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Supporting Information

Structure Elucidation and Spectroscopic Analysis of Chromophores Produced by Oxidative Psilocin Dimerization

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Experimental Procedures

Materials: Chemicals and solvents were purchased from Deutero, Roth, Sigma-Aldrich, and VWR. All solvents used were of HPLC grade, deuterated solvents were of > 99.8 % purity. Solvents were dried by 3Å molecular sieves. **1** was synthesized as described.[1,2]

Analytical instrumentation and techniques: 1D and 2D NMR spectra were recorded on Bruker Avance III 500 or 600 MHz instruments at 300 K. For internal calibration, solvent signals of acetone-*d*$_6$ (^{1}H 2.05 ppm, ^{13}C 29.9 ppm), methanol-*d*$_4$ (^{1}H 3.31 ppm, ^{13}C 49.1 ppm), or DMSO (^{1}H 2.50 ppm, ^{13}C 39.5 ppm), respectively, were used. High resolution mass spectra were recorded on a Thermo Accela liquid chromatograph coupled to a Q-Exactive Orbitrap spectrometer. An Accucore C_{18} 2.6 µm, 100 × 2.1 mm column was used at 0.2 mL min^{-1} eluent flow (0.1 % formic acid (FA) in acetonitrile (MeCN)/0.1 % FA in H_2O: 2 min 2/98, 8 min 98/2, 10 min 98/2). Analytical liquid chromatography (LC-DAD-MS) was carried out on an Agilent 1290 Infinity II UHPLC instrument, fitted to a 6130 quadrupole mass detector. A Phenomenex Luna Omega Polar C_{18} 1.6 µm, 50 × 2.1 mm column (with guard column) was used at 30 °C and a flow of 1 mL min^{-1} (MeCN/0.1 % FA in H_2O: 0 min 5/95, 1 min 5/95, 8 min 40/60, 9 min 100/0).

Computational methods: Spectral rendering was accomplished by using the algorithm of specrend.[3] Measured absorption spectra were cropped to the region of λ = 380 to 780 nm. Resulting Vis-spectra were normalized to λ_{max} = 1 and subtracted from a theoretical emission spectrum of perfect white light ($E(\lambda) = 1$). The obtained transmission spectra were included within the specrend code, adjusted accordingly. Resulting programs calculate the xyz and RGB color values by using the CIE 1931 color matching functions and the implemented HDTV standard for RGB conversion.[4] Additionally, xyz values returned by specrend were entered into WolframAlpha (Wolfram Mathematica based computational online platform, www.wolframalpha.com) as an alternative approach of CIE xyz to RGB conversion. Actual colors in the Figures will slightly vary depending on the monitor model or printing technique and are mainly meant for illustrative purposes. All quantum chemistry calculations were carried out using GAMESS.[5] For UV/Vis spectra prediction of quinoid dimers, diprotonated (dicationic) structures were pre-optimized in gas-phase (with C2 symmetry restriction, where applicable) at the B3LYP/def2-TZVP level of theory.[6,7] Subsequently, full optimization was carried out in solution using the same functional and basis set, adding implicit water using the solvation model based on density (SMD).[8] Of each obtained ground state structure, the lowest 10 excited states were calculated using TD-DFT, at the same level of theory. Theoretical UV/Vis spectra were derived by summation of gaussian shaped absorption bands corresponding to the obtained vertical excitation energies and oscillator strengths, at a standard derivation of 0.275 eV.

Preparative equipment: Silica column chromatography was run on manually packed silica gel 60 (Merck), (semi-)preparative HPLC was carried out on Agilent 1200 and 1260 chromatographs. Sephadex LH-20 chromatography was run on a GE Healthcare Äkta Pure 25 FPLC system.

Synthetic procedures

a) Synthesis of O-acetylated 4-hydroxyindoles: The general procedure to O-acetylate 4-hydroxyindoles from the respective 1*H*-indole-4-ols followed the procedure described by Lugemwa et al.[9] and was carried out in sieve-dried toluene.

5-Methyl-1*H*-indol-4-yl acetate (10). From 500 mg 5-methyl-1*H*-indol-4-ol **7**, 623 mg off-white solid, 97 %. HRMS: 190.08597 [*M* + H]$^+$, calcd. 190.08626. ^{1}H NMR (600 MHz, acetone-*d*$_6$) δ/ppm 10.26 (1H, s-br, NH-1), 7.26 (1H, dd, J_1=J_2=2.7 Hz, H-2), 7.22 (1H, d, *J*=8.2 Hz, H-7), 6.97 (1H, d, *J*=8.2 Hz, H-6), 6.33 (1H, m, H-3), 2.36 (3H, s, 4-OAc), 2.20 (3H, s, 5-Me).^{13}C NMR (151 MHz, acetone-*d*$_6$) δ/ppm 169.12, 142.69, 137.67, 125.92, 124.88, 123.16, 119.89, 109.93, 99.00, 20.67, 15.75. NMR spectra of **10** are shown in Figures S15a-b.

7-Methyl-1*H*-indol-4-yl acetate (11). From 320 mg 7-methyl-1*H*-indol-4-ol **8**, 379 mg off-white/blueish solid, 92 %. HRMS: 190.08598 [*M* + H]$^+$, calcd. 190.08626. ^{1}H NMR (600 MHz, acetone-*d*$_6$) δ/ppm 10.34 (1H, s-br, NH-1), 7.29 (1H, dd, J_1=J_2=2.7 Hz, H-2), 6.88 (1H, d, *J*=7.7 Hz, H-5), 6.67 (1H, d, *J*=7.7 Hz, H-6), 6.39 (1H, m, H-3), 2.48 (3H, s, 5-Me), 2.31 (3H, s, 4-OAc). ^{13}C NMR (151 MHz, acetone-*d*$_6$) δ/ppm 169.59, 143.21, 138.25, 125.56, 122.49, 122.13, 119.28, 112.28, 99.93, 20.97, 16.69. NMR spectra of **11** are shown in Figures S16a-b.

1*H*-Indol-5-yl acetate (12). From 364 mg 1*H*-indol-5-ol **9**, 422 mg off-white solid, 97 %. HRMS: 176.07051 [*M* + H]$^+$, calcd. 176.07061. ^{1}H NMR (500 MHz, acetone-*d*$_6$) δ/ppm 10.37 (1H, s-br, NH-1), 7.41 (1H, d, *J*=8.7 Hz, H-7), 7.37 (1H, dd, J_1=J_2=2.7 Hz, H-2), 7.27 (1H, d, *J*=2.2, H-4), 6.85 (1H, dd, J_1=8.8 Hz, J_2=2.2 Hz), 6.46 (1H, m, H-3), 2.24 (3H, s, 5-OAc). ^{13}C NMR (126 MHz, acetone-*d*$_6$) δ/ppm 169.80, 144.71, 134.35, 128.53, 126.45, 115.93, 112.54, 111.71, 101.93, 20.47. NMR spectra of **12** are shown in Figures S17a-b.

b) Synthesis of 4- or 5-acetoxy-*α*,*β*-dioxo-*N*,*N*-dimethyltryptamines: 1 mmol of the respective acetylated hydroxyindole in 3.3 mL sieve dried THF were added dropwise under inert atmosphere to a stirring solution of 340 µl $(COCl)_2$ (2.11 mmol, 4 eq) in 750 µL dry THF cooled on ice. The reaction progress was checked by TLC. After complete turnover of starting material, mixture was diluted with 3.8 mL dry THF, $HNMe_2$ (2 M solution in THF) was added very slowly with continued cooling, until moist pH paper gave a basic reaction. The mixture was evaporated in a rotary evaporator, and the product was isolated by step gradient column chromatography on silica gel. For final purification the obtained product was crystallized from EtOAc.

5-Methyl-3-(2-dimethylamino-2-oxoacetyl)-1*H*-indol-4-yl acetate (13). From 308 mg **10**, reaction time 16 h, column using 1 % triethylamine in CH_2Cl_2:MeOH (40:1 to 20:1). Yield: 341 mg, off-white solid, 72 %. HRMS: 289.11775 [*M* + H]$^+$, calcd. 289.11828. ^{1}H NMR (600 MHz, acetone-*d*$_6$) δ/ppm 11.42 (1H, s-br, NH-1), 8.02 (1H, s, H-2), 7.35 (1H, d, *J*=8.2 Hz, H-7), 7.18 (1H, d, *J*=8.2 Hz, H-6), 3.00 (3H, s, N-Me), 2.94 (3H, s, N-Me), 2.42 (3H, s, 4-OAc), 2.26 (3H, s, 5-Me). ^{13}C NMR (151 MHz, acetone-*d*$_6$) δ/ppm 187.4, 170.1, 169.3, 144.0, 139.6, 139.4, 127.8, 124.9, 120.3, 114.8, 111.2, 37.6, 34.2, 21.8, 16.6. NMR spectra of **13** are shown in Figures S18a-b.

7-Methyl-3-(2-dimethylamino-2-oxoacetyl)-1*H*-indol-4-yl acetate (14). From 283 mg **11**, reaction time 14 h, column using 1 % triethylamine in CH_2Cl_2:MeOH (30:1 to 15:1). Yield: 250 mg, white solid, 58 %. HRMS: 289.11818 [*M* + H]$^+$ calcd. 289.11828. ^{1}H NMR (500 MHz, methanol-*d*$_4$): δ/ppm 7.97 (1H, s, H-2), 7.11 (1H, d, *J*=7.9 Hz, H-6), 6.83 (1H, d, *J*=7.9 Hz, H-5), 3.07 (3H, s, *N*-Me), 2.98 (3H, s, *N*-Me), 2.53 (3H, s, 7-Me), 2.40 (3H, s, OAc). ^{13}C NMR (126 MHz, methanol-*d*$_4$): δ/ppm 187.25, 172.37, 170.29, 143.95, 140.03, 139.74, 126.14, 121.44, 119.31, 116.98, 114.89, 37.75, 34.32, 21.53, 16.36. NMR spectra of **14** are shown in Figures S19a-b.

3-(2-Dimethylamino-2-oxoacetyl)-1H-indol-5-yl acetate (15). From 316 mg **12**, reaction time 2 h, column using 1 % triethylamine in CH_2Cl_2:MeOH (30:1 to 15:1). Yield 326 mg, white solid, 66 %. HRMS: 275.10251 [*M* + H]$^+$, calcd. 275.10263. ^{1}H NMR (500 MHz, methanol-*d*$_4$): δ/ppm 8.06 (1H, s, H-2), 7.89 (1H, d, *J*=2.2 Hz, H-4), 7.50 (1H, d, *J*=8.8 Hz, H-7), 7.05 (1H, dd, *J*$_1$=8.8 Hz, *J*$_2$=2.2 Hz, H-6), 3.10 (3H, s, *N*-Me), 3.03 (3H, s, *N*-Me), 2.31 (3H, s, OAc). ^{13}C NMR (126 MHz, methanol-*d*$_4$): δ/ppm 187.94, 172.03, 169.86, 148.57, 139.24, 136.55, 127.16, 119.65, 115.11, 115.09, 114.04, 37.97, 34.56, 21.11. NMR spectra of **15** are shown in Figures S20a-b.

c) Reduction of 13, 14, and 15. 0.41 mmol of substrate dissolved in 2.8 mL dry 2-methyl-THF were placed in a dried flask with fitted Liebig cooler and the system was purged with argon. The solution was cooled by an ice bath. A suspension of 63 mg $LiAlH_4$ (1.66 mmol, 4 eq) in 850 µL 2-methyl-THF was added slowly and under stirring by a syringe through the septum at the top of the condenser. Another 400 µL 2-methyl-THF were added, using the same syringe, to rinse the glass walls inside. Subsequently, the ice bath was removed and the reaction was heated to reflux for several hours (see below). After cooling down to 0 °C, the reaction was quenched by slow and cautious addition of 200 µL THF:H_2O (27:100). After stirring for a few minutes, 400 mg anhydrous NaS_2O_4, 200 mg silica and 1.2 mL CH_2Cl_2 were added. The slurry was filtered on a glass frit, and solids were washed with portions of CH_2Cl_2:MeOH (9:1) until the eluting filtrate was virtually free of product (as analyzed by TLC). The product was obtained after evaporation of the filtrate or, if necessary, after silica column chromatography. Solvent-free solids were obtained by applying a reduced pressure (0.5 to 1 mbar). Individual details for the syntheses of **3**, **4**, and **5** are provided below.

Bufotenin (3). From 240 mg of **15**, reflux time 4 h. The product was obtained after column chromatography 1 % triethylamine in CH_2Cl_2:MeOH (5:1) and was taken up in 50 mL acetone and filtered on a glass frit, the solvent was evaporated. Yield: 74 mg, off-white amorphous solid, 41 %. HRMS: 205.13356 [*M* + H]$^+$, calcd. 205.13354. ^{1}H NMR (500 MHz, acetone-*d*$_6$): δ/ppm 9.67 (1H, s-br, NH-1), 7.17 (1H, d, *J*=8.6 Hz, H-7), 7.07 (1H, d, *J*=2.3 Hz, H-2), 6.95 (1H, d, *J*=2.3 Hz, H-4), 6.68 (1H, dd, *J*$_1$=8.6 Hz, *J*$_2$=2.3 Hz, H-6), 2.81 (2H, t, *J*=7.9 Hz, *N*-*α*-CH_2), 2.54 (2H, t, *J*=7.9 Hz, *N*-*β*-CH_2), 2.26 (6H, s, *N*-Me_2). ^{13}C NMR (126 MHz, acetone-*d*$_6$) δ/ppm 151.54, 132.56, 129.50, 123.75, 113.66, 112.50, 112.26, 103.56, 61.32, 45.75, 24.55. ^{1}H and ^{13}C NMR spectra are provided in Figures S9a and S9b.

5-Methylpsilocin (4). The synthesis followed a described procedure.[10] From 117 mg of **13**, reflux time 3 h, yielding 74 mg grey crystals (84 %). HRMS: 219.14926 [*M* + H]$^+$, calcd. 219.14919. ^{1}H NMR (600 MHz, acetone-*d*$_6$): δ/ppm 12.45 (1H, s-br, OH), 9.65 (1H, s-br, NH-1), 6.90 (1H, s, H-2), 6.79 (1H, d, *J*=8.1 Hz, H-6), 6.71 (1H, d, *J*=8.1 Hz, H-7), 2.90 (2H, t, *J*=5.0 Hz, *N*-*α*-CH_2), 2.66 (2H, t, *J*=5.0 Hz, *N*-*β*-CH_2), 2.32 (6H, s, *N*-Me_2), 2.22

(3H, s, 5-Me). ^{13}C NMR (151 MHz, acetone-*d*$_6$): δ/ppm 150.28, 139.27, 125.83, 122.50, 122.34, 118.68, 113.38, 102.89, 62.76, 45.57, 25.94, 16.31. ^{1}H and ^{13}C NMR spectra are provided in Figures S2a and S2b.

7-Methylpsilocin (5). From 150 mg of **14**, reflux time 3.5 h. Column chromatography using 1 % triethylamine in CH_2Cl_2:MeOH (9:1) yielded 68 mg off-white/reddish crystals (60 %). HRMS: 219.14919 [*M* + H]$^+$, calcd. 219.14919. ^{1}H NMR (500 MHz, acetone-*d*$_6$): δ/ppm 11.84 (1H, s-br, OH), 9.68 (1H, s-br, NH-1), 6.94 (1H, s, H-2), 6.67 (1H, d, *J*=7.6 Hz, H-6), 6.27 (1H, d, *J*=7.6 Hz, H-5), 2.92 (2H, t, *J*=5.1 Hz, *N*-*α*-CH$_2$), 2.65 (2H, t, *J*=5.1 Hz, *N*-*β*-CH$_2$), 2.34 (3H, s, 5-Me), 2.30 (6H, s, *N*-Me$_2$). ^{13}C NMR (126 MHz, acetone-*d*$_6$): δ/ppm 151.37, 139.41, 123.58, 122.23, 118.09, 114.84, 111.95, 105.85, 62.42, 45.28, 25.56,16.44. ^{1}H and ^{13}C NMR spectra are provided in Figures S3a and S3b.

Oxidations

a) Analytical scale oxidations of hydroxytryptamines and LC-DAD-MS. 0.25 to 1 mM solutions (H_2O or aq. MeOH) of the respective substrates **1**, **3**, **4**, and **5** were oxidized using 2.4 eq Fe^{III}. Once a discernible hue appeared, the mixture was immediately analyzed by LC-DAD-MS. Reinjections at later timepoints (usually 5-30 minutes) were used to obtain qualitative information on stability of initially formed products. From peaks of interest, related UV/Vis and MS spectra were extracted from chromatograms.

b) Preparative scale oxidation of 4. 15 mg of **4** in 7.5 mL MeOH were oxidized by mixing with 1.65 mL aqueous $FeCl_3$ (100 mM solution, 2.4 eq). The solution deeply colorized instantaneously. After 20 min at RT, the reaction was diluted with 12 mL H_2O. The solution was concentrated by rotary evaporation to remove the majority of the MeOH. A Sep-Pak C_{18} SPE cartridge (Waters 35 cc/10 g) was washed with four column volumes MeOH and equilibrated with four column volumes 2.5 % MeOH in H_2O. The reaction mixture was loaded onto the cartridge, and 2.5 % MeOH in H_2O was added until the pale-yellow salt fraction had eluted from the cartridge which was then washed with two bed volumes (each) MeOH and acetone. After concentration, final purification of the products was accomplished by preparative HPLC (Phenomenex Luna C_{18} column, 250 × 21.2, 10 µm particle size, flow: 20 mL min^{-1}, solvent gradient: MeCN/H_2O (+ 0.1 % TFA), from 5 to 20 % MeCN in 25 min and then to 50 % in 10 min, 25 °C. One major (violet, **4a**, *E*/*Z* isomeric mixture, t_R=31.9 min) and one minor product (yellow, **4b,** t_R=24.4 min) was obtained as the respective hydrotrifluoroacetates.

(*E*/*Z*)-3,3'-Bis(2-(dimethylamino)ethyl)-5,5'-dimethyl-[7,7'-biindolyliden]-4,4'(1*H*,1'*H*)-dione (4a). HRMS: 217.13362 [*M* + 2H]$^{2+}$, 433.25949 [*M* + H]$^+$, calcd. 217.13390, 433.25980. UV/Vis in H_2O λ_{max}/nm (log ε): 579 (4.30), 374 (4.11), 289 (3.77), 217 (4.38), 202 (4.37). ^{1}H NMR (600 MHz, methanol-*d*$_4$): major isomer (86%) δ/ppm 7.65 (2H, s, H-6, H-6'), 7.18 (2H, s, H-2, H-2'), 3.44 (4H, t, *J*=7.7 Hz, 2 × *N*-*α*-CH$_2$), 3.24 (4H, t, *J*=7.7 Hz, 2 × *N*-*β*-CH$_2$), 2.99 (12H, s, 2 × *N*-Me$_2$), 2.17 (6H, s, 5-Me, 5'-Me). Minor isomer (14%), if resolved, δ/ppm 7.62 (H-2, H-2'), 6.99 (H-2, H-2'), 2.16 (5-Me, 5'-Me). ^{13}C NMR (151 MHz, methanol-*d*$_4$): Major isomer δ/ppm 185.37 (C-4, C-4'), 139.28 (C-5, C-5'), 135.49 (C-7a, C-7a'), 133.84 (C-6, C-6'), 128.55 (C-7, C-7'), 126.59 (C-2, C-2'), 122.56 (C-3a, C-3a'), 119.74 (C-3, C-3'), 59.56 (2 × *N*-*α*-C), 43.79 (2 × *N*-Me$_2$), 22.78 (2 × *N*-*β*-C), 16.73 (5-Me, 5'-Me). Minor isomer, if resolved, δ/ppm 185.88 (C-4, C-4'), 137.03 (C-5, C-5'), 135.21 (C-7a, C-7a'), 133.02 (C-

6, C-6’), 127.34 (C-7, C-7’), 125.64 (C-2, C-2’), 16.48 (5-Me, 5’-Me). 1D and 2D NMR spectra are provided in Figures S4a-S4e.

3-(2-(Dimethylamino)ethyl)-5-methyl-1*H*-indole-4,7-dione (4b). HRMS: 233.12824 [*M* + H]$^+$, calcd. 233.12845. UV/Vis in H_2O λ_{max}/nm (log ε): 444 (3.28), 339 (3.43), 266 (4.22), 222 (4.15). ^{1}H NMR (600 MHz, DMSO-d_6): δ/ppm 12.62 (1H, s, NH-1), 10.11 (1H, s-br, NH$^+$), 7.16 (1H, s, H-2), 6.52 (1H, s, H-6), 3.25 (2H, t, *J*=7.8 Hz, 2 × *N*-*α*-CH_2), 3.06 (2H, t, *J*=7.8 Hz, 2 × *N*-*β*-CH_2), 2.79 (6H, s, *N*-Me_2), 1.99 (3H, s, 5-Me). ^{13}C NMR (151 MHz, DMSO-d_6): δ/ppm 184.03 (C-4), 177.25 (C-7), 146.54 (C-5), 132.54 (C-6), 131.38 (C-7a), 125.07 (C-2), 122.04 (C-3a), 119.76 (C-3), 56.05 (*N*-α-C), 42.13 (*N*-Me2), 20.36 (*N*-β-C), 15.40 (5-Me). 1D and 2D NMR spectra are provided in Figures S5a-S5e.

c) Preparative scale oxidation of 7-Methylpsilocin (5). 5 mg **5** was oxidized by 12.4 mg $FeCl_3 \cdot 6\ H_2O$ in 23 mL 50 % aqueous MeOH, initally forming a green solution that fades to pale yellow. After 1 h, the mixture was lyophilized and EtOAc (10 mL, sieve dried), Ac_2O (1 mL) and pyridine (1 mL) were added to the residue. After acetylation overnight, the mixture was dried in 1 mL aliquots under reduced pressure. Re-combined crude product was purified by semi-preparative HPLC (Agilent XDB C_{18} 250 × 9.4 mm column, 5 µm particle size, flow: 2.5 mL min^{-1}, solvent gradient: MeCN/H_2O (+ 0.1 % TFA) from 10 to 35 % MeCN in 20 min, 12 °C), yielding the respective bis-hydrotrifluoroacetate of **5b** (t_R=19.3 min).

3,3’-Bis(2-(dimethylamino)ethyl)-7,7’-dimethyl-1*H*,1’*H*-[5,5’-biindole]-4,4’-diyl diacetate (5b). HRMS: 260.15164 [*M* + 2H]$^{2+}$, 519.29612 [*M* + H]$^+$, calcd. 260.15229, 519.29658. ^{1}H NMR (600 MHz, methanol-d_4): δ/ppm 7.29 (2H, s, H-2, H-2’), 6.84 (2H, s, H-6, H-6’), 3.46 (4H, t, *J*=7.5 Hz, 2 × *N*-*α*-CH_2), 3.15 (4H, t, *J*=7.5 Hz, 2 × *N*-β-CH_2), 2.93 (12H, s, 2 × *N*-Me_2), 2.49 (6H, s, 7-Me, 7’-Me), 1.99 (6H, s, 2 × OAc). ^{13}C NMR (151 MHz, methanol-d_4): δ/ppm 172.09 (2×OAc-C=O), 140.86 (C-4, C-4’), 139.15 (C-7a, C-7a’), 126.76 (C-6, C-6’), 125.79 (C-2, C-2’), 123.25 (C-5, C-5’), 120.49 (C-3a, C-3a’), 120.29 (C-7, C-7’), 109.27 (C-3, C-3’), 59.99 (2 × *N*-*α*-C), 43.90 (2 × *N*-Me_2), 22.97 (2 × *N*-β-C), 20.99 (2 × OAc-Me), 16.61 (7-Me, 7’-Me). 1D and 2D NMR spectra are provided in Figures S6a-S6d.

d) Preparative scale oxidation of 3 and subsequent product isolation and derivatization. In a typical batch, 6.3 mg of **3** was reacted, for 1 minute, with 16.6 mg of $FeCl_3 \cdot 6\ H_2O$ in 2 mL of 10 % aqueous MeOH and then directly loaded onto a Sephadex LH-20 column (900 × 23 mm), eluting with 0.01 M HCl in 10 % aqueous MeOH at a flow of 1 mL min^{-1}. Four main product fractions (A-D) were collected. After LC-DAD-MS analysis, the fractions of interest (B-D) were used for product identification. Fraction B (main product) was lyophilized and subsequently purified by semi-preparative HPLC (Thermo Hypercarb column, 150 × 10 mm, 5 µm particle size, flow: 2.5 mL min^{-1}, solvent gradient MeCN/H_2O (+ 0.1 % TFA), from 10 to 25 % MeCN in 10 min, 25 °C), yielding **3a** as its bis-hydrotrifluoroacetate (t_R=9.4 min). The eluate of fraction C was heated to 60 °C, for 10 h, until the initial product had completely disappeared (ion *m*/*z* 405 [*M* + H]$^+$). *O*-phenylenediamine (32 µg mL^{-1}) was added to the resulting solution and the reaction was kept at RT overnight. After lyophilization, the crude product mixture was purified by semi-preparative HPLC (Phenomenex Synergy Polar-RP, 250 × 10 mm column, 4 µm particle size, flow: 2.0 mL min^{-1}, solvent gradient MeOH/H$_2$O (+ 0.1 % FA), from 10 to 76 % MeOH within 22 min, 25 °C), yielding **3d** (t_R=23.5 min) as its bis-hydroformate. Fraction D was directly reacted with *o*-phenylenediamine (32 µg mL^{1}) overnight at RT. After lyophilization and semi-preparative HPLC (Agilent XDB C$_{18}$ column, 250 × 9.4 mm, 5 µm particle size, flow: 2.5 mL min^{-1}, solvent gradient MeCN/H$_2$O (+ 0.1 % FA) from 10 to 42.5 % MeCN within 13 min, 25 °C) compound **3f** (t_R=12.9 min) was obtained as its hydroformate. Multiple batches were combined to collect an amount sufficient for characterization.

4,4'-Bibufotenin (3a). HRMS: 204.12569 [*M* + 2H]$^{2+}$, 407.24393 [*M* + H]$^+$, calcd. 204.12608, 407.24415. ^{1}H NMR (600 MHz, methanol-*d*$_4$): δ/ppm 7.38 (2H, d, *J*=8.7 Hz, H-7, H-7'), 7.19 (2H, s, H-2, H-2'), 6.94 (2H, d, *J*=8.7 Hz, H-6, H-6'), 2.68 (2H, m, 2 × ½ *N*-α-CH$_2$), 2.59 (2H, m, 2 × ½ *N*-α-CH$_2$), 2.51 (2H, m, 2 × ½ *N*-β-CH$_2$), 2.45 (6H, s, 2 × *N*-Me), 2.40 (6H, s, 2 × *N*-Me), 2.29 (2H, m, 2 × ½ *N*-β-CH$_2$). ^{13}C NMR (151 MHz, methanol-*d*$_4$): δ/ppm 149.69 (C-5, C-5'), 133.75 (C-7a, C-7a'), 128.58 (C-3a, C-3a'), 127.20 (C-2, C-2'), 114.11 (C-4, C-4'), 113.58 (C-7, C-7'), 113.51 (C-6, C-6'), 110.00 (C-3, C-3'), 59.94 (2 × *N*-α-C), 43.85 (2 × *N*-Me), 42.58 (2 × *N*-Me), 22.53 (2 × *N*-β-C). 1D and 2D NMR spectra are provided in Figures S11a-S11d.

