

**Biomimetic Synthesis of Oleocanthal, Oleacein, and Their Analogues Starting from  
Oleuropein, A Major Compound of Olive Leaves.**

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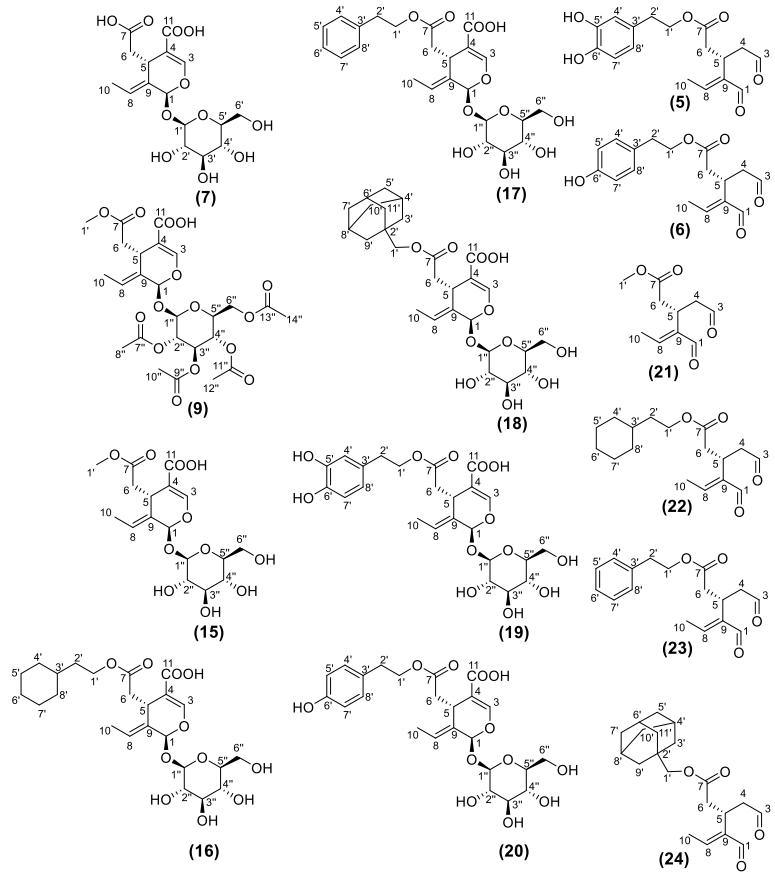


Figure S 1. Structures of semi-synthetic compounds **5**, **6**, **7**, **9** and **15–24**.

Oleoside or (*2S,4S,E*)-4-(carboxymethyl)-3-Ethylidene-2-*{[(2R,3S,4R,5R,6S)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2*H*-pyran-2-yl]oxy}*-3,4-dihydro-2*H*-pyran-5-carboxylic acid (**7**)

Yield: 85%. Rf 0.20 (CH<sub>2</sub>Cl<sub>2</sub>–MeOH 8:2). <sup>1</sup>H NMR (600 MHz, D<sub>2</sub>O) δ 7.68 (s, 1H, H-3), 6.25 (q, *J* = 7.11 Hz, 1H, H-8), 6.04 (s, 1H, H-1), 5.04 (d, *J* = 8.02 Hz, 1H, H-1'), 4.11 (dd, *J* = 9.60, 4.61 Hz, 1H, H-5), 4.01 (dd, *J* = 12.48, 2.20 Hz, 1H, H-6a'), 3.83 (dd, *J* = 12.48, 5.91 Hz, 1H, H-6b'), 3.65–3.62 (m, 1H, H-3'), 3.60 (ddd, *J* = 8.33, 5.91, 2.20 Hz, 1H, H-5'), 3.54–3.52 (m, 1H, H-2'), 3.52–3.50 (m, 1H, H-4'), 2.91 (dd, *J* = 13.85, 4.61 Hz, 1H, H-6a), 2.54 (dd, *J* = 13.85, 9.60 Hz, 1H, H-6b), 1.84 (dd, *J* = 7.06, 1.20 Hz, 3H, H-10); <sup>13</sup>C NMR (151 MHz, D<sub>2</sub>O) δ 176.47 (C-7), 170.50 (C11), 154.62 (C-3), 128.46 (C-9), 125.06 (C-8), 108.68 (C-4), 99.73 (C-1'), 94.96 (C-1), 76.42 (C5'), 75.74 (C-3'), 72.73 (C-2'), 69.55 (C-4'), 60.71 (C-6'), 40.31 (C-6), 30.70 (C-5), 12.88 (C-10); HRMS (ESI-) m/z 389.1091 (calcd for C<sub>16</sub>H<sub>21</sub>O<sub>11</sub> 389.1089).

(*2R,4S,E*)-3-Ethylidene-4-(2-Methoxy-2-oxoethyl)-2-*{[(2R,3S,4R,5S,6S)-3,4,5-triacetoxy-6-(acetoxymethyl)tetrahydro-2*H*-pyran-2-yl]oxy}*-3,4-dihydro-2*H*-pyran-5-carboxylic acid (**9**)

Yield: 78%. Rf 0.23 (cyclohexane–EtOAc 1:1). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>): δ 7.57 (s, 1H, H-3), 6.05 (q, *J* = 7.22 Hz, 1H, H-8), 5.74 (s, 1H, H-1), 5.28–5.25 (m, 1H, H-3''), 5.13–5.12 (m, 1H, H-2''), 5.12–5.10 (m, 1H, H-4''), 5.04 (d, *J* = 7.97 Hz, 1H, H-1''), 4.31 (dd, *J* = 12.37, 4.99 Hz, 1H, H-6a''), 4.14 (dd, *J* = 12.37, 2.37 Hz, 1H, H-6b''), 3.98 (dd, *J* = 8.96, 4.48 Hz, 1H, H-5), 3.78 (ddd, *J* = 7.38, 4.99, 2.37 Hz, 1H, H-5''), 3.63 (s, 3H, H-1') , 2.78

(dd,  $J = 14.55, 4.48$  Hz, 1H, H-6a), 2.44 (dd,  $J = 14.55, 8.96$  Hz, 1H, H-6b), 2.08 (s, 3H, H-8''), 2.03 (s, 3H, H-10''), 2.03 (s, 3H, H-12''), 2.02 (s, 3H, H-14''), 1.75 (dd,  $J = 7.13, 1.40$  Hz, 3H, H-10);  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ ):  $\delta$  171.59 (C-7), 171.47 (C-11), 170.73 (C-13''), 170.29 (C-9''), 169.55 (C-7''), 169.48 (C-11''), 155.20 (C-3), 127.91 (C-9), 125.32 (C-8), 108.05 (C-4), 97.28 (C-1''), 94.10 (C-1), 72.69 (C-5''), 72.42 (C-3''), 70.92 (C-2''), 68.48 (C-4''), 61.97 (C-6''), 51.73 (C-1'), 39.83 (C-6), 30.17 (C-5), 20.79 (C-8''), 20.77 (C-10''), 20.71 (C-12''), 20.69 (C-14''), 13.62 (C-10). HRMS (ESI+) m/z 595.1620 (calcd for  $\text{C}_{25}\text{H}_{33}\text{O}_{15}\text{Na}$  595.1639).

Oleoside 7-methyl ester or (*2S,4S,E*)-3-Ethylidene-4-(2-Methoxy-2-oxoethyl)-2-  
{[(2*R*,3*S*,4*R*,5*R*,6*S*)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2*H*pyran-2-yl]oxy}-3,4-dihydro-2*H*-pyran-5-carboxylic acid (**15**)

Yield: 62%. Rf 0.24 ( $\text{CH}_2\text{Cl}_2-\text{MeOH}$  8:2).  $^1\text{H}$  NMR (600 MHz, methanol –  $d_4$ )  $\delta$  7.47 (s, 1H, H-3), 6.12 (q,  $J = 7.00$  Hz, 1H, H-8), 5.90 (s, 1H, H-1), 4.83 (d,  $J = 8.08$  Hz, 1H, H-1''), 4.05 (dd,  $J = 9.51, 4.46$  Hz, 1H, H-5), 3.91 (dd,  $J = 11.90, 1.47$  Hz, 1H, H-6a''), 3.72 (dd,  $J = 11.90, 5.61$  Hz, 1H, H-6b''), 3.65 (s, 3H, H-1'), 3.45–3.42 (m, 1H, H-3''), 3.37–3.36 (m, 1H, H-5''), 3.35–3.34 (m, 1H, H-4''), 3.34–3.33 (m, 1H, H-2''), 2.86 (dd,  $J = 14.15, 4.46$  Hz, 1H, H-6a), 2.47 (dd,  $J = 14.15, 9.51$  Hz, 1H, H-6b), 1.81 (dd,  $J = 7.12, 1.42$  Hz, 3H, H-10);  $^{13}\text{C}$  NMR (151 MHz, methanol –  $d_4$ )  $\delta$  173.81 (C-7), 171.28 (C11), 153.80 (C-3), 131.16 (C-9), 124.29 (C-8), 111.41 (C-4), 100.95 (C-1''), 94.96 (C-1), 78.38 (C5''), 77.99 (C-3''), 74.83 (C-2''), 71.49 (C-4''), 62.73 (C-6''), 52.05 (C-1'), 41.12 (C-6), 32.23 (C-5), 13.52 (C-10); HRMS (ESI-) m/z 403.1251 (calcd for  $\text{C}_{17}\text{H}_{23}\text{O}_{11}$  403.1246).

Demethyloleuropein or  $(2S,4S,E)$ -4-(2-(3,4-Dihydroxyphenethoxy)-2-oxoethyl)-3-ethylidene-2- $\{[(2R,3S,4R,5R,6S)-3,4,5\text{-trihydroxy-}6\text{-hydroxymethyl)tetrahydro-}2H\text{-pyran-}2\text{-yl]oxy}\}$ -3,4dihydro-2*H*-pyran-5-carboxylic acid (**19**)

Yield: 36%. Rf 0.28 (CH<sub>2</sub>Cl<sub>2</sub>–MeOH 8:2). <sup>1</sup>H NMR (600 MHz, D<sub>2</sub>O) δ 7.48 (s, 1H, H-3), 6.95 (d, *J* = 8.12 Hz, 1H, H-7'), 6.90 (d, *J* = 2.00 Hz, 1H, H-4'), 6.81 (dd, *J* = 8.05, 2.00 Hz, 1H, H-8'), 6.10 (q, *J* = 6.96 Hz, 1H, H-8), 5.81 (s, 1H, H-1), 4.95 (d, *J* = 7.95 Hz, 1H, H-1''), 4.39 (dt, *J* = 10.79, 6.52 Hz, 1H, H-1a'), 4.26 (dt, *J* = 10.79, 6.36 Hz, 1H, H-1b'), 3.99–3.96 (m, 1H, H-5), 3.98 (dd, *J* = 12.30, 1.94 Hz, 1H, H-6a''), 3.82 (dd, *J* = 12.30, 5.26 Hz, 1H, H-6b''), 3.65–3.62 (m, 1H, H-3''), 3.58 (ddd, *J* = 9.97, 5.26, 1.94 Hz, 1H, H-5''), 3.54–3.52 (m, 1H, H-4''), 3.52–3.49 (m, 1H, H-2''), 2.91 (t, *J* = 6.05 Hz, 2H, H-2'), 2.80 (dd, *J* = 13.67, 4.71 Hz, 1H, H-6a), 2.57 (dd, *J* = 13.67, 8.91 Hz, 1H, H-6b), 1.65 (dd, *J* = 7.17, 1.14 Hz, 3H, H-10); <sup>13</sup>C NMR (151 MHz, D<sub>2</sub>O) δ 174.33 (C-7), 172.00 (C-11), 152.66 (C-3), 143.93 (C-5'), 142.98 (C-6'), 131.28 (C-3') 128.89 (C-9), 124.74 (C-8), 121.34 (C-8'), 116.85 (C-4'), 116.38 (C-7'), 110.87 (C-4), 99.59 (C-1''), 94.74 (C-1), 76.34 (C-5''), 75.74 (C-3''), 72.75 (C-2''), 69.51 (C-4''), 66.32 (C-1'), 60.71 (C6''), 39.88 (C-6), 33.42 (C-2'), 30.87 (C-5), 12.61 (C-10); HRMS (ESI-) m/z 525.1620 (calcd for C<sub>24</sub>H<sub>29</sub>O<sub>13</sub> 525.1614).

Demethylligstroside or  $(2S,4S,E)$ -3-Ethylidene-4-(2-(4-Hydroxyphenethoxy)-2-oxoethyl)-2- $\{[(2R,3S,4R,5R,6S)-3,4,5\text{-trihydroxy-}6\text{-hydroxymethyl)tetrahydro-}2H\text{-pyran-2-yl]oxy}\}$ -3,4dihydro-2*H*-pyran-5-carboxylic acid (**20**)

Yield: 39%. Rf 0.35 (CH<sub>2</sub>Cl<sub>2</sub>–MeOH 8:2). <sup>1</sup>H NMR (600 MHz, D<sub>2</sub>O) δ 7.58 (s, 1H, H-3), 7.25 (d, *J* = 7.74 Hz, 2H, H-4'/H-8'), 6.94 (d, *J* = 7.85 Hz, 2H, H-5'/H-7'), 6.12 (q, *J* = 6.85 Hz, 1H, H-8), 5.86 (s, 1H, H-1), 4.96 (d, *J* = 8.04 Hz, 1H, H-1''), 4.39 (dt, *J* = 10.52, 6.73 Hz, 1H, H-1a'), 4.27 (dt, *J* = 10.52, 6.14 Hz, 1H, H-1b'), 3.98 (dd, *J* = 12.38, 1.68 Hz, 1H,

H-6a''), 3.97–3.96 (m, 1H, H-5), 3.82 (dd,  $J = 12.38, 5.51$  Hz, 1H, H-6b''), 3.65–3.62 (m, 1H, H-3''), 3.57 (ddd,  $J = 10.02, 5.51, 1.68$  Hz, 1H, H-5''), 3.55–3.52 (m, 1H, H-4''), 3.52–3.50 (m, 1H, H-2''), 2.95 (t,  $J = 5.98$  Hz, 2H, H-2'), 2.78 (dd,  $J = 13.57, 4.75$  Hz, 1H, H-6a), 2.56 (dd,  $J = 13.57, 8.95$  Hz, 1H, H-6b), 1.66 (d,  $J = 7.10$  Hz, 3H, H-10);  $^{13}\text{C}$  NMR (151 MHz,  $\text{D}_2\text{O}$ )  $\delta$  174.19 (C-7), 170.78 (C-11), 154.08 (C-3), 130.37 (C-3'/C-4'/C-8'), 128.51 (C-9), 124.98 (C-8), 115.51 (C-5'/C-7'), 109.07 (C-4), 99.57 (C-1''), 94.78 (C-1), 76.38 (C-5''), 75.76 (C-3''), 72.77 (C-2''), 69.44 (C-4''), 66.36 (C-1'), 60.77 (C-6''), 39.87 (C-6), 33.29 (C-2'), 30.53 (C-5), 12.68 (C-10); HRMS (ESI-) m/z 509.1670 (calcd for  $\text{C}_{24}\text{H}_{29}\text{O}_{12}$  509.1664).

EDA methyl ester or (3*S*,4*E*)-4-Formyl-3-(2-oxoethyl)hex-4-enoic acid methyl ester (**21**)  
Yield: 39%. Rf 0.41 (cyclohexane-EtOAc 2:3).  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  9.67 (brs, 1H, H-3), 9.29 (d,  $J = 1.97$  Hz, 1H, H-1), 6.71 (q,  $J = 7.04$  Hz, 1H, H-8), 3.69–3.64 (m, 1H, H-5), 3.63 (s, 3H, H-1'), 3.02 (ddd,  $J = 18.12, 8.42, 1.19$  Hz, 1H, H-4a), 2.83 (dd,  $J = 18.12, 5.74$  Hz, 1H, H-4b), 2.75 (dd,  $J = 16.11, 8.57$  Hz, 1H, H-6a), 2.66 (dd,  $J = 16.11, 6.47$  Hz, 1H, H-6b), 2.13 (d,  $J = 7.09$  Hz, 3H, H-10);  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  200.47 (C-3), 195.21 (C-1), 154.34 (C-8), 51.71 (C-1'), 46.44 (C-4), 36.83 (C6), 27.44 (C-5), 15.38 (C-10); HRMS (ESI+) m/z 221.0781 (calcd for  $\text{C}_{10}\text{H}_{14}\text{O}_4\text{Na}$  221.0784).

Oleacein or (3*S*,4*E*)-4-Formyl-3-(2-oxoethyl)-4-hexenoic acid 2-(3,4-dihydroxyphenyl)ethyl ester (**5**)

Yield: 30%. Rf 0.46 (cyclohexane-EtOAc 2:3).  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  9.65 (brs, 1H, H-3), 9.21 (d,  $J$  = 1.88 Hz, 1H, H-1), 6.79 (d,  $J$  = 8.05 Hz, 1H, H-7'), 6.72 (d,  $J$  = 1.95 Hz, 1H, H-4'), 6.67 (q,  $J$  = 7.12 Hz, 1H, H-8), 6.61 (dd,  $J$  = 8.12, 1.95 Hz, 1H, H-8'), 4.25 (dt,  $J$  = 10.92, 6.51 Hz, 1H, H-1a'), 4.18 (dt,  $J$  = 10.92, 6.35 Hz, 1H, H-1b'), 3.66–3.61 (m, 1H, H-5), 2.96 (ddd,  $J$  = 18.20, 8.18, 1.19 Hz, 1H, H-4a), 2.80–2.78 (m, 1H, H-4b), 2.78 (t,  $J$  = 6.19 Hz, 2H, H-2'), 2.75 (dd,  $J$  = 15.59, 8.73 Hz, 1H, H-6a), 2.63 (dd,  $J$  = 15.59, 6.53 Hz, 1H, H-6b), 2.06 (d,  $J$  = 7.07 Hz, 3H, H-10);  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  201.01 (C-3), 195.85 (C-1), 172.00 (C-7), 155.09 (C-8), 143.57 (C-5'), 143.41 (C-9), 142.90 (C-6'), 130.75 (C-3'), 121.46 (C-8'), 116.34 (C-4'), 115.43 (C-7'), 65.33 (C-1'), 46.44 (C-4), 37.14 (C-6), 34.40 (C-2'), 27.37 (C-5), 15.42 (C-10); HRMS (ESI+) m/z 343.1150 (calcd for  $\text{C}_{17}\text{H}_{20}\text{O}_6\text{Na}$  343.1152).

Oleocanthal or (3*S*,4*E*)-4-Formyl-3-(2-oxoethyl)-4-hexenoic acid 2-(4-hydroxyphenyl)ethyl ester (**6**)

Yield: 33%. Rf 0.52 (cyclohexane-EtOAc 2:3).  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  9.62 (brs, 1H, H-3), 9.23 (d,  $J$  = 1.97 Hz, 1H, H-1), 7.04 (d,  $J$  = 8.42 Hz, 2H, H-4'/H-8'), 6.76 (d,  $J$  = 8.45 Hz, 2H, H-5'/H-7'), 6.65 (q,  $J$  = 7.08 Hz, 1H, H-8), 4.24 (dt,  $J$  = 10.86, 6.99 Hz, 1H, H-1a'), 4.20 (dt,  $J$  = 10.86, 6.97 Hz, 1H, H-1b'), 3.63–3.58 (m, 1H, H-5), 2.99 (ddd,  $J$  = 18.26, 8.61, 1.16 Hz, 1H, H-4a), 2.83 (t,  $J$  = 6.92 Hz, 2H, H-2'), 2.75 (dd,  $J$  = 18.26, 5.64 Hz, 1H, H-4b), 2.70 (dd,  $J$  = 15.87, 8.26 Hz, 1H, H-6a), 2.63 (dd,  $J$  = 15.91, 6.66 Hz, 1H, H-6b), 2.07 (d,  $J$  = 7.06 Hz, 3H, H-10);  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  200.62 (C-3), 195.32

(C-1), 172.13 (C-7), 154.64 (C-6'), 154.45 (C-8), 143.49 (C-9), 130.15 (C-3'), 129.82 (C-4'/C-8'), 115.55 (C-5'/C-7'), 65.34 (C-1'), 46.36 (C-4), 37.07 (C-6), 34.32 (C-2'), 27.45 (C-5), 15.35 (C-10); HRMS (ESI+) m/z 327.1200 (calcd for C<sub>17</sub>H<sub>20</sub>O<sub>5</sub>Na 327.1203).

EDA 2-phenylethyl ester or (3*S*,4*E*)-4-Formyl-3-(2-oxoethyl)-4-hexenoic acid 2-phenylethyl ester (**23**)

Yield: 31.5%. Rf 0.57 (cyclohexane-EtOAc 2:3). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 9.62 (brs, 1H, H-3), 9.23 (d, *J* = 1.96 Hz, 1H, H-1), 7.30–7.28 (m, 2H, H-7'/H-5'), 7.23–7.21 (m, 1H, H-6'), 7.19–7.18 (m, 2H, H-4'/H-8'), 6.62 (q, *J* = 6.95 Hz, 1H, H-8), 4.29 (dt, *J* = 10.87, 7.03 Hz, 1H, H-1a'), 4.26 (dt, *J* = 10.87, 6.94 Hz, 1H, H-1b'), 3.63–3.58 (m, 1H, H-5), 2.99 (ddd, *J* = 18.28, 8.64, 1.29 Hz, 1H, H-4a), 2.91 (t, *J* = 6.97 Hz, 2H, H-2'), 2.75 (ddd, *J* = 18.28, 5.45, 0.86 Hz 1H, H-4b), 2.70 (dd, *J* = 15.87, 8.39 Hz, 1H, H-6a), 2.63 (dd, *J* = 15.87, 6.58 Hz, 1H, H-6b), 2.07 (d, *J* = 7.05 Hz, 3H, H-10); <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ 200.43 (C-3), 195.16 (C-1), 172.01 (C-7), 154.21 (C-8), 143.49 (C-9), 137.86 (C-3'), 129.01 (C-4'/C-8'), 128.65 (C-5'/C7'), 126.72 (C-6'), 65.06 (C-1'), 46.35 (C-4), 37.02 (C-6), 35.19 (C-2'), 27.43 (C-5), 15.33 (C-10). HRMS (ESI+) m/z 311.1253 (calcd for C<sub>17</sub>H<sub>20</sub>O<sub>4</sub>Na 311.1254).

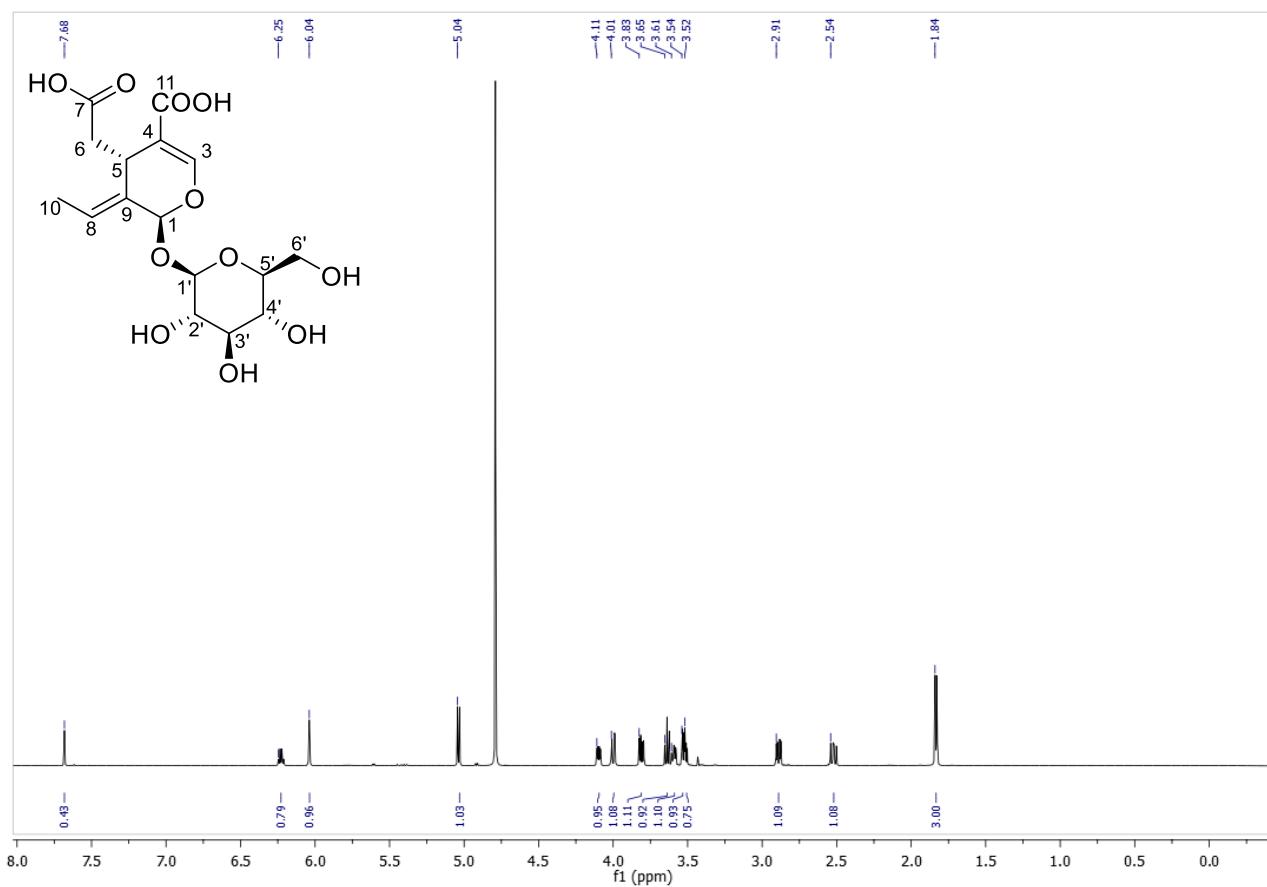


Figure S2.  $^1\text{H}$  NMR spectrum of oleoside (7) in  $\text{D}_2\text{O}$  (600 MHz).

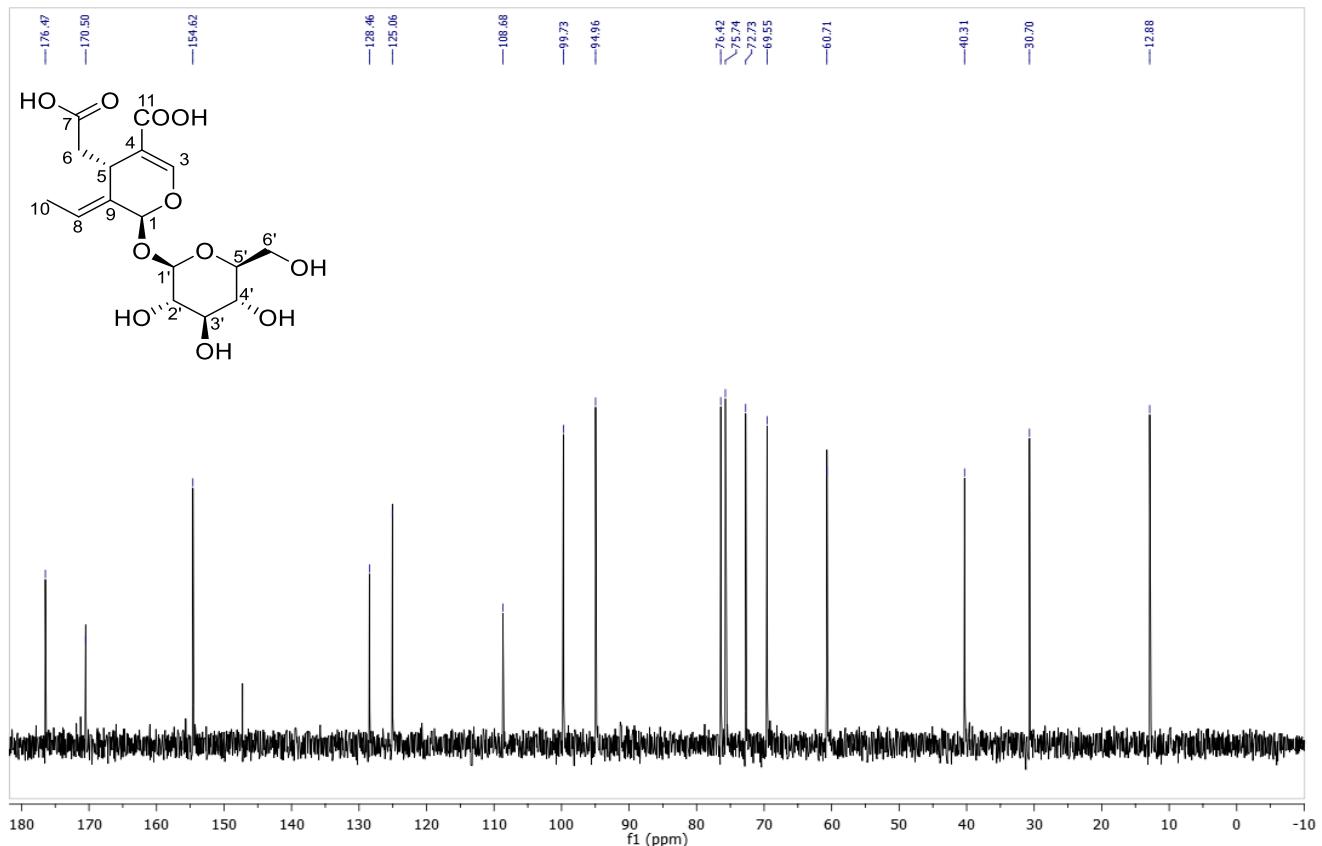


Figure S3. <sup>13</sup>C NMR spectrum of oleoside (7) in  $\text{D}_2\text{O}$  (151 MHz).

