Fractionation and DOSY NMR as Analytical Tools: from Model Polymers to a Technical Lignin

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General Procedures

Chemical reagents were obtained from Sigma-Aldrich, Fischer Scientific and Acros organics and were used as received unless specified. Kraft lignin was sourced from MeadWestvaco Corporation, Richmond, VA. All reactions conducted under inert conditions were carried out in flame dried glassware under a positive atmosphere of nitrogen. The dry solvents used were obtained from a solvent purification system (MBraun, SPS-800). Thin layer chromatography was conducted on glass backed TLC plates. Developed plates were air dried and viewed with a UV lamp 254 & 365 nm); where required the plates were developed with KMnO₄ solution. Mass spectrometry data was acquired through the University of St Andrews School of Chemistry mass spectrometry service or the EPSRC Mass Spectrometry service at Swansea. IR analysis was carried out using a Shimadzu IRAffinity-1 Fourier Transform spectrometer as thin films with only characteristic peaks reported.

NMR Analysis

¹H NMR and ¹³C NMR of small molecules was performed on a Bruker Avance III 500 MHz spectrometer with the residual solvent peak used as the internal standard. Multiplicities were reported as the following: s = singlet, d = doublet, t = triplet, q = quartet and m = multiplet and J values are reported in Hz. NMR spectra used for small molecule assignment were processed on MestReNova 10.0 Windows version.

For polymer samples, ¹H NMR was performed on a Bruker Avance III 700 MHz spectrometer equipped with a nitrogen cooled cryoprobe (Prodigy). The residual solvent peak was used as an internal standard. Quantitative ¹H NMR spectra were acquired with the standard pulse sequence from the Bruker library (zg) and used a 30 s inter-scan (D1) delay.

DOSY experiments were performed using the ledbp gp2s pulse sequence. Gradient amplitude (6.56 G.mm⁻¹) was calibrated using the residual signal of HDO in D₂O. The diffusion delay (∆) and gradient pulse length (δ) were optimized for each sample in order to
achieve ca. 5-10% residual signal at 98% gradient strength (compared to 10% gradient strength) using the 1D DOSY experiment with the ledbpgp2s1d pulse sequence. Each pseudo-2D experiment consisted of series of 32 spectra acquired with 65536 data points. The gradient pulses were incremented from 10% to 98% with a linear ramp. The temperature was set and maintained at 295 K. Data sets were processed by Fourier transformation in $F_2$, using line broadening of 10 Hz, followed by a baseline correction. The DOSY analysis was then performed in Bruker Dynamics Center 2.3. Manual peak picking was performed for each dataset and peak intensities were used to measure the signal decay. Error estimation of the fit was performed at the 95% confidence level. All samples were prepared by dissolving 60 mg of material in 0.7 mL of $d_6$-DMSO. The samples were then sonicated for 30 mins at 35°C and then filtered through a 0.45 µm PTFE syringe filter. All samples were allowed to thermally equilibrate prior to optimizing DOSY parameters ($\Delta$ and $\delta$).

**Continuous wave electron paramagnetic resonance spectroscopy**

EPR spectra were obtained with a Bruker EMX 10/12 spectrometer equipped with an SHQE resonator at an operating frequency of ~9.76 GHz with 100 kHz modulation. Weighed lignin samples were measured in 4 mm OD quartz tubes (Wilmad) closed with rubber septa (Sigma-Aldrich). All spectra were recorded with a time constant and conversion time of 40.96 ms each and an attenuation of 38.0 dB (32 µW power) to avoid saturation. For quantitative analysis, spectra were recorded in triplicate using a 200 G (20 mT) field sweep centred at 3485 G with 1024 points resolution and a modulation amplitude of 2.0 G. A 100 µM solution of TEMPO in toluene was used as external standard for quantification and measured with identical parameters. Wider scans to detect broader signals were recorded for the crude and derivate and the later fractions using a 800 G field sweep centred at 3485 G with 2048 points resolution and a modulation amplitude of 2.0 G. Narrower scans to resolve potential additional structure on the radical signal were recorded for the earlier fractions.
using a 90 G field sweep centred at 3485 G with 1024 points resolution and a modulation amplitude of 0.4 G. Uncertainties in the number of spins per mg sample were estimated from the respective weighing and volumetric errors and the corrected standard deviations of triplicate measurements propagated to spins per weight.

**Synthetic Procedures.**

**Synthesis of alkyl bromo-esters 3(I-VIII)**

To a stirred solution of the bromoacetic acid (6) (1.20 eq.) in cyclohexane (10 mL/g of alcohol) was added the required alcohol (1.00 eq.) and p-toluenesulfonic acid monohydrate (0.01 eq.). The mixture was heated at reflux under Dean-Stark conditions until the reaction was complete (as judged by 1.00 eq. of water removed). After cooling to room temperature, the crude reaction mixture was diluted with cyclohexane (1 vol. eq.) and washed with NaHCO$_3$ (sat. solution), brine, dried over MgSO$_4$ and concentrated *in vacuo* to give the required bromoester in sufficient purity that no further purification was carried out. Quantities of reagents, reactants and solvents are specified for each reaction in the Supplementary Information.

**Synthesis of Monomer Units 4 (I-VIII)**

To a stirred solution of vanillin (1.00 eq.) and K$_2$CO$_3$ (2.00 eq.) in acetone (10 mL/g) was added the bromoester (3(I)-3(VIII)). The mixture was heated at reflux until the reaction was complete (as judged by TLC). The reaction was then cooled, filtered through a pad of celite, and concentrated *in vacuo* to give the crude monomer (4(I)-4(VIII)). Quantities of reagents, reactants, solvents and the purification method employed are specified for each reaction in the Supplementary Information.
Synthesis of all G β-O-4 polymer 1 - (i) Aldol polymerization and (ii) Reduction

**LDA Preparation:** to a solution of diisopropylamine (1.3 eq.) in THF (3 mL/mmol) at -78 °C was added a solution of n-BuLi in hexanes (molarity determined by titration against diphenylacetic acid) (1.2 eq.) dropwise. The mixture was briefly warmed to 0 °C before cooling to -78 °C again prior to use.

(i) **Aldol polymerization:** To a flask containing monomer 4(I)-4(VIII) (1.0 eq.)* in THF (20 v/w) at -15 °C was added dropwise the LDA solution (see above). After addition, the reaction was stirred vigorously for 2 hours. The mixture was then quenched by addition of NH₄Cl (sat. solution), diluted with brine and extracted with ethyl acetate (3x). The organic extracts were combined, washed with brine, dried with MgSO₄ and concentrated *in vacuo* to yield the crude polyester (5(I)-5(VIII)). *the monomer dried by azeotropic distillation using toluene (2x) immediately prior to use.

