Supporting Information

Formal Synthesis of Kingianin A Based Upon a Novel Electrochemically-Induced Radical Cation Diels-Alder Reaction

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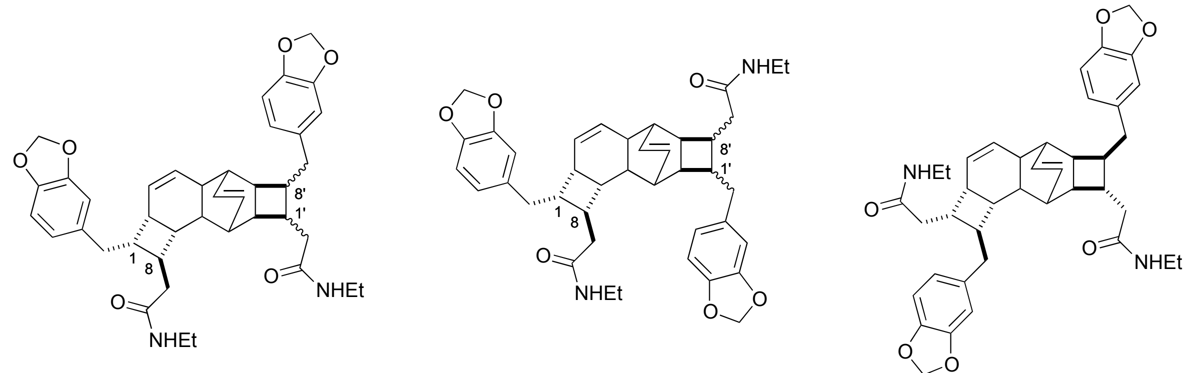
I. Materials and Methods

Reactions were performed in flame-dried glassware under an atmosphere of argon and stirred magnetically unless otherwise stated. CH_2Cl_2 was freshly distilled from CaH_2. All other reagents were obtained commercially and used without further purification. Thin layer chromatography was carried out on aluminium-backed plates pre-coated with silica (0.2 mm, 60 F_{254}, Merck). The plates were visualised using UV light or developed with basic potassium permanganate solution. Flash chromatography was performed using Merck silica gel 60 as the stationary phase.

Electrochemical measurements were performed using an Autolab PGSTAT20 potentiostat with a three-electrode configuration. Bulk electrolysis experiments, at a potential of 1.50 V vs. SCE, were carried out using a two-compartment cell. A reticulated vitreous carbon 80 PPI (The Electrosynthesis Company) working electrode was separated from a wound Pt/Rh gauze secondary electrode by a glass frit. A SCE was bridged to the test solution through a vycor frit that was orientated at the centre of the working electrode. The working electrode compartment was fitted with a magnetic stirrer bar and the test solution was stirred rapidly during electrolysis. Prior to electrolysis a cyclic voltammogram was recorded *in situ* at a Pt disc working electrode.

Compounds previously described in the literature were characterised to levels consistent with that reported. Infra-red spectra were recorded using a Bruker Tensor 27 FT-IR spectrophotometer with a neat film on a NaCl disc. Their absorbances are quoted as ν_{max} (cm^{-1}). ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ at ambient temperature using AV400 (400 MHz), AV3400 (400 MHz) and AV3500 (500 MHz) spectrometers. Data are expressed as chemical shifts in parts per million (ppm) relative to residual solvent signals of $CHCl_3$ (^1H NMR 7.26; ^{13}C NMR 77.0) as the internal standard on the δ scale. The following abbreviations are used to designate the multiplicity of each signal; s, singlet; d, doublet; dd, doublet of doublets; dddd, doublet of doublets of doublets of doublets; dt, doublet of triplets; t, triplet; q, quartet; m, multiplet; br, broad. Coupling constants *J* are given in Hz. High-resolution mass spectra were obtained using a Bruker MicroTOF mass spectrometer operating electrospray ionisation (ESI) in the positive mode.

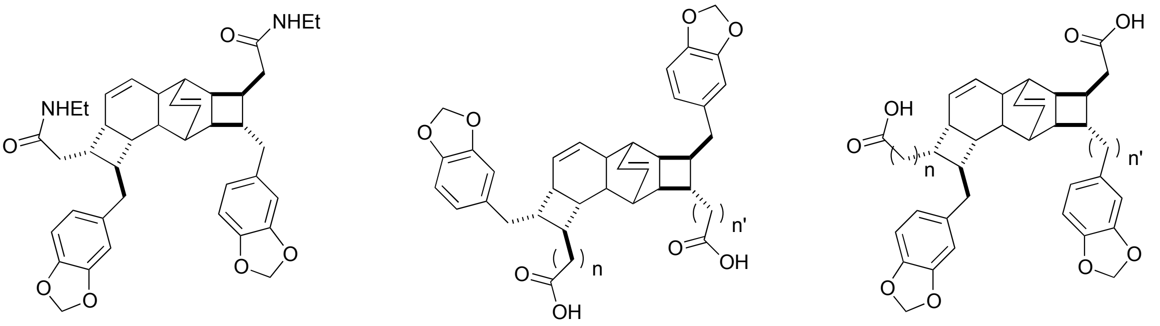
II. Kingianins A-N



kingianin A (**1**): 1'H = β; 8'H = α
kingianin B: 1'H = α; 8'H = β

kingianin C: 1'H = β; 8'H = α
kingianin D: 1'H = α; 8'H = β

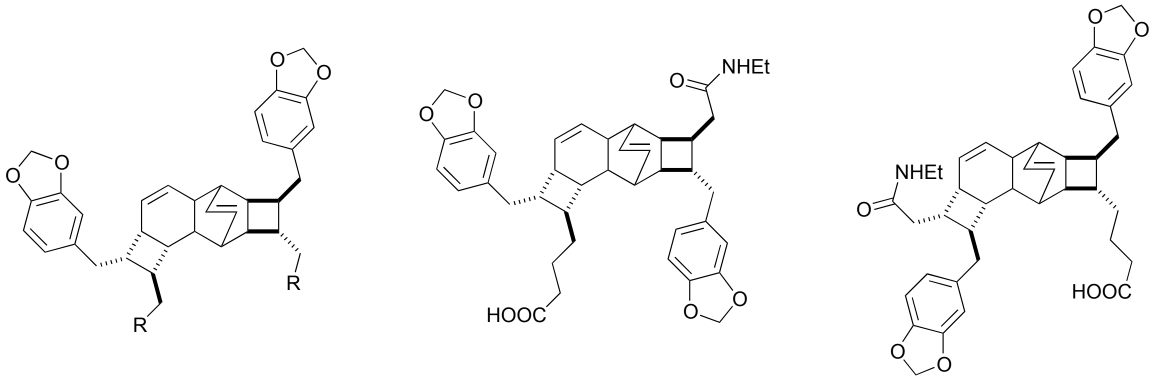
kingianin E



kingianin F

kingianin G: n = 1; n' = 3
kingianin H: n = n' = 3

kingianin I: n = 3; n' = 1
kingianin J: n = n' = 3



kingianin K: R_1 = CONHEt; R_2 = CH_2CH_2COOH
kingianin L: R_1 = CH_2CH_2COOH, R_2 = CONHEt