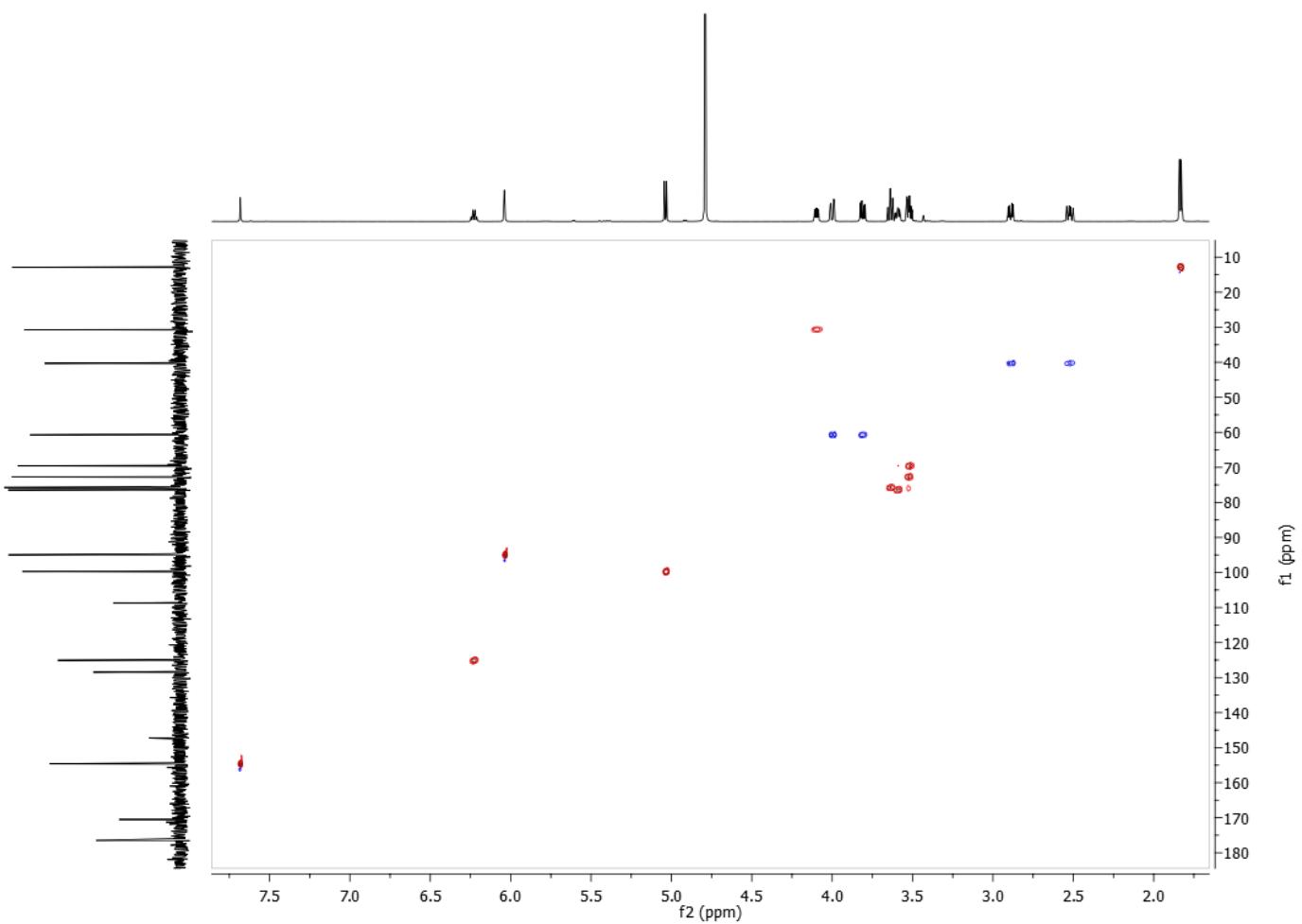


Figure S4. HSQC spectrum of oleoside (7) in  $\text{D}_2\text{O}$  (600 MHz).

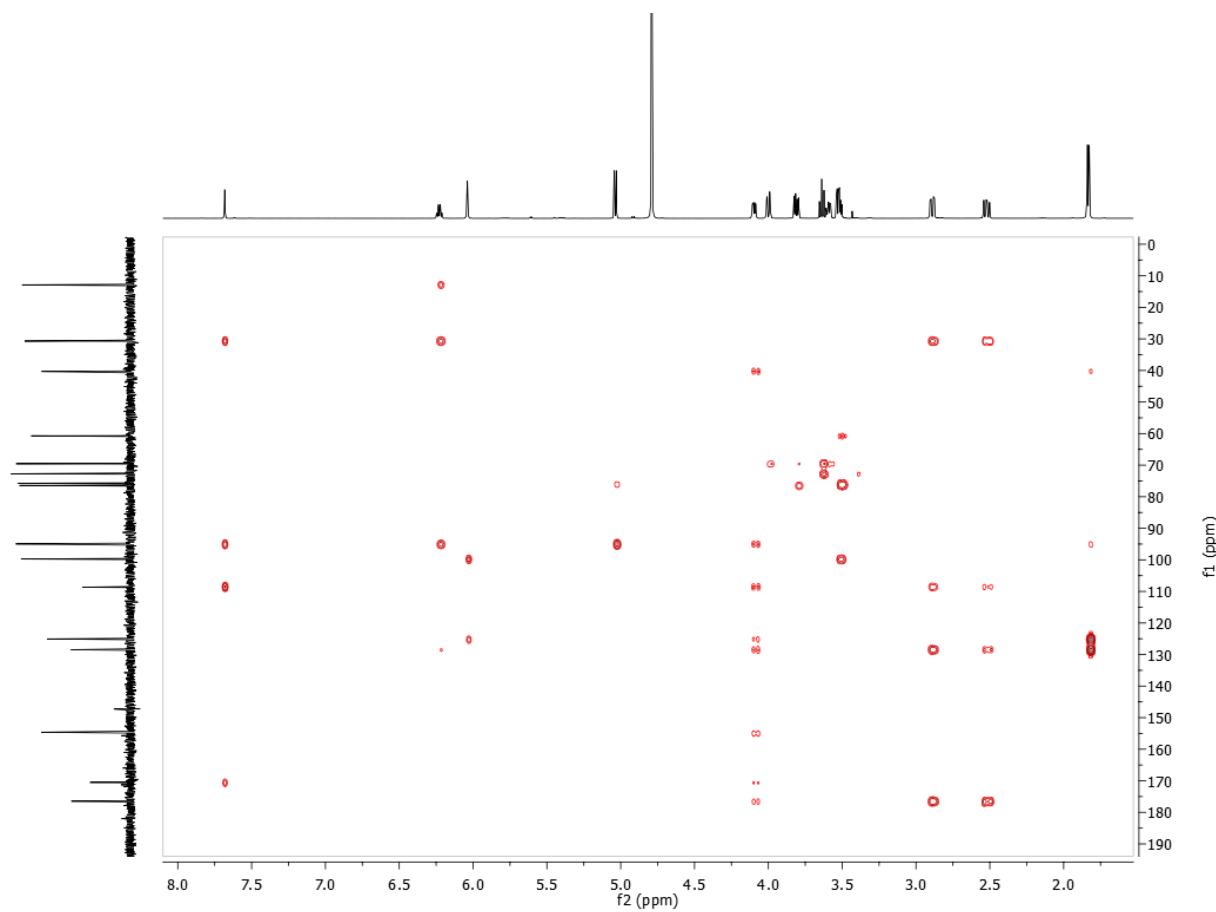


Figure S5. HMBC spectrum of oleoside (**7**) in  $\text{D}_2\text{O}$  (600 MHz).

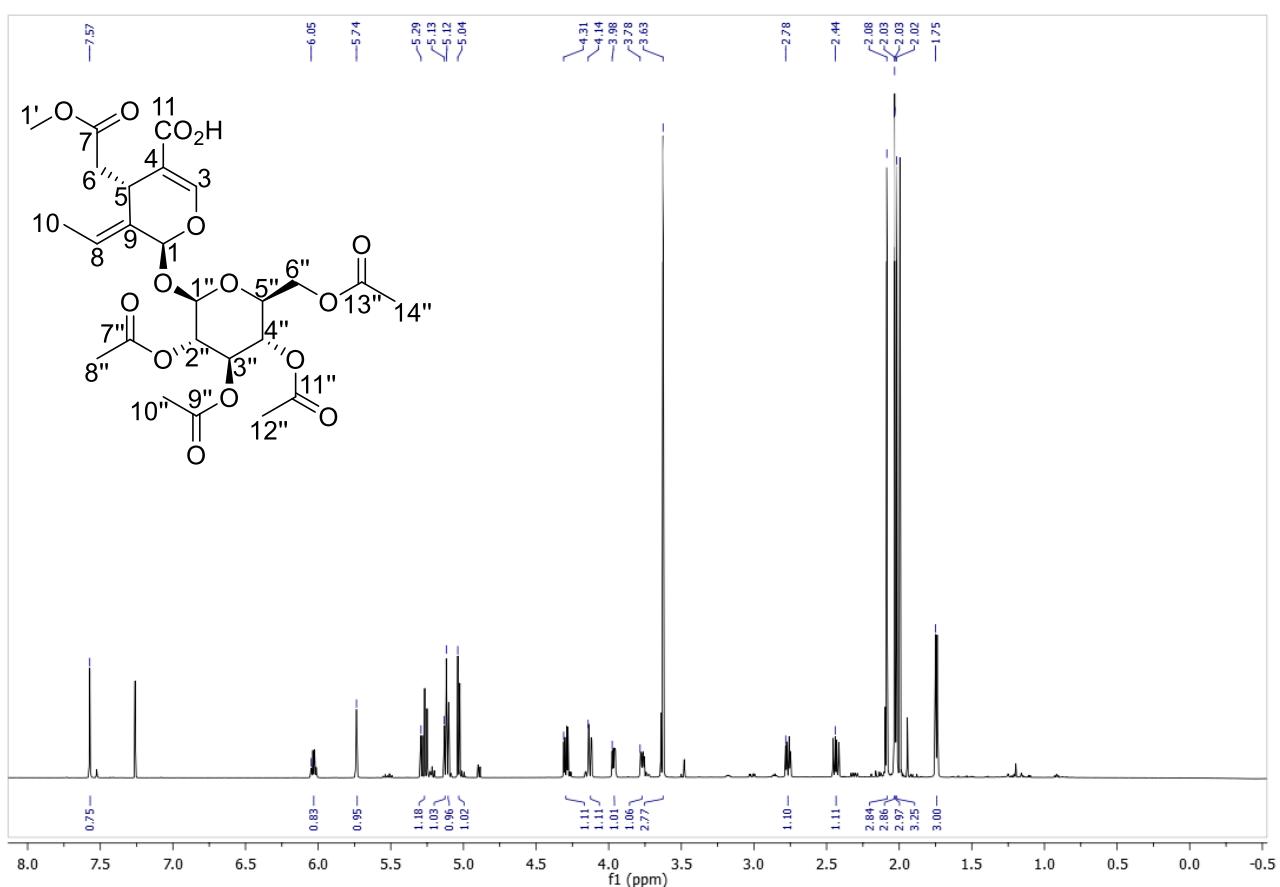


Figure S6. <sup>1</sup>H NMR spectrum of (2*S*,4*S*,*E*)-3-Ethylidene-4-(2-methoxy-2-oxoethyl)-2-{[(2*R*,3*S*,4*R*,5*S*,6*S*)-3,4,5-triacetoxy-6-(acetoxymethyl)tetrahydro-2*H*-pyran-2-yl]oxy }-3,4-dihydro-2*H*-pyran-5-carboxylic acid (**9**) in CDCl<sub>3</sub> (600 MHz).

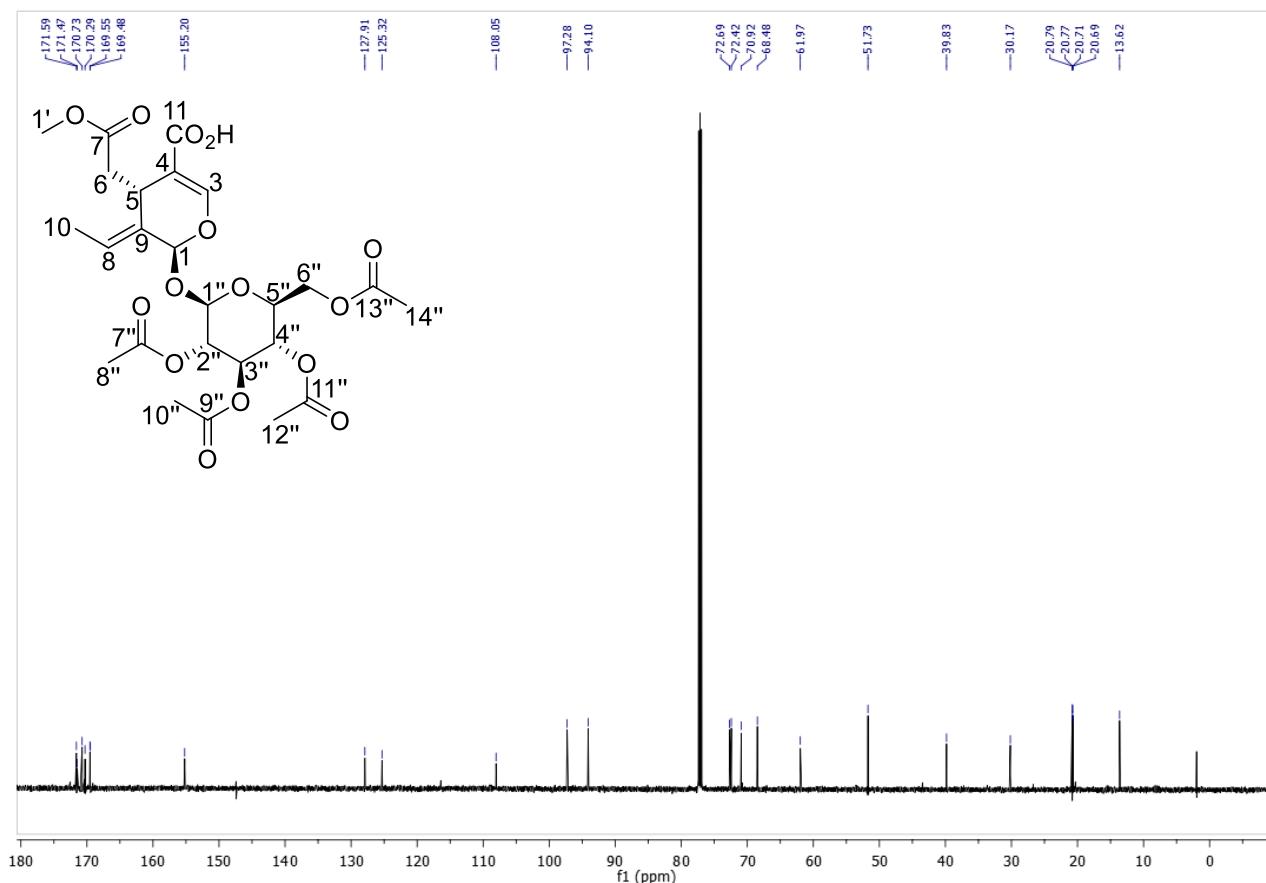


Figure S7.  $^{13}\text{C}$  NMR spectrum of  $(2S,4S,E)$ -3-Ethylidene-4-(2-methoxy-2-oxoethyl)-2- $\{(2R,3S,4R,5S,6S)$ -3,4,5-triacetoxy-6-(acetoxymethyl)tetrahydro-2*H*-pyran-2-yl]oxy}-3,4-dihydro-2*H*-pyran-5-carboxylic acid (**9**) in  $\text{CDCl}_3$  (151 MHz).

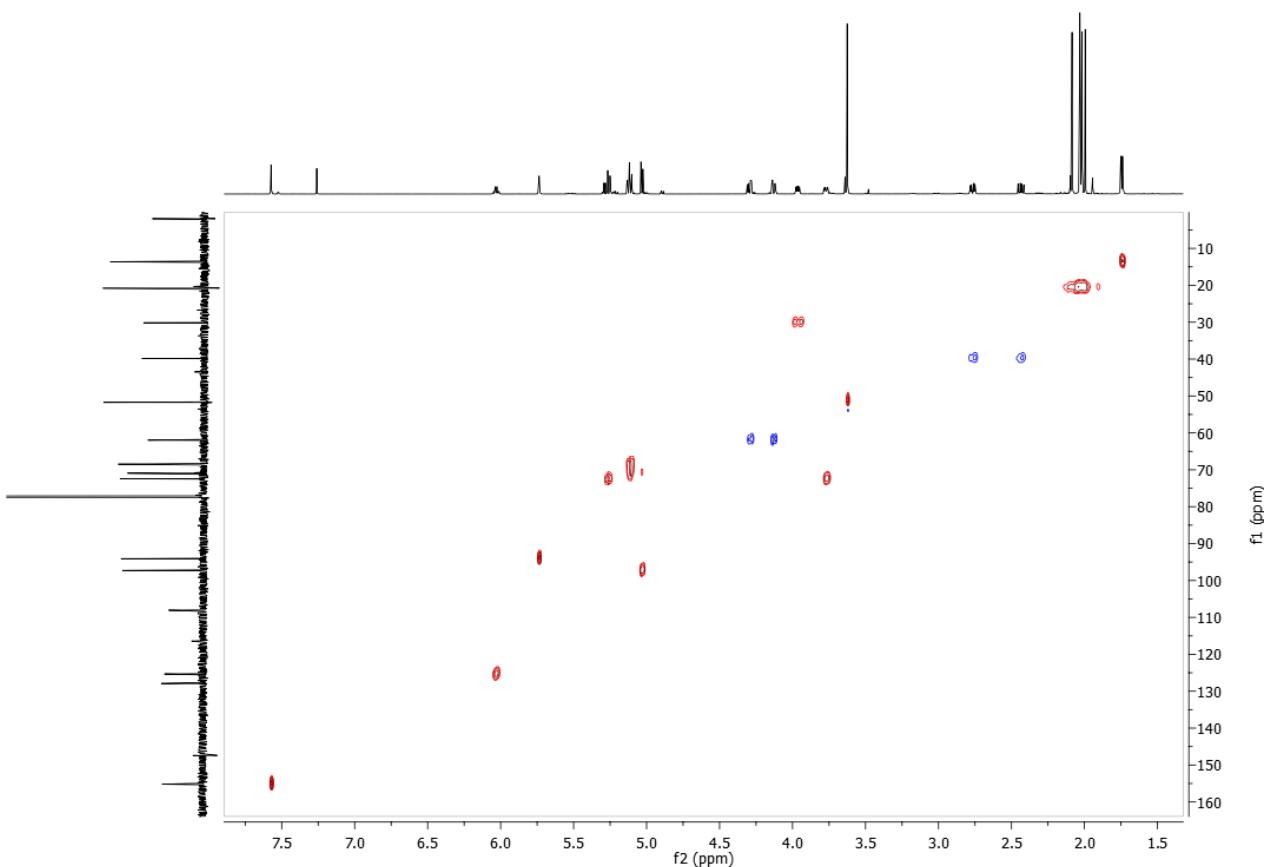


Figure S8. HSQC spectrum of (*2S,4S,E*)-3-Ethylidene-4-(2-methoxy-2-oxoethyl)-2-  
{[(*2R,3S,4R,5S,6S*)-3,4,5-triacetoxy-6-(acetoxymethyl)tetrahydro-2*H*-pyran-2-yl]oxy}-3,4-  
dihydro-2*H*-pyran-5-carboxylic acid (**9**) in CDCl<sub>3</sub> (600 MHz).

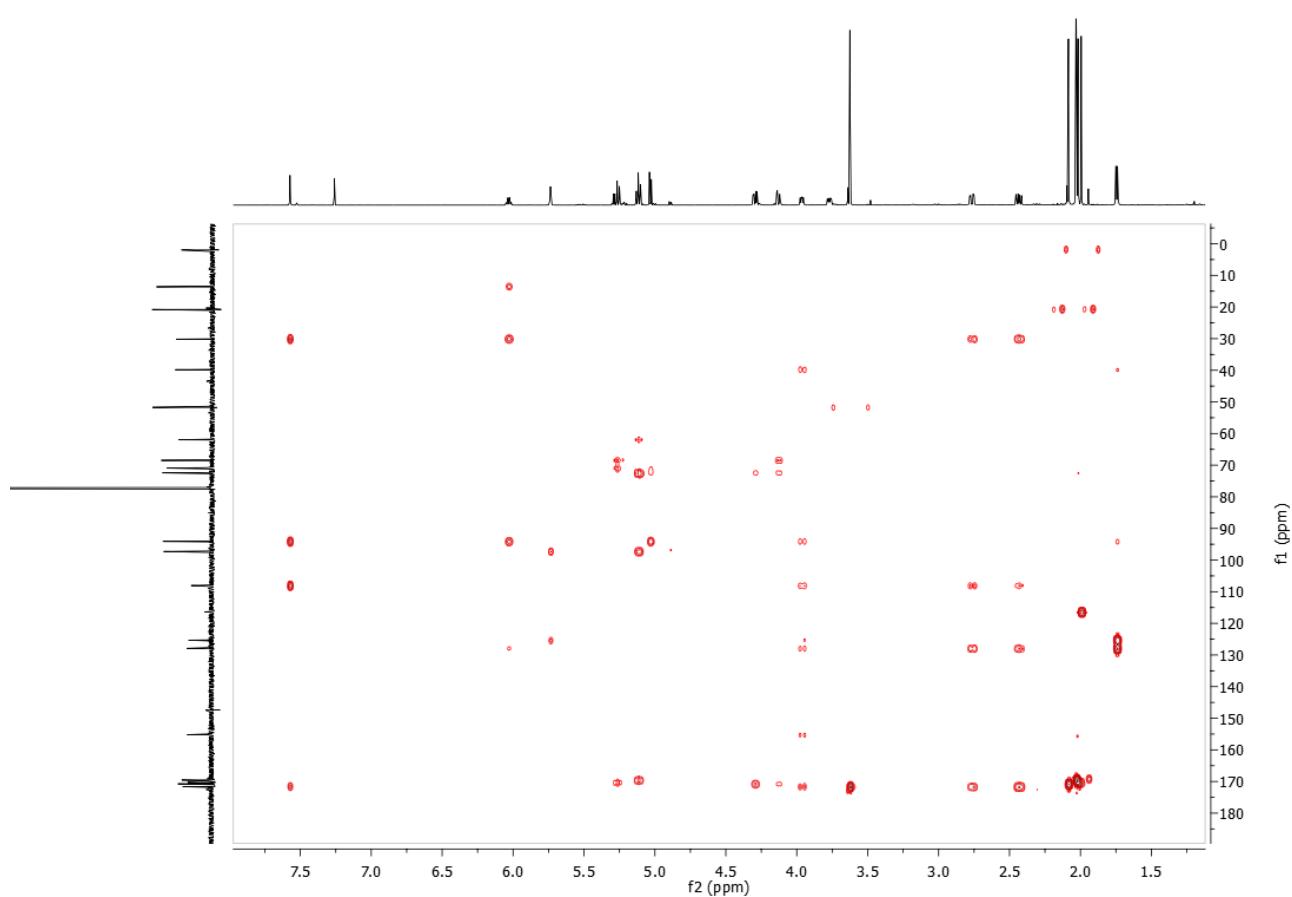


Figure S9. HMBC spectrum of (2*S*,4*S*,*E*)-3-Ethylidene-4-(2-methoxy-2-oxoethyl)-2-  
{[(2*R*,3*S*,4*R*,5*S*,6*S*)-3,4,5-triacetoxy-6-(acetoxymethyl)tetrahydro-2*H*-pyran-2-yl]oxy}-3,4-  
dihydro-2*H*-pyran-5-carboxylic acid (**9**) in CDCl<sub>3</sub> (600 MHz).

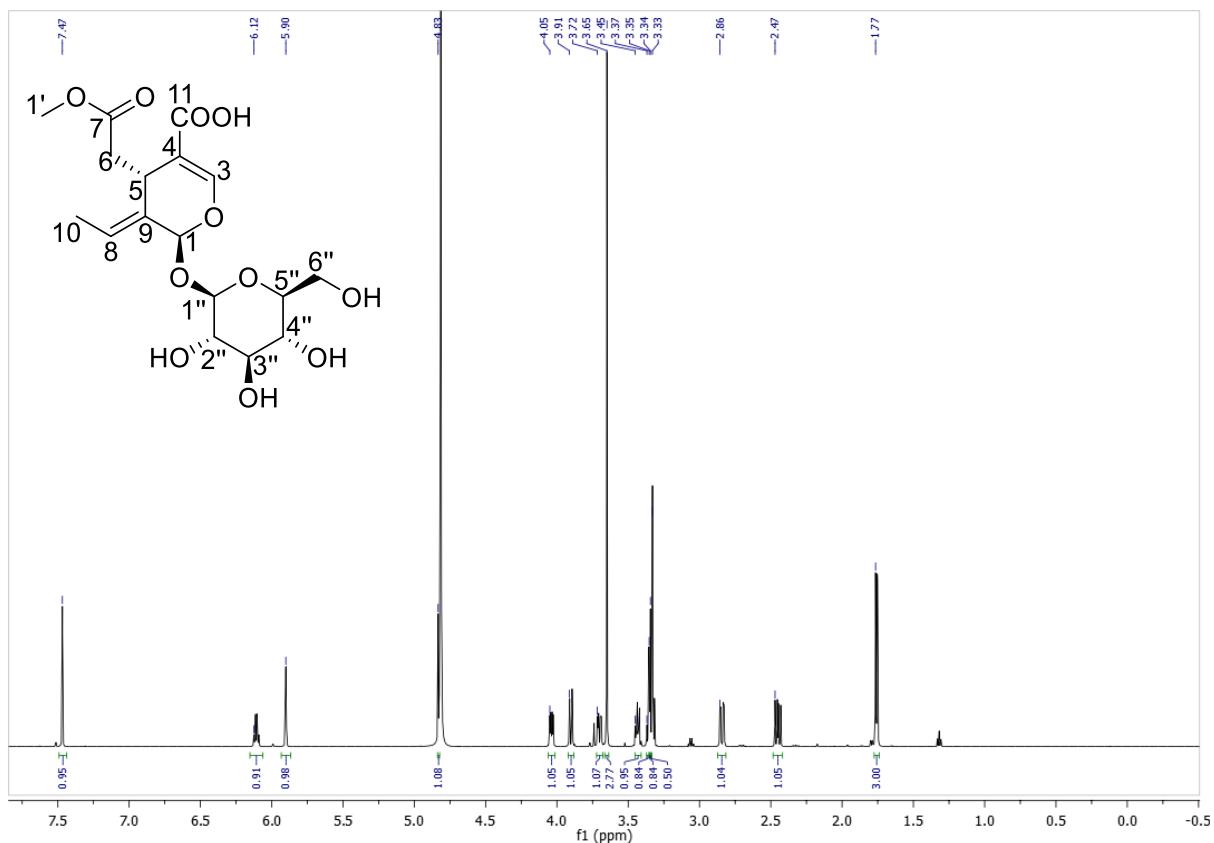


Figure S10.  $^1\text{H}$  NMR spectrum of (*2S,4S,E*)-3-Ethylidene-4-(2-methoxy-2-oxoethyl)-2-  
 $\{[(2R,3S,4R,5R,6S)-3,4,5\text{-trihydroxy-}6\text{-hydroxymethyl})\text{tetrahydro-}2H\text{-pyran-}2\text{-yl}]$ oxy}-  
 3,4dihydro-2*H*-pyran-5-carboxylic acid (**15**) in methanol –  $d_4$  (600 MHz).

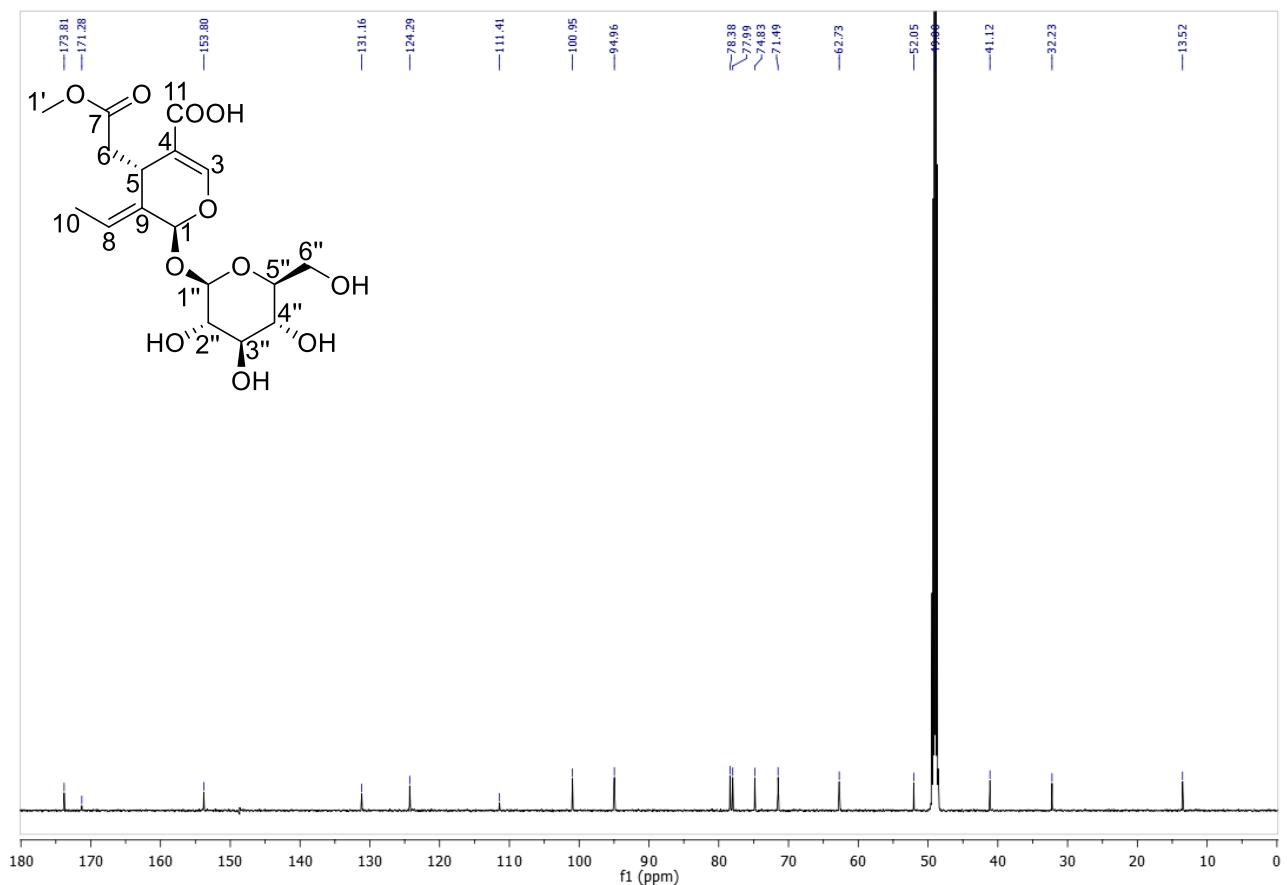


Figure S11.  $^{13}\text{C}$  NMR spectrum of (*2S,4S,E*)-3-Ethylidene-4-(2-methoxy-2-oxoethyl)-2-  
{[(*2R,3S,4R,5R,6S*)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2*H*-pyran-2-yl]oxy}-  
3,4dihydro-2*H*-pyran-5-carboxylic acid (**15**) in methanol –  $d_4$  (151 MHz).

