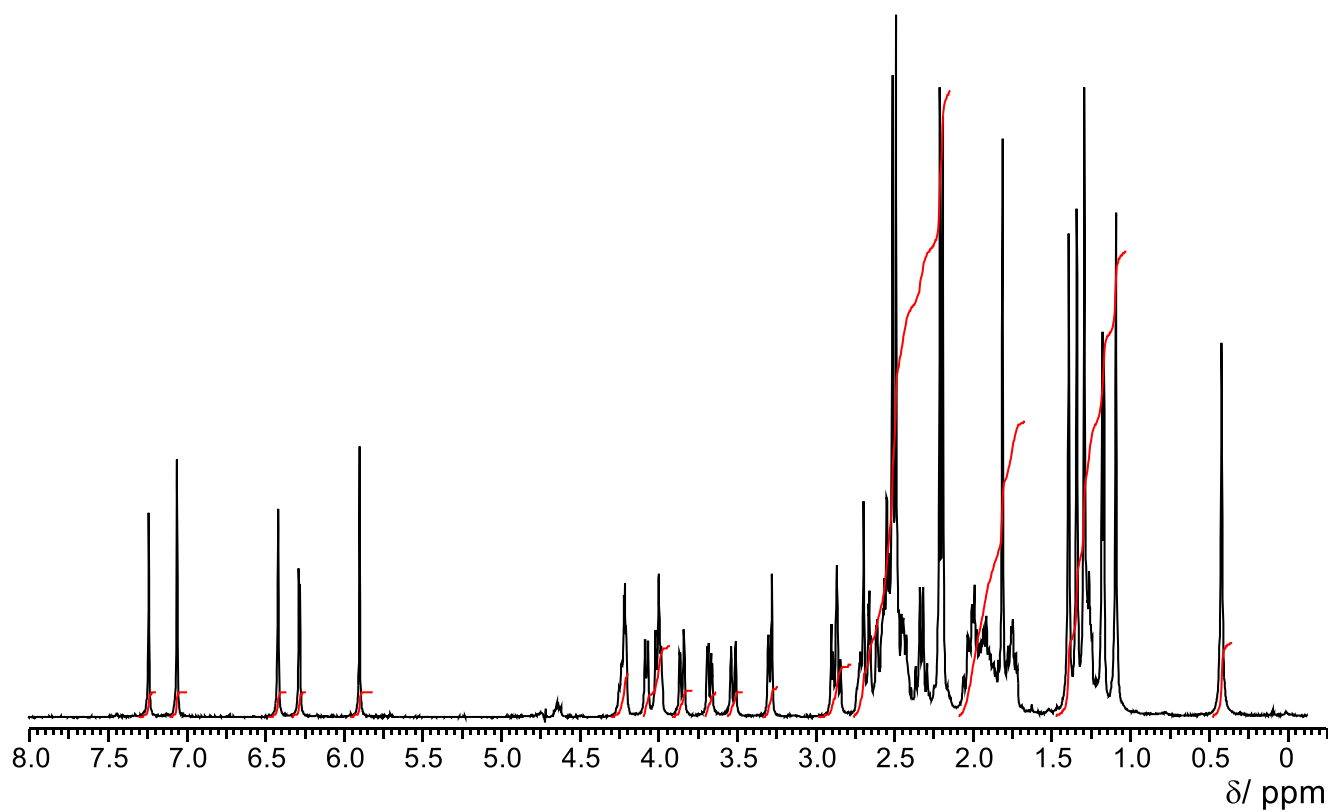


Figure S2. ¹H-NMR spectrum of **2** (500 MHz, D₂O (presat), 298 K, 4.1 × 10⁻³ M).

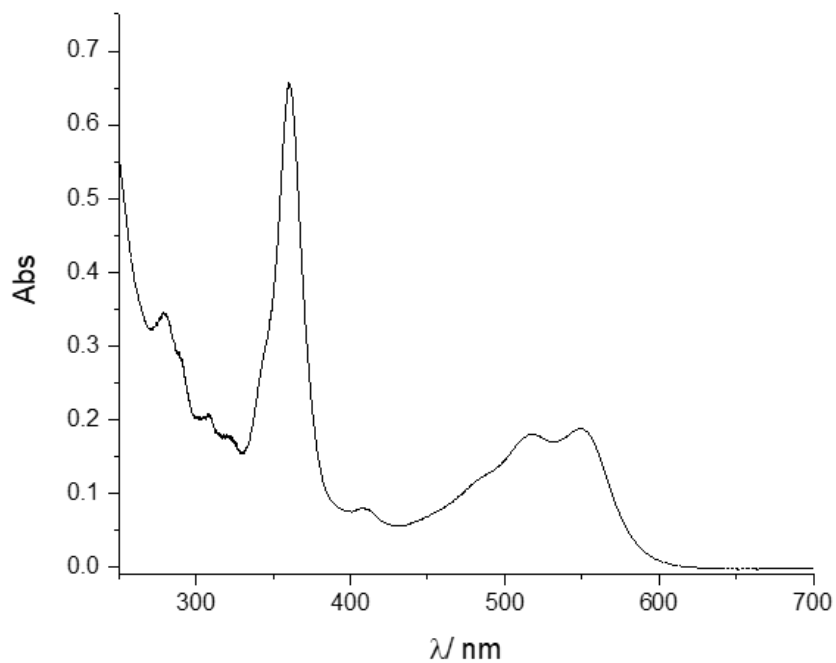


Figure S3. UV/Vis spectrum of **2** (H₂O, 4.1 × 10⁻⁵ M).

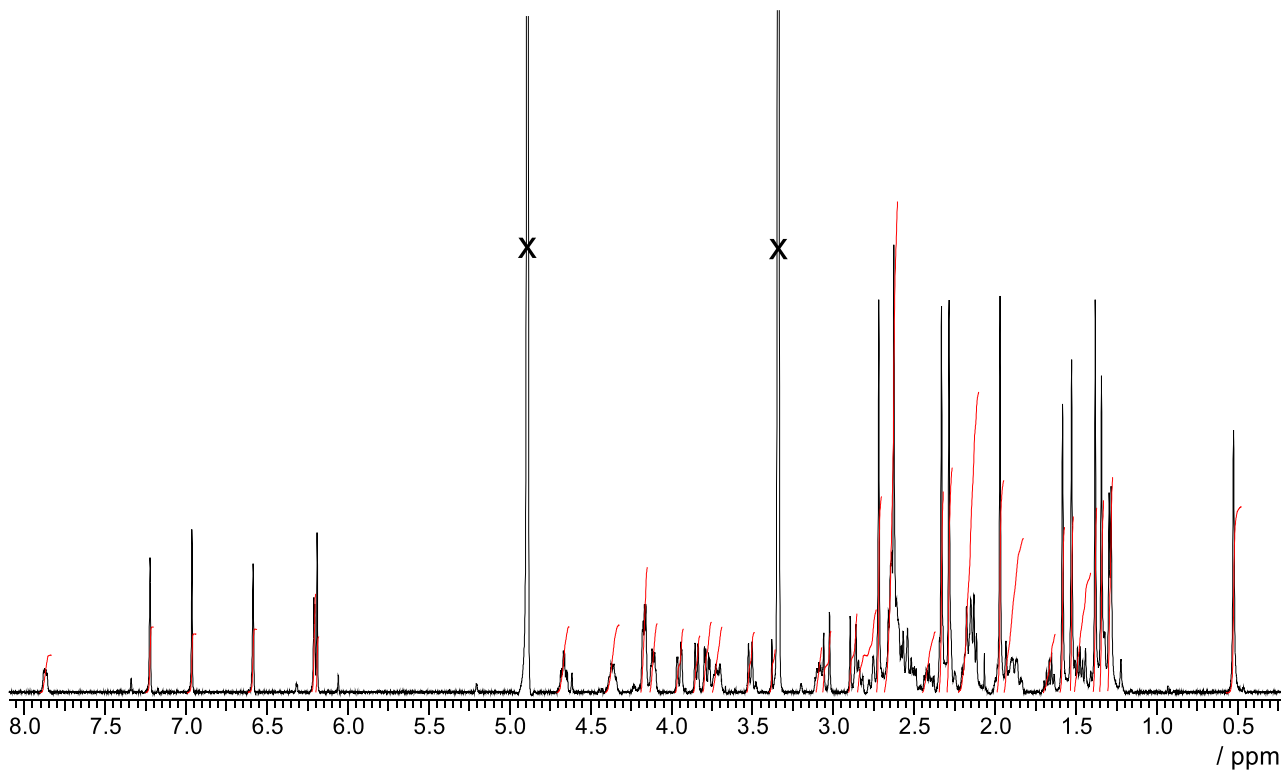


Figure S4. $^1\text{H-NMR}$ spectrum of **3** (500 MHz, CD_3OD , 298 K, $7.3 \cdot 10^{-3}$ M).