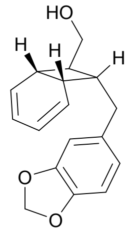
kingianin M

kingianin N

Figure S1. The kingianin family of natural products (kingianins A-N).

III. Experimental Procedures

The alcohols 5 and 8



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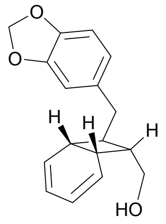


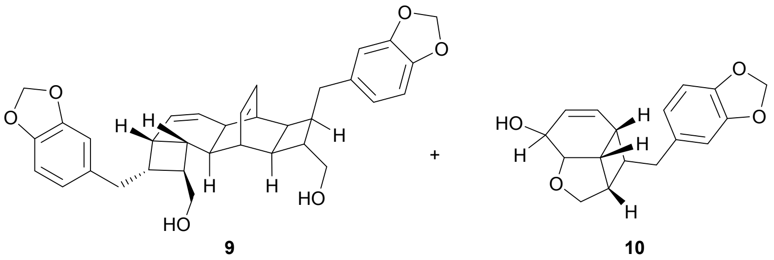
5 **8**

To a solution of boronic ester **7** (100 mg, 0.22 mmol) and vinyl bromide **6** (17 mg, 0.07 mmol) in THF:H_2O (3:1, 1 mL) was added tetrakis(triphenylphosphine)palladium (9 mg, 0.007 mmol) and the solution was stirred for 5 min. Thallium ethoxide (33 mg, 0.13 mmol, 9.4 μL) was added by microsyringe, upon which a yellow precipitate formed. The reaction mixture was heated to 90 °C and stirred for 23 h. After cooling to room temperature, diethyl ether (2 mL) and sodium thiosulfate (10% w/v H_2O, 1 mL) were added and the solution was stirred for 5 min, filtered through a pad of celite and washed with diethyl ether (3 x 5 mL). The organic layer was separated and the aqueous layer extracted with diethyl ether (3 x 5 mL). The combined organic extracts were washed with brine (10 mL) and then H_2O (10 mL) and then dried over anhydrous Na_2SO_4, filtered and volatile solvent removed under reduced pressure. The concentrate was passed through a short pad of silica gel and washed with ethyl acetate and hexane (1:1) (300 mL). The yellow fractions were combined and the volatile solvents were removed under reduced pressure. The crude product was carried directly on to the next step without further purification.

To the crude bicyclo[4.2.0]octadienes was added THF (0.6 mL) and the reaction mixture was cooled to 0 °C. To this solution was added portion wise tetrabutylammonium fluoride trihydrate (70 mg, 0.22 mmol) and the reaction was allowed to warm to room temperature. After stirring for 4 h, the mixture was returned to 0 °C and ammonium chloride (aqueous sat. soln., 0.5 mL) was added. The organic layer was separated and the aqueous layer extracted with ethyl acetate (3 x 5 mL). The combined organic extracts were washed with brine (10 mL), dried over anhydrous $MgSO_4$, filtered and volatile solvent removed under reduced pressure. The crude products were purified by flash silica gel column chromatography (PE:EtOAc = 19:1 to 5:1) to furnish the inseparable bicyclo[4.2.0]octadienyl alcohols **5** and **8** (3:2) as a pale yellow oil (16.6 mg, 83% over two steps). R_f 0.37 (PE:EA = 80:20); ^1H NMR (400 MHz, $CDCl_3$) δ 2.54-2.91 (m, 5H), 3.18-3.28 (m, 1H), 3.33-3.46 (m, 1.2H), 3.58 (dd, *J* = 10.8, 5.7 Hz, 0.4H), 3.72 (dd, *J* = 10.8, 8.2 Hz, 0.4H), 5.45 (dd, *J* = 9.7, 5.5 Hz, 0.4H), 5.57-5.66 (m, 2H), 5.73 (dd, *J* = 9.5, 5.4 Hz, 0.6H), 5.83-5.89 (m, 0.4H), 5.90-5.95 (m, 2.6H), 6.60-6.75 (m, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 32.5, 32.9, 34.5, 36.1, 36.2, 41.6, 48.3, 50.4, 51.7, 53.6, 63.3, 65.3, 100.8 (x2), 108.17, 108.24, 108.95, 109.05, 121.2, 121.4, 121.5, 121.8, 124.3, 124.4, 125.3, 126.2, 126.7, 127.2, 134.3, 134.8, 145.7, 145.8, 147.6, 147.7 ppm; ν_{max} cm^{-1} (Thin film): 3355, 2918, 1502, 1442, 1247 (C-O-C), 1039; HRMS (ESI): Calculated for $C_{17}H_{19}O_3$ [M+H]$^+$ 271.1329 obtained 271.1338, calculated for $C_{17}H_{18}NaO_3$ [M+Na]$^+$ 293.1148, obtained 293.1140.

This data is consistent with that reported by Parker *et al.*[1]

The diol 9 and the ether 10



To a solution of tetrabutylammonium tetrafluoroborate (1.97 g, 5.97 mmol) in CH_2Cl_2 (15 mL) was added the mixture of alcohols **5** and **8** (3:2) (10.0 mg, 0.04 mmol). The reaction mixture was subjected to anodic oxidation at 1.5 V until 3.57 C of charge had been passed. The solution was concentrated under reduced pressure and the resulting solids were ground to a fine powder in a mortar and pestle and then triturated with diethyl ether (5 x 10 mL). The organic washings were combined and dried over anhydrous $MgSO_4$, filtered and volatile solvent removed under reduced pressure. The above procedure was repeated for a second batch of alcohol (10 mg, 0.04 mmol) and the crude products were combined and purified by preparative thin layer chromatography to yield the compounds **9** (1.5 mg, 13%) and **10** (1.3 mg, 16%).