(ii) **Reduction:** To a solution of crude polyester (5(I)-5(VIII)) (1.00 eq.) in ethanol (10 mL/g) was added NaBH₄ (5.00 eq.) and the reaction was heated to 50 °C. Methanol (15.00 eq.) was added slowly and the mixture was left for 1 hour. The mixture was concentrated *in vacuo* to give a gum, re-dissolved in water (15 mL/g) and any alcohol produced during the reaction was extracted with ethyl acetate (3x). The aqueous layer was separated, acidified to pH ~2 using 6N HCl (caution: add slowly, very exothermic) which caused the reduced polymer to precipitate into a gum. The gum was collected and dried in a vacuum oven for 16 hours then taken up in acetone: methanol (9:1, ~10 mL/g) and added dropwise to diethyl ether (10x volume) to give an off-white precipitate of polymer 1(I-VIII).

**Large Scale synthesis of the all G β-O-4 polymer**

The synthesis of octyl bromoacetate (3(V)) and monomer unit 4(V) followed the identical procedures as reported above.
**LDA Preparation:** to a solution of diisopropylamine (9.42 g, 93 mmol, 1.5 eq.) in THF (280 mL) at -78 °C was added a solution of n-BuLi in hexanes (40 ml, 2.31 M (molarity determined by titration against diphenylacetic acid) 1.5 eq.) dropwise. The mixture was briefly warmed to 0 °C before cooling to -78 °C again prior to use.

(i) **Aldol polymerization:** To a flask containing monomer 4(V) (20.6 g, 64.0 mmol, 1 eq.)* in THF (250 mL) at -15 °C was added dropwise the LDA solution (see above). After addition, the reaction was stirred vigorously for 2 hours. The mixture was then quenched by addition of NH₄Cl (sat. solution), diluted with brine and extracted with ethyl acetate (3x 200 mL). The organic extracts were combined, washed with brine, dried with MgSO₄ and concentrated *in vacuo* to yield the crude polyester (5(I)-5(VIII)). * the monomer was dried by azeotropic distillation using toluene (2x 200 mL) immediately prior to use.

(ii) **Reduction:** To a solution of crude polyester 5(V) (20.0 g, 62 mmol, 1.00 eq.) in ethanol (350 mL) was added NaBH₄ (12.1 g, 320 mmol, 5 eq.) and the reaction was heated to 50 °C. Methanol (30.8 g, 960 mmol, 15.0 eq.) was added slowly and the mixture was left for 1 hour. The mixture was concentrated *in vacuo* to give a gum, re-dissolved in water (15 mL/g) and any n-octanol produced during the reaction was extracted with ethyl acetate (3x 200 mL).* The aqueous layer was separated, acidified to pH ~2 using 6N HCl (caution: add slowly, very exothermic) which caused the reduced polymer to precipitate into a gum. The gum was collected and dried in a vacuum oven for 16 hours then taken up in acetone: methanol (9:1, ~10 mL/g) and added dropwise to diethyl ether (10x volumes, v/v) to give an off-white precipitate of polymer 1(V). *In some cases, the separation was inefficient. NaCl was added to the solution and the polymer precipitated out. The precipitate was collected by filtration and dissolved in the minimum amount of 6M NaOH. The resulting solution was neutralized by the addition of 6N HCl with vigorous stirring. The sticky gum obtained was then collected and dried in a vacuum oven for 16 hours then taken up in acetone: methanol
(9:1, ~10 mL/g) and added dropwise to diethyl ether (10 volumes, v/v) to give an off-white precipitate of polymer 1(V) (3.00 g, 25% over 2 steps).

**Gel Permeation Chromatography**

GPC analysis was carried out using a Shimadzu HPLC/GPC system equipped with a CBM-20A communication bus, DGU-20A degassing unit, LC-20AD pump, SIL-20A autosampler, CTO-20A column oven and SPD 20A UV-Vis detector. Samples were analyzed using a Phenogel 5 µm 50A (300 x 7.8 mm) and Phenogel (5 µm 500A (300 x 7.8mm) columns connected in series and eluted with inhibitor free THF (1mL min\(^{-1}\)) with a column oven temperature of 30°C. The system was calibrated using polystyrene standards sourced from Polymer Standards Services (PSS) with \(M_p\) values ranging from 266 Da to 12600 Da. \(M_n\) values were calculated using the equation:

\[
M_n = \frac{\sum h_i M_i}{\sum h_i}
\]

where \(M_i\) is the molecular weight at given point \(i\), according to a calibration and \(h\) is the signal intensity of a given log M measurement point \(i\).

\(M_w\) values were calculated using the equation:

\[
M_w = \frac{\sum h_i M_i^2}{\sum h_i M_i}
\]

**GPC sample preparation**

To a solution of polymer 1(I-VIII) (ca. 7 mg) in pyridine (0.5 mL) was added acetic anhydride (0.5 mL) and the solution was stirred for 16 hours. The mixture was concentrated in vacuo by azeotropic distillation with toluene (3x), ethanol (3x) and dichloromethane (3x). The residue was dissolved in THF (1 mL) and filtered through a 0.45 µm PTFE syringe filter and submitted for analysis. Fractionation samples were already acetylated and so used directly from fractionation process. Samples were prepared by dissolving ca. 7 mg of
material in 1 mL of THF, passed through a 0.45 µm PTFE syringe filter and submitted for analysis. The GPC had been previously calibrated using polystyrene standards sourced from.

**Fractionation and Yield Analysis of Model Polymer and Kraft Lignin**

**Model Polymer Acetylation**

To a solution of polymer \(1(V)\) in pyridine (5 mL g\(^{-1}\), v/w) was added acetic anhydride (5 mL g\(^{-1}\), v/w) and the solution was stirred for 16 hours. The mixture was concentrated in vacuo by azeotropic distillation with toluene (3x), ethanol (3x) and dichloromethane (3x). The residue was dissolved in a minimum amount of DCM and added dropwise to diethyl ether (10 volumes, v/v). The precipitate was collected by filtration and dried *in vacuo*.

**Kraft Lignin Acetylation**

To a solution of Kraft lignin in pyridine (5 ml g\(^{-1}\), v/w) was added acetic anhydride (5 mL g\(^{-1}\), v/w) and the solution was stirred for 16 hours. The mixture was concentrated *in vacuo* by azeotropic distillation with toluene (3x), ethanol (3x) and dichloromethane (3x). The residue was dissolved in the minimum amount of DCM and added dropwise to diethyl ether (10 volumes, v/v). The precipitate was collected by filtration and dried *in vacuo*.

**Fractionation of the acetylated all G β-O-4 polymer (Ac-1(V)) and lignin**

To the purified acetylated polymer / lignin (~10 g), was added a solution of acetone (5%, v/v) in diethyl ether (100 vol/w) and the mixture was allowed to stir vigorously for 1 hour. The insoluble fraction was filtered off and dried under vacuum. The filtrate was concentrated and dried *in vacuo*. This process was repeated with 5% increments of acetone in diethyl ether solution until all material had dissolved. After the last fractionation step, all the fractions were then dried *in vacuo* for a further 8 hours before being weighed. For a schematic representation see Figure S3.
Aldol Polymerisation Reactions: Polyester 5(I)-5(VIII) analysis

All reactions were conducted on a 2 g scale to determine which monomer 4(I)-4(VIII) gave the highest degree of polymerisation (D. o. P.) in comparison to isolated polymer yield at the end of the polymer synthesis.

