Supplementary information

Slight changes in the chemical structure of haemanthamine greatly influence the effect of the derivatives on rumen fermentation in vitro

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Synthesis of compounds 2-10

Compound 2. (3S,4aS,11bS,12R)-3-methoxy-4,4a-dihydro-3H,6H-11b,5-ethano[1,3]dioxolo[4,5-j]phenanthridin-12-yl acetate

Pyridine (1.34 mL, 16.6 mmol) and DMAP (10 mg) were added to a solution of haemanthamine **1** (1.00 g, 3.32 mmol) dissolved in dichloromethane (20 mL). The mixture was cooled (0 °C) and acetic anhydride (0.94 mL, 9.96 mmol) was added slowly. The resultant mixture was stirred until complete consumption of starting material. The reaction was washed with NaOH solution (1 M, 3 x 30 mL) and brine (3 x 30 mL), dried ($MgSO_4$) and evaporated under reduced pressure. The crude product was purified using silica gel flash chromatography (1-5% MeOH in chloroform, gradient elution) to give **2** (1.10 g, 3.20 mmol, 97% yield) as a gum. Rf = 0.48 (10% MeOH in DCM); ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.89 (1H, s, CH), 6.46 (1H, s, CH), 6.34 (1H, d, *J* 10.1 Hz, CH), 6.16 (1H, dd, *J* 4.6, 10.1 Hz, CH), 5.89 (2H, s, CH_2), 4.96 (1H, dd, *J* 3.4, 7.0 Hz, CH), 4.35 (1H, d, *J* 16.8 Hz, CH), 3.83-3.86 (1H, m, CH), 3.73 (1H, d, *J* 16.8), 3.40 (1H, dd, *J* 7.2, 14.5, CH), 3.53 (3H, s, CH_3), 3.13 (1H, dd, *J* 3.6, 14.5 Hz, CH), 2.05 (1H, dd, *J* 4.5, 13.6, CH), 1.97 (3H, s, CH_3), 1.92 (1H, dd, *J* 5.2, 13.6 Hz, CH); ^{13}C NMR (125MHz, $CDCl_3$): δ 170.2, 146.8, 146.6, 134.4, 129.7, 127.8, 126.5, 106.7, 104.1, 101.0, 80.5, 77.2, 72.6, 63.0, 61.3, 60.7, 56.7, 49.3, 28.5, 21.4 ppm; ν_{max} 2932, 2821, 1737, 1483, 1240, 1035, 754 cm^{-1}; MS(CI) 344.2 (100%, [M+H$^+$]) 687.3 (10%, [2M+H$^+$]); HRMS(ES) found 344.1490, $C_{19}H_{22}O_5N$ ([M+H$^+$]) requires 344.1492.

Compound 3. (3S,4aS,11bS,12R)-3-methoxy-4,4a-dihydro-3H,6H-11b,5-ethano[1,3]dioxolo[4,5-j]phenanthridin-12-yl butyrate

Pyridine (1.34 mL, 16.6 mmol) and DMAP (10 mg) were added to a solution of haemanthamine **1** (1.00 g, 3.32 mmol) dissolved in dichloromethane (20 mL). The mixture was cooled (0 °C) and *n*-butanoyl chloride (1.03 mL, 9.96 mmol) was added slowly. The resultant mixture was stirred until complete consumption of starting material. The reaction was washed with NaOH solution (1 M, 3 x 30 mL) and brine (3 x 30 mL), dried ($MgSO_4$) and evaporated under reduced pressure. The crude product was purified using silica gel flash chromatography (1-5% MeOH in chloroform, gradient elution) to give **3** (1.125 g, 3.03 mmol, 92% yield) as a gum. Rf = 0.53 (10% MeOH in DCM); ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.88 (1H, s, CH), 6.44 (1H, s, CH), 6.33 (1H, d,

J 10.1 Hz, CH), 6.12 (1H, dd, *J* 5.0, 10.0 Hz, CH), 5.87 (2H, s, CH_2), 4.96 (1H, dd, *J* 3.5, 7.1 Hz, CH), 4.33 (1H, d, *J* 16.9, CH), 3.83-3.79 (1H, m, CH), 3.69 (1H, d, *J* 16.9 Hz, CH), 3.41-3.53 (1H, m, CH), 3.34 (3H, s, CH_3), 3.28 (1H, dd, *J* 3.5, 14.3 Hz, CH), 2.18 (2H, td, *J* 2.7, 7.4 Hz, CH_2), 2.02 (1H, dd, *J* 4.8, 13.6 Hz, CH), 1.92 (1H, td, *J* 4.2, 13.4 Hz, CH), 1.57 (2H, hextet, *J* 7.39 Hz, CH_2), 0.91 (3H, t, *J* 7.4 Hz, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ 172.7, 146.7, 146.5, 134.5, 129.6, 127.9, 126.7, 106.7, 104.0, 101.0, 80.2, 72.7, 62.9, 61.3, 60.8, 56.6, 49.3, 36.5, 28.5, 18.4, 13.8 ppm; ν_{max} 3020, 2935, 2401, 1730, 1483, 1216, 755 cm^{-1}; MS(CI) 372.2 (100%, $[M+H^+]$) 743.4 (15%, $[2M+H^+]$); HRMS(ES) found 372.1801, $C_{21}H_{26}O_5N$ ($[M+H^+]$) requires 372.1805

Compound 4. (3S,4aS,11bS,12R)-3-methoxy-4,4a-dihydro-3H,6H-11b,5-ethano[1,3]dioxolo[4,5-j]phenanthridin-12-yl pivalate

Triethylamine (1.39 mL, 9.96 mmol) and DMAP (10 mg) were added to a solution of haemanthamine **1** (1.0 g, 3.32 mmol) in dichloromethane (20 mL). The mixture was cooled (0 °C) and pivaloyl chloride (1.22 mL, 9.96 mmol) was added slowly and allowed to stir until complete consumption of the starting material. The sample was then washed subsequently with 1 M NaOH solution (3 x 30 mL) and brine (3 x 30 mL) then dried ($MgSO_4$) and evaporated under reduced pressure. The product was then purified using flash column chromatography (1-10% MeOH in chloroform, gradient elution) to give **4** (520 mg, 1.35 mmol, 41% yield) as a gum. Rf = 0.61 (10% MeOH in DCM); ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.91 (1H, s, CH), 6.47 (1H, s, CH), 6.35 (1H, d, *J* 10.1 Hz, CH), 6.15 (1H, dd, *J* 5.0, 10.0 Hz, CH), 5.89 (2H, s, CH_2), 4.92 (1H, dd, *J* 3.3, 7.1 Hz, CH), 4.36 (1H, d, *J* 16.9 Hz, CH), 3.80-3.86 (1H, m, CH), 3.72 (1H, d, *J* 6.9 Hz, CH), 3.38-3.43 (1H, m, CH), 3.36 (3H, s, CH_3), 3.26 (1H, dd, *J* 3.3, 14.3 Hz, CH), 2.05 (1H, dd, *J* 4.5, 13.7 Hz, CH), 1.94 (1H, td, *J* 4.2, 13.5 Hz, CH), 1.14 (9H, s, 3 x CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ 177.5, 146.7, 146.5, 134.4, 129.5, 127.9, 126.6, 106.7, 104.0, 101.0, 79.9, 72.8, 62.9, 61.3, 60.9, 56.6, 53.5, 49.3, 28.4, 27.2 ppm; ν_{max} 2930, 1725, 1483, 1156 cm^{-1}; MS(CI) 386.2 (100%, $[M+H^+]$) ; HRMS(ES) found 386.1954, $C_{22}H_{28}O_5N$ ($[M+H^+]$) requires 386.1962

Compound 5. (3S,4aS,11bS,12R)-3-methoxy-4,4a-dihydro-3H,6H-11b,5-ethano[1,3]dioxolo[4,5-j]phenanthridin-12-yl hexanoate

Triethylamine (1.39 mL, 9.96 mmol) and DMAP (10 mg) were added to a solution of haemanthamine **1** (1.0 g, 3.32 mmol) in dichloromethane (20 mL). The mixture was cooled (0 °C) and n-hexanoyl chloride (1.39 mL, 9.96 mmol) was added slowly and allowed to stir until complete consumption of the starting material. The sample was then washed subsequently with 1 M NaOH solution (3 x 30 mL) and brine (3 x 30 mL) then dried ($MgSO_4$) and evaporated under reduced pressure. The product was then purified using flash column chromatography (1-10% MeOH in chloroform, gradient elution) to give **5** (1.146 g, 3.03 mmol, 91% yield) as a gum. Rf = 0.73 (10% MeOH in DCM); ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.89 (1H, s, CH), 6.45 (1H, s, CH), 6.33 (1H, d, *J* 10.1 Hz,CH), 6.13 (1H, dd, *J* 5.0, 10.0 Hz, CH), 5.87 (2H, s, CH_2), 4.96 (1H, dd, *J* 3.5, 7.0

Hz, CH), 4.34 (1H, d, *J* 16.8Hz, CH), 3.79-3.84 (1H, m, CH), 3.70 (1H, d, *J* 16.8 Hz, CH), 3.39 (1H, dd, *J* 7.1, 15.4 Hz, CH), 3.34 (3H, s, CH_3), 3.29 (1H, dd, *J* 3.5, 14.4, CH), 2.19 (2H, td, *J* 2.7, 7.4 Hz, CH_2), 2.03 (1H, dd, *J* 4.3, 13.6 Hz, CH), 2.03 (1H, dd, *J* 4.3, 13.6 Hz, CH), 1.93 (1H, td, *J* 4.2, 12.4 Hz, CH), 1.54 (2H, p, *J* 7.44 Hz, CH_2), 1.22-1.33 (4H, m, 2 x CH_2), 0.88 (3H, t, *J* 6.8Hz, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ 172.9, 146.8, 146.6, 134.5, 129.6, 128.0, 126.7, 106.7, 104.1, 101.0, 80.3, 72.7, 62.9, 61.4, 60.8, 56.7, 49.3, 34.6, 31.4, 28.5, 24.7, 22.4, 14.0 ppm; ν_{max} 2957, 2871, 1736, 1484, 1240, 1091, 755 cm^{-1}; MS(CI) 400.2 (55%, [M+H$^+$]); HRMS(ES) found 400.2115, $C_{23}H_{30}O_5N$ ([M+H$^+$]) requires 400.2118

Compound 6. (3R,4aS,11bS,12R)-3-methoxy-2,3,4,4a-tetrahydro-1H,6H-11b,5-ethano[1,3]dioxolo[4,5-j]phenanthridin-12-ol