3-(2-(Dimethylamino)ethyl)-4-(3-(2-(dimethylamino)ethyl)-3H-pyrrolo[2,3-*b*]phenazine-3-yl-1*H*-indol-5-ol (3d). HRMS: 247.13907 [*M* + 2H]$^{2+}$, 493.27087 [*M* + H]$^+$, calcd. 247.13944, 493.27104. ^{1}H NMR (500 MHz, methanol-*d*$_4$): δ/ppm 8.10 (1H, s, H-4'), 8.05 (1H, d, *J*=8.6 Hz, H-9 or H-12), 8.00 (1H, d, *J*=8.6 Hz, H-9 or H-12), 7.79 (1H, dd, J_1=8.6 Hz, J_2=6.8 Hz H-10 or H-11), 7.71 (1H, dd, J_1=8.6 Hz, J_2=6.8 Hz H-10 or H-11), 7.35 (1H, s, H-2), 7.27 (1H, d, *J*=8.7 Hz, H-7), 7.00 (1H, s, H-7'), 6.74 (1H, d, *J*=8.7 Hz, H-6), 6.38 (1H, s, H-2'), 3.85-3.60 (4H, m, *N*-α-CH$_2$, *N*-β-CH$_2$), 3.13 (6H, s, *N*-Me$_2$), 3.02-2.73 (4H, m, *N*-α'-CH$_2$, *N*-β'-CH$_2$), 2.66 (6H, s, *N*-Me$_2$'). ^{13}C-NMR (126 MHz, methanol-*d*$_4$): δ/ppm 155.66 (C-5), 153.86 (C-7a'), 147.14 (C-6'), 146.19 (C-3a'), 144.16 (C-8 or C-13), 142.41 (C-5'), 141.52 (C-8 or C-13), 135.64 (C-7a), 132.03 (C-10 or C-11), 129.86 (C-9 or C-12), 129.63 (C-10 or C-11), 128.70 (C-9 or C-12), 126.08 (C-2), 125.36 (C-4'), 123.90 (C-3a), 116.28 (C-4), 114.38 (C-7), 108.27 (C-3), 107.34 (C-6), 101.98 (C-2'), 98.47 (C-7'), 61.01 (C-3'), 59.74 (*N*-α-C), 55.70 (*N*-α'-C), 44.51 (2×*N*-Me$_2$), 34.96 (*N*-β'-C), 26.14 (*N*-β-C). 1D and 2D NMR spectra are provided in Figures S13a-S13e.

***N*,*N*-Dimethyl-2-(3*H*-pyrrolo[3,2-*a*]phenazine-1-yl)ethan-1-amine (3f).** HRMS: 291.16007 [*M* + H]$^+$, calcd. 291.16042. ^{1}H NMR (600 MHz, methanol-*d*$_4$): δ/ppm 8.30 (1H, d, *J*=8.4 Hz, H-9 or H-12), 8.22 (1H, d, *J*=8.4 Hz, H-9 or H-12), 8.01 (1H, d, *J*=9.2 Hz, H-7), 7.91 (1H, dd, J_1=8.4 Hz, J_2=6.7 Hz, H-10 or H-11), 7.87 (1H, dd, J_1=8.4 Hz, J_2=6.7 Hz, H-10 or H-11), 7.81 (1H, d, *J*=9.2 Hz, H-6), 7.45 (1H, s, H-2), 3.79 (2H, m, *N*-β-CH$_2$), 3.74 (2H, m, *N*-α-CH$_2$), 3.03 (6H, s, *N*-Me$_2$). ^{13}C NMR (151 MHz, methanol-*d*$_4$): δ/ppm 143.38 (C-8 or C-13), 143.36 (C-5), 142.99 (C-4), 141.72 (C-8 or C-13), 136.53 (C-7a), 131.14 (C-10 or C-11), 130.29 (C-9 or C-12), 130.02 (C-9 or C-12), 129.91 (C-10 or C-11), 124.51 (C-2), 123.73 (C-6), 122.80 (C-7), 120.25 (C-3a), 116.95 (C-3), 59.99 (*N*-α-C), 44.11 (*N*-Me$_2$), 24.03 (*N*-β-C). 1D and 2D NMR spectra are provided in Figures S14a-S14d.

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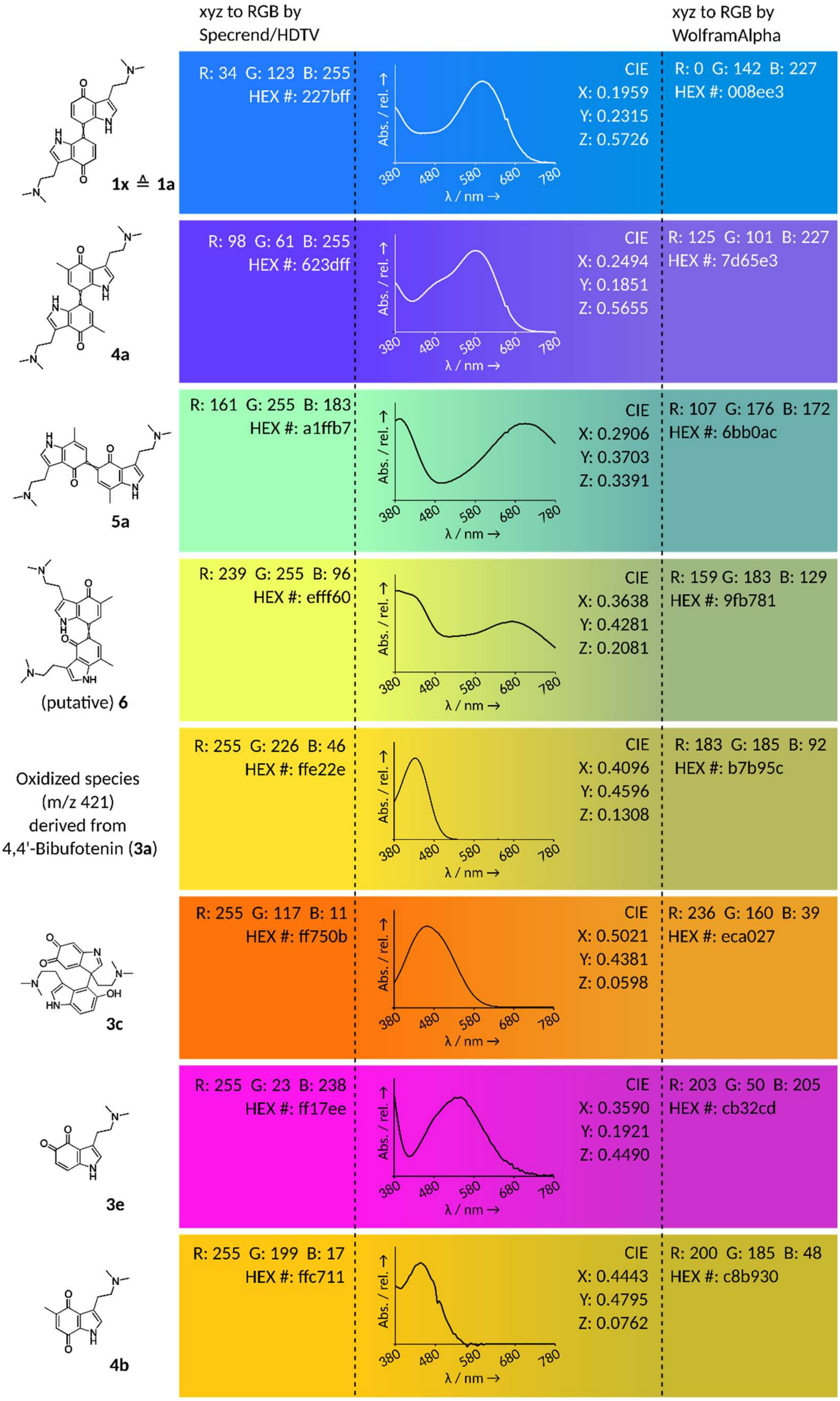

Figure S1. Rendered colors of indoleethylamine oxidation products, derived from LC-DAD visual absorption spectra.

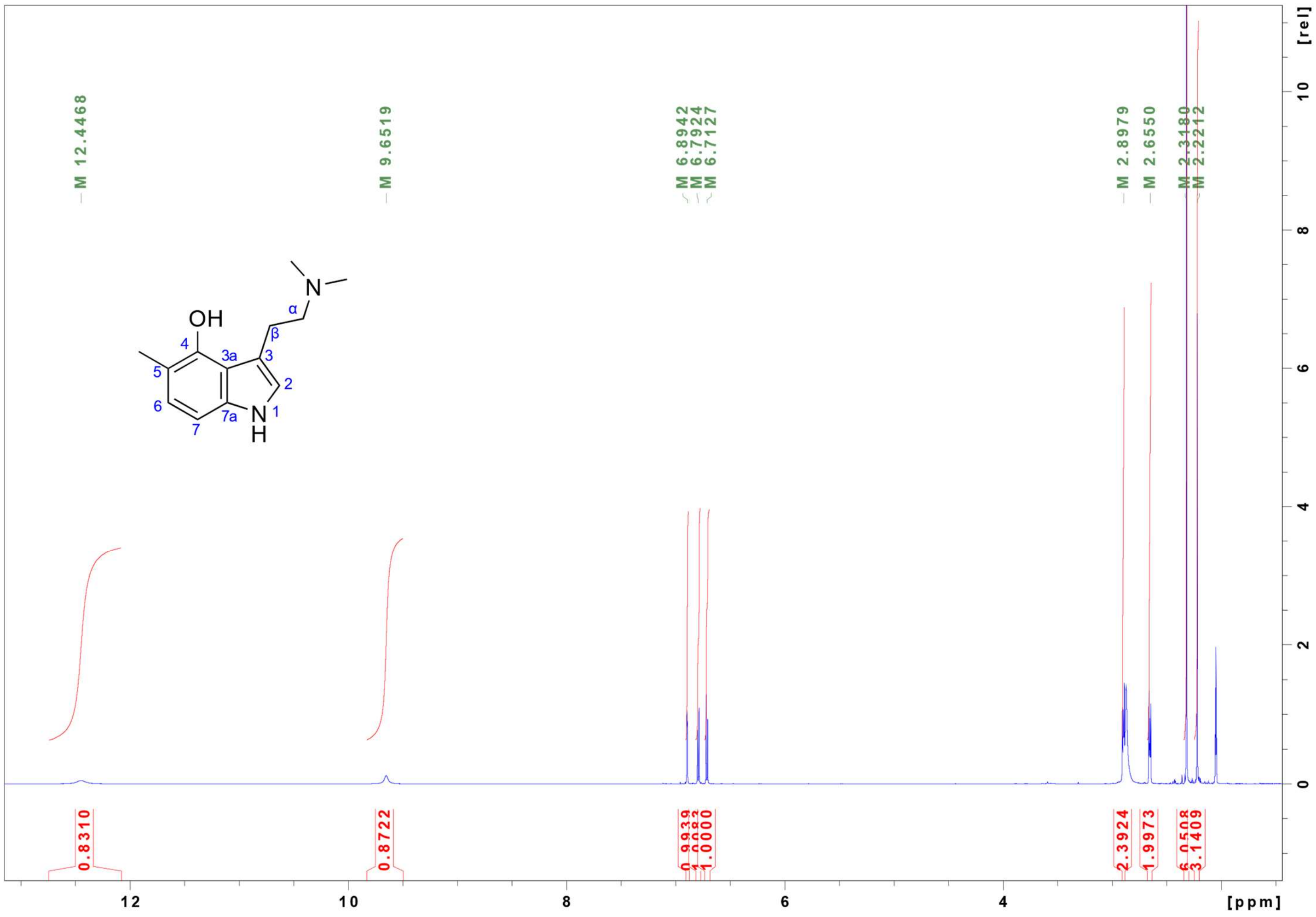

Figure S2a. ^{1}H NMR spectrum of **4** (600 MHz, acetone-*d*$_6$).

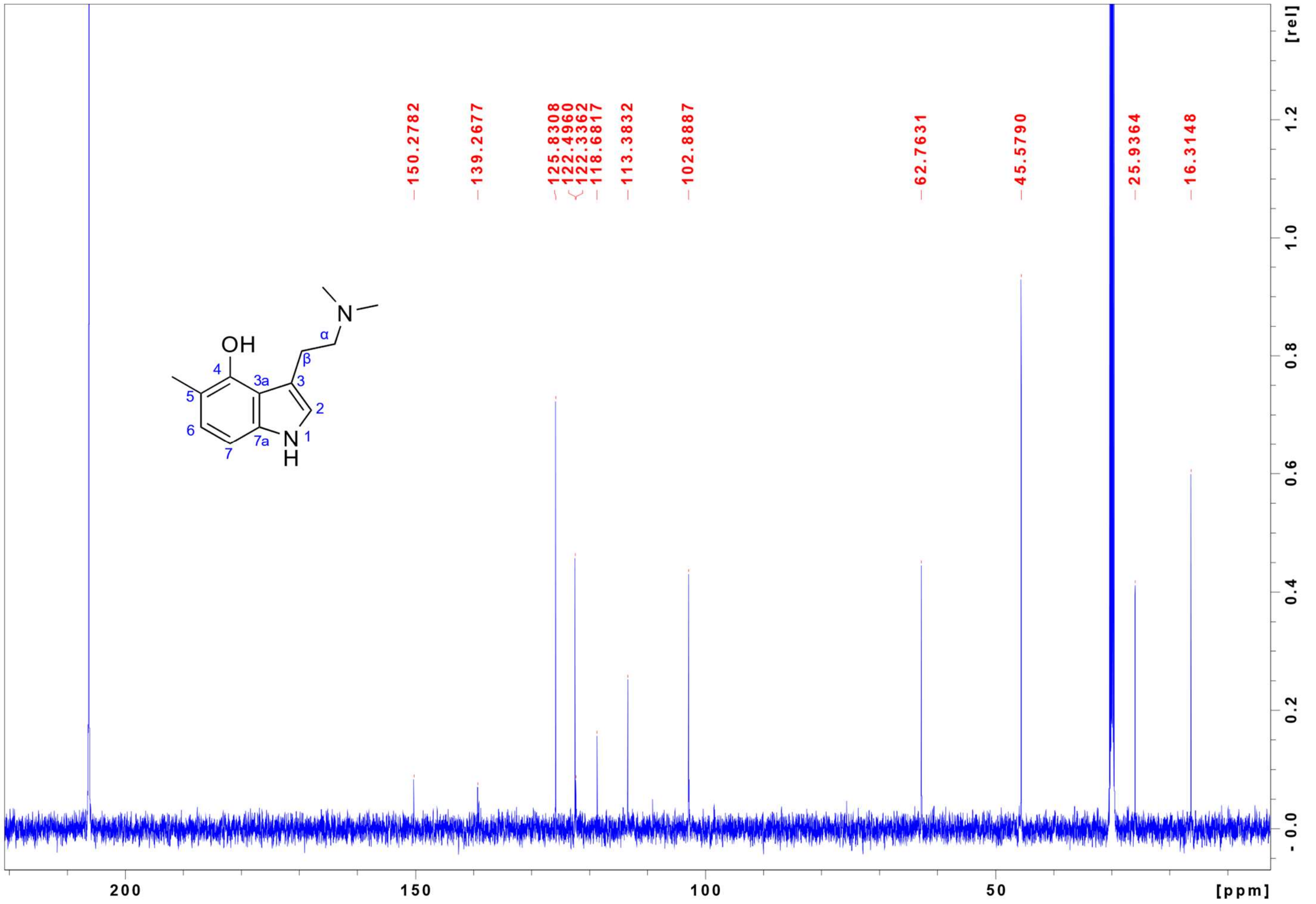

Figure S2b. ^{13}C NMR spectrum of **4** (151 MHz, acetone-d_6).

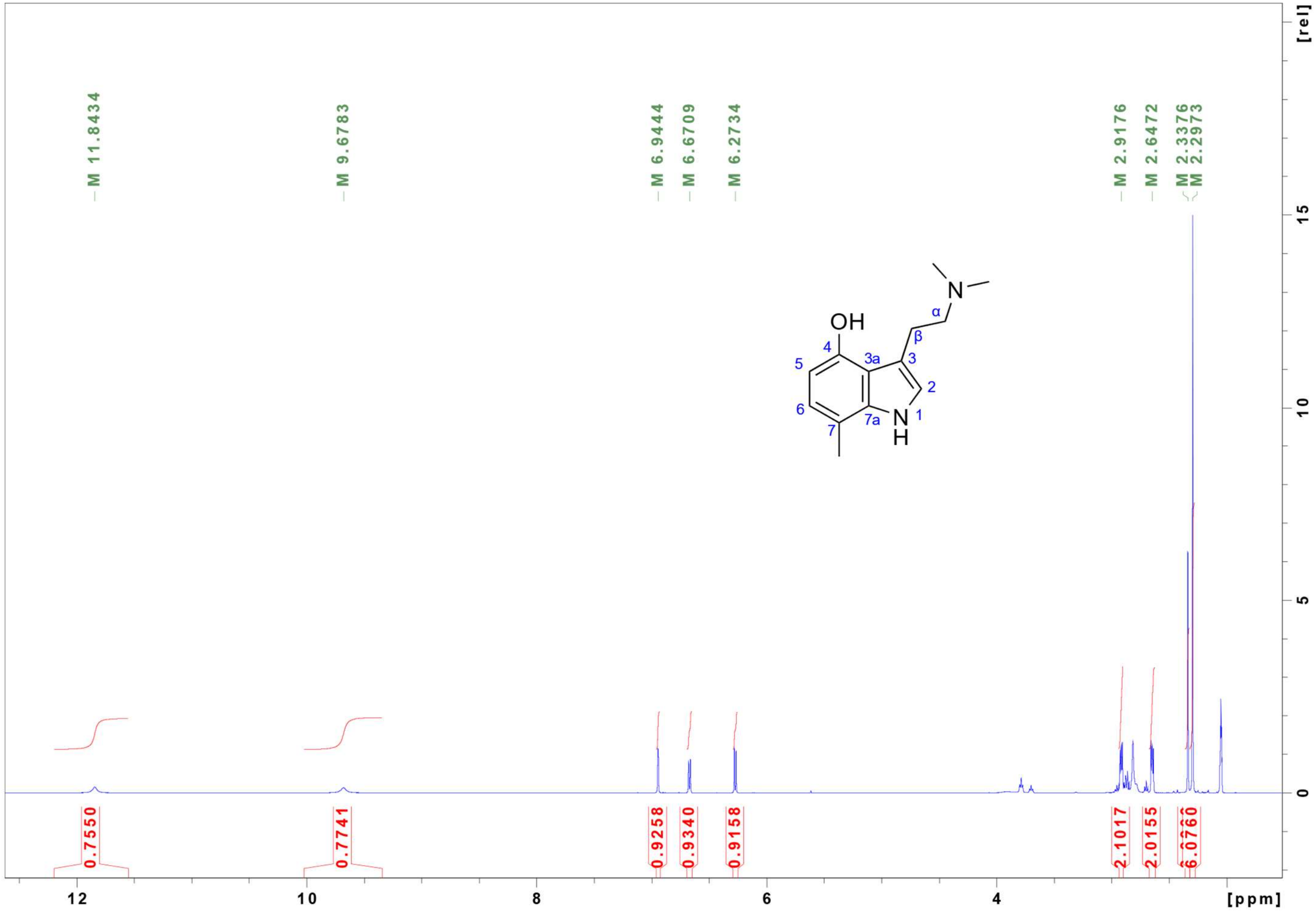

Figure S3a. ^{1}H NMR spectrum of **5** (500 MHz, acetone-d_6).

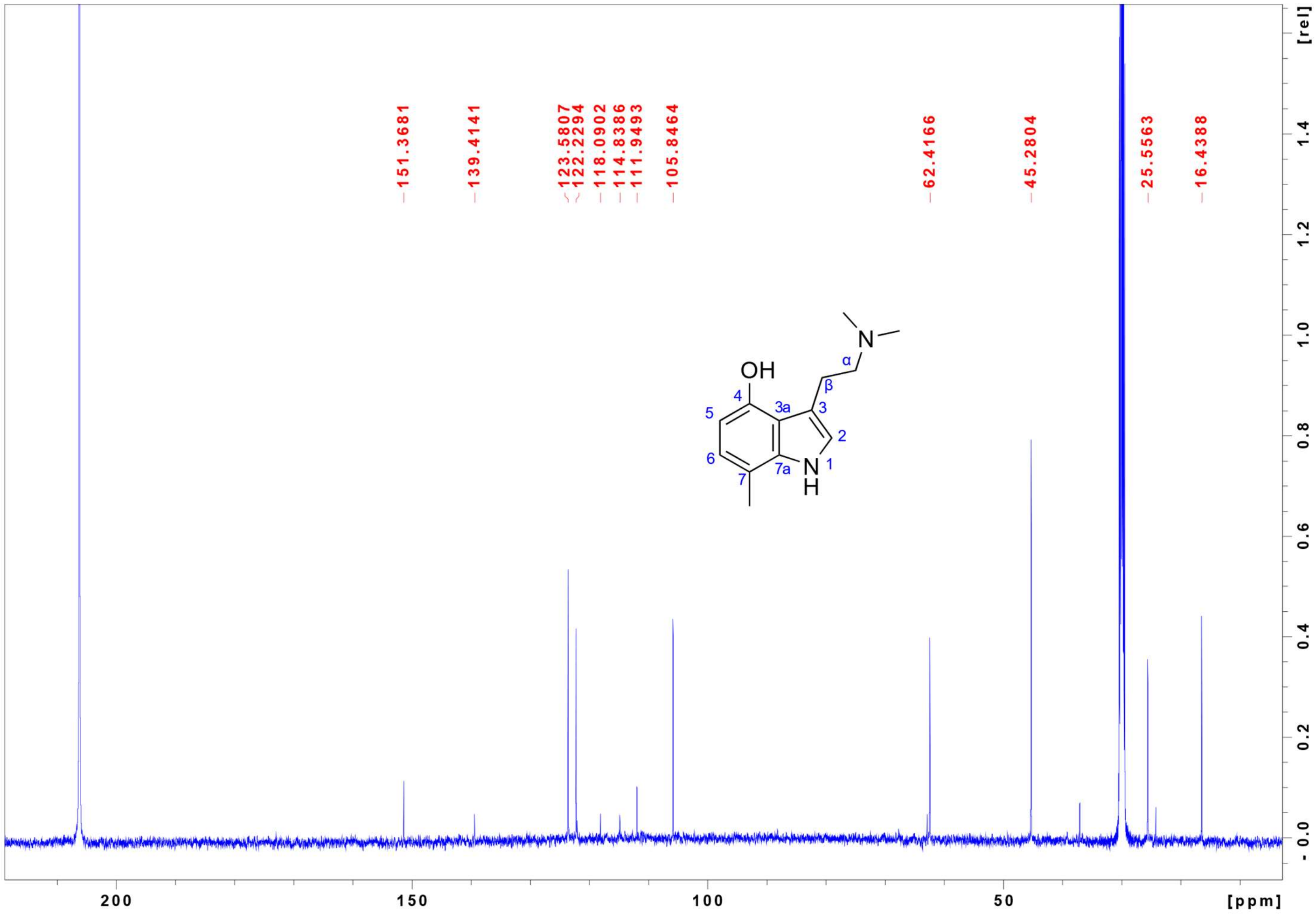

Figure S3b. ^{13}C NMR spectrum of **5** (126 MHz, acetone-d_6).

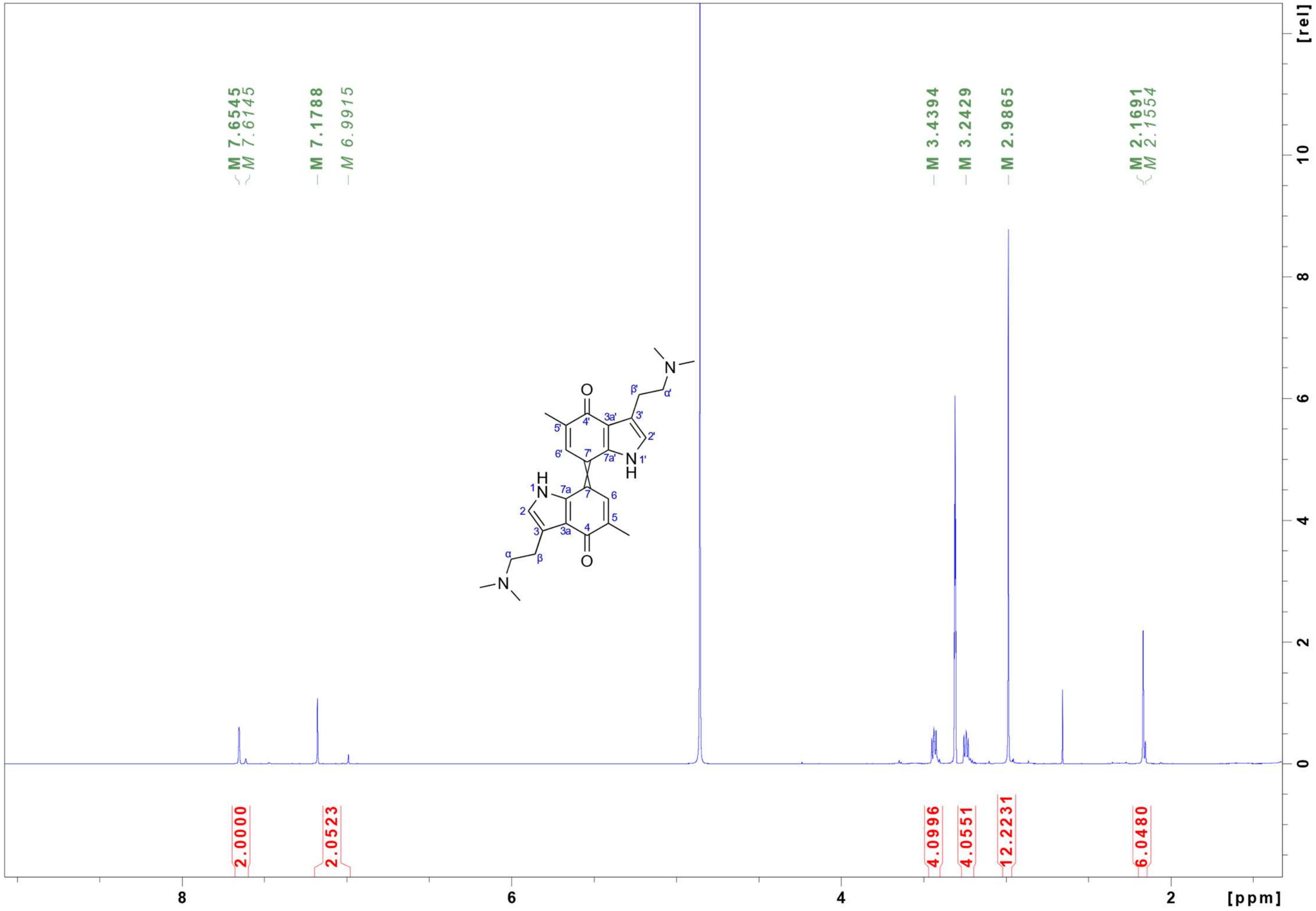

Figure S4a. ^{1}H NMR spectrum of **4a** (600 MHz, methanol-*d*$_4$). Major isomer: bold peak labels, minor isomer (if resolved): italicized peak labels.

