An Efficient and Flexible Synthesis of Model Lignin Oligomers.

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ESI

General Experimental

Chemicals were purchased from Sigma-Aldrich, Alfa Aesar and used without further purification. ^{1}H NMR spectra were recorded at 300 MHz and 400 MHz using Bruker Avance DPX-300 and Bruker Avance 400 MHz instruments. ^{13}C NMR spectra were recorded at 75 MHz and 100 MHz also using these instruments. Tetramethylsilane was used as an internal standard with chloroform-d as the solvent unless otherwise stated. Mass spectra (Electrospray and Electron ionisation) were recorded on VG Autospec spectrometer (EI) and Varian Workstation 1200 (ES). Analytical tlc was performed on Merck Kieselgel 60F_{254} plates, which were visualised using a Davidson & Hardy LTD UVGL-58 handheld UV lamp or vanillin stain. Preparative tlc was carried out using Merck Kieselgel PF_{254}(22 g, 62 mL water) on 20 cm x 20 cm glass plates. Flash chromatography was carried out using Merck Kieselgel 60 (230-400 mesh). Where $MgSO_4$ and Na_2SO_4 are mentioned in the context of drying solvents, it is the anhydrous salts which are being referred to.

Dehydrodiacetovanillone, 4

Acetovanillone, **3**, (20.0 g, 0.12 mole) was dissolved in boiling water (800 mL) with vigorous stirring. To this was added iron (II) sulphate heptahydrate (1.67 g, 0.006 mole) followed immediately by sodium persulphate (14.29 g, 0.06 mole). The clear, pale yellow solution turned brown with precipitate rapidly. This was left to stir for 15 min after which the solution was filtered. The filter cake was suspended in water (500 mL) and the minimum amount of solid sodium hydroxide was added to get the solid to dissolve. The solution was then slowly acidified with conc. HCl until a precipitate formed. The solid product was filtered and washed several times with boiling water and was dried in an oven overnight giving pure dehydrodiacetovanillone (**4**) as a beige, amorphous solid. (Yield: 18.89 g, 95 %)

^{1}H NMR (300 MHz) δ_H (ppm): 2.58 (6H, s, COC<u>H$_3$</u>), 4.02 (6H, s, O<u>Me</u>), 6.32 (2H, s, Ar<u>OH</u>), 7.58 (2H, d, *J*= 1.88 Hz, <u>Ar</u>), 7.62 (2H, d, *J*=1.92 Hz, <u>Ar</u>)

^{13}C NMR (75 MHz, $CDCl_3$) δ_C (ppm): 26.49, 56.67, 109.41, 122.66, 126.09, 130.01, 147.92, 196.98

EI-HRMS (*m/z*)- calc. Mass 330.1104 found 330.1103

Data consistent with the literature.[18]

4,4′-Di-*O*-Benzyl Dehydrodiacetovanillone, 5

Dehydrodiacetovanillone, **4**, (20.0 g, 0.061 mole) was dissolved in acetone (200 mL) and heated to reflux. To this was added K_2CO_3 (16.71 g, 0.121 mole) and benzyl bromide (20.71 g, 0.121 mole). The reaction was allowed to reflux for 24 hrs. It was then cooled and the solid was removed by filtration. The filtrate was concentrated under reduced pressure until it was a viscous, black oil. The resultant oil was then washed with hexane to yield >95 % pure product by NMR which could be used without further purification for the next step. Alternatively it could be placed on a large silica plug. The plug was then washed several times with 1:4 EtOAc:hexane (6 x 200 mL). The solvent was then removed under reduced pressure and the solid residue recrystallized from a minimum amount of hot EtOAc with hexane then added as a counter solvent until its cloud point. This solution was cooled to 4 ^{o}C to give the product as white needles. (Yield: 21.63 g, 70 %)

^{1}H NMR (300 MHz, $CDCl_3$) δ_H (ppm): 2.47 (6H, s, COC$\underline{H_3}$), 3.99 (6H, s, O$\underline{Me}$), 4.87 (4H, s, OC$\underline{H_2}$Ar), 6.99-7.03 (4H, m, $\underline{Ar}$), 7.12-7.20 (6H, m, $\underline{Ar}$), 7.41 (2H, d, J = 2.04 Hz, $\underline{Ar}$), 7.61 (2H, d, J= 2.03 Hz, $\underline{Ar}$)

^{13}C NMR (75 MHz, $CDCl_3$) δ_C (ppm): 26.80, 56.53, 75.06, 111.17, 125.69, 128.24, 128.50, 132.27, 133.01, 137.48, 150.32, 153.46, 197.53

ES-HRMS (*m/z*)- [M+H$^+$] calc. Mass 511.2141 found 511.2121

Data is consistent with literature.[22]

Diethyl 3,3′-(6,6′-di(benzyloxy)-5,5′-dimethoxybiphenyl-3,3′-diyl)di(3-oxopropanoate), 6

The dibenzylated intermediate **5** (15.00 g, 0.029 mole) was dissolved in diethyl carbonate (19.73 g, 0.29 mole) and heated to 80 ^{o}C. To this was added NaH (60 % dispersion in mineral oil, 5.87 g, 0.147 mole) in small portions. The reaction is very exothermic and the release of hydrogen gas means extra care should be employed. The reaction mixture turns from clear and slightly yellow to orange and opaque. The reaction was monitored by NMR. The reaction mixture was cooled to room temperature and carefully quenched with water. Once the excess hydride was quenched the reaction mixture was further diluted with water (300 mL) and extracted with ethyl acetate (150 mL x 3). The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure to give a yellow oil. Residual diethyl carbonate was removed by trituration with hexane. The resulting oil could then be purified by flash chromatography (4:1 hexane:ethyl acetate) and recrystallised from EtOAc:hexane to give colourless, granular crystals. (Yield: 12.88 g, 67 %)