Under a nitrogen atmosphere, palladium on charcoal (10%, 0.1 g) was added to a solution of haemanthamine **1** (5.00 g, 16.6 mmol) dissolved in dry THF (100 mL). After evacuation, the mixture was stirred at rt under a hydrogen atmosphere for 16 hrs following which the reaction was filtered through a celite pad which was washed with excess THF and the filtrate evaporated under reduced pressure. The residue was purified by flash column chromatography (1-5% MeOH in chloroform, graduated elution) to give dihydrohaemanthamine **6** (3.62 g, 11.9 mmol, 72% yield) as a white crystalline solid. Rf = 0.17 ((10% MeOH in DCM); ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.69 (1H, s, CH), 6.39 (1H, s, CH), 5.86 (2H, s, CH_2), 4.26 (1H, d, *J* 16.70 Hz,CH), 4.10-4.04 (1H, m, CH), 3.69 (1H, s, CH), 3.64 (1H, d, *J* 16.71 Hz, CH), 3.35-3.19 (7H, m), 2.34-1.75 (6H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 146.3, 145.6, 139.2, 125.7, 105.9, 103.3, 100.5, 82.1, 75.4, 62.8, 62.4, 60.6, 55.4, 45.9, 29.9, 26.7, 22.6 ppm; ν_{max} 3028, 2924, 1509, 1228, 1045, 822, 724 cm^{-1}; MS(CI) 304.1 (100%, [M+H$^+$]), 607.3 (5%, [2M+H$^+$]); HRMS(ES) found 304.1540, $C_{17}H_{22}O_5N$ ([M+H$^+$]) requires 304.1543

Compound 7. (3R,4aS,11bS,12R)-3-methoxy-2,3,4,4a-tetrahydro-1H,6H-11b,5-ethano[1,3]dioxolo[4,5-j]phenanthridin-12-yl acetate

Pyridine (1.34 mL, 16.6 mmol) and DMAP (10 mg) were added to a solution of dihydrohaemanthamine **6** (1.00 g, 3.32 mmol) dissolved in dichloromethane (20 mL). The mixture was cooled (0 °C) and acetic anhydride (0.94 mL, 9.96 mmol) was added slowly. The resultant mixture was stirred until complete consumption of starting material. The reaction was washed with NaOH solution (1 M, 3 x 30 mL) and brine (3 x 30 mL), dried ($MgSO_4$) and evaporated under reduced pressure. The crude product was purified using silica gel flash chromatography (1-5% MeOH in chloroform, gradient elution) to give **7** (354 mg, 1.02 mmol, 49% yield) as a gum. Rf = 0.44 (10% MeOH in DCM); ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.76 (1H, s, CH), 6.56 (1H, s, CH), 5.94 (2H, d, *J* 3.0 Hz, CH_2), 4.81 (1H, dd, *J* 3.6, 7.5 Hz, CH), 4.13 (1H, d, *J* 17.0 Hz, CH), 3.66 (1H, s, CH), 3.61 (1H, d, *J* 17.1 Hz, CH), 3.33 (4H, s, 2 x CH_2), 3.23-3.31 (1H, m, CH), 3.20 (2H, s, CH_2), 2.98 (2H, m, CH_2), 2.19-2.33 (1H, m, CH), 1.79-1.93 (4H, m, 2 x CH_2), 1.53 (1H, td, *J* 1.2, 14.4 Hz, CH); ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.1, 146.7, 146.5,

134.4, 129,5, 127.7, 126.6, 106.7, 104.0, 100.9, 80.5, 72.6, 62.9, 61.3, 60.6, 56.6, 49.3, 28.4, 21.3 ppm; ν_{max} 3020, 1216, 756 cm^{-1}; MS(CI) 346.2 (100%, $[M+H^+]$), 691.3 (5% $[2M+H^+]$); HRMS(ES) found 346.1641, $C_{19}H_{24}O_5N$ ($[M+H^+]$) requires 346.1649

Compound 8. (3R,4aS,11bS,12R)-3-methoxy-2,3,4,4a-tetrahydro-1H,6H-11b,5-ethano[1,3]dioxolo[4,5-j]phenanthridin-12-yl butyrate

Pyridine (1.34 mL, 16.6 mmol) and DMAP (10 mg) were added to a solution of dihydrohaemanthamine **6** (1.00 g, 3.32 mmol) dissolved in dichloromethane (20 mL). The mixture was cooled (0 °C) and *n*-butanoyl chloride (1.03 mL, 9.96 mmol) was added slowly. The resultant mixture was stirred until complete consumption of starting material. The reaction was washed with NaOH solution (1 M, 3 x 30 mL) and brine (3 x 30 mL), dried ($MgSO_4$) and evaporated under reduced pressure. The crude product was purified using silica gel flash chromatography (1-5% MeOH in chloroform, gradient elution) to give **8** (232 mg, 0.62 mmol, 29% yield) as a gum. Rf = 0.49 (10% MeOH in DCM); ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.71 (1H, s, CH), 6.40 (1H, s, CH), 5.86 (2H, s, CH_2), 5.00 (1H, dd, *J* 3.4, 6.9 Hz, CH), 4.28 (1H, d, *J* 16.9 Hz, CH), 3.70 (1H, s, CH), 3.65 (1H, d, *J* 16.8 Hz, CH), 3.37 (1H, dd, *J* 7.1, 14.3 Hz, CH), 3.27 (3H, s, CH_3), 3.12 (1H, dd, *J* 3.5, 14.5 Hz, CH), 2.27 (3H, t, *J* 7.3 Hz, CH_3), 1.80-2.10 (5H, m), 1.56-1.68 (3H, m), 1.24 (1H, t, *J* 7.1 Hz, CH), 0.94 (3H, t, *J* 7.4 Hz, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.0, 146.7, 146.3, 138.4, 126.3, 106.1, 104.0, 100.9, 82.5, 75.3, 62.8, 61.4, 61.0, 55.8, 45.1, 36.6, 30.4, 26.8, 22.6, 18.5, 13.7; ν_{max} 3020, 2401, 1216, 757, 669 cm^{-1}; MS(CI) 374.2 (100%, $[M+H^+]$), 747.4 (10%, $[2M+H^+]$); HRMS(ES) found 374.1958, $C_{21}H_{28}O_5N$ ($[M+H^+]$) requires 374.1962.

Compound 9. (3R,4aS,11bS,12R)-3-methoxy-2,3,4,4a-tetrahydro-1H,6H-11b,5-ethano[1,3]dioxolo[4,5-j]phenanthridin-12-yl pivalate

Pyridine (1.34 mL, 16.6 mmol) and DMAP (10 mg) were added to a solution of dihydrohaemanthamine **6** (1.00 g, 3.32 mmol) dissolved in dichloromethane (20 mL). The mixture was cooled (0 °C) and pivolyl chloride (1.22 mL, 9.96 mmol) was added slowly. The resultant mixture was stirred until complete consumption of starting material. The reaction was washed with NaOH solution (1 M, 3 x 30 mL) and brine (3 x 30 mL), dried ($MgSO_4$) and evaporated under reduced pressure. The crude product was purified using silica gel flash chromatography (1-5% MeOH in chloroform, gradient elution) to give **9** (554 mg, 1.31 mmol, 61% yield) as a gum. Rf = 0.51 (10% MeOH in DCM); ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.73 (1H, s, CH), 6.41 (1H, s, CH), 5.87 (2H, s, CH_2), 4.88 (1H, dd, *J* 3.2, 6.7 Hz, CH), 4.31 (1H, d, *J* 16.8 Hz, CH), 3.73 (1H, s, CH), 3.67 (1H, d, *J* 15.9 Hz, CH), 3.41 (1H, dd, *J* 7.0, 14.5 Hz, CH), 3.29 (3H, s, CH_3), 3.05 (1H, dd, *J* 3.4, 14.5, CH), 2.32-2.29 (1H, m, CH), 1.98-2.13 (4H, m, 2 x CH_2), 1.57 (1H, t, *J* 13.3 Hz, CH), 1.19 (9H, s, 3 x CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ 178.1, 146.8, 146.4, 138.6, 126.3, 106.2, 104.1, 100.9, 83.0, 75.3, 62.9, 62.0, 61.0, 55.9, 45.1, 38.7, 30.4, 27.4, 26.8, 22.5 ppm; ν_{max} 3020, 1216, 760 cm^{-1}; MS(CI) 388.2 (100%, $[M+H^+]$),

775.4 (15%, [2M+H^+]); HRMS(ES) found 388.2113, $C_{22}H_{30}O_5N$ ([M+H^+]) requires 388.2118.

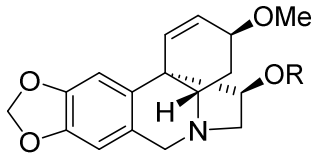
Compound 10. (3R,4aS,11bS,12R)-3-methoxy-2,3,4,4a-tetrahydro-1H,6H-11b,5-ethano[1,3]dioxolo[4,5-j]phenanthridin-12-yl hexanoate

Pyridine (1.34 mL, 16.6 mmol) and DMAP (10 mg) were added to a solution of dihydrohaemanthamine **6** (1.00 g, 3.32 mmol) dissolved in dichloromethane (20 mL). The mixture was cooled (0 °C) and n-hexanoyl chloride (1.39 mL, 9.96 mmol) was added slowly. The resultant mixture was stirred until complete consumption of starting material. The reaction was washed with NaOH solution (1 M, 3 x 30 mL) and brine (3 x 30 mL), dried ($MgSO_4$) and evaporated under reduced pressure. The crude product was purified using silica gel flash chromatography (1-5% MeOH in chloroform, gradient elution) to give 10 (711 mg, 1.77 mmol, 83% yield) as a gum. Rf = 0.55 (10% MeOH in DCM); ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.72 (1H, s, CH), 6.41 (1H, s, CH), 5.87 (2H, s, CH_2), 5.02 (1H, dd, *J* 3.4, 7.0 Hz, CH), 4.32 (1H, d, *J* 16.8, CH), 3.69 (2H, d, *J* 16.6 Hz, CH_2), 3.30-3.40 (2H, m, CH_2), 3.27 (3H, s, CH_3), 3.20 (1H, dd, *J* 3.4, 8.5 Hz, CH), 2.15-2.30 (4H, m), 1.81-2.15 (4H, m), 1.57-1.65 (4H, m), 1.24-1.36 (6H, m), 0.88 (3H, t, *J* 6.9 Hz, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.2, 146.7, 146.3, 138.5, 126.5, 106.1, 104.0, 100.9, 82.6, 75.4, 62.9, 61.6, 61.1, 55.8, 45.2, 34.7, 31.4, 30.5, 26.8, 24.8, 22.6, 22.4, 14.0 ppm; ν_{max} 3020, 2933, 1729, 1482, 1216, 757, 699 cm^{-1}; MS(CI) 402.2 (100%, [M+H^+]); HRMS(ES) found 402.2266, $C_{23}H_{32}O_5N$ ([M+H^+]) requires 402.2275