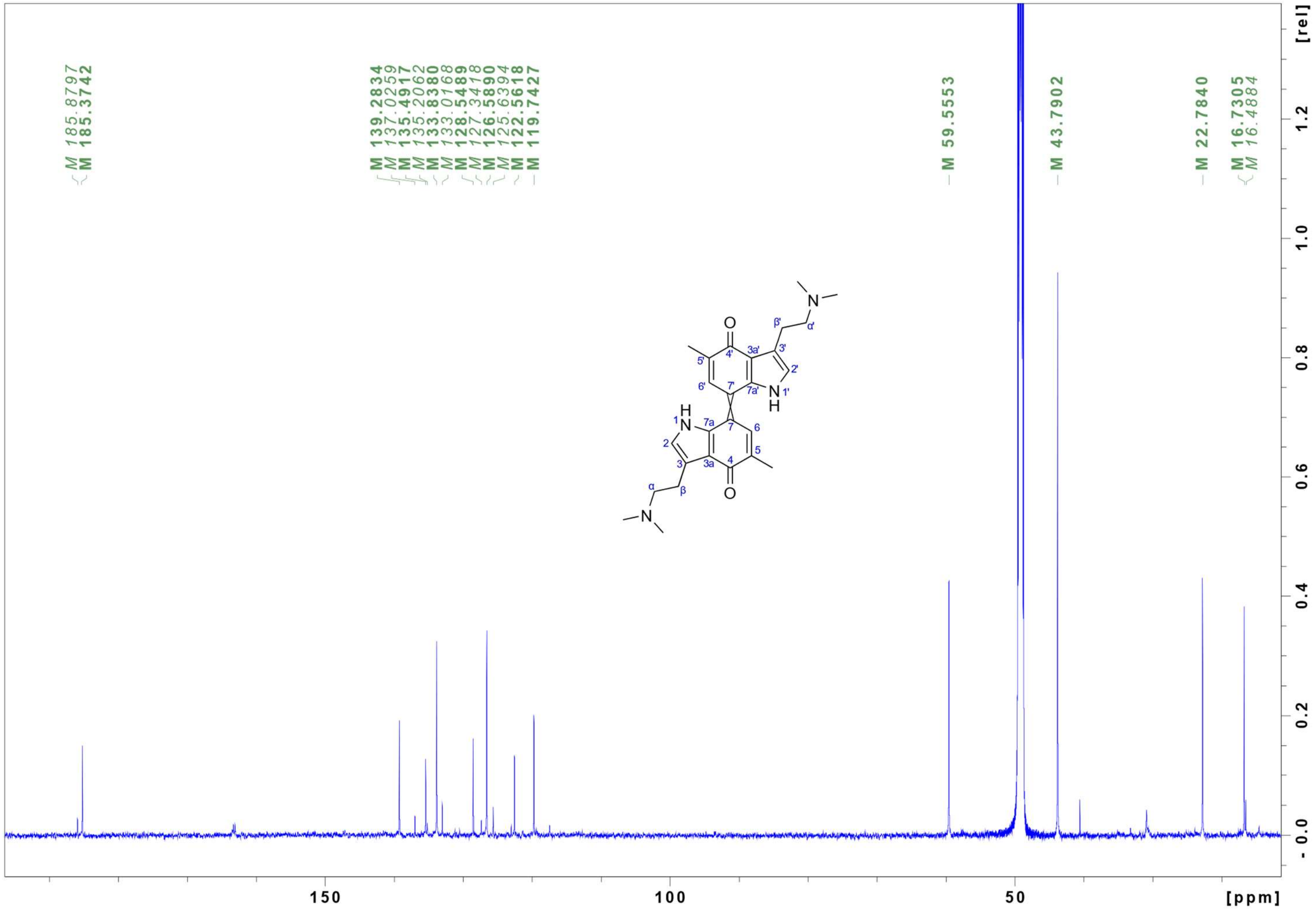

Figure S4b. ^{13}C NMR spectrum of **4a** (151 MHz, methanol-d_4). Major isomer: bold peak labels, minor isomer (if resolved): italicized peak labels.

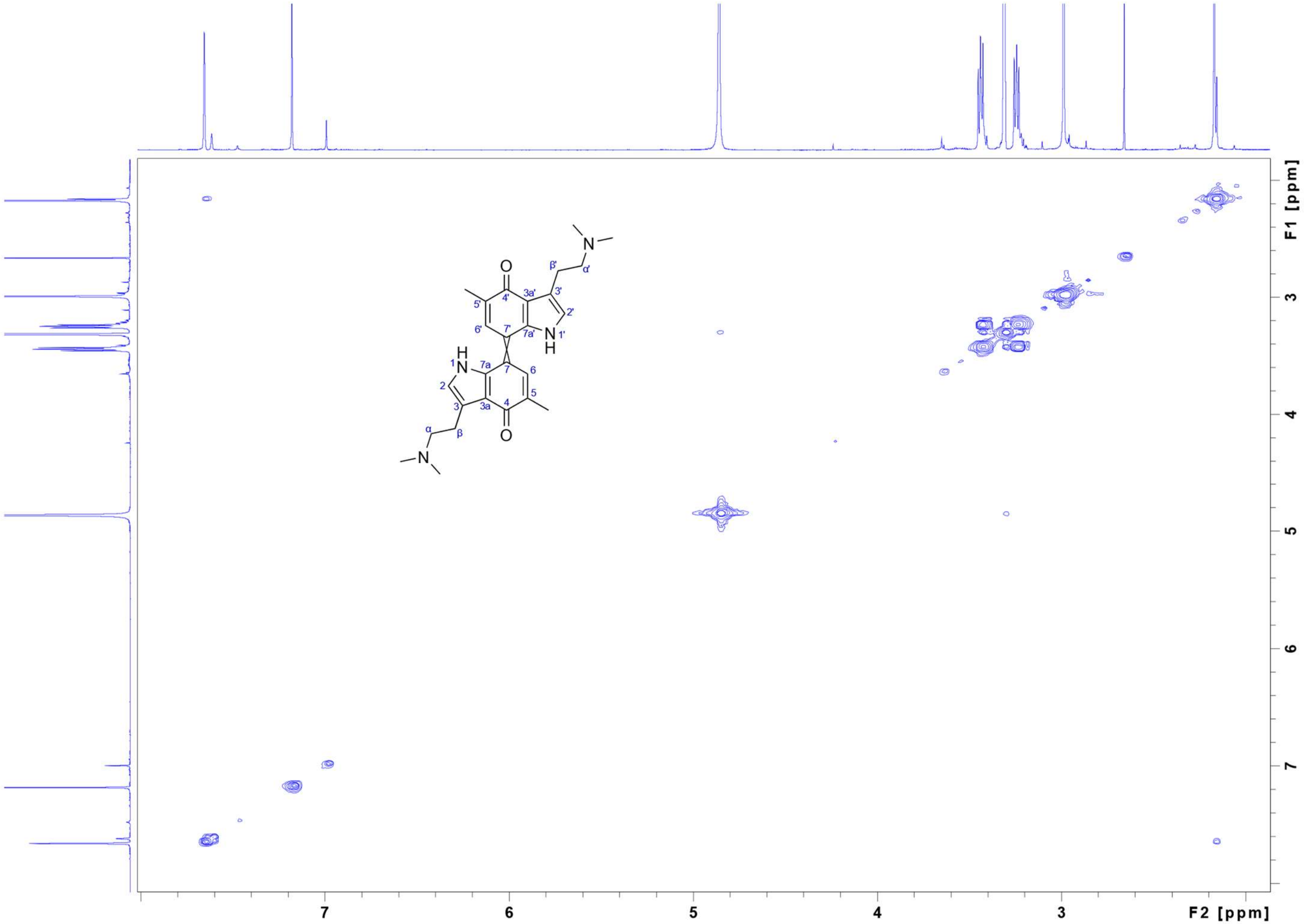

Figure S4c. ^{1}H,^{1}H COSY spectrum of **4a** (600 MHz, methanol-*d*$_4$).

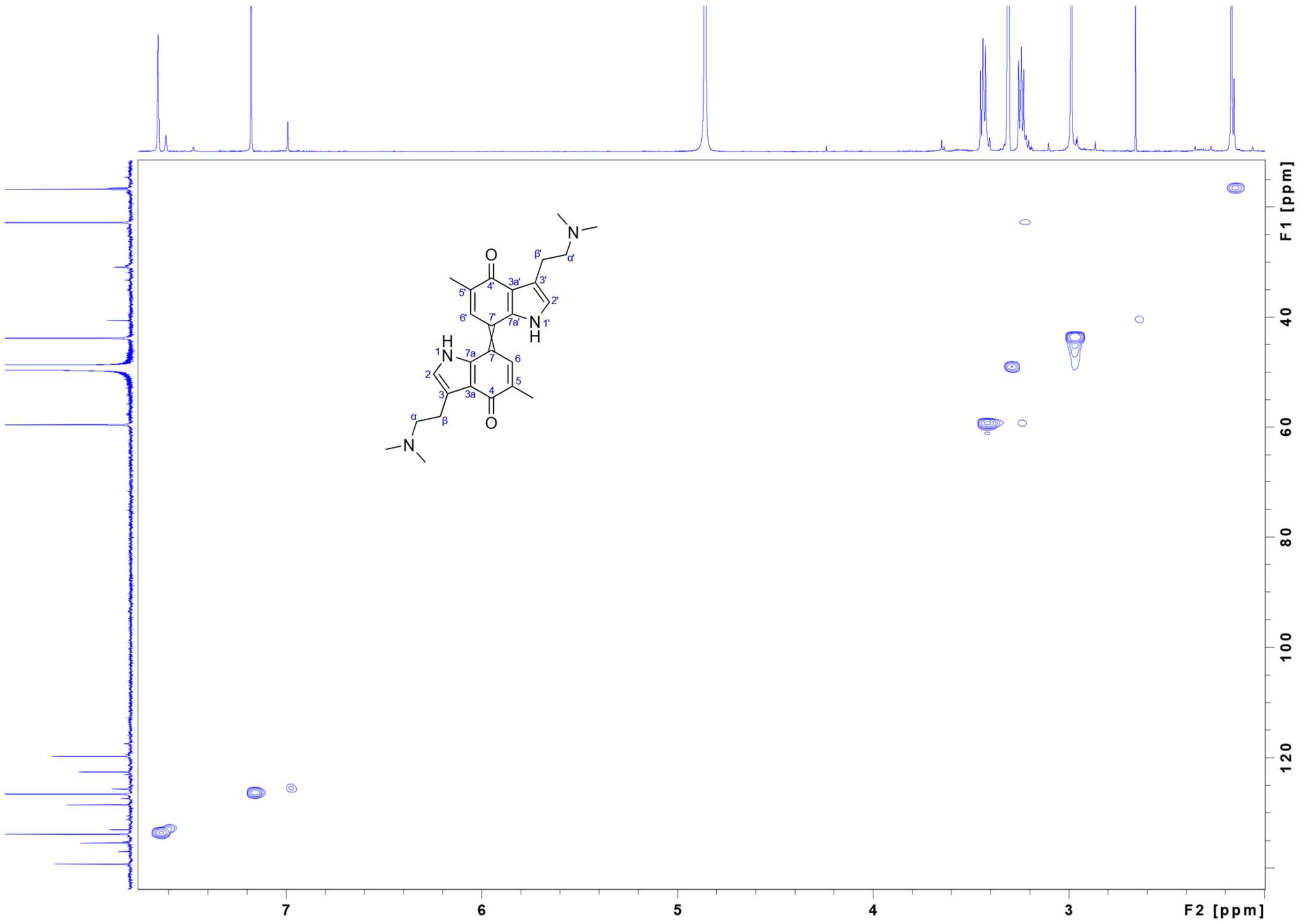

Figure S4d. ^{1}H,^{13}C HSQC spectrum of **4a** (^{1}H: 600 MHz, ^{13}C: 151 MHz, methanol-*d*$_4$).

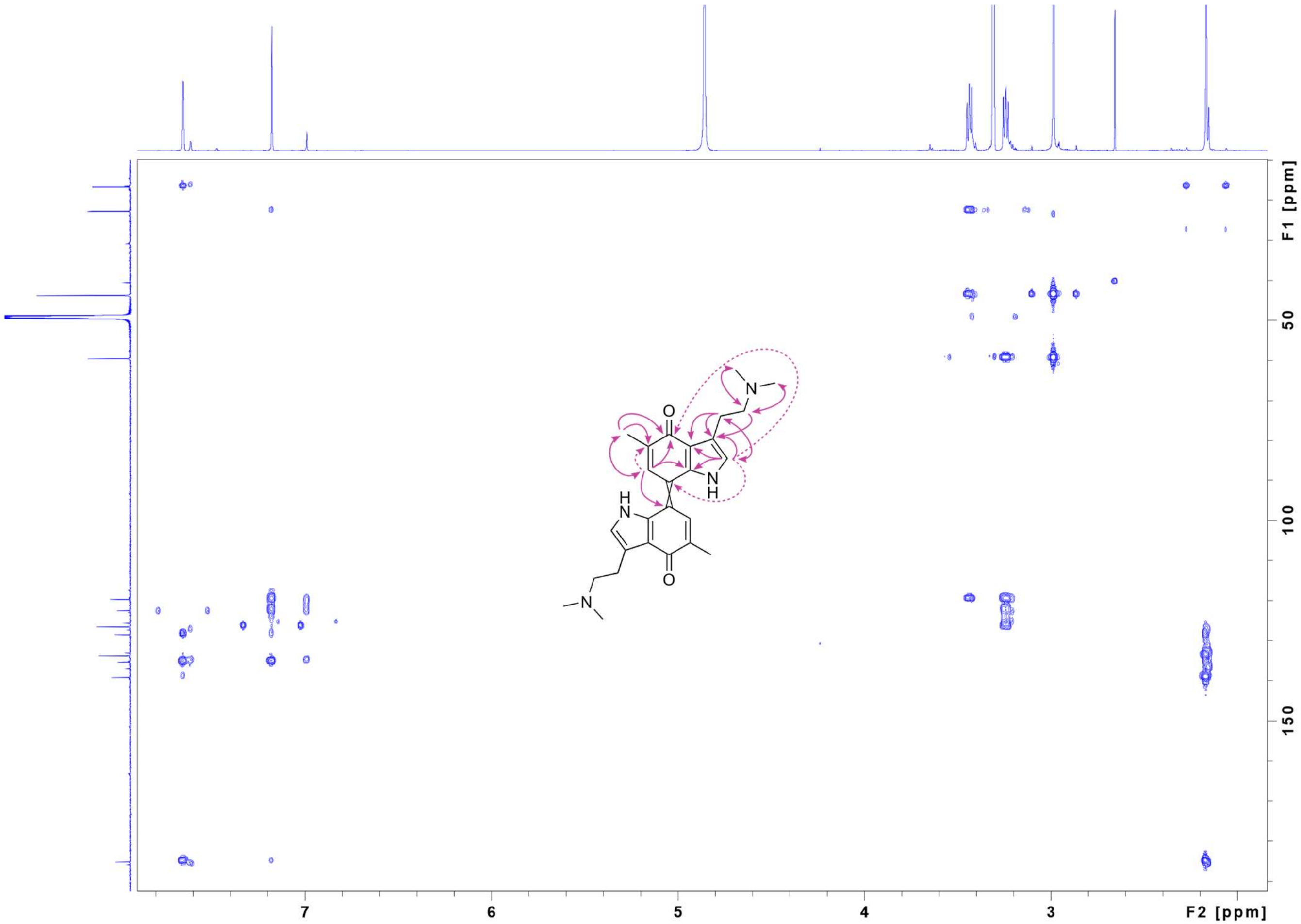

Figure S4e. ^{1}H,^{13}C HMBC spectrum of **4a** (^{1}H: 600 MHz, ^{13}C: 151 MHz, methanol-d_4). Selected correlations shown as pink arrows (dotted arrows: weak correlations).

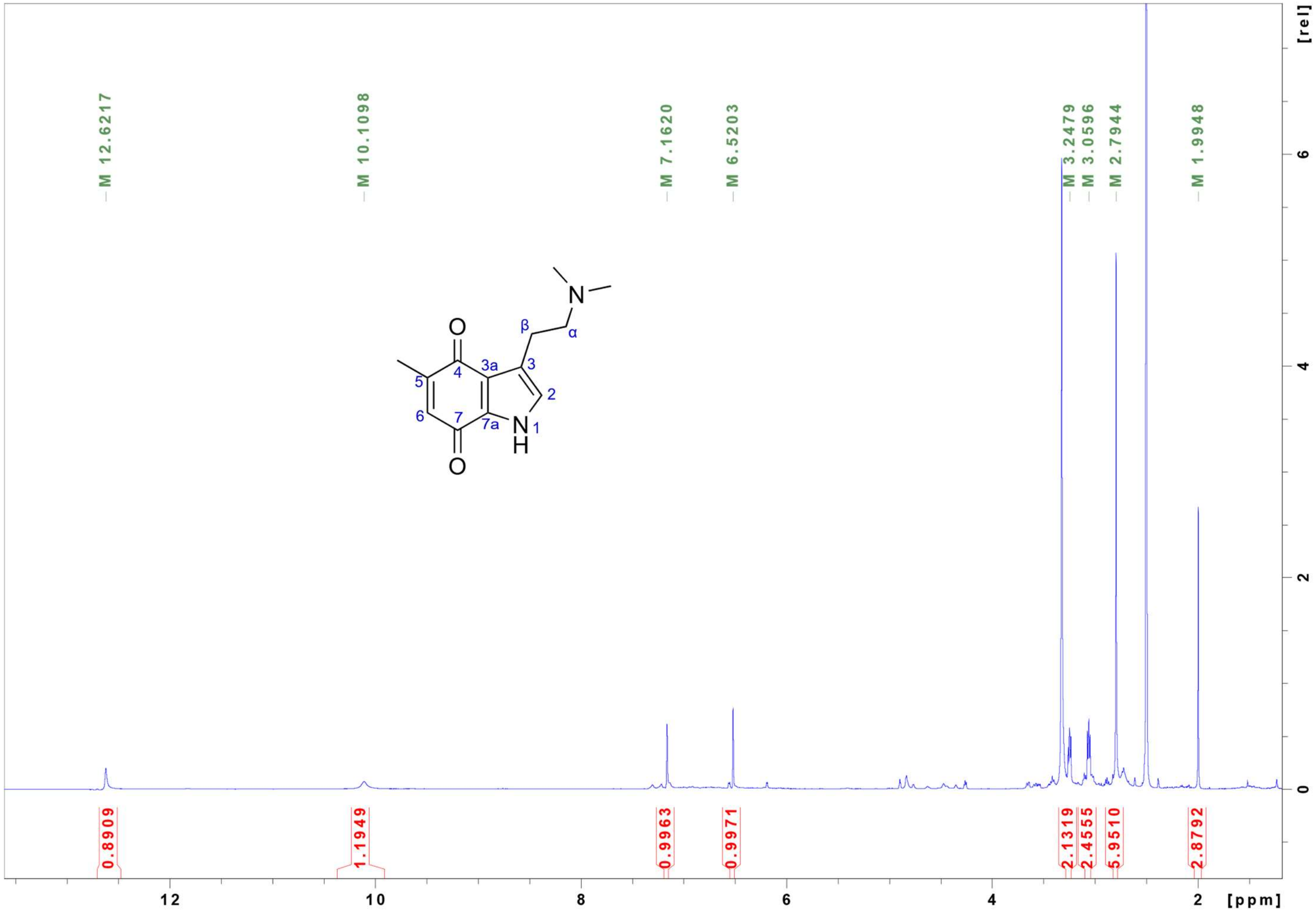

Figure S5a. ^{1}H NMR spectrum of **4b** (600 MHz, DMSO-*d*$_6$).

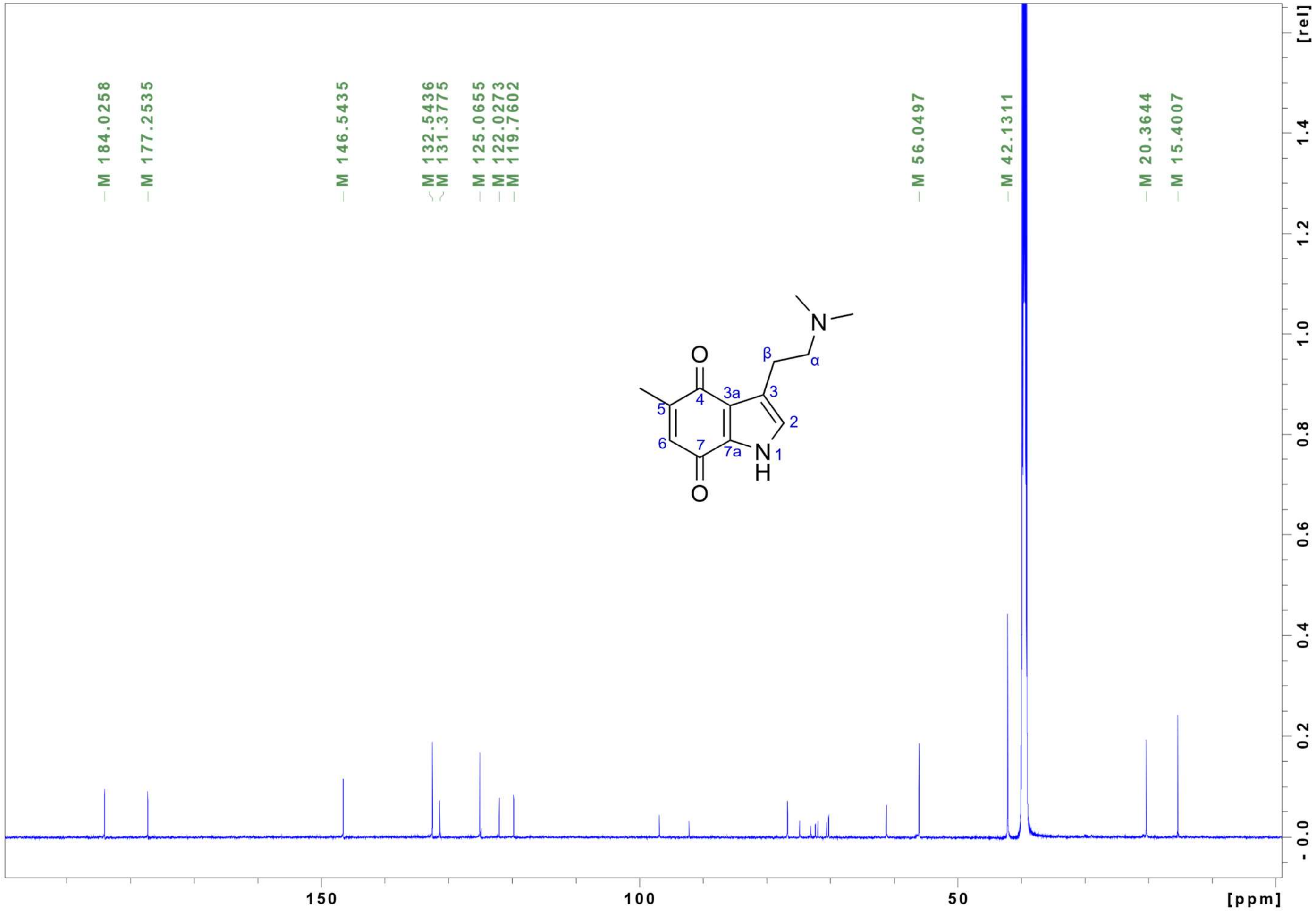

Figure S5b. ^{13}C NMR spectrum of **4b** (151 MHz, DMSO-d_6).

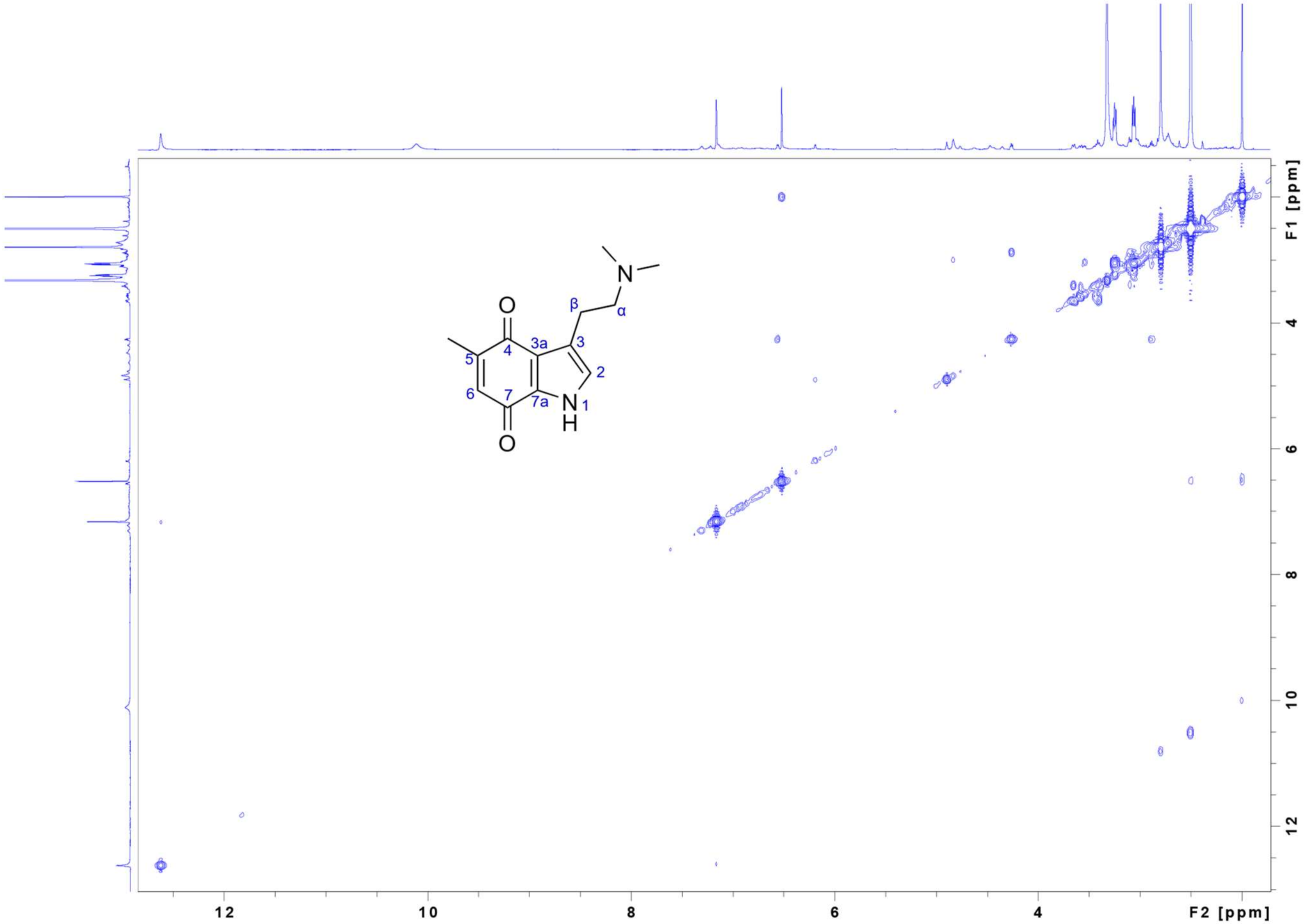

Figure S5c. ^{1}H,^{1}H COSY spectrum of **4b** (600 MHz, DMSO-*d*$_6$).

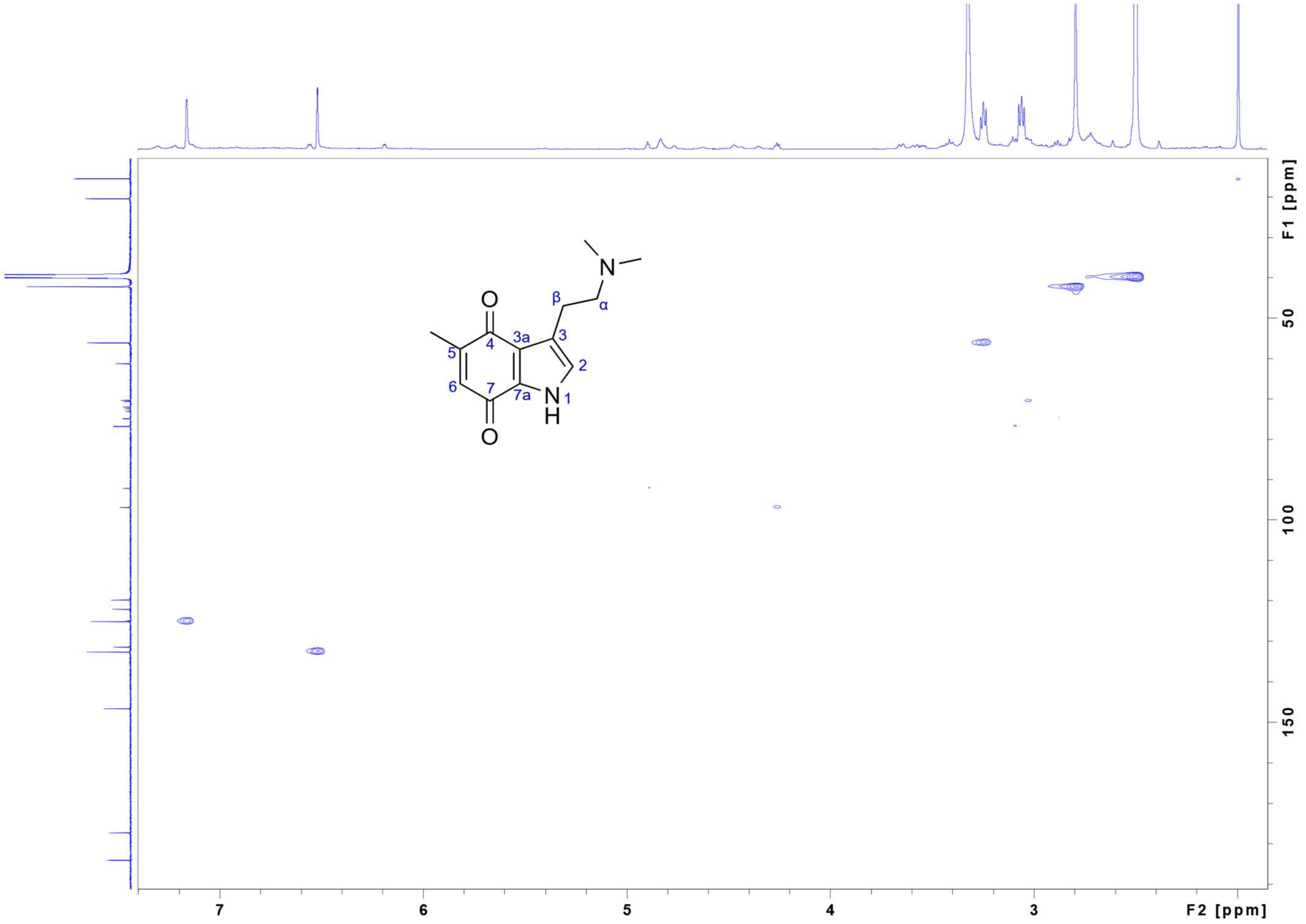

Figure S5d. ^{1}H,^{13}C HSQC spectrum of **4b** (^{1}H: 600 MHz, ^{13}C: 151 MHz, DMSO-d_6).