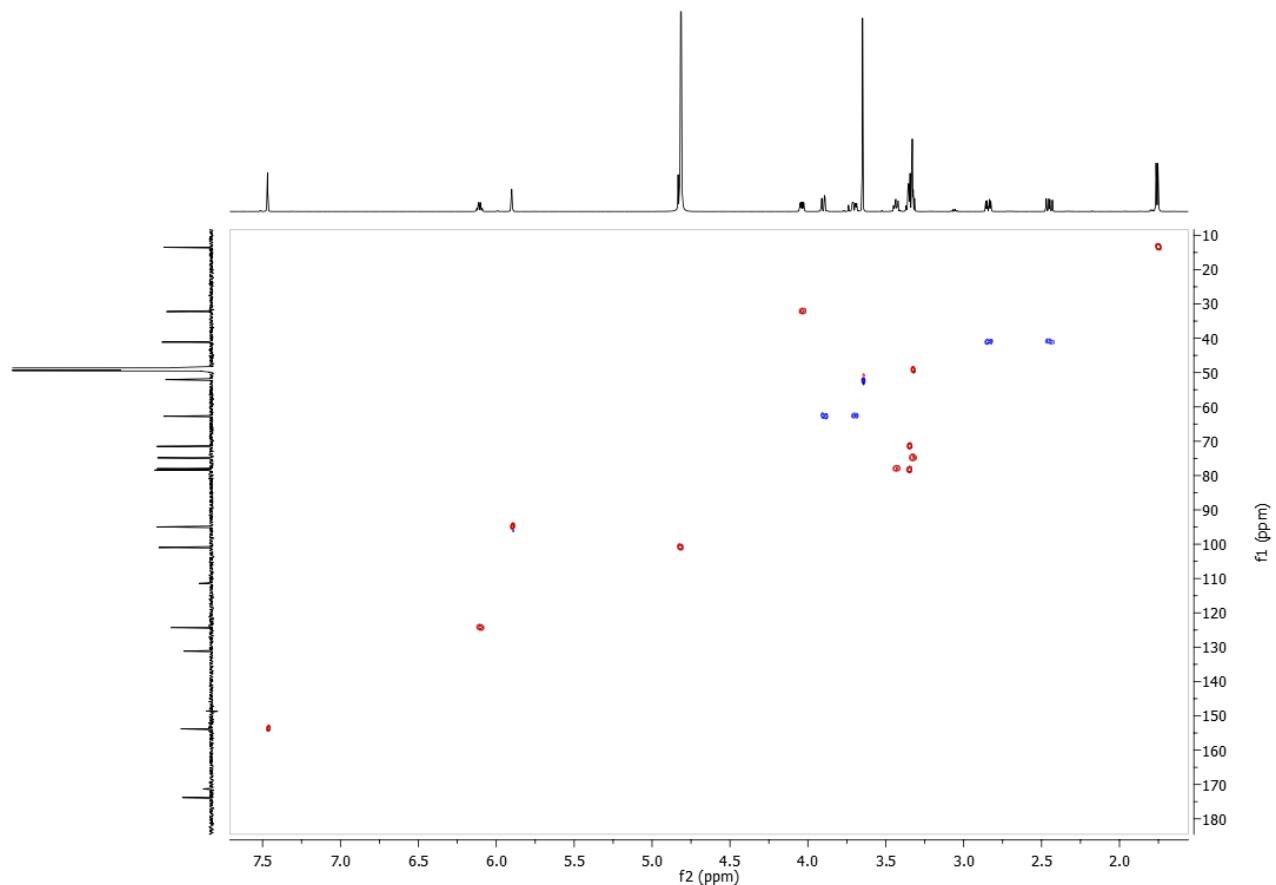


Figure S12. HSQC spectrum of (*2S,4S,E*)-3-Ethylidene-4-(2-methoxy-2-oxoethyl)-2-  
{[(*2R,3S,4R,5R,6S*)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2*H*-pyran-2-yl]oxy}-  
3,4dihydro-2*H*-pyran-5-carboxylic acid (**15**) in methanol – *d*<sub>4</sub> (600 MHz).

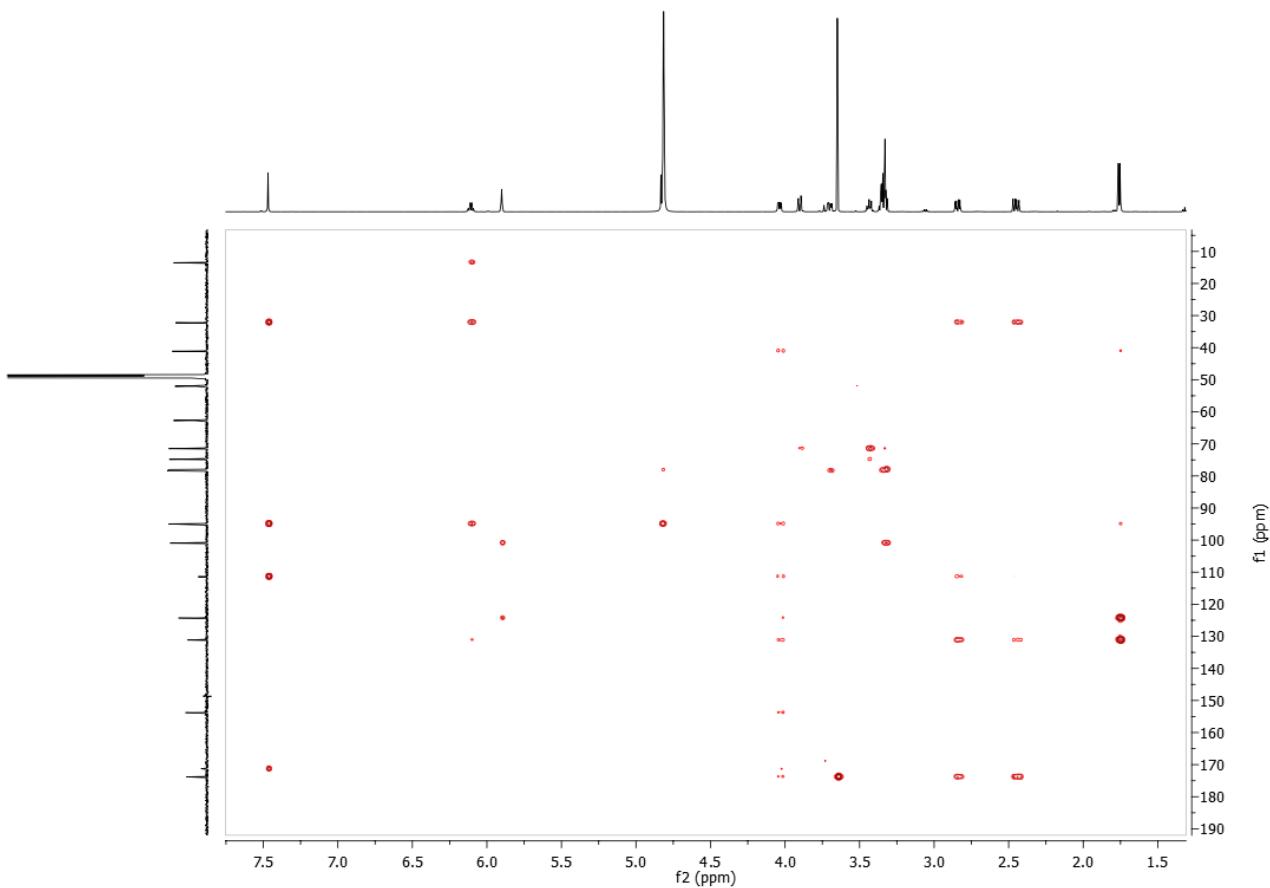


Figure S13. HMBC spectrum of (*2S,4S,E*)-3-Ethylidene-4-(2-methoxy-2-oxoethyl)-2-  
{[(*2R,3S,4R,5R,6S*)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2*H*-pyran-2-yl]oxy}-  
3,4dihydro-2*H*-pyran-5-carboxylic acid (**15**) in methanol – *d*<sub>4</sub> (600 MHz).

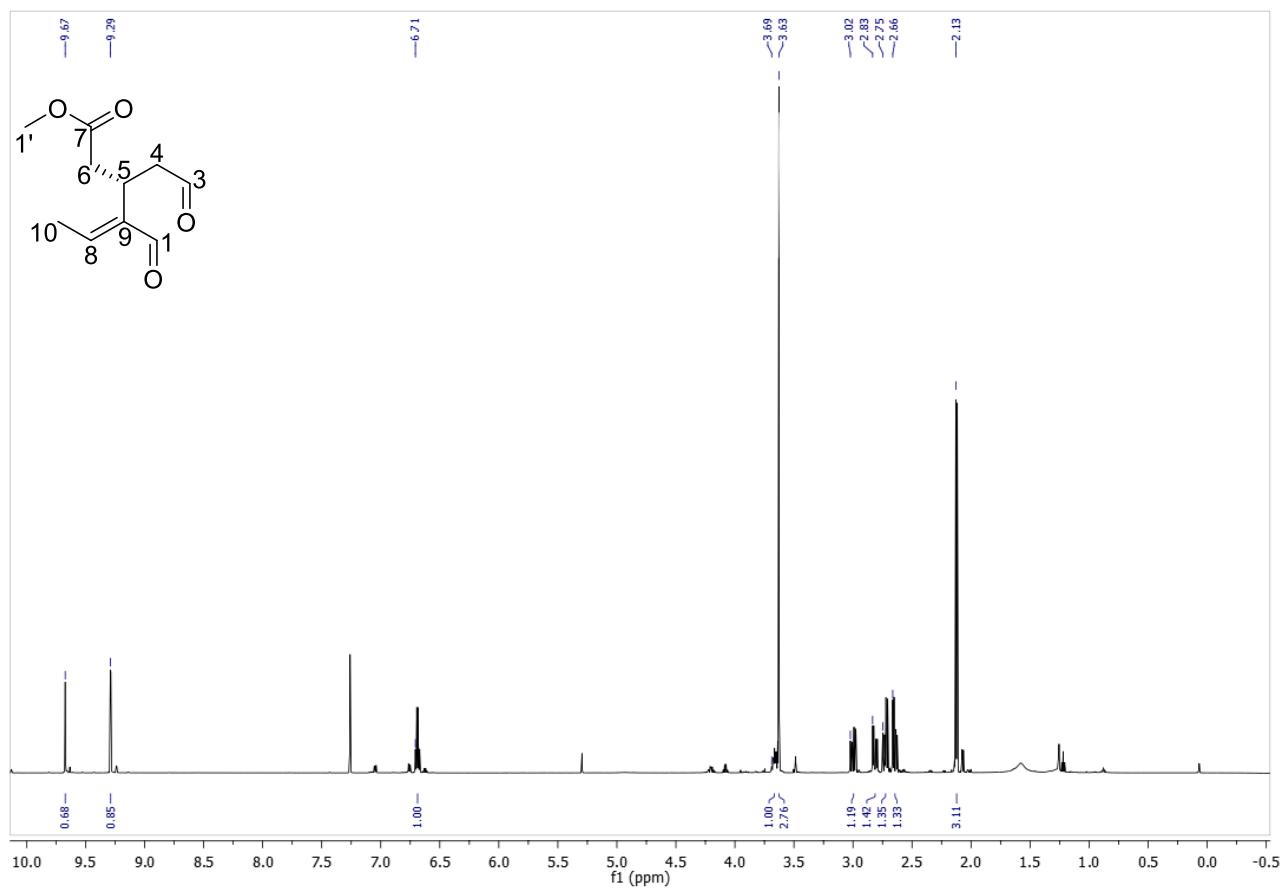


Figure S14. <sup>1</sup>H NMR spectrum of (*S,E*)-Methyl 4-Formyl-3-(2-oxoethyl)hex-4-enoate (**21**)  
in CDCl<sub>3</sub> (600 MHz).

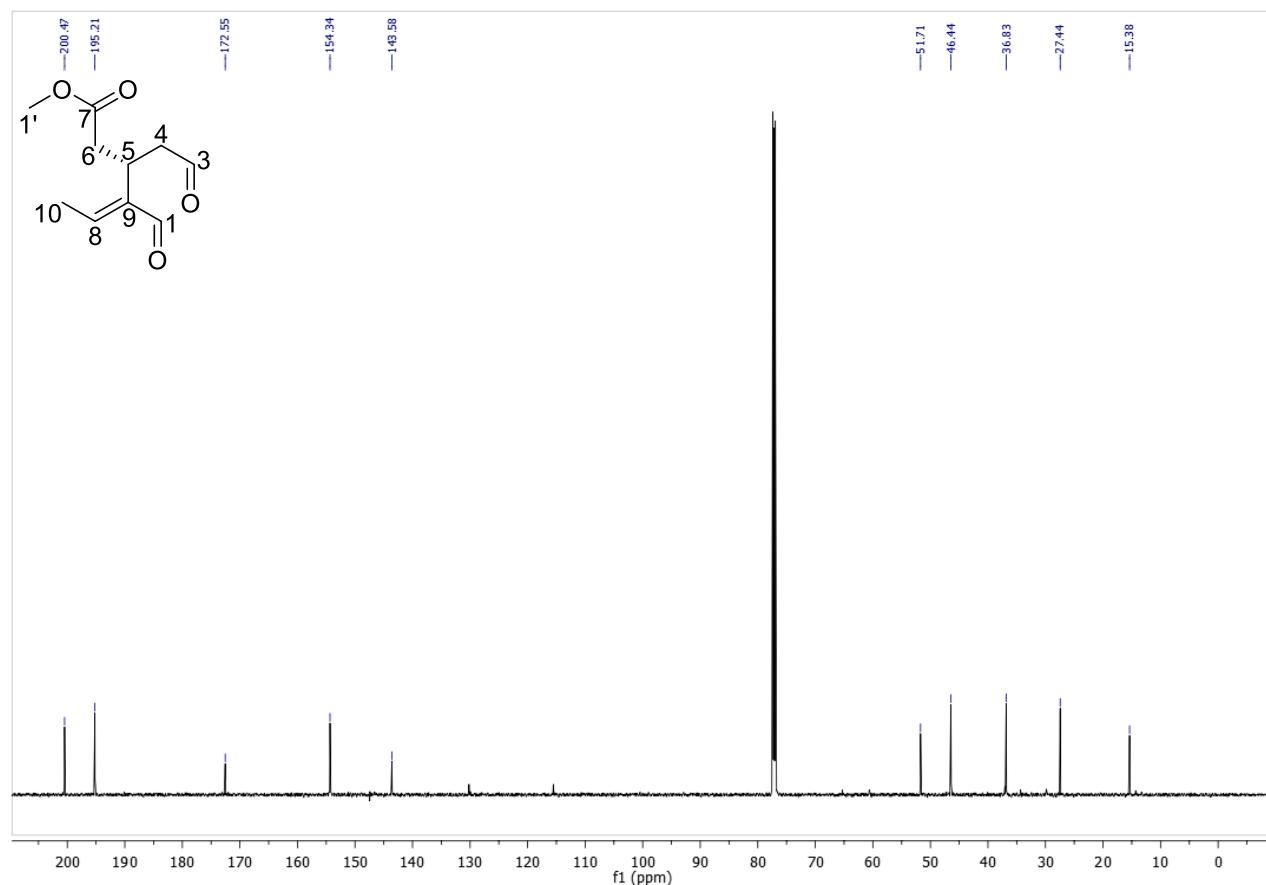


Figure S15.  $^{13}\text{C}$  NMR spectrum of (S,E)-Methyl 4-Formyl-3-(2-oxoethyl)hex-4-enoate (**21**)  
in  $\text{CDCl}_3$  (151 MHz).

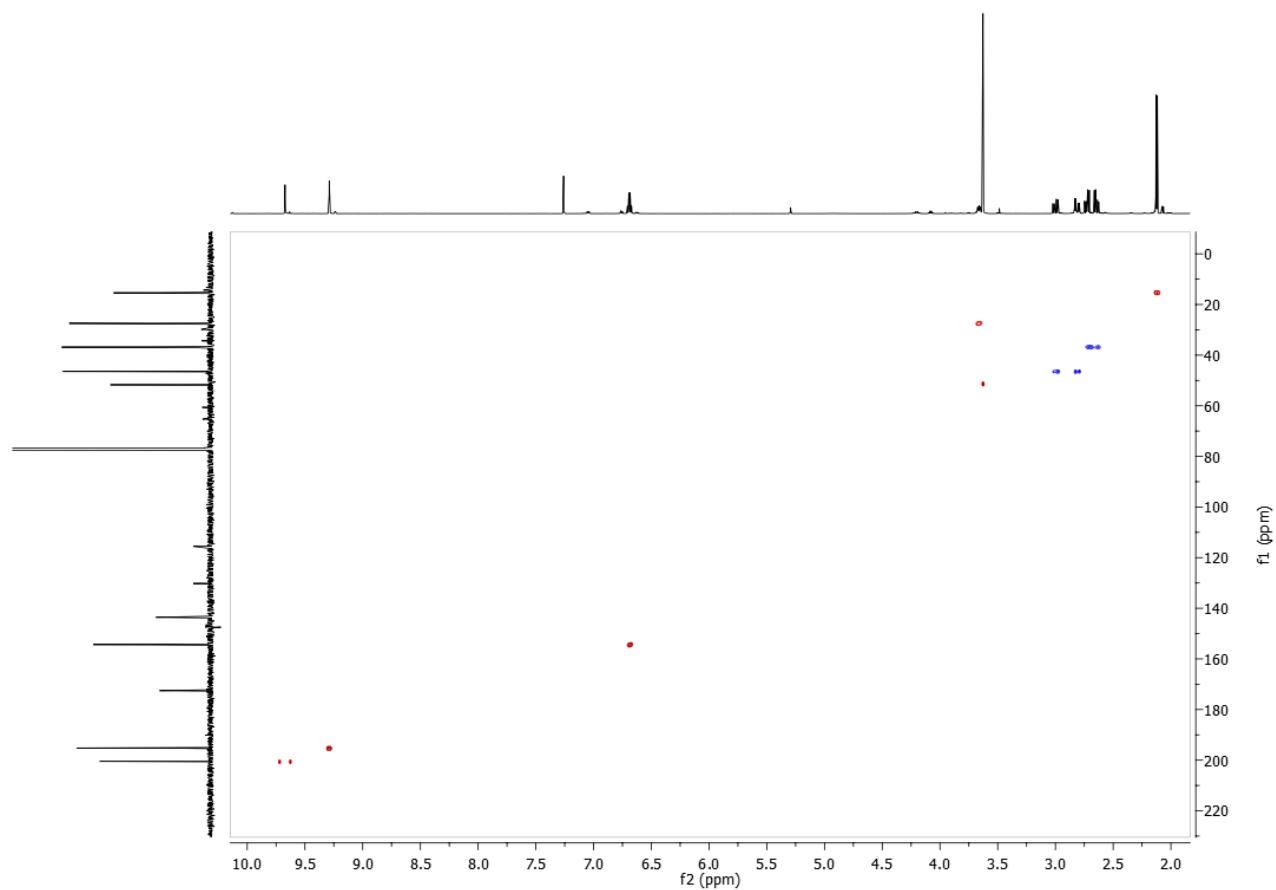


Figure S16. HSQC spectrum of (*S,E*)-Methyl 4-Formyl-3-(2-oxoethyl)hex-4-enoate (**21**) in  $\text{CDCl}_3$  (600 MHz).

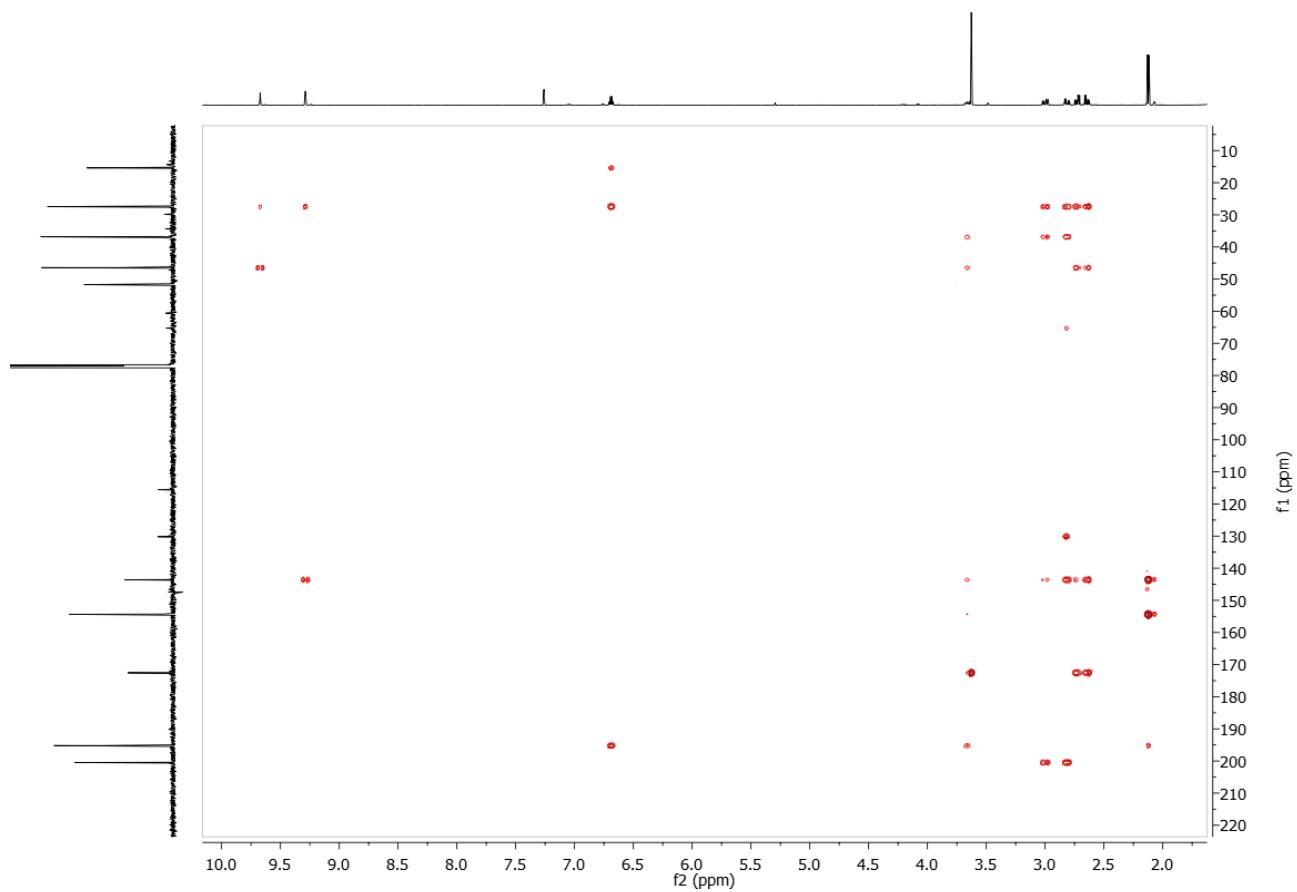


Figure S17. HMBC spectrum of (*S,E*)-methyl 4-Formyl-3-(2-oxoethyl)hex-4-enoate (**21**) in  $\text{CDCl}_3$  (600 MHz).

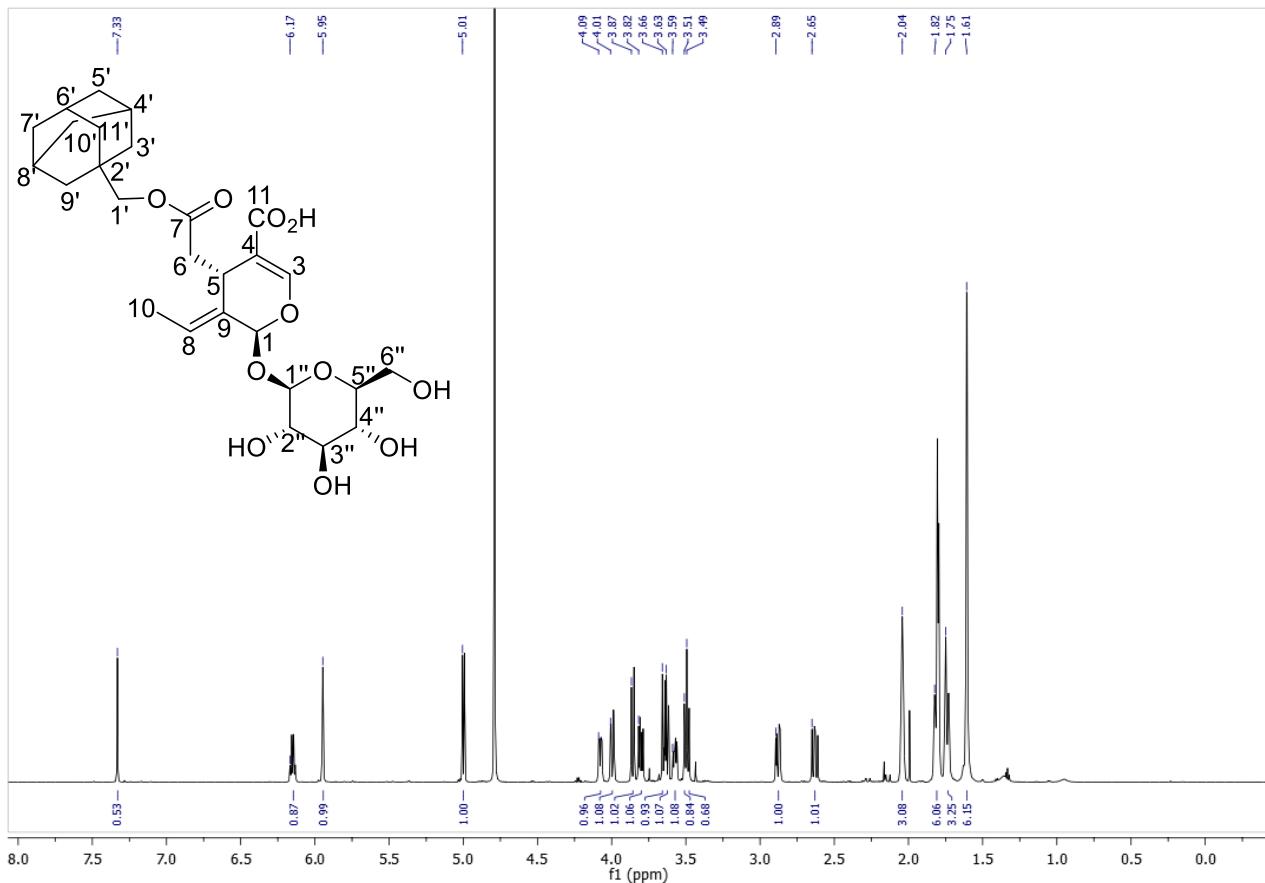


Figure S18. <sup>1</sup>H NMR spectrum of (2*S*,4*S*,*E*)-4-(Adamantan-1-ylmethoxy)-2-oxoethyl)-3-ethylidene-2-{[(2*R*,3*S*,4*R*,5*R*,6*S*)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2*H*-pyran-2-yl]oxy}-3,4-dihydro-2*H*-pyran-5-carboxylic acid (**18**) in D<sub>2</sub>O (600 MHz).

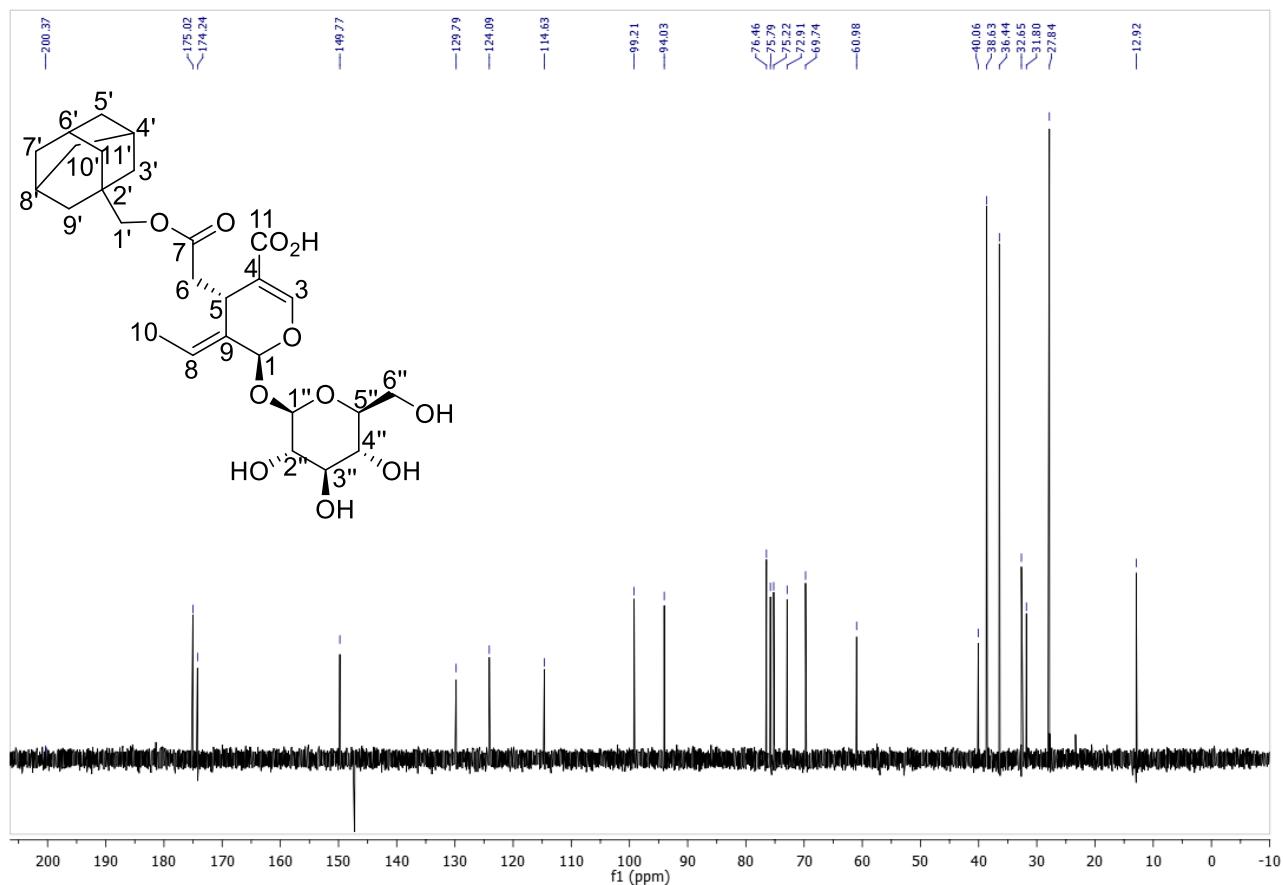


Figure S19.  $^{13}\text{C}$  NMR spectrum of  $(2S,4S,E)$ -4-(2-(Adamantan-1-ylmethoxy)-2-oxoethyl)-3-ethylidene-2- $\{[(2R,3S,4R,5R,6S)-3,4,5\text{-trihydroxy}-6\text{-}(hydroxymethyl)tetrahydro-2H-pyran-2-yl]oxy\}$ -3,4-dihydro-2*H*-pyran-5-carboxylic acid (**18**) in  $\text{D}_2\text{O}$  (151 MHz).