Compound 9

R$_f$ 0.13 (PE:EtOAc = 3:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.73 (d, *J* = 9.0 Hz, 1H), 1.79-1.88 (m, 1H), 1.93-2.03 (m, 2H), 2.16-2.70 (m, 12H), 3.31-3.41 (m, 4H), 5.64 (br d, *J* = 10.3 Hz, 1H), 5.72 (br d, *J* = 10.3 Hz, 1H), 5.91 (s, 2H), 5.92 (s, 2H), 6.14 (t, *J* = 7.0 Hz, 1H), 6.28 (t, *J* = 7.0 Hz, 1H), 6.56-6.74 (m, 6H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 32.8, 35.3, 36.3, 38.0, 38.3, 38.6, 38.8, 39.5, 40.67, 40.73, 41.2, 42.7, 44.1, 47.7, 65.2, 67.0, 100.7 (x2), 108.2 (x2), 108.8, 108.9, 121.0, 121.1, 125.3, 132.0, 132.1, 135.0, 135.1, 135.4, 145.60 (x2), 147.6, 147.7 ppm; ν_{max} cm^{-1} (Thin film): 3429 (O-H), 1646 (C=C); HRMS (ESI): Calculated for $C_{34}H_{36}NaO_6$ [M+Na]$^+$ 563.2404, obtained 563.2392.

This data is consistent with that reported by Parker *et al.*[1]

Compound 10

R_f 0.27 (PE:EtOAc = 3:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.86-1.95 (m, 1H), 2.47 (dddd, J = 8.6, 6.5, 4.5, 1.9 Hz, 1H), 2.61-2.66 (m, 1H), 2.74 (d, J = 8.2 Hz, 2H), 2.96-3.03 (m, 1H), 3.48 (dd, J = 9.3, 4.5 Hz, 1H), 3.66 (d, J = 9.3 Hz, 1H), 3.91 (br dd, J = 6.2, 2.1 Hz, 1H), 4.34 (br s, 1H), 5.67 (dd, J = 10.1, 4.3 Hz, 1H), 5.84-5.90 (m, 1H), 5.93 (s, 2H), 6.61 (dd, J = 7.9, 1.5 Hz, 1H), 6.63-6.66 (m, 1H), 6.73 (d, J = 7.9 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 31.4, 33.3, 41.5, 41.8, 47.3, 62.9, 72.4, 78.8, 100.8, 108.1, 108.9, 121.4, 124.0, 132.1, 133.6, 145.8, 147.6 ppm; ν_{max} cm^{-1} (Thin film): 3425 (O-H), 1641 (C=C); HRMS (ESI): Calculated for $C_{17}H_{18}NaO_4$ $[M+Na]^+$ 309.1097 obtained, 309.1088.

References

1 H. N. Lim and K. A. Parker, *Org. Lett.*, 2013, **15**, 398

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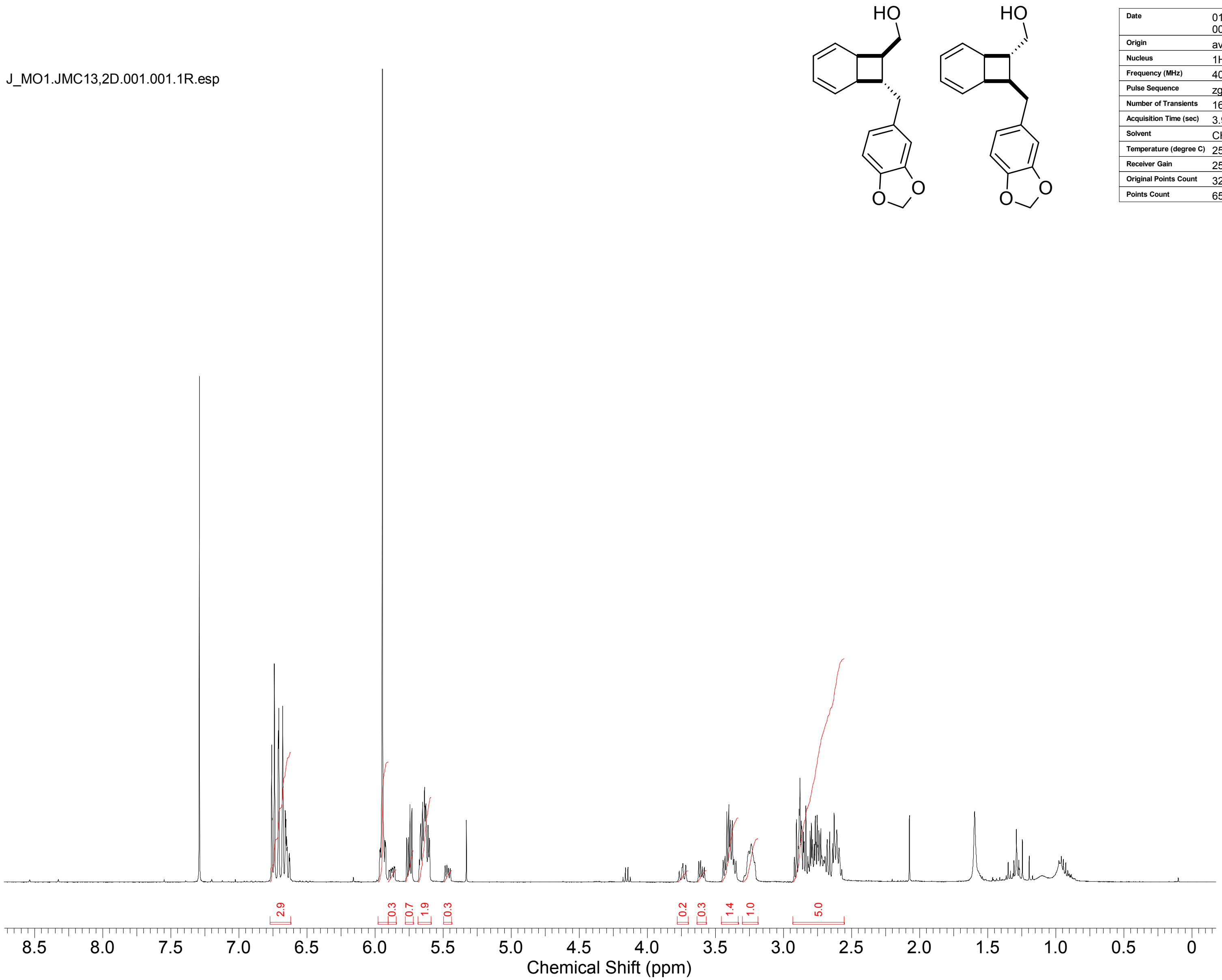