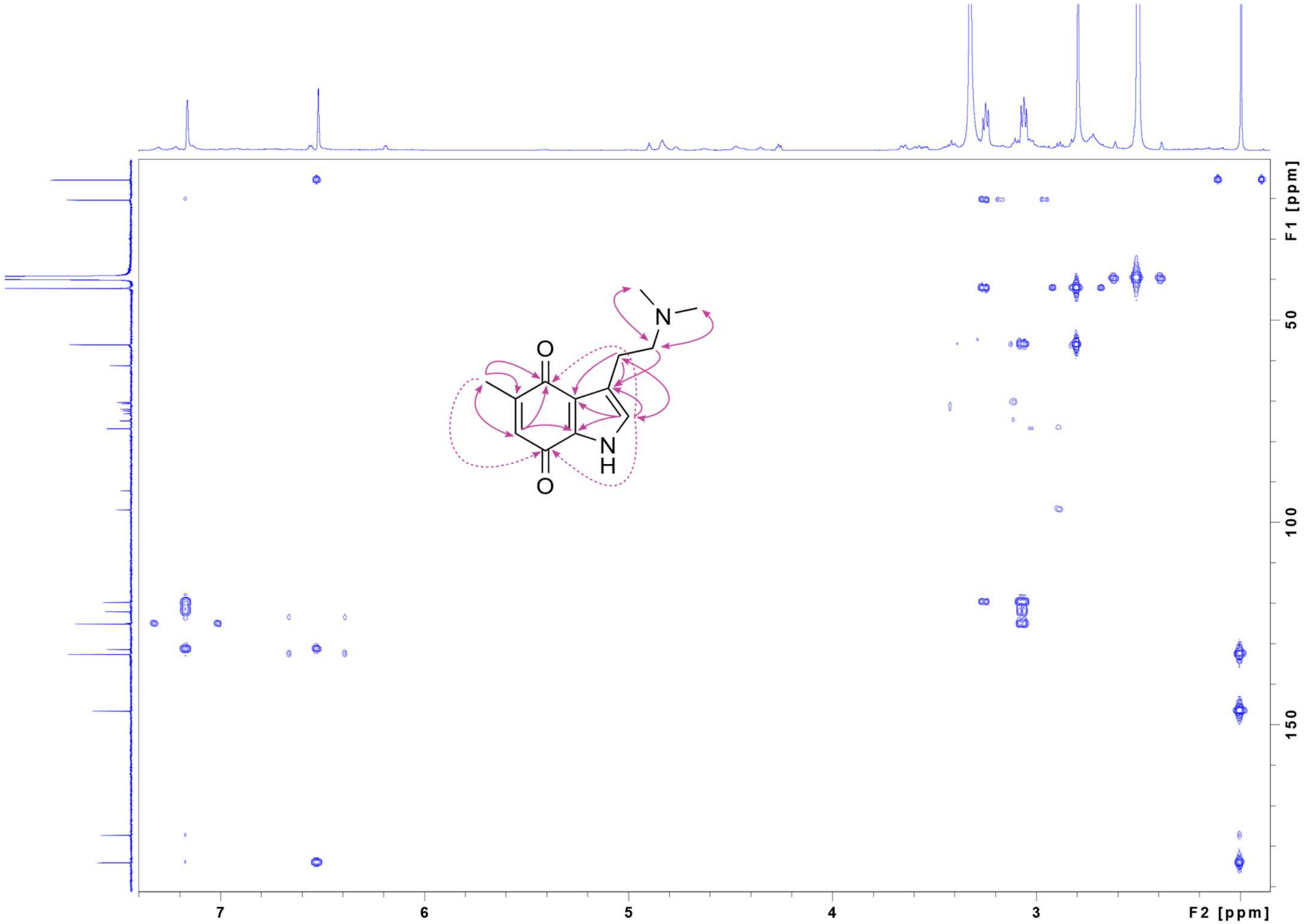

Figure S5e. ^{1}H,^{13}C HMBC spectrum of **4b** (^{1}H: 600 MHz, ^{13}C: 151 MHz, DMSO-*d*$_6$). Selected correlations shown as pink arrows (dotted arrows: weak correlations).

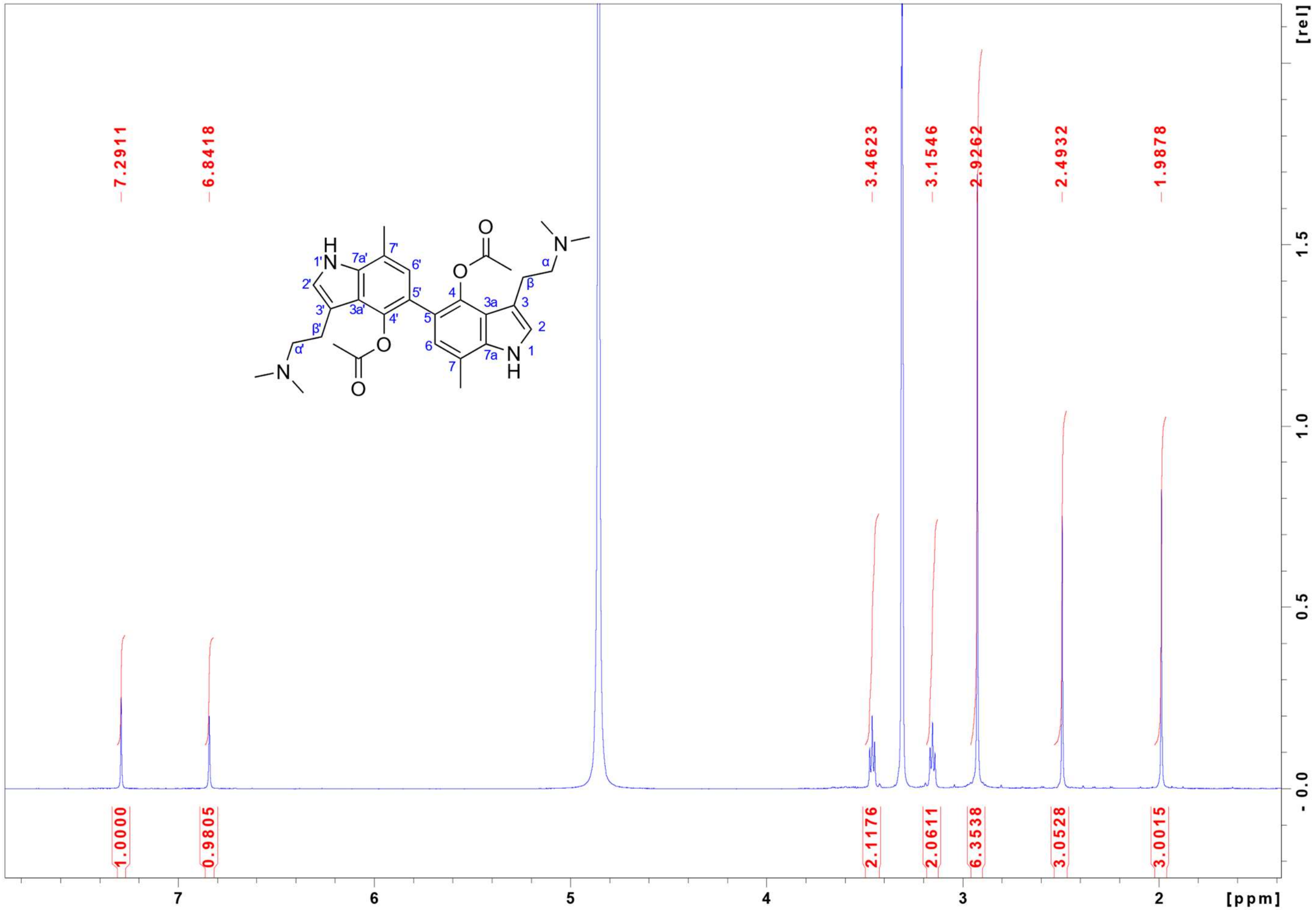

Figure S6a. ^{1}H NMR spectrum of **5b** (600 MHz, methanol-*d*$_4$).

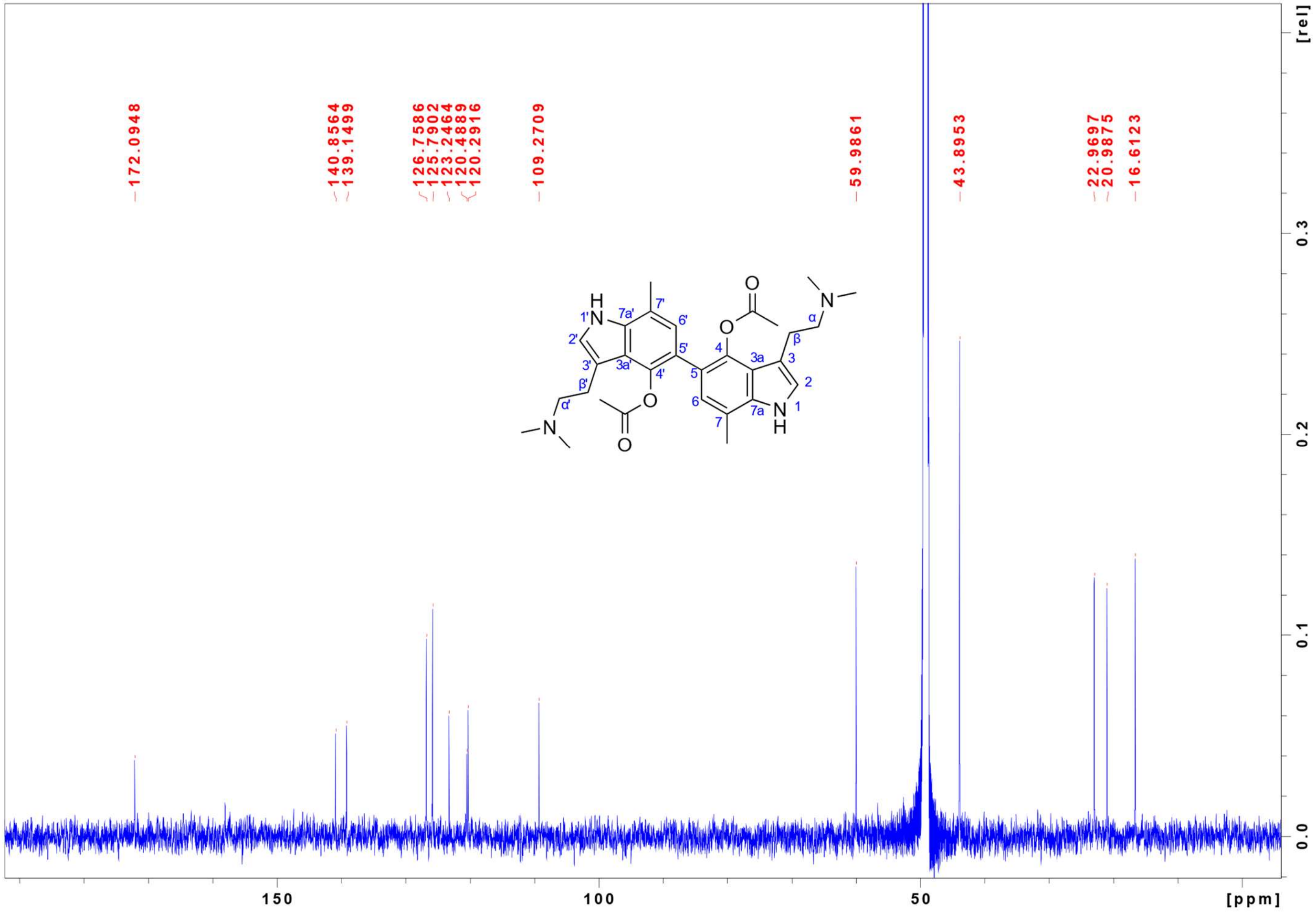

Figure S6b. ^{13}C NMR spectrum of **5b** (151 MHz, methanol-d_4).

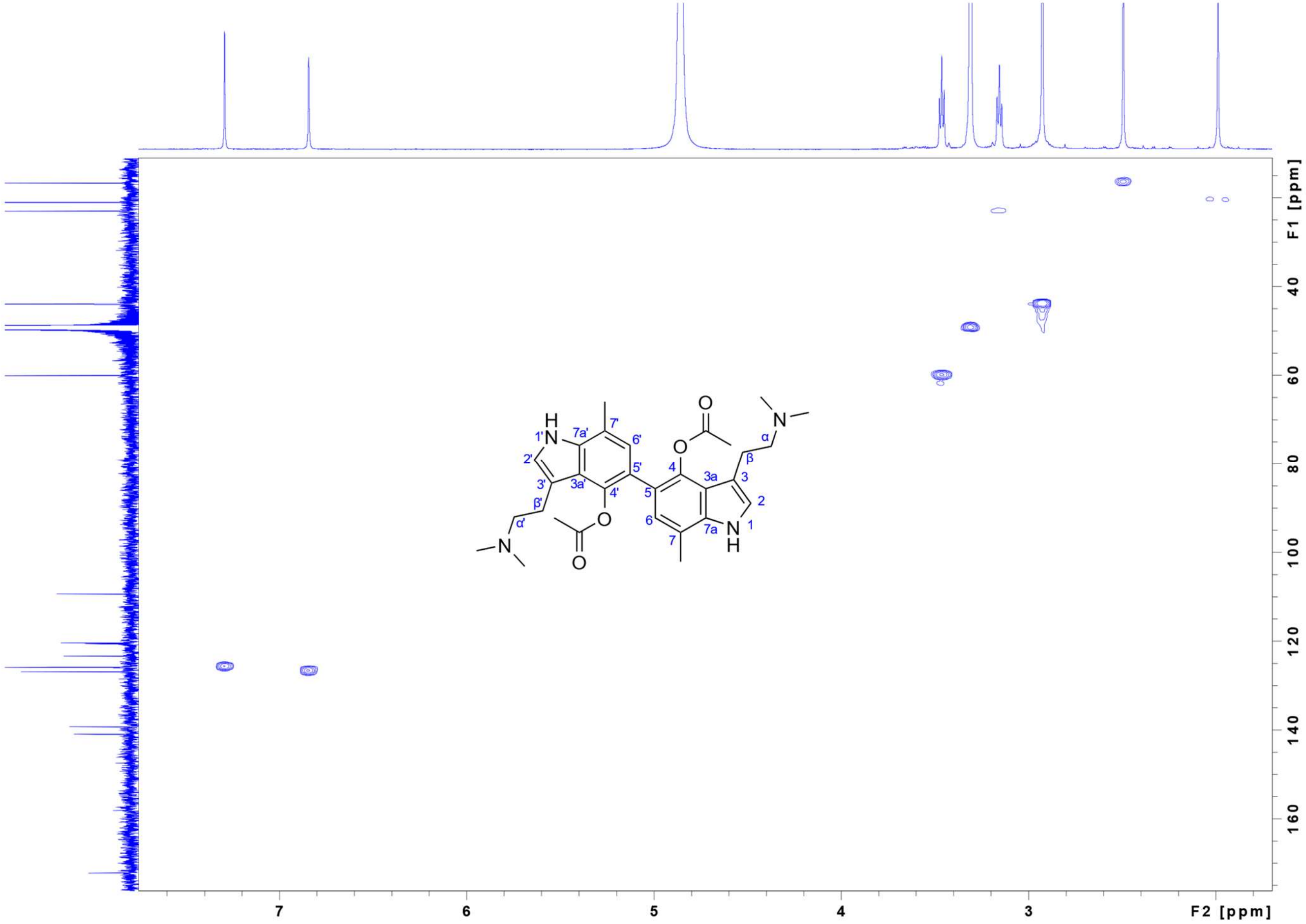

Figure S6c. ^{1}H,^{13}C HSQC spectrum of **5b** (^{1}H: 600 MHz, ^{13}C: 151 MHz, methanol-*d*$_4$).

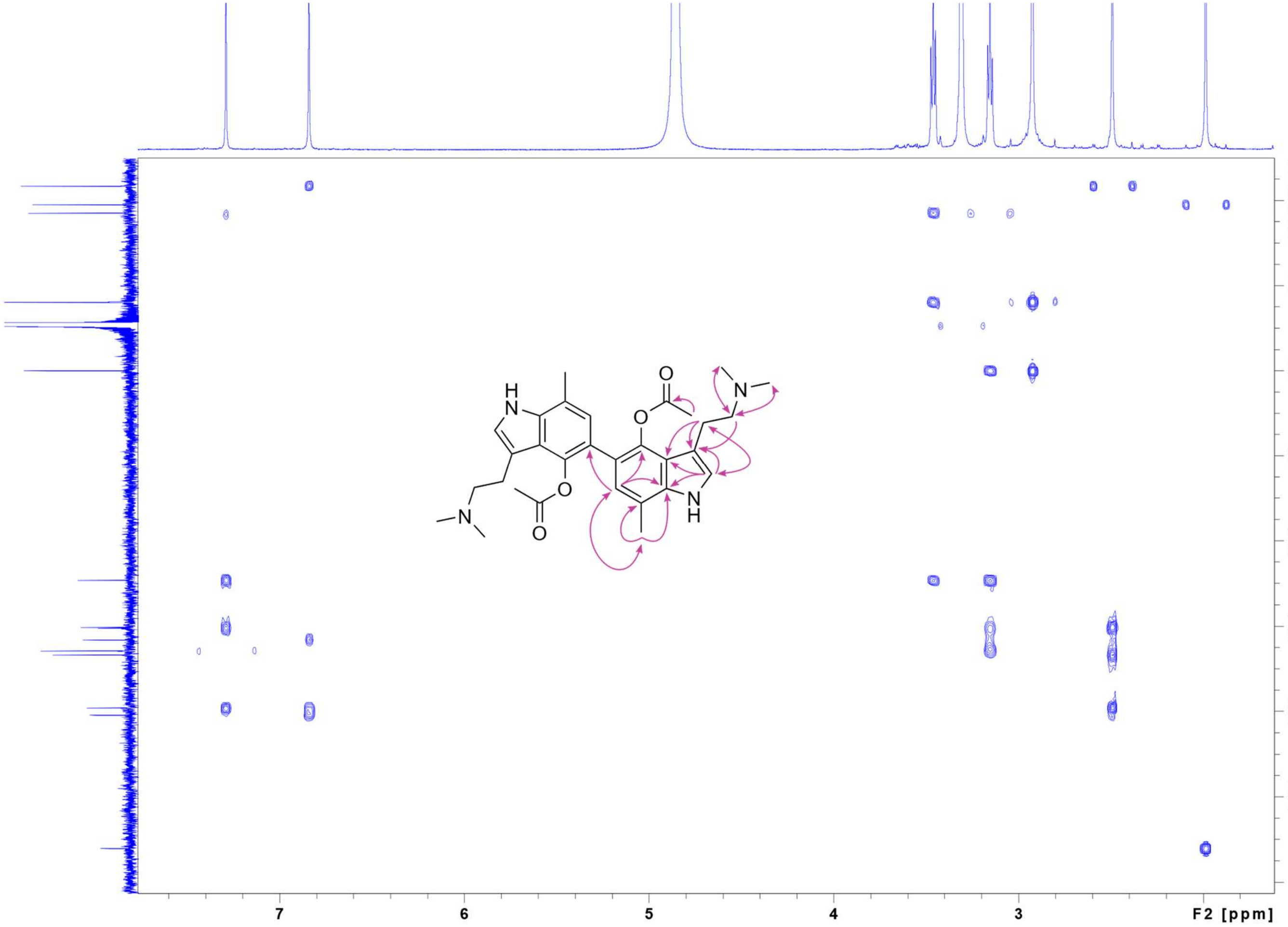

Figure S6d. ^{1}H,^{13}C HMBC spectrum of **5b** (^{1}H: 600 MHz, ^{13}C: 151 MHz, methanol-*d*$_4$). Selected correlations shown as pink arrows.

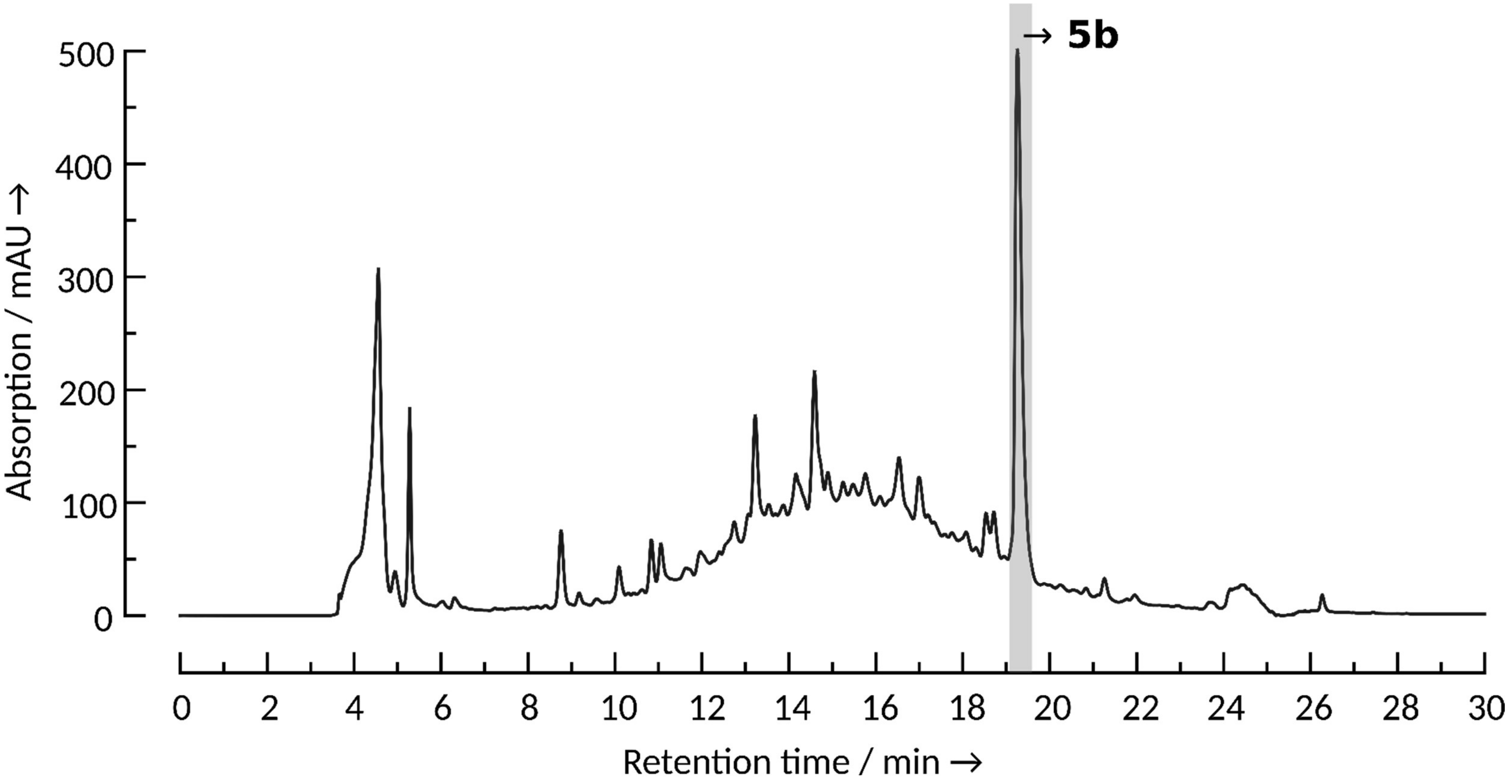

Figure S7. HPLC-UV chromatogram (λ = 280 nm, semi-preparative HPLC, C_{18} column) of acetylated oxidation product mixture derived from **5**. The shaded area indicates the collected fraction to isolate **5b**.

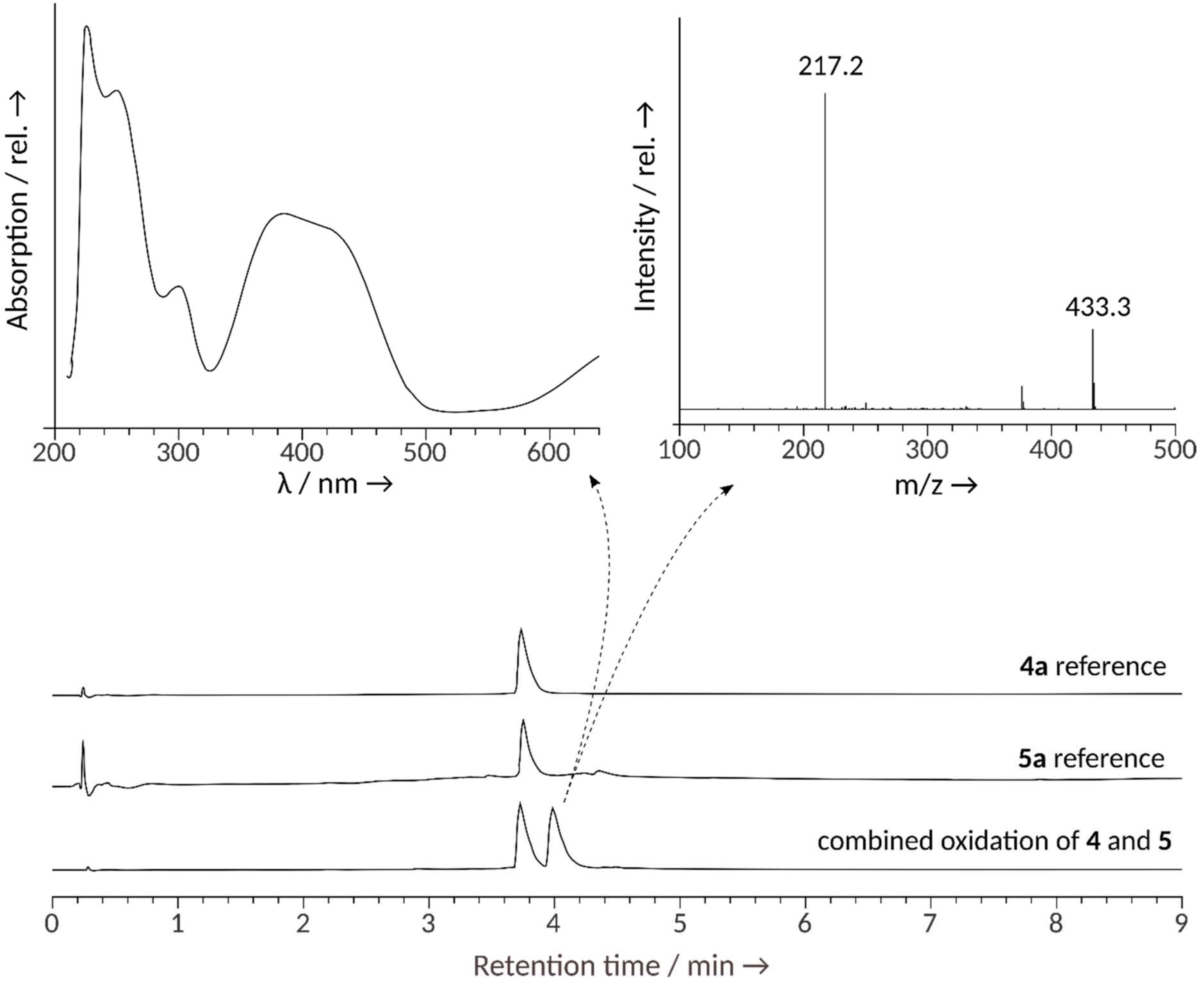

Figure S8. Chromatographic data of the putative heterodimer **6**. The combined oxidation of **4** and **5** yields **6** (t_R=4.0 min). Retention times for references **4a** and **5a** are t_R=3.7 and t_R=3.8 min, respectively. The upper left panel shows the UV/Vis spectrum, the upper right panel the mass spectrum of **6**. Ion assignments: $[M + 2H]^{2+}$ for m/z 217, $[M + H]^{+}$ for m/z 433.