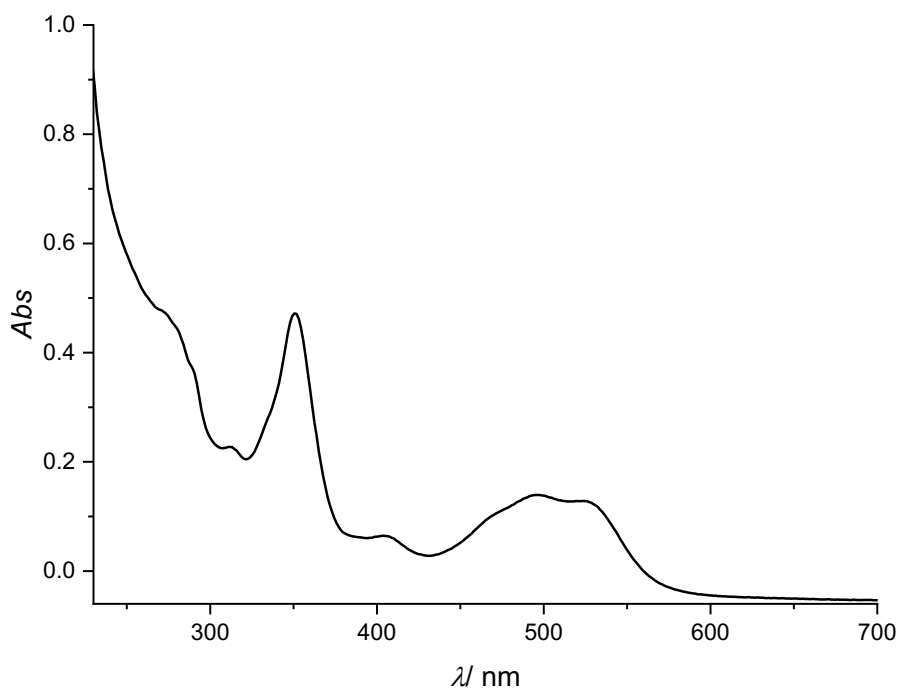


Figure S5. UV/Vis spectrum of **3** (H_2O , $c = 2.2 \cdot 10^{-5}$ M).

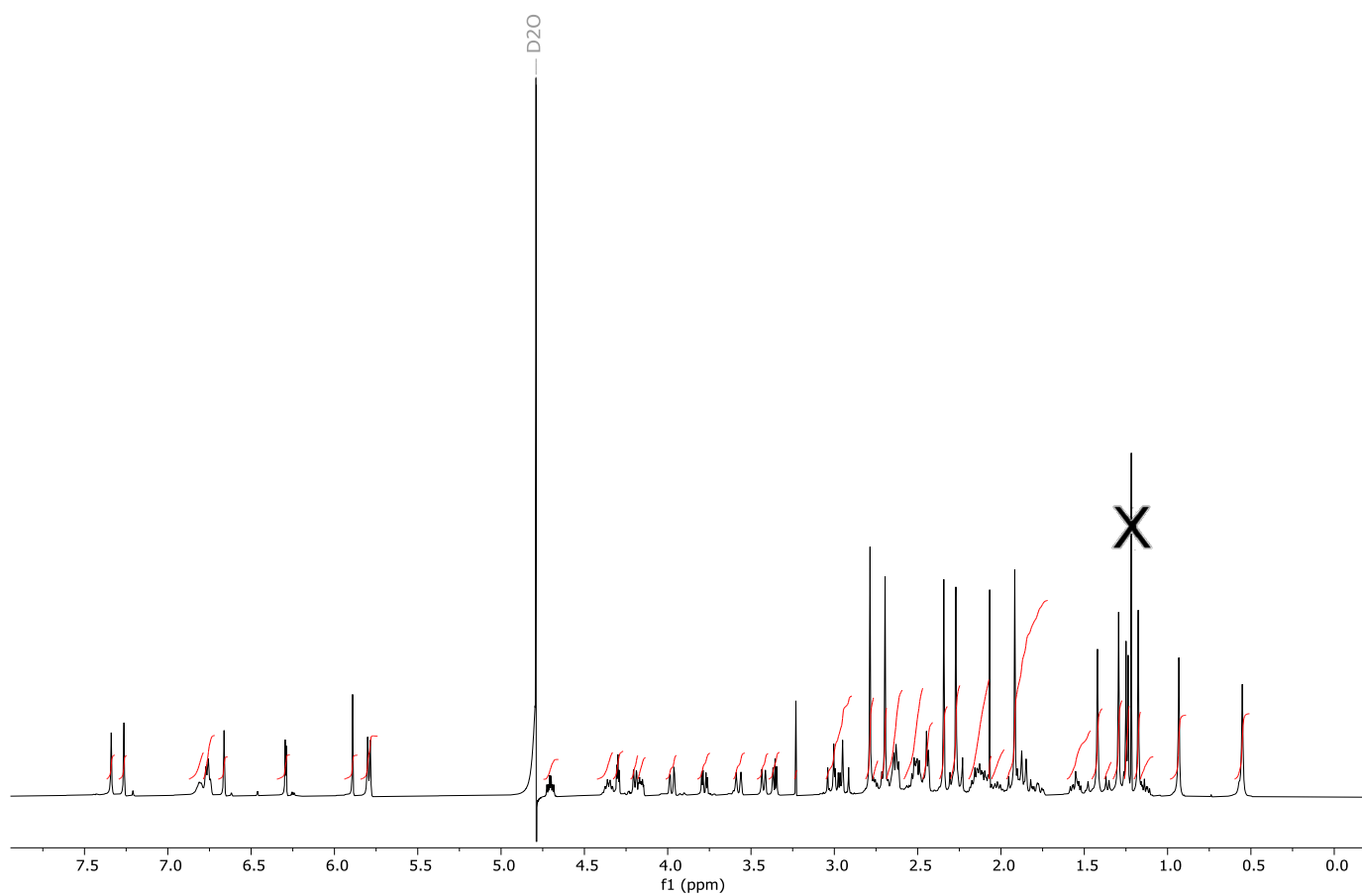


Figure S6. ^1H -NMR spectrum of **4** (500 MHz, D_2O (presat), 298 K, 1.2×10^{-2} M).

