Supporting Information

Total synthesis of acylphloroglucinols and their antibacterial activities against clinical isolates of multi-drug resistant (MDR) and methicillin-resistant strains of *Staphylococcus aureus*

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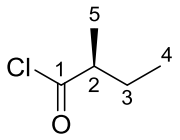


2

(*S*)-2-Methylbutanoyl chloride (2). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 0.95 (3H, t, J = 7.5 Hz, H4), 1.26 (3H, d, J = 7.5 Hz, H5), 1.59 (1H, m, H3a), 1.80 (1H, m, H3b), 2.80 (1H, q, J = 7.0 Hz, H2); ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 11.3 (C4), 16.7 (C5), 26.7 (C3), 53.1 (C2), 177.8 (C1).

Figure 1: ^{1}H NMR spectrum of **2** (500 MHz, $CDCl_3$)

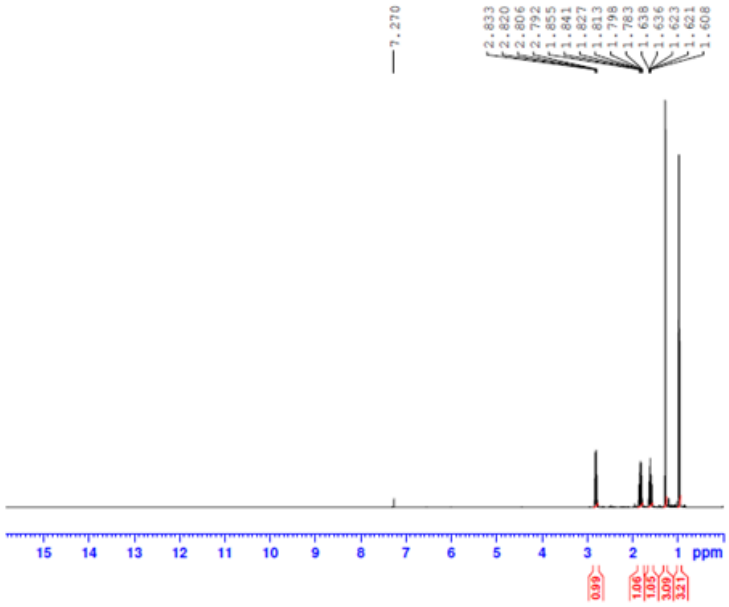
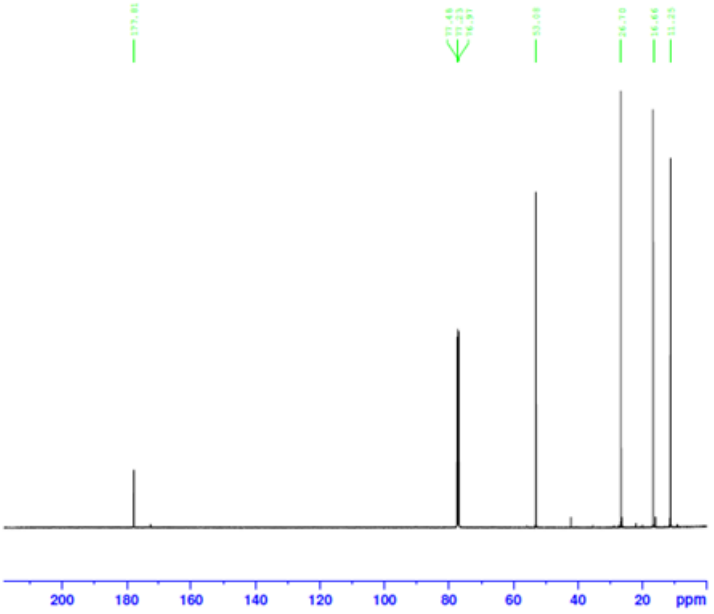
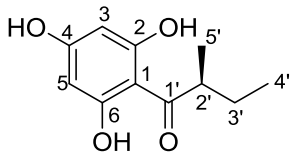


Figure 2: ^{13}C NMR spectrum of **2** (125 MHz, $CDCl_3$)





4

(*S*)-2-Methyl-1-(2,4,6-trihydroxyphenyl)butan-1-one (4). ^{1}H NMR (500 MHz, CD_3OD): δ_H 0.88 (3H, t, J = 7.5 Hz, H4'), 1.11 (3H, d, J = 6.5 Hz, H5'), 1.33 (1H, m, H3'a), 1.78 (1H, m, H3'b), 3.84 (1H, m, H2'), 5.81 (2H, s, H3, H5); ^{13}C NMR (125 MHz, CD_3OD): δ_C 12.4 (C4'), 17.2 (C5'), 28.2 (C3'), 46.7 (C2'), 96.0 (C3, C5), 105.3 (1), 165.8 (C2, C4, C6), 211.4 (C1').

Figure 3: ^{1}H NMR spectrum of **4** (500 MHz, CD_3OD)

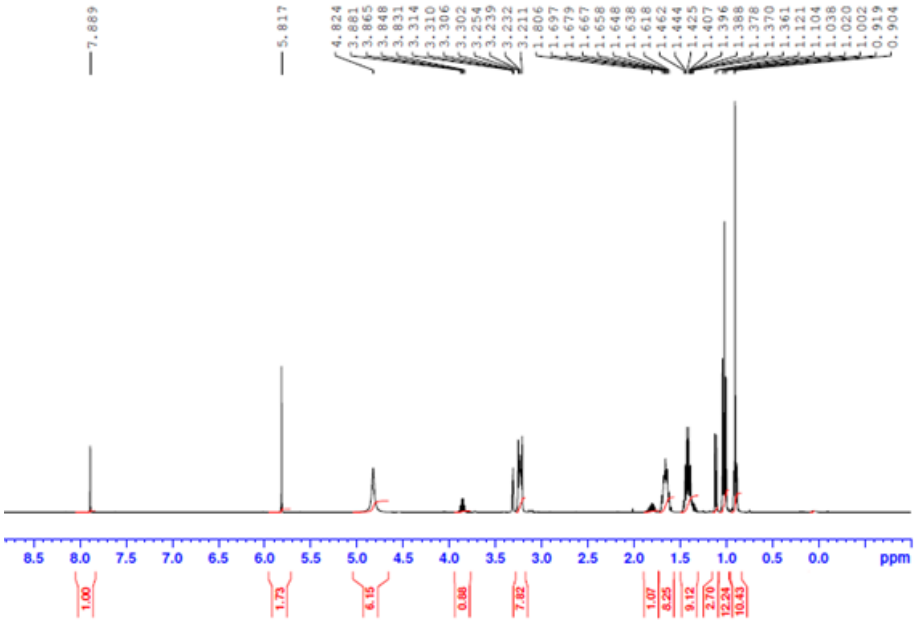
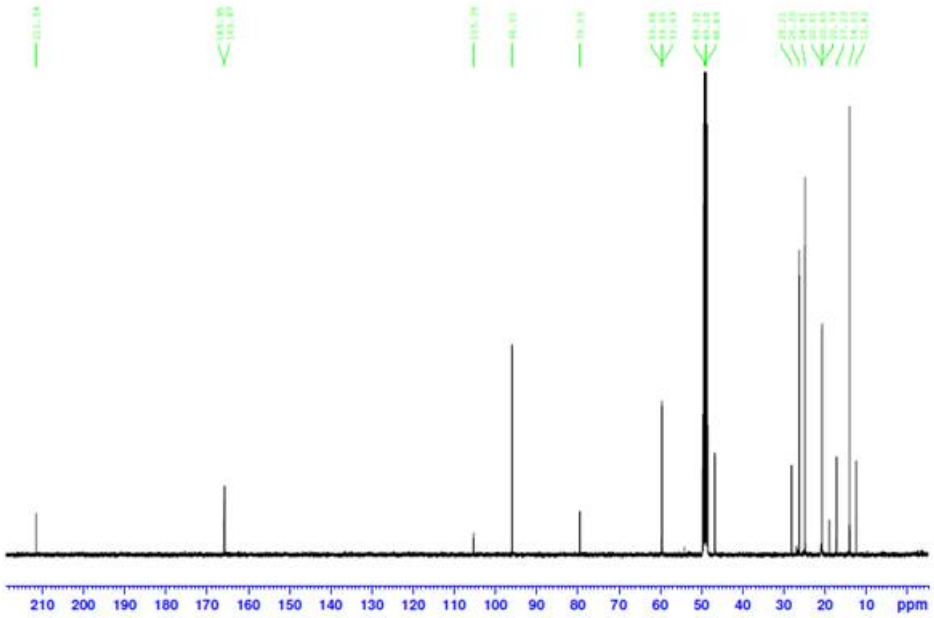
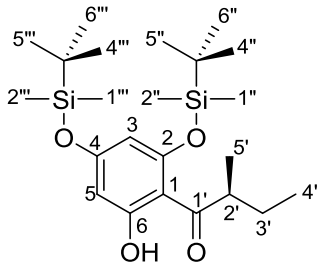


Figure 4: ^{13}C NMR spectrum of **4** (125 MHz, CD_3OD)

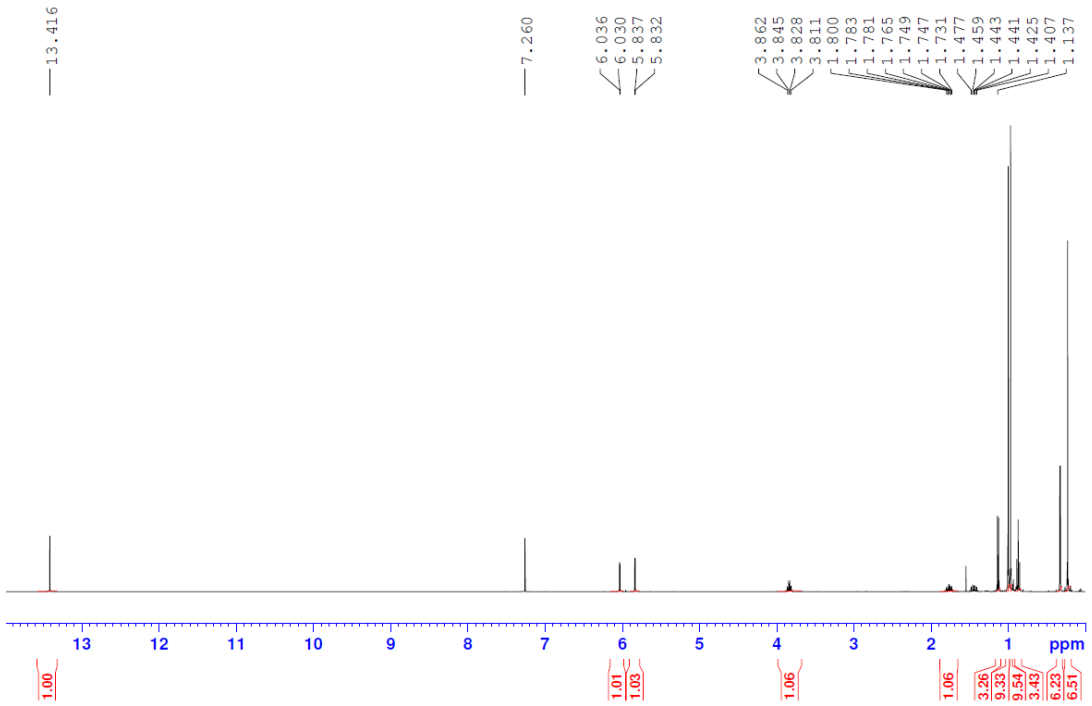


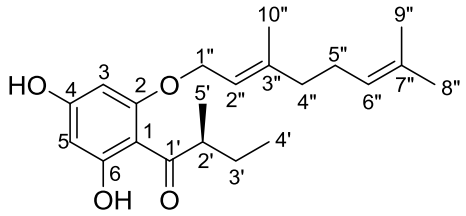


5

(*S*)-1-(2,4-bis((*tert*-Butyldimethylsilyl)oxy)-6-hydroxyphenyl)-2-methylbutan-1-one (5). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 0.23 (2 × 3H, s, H1", H2"), 0.32 (2 × 3H, s, H1'", H2'"), 0.88 (3H, t, J = 7.5 Hz, H4'), 0.97 (3 × 3H, s, H4", H5", H6"), 0.99 (3 × 3H, s, H4'", H5'", H6'"), 1.12 (3H, d, J = 6.5Hz, H5'), 1.43 (1H, m, H3'a), 1.78 (1H, m, H3'b), 3.82 (1H, m, H2'), 5.85 (1H, d, J = 2.0 Hz, H3), 6.04 (1H, d, J = 2.0 Hz, H5), 13.43 (1H, s, OH6); ^{13}C NMR (125 MHz, $CDCl_3$): δ_C -4.2 (C1", C2"), -3.7 (C1'", C2'"), 11.0 (C4'), 16.9 (C5'), 18.1 (C3"), 18.9 (C3'"), 25.5 (C4", C5", C6"), 26.1 (C4'", C5'", C6'"), 26.5 (C3'), 45.0 (C2'), 102.0 (C3), 103.1 (C5), 108.4 (C1), 158.8 (C4), 161.7 (C2), 166.5 (C6), 210.5 (C1').

Figure 5: ^{1}H NMR spectrum of **5** (500 MHz, $CDCl_3$)





6

(*S*,*E*)-1-(2-((3,7-Dimethylocta-2,6-dien-1-yl)oxy)-4,6-dihydroxy-phenyl)-2-methylbutan-1-one (olympicin A) (6). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 0.88 (3H, t, J = 7.5 Hz, H4'), 1.12 (3H, d, J = 6.5 Hz, H5'), 1.36 (1H, m, H3'a), 1.61 (3H, s, H9"), 1.69 (3H, s, H8"), 1.74 (3H, s, H10"), 1.79 m (1H, m, H3'), 2.10 (2H, m, H5"), 2.13 (2H, m, H4"), 3.68 (1H, m, H2'), 4.56 (2H, d, J = 6.5 Hz, H1"), 5.10 (1H, m, H6"), 5.44 (1H, br s, HO4), 5.50 (1H, m, H2"), 5.91 (1H, d, J = 2.0 Hz, H3), 5.98 (1H, d, J = 2.0 Hz, H5), 14.10 (1H, s, HO6); ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 11.9 (C4'), 16.5 (C5'), 16.6 (C10"), 17.7 (C9"), 25.7 (C8"), 26.2 (C5"), 26.9 (C3'), 39.5 (C4"), 46.2 (C2'), 65.6 (C1"), 91.5 (C3), 96.5 (C5), 105.9 (C1), 118.2 (C2"), 122.6 (C6"), 132.0 (C7"), 142.4 (C3"), 161.9 (C4), 162.6 (C2), 167.5 (C6), 210.4 (C1').

Figure 6: ^{1}H NMR spectrum of **6** (500 MHz, $CDCl_3$)

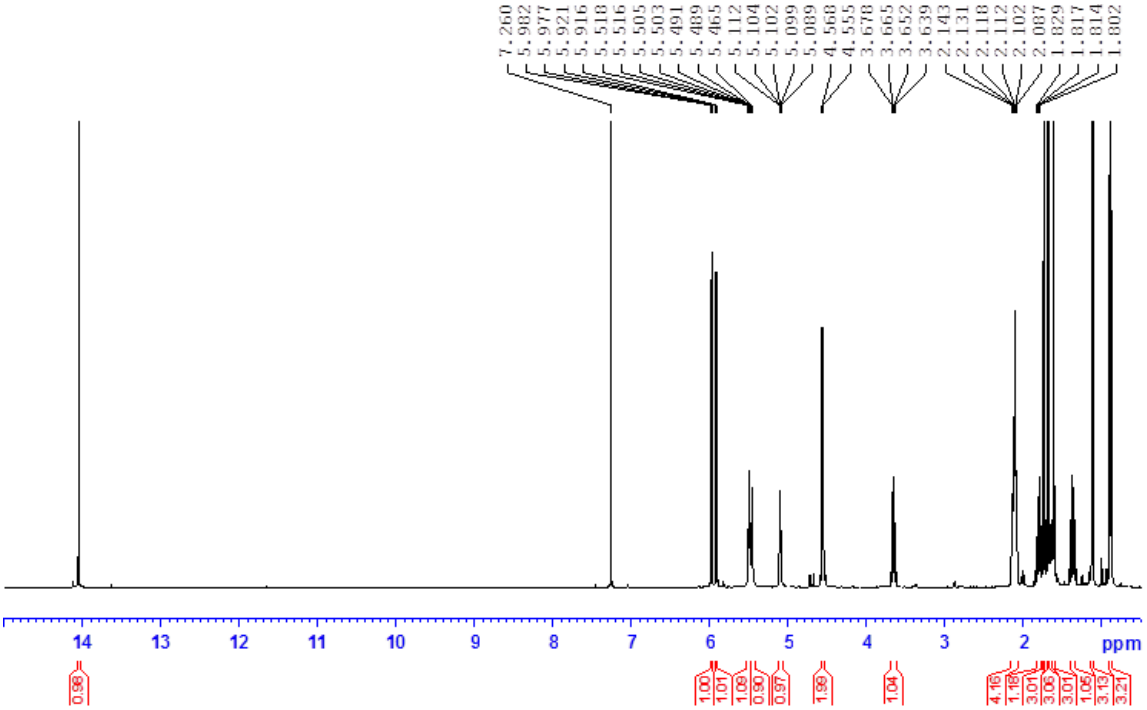
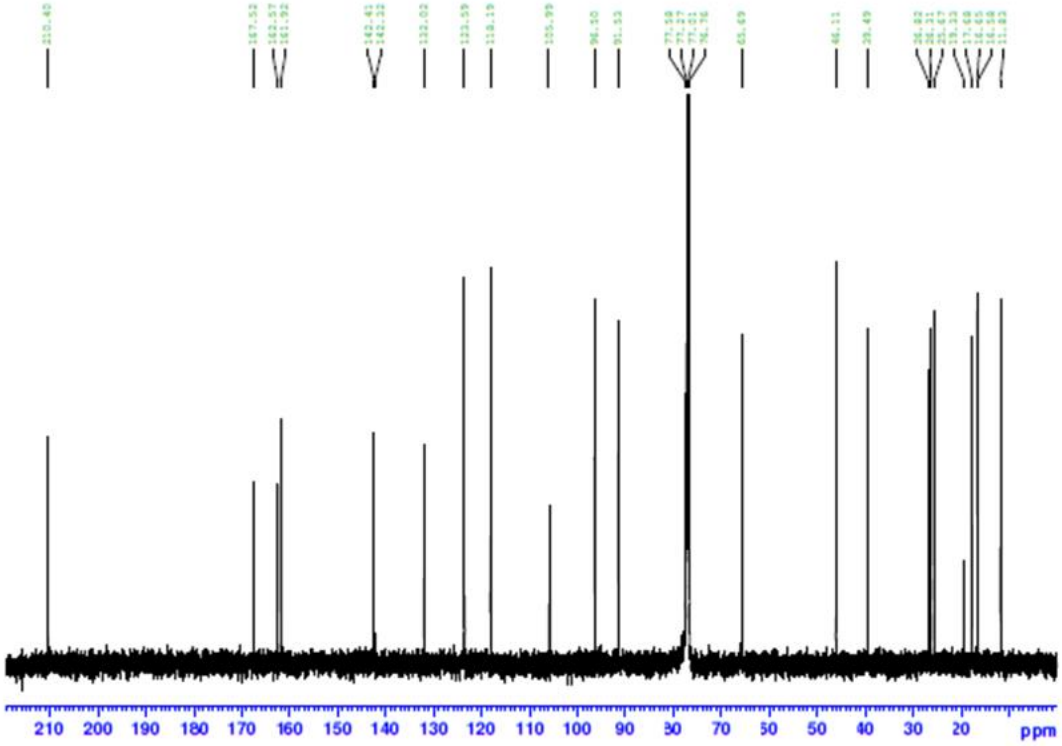
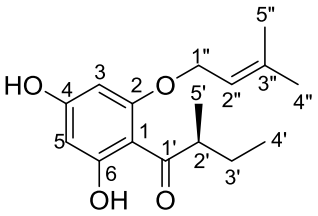


Figure 7: ^{13}C NMR spectrum of **6** (125 MHz, $CDCl_3$)





7

(*S*)-1-(2,4-Dihydroxy-6-((3-methylbut-2-en-1-yl)oxy)phenyl)-2-methylbutan-1-one (7). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 0.88 (3H, t, J = 7.5 Hz, H4'), 1.13 (3H, d, J = 6.5 Hz, H5'), 1.33 (1H, m, H3'a), 1.76 (3H, s, H5"), 1.78 (1H, m, H3'), 1.82 (3H, s, H4"), 3.66 (1H, m, H2'), 4.55 (2H, d, J = 6.5 Hz, H1"), 5.51 (1H, t, J = 6.5 Hz, H2"), 5.70 (1H, br s, HO4), 5.93 (1H, d, J = 2.0 Hz, H3), 6.00 (1H, d, J = 2.0 Hz, H5), 14.07 (1H, br s, HO6); ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 12.0 (C4'), 16.7 (C5'), 18.4 (C5"), 25.9 (C4"), 27.1, (C3'), 46.3 (C2'), 65.8 (C1"), 91.7 (C3), 96.7 (C4), 106.1 (C1), 118.6 (C2"), 139.3 (C3"), 162.3 (C4), 162.8 (C2), 167.7 (C5), 210.6 (C1').