Figure S1. ^1^H NMR (700 MHz, CDCl$_3$) of crude polyester 5(I)-5(VIII) mixtures. Analysis included Bernstein polynomial baseline correction followed by Lorentzian line-fitting analysis using MestReNova 10.0 for Mac. Degree of polymerisation was calculated by comparison of the integration of the aldehyde region (set equivalent to 1H - end-group) with the integration all aromatic peaks (scaled to account for the fact that it is equivalent to 3 hydrogens). The results of this analysis are presented in Table 1 of the manuscript.
**Table S1** Synthesis yields and molecular weight characterisation of large scale synthetic batches of model polymer 1(V). SB-1 was made by polymerising 200 g of monomer 4(V) to give 30 g of polymer 1(V) (25% yield). SB-2 produced 1.5 g of polymer 1(V) from 10 g of 4(V) with SB-3 giving 3.0g of 1(V) from 20g of 4(V). Molecular weight analysis was performed on acetylated samples of polymer 1(V) (Ac-1(V)) to ensure sufficient solubility.

| Synthetic Batch | Yield of 1(V) (g) | Ac-1(V) $M_n$ (GPC)$^a$ | Ac-1(V) $M_w$ (GPC)$^a$ | Ac-1(V) PDI | Ac-1(V) $M_n$ (Q-3H NMR)$^b$ |
|-----------------|-------------------|-------------------------|-------------------------|-------------|-----------------------------|
| SB-1            | 30 (25%)          | 2000                    | 2800                    | 1.4         | 2420                        |
| SB-2            | 1.5 (25%)         | 2600                    | 4100                    | 1.6         | 2625                        |
| SB-3            | 3.0 (25%)         | 2800                    | 4400                    | 1.6         | 2884                        |

$^a$ GPC integrations were taken from where the UV response left the baseline to where it returned to the baseline. $^b$ NMR end group analysis was performed by measuring the integral of the $\beta$-O-4 $\alpha$ proton relative to the benzylic CH$_2$ end group (see Figure S4). Material from SB-1 was used for the G-1 and G-2 fractionation experiments.
Figure S2. Characterisation of the all G β-O-4 polymer. Cross peaks have been colour coded to the structural feature they belong. Sample was prepared by dissolving 60 mg of material in 0.7 mL of $d_6$-DMSO and passing the solution through a 0.45 µm PTFE syringe filter. Data was acquired on a Bruker 700 MHz Avance III spectrometer equipped with a nitrogen cooled $[^{1}H/^{13}C/^{15}N]$ triple resonance cryo probe TCI (prodigy). The hsqedttgsp.3 pulse sequence was used with a spectra width of 180 ppm and 256 points in the indirect dimension ($D_2 = 1$ s, $ns = 1$). Aromatic and linkage regions are shown.
Fractionation protocol and yield analysis

**Figure S3.** Schematic representation of the fractionation process. Acetylated material was stirred at room temperature for 1 hour in a solvent system. The insoluble fraction was filtered off, dried under vacuum and taken forward into the next solvent system. The soluble fractions were concentrated and dried under vacuum. Once all material had been dissolved, the fractions were left under vacuum for 8 hours.
Table S2. Fraction yield analyses for 2 fractionations of the all G β-O-4 model polymer Ac-1(V) (each fractionation was assigned a code – G#), Kraft lignin fractionation 1 (KL-1) and Kraft lignin fractionation 2 (KL-2). The “Initial Mass” corresponds to the mass of the acetylated material Ac-1(V) before fractionation. The “Total Recovered Mass” corresponds to the sum of the yields of all the soluble fractions generated during the fractionation process. The “Yield” corresponds to the recovered mass as a percentage of the initial mass. Acetone:diethyl ether ratios used in each step of the fractionation are shown.

| Fraction | Acetone : Et₂O Ratio (v/v) | Fraction Yields (g) |
|----------|-----------------------------|---------------------|
|          |                             | G-1     | G-2     | KL-1    | KL-2    |
| F1       | 05 : 95                     | 0.099   | 0.415   | 0.253   | 0.261   |
| F2       | 10 : 90                     | 0.348   | 0.935   | 0.341   | 0.288   |
| F3       | 15 : 85                     | 1.006   | 1.230   | 0.472   | 0.366   |
| F4       | 20 : 80                     | 1.140   | 1.160   | 0.511   | 0.463   |
| F5       | 25 : 75                     | 1.676   | 0.780   | 0.430   | 0.546   |
| F6       | 30 : 70                     | 0.880   | 0.060   | 0.670   | 0.511   |
| F7       | 35 : 65                     | 0.267   | 0.088   | 0.345   | 0.788   |
| F8       | 40 : 60                     | n/a     | n/a     | 0.225   | 0.163   |
| F9       | 45 : 55                     | n/a     | n/a     | 0.300   | 1.129   |
| F10      | 50 : 50                     | n/a     | n/a     | 2.269   | 1.643   |
| F11      | 55 : 45                     | n/a     | n/a     | 1.086   | 1.433   |
| F12      | 60 : 40                     | n/a     | n/a     | 0.477   | 0.680   |
| F13      | 65 : 35                     | n/a     | n/a     | 0.163   | 0.186   |
| F14      | 70 : 30                     | n/a     | n/a     | 0.046   | 0.111   |
|          | Total Recovered Mass (g)    | -       | 5.417   | 4.668   | 7.600   | 8.568   |
|          | Initial Mass (g)            | -       | 6.171   | 4.902   | 8.860   | 10.530  |
| Yield (%) |  -  | 88  | 95  | 86  | 81  |
|-----------|-----|-----|-----|-----|-----|

GPC Analysis of Model Polymer Ac-1(V) G-1

See Experimental Section of manuscript for an additional description of how the GPC analysis was carried out.