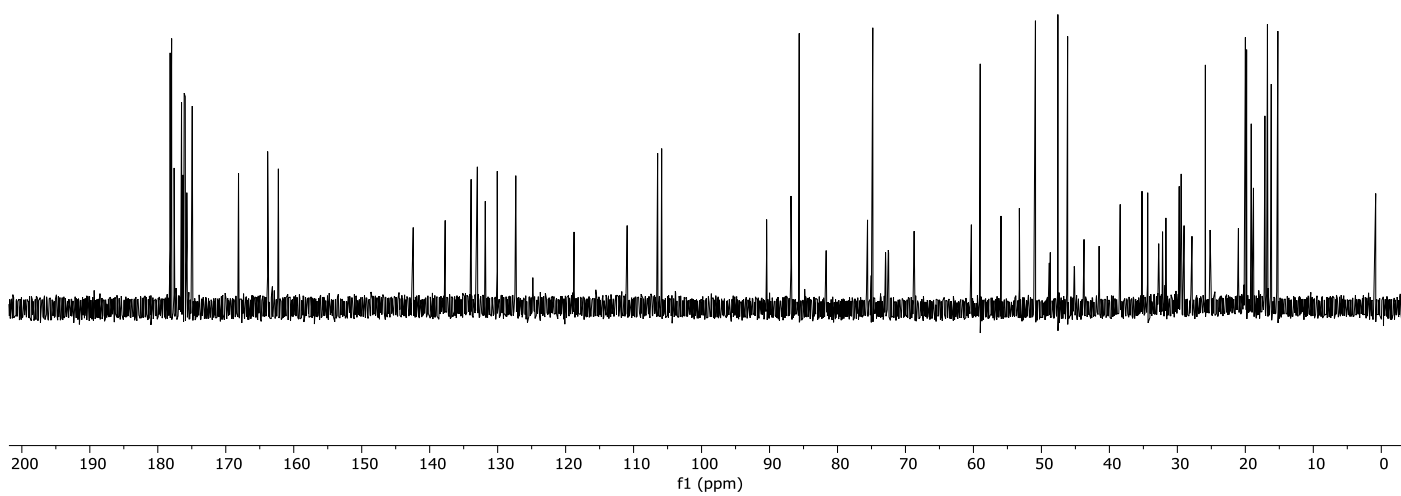


Figure S7. ^{13}C -NMR spectrum of **4** (126 MHz, D_2O , 298 K, 1.2×10^{-2} M).

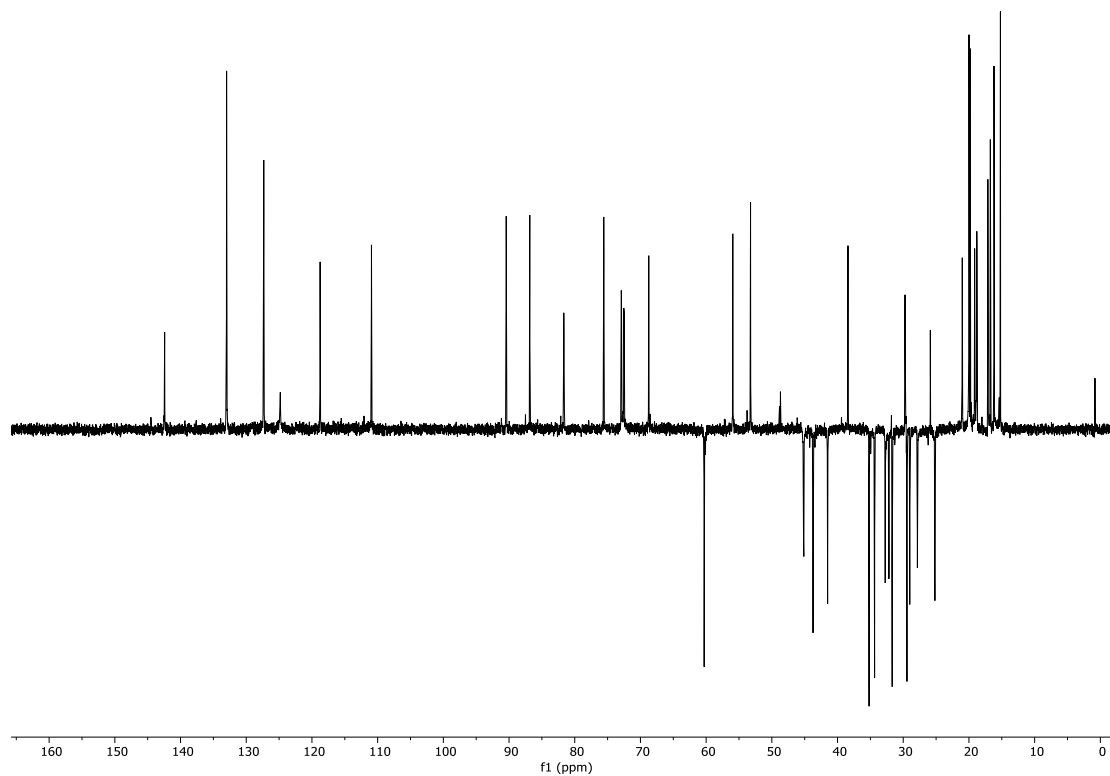


Figure S8. DEPT 135-NMR spectrum of **4** (126 MHz, D₂O, 298 K, 1.2 x 10⁻² M).

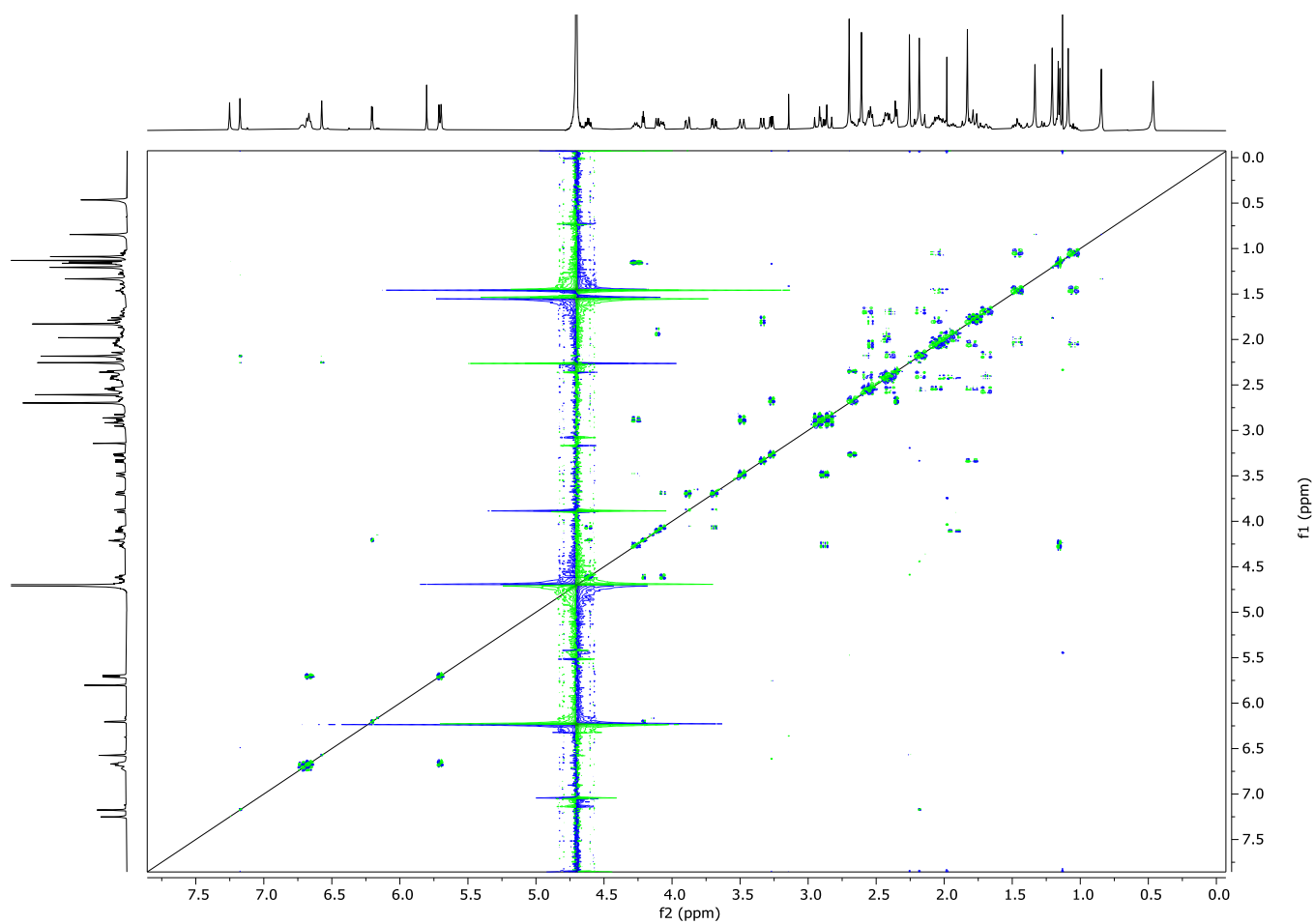


Figure S9. ¹H-¹HDFQ-COSY spectrum of **4** (500 MHz, D₂O, 298 K, 1024 x 2560 p, 12 scans, 1.2 x 10⁻² M).