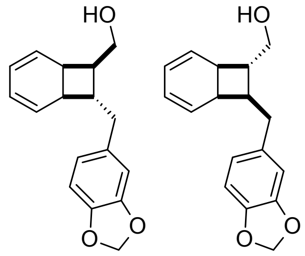

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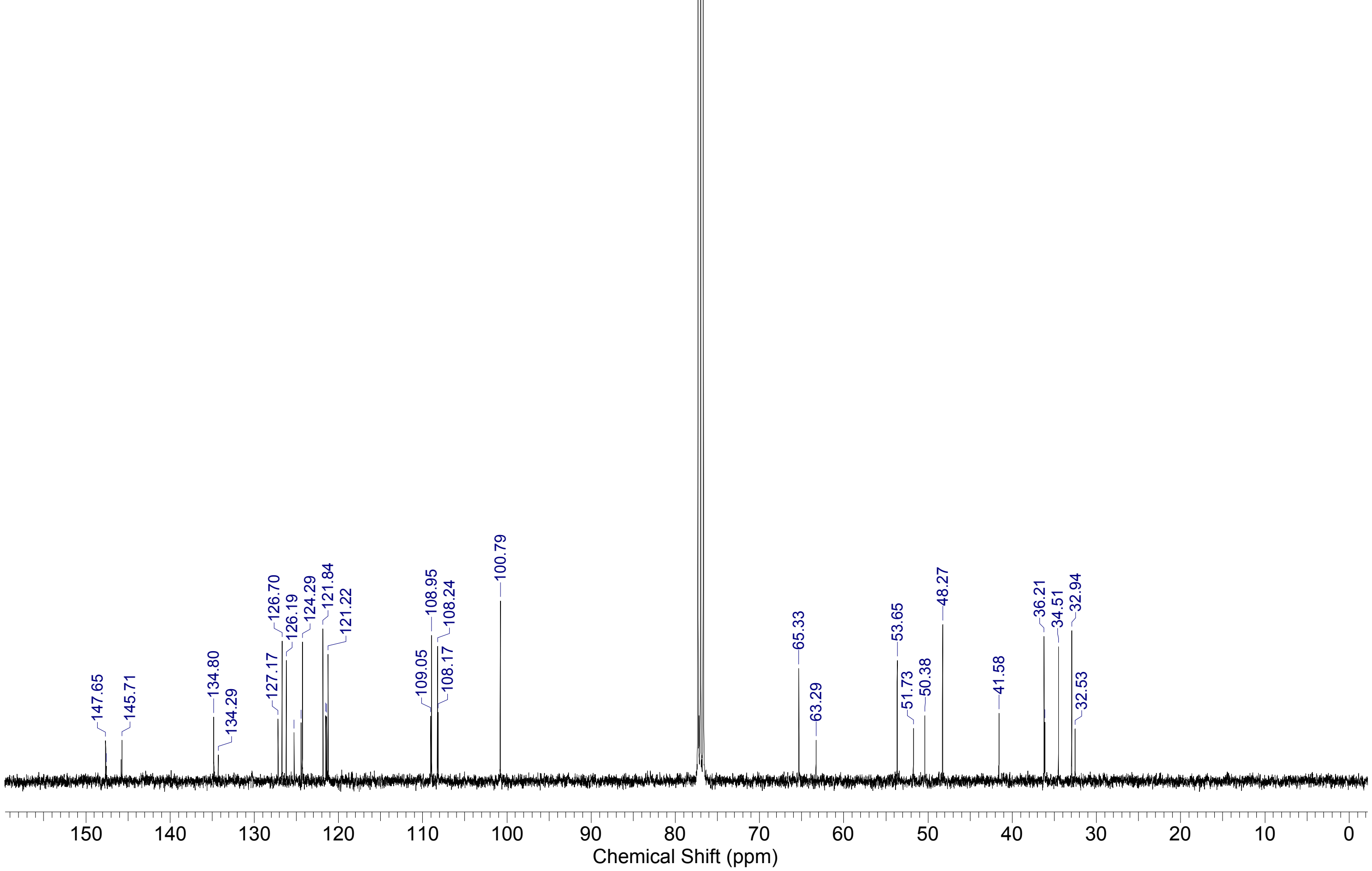

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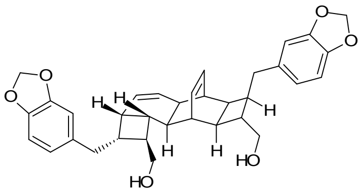