^{1}H NMR (300 MHz, $CDCl_3$) δ_H (ppm): 1.24 (6H, t, J = 7.11 Hz, $CH_2C\underline{H_3}$), 3.83 (4H, s, , J = 7.11 Hz, COC$\underline{H_2}$COOEt), 3.98 (6H, s, O$\underline{Me}$), 4.18 (4H, q, J = 7.14 Hz, COOC$\underline{H_2}CH_3$), 4.88 (4H, s, C$\underline{H_2}$Ar),

6.97-7.00 (4H, m, Ar), 7.14-7.20 (6H, m, Ar), 7.29 (2H, d, J = 2.03 Hz, Ar), 7.61 (2H, d, J = 1.93 Hz, Ar)

^{13}C NMR (75 MHz, $CDCl_3$) δ_C (ppm): 14.53, 46.00, 56.54, 61.83, 75.07, 111.65, 125.43, 128.32, 128.49, 128.54, 131.82, 132.34, 137.35, 150.86, 153.53, 167.91, 191.88

ES-HRMS (m/z)- [M+H$^+$] calc. Mass 655.2543 found 655.2546

FTIR (Thin film) ν_{max} (cm^{-1}): 3470, 3065, 3030, 2979, 2939, 2905, 2842, 1741, 1681, 1619, 1578, 1496, 1453, 1462, 1405, 1366, 1319, 1257, 1193, 1147, 1093, 1058, 1032, 973, 912, 895, 871, 852, 785, 760, 734, 698, 641, 600

Crystal data: $C_{38}H_{38}O_{10}$, M=654.68, triclinic, a= 10.1930 (10), b= 11.524 (2), c= 15.213 (10) Å, U= 1716.0(4) Å^3, Mo-Kα radiation, Z=4, λ=0.70073 Å, space group P-1, F(000)=692, Dx=1.267 g cm^{-3}, μ=0.092 mm^{-1}. Data were measured on a Seimens P4 diffractometer at 293(2) K, measured/observed reflections: 6372/6008, R_{int}= 0.0476, direct methods solution, full-matrix, least squares refinement on F_o^2, anisotropic displacement parameters for non hydrogen atoms; all hydrogen atoms were observed at positions calculated from the geometry of the molecule using the riding model. R_1=0.749 for 3761 data with 425 parameters, ωR_2=0.2063, GoF=1.045, $\Delta\rho_{min/max}$=-0.301/0.633 eÅ^{-3}

$C_{38}H_{38}O_{10}$: requires C-67.71%, H-5.85% found C-69.46%, H-5.81%

Diethyl 3,3′-(6,6′-di(benzyloxy)-5,5′-dimethoxybiphenyl-3,3′-diyl)di(2-bromo-3-oxopropanoate), 7

To a solution of **6** (10.00 g, 0.015 mole) in EtOAc (200 mL) was added Amberlyst A15 resin (2.0 g) and *N*-bromosuccinimide (5.34 g, 0.03 mole). The reaction mixture was stirred at room temperature until TLC showed the disappearance of starting material (1: 4 EtOAc:hexane). The Amberlyst resin was filtered off and the solvent removed under reduced pressure. The residue was then purified using flash chromatography (4:1 hexane:ethyl acetate) to give **7** as a yellow oil. (Yield- 9.73 g, 79 %)

^{1}H NMR (300 MHz, $CDCl_3$) δ_H (ppm): 1.23 (6H, t, J = 7.17 Hz, $COOCH_2CH_3$), 3.98 (6H, s, OMe), 4.25 (4H, q, J = 7.17 Hz, $COOCH_2CH_3$), 4.91 (4H, broad s, CH_2Ar), 5.52 (2H, overlapping singlets from diastereoisomers, CHBr), 6.99-7.02 (4H, m, Ar), 7.13-7.20 (6H, m, Ar), 7.39 (2H, d, J = 2.07 Hz, Ar), 7.64 (2H, d, J = 7.64 Hz, Ar)

^{13}C NMR (75 MHz, $CDCl_3$) δ_C (ppm): 14.34, 46.26, 56.57, 63.69, 75.18, 112.76, 125.79, 128.34, 128.46, 128.56, 129.00, 132.30, 137.25, 151.40, 153.59, 165.51, 187.49

ES-HRMS (m/z)- [M+H$^+$] calc. Mass 811.0753 found 811.0787

FTIR (Thin film) ν_{max} (cm^{-1}): 1760, 1739, 1680, 1578, 1497, 1481, 1455, 1405, 1366, 1300, 1283, 1233, 1195, 1152, 1093, 1056, 1025, 971, 911, 734, 698

$C_{38}H_{36}O_{10}Br_2$: requires C-56.17%, H-4.47% found C-55.95%, H-4.08%

Dehydrodiisoeugenol, 9

Isoeugenol, **8**, (50.0 g, 0.305 mole) was dissolved in ethanol (572 mL) and water (252 mL). Iron (III) chloride (29.68 g, 0.183 mole) was dissolved in water (304 mL) and added to the isoeugenol solution, turning the solution dark green. The reaction flask was stoppered, shaken briefly and then left to stand for 48 h during which time the reaction mixture turned yellow and white crystals precipitated. The reaction mixture was filtered and the crystals washed with ice cold ethanol. The crystals were then dissolved in dichloromethane (DCM) and passed through a silica plug. The solvent was then removed and the off white solid product could then be used in the next step or recrystalized from ethanol. (Yield: 14.92 g, 30 %)

^{1}H NMR (300 MHz, $CDCl_3$) δ_H (ppm): 1.38 (3H, d, *J* = 6.77 Hz, γ′ -H), 1.87 (3H, d, *J* = 6.54 Hz, γ′′-H), 3.45 (1H, m, β′-H), 3.88 (3H, s, OMe), 3.89 (3H, s, OMe), 5.1 (1H, d, *J* = 9.50 Hz, α′-H), 5.63 (1H, s, OH), 6.13 (1H, dq, *J* = 6.57, 15.62 Hz, β′′-H), 6.36 (1H, d, *J* = 14.32 Hz, α′′-H), 6.77 (2H, d, *J* = 5.59 Hz, Ar), 6.89 (2H, s, Ar), 6.97 (1H, s, Ar)