Figure 8: ^{1}H NMR spectrum of **7** (500 MHz, $CDCl_3$)

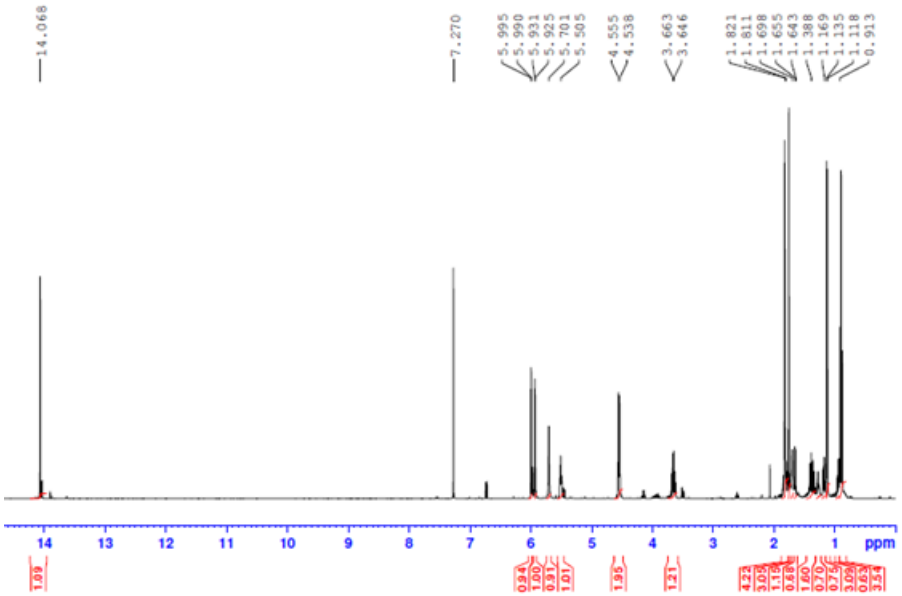
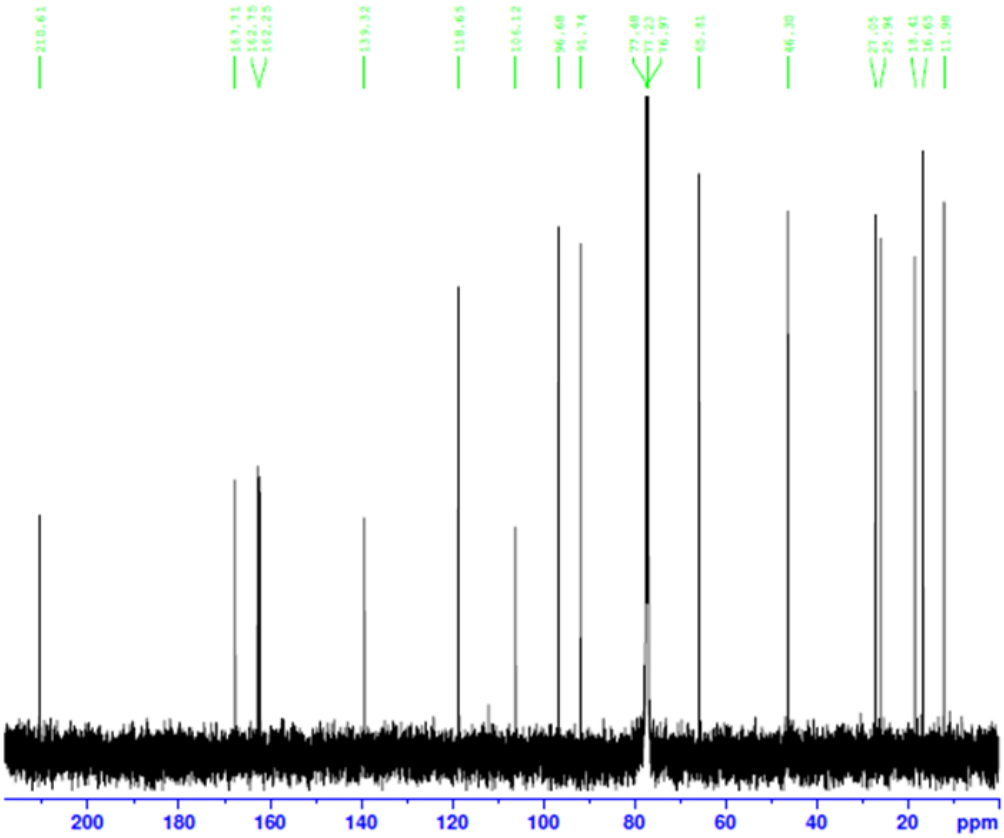
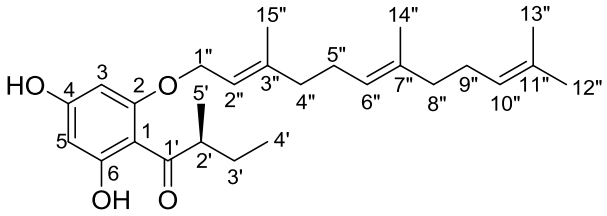


Figure 9: ^{13}C NMR spectrum of **7** (125 MHz, $CDCl_3$)





8

(*S*)-1-(2,4-Dihydroxy-6-(((2*E*,6*E*)-3,7,11-trimethyldodeca-2,6,10-trien-1-yl)oxy)phenyl)-2-methylbutan-1-one (8). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 0.90 (3H, t, J = 7.5 Hz, H4'), 1.13 (3H, d, J = 6.5 Hz, H5'), 1.37 (1H, m, H3'), 1.61 (3H, s, H13"), 1.62 (3H, s, H14"), 1.69 (3H, s, H12"), 1.75 (3H, s, H15"), 1.80 (1H, m, H3'), 1.99 (2H, s, H8"), 2.07 (2H, s, H9"), 2.11 (2H, m, H5"), 2.13 (2H, m, H4"), 3.67 (1H, m, H2'), 4.57 (2H, d, J = 6.5 Hz, H1"), 5.08 (1H, m, H10"), 5.12 (1H, m, H6"), 5.52 (1H, m, H2"), 5.93 (1H, d, J = 2.5 Hz, H3), 5.99 (1H, d, J = 2.5 Hz, H5), 14.05 (1H, s, HO6); ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 12.1 (C4'), 16.2 (C13"), 16.8 (C5'), 16.9 (C15"), 17.9 (C14"), 25.9 (C12"), 26.5 (C5"), 26.9 (C9"), 27.0 (C3'), 39.7 (C4"), 39.9 (C8"), 46.3 (C2'), 65.9 (C1"), 91.8 (C3), 96.7 (C5), 106.1 (C1), 118.4 (C2"), 123.7 (C6"), 124.5 (C10"), 131.6 (C11"), 135.9 (C7"), 142.7 (C3"), 162.3 (C4), 162.8 (C2), 167.7 (C6), 210.6 (C1').

Figure 10: ^{1}H NMR spectrum of **8** (500 MHz, $CDCl_3$)

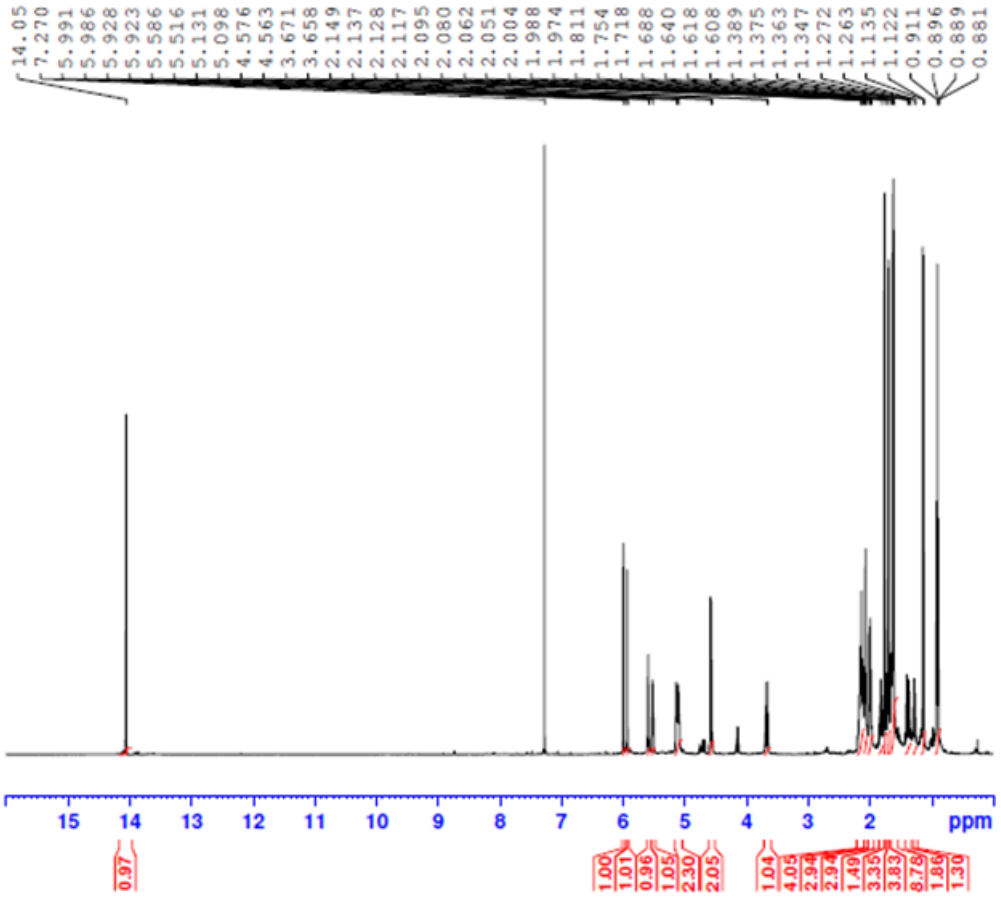
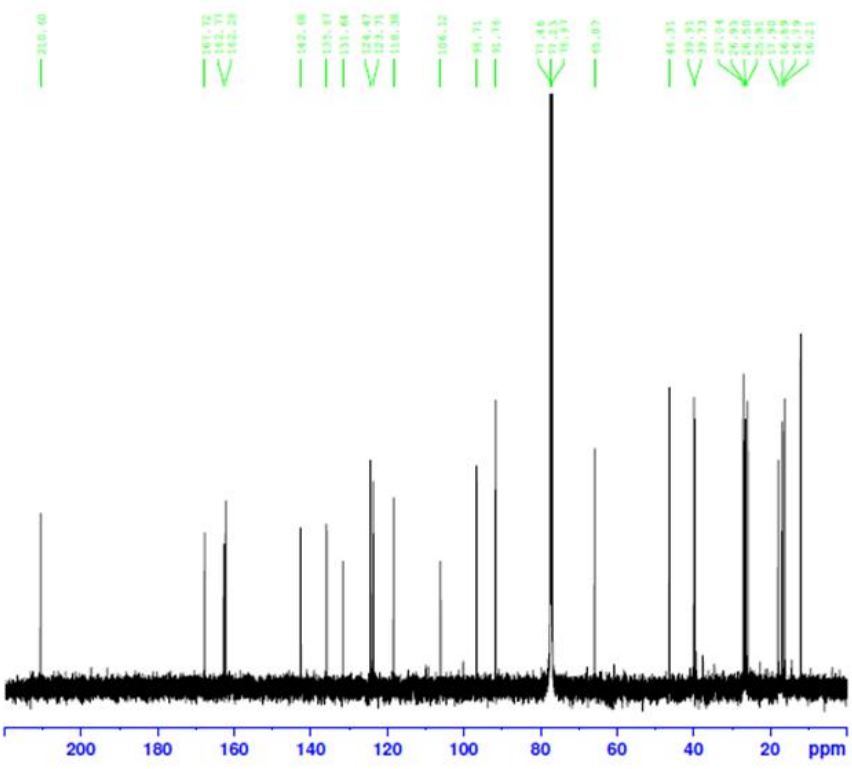
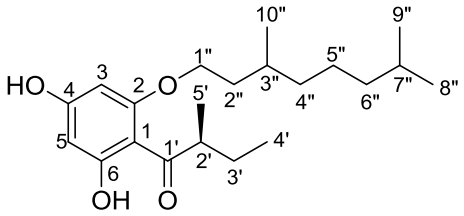


Figure 11: ^{13}C NMR spectrum of **8** (125 MHz, $CDCl_3$)

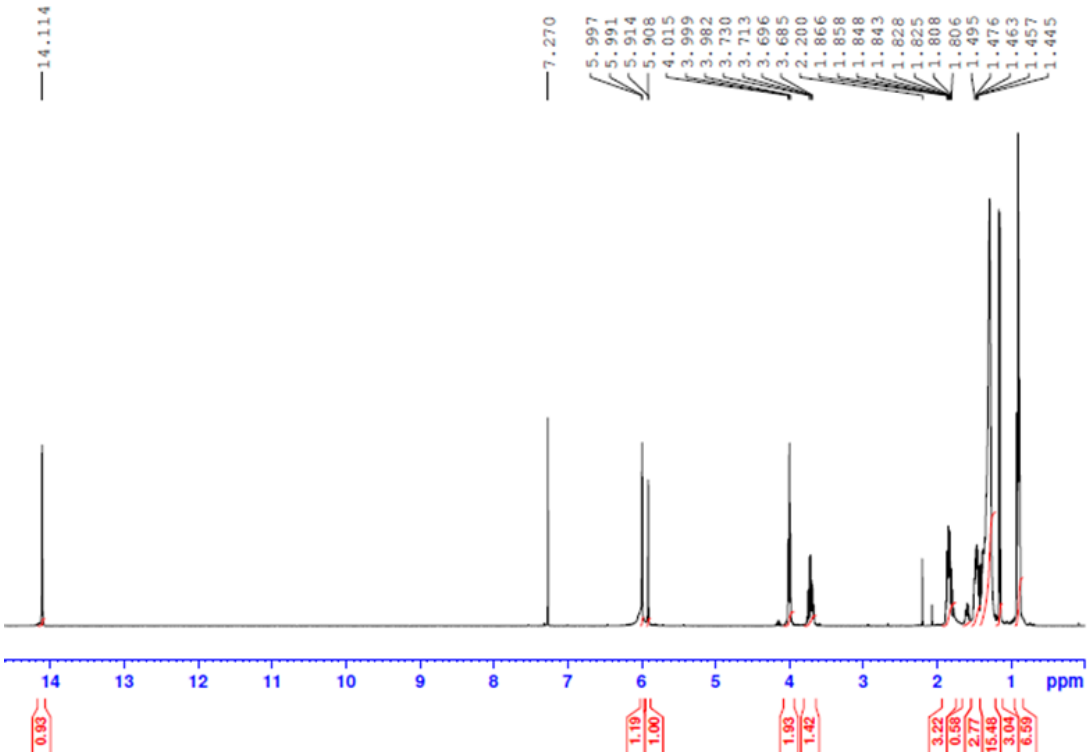

210.40
167.72
162.77
162.20
142.48
135.97
133.64
124.47
123.71
118.38
106.12
95.71
91.76
81.46
81.25
81.07
65.07
46.35
39.91
39.73
27.04
26.93
26.80
26.61
17.91
16.89
16.79
16.21
200
180
160
140
120
100
80
60
40
20
ppm

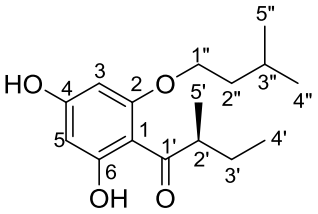


9

(2*S*)-1-(2-((3,7-Dimethyloctyl)oxy)-4,6-dihydroxyphenyl)-2-methylbutan-1-one (9). ^{1}H NMR ($CDCl_3$): δ_H 0.88 (3H, t, J = 7.5 Hz, H4'), 0.89 (6H, d, J = 6.5 Hz, H8" and H9"), 0.97 (3H, d, J = 6.5 Hz, H10"), 1.15 (3H, d, J = 6.5 Hz, H5'), 1.18 (2H, m, H6"), 1.19 (1H, m, H2"a), 1.35 (3H, m, H3'a, H5"), 1.43 (1H, m, H2"b), 1.54 (1H, m, H7"), 1.66 (3H, m, H3", H4"a), 1.82 (1H, m, H3'b), 1.89 (1H, m, H4"b), 3.72 (1H, m, H2'), 4.04 (2H, d, J = 6.5 Hz, H1"), 5.36 (1H, br s, HO4), 5.93 (1H, d, J = 2.0 Hz, H3), 5.99 (1H, d, J = 2.0 Hz, H5), 14.05 (1H, s, HO6); ^{13}C NMR ($CDCl_3$): δ_C 11.7 (C4'), 16.8 (C5'), 19.6 (C10"), 22.6 (C8" and C9"), 24.6 (C5"), 26.6 (C3'), 28.0 (C7"), 29.9 (C3"), 36.0 (C4"), 37.5 (C2"), 39.2 (C6"), 46.0 (C2'), 66.7 (C1"), 91.5 (C3), 96.5 (C5), 105.8 (C1), 162.4 (C4), 162.8 (C2), 167.4 (C6), 210.4 (C1').

Figure 12: ^{1}H NMR spectrum of **9** (500 MHz, $CDCl_3$)

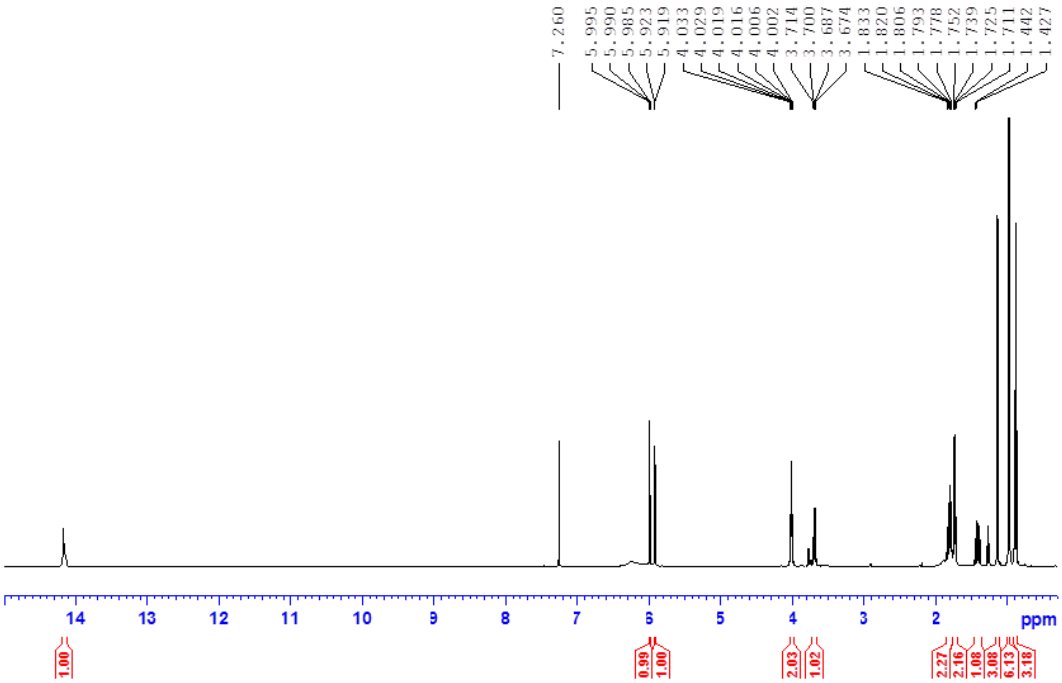


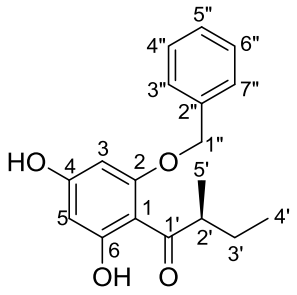


10

(*S*)-1-(2,4-Dihydroxy-6-(isopentyloxy)phenyl)-2-methylbutan-1-one (10). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 0.89 (3H, t, *J* = 7.5 Hz, H4'), 0.98 (6H, d, *J* = 6.5 Hz, H4" and H5"), 1.14 (3H, d, *J* = 6.5 Hz, H5'), 1.41 (1H, m, H3'a), 1.73 (2H, m, H2"), 1.80 (1H, m, H3"), 1.81 (1H, m, H3'b), 3.69 (1H, m, H2'), 4.02 (2H, d, *J* = 6.5 Hz, H1"), 5.40 (1H, br s, HO4), 5.92 (1H, d, *J* = 2.0 Hz, H3), 5.99 (1H, d, *J* = 2.0 Hz, H5), 14.17 (1H, s, HO6); ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 11.7 (C4'), 16.8 (C5'), 22.5 (C4" and C5"), 25.2 (C3"), 26.6 (C3'), 37.7 (C2"), 46.0 (C2'), 67.5 (C1"), 91.5 (C3), 96.5 (C5), 105.8 (C1), 162.4 (C4), 162.8 (C2), 167.4 (C6), 210.4 (C1').