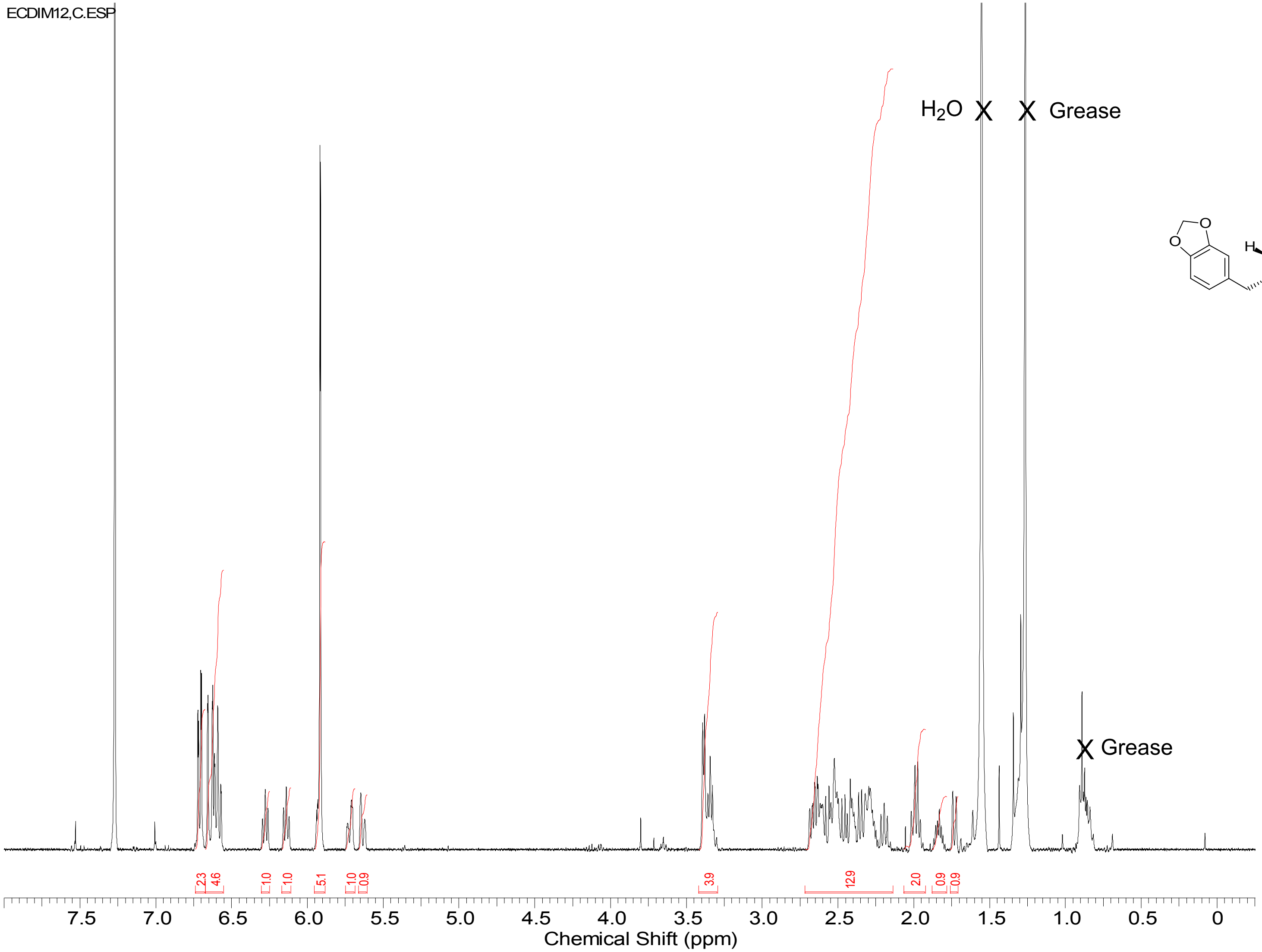

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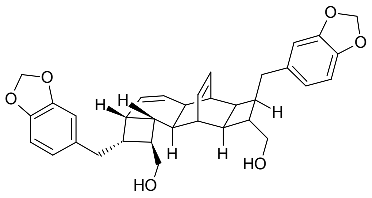

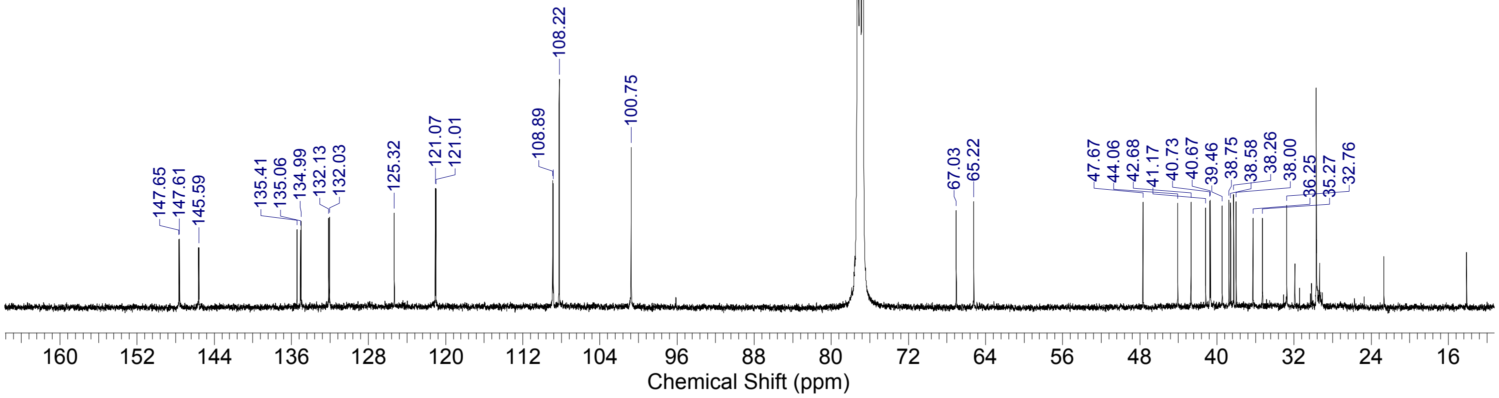

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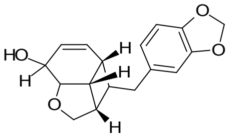