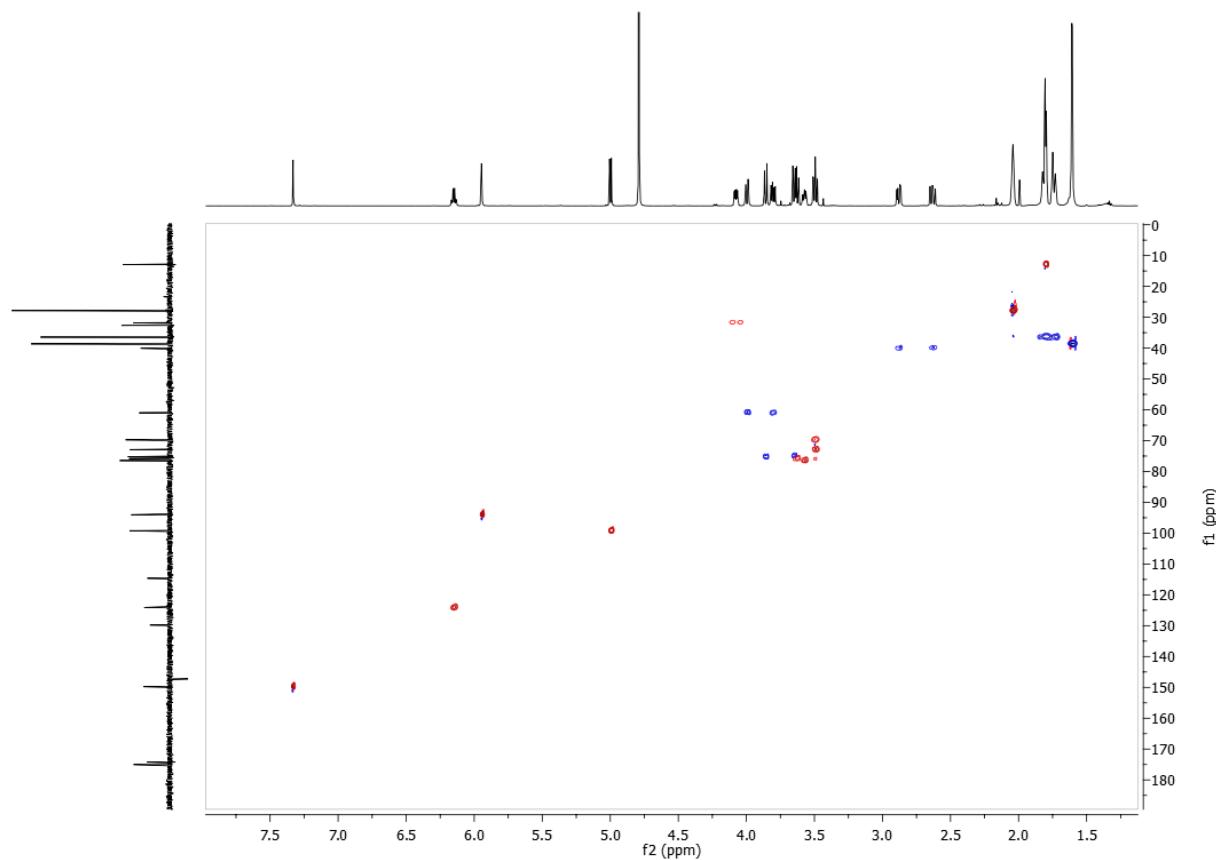


Figure S20. HSQC spectrum of (*2S,4S,E*)-4-(2-(Adamantan-1-ylmethoxy)-2-oxoethyl)-3-ethylidene-2-[(*2R,3S,4R,5R,6S*)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2H-pyran-2-yl]oxy}-3,4-dihydro-2H-pyran-5-carboxylic acid (**18**) in D<sub>2</sub>O (600 MHz).

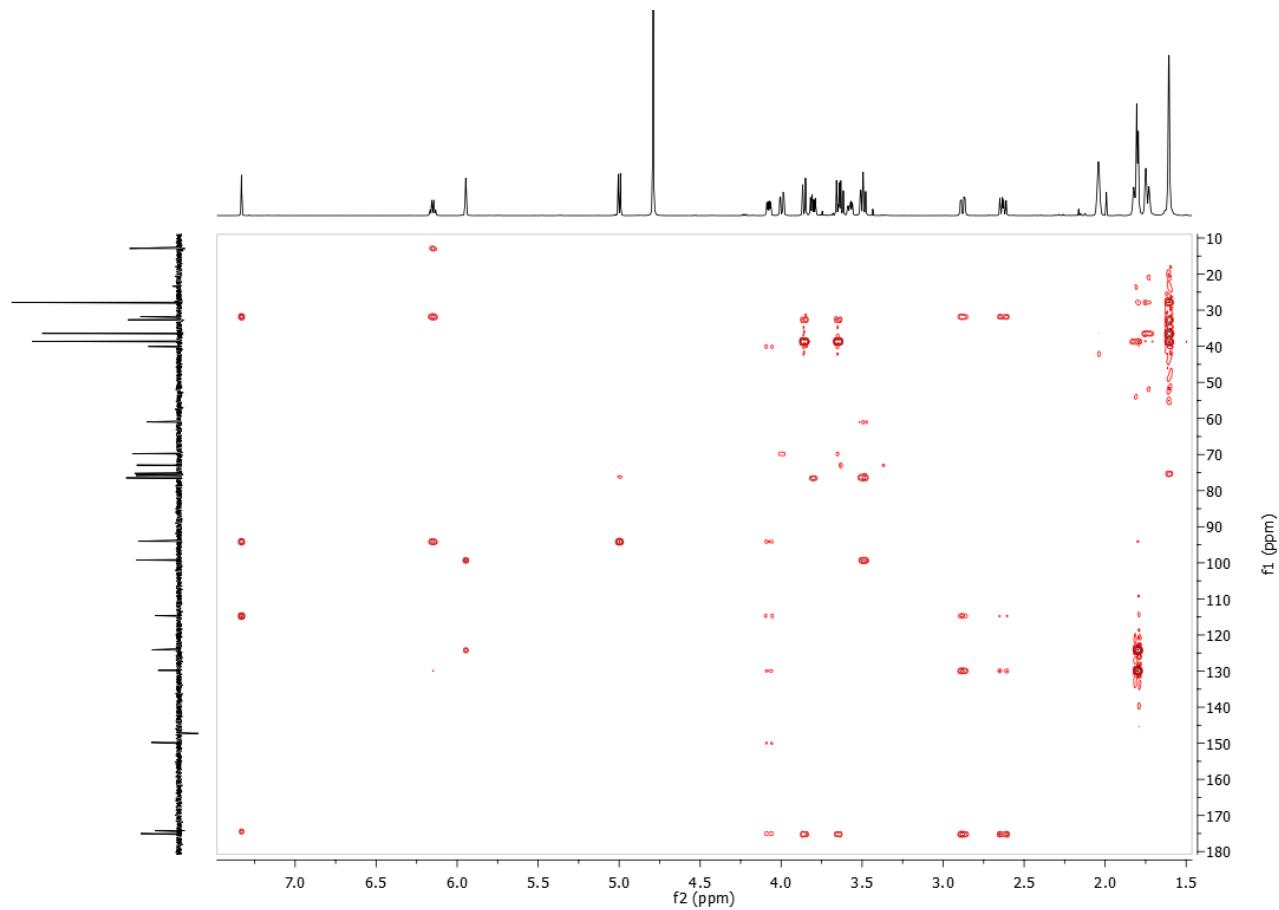


Figure S21. HMBC spectrum of (*2S,4S,E*)-4-(Adamantan-1-ylmethoxy)-2-oxoethyl)-3-ethylidene-2-[(*2R,3S,4R,5R,6S*)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2*H*-pyran-2-yl]oxy}-3,4-dihydro-2*H*-pyran-5-carboxylic acid (**18**) in  $\text{D}_2\text{O}$  (600 MHz).

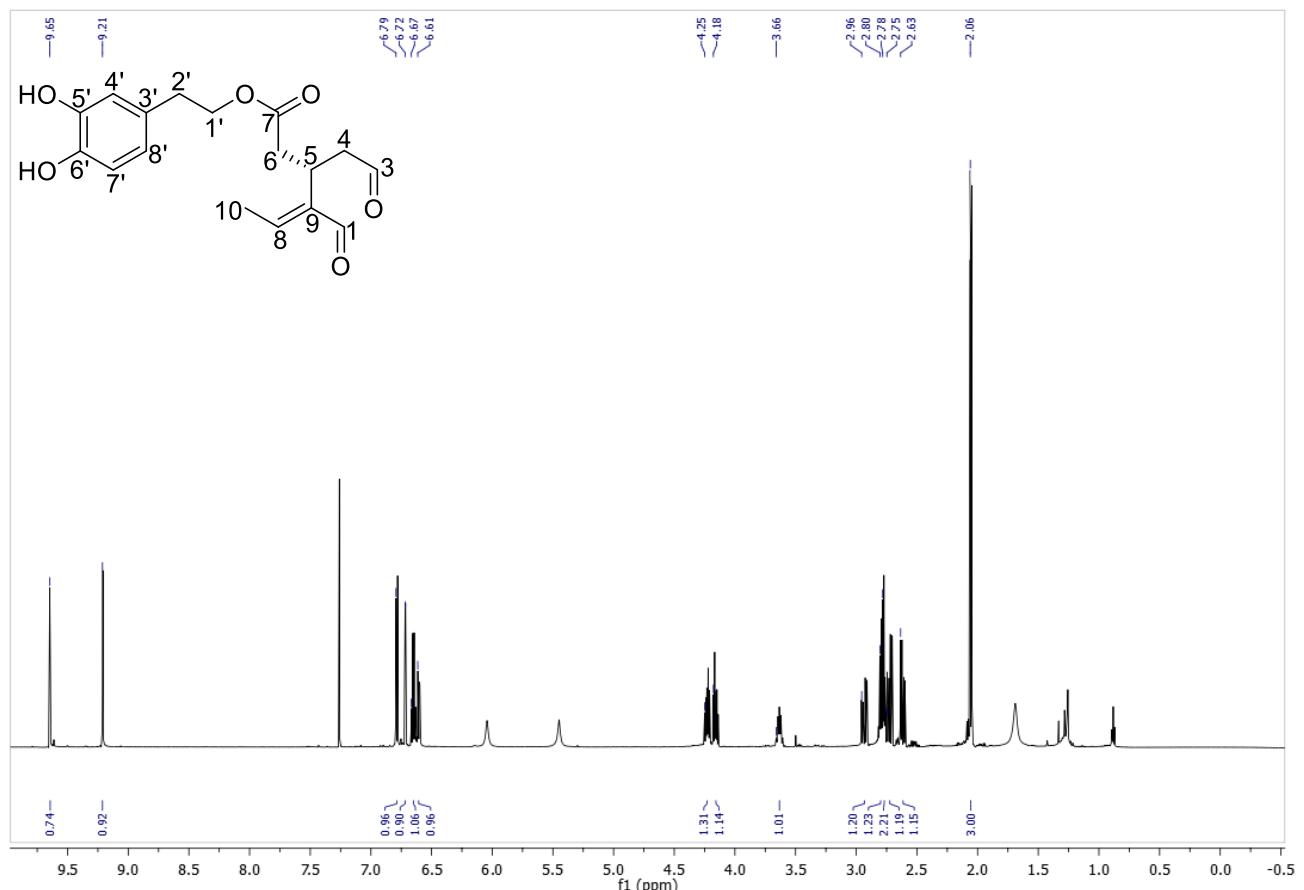


Figure S22. <sup>1</sup>H NMR spectrum of oleacein (**5**) in CDCl<sub>3</sub> (600 MHz).

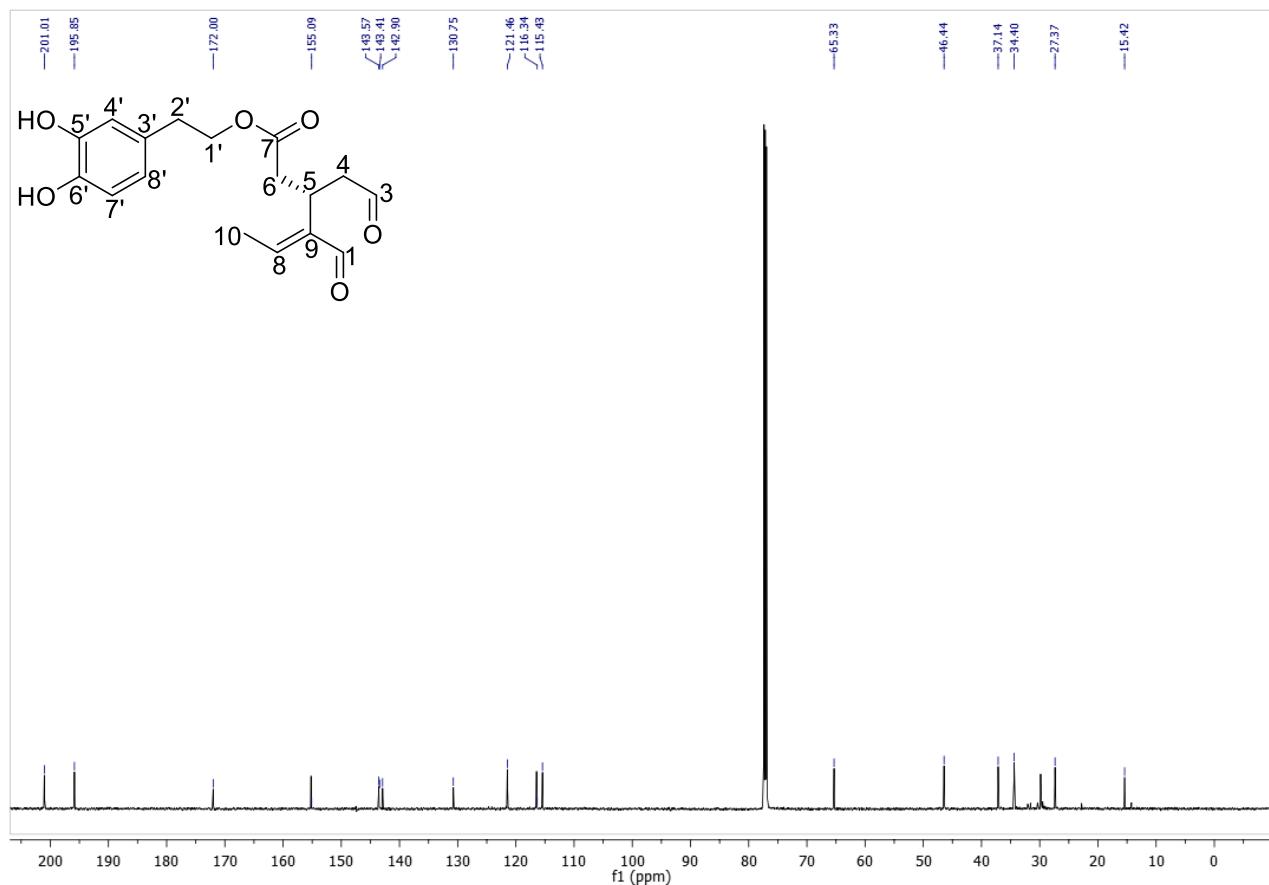


Figure S23.  $^{13}\text{C}$  NMR spectrum of oleacein (**5**) in  $\text{CDCl}_3$  (151 MHz).

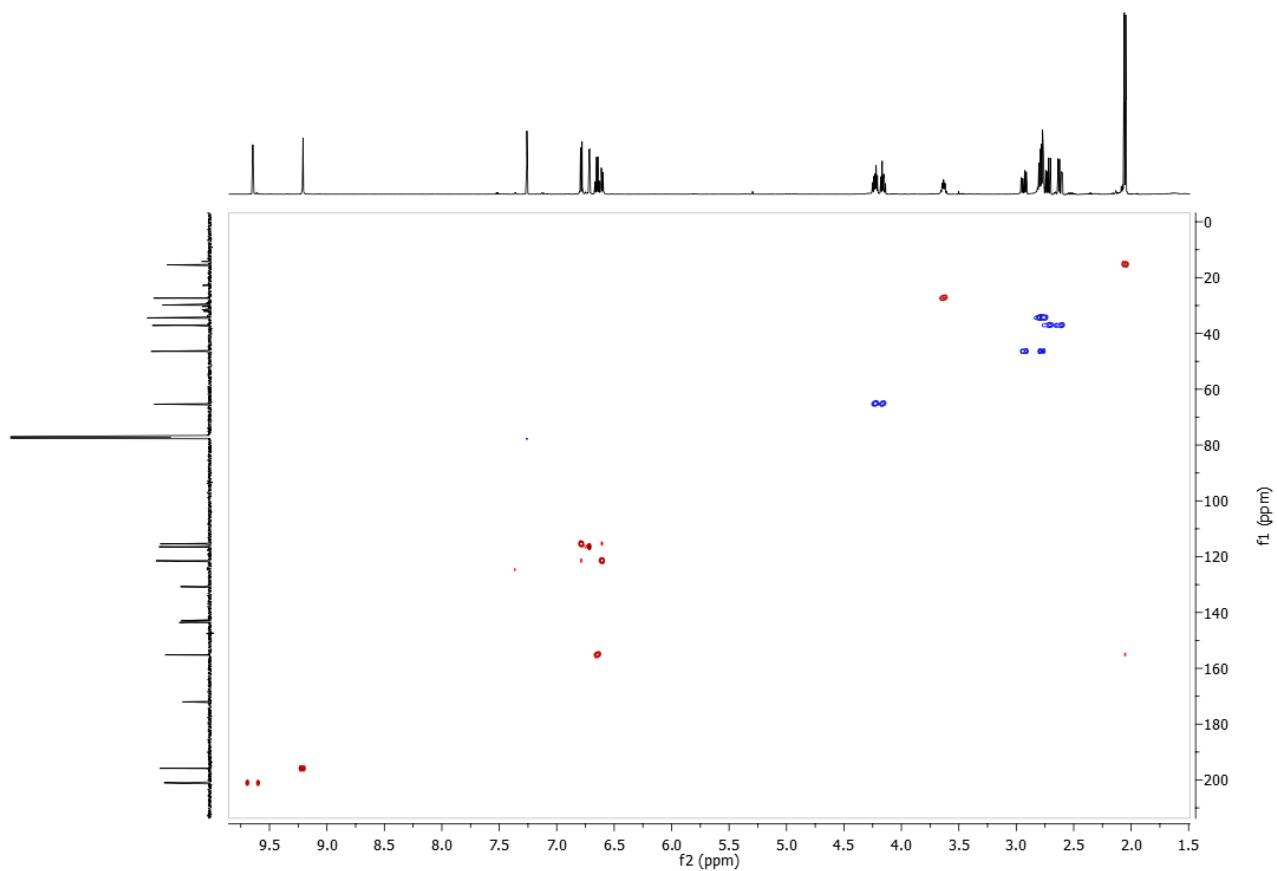


Figure S24. HSQC spectrum of oleacein (**5**) in  $\text{CDCl}_3$  (600 MHz).

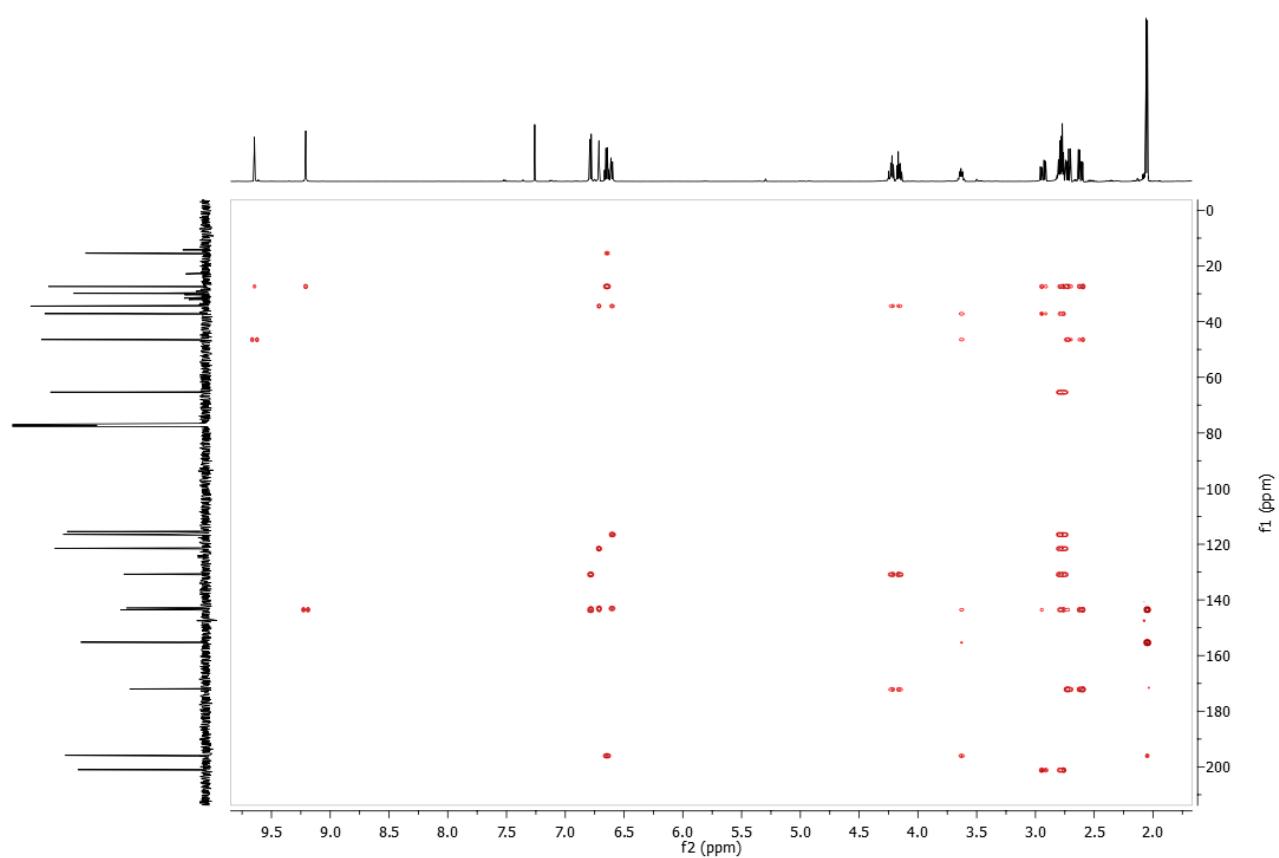


Figure S25. HMBC spectrum of oleacein (**5**) in  $\text{CDCl}_3$  (600 MHz).

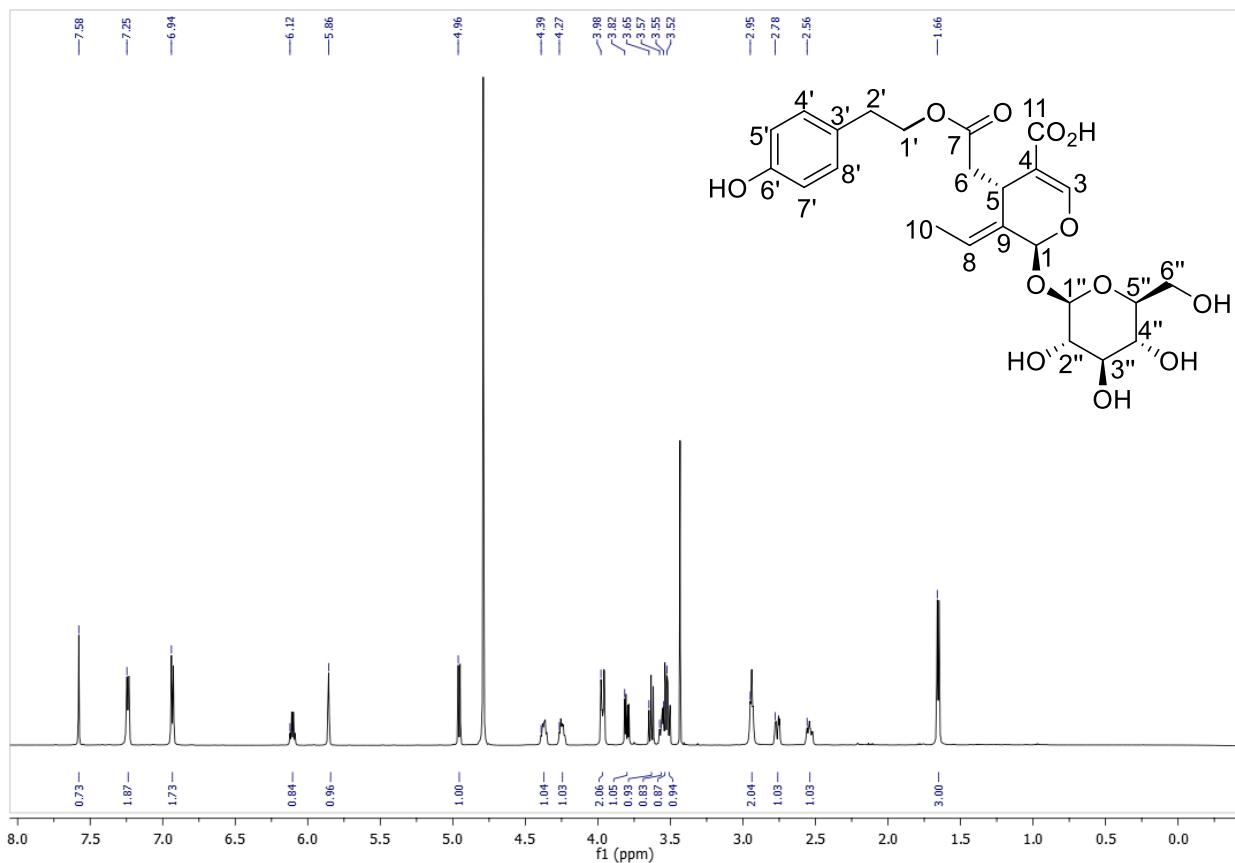


Figure S26. <sup>1</sup>H NMR spectrum of (2*S*,4*S*,*E*)-3-Ethylidene-4-(2-(4-hydroxyphenethoxy)-2-oxoethyl)-2-[(2*R*,3*S*,4*R*,5*R*,6*S*)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2*H*-pyran-2-yl]oxy}-3,4-dihydro-2*H*-pyran-5-carboxylic acid (**20**) in  $\text{D}_2\text{O}$  (600 MHz).

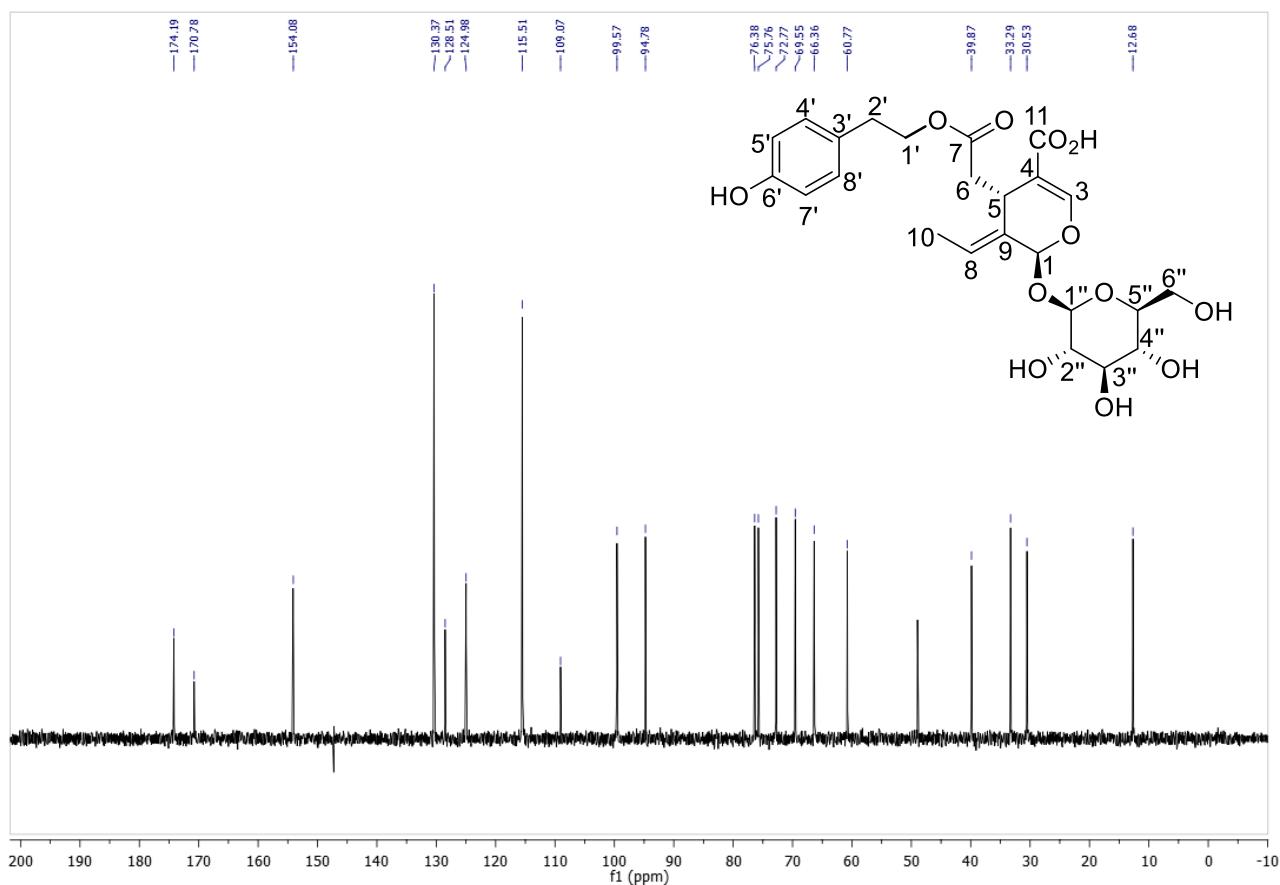


Figure S27.  $^{13}\text{C}$  NMR spectrum of  $(2S,4S,E)$ -3-Ethylidene-4-(2-(4-hydroxyphenethoxy)-2-oxoethyl)-2- $\{[(2R,3S,4R,5R,6S)-3,4,5\text{-trihydroxy-}6\text{-(hydroxymethyl)tetrahydro-}2H\text{-pyran-}2\text{-yl}]$ oxy}-3,4-dihydro-2H-pyran-5-carboxylic acid (**20**) in  $\text{D}_2\text{O}$  (151 MHz).