Figure 13: ^{1}H NMR spectrum of **10** (500 MHz, $CDCl_3$)





11

(*S*)-1-(2-(Benzyloxy)-4,6-dihydroxyphenyl)-2-methylbutan-1-one (11). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 0.68 (3H, t, J = 6.5 Hz, H4'), 1.00 (3H, d, J = 6.5 Hz, H5'), 1.29 (1H, m, H3'), 1.71 (1H, m, H3'), 3.57 (1H, m, H2'), 5.08 (2H, s, H1"), 6.00 (1H, d, J = 2.0 Hz, H3), 6.01 (1H, d, J = 2.0 Hz, H5), 7.38-7.42 (5H, m, H3"-7"), 14.00 (1H, s, HO6); ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 11.7 (C4'), 16.8 (C5'), 26.9 (C3'), 46.2 (C2'), 71.6 (C1"), 92.0 (C5), 97.1 (C3), 106.1 (C1), 128.4 (C3" and C7"), 128.8 (C5"), 129.0 (C4" and C6"), 135.6 (C2"), 162.2 (C4), 162.5 (C6), 167.8 (C2), 210.6 (C1').

Figure 14: ^{1}H NMR spectrum of **11** (500 MHz, $CDCl_3$)

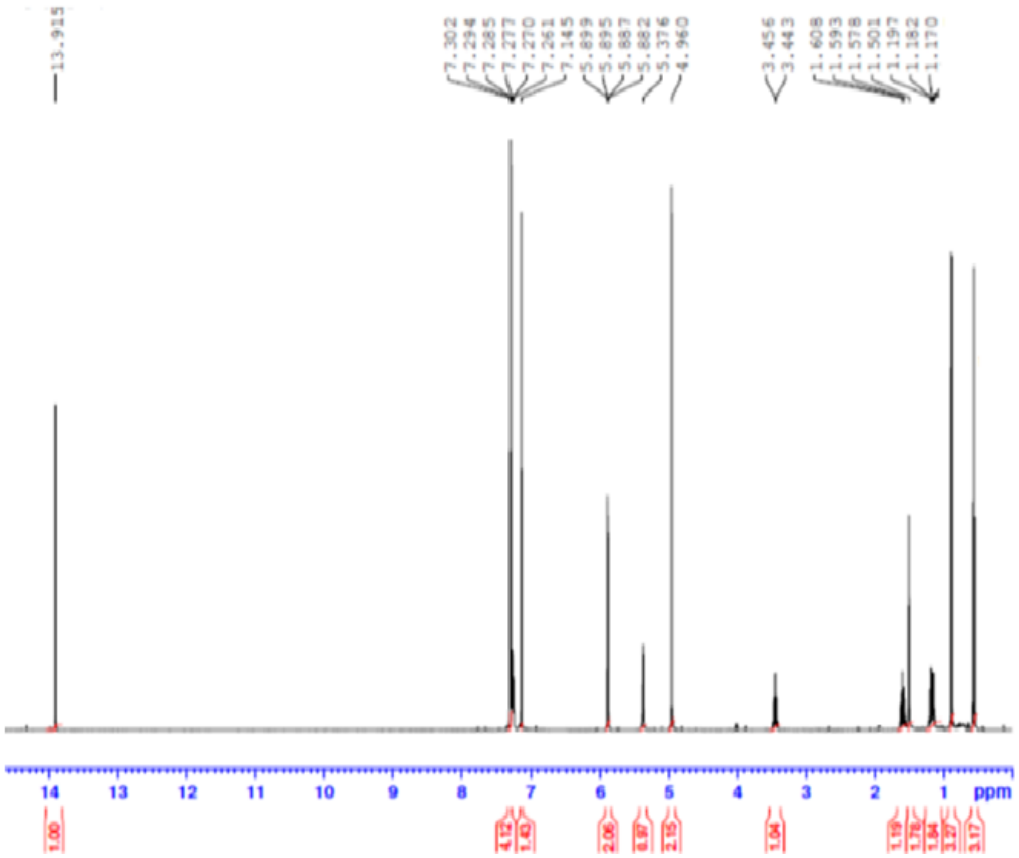
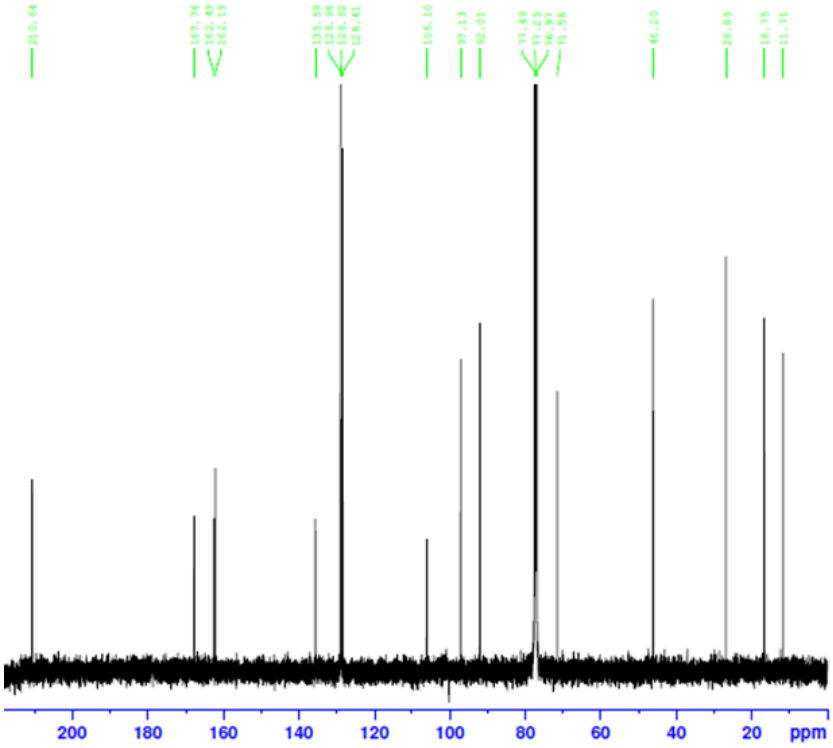
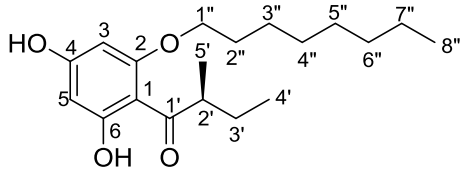


Figure 15: ^{13}C NMR spectrum of **11** (125 MHz, $CDCl_3$)





12

(*S*)-1-(2,4-Dihydroxy-6-(octyloxy)phenyl)-2-methylbutan-1-one (12). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 0.89 (3H, t, J = 7.5 Hz, H8"), 0.90 (3H, t, J = 7.5 Hz, H4'), 1.16 (3H, d, J = 7.0 Hz, H5'), 1.26-1.40 (8H, m, H3"-H6"), 1.38 (1H, m, H3'), 1.46 (2H, m, H2"), 1.81 m (1H, m, H3'), 1.85 (2H, m, H7"), 3.72 (1H, q, J = 6.5 Hz, H2'), 4.00 (2H, t, J = 6.5 Hz, H1"), 5.42 (1H, br s, HO4), 5.91 (1H, d, J = 2.0 Hz, H3), 5.99 (1H, d, J = 2.0 Hz, H5), 14.06 (1H, s, HO6); ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 12.0 (C4'), 14.3 (C8"), 17.1 (C5'), 22.8 (C7"), 26.5 (C3'), 26.9, 29.3, 29.4, 29.5, 32.0 (C2"-C6"), 46.3 (C2'), 69.4 (C1"), 91.5 (C3), 96.8 (C5), 106.2 (C1), 162.2 (C4), 163.0 (C2), 167.8 (C6), 210.5 (C1').

Figure 16: ^{1}H NMR spectrum of **12** (500 MHz, $CDCl_3$)

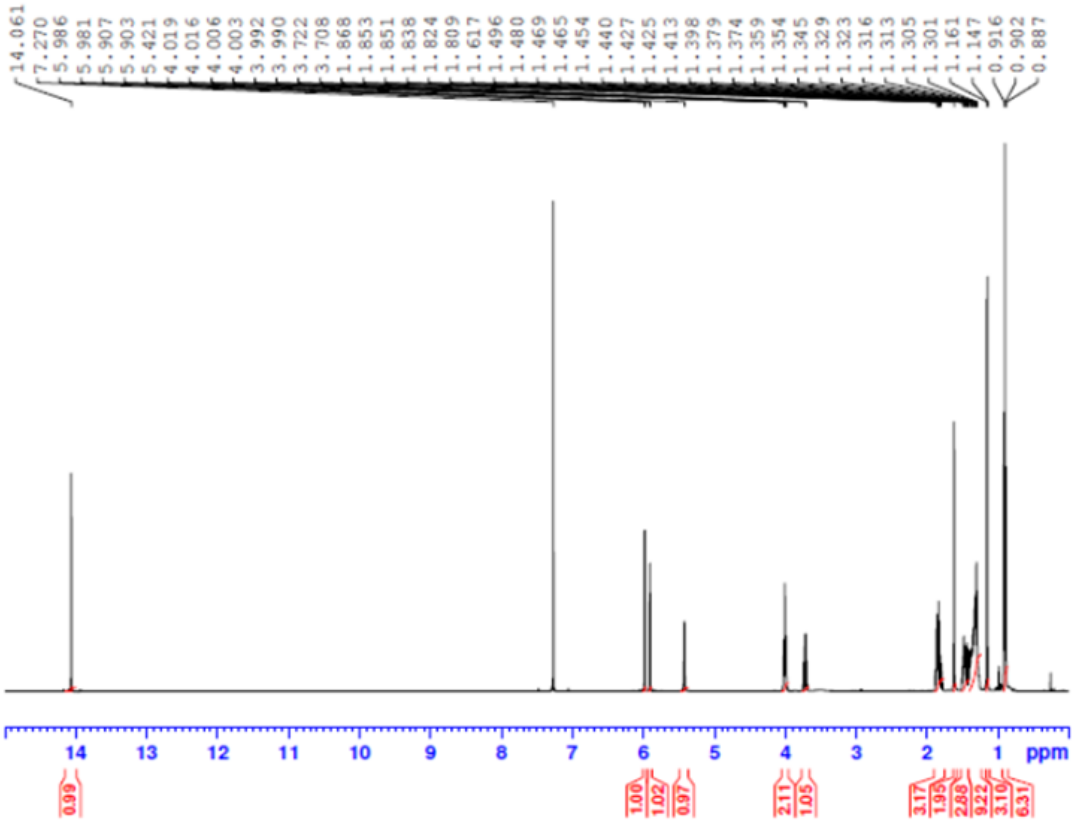
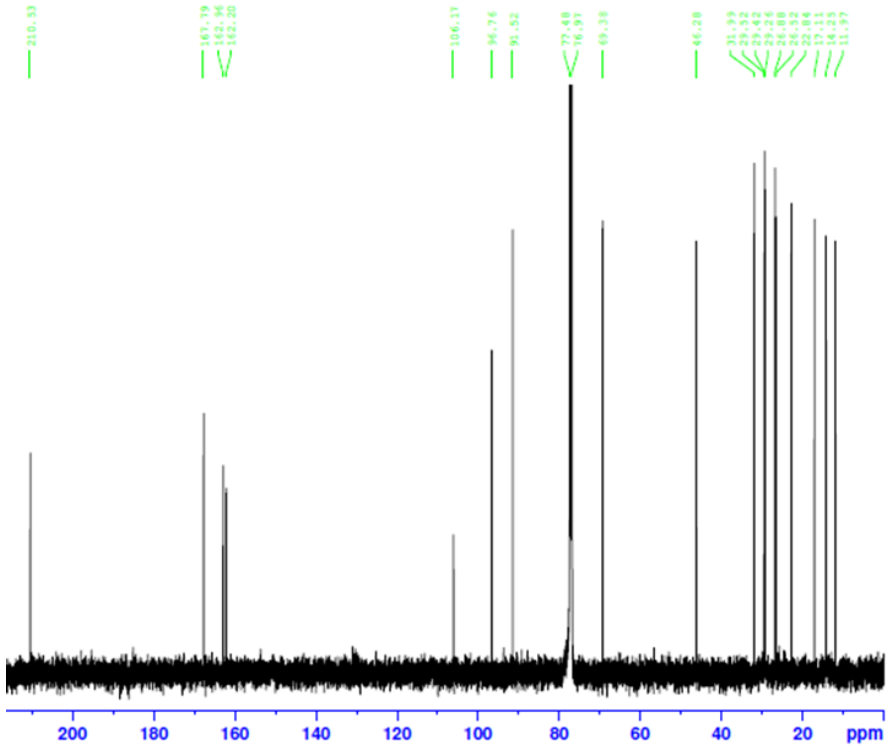
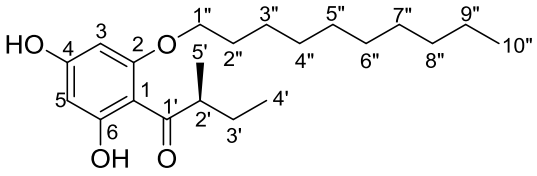


Figure 17: ^{13}C NMR spectrum of **12** (125 MHz, $CDCl_3$)

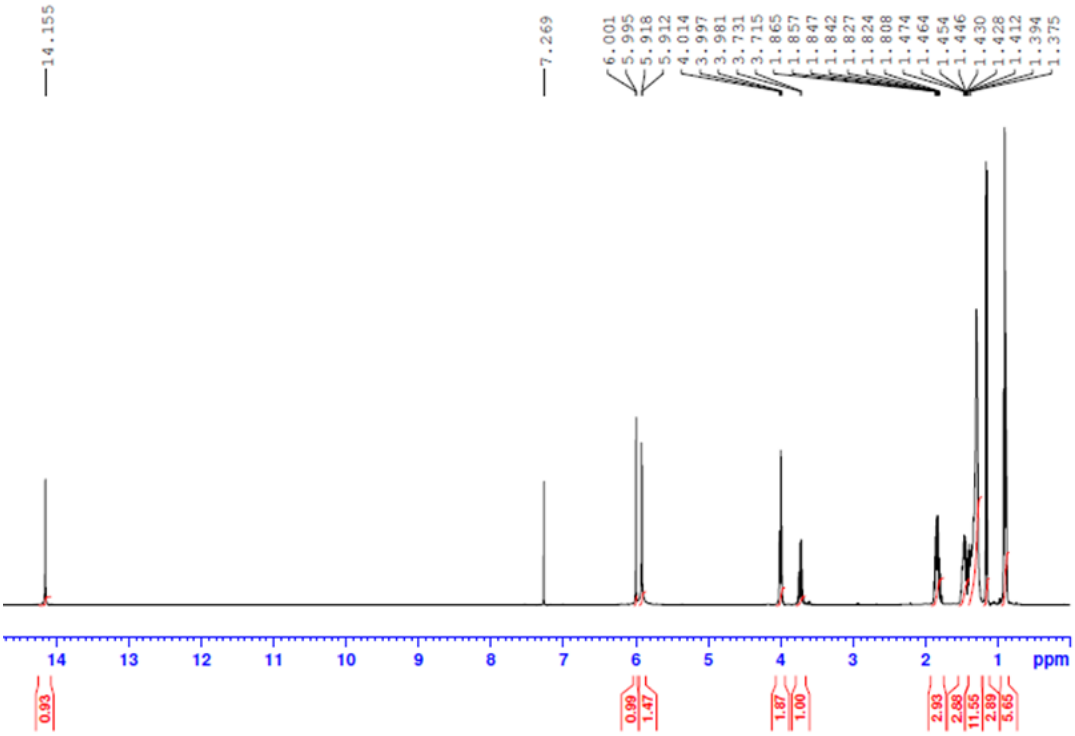


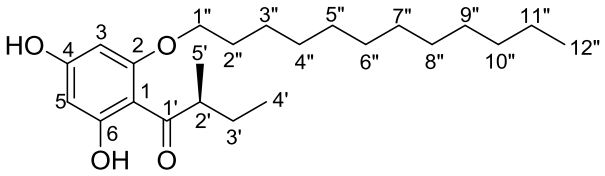


13

(*S*)-1-(2-(Decyloxy)-4,6-dihydroxyphenyl)-2-methylbutan-1-one (13). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 0.88 (3H, t, *J* = 7.5 Hz, H4'), 0.89 (3H, t, *J* = 7.5 Hz, H10"), 1.17 (3H, d, *J* = 6.5 Hz, H5'), 1.28-1.31 (12H, m, H3"-8"), 1.34 (1H, m, H3'), 1.46 (2H, m, H2"), 1.81 (1H, m, H3'), 1.84 (2H, m, H9"), 3.72 (1H, q, *J* = 6.5 Hz, H2'), 4.00 (2H, t, *J* = 6.5 Hz, H1"), 5.92 (1H, d, *J* = 2.0 Hz, H3), 6.00 (1H, d, *J* = 2.0 Hz, H5), 14.16 (1H, s, HO6); ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 12.0 (C4'), 14.3 (C10"), 17.3 (C5'), 26.5, 26.6, 29.1, 29.4, 29.5, 29.6, 29.8, 29.9, 32.0 (C2"-C9"), 46.3 (C2'), 69.3 (C1"), 91.6 (C3), 96.8 (C5), 106.2 (C1), 162.3 (C4), 163.0 (C2), 167.7 (C6), 210.6 (C1').

Figure 18: ^{1}H NMR spectrum of **13** (500 MHz, $CDCl_3$)





14

(*S*)-1-(2-(Dodecyloxy)-4,6-dihydroxyphenyl)-2-methylbutan-1-one (14). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 0.88 (3H, t, J = 7.5 Hz, H4'), 0.89 (3H, t, J = 7.5 Hz, H12"), 1.16 (3H, d, J = 6.5 Hz, H5'), 1.28-1.30 (16H, m, H3"-10"), 1.35 (1H, m, H3'), 1.46 (2H, m, H2"), 1.83 m (1H, m, H3'), 1.86 (2H, m, H11"), 3.73 (1H, q, J = 6.5 Hz, H2'), 4.00 (2H, t, J = 6.5 Hz, H1"), 5.92 (1H, d, J = 2.0 Hz, H3), 6.00 (1H, d, J = 2.0 Hz, H5), 6.02 (1H, br s, HO4), 14.19 (1H, s, HO6); ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 12.0 (C4'), 14.3 (C12"), 17.1 (C5'), 22.9 (C2"), 26.9 (C3'), 26.5, 29.3, 29.5, 29.6, 29.77 (2C), 29.8, 29.9, 32.1 (C3"-C11"), 46.3 (C2'), 69.4 (C1"), 91.7 (C3), 96.8 (C5), 106.1 (C1), 162.5 (C4), 163.0 (C2), 167.7 (C6), 210.7 (C1').