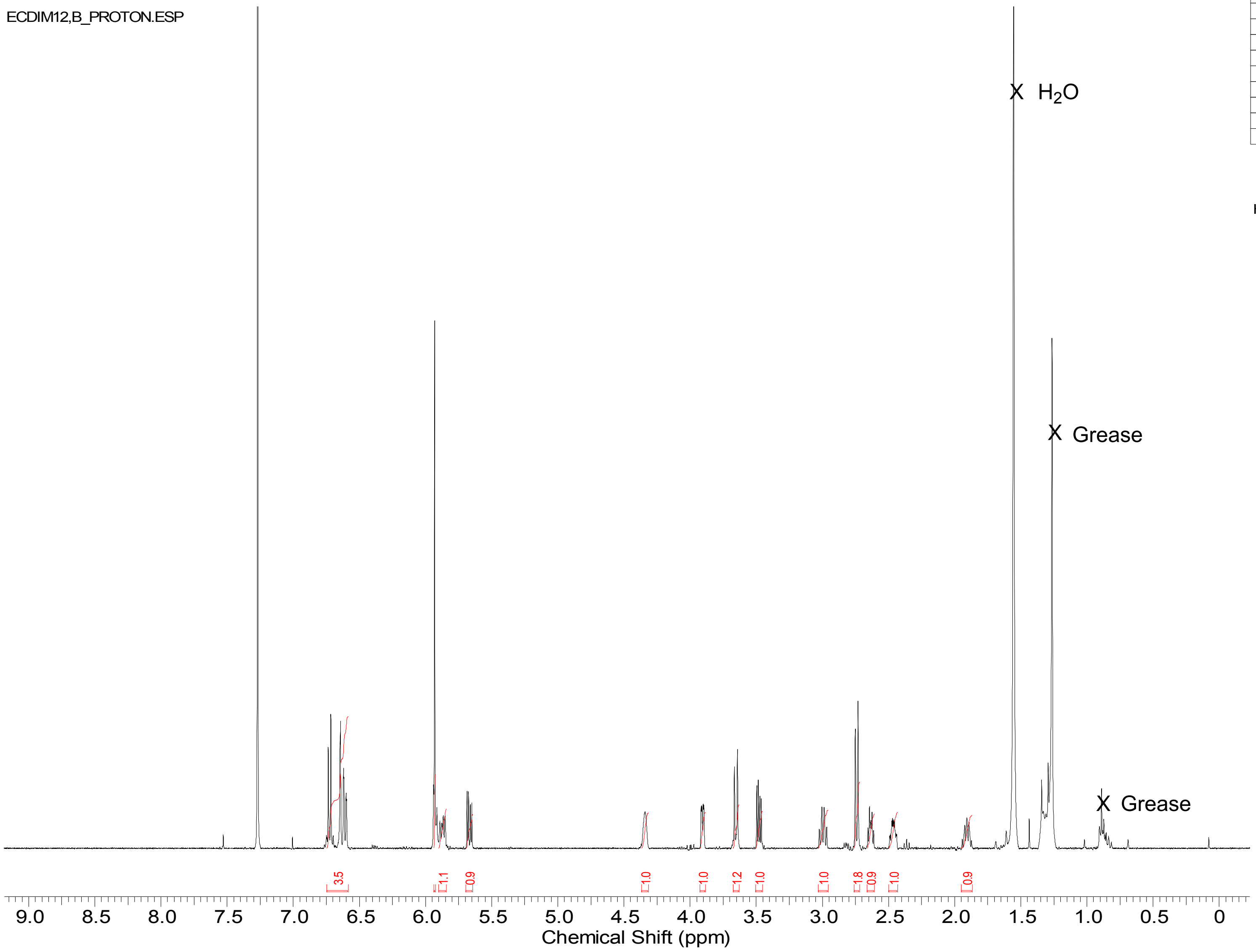

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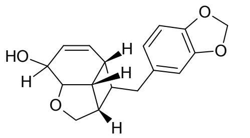

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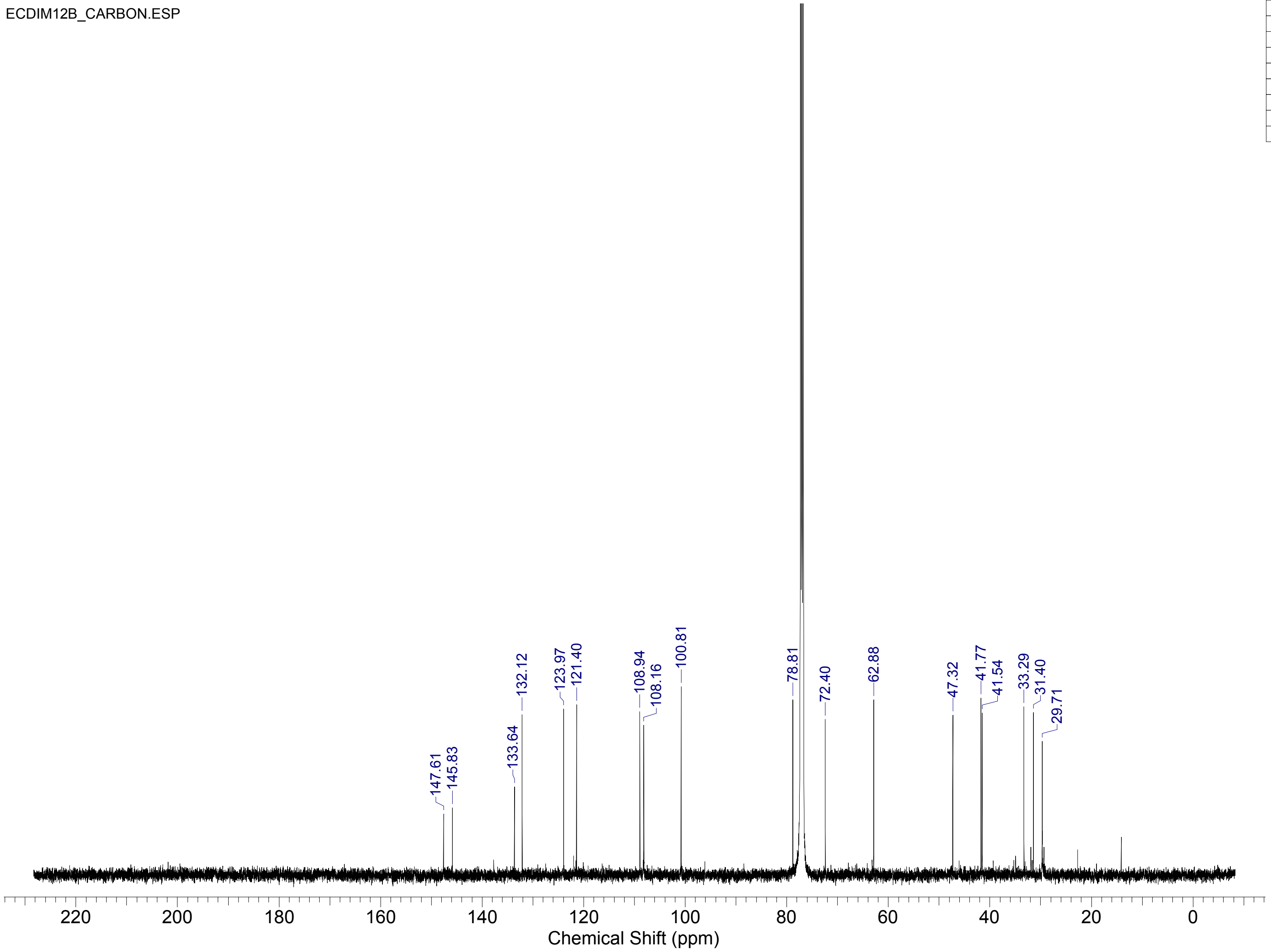