Table S3. Fractionation G-1 GPC triplicate data showing the measured $M_n$ (g mol$^{-1}$), $M_w$ (g mol$^{-1}$) and associated PDI for each fraction. Three individual samples were prepared for each fraction.

| Fraction | G-1(1) | G-1(2) | G-1 (3) | Average |
|----------|--------|--------|---------|---------|
|          | $M_n$  | $M_w$  | PDI     | $M_n$  | $M_w$  | PDI     | $M_n$  | $M_w$  | PDI     |
| F1       | 1800   | 2400   | 1.3     | -      | -      | -       | -      | -      | -       | 1800*   | 2400*   | 1.3     |
| F2       | 2000   | 2600   | 1.3     | 2000   | 2500   | 1.3     | 2000   | 2500   | 1.3     | 2000 (28) | 2600 (26) | 1.3     |
| F3       | 2200   | 2800   | 1.3     | 2200   | 2800   | 1.3     | 2200   | 2800   | 1.3     | 2200 (2) | 2800 (9) | 1.3     |
| F4       | 2400   | 3200   | 1.3     | 2400   | 3200   | 1.3     | 2400   | 3200   | 1.3     | 2400 (8) | 3200 (5) | 1.3     |
| F5       | 2800   | 3900   | 1.4     | 2800   | 3900   | 1.4     | 2900   | 3900   | 1.4     | 2800 (42) | 3900 (31) | 1.4     |
| F6       | 3300   | 4700   | 1.4     | 3300   | 4700   | 1.4     | 3200   | 4700   | 1.5     | 3300 (14) | 4700 (4) | 1.5     |
| F7       | 3600   | 5900   | 1.6     | 3800   | 6000   | 1.6     | 3700   | 6000   | 1.6     | 3700 (59) | 5900 (23) | 1.6     |

*Insufficient material was available to perform analysis in triplicate. Integrated regions were set to where the UV response left and returned to the baseline. Standard deviations (σ) are shown in parentheses.
Table S4 GPC-determined molecular weights of fractions from G-1 and G-2 fractionation series (g mol\(^{-1}\)). Integrations were taken from where the UV response left to where it returned to the baseline. PDIs were calculated by taking the ratio of the measured average molecular weights (\(M_w/M_n\)).

| Fraction | G-1\(^a\) | G-2 |
|----------|-----------|-----|
|          | \(M_n\)   | \(M_w\) | PDI | \(M_n\) | \(M_w\) | PDI |
| F1       | 1800\(^a\) | 2400\(^a\) | 1.3 | 1400 | 1800 | 1.3 |
| F2       | 2000 | 2600 | 1.3 | 1600 | 2000 | 1.3 |
| F3       | 2200 | 2800 | 1.3 | 2000 | 2600 | 1.3 |
| F4       | 2400 | 3200 | 1.3 | 2500 | 3200 | 1.3 |
| F5       | 2800 | 3900 | 1.4 | 3100 | 4200 | 1.3 |
| F6       | 3300 | 4700 | 1.5 | 2900 | 4500 | 1.5 |
| F7       | 3700 | 5900 | 1.6 | 3000 | 5000 | 1.7 |
| Bulk     | 2000 | 2800 | 1.4 | 2000 | 2800 | 1.4 |

\(^a\) G-1 values given are the averages from the triplicate data shown in Table S3.

The observed polydispersity increases, eventually to values above the initial bulk material (F6 and F7) across all fractionation. This is thought to result from the significant tailing that can be seen in the GPC profiles (seen in all fractionations) of these fractions (Figure 2, manuscript and FigureS4 below). As tailing leads to a lower number average molecular weight (\(M_n\)), a higher PDI is expected for fractions with increased tailing. If this is the case, the number average molecular weight (\(M_n\)) will be more significantly affected leading to a higher PDI values. It is important to note however that the high molecular weight material expected to dissolve at later steps in the fractionation process, represent a small weight fraction of the initial bulk material (Table S2 & Figure S4). Any lower molecular weight contaminants that were not extracted in a previous, higher yielding step, are likely to significantly reduce the measured number average and generate higher PDI than the initial bulk material.
Figure S4. Overlay of GPC elution time profiles of fractionated Ac-I(V) (from fractionation G-1). Fractions have been colour coded. The bulk material is shown in black. Fraction profiles have been normalised and multiplied by the mass fraction (% recovered material) to illustrate the relative abundances across the molecular weight distribution. The fraction (coloured) profiles have each been multiplied by two for clarity.
Figure S5. A) Sections of $^1$H NMR spectrum of fraction F1 (G-1) showing i) $\alpha$-proton signal and ii) benzylic CH$_2$ end group signal. B) Structure of a representative polymer chain that contains 3 aromatic rings linked together by 2 $\beta$-O-4 units with an overall molecular weight of 842.844 g mol$^{-1}$. C) Schematic representation of a polymer Acf-1(V) chain containing 3 aromatic units and 2 $\beta$-O-4 linkages broken down into fragments that were used to calculate the $M_n$ by quantitative $^1$H NMR. Integrals were normalised so that the benzylic CH$_2$ end group integral (*) = 2. The $\alpha$-proton integral was then taken as $n$ (for fraction F1, G-I $n=5.23$, see A(i)), and used to calculate the average number of linkages in the polymer chains. This value was then multiplied by the molecular weight of one unit (blue fragment) and summed with molecular weights of the two end groups.
Table S5 Quantitative $^1$H NMR analysis of Ac-I(V) G-1 fractions performed in triplicate. Samples were prepared by dissolving 60 mg of material in 0.7 mL of $d_6$DMSO and sonicating for 30 mins in a water bath set to 30°C. The solutions were then filter through a 0.45 µm PTFE syringe filter. Data was acquired on a Bruker Avance III 700 MHz spectrometer equipped with a nitrogen cooled, $[^1$H/$^{13}$C/$^{15}$N] triple resonance cryoprobe TCI (prodigy). The standard Bruker zg pulse sequence was used (ns = 4 & $D_1 = 30$ s). Integrals were normalised so that the signal for the benzylic CH$_2$ end group was equal to 2. The integral intensity of the α proton of the β-O-4 unit was then taken and used to calculate the $M_n$ of the Ac-I(V) G-1 fractions (see above). Average values of the $M_n$ triplicate data were then generated and the associated standard deviations (σ) are given in square brackets.

|     | Integral α$_H$β-O-4 | Molecular Weight (g mol$^{-1}$) | Average (g mol$^{-1}$) | [σ] |
|-----|---------------------|-------------------------------|-------------------------|-----|
|     | 1       | 2       | 3       | 1  | 2  | 3 |  |     |
| F1  | 5.18    | 5.21    | 5.29    | 1734 | 1743 | 1765 | 1747 | 16 |
| F2  | 5.78    | 5.73    | 5.77    | 1902 | 1888 | 1899 | 1897 | 7  |
| F3  | 6.87    | 6.73    | 7.05    | 2208 | 2169 | 2258 | 2212 | 45 |
| F4  | 8.12    | 8.09    | 7.83    | 2558 | 2550 | 2477 | 2528 | 45 |
| F5  | 10.70   | 10.15   | 10.15   | 3281 | 3127 | 3127 | 3178 | 89 |
| F6  | 12.45   | 12.56   | 12.38   | 3772 | 3803 | 3752 | 3775 | 25 |
| F7  | 14.84   | 14.26   | 14.18   | 4442 | 4279 | 4257 | 4326 | 101 |
End group NMR data measured on a 700 MHz spectrometer fitted with a nitrogen cooled cryoprobe (TCI). Samples were prepared by dissolving 60 mg of material in 0.7 ml $d_6$-DMSO. $^1$H NMR spectra were processed in MestReNova 11.0.3 software package. Global spectral deconvolution (GSD) was used to measure the integrals of the peaks of interest. a) magnitude of the integral of the $\beta$-O-$\alpha$ proton relative to the benzylic CH$_2$ end group. $M_n$ is the number average molecular weight calculated from molecular weights of the fragments (see Figure S4) and the relative integrals of the $\beta$-O-$\alpha$ proton. *Fractions did not provide enough material for DOSY analysis at the required concentration.