Figure 19: ^{1}H NMR spectrum of **14** (500 MHz, $CDCl_3$)

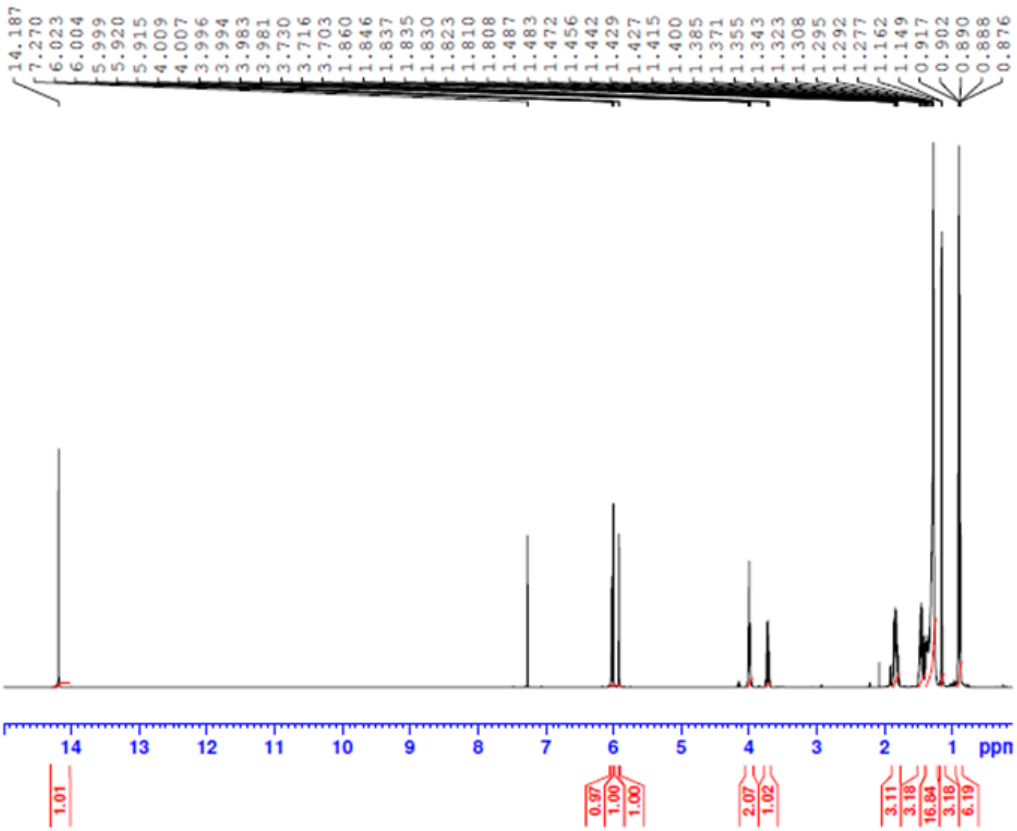
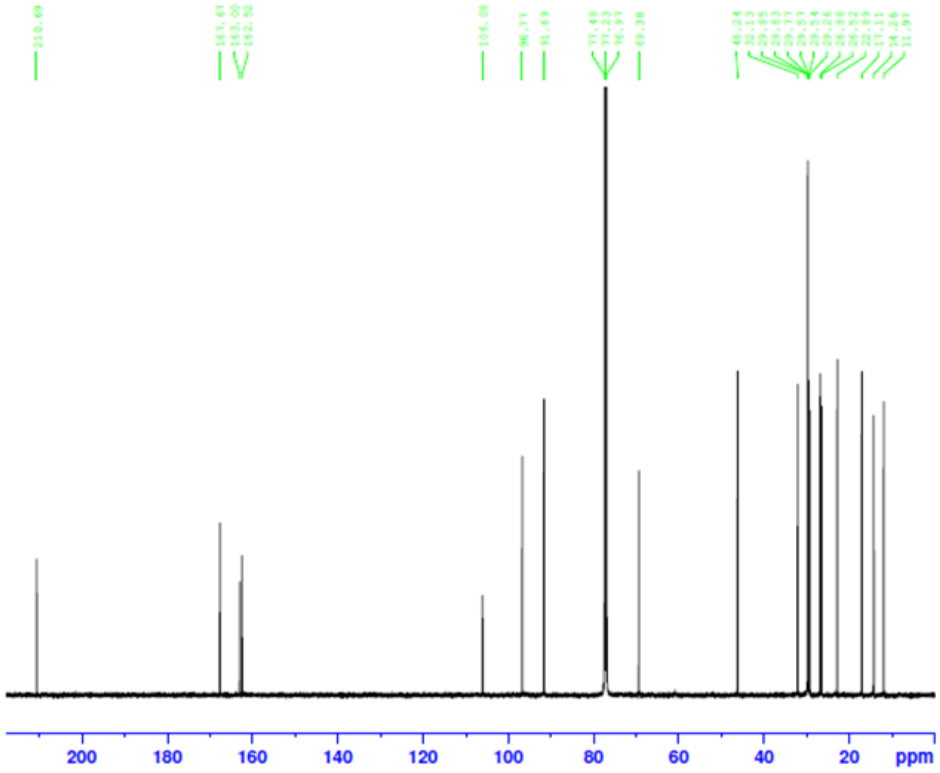
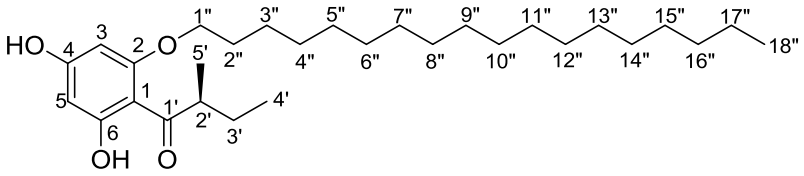


Figure 20: ^{13}C NMR spectrum of **14** (125 MHz, $CDCl_3$)





15

(*S*)-1-(2,4-Dihydroxy-6-(octadecyloxy)phenyl)-2-methylbutan-1-one (15). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 0.89 (3H, t, J = 7.5 Hz, H4'), 0.91 (3H, t, J = 7.5 Hz, H18"), 1.16 (3H, d, J = 6.5 Hz, H5'), 1.27-1.33 (28H, m, H3"-16"), 1.42 (1H, m, H3'), 1.46 (2H, m, H2"), 1.81 (1H, m, H3'), 1.85 (2H, m, H17"), 3.73 (1H, q, J = 6.5 Hz, H2'), 4.00 (2H, t, J = 6.5 Hz, H1"), 5.92 (1H, d, J = 2.0 Hz, H3), 6.00 (1H, d, J = 2.0 Hz, H5), 6.07 (1H, br s, HO4), 14.12 (1H, s, HO6); ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 12.0 (C4'), 14.3 (C18"), 17.1 (C5'), 22.9 (C3"), 26.5 (C3'), 26.9, 29.3, 29.6, 29.8-29.9 (C4"-C17"), 32.2 (C2"), 46.3 (C2'), 69.4 (C1"), 91.6 (C3), 96.8 (C5), 106.1 (C1), 162.3 (C4), 163.0 (C2), 167.8 (C6), 210.6 (C1').

Figure 21: ^{1}H NMR spectrum of **15** (500 MHz, $CDCl_3$)

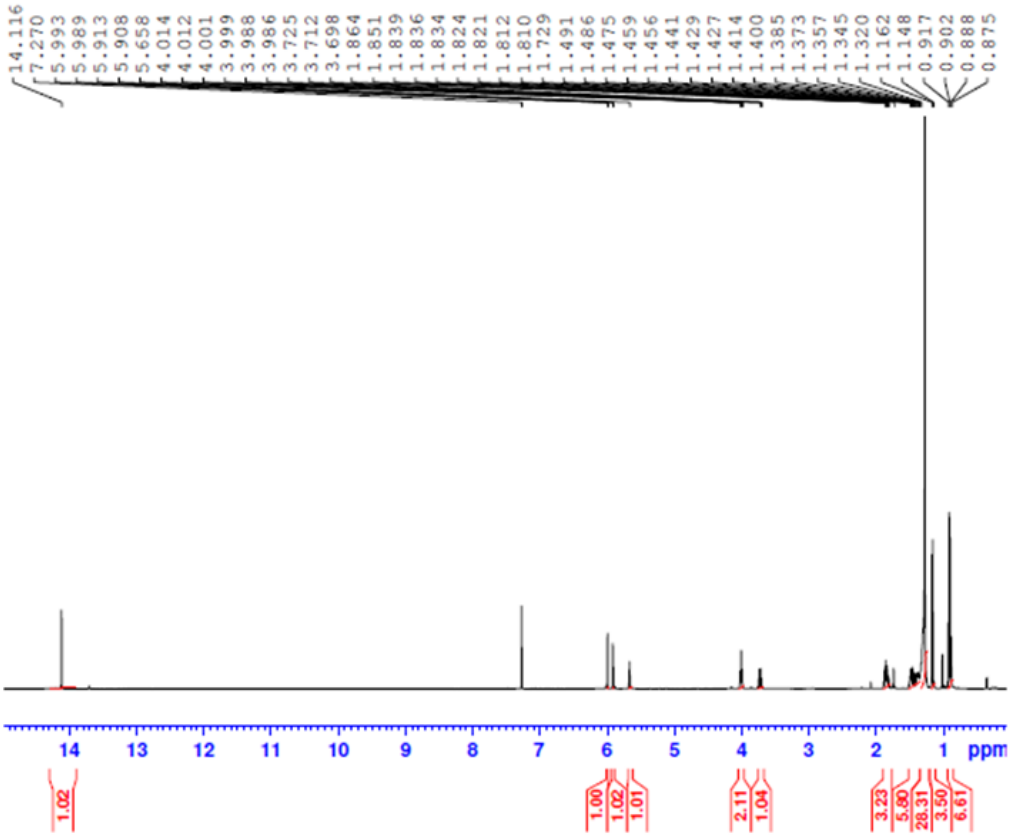
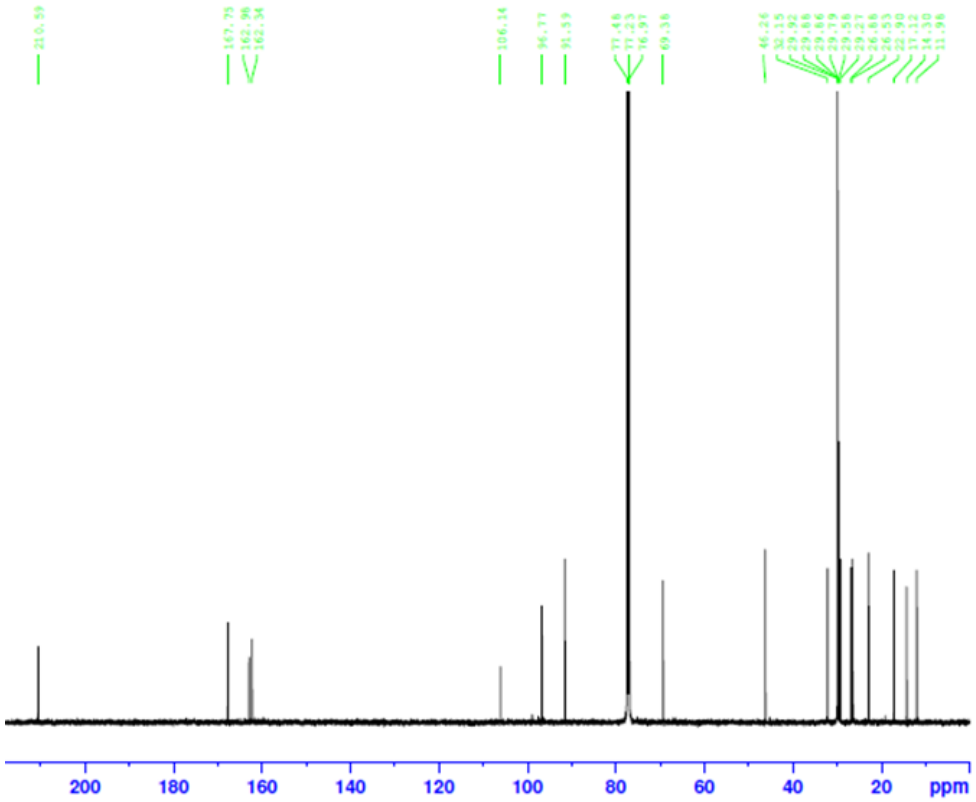
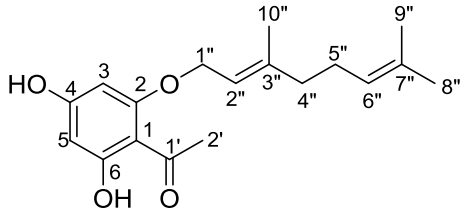


Figure 22: ^{13}C NMR spectrum of **15** (125 MHz, $CDCl_3$)





18

(*E*)-1-(2-((3,7-Dimethylocta-2,6-dien-1-yl)oxy)-4,6-dihydroxyphenyl)ethanone (18). ^{1}H NMR (500 MHz, $(CD_3)_2CO$): δ_H 1.59 (3H, s, H10"), 1.64 (3H, s, H9"), 1.77 (3H, s, H8"), 2.11-2.16 (4H, m, H4", H5"), 2.55 (3H, s, H2'), 4.64 (2H, d, J = 6.5 Hz, H1"), 5.11 (1H, m, H6"), 5.56 (1H, m, H2"), 5.93 (1H, d, J = 2.0 Hz, H3), 6.03 (1H, d, J = 2.0 Hz, H5), 13.91 (1H, s, HO6); ^{13}C NMR (125 MHz, $(CD_3)_2CO$): δ_C 16.7 (C10"), 17.8 (C9"), 25.9 (C8"), 27.0 (C5"), 33.2 (C2'), 40.1 (C4"), 66.4 (C1"), 92.8 (C3), 96.6 (C5), 106.1 (C1), 119.9 (C2"), 124.7 (C6"), 132.2 (C7"), 142.6 (C3"), 164.0 (C4), 166.0 (C2), 168.3 (C6), 203.5 (C1').

Figure 23: ^{1}H NMR spectrum of **18** (500 MHz, $(CD_3)_2CO$)

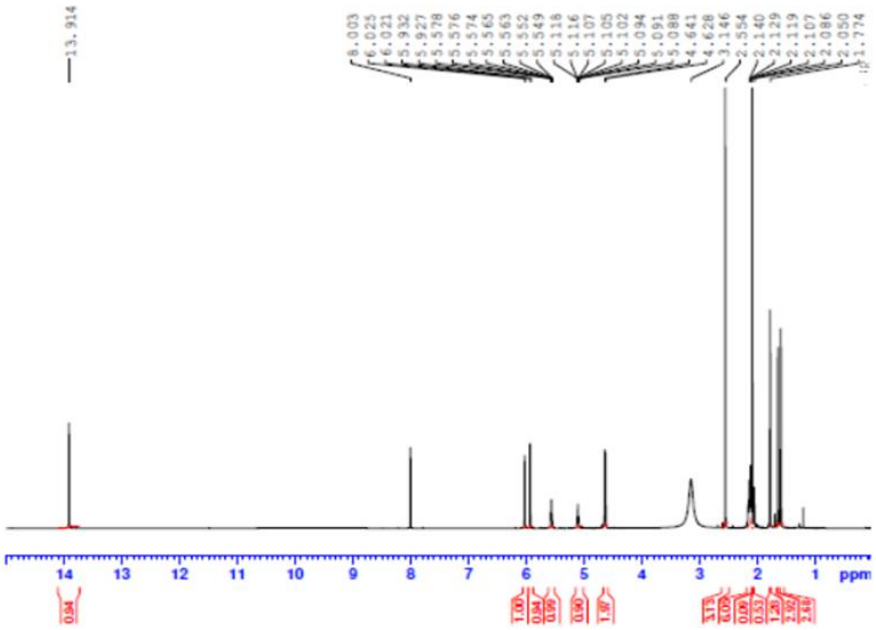
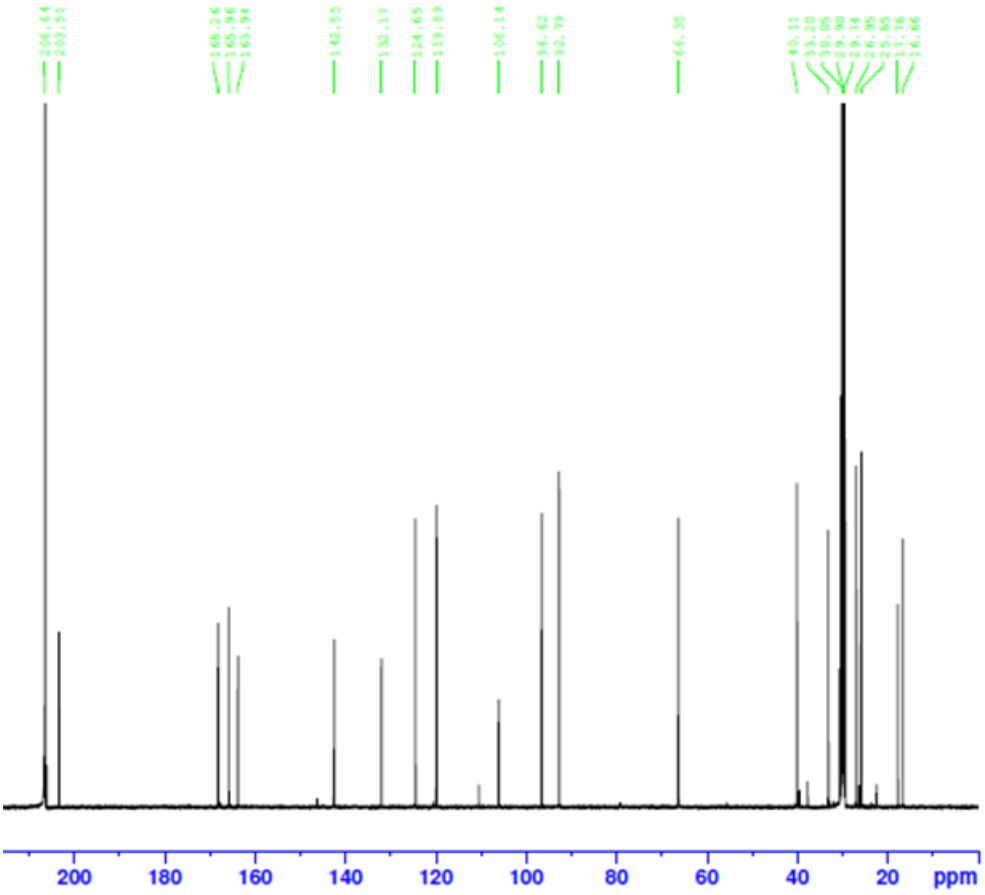
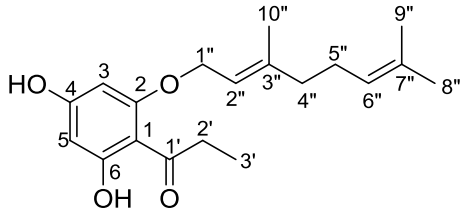


Figure 24: ^{13}C NMR spectrum of **18** (125 MHz, $(CD_3)_2CO$)





19

(*E*)-1-(2-((3,7-Dimethylocta-2,6-dien-1-yl)oxy)-4,6-dihydroxyphenyl)propan-1-one (19). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 1.15 (3H, t, J = 7.0 Hz, H3'), 1.61 (3H, s, H9"), 1.68 (3H, s, H8"), 1.74 (3H, s, H10"), 2.10 (2H, m, H5"), 2.13 (2H, m, H4"), 3.03 (2H, q, J = 7.0 Hz, H-2'), 4.57 (2H, d, J = 6.5 Hz, H1"), 5.10 (1H, m, H6"), 5.51 (1H, m, H2"), 5.53 (1H, s, HO4), 5.91 (1H, d, J = 2.0 Hz, H3), 5.98 (1H, d, J = 2.0 Hz, H5), 14.05 (1H, s, HO6); ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 9.0 (C3'), 16.9 (C10"), 18.0 (C9"), 25.9 (C8"), 26.5 (C5"), 37.8 (C2'), 39.7 (C4"), 66.0 (C1"), 91.7 (C3), 96.6 (C5), 106.3 (C1), 118.6 (C2"), 123.8 (C6"), 132.3 (C7"), 142.4 (C3"), 162.4 (C4), 163.2 (C2), 167.4 (C6), 207.0 (C1').

Figure 25: ^{1}H NMR spectrum of **19** (500 MHz, $CDCl_3$)

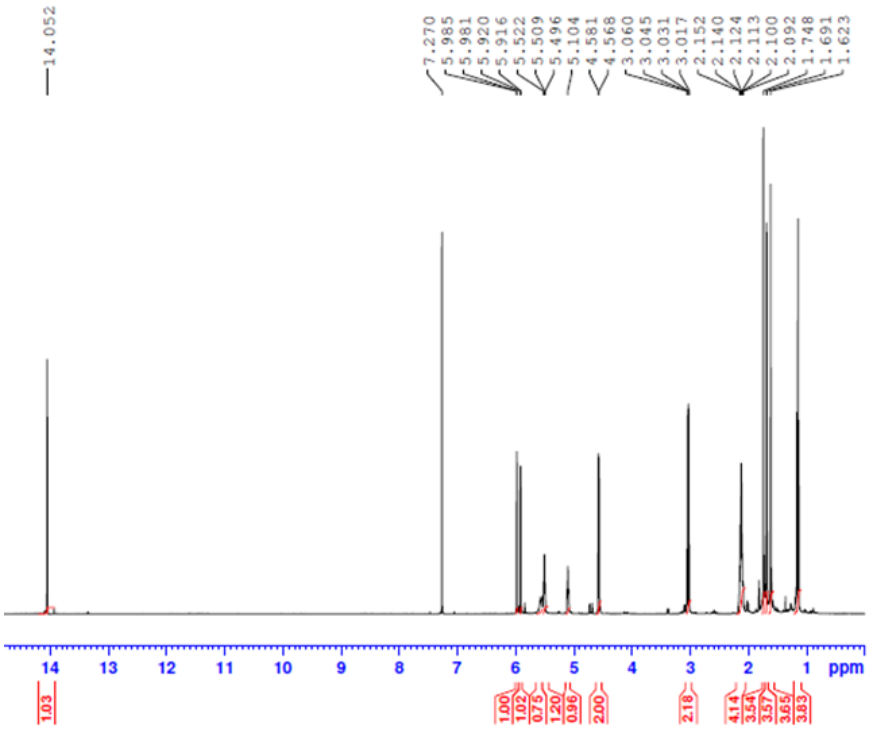
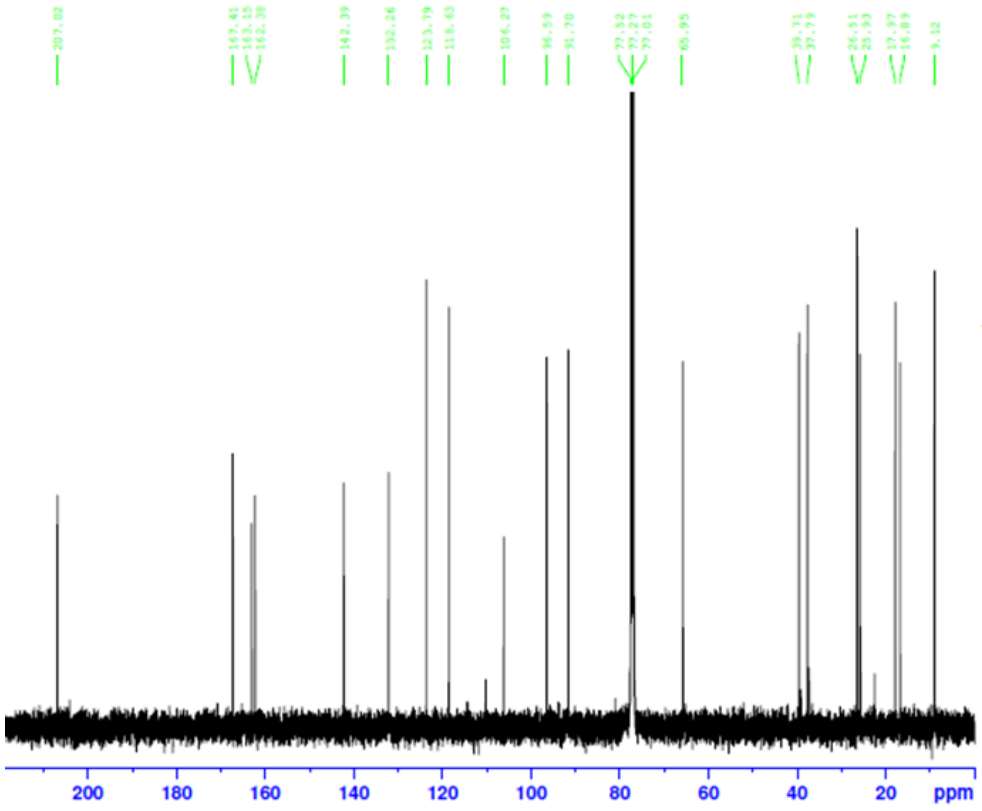
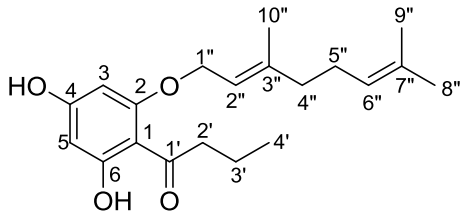


Figure 26: ^{13}C NMR spectrum of **19** (125 MHz, $CDCl_3$)





20

(*E*)-1-(2-((3,7-Dimethylocta-2,6-dien-1-yl)oxy)-4,6-dihydroxyphenyl)butan-1-one (20). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 0.97 (3H, t, J = 6.5 Hz, H4'), 1.61 (3H, s, H9"), 1.69 (3H, s, H8"), 1.71 (2H, s, H3'), 1.74 (3H, s, H10"), 2.10 (2H, m, H5"), 2.13 (2H, m, H4"), 2.97 (2H, t, J = 7.0 Hz, H-2'), 4.54 (2H, d, J = 6.5 Hz, H1"), 5.10 (1H, m, H6"), 5.50 (1H, t, J = 6.5Hz, H2"), 5.91 (1H, s, HO4), 5.93 (1H, d, J = 2.0 Hz, H3), 5.99 (1H, d, J = 2.0 Hz, H5), 14.10 (1H, s, HO6); ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 14.2 (C4'), 16.9 (C10"), 17.9 (C9"), 18.9 (C2'), 25.9 (C8"), 26.5 (C5"), 39.7 (C4"), 46.5 (C3'), 65.9 (C1"), 92.1 (C3), 96.6 (C5), 106.0 (C1), 118.4 (C2"), 123.8 (C6"), 132.2 (C7"), 142.7 (C3"), 162.3 (C4), 163.4 (C2), 167.3 (C6), 206.9 (C1').