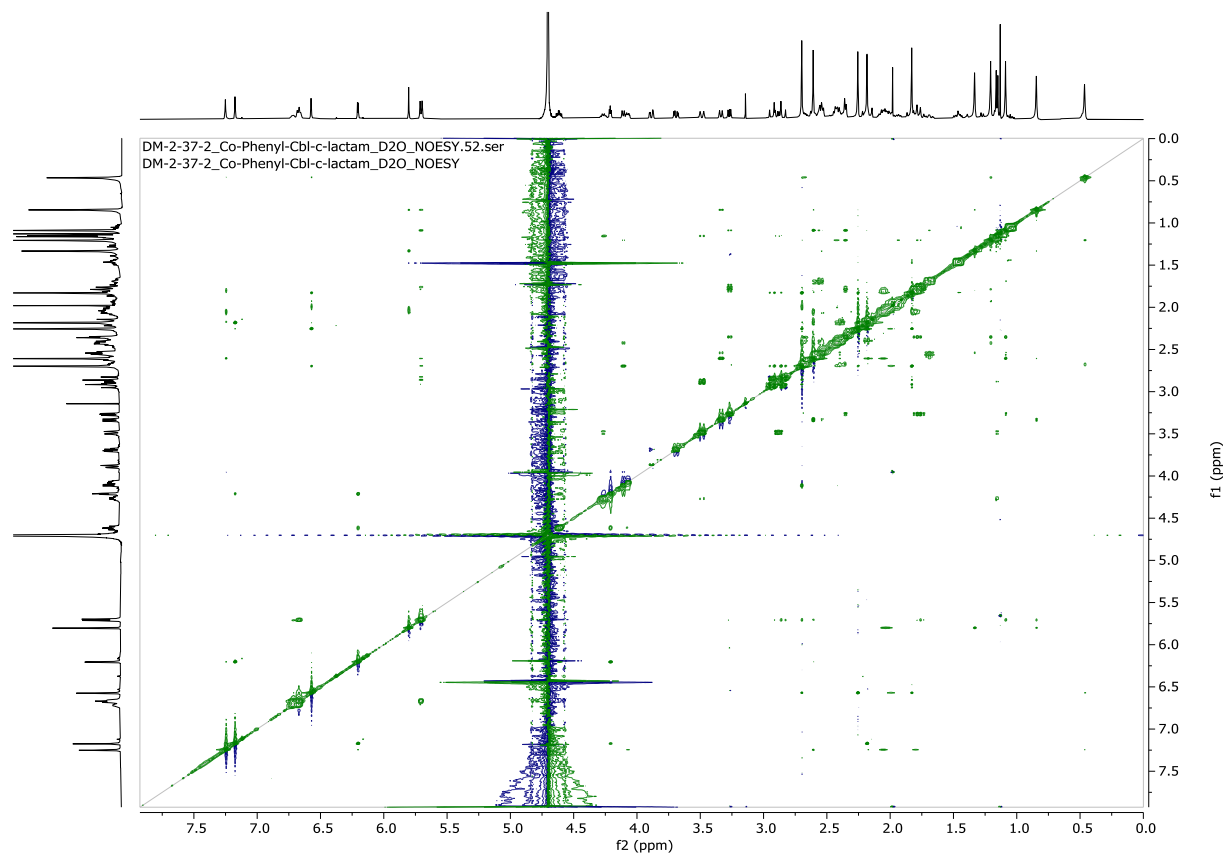


Figure S10. ^1H - ^1H NOESY spectrum of **4** (500 MHz, D_2O , 298 K, 1024 x 1884 p, 16 scans, 1.2×10^{-2} M).

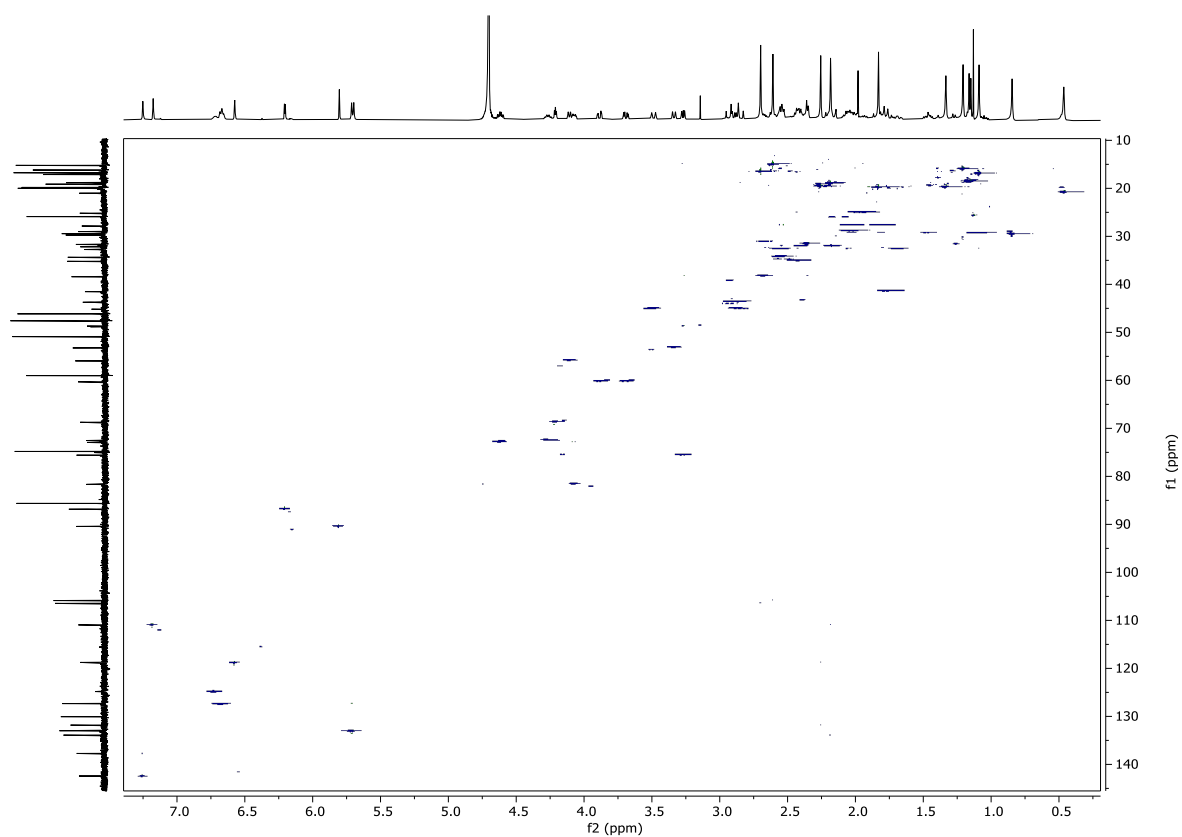


Figure S11. ^1H - ^{13}C HSQC spectrum of **4** (500 MHz, 126 MHz, D_2O (presat), 298 K, 1024 x 5120 p, 18 scans, 1.2×10^{-2} M).