| Fraction | G-1 | G-2 |
|----------|-----|-----|
|          | a)  | $M_n$ | a)  | $M_n$ |
| F1       | 5.2 | 1700  | 3.8 | 1400  |
| F2       | 5.8 | 1900  | 5.2 | 1700  |
| F3       | 6.9 | 2200  | 10.6| 230   |
| F4       | 8.0 | 2500  | 9.2 | 2900  |
| F5       | 10.3| 3200  | 11.6| 3500  |
| F6       | 12.5| 3800  | *   | *     |
| F7       | 14.4| 4300  | *   | *     |
| F8       | -   | -     | -   | -     |
| F9       | -   | -     | -   | -     |
Table S7. The mean values of the triplicate analysis of G-1 fractionation showing the weight average molecular weight ($M_w$) measured by GPC (1), number average molecular weight ($M_n$) measured by GPC (2), polydispersity index ($M_w/M_n$) measured by GPC (3) and number average molecular weight calculated from end group analysis (4), PDI calculated using ($M_w$(GPC)/$M_n$(NMR)) (5). Integrations for the GPC were taken from where the UV response left to where it returned to the baseline. Values in parentheses correspond to the standard error associated with each fraction. Only one GPC data point could be measured for fraction F1 (5 %) due to availability of the material.

| Entry | Acetone Concentration (% v/v) | 5%   | 10%   | 15%   | 20%   | 25%   | 30%   | 35%   |
|-------|--------------------------------|------|-------|-------|-------|-------|-------|-------|
| 1     | $M_w$(GPC) [g.mol$^{-1}$]     | 2400*| 2600  | 2800  | 3200  | 3900  | 4700  | 5900  |
| 2     | $M_n$(GPC) [g.mol$^{-1}$]     | 1800*| 2000  | 2200  | 2400  | 2800  | 3300  | 3700  |
| 3     | PDI (GPC)                      | 1.3* | 1.3   | 1.3   | 1.3   | 1.4   | 1.5   | 1.6   |
| 4     | $M_n$(NMR) [g.mol$^{-1}$]     | 1700*| 1900  | 2200  | 2500  | 32    | 3800  | 4300  | (9.20)  | (4.28)  | (25.96)  | (25.81)  | 32    | 3800  | 4300  | (58.28)  |
| 5     | PDI*                           | 1.3  | 1.3   | 1.3   | 1.3   | 1.2   | 1.3   | 1.4   |
| 6     | % Difference $M_n$ (NMR-GPC)   | 4.5  | -4.4  | 2.6   | 4.1   | 12.7  | 15.6  | 16.7  |

*PDI = $M_w$(GPC)/$M_n$(NMR)
Table S8. The values of the analysis of G-2 fractionation showing the weight average molecular weight ($M_w$) measured by GPC (1), number average molecular weight ($M_n$) measured by GPC (2), polydispersity index ($M_w/M_n$) measured by GPC (3) and number average molecular weight calculated from end group analysis (4), PDI calculated using ($M_w$(GPC)/$M_d$(NMR)) (5). Integrations for the GPC were taken from where the UV response left to where it returned to the baseline.

| Entry | Acetone Concentration (% v/v) | 5%  | 10%  | 15%  | 20%  | 25%  | 30%  | 35%  |
|-------|-------------------------------|-----|------|------|------|------|------|------|
| 1     | $M_w$(GPC) [g.mol$^{-1}$]     | 1800| 2000 | 2600 | 3200 | 4200 | 4500 | 5000 |
| 2     | $M_n$(GPC) [g.mol$^{-1}$]     | 1400| 1600 | 2000 | 2500 | 3100 | 2900 | 3000 |
| 3     | PDI (GPC)                     | 1.3 | 1.3  | 1.3  | 1.3  | 1.3  | 1.6  | 1.7  |
| 4     | $M_n$(NMR) [g.mol$^{-1}$]     | 1400| 1700 | 2300 | 2900 | 3500 | *    | *    |
| 5     | PDI *                         | 1.3 | 1.2  | 1.1  | 1.1  | 1.2  | *    | *    |
| 6     | % Difference $M_n$ (NMR-GPC)  | 2.0 | 7.7  | 12.3 | 15.2 | 14.2 | *    | *    |

*PDI = $M_w$(GPC)/$M_d$(NMR)
DOSY Analysis: See Experimental Section of manuscript for an additional description of how the DOSY analysis was carried out.

Figure S6. Outline of how the DOSY NMR data was processed and analysed. A) Peak picking used in DOSY analysis of acetylated polymer Ac-I(V) (fraction F7, G-1) fractions. B) Pseudo 2D DOSY data set showing signal intensity decay in the PFG dimension. C) Processed DOSY spectrum showing the diffusion coefficient of each signal in the peak picked in the $^1$H Spectrum. D) Plot of the average diffusion coefficient derived from all signals peak picked in the spectrum plotted against the concentration of acetone used to isolate the fraction being studied. Error bars correspond to the standard error associated with the average diffusion coefficient of each fraction. DMSO diffusion coefficient added to show the order of magnitude difference between the residual solvent and polymer signals. Samples were run on a Bruker 700 MHz spectrometer equipped with a nitrogen cooled TCI cryoprobe (prodigy). Samples were prepared by dissolving 60 mg of material in 0.7 mL of $d_6$-DMSO. DOSY parameters ($\Delta$ and $\delta$), were optimised so that the residual signal at high (98%) gradient strength was ca. 5% of the low (10%) gradient strength for each fraction being studied. Line broadening (LB) of 6 Hz was applied prior to the Fourier transform. Each fraction dataset was manually phased and a baseline correction was applied in the F2 dimension. DOSY analysis was performed in the Bruker Dynamics Centre version 2.3 software package.
Table S9. Average diffusion coefficients ($D$) for model polymer (G-1 & G-2) and Kraft fractionations (KL-1 & KL-2). The values were produced by taking average diffusion coefficient of peak picked signals for each fraction (See Figure S5). Average log $D$ values were produced by taking the log of the average diffusion coefficients. Concentration of samples was strictly controlled to 86 mg mL$^{-1}$. * samples that did not allow for an accurate concentration of solution to be made due to the abundance or properties of the material.