Figure 27: ^{1}H NMR spectrum of **20** (500 MHz, $CDCl_3$)

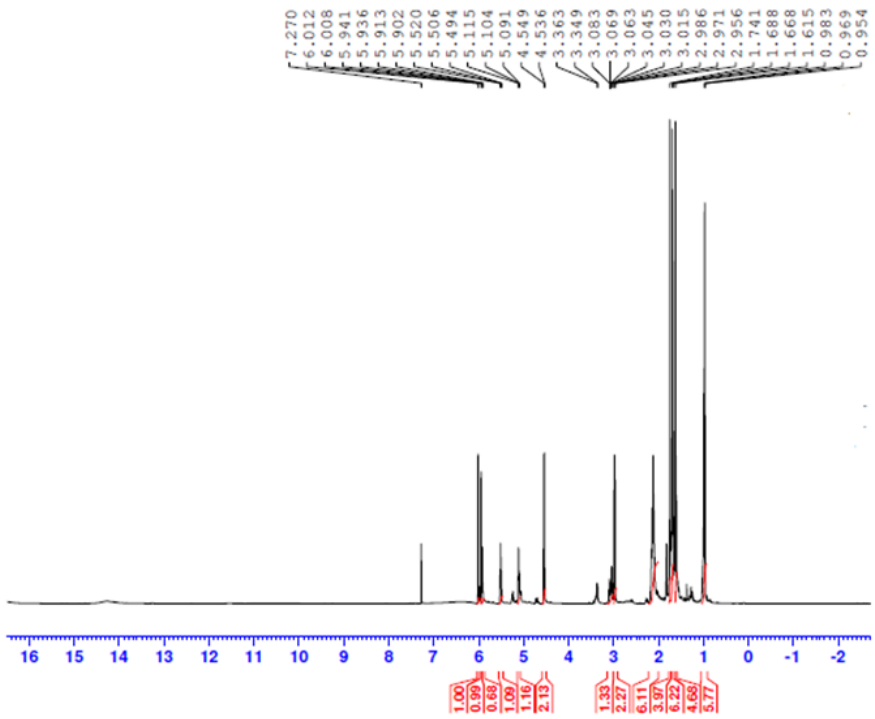
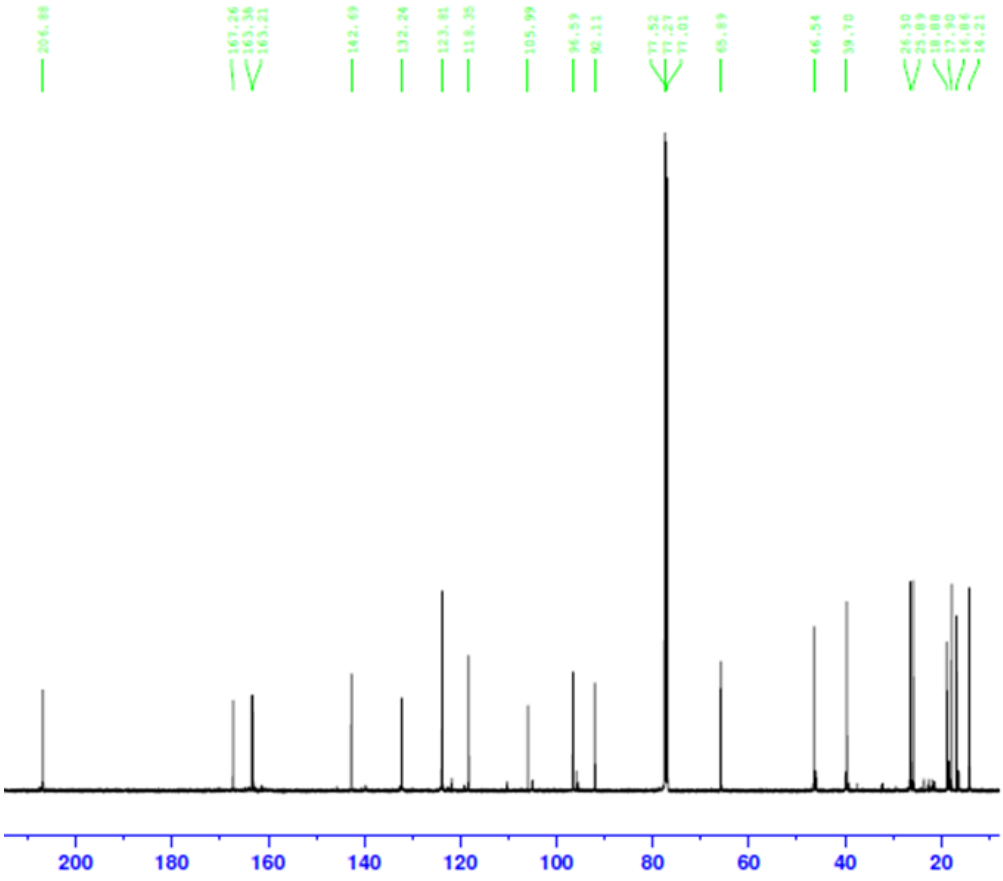
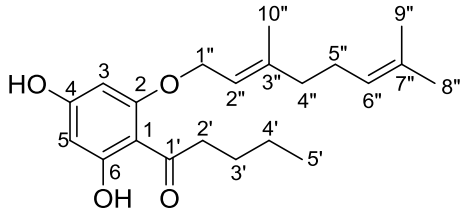


Figure 28: ^{13}C NMR spectrum of **20** (125 MHz, $CDCl_3$)





21

(*E*)-1-(2-((3,7-Dimethylocta-2,6-dien-1-yl)oxy)-4,6-dihydroxyphenyl)pentan-1-one (21). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 0.92 (3H, t, J = 6.5 Hz, H5'), 1.37 (2H, q, J = 6.5 Hz, H4'), 1.61 (3H, s, H9"), 1.64 (2H, m H3'), 1.69 (3H, s, H8"), 1.74 (3H, s, H10"), 2.10 (2H, m, H5"), 2.13 (2H, m, H4"), 3.00 (2H, m, H-2'), 4.55 (2H, d, J = 6.5 Hz, H1"), 5.10 (1H, t, J = 6.5 Hz, H6"), 5.50 (1H, t, J = 6.5 Hz, H2"), 5.92 (1H, d, J = 2.0 Hz, H3), 5.99 (1H, d, J = 2.0 Hz, H5), 6.38 (1H, s, HO4),14.04 (1H, s, HO6); ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 14.2(C5'), 16.9 (C10"), 17.9 (C9"), 22.8 (C4'), 25.9 (C8"), 26.5 (C5"), 27.4 (C3'), 39.6 (C4"), 44.4 (C2'), 65.9 (C1"), 91.9 (C3), 96.6 (C5), 106.1 (C1), 118.4 (C2"), 123.8 (C6"), 132.2 (C7"), 142.6 (C3"), 162.9 (C4), 163.1 (C2), 167.4 (C6), 206.8 (C1').

Figure 29: ^{1}H NMR spectrum of **21** (500 MHz, $CDCl_3$)

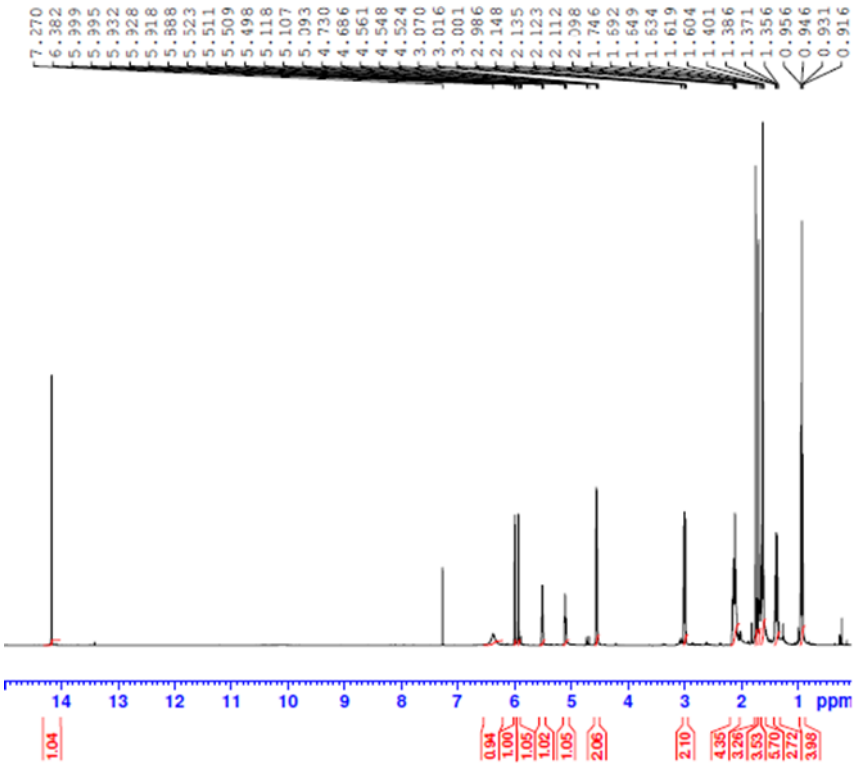
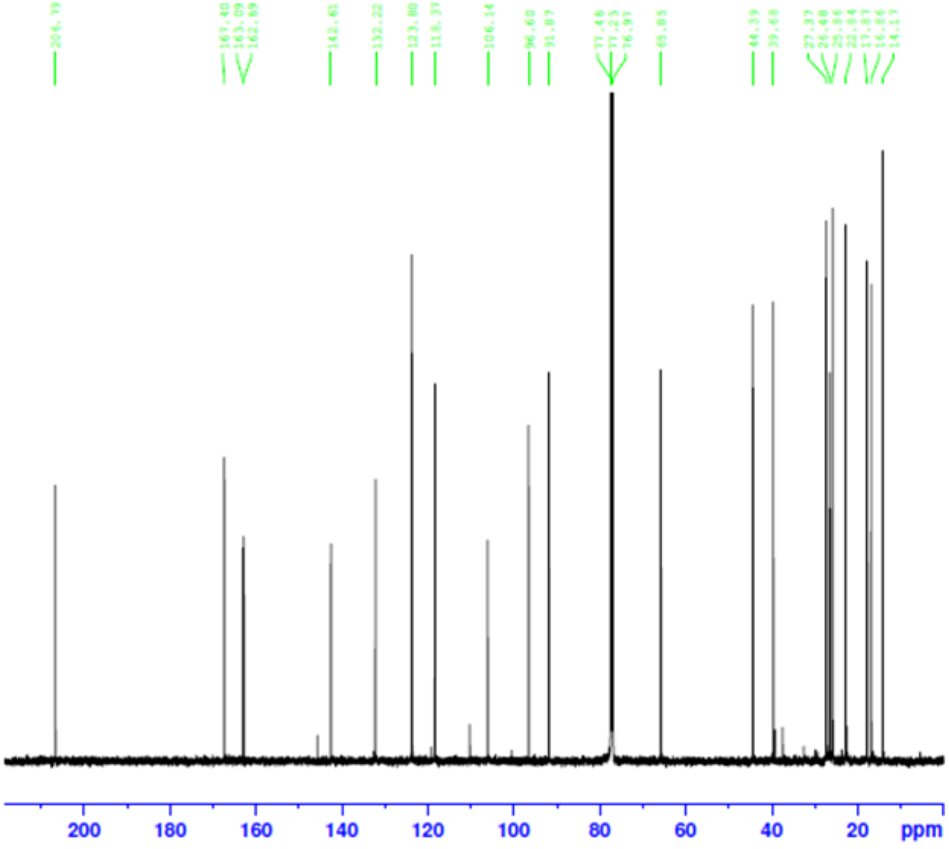
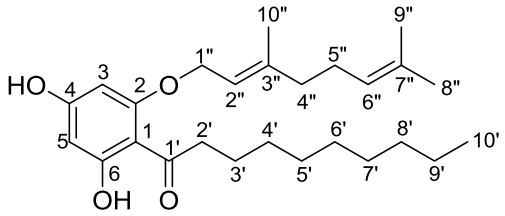


Figure 30: ^{13}C NMR spectrum of **21** (125 MHz, $CDCl_3$)





22

(*E*)-1-(2-((3,7-Dimethylocta-2,6-dien-1-yl)oxy)-4,6-dihydroxyphenyl)decan-1-one (22). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 0.88 (3H, t, J = 6.5 Hz, H10'), 1.26 (12H, br s, H3'-H9'), 1.35 (2H, m, H3'), 1.61 (3H, s, H9"), 1.68 (3H, s, H8"), 1.74 (3H, s, H10"), 2.09 (2H, m, H5"), 2.13 (2H, m, H4"), 2.99 (2H, t, J = 7.6 Hz, H-2'), 4.56 (2H, d, J = 6.4 Hz, H1"), 5.11 (1H, t, J = 6.8 Hz, H6"), 5.51 (1H, t, J = 6.8 Hz, H2"), 5.92 (1H, d, J = 2.4 Hz, H3), 5.99 (1H, d, J = 2.4 Hz, H5), 14.10 (1H, s, HO6); ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 14.4 (C10'), 16.9 (C10"), 17.9 (C9"), 22.9 (C9'), 25.4 (C3'), 25.9 (C8"), 26.6 (C5"), 29.6 (C4'), 29.7-29.8 (C5'-C7'), 32.2 (C8'), 39.8 (C4"), 44.7 (C2'), 65.9 (C1"), 91.9 (C3), 96.6 (C5), 106.1 (C1), 118.5 (C2"), 123.8 (C6"), 132.2 (C7"), 142.5 (C3"), 163.0 (C4), 163.1 (C2), 167.5 (C6), 206.5 (C1').

Figure 31: ^{1}H NMR spectrum of **22** (500 MHz, $CDCl_3$)

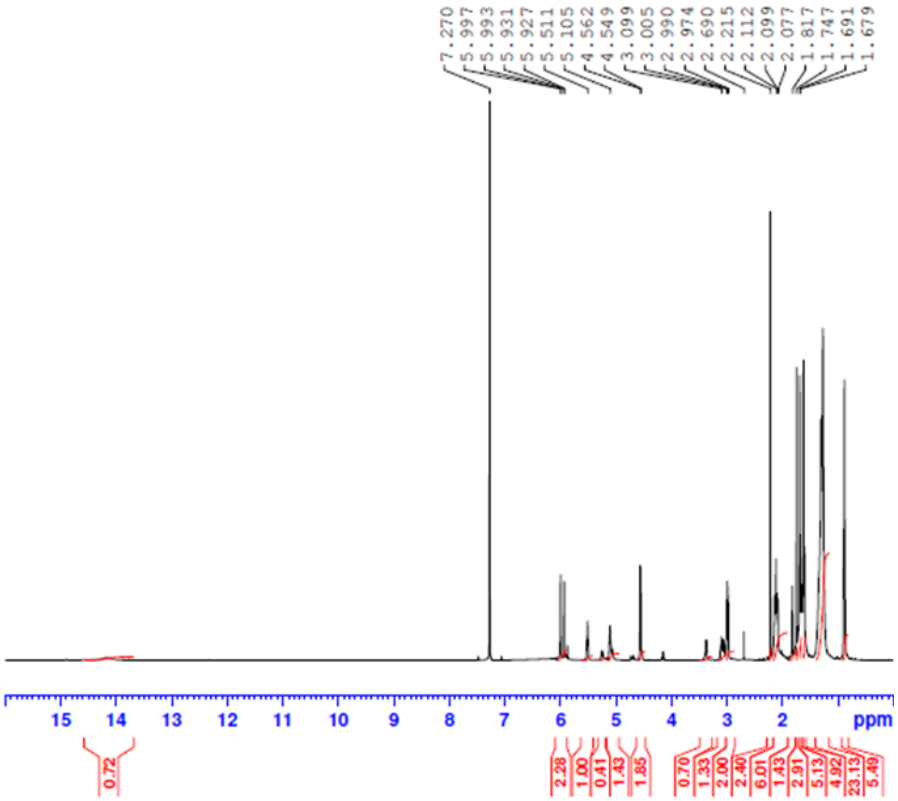
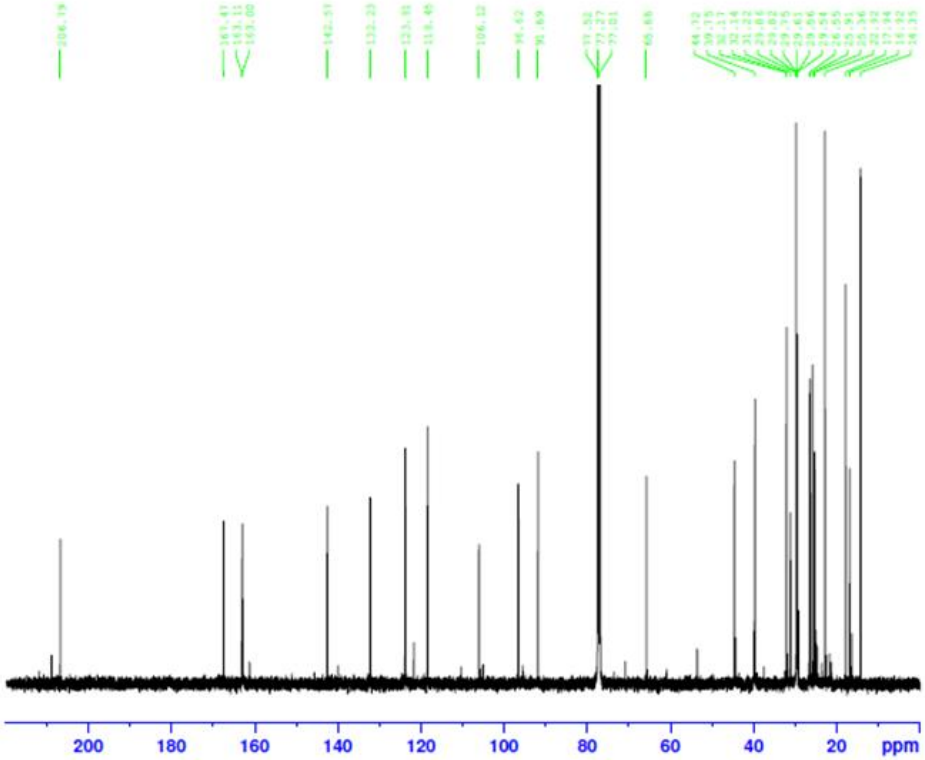
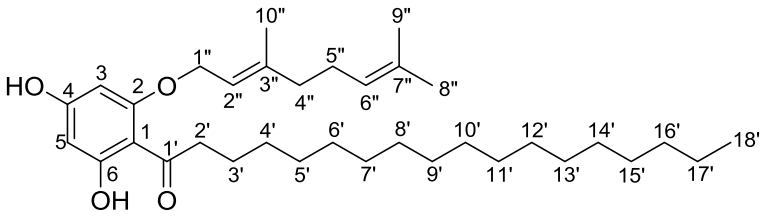


Figure 32: ^{13}C NMR spectrum of **22** (125 MHz, $CDCl_3$)





23

(*E*)-1-(2-((3,7-Dimethylocta-2,6-dien-1-yl)oxy)-4,6-dihydroxyphenyl)octadecan-1-one (23). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 0.89 (3H, t, J = 6.8Hz, H18'), 1.26-1.35 (34H, br s, H3'-H17'), 1.62 (3H, s, H9"), 1.69 (3H, s, H8"), 1.75 (3H, s, H10"), 2.10 (2H, m, H5"), 2.13 (2H, m, H4"), 2.99 (2H, m, H-2'), 4.55 (2H, d, J = 6.5 Hz, H1"), 5.10 (1H, t, J = 6.5 Hz, H6"), 5.50 (1H, t, J = 6.5 Hz, H2"), 5.91 (1H, d, J = 2.0 Hz, H3), 5.98 (1H, d, J = 2.0 Hz, H5), 14.12 (1H, s, HO6); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 14.3 (C10'), 16.9 (C10"), 17.9 (C9"), 22.9 (C9'), 25.3 (C3'), 25.9 (C8"), 26.5 (C5"), 29.6 (C4'), 29.8-29.9 (C5'-C17'), 32.1 (C8'), 39.7 (C4"), 44.7 (C2'), 65.9 (C1"), 91.7 (C3), 96.6 (C5), 106.3 (C1), 118.5 (C2"), 123.8 (C6"), 132.2 (C7"), 142.5 (C3"), 162.6 (C4), 163.1 (C2), 167.5 (C6), 206.7 (C1').

