Supporting Information for

The Chemistry of Pyrrolo[1,2-*a*]indole and Pyrido[1,2-*a*]indole – Based Quinone Methides. Mechanistic Explanations for differences in Cytostatic/ Cytotoxic Properties.

*Omar Khdour and Edward B. Skibo**

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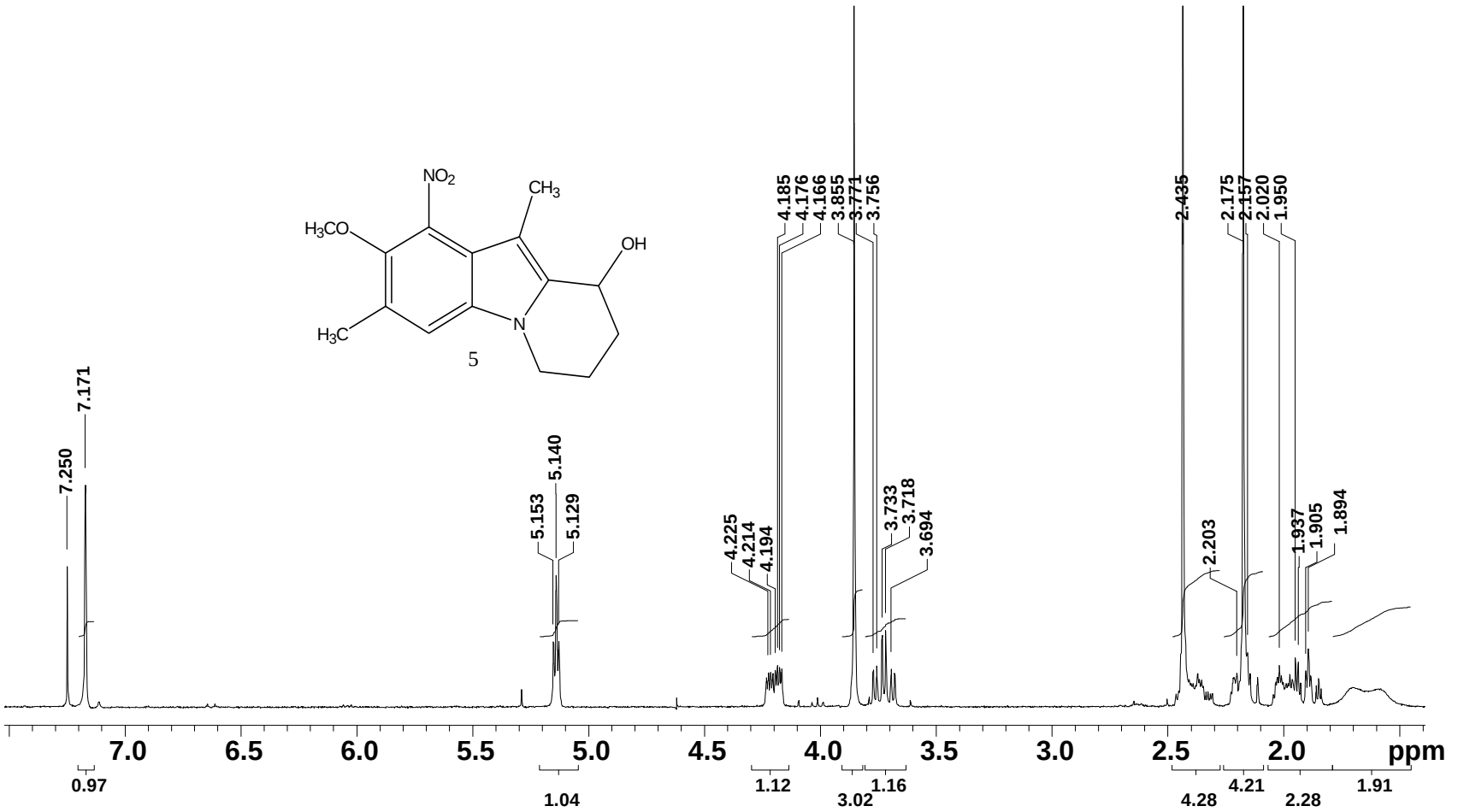
General Experimental Methods