^{13}C NMR (75 MHz, $CDCl_3$) δ_C (ppm): 17.58, 18.37, 45.63, 55.96, 56.00, 93.80, 108.94, 113.32, 114.08, 119.99, 123.51, 130.94, 132.11, 133.68, 144.17, 145.80, 146.68

ES-HRMS (*m/z*)- [$M+H^+$] calc mass 327.1596 mass found 327.1611

Data is consistent with literature.[24]

(*E*)-Diethyl 3,3′-(6,6′-di(benzyloxy)-5,5′-dimethoxybiphenyl-3,3′-diyl)di(2-(2-methoxy-4-(7-methoxy-3-methyl-5-((*E*)-prop-1-enyl)-2,3-dihydrobenzofuran-2-yl)phenoxy)-3-oxopropanoate), 10

Dehydrodiisoeugenol, **9**, (3.38 g, 0.01 mole) was dissolved in acetone (20 mL) and the solution heated to 60 ^oC. To this was added K_2CO_3 (1.38 g, 0.01 mole). Brominated intermediate **7** (4.21 g, 0.005 mole) was dissolved in acetone (20 mL) and was added to the solution of **9**. The reaction mixture was stirred until all of compound **9** was consumed which was monitored *via* tlc (1:4 EtOAc:hexane). The reaction mixture was then cooled to room temperature and filtered. The solvent was removed under reduced pressure and the crude product purified using flash chromatography (4:1 hexane:ethyl acetate) to give a cream solid after drying under reduced pressure. (Yield: 4.05 g, 60 %)

^{1}H NMR (400 MHz, $CDCl_3$) δ_H (ppm): 1.17 (6H, t, *J* = 7.76 Hz, COOC$\underline{H_2}CH_3$), 1.34 (6H, d, *J* = 7.52 Hz, γ′-H), 1.86 (6H, two doublets superimposed, J= 6.76 Hz γ′′-H), 3.37 (2H, m, β′-H), 3.62-3.94 (multiple singlets corresponding to ArOMe), 4.18 (4H, q, *J*= 7.00 Hz, COOC$\underline{H_2}CH_3$), 4.88 (4H, overlapping singlets, O$\underline{CH_2}$Ar), 5.06 (2H, 3 sets of overlapping doublets, *J*= 9.04 Hz, α′-H), 5.75 (2H, two overlapping singlets, β-H), 6.09 (2H, dq, *J*= 6.9, 9.00 Hz, β′′-H), 6.35 (2H, d, *J*= 6.35 Hz, α′′-H), 6.73-7.11 (20H, m, Ar), 7.70 (2H, m, Ar), 7.79 (2H, m, Ar)

^{13}C NMR (100 MHz, $CDCl_3$) δ_C ppm- 14.16, 17.92, 18.51, 45.75, 45.78, 55.83, 56.07, 56.20, 62.25, 74.71, 82.47, 93.34, 109.40, 110.63, 110.73, 113.16, 113.46, 119.03, 119.14, 123.69, 125.97, 127.83, 127.92, 127.99, 128.03, 128.16, 129.63, 131.04, 132.45, 132.59, 132.62, 133.22, 136.43, 137.30, 144.28, 146.15, 146.62, 150.72, 150.79, 151.13, 152.89, 167.01, 190.32

ES-HRMS (*m/z*)- [M+NH_4^+] calc. Mass 1320.5532 found 1320.5535

FTIR (Thin film) ν_{max} (cm^{-1}): 3466, 2962, 2935, 1759, 1683, 1600, 1510, 1497, 1463, 1452, 1422, 1409, 1367, 1337, 1270, 1210, 1158, 1144, 1093, 1033, 963, 910, 856, 819, 733, 698

$C_{78}H_{78}O_{18}$: requires C-71.87%, H-6.03% found C-71.49%, H-5.99%

(*E*)-1,1′-(6,6′-bis(benzyloxy)-5,5′-dimethoxybiphenyl-3,3′-diyl)bis(2-(2-methoxy-4-(7-methoxy-3-methyl-5-((E)-prop-1-enyl)-2,3-dihydrobenzofuran-2-yl)phenoxy)propane-1,3-diol), 11

Compound **10** (1 g, $7.67x10^{-4}$ mole) was dissolved in chloroform (20 mL) and to this was added methanol (20 mL). To this solution lithium borohydride (0.167 g, $7.67x10^{-4}$ mole). The reaction was monitored by TLC (5 % methanol in DCM). Once **10** had been consumed the reaction mixture was then separated between water and chloroform. The organic layer was then dried with $MgSO_4$ and the solvent removed. The residue was then purified using flash chromatography (1:49 methanol:DCM). A white solid was obtained. (Yield- 76 %, 0.713 g)

^{1}H NMR (400 MHz, $CDCl_3$) δ_H ppm – 0.88 (d, *J*= 7.2 Hz, γ′-H-*cis*)1.38 (6H, two overlapping doublets, *J*= 6.80 Hz, γ′-H) , 1.86 (6H, two overlapping doublets, *J*= 6.52 Hz, γ′′-H), 3.43 (m, 2H, *J*= 7.04 Hz, β′-H) , 3.49-3.79 (region is shown to be overlapping γ-H from a mixture of *erythro* and *threo* diastereoisomers as well as containing β′-H-*cis* hydrogen) , 3.82-3.88(multiple singlets corresponding to ArOMe), 3.98 (m, β-H from *Threo* diastereoisomer), 4.12(broad m, A ring β-H from *Erythro* diastereoisomer), 4.76 (4H, overlapping signals, C$\underline{H_2}$Ar), 4.95 (2H, overlapping doublets, *J*= 5.10 Hz, α′-H), 5.10 (2H, overlapping signals, β-H),5.74 (d, *J*=7.2 Hz, α′-H *cis*), 6.11(2H, overlapping doublet of quintets, *J*= 6.52, 15.56 Hz, β′′-H), 6.35 (2H, overlapping doublets, *J*= 15.56 Hz, α′′-H), 6.75-7.14 (m, Ar)