| Fraction | G-1 | G-2 | KL-1 | KL-2 |
|----------|-----|-----|------|------|
|          | $D$ | Log $D$ | $D$ | Log $D$ | $D$ | Log $D$ | $D$ | Log $D$ |
| F1       | 6.05 | -10.22 | 8.26 | -10.08 | 11.76 | -9.93 | 9.17 | -10.04 |
| F2       | 5.60 | -10.25 | 7.75 | -10.11 | 8.87 | -10.05 | 9.68 | -10.01 |
| F3       | 5.23 | -10.28 | 6.27 | -10.20 | 8.35 | -10.08 | 7.62 | -10.12 |
| F4       | 4.82 | -10.32 | 5.16 | -10.29 | 7.41 | -10.13 | 6.99 | -10.16 |
| F5       | 4.31 | -10.37 | 4.63 | -10.33 | 6.31 | -10.20 | 5.99 | -10.22 |
| F6       | 3.62 | -10.44 | -a  | -a  | 5.78 | -10.24 | 5.36 | -10.27 |
| F7       | 3.19 | -10.50 | -a  | -a  | 4.46 | -10.35 | 4.75 | -10.32 |
| F8       | n/a | n/a | n/a | n/a | 5.46 | -10.26 | 4.53 | -10.34 |
| F9       | n/a | n/a | n/a | n/a | 4.75 | -10.32 | 4.53 | -10.34 |
| F10      | n/a | n/a | n/a | n/a | 3.76 | -10.42 | 3.73 | -10.43 |
| F11      | n/a | n/a | n/a | n/a | 3.14 | -10.50 | 3.30 | -10.48 |
| F12      | n/a | n/a | n/a | n/a | 2.23 | -10.65 | 1.57 | -10.81 |
| F13      | n/a | n/a | n/a | n/a | -a  | -a  | 1.22 | -10.91 |
| F14      | n/a | n/a | n/a | n/a | -a  | -a  | 1.08 | -10.97 |
Figure S7. G-2 Fractionation DOSY analysis plotting the log $D$ against the Log molecular weight from different sources (orange $M_n$ (NMR); blue ($M_w$ (GPC) and red $M_n$ (GPC)). Linear correlations were seen with good agreement between NMR and GPC analysis of $M_n$.

Table S10 Scaling factors $\alpha$ for various types of polymer solvent systems.$^1$

| $\alpha$ | Polymer solvent system                      |
|----------|---------------------------------------------|
| < 0.5    | Branched polymers                           |
| 0.5      | $\Theta$ conditions - closely coiled linear polymer, no interaction with solvent |
| 0.5 – 0.8| Flexible linear polymers in "good" solvent   |
| > 0.8    | Semi flexible linear polymers               |
| = 2      | Polymers with rigid rod structure            |
Kraft Fraction GPC Data

Table S11 GPC determined molecular weights of fractions from Kraft fractionation 1 (KL-1) and Kraft fractionation 2 (KL-2), with the associated PDIs. Integrations were taken from where the UV response left to where it returned to the baseline. PDIs were calculated by taking the ratio of the measured average molecular weights ($M_n/M_w$). *Insufficient material to perform GPC analysis at the required concentrations.

| Fraction | KL-1 | | KL-2 | | |
|----------|------|------|------|------|------|
|          | $M_n$ (g mol$^{-1}$) | $M_w$ (g mol$^{-1}$) | PDI | $M_n$ (g mol$^{-1}$) | $M_w$ (g mol$^{-1}$) | PDI |
| F1       | 600  | 900  | 1.5 | 800  | 1400 | 1.8 |
| F2       | 800  | 1200 | 1.5 | 900  | 1300 | 1.5 |
| F3       | 900  | 1500 | 1.7 | 1100 | 1700 | 1.5 |
| F4       | 1200 | 1900 | 1.6 | 1400 | 2000 | 1.5 |
| F5       | 13   | 2300 | 1.8 | 1800 | 2900 | 1.6 |
| F6       | 1500 | 2900 | 1.9 | 2200 | 3100 | 1.4 |
| F7       | 1800 | 3600 | 2.0 | 2600 | 3700 | 1.4 |
| F8       | 1900 | 4400 | 2.3 | 3100 | 4600 | 1.5 |
| F9       | 1100 | 4800 | 4.4 | 3100 | 4800 | 1.6 |
| F10      | $a$  | 5300 | $a$ | 3400 | 5500 | 1.6 |
| F11      | $a$  | 6600 | $a$ | 4000 | 7200 | 1.8 |
| F12      | $a$  | 8400 | $a$ | 3700 | 8900 | 2.4 |
| F13      | $b$  | $b$  | $b$ | 3600 | 9700 | 2.7 |
| F14      | $b$  | $b$  | $b$ | 3700 | 10300| 2.8 |

*a* $M_n$ values obtained for this material were not reliable due to the broadness of the peaks. As a result, PDIs could not be calculated for these fractions.

*b* Fraction did not provide enough material to make an accurate concentration for NMR analysis.
Figure S8. Overlay of $^1$H NMR spectra of KL-2 fractions (F1, F7 and F14). Samples were prepared by dissolving 60 mg of material in 0.7 ml $d_6$-DMSO. Higher molecular weight lignin chains (F14 showed noticeably less intense and broader line shapes than lower molecular weight fractions (F7 and F1) illustrating the effect of the $T_2$ relaxation.
Figure S9. The aromatic ($\delta_H$ 6.2-7.8 ppm, $\delta_C$ 103-132 ppm) and linkage ($\delta_H$ 3.2-5.8 ppm, $\delta_C$ 53-90 ppm) regions of the HSQC spectrum of Kraft lignin (11 $\beta$-O-4 per 100 C$_9$ units). The cross-peaks are colour coordinated for the structures they belong.
**Figure S10.** KL-1 Average $T_1$ relaxation times of fractions F2 to F12. $T_1$ relaxation times were measured using the *t1ir* pulse sequence with 16 increments variable delays between 0.05 s and 15 s and an inter scan delay of 20 seconds. Average relaxation times were calculated by measuring the $T_1$ relaxation at 16 points along the 1D $^1$H spectrum and taking the mean. Error bars shown in the figure represent the standard error of the calculated mean relaxation time. Heavier fractions present longer relaxation $T_1$ relaxation times and therefore will be under represented in the spectrum of the bulk (unfractionated) material.
Bromoester and monomer synthesis

Methyl 2-bromoacetate (S1)

\[
\text{Br} \quad \text{O} \\
\text{O}
\]

S1 was used as received from Alfa Aesar (UK)

Ethyl 2-bromoacetate (S2)

\[
\text{Br} \quad \text{O} \\
\text{O}
\]

S2 was used as received from Acros Organics (UK)

\(n\)-Butyl 2-bromoacetate (S3)

\[
\text{Br} \quad \text{O} \\
\text{O}
\]

S3 was prepared from \(n\)-butanol (8.89 g, 120 mmol, 1 eq.), bromoacetic acid (20 g, 144 mmol, 1.2 eq.) and TsOH.H₂O (0.228 g, 12 mmol 0.01 eq.) in cyclohexane (80 ml) using General Procedure A. Compound S3 was obtained as a colourless oil (19.90 g, 102 mmol, 85%). \(^1\)H NMR (500 MHz, Chloroform-\(d\)) \(\delta = 4.17\) (t, \(J=6.7\), 2H), 3.83 (s, 2H), 1.64 (dq, \(J=7.9, 6.7\), 2H), 1.44 – 1.33 (m, 2H), 0.93 (t, \(J=7.4\), 3H). Analytical data in accordance with literature.