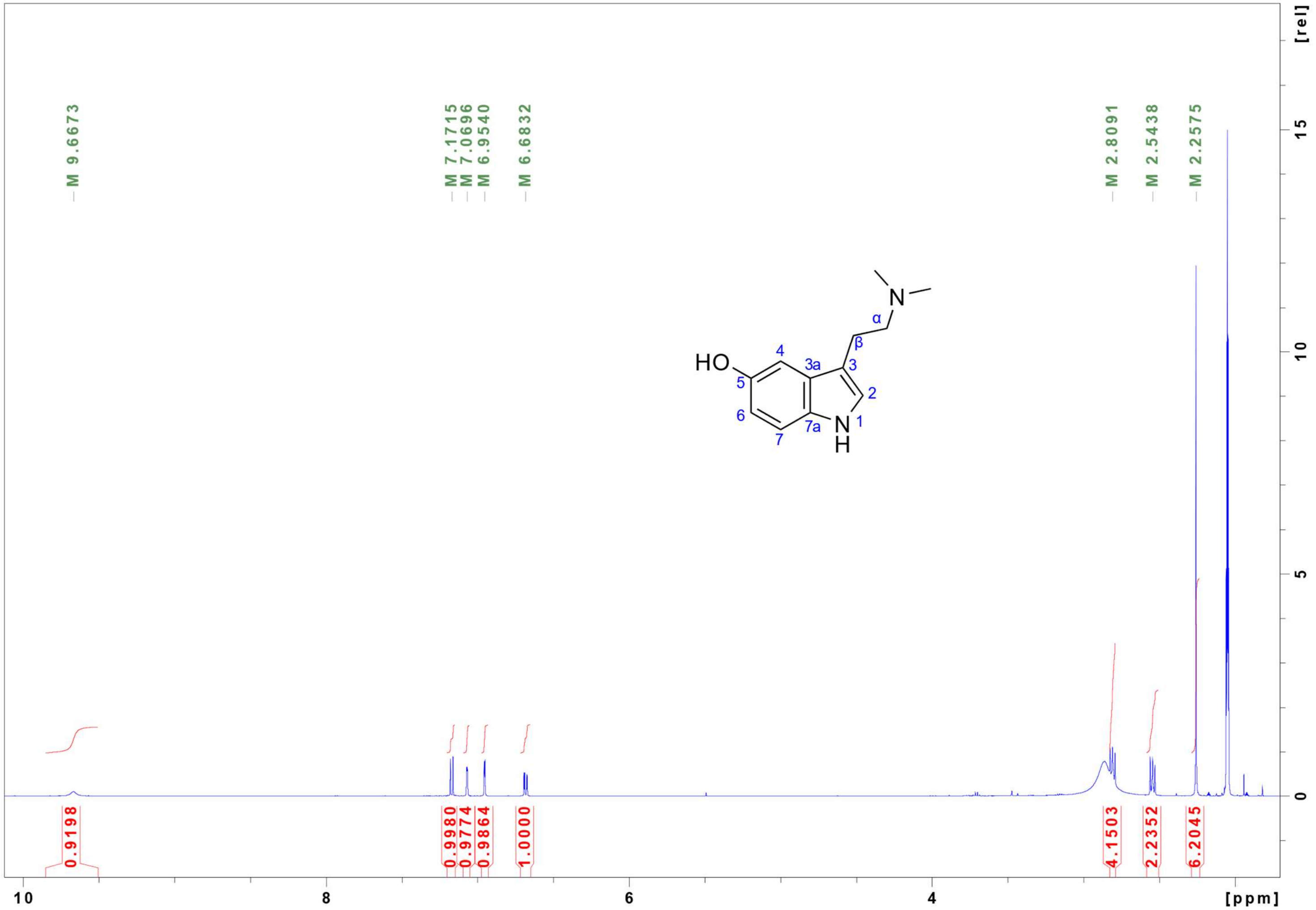

Figure S9a. ^{1}H NMR spectrum of **3** (500 MHz, acetone-d_6).

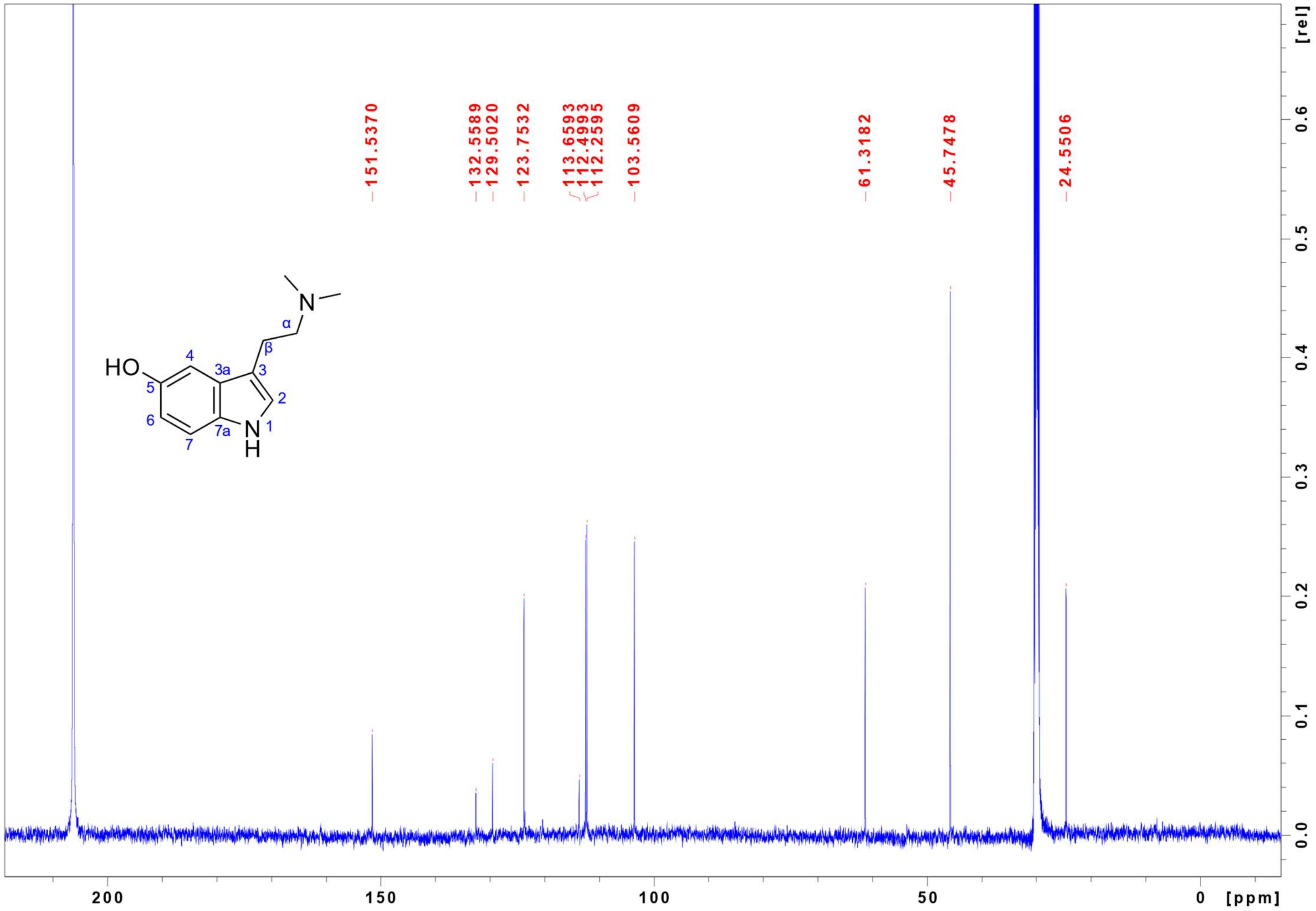

Figure S9b. ^{13}C NMR spectrum of **3** (126 MHz, acetone-d_6).

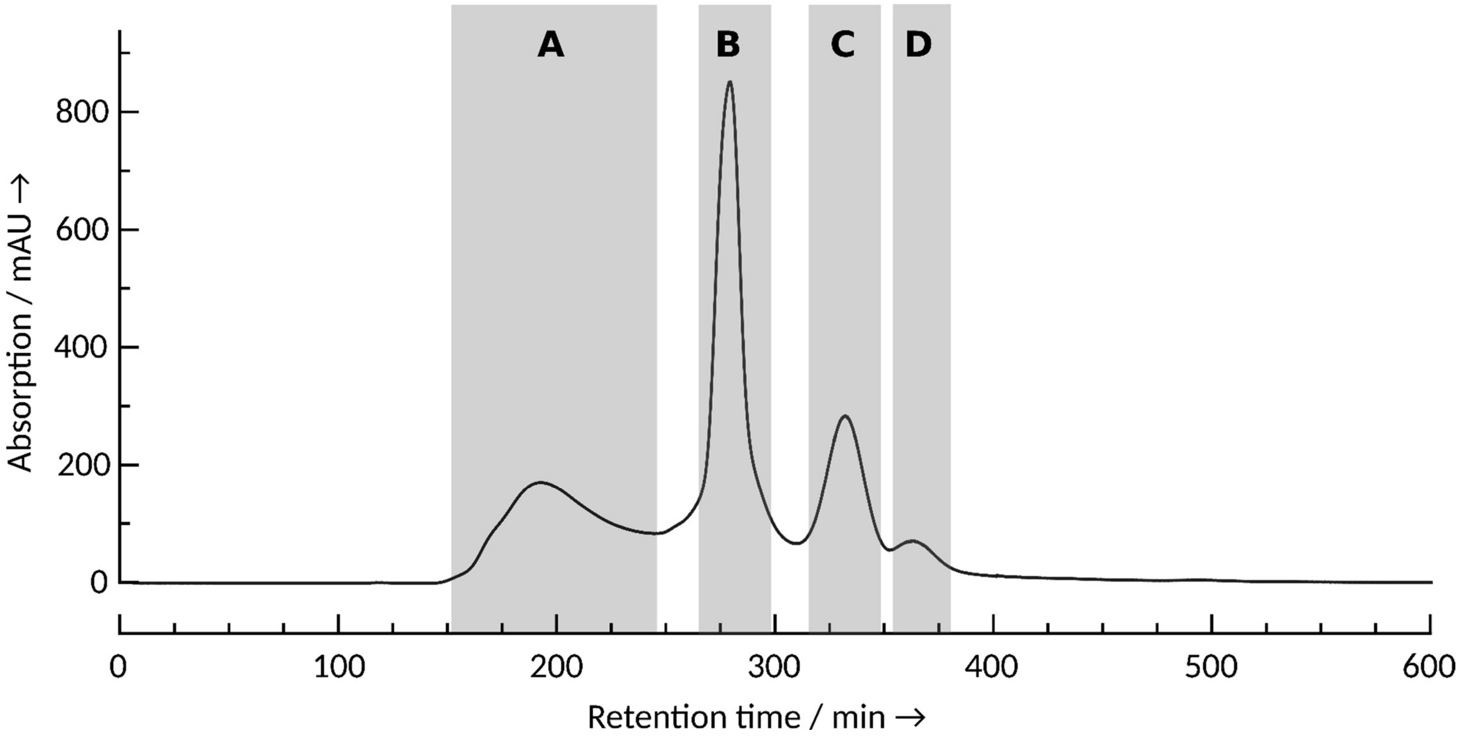

Figure S10. FPLC-UV chromatogram (λ = 280 nm, Sephadex LH-20 column) of crude oxidation product mixture derived from **3**. Shaded areas indicate collected fractions A-D. Main components as indicated by LC-DAD-MS analysis and/or isolated compounds: Fraction A: various higher oligomers; B: **3a**; C: **3b**, **3c**; D: **3e**.

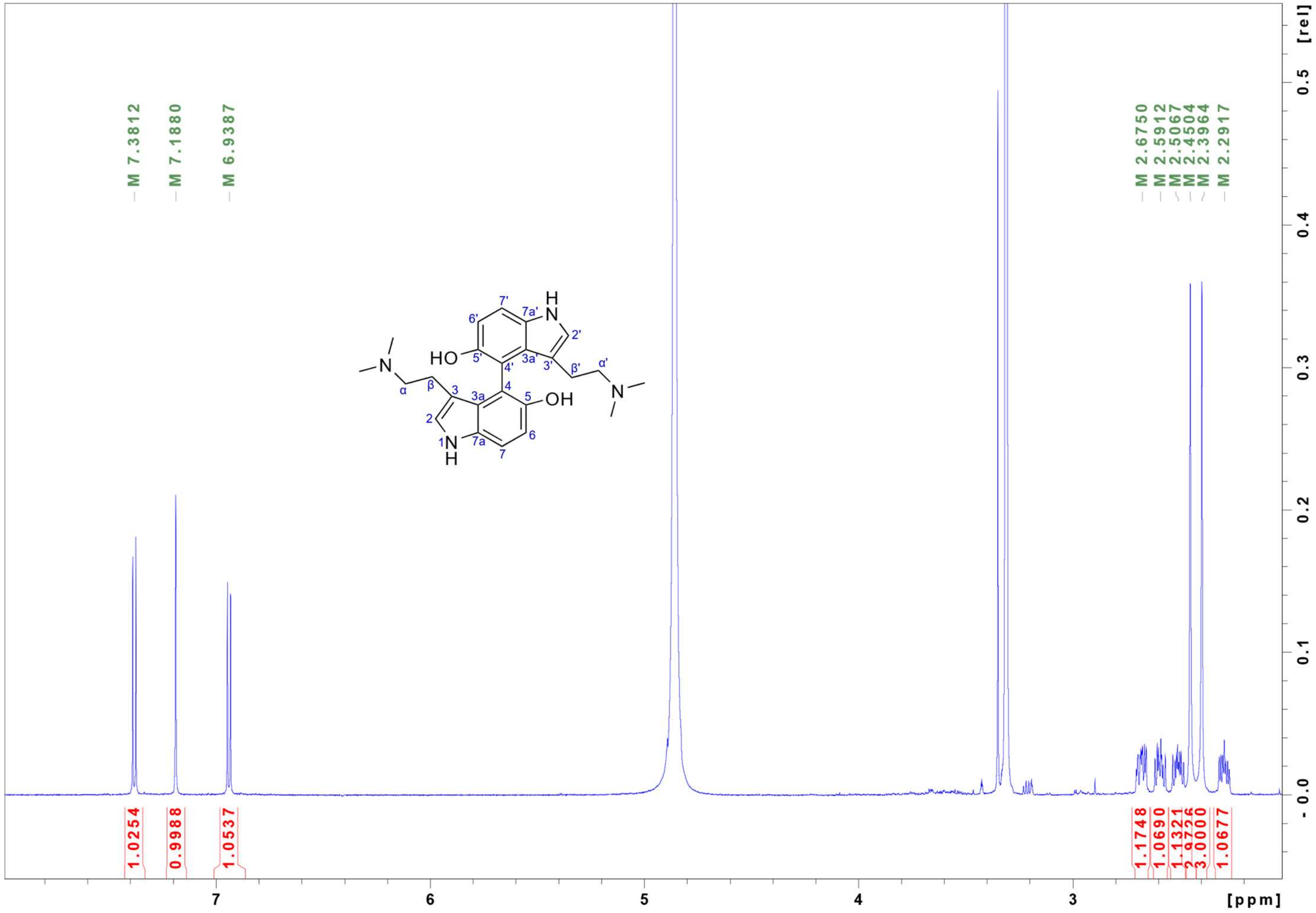

Figure S11a. ^{1}H NMR spectrum of **3a** (600 MHz, methanol-*d*$_4$).

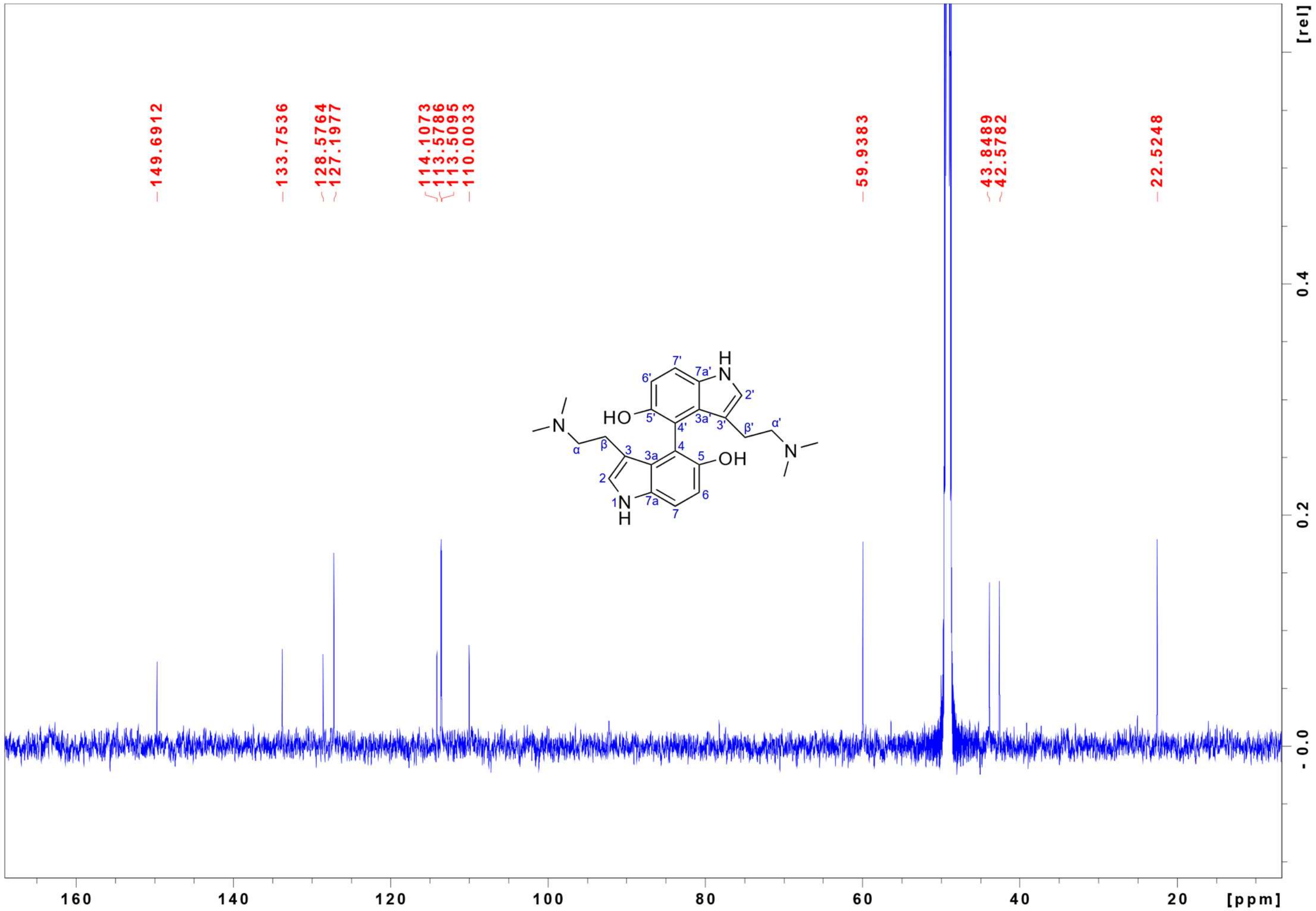

Figure S11b. ^{13}C NMR spectrum of **3a** (151 MHz, methanol-*d*$_4$).

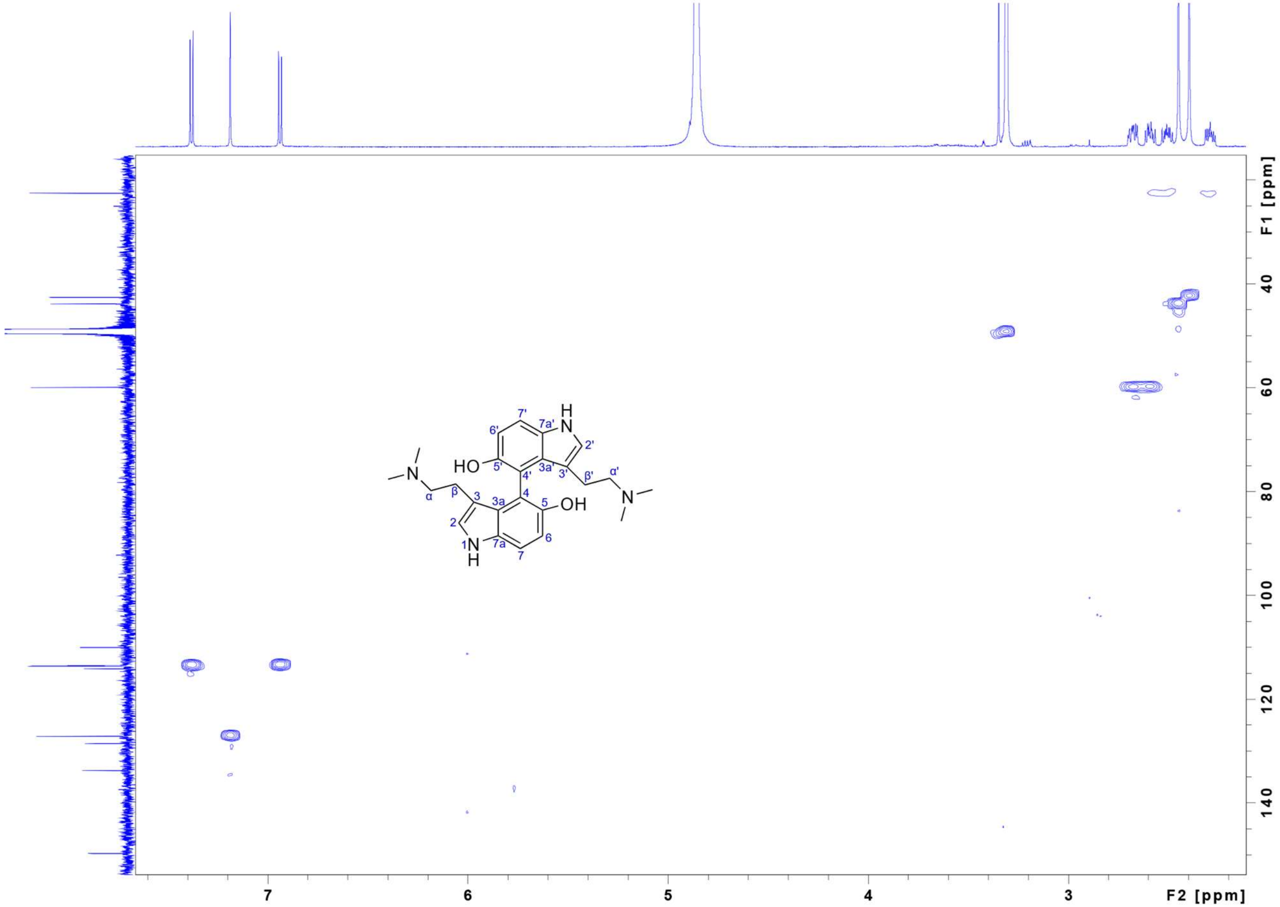

Figure S11c. ^{1}H,^{13}C HSQC spectrum of **3a** (^{1}H: 600 MHz, ^{13}C: 151 MHz, methanol-d_4).

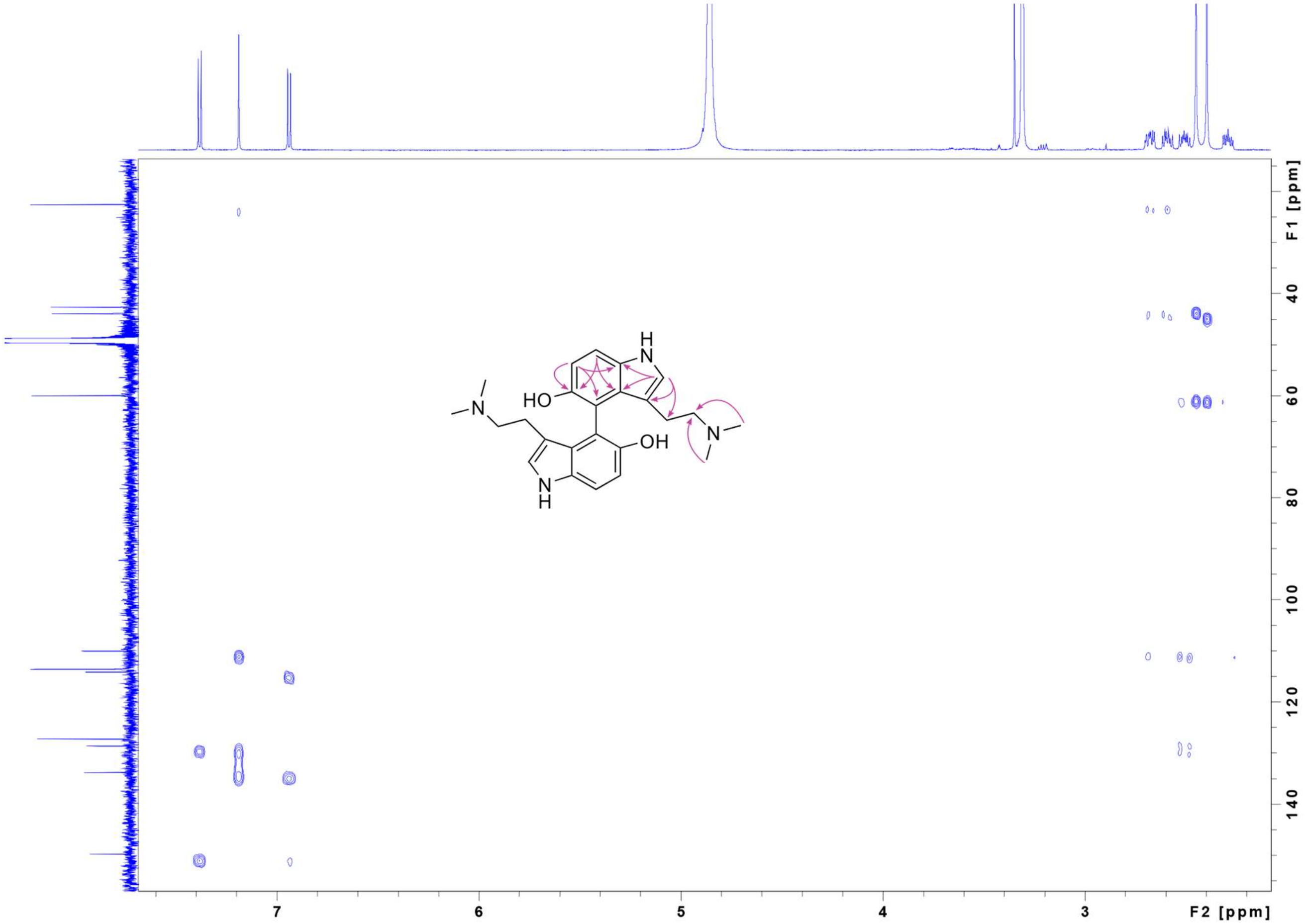

Figure S11d. ^{1}H,^{13}C HMBC spectrum of **3a** (^{1}H: 600 MHz, ^{13}C: 151 MHz, methanol-d_4). Selected correlations shown as pink arrows.