^{13}C NMR (100 MHz, $CDCl_3$) δ_C ppm- 17.88, 18.44, 45.71, 45.75, 56.01, 56.05, 56.13, 60.77, 72.90, 72.98, 74.59, 87.03, 93.24, 93.33, 109.37, 109.40, 109.71, 110.22, 110.27, 110.33, 113.42, 119.85, 119.90, 120.49, 121.25, 123.64, 127.53, 127.75, 127.85, 127.94, 128.06, 130.97, 132.44, 132.73, 133.16, 136.24, 137.89, 144.21, 145.13, 146.53, 146.88, 151.57, 151.64, 153.16

ES-HRMS (*m/z*)- [$M+NH_4^+$] calc. Mass 1240.5634 found 1240.5656

FTIR (Thin film) ν_{max} (cm^{-1}): 3465, 2961, 2936, 1648, 1608, 1511, 1497, 1463, 1452, 1420, 1375, 1336, 1268, 1219, 1143, 1033, 733, 698

1,1′-(6,6′-dihydroxy-5,5′-dimethoxybiphenyl-3,3′-diyl)bis(2-(2-methoxy-4-(7-methoxy-3-methyl-5-propyl-2,3-dihydrobenzofuran-2-yl)phenoxy)propane-1,3-diol), 12

In a round bottom flask **11** (139 mg, $1.33x10^{-4}$ mole) was dissolved in a 1:1 ethanol/ethyl acetate mixture (10 mL). To this palladium on carbon 10 % (14 mg) was added. The flask was sealed and purged with hydrogen using a balloon. The reaction was allowed to stir under hydrogen for 3 h and monitored via tlc (1:49 methanol:DCM an eluent). Once the starting material was consumed the reaction mixture was filtered and the solvent removed using a rotary evaporator. The residue was purified using preparative layer chromatography (1:49 methanol:DCM) to yield the desired product as a white solid, foam. (Yield- 111 mg, 93 %)

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.79 (d, *J*= 7.3 Hz, γ′-H-*cis*), 0.96 (6H, t, *J*=7.28 Hz, γ′′-H), 1.38 (6H, two doublets superimposed, *J*=6.52, 6.76 Hz, γ′-H), 1.64 (4H, pseudo-quintet, *J*=7.80, 7.52, 7.28 Hz, β′′-H), 2.55 (4H, pseudo-triplet, *J*= 7.28, 8.04 Hz, α′′-H), 3.44 (2H, m, β′-H), 3.55 (superimposed, β′-H-*cis)*, 3.55-3.95 (m, γ-H), 3.84-3.89 (multiple singlets corresponding to ArOMe and overlapping γ-H from a mixture of *erythro* and *threo* diastereoisomers as well as containing β′-H-*cis* hydrogen), 4.05 (m, β-H from *threo* diastereoisomer), 4.18 (broad m, β -H from *erythro* diastereoisomer), 4.98 (broad m, 2H, α-H), 5.09 (2H, two doublets superimposed, *J*=9.52 and 9.28 Hz, α′-H), 6.15 (four singlets, ArOH), 6.60 (d, 4H, Ar, *J*=14.28 Hz), 6.88-7.10 (m, 10H, Ar)

^{13}C NMR (100 MHz, $CDCl_3$) δ_C ppm- 13.93, 17.60, 25.10, 29.27, 38.09, 45.82, 55.97, 55.99, 56.21, 60.95, 72.87, 87.17, 92.96, 108.45, 110.33, 111.86, 115.43, 120.03,120.51, 121.22, 122.24, 124.12, 131.78, 132.97, 136.55, 142.16, 142.60, 143.87, 145.23, 146.81, 146.89, 147.44, 151.26, 151.53

HRMS ES : ($M+NH_4^+$) calc. Mass 1064.5008, found 1064.5009

FTIR (Thin film) ν_{max} (cm^{-1}):3472, 2959, 2932, 2870, 1604, 1511, 1497, 1463, 1453, 1422, 1376, 1345, 1326, 1267, 1219, 1141, 1031, 910, 853, 816, 732

β-keto ester 14

O-Benzyl acetovanillone **13** (10.00 g, 0.039 mole) was dissolved in diethyl carbonate (30 mL) and heated to 80 °C. To this was added NaH (60% dispersion in mineral oil, 7.79 g, 0.195 mole) in small portions. The reaction is exothermic and the release of hydrogen gas means extra care should be employed. The reaction mixture turns from clear and slightly yellow to orange and opaque. The reaction was monitored by NMR. The reaction mixture was cooled to room temperature and carefully quenched with water. Once the excess hydride was quenched the reaction mixture was further diluted with water (300 mL) and extracted with ethyl acetate (150 mL x 3). The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure to give a yellow oil. Residual diethyl carbonate was removed by trituration with hexane. The resulting oil could then be purified by flash chromatography (4:1 hexane:ethyl acetate) and recrystallised from EtOAc:hexane to give colourless, granular crystals. (Yield: 8.96 g, 70 %)

^{1}H NMR (300 MHz, $CDCl_3$) δ_H (ppm): 1.26 (3H, t, *J*= 7.1 Hz, $CH_2C\underline{H}_3$), 3.93 (2H, s, βH), 3.94 (3H, s, OMe), 4.20 (2H, q, *J*= 7.1 Hz, $C\underline{H}_2CH_3$), 5.23(2H, s, $OC\underline{H}_2Ar$), 6.90 (1H, d, *J*= 8.4 Hz, Ar), 7.32-7.49 (7H, m, Ar), 7.55 (1H, d, *J*= 2.0 Hz Ar)