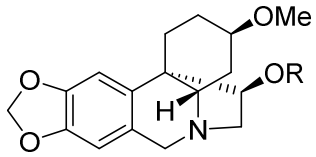
Supplementary Table S1. Effect of dihydrohaemanthamine **6** and derivatives of haemanthamine **1** and dihydrohaemanthamine **6**, added at 0.125, 0.250, 0.5 or 1 g/L, on rumen protozoa activity assessed in vitro as the amount of 14C-labelled bacteria broken down by rumen protozoa (% of the initial radioactivity released per hour)

	Dose (g/L)						
	0	0.125	0.25	0.5	1	SED	P
Haemanthamine derivatives							
2	1.44^{d}	1.22^{cd}	1.09^{bc}	0.871^{b}	0.495^{a}	0.123	<.001
3	1.44^{b}	1.58^{b}	1.32^{b}	0.383^{a}	0.270^{a}	0.154	<.001
4	1.44^{c}	1.34^{c}	0.735^{b}	0.277^{a}	0.280^{a}	0.128	<.001
5	1.44^{b}	1.42^{b}	1.25^{b}	0.653^{a}	0.426^{a}	0.130	<.001
Dihydrohaemanthamine derivatives							
6	1.44^{d}	1.17^{c}	1.06^{c}	0.810^{b}	0.363^{a}	0.111	<.001
7	1.44c	1.51c	1.39c	0.958b	0.483a	0.123	<.001
8	1.44^{c}	1.38^{c}	0.942^{b}	0.249^{a}	0.249^{a}	0.117	<.001
9	1.44^{b}	1.19^{b}	0.438^{a}	0.137^{a}	0.201^{a}	0.161	<.001
10	1.44^{c}	0.844^{b}	0.299^{a}	0.279^{a}	0.219^{a}	0.151	<.001

$^{a-d}$ Means with different superscript differ (n=4)



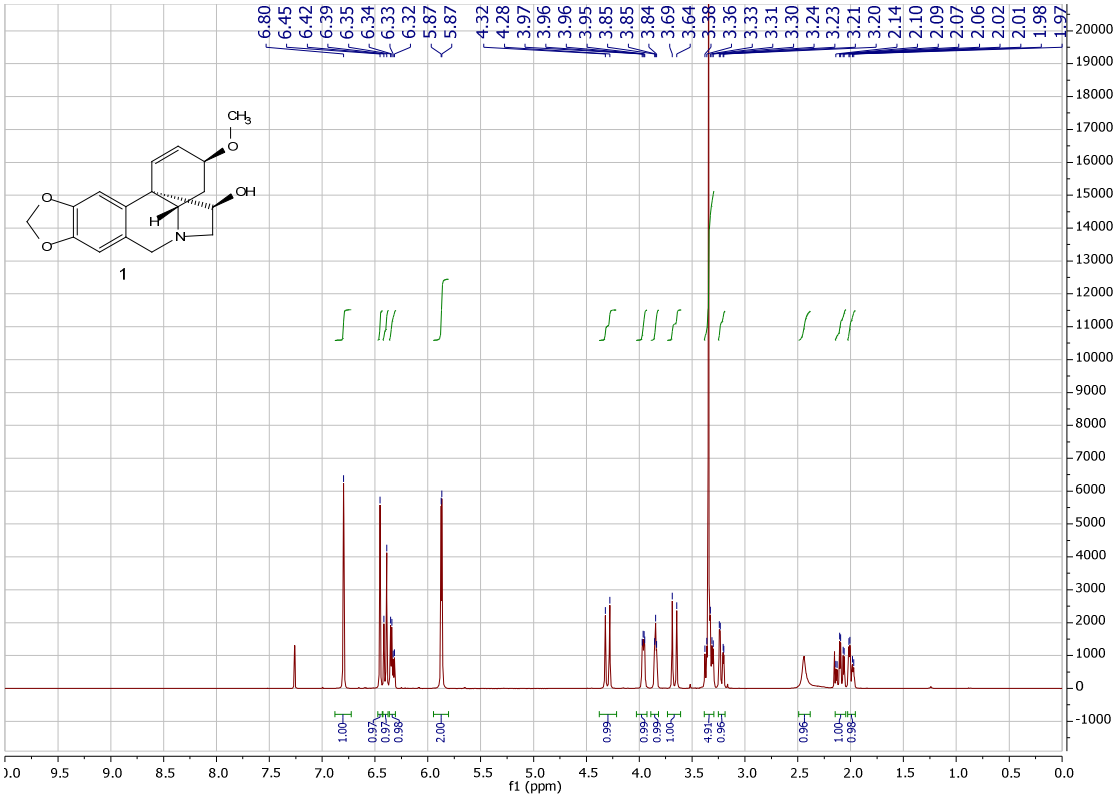
No	R	Name
1	H	(3S,4aS,11bS,12R)-3-methoxy-4,4a-dihydro-3H,6H-11b,5-ethano[1,3]dioxolo[4,5-j]phenanthridin-12-ol
2	Ac	(3S,4aS,11bS,12R)-3-methoxy-4,4a-dihydro-3H,6H-11b,5-ethano[1,3]dioxolo[4,5-j]phenanthridin-12-yl acetate
3	CO*n*Pr	(3S,4aS,11bS,12R)-3-methoxy-4,4a-dihydro-3H,6H-11b,5-ethano[1,3]dioxolo[4,5-j]phenanthridin-12-yl butyrate
4	CO*t*Bu	(3S,4aS,11bS,12R)-3-methoxy-4,4a-dihydro-3H,6H-11b,5-ethano[1,3]dioxolo[4,5-j]phenanthridin-12-yl pivalate
5	COC_5H_{11}	(3S,4aS,11bS,12R)-3-methoxy-4,4a-dihydro-3H,6H-11b,5-ethano[1,3]dioxolo[4,5-j]phenanthridin-12-yl hexanoate

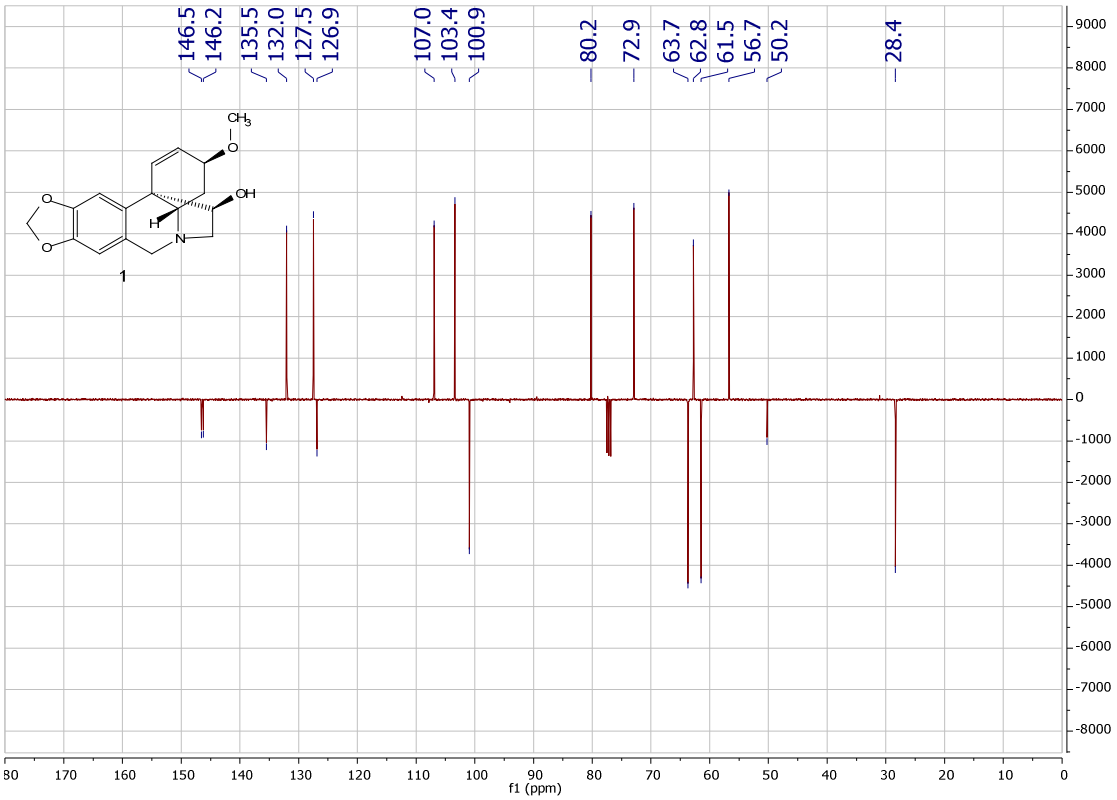


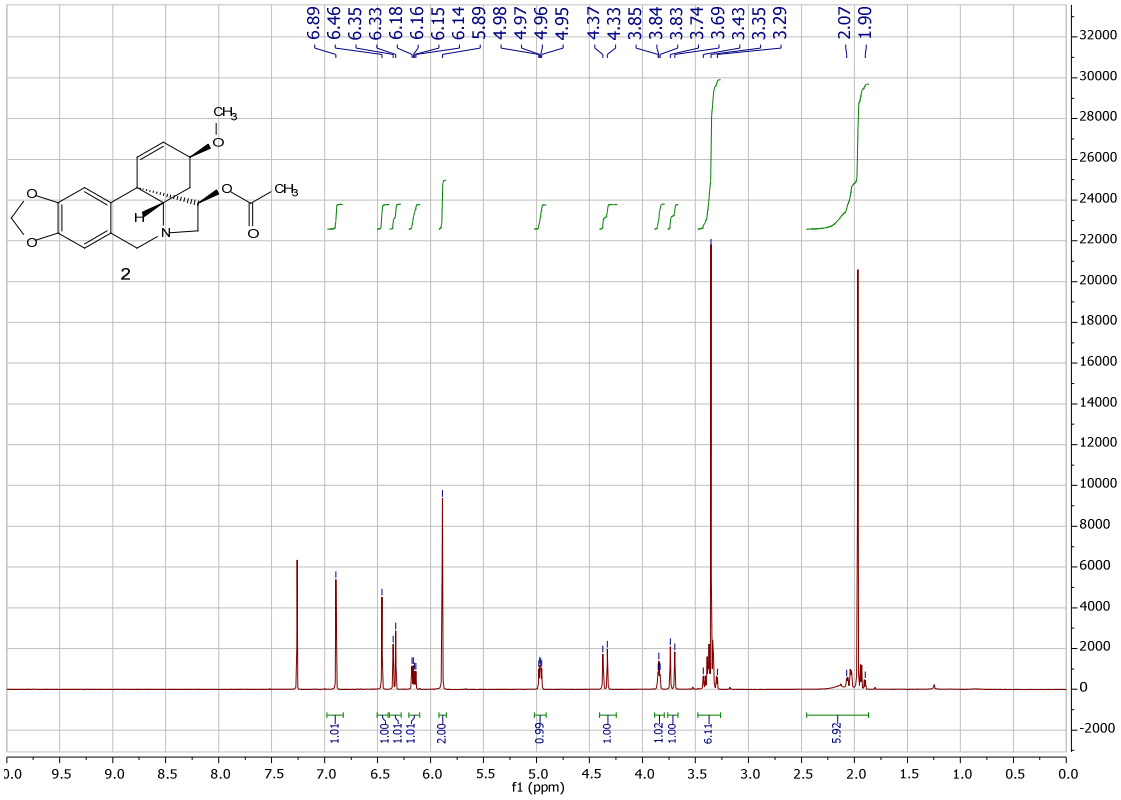
No	R	Name
6	H	(3R,4aS,11bS,12R)-3-methoxy-2,3,4,4a-tetrahydro-1H,6H-11b,5-ethano[1,3]dioxolo[4,5-j]phenanthridin-12-ol
7	Ac	(3R,4aS,11bS,12R)-3-methoxy-2,3,4,4a-tetrahydro-1H,6H-11b,5-ethano[1,3]dioxolo[4,5-j]phenanthridin-12-yl acetate
8	CO*n*Pr	(3R,4aS,11bS,12R)-3-methoxy-2,3,4,4a-tetrahydro-1H,6H-11b,5-ethano[1,3]dioxolo[4,5-j]phenanthridin-12-yl butyrate
9	CO*t*Bu	(3R,4aS,11bS,12R)-3-methoxy-2,3,4,4a-tetrahydro-1H,6H-11b,5-ethano[1,3]dioxolo[4,5-j]phenanthridin-12-yl pivalate
10	COC_5H_{11}	(3R,4aS,11bS,12R)-3-methoxy-2,3,4,4a-tetrahydro-1H,6H-11b,5-ethano[1,3]dioxolo[4,5-j]phenanthridin-12-yl hexanoate