Figure 33: ^{1}H NMR spectrum of **23** (500 MHz, $CDCl_3$)

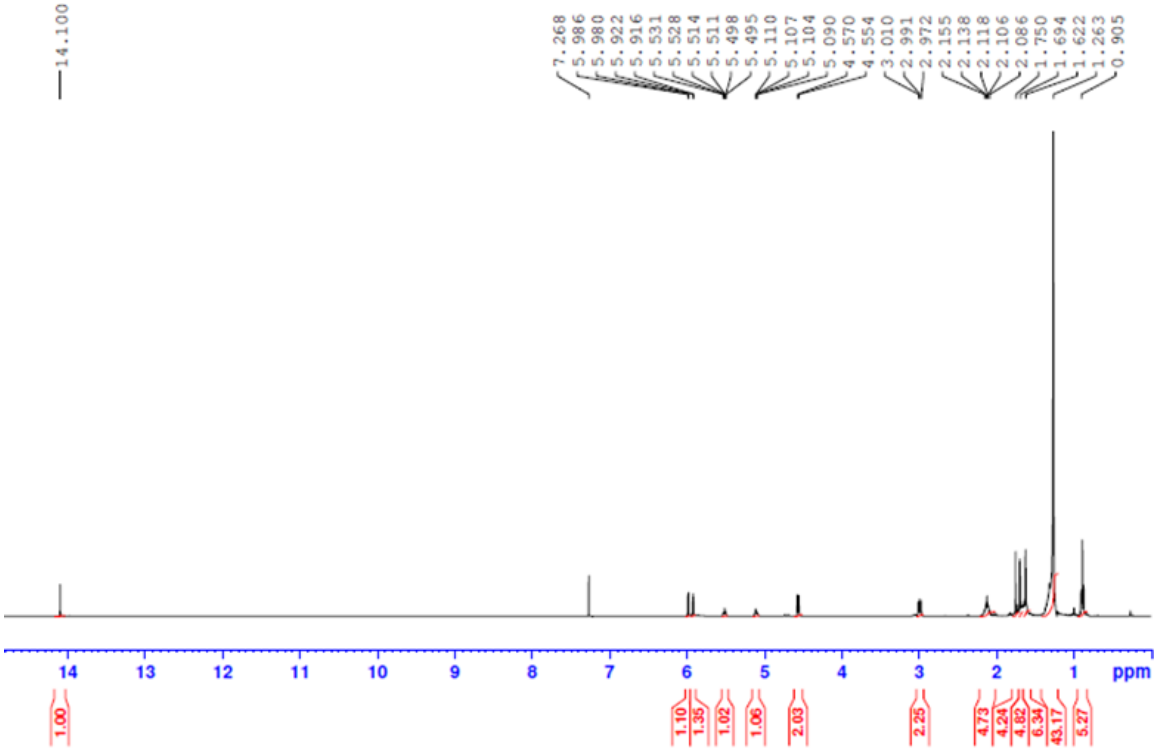
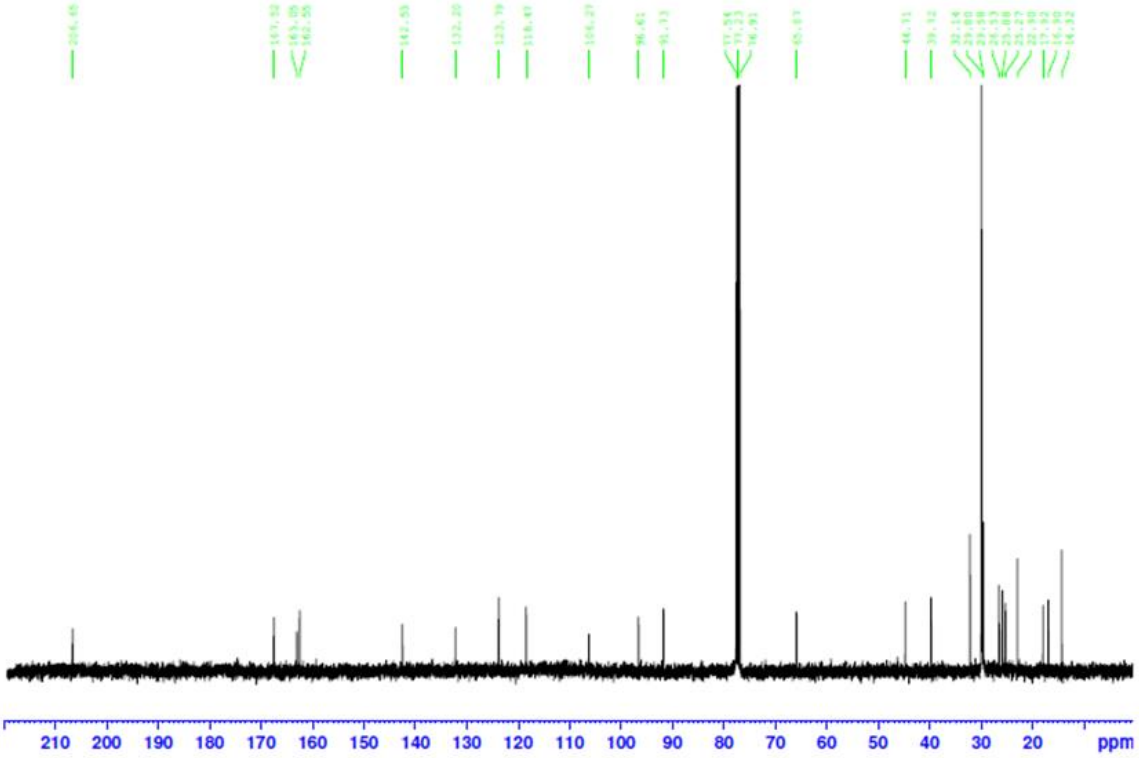
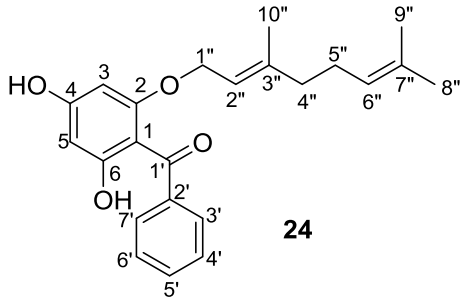


Figure 34: ^{13}C NMR spectrum of **23** (125 MHz, $CDCl_3$)





24

(*E*)-(2-((3,7-Dimethylocta-2,6-dien-1-yl)oxy)-4,6-dihydroxyphenyl)(phenyl)-methanone (24). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 1.52 (3H, s, H9"), 1.61 (3H, s, H8"), 1.71 (3H, s, H10"), 1.85 (2H, m, H4"), 1.94 (2H, m, H5"), 4.21 (2H, d, *J* = 6.5 Hz, H1"), 4.61 (1H, t, *J* = 6.5 Hz, H2"), 5.05 (1H, m, H6"), 5.89 (1H, d, *J* = 2.0 Hz, H3), 6.07 (1H, d, *J* = 2.0 Hz, H5), 7.36 (2H, dt, *J* = 8.0, 1.5 Hz, H4' and H6'), 7.42 (1H, d, *J* = 8.0 Hz, H5'), 7.49 (2H, dt, *J* = 8.0, 1.5 Hz, H3' and H7'), 12.27 (1H, s, HO6); ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 16.8 (C10"), 17.9 (C9"), 25.9 (C8"), 26.4 (C5"), 39.4 (C4"), 65.5 (C1"), 92.4 (C3), 96.5 (C5), 106.1 (C1), 118.1 (C2"), 124.0 (C6"), 127.6 (C4', 6'), 127.8 (C3', C7'), 130.7 (C5'), 132.0 (C7"), 140.7 (C3"), 142.5 (C2'), 162.4 (C2), 163.5 (C4), 165.9 (C6), 200.1 (C1').

Figure 35: ^{1}H NMR spectrum of **24** (500 MHz, $CDCl_3$)

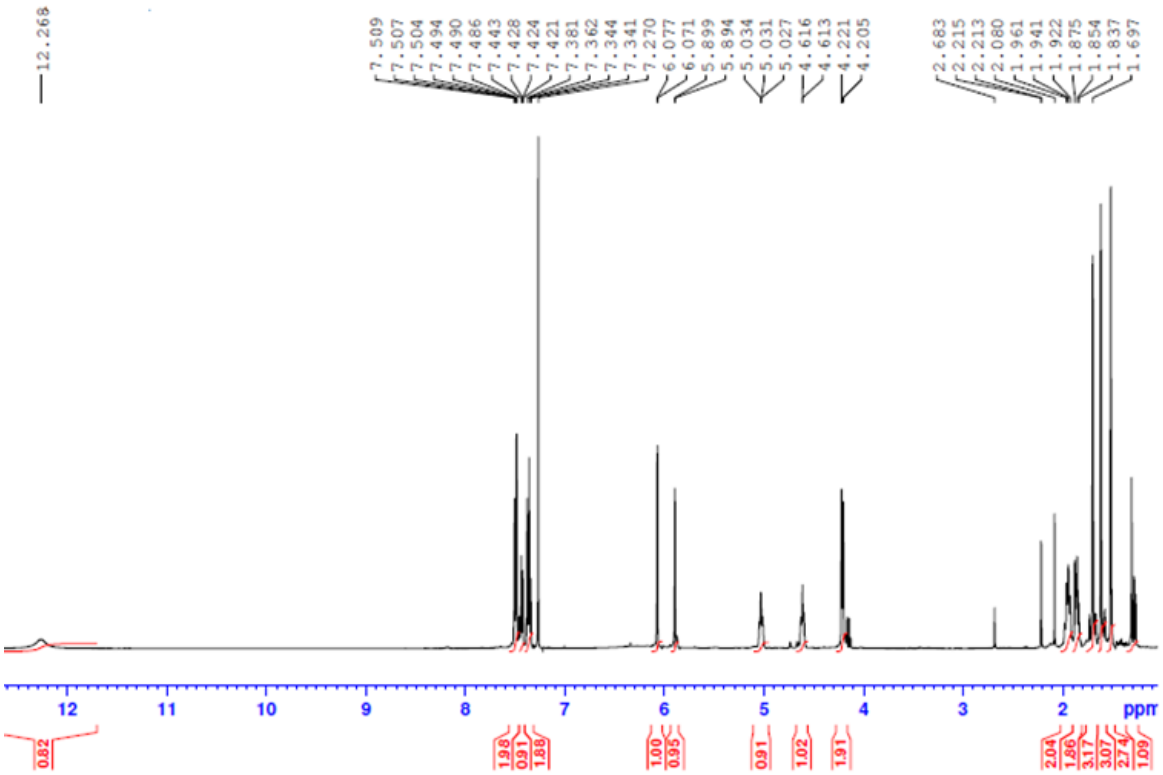
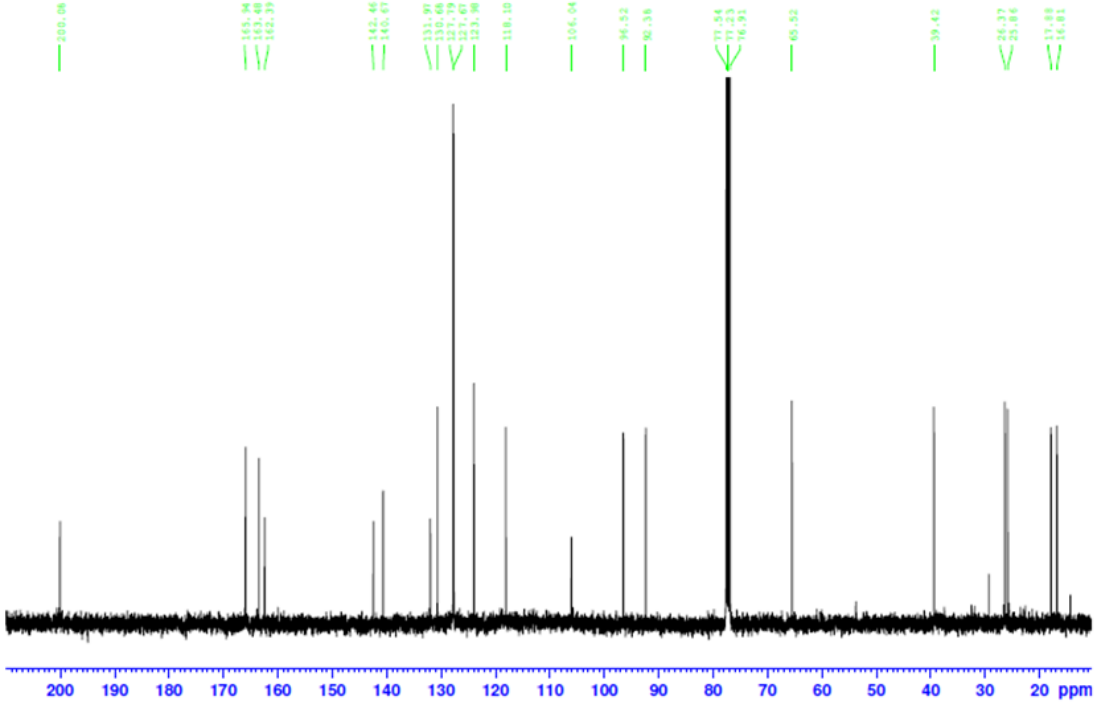


Figure 36: ^{13}C NMR spectrum of **24** (125 MHz, $CDCl_3$)



General procedure for the Friedel-Crafts acylation of phloroglucinol. A solution of phloroglucinol (**3**; 5.00 g, 39.7 mmol) in carbon disulphide (50 mL) was transferred into a two-necked round-bottomed flask and allowed to stir while aluminium trichloride (21.68 g, 162.7 mmol, 4.1 equiv) was added. Nitrobenzene (20 mL) was then added to the solution over 30 min. The solution was heated under reflux at 55 °C for 30 min. A solution of acyl chloride (39.7 mmol, 1.0 equiv) dissolved in 5 mL nitrobenzene was added to the reaction mixture over 30 min, followed by heating for another 30 min. The reaction mixture was allowed to cool with stirring and then poured into an ice-water bath (200 mL). 50 mL of 3 M hydrochloric acid was then added and the mixture extracted with diethyl ether (3 × 250 mL). The organic solvents were removed under reduced pressure. The oily residue containing the acylphloroglucinol (**16**) was subjected to VLC over SiGel PF254 using hexane and EtOAc of increasing polarity. The target acylphloroglucinols typically eluted with 20-45% EtOAc in hexane and were isolated in yields between 50% and 60% (see Table S1 for the actual yields of each acylphloroglucinol **16b-16g**).

General procedure for the TBDMS protection of acylphloroglucinols. Acylphloroglucinol **16** (*ca.* 20.0 mmol) was dissolved in dry acetone (typically 10 mL, but up to 70 mL may be required) and transferred into a suitably-sized round bottom flask. Imidazole (3 equiv) was added to the solution and the reaction mixture stirred for 5 min, followed by the addition of TBDMS-Cl (2.1 equiv). The reaction mixture was stirred for 2 h at room temperature. Acetone was removed from the reaction mixture under reduced pressure and the residue taken up in chloroform and washed with 1 M HCl (150 mL). The organic layer was dried using anhydrous magnesium sulphate, filtered and the solvent was removed under reduced pressure. The crude product purified by VLC over silica gel using hexane and EtOAc of increasing polarity. The target TBDMS-protected acylphloroglucinols typically eluted with 3-10% EtOAc in hexane

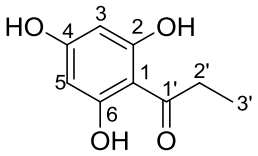
and were isolated in yields between 40% and 85% (see Table S1 for the actual yields of each acylphloroglucinol **17a**-**17g**).

General procedure for the simultaneous *O*-geranylation and deprotection of TBDMS-protected acylphloroglucinols. TBDMS-protected acylphloroglucinol **17** (*ca.* 2 mmol) was dissolved in dry DMF (10 mL) and anhydrous potassium carbonate (1.5 equiv) was added. The mixture was stirred for approximately 5 min followed by the addition of geranyl bromide (1.2 equiv). The mixture was heated at 80 °C for 3 h with stirring. The reaction mixture was poured over water and extracted with chloroform. The solvent in the organic layer was removed under reduced pressure. The crude product was purified by chromatography over silica gel by VLC. The target geranylated acylphloroglucinols typically eluted with 4-20% EtOAc in hexane and were isolated in yields between 5% and 45% (see Table S1 for the actual yields of each geranylated acylphloroglucinol **18**-**24**).

Table S1. Yields of the individual Friedel-Crafts acylation, TBDMS protection and geranylation steps in the synthesis of **18**-**24**.

Acylation of phloroglucinol (**3**)		TBDMS protection of acylphloroglucinol **16**		Geranylation and deprotection of **17**		Acyl group
Compound	Yield (%)	Compound	Yield (%)	Compound	Yield (%)	
16a[a]	n/a	**17a**	40	**18**	11	acetyl
16b	60	**17b**	68	**19**	6.4	propanoyl
16c	56	**17c**	73	**20**	14	butanoyl
16d	55	**17d**	46	**21**	22	pentanoyl
16e	51	**17e**	82	**22**	10	decanoyl
16f	60	**17f**	69	**23**	46	octadecanoyl
16g	54	**17g**	58	**24**	32	benzoyl

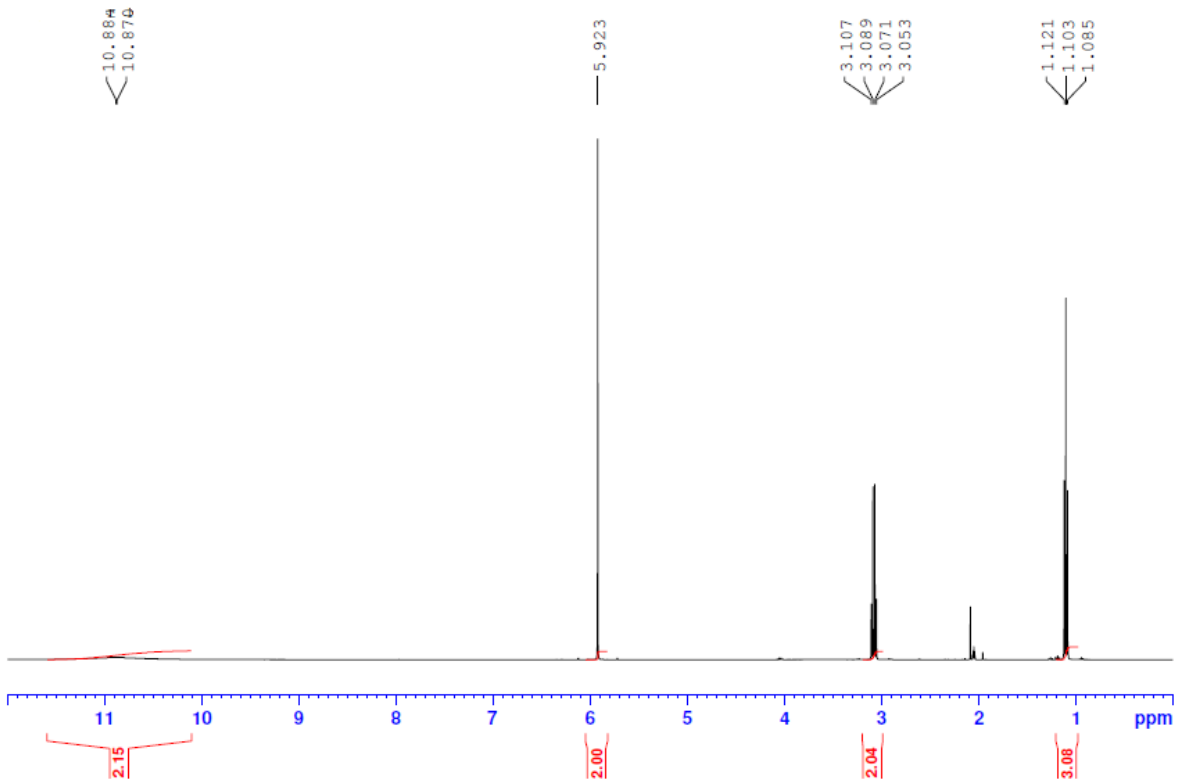
[a]Acetylphloroglucinol **16a** is commercially available

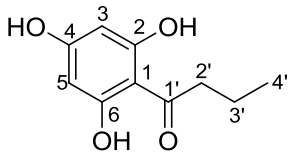


16b

1-(2,4,6-Trihydroxyphenyl)propan-1-one (16b). ^{1}H NMR (400 MHz, $(CD_3)_2CO$): δ_H 1.10 (3H, t, J = 7.2 Hz, H3'), 3.08 (2H, q, J = 7.2 Hz, H2'), 5.92 (2 × 1H, s, H3 and H5), 10.88 (3 × 1H, br s, HO2, HO4 and HO6).