All analytically pure compounds were dried under high vacuum in a drying pistol over refluxing methanol. Elemental analyses (CHN) were obtained for intermediates and final products. Melting points and decomposition points were determined for all intermediates and final products. All TLCs were performed on silica gel plates using a variety of solvent systems and a fluorescent indicator for visualization. IR spectra were taken as KBr pellets and only the strongest absorbances were reported. H NMR spectra were obtained with a 300 or 500 MHz spectrometer. All chemical shifts are reported relative to TMS. High- resolution mass spectra were obtained using MALDI or EI mode.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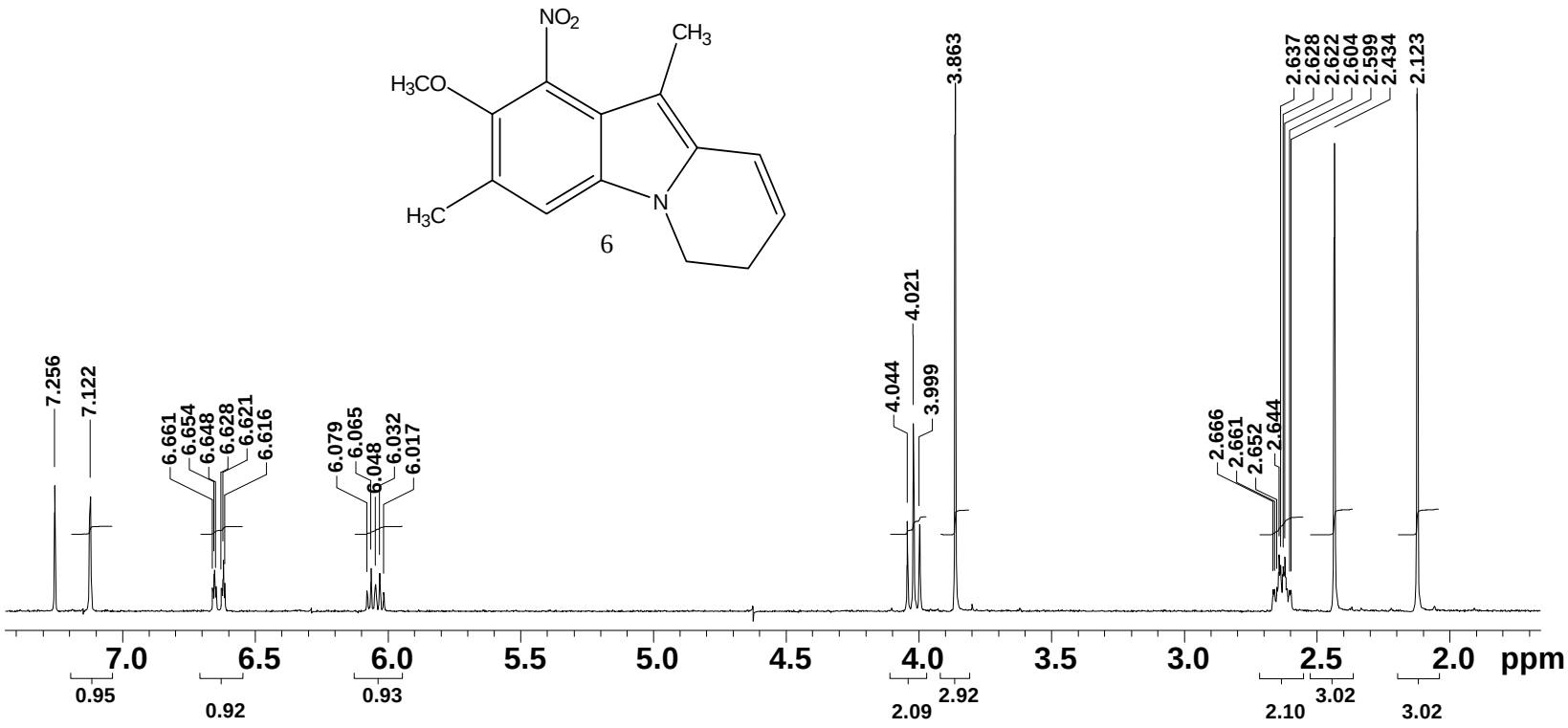
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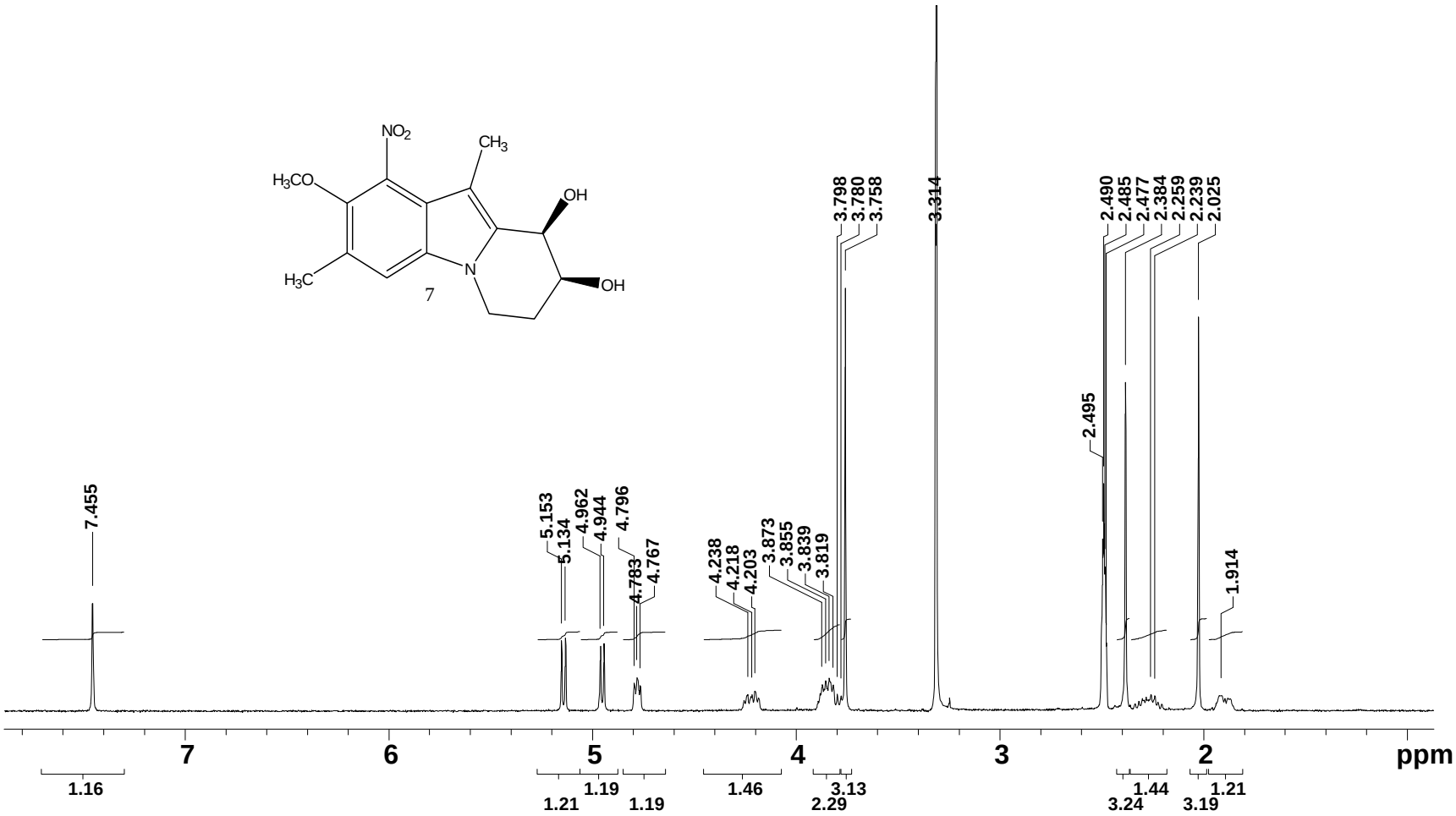
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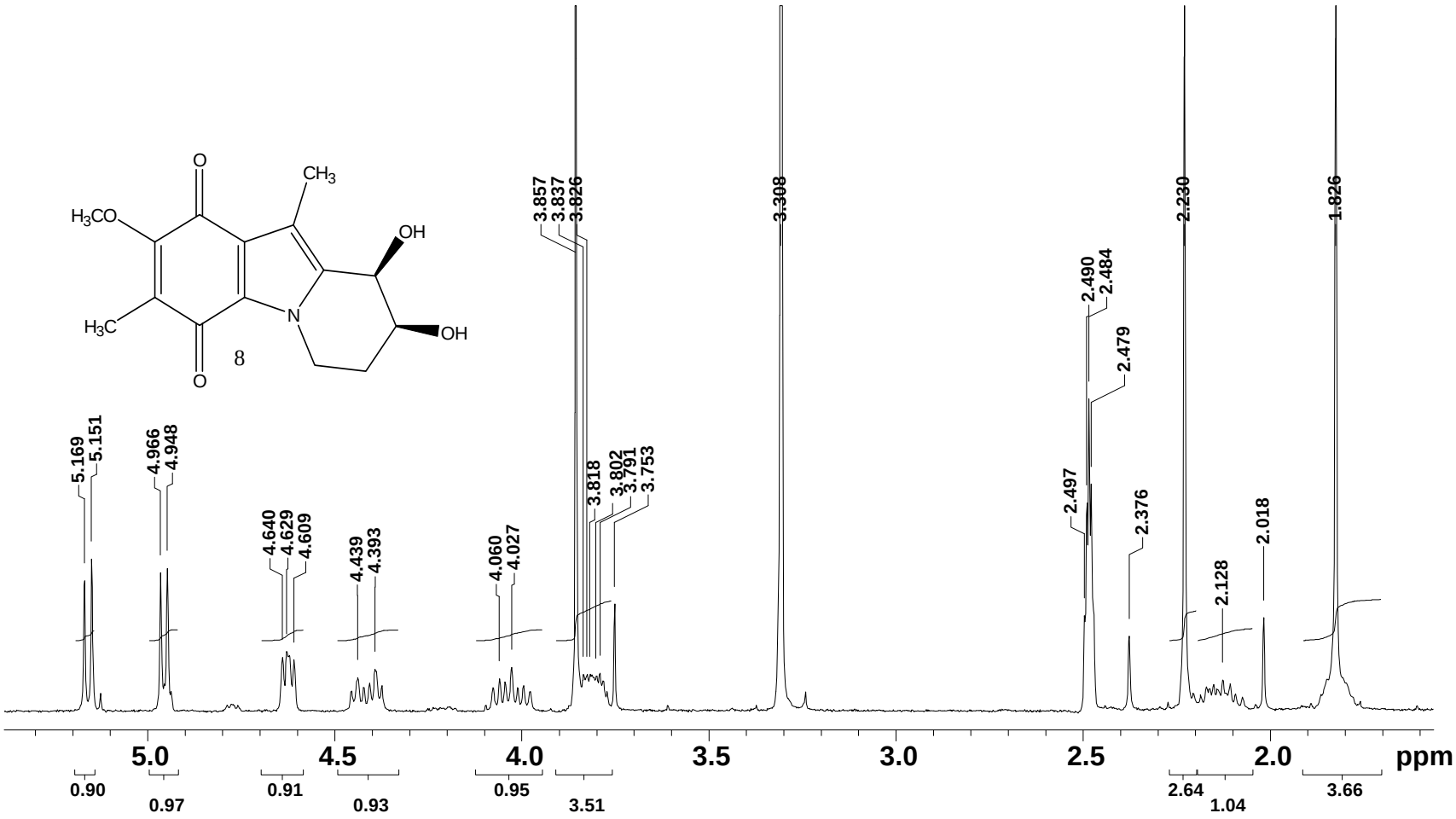
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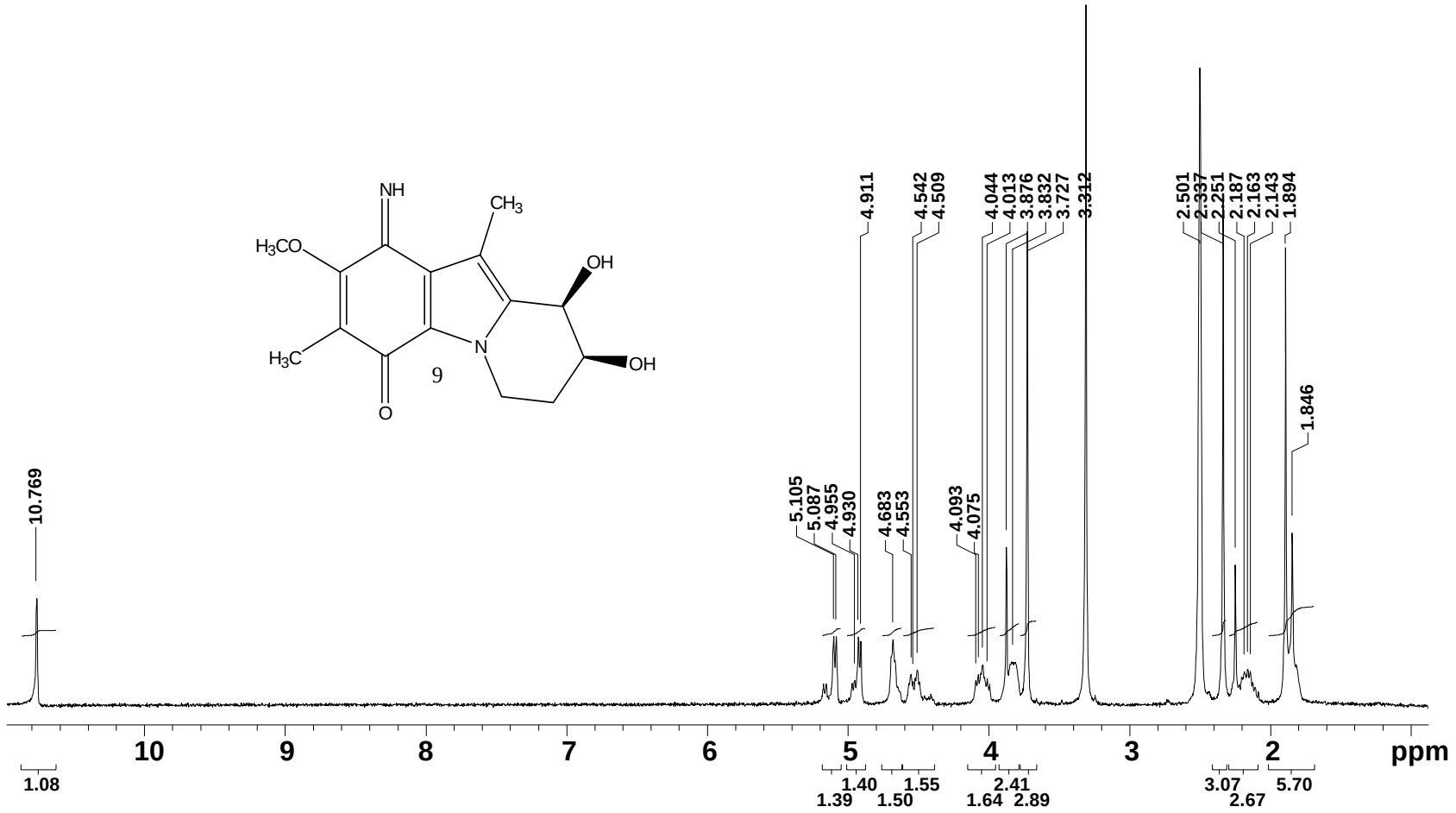
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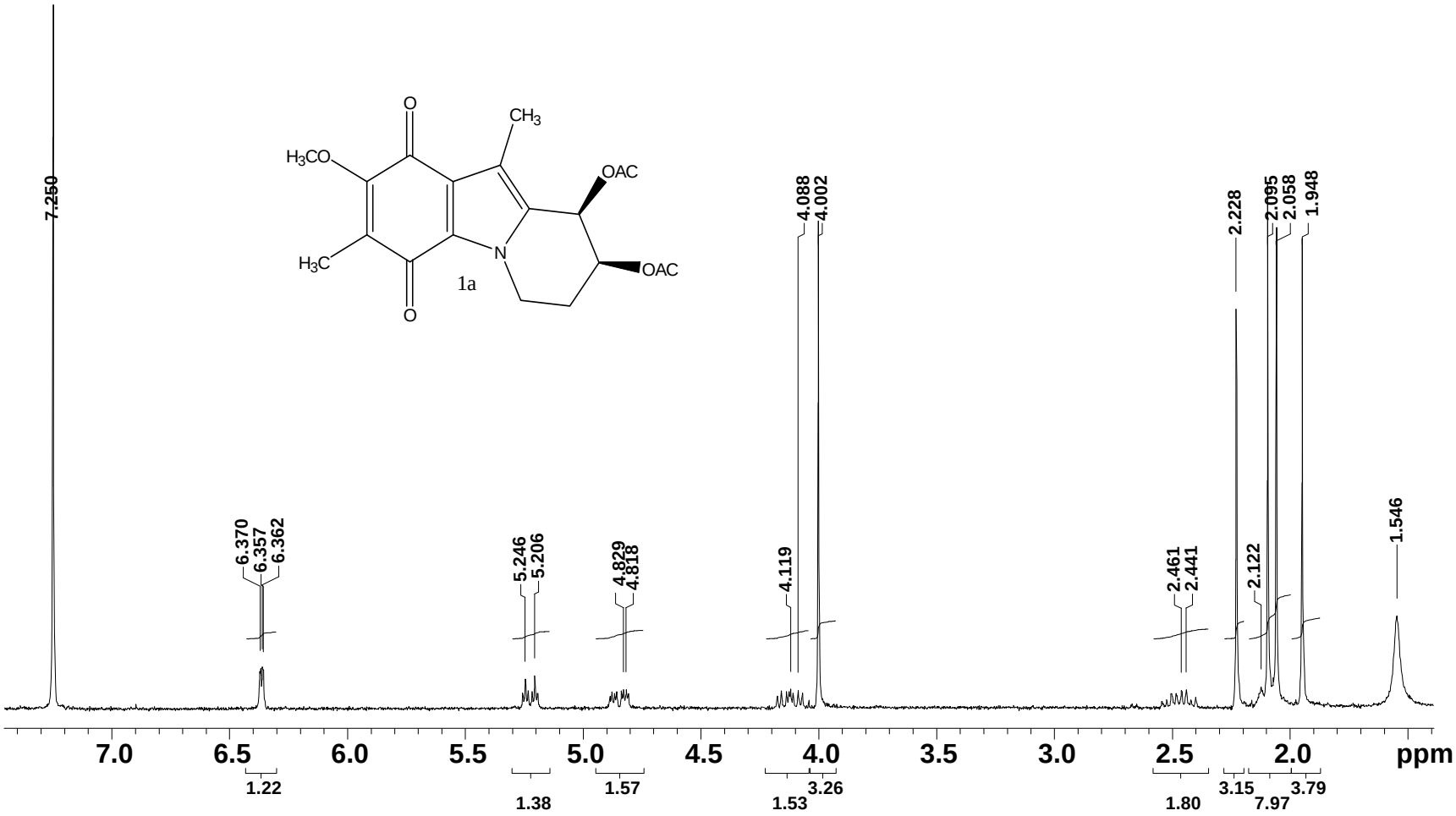
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OAC