^{13}C NMR (75 MHz, $CDCl_3$) δ_C (ppm): 14.28($CH_2\underline{C}H_3$), 45.92(βC), 56.24(OMe), 61.61($\underline{C}H_2CH_3$), 71.01($C\underline{H}_2Ar$), 110.94, 112.32, 123.50, 127.38, 128.36, 128.90, 129.68, 136.28, 149.84, 153.15, 167.91($\underline{C}OOEt$), 191.23($\underline{C}O$)

$[M]^+$ calc. 328.1311 found 328.1289

α-Bromo-β-keto ester 15

To a solution of β-keto ester **14** (7.00 g, 0.021 mole) in EtOAc (200 mL) was added Amberlyst A15 resin (2.0 g) and *N*-bromosuccinimide (3.79 g, 0.021 mole). The reaction mixture was stirred at room temperature until TLC showed the disappearance of starting material (1: 4 EtOAc:hexane). The Amberlyst resin was filtered off and the solvent removed under reduced pressure. The residue was then purified using flash chromatography (4:1 hexane:ethyl acetate)to give **15** as a yellow oil. (Yield-7.27 g, 85 %)

^{1}H NMR (300 MHz, $CDCl_3$) δ_H (ppm): 1.26 (3H, t, *J*= 7.1 Hz, $CH_2C\underline{H}_3$), 3.94 (3H, s, OMe), 4.20 (2H, q, *J*= 7.1 Hz, $C\underline{H}_2CH_3$), 5.23(2H, s, $OC\underline{H}_2Ar$), 5.62 (2H, s, βH), 6.90 (1H, d, *J*= 8.4 Hz, Ar), 7.35-7.49 (6H, m, Ar), 7.55 (2H, m, Ar)

^{13}C NMR (75 MHz, $CDCl_3$) δ_C (ppm): 14.12($CH_2\underline{C}H_3$), 46.44(βC), 56.31(OMe), 63.45($\underline{C}H_2CH_3$), 71.10($C\underline{H}_2Ar$), 111.84, 112.34, 124.07, 126.76, 127.41, 136.13, 150.00, 153.67, 162.45, 165.55($\underline{C}OOEt$), 186.91($\underline{C}O$)

$[M+NH_4]^+$ calc. 424.0759 found 424.0789

Trimer 16

Compound **15** (9.34 g, 0.023 mole) was dissolved in acetone. To this was added dehydrodiisoeugenol **9** (7.50 g, 0.023 mole) and K_2CO_3 (3.17 g, 0.023 mole). The reaction was refluxed and monitored by TLC. Once compound **15** was consumed the reaction was allowed to cool to room temperature and filtered. The crude mixture was then purified using flash chromatography (80:20 hexane: ethyl acetate) to give the product as an amorphous white solid. (9.63 g, 64 %)

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.22(3H, t, *J*= 7.2Hz, $C\underline{H}_2CH_3$), 1.37(3H, d, *J*= 6.8 Hz, B ring γH), 1.86(3H, dd, *J*= 1.6, 6.6Hz, B ring γH), 3.42(1H, m, B ring βH), 3.78(3H, s, ArOMe), 3.88(3H, s, ArOMe), 3.93(3H, s, ArOMe), 4.25(2H, q, *J*= 7.00 Hz, $C\underline{H}_2CH_3$), 5.09(1H, d, *J*=9.1 Hz, B ring αH), 5.23(2H, s, $OC\underline{H}_2Ar$), 5.74(1H, overlapping isomers d, *J*= 2.9 Hz, A ring βH), 6.10(1H, dq, *J*= 6.6, 15.7 Hz, C ring βH), 6.35(1H, dd, *J*= 1.6, 15.7 Hz, C ring αH) , 6.75(1H, s, Ar), 6.78(1H, s, Ar), 6.84-6.93(3H, m, Ar), 6.98(1H, d, *J*= 1.7 Hz, Ar), 7.31-7.44(5H, m, Ar), 7.70(1H, d, *J*= 2.0 Hz, Ar), 7.78(1H, dd, *J*= 2.0, 8.5 Hz, Ar)

^{13}C NMR (100 MHz, $CDCl_3$): 14.25($CH_2\underline{C}H_3$), 17.96(B ring γC), 18.00(B ring γC), 18.56(C ring γC), 45.84(B ring βC), 45.86(B ring βC), 56.10(ArOMe), 56.12(ArOMe), 56.2(ArOMe)1, 62.32($\underline{C}H_2CH_3$), 71.00($O\underline{C}H_2Ar$), 82.87(A ring βC), 82.92(A ring βC), 93.43(B ring αC), 93.47(B ring αC), 109.45, 110.84, 110.93, 112.22, 112.32, 113.51, 118.36, 119.19, 123.78, 124.87, 127.40,

131.09, 132.55, 136.32, 144.36, 146.40, 149.59, 153.41, 167.20(COOEt), 167.21(COOEt), 190.18(CO), 190.21(CO)

$[M+H]^+$ calc mass 653.2751 found 653.2721

Debenzylated Trimer 17

Trimer **16** (7.00 g, 0.01 mole) was dissolved in THF (100 mL) in a RBF. To this palladium on carbon 10 % (1.0 g) was added. The flask was sealed and purged with hydrogen using a balloon. The reaction was allowed to stir under hydrogen for 3 h and monitored via tlc (6:4 EtOAc : Hexane). Once the starting material was consumed the reaction mixture was filtered and the solvent removed using a rotary evaporator. The residue was purified using flash chromatography (6:4 EtOAc : Hexane) to yield the desired product as a white solid, foam. (Yield- 5.25 g, 93 %)