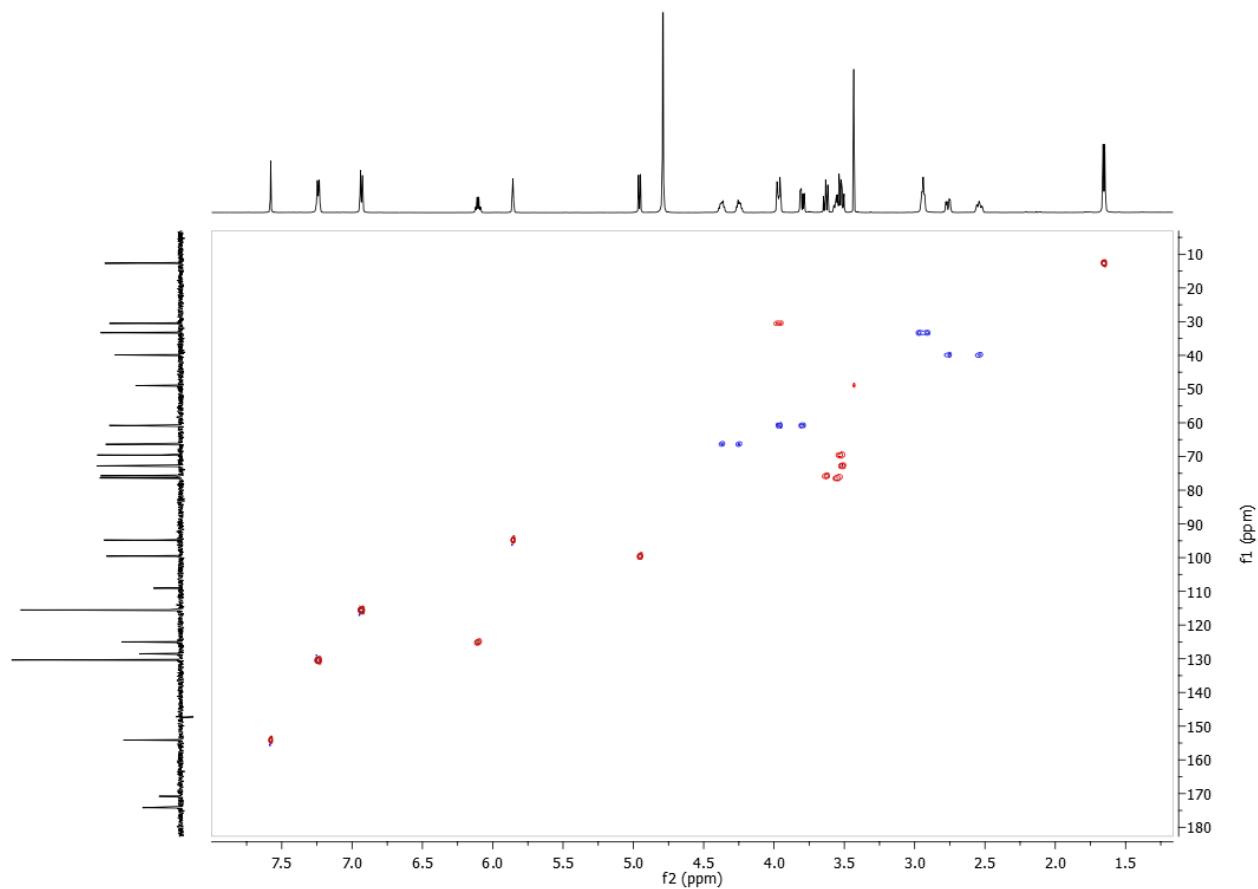


Figure S28. HSQC spectrum of (*2S,4S,E*)-3-Ethyldene-4-(2-(4-hydroxyphenethoxy)-2-oxoethyl)-2-[(*2R,3S,4R,5R,6S*)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2*H*-pyran-2-yl]oxy}-3,4-dihydro-2*H*-pyran-5-carboxylic acid (**20**) in D<sub>2</sub>O (600 MHz).

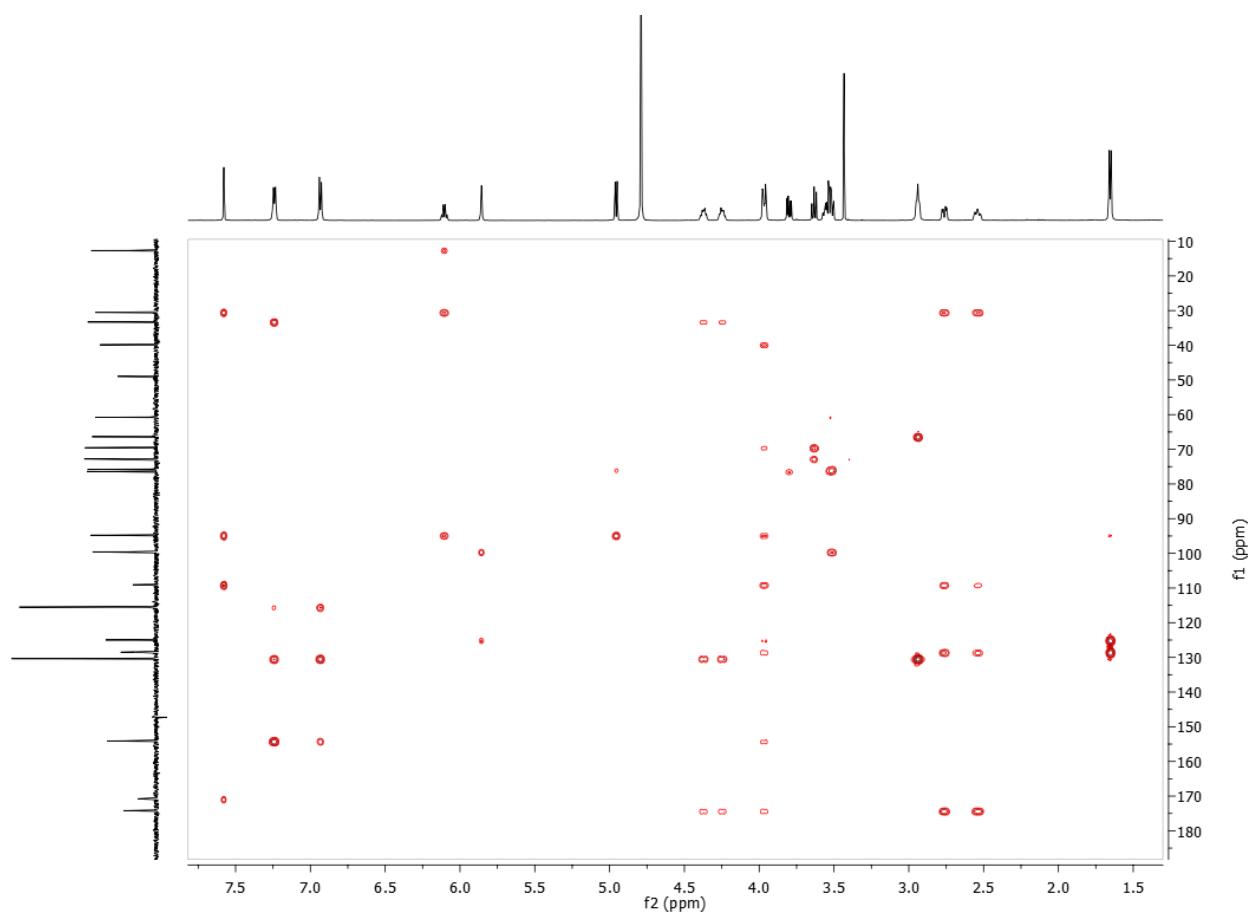


Figure S29. HMBC spectrum of (*2S,4S,E*)-3-Ethylidene-4-(2-(4-hydroxyphenethoxy)-2-oxoethyl)-2-[(*2R,3S,4R,5R,6S*)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2*H*-pyran-2-yl]oxy}-3,4-dihydro-2*H*-pyran-5-carboxylic acid (**20**) in D<sub>2</sub>O (600 MHz).

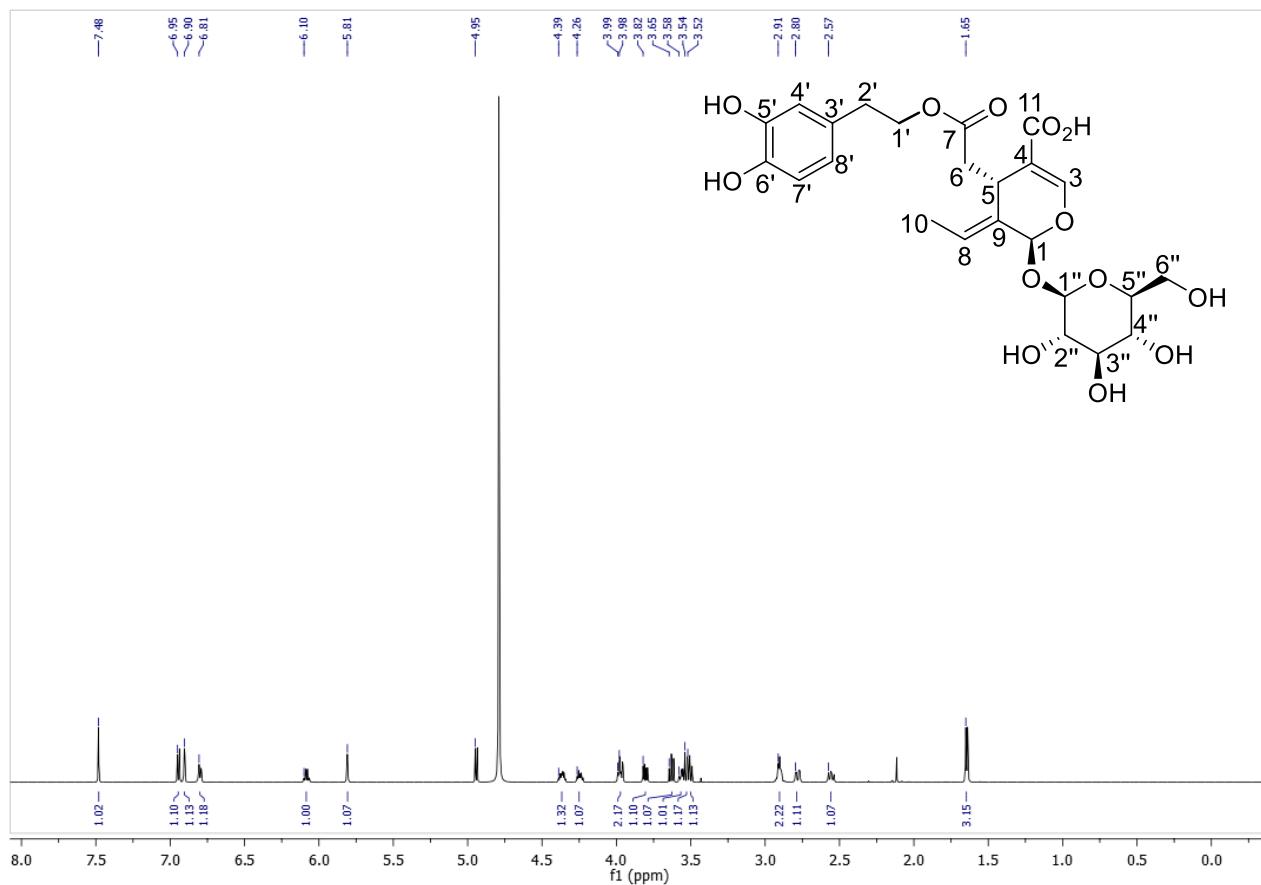


Figure S30. <sup>1</sup>H NMR spectrum of (2*S*,4*S*,*E*)-4-(2-(3,4-Dihydroxyphenethoxy)-2-oxoethyl)-3-ethylidene-2-{{[(2*R*,3*S*,4*R*,5*R*,6*S*)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2*H*-pyran-2-yl]oxy}-3,4-dihydro-2*H*-pyran-5-carboxylic acid (**19**) in D<sub>2</sub>O (600 MHz).

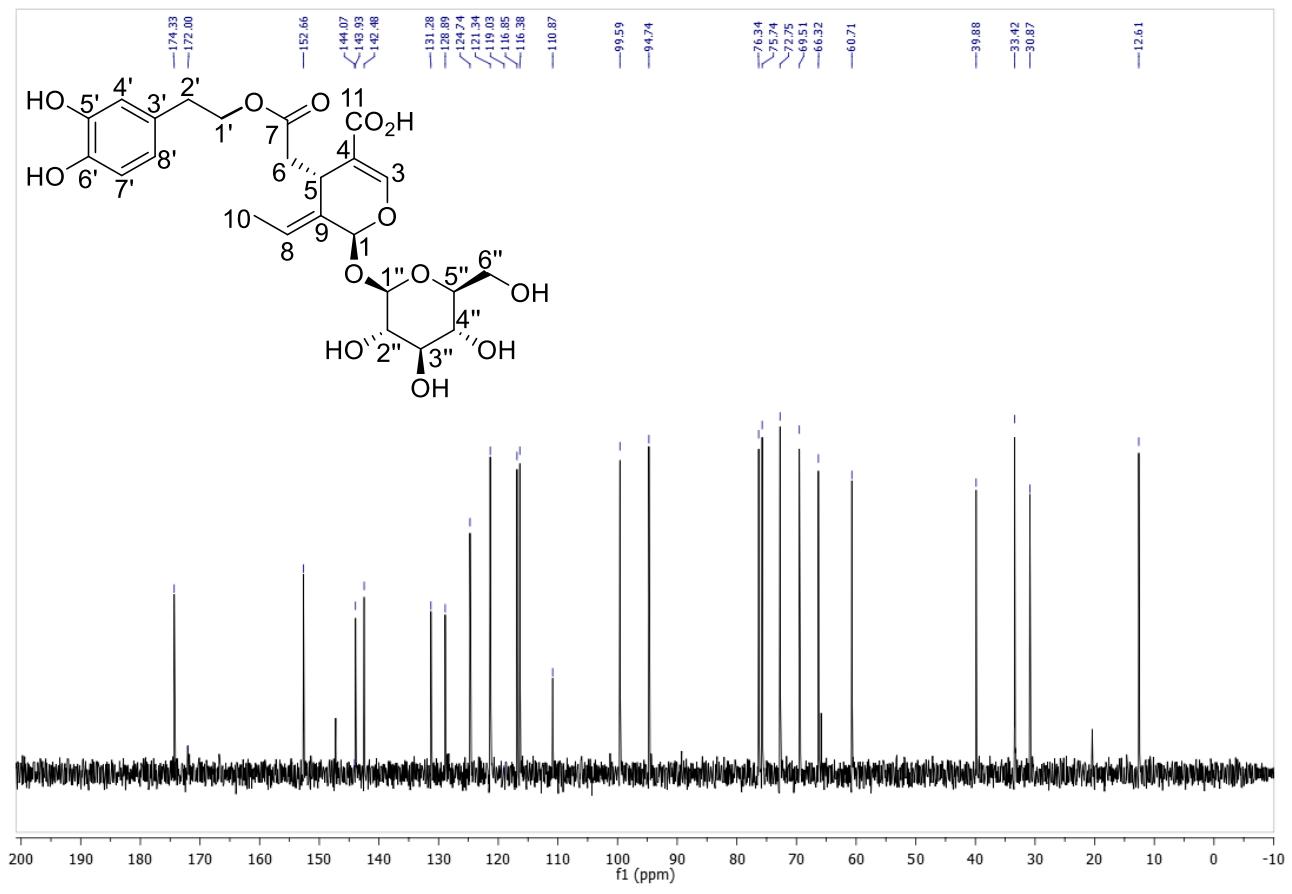


Figure S31.  $^{13}\text{C}$  NMR spectrum of  $(2S,4S,E)$ -4-(2-(3,4-Dihydroxyphenethoxy)-2-oxoethyl)-3-ethylidene-2- $\{(2R,3S,4R,5R,6S)\text{-}3,4,5\text{-trihydroxy-6-(hydroxymethyl)tetrahydro-2}H\text{-pyran-2-yl}\text{oxy}\}$ -3,4-dihydro-2*H*-pyran-5-carboxylic acid (**19**) in  $\text{D}_2\text{O}$  (151 MHz).

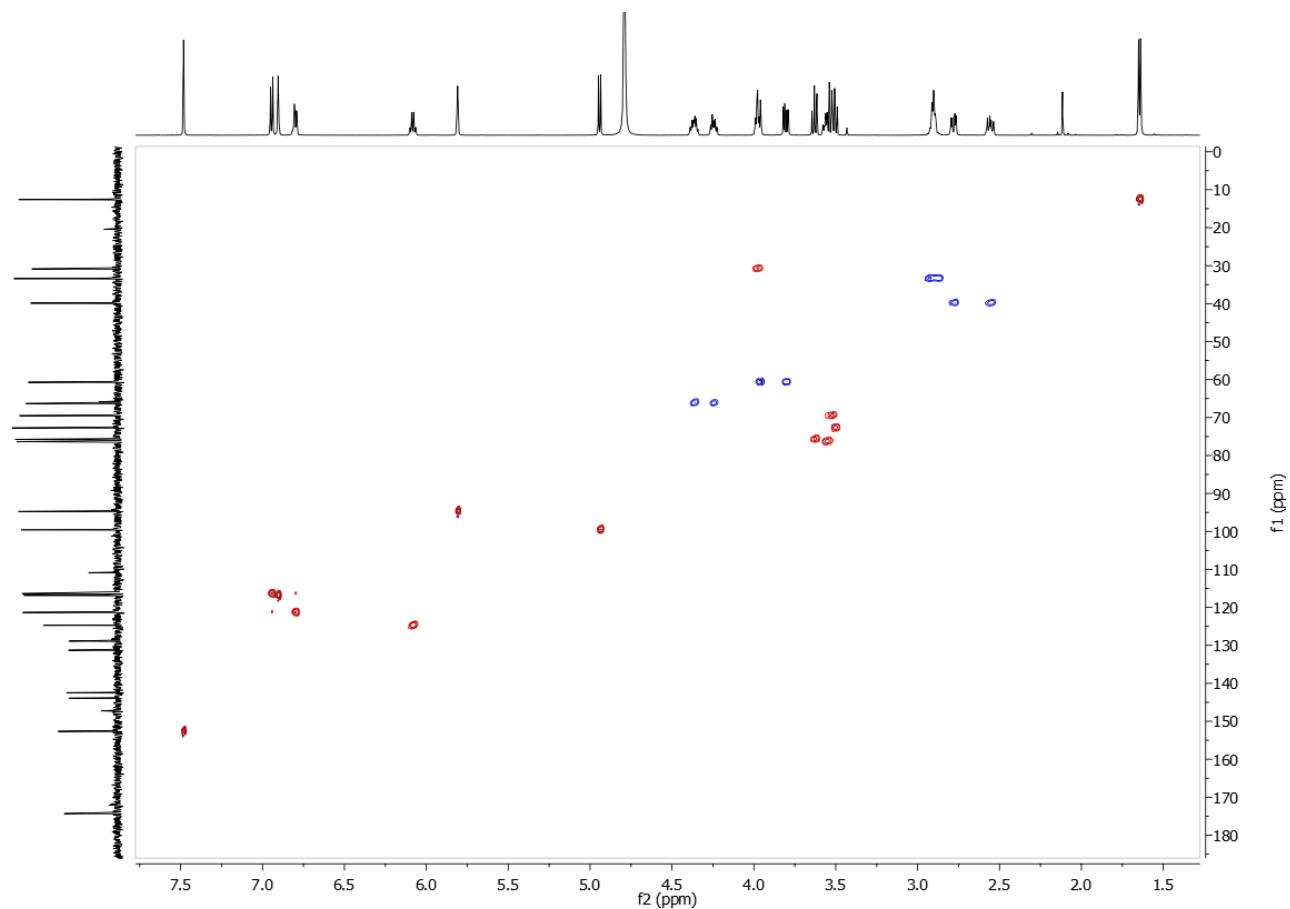


Figure S32. HSQC spectrum of (*2S,4S,E*)-4-(2-(3,4-Dihydroxyphenethoxy)-2-oxoethyl)-3-ethylidene-2-[(*2R,3S,4R,5R,6S*)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2*H*-pyran-2-yl]oxy}-3,4-dihydro-2*H*-pyran-5-carboxylic acid (**19**) in D<sub>2</sub>O (600 MHz).

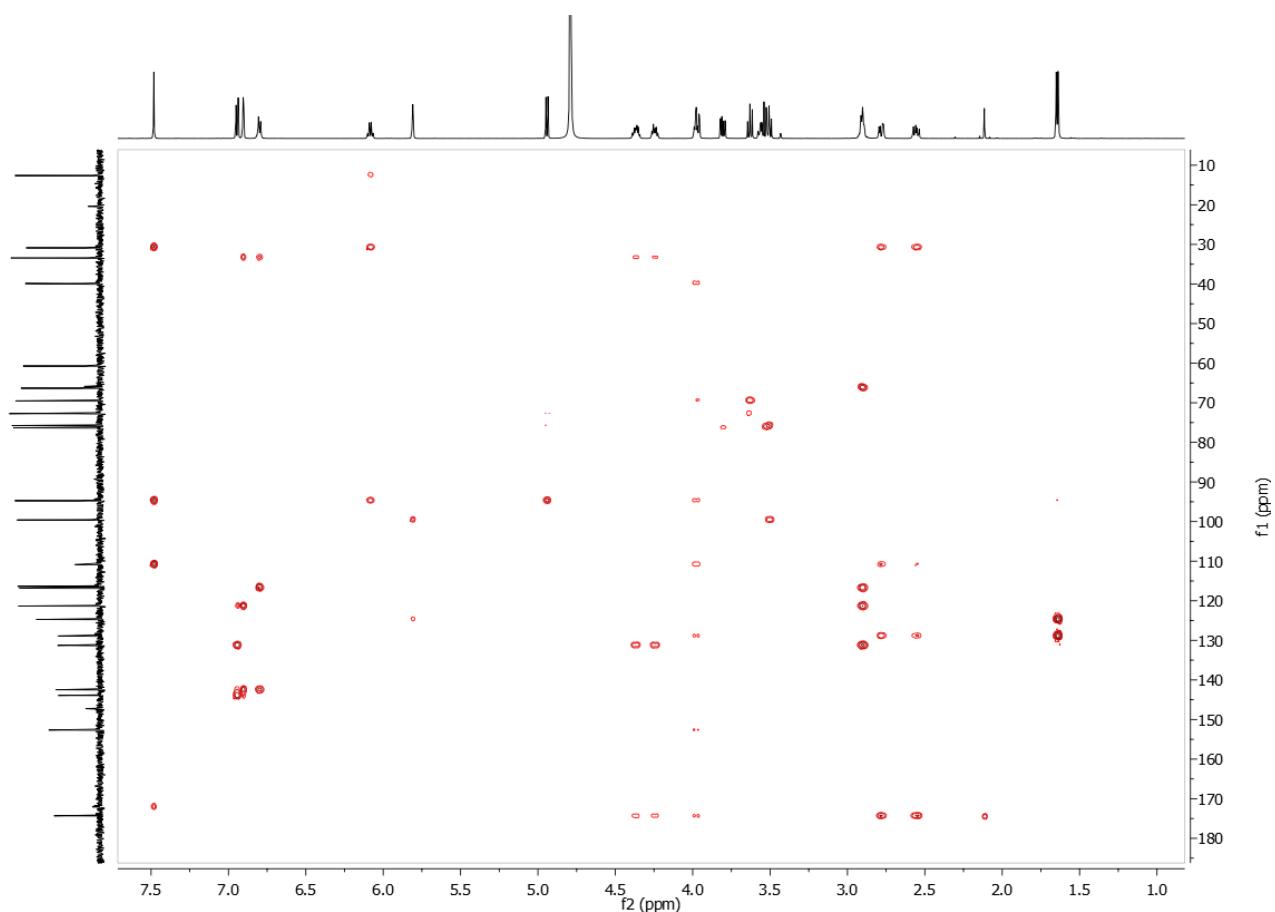


Figure S33. HMBC spectrum of (*2S,4S,E*)-4-(2-(3,4-Dihydroxyphenethoxy)-2-oxoethyl)-3-ethylidene-2-[(*2R,3S,4R,5R,6S*)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2*H*-pyran-2-yl]oxy}-3,4-dihydro-2*H*-pyran-5-carboxylic acid (**19**) in D<sub>2</sub>O (600 MHz).

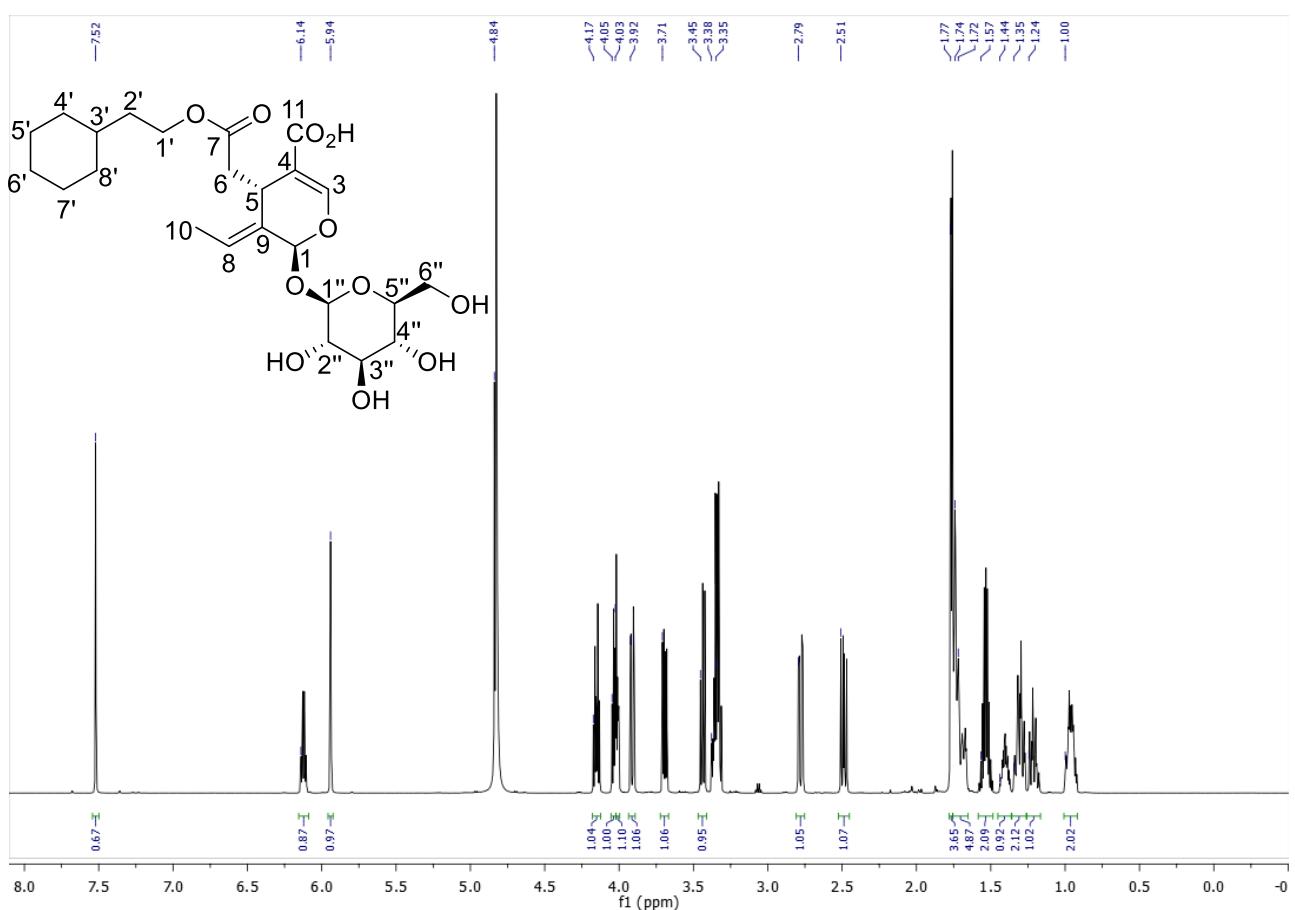


Figure S34.  $^1\text{H}$  NMR spectrum of  $(2S,4S,E)$ -4-(2-(2-Cyclohexylethoxy)-2-oxoethyl)-3-ethylidene-2- $\{(2R,3S,4R,5R,6S)$ -3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2*H*-pyran-2-yl]oxy}-3,4-dihydro-2*H*-pyran-5-carboxylic acid (**16**) in methanol- $d_4$  (600 MHz).