Figure 37: ^{1}H NMR spectrum of **16b** (400 MHz, $(CD_3)_2CO$)

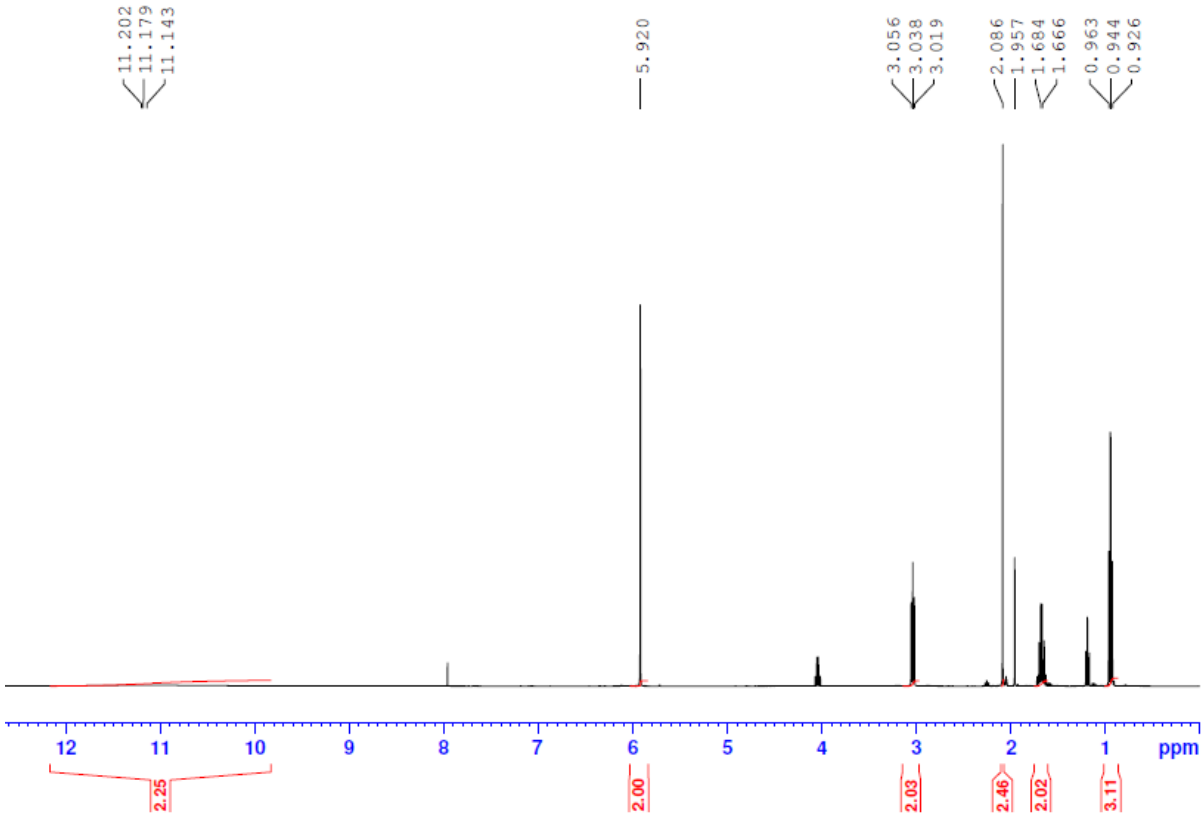


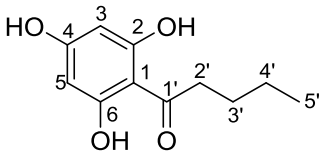


16c

1-(2,4,6-Trihydroxyphenyl)butan-1-one (16c). ^{1}H NMR (400 MHz, $(CD_3)_2CO$): δ_H 0.91 (3H, t, J = 7.2 Hz, H4'), 1.65 (2H, m, H3'), 3.00 (2H, t, J = 7.2 Hz, H2'), 5.88 (2 × 1H, s, H3 and H5), 11.14 (3 × 1H, br s, HO2, HO4 and HO6).

Figure 38: ^{1}H NMR spectrum of **16c** (400 MHz, $(CD_3)_2CO$)

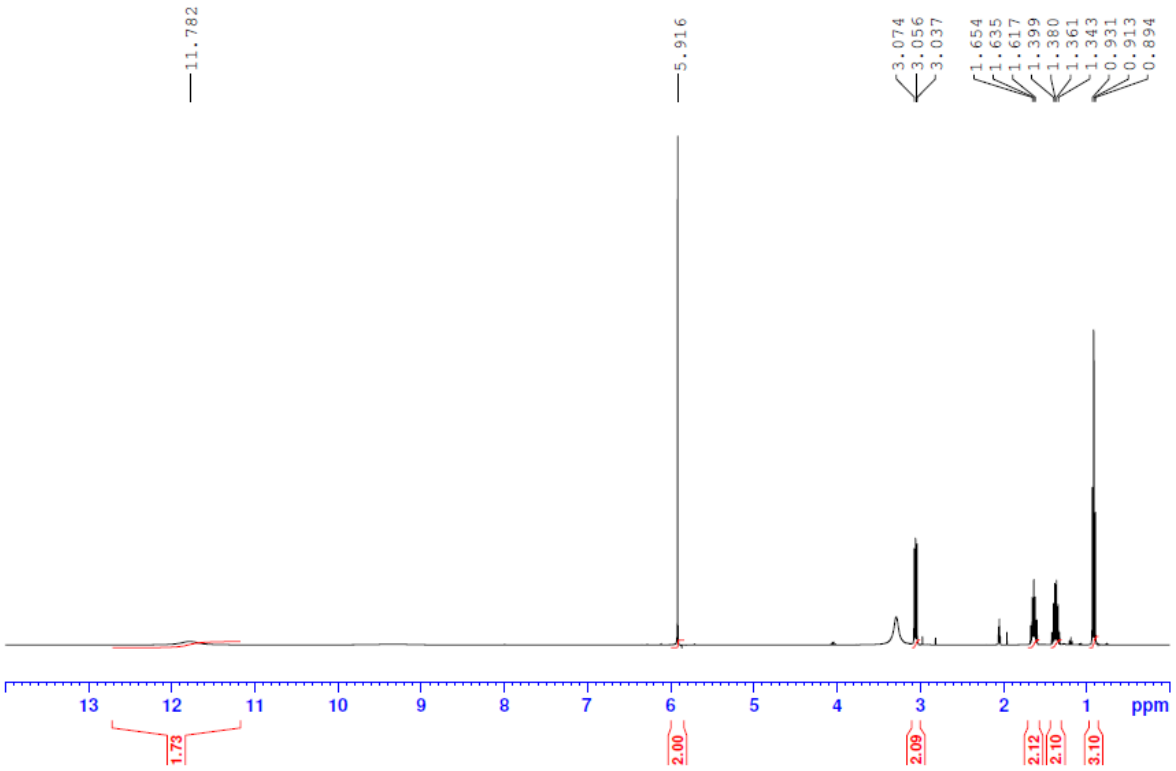


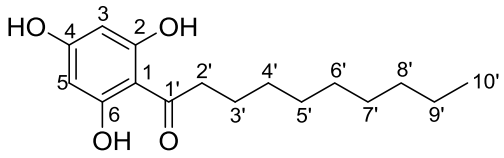


16d

1-(2,4,6-Trihydroxyphenyl)pentan-1-one (16d). ^{1}H NMR (400 MHz, $(CD_3)_2CO$): δ_H 0.91 (3H, t, J = 7.2 Hz, H5'), 1.37 (2H, m, H4'), 1.63 (2H, m, H3'), 3.06 (2H, t, J = 7.2 Hz, H2'), 5.92 (2 × 1H, s, H3 and H5), 11.78 (3 × 1H, br s, OH2, OH4 and OH6).

Figure 39: ^{1}H NMR spectrum of **16d** (400 MHz, $(CD_3)_2CO$)

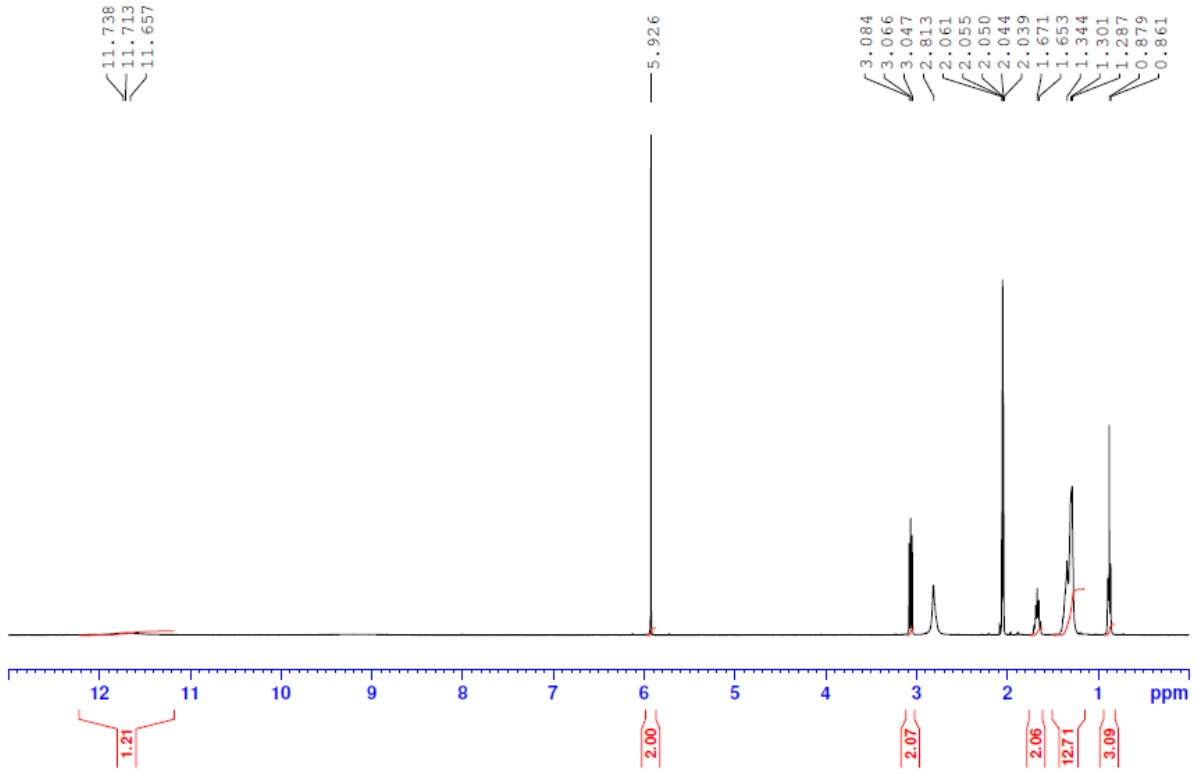


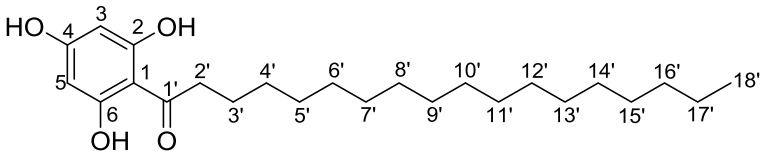


16e

1-(2,4,6-Trihydroxyphenyl)decan-1-one (16e). ^{1}H NMR (400 MHz, $(CD_3)_2CO$): δ_H 0.88 (3H, t, J = 7.2 Hz, 10'), 1.30 (6 × 2H, m, H4'-9'), 1.67 (2H, m, H3'), 3.07 (2H, t, J = 7.2 Hz, H2'), 5.92 (2 × 1H, s, H3 and H5), 11.71 (3 × 1H, br s, OH2, OH4 and OH6).

Figure 40: ^{1}H NMR spectrum of **16e** (400 MHz, $(CD_3)_2CO$)

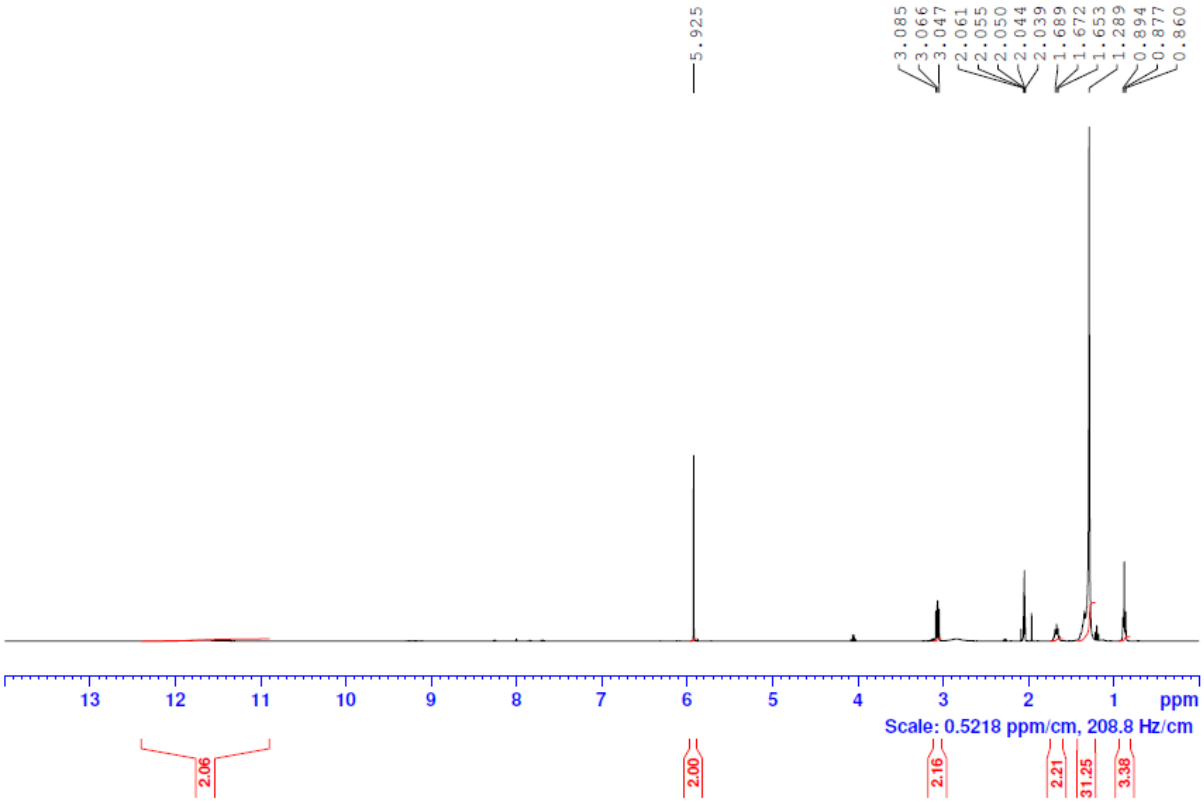


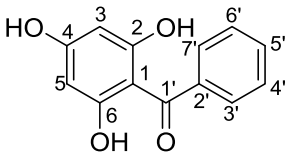


16f

1-(2,4,6-Trihydroxyphenyl)octadecan-1-one (16f). ^{1}H NMR (400 MHz, $(CD_3)_2CO$): δ_H 0.88 (3H, t, J = 7.2 Hz, 18'), 1.29 (14 × 2H, m, H4'-17'), 1.67 (2H, m, H3'), 3.07 (2H, t, J = 7.2 Hz, H2'), 5.93 (2 × 1H, s, H3 and H5), 11.64 (3 × 1H, br s, OH2, OH4 and OH6).

Figure 41: ^{1}H NMR spectrum of **16f** (400 MHz, $(CD_3)_2CO$)

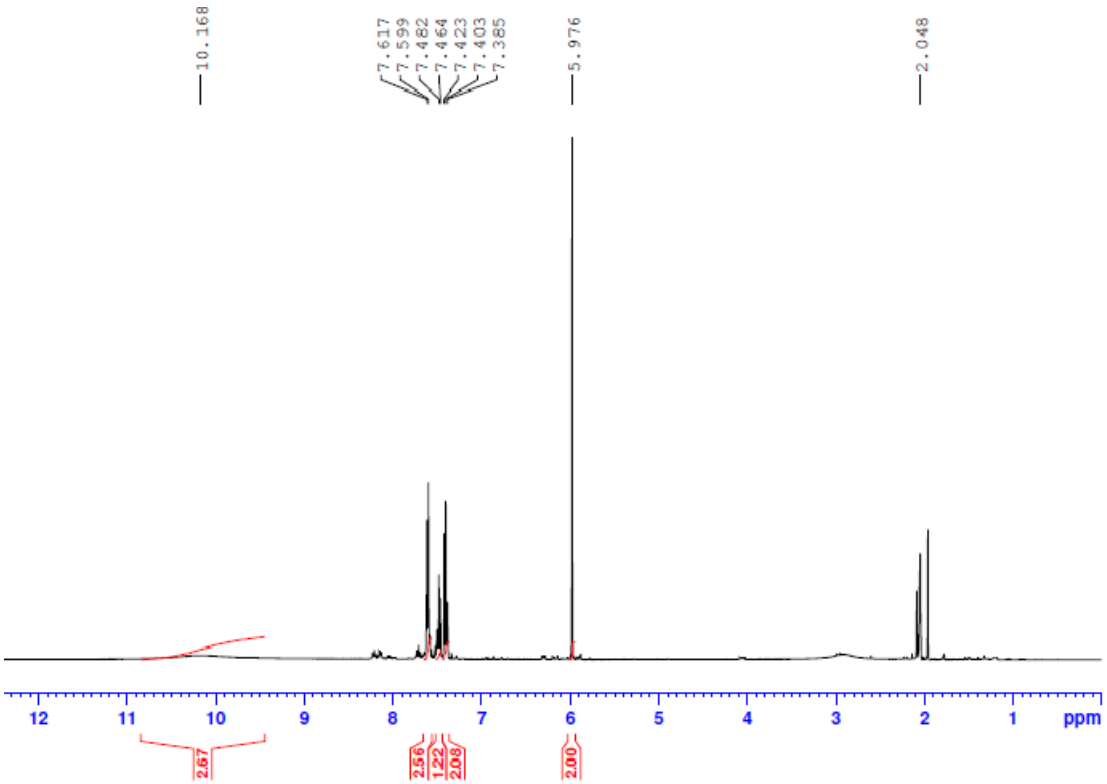


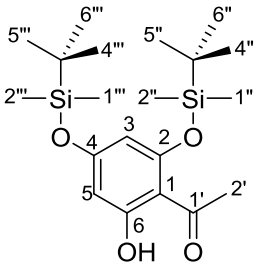


16g

1-(2,4,6-Trihydroxyphenyl)phen-1-one (16g). ^{1}H NMR (400 MHz, $(CD_3)_2CO$): δ_H 5.98 (2 × 1H, s, H3 and H5), 7.40 (2 × 1H, d, J = 8.0 Hz, H4', H6'), 7.47 (1H, t, J = 8.0 Hz, H5'), 7.61 (2 × 1H, d, J = 8.0 Hz, H3' and H7'), 10.17 (3 × 1H, br s, HO2, HO4 and HO6).