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.96(3H, t, *J*= 7.3Hz, C ring γH), 1.23(3H, t, *J*= 7.2Hz, $C\underline{H}_2CH_3$), 1.36(3H, d, *J*= 6.7Hz, B ring γH), 1.62(2H, m, C ring βH), 2.54(1H, m, C ring αH), 3.41(1H, m, B ring βH), 3.80(3H, s, ArOMe), 3.87(3H, s, ArOMe), 3.95(3H, s, ArOMe), 4.26(2H, q, *J*= 7.15Hz, $C\underline{H}_2CH_3$), 5.07(1H, d, *J*=9.6 Hz, B ring αH), 5.75(1H, 2 singlets, βH), 6.13(1H, s, ArOH), 6.57(1H, s, Ar), 6.61(1H, s, Ar), 6.88-6.96(3H, m, Ar),7.01(1H, d, *J*=1.9 Hz) 7.71(1H, d, *J*= 1.9 Hz, Ar), 7.82(1H, dt, *J*= 2.0, 8.2 Hz, Ar)

^{13}C NMR (100 MHz, $CDCl_3$) δ_C ppm- 14.11(C ring γC), 14.27($CH_2\underline{C}H_3$), 17.83(B ring γC), 17.86(B ring γC), 25.27(C ring βC), 38.29(C ring αC), 46.02(B ring βC), 46.05(B ring βC), 56.15(ArOMe), 56.20(ArOMe), 56.31(ArOMe), 62.33($\underline{C}H_2CH_3$), 82.87(A ring βC), 93.29(B ring αC), 93.32(B ring αC), 110.95, 111.03, 111.71, 112.05, 114.26, 118.41, 118.45, 119.34, 125.72, 125.74, 132.98, 136.54, 136.68, 144.08, 145.51, 146.37, 146.71, 150.74, 150.76, 151.45, 167.25 (COOEt), 167.27(COOEt), 190.12(CO)

$[M+Na]^+$ calc mass 573.2101 found 573.2129

β-keto ester Octamer 18

Trimer **17** (5.55 g, 9.8×10^{-3} mole) was dissolved in acetone (100 mL) in a 250 mL RBF. To this was added compound **7** (3.22 g, 4.9×10^{-3} mole) dissolved in acetone (50 mL) and K_2CO_3 (1.36 g, 9.8×10^{-3} mole). The RBF was then fitted with a reflux condenser and the reaction mixture refluxed. The conversion of starting materials was monitored by TLC (6:4 EtOAc:Hexane). Once full conversion was observed (approximately 3 hours) the reaction mixture was cooled to room temperature before being filtered. The acetone was then removed using a rotary evaporator and the residue was dissolved in chloroform (200 mL) and washed with water (3 x 100 mL). The organic layer was then dried with

$MgSO_4$ and the solvent removed. The crude oil was then purified using flash chromatography (gradient up to 6:4 EtOAc:Hexane). (3.83 g, 43 %, cream solid)

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.96(6H, t, *J*= 7.3 Hz, D ring γH), 1.19(6H,overlapping multiplets, $CH_2C\underline{H}_3$), 1.36(6H, d, *J*= 6.7Hz, C ring γH), 1.63(4H, m, D ring βH), 2.54(2H, m, D ring βH), 3.40(2H, m, C ring βH), 3.74-3.94(multiple over lapping singlets, ArOMe), 4.22(4H, q, *J*= 7.15Hz, $C\underline{H}_2CH_3$), 4.73-4.88(4H, multiple singlets, OBn), 5.07(2H, d, *J*=9.5 Hz, C ring αH), 5.71(2H, multiple singlets, B ring βH) , 5.84(2H, multiple singlets, A ring βH), 6.57(2H, s, Ar), 6.61(2H, m, Ar), 6.79-7.10(19H, m, Ar), 7.63-7.80(8H, m, Ar)

^{1}H NMR (400 MHz, $CDCl_3$): δ 14.10(D ring γC), 14.20($CH_2\underline{C}H_3$), 14.24($CH_2\underline{C}H_3$), 17.85(C ring γC), 25.26(D ring βC), 38.28(D ring αC), 46.05(C ring βC), 56.02(ArOMe), 56.09(ArOMe), 56.16(ArOMe), 56.20(ArOMe), 62.35($\underline{C}H_2CH_3$), 62.67($\underline{C}H_2CH_3$), 74.83($C\underline{H}_2$Ar), 81.90 (A ring βC), 82.95(A ring βC), 83.00(A ring βC), 93.25(C ring αC), 109.94, 110.91, 110.96, 111.65, 112.05, 113.26, 113.31, 115.65, 116.23, 116.29, 118.55, 119.23, 119.29, 119.32, 124.31, 126.06, 127.95, 128.02, 128.14, 128.18, 128.24, 129.34, 129.79, 132.58, 132.60, 132.97, 136.68, 136.68, 136.71, 137.27, 144.08, 145.50, 146.28, 149.99, 150.19, 150.72, 150.76, 151.00, 151.26, 151.40, 153.03, 166.28 ($\underline{C}$OOEt),167.03($\underline{C}$OOEt), 189.29, 190.16, 190.18($\underline{C}$O)

$[M+Na]^+$ calc mass 1798.6489 found 1798.9442

Alcohol Octamer 19

Octamer **18** (1.0 g, $5.62x10^{-4}$ mole) was dissolved in chloroform (40 mL) and methanol (20 mL). To this $NaBH_4$ (0.21 g, $5.62x10^{-3}$ mole) with stirring. The reaction was monitored by TLC (5% methanol:DCM). If conversion was incomplete more $NaBH_4$ was added. Once starting material had been consumed the reaction mixture was diluted with chloroform (100 mL) and washed with water (2 x 50 mL). The water layers were combined and washed with chloroform (100 mL). The combined organic layers were dried with $MgSO_4$ and the solvent removed. The crude oil was then purified using flash chromatography (gradient up to 5 % methanol:DCM). (0.463 g, 51 %, white solid)