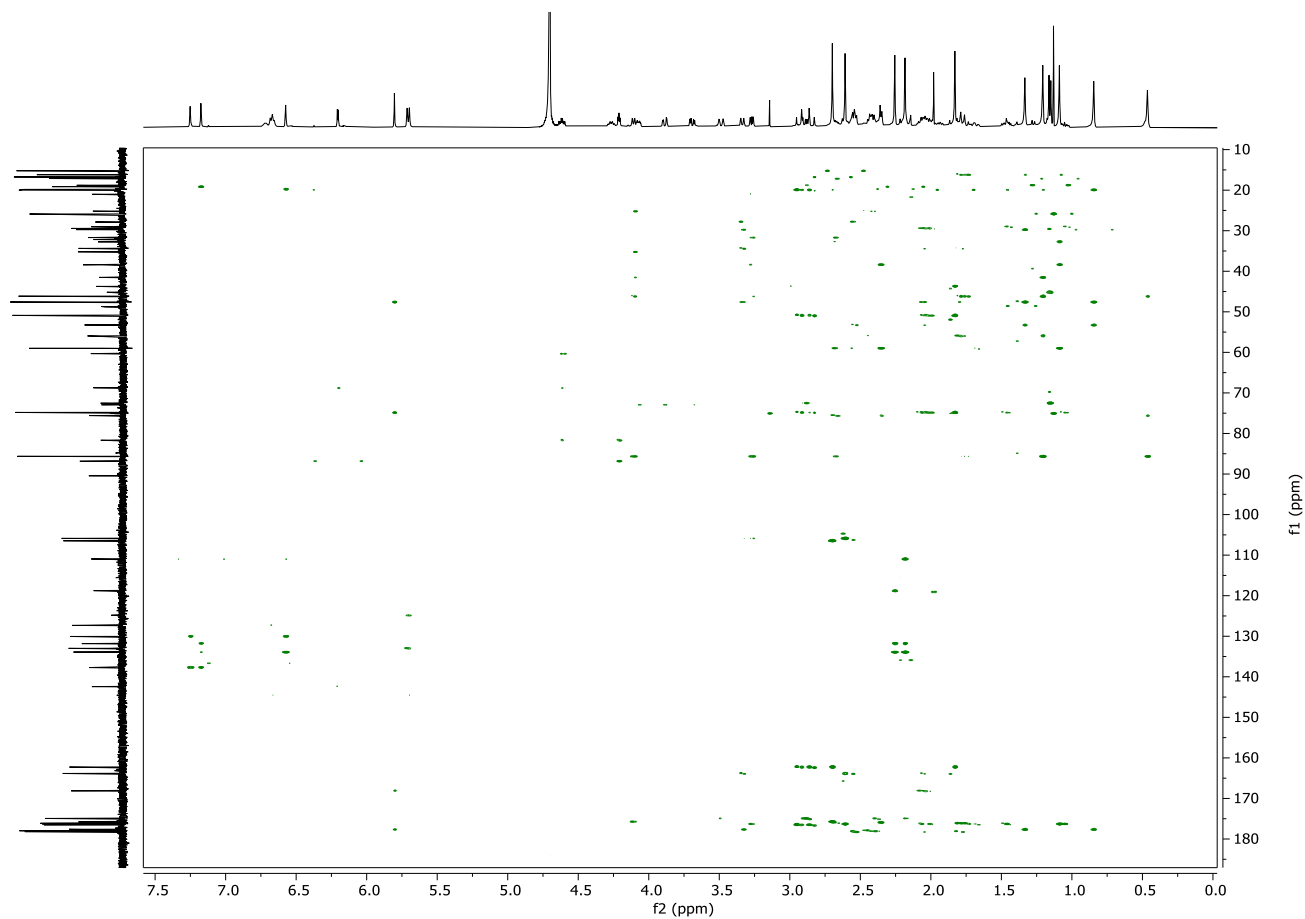


Figure S12. ^1H - ^{13}C -HMBC spectrum of **4** (500 MHz, 126 MHz, D_2O , 298 K, 1024 x 3000 p, 12 scans, 1.2×10^{-2} M).

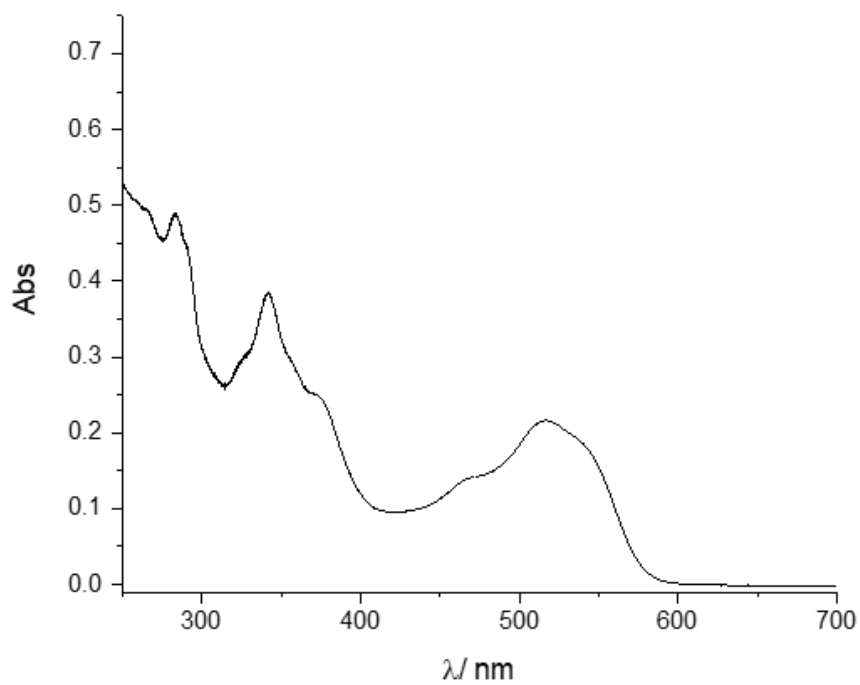


Figure S13. UV/Vis spectrum of **4** (H_2O , 3.9×10^{-5} M).

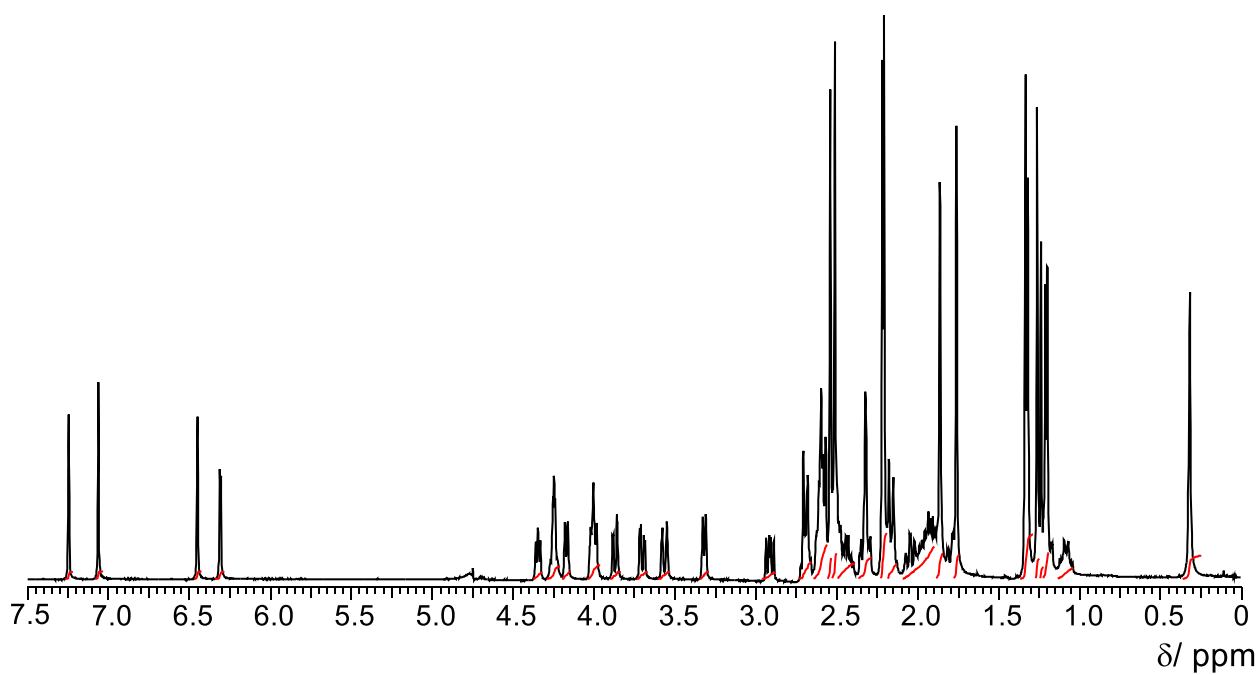


Figure S14. ¹H-NMR spectrum of **5** (500 MHz, D₂O (presat), 298 K, 4.9 × 10⁻³ M).