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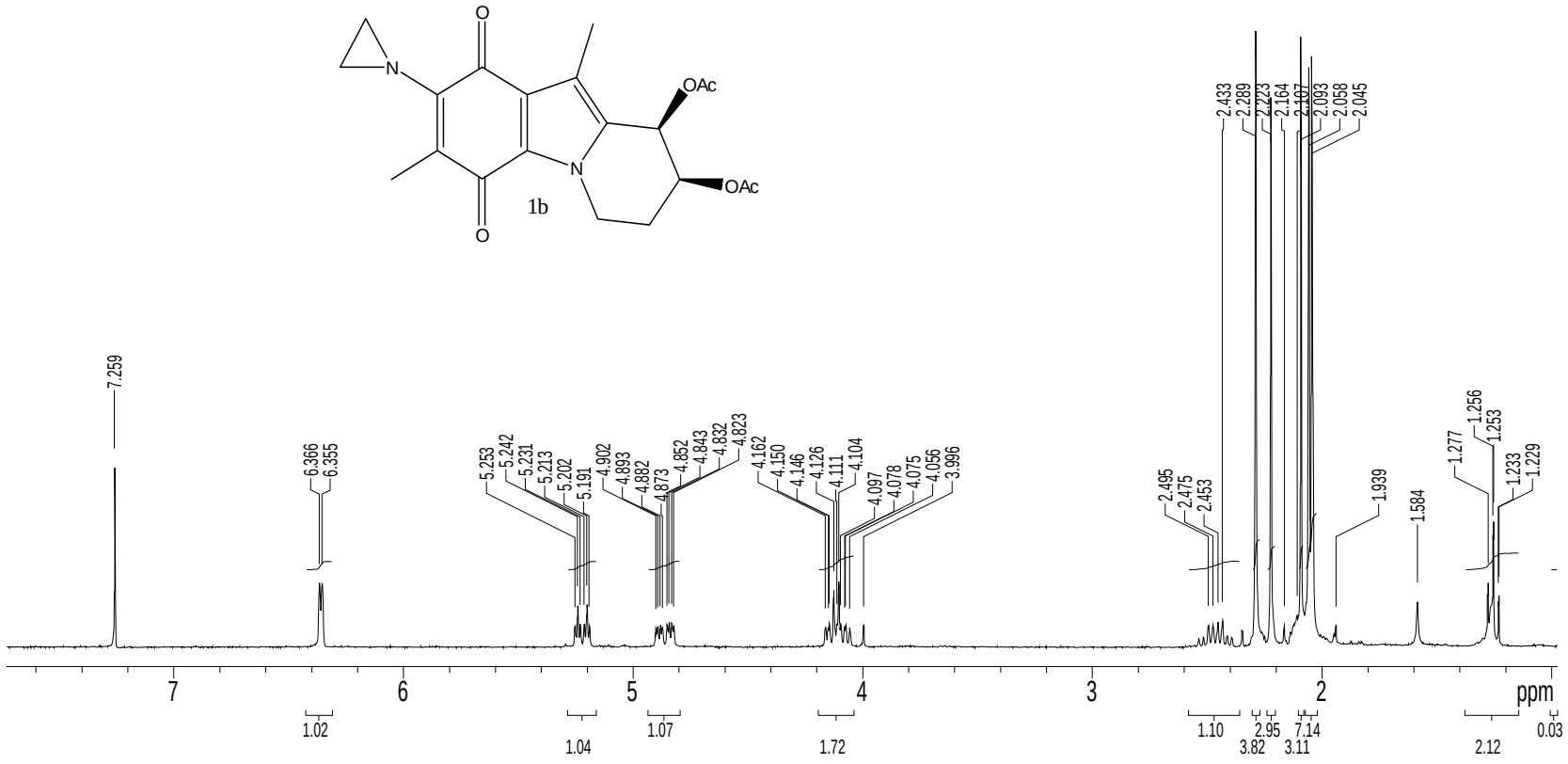
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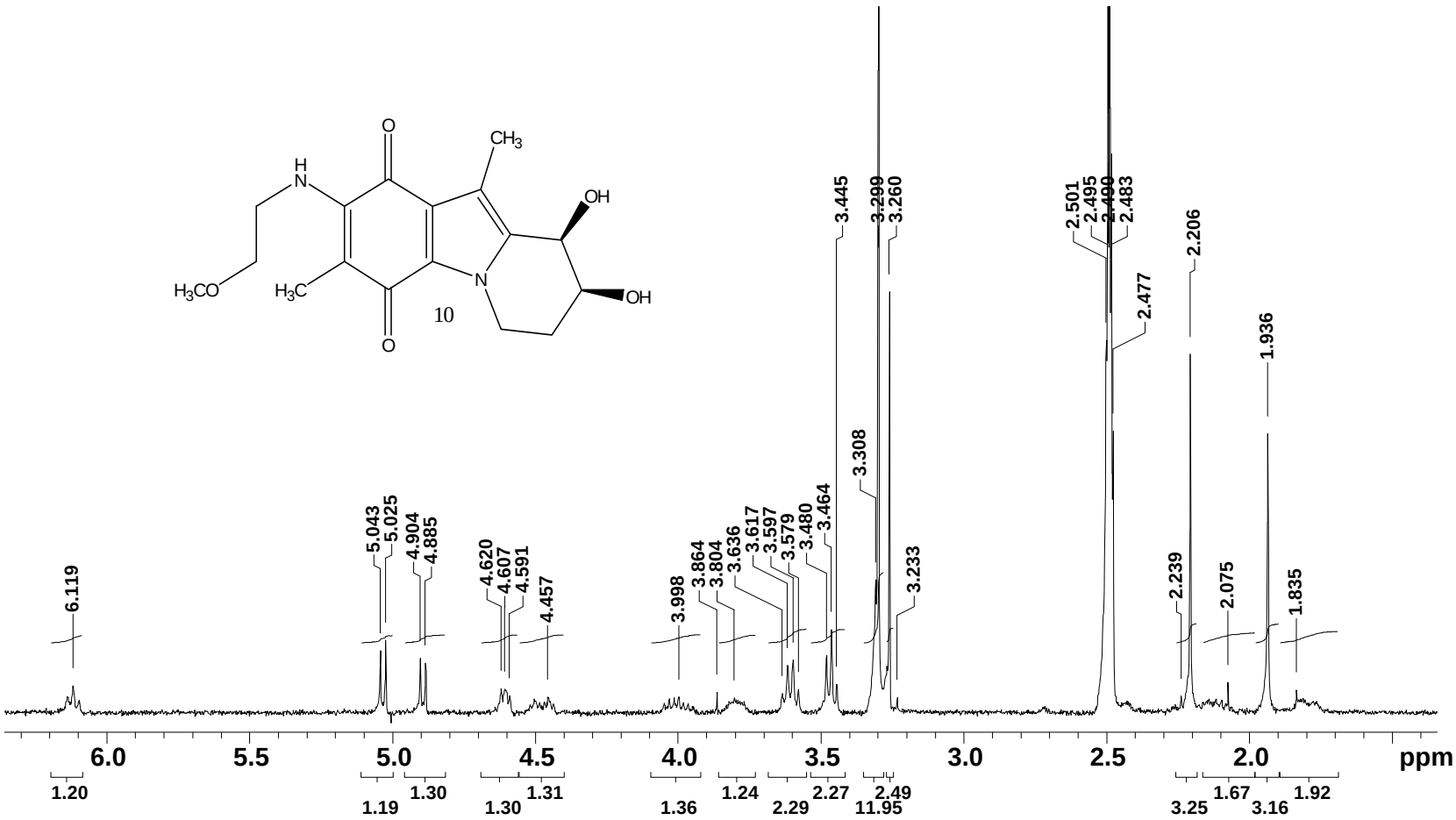
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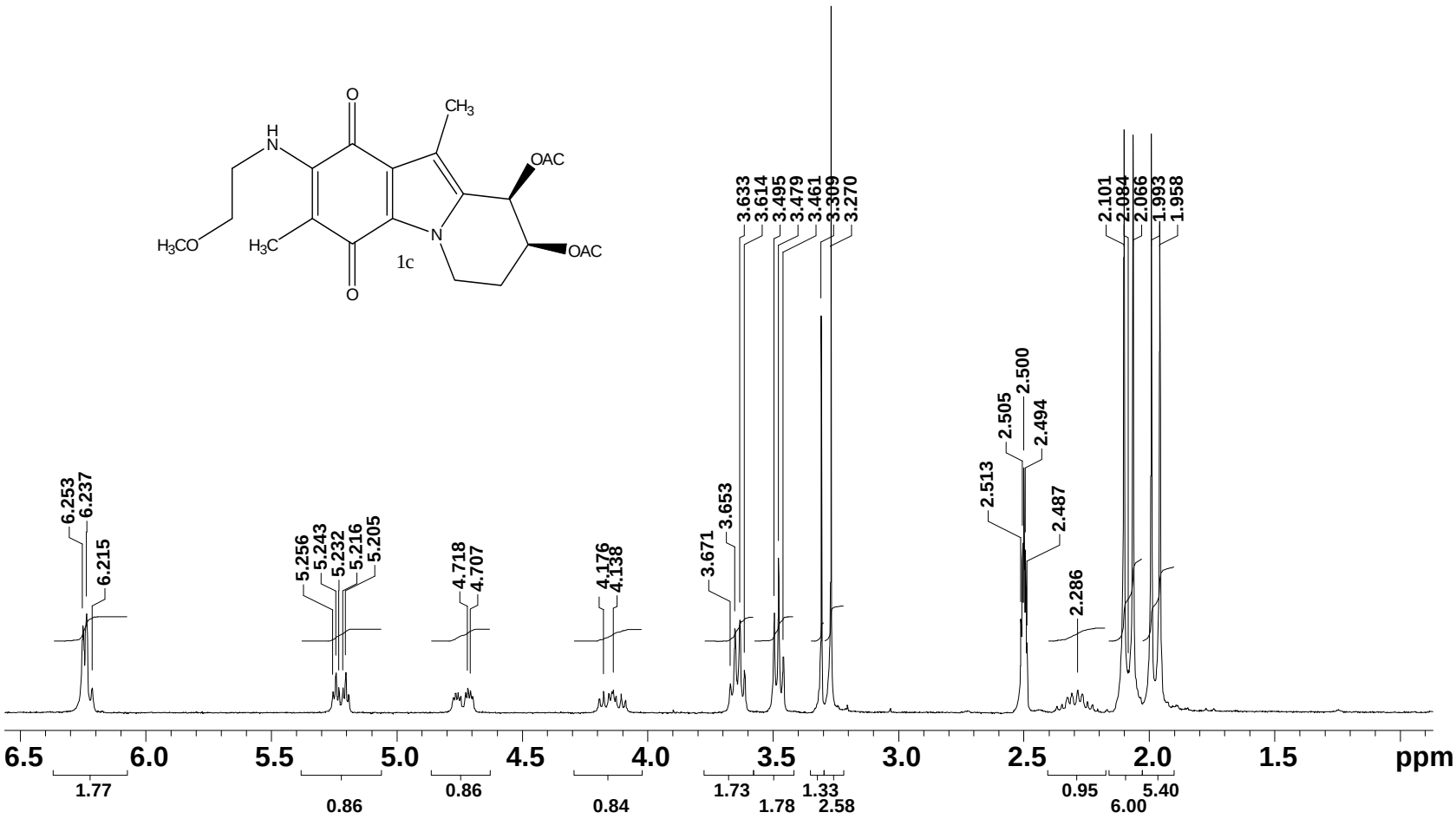
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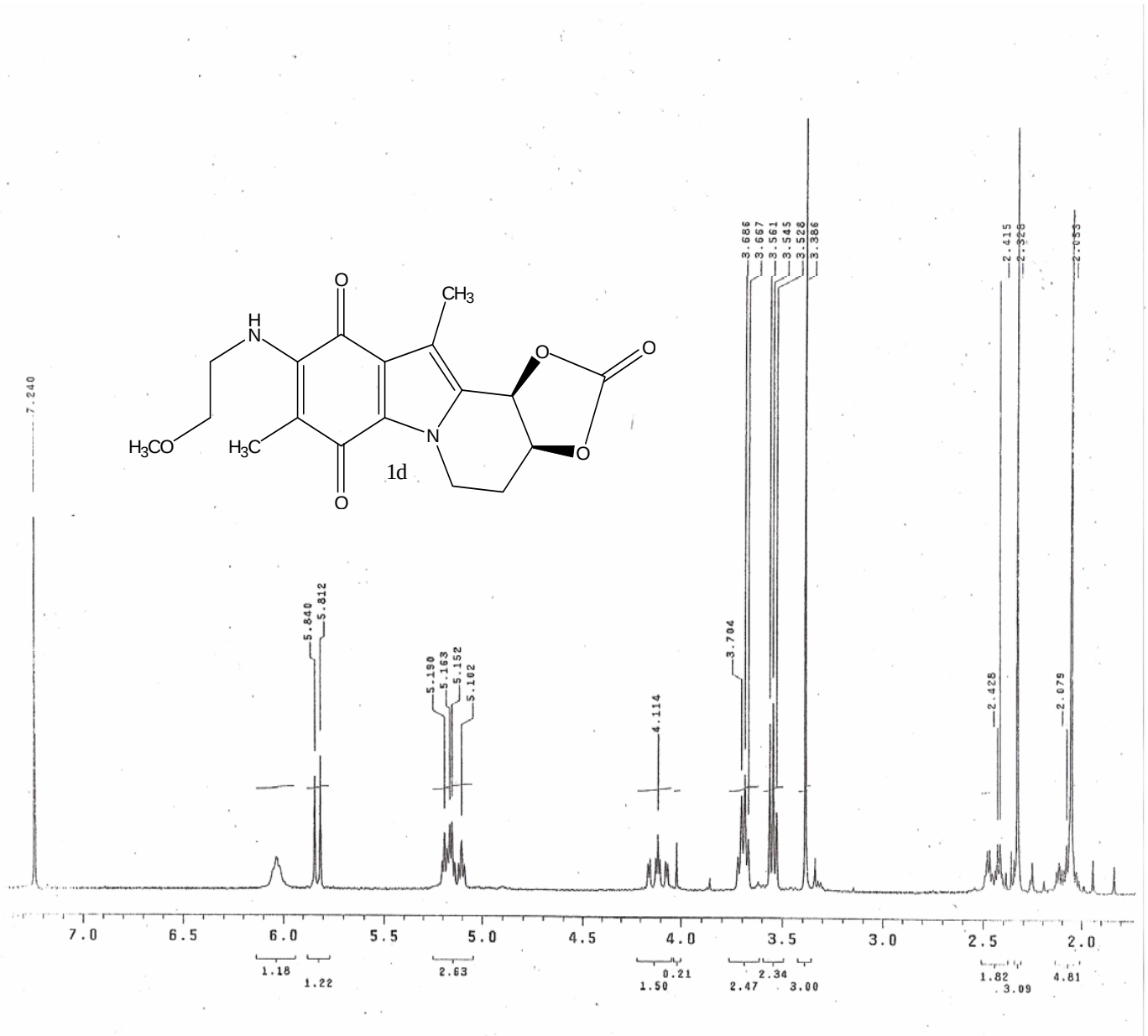
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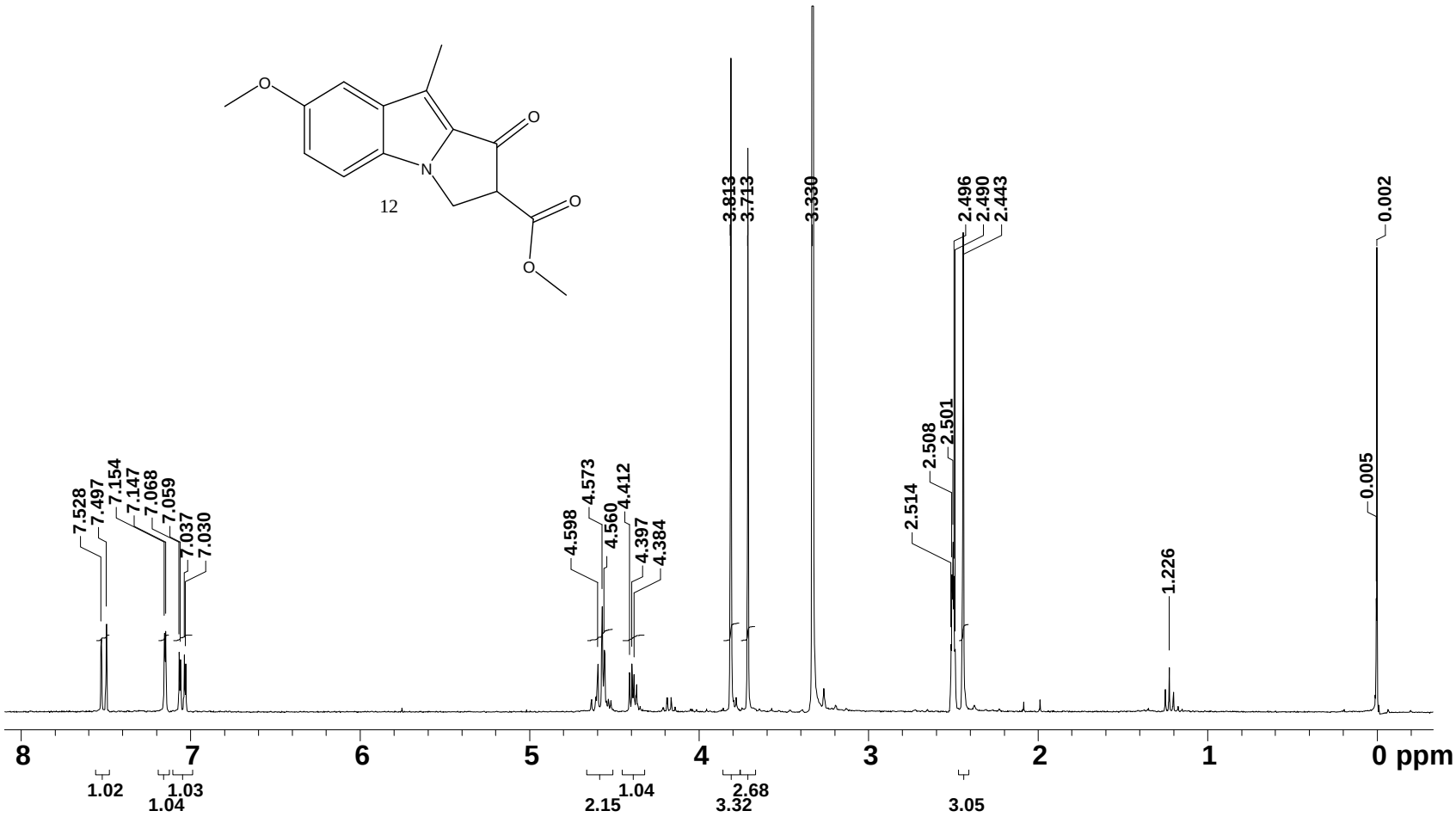
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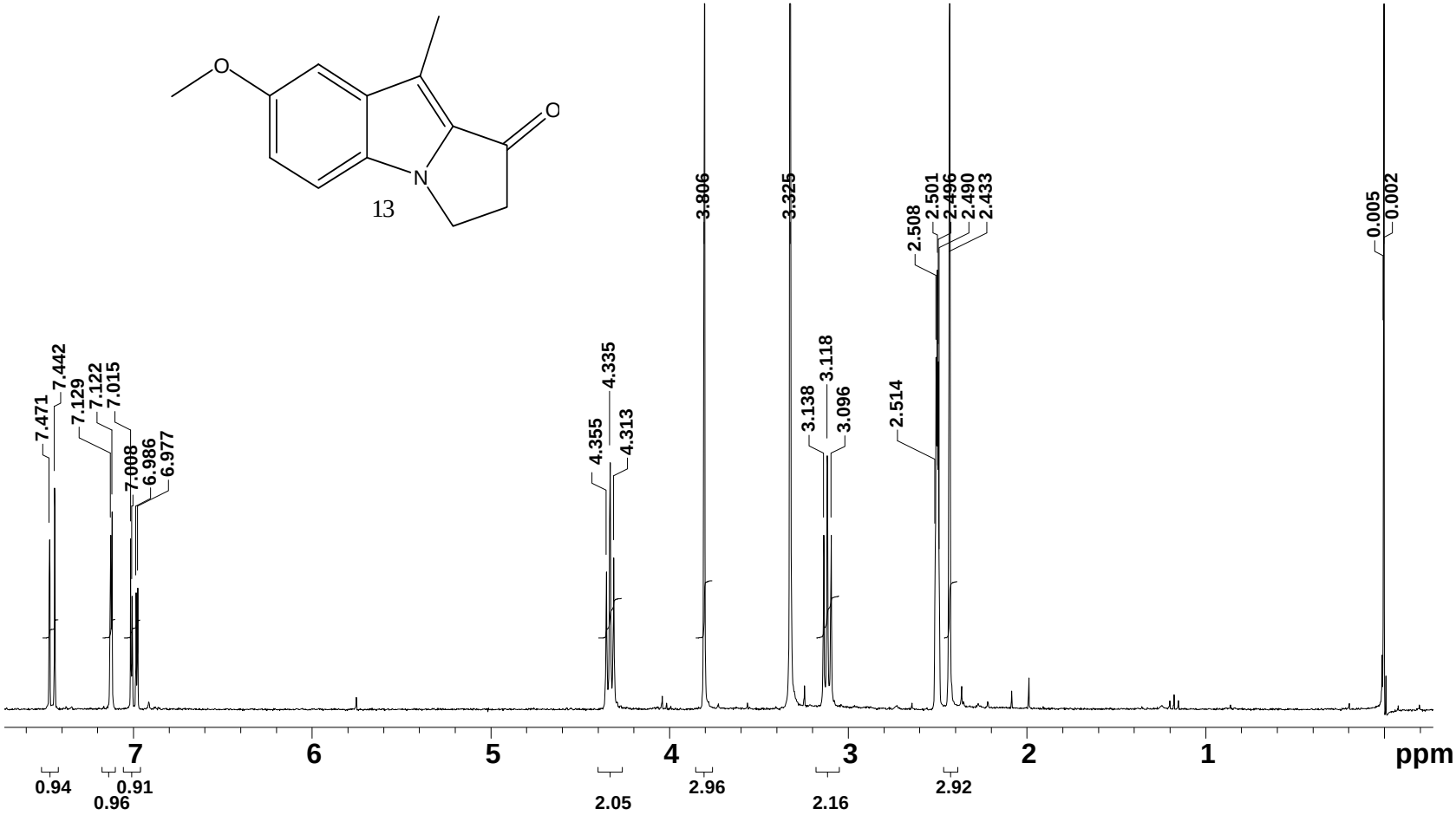
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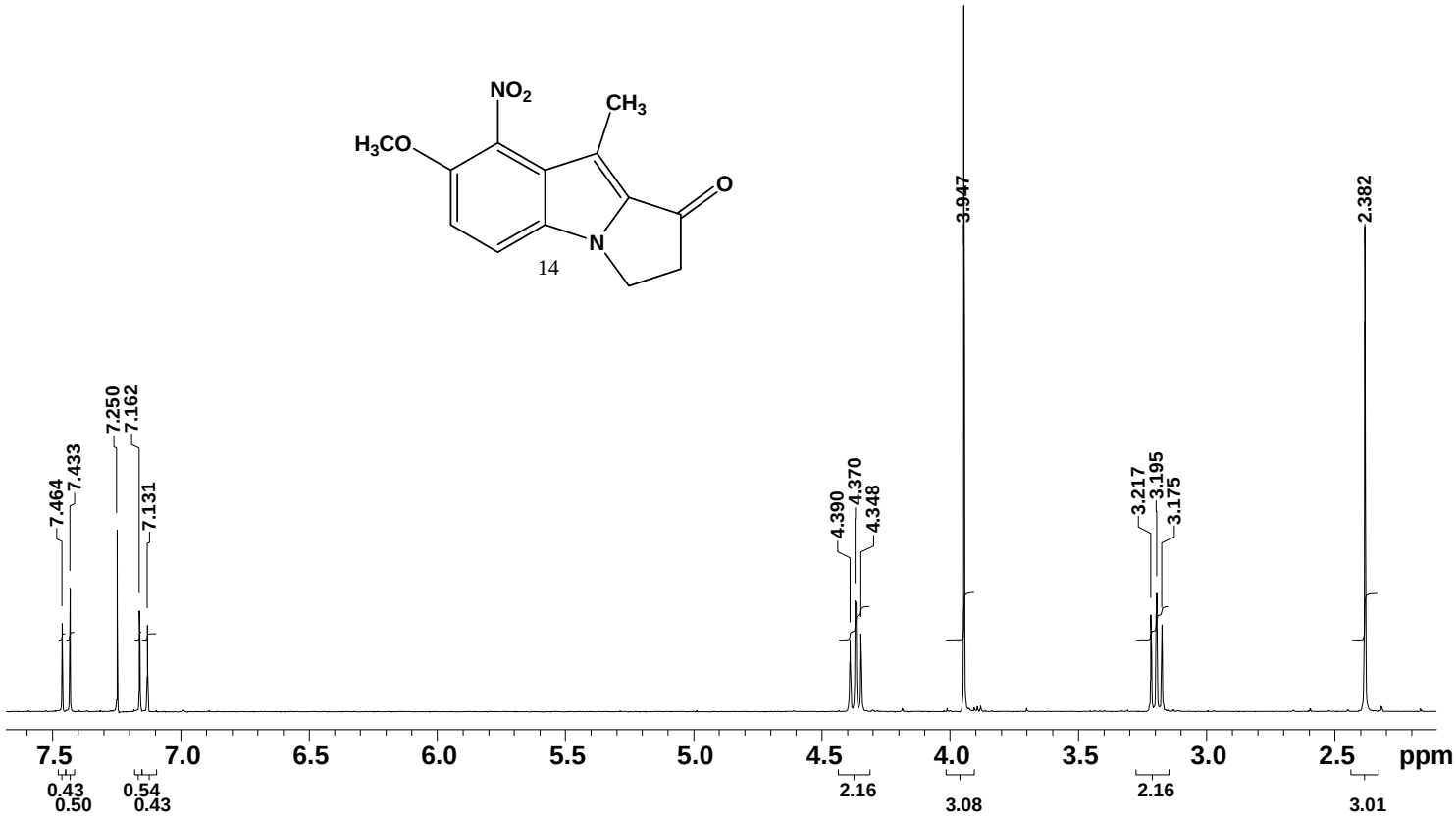
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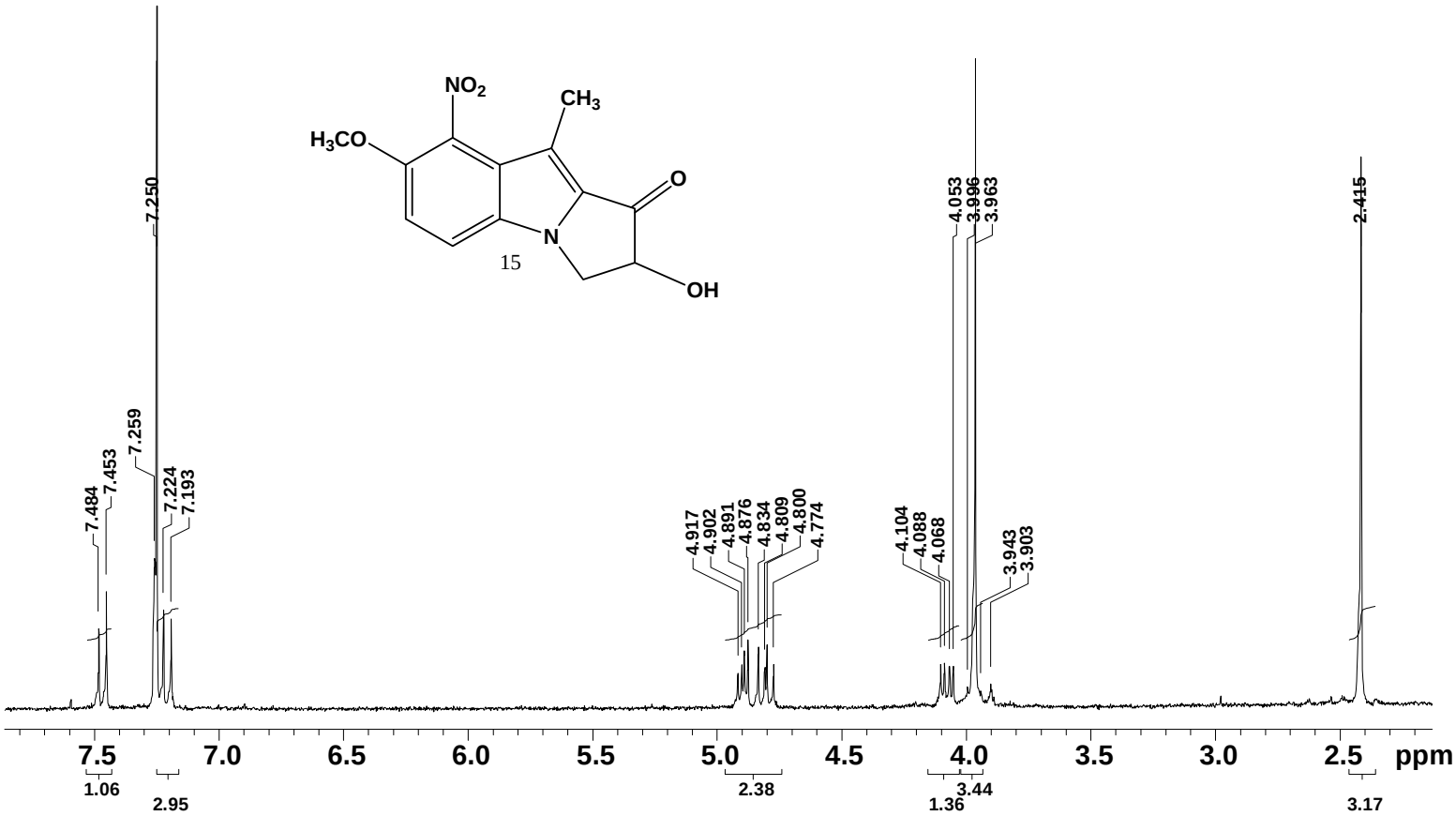
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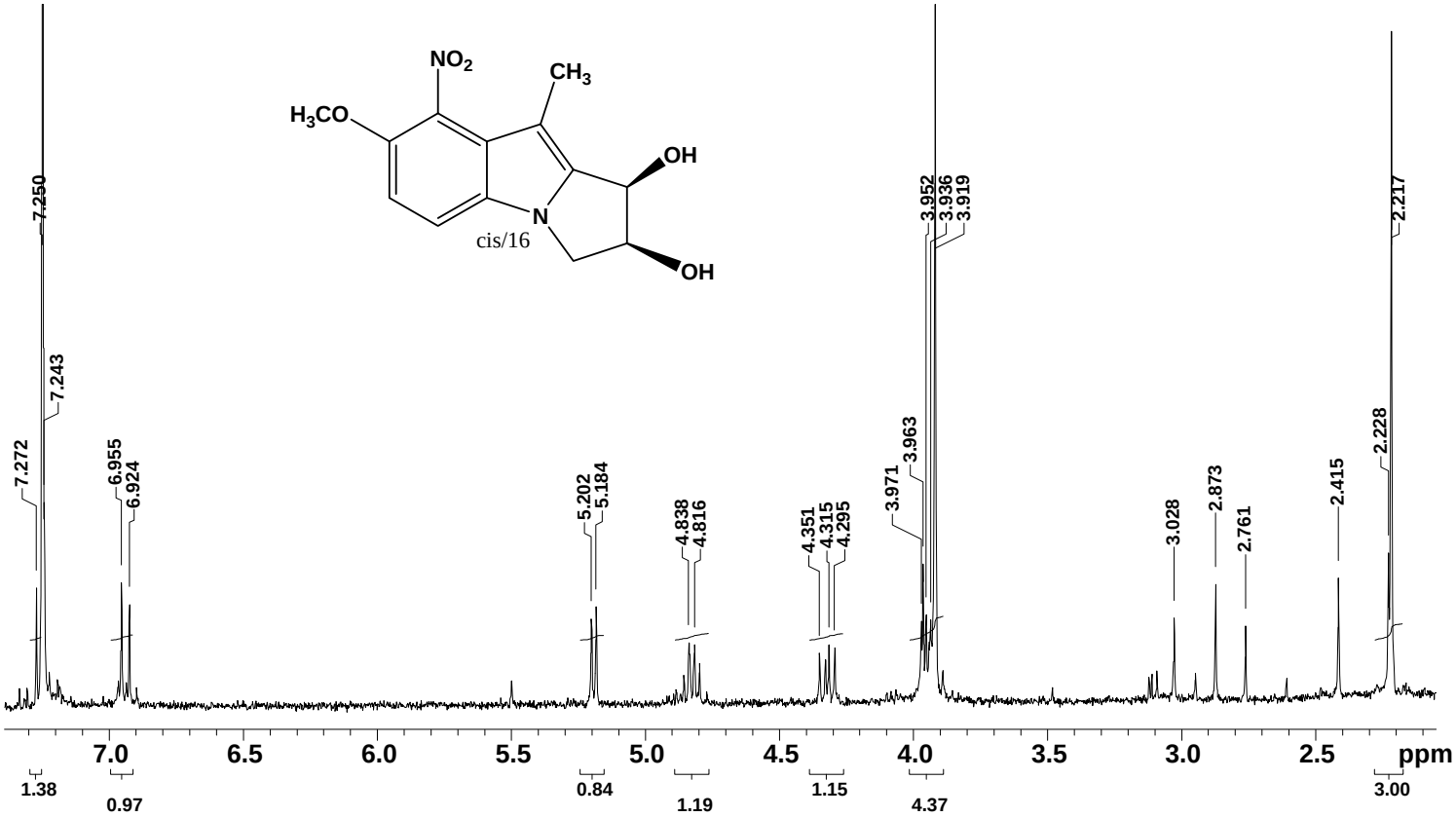
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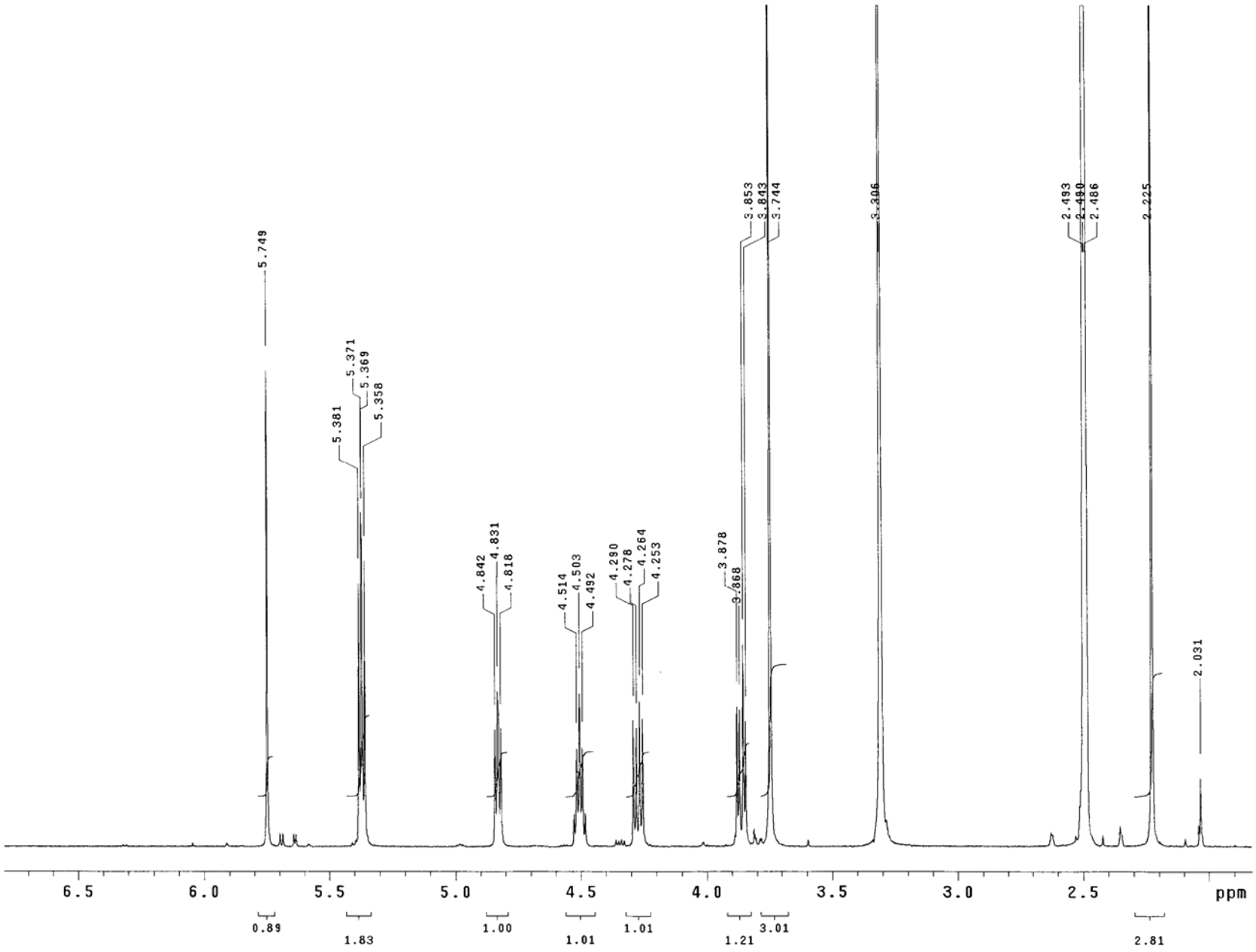
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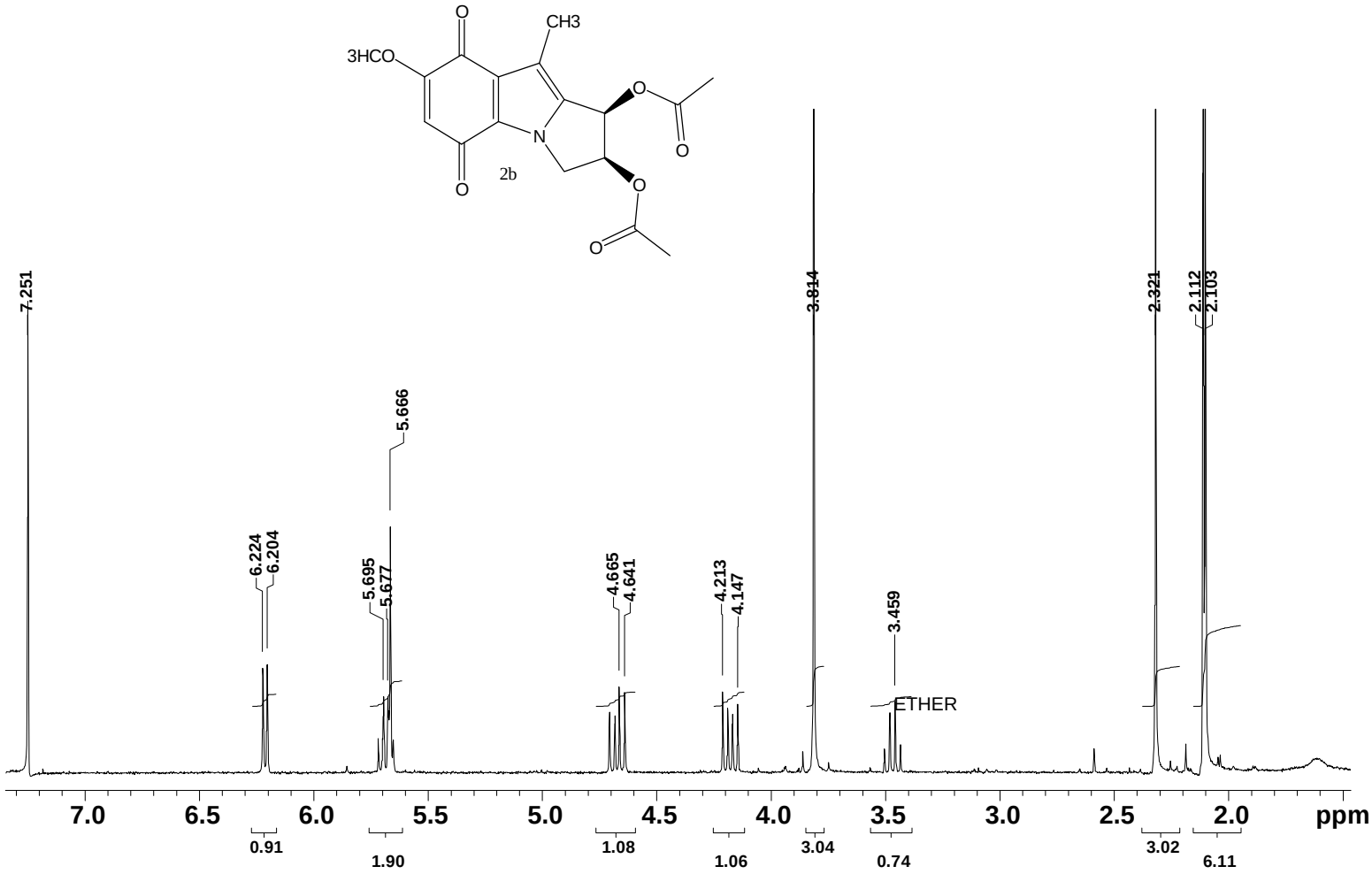
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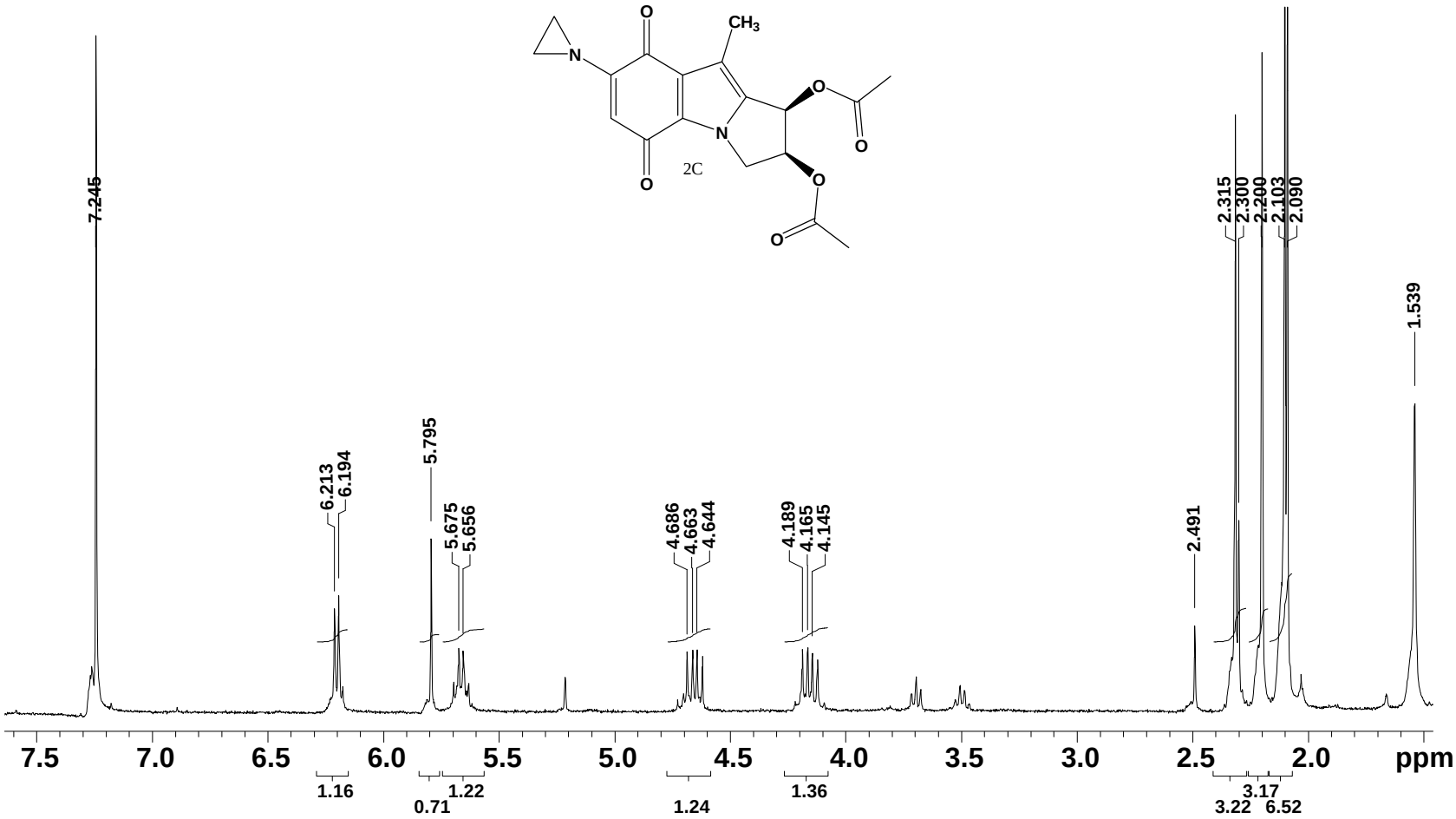
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2.300