Suplementary Figure S1. Structure of haemanthamine and dihydrohaemanthamine derivatives.

NMR data for compounds 1-10



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6.14
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4.98
4.97
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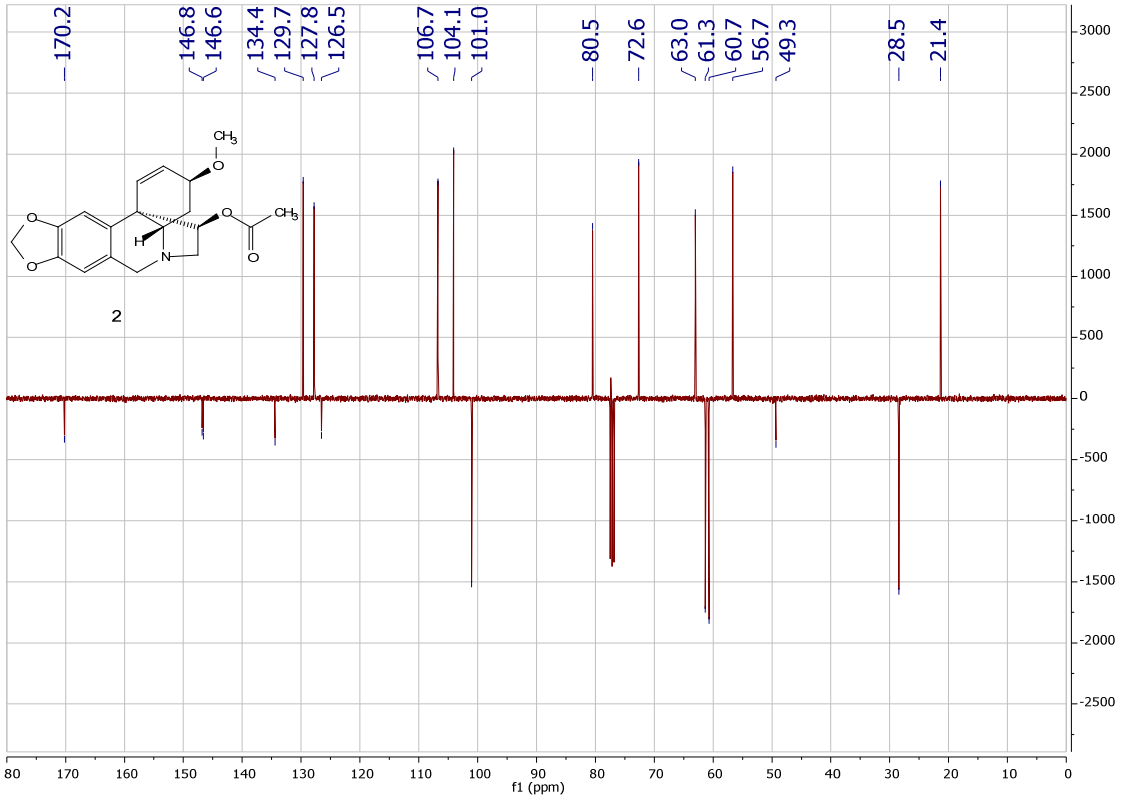
4.95
4.37
4.33
3.85
3.84
3.83
3.74
3.69
3.43
3.35
3.29
2.07
1.90
2
f1 (ppm)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127.8
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106.7
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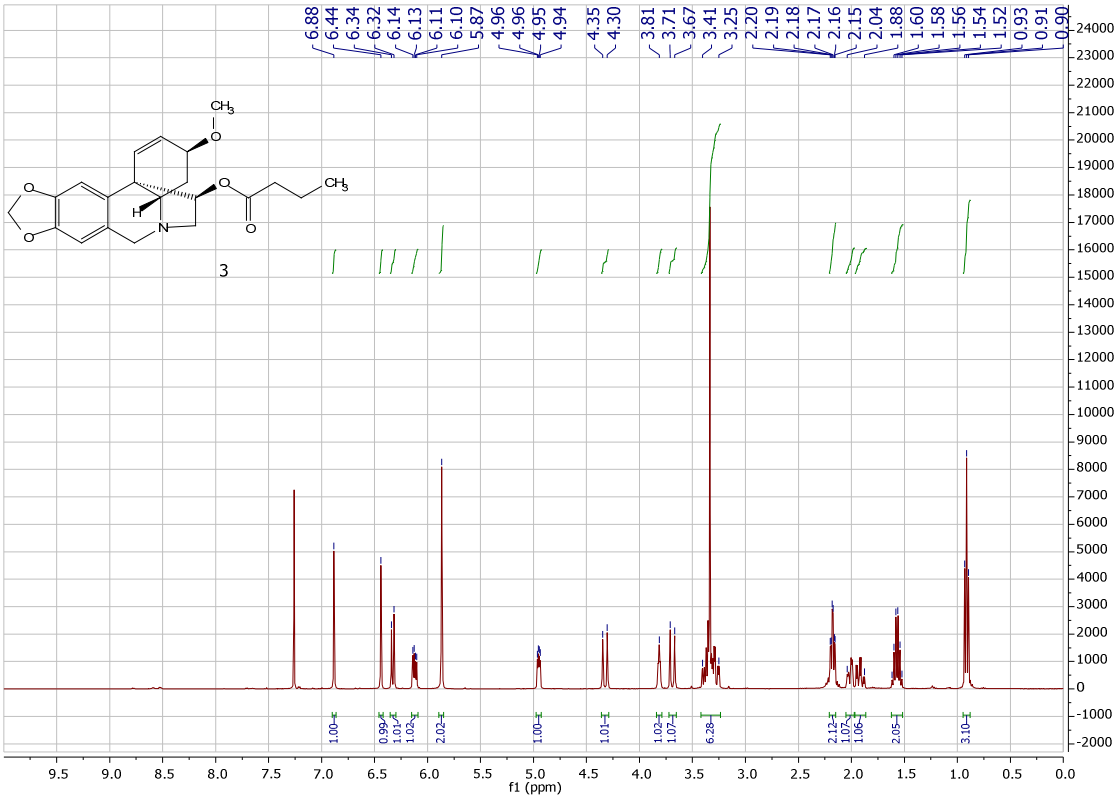
63.0
61.3
60.7
56.7
49.3
28.5
21.4
2
f1 (ppm)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6.10
5.87
4.96
4.96
4.95
4.94
4.35
4.30
3.81
3.71
3.67
3.41
3.25
2.20
2.19
2.18
2.17