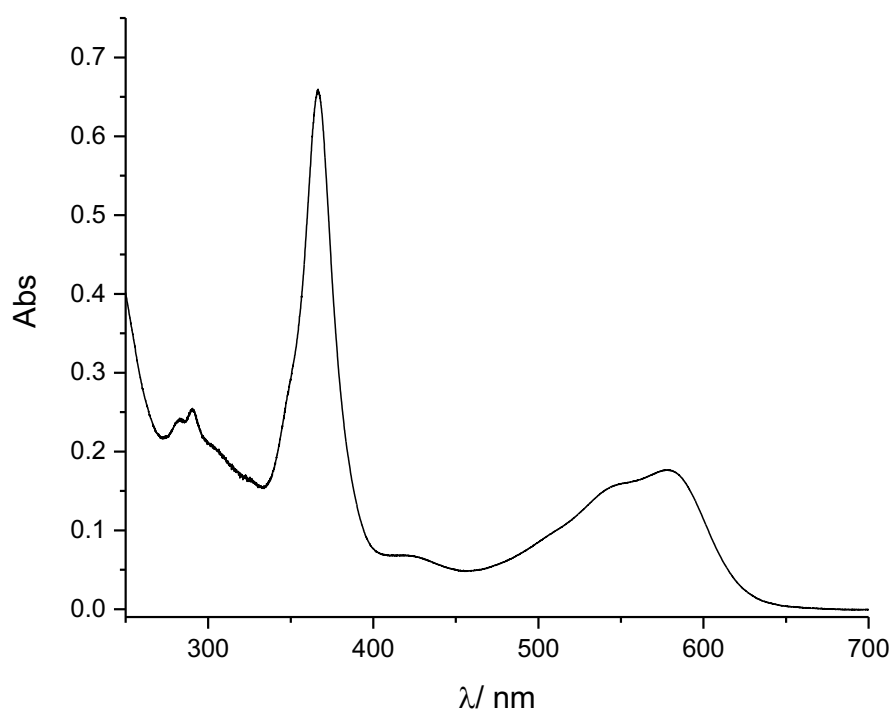


Figure S15. UV/Vis spectrum of **5** (H₂O, 4.9 × 10⁻⁵ M).

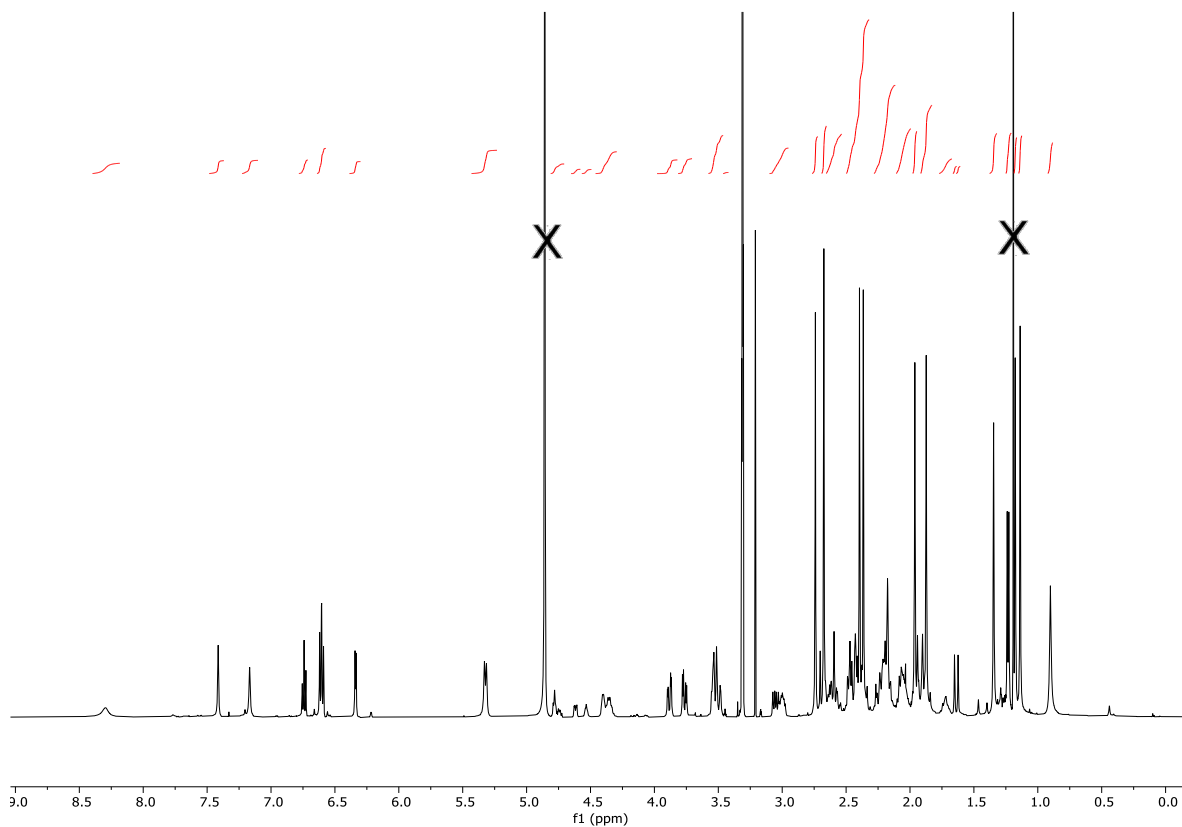


Figure S16. ^1H -NMR spectrum of **7** (500 MHz, CD_3OD (presat), 298 K, 8.7×10^{-3} M).

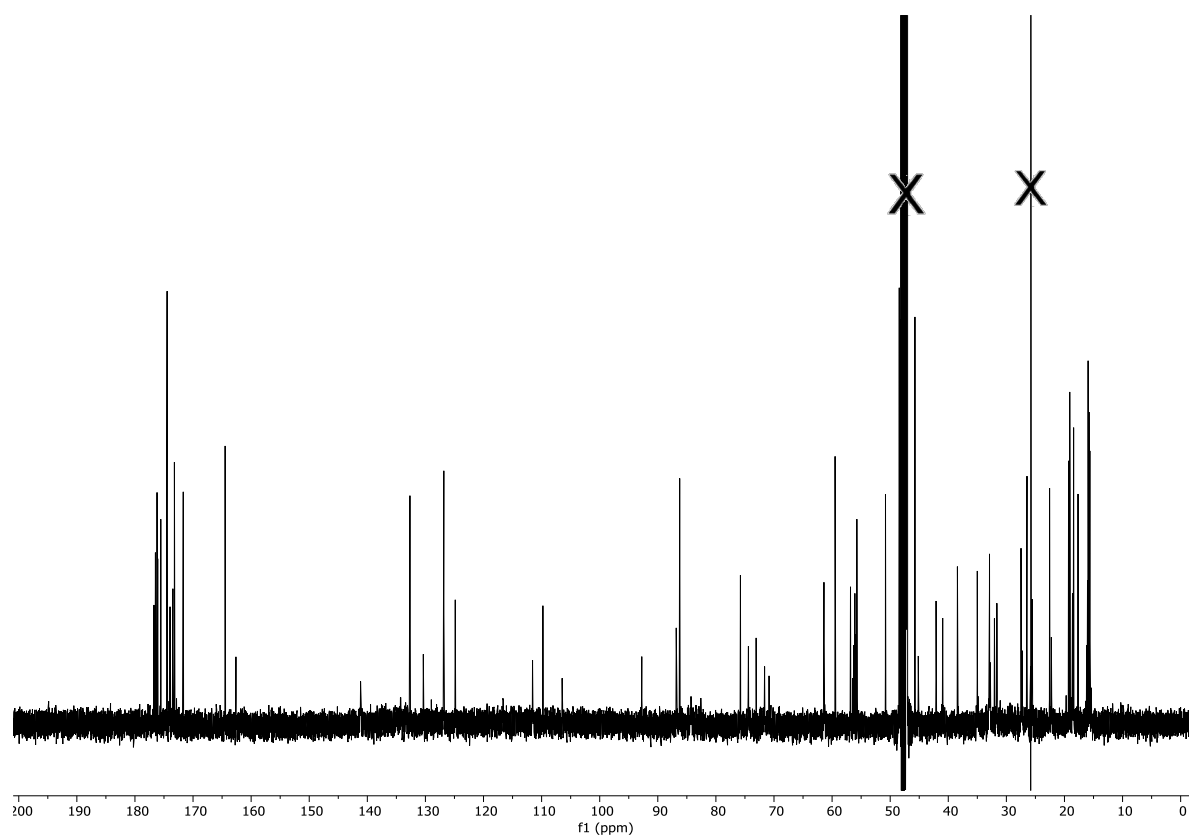


Figure S17. ^{13}C -NMR spectrum of **7** (126 MHz, CD_3OD (presat), 298 K, 8.7×10^{-3} M).