2.200
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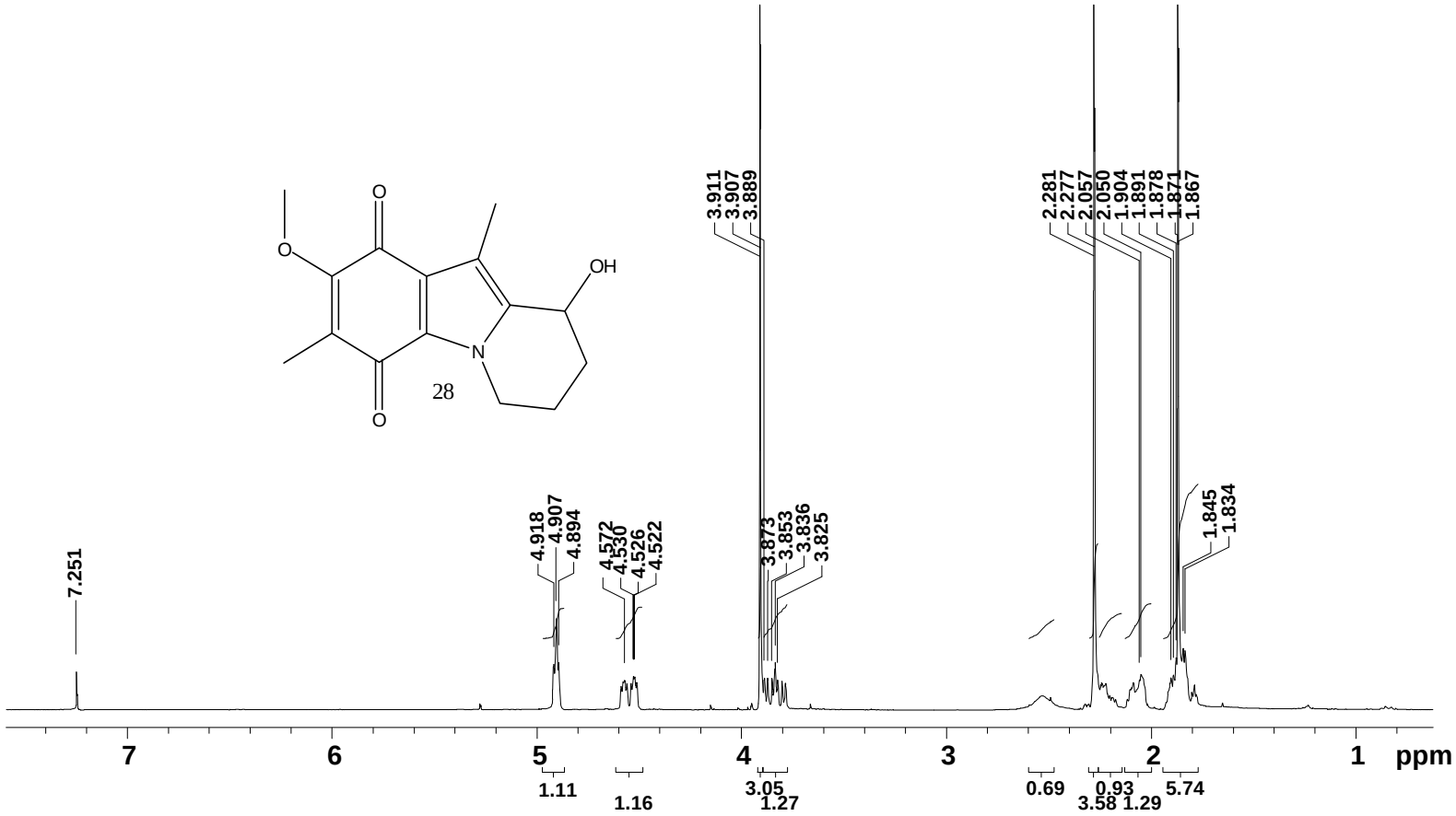
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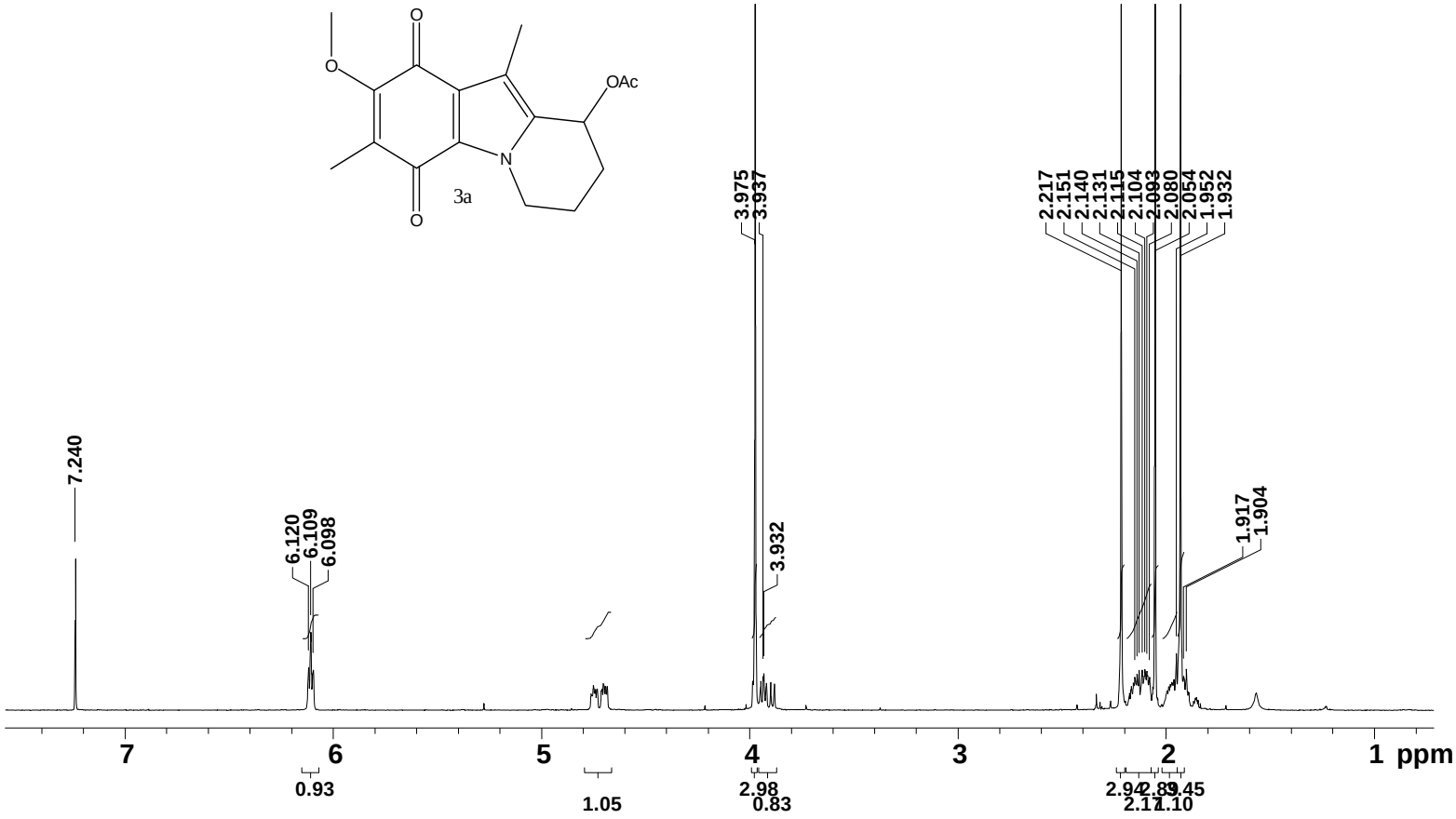
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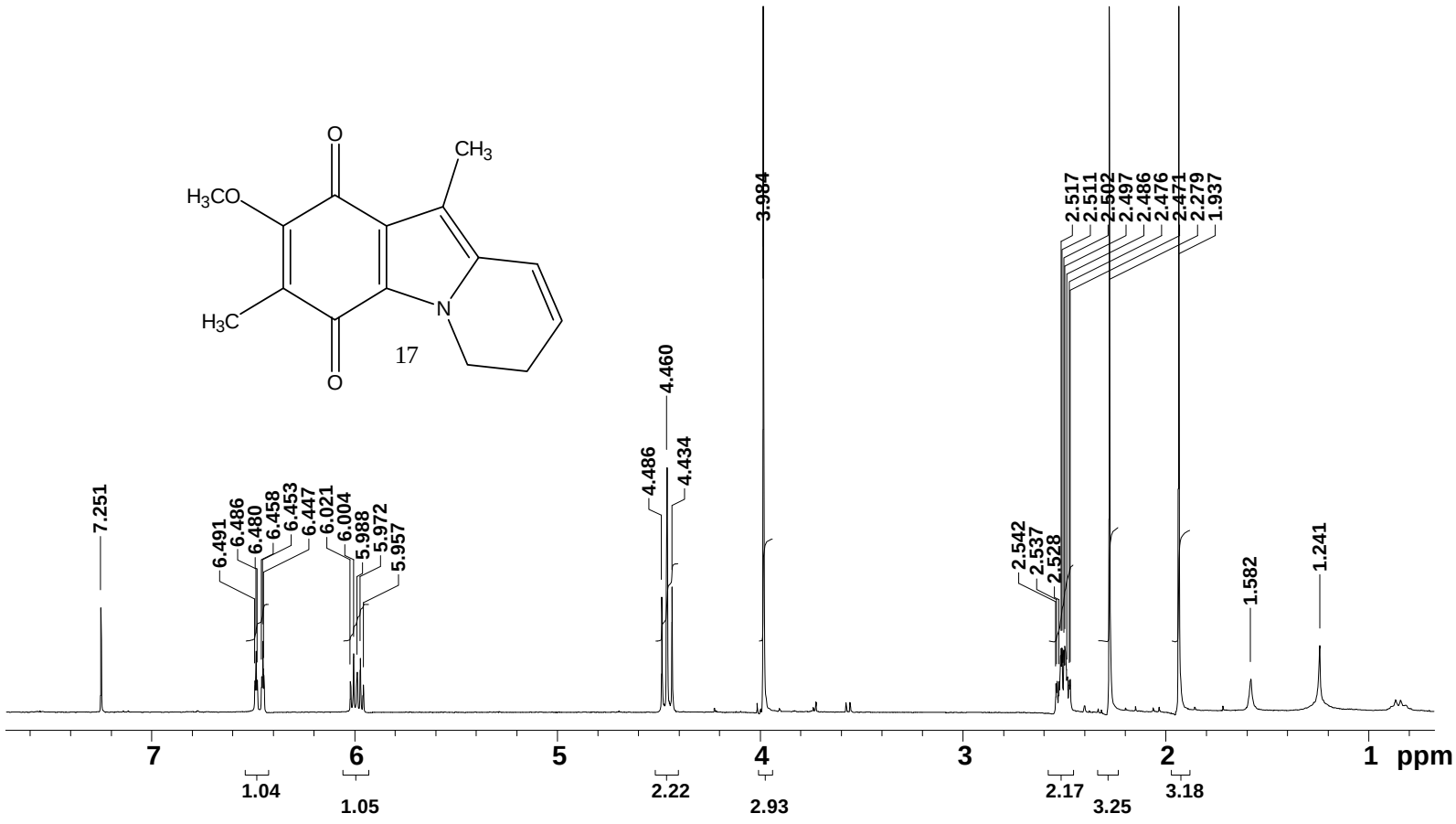
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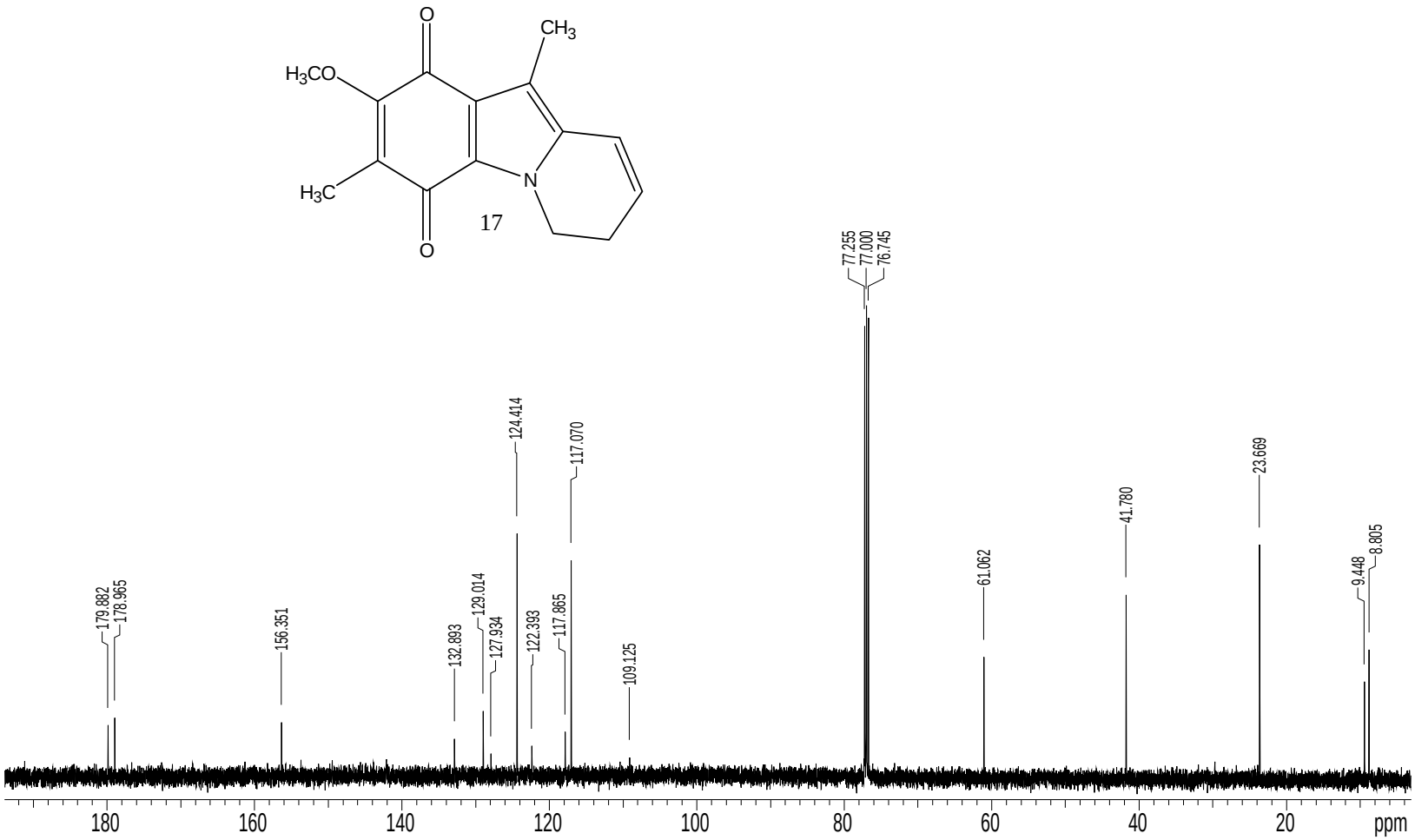
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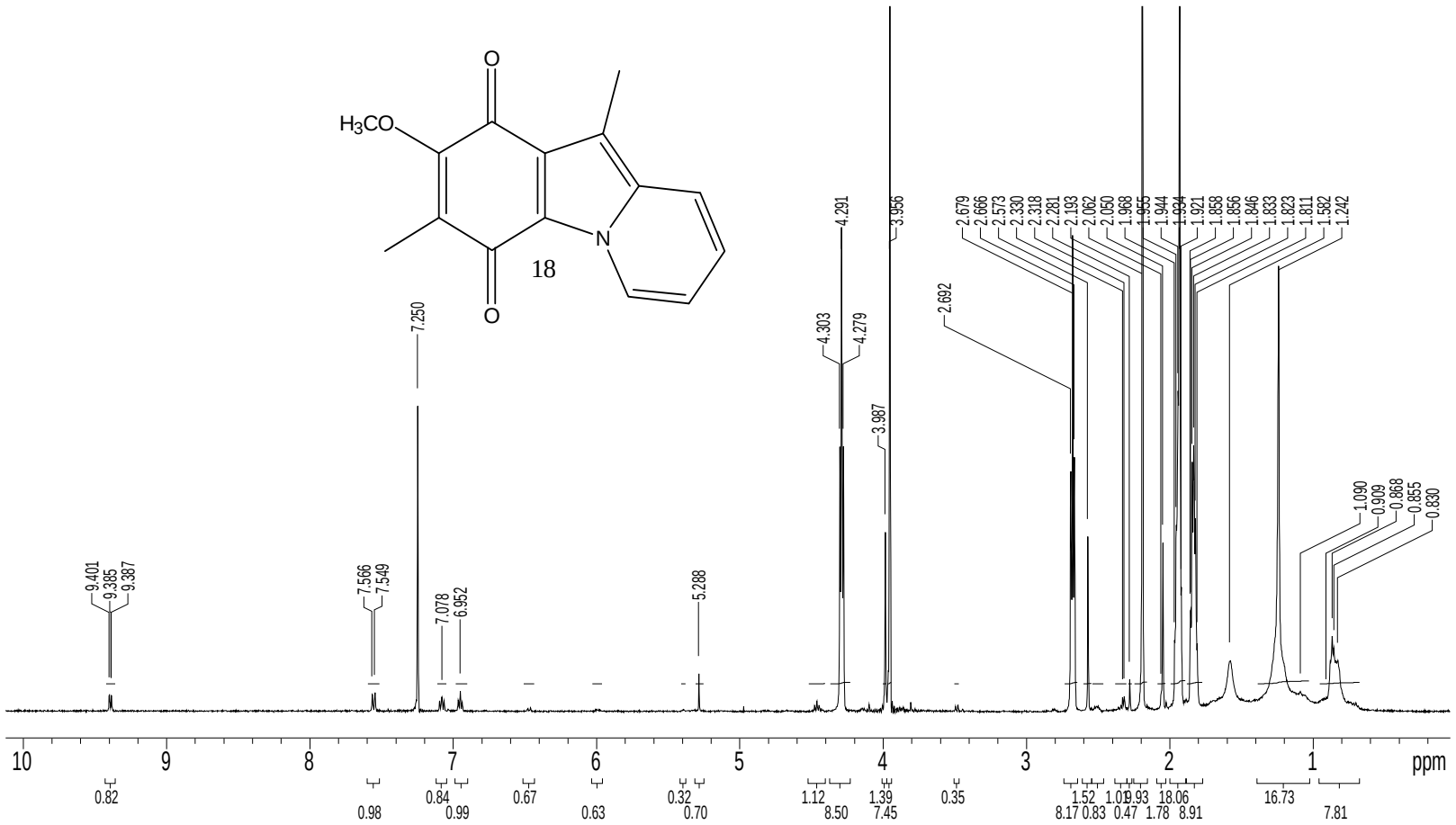
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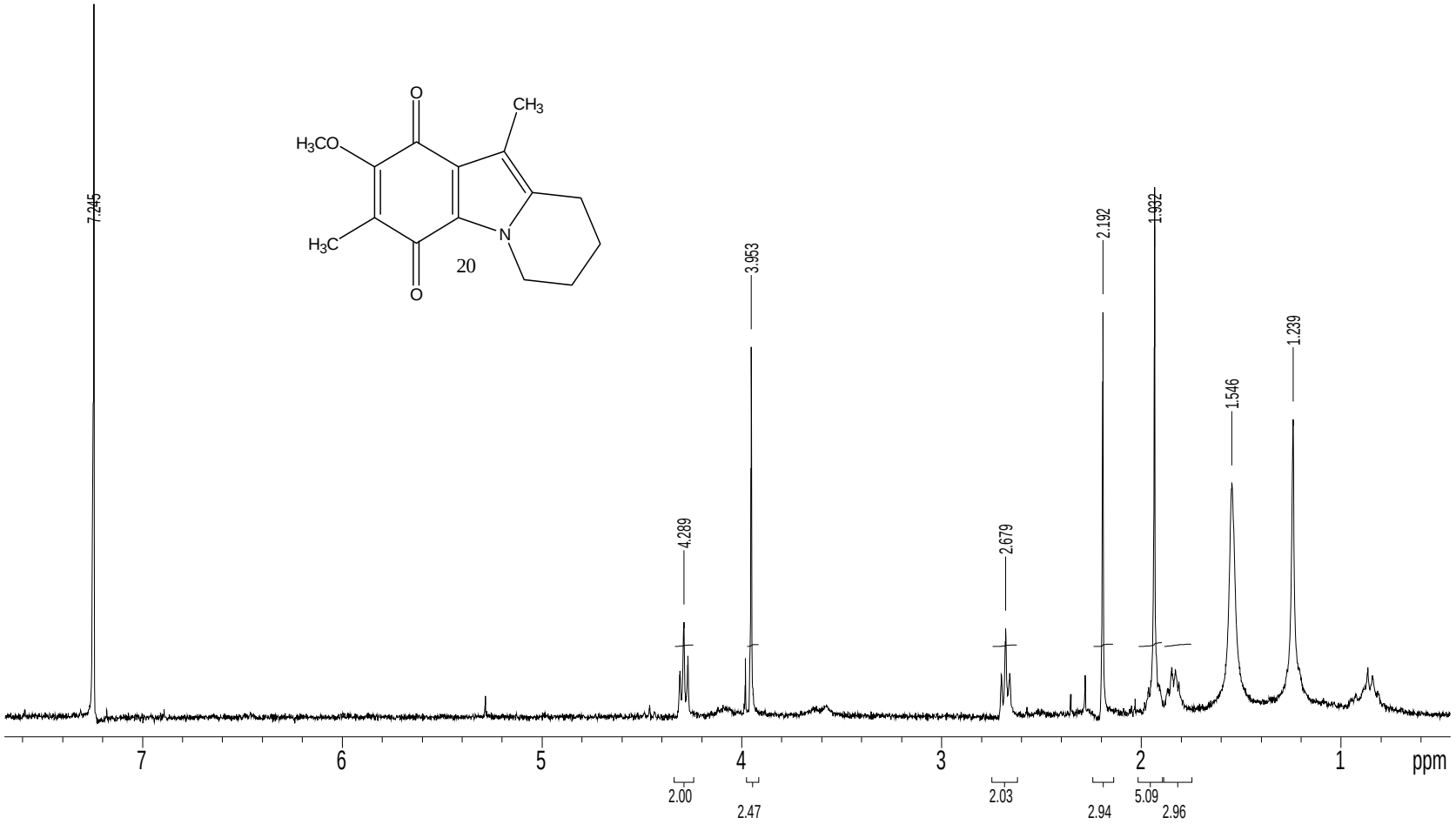
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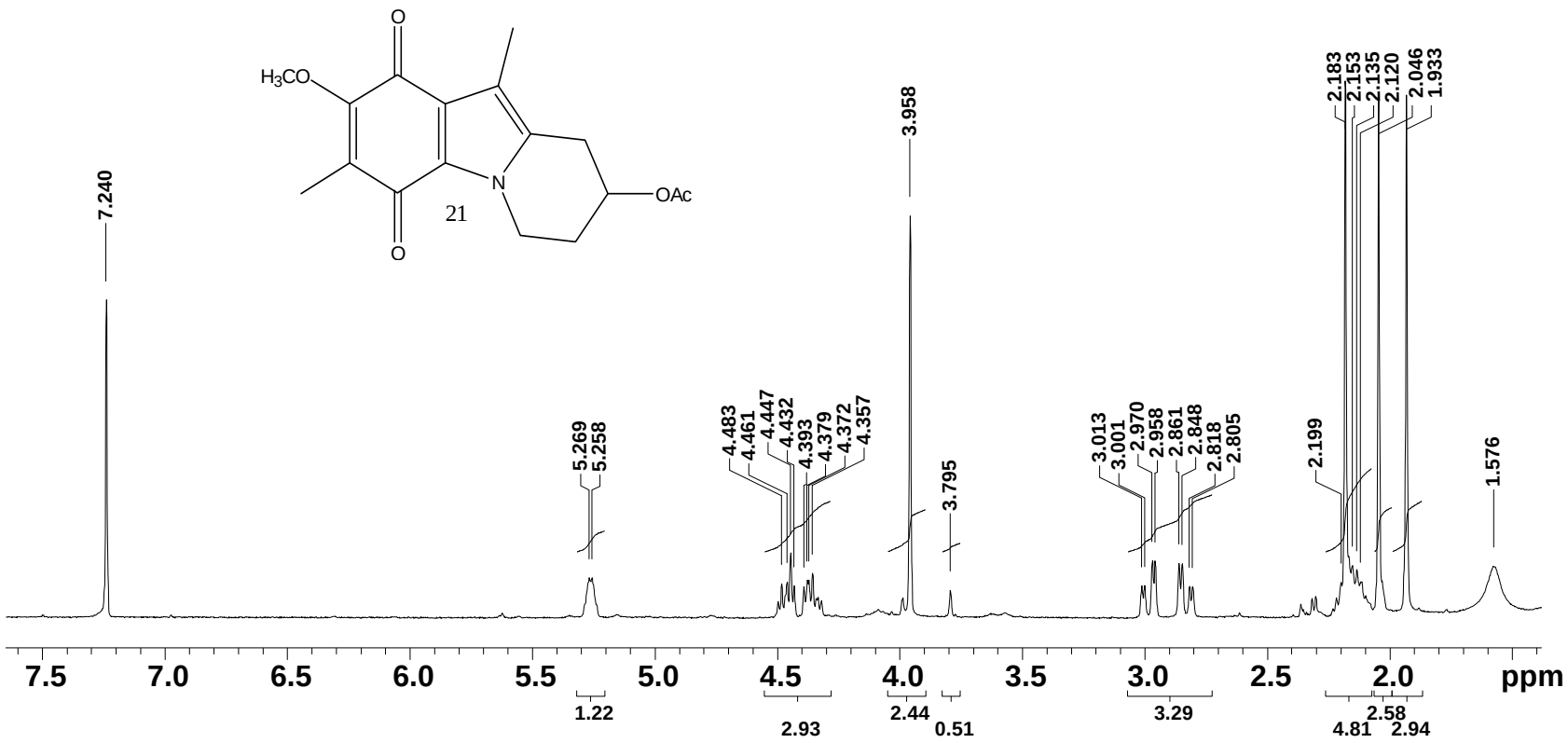
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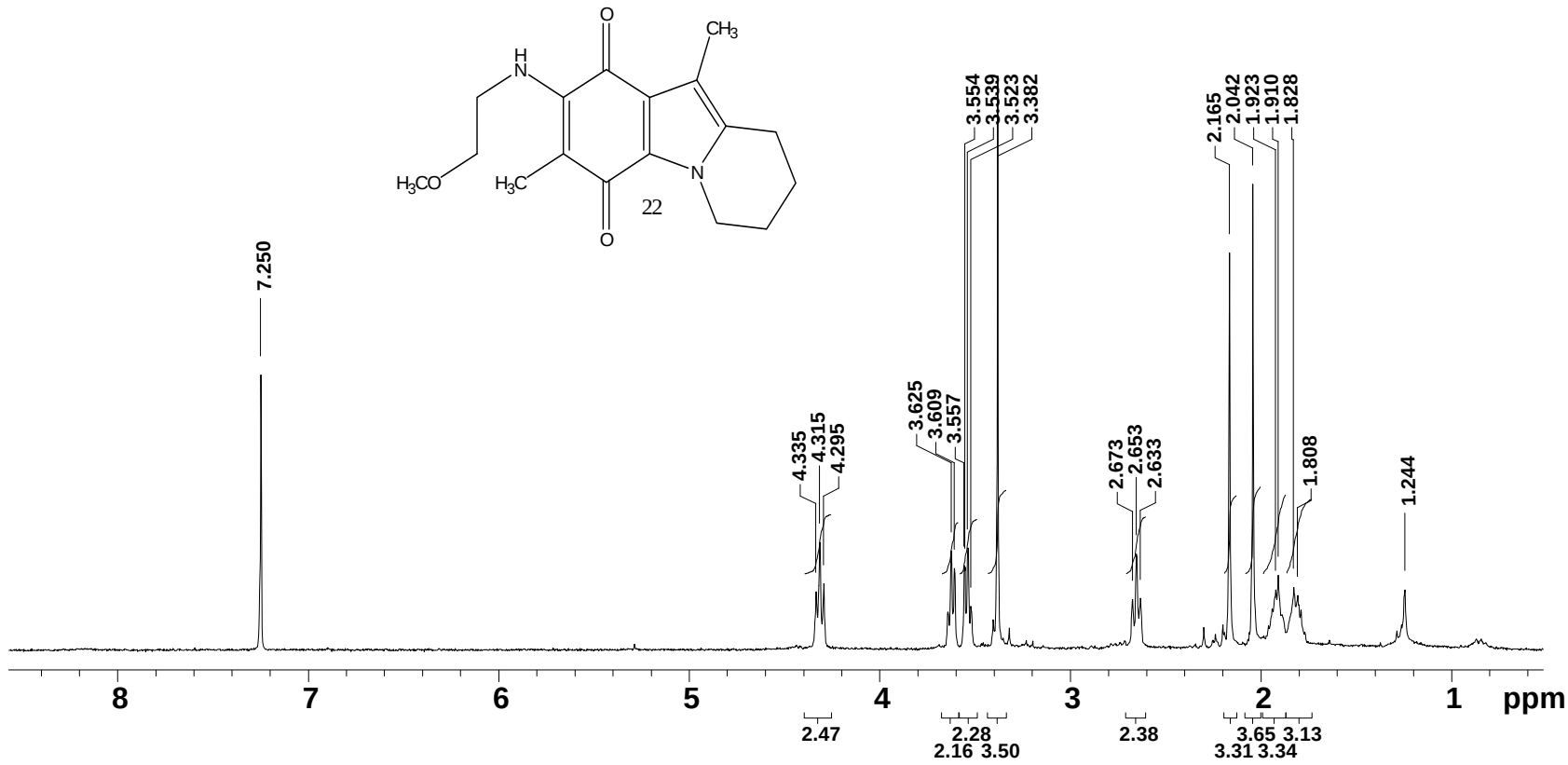
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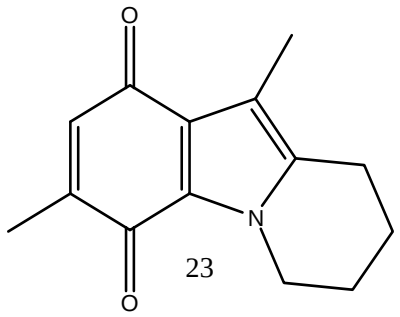
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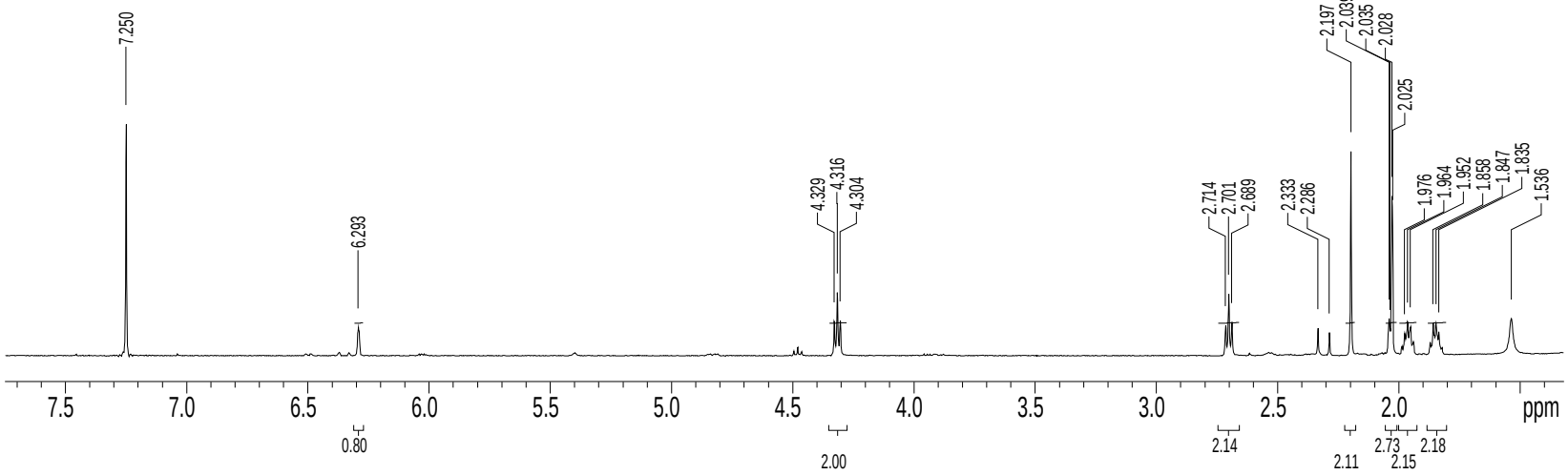
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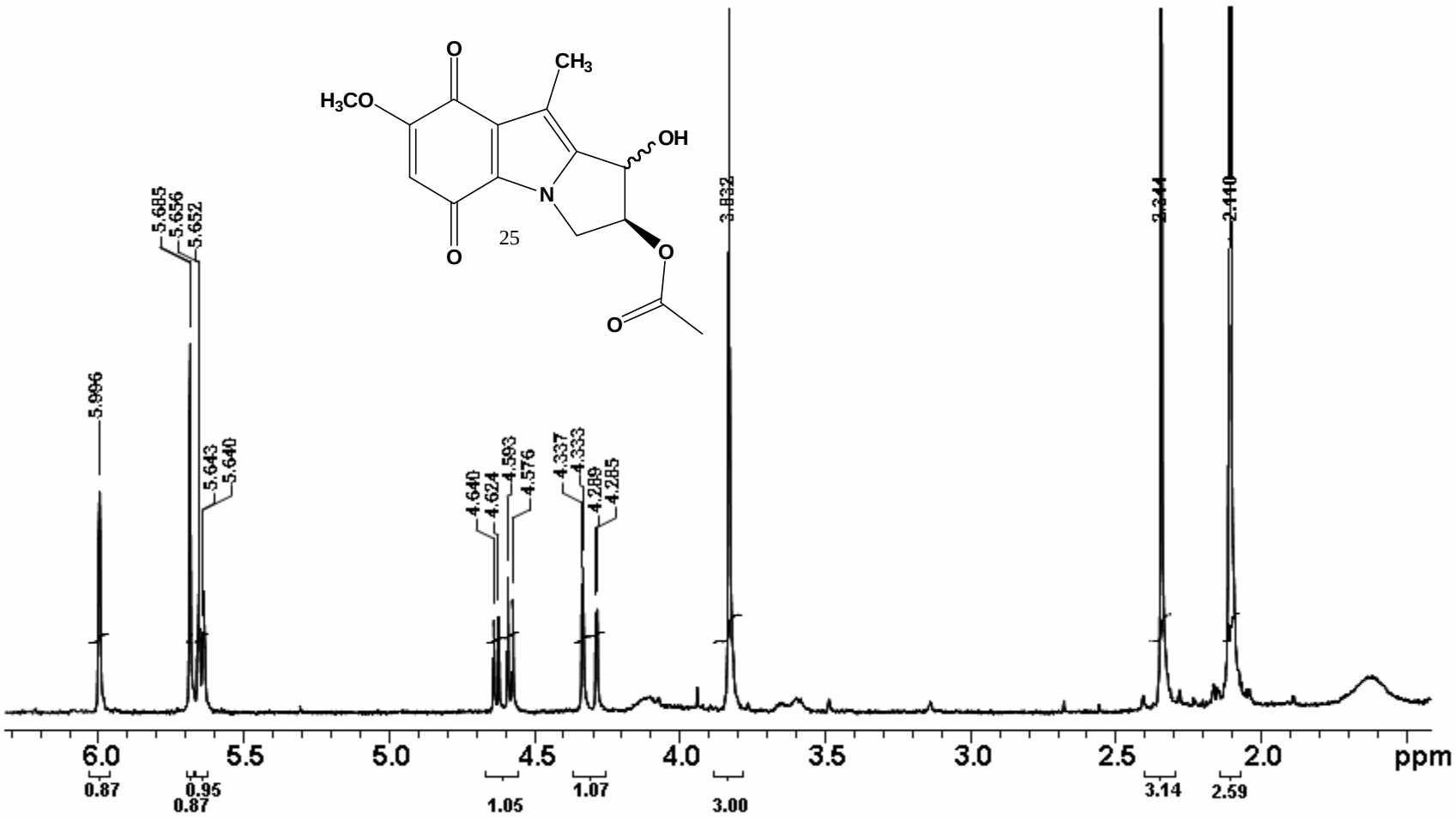
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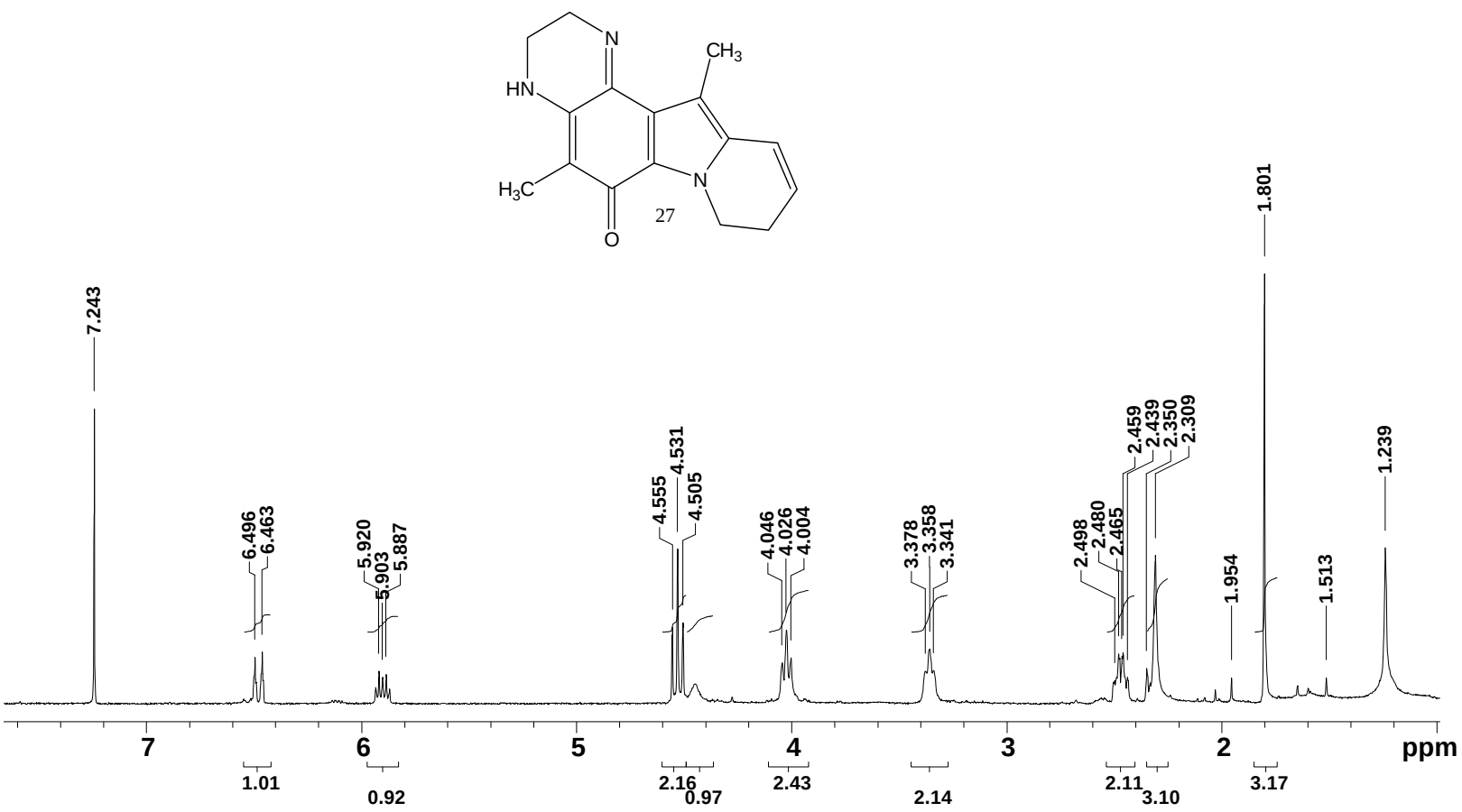
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3.17