2.16
2.15
2.04
1.88
1.60
1.58
1.56
1.54
1.52
0.93
0.91
0.90
CH3
O
O
O
O
H
N
O
CH3
3
1.00
0.99
1.01
1.02
2.02
1.00
1.01
1.02
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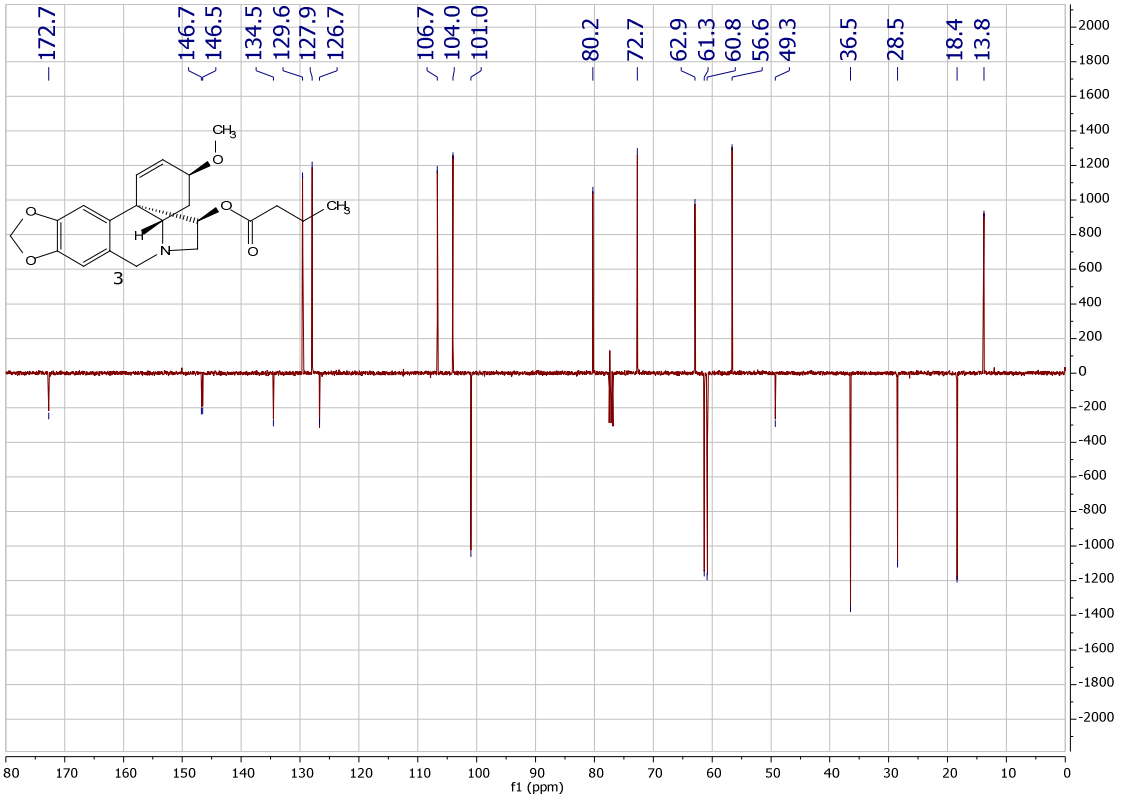
6.28
2.12
1.07
1.06
2.05
3.10
f1 (ppm)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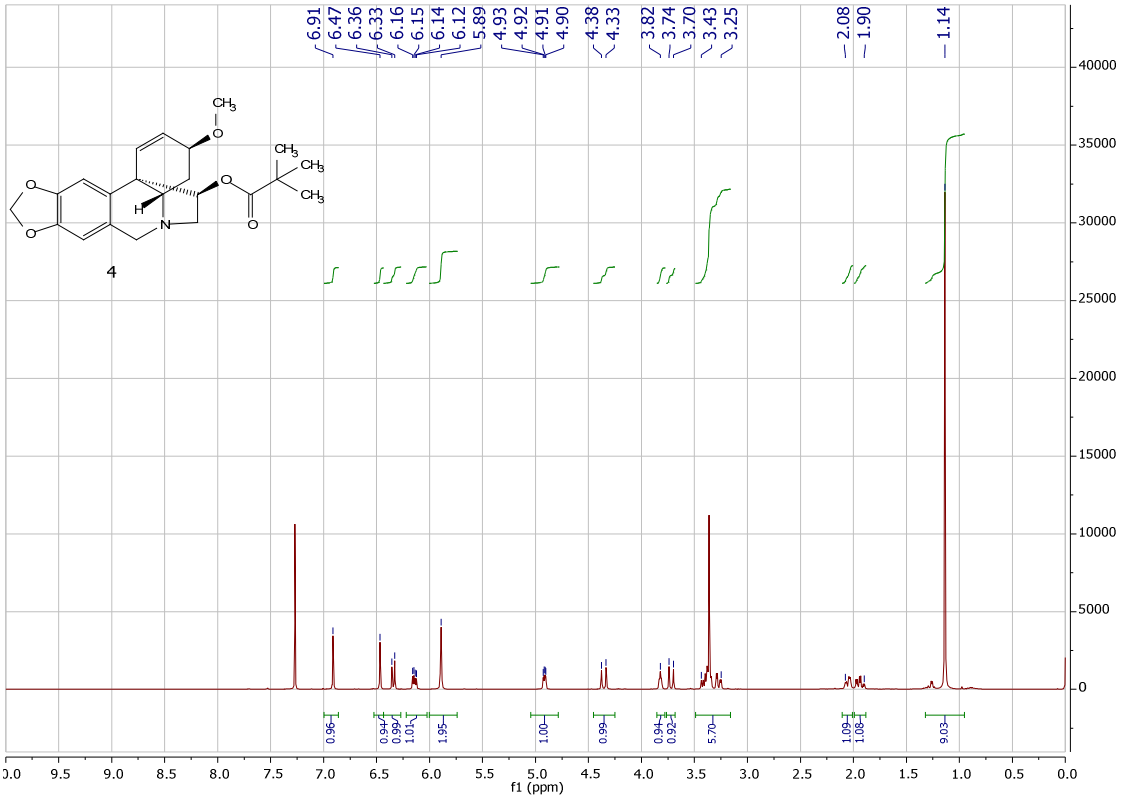
129.6
127.9
126.7
106.7
104.0
101.0
80.2
72.7
62.9
61.3
60.8
56.6
49.3
36.5
28.5
18.4
13.8
CH3
O
O
O
O
H
N
O
CH3
3
f1 (ppm)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6.33
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6.15
6.14
6.12
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4.92
4.91
4.90
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4.33
3.82
3.74
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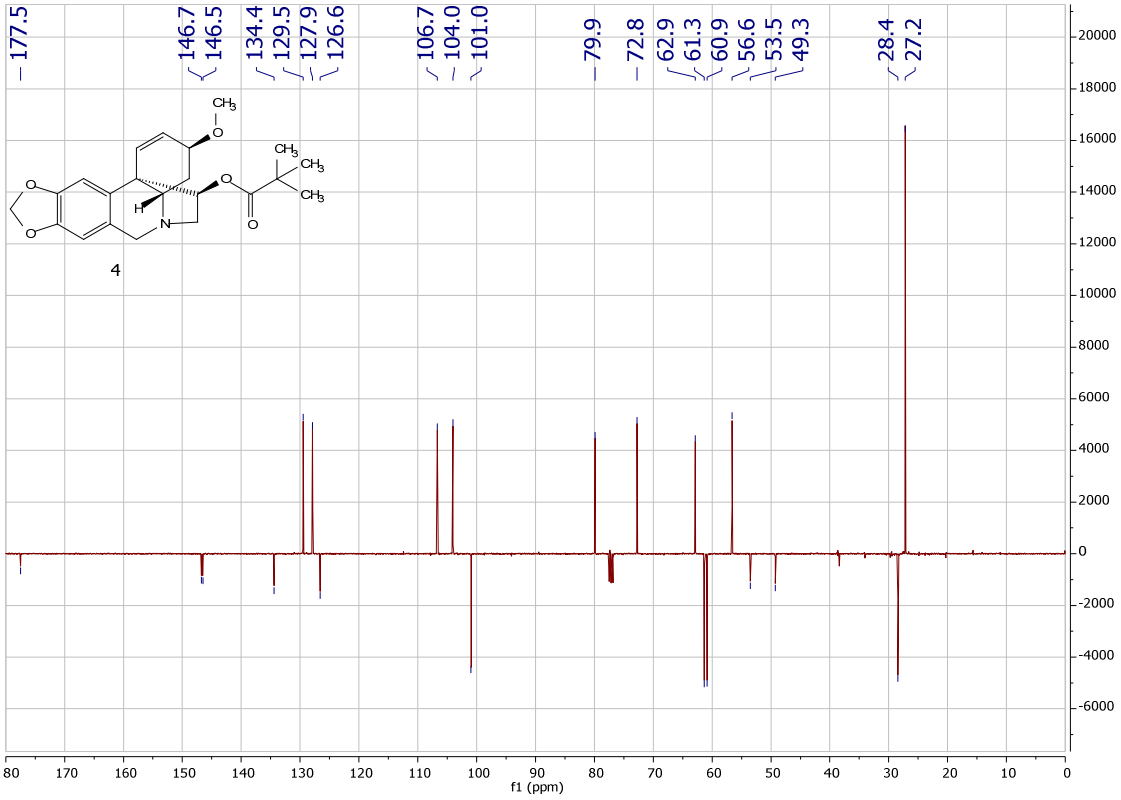