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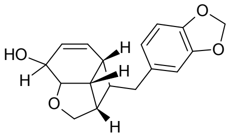

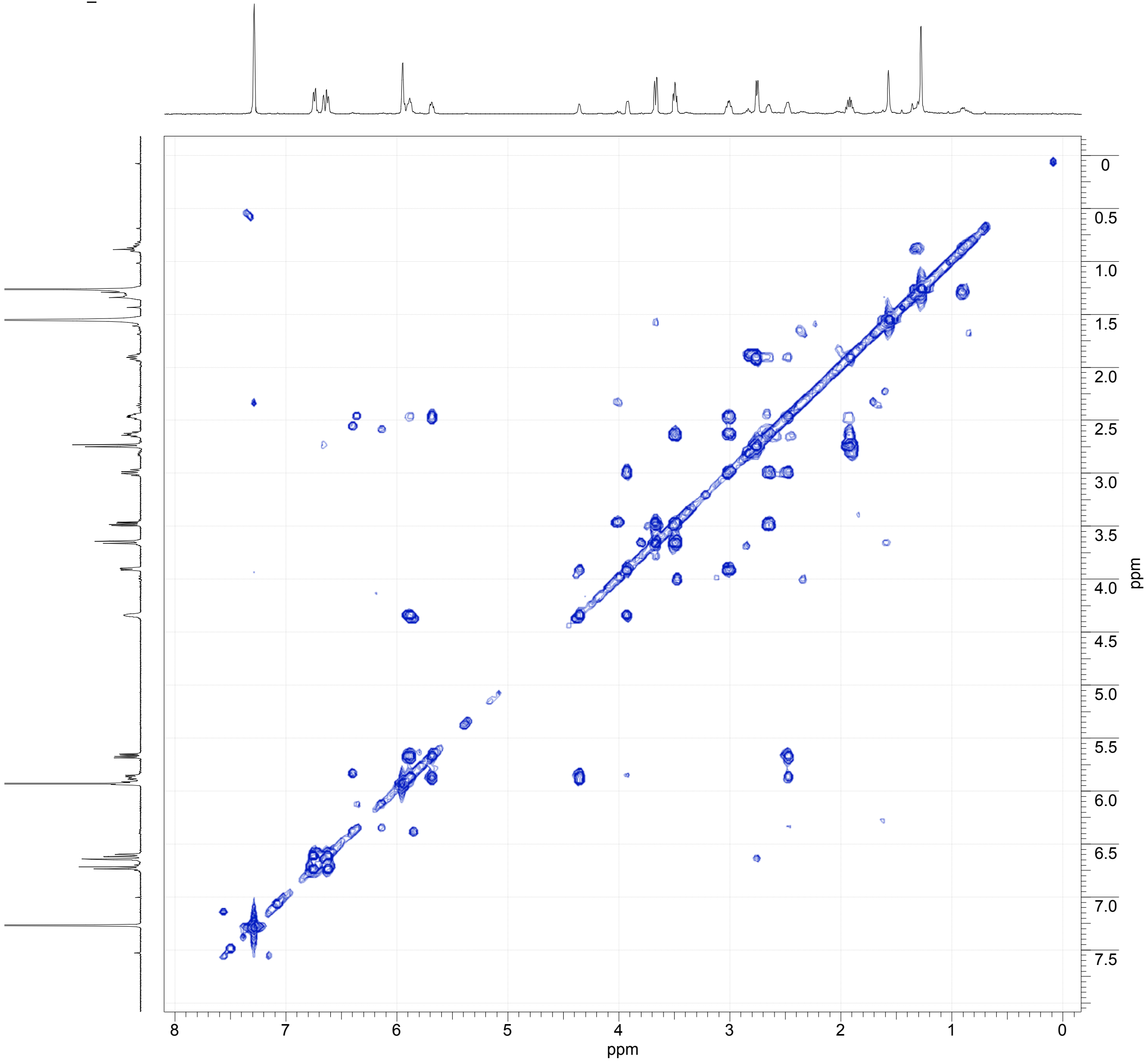

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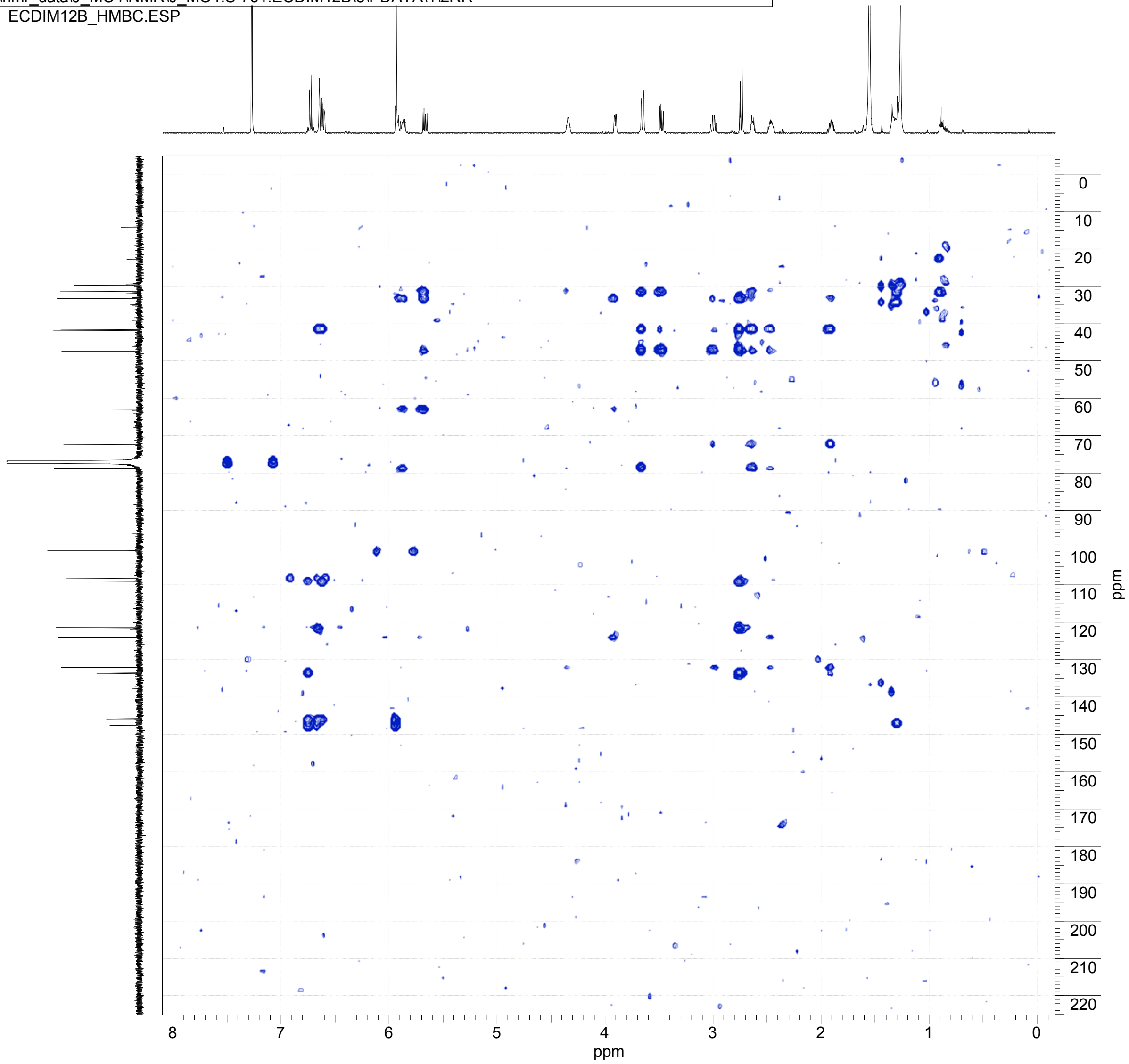