Ethyl 5-Methoxy-3-methylindole-2-carboxylate (11). To a slurry of potassium *t*-butoxide (16.95 g, 0.15 mol) in 100 mL of dry benzene under nitrogen, was added of 20.5 mL of diethyl oxalate. A solution of 3-methyl-4-nitroanisole (25 g, 0.15mol) in 300 ml of dry benzene was added dropwise and a red solid formed immediately. The reaction mixture was then stirred at room temperature for 45 min. The red solid precipitate was collected by filtration washed with benzene to afford 29 g of the potassium salt 3-(5-Methoxy-2-nitro-phenyl)-2-oxo-propionic acid ethyl ester (63%).

To a stirred mixture of 20.0 g (65.5 mmol) of the ketoester salt prepared above and 300 mL of dry acetone was slowly added 18.0 g (127 mmol) of methyl iodide at room temperature.[29] After completion of addition, stirring was continued for 4 h. The reaction mixture was filtered and the solid was washed two times with 50-mL portions of acetone. The filtrates and washing were combined and evaporated to red oil which was dissolved in 200 mL of glacial acetic acid and treated with 25 g of zinc dust under efficient mechanical stirring at 40-45 ºC. The reaction was stirred for 3 h, before was filtered, and the solid residue was washed two times with 25-mL portions of acetic acid. The filtrate and washings were diluted with 800 mL of ice-cold water and extracted two times with 200-mL portions of ethyl acetate. The extracts were washed with water and dried (Na_2SO_4). Dried extracts were concentrated to a residue and purified by flash chromatography on silica gel using CH_2Cl_2 as the eluent. Recrystallization from methanol afforded (**11**) as white crystals: 3.8 g (25%) yield; mp 151-162 ºC; IR (KBr pellet) 3327, 2988, 1672, 1535,1470,1284,1251, 1202, 1017 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.39 (1H, bs, -NH proton), 7.31 (1H, d), 7.01 (2H, m), 4.42 (2H, q, J = 7.2 Hz, methylene protons), 3.88 (3H, s methoxy), 2.58 (3H, s), 1.39 (3H, t, J = 7.2 Hz); mass spectrum (EI), *m/z* 233 (M^+), 187 (M^+-CH_3CH_2OH),