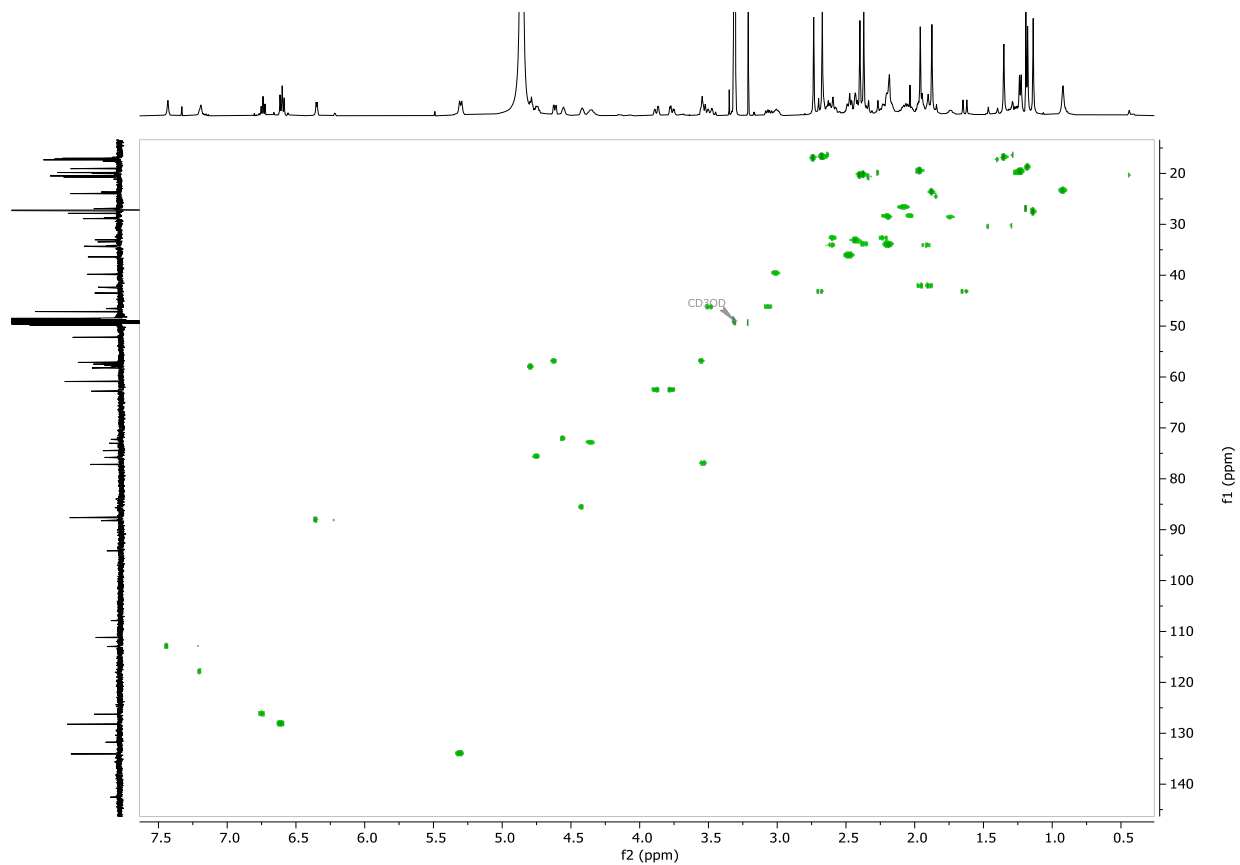


Figure S18. ^1H - ^{13}C HSQC spectrum of **7** (500 MHz, 126 MHz, CD_3OD , 298 K, 1024 x 1024 p, 32 scans, 8.7×10^{-3} M).

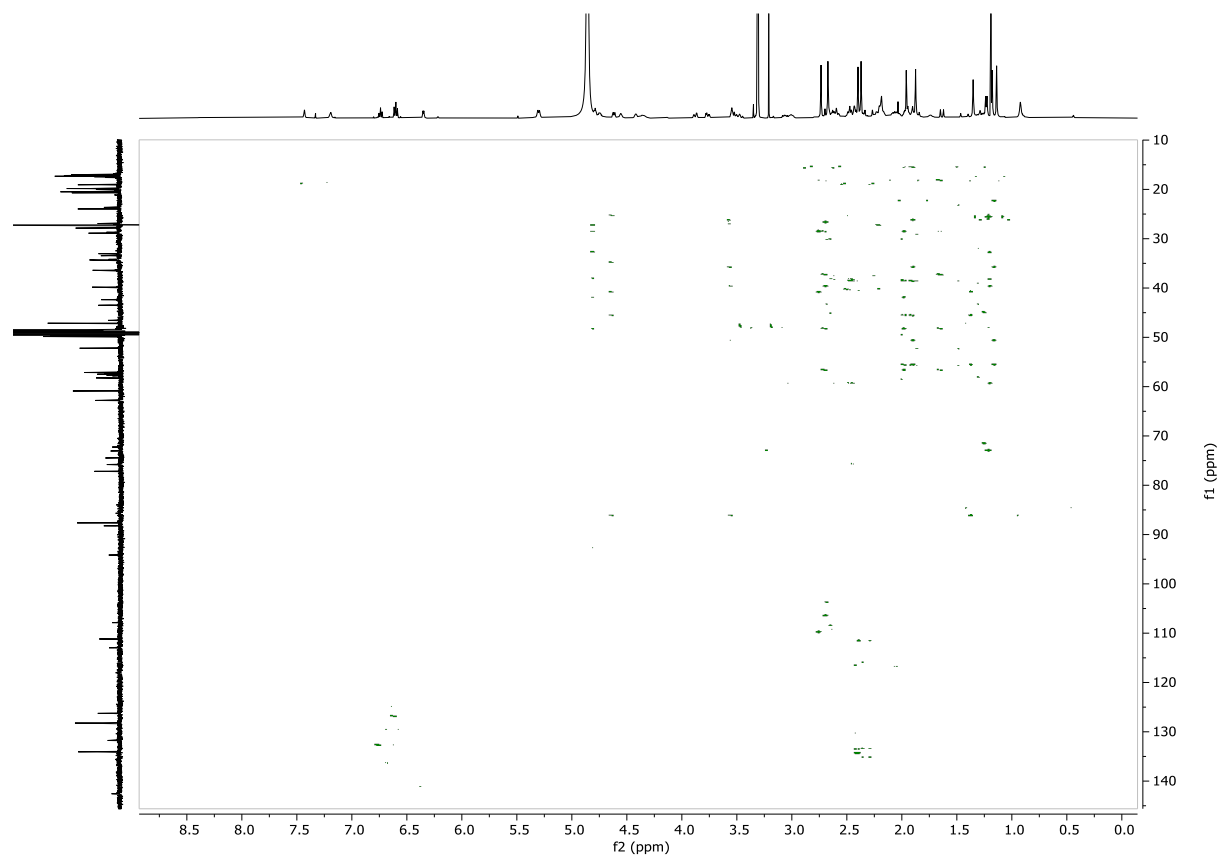


Figure S19. ^1H - ^{13}C HMBC spectrum of **7** (500 MHz, 126 MHz, CD_3OD , 298 K, 1024 x 2341 p, 12 scans, 8.7×10^{-3} M).