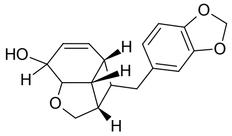

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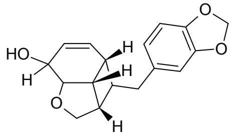

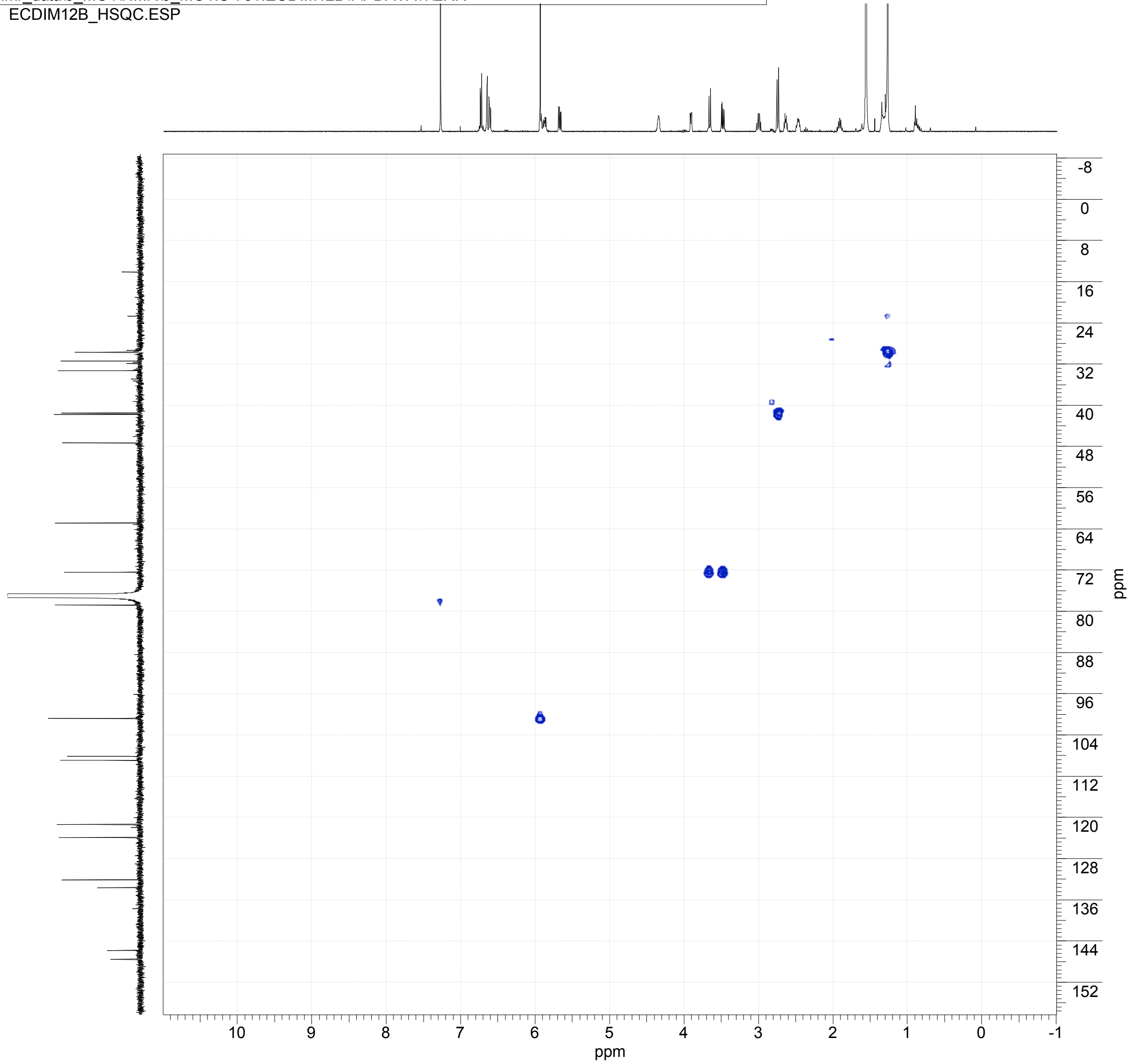

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