172, 140. Anal calcd. for $C_{13}H_{15}NO_3$: C, 66.94; H, 6.48; N, 6.00. Found: C, 66.82; H, 6.44; N, 6.96.

Methyl 2, 3-Dihydro-7-methoxy-9-methyl-1-oxo-1H-pyrrolo [1, 2 - *a*] indole-2-carboxylate (12). To a mechanically stirred suspension of 2.0 g (17.8 mmol) of potassium tert-butoxide in 40 ml of dry benzene were added a solution of 4.0 g (17.14 mmol) of **11** in 100 mL of dry benzene and then 3.0 g (34.8 mmol) of methyl acrylate. The reaction mixture was refluxed for 4 h and then stirred at room temperature for 48 h. The reaction was treated with 400 mL of water and acidified with concentrated hydrochloric acid to pH 4. The acidified mixture was extracted two times with 200 mL portions of CH_2Cl_2 and then the extracts were washed with water and dried (Na_2SO_4). Dried extracts were concentrated to a white solid that was recrystallized from methanol: 2.6 g (50 %) yield; mp 158-160 ºC; IR (KBr pellet) 3071, 3000, 2956,2918,2820, 1738, 1705, 1569, 1339, 1241,1164,1039, 804 cm^{-1}; ^1H NMR (DMSO-d_6) δ 7.52 (1H, d, J = 9.3 Hz), 7.14 (1H, d, J = 2.1 Hz), 7.06 (1H, dd, J = 2.7 , 6.6 Hz), 4.59 (2H, m), 4.41(1H, m), 3.81 (3H, s), 3.71(3H, s), 2.44(3H, s); MALDI *m/z* calcd for $C_{15}H_{16}NO_4$ (M+1) 273.100, found 273.102. Anal. Calcd for $C_{15}H_{15}NO_4$: C, 65.92; H, 5.53; N, 5.13. Found: C, 66.09; H, 5.63; N, 5.11.