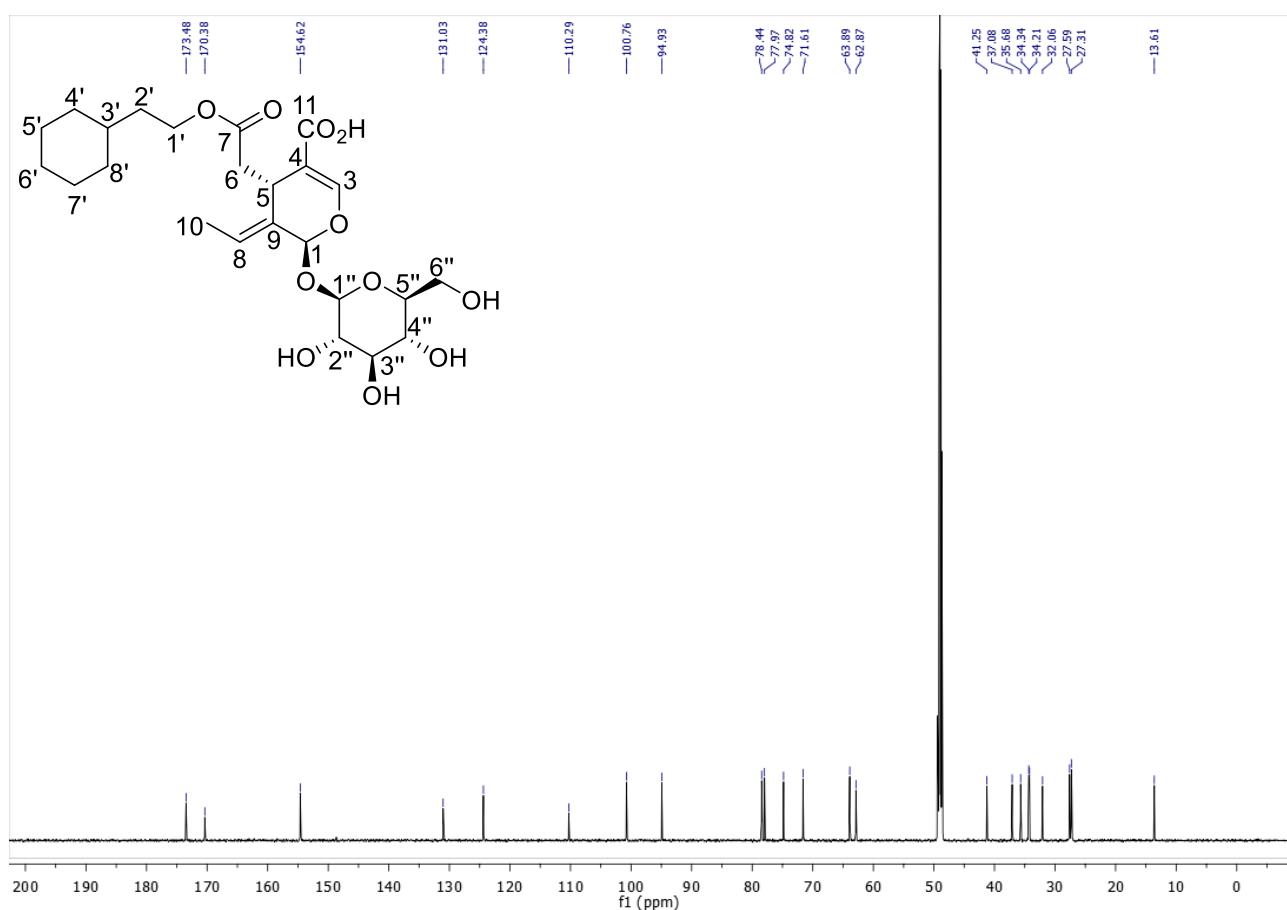
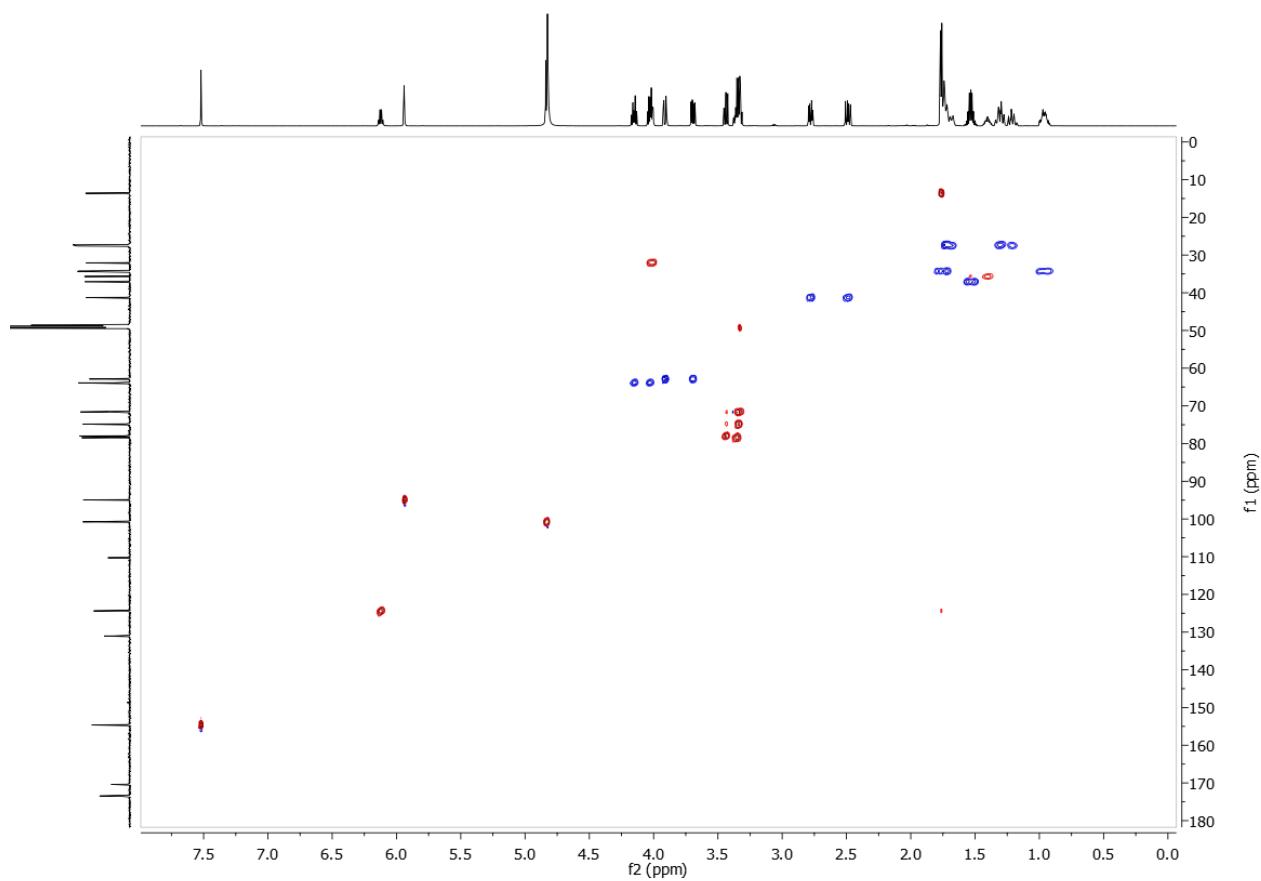


Figure S35. <sup>13</sup>C NMR spectrum of (2*S*,4*S*,*E*)-4-(2-(2-Cyclohexylethoxy)-2-oxoethyl)-3-ethylidene-2-[(2*R*,3*S*,4*R*,5*R*,6*S*)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2*H*-pyran-2-yl]oxy}-3,4-dihydro-2*H*-pyran-5-carboxylic acid (**16**) in methanol – *d*<sub>4</sub> (151 MHz).



*Figure S36.* HSQC spectrum of (2*S*,4*S*,*E*)-4-(2-(2-Cyclohexylethoxy)-2-oxoethyl)-3-ethylidene-2-[(2*R*,3*S*,4*R*,5*R*,6*S*)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2*H*-pyran-2-yl]oxy}-3,4-dihydro-2*H*-pyran-5-carboxylic acid (**16**) in methanol – *d*<sub>4</sub> (600 MHz).

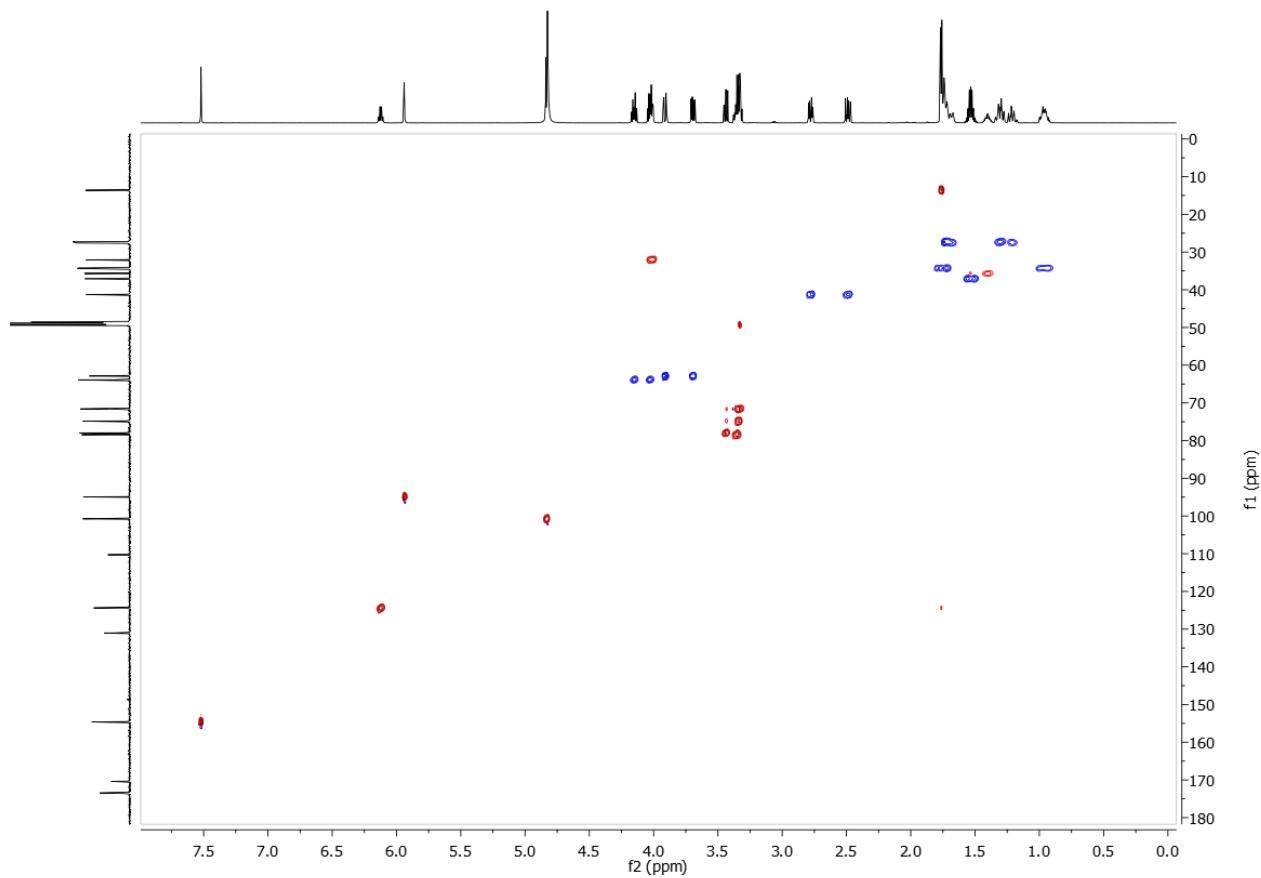


Figure S37. HSQC spectrum of (*2S,4S,E*)-4-(2-(2-Cyclohexylethoxy)-2-oxoethyl)-3-ethyldene-2-[(*2R,3S,4R,5R,6S*)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2*H*-pyran-2-yl]oxy}-3,4-dihydro-2*H*-pyran-5-carboxylic acid (**16**) in methanol – *d*<sub>4</sub> (600 MHz).

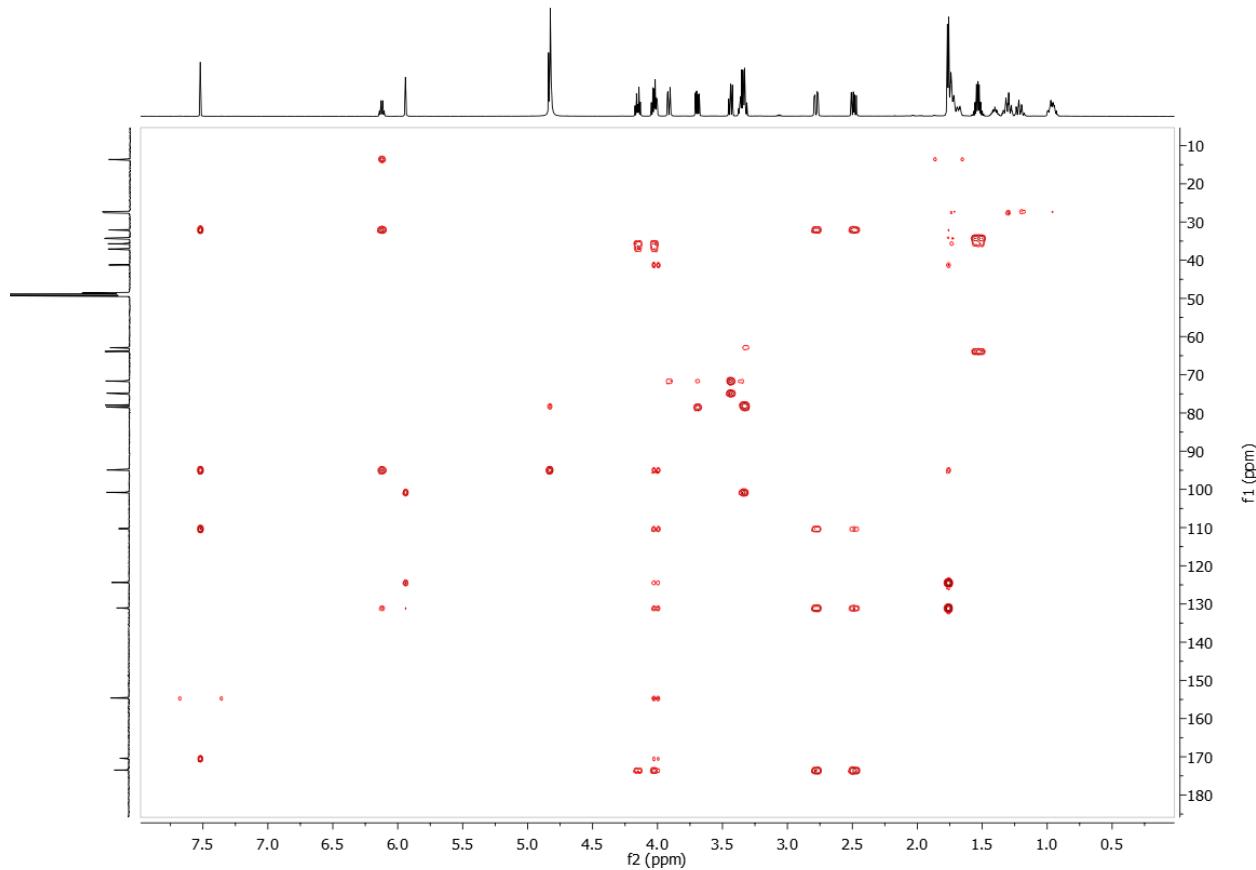


Figure S38. HMBC spectrum of (*2S,4S,E*)-4-(2-(2-Cyclohexylethoxy)-2-oxoethyl)-3-ethylidene-2-[(*2R,3S,4R,5R,6S*)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2*H*-pyran-2-yl]oxy}-3,4-dihydro-2*H*-pyran-5-carboxylic acid (**16**) in methanol – d<sub>4</sub> (600 MHz).

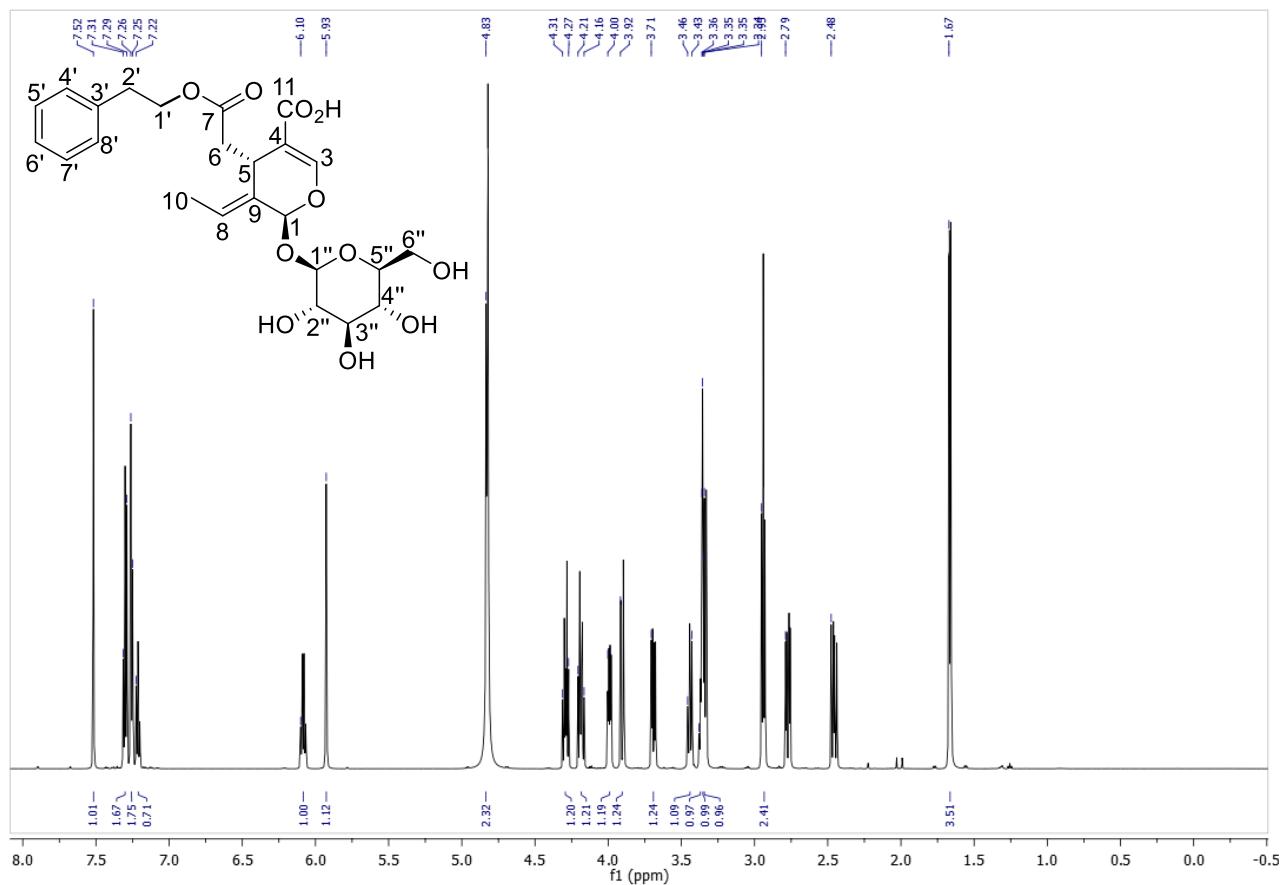


Figure S39.  $^1\text{H}$  NMR spectrum of  $(2S,4S,E)$ -3-Ethylidene-4-(2-oxo-2-phenethoxyethyl)-2-  
 $\{[(2R,3S,4R,5R,6S)-3,4,5\text{-trihydroxy-}6\text{-}(\text{hydroxymethyl})\text{tetrahydro-}2H\text{-pyran-}2\text{-yl}]o\text{x}\text{y}\}$ -  
3,4-dihydro-2*H*-pyran-5-carboxylic acid (**17**) in methanol –  $d_4$  (600 MHz).

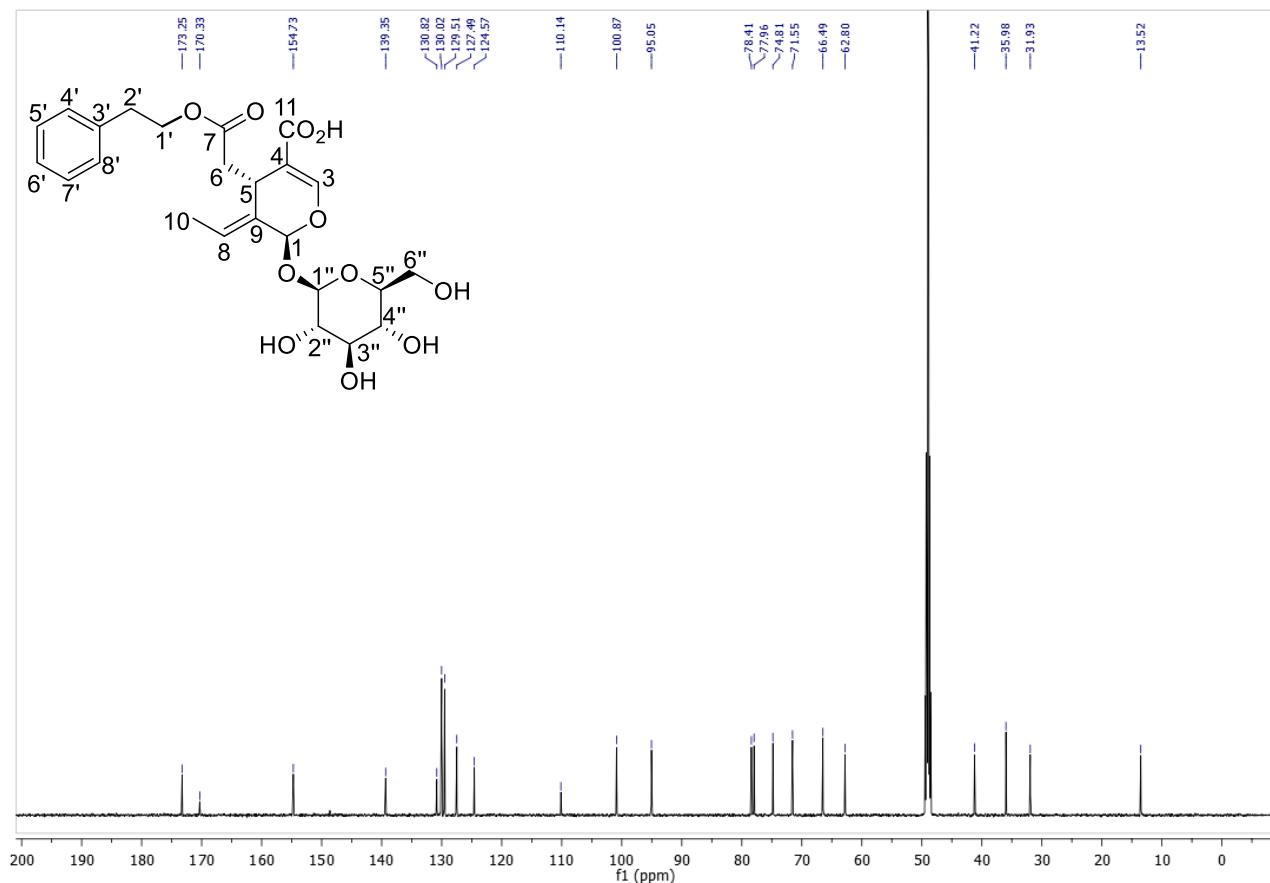


Figure S40. <sup>13</sup>C NMR spectrum of (*2S,4S,E*)-3-Ethylidene-4-(2-oxo-2-phenethoxyethyl)-2-  
{[(*2R,3S,4R,5R,6S*)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2*H*-pyran-2-yl]oxy}-  
3,4-dihydro-2*H*-pyran-5-carboxylic acid (**17**) in methanol – *d*<sub>4</sub> (151 MHz).

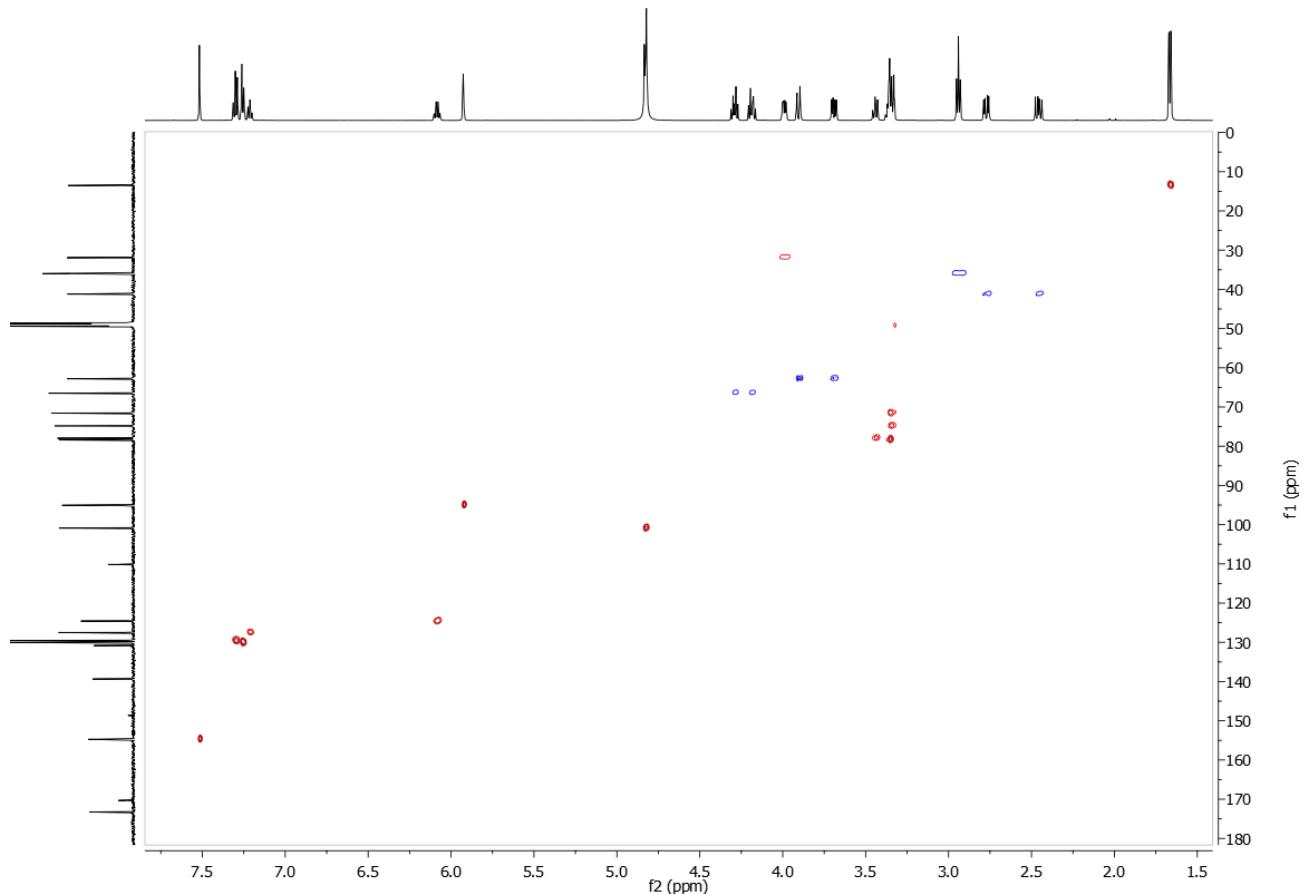


Figure S41. HSQC spectrum of (*2S,4S,E*)-3-Ethyldene-4-(2-oxo-2-phenethoxyethyl)-2-  
{[(*2R,3S,4R,5R,6S*)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2*H*-pyran-2-yl]oxy}-  
3,4-dihydro-2*H*-pyran-5-carboxylic acid (**17**) in methanol –  $d_4$  (600 MHz).

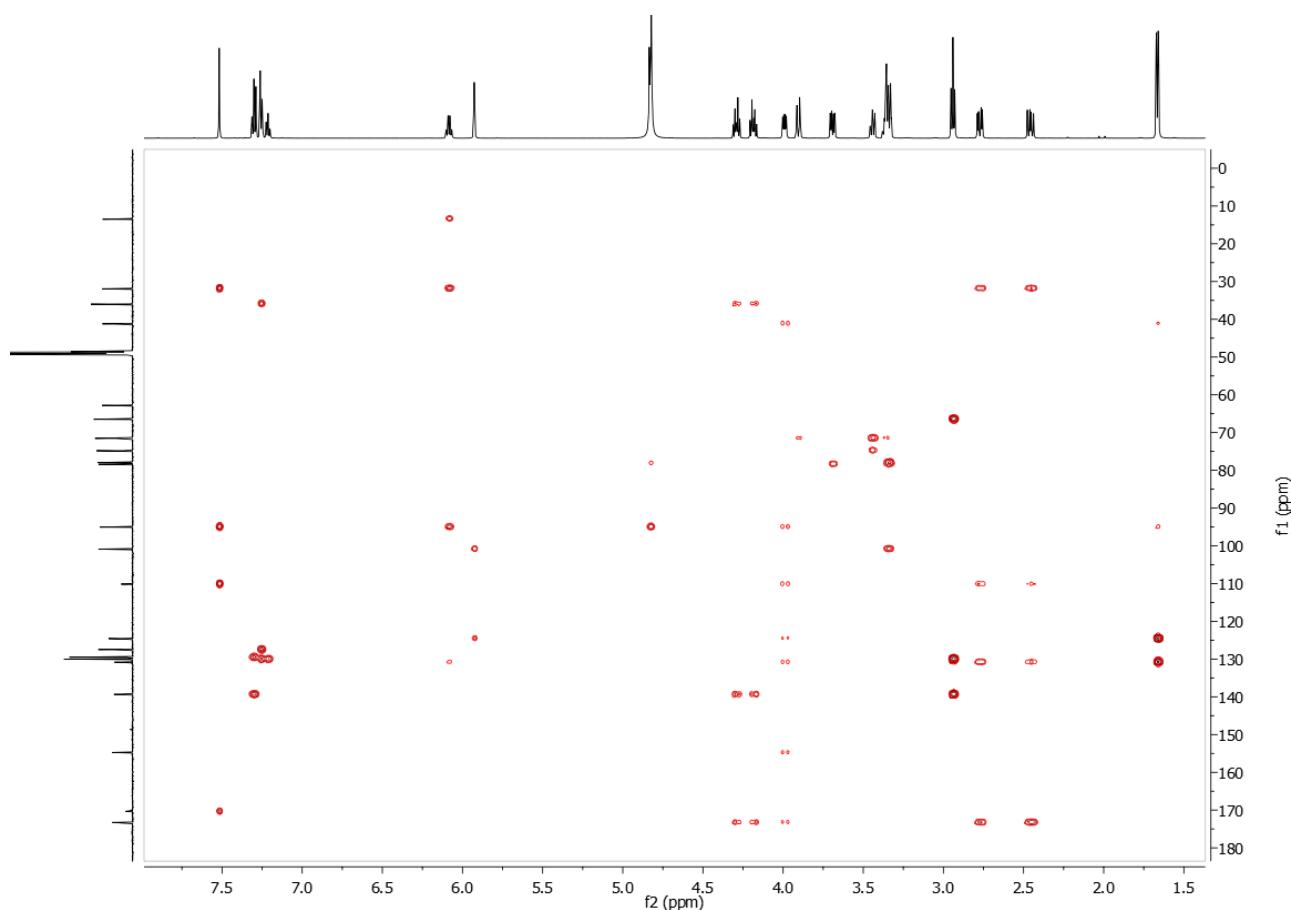


Figure S42. HMBC spectrum of (*2S,4S,E*)-3-Ethylidene-4-(2-oxo-2-phenethoxyethyl)-2-  
{[(*2R,3S,4R,5R,6S*)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2*H*-pyran-2-yl]oxy}-  
3,4-dihydro-2*H*-pyran-5-carboxylic acid (**17**) in methanol – *d*<sub>4</sub> (600 MHz).