3.25
2.08
1.90
1.14
4
f1 (ppm)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106.7
104.0
101.0
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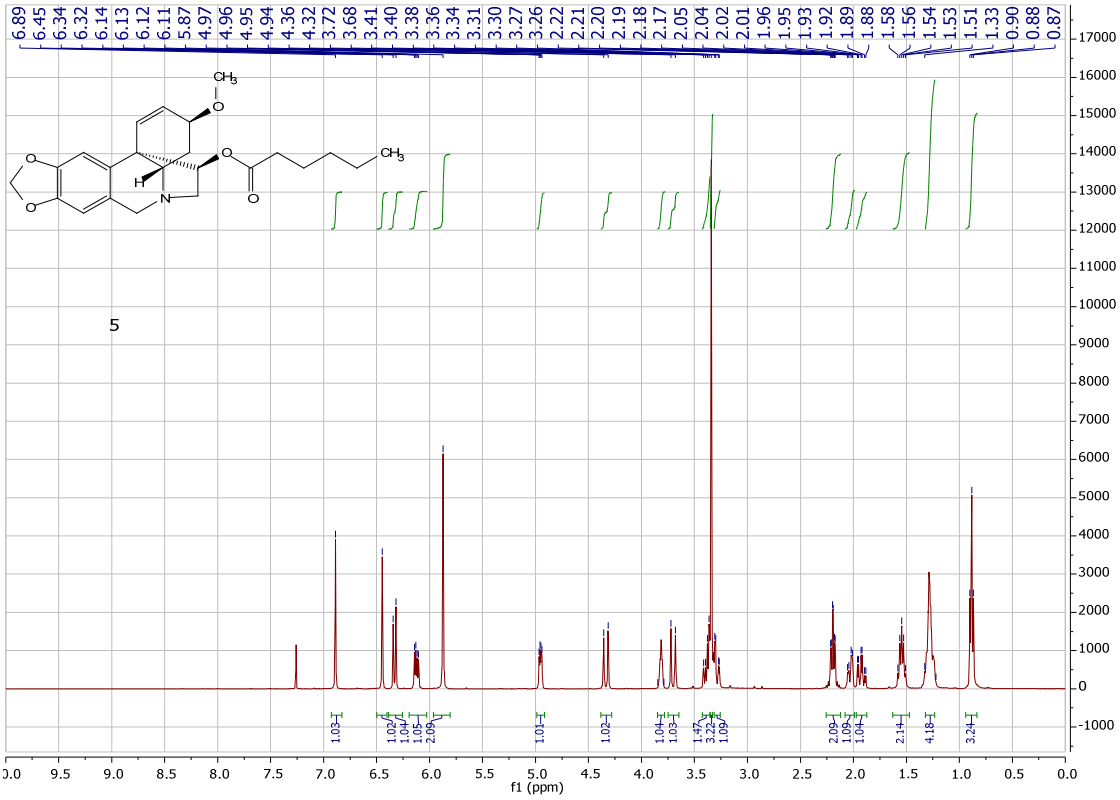
62.9
61.3
60.9
56.6
53.5
49.3
28.4
27.2
4
f1 (ppm)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CH3
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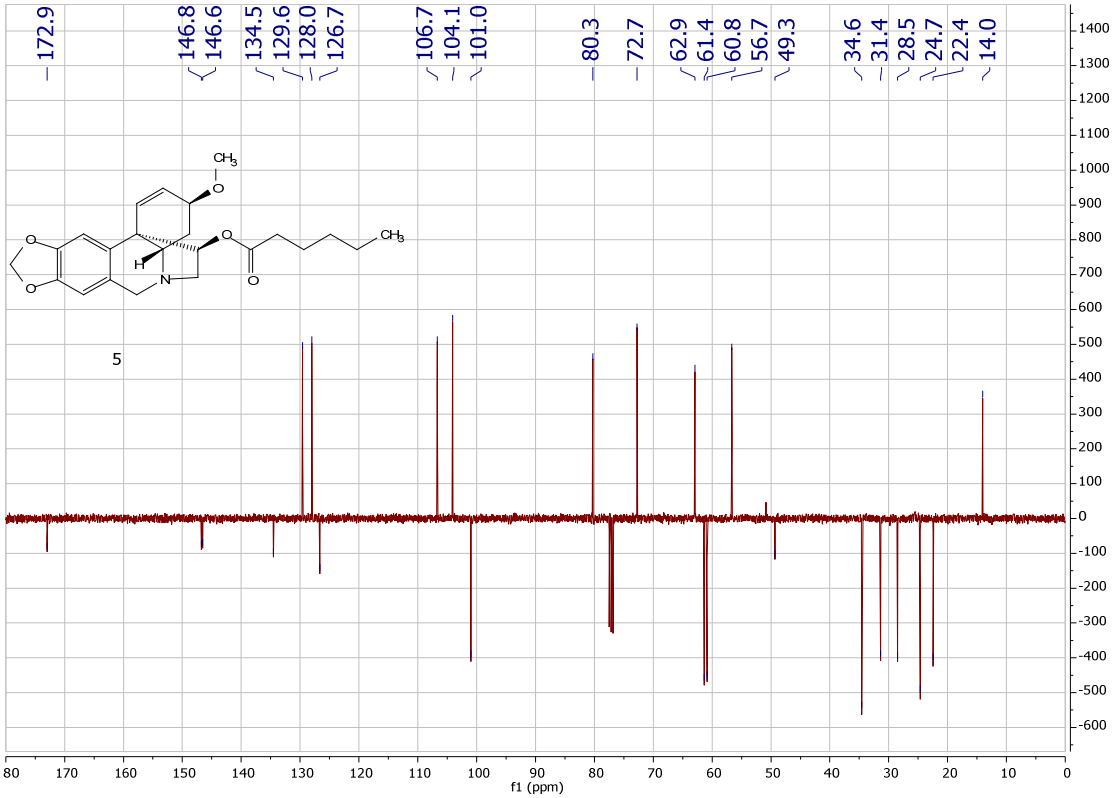
O
O
O
H
N
O
CH3
5
f1 (ppm)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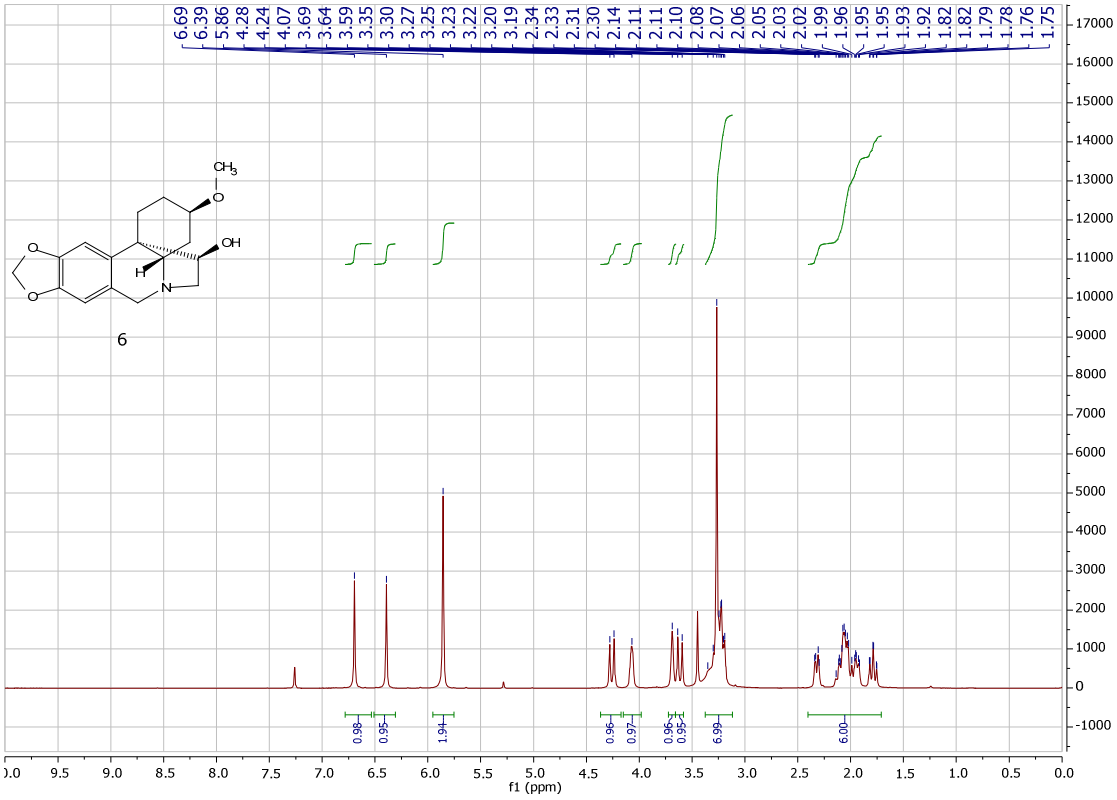
106.7 104.1 101.0
80.3 72.7
62.9 61.4 60.8 56.7 49.3
34.6 31.4 28.5 24.7 22.4 14.0
CH3
O
O
O
O
H
N
O
CH3
5
f1 (ppm)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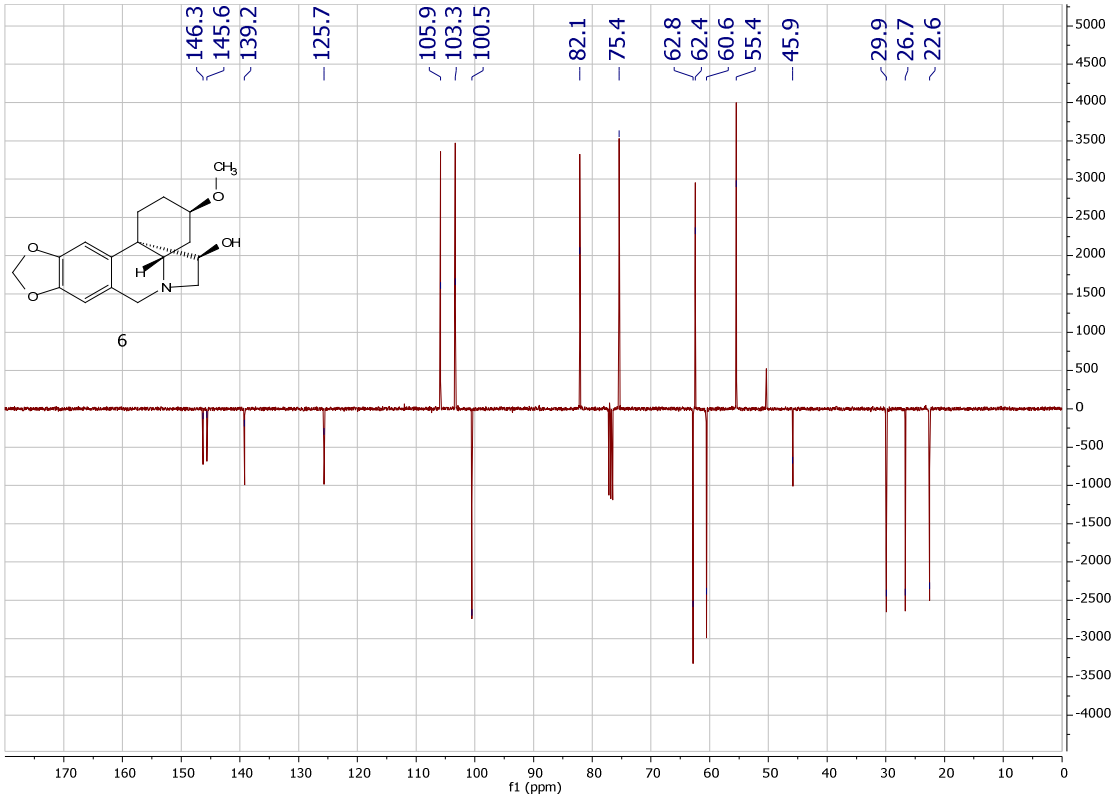
CH3
O
OH
H
N
O
O
6
0.98 0.95 1.94 0.96 0.97 0.96 0.95 6.99 6.00