2, 3-Dihydro-7-methoxy-9-methyl-1H-pyrrolo [1, 2 - *a*] indol-1-one (13). A solution of **12,** 2.0 g (7.3 mmol), in 20 mL of ethanol and 20 mL of 6M HCl was heated at 80 ºC for 2 h. The solvents were removed by evaporation and the residue was extracted with Et_2O (100 mL). The ethereal extract was washed with $NaHCO_3$ solution (50 mL), dried (Na_2SO_4) and concentrated under reduced pressure to a white solid which was recrystallized from (CH_2Cl_2/hexane): 1.37 g (87%) yield; mp 197-199 ºC; IR (KBr pellet) 2954, 2907, 1689, 1618, 1563, 1487, 1405, 1383, 1328, 1164, 1039, 798 cm^{-1}; ^1H NMR (DMSO-d6) 7.47 (1H, d, J = 8.7 Hz), 7.12 (1H, d, J = 2.1

Hz), 7.01 (1H, dd, *J* = 2.1, 6.6 Hz),, 4.35 (2H, t, *J* = 6 Hz), 3.80 (3H, s), 3.32 (2H, t, *J* = 6 Hz), 2.43 (3H, s); MALDI *m/z* calcd. for $C_{13}H_{13}NO_2$ 215.0946, found 215.106 .

2, 3-Dihydro-7-methoxy-9-methyl-8-nitro-1H-pyrrolo [1, 2-*a*] indol-1-one (14). To a mixture of 2.0 g (9.3 mmol) of (**13**) and 60 mL of glacial acetic acid was added 3 mL of 70% nitric acid dropwise with stirring while maintaining a temperature of 10-15 ºC. Reaction was stirred for 10 min at this temperature range. 200 mL of ice water was added, the reaction was extracted two times with 100-mL portions of dichloromethane. The extracts were washed with water and dried (Na_2SO_4). Dried extracts were concentrated to a residue and purified by flash chromatography on silica gel using chloroform as the eluent. Recrystallization from ethyl acetate afforded (**14**) as a yellow crystalline solid: 1.25 g (52%) yield; mp 185-187 ºC; IR (KBr pellet) 3033, 2983, 2940, 1722, 1623, 1552, 1525, 1355, 1323, 1279, 1055, 787 cm^{-1}; ^1H NMR (DMSO-d_6) δ 7.46 (1H, d, *J* = 9.3 Hz), 7.25 (1H, d, *J* = 9.3 Hz), 4.39 (2H, t), 3.94 (3H, s), 3.21 (2H, t), 2.38 (3H, s). MALDI *m/z* calcd for $C_{13}H_{13}N_2O_4$(M+1) 261.0875, found 261.088. Anal. Calcd for $C_{13}H_{12}N_2O_4$: C, 60.00; H, 4.65; N, 10.76. Found: C, 59.94; H, 4.70; N, 10.72.

2, 3-Dihydro-2-hydroxy-7-methoxy-9-methyl-8-nitro-1H-pyrrolo [1, 2-*a*] indol-1-one (15). A solution of **14**, 500 mg (1.9 mmol), in 80 mL of DMF was added 800 mg $CuBr_2$ and 200 mg of LiBr. The mixture was heated at 85 ºC. for 32 hours and then the reaction was cooled to room temperature and acidified with aqueous 1N HCl to pH 3.00. Extraction with 3x 50 mL portions of CH_2Cl_2 then the extracts were washed with water and dried (Na_2SO_4). Dried extracts were concentrated to a residue and purified by flash chromatography on silica gel using chloroform as the eluent: 210 (39%) yield; mp dec. ≥ 159 ºC ; IR (KBr pellet) 3369, 2924, 1697, 1523, 1357, 1275, 1118 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.48 (1H, d, *J*= 9.3 Hz), 7.22 (11H, d, *J*= 9.3 Hz), 4.91 (2H, m), 4.10 (1H, m), 3.96 (3H, s), 2.41(3H, s). MALDI *m/z* calcd. for $C_{13}H_{13}N_2O_5$ (M+1) 277.

081, found 277.082. Anal. Calcd for $C_{13}H_{12}N_2O_4$: C, 56.52; H, 4.38; N, 10.14. Found: C, 55.87; H, 4.32; N, 9.93.

2, 3-Dihydro-7-methoxy-9-methyl-8-nitro-1H-pyrrolo [1, 2 - *a*] indole-*cis*-1, 2-diol (*cis*-16). Sodium borohydride 0.3 g, (7.9 mmol) was added portionwise upon cooling to a solution of (**15**) 0.5 g, (1.8 mmol) in methanol (50 mL) at 0 ºC. The reaction mixture was stirred at room temperature for 10 minute. Reaction was quenched with iced water, the reaction then extracted with methylene chloride (3x 50 mL). The combined organic layers were dried over Na_2SO_4, filtered, and evaporated. Crude product was purified by silica gel chromatography (methylene chloride) as the eluent. Two fractions were collected, the major was the title compound cis-isomer and the minor was the trans- isomer: 325 mg (cis-isomer) (65%) yield ; mp dec. ≥ 163 ºC ; IR(KBr pellet) 3350, 2941, 1653, 1521, 1367, 1124 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.27 (1H, d, J = 8.7 Hz), 6.95 (1H, d, J = 9.3 Hz), 5.20 (1H, d, J = 5.4 Hz), 4.83 (1H, m), 4.35 (1H, m), 3.97 (1H, m), 3.91(3H, s), 2.21 (3H, s); MALDI m/z calculated 278.0903 (M^+) $C_{13}H_{14}N_2O_5$. Found 278.092 (M+). 105 mg (trans-isomer) (21%) yield.

2, 3-Dihydro-cis-1, 2-dihydroxy-7-methoxy-9-methyl-1H-pyrrolo[1, 2 - *a*]indole-5, 8-dione (2a). A solution of 150 mg (0.54 mmol) of (**cis-16**) in 100 ml of methanol containing of 5% Pd on carbon was shaken under 50 psi of H_2 for 45 min. The reaction mixture was filtered through Celite, and the filtrate was washed with 15 ml of methanol. The filtrate was concentrated to afford the crude amine product, which was used in the next step without purification.

The amine was dissolved in 2 mL of MeOH followed by 20 mL of phosphate buffer (monobasic potassium phosphate) (0.1 M), pH = 3.20. To this solution was added a solution

consisting of 4 g of Fremy's salt in 100 mL phosphate buffer (monobasic potassium phosphate, 0.1M, pH = 3.20). The reaction mixture was stirred at room temperature for 50 min and then extracted (4x 50 mL) portions of chloroform. The dried (Na_2SO_4) extracts were concentrated. Flash column chromatography of the crude product on silica gel using (CH_2Cl_2/MeOH: 96:4) as the eluent. The isolated cis-diol (**2a**) was crystallized from (CH_2Cl_2/hexane) to afford the product as light red solid. 75 mg (53%) yield; mp dec. ≥ 169 ºC; IR (KBr pellet) 3410, 3298, 2933, 1653, 1640, 1503, 1447, 1327, 1102, 1002 cm^{-1}; ^1H NMR (DMSO-d6) δ 5.73 (1H, s), 5.37 (2H, m), 4.83 (1H, t, *J* = 7.6 Hz), 4.49 (1H, t, *J* = 7.6 Hz), 4.29 (1H, m), 3.87 (1H, m), 3.73 (3H, s), 2.21 (3H, s); MALDI *m/z* calcd for $C_{13}H_{14}NO_5$ (M+1) 264.0867, found 264.090. Anal. Calcd for $C_{13}H_{13}NO_5 \bullet 0.2\ H_2O$: C, 58.51; H, 5.06; N, 5.25. Found: C, 58.20; H, 4.94; N, 5.23.

***cis*-1, 2-Diacetoxy- 2, 3-Dihydro-7-methoxy-9-methyl-1H-pyrrolo [1, 2-a] indole-5, 8-dione (2b).** To a stirred solution of **2a,** 80 mg (0.30 mmol), in 30 mL of dry methylene chloride, cooled to 0 ºC, was added 30 mg of DMAP followed by 0.2 mL of acetic anhydride. The reaction was stirred for 5 min at room temperature and then solvent was evaporated to yield solids. The crude product was purified by flash silica gel chromatography using methylene chloride as the eluent. Recrystallization from methylene chloride/hexane afforded **2b** as a light yellow solid: 86 mg (82%) yield; mp 188-190ºC; IR (KBr pellet) 2942, 1739, 1645, 1505, 1371,1250, 1027 cm^{-1} ; ^1H NMR ($CDCl_3$) δ 6.22 (1H, d, *J* = 6 Hz)), 5.69 (1H, m), 5.66 (1H, s), 4.66 (1H, q), 4.21 (1H, q), 3.81 (3H, s), 2.32 (3H, s), 2.11 (3H, s), 2.10 (3H, s); MALDI *m/z* calcd for $C_{17}H_{19}NO_7$ (M+2, hydroquinone) 349.115, found 349.123. Anal. Calcd for $C_{17}H_{17}NO_7$: C, 58.79; H, 4.93; N, 4.03. Found: C, 58.66; H, 4.99; N, 4.17.