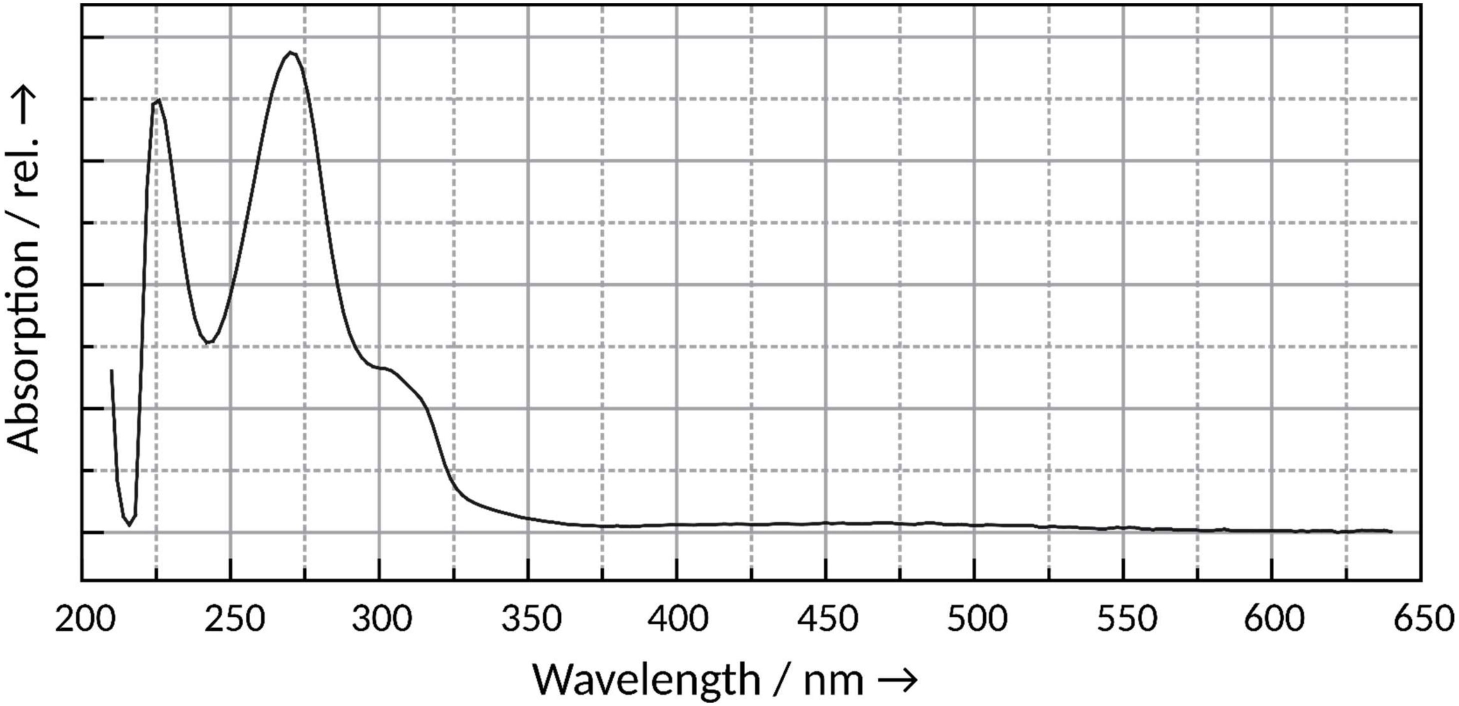

Figure S12. UV/Vis spectrum of **3b**, derived from DAD data.

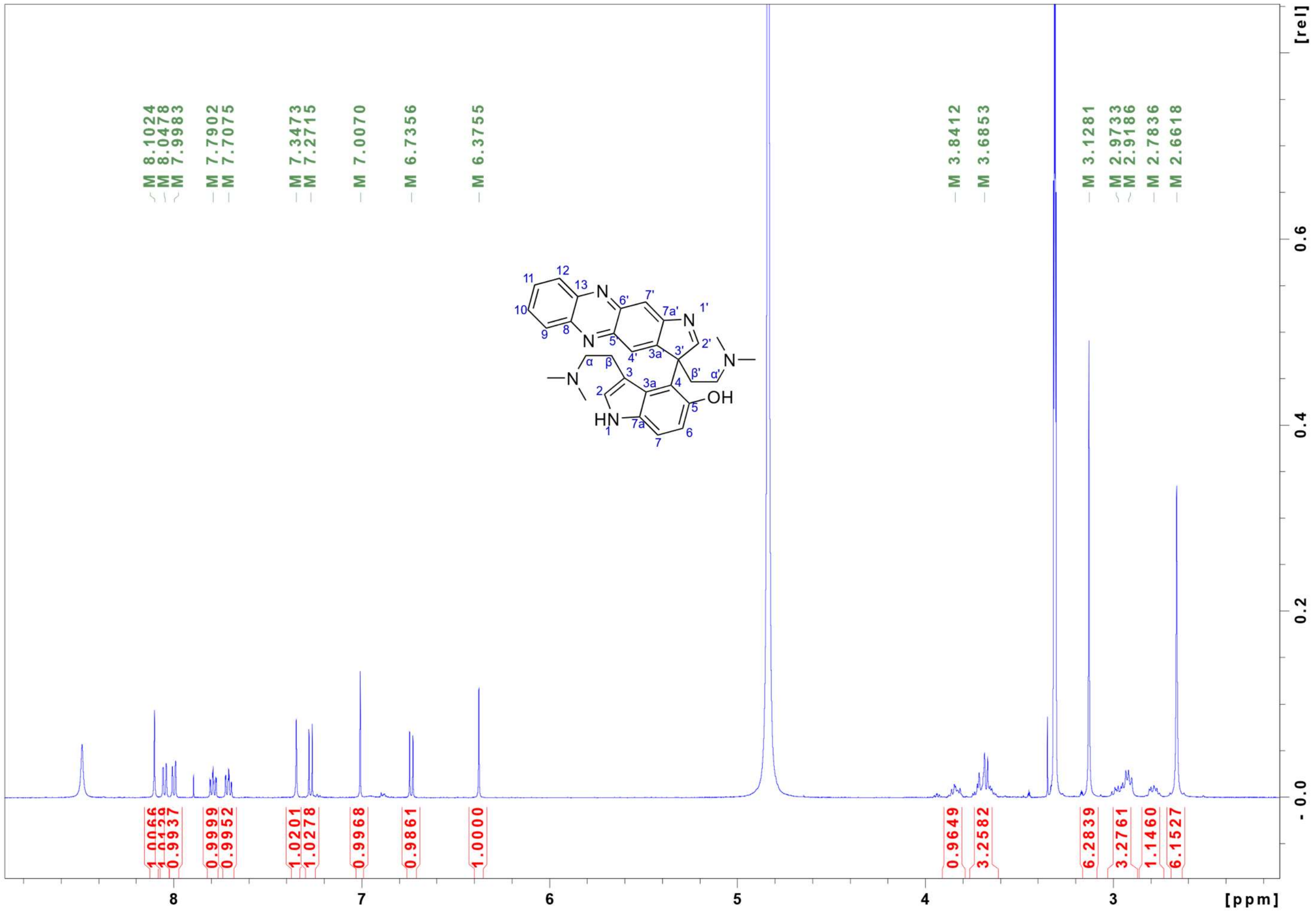

Figure S13a. ^{1}H NMR spectrum of **3d** (500 MHz, methanol-d_4).

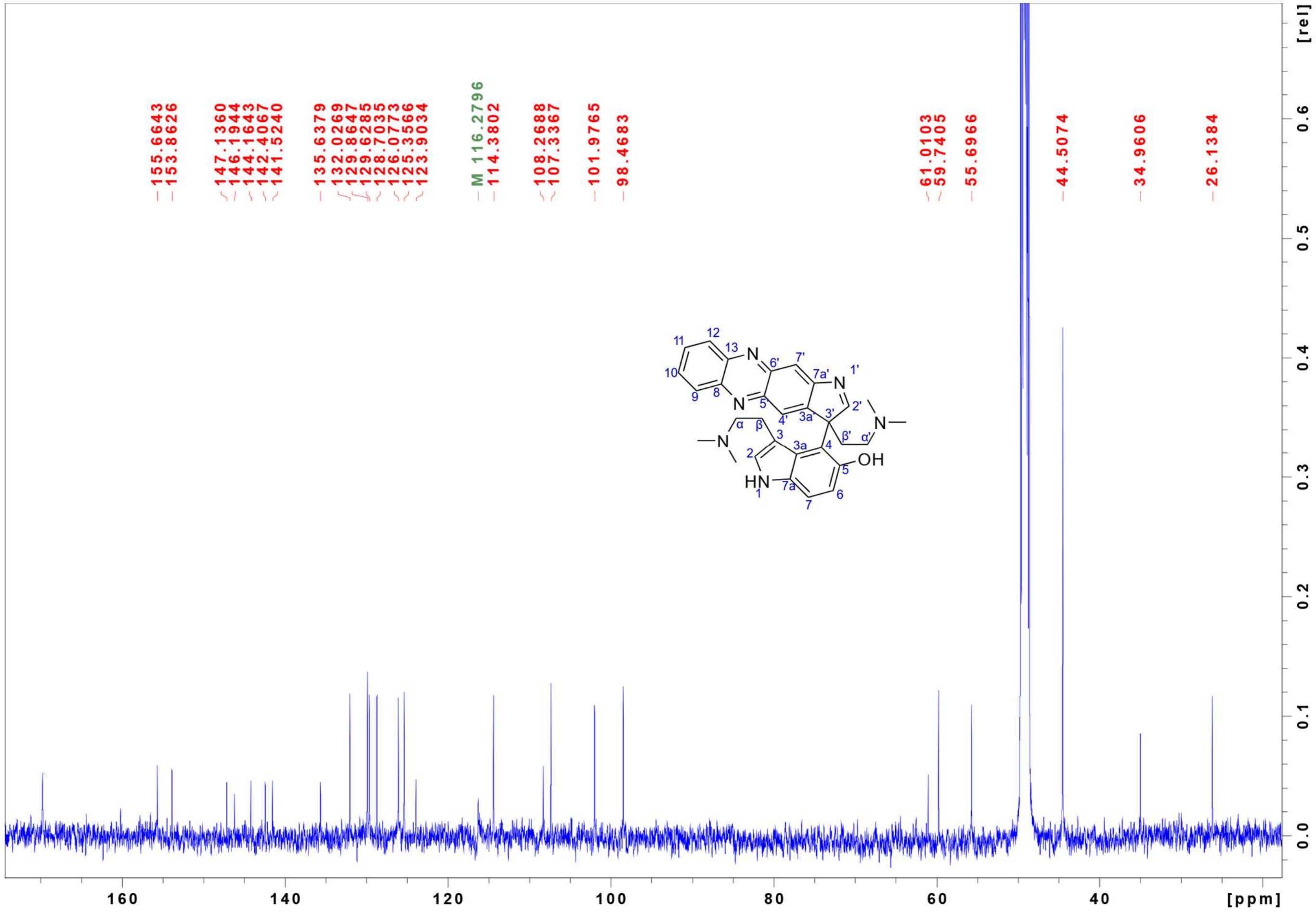

Figure S13b. ^{13}C NMR spectrum of **3d** (126 MHz, methanol-*d*$_4$).

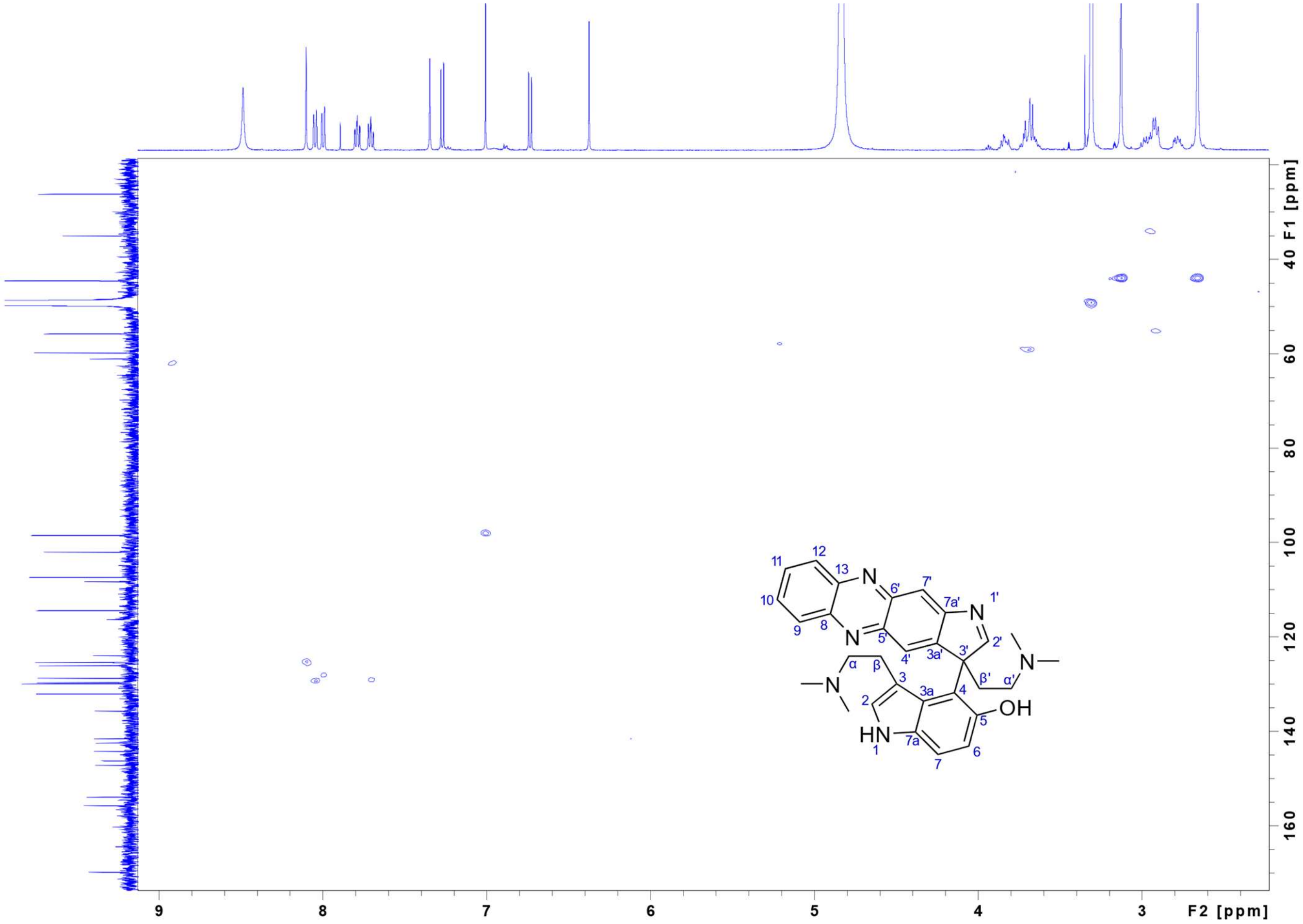

Figure S13c. ^{1}H,^{13}C HSQC spectrum of **3d** (^{1}H: 500 MHz, ^{13}C: 126 MHz, methanol-*d*$_4$).

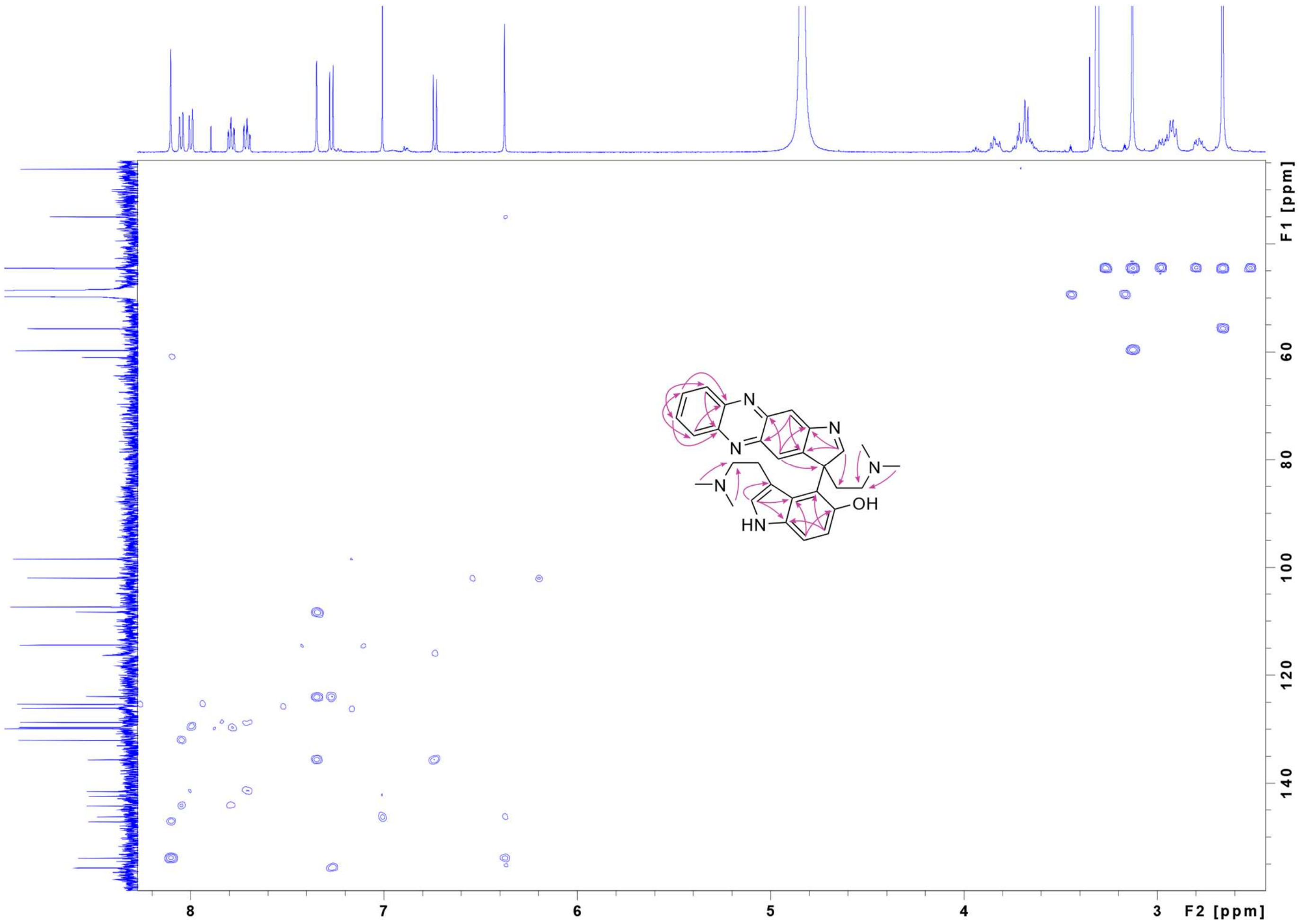

Figure S13d. ^{1}H,^{13}C HMBC spectrum of **3d** (^{1}H: 500 MHz, ^{13}C: 126 MHz, methanol-d_4). Selected correlations shown as pink arrows.

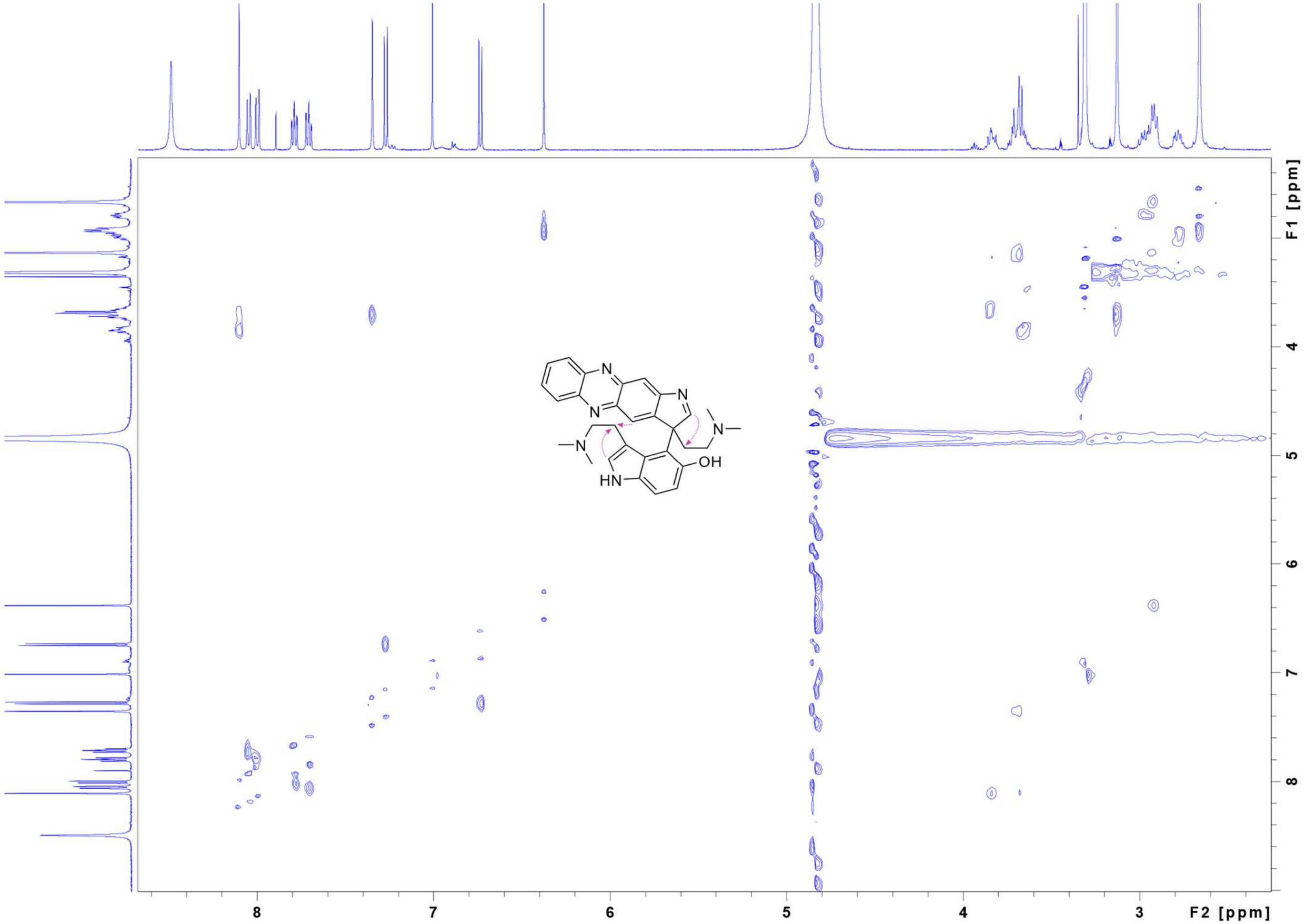

Figure S13e. ^{1}H,^{1}H NOESY spectrum of **3d** (500 MHz, methanol-*d*$_4$). Selected correlations shown as dotted pink arrows.

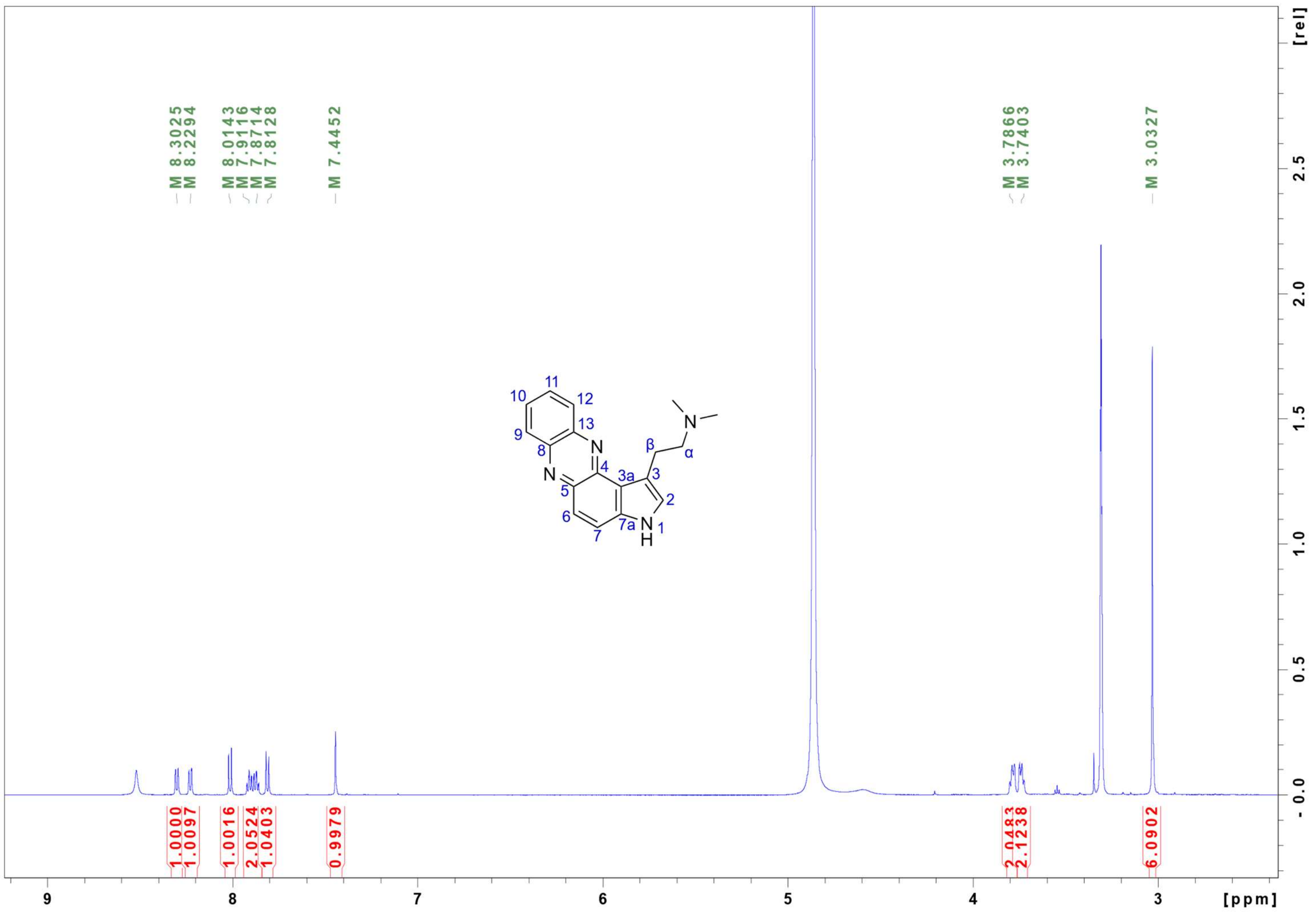

Figure S14a. ^{1}H NMR spectrum of **3f** (600 MHz, methanol-d_4).