f1 (ppm)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OH
H
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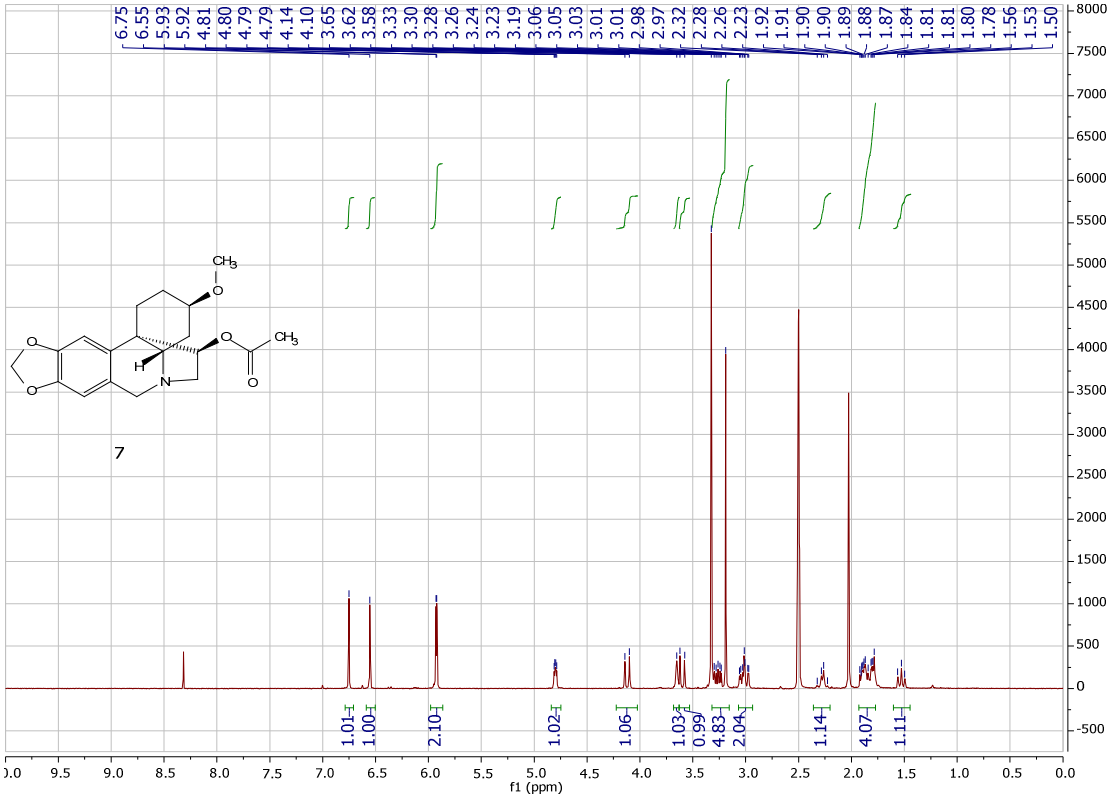
O
O
6
f1 (ppm)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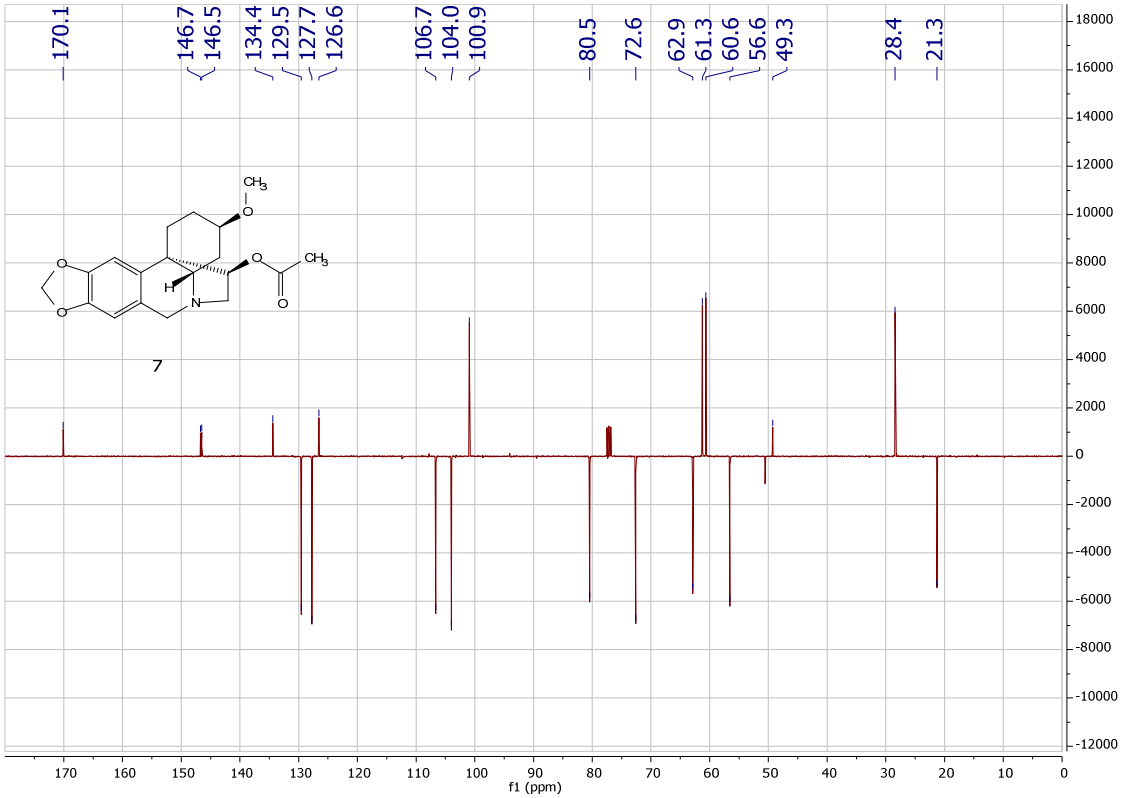
1.01 1.00 2.10 1.02 1.06 1.03 0.99 4.83 2.04 1.14 4.07 1.11
f1 (ppm)
7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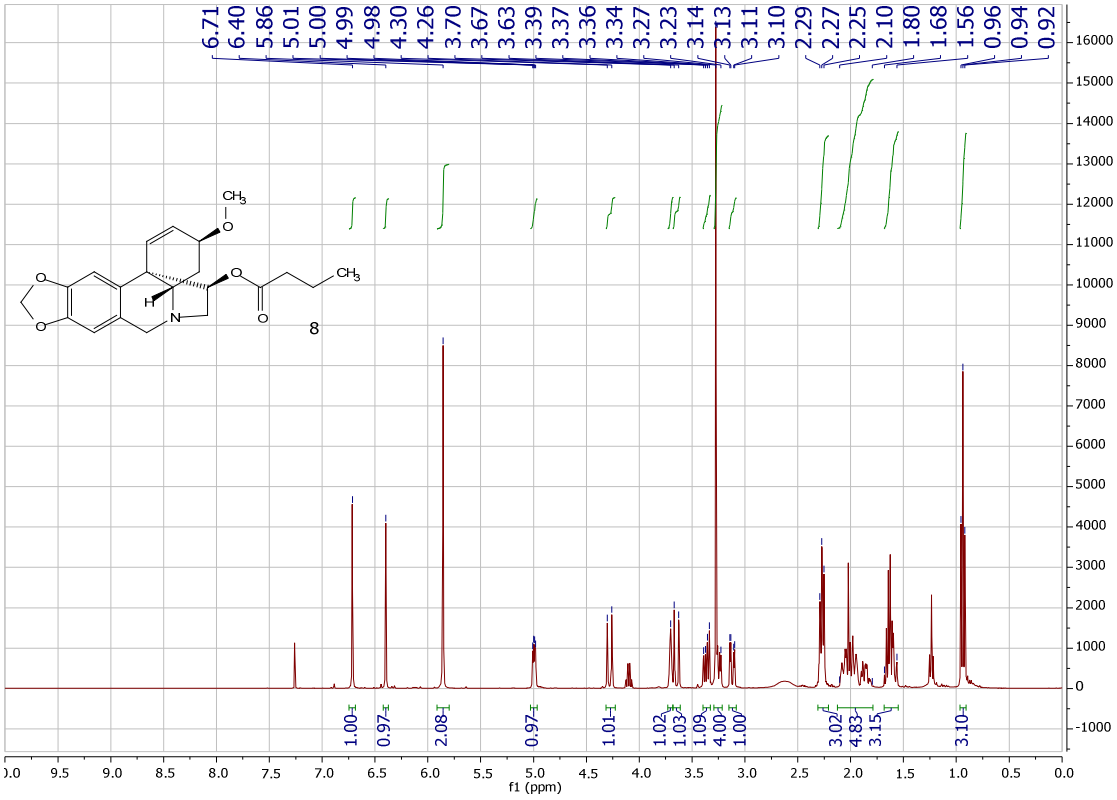
f1 (ppm)
7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4.30
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3.67
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3.37
3.36
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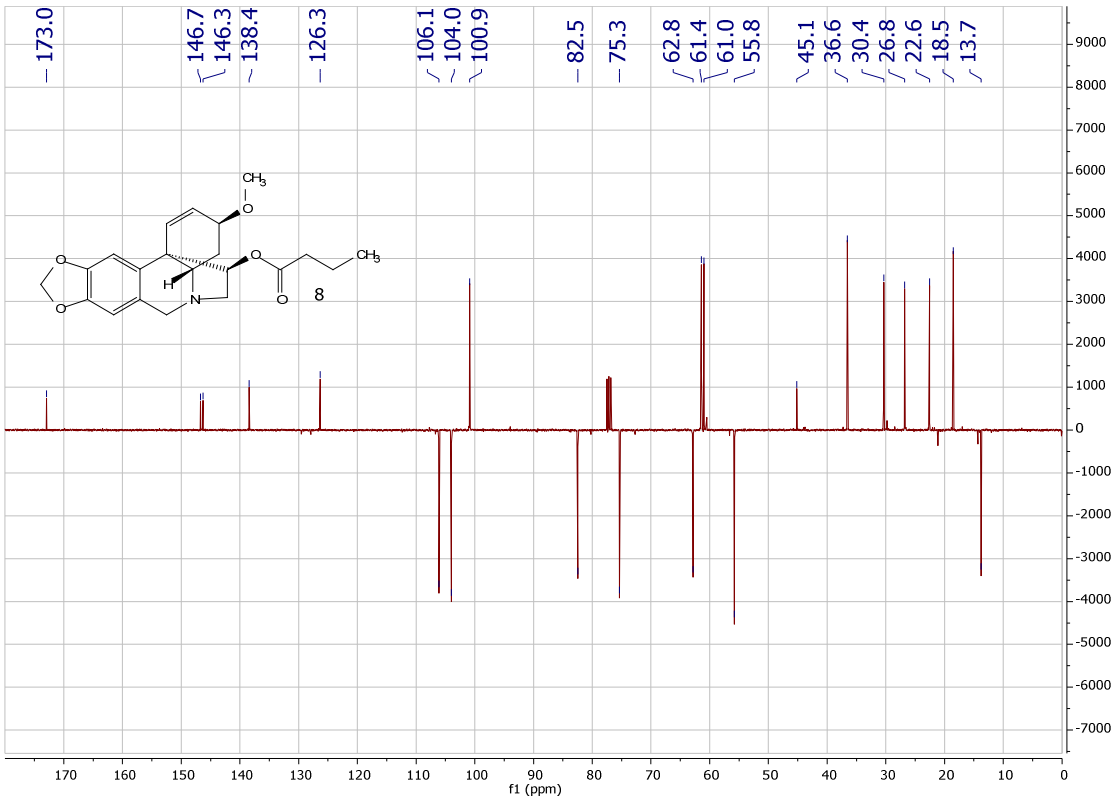
3.13
3.11
3.10
2.29
2.27
2.25
2.10
1.80
1.68
1.56
0.96
0.94
0.92
1.00
0.97
2.08
0.97