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.96(6H, t, *J*= 7.3Hz, D ring γH), 1.37(6H, d, *J*= 6.7Hz, C ring γH), 1.64(4H, m, D ring βH), 2.55(2H, m, D ring βH), 3.45(2H, m, C ring βH), 3.63(2H, A and B ring γH), 3.85(multiple over lapping singlets, ArOMe and A and B ring γH), 4.11(4H, A and B ring βH), 4.75(4H, multiple singlets, OBn), 4.91(4H, A and B ring αH), 5.08(2H, d, *J*=9.5 Hz, C ring αH), 6.58(2H, s, D ring Ar), 6.62(2H, s, D ring Ar), 6.78(3H, m, Ar), 6.95(3H, m, Ar), 7.05(3H, m, Ar), 7.15(3H, s, Ar)

^{13}C NMR (100 MHz, $CDCl_3$) δ_C ppm- 14.01(D ring γC), 17.83(C ring γC), 25.28(D ring βC), 38.29(D ring αC), 46.04(C ring βC), 56.16(ArOMe), 56.22(ArOMe), 56.28(ArOMe), 60.93(A and B

ring γH), 61.27(A and B ring γH), 72.83(A and B ring αH), 72.88(A and B ring αH), 73.28(A and B ring αH), 74.75(C$\underline{H}_2$Ar), 86.96(A ring βC), 87.02(A ring βC), 87.10(A ring βC),93.29(C ring αC), 100.20, 110.18, 110.29, 110.38, 110.50, 110.61, 111.97, 115.65, 119.30, 119.55, 120.12, 120.70, 120.76, 121.45, 127.68, 128.10, 129.21, 132.89, 132.94, 135.53, 136.79, 138.05, 144.07, 145.35, 146.41, 146.51, 146.90, 146.98, 151.54, 151.77,

$[M+NH_4]^+$ calc. 1636.7417 found 1636.7485

Debenzylated Octamer 20

Octamer **19** (0.463 g, 3.22 x 10^{-4}) was dissolved in THF (100 mL) in a RBF. To this palladium on carbon 10 % (14 mg) was added. The flask was sealed and purged with hydrogen using a balloon. The reaction was allowed to stir under hydrogen for 3 h and monitored via tlc (6:4 EtOAc : Hexane). Once the starting material was consumed the reaction mixture was filtered and the solvent removed using a rotary evaporator. The residue was purified using flash chromatography (6:4 EtOAc : Hexane) to yield the title product as a white solid, foam. (Yield- 0.431 g, 93 %)

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.96(6H, t, *J*= 7.3Hz, D ring γH), 1.37(6H, d, *J*= 6.6Hz, C ring γH), 1.64(4H, m, D ring βH), 2.55(2H, m, D ring βH), 3.45(2H, m, C ring βH), 3.61(2H, A and B ring γH), 3.78(multiple over lapping singlets, ArOMe and A and B ring γH), 4.11(4H, A and B ring βH), 4.89(4H, A and B ring αH), 5.07(2H, d, *J*=9.5 Hz, C ring αH), 6.58(2H, s, D ring Ar), 6.62(2H, s, D ring Ar), 6.78-7.02 (8H, m, Ar)

^{13}C NMR (100 MHz, $CDCl_3$) δ_C ppm- 14.11(D ring γC), 17.82(C ring γC), 25.29(D ring βC), 38.29(D ring αC), 46.02(C ring βC), 56.16(ArOMe), 56.35(ArOMe), 60.98 (A and B ring γH), 61.62 (A and B ring γH), 72.83(A and B ring αH), 73.34(A and B ring αH), 86.78(A ring βC), 87.14(A ring βC), 93.30(C ring αC), 108.87, 109.03, 110.29, 110. 47, 110.58, 111.97, 115.65, 119.28, 119.41, 119.45, 120.10,120.24, 120.38, 120.53, 120.58, 120.62, 120.57, 124.51, 132.90, 135.92, 136.61, 136.77, 142.37, 144.06, 145.41, 146.61, 146.97, 147.05, 147.55, 151.23, 151.67

$[M+NH_4]^+$ calc. 1456.6479 found 1456.6409

Diethyl diferulate 21

Ethyl ferulate (13.00 g, 0.058 mole) was dissolved in benzene (150 mL). Silver (I) oxide (8.13 g ,0.035 mole) was added with stirring to the solution. The flask was then purged with nitrogen and the reaction allowed to stir for 5 hours. After this time a small sample was taken, the solvent removed and an NMR run. Once the ratio of starting material to product was judged to be constant by the 6.11 ppm shift of the product the reaction solution was passed through a short celite plug which was washed with EtOAc (100 mL). The solvent was removed to yield a yellow oil which was purified using flash

chromatography with a gradient eluant 8:2 to 6:4 hexane:EtOAc. The product could be recrystallized from the minimal amount of hot EtOAc and then room temperature hexane as the antisolvent. (5.44 g, 42 % yield, white crystals)

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.34(3H, t, *J*=7.1Hz, $CH_2C\underline{H}_3$), 3.88(3H, s, OMe), 3.92(3H, s, OMe), 4.25(4H, q overlapping, *J*=7.1 Hz, $C\underline{H}_2CH_3$), 4.32(1H, d, *J*=9.3 Hz, A ring βH), 5.67(1H, s, ArOH), 6.11(1H, d, *J=8.3* Hz, A ring αH), 6.31(1H, d, *J*= 15.9 Hz, B ring βH), 6.90(3H, s, Ar), 7.03 (1H, s, Ar), 7.19(1H, s, Ar), 7.6 4(1H, d, *J*= 15.9 Hz, B ring αH)

^{13}C NMR (100 MHz, $CDCl_3$) δ_C ppm- 14.50($CH_2\underline{C}H_3$), 14.57($CH_2\underline{C}H_3$), 55.80(A ring βC), 56.24(ArOMe), 56.34(ArOMe), 60.63($\underline{C}H_2CH_3$), 62.09($\underline{C}H_2CH_3$), 87.71(A ring αH), 108.97, 112.16, 114.73, 116.19(B ring βC), 118.11, 119.70, 126.10, 128.86, 131.70, 144.75(B ring αC), 144.94, 146.27, 146.92, 150.15, 167.43 ($\underline{C}$OOEt), 170.45($\underline{C}$OOEt)