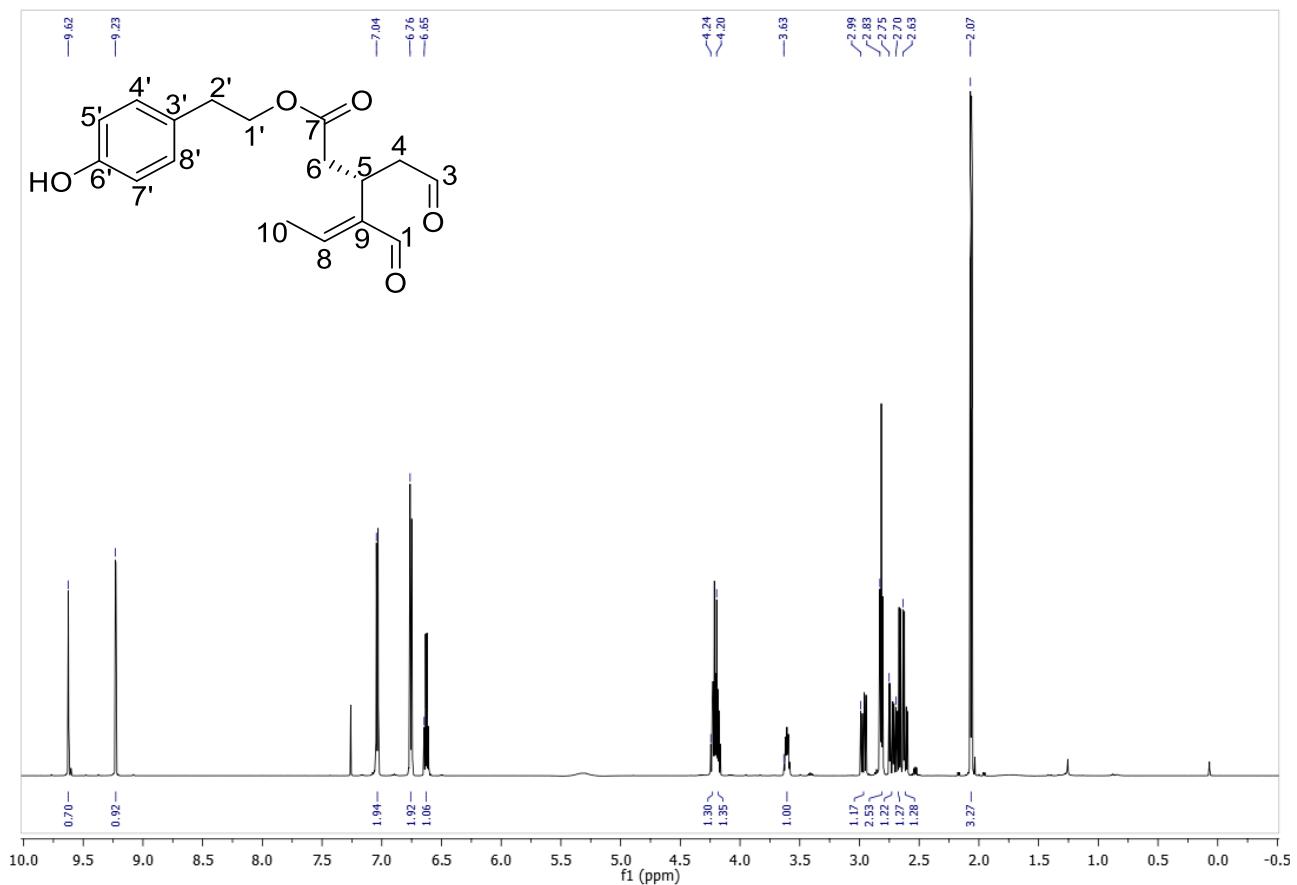


Figure S43.  $^1\text{H}$  NMR spectrum of oleocanthal (**6**) in  $\text{CDCl}_3$  (600 MHz).

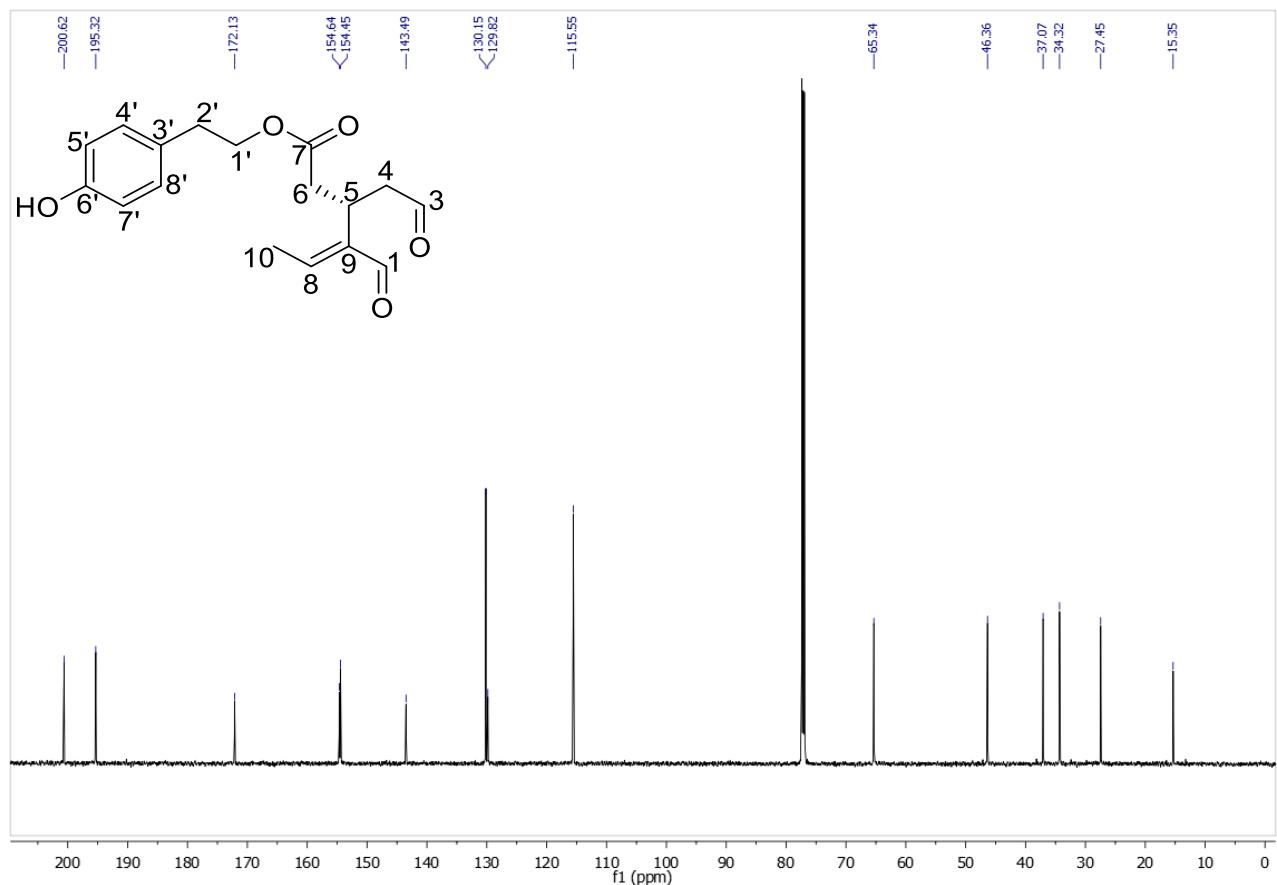


Figure S44.  $^{13}\text{C}$  NMR spectrum of oleocanthal (**6**) in  $\text{CDCl}_3$  (151 MHz).

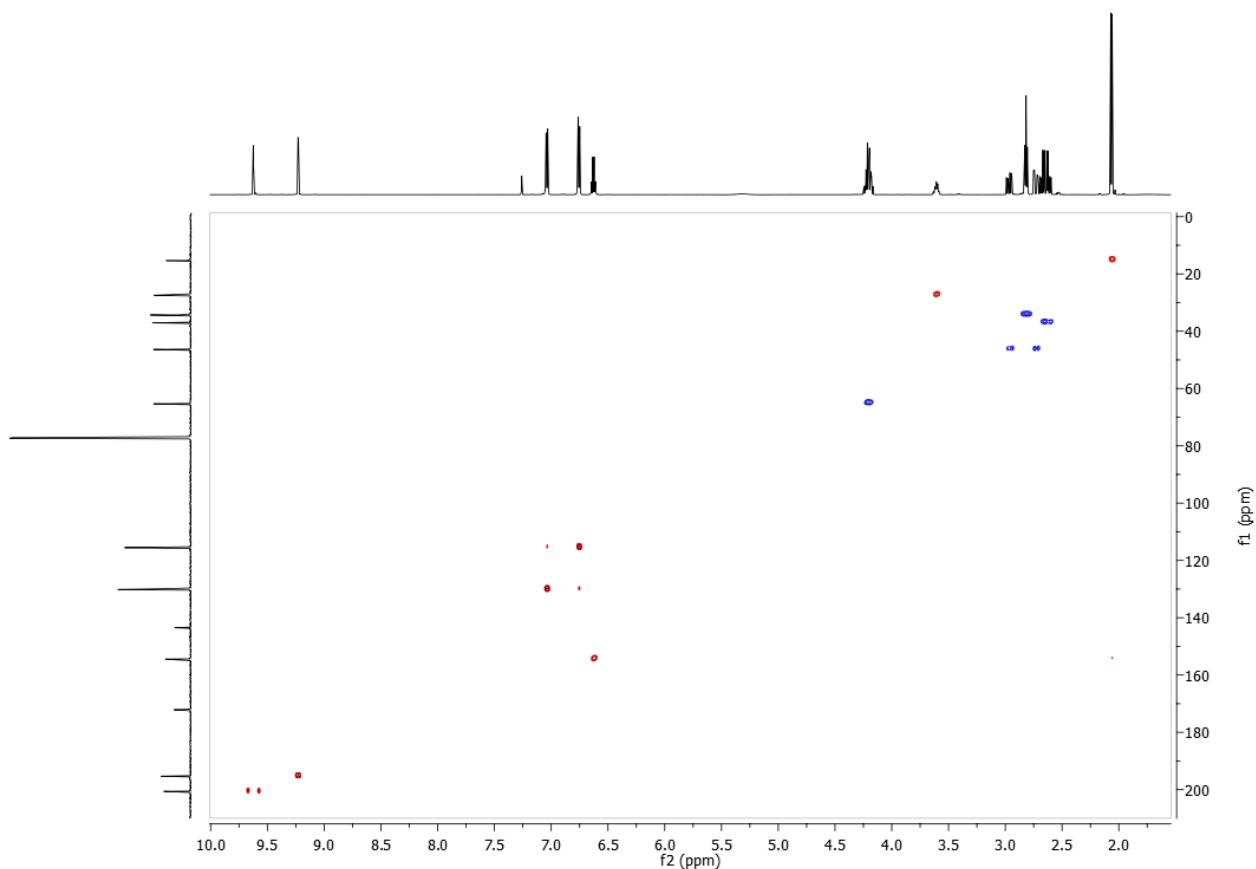


Figure S45. HSQC spectrum of oleocanthal (**6**) in  $\text{CDCl}_3$  (600 MHz).

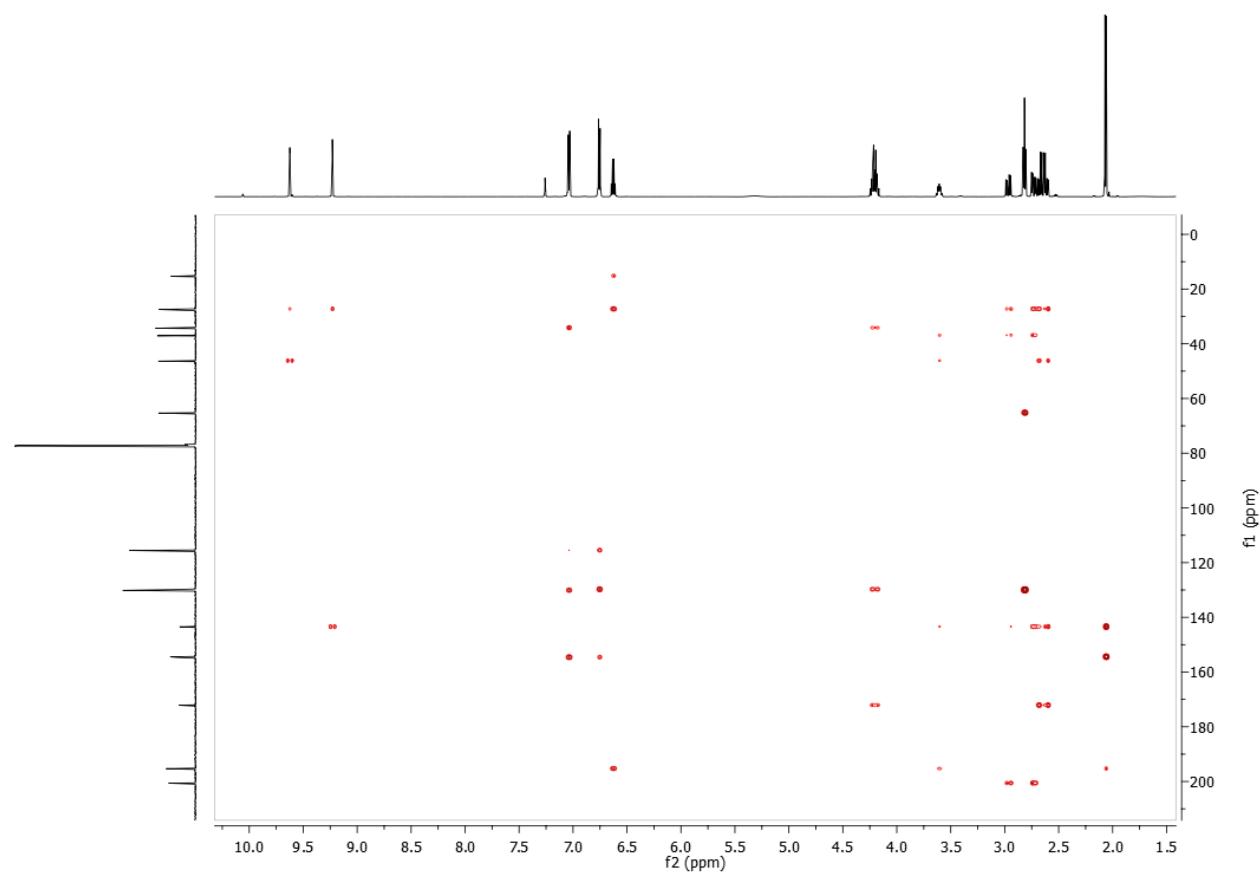


Figure S46. HMBC spectrum of oleocanthal (**6**) in  $\text{CDCl}_3$  (600 MHz).

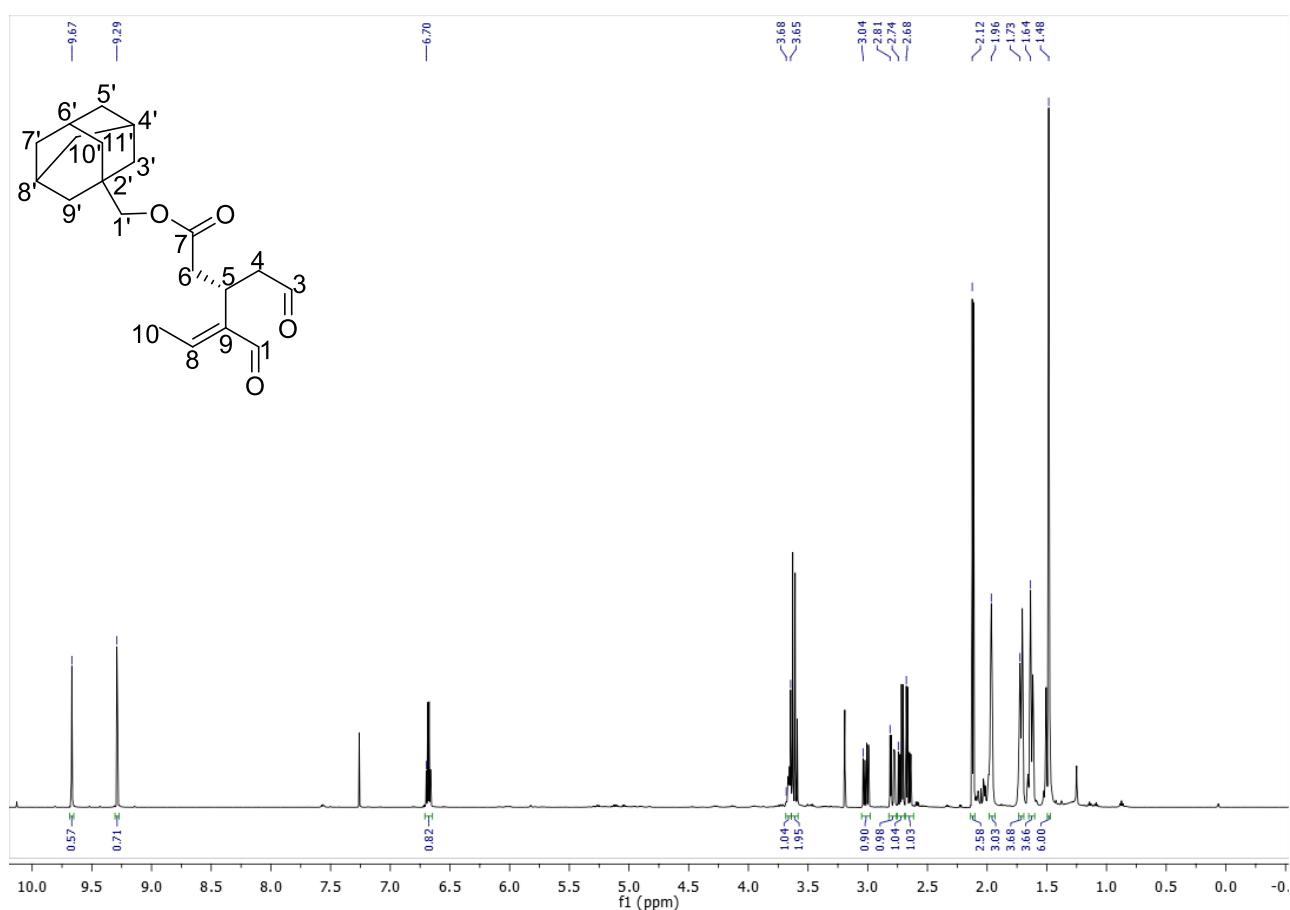


Figure S47.  $^1\text{H}$  NMR spectrum of  $(3S,4E)$ -4-Formyl-3-(2-oxoethyl)hex-4-enoic acid adamantan-1-ylmethyl ester (**24**) in  $\text{CDCl}_3$  (600 MHz).

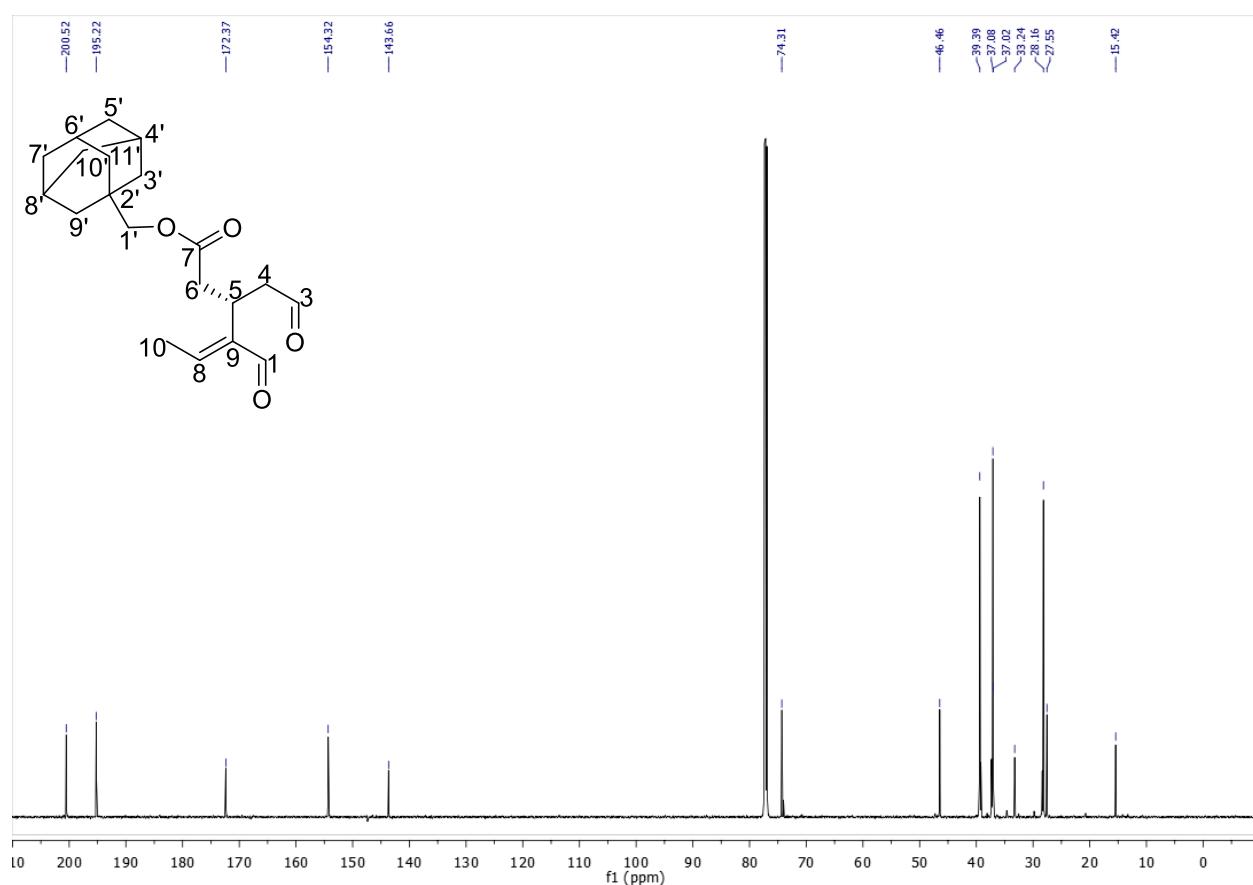


Figure S48.  $^{13}\text{C}$  NMR spectrum of (3*S*,4*E*)-4-Formyl-3-(2-oxoethyl)hex-4-enoic acid adamantan-1-ylmethyl ester (**24**) in  $\text{CDCl}_3$  (151 MHz).

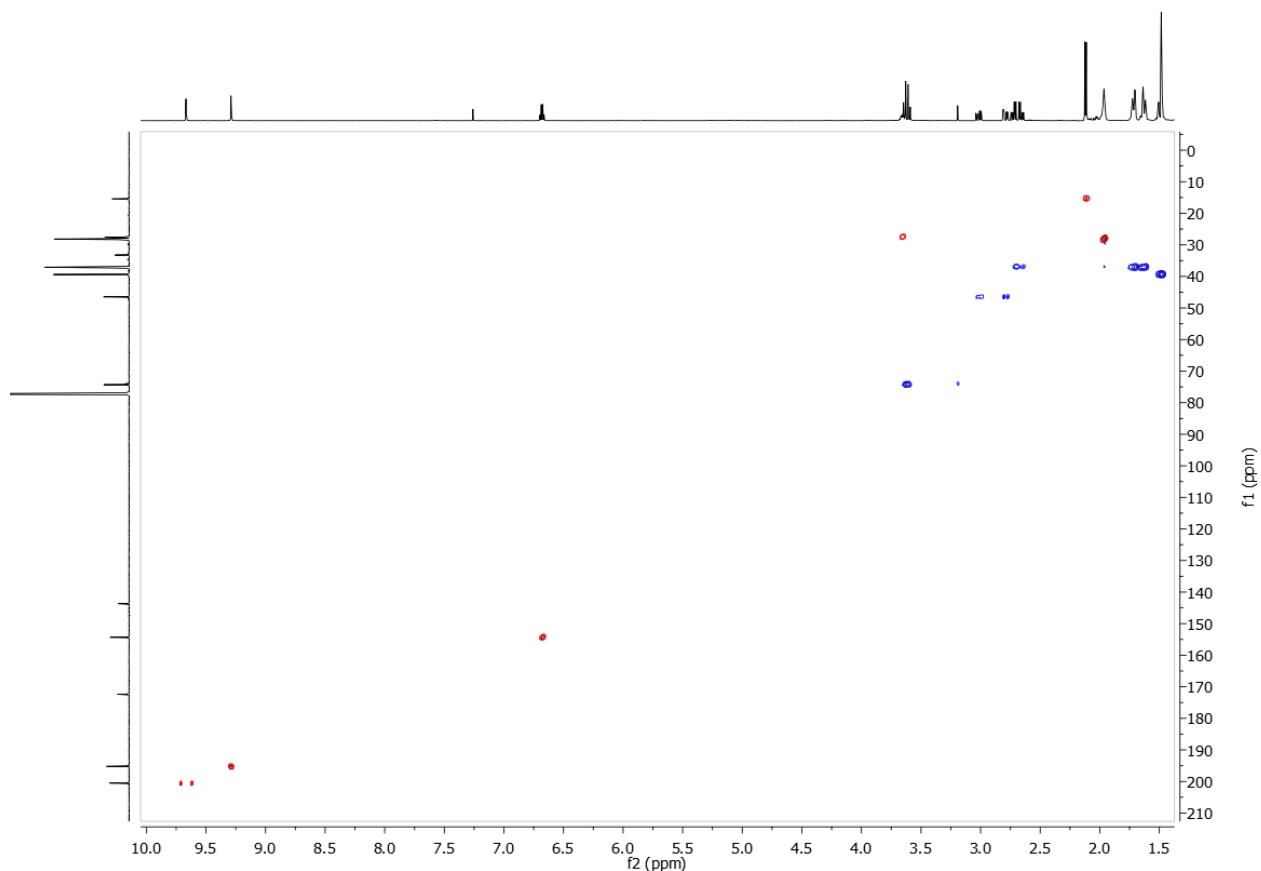


Figure S49. HSQC spectrum of (3*S*,4*E*)-4-Formyl-3-(2-oxoethyl)hex-4-enoic acid adamantan-1-ylmethyl ester (**24**) in CDCl<sub>3</sub> (600 MHz).

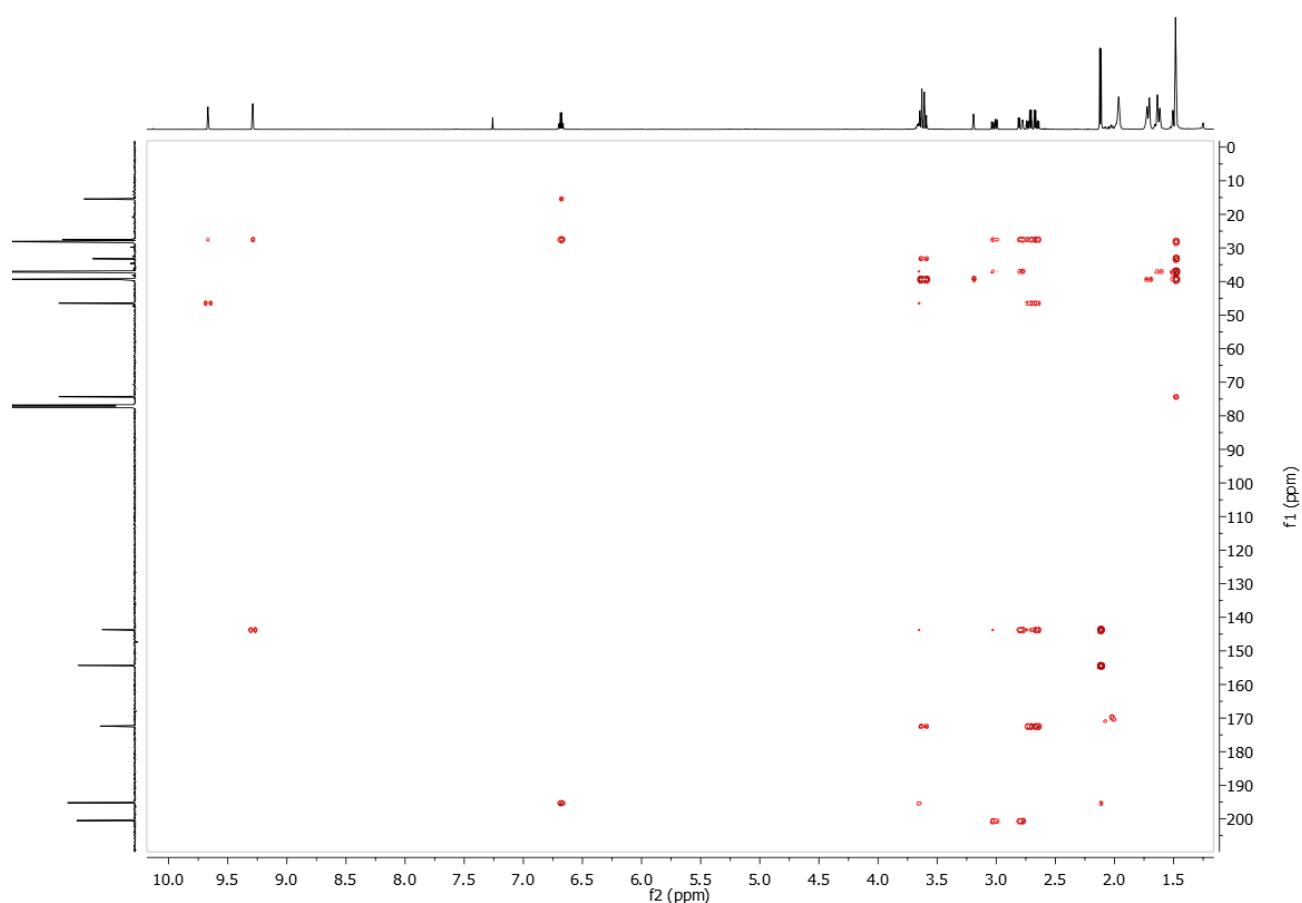


Figure S50. HMBC spectrum of (*3S,4E*)-4-Formyl-3-(2-oxoethyl)hex-4-enoic acid adamantan-1-ylmethyl ester (**24**) in  $\text{CDCl}_3$  (600 MHz).