\(n\)-Pentyl 2-bromoacetate (S4)

\[
\text{Br} \quad \text{O} \\
\text{O}
\]

S4 was prepared from pentanol (7.78 g, 88.2 mmol, 1.00 eq.), bromoacetic acid (14.50 g, 104 mmol, 1.18 eq.) and TsOH.H₂O (0.17 g, 0.9 mmol, 0.01 eq.) in cyclohexane (75 mL) using General Procedure A. Compound S4 was obtained as a colourless oil (17.29 g, 82.7 mmol, 93%). \(^1\)H NMR (500 MHz, Chloroform-\(d\)) \(\delta = 4.16\) (t, \(J=6.7\), 2H), 3.83 (s, 2H), 1.71 – 1.56 (m, 2H), 1.38 – 1.29 (m, 4H), 0.94 – 0.84 (m, 3H). Analytical data in accordance with literature.

Octyl 2-bromoacetate (S5)
**S5** was prepared from octanol (6.50 g, 50 mmol, 1 eq.), bromoacetic acid (8.32 g, 59 mmol, 1.2 eq.) and TsOH.H$_2$O (0.1 g, 0.5 mmol, 0.01 eq.) in cyclohexane (50 ml) using General Procedure A. Compound **S4** was obtained as a colourless oil (11.9 g, 47.4 mmol, 95%).  $^1$H NMR (500 MHz, Chloroform-$d$) $\delta = 4.16$ (t, $J=6.7$, 2H), $3.83$ (s, 2H), $1.71 – 1.58$ (m, 2H), $1.40 – 1.20$ (m, 10H), $0.87$ (t, $J=6.9$, 3H). Analytical data in accordance with literature.$^3$

**Decyl 2-bromoacetate (S6)**

S6 was prepared from decanol (11.2 g, 70.7 mmol, 1.00 eq.), bromoacetic acid (11.8 g, 84.9 mmol, 1.20 eq.) and TsOH.H$_2$O (0.16 g, 0.9 mmol, 0.01 eq.) in cyclohexane (110 mL) using General Procedure A. Compound **S6** was obtained as a colourless oil (19.3 g, 69.1 mmol, 98%).  $^1$H NMR (500 MHz, Chloroform-$d$) $\delta = 4.15$ (t, $J=6.7$, 2H), $3.82$ (s, 2H), $1.65$ (dq, $J=8.2$, 6.6, 2H), $1.39 – 1.20$ (m, 14H), $0.87$ (t, $J=6.9$, 3H). Analytical data in accordance with literature.$^4$

**Dodecyl 2-bromoacetate (S7)**

S7 was prepared from dodecanol (10.71 g, 57.5 mmol, 1.00 eq.), bromoacetic acid (9.60 g, 69.0 mmol, 1.20 eq.) and TsOH.H$_2$O (0.16 g, 0.9 mmol, 0.01 eq.) in cyclohexane (110 mL) using General Procedure A. Compound **S7** was obtained as a colourless oil (17.4 g, 56.6 mmol, 98%).  $^1$H NMR (500 MHz, Chloroform-$d$) $\delta = 4.16$ (t, $J=6.7$, 2H), $3.83$ (s, 2H), $1.64$ (dt, $J=8.2$, 6.6, 2H), $1.43 – 1.16$ (m, 18H), $0.87$ (t, $J=6.9$, 3H). Analytical data in accordance with literature.$^4$

**tert-butyl 2-bromoacetate (S8)**

S8 was used as received from Chemada Fine Chemicals.
Monomer Synthesis

Methyl 2-(4-formyl-2-methoxyphenoxy)acetate (S9)

S9 was prepared from vanillin (10.0 g, 65.7 mmol, 1 eq), K₂CO₃ (18.2 g, 131.7 mmol, 2 eq.), S1 in acetone (50 ml) using General Procedure B.

¹H NMR (500 MHz, Chloroform-d) δ = 9.86 (s, 1H), 7.48 – 7.38 (m, 2H), 6.87 (d, J=8.1, 1H), 4.80 (s, 2H), 3.95 (s, 3H), 3.81 (s, 3H). Analytical data in accordance with literature.⁵

Ethyl 2-(4-formyl-2-methoxyphenoxy)acetate (S10)

S10 was prepared from vanillin (10.0 g, 65.7 mmol, 1 eq), K₂CO₃ (18.2 g, 131.7 mmol, 2 eq) S2 (10.2 g, 65.7 mmol, 1 eq) in acetone (50 mL) using General Procedure B.

¹H NMR (500 MHz, Chloroform-d) δ = 9.85 (s, 1H), 7.51 – 7.35 (m, 2H), 6.86 (d, J=8.1, 1H), 4.77 (s, 2H), 4.26 (q, J=7.1, 2H), 3.94 (s, 3H), 1.27 (t, J=7.1, 3H). Analytical data in accordance with literature.⁶

Butyl 2-(4-formyl-2-methoxyphenoxy)acetate (S11)

S11 was prepared from vanillin (7.43 g, 48.8 mmol, 1.00 eq.), K₂CO₃ (13.50 g, 97.7 mmol, 2.00 eq.), S3 (10.00 g, 51.3 mmol, 1.05 eq.) in acetone (75 mL) using General Procedure B. Compound S11 was recovered pure from trituration with petroleum ether as an off-white precipitate (12.02 g, 45.1 mmol, 92%). HRMS: (NSI+) m/z [M + H⁺] calcd for C₁₄H₁₈O₅H⁺ 266.1154; found 267.1222. M.p. 53-54 °C. IR (FTIR)νmax: 2960, 2935, 1763, 1676, 1583, 1508, 1460 cm⁻¹.¹

¹H NMR (500 MHz, Chloroform-d) δ = 9.86 (s, 1H), 7.49 – 7.38 (m, 2H), 6.86 (d, J=8.1, 1H), 4.79 (s, 2H), 4.20 (t, J=6.7, 2H), 3.95 (s, 3H), 1.65 – 1.57 (m, 2H), 1.32 (h, J=7.4, 2H), 0.90 (t, J=7.4, 3H).¹³C NMR: (126 MHz, CDCl₃) δ = 190.97, 168.25, 152.65, 150.06, 131.21, 126.29, 112.32, 109.90, 65.99, 65.58, 56.22, 30.60, 19.09, 13.74.
pentyl 2-(4-formyl-2-methoxyphenoxy)acetate (S12)