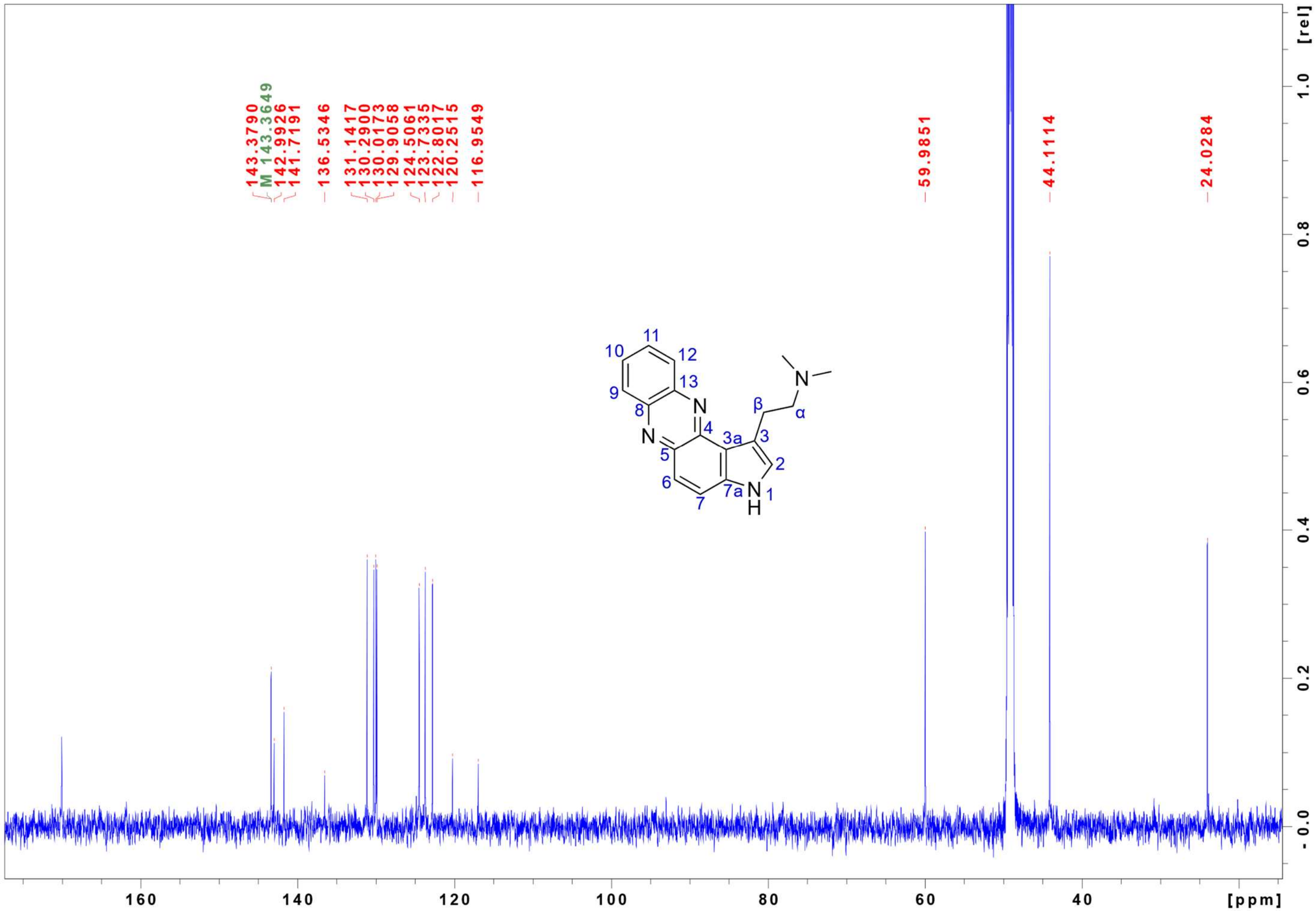

Figure S14b. ^{13}C NMR spectrum of **3f** (151 MHz, methanol-*d*$_4$).

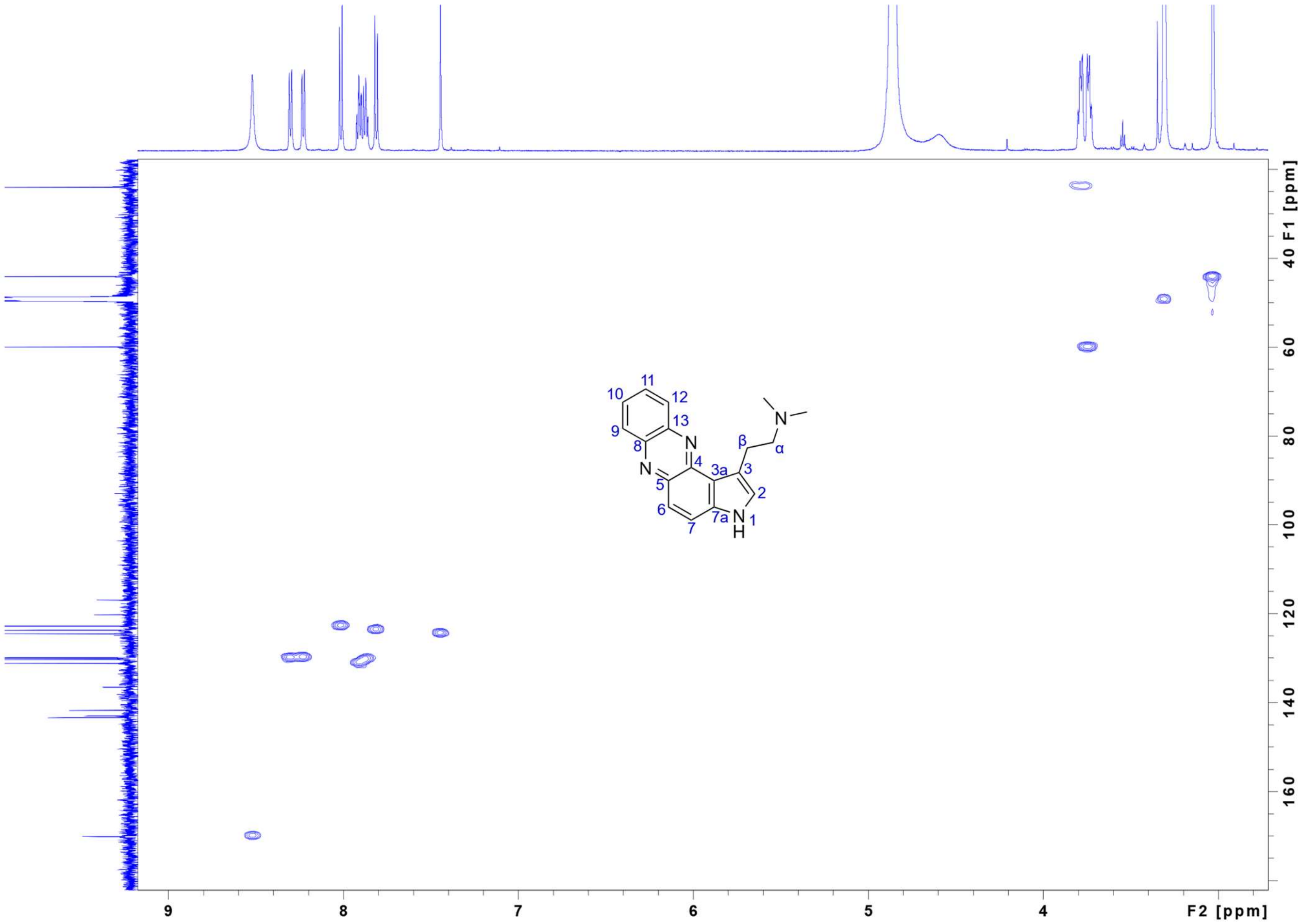

Figure S14c. $^1H,^{13}C$ HSQC spectrum of **3f** (^1H: 600 MHz, ^{13}C: 151 MHz, methanol-*d*$_4$).

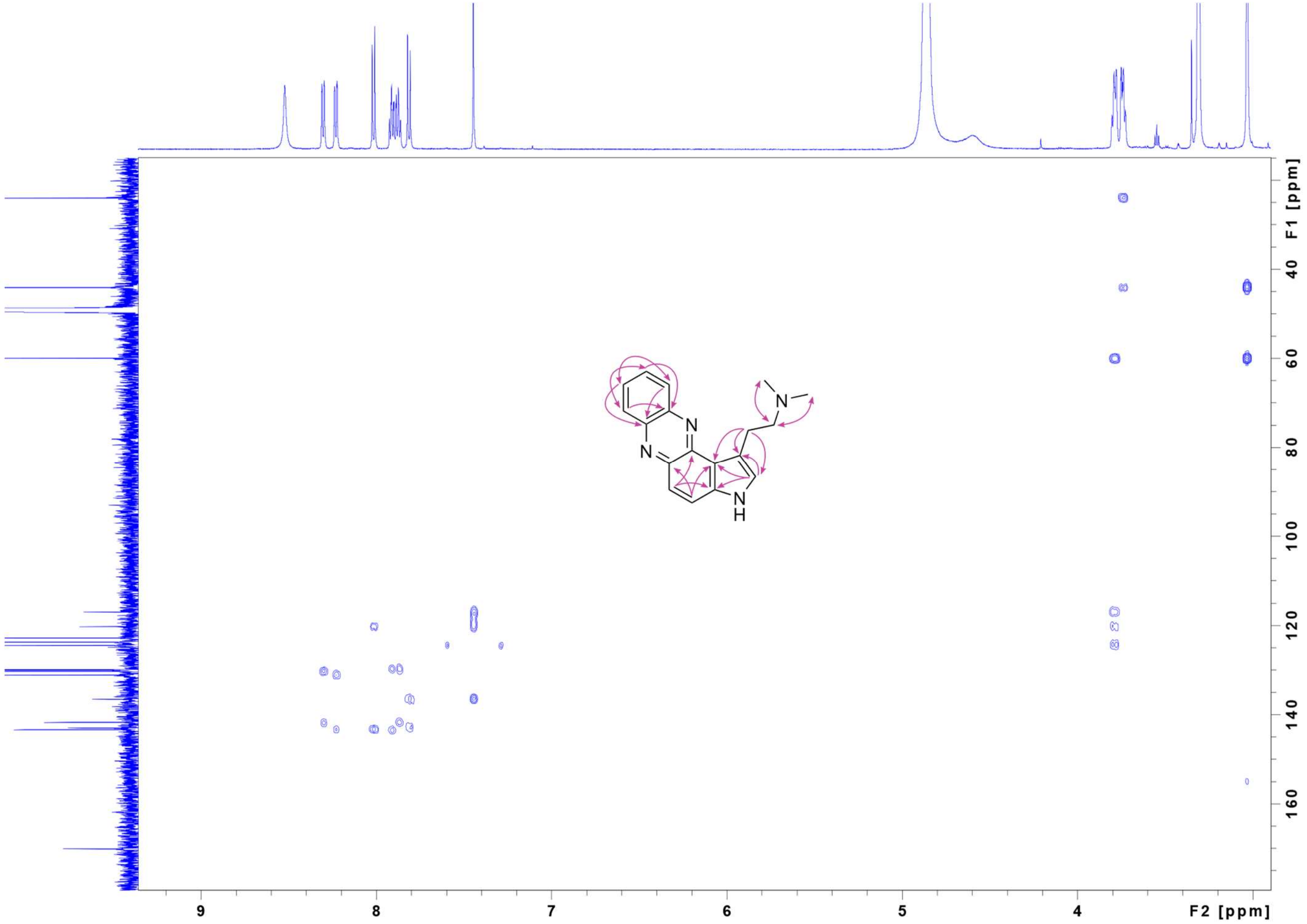

Figure S14d. ^{1}H,^{13}C HMBC spectrum of **3f** (^{1}H: 600 MHz, ^{13}C: 151 MHz, methanol-*d*$_4$). Selected correlations shown as pink arrows.

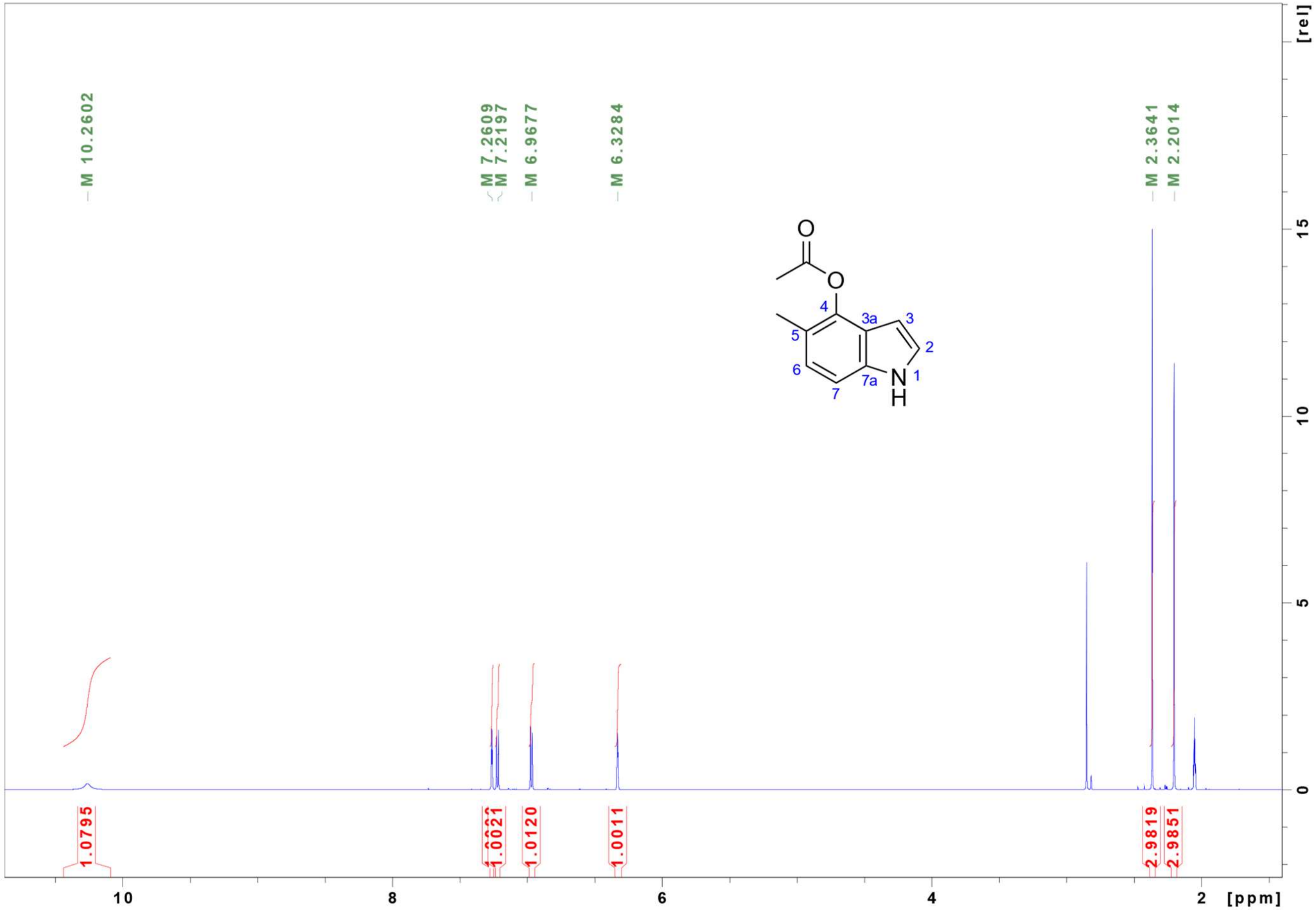

Figure S15a. ^{1}H NMR spectrum of **10** (600 MHz, acetone-d_6).

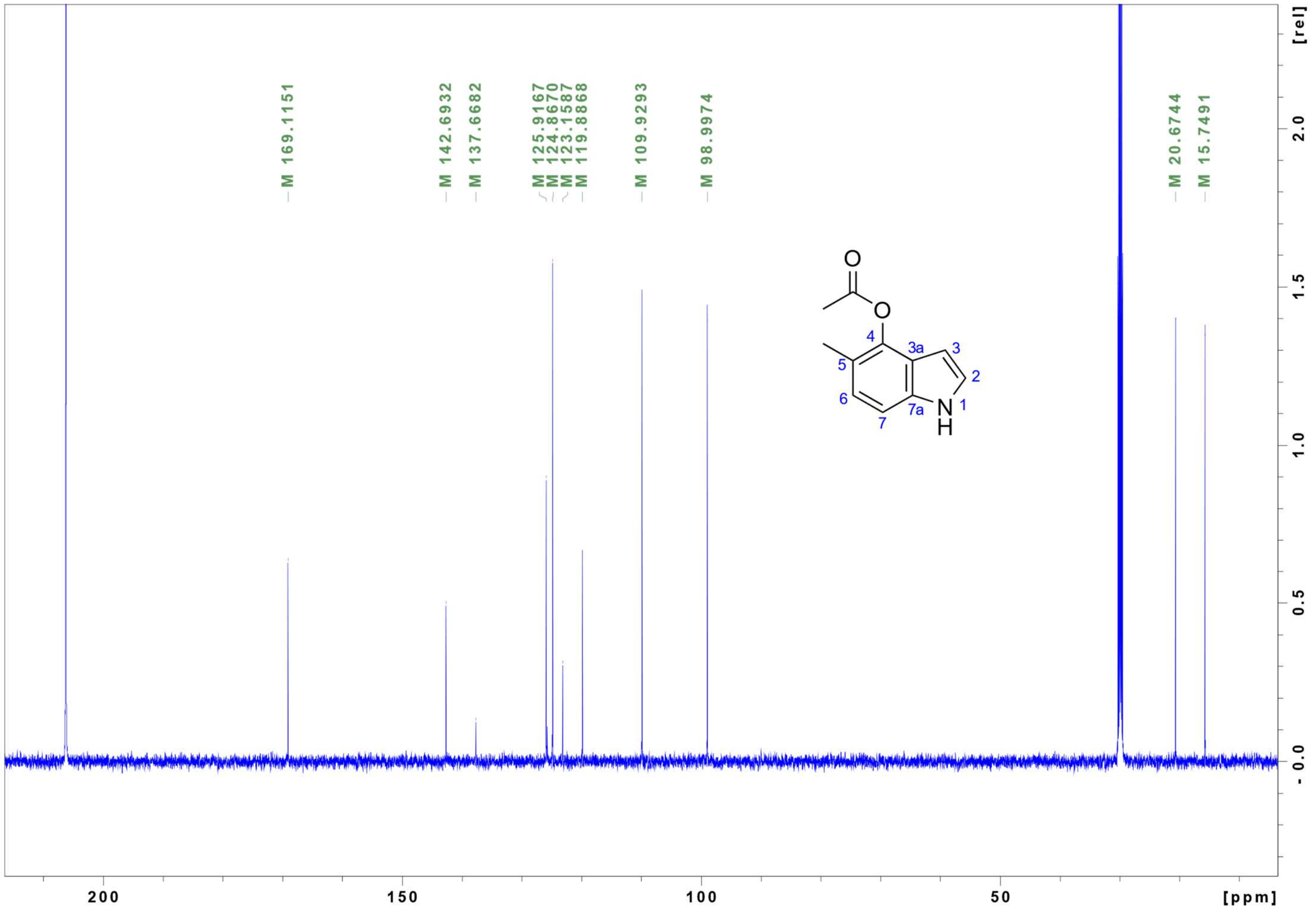

Figure S15b. ^{13}C NMR spectrum of **10** (151 MHz, acetone-d_6).

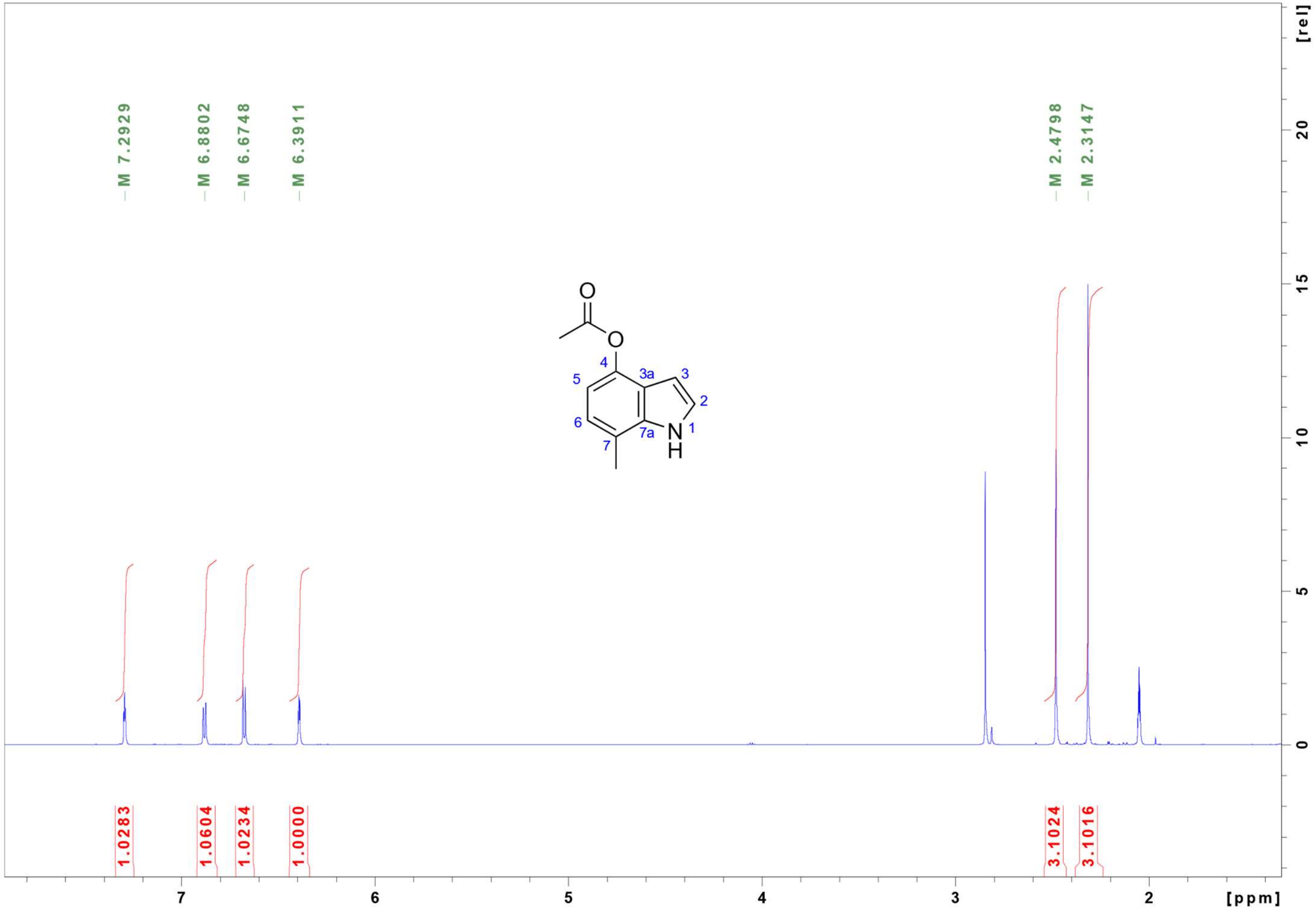

Figure S16a. ^{1}H NMR spectrum of **11** (600 MHz, acetone-d_6).

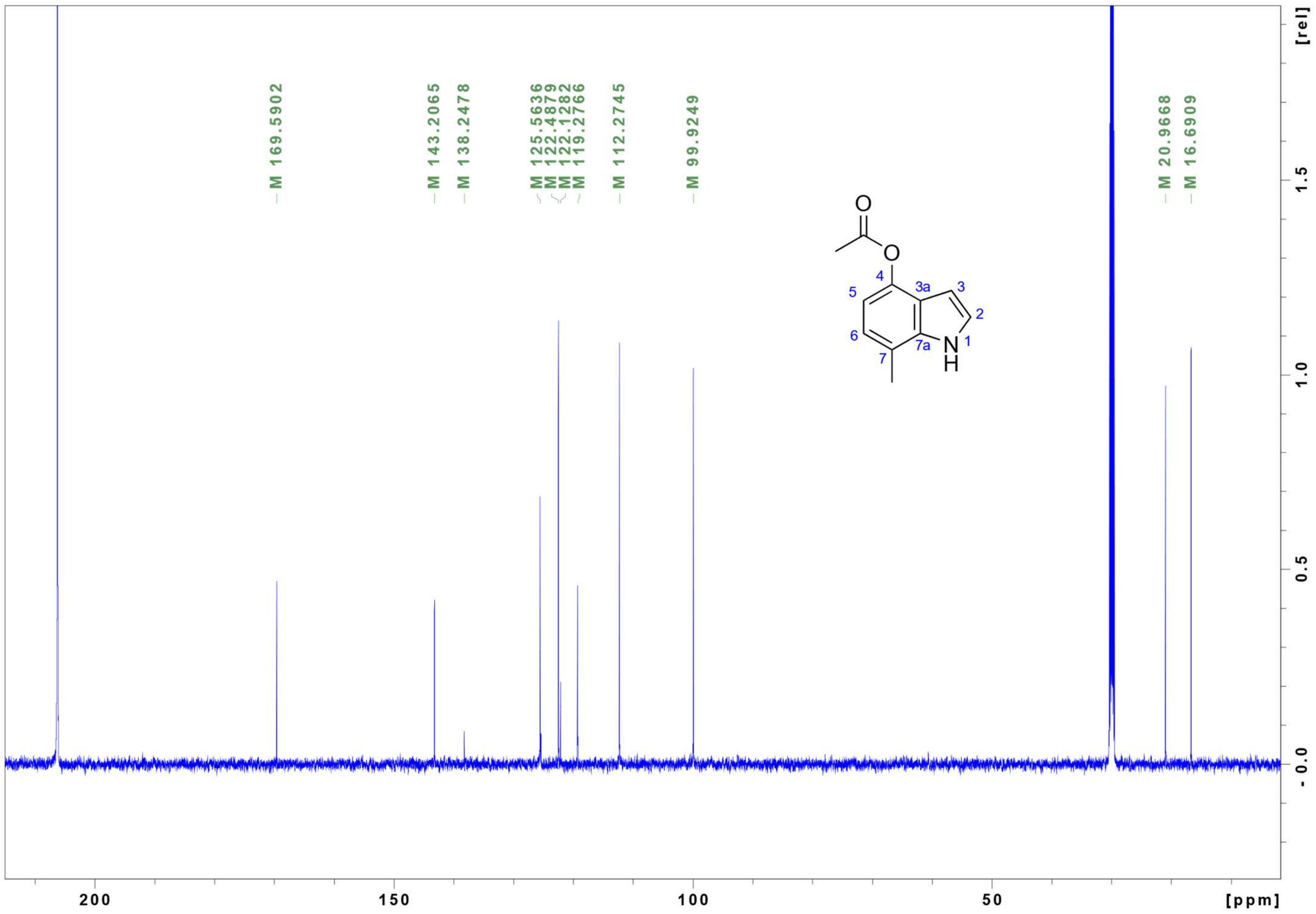

Figure S16b. ^{13}C NMR spectrum of **11** (151 MHz, acetone-d_6)..

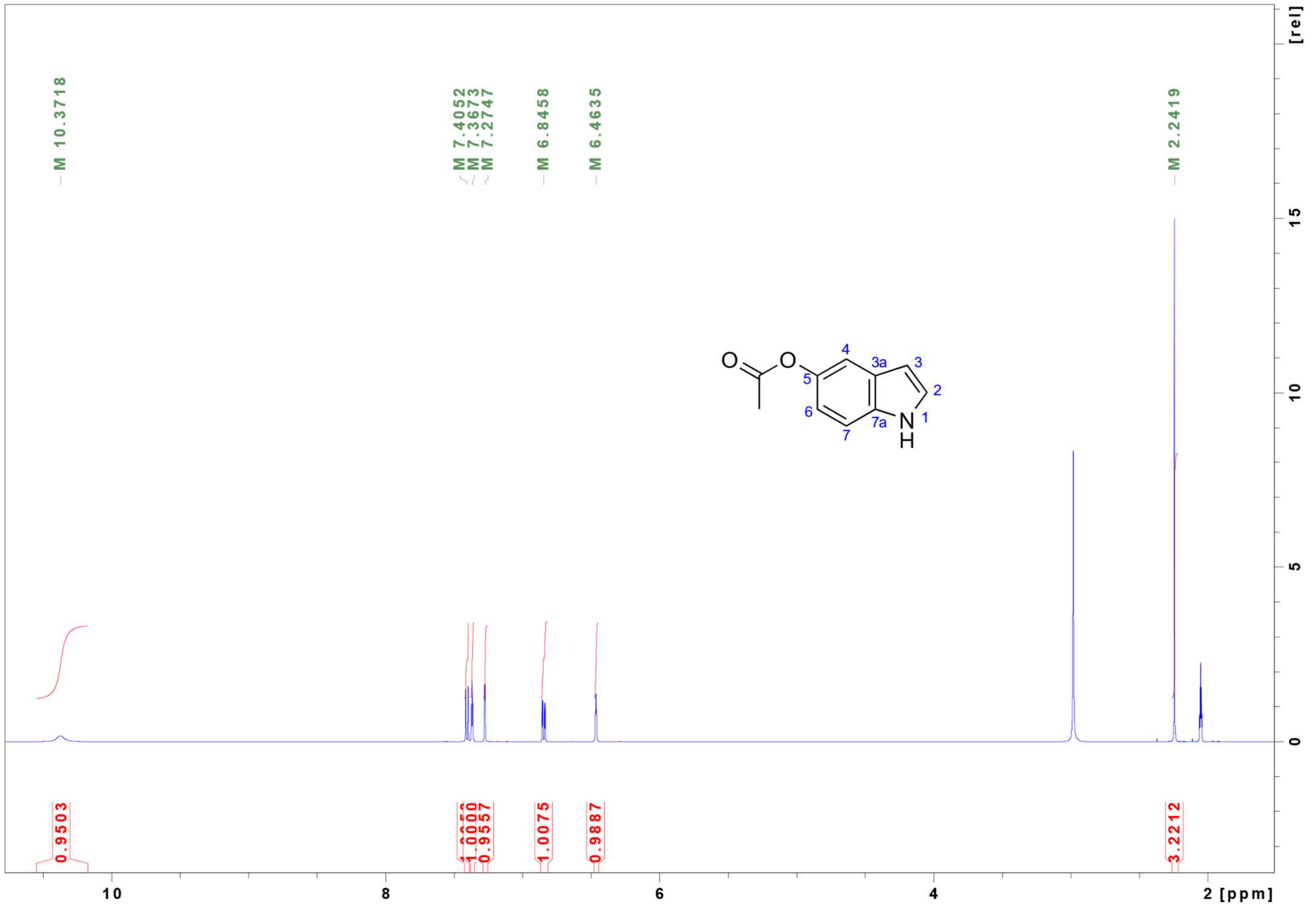

Figure S17a. ^{1}H NMR spectrum of **12** (500 MHz, acetone-d_6).