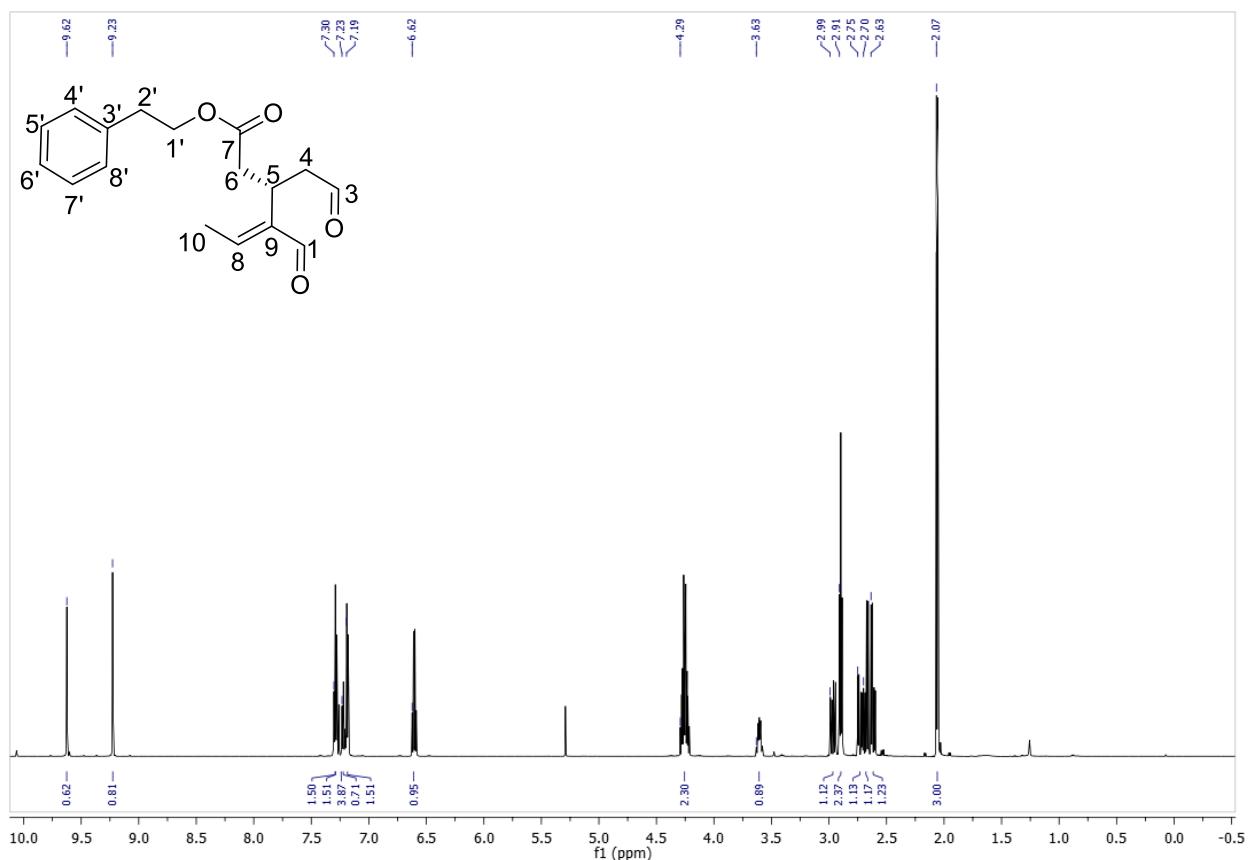


Figure S51.  $^1\text{H}$  NMR spectrum of (3*S*,4*E*)-4-Formyl-3-(2-oxoethyl)-4-hexenoic acid 2-phenylethyl ester (**23**) in  $\text{CDCl}_3$  (600 MHz).

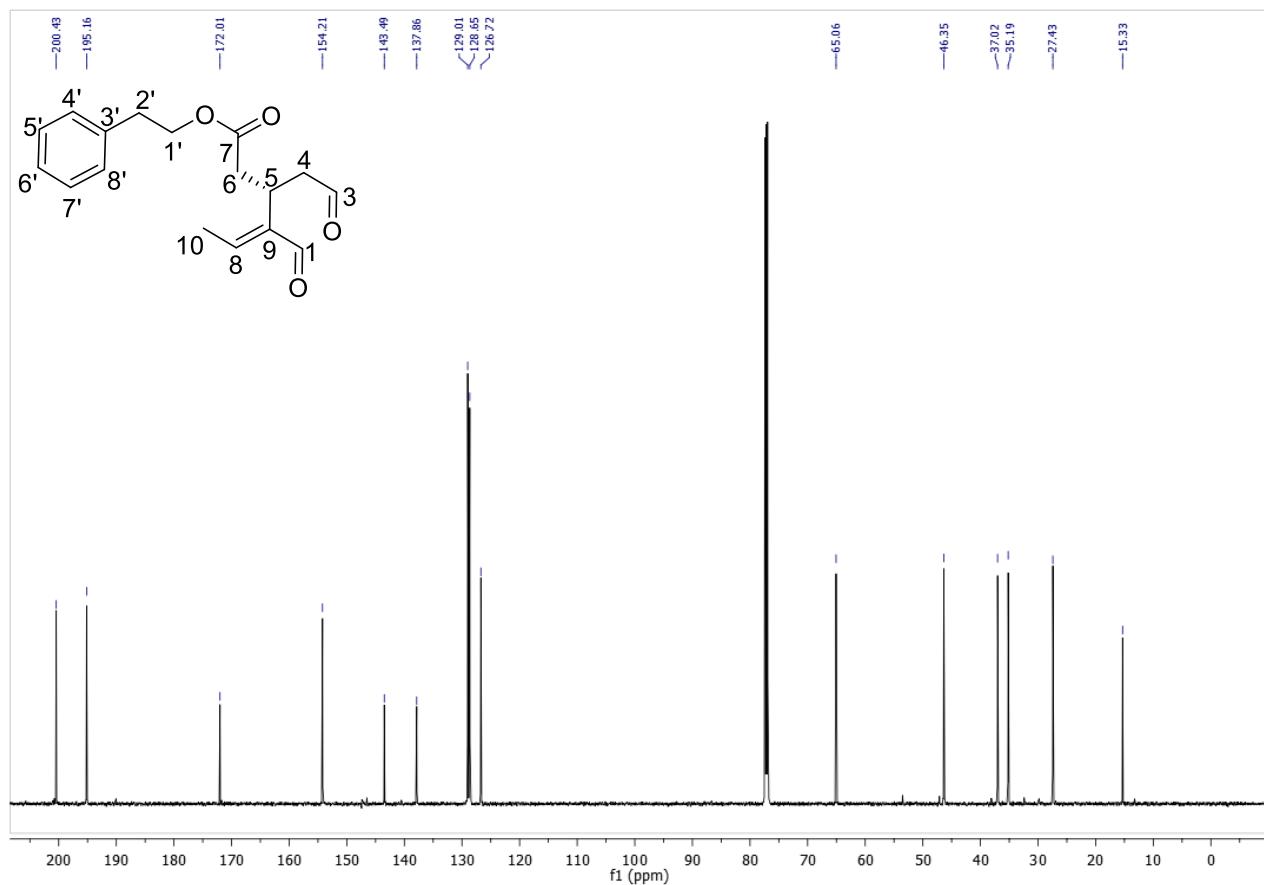


Figure S52.  $^{13}\text{C}$  NMR spectrum of (3*S*,4*E*)-4-Formyl-3-(2-oxoethyl)-4-hexenoic acid 2-phenylethyl ester (**23**) in  $\text{CDCl}_3$  (151 MHz).

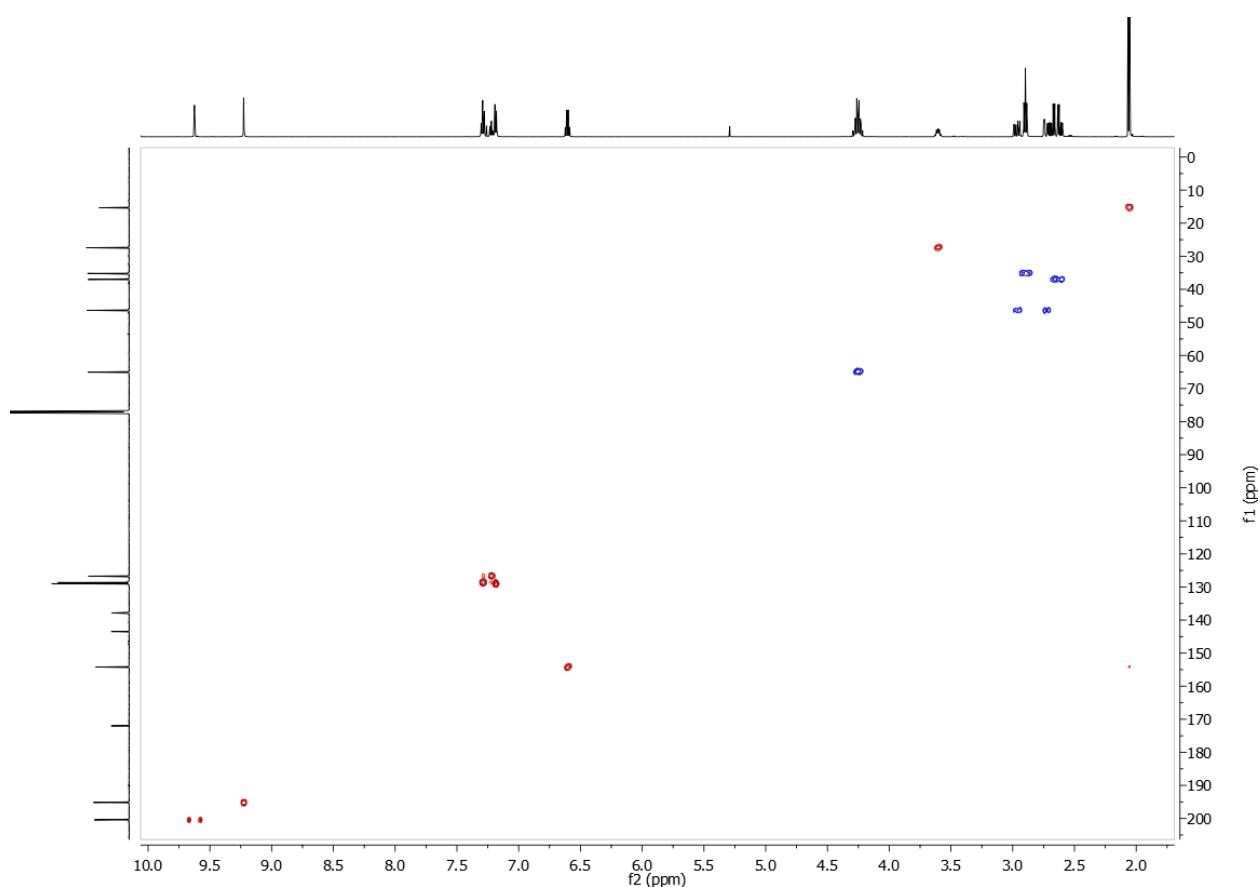


Figure S53. HSQC spectrum of (*3S,4E*)-4-Formyl-3-(2-oxoethyl)-4-hexenoic acid 2-phenylethyl ester (**23**) in CDCl<sub>3</sub> (600 MHz).

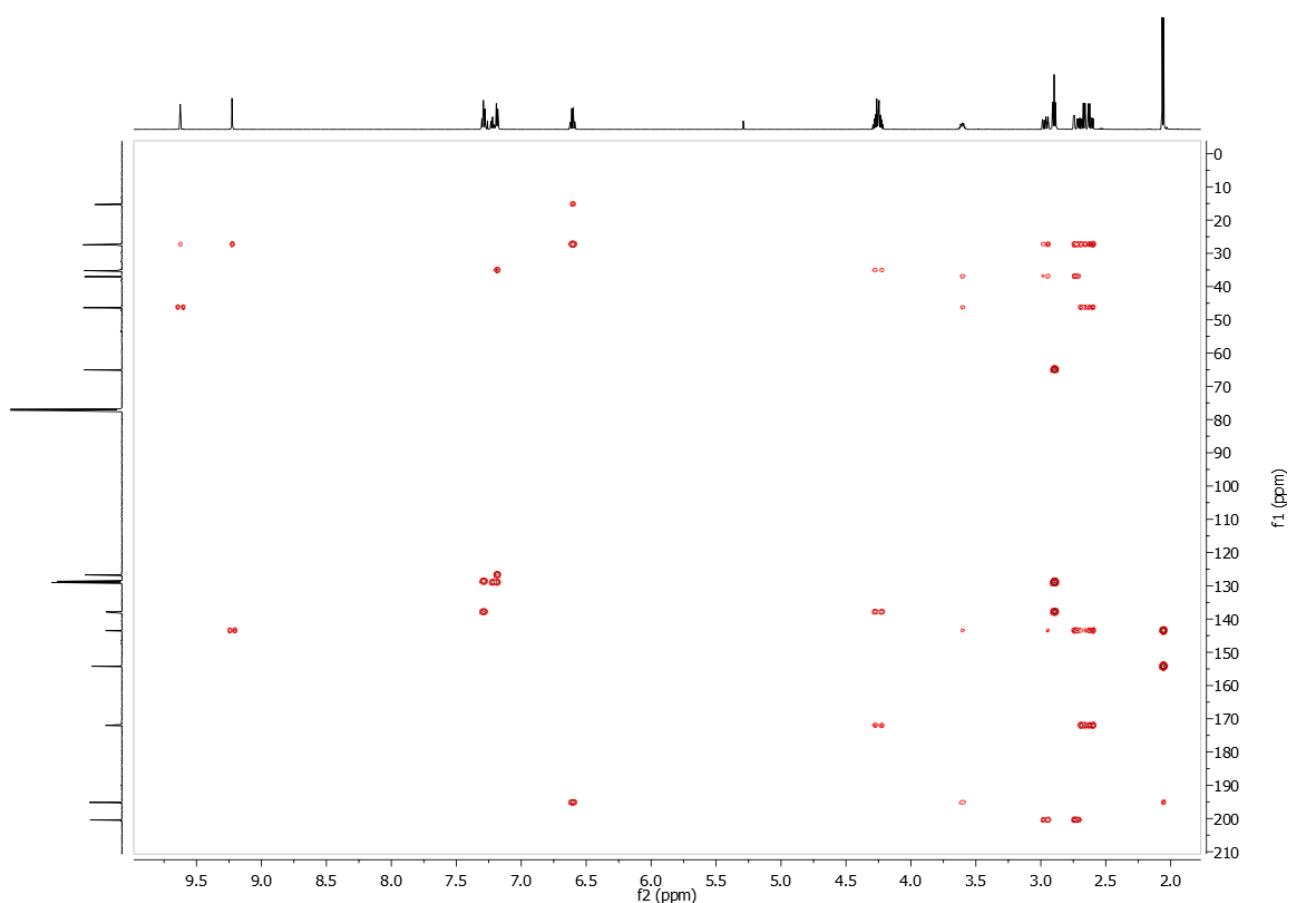


Figure S54. HMBC spectrum of (*3S,4E*)-4-Formyl-3-(2-oxoethyl)-4-hexenoic acid 2-phenylethyl ester (**23**) in CDCl<sub>3</sub> (600 MHz).

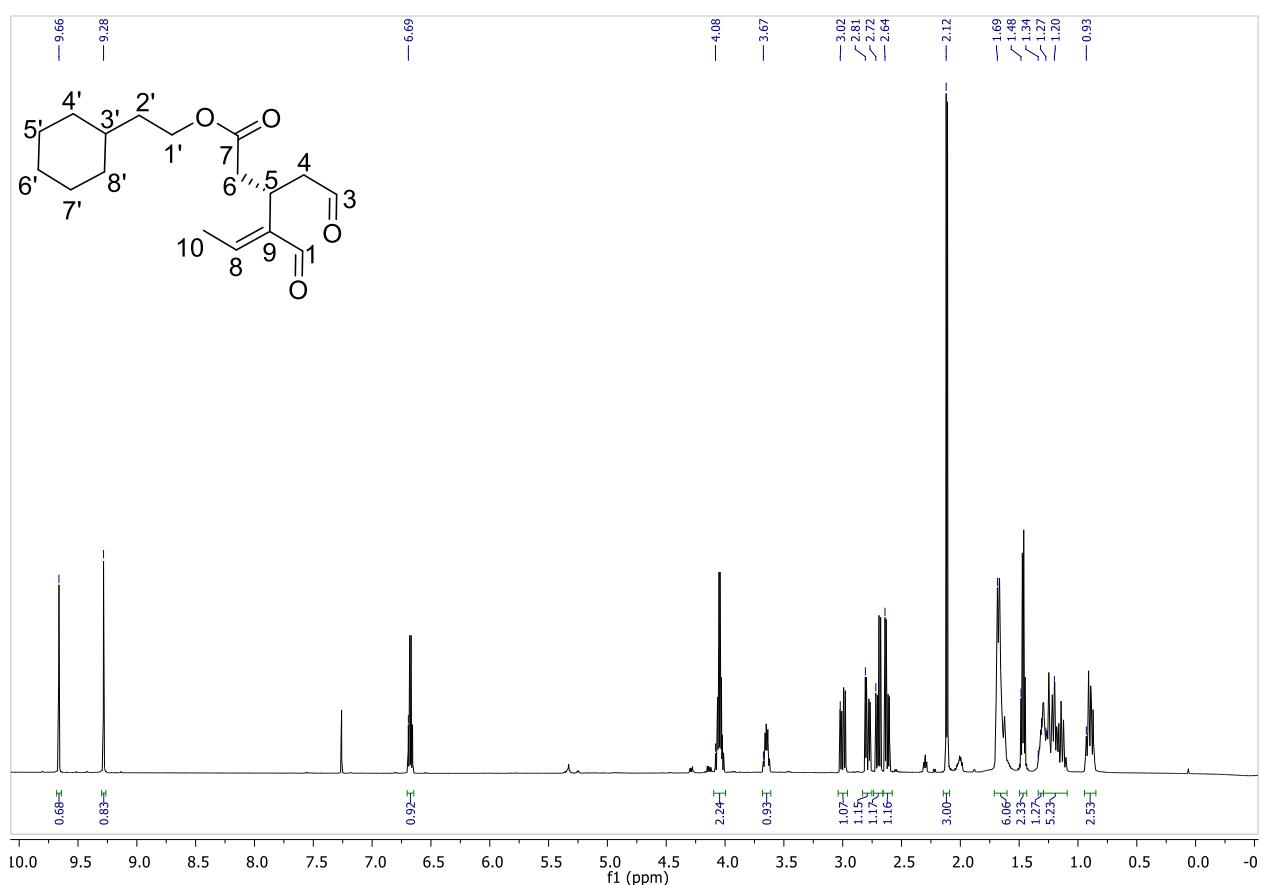


Figure S55. <sup>1</sup>H NMR spectrum of (3*S*,4*E*)-4-Formyl-3-(2-oxoethyl)-4-hexenoic acid 2-cyclohexylethyl ester (**22**) in CDCl<sub>3</sub> (600 MHz).

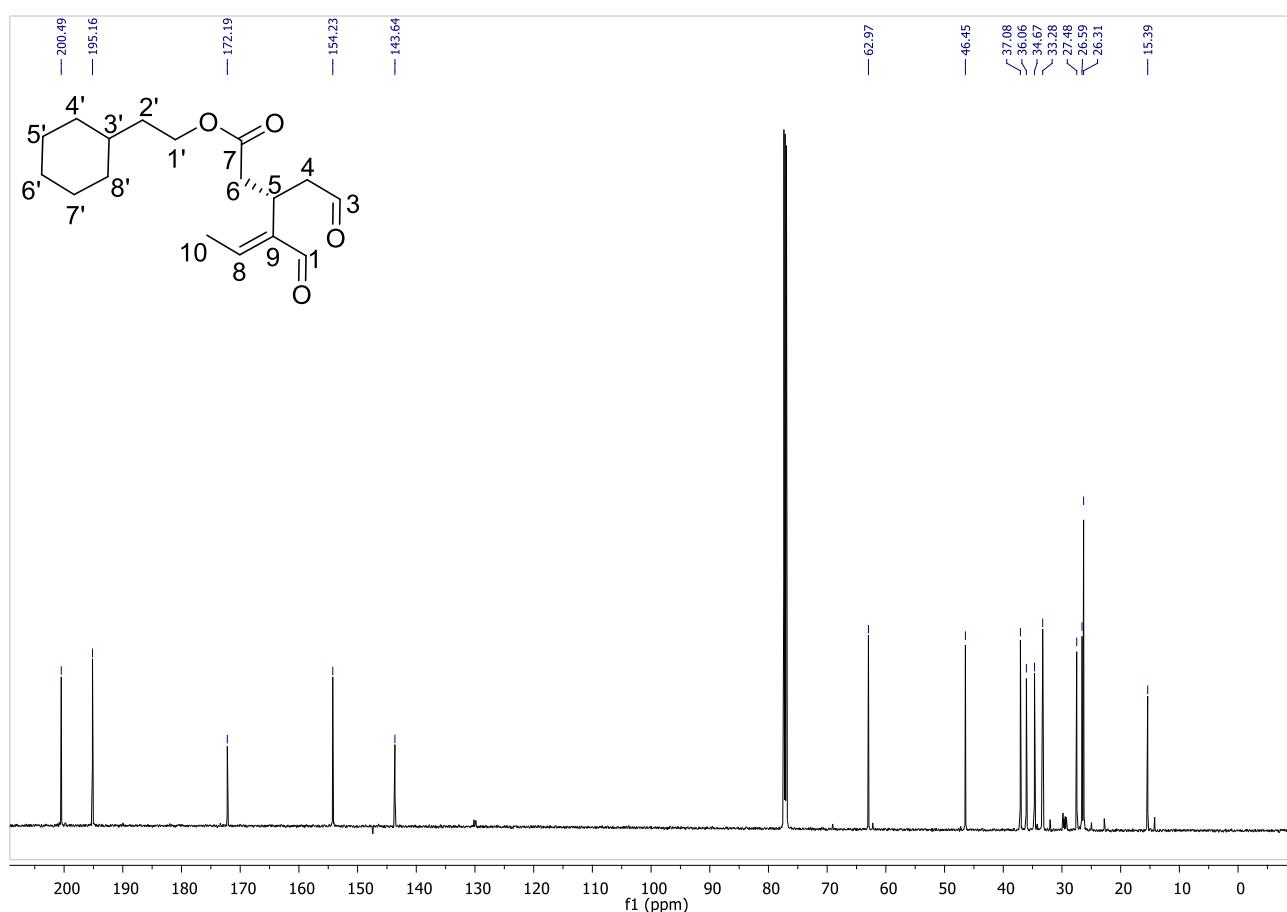


Figure S56.  $^{13}\text{C}$  NMR spectrum of (*3S,4E*)-4-Formyl-3-(2-oxoethyl)-4-hexenoic acid 2-cyclohexylethyl ester (**22**) in  $\text{CDCl}_3$  (151 MHz).

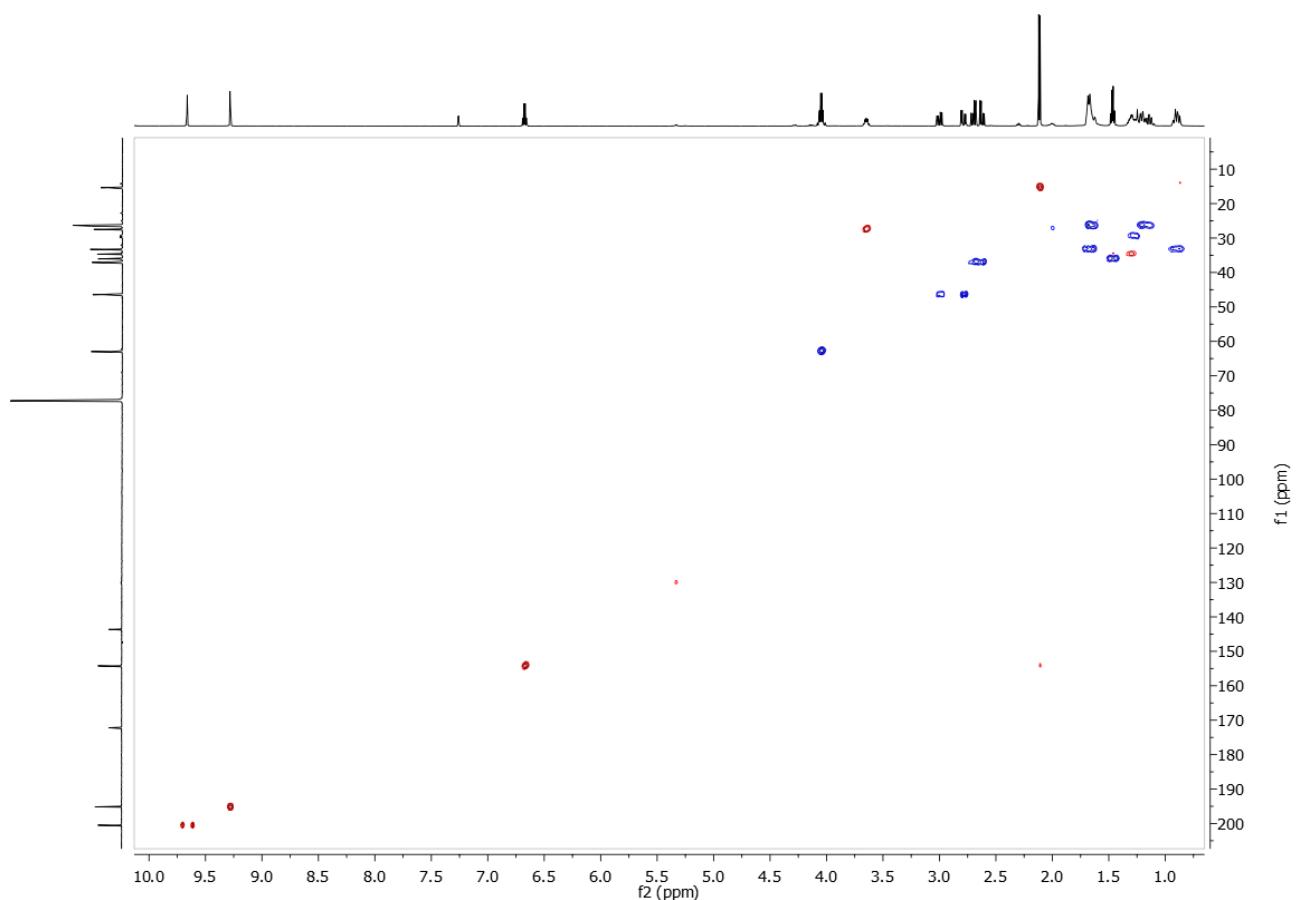


Figure S57. HSQC spectrum of (*3S,4E*)-4-Formyl-3-(2-oxoethyl)-4-hexenoic acid 2-cyclohexylethyl ester (**22**) in  $\text{CDCl}_3$  (600 MHz).

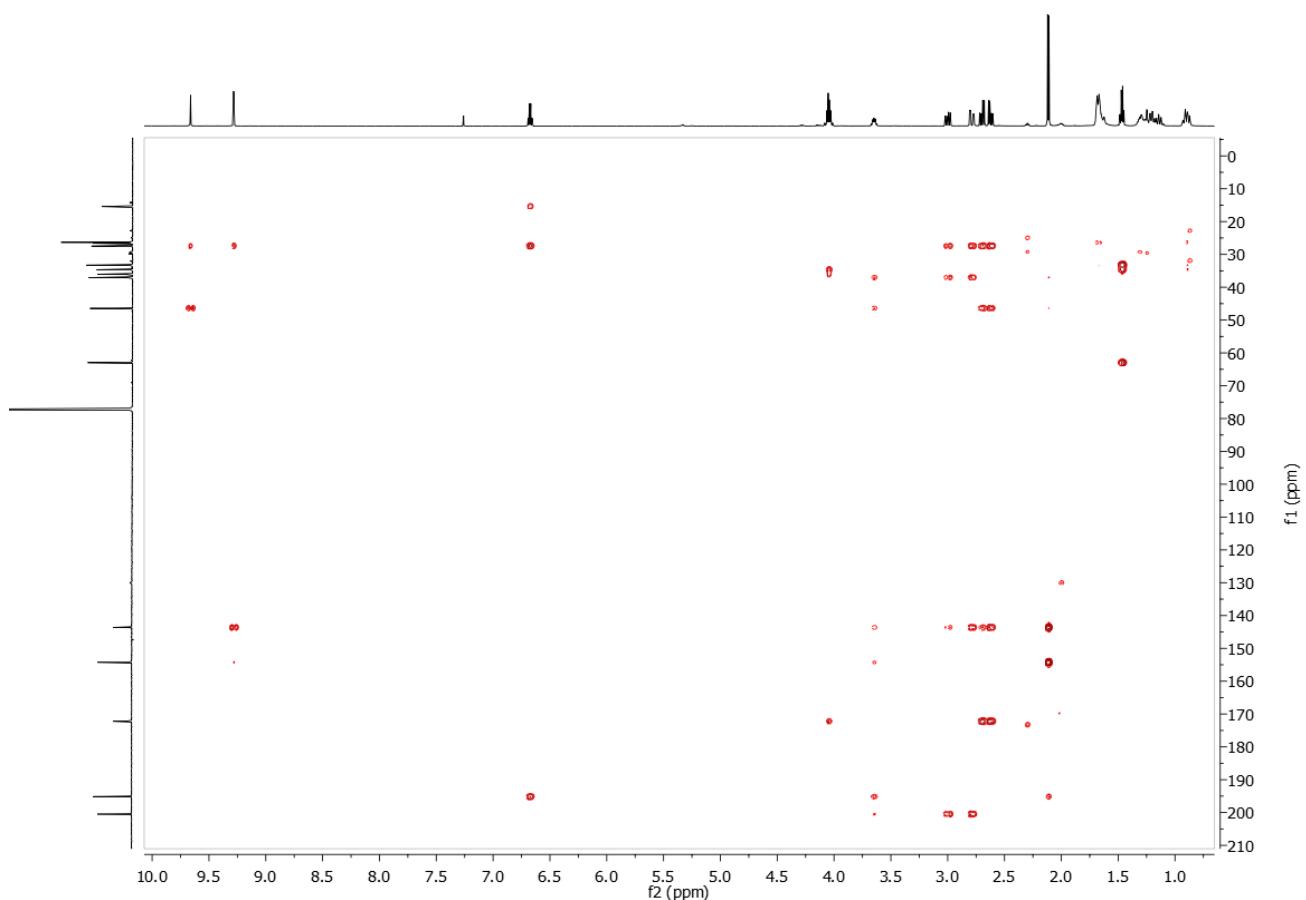


Figure S58. HMBC spectrum of (*3S,4E*)-4-Formyl-3-(2-oxoethyl)-4-hexenoic acid 2-cyclohexylethyl ester (**22**) in CDCl<sub>3</sub> (600 MHz).