1.01
1.02
1.03
1.09
4.00
1.00
3.02
4.83
3.15
3.10
f1 (ppm)
8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82.5
75.3
62.8
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61.0
55.8
45.1
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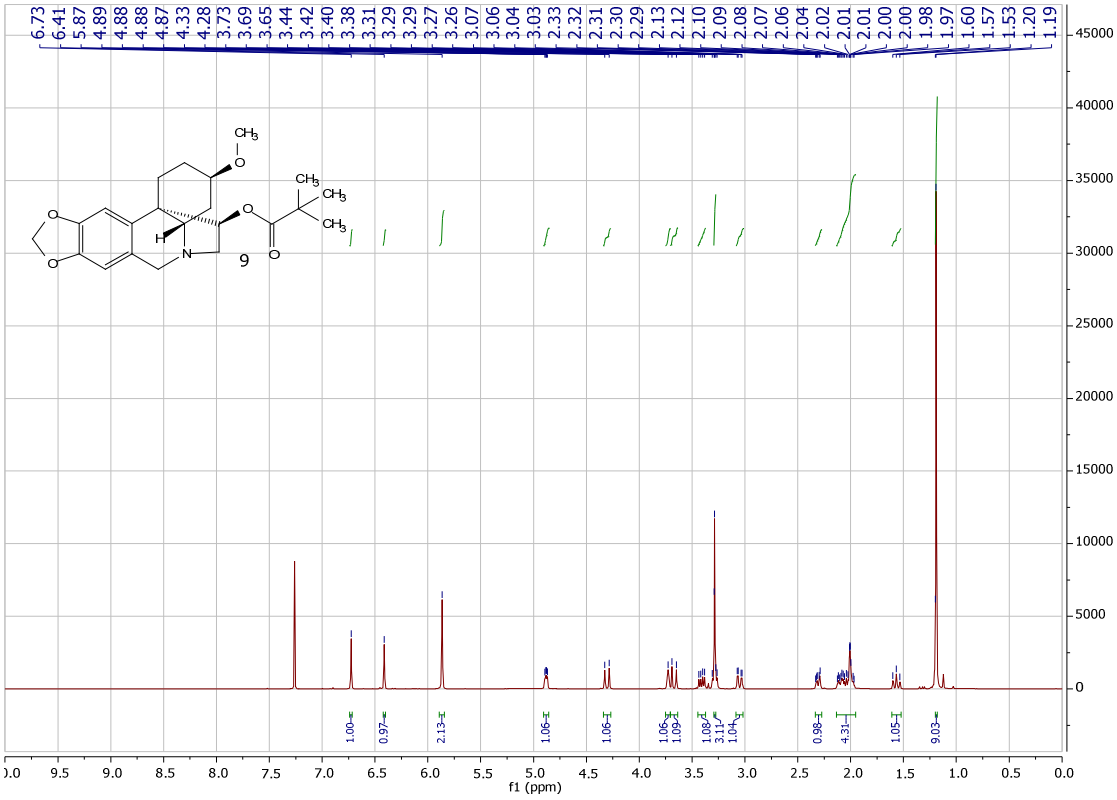
30.4
26.8
22.6
18.5
13.7
f1 (ppm)
8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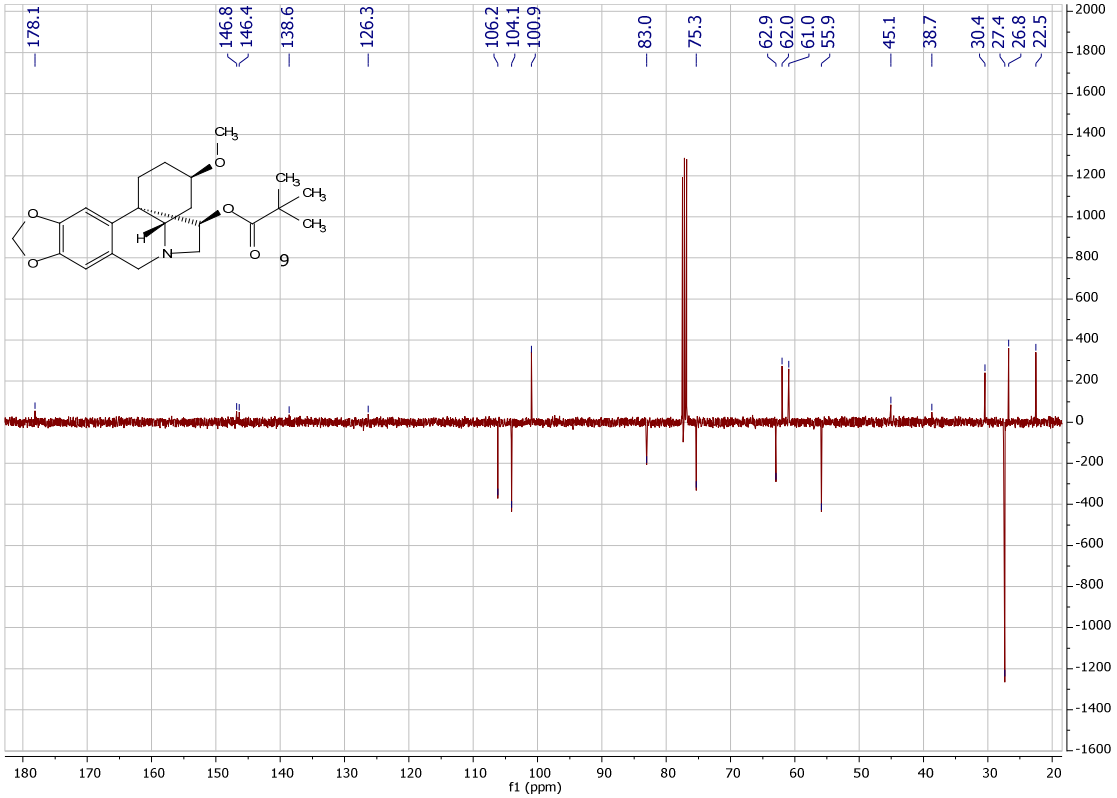
9
f1 (ppm)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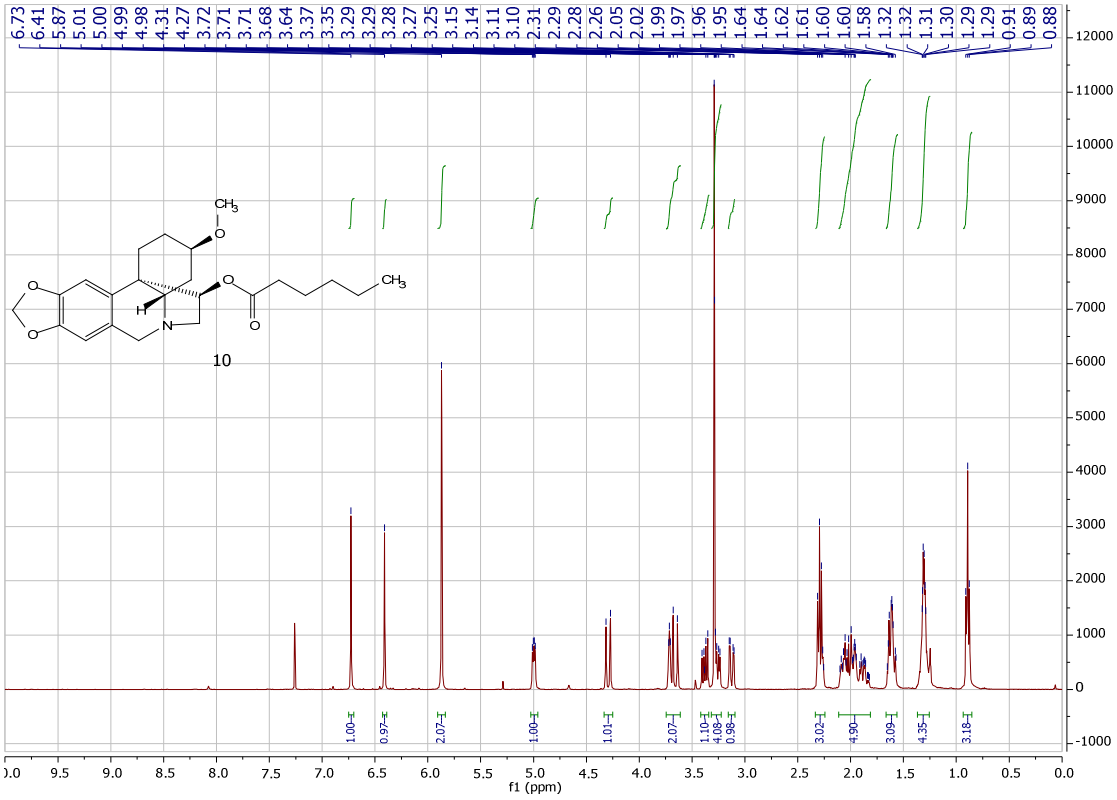
9
f1 (ppm)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1.00 0.97 2.07 1.00 1.01 2.07 1.10 4.08 0.98 3.02 4.90 3.09 4.35 3.18
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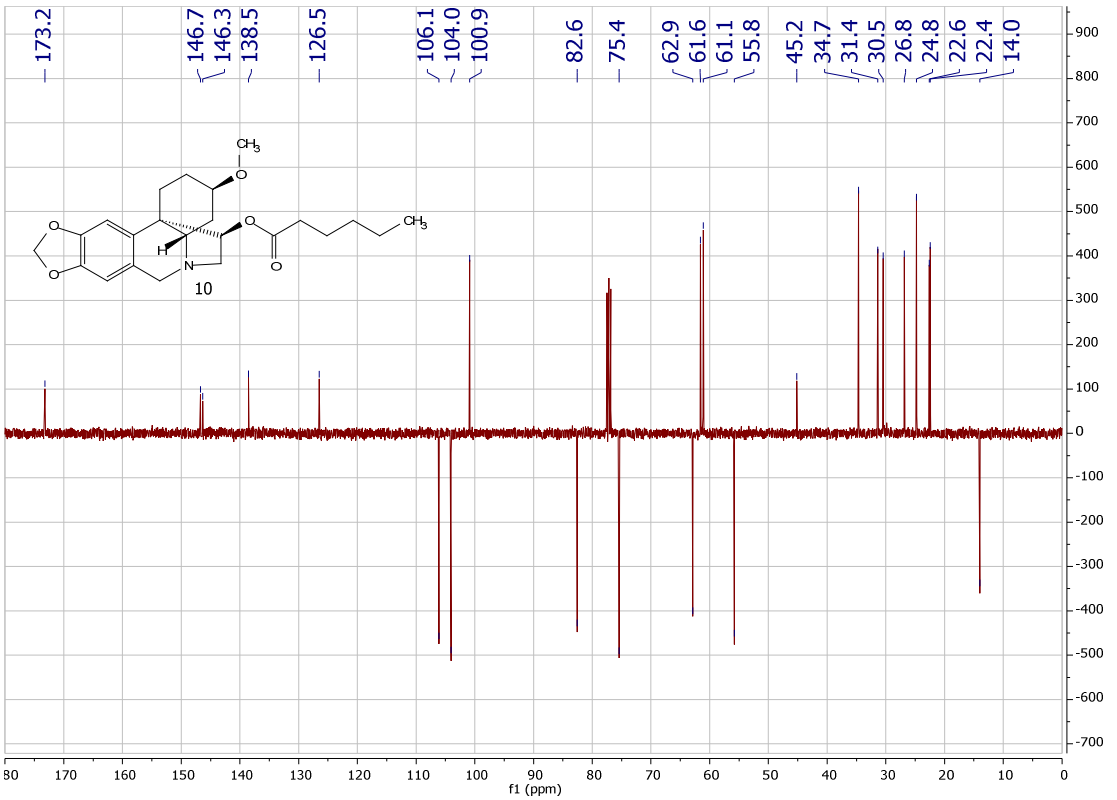
10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