S12 was prepared from vanillin (10.00 g, 65.7 mmol, 1.00 eq.), K₂CO₃ (18.16 g, 131.4 mmol, 2.00 eq.), S4 (14.43 g, 69.0 mmol, 1.05 eq.) in acetone (100 mL) using General Procedure B. Compound S12 was recovered pure from flash column chromatography (10-20% ethyl acetate in petroleum ether) as a pale yellow oil (14.59 g, 52 mmol, 79%). HRMS: (NSI+) m/z [M + H⁺] calcd for C₁₅H₂₀O₅H⁺ 281.1384; found 281.1385. IR (FTIR)ν_max: 2958, 2933, 1755, 1681, 1587, 1506 cm⁻¹. ¹H NMR (500 MHz, Chloroform-d) δ = 9.85 (s, 1H), 7.49 – 7.34 (m, 2H), 6.86 (d, J=8.1, 1H), 4.78 (s, 2H), 4.19 (t, J=6.7, 2H), 3.94 (s, 3H), 1.68 – 1.58 (m, 2H), 1.38 – 1.19 (m, 4H), 0.86 (t, J=7.0, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 190.96, 168.24, 152.63, 150.03, 131.19, 126.28, 112.28, 109.89, 65.97, 65.84, 56.20, 28.28, 27.98, 22.33, 14.05.

Octyl 2-(4-formyl-2-methoxyphenoxy)acetate (S13)

S13 was prepared from vanillin (15.0 g, 98.6 mmol, 1 eq.), K₂CO₃ (27.3 g, 197.6 mmol, 2 eq.), S5 (24.8 g, 98.6 mmol, 1 eq.) in acetone (50 ml) using General Procedure B. HRMS: (NSI+) m/z [M + H⁺] calcd for C₁₈H₃₀O₂⁺ 323.1853; found 323.1856. M.p. 46-48 °C. IR (FTIR)ν_max: 2924, 2854, 1739, 1683, 1587, 1506 cm⁻¹. ¹H NMR (500 MHz, Chloroform-d) δ = 9.86 (s, 1H), 7.49 – 7.38 (m, 2H), 6.87 (d, J=8.1, 1H), 4.79 (s, 2H), 4.20 (t, J=6.7, 2H), 3.96 (s, 3H), 1.63 (p, J=6.9, 2H), 1.34 – 1.20 (m, 10H), 0.87 (t, J=7.0, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 190.97, 168.27, 152.67, 150.07, 131.23, 126.32, 112.30, 109.91, 66.01, 65.90, 56.24, 31.88, 29.29, 29.26, 28.62, 25.89, 22.77, 14.24.

Decyl 2-(4-formyl-2-methoxyphenoxy)acetate (S14)

S14 was prepared from vanillin (5.18 g, 34.0 mmol, 1.00 eq.), K₂CO₃ (9.42 g, 68.2 mmol, 2.00 eq.), S6 (9.99 g, 35.8 mmol, 1.05 eq.) in acetone (50 mL) using General Procedure B. Compound S14 was recovered pure from flash column chromatography (10-20% ethyl acetate in petroleum ether) as an amorphous white solid (7.94 g, 22.7 mmol, 67%). HRMS (NSI+) m/z [M + H⁺] calcd for C₂₀H₃₆O₂H⁺
351.2166; found 351.2167. **IR (FTIR)** $\nu_{\text{max}}$: 2922, 2900, 1739, 1683, 1587, 1506, 1458 cm$^{-1}$. **$^1$H NMR** (500 MHz, Chloroform-$d$) $\delta = 9.85$ (s, 1H), 7.49 – 7.38 (m, 2H), 6.86 (d, $J=8.2$, 1H), 4.78 (s, 2H), 4.19 (t, $J=6.7$, 2H), 3.95 (s, 3H), 1.62 (p, $J=6.8$, 2H), 1.25 (m, 14H), 0.87 (t, $J=6.9$, 4H). **$^{13}$C NMR** (126 MHz, CDCl$_3$) $\delta$ 190.94, 168.24, 152.64, 150.04, 131.20, 126.29, 112.29, 109.89, 65.98, 65.87, 56.21, 31.99, 29.61, 29.41, 29.27, 28.65, 28.60, 25.86, 22.80, 14.24.

Dodecyl 2-(formyl-2-methoxyphenoxy)acetate (S15)

S15 was prepared from vanillin (4.72, 31.0 mmol, 1.00 eq.), K$_2$CO$_3$ (8.55 g, 62 mmol, 2.00 eq.), S7 (10.00 g, 32.6 mmol, 1.05 eq.) in acetone (50 mL) using General Procedure B. Compound S15 was recovered pure from trituration with petroleum ether as a white precipitate (8.98 g, 23.7 mmol, 76%). **HRMS** (NSI$^+$) $m/z$ [M + H$^+$] calcd for C$_{22}$H$_{34}$O$_4$H$^+$ 379.2479; found 379.2479. **M.p.** 59–61 °C. **IR (FTIR)** $\nu_{\text{max}}$: 2954, 2900, 1739, 1683, 1672, 1587, 1471 cm$^{-1}$. **$^1$H NMR** (500 MHz, Chloroform-$d$) $\delta = 9.86$ (s, 1H), 7.53 – 7.41 (m, 2H), 6.87 (d, $J=8.1$, 1H), 4.79 (s, 2H), 4.20 (t, $J=6.7$, 2H), 3.96 (s, 3H), 1.63 (p, $J=7.0$, 2H), 1.32 – 1.21 (m, 20H), 0.88 (t, $J=6.9$, 3H). **$^{13}$C NMR** (126 MHz, CDCl$_3$) $\delta$ 190.96, 167.10, 152.76, 149.97, 130.98, 126.30, 126.32, 112.31, 109.91, 66.01, 65.90, 56.24, 32.06, 29.77 (x2), 29.69, 29.64, 29.49, 29.30, 28.63, 25.89, 22.84, 14.28.

**tert-butyl 2-(formyl-2-methoxyphenoxy)acetate (S16)**

S16 was prepared from vanillin (3.00 g, 19.7 mmol, 1.00 eq.), K$_2$CO$_3$ (4.00 5.44 g, 2.00 eq.), S8 (4.04 g, 20.7 mmol, 1.05 eq.) in acetone (30 mL) using General Procedure B. Compound S16 was recovered pure from after work-up to give a beige precipitate (5.23 g, 19.6 mmol, 99%). **$^1$H NMR** (500 MHz, Chloroform-$d$) $\delta = 9.85$ (s, 1H), 7.49 – 7.35 (m, 2H), 6.84 (d, $J=8.0$, 1H), 4.67 (s, 2H), 3.94 (s, 3H), 1.46 (s, 9H). **$^{13}$C NMR** (126 MHz, CDCl$_3$) $\delta$ 190.99, 167.10, 152.76, 149.97, 130.98, 126.30, 112.01, 109.83, 82.99, 66.17, 56.20, 28.13. Analytical data in accordance with literature.?
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NMR Spectra

1H NMR 1-buty1 bromoester
Solvent: CDCl3
500.13 MHz

1H NMR propyl bromoester
Solvent: CDCl3
500.13 MHz