Hexamer 22

Diethyldiferulate, **21**, (1.65 g, $3.73x10^{-3}$ mole) was dissolved in acetone (10 mL) and the solution heated to 60 °C. To this was added K_2CO_3 (0.515 g, $3.73x10^{-3}$ mole). Brominated intermediate **7** (1.22 g, $1.86x10^{-3}$ mole) was dissolved in acetone (10 mL) and was added to the solution of **21**. The reaction mixture was stirred until all of compound **7** was consumed which was monitored *via* tlc (1:4 EtOAc:hexane). The reaction mixture was then cooled to room temperature and filtered. The solvent was removed under reduced pressure and the crude product purified using flash chromatography (1:1 hexane:ethyl acetate) to give a yellow solid after drying under reduced pressure. (Yield: 1.53 g, 53 %)

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.17(6H, m, A ring γ $COOCH_2C\underline{H}_3$),1.34 (9H, m, B and C ring γ $COOCH_2C\underline{H}_3$), 3.66 (18H, multiple overlapping singlets, OMe), 4.17-4.25 (14H, m, overlapping $COOC\underline{H}_2CH_3$ and B ring βH), 4.88-4.90 (4H, overlapping singlets, $OC\underline{H}_2Ar$), 5.74-5.75 (2H, overlapping singlets, A ring αH), 6.07(2H, overlapping doublets, *J*= 8.0 Hz, , B ring αH), 6.30(2H, d, *J*= 15.9 Hz, C ring βH), 6.71-7.17 (20H, m, Ar), 7.63(2H, d, *J*=15.6 Hz, C ring αH), 7.70 (2H, bs, Ar), 7.79(2H, bs, Ar)

^{13}C NMR (100 MHz, $CDCl_3$) δ_C ppm- 14.19($CH_2\underline{C}H_3$), 14.30($CH_2\underline{C}H_3$), 14.46($CH_2\underline{C}H_3$), 14.54($CH_2\underline{C}H_3$), 55.65(ArOMe). 55.86(B ring βC), 55.93(ArOMe), 56.25(ArOMe), 56.29(ArOMe), 60.60($\underline{C}H_2CH_3$), 62.11($\underline{C}H_2CH_3$), 62.29($\underline{C}H_2CH_3$), 62.34($\underline{C}H_2CH_3$), 74.75($O\underline{C}H_2Ar$), 82.15(A ring βC), 82.47(A ring βC), 87.06(B ring αC), 110.51, 110.62, 111.37, 112.13, 112.87, 113.12, 113.18, 114.47, 115.74, 116.23(C ring βC), 117.09, 117.77, 118.63, 118.63, 118.73, 119.09, 122.16, 124.34, 125.85, 126.04, 127.86, 127.89, 128.02, 128.09, 128.19, 128.93, 129.60, 132.62, 132.67, 135.77, 144.26, 144.66(C ring αC), 145.40, 145.46, 146.21, 146.37, 149.36, 150.01, 150.82, 150.86, 151.21,

152.95, 166.67(COOEt), 166.89(COOEt), 167.21(COOEt), 167.37(COOEt), 170.29(COOEt), 190.21(A ring α CO), 190.28(A ring α CO)

$[C_{86}H_{86}O_{26} + NH_4]^+$ calc.1552.5751 found 1552.5699

Partially reduced hexamer 23

Hexamer **22** (0.2 g, $1.30x10^{-4}$ mole) was dissolved in chloroform (5 mL) and to this was added methanol (15 mL). To this solution sodium borohydride (0.05 g, $1.30x10^{-3}$ mole). The reaction was monitored by TLC (5 % methanol in DCM). Once **22** had been consumed the reaction mixture was then separated between water and chloroform. The organic layer was then dried with $MgSO_4$ and the solvent removed. The residue was then purified using preparative TLC (7:93 methanol:chloroform). A white solid was obtained. (Yield- 40 %, 0.071 g)

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.33(6H, m, C ring γ $COOCH_2CH_3$), 2.31(2H, bs, B ring γ OH), 2.88(2H, bs, A ring γ OH), 3.54(B ring βH), 3.66-3.89(overlapping signals from OMe and A and B ring γ CH_2), 4.13(2H, bs, A ring βH), 4.25(4H, q, , *J*=7.1 Hz, $COOCH_2CH_3$) 4.73(4H, s, OCH_2Ar), 4.87(2H, bs, A ring αH), 5.58(2H, overlapping doublets, *J*= 7.4Hz, B ring αH), 6.28(2H, d, *J*=15.9 Hz, C ring βH), 6.26-7.15(24H, m, Ar), 7.60(2H, d, *J*=15.9 Hz, C ring αH)

^{13}C NMR (100 MHz, $CDCl_3$) δ_C ppm- 14.55(CH_2CH_3), 51.85, 53.51(B ring βC), 53.55(ArOMe), 56.18(ArOMe), 56.23(ArOMe), 60.62(CH_2CH_3), 61.23(A ring γ), 61.39(A ring γ), 61.48, 64.32, 64.47(B ring γ), 73.15(A ring α), 73.30(A ring α), 74.81(OCH_2Ar), 86.47(A ring βC), 86.72(A ring βC), 86.78(A ring βC), 88.57(B ring αC), 88.72(B ring αC), 110.06, 110.19, 111.98, 112.08, 115.45(C ring βC), 115.94, 117.61, 119.08, 120.40, 121.38, 127.74, 127.80, 128.14, 128.22, 128.74, 132.83, 132.90, 135.63, 135.66, 136.70, 137.90, 137.97, 144.77(C ring αC), 144.83(C ring αC), 145.15, 145.23, 145.26, 147.04, 147.10, 150.59, 150.65, 151.36, 151.49, 153.14, 153.20, 167.52(COOEt), 167.58(COOEt)

$[C_{86}H_{82}O_{22} + NH_4]^+$ calc.1388.5641 found 1388.5625

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