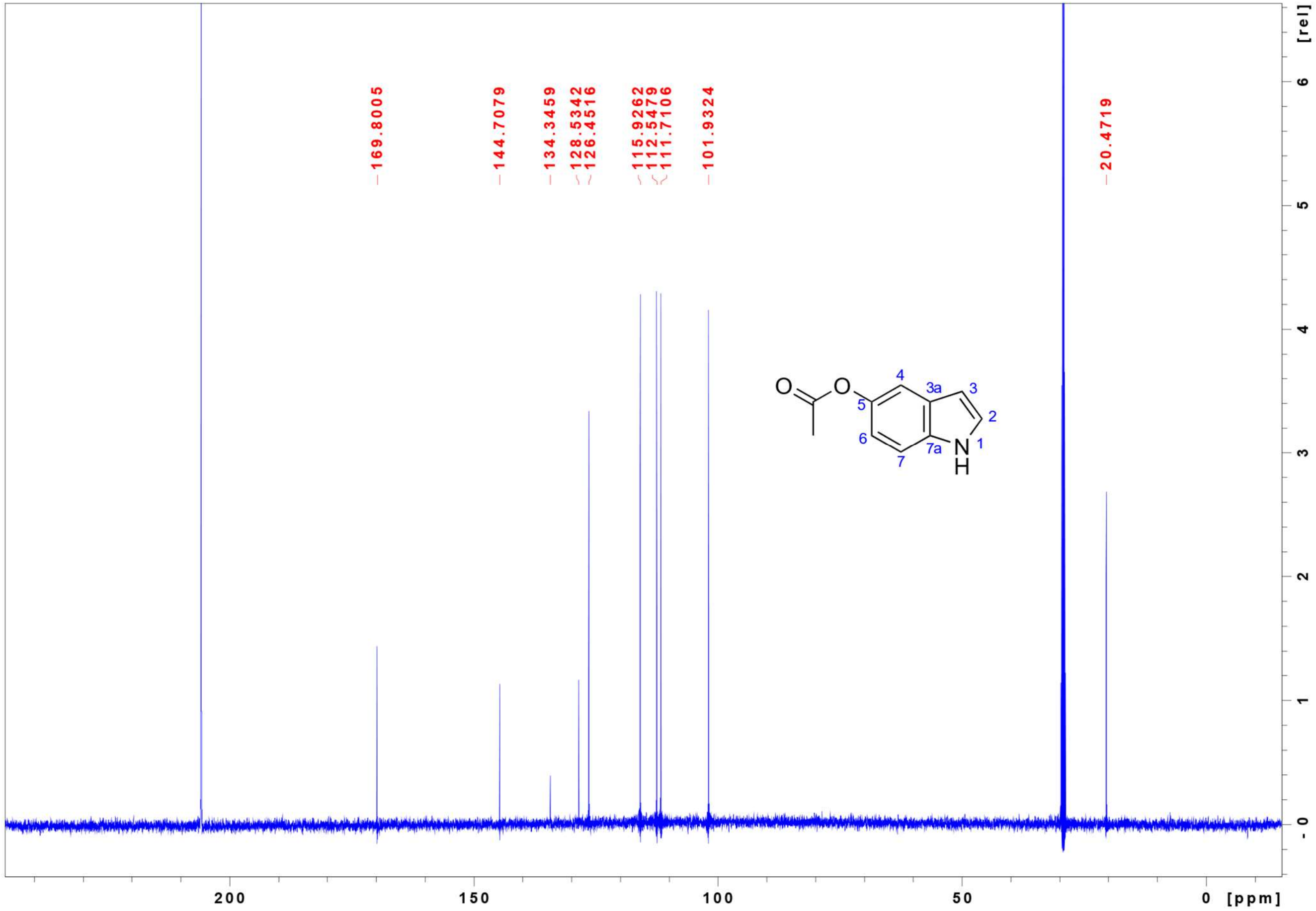

Figure S17b. ^{13}C NMR spectrum of **12** (126 MHz, acetone-d_6).

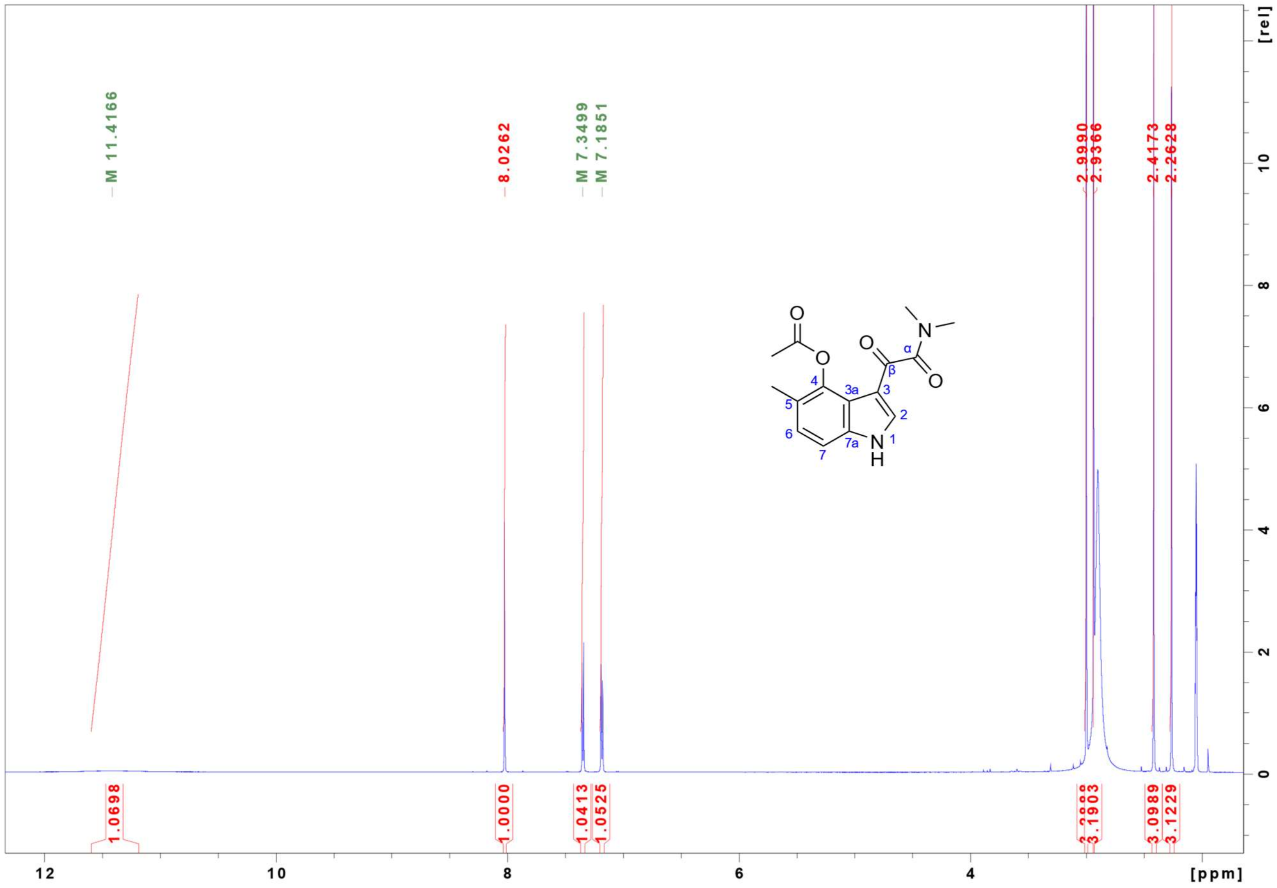

Figure S18a. ^{1}H NMR spectrum of **13** (600 MHz, acetone-d_6).

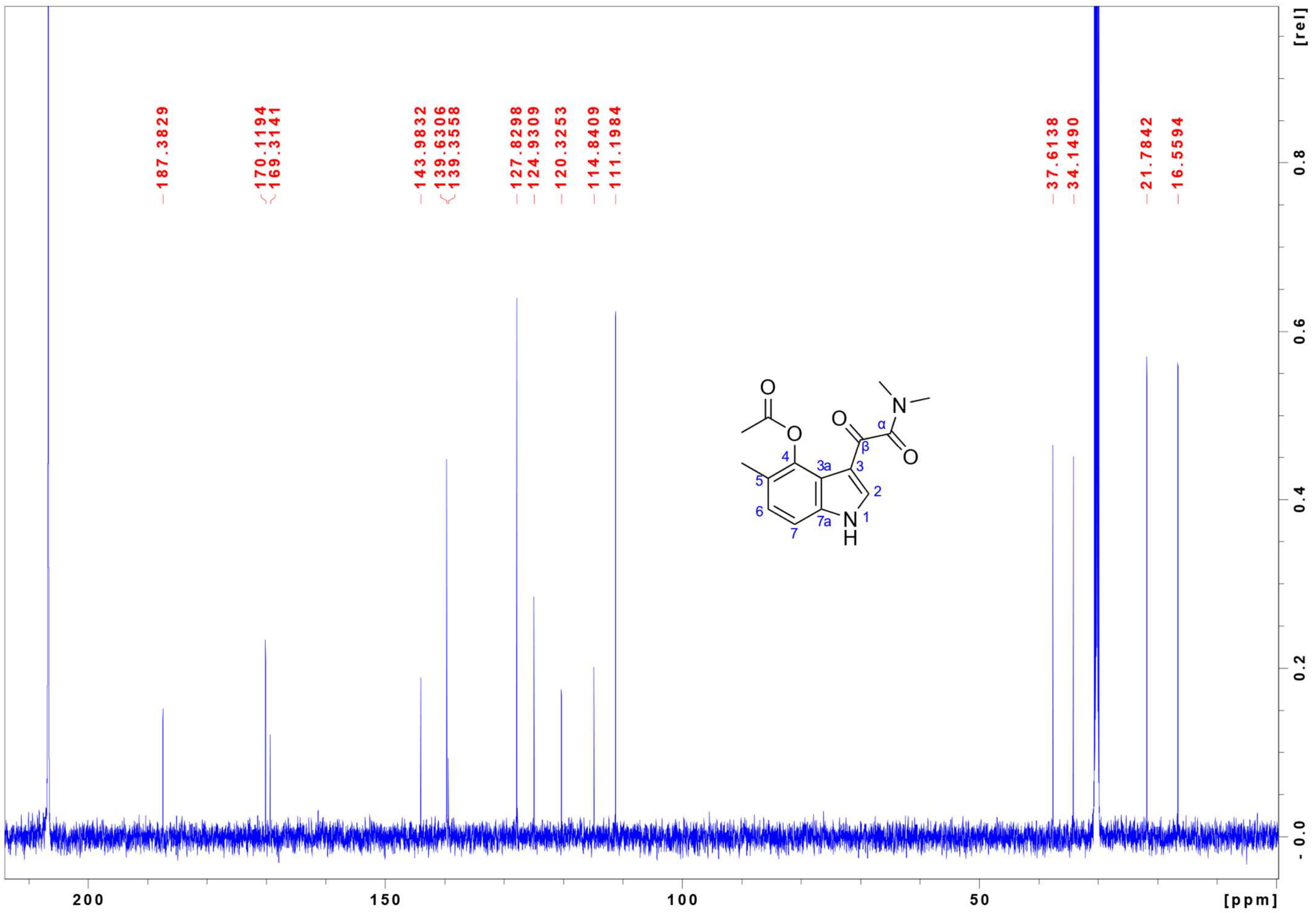

Figure S18b. ^{13}C NMR spectrum of **13** (151 MHz, acetone-*d*$_6$).

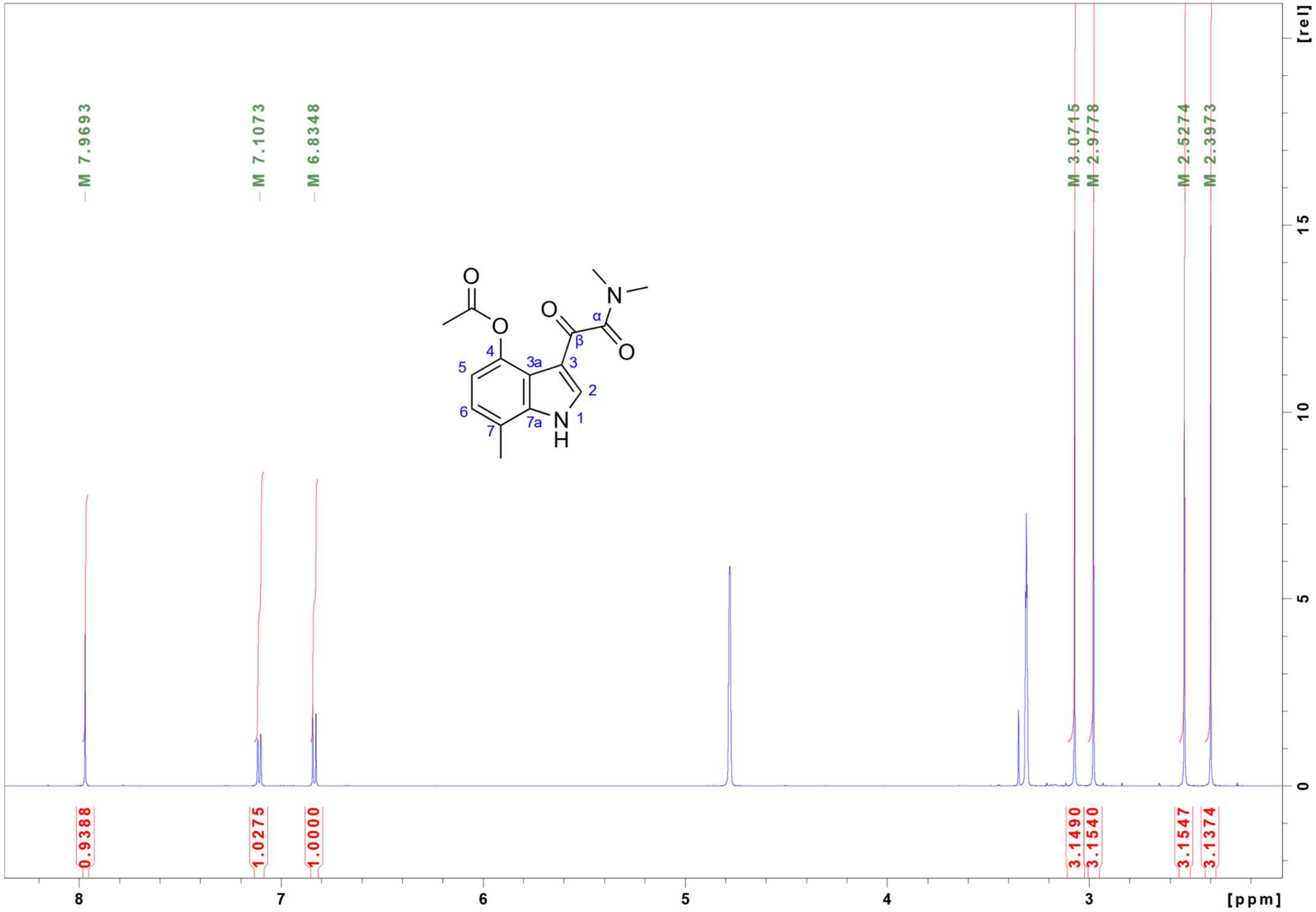

Figure S19a. ^{1}H NMR spectrum of **14** (500 MHz, methanol-d_4).

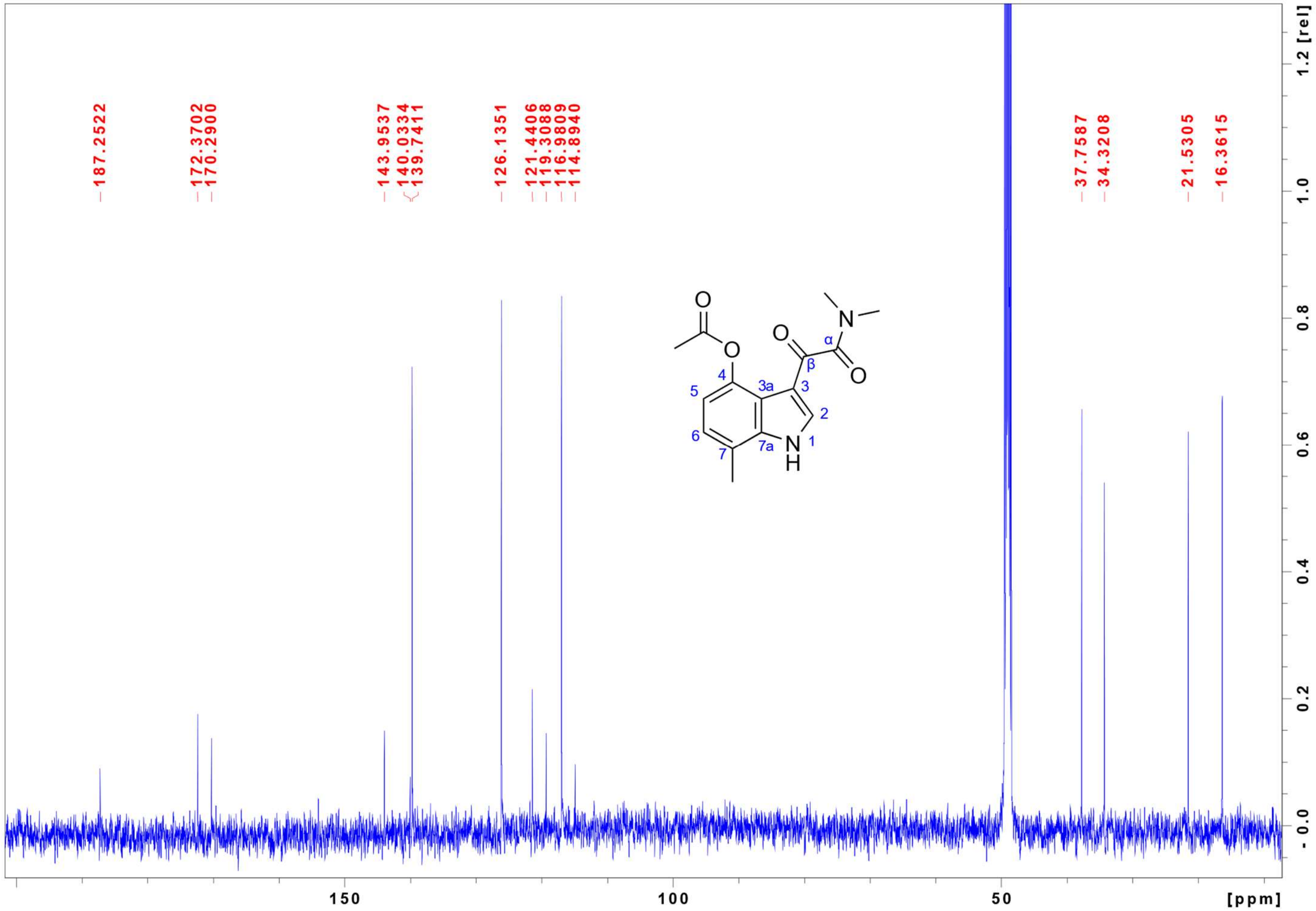

Figure S19b. ^{13}C NMR spectrum of **14** (126 MHz, methanol-d_4).

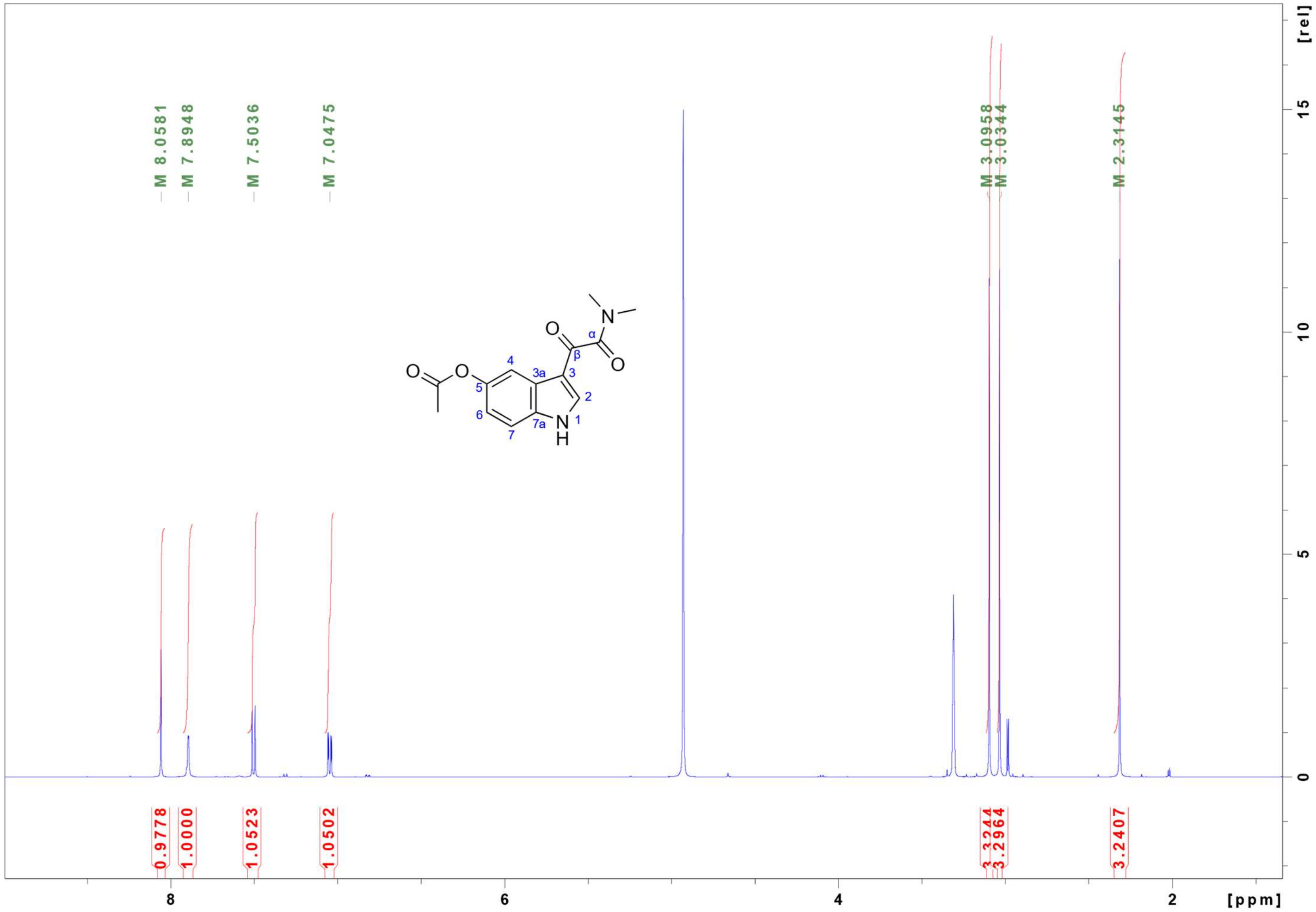

Figure S20a. ^{1}H NMR spectrum of **15** (500 MHz, methanol-d_4).

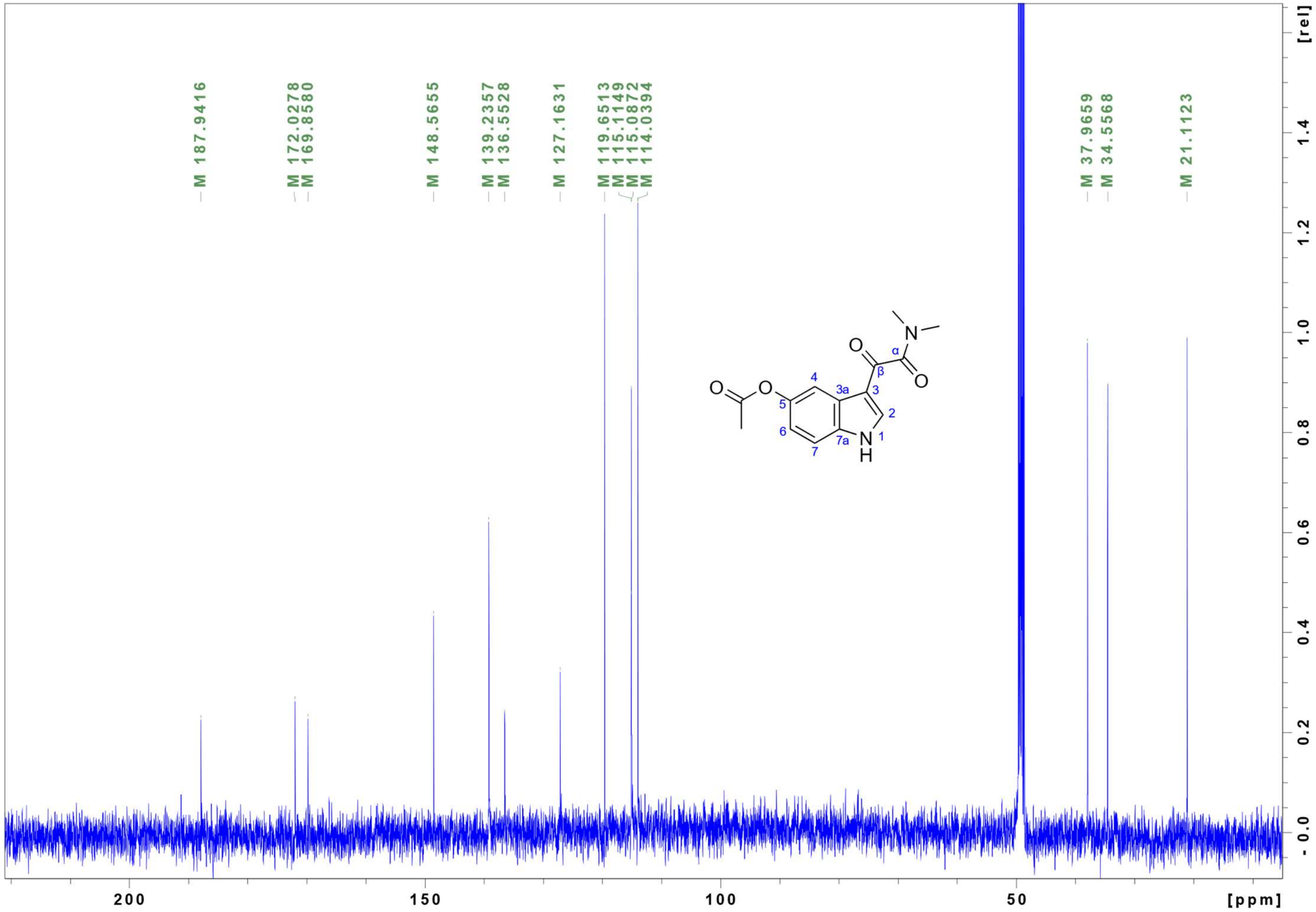

Figure S20b. ^{13}C NMR spectrum of **15** (126 MHz, methanol-d_4).