Figure 42: ^{1}H NMR spectrum of **16g** (400 MHz, $(CD_3)_2CO$)

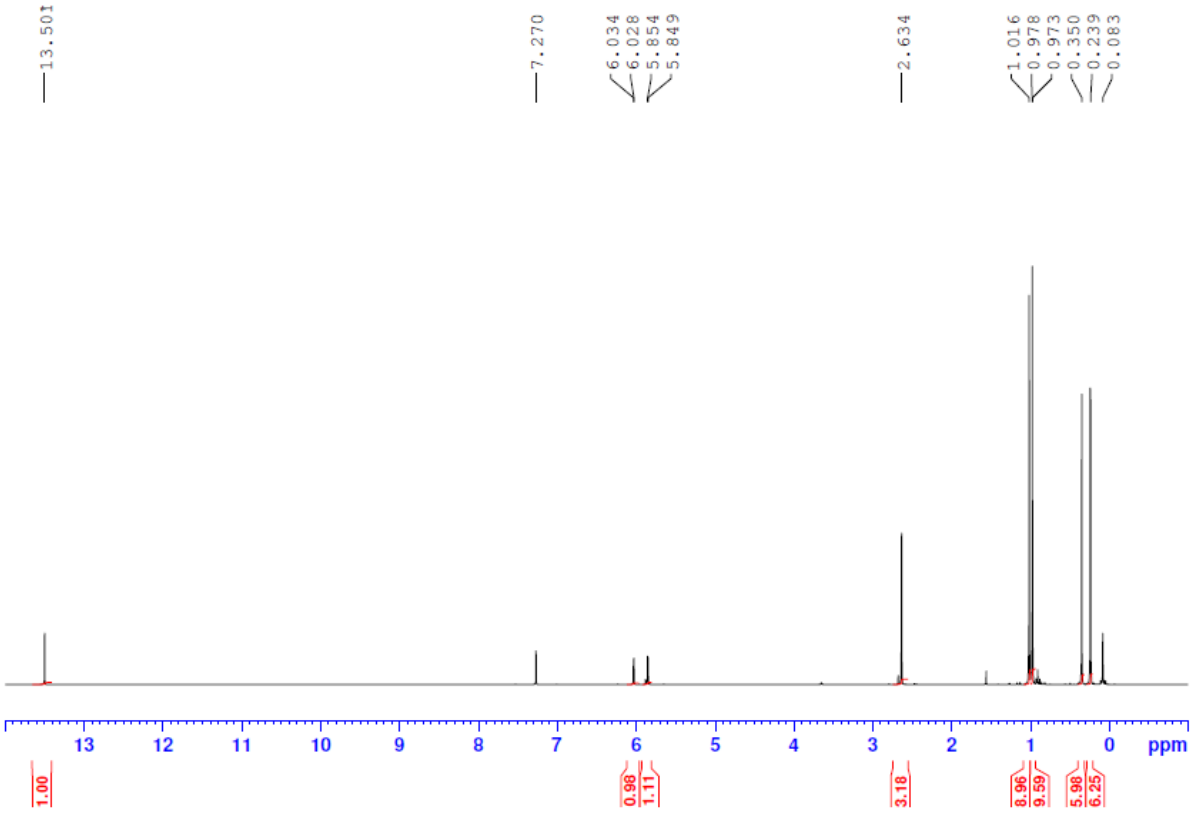


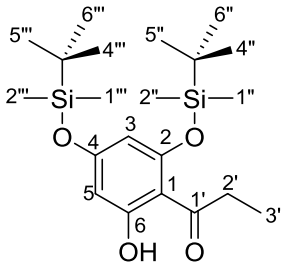


17a

1-(2,4-bis((*tert*-Butyldimethylsilyl)oxy)-6-hydroxyphenyl)-2-ethan-1-one (17a). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 0.24 (2 × 3H, s, H1", H2"), 0.35 (2 × 3H, s, H1'", H2'"), 0.97 (3 x 3H, s, H4", H5", H6"), 1.01 (3 × 3H, s, H4'", H5'", H6'"), 2.63 (3H, s, H2'), 5.85 (1H, d, J = 2.0 Hz), H3, 6.03 (1H, d, J = 2.0 Hz, H5), 13.50 (1H, s, OH6).

Figure 43: ^{1}H NMR spectrum of **17a** (400 MHz, $CDCl_3$)

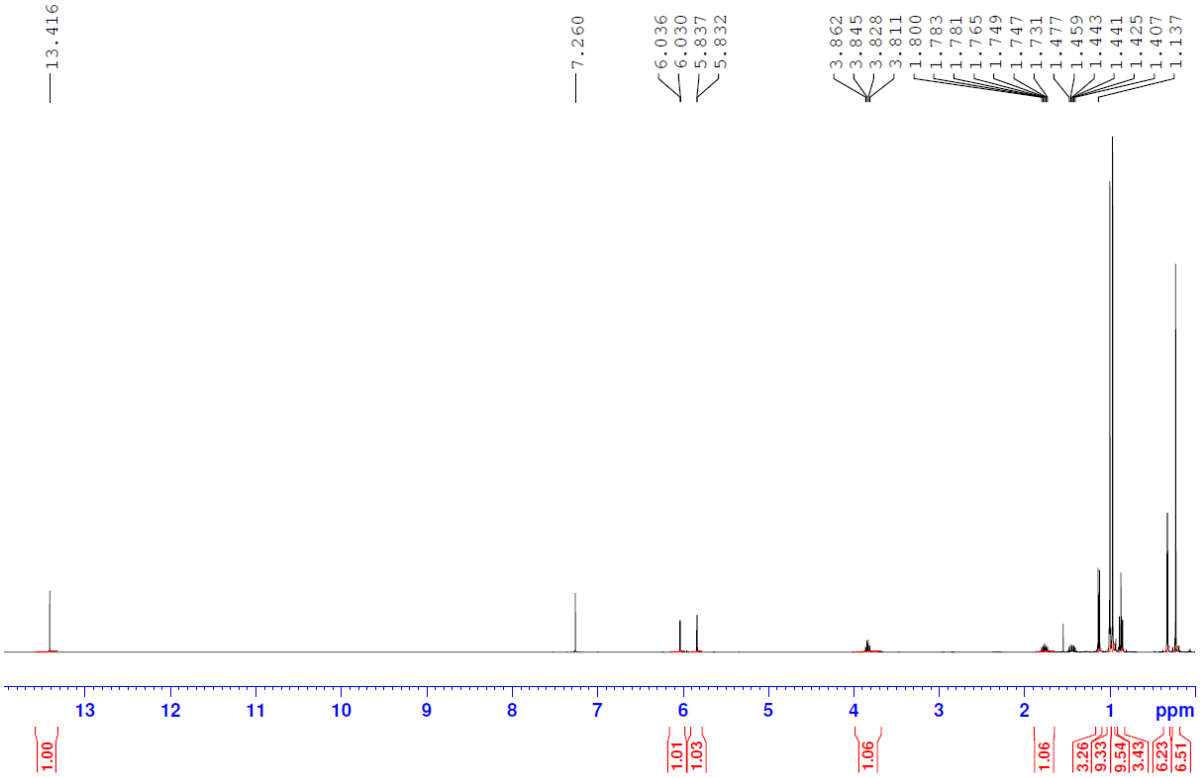


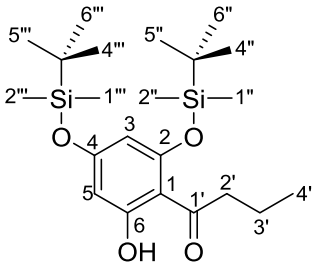


17b

1-(2,4-bis((*tert*-Butyldimethylsilyl)oxy)-6-hydroxyphenyl)-2-propan-1-one (17b). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 0.23 (2 × 3H, s, H1", H2"), 0.35 (2 × 3H, s, H1'", H2'"), 0.97 (3H, t, J = 7.2 Hz, H3'), 1.14 (3 × 3H, s, H4", H5", H6"), 1.41 (3 × 3H, s, H4'", H5'", H6'"), 1.78 (1H, m, H2'b), 3.83 (1H, m, H2'a), 5.83 (1H, d, J = 2.0 Hz, H3), 6.04 (1H, d, J = 2.0 Hz, H5), 13.42 (1H, s, OH6).

Figure 44: ^{1}H NMR spectrum of **17b** (400 MHz, $CDCl_3$)

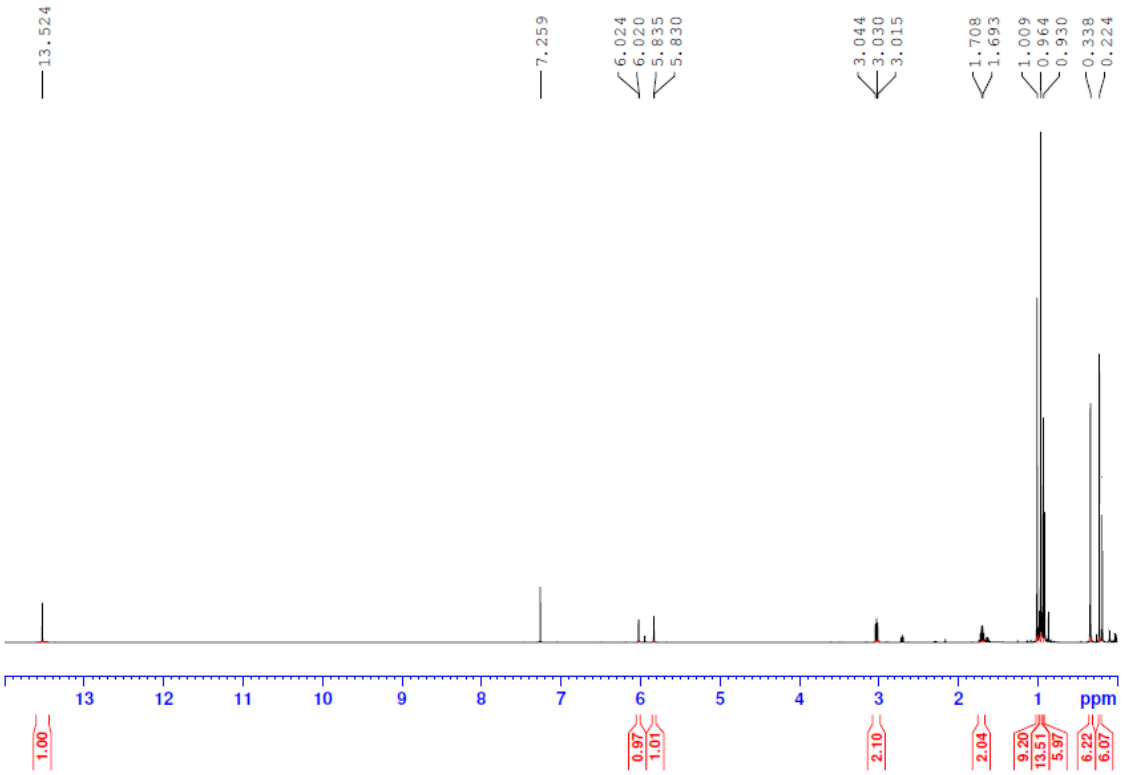


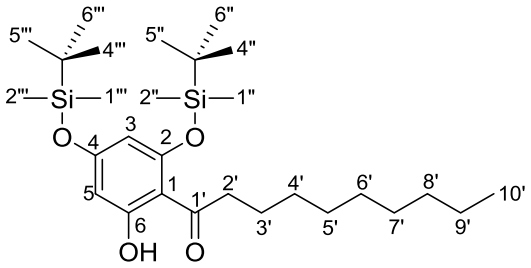


17c

1-(2,4-bis((*tert*-Butyldimethylsilyl)oxy)-6-hydroxyphenyl)-2-butan-1-one (17c). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 0.22 (2 × 3H, s, H1", H2"), 0.34 (2 × 3H, s, H1'", H2'"), 0.95 (3H, t, J = 6.8Hz, H4'), 0.96 (3 × 3H, s, H4", H5", H6"), 1.01 (3 × 3H, s, H4'", H5'", H6'"), 1.70 (2H, m, H3'), 3.03 (2H, t, J = 6.0Hz, H2'), 5.84 (1H, d, J = 2.0 Hz, H3), 6.02 (1H, d, J = 2.0 Hz, H5), 13.52 (1H, s, OH6).

Figure 45: ^{1}H NMR spectrum of **17c** (400 MHz, $CDCl_3$)

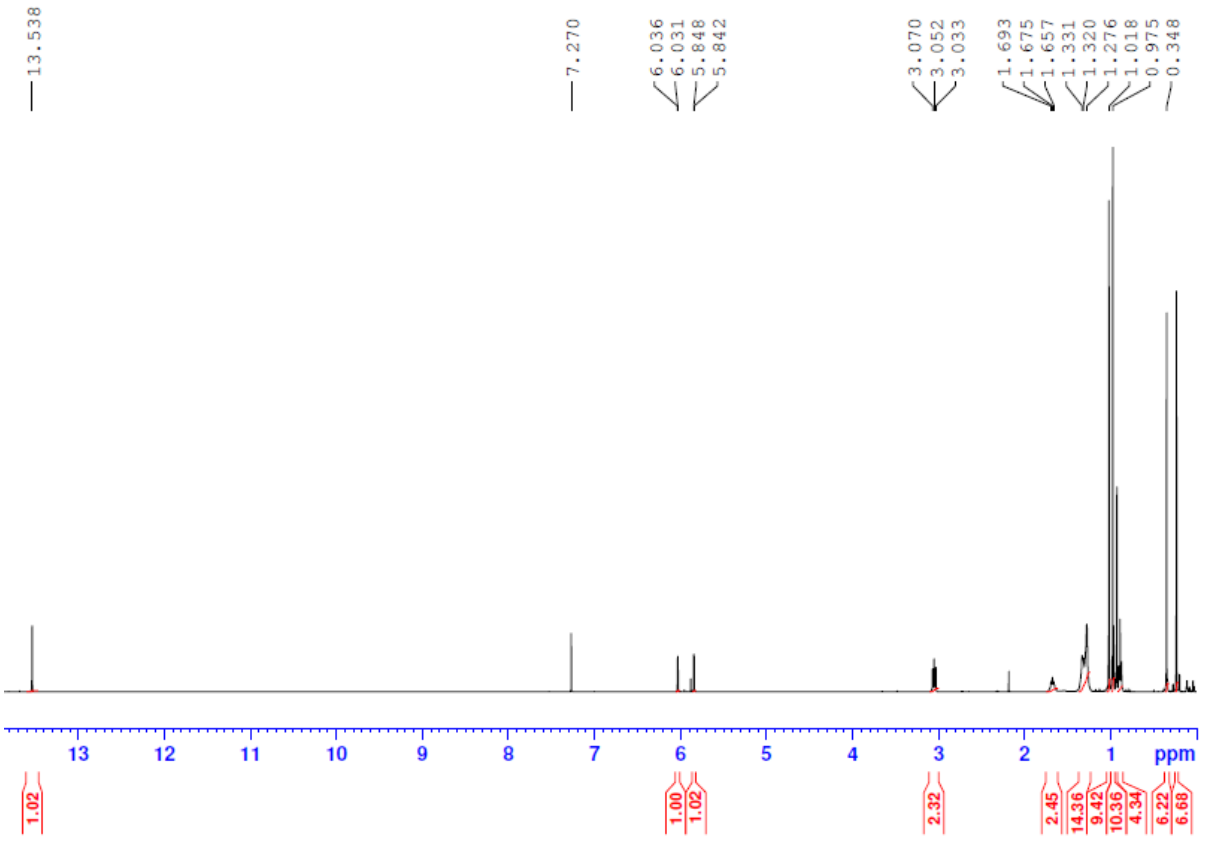


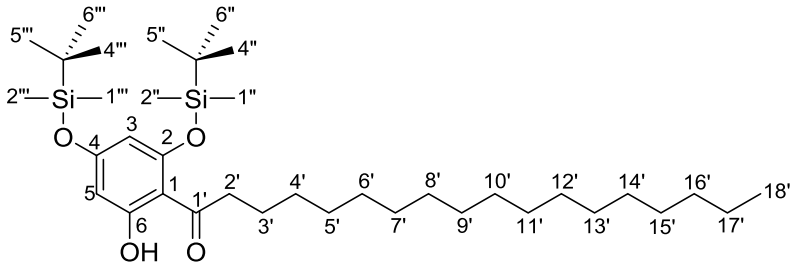


17e

1-(2,4-bis((*tert*-Butyldimethylsilyl)oxy)-6-hydroxyphenyl)-2-decan-1-one (17e). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 0.23 (2 × 3H, s, H1", H2"), 0.35 (2 × 3H, s, H1'", H2'"), 0.91 (3H, t, J = 7.2 Hz, H10'), 0.97 (3 × 3H, s, H4", H5", H6"), 1.02 (3 × 3H, s, H4'", H5'", H6'"), 1.27-1.33 (br s, 6 × 2H, H3'-H9'), 3.05 (2H, J = 7.2 Hz, H2'), 5.85 (1H, d, J = 2.0 Hz, H3), 6.04 (1H, d, J = 2.0 Hz, H5), 13.54 (1H, s, OH6).

Figure 46: ^{1}H NMR spectrum of **17e** (400 MHz, $CDCl_3$)

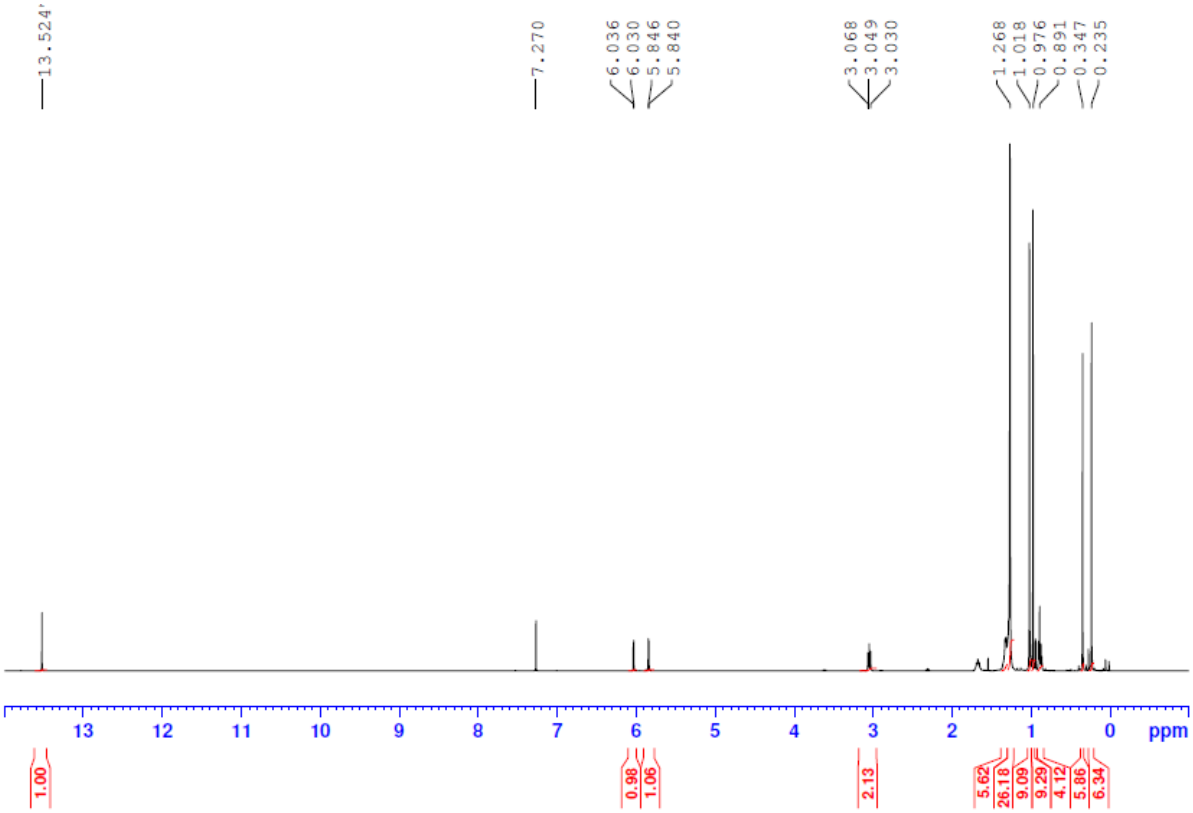


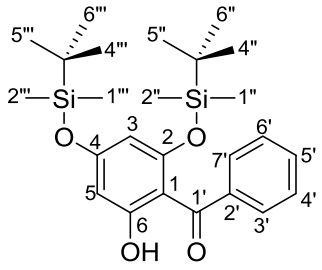


17f

1-(2,4-bis((*tert*-Butyldimethylsilyl)oxy)-6-hydroxyphenyl)-2-octadecan-1-one (17f). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 0.23 (2 × 3H, s, H1", H2"), 0.35 (2 × 3H, s, H1'", H2'"), 0.89 (3H, t, J = 7.2 Hz, H18'), 0.98 (3 × 3H, s, H4", H5", H6"), 1.02 (3 × 3H, s, H4'", H5'", H6), 1.27 (br s, 13 × 2H, H3'-H17'), 3.05 (2H, J = 7.2 Hz, H2'), 5.85 (1H, d, J = 2.0 Hz, H3), 6.04 (1H, d, J = 2.0 Hz, H5), 13.52 (1H, s, OH6).

Figure 47: ^{1}H NMR spectrum of **17f** (400 MHz, $CDCl_3$)





17g

1-(2,4-bis((*tert*-Butyldimethylsilyl)oxy)-6-hydroxyphenyl)-2-phen-1-one (17g). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 0.10 (2 × 3H, s, H1", H2"), 0.27 (2 × 3H, s, H1"', H2"'), 0.62 (3 × 3H, s, H4", H5", H6"), 1.00 (3 × 3H, s, H4"', H5"', H6"'), 5.87 (1H, d, J = 2.5 Hz, H3), 6.16 (1H, d, J = 2.5 Hz, H5), 7.40 (2H, dd, J = 10.0, 2.5 Hz, H4',6'), 7.47 (1H, dt, J = 10.0, 2.5 Hz, H5'), 7.68 (2H, dd, J = 10.0, 2.5 Hz, H3', H7'), 11.17 (1H, s, OH6).

Figure 48: ^{1}H NMR spectrum of **17g** (400 MHz, $CDCl_3$)