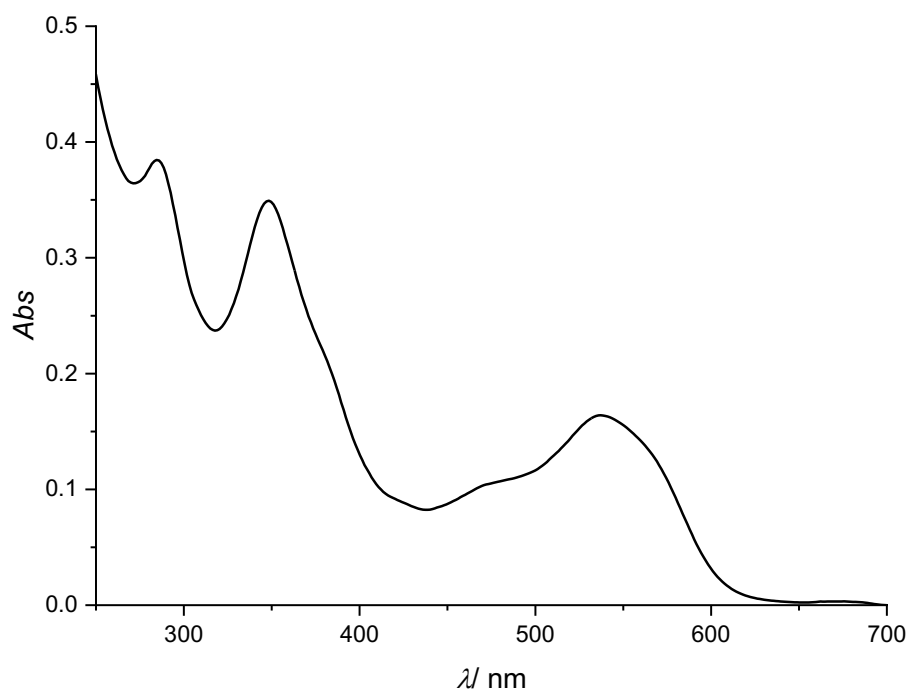


Figure S20. UV/Vis spectrum of **7** (H₂O, 3.5 × 10⁻⁵ M).

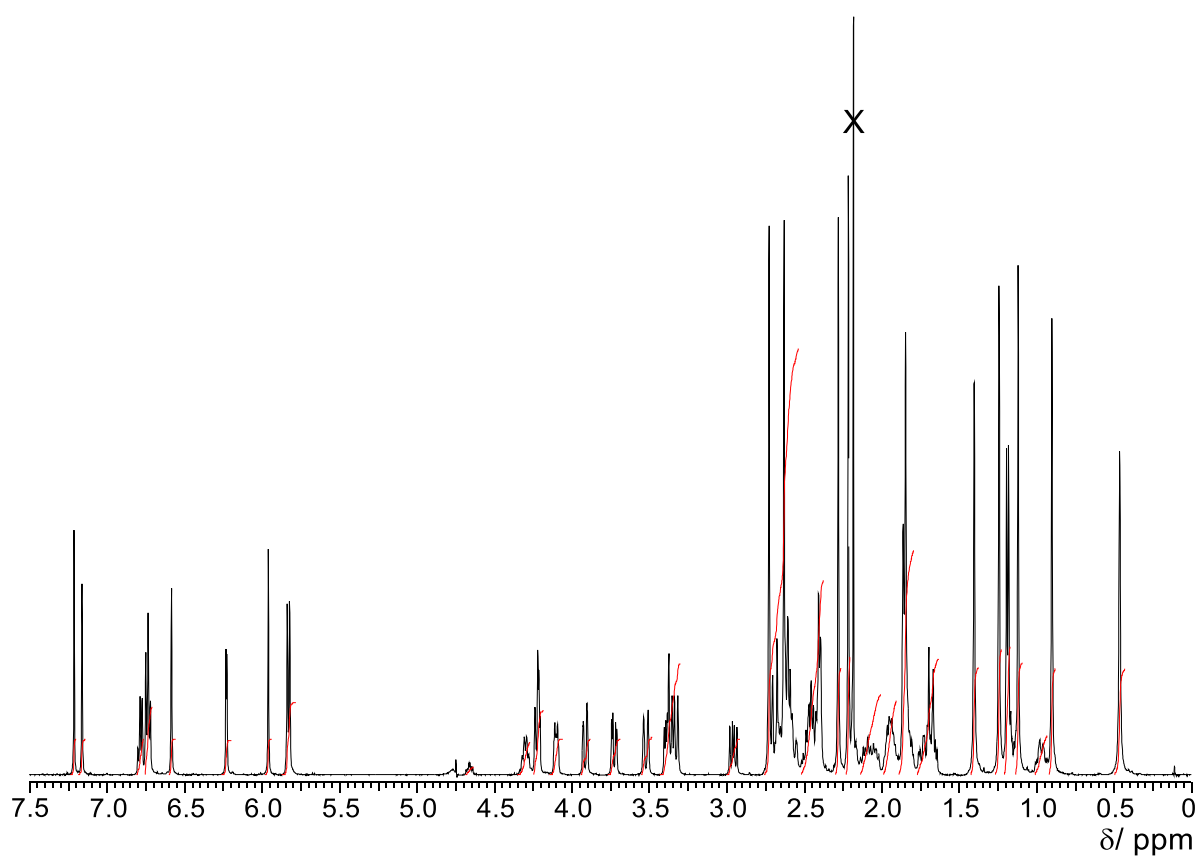


Figure S21. ¹H-NMR spectrum of **8**, **β-PhCbl** (500 MHz, D₂O (presat), 298 K, 3.2 × 10⁻³ M).

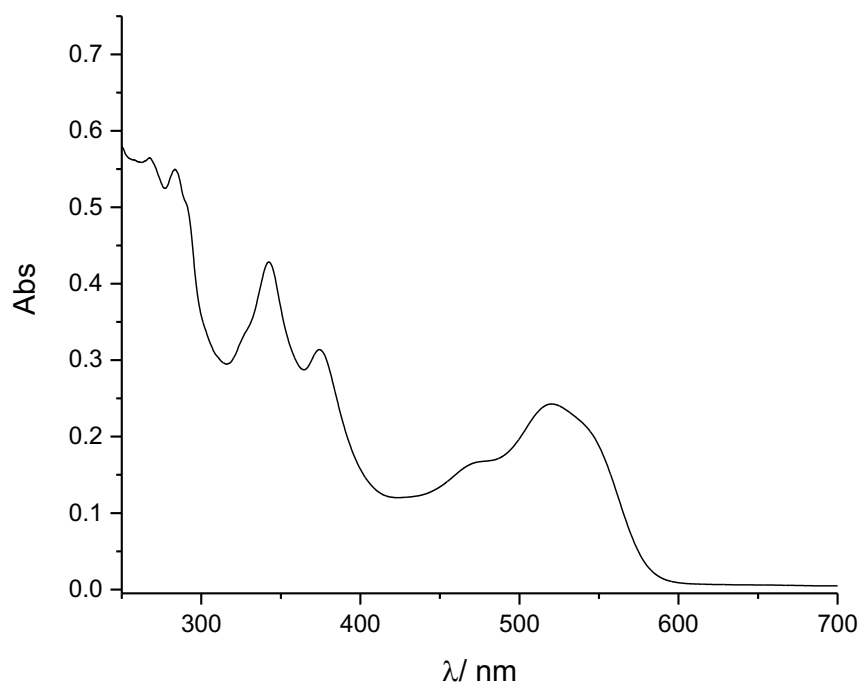


Figure S22. UV/Vis spectrum of **8**, β -PhCbl (H₂O, 6.3×10^{-5} M).