***cis*-1, 2-Diacetoxy -7-aziridinyl-2, 3-dihydro-9-methyl-1H-pyrrolo[1, 2 - *a*]indole-5, 8-dione (2c).** To a solution of **2a,** 60 mg (0.17 mmol), in 20 ml of methanol, cooled to 0 ºC , was

added 0.7 ml of aziridine. The reaction was stirred at 0ºC for 30 min and then at room temperature for 1h. The solvent was then removed in vacuo to afford an orange solid that was purified by flash silica gel chromatography using methylene chloride / ethyl acetate (95:5) as the eluent. Compound **2c** was recrystallized from methylene chloride/hexane to afford an orange crystalline solid: 38 mg (61%) yield; mp189-191 ºC; IR (KBr pellet), 2948, 1739, 1644, 1370, 1250, 1026 cm^{-1}; ^1H NMR ($CDCl_3$) δ) 6.21 (1H, d, *J* = 5.7 Hz), 5.79 (1H, s), 5.67 (1H, q, *J* = 5.7 Hz), 4.68 (1H, m),4.18 (1H, m), 2.31 (3H, s), 2.20 (4H, s), 2.10 (3H, s), 2.09 (3H, s); MALDI m/z calcd for $C_{18}H_{19}N_2O_6$ (M+1) 359.123, found 359.117. Anal. Calcd for $C_{18}H_{18}N_2O_6 \bullet 0.2\ H_2O$: C, 59.73; H, 5.12; N, 7.74. Found: C, 59.52; H, 5.68; N, 7.76.

9-Hydroxy- 6, 7, 8, 9-tetrahydro-3, 10-dimethyl-2-methoxypyrido[1, 2 - *a*]indole-1, 4-dione (28). A solution of **5**, 200 mg (0.69 mmol), in 100 mL of methanol containing 200 mg of 5 % Pd on charcoal was shaken under 50 psi of H_2 for 6 h. The reaction mixture was filtered through Celite and washed two times with 20 mL portions of methanol. The combined filtrates were concentrated to afford the crude amine product, which was used in the next step without purification.

To a solution of 2.2 g of Fremy salt and 2.5 g of potassium dihydrogen phosphate in 150 ml of water was added a solution of the crude amine in 50 ml of acetone. The reaction was stirred for 4 h and then diluted with 200 ml of water. The resulting solution was extracted with of chloroform (3 x 100 ml). The extracts were washed with water, dried (Na_2SO_4), and concentrated to afford a red solid. The crude product was purified by flash silica gel chromatography using hexane/ethyl acetate (40:60) as the eluent. The purified product was crystallized from methylene chloride/hexane to afford an orange crystalline solid: 120 mg (63%) yield; mp 202-204ºC ; IR (KBr), 3489, 2938, 1637, 1126, 1006, 751 cm^{-1}; ^1H NMR ($CDCl_3$) δ

4.91 (1 H, t, *J* = 3.3 Hz), 4.57 (1 H, m), 3.91 (3 H, s), 3.87 (1 H, m), 2.5 (1 H, bs), 2.28 (3 H, s), 2.25 (1 H, m), 2.05 (1 H, m), 1.90-1.83 (5 H); MALDI m/z calcd for $C_{15}H_{18}NO_4$ (M+1) 276.1236, found 276.126.

9-Acetoxy-6, 7, 8, 9-tetrahydro-2-methoxy-3, 10-dimethylpyrido [1, 2 - *a*]indole-1, 4-dione (3a). To a stirred solution of **28**, 100 mg (0.36 mmol), in 50 mL of dry methylene chloride under a nitrogen atmosphere and cooled to 0 ºC, was added 30 mg of DMAP followed by dropwise addition of 0.5 mL of acetic anhydride. Reaction was stirred for 5 min at room temperature and then the solvent was evaporated in vacuo. Crude product was purified by flash silica gel chromatography using methylene chloride as the eluent. Compound **3a** was recrystallized from methylene chloride/hexane to afford an orange crystalline solid: 90 mg (82%); mp 170-171 ºC; IR (KBr pellet) 2954, 1733, 1637, 1238, 1126, 926 cm^{-1} ; ^1H NMR ($CDCl_3$) δ 6.12 (1 H, t, *J* = 3.3 Hz), 4.75 (1 H, m), 3.97 (3 H, s), 3.93 (1 H, m), 2.21 (3 H, s), 2.15 (2 H, m), 2.05 (3 H, s), 1.95 (2 H, m), 1.93 (3 H, s); MALDI *m/z* calculated for $C_{17}H_{20}NO_5$ (M+1) 318.133, found 318.127.

Hydrolysis of 1aH_2 in Anaerobic pH 7.4 Aqueous Buffer. A solution consisting of 10 mL of DMSO and 25 mg (0.067 mmol) of **1a** was added to 30 mL of 0.1 M pH 7.4 phosphate buffer held at μ=1 with KCl. To this solution was added 5 mg of 5% Pd on carbon and the mixture was then deaerated with nitrogen for 30 min. Hydrogen gas was then bubbled into the reaction mixture for 5 min. and then nitrogen was bubbled into the reaction mixture for 30 min to remove the excess hydrogen. The reaction mixture was incubated at 30 ºC for 24 h and then opened to the air. The catalyst was filtered off and the filtrate extracted (3x 20 mL) with methylene chloride. The extracts were dried (Na_2SO_4) and concentrated to a red solid, which was subjected

to preparative silica gel thin-layer chromatographic separation using methylene chloride as the eluent. The physical properties of hydrolysis products (**17**) and (**18**) are provided below:

6, 7-Dihydro-2-methoxy-3, 10-dimethylpyrido[1, 2-*a*]indole-1,4-dione (17): 10 mg (58%) yield; TLC (CH_2Cl_2), R_f = 0.48; IR (KBr pellet), 2962, 2923, 2852, 1667, 1634, 1503, 1306, 1213, 1115, 935, 738 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.48 (1H, doublet of triplets, J = 9.9, 1.5 Hz), 6.0 (1H, doublet of triplets, J = 9.9, 4.2 Hz), 4.48 (2H, t, J =7.8 Hz), 3.98 (3H, s), 2.54 (2H, m), 2.47 and 1.93 (6H, 2s); ^{13}C NMR ($CDCl_3$) δ 179.8, 178.9, 156.3, 132.8, 129.0, 127.9, 124.4, 122.3, 117.8, 117.0, 61.0, 41.7, 23.6, 9.4, 8.8; HREI MS *m/z* calcd for $C_{15}H_{15}NO_3$ 257.1052, found 257.1048.

2-methoxy-3, 10-Dimethylpyrido[1, 2 - *a*]indole-1, 4-dione (18): 2.8 mg (16 %) yield; TLC (CH_2Cl_2), R_f = 0.36; IR (KBr pellet), 3002, 2929, 2852, 1656, 1634,1323,1143,110 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.4 (1H, d, J = 7.2 Hz), 7.57 (1H, d, J = 7.2 Hz), 7.07 (1H, t, , J = 7.2 Hz), 6.95 (1H, t, J = 7.2 Hz), 3.95 (3H, s), 2.58 and 2.06 (6H, 2s); HREI MS *m/z* calcd for $C_{15}H_{13}NO_3$ 255.0895, found 255.0897.

Hydrolysis of (1aH_2) in Anaerobic Methanol. To a mixture consisting of 20 mg of **1a** and 5 mg of Pd on carbon was added 50 mL of methanol. The mixture was deaerated with nitrogen for 30 min, followed by bubbling hydrogen gas for 5 min to facilitate quinone reduction. The reaction mixture was transferred to the glove box (N_2), where the Pd on carbon catalyst was filtered off using Millipore (MILLEX^R-PF) filter. The filtrate was incubated at 30 ºC for 16 h and then combined with air and stirred for 5 min. The filtrate was concentrated to red solid, which was subjected to preparative silica gel thin- layer chromatographic separation using

dichloromethane as eluent. The physical properties of products (**17**), (**18**), (**19**), (**20**) and (**21**) are provided below.

6,7-Dihydro-2-methoxy-3, 10-dimethylpyrido[1, 2 - *a*]indole-1,4-dione (17): 7.0 mg (55%) yield; the physical properties were the same as reported above.

2-Methoxy-3, 10-Dimethylpyrido[1, 2 - *a*]indole-1, 4-dione (18): 2.6 mg (19 %) yield; the physical properties were the same as reported above.

8-Acetoxy- 6, 7, 8, 9-tetrahydro-2, 9-dimethoxy-3, 10-dimethylpyrido [1, 2 - *a*] indole-1, 4-dione (19): trace yield; HREI MS *m/z* calcd for $C_{18}H_{21}NO_6$ 247.1369, found 347.1366.

6, 7, 8, 9-Tetrhydro-2-methoxy-3, 10-dimethylpyrido [1, 2 - *a*]indole-1, 4-dione (20): 1.2 mg (8.5 %) yield; TLC (CH_2Cl_2), R_f = 0.50; IR (KBr pellet), 2916, 1655, 1621, 1499,1332,1143, 1081 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.28 (2H, t, J = 6 Hz), 3.95 (3H, s), 2.67 (2H, t, J = 6 Hz), 2.19 (3H, s), 1.93 (3H, s), 1.92 and 1.84 (4H, 2m); HREI MS *m/z* calcd for $C_{15}H_{17}NO_3$ 259.1208, found 259.1198.

8-Acetoxy- 6, 7, 8, 9-tetrahydro-2-methoxy-3, 10-dimethylpyrido [1, 2 - *a*] indole-1, 4-dione (21): 1.4 mg (8%) yield: mp 145-147 ºC; IR (KBr pellet) 2952, 1730, 1635, 1237, 1127, 924 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5,29 (1 H, m), 4.51- 4,41 (2 H, m), 3.98 (3 H, s), 3.04 (1 H, dd, J = 17.2, 4.8 Hz), 2.88 (1 H, dd, J = 17.2, 4.8 Hz), 2.20 (3 H, s), 2.18 (2 H, m), 2.07 (3 H, s), 1.95 (3 H, s); MALDI *m/z* calcd. for $C_{17}H_{20}NO_5$ (M+1) 318.133, found 318.124.

Hydrolysis of 1cH_2 in Anaerobic Aqueous Buffer. This reaction was carried out as described above for the hydrolysis of **1aH_2**. The physical properties of hydrolysis products (**22**), (**23**) and (**24**) are provided below:

6, 7, 8, 9-Tetrahydro-2-(2-methoxyethylamino)-3, 10-dimethylpyrido[1, 2 - *a*]indole-1, 4-dione (22): 5.5 mg (38%) yield; IR (KBr pellet), 3426, 2934, 1661, 1612, 1246, 1170, 1110 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.28 (1H, b), 4.33 (2H, m), 3.62 (2H, m), 3.55 (2H, m), 3.38 (3H, s), 2.67 (2H, m), 2.16 (3H, s), 2.04 (3H, s), 1.92 (2H, m), 1.82 (2H, m); HREI MS *m/z* calcd for $C_{17}H_{22}N_2O_3$ 302.1631, found 302.1638.

6, 7, 8, 9-Tetrahydro-3, 10-dimethylpyrido[1, 2 - *a*]indole-1, 4-dione (23): 2.1 mg (19%) yield; IR (KBr pellet), 2923, 2852, 1640, 1607, 1481, 1383 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.29 (1H, s), 4.32 (2H, m), 2.71 (2H, m), 2.19 (3H, s), 2.03 (3H, s), 1.87 (2H, m), 1.85 (2H, m); HREI MS *m/z* calcd for $C_{14}H_{15}NO_2$ 229.1103, found 229.1101.

8-Acetoxy- 6, 7, 8, 9-tetrahydro-2-(2-methoxyethylamino)-3, 10-dimethylpyrido[1, 2 - *a*]indole-1, 4-dione (24): trace yield; HRFAB MS *m/z* calcd. for $C_{19}H_{24}N_2O_5$ 360.1685, found 360.1687.

Hydrolysis of $2bH_2$ in Anaerobic Aqueous Buffer (pH 7.4). This reaction was carried out as described above for the hydrolysis of **$1aH_2$**. The physical properties of hydrolysis products (**25**) and (**26**) are provided below and 4.8 mg of starting material **2b** was recovered:

2-Acetoxy- 2, 3-dihydro-1-hydroxy-7-methoxy-9-methyl-1H-pyrrolo[1, 2-*a*]indole-5, 8-dione (25): 1.1 mg (42 %) yield; IR (KBr pellet) 3396, 2952, 1730, 1635, 1237, 1127, 924 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.99 (1H, d, J = 5.4 Hz), 5.68 (1H, s), 5.65 (1H, q, J = 5.4 Hz), 4.64 (1H, dd , J = 4.8, 14.2 Hz), 4.33 (1H, dd, J = 71.2, 14.4 Hz), 3.83 (3H, s), 2.34 (3H, s), 2.11 (3H, s); MALDI *m/z* calcd for $C_{15}H_{16}NO_6$ (M+1) 306.0972, found 306.095.

2-Acetoxy-2, 3-dihydro-7-methoxy-9-methyl-1H-pyrrolo[1, 2 - *a*]indole-5, 8-dione (26). Trace yield; MALDI *m/z* calcd for $C_{15}H_{17}NO_5$ (M+2) 291.1096, found 291.111.

Hydrolysis of $3aH_2$ in Anaerobic Aqueous Buffer (pH 7.4 phosphate). This reaction was carried out as described above for the hydrolysis of **$1aH_2$**. The physical properties of hydrolysis products (**28**), (**20**) and (**17**) are provided below:

6, 7, 8, 9-Tetrahydro- 9-hydroxy-2-methoxy- 3, 10-dimethylpyrido [1, 2 - *a*]indole-1, 4-dione (28): 11.5 mg (53 %) yield; the physical properties were the same as reported above.

6, 7-Dihydro-2-methoxy-3, 10-dimethylpyrido[1, 2 - *a*]indole-1, 4-dione (17): 3.7 mg (18 %) yield; the physical properties were the same as reported above.

6, 7, 8, 9-Tetrahydro-3, 10-dimethyl-2-methoxypyrido [1, 2 - *a*]indole-1,4-dione (20): 3.5 mg (20 %) yield; the physical properties were the same as reported above.

Hydrolysis of $3aH_2$ in Anaerobic Aqueous Buffer (pH 9.00). This reaction was carried out as described above for the hydrolysis of **$1aH_2$** except pH 9.00 0.1 M borate buffer was used as solvent. his reaction afforded **28** as a major product (yield 83%) and **17** as a minor product (yield 5%)**;** the physical properties were the same as reported above.

Hydrolysis of $3bH_2$ in Anaerobic Aqueous Buffer (pH 7.4 phosphate). This reaction was carried out as described above for the hydrolysis of **$1aH_2$**. The physical properties of hydrolysis products (**29**) and (**30**) are the same as reported previously in this laboratory.[29]

2,3-Dihydro-1-hydroxy-7-methoxy-6, 9-dimethyl-1H-pyrrolo[1, 2 - *a*]indole-5, 8-dione (29). 18 mg (83 %) yield; the physical properties were the same as reported.

2,3-Dihydro-7-methoxy-6,9-dimethyl-1H-pyrrolo[1, 2 - a]indole-5, 8-dione (30). Trace yield; the physical properties were the same as reported.

2, 3, 7, 8-Tetrahydro-11-methyl-indolizino[2, 3 - *f*]quinoxaline-6-one (27). To a stirred solution of **17,** 20 mg (0.078 mmol), in 5 mL of methanol was added 5 μL of ethylenediamine. The reaction was stirred 5 h at room temperature,and then solvent was evaporated. The crude product was subjected to preparative silica gel thin- layer chromatographic separation using dichloromethane/ methanol (95:5) as eluent : 16 mg (77% yield); mp dec. ≥ 198 ºC; IR (KBr pellet) cm^{-1}; H-NMR ($CDCl_3$) δ 6.49 (1H, d, *J* = 9.6 Hz), 5.91 (1H, m), 4.55 (2H, t, *J* = 7.2Hz), 4.42 (1H, b), 4.04 (2H, t, *J* = 6 Hz), 3.37 (2H, t, *J* = 4.8 Hz), 2.47 (2H, m), 2.30 (3H, s), 1.79 (3H, s); MALDI *m/z* calcd for $C_{16}H_{18}N_3O$ (M+1) 268.1444, found 268.160; HREI MS *m/z* calcd for $C_{16}H_{17}N_3O$ 267.1355, found 267.1372.

Hydrolysis of $3aH_2$ in Anaerobic Aqueous Buffer (pH 7.4 phosphate). This reaction was carried out as described above for the hydrolysis of **$1aH_2$**. The physical properties of hydrolysis products (**28**), (**20**) and (**17**) are provided below:

6, 7, 8, 9-Tetrahydro- 9-hydroxy-2-methoxy- 3, 10-dimethylpyrido [1, 2 - *a*]indole-1, 4-dione (28): 11.5 mg (53 %) yield; the physical properties were the same as reported above.

6, 7-Dihydro-2-methoxy-3, 10-dimethylpyrido[1, 2 - *a*]indole-1, 4-dione (17): 3.7 mg (18 %) yield; the physical properties were the same as reported above.

6, 7, 8, 9-Tetrahydro-3, 10-dimethyl-2-methoxypyrido [1, 2 - *a*]indole-1,4-dione (20): 3.5 mg (20 %) yield; the physical properties were the same as reported above.

Hydrolysis of $3aH_2$ in Anaerobic Aqueous Buffer (pH 9.00). This reaction was carried out as described above for the hydrolysis of **$1aH_2$** except pH 9.00 0.1 M borate buffer was used as

solvent. his reaction afforded **28** as a major product (yield 83%) and **17** as a minor product (yield 5%)**;** the physical properties were the same as reported above.

Hydrolysis of 3bH_2 in Anaerobic Aqueous Buffer (pH 7.4 phosphate). This reaction was carried out as described above for the hydrolysis of **1aH_2**. The physical properties of hydrolysis products (**29**) and (**30**) are the same as reported previously in this laboratory.[29]

2,3-Dihydro-1-hydroxy-7-methoxy-6, 9-dimethyl-1H-pyrrolo[1, 2 - *a*]indole-5, 8-dione (29). 18 mg (83 %) yield; the physical properties were the same as reported.

2,3-Dihydro-7-methoxy-6, 9-dimethyl-1H-pyrrolo[1, 2 - a]indole-5, 8-dione (30). Trace yield; the physical properties were the same as reported.